Annals of the Rheumatic Diseases

Annual European Congress of Rheumatology

EULAR 2019

Madrid, 12-15 June 2019

Abstracts

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New avenues of OA & osteoporosis management

Francis Berenbaum. Sorbonne Universite, France

All recommendations on the management of osteoarthritis (OA), including EULAR, consider that its treatment should include pharmaceutical and non-pharmacological treatments. In this lecture, the most recent advances in both fields will be addressed. Some of them can change our current practice like recommendations on physical activity or on the choice of analgesics. Moreover, this lecture will highlight some of the drugs and cell therapies in development that could be on the market in the very close years.

Disclosure of interests: None declared


HOT: OSTEOPOROSIS @2019

Serge Ferrari. Geneva University Hospital, Medecine, Geneva, Switzerland

Background: The goal of osteoporosis therapy is to quickly prevent fragility fractures in subjects at risk and on the longer term to restore bone mass (Bone mineral density, BMD) to levels of appropriate bone strength. Currently approved drugs for treatment of osteoporosis in Europe, namely bisphosphonates, denosumab, and teriparatide all decrease vertebral fracture risk within one year, whereas the benefits on non-vertebral fractures may take nearly two years to appear.

Objectives: To provide an update of recent trials regarding osteoporosis treatment.

Methods: Literature review and expert insights into recent analyses of clinical trials.

Results: New H2B trials, notably with teriparatide compared to risudronate, have shown the superiority of the anabolic therapy in preventing fractures in high risk patients. In GIOP, denosumab increased BMD more than risudronate. More importantly, romosozumab, a monoclonal Ab against sclerostin, was superior to alendronate to reduce fractures in high risk subjects, whereas the sequence of romosozumab and denosumab was superior to placebo followed by denosumab and increased BMD over just two years equivalent to seven years of continuous denosumab. New analyses of long-term denosumab, up to ten years of continuous therapy, have shown continuous BMD gains and further reduction in fracture rates, with T-scores at hip near -1.5 achieving the lowest fracture risk. However several case reports as well as a post-hoc analysis of subjects discontinuing denosumab in the FREEDOM trial have reported an increased risk of multiple vertebral fractures, which may be prevented by a 1-2 yrs consolidation by a bisphosphonate following denosumab therapy (guidelines).

Conclusion: In summary, while new data and more potent drugs are emerging (romosozumab), fueling the concept that anabolics should be used earlier in the disease (romosozumab), bisphosphonates, denosumab, and teriparatide all decrease vertebral fracture risk within one year, whereas the benefits on non-vertebral fractures may take nearly two years to appear.

Disclosure of interests: None declared


Managing patients with axSpA: What are the quality standards?

Uta Klitz. Rheumazentrum Ruhrgebiet at Ruhr-University Bochum, Rheumatology, Heme, Germany

Background: There is wide variation in the management of patients with axial spondyloarthritis (axSpA) worldwide with significant unmet needs such as delayed diagnosis and inequity in bMARD prescription. Assessing the quality of care provided to patients with axSpA is important not only to patients and physicians, but also to providers and purchasers of health care. There is no agreed methodology to quantify quality of care but several approaches have been proposed aiming to assess quality in a measurable construct, e.g. quality indicators, performance measures or quality standards. Definition of quality standards (QS) enable society to identify resources and processes which may need to be optimised in patients with axSpA.

Objectives: A major goal of the international organization Assessment of SpondyloArthritis International Society (ASAS) is to improve quality of care and health outcomes in patients with axSpA. Recognized gaps in current care prompted ASAS in 2016 to start developing a quality standard set (ASAS QS) to optimize access, treatment and patient outcomes in axSpA.

Methods: An ASAS task force developed a set of ASAS QS step-wise. First, key areas for quality improvement were proposed, discussed, rated and agreed on. Thereafter, key areas were prioritized and statements for the most important key areas were phrased on consensus. Appropriate tools were selected and measures developed to be able to assess and quantify the quality of care on the community level.

Results: The ASAS task force, consisting of 20 rheumatologists, 2 physiotherapists, and 2 patients, selected and proposed 34 potential key areas for quality improvement which were commented by 140 ASAS survey participants (86 physicians, 42 patients). Within that process 3 new key areas came up, which led to a reevaluation of all 37 key areas by 120 participants (86 physicians, 29 patients). Five key areas were identified as most important to determine quality of care: referral including rapid access, monitoring, treatment, education including patient information and comorbidities. On that background, 9 QS were agreed on and finally endorsed by ASAS.

Conclusion: ASAS successfully developed the first QS set for improvement of health care for adult patients with axSpA. All QS are measurable achievable in daily care in an optimized situation and intend to minimize variation in quality of care.

Disclosure of interests: Uta Klitz Grant/research support from: AbbVie, Chugai, Eli Lilly, Grünenthal, Janssen, MSD, Novartis, Pfizer, Roche, and UCB. Consultant for: AbbVie, Chugai, Eli Lilly, Grünenthal, Janssen, MSD, Novartis, Pfizer, Roche, and UCB.


Managing patients with axSpA: what are the quality standards?
ANCA-associated vasculitides (AAVs) are a group of diseases with frequent relapses that can sometimes be severe. Treatment comprises an induction-remission phase followed by a maintenance regimen. Induction-remission therapy is effective and now well-established, mainly based on the combination of corticosteroids (CS) and cyclophosphamide or rituximab. For decades, maintenance therapy was compulsory and consisted of azathioprine or methotrexate, combined or not with low-dose CS. That regimen was prescribed for at least 18 months but was sometimes taken for several years. Criteria for stopping treatment have never been codified. Since rituximab has been widely prescribed for induction, the indication for azathioprine maintenance has been challenged because its relapse rate at 18 months (29%) was comparable to that of placebo (32%) given in its stead. However, we considered those relapse rates unacceptably high and have tried to devise a different therapeutic approach to maintenance, with semestral evaluation of the indication of rituximab infusion over 18 months. MAINRITSAN1-trial results demonstrated the superiority of rituximab to maintain remission with a 5% relapse rate at 28 months vs 29% for azathioprine recipients. The 60-month follow-up of that trial confirmed the superiority of rituximab over azathioprine (37% vs 57%), even though rituximab did not abrogate relapses. Since the publication of those results, it is now clear that AAV remission-maintenance therapy should be rituximab—and not azathioprine or another equally effective immunosuppres sant like methotrexate.

Maintaining remission should now also be based on other factors predictive of relapse: vasculitis type, ANCA subtype and/or ANCA presence or absence at the end of the induction regimen. Granulomatosis with polyangiitis relapses more frequently than microscopic polyangiitis or eosinophilic granulomatosis with polyangilits. Relapse rates of the former two are probably linked mainly to ANCA type, anti-PR3 or anti-MPO, with the latter relapsing less frequently. The long-term MAINRITSAN1-trial results identified anti-PR3 presence 1 year after ending induction treatment and/or their persistence were predictor(s) of relapse. We also designed a study comparing fixed-schedule rituximab infusions to re-infusions(4) guided by ANCA titer and/or CD19+ circulating B lymphocytes. Results of that prospective study demonstrated that fewer rituximab infusions should be given but that ANCA titer and the circulating CD19+B cell level are not good predictors of relapse. ANCA presence—indeedently of their titer—is more frequently associated with relapse.

The optimal rituximab-administration duration has not yet been established. Our group is now awaiting the imminent results of a prospective trial comparing 4 vs 8 rituximab infusions at 6-month intervals after obtaining remission.

Conclusions: Major advances have been made in the therapeutic strategy for AAVs. After induction is obtained: 1) AAVs require maintenance therapy. 2) rituximab is superior to immunosuppressants, 3) the presence, persistence and/or reoccurrence of anti-PR3 ANCA predict relapses, 4) the 500-mg rituximab dose/infusion seems well-adapted. The optimal treatment duration remains to be elucidated.

Tailoring maintenance therapy is now the main therapeutic objective for AAV management. Future trials will attempt to evaluate very long-term maintenance treatment of AAVs with the goal of eradicating relapses.

Disclosure of Interests: None declared

SP0008  MANAGEMENT OF CPPD DISEASE
Abibhush Abhishek, The University of Nottingham, Academic Rheumatology, Nottingham, United Kingdom

Background: Calcium pyrophosphate deposition disease (CPPD) is a common cause of arthritis. Its prevalence increases with ageing, and it manifests with asymptomatic chondrocalcinosis, acute crystal synovitis, and chronic arthritis.

Objectives: The objectives of this talk are to summarize the treatment options for the management of CPPD, and to review the evidence base supporting them.

Methods: A systematic literature search was performed to identify all studies published in the English language, and, reporting on the treatment of acute and chronic manifestations of CPPD. All published studies were included with the exception of case reports and conference abstracts. Similarly, a literature search was performed to identify the metabolic and hereditary risk-factors of CPPD. The findings of the systematic literature search are described in a narrative manner. Interventions for which there is no published data are recommended based on clinical experience and expert opinion.

Results: Based on clinical experience, oral or intra-articular corticosteroids are effective and recommended for the management of CPPD. Colchicine and interleukin-1 antagonists are effective and recommended for the management of acute CPP crystal arthritis. Interleukin-1 antagonists should be reserved for use in refractory cases. Oral NSAIDs should be avoided as people with CPPD are frequently elderly. Low-
Comorbidities in psoriatic arthritis

**SP0009**

**CARDIOVASCULAR RISK IN PSORIASIS AND PSORIATIC ARTHRITIS**

Iain McInnes, University of Glasgow, Institute of Infection, Immunity, and Inflammation, Glasgow, United Kingdom

**Background:** Psoriasis and psoriatic arthritis are associated with increased cardiovascular and cardio metabolic risk.

**Objectives:** To describe the prevalence and magnitude CV risk in psoriasis and psoriatic arthritis and to comment on the clinical therapeutic implications of this risk in our practice.

**Methods:** Review of literature concerning CV risk and interpretation of the same.

**Results:** MACE are elevated over time in people with psoriasis and PsA. The mechanisms driving this are currently unclear but likely include both the impact of traditional risk factors e.g. dyslipidaemia, hypertension, obesity and novel risk factors e.g. mediated via increased inflammatory burden. Increased vigilance is required to detect this risk and a low index of suspicion should be introduced in practice. Aggressive management of CV risk should improve outcomes.

**Conclusion:** Recognising and treating factors mediating CV risk in psoriasis and psoriatic arthritis should comprise part of our routine clinical practice.

**Disclosure of Interests:** Iain McInnes Grant/research support from: AstraZeneca and Oxford Immunotec, Consultant for: Abbvie, Celgene, Galvani, Lilly, Novartis, Pfizer, UCB Pharma

**DOI:** 10.1136/annrheumdis-2019-eular.8410

**SP0010**

**INFECTIOUS RISK AND MANAGEMENT OF VACCINATION**

Nico Wulffraat, Wilhelmina Children’s hospital/UMC Utrecht, Pediatric rheumatology and Immunology, Utrecht, Netherlands

**Background:** Over the years, awareness of vaccine-preventable infection in rheumatic diseases has increased. At the same time, the safety of vaccines is still a hot topic in the public arena. Large-scale registries with data on juvenile idiopathic arthritis or RA taking the combination of methotrexate and biologics have demonstrated an increased incidence of infections. EULAR recommendations for both vaccination in pediatric patients and adults with rheumatic diseases, provide evidence-based guidance based on data from published studies on safety and efficacy of vaccinations in adults and children with rheumatic conditions. Especially in children, few data exist on safety and efficacy of live-attenuated vaccines such as MMR. This is relevant given the decreasing vaccination coverage and occurrence of measles outbreaks.

**Objectives:** To provide an overview of vaccines used in patients groups with rheumatic conditions under medication such as MTX or and biologicals. Also we seek for evidence on adverse events, protection rates and persistence of protective antibody titers over time. From these studies general guidelines are proposed.

**Methods:** Literature review of vaccination studies performed in adults and children. In addition the clinical practice of boostering of MMR in JIA patients under immunosuppressive therapy was investigated in several large academic pediatric centers across Europe.

**Results:** EULAR recommendations are updated for children and adults. For most vaccines it is advised to follow the national vaccination guidelines. Non-live vaccines can be safely provided to AIIRD patients under immunomodulating treatment, whereas the administration of live attenuated vaccines should be avoided under immunomodulating treatment, with the possible exceptions of herpes zoster and MMR. In 234 children with JIA who received the MMR booster while using MTX and or a Biological only 7 of adverse events were reported. Adverse events reported were mild (skin reaction, mild fever, urinary tract infection). There was no relation between disease activity, disease type or duration, sex, age and outcome of vaccinations.

**Conclusion:** The EULAR recommendations of 2011 are currently updated and will provide an up-to-date guidance on the management of vaccinations in patients with inflammatory rheumatic conditions. There is still a scarcity of data on safety and efficacy of live attenuated vaccines under biologicals. The next challenge is the implementation into the clinical practice of health professionals across Europe.

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.8622

**SP0011**

**HOW THE GUT INFLUENCES THE IMMUNE SYSTEM**

Mario Zaiss, Friedrich-Alexander University Erlangen-Nuremberg and Universitätsklinikum Erlangen, Department of Internal Medicine 3 – Rheumatology and Immunology, Erlangen, Germany

**Background:** A disturbed gut microbiota composition has been associated with autoimmune diseases. Recent findings support the hypothesis that the onset of RA might be linked with the gut microbiota. Moreover, we could recently show that high fiber diets change the microbiota, increase SCFA levels and attenuate inflammatory arthritis and bone destruction (1). However, direct mechanistic links between the gut microbiota and onset of autoimmune diseases remain largely unknown.

**Objectives:** Herein, we intended to identify if the intestinal barrier integrity could serve as a key checkpoint translating autoimmunity to inflammation.

**Results:** Restoration of the intestinal barrier in the pre-phase of arthritis using different approaches inhibited the development of arthritis.

**Conclusion:** In summary, our data identify a new preventive approach for the onset of autoimmunity disease by specifically targeting impaired intestinal barrier function.

**REFERENCE:**

Background and Aims: The frequency of autoimmune diseases has increased significantly in recent decades in developed countries. The hygiene hypothesis provides a possible explanation for this increase. The hypothesis is based on the observation of a concomitant decrease in the frequency of infectious diseases and an increase in the frequency of autoimmune diseases. It is also based on the geographical disparity in the frequency of autoimmune diseases, much more prevalent in the north than in the south of the northern hemisphere, a disparity that is not explained by genetics.

Method: The disease frequency which is very low in southern countries increases from the first generation among subjects migrating northward. The causal relationship between the decline in infections and the increase in autoimmune diseases remains to be proven. Most of the evidence is based on spontaneous experimental models of autoimmune diseases that show the higher frequency of these diseases in a clean sanitary environment and their prevention through the administration of various bacteria, viruses or parasites.

Results: The underlying mechanisms are beginning to be revealed. An important place is given to pathogens and more particularly to their TLR ligands. Some arguments suggest that commensal bacteria in the intestinal microbiota also play a role. At the cellular level, the stimulation of certain regulatory cells and more particularly those producing TGF beta is well documented.

Conclusion: These considerations are important for understanding the epidemiology and pathophysiology of autoimmune diseases but can also provide new guidance on their treatment and especially their prevention. The problem is, however, complicated by the fact that the theory applies to varying degrees depending on the disease, for instance more in systemic lupus erythematosus than rheumatoid arthritis.

Disclosure of Interests: None declared

Wednesday, 12 June 2019
14:15:00 – 15:45:00
Pharmaceutical pipeline in OA

GROWTH FACTORS AND CARTILAGE: FROM MECHANISMS TO DMARDS
Marc Hochberg, University of Maryland, School of Medicine, United States of America

Background: Growth factors are biologically active molecules that can stimulate cellular division, growth and differentiation and, in articular cartilage, can regulate development, homeostasis and regeneration of matrix. These anabolic factors can stimulate synthesis of proteoglycans, aggrecan and type II collagen, induce mesenchymal stem cell (MSC) proliferation and drive differentiation of MSCs into chondrocytes and decrease catabolic effects of cytokines and matrix metalloproteinases (MMPs). Growth factors would not, however, be expected to have a direct anabolic effect in patients with symptomatic knee osteoarthritis.

Objectives: To review the role of growth factors in articular cartilage, identify specific growth factors and review data from phase 1 and 2 studies of selected growth factors in subjects with knee osteoarthritis.

Methods: A PubMed search was performed using key words “cartilage or chondrocyte” and “growth factor”. The search included both original manuscripts and review articles as well as clinical trials but was limited to English language. From these searches, I selected review articles and clinical trials and excluded articles that solely examined molecular mechanisms of action of growth factors on chondrocytes.

Results: Growth factors for articular cartilage include molecules in the transforming growth factor-β (TGF-β) superfamily (including TGF-β1, bone morphogenetic protein [BMP]-2 and BMP-7), insulin-like growth factor-I, fibroblast growth factor (FGF) family (including FGF-2 and FGF-18), platelet-derived growth factor (PDGF) and Wnt ligands as well as platelet-rich plasma (PRP).

Conclusion: Data will be presented from phase 1 and 2 studies of rhFGF-18 and (PDGF) and Wnt ligands as well as platelet rich plasma (PRP).

REFERENCES:


Wednesday, 12 JUNE 2019
14:15:00 – 15:45:00
What’s new: Latest news on biological treatment

GROWTH FACTORS AND CARTILAGE: FROM MECHANISMS TO DMARDS
Marc Hochberg, University of Maryland, School of Medicine, United States of America

Biologic medications have revolutionized the treatment of many rheumatologic diseases, but their high cost often limits patient access to these effective treatments. Biosimilars are legitimate copies of biopharmaceuticals, which no longer are protected by patent, that have undergone rigorous analytical and clinical assessment in comparison to their reference products and have been approved by a regulatory authority in a highly regulated area according to a specific pathway for biosimilar evaluation. In 2005, the European Medicines Agency (EMA) established a pathway for the review and approval of biosimilars and, one year later, approved the human growth hormone Omnitrope as the first biosimilar. As of March 2019, 56 of 60 biosimilars approved by the EMA were commercially available in the European Union, of which 6 were of rituximab and 15 were of TNF inhibitors to treat rheumatologic diseases.

Commercially available lots of a reference product are not identical to one another. All biologic medications are subject to normal batch-to-batch variability and are monitored to ensure that this variation is within “proven acceptable ranges” so that patients are not subjected to risks of lesser safety or efficacy. Since biosimilars have been compared extensively to their reference products and been shown to have highly similar structure, equivalent efficacy, and comparable safety, an approved biosimilar can be considered to be like another batch of its reference product. Thus, patients need not be apprehensive about using an approved biosimilar in place of its reference product.

The “nocebo effect” refers to the misattribution of bodily symptoms to a medication and may result in discontinuation of a treatment that is not actually causing the perceived symptoms. Studies have suggested that the nocebo effect may result in discontinuation of treatment with a biosimilar because of subjective perceptions. This may be addressed by providing encouragement and reassurance through education and open collaborative discussion between providers and patients. By taking this approach to counseling patients, the rate of biosimilar discontinuation may be reduced.

The NOR-SWITCH study demonstrated that patients with inflammatory diseases controlled on treatment with reference infliximab do not experience greater worsening of disease activity when switched to biosimilar infliximab CT-P13 than when continued on treatment with the reference product. Thus, when the cost of the biosimilar is significantly lower than that of its reference product, substituting the biosimilar for the reference product may provide an economic advantage with no loss of clinical benefit. In Norway, where there is an annual “winner takes all” competitive tender process for hospital administered medications, the price of bio- similar infliximab in 2015 was 69% lower than that of its reference product. Thus, in most countries, it is safe, effective, and cost-effective to switch to a biosimilar. However, competition from biosimilars has occasionally driven down the price of a reference product, as in Sweden where the price of reference adalimumab was reduced by 80% in 2018 and became lower than that of adalimumab biosimilars.

The availability of lower-priced biosimilars should decrease the cost of treating patients by introducing market competition. Biosimilars should be more readily available to patients for whom the reference product had been inaccessible because of cost. Greater global access to effective biologic medications should reduce disability, morbidity, and mortality associated with rheumatologic diseases.

Disclosure of Interests: Jonathan Kay Grant/research support from: Gilead Sciences, Pfizer, UCB Pharma, Consultant for: AbbVie, Boehringer Ingelheim GmbH, Celtrion Healthcare, Merck Sharp & Dohme Corp., Novartis Pharmaceuticals, Pfizer, Samsung Bioepis, Sandoz, UCB Pharma.
How to perform low-budget high-quality research

**SP0016 YOUR VERY FIRST STEPS ON SYSTEMATIC REVIEW**
Loreto Carmona, Instituto de Salud Musculosqueletica, Research, Madrid, Spain

Systematic reviews (SR) are a type of clinical research, and thus they follow the hypothetical-deductive or scientific method. Their objective is to answer clinical questions and they do it based on a specific structure (protocol) and working through inferences. Interestingly, a SR is a type of study design that can answer all types of questions, from efficacy to incidence. They manage the information from previous studies in a newly established reproducible way, as unbiased as possible. They provide quick answers. However, they should be performed and interpreted with caution: a poor systematic review is much worse than a narrative review, as it gives the false impression of "science". This is even worse if the studies were combined in a meta-analysis.

In this lecture, we will review the protocol of a SR, the importance of rephrasing the question, the search strategy, selection criteria, and procedures of studies selection, primary endpoints, and quality and risk of bias. The last part of any SR is the analysis, which is always qualitative, supported by the evidence table, and following a synthetic discourse with the PICO order, and sometimes quantitative (meta-analysis). We will review some methods to evaluate publication bias, to combine results, and to explore heterogeneity. In this sense, it is essential to note that if we cannot find a valid explanation for heterogeneity, our results may not be valid.

**Disclosure of Interests:** Loreto Carmona Grant/research support from: Abbvie, Actelion, Astellas, BMS, Eisay, Gebro Pharma, Grünenthal, Leo Pharma, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi-Aventis and UCB Pharma, Paid instructor for: Novartis


**SP0017 USING AVAILABLE DATASETS TO ANSWER NEW RESEARCH QUESTIONS**
Daniel Prieto-Alhambra, University of Oxford, NDORMS, Oxford, United Kingdom

**Background:** Clinical data are continuously recorded in clinical encounters in the form of electronic medical records, registries, audits and similar databases. Such large datasets are available to researchers, and provide unique opportunities. However, challenges arise from the use of routinely collected data, that need special attention and specific skills to minimize a waste in research.

**Objectives:** To discuss available data sources (data discovery), their advantages and limitations, their uses, and to cover examples of research conducted using routinely collected datasets.

**Methods:** We will discuss a list of data sources at high level (types of data), their main pros and cons, and then cover challenges and solutions through a number of previously published examples.

**Disclosure of Interests:** Daniel Prieto-Alhambra Grant/research support from: Grants from Amsen, UCB Biopharma and Servier outside the submitted work, Consultant for: UCB Biopharma, Speakers bureau: Amsen


Health Professional Welcome session

**SP0018 WHAT YOU SHOULDN'T MISS FROM THE HPR PROGRAMME AS A CLINICIAN**
Maria Bergström, Linköping University, Department of Social and Welfare Studies, Division of Occupational Therapy, Norrköping, Sweden

As a health professional, the EULAR congress is the place where I can get access to new and fresh rheumatology research of good quality. My presentation will take you through the possibilities the congress offers clinicians when it comes to different topics within the area of rheumatology. Further, my aim and hope is to give you a sense of what is in store for you during this year’s EULAR congress. People with rheumatic diseases today live their lives to a great extent having the diagnosis affecting their everyday life. The ability to work, interact with others or engaging in activities they want to, can be limited. So what do we need to know about them in order to provide the best possible treatment and rehabilitation? As a health professional clinician, I look forward to finding some of the answers to this during this congress.

During the EULAR congress, we as health professionals have the possibility to contribute to and acquire research of good quality in rheumatology, on our way to giving our patients the best possible treatment. Also, we have the possibility to contribute to the patients' health, and I look forward to sessions touching health topics such as exercise. The quality of research and the variety of topics during this EULAR congress can give us a bigger set of tools to work with when we get back to our patients and continue our path towards the best possible treatment and health for this big and important group of patients. I hope that this session can provide an overview of what this years’ congress can offer from a clinical perspective.

**Disclosure of Interests:** None declared


**SP0019 PRES HPR: DONT DELAY, COLLABORATE TODAY**
Jeanette Cappon1, PReS Committee for Health Professionals1, Department of pediatric rehabilitation, Reade Center for rehabilitation and rheumatology2, Dutch Health Professionals in Pediatric Rheumatology3, Reade Center for Rehabilitation and Rheumatology, Pediatric Rehabilitation, 1056AB Amsterdam, Netherlands

**Background:** The Pediatric Rheumatology European Society (PReS) is an international organization based in Europe which is dedicated to advance the care and improve the health and well-being of children and young people with rheumatic conditions, helping them to reach their full potential. Full PReS membership is extended to individuals from all European countries, whether they are within the EU or not, and includes countries in the middle east and from other parts of the world as associate members to enrich the collective experience and knowledge. PReS welcomes every practitioner/researcher in the field of pediatric rheumatology.

The PReS committee for Health Professionals in Pediatric Rheumatology aims to bring together nurses, physical therapists, occupational therapists, social workers, psychologists, pediatricians and other health professionals (HP) to foster dialogue, to set standards of clinical practice, education and research.

Collaboration between PReS and Eular Health Professionals starts today, here in Madrid. Collaboration in general starts with a shared goal to work on together. Our young patients of today might be your patients of tomorrow: what should you know about what they have been through? Your patients of today might have been our young patients of yesterday: what can we learn from their experiences of the past being a child with a rheumatic condition? Did they receive comprehensive care that sustained into their adulthood?

**Objectives:** To find shared goals between HP Eular and HP PReS to deliver comprehensive care for people with rheumatic diseases during their full life.

To find common interests to discuss between HP Eular and HP PReS.

**Methods:** Examples of common interests e.g. supporting self management of pain and health and illness education are presented.

Shared goals for collaboration are proposed and collected from the audience.

**Results:** Health Professionals from Eular and PReS experience common interests and shared goals. Positive relations are expected to develop upcoming years.

**Conclusion:** Collaboration between Eular and PReS can start today

**Disclosure of Interests:** None declared


EULAR Projects in paediatric rheumatology

**SP0020 THE GLOBAL CHALLENGE AND OPPORTUNITY FOR PAEDIATRIC RHEUMATOLOGY**
Christian Scott, University of Cape Town, Red Cross War Memorial Children’s Hospital, Paediatric Rheumatology, Cape Town, South Africa

**Background:** Poorly developed healthcare systems and the overwhelming burden of communicable diseases have limited the growth and development of Paediatric Rheumatology in non central and less resourced countries.1,2 Most children on earth reside in these less resourced environments and suffer from disproportionately poor access to adequate care for paediatric rheumatic diseases. Emerging evidence suggests that rates of rheumatic diseases are not likely to be different to European and North American children but that diseases severity and
outcomes may be worse and that children in these countries face the additional burdens of poverty, socio-political instability and communicable diseases. 3, 4

Objectives: To review the current situation and challenges faced by the children in less resourced countries with rheumatic diseases and those who provide medical care for them, and to explore opportunities that will drive the global development of paediatric rheumatology to the benefit of all children with rheumatic diseases.

Methods: A thorough review of published literature and gaps in knowledge on the epidemiology and outcomes of childhood rheumatic diseases from less resourced countries. A review of current and planned global initiatives to improve Paediatric Rheumatology care in less resourced countries.

Results: Despite increasing emerging data on paediatric rheumatic diseases from less resourced countries, data on paediatric rheumatic diseases from less resourced countries are sparse. Paediatric rheumatology services in most countries remain inadequate or non-existent to serve the needs of the population, despite encouraging growth in some areas. Improvements in healthcare systems in these countries offer opportunities for the growth of paediatric rheumatology care. Greater genetic diversity and different disease profiles offer opportunities for the advancement of genetic and environmental influences on rheumatic diseases.

Conclusion: An organised effort from the paediatric rheumatology global community can play an important role in the development of education, networks, services and research capabilities that could lead to increased scientific growth and clinical benefits for all children with rheumatic diseases, regardless of their geographical or socio economic position.

REFERENCES:

Disclosure of Interests: None declared


SP0021 DELIVERING FUTURE GLOBAL RESEARCH CHALLENGES IN PAEDIATIC RHEUMATOLOGY

Nicolino Ruperto, Istituto Gaslini, Clinica Pediatrica e Reumatologia-PRINTO, Genoa, Italy

The treatment of pediatric rheumatic diseases has improved tremendously in the last 20 years thanks to appropriate legislative initiatives, the existence of very large collaborative networks and the availability of new potent medications. In particular, JIA has transformed from a tremendous impairment of patients with juvenile idiopathic arthritis (JIA) with over 3500 children enrolled in trials with registriative purposes. For JIA now the tendency is to concentrate on oral therapies and on drugs targeting specific JIA categories. Also in juvenile systemic lupus erythematosus (SLE) the childhood counterpart of SLE there are several potential targets to be tested in children. In addition the field of paediatric rheumatology has provided an excellent example of large scale academic studies which, through the Paediatric Rheumatology International Trials Organisation (PRINTO) have enrolled over 38,000 children from over 60 countries.

Further improvement in future years will stem from a better definition of the paediatric disease entities, the discovery of laboratory and imaging biomarkers that could help the tuning of therapy, a smoother implementation of future clinical trials, a more standardized link between academia (clinical and basic science), regulatory authorities, learned societies such as the Pediatric Rheumatology European Society (PRES) and family organisations for the planning of future trials.

This lecture will present a general overview and a perspective for the future (mainly academic) work to align clinical data collection with basic researchers, PRES, and family associations in order to foster and facilitate drug evaluation in pediatric rheumatic diseases as well as academic research.

REFERENCES:
INTRODUCTORY TALK ON CRYSTAL ANALYSIS

RELIABILITY IN THE LAST 10 YEARS: OBJECTIVES:

1. Intra-observer reliability has been shown in several studies to be higher than inter-observer.
2. Assessment of ‘evaluability’ varies between observers and therefore also needs to be taken into account when assessing reliability.
3. Subject to evaluability, certain parameters demonstrate high intra- and inter-observer reliabilities. Reliability differs across different capillaroscopic parameters.

Conclusion: Recent studies examining reliability of capillaroscopy suggest that certain parameters, including image grade, capillary density and apex width have high intra-and inter-observer reliabilities (subject to nailfold image evaluability, which remains a major challenge). Standardisation training is likely to improve reliability.

REFERENCES:

Methods and tools for quantization of capillaroscopic morphological changes

Alberto Sulis, University of Genoa, Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, IRCCS Polyclinic Hospital San Martino, Genova, Italy

Capillaroscopy is routinely used in clinical practice to assess nailfold microvascular structure. Unlike laser techniques that give functional information, capillaroscopy allows a morphological assessment of nailfold capillary bed. It is a recognized tool to early differentiate primary from secondary Raynaud’s phenomenon, as well as to follow scleroderma microangiopathy. As microangiopathy extent correlates with organ involvement degree, nailfold capillaroscopy abnormalities are also considered a possible biomarker in systemic sclerosis.1,2 Several tools may be used to quantitate morphological capillary changes, from devices with low magnification (20x), to instruments with high magnification (200x or more).3-5 The instruments with low magnification allow a global evaluation of the entire nailfold area (wide-field capillaroscopy), and they provide a panoramic vision of the whole nailfold microvascular network. Magnifying glass, ophthalmoscope and dermatoscope are example of optical instruments with low magnification. Obtaining a high-quality documentation may be difficult by these tools, as well as the identification of early capillary changes; furthermore, storing capillary images is not possible.

Stereomicroscope, usb-microscope or videocapillaroscope allow a sequential higher magnification up to 600x which enable detailed observation of small nailfold areas or single capillaries. However, by using a microscope, patient’s fingers must be placed under the lens, and this may make the exam sometimes difficult, for example in the presence of either finger contractures or arm disabilities.

The optical probe videocapillaroscope is currently considered the gold-standard for nailfold videocapillaroscopy, as it has the advantage to be moved to the finger of the patient at direct contact with the nailfold: this facilitates examination of patients with systemic sclerosis and finger flexion contractures, simply by moving the probe. The use of videocapillaroscope has a high sensitivity, a short time of execution after an easy operator training, allows early diagnosis of secondary Raynaud’s phenomenon by very early detection of microvascular changes, and also allows the counting and scoring of capillaroscopic parameters. Connection of the instrument with a software enable image recording, report writing and automated capillary number counting.

To quantitate capillaroscopic morphological changes (mainly capillary number, capillary dilations, giant capillaries, microhemorrhages, abnormal shape/ramified capillaries, capillary bed disorganization) a simple rating scale may be adopted to score each capillary abnormalities (score 0-3) (score 0 = no changes; score 1 = less than 33% of capillary alterations/reduction; score 2 = 33-66% of capillary alterations/reduction; score 3 = more than 67% of capillary alterations/reduction, per linear millimetre. Reduction = capillary number per linear millimetre ×0.5). The mean score value for each capillaroscopic parameter is calculated from the analysis of at least two millimetres in the centre of the nailfold, by evaluating the first row of capillaries in each finger from 2nd to 5th. The Microangiopathy Evolution Score (MES) (sum of scores of progression parameters: capillary number, abnormal shape/ramified capillaries, capillary bed disorganization - Score 0-9) may be calculated to follow the scleroderma microvascular damage.6,7 However, at least the simple capillary number per linear millimetre should be counted, as well as larger capillary diameters measured, to monitor microangiopathy in systemic sclerosis.1,2

References:


Disclosure of Interests: None declared

**SP0029 RHEVITAL: CONTROLLING YOUR DISEASE ACTIVITY WITH AN APP**

Corrina Elling-Audersch, German Leage against Arthritis, NRW, Solingen, Germany

**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory disease requiring long-term treatment with regular monitoring of the ongoing therapeutic process by a rheumatologist to achieve good health outcomes and prevent negative disease impacts.

**Objectives:** The RheVITAL App is the product of a new and multilayered concept of treatment. A combination of a team of rheumatologists, physiotherapists, IT specialists and research partners from the German League against Arthritis have all contributed to the development of this research project.

**Methods:** The presentation will show how this monitoring system improves the treatment of RA individually, monitors the patients on their way to self-empowerment and promotes participative collaboration between patients and rheumatologists.

**Results:** The patients play an active role in the whole system. The patients are trained about their diseases, their treatment and the medicine they are taking. Furthermore they are given much more information about the German patient organisation.

**Conclusion:** My talk will consider the function and management of the app, the difficulties as well as the efforts of data security and the role of the patient organisation as a research partner involved in this project.

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.8469

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**SP0030 DEVELOPING E-HEALTH SOLUTIONS FOR PATIENTS WITH PATIENTS**

Susanne Karlfeld, Karolinska Institutet, Academic Specialist Center, Center for Rheumatology, Stockholm, Sweden

**Background:** At the Center for Rheumatology the Patient’s voice and needs are always central in the planning and development of the organization and its services and structure. The Patient Council at the unit, with representatives from 14 different patient organizations, is a core facility that is always addressed when decisions are to be made that affects the patients. The need of a structure for digital re-visits at the clinic was raised in the Patient Council meeting.

**Objectives:** To develop a structure for a fully digital re-visit where all the preparations, the actual visit and the documentation and follow up could be conducted using different e-Health solutions and digital tools.

**Methods:** By first asking the involved patient representatives about desired interfaces and features of the end solution, we could decide on which available tools and structures we could build the digital re-visit around. A working group including patients, health care providers at the unit and technical staff, together formed the end product.

**Results:** A fully digitalized structure for re-visits to different health care providers (physicians, nurses, physiotherapists etc) is now up and running with an increasing number of visits every week.

**Conclusion:** By asking the patients about what is most important for them we focus on solutions and services that the patients really need and ask for. If we involve patients in the process from the very beginning, we know that we are doing the right thing and that we use our resources in the best way.

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.8510

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**SP0031 NEWS IN THE WORLD OF REHABILITATION**

Ann Bremerland, Ranb Spenshult, Sweden

The ageing population and the increasing prevalence of chronic diseases is a great challenge for future health care systems. There will be a growing demand for rehabilitation services and a need to strengthen rehabilitation in the health system. According to the World Health Organization (WHO), rehabilitation is “the key for health in the 21st century”. In the document Rehabilitation in health systems (2017), the WHO presents a number of overarching principles for rehabilitation services: the provision of person-centred care, the continuum of care across different levels of the health care system, and the importance of accessible, affordable care of high quality to everyone in need of rehabilitation. With reference to the WHO overarching principles, I will shortly address and discuss some achievements and challenges in the delivery of rehabilitation services supported by recent and ongoing studies. Rheumatic and musculoskeletal diseases (RMDs) include over 200 diagnoses why the talk will include examples from rehabilitation services given to people with inflammatory arthritis (IA). Over the last decades, pharmacological interventions has contributed to improved quality of life for a large number of people with inflammatory arthritis (IA). However, a relatively large group of people with IA lives with a persistent disease and experience pain, fatigue, physical disability, impaired work ability and decreased quality of life, emphasizing the need of rehabilitation services. I will discuss advancements and challenges in providing person centered care, in bridging the gap between health care sectors, the challenge to provide evidence of an effective rehabilitation service of high quality and if we provide accessible rehabilitation services according to the need of people with rheumatic diseases.

**REFERENCE:**


**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.8435

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**SP0032 HOW TO MEASURE REHABILITATION**

Alison Hammond, University of Salford, Centre for Health Sciences Research, Salford, United Kingdom

**Background:** Measuring outcomes is fundamental to rehabilitation. A wide range of subjective and objective outcome are available to health professionals, with patient reported outcomes (PROs) being widely used. Fundamental to their use is understanding how to select appropriate measures and interpret results.

**Objectives:** This talk addresses: how to identify and select patient reported outcomes measures; the COSMIN taxonomy; understanding measurement properties; evaluating fitness for purpose; and understanding cross-cultural and linguistic validation of PROs, to enable PROs to be used across countries. This will be illustrated with an example of a Swedish – English-Dutch-German PRO, the Evaluation of Daily Activity Questionnaire.

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.8491

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**SP0033 RHEUMATOLOGICAL REHABILITATION, WHAT’S NEXT**

Thea Viert Vieland, Leiden University Medical Center, Orthopaedics, Rehabilitation and Physiotherapy, 2300 RC Leiden, Netherlands

Over the past years, there have been major changes in the delivery of rheumatology rehabilitation and advances in its evidence base. To make rheumatology rehabilitation future-proof, a number of developments in the medical treatment of people with rheumatic and musculoskeletal diseases (RMDs), health systems and society as a whole need to be taken into account with the planning of services and their evaluation and the training of health professionals in rheumatology (HPRs).

Regarding the health status and needs of people with RMDs, their profile has changed markedly over the past decades, to a large extent due to improvements in the medical treatment. But some patients may not respond well to treatment, and for those who do, there may still be challenges to keep up with the increasing demands of our society.

For reasons of transparency, quality and efficiency there is a need to demonstrate the added value of rehabilitation, by working along defined rehabilitation care pathways. But care also needs to be personalized, tailored to a person’s individual situation, abilities and needs. This includes, among others, that people with RMDs must be involved in any treatment decision, requiring a specific level of health literacy.

The actual delivery of rehabilitation services by means of extensive inpatient or outpatient trajectories is under pressure in many health care systems, for economic reasons but also because treatment in one’s own environment whenever possible, is preferred by many people with RMDs. For that purpose, adequate use of digital interventions, but also seamless care involving primary care clinicians with specific expertise is needed.

All of the abovementioned developments require specific competences of HPRs, not only including the optimal assessment and treatment of individual people with RMD, but also makes a strong appeal to e.g. their communication, advocacy and organizational skills and abilities to monitor the quality of their practices and redesign when needed.

This presentation addresses current and future challenges for HPRs in rheumatology rehabilitation and how they can anticipate to be prepared for the next phase.
RA-MAP. PATIENT STRATIFICATION IN RA

John Isaacs, Newcastle University, Institute of Cellular Medicine, Newcastle upon Tyne, United Kingdom

Background: When we assess rheumatoid arthritis in the clinic we quantify inflammation. Apart from measuring auto-antibodies we do not assess the immune system.

Objectives: The MRC/ABPI RA-MAP study was an academia-industry consortium designed to characterise the immune dysregulation that presents clinically as RA. Key questions were:
- Are there baseline immune markers of prognosis/therapeutic response?
- What is the molecular signature of the disease state (is there an immune correlate of inflammation)?
- Can RA be defined in terms of immune dysregulation and are there distinct subtypes?

Methods: RA-MAP was a systems immunology analysis of 275 patients with seropositive, treatment-naive early RA (the TACERA cohort). Patients were assessed at baseline and every 3 months for up to 18 months. At each visit, clinical samples were collected for transcriptomic (blood), proteomic (blood and urine) analyses. Peripheral blood mononuclear cells were characterised by flow cytometry. Clinical and demographic information was collected at each visit. Primary analyses addressed the key questions by seeking associations between immune parameters and disease activity or disease state.

Results: Latent class analysis of clinical data revealed three main disease trajectories. Transcriptomic and systems approaches highlighted at least two subtypes of seropositive RA. Proteomic analyses also supported multiple RA subtypes. Metabolomic analyses revealed prognostic baseline signatures. Flow cytometry revealed a reduction in peripheral blood mononuclear cell complexity as disease became less active. Combinatorial analyses of different datasets is currently underway.

Conclusion: RA-MAP has provided important insights into the immunological and molecular heterogeneity of RA. Our findings require replication and validation, and some analyses are ongoing. RA is the consequence of dysregulated immunity characterized by distinct molecular ‘endotypes’.

REFERENCES:


SP0036 MASTERPLANS – TAILORING SLE FOR THERAPY

Ian N. Bruce, University of Manchester, United Kingdom

Background: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease which is highly heterogeneous in its clinical manifestations and also in its response to specific therapies. Across a number of trials of novel agents, overall response rates are approximately 40-60% and in the past almost 60 years only one drug (belimumab) has been licensed for use in SLE. Current therapy is therefore based on a ‘trial and error’ approach frequently involving glucocorticoid co-therapy. Delayed and poor control of inflammation results in organ damage, cardiovascular disease and glucocorticoid toxicity. We established a consortium of academia and industry partners (Maximizing SLETherapeutic Potential, by Applicating Novel and Stratified approaches (MASTERPLANS)) with the aim of identifying key endotypes associated with response and low disease activity on particular therapies.

Objectives: Our consortium is addressing the hypothesis that strata exist within SLE populations that will enable more targeted use of existing and novel therapeutic agents and improve response rates. Specifically, B-cell related biomarkers including dynamics and function predict responses to mycophenolate mofetil (MMF) and B-cell targeted biologics and interferon signature/pathway dynamics identifies patients with poorer responses to these agents.

Methods: Our approach will firstly be to re-analyse data already available from large studies and trials to identify key predictive factors of response. Also, using data from a large UK cohort, the BILAG-Biologics Register, we will assess clinical factors and biomarkers that predict response and low disease activity. Combining results from these studies with that gained from previous studies will enhance our ability to identify endotypes of response.

Conclusion: Identifying biomarkers of response will allow better selection of therapeutic agents for individual patients. Using the right drug at the right time will improve control of inflammation for patients with SLE and contribute to improving long-term outcomes.

Disclosure of Interests: Ian N. Bruce Grant/research support from: Genzyme Sanofi, GlaxoSmithKline, Consultant for: AstraZeneca, Eli Lilly, GlaxoSmithKline,
USING GENETICS IN PERSONALISED MEDICINE IN RHEUMATIC DISEASES

Anne Barton.
University of Manchester, Centre for Musculoskeletal Research, Manchester, United Kingdom

Background: For all treatments available for rheumatoid arthritis (RA), none are effective for all patients. For many drugs, patients are given 3-6 months of treatment before a decision is made regarding efficacy and, for those in whom the treatment does not work, that can be a period of on-going disease activity, exposure to the risk of side effects and possible accumulation of joint damage, all of which impact quality of life. Straited medicine approaches aim to better target treatments to those most likely to respond. However, currently, CRP/ESR are the only biological markers (biomarkers) routinely used to inform whether therapy is required and RF/ACPA status are often considered.

Objectives: To update in progress of using genomic approaches to inform treatment selection in rheumatoid arthritis

Methods: National and international precision/stratified medicine programmes are investigating whether genetic and epigenetic biomarkers could help in the selection of therapy and progress will be reviewed.

Results: Recent studies have developed new outcome measures to assess treatment efficacy for controlling synovitis, confirming previous findings from genetic studies of heritability. Issues around the best tissue to sample, the predictive ability of a test and confounding factors including adherence will be considered and emerging biomarkers reviewed.

Conclusion: Matching the right treatments to the right patients is the goal of personalised medicine and potential biomarkers are starting to emerge. However, caution is required as none have so far been proven to be clinically useful or cost-effective.

REFERENCE:

Disclosure of Interests: None declared

SP0038 FACTORS IMPORTANT FOR MEDICAL ADHERENCE

Bart van den Berst.
Sint Maartenskliniek, Netherlands

Factors important for medical adherence in rheumatic diseases

Disease-modifying antirheumatic drugs (DMARDs) are the cornerstone for the treatment of inflammatory arthritis and fundamental to prevent radiologic progression in patients with rheumatoid/pсорiatic arthritis. However, the full benefit of DMARDs can only be achieved if patients follow prescribed treatment regimes. Adherence, or the extent to which patients take medications as prescribed, is however low in chronic medical conditions: approximately 50% of all people with chronic medical conditions do not adhere to their prescribed medication regimens [1,2]. Previous research in patients with rheumatic diseases vary from 30% to 107%, depending on the used measurement method [7].

Thus, improving adherence to DMARDs could dramatically improve the efficacy of drug therapy in rheumatic diseases and reduce costs. However, so far, interventions designed to improve medication adherence are only partly effective in changing medication-taking behaviour [2-5].

To be able to improve adherence, factors should be known that are associated with medication adherence in RA. This will help us to target non-adherent patients and design interventions to improve adherence. Although several studies have examined factors associated with adherence to treatment with DMARDs, hardly any variable was found to be consistently and strongly related to adherence [6-7]. Despite this, there is evidence that especially patient’s need to take medication, prior DMARD use, patient’s self-efficacy and information delivered to the patient might be associated with medication adherence.

Overall, two types of non-adherent behaviour are commonly observed: unintentional (due to forgetfulness, regimen complexity or physical problems) and intentional (when the patient decides not to take the treatment as instructed). In case of intentional non-adherence, the decision to take medication is based on a cost-benefit analysis weighing the costs/risks of the treatment against the perceived benefits. This implicates that health care professionals should individually assess patient’s (un)intentional barriers to take medication and target medication adherence interventions on patient’s individual barriers. Thus, besides tackling (un)intentional) practical barriers, such as forgetfulness (with for example reminder services), clinicians should also be sensitive to patient’s personal beliefs that might impact medication adherence, and should discuss with their patient any concerns that they raise about prescribed medications. This lecture will give insight in the latest insights in the research of factors important for medication adherence and their practical consequences for adherence improving interventions in clinical practice.

REFERENCE:

Disclosure of Interests: Bart van den Berst Grant/research support from: UCB, Pfizer, Abbvie; Speakers bureau: Pfizer, Abbvie, UCB, Biogen, Sandoz, Consultant for: UCB, Novartis and Pfizer

THURSDAY, 13 JUNE 2019
10:15:00 – 11:45:00
Advances in understanding and treating of SLE

SP0039 WIN: DE-CONVOLUTING THE COMPLEXITIES OF SLE – RECENT INSIGHTS INTO THE PATHOPHYSIOGENESIS

Mary K. Crow.
Hospital for Special Surgery, Weill Cornell Medical College, Mary Kirkland Center for Lupus Research, United States of America

Background: SLE remains one of the most complex diseases in medicine, with protein alterations in immune system function contributing to autoimmunity, tissue inflammation and damage, and diverse clinical manifestations. While considerable advances in understanding the molecular pathways and mediators involved in SLE have led to identification of rational therapeutic targets, a full understanding of the upstream etiologic drivers of the disease and how genetic risk and environmental stimuli shape the evolution of the disease and its clinical heterogeneity requires continued investigation.

Objectives: To review recent literature relevant to the etiology, pathogenesis and heterogeneity of SLE.

Methods: Review and synthesis of recent literature.

Results: Recent advances in characterizing the mechanisms of regulation and degradation of endogenous nucleic acids, particularly invariants derived from disorders based on a variety of single gene mutations that result in production of type I interferon, suggest potential drivers of type I interferon production in SLE. The functional alterations in many aspects of T and B cell function in patients with SLE, some attributable to type I interferon, continue to be identified. Potential contributions of the microbiome expand our view of candidate disease-enhancing factors. Interest in defining patients at risk for evolving from pre-clinical to clinical disease...
that fulfills classification criteria for SLE may help to identify the essential elements of lupus pathogenesis and suggest approaches for disease prevention.

**Conclusion:** Endogenous nucleic acids have emerged as compelling candidates for drivers of lupus pathogenesis, along with their traditional role as antigenic targets of lupus autoantibodies. Although the clinical heterogeneity of SLE has contributed efforts to successfully test new therapies, advances in identifying sources of nucleic acids stimulating type I interferon and alterations in adaptive immune system function help us move toward a synthetic understanding of disease pathogenesis and suggest that therapeutic regimens targeting both innate and adaptive immune systems might be required to control or prevent disease.

**REFERENCES:**


Disclosure of Interests: None declared

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**SP0040 HOT: NOVEL PARADIGMS IN THE MANAGEMENT OF SLE**

**Thomas Dörner,** Charité Berlin, Berlin, Germany

Heterogeneity of systemic lupus erythematosus (SLE) remains challenging and, thus, many unmet needs remain, including the development of safer and more efficacious therapies to better control SLE activity resulting in improved outcomes. To develop innovative therapies, we need a far better understanding of its pathogenesis including delineation of clinical phenotypes. Recently, the lupus community has developed new classification criteria, T2T principles as well as low lupus disease activity and remission definitions to overcome obstacles created by SLE heterogeneity and improve outcomes. New proposals for the histologic classification of lupus nephritis have also been put forward and undergo evaluation. Recent therapeutic advances and clinical developments hold promise for improved treatments in this challenging disease and will be discussed.

**Disclosure of Interests:** Thomas Dörner Grant/research support from: Eli Lilly, Janssen, Roche, UCB Pharma, Consultant for: Eli Lilly, Janssen, Roche, UCB Pharma, Speakers bureau: Eli Lilly, Janssen

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**THURSDAY, 13 JUNE 2019**

**10:15:00 – 11:45:00**

**From child to adult care – breaking down the barriers of transition**

**SP0041 TACKLING TRANSITION: THE CURRENT LANDSCAPE, AND WHERE WE ARE HEADING**

**Stephen Bait,** Manchester University Foundation Trust, Specialist Medicine, Manchester, United Kingdom

The transition from childhood to adulthood is a key life stage. While the time course of the bio-psycho-social development of young people is continuous, many of the health and social care services with which they may be involved have relatively fixed, rigid structures. This can be challenging for young adults: leading to a sense of marginalisation and alienation. Young people with long term health conditions who are not equivalent, a developmentally appropriate approach to transition has clear benefits: seeing the process as being outcome and skills-based, rather than time-based.

Adolescence and early adulthood are times when life-long health behaviours are set in place; good health for young people is a foundation for good health in later life. There is a need to invest in age appropriate health promotion and youth-friendly health services if we are truly committed to improving young people’s health outcomes and the health of the adult population they will go on to form. There is an opportunity to develop and sustain a generational shift in health literacy and health-related behaviours: a real legacy; and an investment in the future.

**REFERENCE:**


Disclosure of Interests: None declared

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**SP0042 FROM PAEDIATRIC CARE TO ADULT CARE – THE NEEDS OF YOUNG PEOPLE, AND HOW HEALTHCARE PROFESSIONALS CAN FACILITATE OPTIMAL TRANSITION**

**Judy Ammerlaan,** University Medical Center Utrecht, Rheumatology and Clinical Immunology, Utrecht, Netherlands

In this presentation, the learning experiences and reflections of a healthcare team on redeveloping the transitional care for young adults with RMD’s are shared. In the process of redeveloping care, the healthcare team experienced that small steps, driven by patient stories and involvement of patients in all phases from development to evaluation, led to meaningful results. The eHealth interventions, developed to support the transition and to increase self-management were found to be feasible and evaluated positively by the young adult group. But the healthcare team also experienced that the focus on the patient alone, is not enough to implement self-management interventions and sustain patient centered care in daily practice. How healthcare professionals personally think and feel about patient centered care is essential and needs to be discussed in daily care. It determines the way of being present with attention and commitment in daily health care. It affects the hands, head and heart. A daily reflection on shared answers of the patient and the health care professional to the question ‘what is the most important to you?’ may help to implement patient centered care in health practice.

Disclosure of Interests: None declared

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**SP0043 MY IDEAL TRANSITION**

**Indra Beer,** Rheuma – Liga Bundesverband e.V., Projekt “Mein Rheuma wird erwachsen!”, 53111 Bonn, Germany

In my lecture I will present the barriers of transition from the young patient’s point of view and show possible solutions. Every year 2,000 young people aged between 16 and 19 arrive at the transition phase in Germany. One third of these young rheumatic patients stop or interrupt their therapy when they have to change from the paediatric rheumatologist to the adult rheumatologist.

In my talk I will focus on significant changes in the lives of young people. This includes e.g. the changes due to education and training, the first partnership or just moving out of the parents’ house.

Especially in the difficult phase of transition young people should be strengthened and be made aware of the differences between the doctors treating them and the barriers they will be facing. They should learn to manage themselves and be made sensitive that long-term damage can be avoided.

So, based on my experience I will outline the various support services that are necessary to prepare and accompany young people in that transition phase. Only then, in addition to evidence-based medical care, young people with a rheumatic disease can achieve a successful long-term healthcare outcome that will enable full participation in life.

Disclosure of Interests: None declared
Spondyloarthritides and vasculitis – new perspectives on outcome.

Raashid Luqmani
University of Oxford, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom

Background: Cyclophosphamide and more recently rituximab have transformed the outcome for granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA), resulting in survival in most cases. However, patients are at risk of frequent relapses, low grade gumprone disease, drug toxicity and worsening co-morbidity. Historically, prolonged courses of cyclophosphamide (used for both induction and maintenance) increased the risk of malignancy (especially bladder cancer). More limited use of cyclophosphamide, or the use of other agents including rituximab or methotrexate (for milder forms) offer safer but still effective options. The high relapse risk in AAV (especially in GPA) means that maintenance therapy is necessary but there is uncertainty over the most effective, safe long term choice. Maintenance RTX (fixed dose at fixed intervals of 4-6 months) is superior to azathioprine, but it is not clear if combination maintenance is superior to RTX alone. Long term side effects of RTX include hypogammaglobulinemia and potential for reactivation of JC virus. Reducing the glucocorticoid burden in AAV remains a challenge. We still do not know how long to continue therapy in AAV. Two recent studies provide conflicting opinion on the duration of maintenance therapy using azathioprine on risk of future relapse. The use of low doses of rituximab has recently explored in AAV: in thyroid eye disease, 100mg rituximab is effective. Less frequent dose intervals, as used in rheumatoid arthritis, will not control AAV. Future studies could address optimal long term management of patients with AAV, in order to improve their quality of survival and well-being.

Objectives: To assess the risk of relapse of vasculitis and to review the evidence for the use, effectiveness and toxicity of different maintenance strategies in systemic vasculitis

Methods: A review of published studies of long term outcome in vasculitis and of maintenance therapy in systemic vasculitis

Results: Once remission has been achieved, relapse is increasingly common, perhaps over 70% in some forms of ANCA associated vasculitis such as GPA. A strategy of induction therapy for one year, without any maintenance results in relapse in most cases of limited GPA. A maintenance regimen is recommended in order to avoid recurrence of the disease, but the evidence base for use of maintenance therapies remains limited. Maintenance is different from treatment of a relapse, usually aiming to prevent recurrence of clinical evidence of disease. We will show the evidence for different types of maintenance regimens and the outcomes in terms of relapse and toxicity with a focus on recently completed clinical trials and observational cohorts in a variety of forms of systemic vasculitis

Conclusion: The management disease in systemic vasculitis requires induction therapy but increasingly recognised is the importance of a maintenance regimen. Current and future strategies should explore a mechanism based approach, to selectively modify the underlying immunopathogenic mechanisms.

REFERENCES:

Disclosure of Interests: Raashid Luqmani Grant/research support from: Roche, Vifor and GSK

The exact role for new imaging technologies in osteoarthritis (OA) depends in part on the setting (clinical trials or routine care) and also on the tissues we decide are important to be studied.

In clinical practice, modern imaging such as ultrasound provides a useful adjunct for patients where there is diagnostic uncertainty - the EULAR recommendations for the use of imaging in the clinical management of peripheral joint OA provide an evidence-based background to this use of imaging. The impact of imaging is minimal in guiding choice of therapy as our therapeutic options (outside of surgery) are very limited.

In clinical studies and trials, there are a number of imaging modalities that provide insights into a range of OA tissues, for both quantification and characterisation. Most techniques have been based on MRI because of its soft-tissue advantages. In OA trials, MRI-based quantification methods provide improved responsiveness advantages over semi-quantitative scores, which have served an important role in highlighting the multi-tissue nature of OA and frequency of pathology. Using appropriate sequences, manual segmentation of cartilage or contrast-enhancing synovium can be quantified, and dynamic-contrast enhanced images can also be used to provide volumetric and pharmacokinetic assessments of the synovium. Using such information, we now know how to power studies for cartilage thickness endpoints.

A number of MRI techniques have been developed to study cartilage composition, such as T2mapping and T1rho. They have provided insights into structural deterioration, but are limited by technical aspects which make them difficult to apply in multicentre clinical trials.

Artificial intelligence and supervised machine learning have promised much in medicine, but in MSK imaging there has been some useful applications. Early technology applied 2D statistical shape models (SSMs) to X-rays, usually of the hip, providing novel information on bone shape. However the advent of 3D MRI or CT-based SSM technology has provided the ability to do automated quantification of large OA datasets. One of the most interesting tissues studied to date has been 3D bone shape. Studies have shown changes in bone shape are more responsive than radiographic joint space narrowing or even MRI quantitative cartilage thickness, predict incident radiographic OA, and that bone shape is associated with subsequent joint replacement. Recent work has shown a relationship between bone shape and bone marrow lesions, though these likely represent different elements of subchondral bone pathology. Work is just beginning on other relevant tissues such as the meniscus, and on other OA joints.

Disclosure of Interests: Philip G Conaghan Consultant for: Flexion Therapeutics, AbbVie, Medivir, Merck Serono, Novartis, GlaxoSmithKline

THURSDAY, 13 JUNE 2019
13:30–00:00

Can drugs and surgery help people with joint pain increase activity?

Speaker Abstracts


CASE 1 PRESENTER: ALL THESE PAINKILLERS AND STILL NOT GOING ANYWHERE

Kristine Røren Nordén. Diakonhjemmet hospital, Norwegian National Advisory Unit on Rehabilitation in Rheumatology and Norwegian National Unit for Rehabilitation for Rheumatic Patients with Special Needs, Oslo, Norway

Background: The session will present a case history of a 24 year-old male presenting with axial Spondyloarthritis and extensive pain problems. He had been treated with biological medication for a while, had a few inflammatory burden, but experienced persistent pain. Furthermore, he was on sick leave from his job as an electrician and had a very low physical activity level. The patient was admitted for a 3-week in-patient rehabilitation stay at the Norwegian National Unit for Rehabilitation for Rheumatic Patients with Special Needs. The unit offers person-centered, specialized interdisciplinary in-patient rehabilitation for patients with inflammatory rheumatic disease. Target group is patients with complex illness challenges and increasing function- or activity problems.

The rehabilitation was planned and organized through close cooperation between the patient and the specialized interdisciplinary team. Relationship between analgesics, pain and physical activity was a central issue in the rehabilitation process. The session will outline the patient response to comprehensive treatment modalities including changes in medication and participation in physical activity and exercise.

Objectives:
• To present the patient history
• To present results of the interdisciplinary examination
• To present the patient’s specific goals for the rehabilitation process
• To present experiences with pharmacological and non-pharmacological treatment modalities for this patient

Disclosure of Interests: None declared

CASE 2 PRESENTER: SITTING AROUND ON A NEW JOINT

Maaike Gademan. LUMC, Orthopaedics and Clinical Epidemiology, Leiden, Netherlands

The end-stage treatment for hip and knee osteoarthritis is arthroplasty. The main aims of this treatment are to improve pain and joint functioning. It is thereby conceivable that patients should become more physically active after surgery.

REFERENCES:
[3] Cook MJ, Bellou E, Bowes J, et al. The prevalence of co-morbidities such as cardiovascular diseases, diabetes and osteoporosis, and has beneficial effects on psychological health. The aim of this lesson will be to present a case history of a patient with extensive pain problems and discuss the treatment options based on relationship between analgesics, pain and physical activity.

Objectives:
• To discuss the effect of analgesics on activity
• To discuss the use of painkillers in connection with exercise
• To discuss pain tolerance during exercise
• To discuss the effect of physical activity on pain

Disclosure of Interests: None declared
Although the literature on the outcomes of total hip and knee arthroplasty (THA and TKA) is vast, relatively little is known about physical activity levels of OA patients undergoing surgery. This presentations summarizes the state-of-the-art literature on the physical (in) activity level of patients with an indication for THA or TKA and the changes of physical (in)activity levels after surgery. These results are presented taking into account the activity levels of the general population. The presentation will end with an informal quiz on physical (in)activity in THA and TKA patients.

REFERENCES:

Disclosure of Interests: None declared

Thea Vliet Vlieland.
Leiden University Medical Center, Orthopaedics, Rehabilitation and Physiotherapy, 2300 RC Leiden, Netherlands

The literature on the effect of total hip and knee arthroplasty (THA and TKA) on the amount of physical activity is scanty, with various studies suggesting that physical activity levels do not increase after surgery. These results raise several questions, such as: Are patients who will undergo or underwent THA or TKA more or less physically active than the general population? And, if not, should they become more physically active, what are barriers and facilitators for physical activity levels, what would be the potential benefits? Who are the stakeholders that should be involved in the promotion of physical activity in this patient group? These, and other questions will be highlighted in an interactive discussion with the attendees of the session.

REFERENCES:

Disclosure of Interests: None declared

THURSDAY, 13 JUNE 2019
13:30:00 – 15:00:00

My joints hurt and I’m overwhelmingly tired – fatigue in rheumatoid arthritis

José António P. da Silva. Centro Hospitalar e Universitário de Coimbra, Rheumatology, Coimbra, Portugal

Background: Fatigue is a frequent and important symptom in rheumatoid arthritis (RA), and it is associated with significantly reduced health-related quality of life, thus contributing to the impact of disease upon patients’ lives.

Objectives: To collect, summarise and interpret available evidence on the nature of fatigue and the best ways to assess it in Rheumatoid Arthritis

Methods: A systematic literature research was performed in trying to (i) to synthesise the size of fatigue in the global impact of rheumatoid arthritis; (ii) describe validated instruments and their psychometric properties as measures of fatigue, among patients with RA; and finally (iii) propose a clinically meaningful, valid and feasible process to measure fatigue in clinical practice.

Results: Fatigue has a major relevance in the overall burden of disease in RA. Several instruments have been validated to measure it, but no consensus has yet been reached to recommend a “gold-standard”.

Conclusion: Although fatigue is recognized by the rheumatology community as an important consequence of RA and a major gap in its current management of the disease, it has not been easy to measure and grasp. The problem seems to reside in the multidimensional causality and subjective nature of this phenomenon, which may warrant dedicated measures and interventions.

Disclosure of Interests: None declared

HOW TO PREVENT AND MANAGE FATIGUE IN PATIENTS WITH RA

James Galloway. King’s College London, Inflammation Biology, London, United Kingdom

Background: Fatigue is, similar to pain, a subjective symptom that occurs in many different diseases, particularly in patients with RA. Indeed, RA patients consistently report fatigue as one of the most disabling features of the disease (second only to pain). Fatigue is multifactorial in origin and reflects a complex construct of psychological, biochemical and physiological processes.

Objectives: If we are to effectively support our patients with RA, we must address fatigue. This requires understanding of which of our interventions work. At the end of the talk you should be familiar with how you can help manage fatigue, know which non-pharmacological interventions have a robust evidence and be aware of the impact of our different mode of action targeted RA therapies upon fatigue. For most our patients, a multimodal approach is needed.

Methods: This talk will present a narrative review of the evidence base around fatigue interventions in RA.

Disclosure of Interests: James Galloway Consultant for: Pfizer Inc

DECONVOLUTION OF THE IMMUNE RESPONSE

Lars Rogge. Institut Pasteur, Immunoregulation Unit, Immunology Department, 75015 Paris, France

Background: Anti-TNF therapy has revolutionized treatment of many chronic inflammatory diseases, including rheumatoid arthritis, Crohn’s disease and spondyloarthritids (SpA). However, clinical efficacy of TNF-inhibitors (TNFI) is limited by a high rate of non-responsiveness (30-40%) both in SpA and other diseases, which exposes a substantial fraction of patients to important side-effects without clinical benefit. Despite TNFI having been used extensively for many years, it is still not possible to determine which patients will respond to TNFI before treatment initiation.

Objectives: In this study, we have tested the hypothesis that the functional analysis of immune responses of patients before and after anti-TNF therapy may not only improve our understanding of the molecular mechanisms of TNF-blocker activity, but also identify correlates of therapeutic responses in SpA patients.

Methods: To facilitate the potential translational of our findings into a clinical setting, we have used standardized whole-blood stimulation assays (“TruCulture” assays; Duffy et al., 2014), and have minimized sources of pre-analytical variability, implementing a highly sensitive and robust pipeline to assess immune functions in patients.

Results: We show that anti-TNF therapy induces profound changes in patients’ immune responses, affecting predominantly several innate immune pathways. Of note, all these effects could be measured in stimulated, but not in resting immune cells, and were already detectable early, after a single TNFI injection. Modular transcriptional repertoire analysis revealed that TNFI affect immune responses via multiple mechanisms, such as directing monocyte/macrophage polarization and the inhibition of a TNF- and IL-1-dependent feed-forward loop of NF-kB activation.

On the other hand, the action of anti-TNF treatment was surprisingly selective, in that it did not affect the IL-6/Th17 or Th1 arm of the patients’ immune response. These findings have important implications for therapy, given the recent approval of anti-IL-17 antibodies as an alternative agent for the treatment of several chronic inflammatory diseases.

To investigate the concept that the immune status of a patient will define their response to TNFI treatment, we have used machine-learning algorithms to identify, in whole-blood stimulation assays, immunological transcripts that correlate with clinical efficacy of TNFI. We found that high expression, before treatment initiation, of molecules associated with leukocyte invasion/migration and inflammatory processes predisposes to favorable outcome of anti-TNF therapy, while high-level expression of cytotoxic molecules was associated with poor therapeutic responses to TNF-blockers.

Conclusion: These findings suggest that SpA patients whose immune response is characterized by strong, NF-kB-mediated inflammation are more likely to benefit
It is becoming clear that the field of medicine needs to change to stay affordable. One way of doing that is by optimizing the patients’ journey with true personalized medicine approaches. In other words, how to give every patient the right drug, at the right moment for the optimal duration. Recent advances in molecular techniques have truly revolutionized research into molecular fingerprinting—classification of clinical phenomena on the basis of a molecular basis rather than a diagnosis based on organ, symptoms or clinical criteria. This makes personalized medicine reachable within the coming years.

In my presentation I will dive in to the various molecular technologies (multi-omics) to achieve molecular fingerprinting of patients. Next, I will explain the computational techniques necessary to process the big data originating from the molecular processes enabling researchers to visualize big data from clinicians and patients. Finally, I will provide several examples of how these exercises might improve care for patients covering the space of rheumatic and musculoskeletal diseases (RMDs).

At the end of my presentation I will show how big data can be used for drug discovery, immune monitoring in clinical trials and/or daily clinical practice as well as drug repurposing. Together, I will provide a glimpse of the future on personalized healthcare within the field of RMDs.

Disclosure of Interests: None declared
TOWARDS OPTIMAL INTENSITY

George Melkos. University of Glasgow, Institute of Infection, Immunity, and Inflammation, Glasgow, United Kingdom

Background: There is ample evidence now to suggest that exercise can help ameliorate RMD symptoms and comorbidities. Similar to the prescription of medication, the dosage of exercise should be optimized to achieve the best health benefits. However, a consensus on the dosage of exercise prescription for RMD patients is currently missing.

Objectives: This talk will explore the data required from RMD patients to develop the best exercise prescription, exercise principles and current state-of-the-art, as well as how we can use the current evidence to identify the optimum dosage for the exercise prescription in people with RMDs.

Methods: Suggestions have been synthesized using existing evidence-based resources, including recent systematic reviews and meta-analyses (EULAR, Cochrane Library and peer-reviewed journals publications) as well as randomized controlled trials. Data for the effectiveness of exercise dosage on various different outcomes has been extracted and will be explored.

Results: Different dosages of exercise have differing effects on symptoms of RMDs. The optimal dosage depends on various factors and on the outcome that the exercise prescription aims to improve.

Conclusion: Despite the increasing research on exercise in RMDs, a currently a consensus for the optimal exercise dosage is currently missing. More interdisciplinary research, with a heavy patient involvement, is required in the area.

Disclosure of Interests: None declared

Getting a grip on the co-morbidities in gout

Edward Roddy. Keele University, Research Institute for Primary Care and Health Sciences, Keele, United Kingdom

Patients with gout very commonly have multiple co-existent comorbidities. Associations between gout and hypertension, obesity, chronic kidney disease and cardiovascular disease have long been recognised whereas several new comorbidity disease associations, such as sleep apnoea and mental health problems, have been described more recently, including lower risk of neurodegenerative diseases. These associations are complex with some comorbidities such as obesity and sleep apnoea predisposing to the development of gout, whereas gout is a risk factor for incident cardiovascular disease and erectile dysfunction. The management of gout is often more complex in the presence of comorbidity and can present a significant therapeutic challenge. This talk will provide an update on the co-morbidities that are associated with gout and discuss their implications for the management of gout, in particular for long-term urate-lowering therapy.

Disclosure of Interests: None declared

COSTA RHEUMATOLOGY – AN LIFESTYLE INTERVENTION

Jorge M. Rodriguez. Hospital General Universitario de Alicante-ISAIBAL, Sección de Reumatología, Alicante, Spain

Background: Gout is an independent cardiovascular risk factor. Patients suffering from gout show a higher incidence of all forms of the atherosclerotic disease, as well as cardiovascular and all-cause mortality. This associates with both comorbidities and urate crystal-led inflammation. Thus, gout, along with being the most common form of inflammatory arthritis in rich countries, carries with significant morbidity and mortality. Proper management is essential. The purpose of this lecture is to analyse the potential strategies aimed to control the cardiovascular risk in patients with gout.

Disclosure of Interests: None declared

REFERENCES:
THURSDAY, 13 JUNE 2019
13:30:00 – 15:00:00
EULAR SCHOOL OF RHEUMATOLOGY 2019: A NEW ERA FOR EDUCATION

Annamaria Iagnocco, Academic Rheumatology Unit Università degli Studi di Torino, Academic Rheumatology Centre, Turin, Italy

The first strategic aim of EULAR for the period 218-2023 is to be the leading provider of education in Rheumatic and Musculoskeletal Diseases (RMDs). The benefits that the rheumatology community gets from high levels of education in the field of RMDs result in an increased knowledge of them as well as in the optimization of their management. This leads to a significant relief to the lives of people with RMDs.

EULAR has traditionally been a strong supplier of education in rheumatology and the launch of the EULAR School of Rheumatology has further increased the EULAR’s educational offering and its quality, by providing tailored learning materials, improving access to high quality education in the field of RMDs and developing innovative learning methods and recognised EULAR certifications.

The School of Rheumatology is as a fully integrated operational entity contained within EULAR which combines all educational offers, whether they are live activities and material addressed to rheumatologists, undergraduates, trainees, teachers, researchers, health professionals, and people with RMDs.

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This presentation provides some theoretical and practical insights into “aktiv-hoch-r”.

Nicole Stefan-Schick
Sports Science consultant, Deutsche Rheuma-Liga Bundesverband e.V.

Disclosure of Interests: None declared

THURSDAY, 13 JUNE 2019
13:30:00 – 15:00:00
Ultrasound basic I

Loreto Carmona, Instituto de Salud Musculoesquelética, Research, Madrid, Spain

This is not an easy task to do in 20 minutes, but we will try to engage the attendee and to pass the message through. The most important take home message of this lecture will be that “it is the learning, not the teaching, what we must master”.

Good teachers are, therefore, mere facilitators of the learning process, not the stars. This lecture will have two parts, one dedicated to teaching in general and a second one on assessment (because assessment style drives learning behaviour).

Four are the principles of teaching in medicine: 1) orientation not only to knowledge but to problem solving, 2) adaptation to needs, 3) evaluation of the efficacy of teaching, and 4) learning should be enjoyable. We will review each one of these principles and how to implement them in our daily teaching. Things like preparing a lesson plan, or tips to engage learners, will be part of this lecture.

In the second part we will outline how to improve assessment and generate good questions.

Disclosure of Interests: Loreto Carmona Grant/research support from: Abbvie, Actelion, Astellas, BMS, Eisai, Gebo Pharma, Grünenthal, Leo Pharma, Lilly, MSD, Novartis, Pfizer, Roche, Sanofi-Aventis and UCB Pharma, Paid instructor for: Novartis

THURSDAY, 13 JUNE 2019
13:30:00 – 15:00:00
HOW TO ASSESS US LESIONS FOR GOUT + DEMO

Sara Nyssom, Center for Rheumatology and Spine Diseases, Rigshospitalet, Glostrup, Copenhagen Center for Arthritis Research (COPECARE), Glostrup, Denmark

Gout is the most common inflammatory joint disease in Western developed countries. Diagnosis and monitoring have historically been based upon clinical assessment combined with biochemical results (primarily p-urate) but over the last decade ultrasonography (US) has received increasing attention for these purposes. US has been shown able to detect monosodium urate deposits in both joints and tendons. In 2015 the Outcome Measures in Rheumatology (OMERACT) US Working Group developed definitions of structural lesions in gout. These include double contour sign (deposits of crystals on the surface of cartilage), tophus (larger hyper-echoic aggregation of crystals), aggregates (small hyper-echoic deposits) and erosion (1). The double contour sign has been included in the ACR/EULAR 2015 gout classification criteria as a way to visualize urate deposits in joints (2). Furthermore, US can visualize potential concomitant inflammatory aspects of gout since it can visualize both joint inflammation and tenosynovitis.

In this talk the diagnostic properties of US will be described and the potential risk of false positive results due to artefacts or misinterpreted lesions will be discussed. Furthermore, the potential role of US in monitoring of treatment response will be explored.

REFERENCES:

Disclosure of Interests: None declared
Background: Greater trochanteric pain syndrome (GTPS) is a clinical diagnosis with the typical presentation of chronic intermittent lateral hip/thigh/buttock pain, aggravated with activity and when lying on the affected side. There is a lack of valid/speciﬁc diagnostic criteria for GTPS. GTPS can be attributed to a multitude of causes ranging from tendinopathy and/or rupture of the gluteal tendons and/or bursitis, to pathological alterations of the iliotibial band/fascia lata and other nearby anatomical structures located on the lateral part of the hip. To further complicate the diagnostic process, according to different studies, the prevalence of GTPS in adults with lower back pain has been found to be between 20-30%. Alterations of the lumbar biomechanics may interfere in the range of internal rotation of the hip and consequently produce a GTPS and vice versa. Changes in hip range of motion will trigger changes in the dynamics of lower extremities and the spine. Generalized myofascial pain can also be a source of confusion when evaluating patients with GTPS.

Objectives: Understand the clinical anatomy of the lateral hip. Interpret the US images of the lateral hip. Identify potential pain generators of the lateral hip.

Methods: The study of the static and dynamic sonoanatomy of the different components of the lateral region of the hip can contribute in a relevant way to clarify the diagnosis. In the eular guidelines of sonographic musculoskeletal (MSUS) exam published in 2017, the sonoanatomic exam of the lateral hip has been developed in detail and will be discussed during this lecture.

The anatomy against what is often thought is not stagnant knowledge but evolves over the years providing new and useful data applicable in daily clinical practice. The anatomy, both static and dynamic, of the trochanteric region, is complex. For example, the subgluteus maximus bursa, which is frequently incriminated in the GTPS, is located in the posterior facet of the greater trochanter and is related to the iliotibial tract, the fascial contributions of the gluteus maximus and the tensor of the fascia lata muscle to the iliotibial tract and the origin of the vastus lateralis. In order to understand the multifunction and relationships of the different structures of this region means one has to have seen images of them and for that purpose, the human cadaveric dissection is the best tool. Thanks to the fact that the speaker is involved as a professor in the anatomy department at the University of Barcelona, Belvitge campus, directed by prof M Miguel, the clinical anatomy part will be developed with real dissections made specifically for this lecture.

Results:

Conclusion: Knowledge of the clinical anatomy needed to understand the relationships between the different structures, the clinical history, and physical examination of GTPS patients and the therapeutic possibilities including ultrasound-guided injections are other steps that lead to an accurate diagnosis of GTPS.

REFERENCES:
[1] anatomy and anthropology: Maribel Miguel, Mike Benjamin
[2] Clinical anatomy: Juan Canoso
[3] Regional musculoskeletal ultrasound: Carlo Martinoli

Disclosure of Interests: None declared
Interstitial lung disease in rheumatic diseases and systemic sclerosis

Yannick Allare, France

Interstitial lung diseases (ILDs) are a group of heterogeneous disorders, either idiopathic (idiopathic pulmonary fibrosis-IPF) or associated with other diseases, particularly autoimmune diseases, from which systemic sclerosis is the leading disease at risk of developing ILD. It has been proposed that for clinical research and patient management various subsets of fibrosing ILD that have similar biological and clinical behaviours could be merged into a single entity although specificities within each disease remain, with various patterns of lung injury. Nevertheless, the shared part relates to progressive fibrosing ILD leading to progressive decline in lung function and early mortality. In SSC, a recent report from EUSTAR network showed that ILD was nowadays the first cause of death identified as contributing to 17% of deaths (1).

No drugs are licensed for the treatment of ILDs related to autoimmune diseases. Treatment guidelines issued by the European League Against Rheumatism (EULAR) recommend tailored therapy with cyclophosphamide (CYC) for SSC-ILD, in particular for patients with progressive ILD (2). Indeed, 3 randomized controlled trials showed some benefits of using CYC either orally or by infusion route although the effect size was small and the clinical translation of the findings was difficult to establish. The limitations of CYC trials in SSC-ILD led the experts to add that dose and duration of treatment need to be tailored individually dependent on the clinical condition and response. Furthermore, with regards to safety, potential risks of bone marrow suppression, teratogenicity, gonadal failure and haemorrhagic cystitis must be always considered. Beyond standard immunosuppression, the use of high dose CYC with or without irradiation, but using rescue with stem cells showed some effects on ILD measured through lung function and imaging. Nevertheless, considering the risk of potential treatment-related mortality and morbidity, the EULAR recommends that HSCT should be considered for the treatment of selected patients with rapidly progressive SSC at risk of organ failure, two domains which remain to be delineated. Altogether these results suggest that immunosuppressants might be beneficial in the context of SSC-ILD although the right drug, the right dosing and the right patients still need to be defined. In practice, because of SLSS trial, mycophenolate mofetil has emerged as the leading drug used when a physician aims at treating SSC-ILD. The understanding of SSC and SSC-ILD have improved in the recent years and subset at risk and candidate biomarkers have emerged. Indeed, interleukin 6 has been shown to predict some disease progression including lung involvement. Therefore, targeted therapy against IL6 is an appealing strategy to improve SSC outcomes. If the pivotal trials using tocilizumab had skin as a primary outcome and failed to meet the primary end-point, secondary analyses revealed stimulating lung results that will be showed during EULAR 2019 and discussed within the ILD session. B-cells role has also been scrutinized in SSC with promising data. Therefore, rituximab is used in some SSC patients with various indications according to physician views and experience. EUSTAR has assembled a large group of rituximab treated patients and performed a well-designed observational study that did not show clear evidence supporting some efficacy of rituximab on SSC-ILD although some clues emerged. The role of anti-fibrotic drugs (nintedanib, pirfenidone), that showed to slow disease progression in patients with IPF, in patients in other forms of fibrosing ILD remains to be determined. However, several trials are ongoing and the results of the SENSCIS trial evaluating nintedanib in SSC-ILD will be presented during EULAR 2019 and discussed during the ILD session. Altogether, the available results show some progresses made in the management of SSC-ILD, so far mainly through the use of treatment targeting immune disturbances. Considering the severity and the complexity of SSC pathogenesis and related lung complication, one might anticipate that if trials of biologic therapies are positive, the treatment of SSC-ILD, and maybe of all fibrosing autoimmune ILDs, might involve combination of immunosuppression and anti-fibrotic therapies.

References:

Disclosure of Interests: None declared

Diagnostic challenges in vasculitis

Wolfgang Schmidt, Immanuel Krankenhaus Berlin, Medical Center for Rheumatology Berlin-Buch, 13125 Berlin, Germany

Background: Giant cell arteritis (GCA) and Takayasu arteritis (TAK) are large-vessel vasculitides (LVV). Recommendations demanded so far to confirm the diagnosis histologically, particularly in suspected GCA. Biopsy is however invasive, and results are not immediately available. Technology has rapidly improved; and many recent studies suggest that imaging may have comparable diagnostic accuracy.

Objectives: To provide an overview of new developments for ultrasound, magnetic resonance imaging (MRI), computed tomography (CT) and 18-fluorodeoxy-glucose positron emission tomography (PET) in diagnosis of LVV and to present new EULAR recommendations on imaging in LVV.

Methods: A systematic literature review and meta-analysis of diagnostic and prognostic studies enrolling >20 patients and investigating ultrasound, MRI, CT or PET in patients with suspected and/or established primary LVV was conducted (1). On this basis, a group of imaging experts, rheumatologists, patients and health care professionals developed EULAR recommendations on imaging in LVV (2). This review refers also to new data after the EULAR recommendations had been published.

Results: In suspected GCA, imaging should be done early, but without delaying treatment. No further diagnostic test (histology or other imaging) is necessary if results of imaging and clinical presentation correspond. Ultrasound of temporal and axillary artery arteries showing a non-compressible ‘halo-sign’ is the method of first choice in suspected cranial GCA. The meta-analysis showed positive and negative likelihood ratios of 19 and 0.2, respectively, for a final diagnosis of GCA. Good data is also available on MRI of cranial arteries. Ultrasound, MRI, CT or PET can be applied for confirming extracranial GCA. Ultrasound is of limited value for assessing particularly the thoracic aorta. MRI is first choice for suspected Takayasu arteritis, but ultrasound, CT or PET can be also applied. Conventional angiography is not recommended instead for interventions. Imaging might be used in suspected flare and to monitor damage. There is no convincing evidence to recommend routine monitoring in remission. Imaging should be done by a trained specialist using appropriate equipment. Particularly ultrasound of cranial arteries showed high diagnostic accuracy in a study for developing new classification criteria. Measuring intima thickness (cut-offs of around 0.4 mm for temporal and 1.0 mm for axillary arteries) may help to improve diagnostic accuracy and to use ultrasound for disease monitoring in trials (3). Reliabilities of sonographers both for evaluating videos and for examining patients directly were very high (4,5). Newer PET technology now allows to also show inflamed temporal, maxillary and vertebral arteries (6). The significance of positive imaging findings in follow-up studies still remains unclear. The incidence of vision loss decreased with the introduction of fast-track clinics. These clinics are increasingly established in centres. They include referral within one working day to a rheumatologist followed by immediate imaging for establishing the diagnosis. Imaging can be done by the rheumatologist (most commonly ultrasound) or by a collaborating department.

Conclusion: Ultrasound, MRI, CT and PET allow to confirm or exclude LVV provided that it is performed by a trained specialist using appropriate equipment. Fast-track clinics using ultrasound are increasingly established in rheumatology.
Ultrasound showed high diagnostic accuracy. Modern PET equipment may also delineate vasculitic temporal, maxillary and vertebral arteries. The significance of follow-up imaging studies in L UV still needs to be determined.

REFERENCES:

Disclosure of Interests: Wolfgang Schmidt Grant/research support from: GSK, Roche, Novartis, Sanofi, Consultant for: GSK, Roche, Novartis, Sanofi

SP0073 DIAGNOSIS OF GASTROINTESTINAL VASCULITIS
Maria C Cid. Hospital Clinic. University of Barcelona. IDIBAPS, Autoimmune Diseases, Barcelona, Spain

The gastrointestinal vasculature can be involved by a variety of vasculitis affecting large, medium, small or variable vessel size according to the 2012 revised Chapel Hill consensus nomenclature. Gastrointestinal involvement (GI) is one of the most severe complications of vasculitis requiring intensive immunosuppressive therapy and sometimes revascularization techniques or emergency surgery and may affect a variety of organs including large or small intestines, liver, biliary tract, pancreas, and less frequently, stomach or oesophagus. It can complicate the course of patients with known or with overt suspicion of vasculitis or be the main or even the only manifestation of these diseases.

Clinical manifestations range from abdominal pain, sometimes colicky, that usually worsens after eating to overt signs of bowel ischaemia or perforation with diffuse and constant abdominal pain, reduced peristalsis, abdominal defence and distension, and signs of peritoneal irritation. GI bleeding, frequently in the form of occult blood loss or haematochezia and less frequently melena or rectalasia, is common. Non-specific symptoms such as nausea, vomiting or diarrhoea may be observed. Pancreatitis, cholecystitis or appendicitis may also occur.

In large-vessel vasculitis, including giant-cell arteritis (GCA) and Takayasu disease (TAK), inflammation usually affects the proximal portion of the celiac trunk, hepatic or mesenteric arteries. GI involvement is rare in GCA with only isolated cases or small series having been reported. About 30% of patients with GCA have elevated hepatic enzymes as part of the acute phase response and rarely reflect involvement of the hepatic vasculature. Imaging techniques disclose stenotic or occlusive lesions in 25% of patients with TAK but clinically manifest involvement occur in about 16% of patients. Abdominal pain suggestive of vascular insufficiency is present in about 16% of patients; abdominal bruits can be perceived in 14% but only 4% present with overt signs of mesenteric ischaemia. Due to the involvement of the proximal portion of the GI branches, the ischemic territories may be extensive but usually progression of vascular occlusion is not abrupt, and due to the size of vessels involved, patients may benefit from percutaneous revascularization procedures if immunosuppressive treatments are not sufficient. Interest-

PPS1208 A PHASE 3 RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF LA-015 IN PATIENTS WITH SYSTEMIC VASCULITIS WHO ARE NOT SUFFICIENTLY RECOVERING FROM AN ANEURYSMAL COMPLICATION
Maria Cid. Hospital Clinic. University of Barcelona. IDIBAPS, Autoimmune Diseases, Barcelona, Spain

In large-vessel vasculitis, including giant-cell arteritis (GCA) and Takayasu disease (TAK), inflammation usually affects the proximal portion of the celiac trunk, hepatic or mesenteric arteries. GI involvement is rare in GCA with only isolated cases or small series having been reported. About 30% of patients with GCA have elevated hepatic enzymes as part of the acute phase response and rarely reflect involvement of the hepatic vasculature. Imaging techniques disclose stenotic or occlusive lesions in 25% of patients with TAK but clinically manifest involvement occur in about 16% of patients. Abdominal pain suggestive of vascular insufficiency is present in about 16% of patients; abdominal bruits can be perceived in 14% but only 4% present with overt signs of mesenteric ischaemia. Due to the involvement of the proximal portion of the GI branches, the ischemic territories may be extensive but usually progression of vascular occlusion is not abrupt, and due to the size of vessels involved, patients may benefit from percutaneous revascularization procedures if immunosuppressive treatments are not sufficient. Interest-

REFERENCES:
Among all forms of vasculitis, perhaps that affecting the CNS (CNS-V) poses the greatest challenge in diagnosis given the lack of any non invasive high specificity test, the complex and extensive list of mimicking conditions, its inaccessibility for biopsy and its genuine rarity. The diagnosis still requires the presence of an unexplained neurologic sign or symptom(s) following an exhaustive evaluation, evidence of vascular involvement (by direct or indirect angiography) or biopsy and most importantly the meticulous exclusion of all those conditions capable of producing mimicking clinical, radiographic or histologic findings that would confound accurate diagnosis. Despite these challenges CNS-V has been increasingly reported due to a combination of increased diagnostic awareness and advances in diagnostics. Two of these major advances will be discussed including the use of direct vascular wall imaging to differentiate vascular inflammation from atherosclerosis and the use of next generations sequencing to identify infectious etiologies and obviate the use of biopsy. Clinical examples will be presented.

REFERENCES:


THURSDAY, 13 JUNE 2019
15:30:00 – 17:00:00
How to manage and treat childhood onset lupus? A multidisciplinary point of view

CASE PRESENTER: CHILDHOOD ONSET OF NEUROLUPUS

Eve Smith, Alder Hey Children’s NHS Foundation Trust, Paediatric Rheumatology, Liverpool, United Kingdom

Background: In the series of talks ‘How to manage and treat childhood onset lupus?’ A multidisciplinary point of view’ the first talk focuses on achievement of the initial diagnosis of Lupus within the childhood period, including some potential pitfalls and how these can be avoided. Initial and ongoing treatment within the childhood period, alongside paediatric specific therapeutic considerations will be discussed. The role of the multidisciplinary team of doctors, nurses, physiotherapists, occupational therapists, psychologists and sub-specialists will be highlighted. The impact of the diagnosis on the child, family, education and social activities will also be described. This talk will be followed by a subsequent talks following the patient through transition and into adulthood.

Disclosure of Interests: None declared


CASE PRESENTER: TRANSITION OF NEUROLUPUS PHASE INTO ADULTHOOD

Lovro Lamot. The University of British Columbia and British Columbia Children’s Hospital Research Institute, Department of Pediatrics, Division of Rheumatology, Vancouver, Canada

Childhood-onset SLE (cSLE) accounts for approximately 20% of all SLE cases and is often regarded as one of the most complex rheumatic diseases. With the increase of five-year survival rate of cSLE patients to over 95%, there is a growing number of adolescents and young adults (AYA) transferring from pediatric to adult care. Even in the best-case scenario, there is often considerable challenges regarding this transition. Hence, it is not surprising that morbidity, mortality and disease activity in cSLE, as well as in many other chronic illnesses and conditions, worsen during or just after the transition. The reasons for these deteriorations are numerous, with most prominent arising from the nature of the disease and changes during the tumultuous period of adolescence, but also the differences between pediatric and adult clinical and healthcare settings. Besides, the AYA patients with chronic conditions often feel they are not well prepared for the transition to adult care, while the adult rheumatologists commonly report concerns about assuming the responsibility of patients with the pediatric-onset disease. Some of these concerns are probably motivated by increased vulnerability of AYA patients with cSLE, who are more likely than their adult counterparts to develop lupus nephritis and neuropsychiatric manifestations, as well as other organs involvement and atherosclerosis. Moreover, due to the severity of the disease, patients with cSLE are treated more aggressively, accumulating more drug-related toxicity than patients with adult-onset SLE, which results in significant SLE-related damage and complications such as osteoporosis during the childhood. On the other hand, there is decreased medication adherence in AYA, further complicated by the neurocognitive and memory impact of the disease, as well as high rates of comorbid depression and anxiety. Some additional problems in cSLE patients at transition age are sexuality, fertility, and pregnancy. All this makes patients with cSLE require specialized and multidisciplinary care at the transition, that is capable of addressing medical, psychosocial, educational and vocational needs.

This presentation will be part of the comprehensive session discussing distinct features of the SLE during the different phases of life. It will emphasize specific challenges of the transition from pediatric to adult care, with the use of a compelling clinical case as an example.

REFERENCES:

Disclosure of Interests: None declared

with a suspected diagnosis of neuropsychiatric pSLE. Underlying factors including infections, hypertension, metabolic abnormalities or adverse effects of medication should be excluded before considering a lupus-related neurological involvement. Finally, the diagnosis of pSLE should also be considered in case of severe complications such as macrophage activation syndrome or alveolar hemorrhage. Monogenic SLE should be suspected in early-onset SLE (<5-year-old) and mainly comprise complement deficiencies, genetic overproduction of interferon-α, B-cell apoptosis defects and rare inherited immunodeficiencies. Each of these conditions is associated with specific features: 1) Primary complement defects are associated with recurrent pyogenic or neisserial infections 2) type-1 interferonopathies are often associated with spasticity, cerebral calcifications, encephalopathy, skin ulcers and chills, and, in some cases, with a growth delay (spondyloenchondrodysplasia) 3) B-cell apoptosis defects (mutation in PRKCD gene) is associated with a lymphoproliferative disease. A proper diagnosis of SLE must therefore be based upon a complete family medical history as well as on clinical evaluation with details history of both present and past illnesses, analysis of growth chart as well as laboratory tests for SLE. The search for auto-antibodies towards nuclear antigens is a key step in the diagnosis strategy, keeping in mind that antinuclear antibodies are not specific for SLE. Screening for complement deficiencies via CH50, AP50, C3 and C4 is recommended in order to facilitate appropriate treatment of comorbidities including infections in pSLE patients.

Conclusion: The diagnosis of pSLE should be suspected in teenagers with acute unexplained symptoms, especially in case of abdominal pain or neuropsychiatric involvement. A monogenic predisposition to SLE should be considered in early-onset SLE, especially in patients with SLE family history, consanguinity, recurrent infections, and/or encephalopathy with spasticity.

REFERENCES:

Disclosure of Interests: None declared

CASE PRESENTER: LONGSTANDING NEURO LUPUS IN ADULT LIFE
Antonis Fanouriakis, "Atikou" University Hospital, Rheumatology and Clinical Immunology, Athens, Greece

Background: Juvenile-onset systemic lupus erythematosus (SLE) poses significant challenges for pediatric and adult rheumatologists. Longstanding disease in adult life carries the sequelae of the protracted course of the disease, as well as of the various treatments received.

Objectives: To present a didactic case of long-standing SLE of childhood onset, with the purpose to familiarise the audience with the multifaceted aspects of the disease, following transition from adolescence into adulthood.


Results: A 25-year old lady was diagnosed with SLE at the age of 9, due to generalised toxic-clonic seizures (status epilepticus), photosensitive rash and positive serology for SLE (ANA, anti-dsDNA, low complements). She was treated with high-dose glucocorticoids and cyclophosphamide with a good neuropsychiatric response. At the age of 15, she developed hematuria and nephrotic proteinuria; a kidney biopsy was compatible with class IV lupus nephritis (LN), with few crescents. She received mycophenolate mofetil (MMF), again with glucocorticoids, with complete response at 12 months. After entering adult life, 5 years later, at the age of 21, she had a severe renal flare with recurrence of nephrotic proteinuria and active urinary sediment. A second kidney biopsy was performed, which showed histologic transformation into mixed class IV + V LN, and increase in chronicity index. Readiministration of MMF failed to provide at least partial response; to this end, high-dose intravenous cyclophosphamide was administered, again with no response after 6 months. Finally, the patient was treated with rituximab, in combination with MMF, which managed to achieve partial remission, with proteinuria levels ~1.5 gr/day and normal renal function. Sixteen years following her initial diagnosis, apart from her ongoing renal inflammation, our patient has suffered significant side-effects from long-term glucocorticoid therapy and her quality of life is significantly affected.

Conclusion: This case illustrates the formidable challenges faced by both patients and treating physicians, for a patient diagnosed with SLE in childhood and had frequent flares during transition into adulthood and later in adult life.

Disclosure of Interests: Antonis Fanouriakis Paid instructor for: Amgen, GSK, Speakers bureau: Abbvie, Enorasis, Genesys Pharma
spine is the worst long-term outcome of this disease, although this occurs less frequently nowadays if compared to former decades. This fact might be related either to the natural course of the disease that becomes milder over time or to a consequent anti-inflammatory treatment initiated earlier in patients with axSpA.

Structural damage in the spine in axSpA is usually assessed on plain radiographs of the spine and, therefore, is frequently referred to as radiographic spinal progression. In the presentation, pathophysiology, assessment and ways of prevention and/or retardation of structural damage progression in the spine in patients with axSpA will be discussed.

Disclosure of Interests: Denis Podddubny Grant/research support from: Abbvie, Merck Sharp & Dohme, Novartis, Consultant for: AbbVie, Bristol-Myers Squibb, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, Roche, UCBB Pharma, Speakers bureau: AbbVie, Bristol-Myers Squibb, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, Roche, UCBB Pharma


SP0081 STRUCTURAL DAMAGE PROGRESSION IN PSA

Philip Hellwell. University of Leeds, Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom

Psoriatic arthritis is a multifaceted disease in which the arthritis tends to be less frequent than in rheumatoid arthritis. This provides a challenge to measure radiographic progression using the simple and time-honoured fashion of assessing the hands and feet. Further, radiographic progression is slower in PSA and changes over a short time period, such as the placebo controlled phase of a trial, are minimal. Newer imaging, such as ultrasound and MRI may be more sensitive and responsive but data on these techniques are limited. These challenges, and how to overcome them, will be discussed.

Disclosure of Interests: Philip Hellwell Grant/research support from: Paid to charity: from AbbVie, Janssen and Novartis, Consultant for: Paid to charity: from AbbVie, Agen, Pfizer, and UCBB and Celpene. Paid to self: from Celpgene and Galapagos


THURSDAY, 13 JUNE 2019
15:30:00 – 17:00:00

Difficult to manage Sjögren’s syndrome and Myositis

SP0082 SCREENING FOR MALIGNANCIES IN SJÖGREN SYNDROME AND MYOSITIS

Albert Selva-O’Callaghan. Vall d’Hebron General Hospital. Universitat Autonoma de Barcelona, Internal Medicine Dept, Barcelona, Spain

Both myositis and Sjögren syndrome may be associated with cancer. However, there are differences between the cancer-associated myositis and cancer that appears in patients with Sjögren syndrome, and these differences make for a distinct tumor screening approach. The fact that any type of cancer – mainly of the adenocarcinoma type - can be associated with myositis -dermatomyositis, either classical or amyopathic, immune-mediated necrotizing myopathy, or polymyositis phenotypes- makes more difficult to know if an occult malignancy is present. Nevertheless, in recent years biological markers such as several autoantibodies, phenotypes- makes more difficult to know if an occult malignancy is present. Alternatively, the clinical situation and screening approaches in Sjögren syndrome are more focused in the detection of lymphoproliferative disorders, mostly in salivary glands (MALT type lymphoma) but also marginal zone or diffuse large B cell lymphomas. Several approaches for detecting MALT-type lymphoma or generalized lymphomas, beyond the well-known parameters such as low complement levels, cytopenias, cryoglobulins or persistent enlargement of salivary glands, are also discussed.

REFERENCES:

Disclosure of Interests: None declared


THURSDAY, 13 JUNE 2019
15:30:00 – 17:00:00

Anergy, exhaustion or post-activation in autoimmunity; Facts and future consequences

George Tsokos. Beth Israel Deaconess Medical Center/Harvard Medical School, Medicine, Boston, United States of America

The distribution and function of T cell subsets in patients with systemic lupus erythematosus (SLE) is aberrant. Distinct molecular and metabolic events dictate the numbers and function of T cells. Specifically, the transcriptional repressor cAMP response element modulator alpha (CREMα), which is increased in cells from patients with SLE, accounts for the decreased expression of the interferon (IFN)-γ receptor interferon (IL)-12 and the increased expression of IL-17 through distinct epigenetic processes. CREMα promotes Th17 cell expansion by promoting the expression of G1s1, the first enzyme in glutaminylation and by suppressing the expression of pyruvate dehydrogenase phosphatase catalytic subunit 2 that enables entry of pyruvate into the Krebs cycle. In parallel, calcium calmodulin kinase 4 which is responsible for the increased binding of CREMα to cAMP response elements of the IL-2and IL-17 loci, promotes the activity of pyruvate kinase M2 and promotes glycolysis and TH17 generation while suppressing the numbers of regulatory T cells. Understanding the exact molecular and metabolic processes that control T cell function in SLE enables therapeutic considerations.

Disclosure of Interests: George Tsokos Grant/research support from: Janssen Research & Development, LLC


SP0084 POST-ACTIVATED B CELLS IN AUTOIMMUNITY

Andrea Lin. Rheumatology and Clinical Immunology, Department of Medicine, Charité Universitätsmedizin Berlin and German Rheumatism Research Center Berlin (DRFZ), Berlin, Germany

Background: B cells are key players in autoimmune diseases such as systemic lupus erythematosus (SLE), primary Sjögren’s syndrome (pSS) and rheumatoid arthritis (RA). In the past, it was believed that B cells from these patients were hyper-responsive to B cell receptor (BCR) and Toll-like receptor (TLR) signaling. New insights suggest that B cells from these patients present a post-activated functiotype.

Objectives: We aim at characterizing B cells and B cell responses of SLE, pSS and RA patients to understand which venues can be taken towards new therapies for these diseases.

Methods: B cells and B cell subsets from peripheral blood samples from SLE, pSS and RA patients and healthy donors (HD), as well as few autoimmune tissues, were analyzed for: phosphotyrosine kinase (PTK) phosphorylation kinetics, protein phosphatase activity, expression of phosphatases or of checkpoint molecules, such as e.g. PD-1, before and after BCR engagement, alone or together with TLR9 and CD40 stimulation, differentiation and proliferation. Expression of transcription factors, such as e.g. STAT1, and the effect of interferons in their expression in B cells from patients were also evaluated.

Results: B cell responses upon BCR engagement in SLE, pSS, RA patients were abnormal with diminished BCR downstream PTK phosphorylation. TLR9, but not CD40 responses were also abnormal. Part of the abnormality related to diffuse up-regulation of phosphatases that apparently counteracted PTK signaling. The abnormality was partially mimicked by repeated signaling through the BCR of HD B cells and could be overcome by CD40 engagement. Check-point molecules, such as e.g. PD-1, was differentially expressed in SLE naïve and memory B cells. SLE naïve and memory B cells expressed higher amounts of STAT1 compared to those of pSS, RA and HD.

Conclusion: Post-activated B cells are characterized by a phenotype of dysregulated expression of certain check-point molecules, such as PD-1, some transcription factors, like STAT1 and certain phosphatases (figure 1). Our data suggest that CD40 activation is involved in modulating BCR responses in post-activated B cells. This has implications for innovative therapies since blocking BCR signaling pathways and CD40 activation as well as targeting certain phosphatases may have synergistic value for treating systemic autoimmunity.
WHO TO IDENTIFY AND INVITE TO AN FLS? WHO IS THAT FRACTURE PATIENT?

Bo Abrahamsson, x, x, Denmark

Background: Though osteoporosis can be diagnosed through the presence of fragility fractures in the absence of other aetiology such as myeloma or metastases, patients with osteoporosis are also at increased risk of high impact traumatic fractures. Further, distinguishing between fracture mechanisms through chart review is often difficult and may lead to patients with osteoporosis being missed. On the other hand, focusing on identifying and treating patients at high imminent fracture risk rather than milder degrees of osteoporosis makes for better cost utility.

Objectives: To review the demographics of patients presenting with fragility fractures and the evidence for targeting osteoporosis assessment for each category of fracture in order to balance the need for maximum risk reduction with the requirement for an evidence based strategy.

Methods: Narrative review of recent epidemiology studies and national and international guidelines.

Results: Based on epidemiology data from Iceland[1] and Denmark[2,3], the risk of subsequent fractures following a sentinel fracture event is critically dependent on the recency and the site of the initial fracture, with the risk of new fractures being particularly high after major osteoporotic fractures[1] and pelvic fractures but less so after lower leg fractures[2].

In Danish women[2], 29.5% of patients suffering a pelvic fracture went on to sustain a hip fracture in the next ten years, compared with 25.9% after a vertebral fracture but only 12.5% after a lower leg fracture. Further, despite the high recurrent fracture risk in the FLS setting, it is important to appreciate that the majority of hip fracture patients have not consulted with a prior fracture in the last ten years prior to their hip fracture[3].

The following issues will be addressed in more detail
1) Demographics of fracture patients with particular emphasis on age, sex and BMD.
2) Which fracture types are indicators of elevated risk of subsequent major osteoporotic fractures?
3) Which fracture types will respond to osteoporosis treatment?
4) What is the role of DXA in FLS?
5) Identifying vertebral fractures

Conclusion: FLS patients are at elevated risk of sustaining additional fractures both in the long term and in the short term, with risks being particularly high in the first years after the sentinel fracture and especially if the initial fracture is a pelvic fracture or a major osteoporotic fracture.

REFERENCES:

Disclosure of Interests: None declared
Systemic lupus erythematosus (SLE) is also associated with smoking. A strong and specific connection of current smoking and >10 pack-years of smoking with dsDNA+ SLE has been observed. In patients with SLE, smoking exposure has deleterious effects on lupus morbidity and is related to cumulative chronic damage, and patients with SLE, smoking has a negative impact on the efficacy of belimumab and a 2-fold decrease in the proportion of patients achieving cutaneous improvement with antimalarials. Published data indicate that smoking has a dose-dependent impact on structural damage progression in Ankylosing Spondylitis.

In a large UK cohort, smoking was positively associated with the risk of psoriatic arthritis in the general population, but negatively associated among patients with psoriasis. In addition, smokers with psoriatic arthritis had a poorer response to TNFIs compared to non-smokers.

Regarding well-established risks of cardiovascular and respiratory diseases, this finding has eventually lead to incorporation of this risk factor into FRAX®. The impact of smoking on bone status is mainly associated with the number of smoking years. In a few reports, it has been observed an association between smoking and carpal tunnel syndrome and inflammatory bowel disease. Finally, current smoking in patients with fibromyalgia is associated with greater pain, possibly as a function of disease severity.

Disclosure of Interests: Antonio Naranjo Grant/research support from: Amgen,
Consultant for: UCB, Speakers bureau: Amgen, UCB

References:
How to Support Yourself Quitting Smoking

Marios Kouloumpras, Cyprus League Against Rheumatism, Aglantzia, Patient Organization, Nicosia, Cyprus

Background: As a person living with Rheumatoid arthritis (RA) (a chronic inflammatory disease caused by both genetic and environmental factors) for the last 45 years (I have been diagnosed with RA at the age of 10 years old) I have been a smoker from the age of 14 years old. As I grew older, and was educated and involved concerning the management of my disease, I realized that smoking, besides its impact on my overall health, had a significant impact as one of the most important risk factors for RA that can increase the severity of the disease and to worsen symptoms. Smoking can also reduce the effect of treatments, including anti-TNF agents and disease-modifying anti-rheumatic drugs (DMARDs). Hence, quitting smoking will improve my overall health, reduce the severity of my disease and ensure that treatments work and reduce the risk for comorbidities e.g. cardiovascular disease and the progression of the disease (joint destrucions).

Objectives: To quit smoking after 40 years of being a smoker and to regain my health and quality of life as well as increase the efficacy of the RA treatments.

Methods: To succeed I plan to be very well informed and to understand the reasons of quitting smoking as well as the negative impact of smoking and to realize that quitting smoking will improve my health and social life. To inform all people close to me including family members as well as friends and coworkers about my decision to quit smoking. Mentally being prepared to cope with the desire to smoke as well as ridding the thought of “just smoke one”. It is also important to rid the mind and lose the connection of things associated with smoking, for example while drinking coffee. To ask for support if needed and to use tools to stop thoughts of smoking and to cope with the effects of nonsmoking and to try avoiding places that could increase my risk of starting to smoke again e.g. pubs.

Results: I have started to cut down on smoking and to minimize it and finally to fully quit smoking for the last 2 years.

Conclusion: Although, if you ask all smokers how difficult it is to stop smoking, the answer will unanimously be “very hard”, as a former smoker I can say that if you quit smoking, be aware of the reasons and the importance of quitting smoking and you will notice that after all it is not very difficult. Of course, when you set this goal it is important that in case of first time failure to not blame yourself and I can

Disclosure of Interests: None declared


Scientific data visualization: focus on (poster) presentation

Maarten Boers, Amsterdam University Medical Centers; Vrije Universiteit, Epidemiology and Biostatistics; Amsterdam Rheumatology and immunology Center, Amsterdam, Netherlands

This practical skills session introduces the principles of good graph and table design as pioneered by Cleveland1 and Tufte2 and updated by Few3, this year as freely downloadable.4,5

Its learning objectives include:

- choosing the data visualization that best fits the data
- identifying the basics of table and graph design
- choosing tables and graphs that tell the story in the data
- introduction to poster design

The session is linked to a special poster tour devoted to poster design on the next day.

REFERENCES:

Disclosure of Interests: None declared

EULAR POINTS TO CONSIDER ON BIG DATA

Disclosure of Interests: These EULAR points to consider provide a framework for the use of big data in RMDs. They refer to big data as a moving field in need of correct reporting of data collection, discussing privacy by design, use of specific data platforms, and data learning; they cover aspects of data sources and data disciplines including computer science and artificial intelligence. Levels of evidence and strengths of recommendations were allocated.

Methods: Based on a literature review of the current status of big data in RMDs and in other fields of medicine, on individual interviews of selected experts, and on the opinion of experts in a face-to-face meeting, points to consider were formulated, discussed, and finalised by an international group of 14 experts from a range of disciplines including computer science and artificial intelligence.

Results: The document comprises 5 overarching principles and 9 points to consider. The overarching principles address the definition of big data and artificial intelligence, types of big data, and ethical and general principles for dealing with big data in RMDs. The points to consider cover aspects of data sources and data collection, discussing privacy by design, use of specific data platforms, and data sharing; data analyses in particular through artificial intelligence and machine learning; they refer to big data as a moving field in need of correct reporting of methods used and of benchmarking; and data interpretation and implementation in clinical practice.

Conclusion: These EULAR points to consider provide a framework for the use of big data in RMDs.

Disclosure of Interests: None declared


MRI

MRI OF LARGE JOINTS IN ARTHRITIS: HOW TO DO AND HOW THEY ARE DIFFERENT FROM SMALL JOINTS?

Iris Eshed. Sheba Medical Center, Tel Aviv University, Department of Diagnostic Imaging, Ramat Gan, Israel

The appendicular skeleton is frequently involved in patients with rheumatic diseases. Involved joints are affected by inflammation of the synovium and joint’s enthese. Imaging depicts joint derangement and generally mirrors the pathophysiology of the disease. MRI is considered the imaging modality of choice for the detection of acute joint inflammation as well as its structural sequela. Thus, MRI plays an important role in identifying, monitoring disease activity and the patient follow-up.

The MRI features of inflammatory arthritis are well described, especially in the small appendicular joints of the hands and feet and include synovitis, erosions, osteitis, tenosynovitis and erosions. In the current presentation, the typical MRI properties of large joints arthritis in different rheumatic entities will be presented with special focus on the difference from inflammatory findings in smaller appendicular joints.

Disclosure of Interests: None declared


MRI OF ENTHESITIS: HOW TO DO AND WHAT TO LOOK FOR

Mikkel Østergaard. Copenhagen Center for Arthritis Research (COPECARE), Rigshospitalet, University of Copenhagen, Center for Rheumatology and Spine Diseases, Glostrup, Denmark

Enthesitis, inflammation at the insertion site of tendon, ligament or joint capsule into bone, is considered a key pathological feature in spondyloarthritis (SpA) and psoriatic arthritis (PsA)[1]. Compared to conventional assessment of enthesitis using clinical scores, MRI detects both soft tissue and intra-osseous abnormalities in active enthesitis, potentially aiding early diagnosis and outcome measurement in SpA and PsA[2]. With the advent of treat-to-target concept and novel therapies, objective and sensitive monitoring of response of enthesitis to therapy is desirable, and a validated MRI scoring system would be a useful adjunct to clinical practice as well as providing additional information as an outcome measure in clinical trials.

The Outcome Measures in Rheumatology (OMERACT) MRI in Arthritis Working Group recently undertook a systematic literature review (SLR) aiming to critically evaluate the published literature for available methods of evaluating enthesitis using MRI in SpA and PsA patients, describing the MRI variables, definitions and scoring systems used to diagnose and monitor enthesitis[3]. Considerable limitations were found regarding standardisation of MRI enthesitis definitions across studies and validity of available semi-quantitative scores as outcome measures. The findings suggested a need for reliable and validated MRI scoring system for enthesitis.

Subsequently, the OMERACT MRI group developed consensus definitions of key pathologies and three heel enthesitis multi-reader scoring exercises were done, separated by discussion, training and calibration[4]. In a final exercise, median pairwise single-measures intra-class correlation coefficients (ICCs; patient-level) for entheseal inflammation status/change scores were 0.83/0.82 for all readers. For radiologists and selected rheumatologists ICCs were 0.91/0.84 and quadratic-weighted kappas (lesion-level) 0.57-0.91/0.45-0.81. It was concluded that the proposed definitions and enthesis scoring system (OMERACT HEMIRIS) are reliable among trained readers and promising for clinical trials[4].

This talk will briefly review the evidence behind the use of MRI for diagnosis and monitoring enthesitis, describe the recently developed OMERACT consensus definitions of key pathologies, and provide examples of these pathologies, aiming for the attendees to learn to be able to recognize them. Finally, an interactive quiz using cases for audience review will be undertaken to test this ability.

REFERENCES:

Disclosure of Interests: Mikkel Østergaard Grant/research support from: Abbvie, Celgene, Centocor, Merck, Novartis, Consultant for: Abbvie, BMS, Boehringer-Ingelheim, Centogene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, Speakers bureau: Abbvie, BMS, Boehringer-Ingelheim, Centogene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB


CRYSTAL ARTHROPATHIES: IS THERE A ROLE FOR MRI?

Kay-Geert Hermann. Chante – Universitätsmedizin Berlin, Radiology, Germany

The plain radiographic features of gout are well known. However, the sensitivity of plain radiographs alone for the detection of signs of gout is poor in acute disease. Dual-energy computed tomography (DECT) and ultrasonography fill the gap for early stage and specific detection. However, there are instances in which MRI of the painful joints was already acquired. Therefore, it is crucial to know the imaging findings of gout in MRI. MRI per se is not suitable for imaging the calcified bone or soft tissue calcifications. However, there are special techniques such as gradient echo sequences or susceptibility-weighted imaging (SWI) to visualize calcifications. Furthermore, the inflamed joint with all its characteristics such as synovitis, tenosynovitis, and erosions is easily accessible by MRI. Specific findings in the...
MRI DIFFICULT CASES OF THE AXIAL SKELETON
Lennart Jans. Ghent University Hospital, Radiology, Gent, Belgium

MRI has revolutionized the assessment of axial spondyloarthritis (SpA) in clinical practice. MRI of the sacroiliac joint is a cornerstone for diagnosis and classification. MRI of the spine may help with difficult cases as spinal changes may antedate sacroiliac changes and indicate disease burden. In daily practice, the interpretation of axial MRI is challenging. Experience has tempered the initial enthusiasm as the limitations of the ASAS criteria in daily practice become evident.

Firstly, the ASAS criteria are intended to classify patients with 'back pain' of more than 3 months' duration and with onset before 45 years of age as having axial SpA. In other patient groups, however, sacroiliitis on MRI as defined by ASAS has a lower sensitivity and specificity.

Secondly, the definition of a 'positive' MRI for sacroiliitis is validated to limited extend only. MRI of the sacroiliac joint requires inflammatory changes to meet the criteria, without a clear quantitative requirement. Bone marrow oedema lacks sensitivity and specificity as MRI findings suggestive of sacroiliitis may be produced by non-inflammatory disorders, a point that remains poorly investigated.

Thirdly, structural changes in the sacroiliac joints are not taken into account in the ASAS criteria. The diagnostic performance of MRI of the sacroiliac joint could be improved by including structural lesions, but to date this is not the case.

Fourthly, spinal imaging is not included in the ASAS criteria. MRI of the spine is considered 'positive' when at least 3 inflammatory or several structural lesions are present, with a sensitivity and specificity similar to those of the sacroiliac joints. The difficulty here is the lack of data. It has not been reliably shown that inflammation proceeds synovial fluid formation and MRI seems incapable of accurately evaluating treatment response. Only about 4% of patients with negative sacroiliac MRI have sacroiliitis.

Clinicians should be aware of unreasonable expectations on MRI. If MRI findings are considered in isolation the findings are not reliable. The diagnosis of SpA can only be made by an expert if patient's history, clinical examination, laboratory findings, and imaging studies converge. When solving difficult cases, collaboration is key: clear communication between rheumatologist and radiologist is mandatory. Radiologists should withstand the pressure to call if a patient has SpA or not based on MRI alone.

REFERENCE:

Disclosure of Interests: None declared

THURSDAY, 13 JUNE 2019
15:30:00 – 17:00:00
Ultrasound advanced I

SP0101 US FOR ASSESSING LUNG INVOLVEMENT IN RHEUMATIC DISEASES – CLINICAL USE + DEMO
Andrea Delle Sedie. University of Pisa, Rheumatology Unit, Pisa, Italy

Background: Evaluation of interstitial lung disease (ILD) is always difficult (low sensitivity for X-ray and pulmonary function tests or high level of radiation for HRCT); ultrasound (US) has recently shown interesting results on truth, discrimination and feasibility. Due to the thickening of interlobular septa for edema or fibrosis, US beam can interact with those structure and produce artifacts on the screen: B-lines (BL) and pleural line irregularity (PLI). A positive correlation between BL and HRCT has been established both in systemic sclerosis patients and in other patients with ILD; more recently similar results have been published by using PLI as a finding for US assessment in patients.

BL has been recently defined by the EULAR as a vertical hyperchoic reverberation artifact that arise from the pleural line, extend to the bottom of the screen without fading, and move synchronously with lung sliding, while PLI has been defined as a loss of regularity that may be associated with an increase in thickness, focal, diffuse, or nodular.

A low number of BLs has been described in healthy subjects but they are generally confined to the posterior and lower part of the thorax. Up to now, many different scanning protocols have been used to assess BL or PLI in patients, providing similar results.

Conclusion: US lung evaluation is a useful and feasible imaging technique.

Disclosure of Interests: Andrea Delle Sedie Speakers bureau: Abbvie, UCB, Celgene, MSD

SP0102 US FOR SYNOVIAL BIOPSIES – CLINICAL RELEVANCE AND SAFETY + DEMO
Andrew Filer. University of Birmingham, Institute of Inflammation and Ageing, Birmingham, United Kingdom

Background: The introduction of ultrasound guidance to access synovial tissue samples has facilitated a rapid growth in tissue-related research. Ultrasound guidance enables operators to use less invasive approaches compared to a gold standard direct vision arthroscopy procedure while maintaining the quality of samples obtained. Patients find the procedures easy to tolerate and are willing to undergo repeat biopsy, facilitating the analysis of tissue samples in clinical trials and experimental medicine studies. Advanced analytic techniques including single cell analytics are now being used to exploit the tissue samples obtained in order to provide dramatic leaps in understanding of synovial pathology.

Objectives: In this session the key aspects of the dominant techniques in use will be presented, including safety, patient tolerability and quality of output. The research and clinical utility of synovial biopsy will be discussed. Sonographic approaches to the major techniques will then be illustrated through video demonstrations, and competencies required to undertake training will be discussed alongside current EULAR initiatives for training. Finally, examples of research outputs generated through synovial biopsy will be explored alongside the logistics required to deliver such clinical studies.

Disclosure of Interests: None declared

THURSDAY, 13 JUNE 2019
17:30:00 – 19:00:00
Fighting and fixing: from initiation to resolution of inflammation

SP0103 T LYMPHOCYTES AND INNATE IMMUNE CELLS BALANCE MUSCLE REGENERATION AND AUTOIMMUNITY
Patrizia Rovere-Querini. IRCCS Ospedale San Raffaele and Università Vita-Salute San Raffaele, Laboratory of Innate Immunity and Tissue Remodelling, Italy

Background: The skeletal muscle is the largest cellular compartment of the organism. It represents an immunologically unique or a “non classical” immunological privileged site, being normally protected from the noxious effects of inflammation. The molecular events that control the homeostatic response to acute muscle injury are however poorly understood. The available information indicates that it involves the cross-talk among various cell populations, which i) perceive the muscle damage and release alert signals, which attract and activate inflammatory cells and progenitor cells ii) organize and maintain regeneration and tissue repair. The scenario is possibly even more complex during inflammatory idiopathic myositis (IBM) in which the immune privilege fails to protect the environment and
muscle cells undergo continuous cycles of death and regeneration as a consequence of the pressure of the immune respose targeting antigens preferentially expressed within regenerating fibers (1, 2).

Objectives: I will review recent evidence on the relative role of unconventional cellular and molecular pathways activated in the tissues of subjects with IMM and in relevant experimental models of skeletal muscle regeneration and autoimmunity, focusing on the action of antigen-specific and regulatory T cells and immune cell populations of innate cells.

Methods: Review of available published data and of data recently generated on the topic.

Results: Muscle necrosis and the ensuing inflammation was consistently associated in mice with up-regulated expression of bona fide autoantigens targeted in particular with histidyl-transfer RNA synthetase (HisRS), Phagocytosis of HisRS-expressing apoptotic myoblasts and appropriate inflammatory costimuli are necessary to elicit the production of anti-HisRS autoantibodies and to jeopardize muscle regeneration. Soluble pattern recognition receptors, and in particular the prototypic long pentraxin PTX3 play a critical role in preventing the accumulation of cell debris in the inflamed skeletal muscle, restricting the immunogenic potential of dying and regenerating myofibers. Conversely the local expression of type I IFN is necessary for the prolonged autoantibody response and for the maintenance and spreading of the immune-mediated muscle damage, as demonstrated using IFNαR1-null mice (3-5). A specialized population of regulatory T (Treg) cells, has been recently characterized in the inflamed and regenerating muscle, which influence both the immune response, by promoting the M1-to-M2 switch, and the activation of precursor/stem muscle cells. Treg cells control the efficacy of muscle repair and might be involved in preventing the systemic effects of the autoimmune response generated as a consequence of the disruption of the immunologically protected environment of the skeletal muscle (6, 7).

Conclusion: Identification of the pathways that are physiologically involved in restricting the onset and accelerating the termination of autoimmune responses targeting the skeletal muscle might be valuable for the identification of novel targets for molecular intervention in patients with IMM.

REFERENCES:

Disclosure of Interests: Patrizia Rovere-Querini Grant/research support from: None declared


THE JANUS-FACED GLADIATOR: NEUTROPHILS IN STERILE INFLAMMATION AND AUTOIMMUNITY

Markus Hofmann
University of Maryland, School of Medicine, United States of America

Background: Neutrophils, and particularly neutrophil extracellular traps (NETs), have been connected with inflammatory and autoimmune diseases, such as RA, SLE, gout and many others. However, the outcome of a deficiency of NET-formation can be observed in chronic granulomatous disease and Papillon-Lefèvre syndrome and is characterized by non-resolving inflammation and frequent autoimmunity.

Objectives: I will give an overview over pro- and anti-inflammatory effects of neutrophils and NETs, respectively, focusing on our results in gout and SLE.

Methods: We investigated the impact of NET-deficiency and/or neutrophil depletion on animal models of SLE (pristane-induced lupus) and gout (MSU crystal-induced arthritis). Mechanistic studies were performed with isolated neutrophils from mice and humans.

Results: In experimental lupus and gouty arthritis neutrophil depletion or neutropenia worsens disease. Also mice strains with normal neutrophil numbers but defects in NET formation (NOX2 or PAD4-deficient mice) have exacerbated and unresolved inflammation. Release of inflammatory mediators by stimulated neutrophils was highest at intermediate cell densities (20–40 × 10^6 cells/cm^3). Above such densities, mediator release by normal neutrophils was outweighed by proteolytic degradation via proteases expressed on aggregated NETs. Additionally, binding to aggregated NETs conferred protection of the serine protease neutrophil elastase (NE) against inactivation by α1-antitrypsin (α1AT).

Conclusion: Although neutrophils are often regarded as archetypical pro-inflammatory cells, evidence is increasing that they can also exert anti-inflammatory and immunoregulatory function. Formation and aggregation of NETs and degradation of inflammatory mediators by serine proteases are important neutrophil tools to resolve gouty arthritis and other forms of localized inflammatory conditions. On the downside, NETs come at the price of collateral tissue damage and may cause occlusion of ductal structures.

REFERENCES:

Disclosure of Interests: None declared


REGULATION OF AUTOANTIBODY ACTIVITY BY T CELL SUBSETS

Gerhard Kröbke
University Hospital Erlangen, Internal Medicine 3, Erlangen, Germany

Our recent data show that the IL-23–Th17 axis controls the intrinsic inflammatory activity of autoantibodies and thereby triggers the clinical onset of autoimmune arthritis in mice and humans suffering from rheumatoid arthritis. TH17 cells regulate expression of sialyltransferases in newly differentiating antibody-producing cells and determine the glycosylation profile and activity of immunoglobulin G (IgG) that is produced by the consecutively emerging plasma cells.

Disclosure of Interests: Gerhard Kröbke Grant/research support from: Lilly, Pfizer, Speakers bureau: Novartis


SEEING IS BELIEVING: NANOTECHNOLOGIES IN TISSUE IMAGING

Matthias Gunzer
University Hospital, University Duisburg-Essen, Institute for Experimental Immunology and Imaging, Essen, Germany

Background: Because bone marrow is the source of all immune cells, knowing the blood supply of bones is essential to understand diverse mechanisms such as arthritic bone inflammation, anti-infectious immune defense or sterile inflammation.

Objectives: We wanted to clarify, how immune cells are able to function inside of the bone and also leave bones for peripheral functions.

Methods: We used a variety of different imaging approaches and animal models as well as insights from clinical studies in humans we have made the bone open to ways of studying, that have not previously possible.

Results: Using these methods we have defined an entirely new concept of how a closed circulatory loop is established in long bones. Thereby we show the mechanistic role of osteoclasts and define, how T cells and neutrophils use the system to fight against viral infection or invade ischemic tissue. This allows an integrated

FRIDAY, 14 JUNE 2019 08:15:00 – 09:45:00
view how the blood circulation inside and outside of bones are interconnected to mediate functional or dysfunctional immunity.

Disclosure of Interests: None declared

SP0107 THE 4-D+ NANOSCOPE: THE RESOLUTION FOR BIOLOGICAL SAMPLES

L. Kling1,2, L. Milb3,4, A. Grüneboom5,6, M. Herrmann4, G. Schett4, A. Maier6, S.H. Christiansen2,3,4, Heilmüh-Zentrum Berlin für Materialien und Energie, Forscherguppe Christiansen, Berlin, Germany; 2Christiansen Research Group, Heilmüh-Zentrum Berlin für Materialien und Energie, Hahn-Meitner-Platz 1, 14109 Berlin, Germany; 3Physics Department, Free University, Berlin, Anni11e14, 14115 Berlin, Germany; 4Max Planck Institute for the Science of Light, Günther-Scharowsky-Str. 1, 91058 Erlangen, Germany; 5Universitätsklinikum der Friedrich-Alexander-Universität Erlangen-Nürnberg, Med. 3, Ulmenweg 18, 91054 Erlangen, Germany; 6Friedrich-Alexander-Universität Erlangen-Nürnberg, Pattern Recognition Lab, Martensstr. 3, 91058 Erlangen, Germany

Background: In ageing societies all over the globe, the number of people suffering from bone disease, e.g. osteoporosis (OP) in the first place, has increased dramatically. OP considerably impairs patients’ life quality, and results in high societal costs. However, current understanding of OP is still insufficient due to the lack of appropriate high resolution tools that permit a thorough analysis of scale bridging bone architectures from macro to nano with statistical significance to support the development of better treatments by drugs or surgical intervention.

Objectives: To revolutionize our knowledge of bone diseases based on an increase in understanding of the underlying bone anatomy, cutting-edge correla-
tive high-resolution microscopy and spectroscopy together with advanced data analysis including machine learning approaches permit reaching the next, so far unprecedented level of understanding.

Methods: Correlative workflows starting from X-ray microscopy (XRM) volume analysis, with voxel sizes of <1μm, over light-sheet fluorescence microscopy and large scale scanning electron microscopy data acquisition, to dual beam micro-
scope analysis (focused electron- and ion beams) permit the scale bridging inves-
tigation of bone architectures and thus merging the “big picture” and the underly-

ing ultrastructure with statistical significance. In combination with addi-
tional analytical add-ons to these microscopes, physical properties such as optical, mechanical, compositional, structural etc. deliver a highly detailed correlated dataset of bone (cf. Figure 2).

The present paper demonstrates novel findings related to various partly age related bone diseases using advanced correlative data acquisition (cf. Figure 2).

Results: Figure 1 shows the different bone fine structures, composed of trabecu-
lar and vascular networks as well as a three-dimensional arrangement of osteo-
lacunae that host osteocytes, as obtained by volume analysis in a new generation of lab-based x-ray microscope (Zeiss XRM Versa 520). These fine structures can be assessed quantitatively with statistical significance and can be correlated with additional modalities as shown in Figure 2. Elucidating examples demonstrating the power of such an approach will be given [ref 1, ref 2, ref 3, ref 4].

Figure 2 shows the an example correlative workflow from sample collection over sample preparation and the acquisition of various image modalities utilizing corre-
lated data from electron-, ion-beam imaging and analytics, probes and focused laser light to study scale bridging bone architectures. We will demonstrate how these correlative workflows will permit to advance the current understanding of bone architectures and function substantially and will show some first systematic correlative microscopy and spectroscopy studies on mouse tibia and human bone [ref1, ref2, ref3, ref4].

Conclusion: Based on our correlative analytics and the data availability, the advanced data interpretation using machine learning approaches will be discus-
csed. Using this approach, all details of bone micro-nano-architecture can be used to provide a novel clinical tool-set for future for early detection of bone diseases.

REFERENCES:

Disclosure of Interests: None declared

SP0108 LSFM AND CATCHING UP IN JOINT IMAGING

Anika Grüneboom1

Background: Bone tissue differs from other organs by its hardness and high optical density. These physical characteristics are challenging in the context of fluo-

descence based imaging studies addressing bone anatomy and physiology. The development of novel imaging technologies, such as light-sheet fluorescence microscopy and X-ray microscopy, and tissue-specific preparation procedures like optical clearing allowed us to reveal a so far unseen network of blood ves-

s in the cortical bone. These trans-cortical vessels (TCVs) directly connect the bone marrow vasculization with the peristeum and make the major contribution to total blood flow in long bones. Furthermore, we could show that immune cells are recruited to the peripheral circulation via TCVs and that TCVs are highly remodelled and inflammatory conditions. In case of chronic arthritis we observed a massive increase in TCV numbers, especially at the metaphysis of long bones. This increase in bone vasculatization confirms observations of previous studies describing increasing numbers of microcanals in the bare area of metacarpal heads in the hands of rheumatoid arthritis patients. These alterations in bone anatomy might hint to an alternative mechanism by which immune cells are recruited into inflamed joint tissue. While current concepts describe the recruit-
ment of immune cells from the systemic circulation, immune cells can potentially infiltrate the articular joints directly from the underlying bone marrow.

Objectives: Clarifying the anatomical routes of cell recruitment as well as explor-
ing the regulatory mechanism guiding immune cells from the bone marrow to the site of inflammation might bear new therapeutic strategies to resolve inflamma-
tion and tissue injury in rheumatoid arthritis.

Methods: 3D optical imaging approaches like Light-sheet fluorescence micro-
scopy and 2-Photon laser-scanning microscopy enable the visualization of entire bones and joints. In combination with tissue-specific preparation procedures and labeling strategies inflammatory mediated changes in vasculatization and cell recruitment can be analyzed.

Results: The joint tissue architecture is massively affected by inflammatory arthritis processes leading to changes in vasculatization, permeability and cellular tissue composition. These processes are directly connected to the onset as well as the resolution of inflammatory arthritis.

Conclusion: Newly available imaging techniques as light-sheet fluorescence microscopy facilitate new insights into bone and joint tissue architecture, function and inflammatory processes. These findings might guide the identification of novel
proresolving mediators to develop therapeutic strategies for managing tissue-damage-induced inflammation.

REFERENCE:

Disclosure of Interests: None declared

FRIDAY, 14 JUNE 2019
10:15:00 – 11:45:00
Paradigm shifts in arthritides

SP0109 HOT: DIAGNOSIS AND TREATMENT OF INFECTION RELATED ARTHRITIDES

Robert Schoen. Yale School of Medicine, Rheumatology, Allergy, Clinical Immunology, New Haven, United States of America

Background: Management of infectious arthritis has evolved because of empiric knowledge, clinical studies, and emerging pathogens. For patients with bacterial arthritis, organism specific, effective anti-microbial therapy is essential, but assessment of co-morbidities, adequate joint drainage, and supportive care are also required. For patients with infectious arthritis an acute intervention is usually necessary, since delay in diagnosis often leads to unsatisfactory outcome. In some situations, the distinction between infection and a post-infectious inflammatory process may be challenging.

Objectives: The goal of this lecture is to review management of septic arthritis in native joints. In addition, I will discuss Lyme arthritis and chronic chikungunya arthritis as examples of the broadening spectrum of infectious arthritis.

Methods: This lecture will rely on my clinical experience and a PubMed literature search.

Results: In this HOT lecture, I will provide practical, up to date information about the diagnosis and management of septic (bacterial) arthritis of native joints. I will discuss longstanding treatment paradigms, as well as advances in management and areas of uncertainty. I will then consider two emerging infections, Lyme arthritis and chronic chikungunya arthritis, that illustrate the changing spectrum of infectious arthritis.

Conclusion: It is the intention of this lecture to assist rheumatologists in management of patients across the spectrum of infectious arthritis. Accurate diagnosis and treatment are often challenging, but critical to satisfactory patient outcome.

REFERENCES:

Disclosure of Interests: None declared

FRIDAY, 14 JUNE 2019
13:30:00 – 15:00:00
Safety First! Infectious complications and pregnancy issues in patients with rheumatic diseases

SP0110 WIN: PREGNANCY ISSUES IN PATIENTS WITH RHEUMATIC DISEASES: THE OB PERSPECTIVE FOR RHEUMATOLOGISTS

Catherine Nelson-Piercy. Guy’s and St. Thomas’ Foundation Trust and Queen Charlotte’s and Chelsea Hospital London, United Kingdom

Pregnancy issues in patients with rheumatic diseases: the OB perspective for rheumatologists

Learning Objectives:

- Understand the importance of pre pregnancy counselling for women with rheumatic disease in pregnancy
- Understand the risk factors for adverse pregnancy outcome in women with rheumatic disease
- Understand the medications which are compatible with use in pregnancy and lactation
- Understand the management of rheumatic disease in pregnancy

Abstract: Rheumatic disease predominantly affects women of child-bearing age and are commonly encountered in obstetric practice. Pregnancy poses an important challenge for doctors looking after these women. Knowledge about medication safety, the effect of pregnancy on the disease, and vice versa, together with pre-conception counselling and multidisciplinary team care, are important to provide the best obstetric and medical care to these women. Women with rheumatic have increased risks of miscarriage, preterm delivery, pre-eclampsia, fetal growth restriction, and disease flare in pregnancy. The main risk factor for adverse pregnancy outcomes in inflammatory arthritis is active disease flare. For women with SLE the risks are lupus nephritis, particularly with CKD class 3-5, anti Ro/La antibodies, active disease and antiphospholipid antibodies. The most important issues of delaying pregnancy until there is quiescent disease, ensuring continued remission by continuation of drugs that are safe in pregnancy and adequately and promptly treating any flare of disease will be discussed. Adequate surveillance of the mother and fetus is imperative, but stratification of women is important to ensure that those with low risk pregnancies are not over-medicalized. There is an understandable reluctance to prescribe drugs, particularly immunosuppressant drugs, in pregnancy and in breast feeding mothers. However much harm can result if drugs are withdrawn, omitted or the dose reduced inappropriately. Active disease has an adverse effect on female fertility and time to pregnancy as well as impacting adversely on pregnancy outcomes. Guidelines from the British Society of Rheumatology and EULAR have reviewed the safety data for antirheumatic drugs in pregnancy. These publications include recommendations for which drugs are compatible with pregnancy and during lactation. These guidelines should reduce errors of omission where important medication for disease control are discontinued prior to or in pregnancy and empower rheumatologists to help women to time their pregnancies during disease remission and with continuation of medications including biologics compatible with pregnancy.

REFERENCES:


Disclosure of Interests: Catherine Nelson-Piercy Consultant for: UCB, Speakers bureau: UCB


FRIDAY, 14 JUNE 2019
13:30:00 – 15:00:00
Immunosuppression in SSc – a matter of timing!

SP0111 POTENTIAL CELLULAR AND MOLECULAR TARGETS

Jöra Distler. University of Erlangen-Nuremberg, Department of Internal Medicine 3, Erlangen, Germany

The pathophysiology of systemic sclerosis (SSc) is characterized by a cascade of microvascular injury with apoptosis of endothelial cells, Th2/M2 biased
immunosuppression or i.v. pulse cyclophosphamide? And if so, on the basis of what criteria should treatment intensity be stepped up? Second, how can patient selection be optimised so as to avoid transplanting dCSSc patients with little chance of responding? Third, is there a window of opportunity where the immune system can be robusted? Last but not least, how can the potentially eligible dCSSc patients access to HSCT? The latter may be the most (de)pressing one, as HSCT is only available in a small number of centres. Until efficacious disease-modifying drugs with a better risk-benefit ratio become available, HSCT will continue to be the only therapeutic option to reverse the disease course in dCSSc patients.

Disclosure of Interests: Jacob M. van Laar Grant/research support from: Genentech, Consultant for: F. Hoffmann-La Roche DOI: 10.1136/annrheumdis-2019-eular.8611

FRIDAY, 14 JUNE 2019
13:30:00 – 15:00:00

Predicting short-term fracture risk: can we foresee the (close) future?

SP0112 IMMUNOSUPPRESSION – ONE FITS ALL VS. INDIVIDUALIZED SELECTION?

Marco Matucci-Cerinic. University of Florence, Division of Rheumatology AUOC, Florence 50138, Italy

Systemic sclerosis (SSc) is an autoimmune disease characterised by skin, vascular and internal organ involvement leading eventually to tissue fibrosis and atrophy. The best control of the disease is usually achieved in the early phase which is characterised by a diffuse tissue inflammation and vasculopathy, of the tissues. In this phase an immunosuppressive strategy can in fact lead to disease remission even if some cases may escape control and progress inexorably to fibrosis.

Classically, the clinical profile of the patient needs to be achieved. The subset, the disease activity and the main clinical features should be defined in order to have the precise profile of the disease. The knowledge of the clinical conditions may therefore help in deciding the drug and shaping the therapeutic regimen and its intensity. Usually, the use of Cyclophosphamide (CYC) and Micophenolate (MMF) may fit the necessity of the largest part of the SSc population. In practice, CYC may be employed as an induction treatment, etile or intravenous, while MMF may be used as a maintenance therapy. Both drugs have been demonstrated to be useful in the treatment of SSc either on the cutaneous or on the lung involvement.

However, the most severe and refractory cases may be today considered for a hematopoietic stem cell transplantation (HSCT). In this case, an individualised selection is performed before a patient can be considered fit to receive this kind of therapeutic regimen. Therefore, the treatment is strictly individualised and only after having a thorough clinical evaluation the patient can be accepted for the systemic conditioning with high doses of CYC for bone marrow ablation. In conclusion, the treatment of SSc is today mainly centered on immunosuppression whose intensity must be decided and individualized according to the disease activity. New innovative targeted drugs are on the horizon in the effort to find the right immunosuppressive and antifibrotic therapeutic approach clinically tailored on the SSc patient.


SP0114 CASE 1 PRESENTER: IMMINENT FRACTURE RISK: ASSESSMENT AND DOES IT HELP CLINICAL MANAGEMENT

Nicholas Fuggle. University of Southampton, MRC Lifecourse Epidemiology Unit, Southampton, United Kingdom

A 60 year old female was under long-term follow-up for rheumatoid arthritis, for which she took methotrexate. Ten years previously she had been found to have a single vertebral fracture and her fracture risk, assessed using The WHO Fracture Risk Assessment Tool (FRAX®), was calculated as a 13% risk of major osteoporotic fracture over the next 10 years. According to The National Osteoporosis Guideline Group (NOGG) recommendations, she underwent Dual X-ray Absorptiometry (DXA) which demonstrated a bone mineral density T-score of -1.7 at the femoral neck. Lifestyle, vitamin D and calcium intake were optimised and follow-up was arranged for 6 months. Prior to her next appointment she fell and sustained a fracture of the distal radius.

On fracture liaison review her FRAX® risk of fracture was 14% (rising due to an increased year of age) despite the recent change in clinical circumstances.

This case serves to emphasise the clinical conundra associated with imminent fracture risk (the 2 years after a fracture when the patient is at a significantly higher risk of fracture) and the difficulties with the decision to treat.


SP0115 CASE 1 DISCUSSANT: IMMINENT FRACTURE RISK: ASSESSMENT AND DOES IT HELP CLINICAL MANAGEMENT

Cyrus Cooper. University of Southampton, MRC Lifecourse Epidemiology Unit, Southampton, United Kingdom

With an estimated 520,000 fragility fractures every year in the UK, delivering effective and efficient healthcare for this patient group has significant consequences for patients, families, the NHS, and society. A fragility fracture is a major risk factor for further fractures, and healthcare systems are now beginning to recognise the benefits of secondary fracture prevention. Despite this, less than 50% of patients receive effective secondary fracture prevention after a fragility fracture. This has led to national and international initiatives to improve clinical services by implementing fracture liaison services (FLSs). Successful funding of a new FLS is usually influenced by the number of fractures it is expected to prevent in the first few years after an index fracture. The expected number of fractures prevented is in turn determined by the baseline risk of subsequent fracture, the number of patients at high enough fracture risk to warrant anti-osteoporosis medication (AOM), and the degree of fracture risk reduction by AOMs. Underestimating fracture risk in the post-fracture period will lead to fewer expected fractures prevented and lower perceived benefit of the FLS by payers, and importantly also by patients, families, healthcare providers, and payers. Tools are available to determine the long-term risk of fracture based on patient factors, including previous fracture. Of these, FRAX® and QFracture have been incorporated within UK NICE clinical guidance, and the FRAX-derived intervention threshold is used to guide therapeutic options for AOM in the NHS.

CASE 2 PRESENTER: BREAKING BAD AND TRAGICALLY HIP. A CASE OF A MISSED OPPORTUNITY AFTER VERTEBRAL FRACTURE

Michael Skjødt. Norwegian University of Science and Technology (NTNU), Department of Public Health and Nursing, Trondheim, Norway

Mrs A is a 78-year old woman, admitted to the emergency room after a same level fall in her home earlier the same day. She has a history of Chronic Obstructive Pulmonary Disease with recurrent exacerbations, and hysterectomy at the age of 41. At admittance, she is complaining of agonising pain localised to her right hip, and she is unable to move the leg. Upon the physical examination, the right leg is shortened and outwardly rotated. Upon further questioning, Mrs A reveals that she has lost four or five cm of height during the past years. An X-ray of the hip demonstrates a neck of the femur fracture. Mrs A has surgery the following day and two screws are inserted. Due to a hospital-acquired pneumonia, Mrs A stays in the hospital for an additional 9 days after the operation, upon which she is discharged for a temporary placement at a nursing home for further rehabilitation.

Two months following discharge, Mrs A was called for a clinical evaluation by the hospital Fracture Liaison Service. Assessment with DXA confirms the osteoporosis diagnosis and VFA shows lower thoracic vertebral fractures. The FLS coordinator noted that Mrs A, related to a hospital admission for an acute exacerbation of her COPD 3 years before, had had a chest x-ray performed, on which vertebral fractures of the thoracic spine could be seen to be present. Mrs A has never previously been assessed nor treated for osteoporosis.

Disclosure of Interests: None declared

CASE 2 DISCUSSANT: AUTOMATED (IMPLEMENTED IN THE PRESENCE OF VERTEBRAL FRACTURES)

Bo Abrahamsen. x, x, x. Denmark

Identification of patients at high risk of osteoporotic fractures is commonly based on fracture history, bone mineral density or a combination of the two. However, vertebral fractures are very often either missed or not acted upon by our health systems and DXA scanning to measure BMD in itself requires a coherent case finding strategy. Current EPR systems may have built-in features to capture signs of sepsis or warnings to alert clinicians to cases with a diagnosis of atrial fibrillation with no apparent prescription for anti-coagulation. Building on the same principle, EPR systems or even national databases can be set up with appropriate decision rules to alert physicians to diagnoses such as RA, AS or COPD that we know strongly increases the risk of osteoporosis and to flag out medication patterns known to predict a high risk of osteoporotic fractures. This can then be checked against the presence of referrals for DXA and/or prescriptions for anti-osteoporosis medicines and a clinical decision aid triggered to alert healthcare professionals. The mechanism powering such a tool can be an existing clinical risk algorithm such as QFracture, FRACT, FREM, Garvan FRC or others, depending on the nature of routinely collected data, the setting and the timescale required, or a bespoke risk tool developed for the healthcare system in question. It is important to appreciate that risk tools need careful calibration to be appropriate across countries and clinics and that the trigger risk level is ultimately a trade-off between clinical judgment and health economics.

Vertebral fractures represent a particular challenge. It has been established in the past that vertebral fractures often are not mentioned in radiology reports even if clearly present, or reported using unclear terminology that does not make it sufficiently clear to clinicians that a vertebral fracture is present. Moreover, even when vertebral fractures are called out in the radiology report it is not uncommon for this to go unnoticed. Opportunistic identification of vertebral fractures by software tools is a possible new avenue for narrowing the treatment gap in osteoporosis. With increasing integration of DICOM images into EPR systems, DICOMs of CT scans and other modalities containing spine images could be used either for automated case finding with alert boxes in the EPR system itself or employed in radiology departments to automatically populate reports with additional information about the presence of vertebral fractures.

REFERENCES:

Disclosure of Interests: None declared

FRI Day, 14 June 2019
13:30:00 – 15:00:00
Primary and secondary fibromyalgia; are they different?

FIBROMYALGIA: AN ACCEPTABLE DIAGNOSIS?

Rinie Goege, Utrecht University, Department of Psychology, Utrecht, Netherlands

Background: Neither patients nor clinicians and researchers fully embrace the fibromyalgia diagnosis. A core objection relates to the huge overlap with other polysymptomatic distress disorders such as somatic symptom disorder and chronic fatigue syndrome. Another objection has to do with the classification of fibromyalgia as a rheumatic disease, which may hamper research and treatment of psychological factors.

Objectives: To get insight into the pros and cons of the fibromyalgia diagnosis. Methods: The scientific literature was reviewed with a focus on homogeneity and heterogeneity within the group diagnosed as fibromyalgia.

Results: That fibromyalgia is not a stable diagnosis of a homogeneous group is reflected in the ongoing development of new classification and diagnostic criteria; the newest including diagnostic criteria, common features, comorbidities, consequences, and putative mechanisms (Arnold et al., 2019). Moreover, treatment recommendations progressed from a focus on pharmacological treatment in 2008 to a focus on nonpharmacological therapies in 2017 (Macfarlane et al., 2017). Also, several studies showed that the group is quite heterogeneous with respect to type, number and severity of symptoms and comorbidities (e.g., Davis et al., 2018) as well as with respect adaptation profiles covering a spectrum of severely maladjusted to quite well adjusted in terms of objective and subjective management (Estevez-Lopez et al., 2018).

Conclusion: Although diagnostic classifications such as fibromyalgia help to examine underlying mechanisms and interventions and to define treatment recommendations, in clinical practice and research account should be taken of heterogeneity of patients in terms of symptoms and disorder-transcending biopsychosocial factors that influence the disorder. This suggests that fibromyalgia is an acceptable diagnosis to the extent that individually is accepted as part of the diagnosis.

REFERENCES:

Disclosure of Interests: None declared

SEARCHING FOR PATHOLOGY; HOW HARD SHOULD WE LOOK?

Ernest Choy. CREATE Centre, United Kingdom

Background: The 1990 American College of Rheumatology (ACR) classification criteria for Fibromyalgia (FM) was intended to facilitate research by defining a homogeneous patient population [1]. Two key features of the criteria are tender point examination and exclusion of other conditions that may cause widespread pain. This led to the view that FM is a diagnosis of exclusion. This is no longer the case in 2019.

Results: In 2010, the ACR published provisional criteria for the diagnosis of FM [2]. These allowed FM to be diagnosed by using questionnaire removing the need for tender point examination. One of the major advantages of the criteria is that the diagnosis of FM can be made by primary care physician and the first-line treatment be initiated without referral to secondary care. Such an approach was
recommended by the Canadian guidelines [3], which recommended “patients should undergo a physical examination which should be within normal limits except for tenderness on pressure of soft tissues however the specific tender point examination according to the 1990 ACR diagnostic criteria is not required to confirm a clinical diagnosis of fibromyalgia”. Furthermore, it stated that “Fibromyalgia should be diagnosed as a clinical construct, without any confirmatory laboratory test, and with testing limited to simple blood testing including a full blood count, erythrocyte sedimentation rate, C-reactive protein, creatine kinase, and thyroid stimulating hormone. Any additional laboratory or radiographic testing should depend on the clinical evaluation in an individual patient that may suggest some other medical condition.” However, many primary care physicians do not feel competent/confident to exclude other rheumatic conditions by physician examination.

Over the last decade, comorbid FM is increasingly recognized in many chronic musculoskeletal diseases including patients with inflammatory arthritis. A systematic review found that the prevalence of FM is 21%, 13% and 18% in RA, axSpA and PsA respectively [4]. Patients with comorbid FM have higher diseases activity score and more severe pain. In 2016, the ACR diagnostic criteria for FM were modified and stated that “A diagnosis of fibromyalgia is valid irrespective of other diagnoses. A diagnosis of fibromyalgia does not exclude the presence of other clinically important illnesses.” [5].

Conclusions: The motion that “FM is a diagnosis of exclusion” is no longer valid. FM should be a positive diagnosis and does not exclude other rheumatic diagnosis.

REFERENCES:

Disclosure of Interests: Ernest Choy Grant/research support from: Amgen, BioCancer, Chugai Pharma, Ferring Pharmaceuticals, Novimmune, Pfizer, Roche, and Union Chimique Belge, Consultant for: Abbvie, Amgen, AstraZeneca, Biogen, BMS, Boehringer Ingelheim, Celgene, Chelsea Therapeutics, Chugai Pharma, Daichi Sankyo, Eli Lilly, Ferring Pharmaceutical, GlaxoSmithKline, Hospita, Isis, Jazz Pharmaceuticals, Janssen, MedImmune, MerckMaPharmaceutical, Merck Sharp & Dohme, Napp, Novimmune, Novartis, ObsEva, Pfizer, Regeneron, Roche, R-Pharm, SynAct Pharma, Sanofi-Genzyme, Torax and Union Chimique Belge. Speakers bureau: Amgen, BMS, Boehringer Ingelheim, Chugai Pharma, Eli Lilly, Hospira, Merck Sharp & Dohme, Novartis, Pfizer, Regeneron, Roche, Sanofi-Aventis, and Union Chimique Belge.


SP0120 PERSONALISED TREATMENT FOR FIBROMYALGIA; THE IMPACT OF COMORBIDITIES
Serge Perrot, France, France

Background: The heterogeneity of the clinical presentation, the co-morbidities and the pathophysiologic mechanisms associated with fibromyalgia (FM), and the modest results on average for any therapy, call for a more individualized management strategy.

How to develop personalized treatment?

Individualized treatment can be developed on the basis of subgrouping of patients according to associated conditions and co-morbidities (mental health problems, chronic overlapping pain conditions, other somatic diseases) or on disease severity. Personalizing treatment needs to classify FM in specific subgroups. It can be proposed on the basis of clinical assessment (e.g. degree of daily functioning), on co-morbidities or on dedicated questionnaires. Lastly, shared decision-making regarding treatment options can be directed according to patient preferences, co-morbidities, and availability in various health care settings.

What is currently recommended as a personalized approach?

The European League Against Rheumatism guidelines recommend a tailored approach directed by FM key symptoms (pain, sleep disorders, fatigue, depression, disability), whereas the German guidelines recommend management tailored to disease severity, with mild disease not requiring any specific treatment, and more severe disease requiring multicomponent therapy (combination of drug treatment with aerobic exercise and psychological treatments). When indicated, treatments should follow a stepwise approach beginning with easily available therapies such as aerobic exercise and amitriptyline. We will present how successful application of a tailored treatment approach that is informed by individual patient characteristics can improve outcome of FM.

Key points: This presentation will presents suggestions for an individualized treatment strategy for FM patients on the basis of symptoms, disease severity and co-morbidities.

Disclosure of Interests: None declared


FRIDAY, 14 JUNE 2019
13:30:00 – 15:00:00
Joint EULAR – EFIS: Combatting or harnessing ILC in the battle against autoimmunity

SP0121 DEBATE: ILC AS INNOCENT BYSTANDER
Mikael Ebbo, Hôpital de la Timone, AP-HM, Aix-Marseille Université, Internal Medicine, Marseille, France

None declared


FRIDAY, 14 JUNE 2019
13:30:00 – 15:00:00
Optimizing the access to new treatments for RMD patients

SP0122 OPTIMIZING HOLISTIC TREATMENTS: THE CHALLENGE OF IMPLEMENTATION
Krysta Dziiedzic, Keele University, School for Primary, Community and Social Care, Stoke on Trent, United Kingdom

International guidelines present recommendations for holistic care for RMDs, building upon best evidence. However, there is still a gap between what we know about best care and what we do to implement best care in our clinical services. Having EULAR guidelines alone (and multiple updates and revisions) is not enough to change complex systems. European funders are now investing in projects to accelerate the uptake of best care across multiple European partners.
Using one example of a completed EIT-Health funded implementation project, JIGSAW-E (Joint Implementation of Guidelines for oSteoArthritis in Western Europe), this presentation will highlight some of the challenges of implementation such as: understanding the context; competing priorities; lack of time and funding; stability of the workforce; and differing health care systems. It will describe the use of Knowledge Mobilization and Communities of Practice as methods for overcoming these challenges and optimizing holistic treatments.

The presentation will offer some of the key factors for implementation such as ‘leading from the middle’ and brokering across silos; working with patients and the public. ‘Patients are the most under-used resource in any health care system’: using theories, models and frameworks to plan, understand and evaluate implementation; using pilot sites to build momentum with dedicated Communities of Practice; and agreeing what success should look like.

Disclosure of Interests: None declared


SP0123 NEW TREATMENTS: WHY SHOULD WE WAIT?

Daniel Morales. University of Dundee, Population Health and Genomics, Dundee, United Kingdom

Background: Improving access to new and established medicines for rheumatological disease is of public health importance. However, drug development processes, medicines regulation and health technology requirements may significantly impact on when a new medicine become available to be used by health care professionals.

Objectives: The objectives of this session are to present some of the challenges and opportunities for accessing new and established medicines for rheumatological disease.

Methods: Drug development processes, medicines regulation and health technology requirements may significantly impact on when a new medicine become available to be used by health care professionals. Although these requirements may be perceived as barriers, many of these requirements are in place to ensure a medicines benefit risk profile is favorable and is cost effective in terms of quality of life. This session will briefly discuss issues around the process of making medicines newly available from drug development to gaining new market approvals with an emphasis on rheumatological disease, including the post-authorization safety requirements that are in place to safe guard public health.

Disclosure of Interests: None declared


FRIDAY, 14 JUNE 2019
13:30:00 – 15:00:00
New assessments in clinical practice

SP0124 WHICH MEASURES TO USE TO ASSESS REMISSION IN RHEUMATOID ARTHRITIS

Annamaria Iagnocco. Academic Rheumatology Unit Università degli Studi di Torino, Academic Rheumatology Centre, Turin, Italy

Remission is the ideal target of treatment in rheumatoid arthritis (RA) patients. However, the definition and characterization of remission is still a theme of discussion and its assessment can be a challenging issue in RA clinical practice. Indeed, nonetheless the new treatments and therapeutic strategies for RA make remission possible, sub-clinical inflammation can still be present both at the joint site and at the patient level, leading to damage progression and to occurrence of flares.

Clinically, remission entails persistent absence of any sign of joint and systemic inflammation. However, the presence of some residual joint inflammatory activity can be accepted by current clinical indexes such as DAS28, SDAI, CDAI and Boolean remission, although the latter is clearly based on more stringent parameters (1,2). Based on those criteria, and particularly with the use of SDAI and Boolean cut-off values, complete and persistent remission is then quite uncommon in late RA, while it seems to be more easily possible in early disease (3). Another interesting issue to consider in clinical practice is the presence of sustained remission which seems to occur less frequently than remission at different point times and with only a minority of cases reaching a complete disease recovery (4).

Depending on the modality that is used, the assessment of remission by imaging encompasses the evaluation of a wide spectrum of lesions. While ultrasound is able to show intra- and peri-articular signs of inflammation and to differentiate active from inactive synovitis with the use of Doppler modes, MR shows also bone marrow inflammatory-related abnormalities. Moreover, ultrasound detects inflammation at multi-site level and allows the measurement of stable remission over time on longitudinal evaluation. Interestingly, also tenosynovial Doppler inflammation has been demonstrated to be a frequent finding in patients in clinical remission and, compared to joint synovitis, it is more associated with self-perceived unstable remission (5). In addition, tenosynovial and joint Doppler positivity has been demonstrated to be an independent risk factor of flare in RA patients in remission (6). Residual joint inflammation in patients in remission can be demonstrated also by other imaging techniques, such as PET which shows enhanced tracer uptake at different joint sites (3). Basically, the capability of imaging to demonstrate sub-clinical disease activity even in patients in clinical remission, by allowing the detection of residual inflammation at different joint sites and at different disease stages gives it an added value compared to clinical assessment alone.

In conclusions, clinical evaluation of remission alone appears frequently inadequate to capture a real persistent lack of inflammation at different joint sites. Imaging can complement the assessment of patients in clinical remission, offering additional data that may still reveal a certain amount of sub-clinical disease activity. With new therapeutic strategies RA management has become increasingly complex over the last years (7). The relevance of this information is then substantial, being structural damage the result of both previous and current phases of disease activity.

REFERENCES:

Disclosure of Interests: None declared


SP0125 HOW TO ASSESS PATIENT WITH SUSPECTED VASCULITIS

Presshil Limpar. University of Oxford, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom

Background: Systemic vasculitides are multi-organ, multi-system conditions which can mimic many other diseases. They are rare but very significant because they can rapidly lead to end organ damage or death if left untreated. The difficulty faced by clinicians in diagnosing a patient with vasculitis is further compounded by the presentation of limited forms of vasculitis, which can be difficult to recognise as due to vasculitis, the effects of co-existing co-morbidity and the use of drugs either for medicinal or recreational purposes. Giant cell arteritis is one of the most common serious forms of vasculitis in adults, leading to blindness if untreated. In view of this risk, many clinicians will initiate treatment of any patients with suspected giant cell arteritis before definitive investigations have been performed. Unfortunately this can result in inadequate outcomes form diagnostic tests such as ultrasound or biopsy of the temporal artery. There are no diagnostic criteria for most forms of vasculitis apart from Behcet’s syndrome. Some tests can be very useful in ruling out other causes as well as helping to confirm a diagnosis of vasculitis. We will review some of the strategies for diagnosing vasculitis, complementing a thorough history and examination with selected investigations to improve diagnostic certainty.

Objectives: To consider the strategies used to assist the diagnosis of systemic vasculitis, to assess the frequency of multi-system involvement in systemic vasculitis; to critically evaluate the role of diagnostic testing in systemic vasculitis.

Methods: A review of current literature on the approach to diagnosis and classification of vasculitis.

Results: Table 1 summarises the clinical manifestations of some forms of primary systemic vasculitis, comparing the different frequencies of the common presenting features. Patients with large vessel vasculitis are usually more distinct as a clinical group from other forms of vasculitis but increasingly we see an overlap between GCA and older patients with Takayasu arteritis. There is considerable overlap of clinical features amongst the small vessel vasculitides, despite different immune-pathogenetic pathways. Amongst the anti-neutrophil cytoplasm antibody (ANCA) associated vasculitides (AAV), the presence of active nephritis characterises most patients with MPA; it is less common in GPA and least common in EGPA. Lung involvement is prevalent in all these forms of AAV, but has different characteristics: bronchial wall inflammation with ulceration plus nodules and infiltrates in GPA; transient infiltrates and bronchospasm in EGPA; lung haemorrhage at presentation in MPA, with subsequent risk of developing lung fibrosis. The different patterns of disease activity help in differentiating
individual forms of vasculitis, but it is important to remember that many features associated with medication and co-morbidity may make this patient group more homogeneous, especially if the original disease manifestations are now quiescent. We will explore the potential use of classification criteria as substitutes for diagnostic criteria in different forms of vasculitis and evaluate the role of specific tests to assist in the diagnosis, with a focus on ANCA testing in small vessel vasculitis and on imaging in large vessel vasculitis.

**Conclusion:** A rational approach to diagnosis in vasculitis is required, based on a combination of clinical features together with relevant investigations. Diagnostic certainty can vary in the absence of definitive evidence from investigations, especially if patients have already been partly treated prior to completing all relevant investigations. Diagnostic testing is improving and with the development of new criteria for classification, this forms a stronger basis to develop a more sound approach to diagnosis. However, we should always be prepared to apply a provisional diagnosis and reconsider any emerging evidence to suggest an alternative condition.

**REFERENCES:**


[4] Start RJHA; Writing group; Reviewer group; Members of EANM Cardiovascular; Members of EANM Infection & Inflammation; Members of Committees, SNMMI Cardiovascular; Members of Council, PET Interest Group; Members of ASNC; EANM Committee Coordinator. FDG-PET/CT(A) imaging in large vessel vasculitis and polymyalgia rheumatica: joint procedural recommendation of the EANM, SNMMI, and the PET Interest Group (PiG), and endorsed by the ASNC. Eur J Nucl Med Mol Imaging. 2018 Jul 45(7):1250-1269.

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.8528

**FRIDAY, 14 JUNE 2019 13:30:00 – 15:00:00**

The benefits of involving patients in health technology assessment

**SP0127**  
**PATIENT ENGAGEMENT WITHIN THE EUROPEAN MEDICINES AGENCY**

Nathalie Bere, European Medicines Agency (EMA), Public engagement Department, London, United Kingdom

The European Medicines Agency (EMA) is the European regulatory body whose role is to evaluate and supervise medicines across the European Union. EMA has been engaging with patients and consumers for many years and today, patient involvement is an integral part of the work at EMA, with a diverse range of opportunities in place to include the patient’s voice at various stages along the medicines regulatory life-cycle. Key to successful engagement has been the need for flexibility, a range of well-tested methodologies and a robust system of support and training.

Patients and caregivers’ real-life perspectives and unique insights complement the scientific data within EMA reviews; they provide input on proposed protocol designs and participate in expert meetings and written consultations on medicines evaluation. They are voting members of EMA committees and they review medical information written for the public. Evidence has shown their contributions make a difference and ultimately help ensure that the Agency’s outcomes are as meaningful and relevant as possible for all concerned.

Some of the key challenges and conclusions of our journey will be highlighted to serve as a guide to those considering a similar, rewarding path.

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.8427
THE VARIOUS ROLES OF PATIENT PARTICIPATION IN HTA BY THE EXAMPLE OF IQWiG

Virginia Seiffart. Institute for Quality and Efficiency in Health Care (IQWiG), Drug Assessment, S0670 Köln, Germany

Background: The involvement of affected persons in preparing systematic reviews and HTA represents an established international standard of benefit assessment. The Institute of Quality and Efficiency in Health Care (IQWiG) is a professionally independent scientific institute founded within the framework of the German Health Care Reform of 2004 as an establishment of the Foundation for Quality and Efficiency in Health Care. IQWiG provides benefit assessments addressing issues concerning the statutory health insurance services. Its responsibilities include among others the preparation of scientific reports, expert opinions and recommendations for quality and efficiency issues taking age, gender, personal circumstances into account.

Objectives: The goal of this presentation is to provide an overview on different paths of involvement of patients and affected persons at IQWiG.

Methods: IQWiG’s legal basis and responsibilities are anchored in the Social Code Book Fifth Book – Statutory Health Insurance (SGB V) and have been adapted and extended several times in the course of further health care reforms. The Institute’s work is commissioned by the Federal Joint Committee or by the Federal Ministry of Health. The information for this presentation stems from IQWiG’s General Methods (currently in version 5.0), a publicly available paper provided on the Institute’s website, which explains the groundwork for its assessments.

Results: The involvement of affected persons at IQWiG primarily takes place during the initial work on a report within the framework of patient-relevant outcomes and relevant subgroups. Moreover, involvement can also include partaking in hearings. Affected persons include in particular patients (represented by parents or relatives, when appropriate) as well as potential participants in prevention measures. Affected persons are found via the patient representation of the Federal Joint Committee, as well as national or local self-help organizations or groups, hospitals or medical practices, external experts or other routes. The involvement can consist of a personal consultation or providing information in writing (through questionnaires or reports on personal experience), in both cases with documents indicating potential conflicts of interest.

Conclusion: As representatives of patients or self-help groups are sometimes not always present and cannot directly account for symptoms or their impact on the quality of life, focus is placed on involving persons directly affected. Different assessments require distinct types of involvement depending on the available time and the confidentiality of the topic.

Disclosure of Interests: None declared

A PATIENT’S VIEW ON PATIENT INVOLVEMENT

Souzi Makri. CYPLAR, Limassol, Cyprus

Background: HTA as defined by the EUPATI:
Health technology assessment aims to inform decision making by health care policy makers. It is a systematic process that considers health technologies (such as medicines) and can involve a review of: Clinical evidence compared to existing models of care, Cost effectiveness, Social and ethical impacts on the health care system and the lives of patients EUPATI Overarching principle: We recommend close cooperation and partnership between the various stakeholders including healthcare professionals’ organisations, contract research organisations, patient’s and consumers’ organisations, academia, scientific and academic societies, regulatory authorities and HTA bodies and the pharmaceutical industry. Experience to date demonstrates that the involvement of patients has resulted in increased transparency, trust and mutual respect between them and other stakeholders. It is acknowledged that the patients’ contribution to the discovery, development and evaluation of medicines enriches the quality of the evidence and opinion available.

Objectives: Inform decision making by health care policy makers. It is a systematic process that considers health technologies (such as medicines) and can involve a review of:
1. Clinical evidence compared to existing models of care,
2. Cost effectiveness,
3. Social and ethical impacts on the health care system and the lives of patients

EUPATI Overarching principle:
“We recommend close cooperation and partnership between the various stakeholders including healthcare professionals’ organisations, contract research organisations, patients’ and consumers’ organisations, academia, scientific and academic societies, regulatory authorities and HTA bodies and the pharmaceutical industry. Experience to date demonstrates that the involvement of patients has resulted in increased transparency, trust and mutual respect between them and other stakeholders. It is acknowledged that the patients’ contribution to the discovery, development and evaluation of medicines enriches the quality of the evidence and opinion available.”

Disclosure of Interests: None declared

STANDARDISATION OF NORMAL VERSUS ABNORMAL AND PATHOLOGICAL CAPILLAROSCOPIC IMAGES

V. Smith1,2,3, on behalf of the EULAR Study Group on Microcirculation in Rheumatic Diseases. 1Department of Rheumatology, Ghent University Hospital, 2Department of Internal Medicine, Ghent University, "Unit for Molecular Immunology and Inflammation, VIB Flemish Institute for Biotechnology (VIB), Ghent, Belgium

Medical doctors frequently get patients with Raynaud’s phenomenon (RP), a frequent symptom in the general population, referred. The importance of
distinguishing normal capillaroscopic findings from (pathognomonic) abnormal (pathological) findings (scleroderma pattern), lies in the fact that this distinction allows the differentiation between a primary RP (not connected to any connective tissue disease [CTD]) from a secondary RP due to systemic sclerosis (SSc) and diseases of the scleroderma spectrum.

What is normal in primary RP?

A normal capillaroscopic pattern, by qualitative assessment, is characterized by a homogeneous distribution of hairpin shaped capillaries as a “comb-like structure”, with a density of >7 capillaries per mm, with a normal dimension and absence of large hemorrhages. Yet, there exists a wide intra- and inter-individual variety in a normal population which will be discussed in this session.

What is pathognomonic abnormal in patients with RP due to SSc?

Patients with the RP who have an underlying clinically recognizable (= with skin involvement) SSC show a very characteristic combination of capillary abnormalities in the nailfold, which can easily be assessed through qualitative assessment (= pattern recognition). Maricq et al. described last century, with the widefield technique (magnification X12–14) the scleroderma pattern. This pathognomonic combination contains the following: a striking widening of all three segments of the capillary loop (arterial, venous and intermediate), loss of capillaries and disorganization of the nailfold capillary bed. Many branched “bushy” capillaries may also be observed.

In 2000, Cutolo et al. qualitatively assessed the nailfolds of an SSc cohort with patients fulfilling the American College of Rheumatology (ACR) criteria for SSc with the nailfold videocapillaroscopy (NVC) technique (magnification X200). According to the different proportions of the hallmark parameters of the scleroderma pattern (giants, capillary loss, hemorrhages and abnormal shapes: (neo)angiogenesis), Cutolo et al. defined three patterns: “early”, “active” and “late”.

The central role of capillaroscopy in distinction between a primary and secondary RP due to SSc is reflected by the fact that capillaroscopy is one of the new ACR/EULAR criteria for classifying a patient as having SSc. In this lecture the standard “FAST TRACK” recognition system of the EULAR Study Group on Microcirculation in Rheumatic Diseases to discern scleroderma patterns from non-scleroderma patterns will be taught to the attendees.

Suggested further reading:

Disclosure of Interests: None declared
DOI: 10.1136/rheumatoid-2019-eular.8591

SP0132

METHODS AND TOOLS FOR QUANTIZATION OF CAPILLAROSCOPICT MORPHOLOGICAL CHANGES

Francesca Ingegni, Academic Rheumatology Unit University degli Studi di Torino, Academic Rheumatology Centre, Turin, Italy

Nailfold capillaroscopy is the one most used technique in both clinical and research settings by adult physicians and paediatric rheumatologists to assess patients with Raynaud’s phenomenon as shown by an international survey on non-invasive techniques to assess the microcirculation performed under the aegis of members of the EULAR Study Group on Microcirculation in Rheumatic diseases [1].

Nailfold capillaroscopy is a simple non-invasive imaging technique mainly used to observe capillaries on the skin surface. After application of a drop of immersion oil, capillaries can be observed with a magnification lens because they run parallel to the epidermis at the nailbed area [2]. A number of different instruments can be used to perform the exam. They have different characteristics in terms of their cost, quality of images, magnifications, training period, portability, software for image analysis and storage.

Some of these instruments can be used both in clinical and research settings such as the stereomicroscope and the videocapillaroscopy. The stereomicroscope allows the widefield visualization of the nailfold with low magnifications, the training is relatively short, but the examination is difficult to perform in patients with digital flexion contractures.

There appears to be consensus regarding the use of videocapillaroscopy that allows a detailed visualization of capillary morphology using higher magnifications (100-300x). Contact probe with polarized light microscopy permits easier observation of the skin surface, and the training period is briefer. Specific software are available for images analysis, storage, and complete medical reports (text + images) can be produced. By contrast, in a clinical setting, nailfold capillaries can generally be visualized using more simple, but also efficient tools such as a dermatoscope, USB microscope, ophthalmoscope or smartphone device. The quality of images can be quite good, although the lower magnification means that some details are unlikely to be seen, and they often lack the possibility of image storage and measurement. In particular, the dermatoscope with magnification of the order of x10 is a small, inexpensive and easily portable piece of equipment that has been suggested to be comparable to videocapillaroscopy within routine clinical practice. As the study of capillary morphology provides clinically relevant information in the management of patients with scleroderma-spectrum diseases, the development of specific software to standardize and automate the analysis is ongoing [3-4].

REFERENCES:
Gout is the most common inflammatory joint disease in Western developed countries. Diagnosis and monitoring have historically been based upon clinical assessment combined with biochemical results (primarily p-urate) but over the last decade ultrasonography (US) has received increasing attention for these purposes. US has been shown able to detect monosodium urate deposits in both joints and tendons. In 2015 the Outcome Measures in Rheumatology (OMERACT) US Working Group developed definitions of structural lesions in gout. These include double contour sign (deposits of crystals on the surface of cartilage), tophus (larger hyper-echoic aggregation of crystals), aggregates (small hyper-echoic deposits) and erosion (1). The double contour sign has been included in the ACR/EULAR 2015 gout classification criteria as a way to visualize urate deposits in joints (2). Furthermore, US can visualize potential concomitant inflammatory aspects of gout since it can visualize both joint inflammation and tenosynovitis.

In this talk the diagnostic properties of US will be described and the potential risk of false positive results due to artefacts or misinterpreted lesions will be discussed. Furthermore, the potential role of US in monitoring of treatment response will be explored.

REFERENCES:

Conclusion: Knowledge of the clinical anatomy needed to understand the relationships between the different structures, the clinical history, and physical examination of GTPS patients and the therapeutic possibilities including ultrasound-guided injections are other steps that lead to an accurate diagnosis of GTPS.

REFERENCES:
[1] anatomy and anthropology: Maribel Miguel, Mike Benjamin
[2] Clinical anatomy: Juan Canoso
[3] Regional musculoskeletal ultrasound: Carlo Martinoli

Disclosure of Interests: None declared
Defining the concept of US-detected ‘minimal disease’ is crucial to enable investigators to identify a threshold (or cut-off) to differentiate normal physiological from minimal pathological changes at the joint level. This threshold, subsequently, will be used to evaluate the best sensitivity to detect changes in therapeutic response and assess remission, as well as facilitate diagnosis of early disease. In order to address this important research question, the OMERACT US SIG has formed the US Minimal Disease Taskforce at the OMERACT 2016 meeting. This collaboration between 24 OMERACT ultrasound centres in 11 countries has successfully recruited more than 600 subjects into the Minimal Disease Study. US data of healthy individuals encompassing synovial hypertrophy, synovial effusion, and Doppler enhancement will be presented.

Disclosure of Interests: None declared

**SP0136**

HOW TO PERFORM US-GUIDED INTERVENTIONS + DEMO

Juhanni Keski, Mikkel Central Hospital, Internal Medicine, Mikkel, Finland

Background: Aspiration and injection of joints and soft tissues is an indispensable skill used in everyday practice by the clinical rheumatologist. These tasks are usually conducted by palpation-guided techniques. These procedures are not always successful [1] and thus US-guided interventions have been developed. Objectives: to explain the effect of needle and sound beam angle on needle visualization, describe different techniques of needle insertion under US guidance, to identify different approaches to the target under US guidance and finally to discuss about the accuracy and efficacy of the ultrasound guided technique.

Methods: There are two common methods for US puncturing: semi-guided or indirect method (skin surface marking) and needle guidance under direct sonomic vision (2,3). The scanning plane is optimized for visualization of the target and penetration of the needle should be at least 0.5cm from the transducer. The movement of the needle in the soft tissue should be followed on the screen during the procedure. The needle appears as a bright echogenic line if the transducer is oriented longitudinally on the needle, and the needle tip may be followed as it reaches the target. If the ultrasound beam is transverse to the needle, the needle is seen as a bright echogenic dot. In case of no visualization of the needle several means are available: steering of the ultrasound beam against the needle (in new machines), curved or virtual convex probe, toeing-in of the probe, shaken the needle slightly and moving the probe a bit from side to side.

Results: According to the clinical and cadaveric studies the ultrasound guided technique is more accurate than the landmark guided technique in the glenohumeral, acromioclavicular, wrist, hand, hip, knee and foot joints and in the tendons of the biceps, wrist, hand hip, knee and ankle (4). Synovial biopsies are more accurate using an ultrasound guided method (5).

Conclusion: Ultrasound is the most applicable and feasible imaging modality for routine clinical use in guiding musculoskeletal procedures. Though many studies have examined the role of imaging guidance for injection there needs to be more examination of how the use of ultrasound prior to injection can alter the pathological and anatomical diagnosis. There is a trend towards an expanded number of advanced applications of interventional musculoskeletal ultrasound which can also be performed by a rheumatologist like nerve blocks or needling of calcifications. Which ultrasound guided technique (direct or semi-guided) is the most appropriate in different anatomical areas and clinical settings remains to be studied. More studies are needed to show the accuracy and efficacy of ultrasound guided injections in different anatomical areas (4).

REFERENCES:

Disclosure of Interests: None declared

**SP0137**

**CORE COMPETENCIES**

Theda Vliet Vlieland, Leiden University Medical Center, Orthopaedics, Rehabilitation and Physiotherapy, 2300 RC Leiden, Netherlands

Background: To maintain and optimize the quality of care provided by health professionals in rheumatology (HPRs), adequate educational offerings are needed. Ideally, these are based on defined core competences.

Objectives: A task force (TF) aimed to develop evidence-based recommendations for the generic core competences of nurses, physical therapists (PTs) and occupational therapists (OTs) to serve as a basis for their postgraduate education.

Methods: The EULAR standardised operating procedures for the development of recommendations were followed. A TF including rheumatologists, nurses, PTs, OTs, patient-representatives, an educationalist, methodologists and researchers from 12 countries met twice. In the first TF meeting, 13 research questions were defined to support a systematic literature review (SLR). In the second meeting, the SLR evidence was discussed and recommendations formulated. Subsequently, level of evidence and strength of recommendation were assigned and level of agreement (LoA) determined (0-10 rating scale).

Results: Three overarching principles and 10 recommendations for the generic core competences of HPRs were developed supported by the SLR and expert opinion. The SLR included 79 full-text papers, 20 of which addressed the competences, knowledge, skills, attitudes or educational needs of HPRs from multiple professions. The average LoA for each recommendation ranged from 9.42 to 9.79. Consensus was reached on education and research agendas.

Conclusion: Evidence and expert opinion informed a set of recommendations providing guidance on the generic core competences of nurses, PTs and OTs in rheumatology. Implementation of these recommendations in the postgraduate education of HPRs at the national and international level is advised, considering variation in health care systems and professional roles.


REFERENCE:

Disclosure of Interests: None declared

**SP0138**

WHAT WE ARE BRILLIANT AT: OT PERSPECTIVE

Ingrid Kleven, Norwegian Advisory Unit on Rehabilitation in Rheumatology, Department of Rheumatology, Díakonhjemmet Hospital, 0370 Oslo, Norway

The unique contribution of occupational therapy is its focus on occupation, which may be defined as “groups of activities and tasks of everyday life, named, organized and given value and meaning by individuals and a culture. Occupation is everything people do to occupy themselves, including looking after themselves (self-care), enjoying life (leisure), and contributing to the social and economic fabric of their communities (productivity).” Occupation is further being influenced by the environment, one’s social roles and one’s developmental level; being client-defined; and consisting of both a performance (objective) dimension and a satisfaction (subjective) dimension (1). Knowledge of the International Classification of Functioning (ICF), occupational performance covers the domain of Activity and Participation in the ICF model.

In clinical practice, occupational therapists use assessment and interventions to determine, recover, or maintain meaningful occupations of individuals, groups, or communities. Lately, occupational therapists have also been increasingly concerned with occupational injustice, which relates to conditions wherein people are deprived, excluded or denied of occupations that are meaningful to them. Within rheumatology, the most frequently applied occupational therapy interventions are patient education concerning ergonomic principles and activity pacing, therapeutic exercise and activity programs, provision of orthoses and assistive technology, and environmental and task modifications.
In the presentation, patient cases will be used to illustrate how occupational therapists may work to enhance occupation in individual clients with a rheumatic condition, and evidence for some of the core interventions will be discussed.

REFERENCE:

Disclosure of Interests: None declared

SP0139 WHAT WE ARE BRILLIANT AT; NURSING PERSPECTIVE
Ricardo Ferreira, Centro Hospitalar e Universitário de Coimbra, EPE, Rheumatology, Coimbra, Portugal

The challenges confronting health care delivery systems worldwide are rapidly changing, and this calls for practice-defined competencies for nurses and other health care workers (Zhang, Luk, Arthur, & Wong, 2001). The definition of competency or competence in nursing has been a subject of debate (Axley, 2008; Fukada, 2018; Zhang et al., 2001). Its clarification is important and still needed to establish a foundation for realistic working behaviours, for nursing education and management.

Although there has been an extensive and valuable work in the definition of core competencies of nursing profession, which includes both autonomous and inter-dependent activities within the multidisciplinary team, little scientific research has been done to clarify the way in which nursing profession is unique.

This presentation will address the following questions:

- What are nurses (collectively) really brilliant at?
- What leads them to develop unique characteristics?
- How do they bring into care, that matches or complements other health professions to result in better quality care?

The presentation is informed by a scoping review, a survey of international nurse leaders and researchers.

REFERENCES:

Disclosure of Interests: None declared

FRIDAY, 14 JUNE 2019
15:30:00 – 17:00
Overdiagnosis and overtreatment in inflammatory arthritis

SP0141 DOES IMAGING LEAD TO OVERDIAGNOSIS AND OVERTREATMENT?
Duncan Porter, Garthavell General Hospital, Rheumatology, Glasgow, United Kingdom

Background: The use of musculoskeletal ultrasound (MSUS) and magnetic resonance (MR) imaging is widespread in the diagnosis and management of patients with rheumatoid disease. Interpreting the images, and their implication for clinical management is challenging, particularly in the community, in mild/early disease, when there is discordance between clinical and imaging findings, and in the presence of co-morbid joint disease.

Objectives: – to review the evidence about whether the use of imaging results in over-diagnosis and over-treatment
Specifically, the following issues will be addressed, using rheumatoid arthritis as the exemplar:

- To review the prevalence of ‘abnormal’ MSUS and MR findings in the general population
- To understand the prevalence and significance of sub-clinical joint inflammation
- To summarise the evidence from clinical trials about the risks/benefits of treating to a target of imaging (rather than clinical) remission

Methods: If clinicians are to interpret the available imaging correctly, several issues are pertinent. Firstly, it is important to understand the prevalence of erosions, synovitis and bone marrow oedema in the general population, in different joints, at different ages and in the presence of co-morbid conditions such as osteoarthritis. Secondly, in RA what are the implications of sub-clinical inflammatory changes for disease progression? Thirdly, do clinical trials support the hypothesis that ‘treat to target’ strategies should aim at a target of ‘imaging remission’ rather than clinical remission? The results of the TaSER, ARCTIC and RA-IMAGINE trials will be reviewed to identify if the systematic, routine use of imaging results in over-treatment or clinical harm. Lastly, the possibility that imaging could have a role in reducing over-treatment will be discussed.

Conclusion: It is impossible to interpret the results of imaging correctly, without knowing the clinical context. Clinicians need to understand the value and the limitations of imaging, and should not pursue a simplistic or binary approach when interpreting the results - otherwise over-diagnosis and over-treatment will be the result. To date, the evidence from RCTs in the management of RA suggest that a ‘treat-to-target’ approach should aim for clinical and not imaging remission.

REFERENCES:
Conventional Treat-to-Target Strategies on Disease Activity Remission and Radiographic Progression in Rheumatoid Arthritis: The IMAGINE-RA Randomized Clinical Trial Effect of MRI vs Conventional Treat-to-Target Strategies on Disease Activity Remission in RA: Effect of MRI vs Conventional Treat-to-Target Strategies on Disease Activity Remission in RA JAMA. 2019 Feb 5;321(5):461–72


Disclosure of Interests: None declared

FRIDAY, 14 JUNE 2019
15:30:00 – 17:00:00
The multiple rheumatological faces of PsA (or PsA is more than just poly-arthritis? – Consequences for management in daily practice)

SP0142
CASE 1 PRESENTER: A PATIENT WITH PERSISTING MONO/OLIGO-ARTHRITIS (ETHER AT START OR REMAINING AFTER TREATMENT OF POLY-ARTICULAR DISEASE)
William Tillett. Royal National Hospital for Rheumatic Diseases, Rheumatology, Bath, United Kingdom

Background: The varied clinical phenotypes of psoriatic arthritis present treat-ment challenges in clinical practice. The dominant phenotype represented in clini-cal trials is polyarthritis with little representation of oligoarticular or monoarticular disease.

Objectives: To review the phenotypes of psoriatic disease and treatment of resistant oligo/monoarthritis in the context of a clinical case.

Methods: Clinical case history

Conclusion: The clinical phenotype of articular disease in psoriatic arthritis can evolve over time. There is limited data to inform the treatment of resistant oligo/ monoarthritis


SP0143
CASE 1 DISCUSSANT: HOW IS TACKLING OLIGO-ARTICULAR DISEASE DIFFERENT FROM POLYARTHRITIS? CAN WE USE TRIAL RESULTS FROM POLY-ARTICULAR PSA IN A PATIENT WITH MONO/ OLIGO-ARTHRITIS?
Laura C Coates. University of Oxford, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, Oxford, United Kingdom

Background: Oligoarthritis is a well recognised phenotype in psoriatic arthritis (PsA) where less than 5 joints are involved with active arthritis. In cohort studies, the proportion of patients presenting with mono/oligoarthritis varies from 20-70% depending on the timeframe studied and duration of disease. However most studies of therapeutic agents in PsA have focused on polyarthritis disease. Although the majority of studies accept a minimum of 3 active joints for inclusion, the average tender and swollen joint counts are usually over 10 at baseline.

Objectives: To review data supporting treatment of psoriatic mono/oligoarthritis including comparisons of response rates in therapeutic trials in PsA and the differential performance of outcome measures in this subtypes of disease.

Results: When considering the applicability of RCT data to mono/oligoarthritis in PsA it is important to address the populations included in these studies. Nearly all large therapeutic studies exclude monoarthritis, and while some oligoarthritis patients are eligible for inclusion in most RCTs, the demographics of the population included suggest that this is a minority. Unfortunately most clinical trials have not reported the efficacy results separately for oligoarthritis and polyarthritis patients. The other key consideration is that the outcome measures used in the majority of trials are developed and validated on patients with polyarticular PsA. Thus assessing effectiveness of therapies may be limited in the oligoarthritis population as the response measures are less sensitive to change.

Conclusion: Although data from polyarticular RCT populations is often used to choose therapies in oligoarticular PsA, there is a real paucity of data to ensure that we are treating these patients optimally. Future research is needed to address the variable prognosis seen in mono/oligoarticular PsA, to ensure that appropriate outcome measures are used to test different therapies and to provide clear evidence on the efficacy of drugs in this important subtype of disease.

Disclosure of Interests: Laura C Coates Grant/research support from: AbbVie, Celgene, Lilly, Novartis and Pfizer, Consultant for: AbbVie, Amgen, BMS, Celgene, Galapagos, Gilead Sciences Inc., Janssen, Lilly, Novartis, Pfizer, Prothena Corp and UCB

SP0144
CASE 2: SOLITARY ENTHESIS AS A THERAPEUTIC CHALLENGE
Philipe Carron. Ghent University Hospital, Rheumatology, Gent, Belgium

The enthesis is a site crucial for mobility of the musculoskeletal system yet it is also commonly a target of inflammation, especially in spondyloarthritis. Because the enthesis is prone to high biomechanical forces, it has been hypothesized that biomechanical forces may be implicated in the onset of the enthesis and spondyloarthritis in general. However, treatment recommendations involve exercise ther-apy which at first glance appears to pose a paradox. Using a case, we will discuss the current knowledge on enthesitis, the link with mechanical stress and the impli-cations thereof in diagnosis and management of spondyloarthritis.

Disclosure of Interests: None declared

SP0145
CASE 2 DISCUSSANT: ENTHESIS AND THE CONCEPT OF MECHANICAL STRESS
Dirk Elewaut. Ghent University Hospital, Rheumatology, Ghent, Belgium Philippe Carron and Dirk Elewaut. VIB Inflammation Research Institute, Ghent University and Department of Rheumatology, Ghent University Hospital

The enthesis is a site crucial for mobility of the musculoskeletal system yet it is also commonly a target of inflammation, especially in spondyloarthritis. Because the enthesis is prone to high biomechanical forces, it has been hypothesized that biomechanical forces may be implicated in the onset of the enthesis and spondyloarthritis in general. However, treatment recommendations involve exercise ther-apy which at first glance appears to pose a paradox. Using a case, we will discuss the current knowledge on enthesitis, the link with mechanical stress and the impli-cations thereof in diagnosis and management of spondyloarthritis.

Disclosure of Interests: None declared

FRIDAY, 14 JUNE 2019
15:30:00 – 17:00:00
Cannabis for arthritis: hype or hope?

SP0146
BENEFITS OF CANNABIS TO YOUR JOINTS: HYPE OR HOPE?
Serge Perrot. France, France

Cannabis-based medicines have been approved for pain management in a num-ber of countries. However, there are uncertainties and controversies about their role and the appropriate use of these medicines for the management of chronic pain, particularly in musculoskeletal conditions. These ancient drugs are now being rediscovered and considered as modern analgesic approaches in the con-text of cannabis legalization in more and more countries. The fight for cannabis legalization is frequently confused with the search for new analgesics in a medical context. Furthermore, there is a confusion between herbal cannabis, medical can-nabis and cannabinoids. Therefore, it is important to differentiate products and
situations and look beyond prejudice and misconceptions, to discover whether there are pharmacological and clinical data to support the use of medical cannabis and cannabinoids in musculoskeletal conditions and arthritis. Aside from media and social discussions, we will try to answer to the current hot question for a clinician is ‘Is it possible to recommend medical cannabis as a new anagolic option in musculoskeletal conditions?’

Disclosure of Interests: None declared

SP0147

ETHICAL ISSUES IN MEDICAL CANNABIS USE
Steve Alexander. University of Nottingham, School of Life Sciences, Nottingham, United Kingdom

Background: The human history of Cannabis is chequered. We have evidence from the Ebers papyrus of ancient Egypt (1450 BCE) that ‘sh-hm-t’ was used as a medication for what appears to have been topical inflammatory issues. In the Atharva Veda (~1500 BCE), ‘bhang’ was considered one of the five sacred plants of India. The Old Testament refers to ‘kanah-bosm’ as a component of a ceremonial anointing oil. In the UK’s Elizabethan era, Cannabis, as hemp, was grown widely for fibre to make rope and sail for the Royal Navy. In Victorian times, WB O’Shaughnessy brought back from India to the UK the medicinal use of Cannabis preparations for its reputed analgesic, anti-emic, anti-inflammatory and anti-consulant properties. In the modern era, Cannabis is a Schedule 1 drug in many countries - a legal status defined as having high abuse potential with no currently accepted medical value.

Objectives: To consider the ethical issues associated with the use of Cannabis-derived preparations for medicinal purposes.

Conclusion: Cannabis is unique among the Schedule 1 list, because extracts from the plant are licensed medicines in different parts of the world. The two most widely-researched metabolites from the plant are Δ⁹-tetrahydrocannabinol and cannabidiol (THC and CBD). The clinical uses of nabiximols (THC:CBD 1:1, combined with other minor cannabinoids) and nabiximol (a synthetic THC analogue) for multiple sclerosis and aneurism, respectively, as well as cannabinol and dronabinol ((-)-trans-THC) for childhood intractable epilepsy and cachexia, respectively, identify that Cannabis-derived medicinal products have therapeutical value.

Cannabis or THC in acute administration has a remarkably low association with mortality, however, there are a number of potential issues in the use of Cannabis itself rather than the above-mentioned extracts/compounds. Long-term heavy use of Cannabis is associated with the risk of addiction in about 10% of individuals. Severe anxiety attacks and psychotic episodes have been linked to higher doses of THC, although this has not been systematically identified. Both THC and CBD have identified metabolic profiles which might influence the turnover of other drugs.

A major feature of the use of Cannabis itself is the variability observed. In part, this derives from the natural product nature of the plant and the associated variation in the metabolites between different parts of the plant, different plants, different methods of harvesting, storage as well as method, dose and frequency of administration, the subject’s prior exposure to Cannabis and the immediate environment context. Even with the well-controlled clinical trials, there has been identified a variability in plasma levels of the administered agents. In those countries where medicinal Cannabis is more freely available, there are also concerns about patient use of black market sources.

Disclosure of Interests: None declared

FRIDAY, 14 JUNE 2019
15:30 - 17:00

Reproductive issues in rheumatology

SP0148

DOES PREGNANCY REALLY AMELIORATE DISEASE ACTIVITY OF WOMEN WITH CHRONIC ARTHRITIS? OLD BELIEFS VS NEW PARADIGMS
Laura Andreoli. University of Brescia, Spedali Civili of Brescia, Department of Clinical and Experimental Sciences, Brescia, Italy

Rheumatoid arthritis (RA) and Spondyloarthritis (SpA) are chronic inflammatory diseases whose onset can occur during childhood or adolescence. Juvenile Idiopathic Arthritis (JIA) can be active still during adulthood. Therefore, the disease course during pregnancy has been a topic of interest over the decades [1]. The approach towards the management of pregnancy in the rheumatic diseases has greatly changed in the last 30 years, as it became evident that active maternal disease is associated with adverse pregnancy outcomes, such as miscarriage, pre-term birth, small-for-gestational age babies. A well-controlled maternal disease during pregnancy is associated with a better pregnancy outcome: the key-point is the treatment of maternal disease with drugs which are not harmful for the fetus. To achieve this "ideal setting" is of fundamental importance to perform a preconception counselling and to maintain a tailor the management of the patient according to the patient risk stratification [2].

Historically, pregnancy has been considered to have a beneficial effect upon RA, with around 90% of women improving and up to 75% going into remission, following drug flares in puerperium in about 80% [3]. Modern prospective and serial and objective evaluations of disease activity, revealed that the validated measures of disease activity reveal less impressive ameliorative effects of pregnancy on RA [4]. A recent systematic review of prospective studies, using serial and objective evaluations of inflammatory disease, reported that RA improves in 60% of patients through pregnancy and flares in 46.7% of cases after delivery [5].

What are the possible explanations for this shift in the course of RA during pregnancy over decades? 1) methodological issues are obviously present (different study design; different patient population in terms of disease subset, duration, and severity); 2) disease activity as a "self-reported outcome" vs of validated indices [6]; 3) change in treatment strategies over time: in the '80s women with RA were likely to be treated with steroids only and probably those women with active disease despite treatment were not able to carry out a pregnancy, therefore it is possible that only patients with mild disease forms of RA were observed during pregnancy. Conversely, the current wide therapeutic armamentarium to reach disease remission also in patients with aggressive forms of RA, therefore it is likely to observe disease flares (rather than amelioration) during pregnancy if the drug is stopped at conception. Interestingly, among 75 prospectively-followed RA pregnancies, in patients treated with tumor necrosis factors inhibitors before conception, the discontinuation of the TNFI early in pregnancy resulted in increased risk for disease flares during pregnancy [7]. On the other hand, if disease is well controlled with drugs which are maintained during pregnancy, then there is little room to detect any improvement during pregnancy. Spondyloarthropathies (SpA) is a heterogeneous group of diseases and limited data are available about the disease course of different subsets (axial SpA –axSpA and Psoriatic Arthritis –PsA-) during pregnancy. Recently, prospective data from the RInFLus registry showed that the majority of women with axSpA who had stable or low disease activity from preconception period to 1 year after delivery with a small increase in the second trimester [8]. Previous studies reported that axSpA tend to be stable or to get worse [9]. Only one small retrospective work showed that the majority of women with AS displayed a decrease in disease activity during pregnancy [10]. In a recent report of 61 pregnant women with axSpA prospectively followed the discontinuation of TNFI early in pregnancy was a risk factor for flare [7]. Regarding Pa, data are scarce. The only two prospective studies demonstrated improvement during pregnancy and deterioration in the postpartum period [11, 12]. Similarly to axSpA, discontinuation of TNF1 at conception is associated with an increased number of flares during pregnancy [13].

In general, it seems that the changes in management of chronic arthritis has determined a shift in paradigm in the disease course during pregnancy. The major determinant of this change has been the growing confidence in using immunosuppressive drugs during pregnancy and breastfeeding. The increasing evidence about the safety of the majority of anti-rheumatic drugs has been recognized by many national and international working groups under the umbrella of scientific societies which endorsed guidelines and points to consider about this topic [14, 15]. Regarding biologic agents (bDMARDs), they can differ in molecular structure; however, they are all big size proteins which cannot passively diffuse and reach the fetus during the first trimester of gestation. Based on this assumption, unintended pregnancies exposed to these drugs are not a problem. As the active transport of IgG immunoglobulins across the placenta becomes significant after week 16 of gestation, it is understood that these bDMARDs which are IgG monoclonal antibodies will be transferred to the fetus. It was demonstrated that the drug concentration of monoclonal antibodies was higher in the newborn as compared to the mother, as expected for any IgG. Therefore, it is recommended to stop bDMARDs (with different timing according to their structure) in the second trimester- early third trimester in order to minimize the exposure to the drug and avoid that the new born will be immunosuppressed because of the drug received from the mother [14, 15]. Among TNFI, certolizumab pegol (CTZ) does not have the Fc portion needed for transplacental passage and so no minimal drug was detectable in the blood of neonates whose mothers received the drug until delivery [16]. Regarding breastfeeding, it is possible to consider bDMARDs as a homogenous class. They are all large proteins, which are unlikely excreted into breastmilk due to their high molecular weight. But even if they were present in breastmilk, bDMARDs will be degraded in the newborn’s digestive tract with no chance for absorption (consider that bDMARDs are administered intravenously or subcutaneously, not orally). CTZ was shown to be absent in the breastmilk and breastfed babies did not show any particular adverse event [17]. The exposure to immunosuppressive drugs, especially to bDMARDs, during late pregnancy poses the question about the immune competence of the neonate and the approach towards vaccinations. Data from large administrative US databases showed that children exposed during the third trimester to TNFI did not have an
Assisted medical procreation includes all the techniques based on the manipulation of reproductive cells that will allow infertile couples to conceive a child. Main techniques are ovulation induction with or without intrauterine insemination, controlled ovarian stimulation and in vitro fertilization (IVF). Intrauterine insemination: sperm (from partner or donor) is inserted directly into woman’s cervix, or uterus at the time of ovulation. Controlled ovarian stimulation is aimed at stimulate ovarian to allow egg retrieval few hours later. Protocols usually include gonadotropin-releasing hormone agonists or antagonists associated with recombinant follicle-stimulating hormone (with few hours later). Protocols usually include gonadotropin-releasing hormone agonists or antagonists associated with recombinant follicle-stimulating hormone (with concomitant close ovarian monitoring). Controlled ovarian stimulation is generally followed by egg retrieval and then by IVF which is performed in the laboratory by putting into contact collected oocytes with sperm (partner or donor). Intracytoplasmic sperm injection (ICSI) is performed in case of inadequate quality of the partner’s sperm (oligospermia notably). One or 2 embryos are transferred in uterus 2/3 or 5 days later (or during the next cycle), while other good quality embryos are cryopreserved for later use. There is no difference in the rates of ongoing pregnancy between transfers of frozen or fresh embryos [1].

By definition, an IVF procedure is defined by the transvaginal egg retrieval: even if the X obtained embryos are implanted Y times, this is still counted as the same procedure. A retrospective study of 14,469 women undergoing IVF, found that the cumulative live birth rates by procedure steadily increased with the number of collected oocytes, reaching 70% when ≥25 oocytes had been retrieved [2]. Women with auto-immune diseases or inflammatory chronic rheumatisms may have infertility as in the general population or because of previous gonadotoxic treatment as cyclophosphamide. While artificial inseminations and oocyte or embryo donations can be considered equivalent to a natural conception in terms of risk, particular attention is needed during IVF in women with systemic lupus erythematosus (SLE), antiphospholipid syndrome (APS) and/or biology (APS) because of the increased level of estradiol after ovarian stimulation (risk of lupus flare and of thrombosis) [3].

Ovulation induction treatments with in vitro fertilization can be safely used in patients with SLE with stable/inactive disease [4]. Similarly, women with rheuma
toid arthritis or spondyloarthritides can underwent IVF safely. In case of APS or APL, an adaptation of the treatment is usually required, especially around the egg retrieval. Management of pregnancy (both treatment and monitoring) must be planned before IVF [4].

As for a normal pregnancy, pre-counselling is important to adapt the treatment (interruption of contraindicated drugs in pregnancy as mycophenolate mofetil or methotrexate before conception due to their potential teratogenicity or at the end of the second trimester for anti TNF agents) [4]. Some treatments, especially hydroxychloroquine in SLE, have to be maintained during all this period and during pregnancy. In women with APS or APL, prophylactic dose of low weight molecular heparin (LMWH) is recommended during the period of stimulation. In case of treatment with coumadine, switch for curative LMWH is needed. In both cases, short interruption is required for the oocyte puncture. Low dose of aspirin is added after the embryo implantation. Folic supplement is recommended, especially in cases of treatment with methotrexate of current treatment with sulfasalazine. Immunizations are also important. Given its potential to reduce the miscarriage rate, LT4 supplementation is recommended for infertile women with subclinical hypothyroidism or thyroid autoimmunity who are undergoing IVF [5].

Finally, a key role of inflammatory immune response has been shown in reproductive failures but a recent meta-analysis did not find any positive effect of immunotherapy (especially anti-TNF) in improving the live birth rate in women undergoing IVF treatment [6].

REFERENCES:

Disclosure of Interests: None declared

SP0150 THE IMPACT OF RHEUMATIC DISEASES AND ANTI-RHEUMATIC DRUGS ON MALE FERTILITY IN ADULT AND YOUNG PEOPLE
Monika Østensen, Sorlandet Hospital Kristiansand, Rheumatology, Kristiansand, Norway

Background: The chronic, systemic inflammation in rheumatic diseases can impair male fertility by direct effects on the gonads or by affecting the hypothala-
mic-pituitary-gonadal (HPG) axis resulting in hypogonadism. Impaired gonadal function is reflected by reduced sperm quality and sometimes lowered testoster-
one levels. Drugs may impair fertility by impairing spermatogenesis or interfere with the HPG axis.

Objectives: To summarize the knowledge on the impact of rheumatic disease and its therapy on fertility in adult and pediatric patients

Methods: Search of the literature

Results: No impairment of spermatogenesis has been shown for azathioprine, cyclosporine, and mycophenolate mofetil. Risk of permanent infertility is associ-
ated with cytotoxic drugs, particularly the alkylating agent cyclophosphamide. Effects of methotrexate (MTX) on male fertility are related to dose. There is no indi-
cation that low-dose MTX 5 – 25 mg/week impairs male fertility. Case reports of men with psoriasis treated with low-dose MTX have either found completely nor-
mal sperm quality or detected oligo- and azoospermia.

Cyclophosphamide (CYC) is administered to adult and pediatric patients with sys-
temic lupus erythematosus, other connective tissue disease and vasculitides. Gonadal damage by CYC is dose-dependent revealed by oligo- and azoospermia
as well as low testosterone, low inhibin B and elevated FSH levels. Cumulative doses of > 7.5 g/m² carry a high risk of permanent infertility in adults. In survivors of childhood cancer treated with CYC recovery of spermatogenesis was sometimes seen after many years. Sulfasalazine (SZ) can induce transient infertility with oligospermia, abnormal morphology of sperm cells and reduced sperm motility in about 40-86% of treated men. Plasma levels of steroids and gonadotropins remain normal during SZ therapy. Recovery of normal sperm quality is observed one to three months after discontinuation of SZ.

Studies comparing men treated with TNF inhibitors (TNFi) with disease-matched and/or healthy controls did not find impairment of sperm quality neither after short term or long-term treatment. Several studies found significantly better sperm quality in patients receiving long-term TNFi therapy than untreated disease matched controls.

Conclusion: Rheumatic disease has an impact on male fertility both by the disease process and by therapy. Most antirheumatic drugs have no negative effect on reproduction, however, treatment with cyclophosphamide increases the risk of infertility both in adults and pediatric patients. Increasing awareness about reproduction issues and infertility risk is needed among adult and pediatric rheumatologists. Clinicians should actively involve themselves in counseling their patients.

REFERENCES:

Disclosure of Interests: None declared

FRIDAY, 14 JUNE 2019
15:30:00 – 17:00:00
The future of therapeutic strategies

SP0151 MICROFABRICATION TECHNOLOGIES FOR CARTILAGE REPAIR
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Background: Cartilage trauma is a major risk factor for the development of post-traumatic osteoarthritis. Treatment options are limited, are ineffective in the long run or come with disadvantages. Hence unconventional new strategies need to be explored to address this problem.

Objectives: In this lecture, I will present three strategies that are currently explored in my lab and that rely on the integration of biology with micro- and nano-technologies to solve this problem.

Results and Methods: In a first strategy, we invested in the development of injectable and in situ gelating hydrogels that can be used as fillers of a cartilage defect stimulating its regeneration. We developed a panel of natural polymer (e.g. hyaluronic acid, dextran, heparin, gelatin, collagen) – tyramine conjugates which crosslink in a macromolecular network in an enzymatic reaction. The reaction is fast, can be tuned and using this method a wide variety of extracellular matrix mimics can be engineered. Moreover, the crosslinking reaction fixes the gel in the surrounding tissue through covalent bonding between tyramine residues in the hydrogel with lysine residues in extracellular matrix proteins, effectively acting as a glue. The hydrogel can be applied during an arthroscopic procedure. We tested the potential of the hydrogel to facilitate the repair of an acute focal cartilage defect in an equine chondral defect model and evaluated the repair process after 2 weeks, 3 months and 7 months. We compared the repair of a hydrogel-filled defect with the microfabrication procedure, a frequently used but largely ineffective procedure due to the formation of fibrous cartilage instead of hyaline cartilage. After two weeks massive cell ingrowth in the hydrogel was observed. This continued and after 3 months hydrogel treated defects resulted in near complete defect filling with predominantly hyaline cartilage and without noticeable reactions in the subchondral bone. This was in marked contrast to the defects treated with microfabrication, which showed a massive response in subchondral bone and the formation of fibrous tissue. The repair was consolidated after 7 months. Defect filling might be a viable solution for treatment of focal cartilage defects to prevent early onset, post-traumatic osteoarthritis.

In a second strategy, we use the same material platform for cell delivery in the joint. Co-injection of cells with the in situ gelating hydrogels might be beneficial in the repair of particularly large (osteochondral) defects. We have developed microfluidic-based systems for the encapsulation of 10-15 cells in microgels of approximately 100 µm or even at the single cell level in microgels with a diameter of 30 µm slightly larger than the cell itself. We postulated that encapsulation of Mesenchymal Stromal Cells (MSCs) could prolong the retention time in the joint after an intra-articular injection over “naked” MSCs and may, therefore, improve the therapeutic benefit of these cells. We tested this hypothesis in a rat model and indeed showed that, while “naked” near infrared labeled MSC rapidly disappeared from the injected joint, encapsulated cells remained present up to 4 months. We are currently exploring its potential to improve the therapeutic efficacy of the MSCs.

In a third strategy, we use the material platform in combination with cytokine neutralizing antibodies to generate easily injectable microgels that can sequester pro-inflammatory cytokines from the synovial fluid. Rather than using conventional antibodies, we rely on the variable domain of single chain, heavy chain-only antibodies, which can effectively neutralize cytokines in cell assays in vitro and are currently explored for its potential to neutralize cytokines in synovial fluid and after intra-articular injection.

Conclusion: In conclusion, the integration of biology with microfabrication technologies has the potential to generate the next generation of therapies for the treatment of cartilage defects and osteoarthritis.

Disclosure of Interests: None declared

SP0152 3D PRINTED DRUGS
Matthew Peake, Alder Hey Children’s Foundation NHS Trust, Paediatric Medicines Research Unit, Liverpool, United Kingdom

Background: With the advent of personalised medicine, the need for flexible dosing is increasingly important. Conventional pharmaceutical manufacturing processes can be constrained in their ability to offer flexible dosing options to meet patient need. This is particularly important in specific populations, for example children, where available formulations are frequently not age-appropriate and need to be modified to achieve an intended dose. 3D-printing of solid dosage forms offers a disruptive technology which enables solid dosage forms to be manufactured at flexible, precise doses meeting the needs of individual patients. This technology has relevance for manufacture of existing active pharmaceutical ingredients for a range of conditions including inflammatory diseases.

Objectives: To develop 3D-printed oral solid dosage forms of medicines which are age-appropriate for children and young people. To determine the acceptability of 3D-printed medicines to children and young people by conducting intervention studies of tablet administration.

Methods: Tablets containing a range of active pharmaceutical ingredients (API) were produced using two stages: (i) hot melt extrusion of a filament containing API and excipients; (ii) 3D printing of the filament using fused deposition modelling (FDM) to produce the desired shape in a layer-by-layer pattern. Acceptability of 3D-printed tablets to children and young people (CYP) aged 4-12 years was assessed by the swallowability and mouthfeel following administration of different size 3D-printed placebo tablets.

Results: Using hydrocortisone as an exemplar API, Tablets were successfully produced by the FDM 3D printing process. Thermal analysis indicated that HC remained stable below 160°C and the tablets had very high mechanical strength with friability of 0%. This illustrates the ability of the printer to produce a ready-to-use tablet without the need for a drying or finishing step. The disintegration took 9.2–14 min confirming immediate release properties. We administered for the first time globally an ingestible 3D-printed tablet to a child. CYP were able to swallow and ingest 3D-printed bi-convex tablets of either 6mm, 8mm or 10mm diameter. The 3D tablets were reported by CYP to have a slightly more discernible mouthfeel than placebo tablets of the same size manufactured in a GMP facility.

Conclusion: FDM 3D printing offers a disruptive technology for the manufacture of solid dosage forms of medicines of flexible doses with excellent dose precision and pharmaceutical properties. In circumstances where modification of existing dosage forms is hydrogel based, this offers an alternative reliable means of achieving the intended dose. This technology is also suited to the manufacture of solid dosage forms of small molecules which may be particularly important in the treatment of inflammatory diseases.

Disclosure of Interests: None declared
Calming the cytokine storm in children and adults

Jan van Laar, Erasmus MC, University Medical Center Rotterdam, Internal Medicine, Division of Clinical Immunology, Netherlands

Background: Hemophagocytic lymphohistiocytosis (HLH) is a rare and often overlooked clinical manifestation of an aberrant hyperinflammatory immune response leading to a fatal cytokine storm(1). Diagnostic criteria according to The HLH Study Group of the Histiocyte Society include fever, splenomegaly, bicytopenia, hypertriglyceridemia and/or hypofibrinogenemia, hyperferritinemia, low/absent NK activity, increased soluble CD-25 levels and hemophagocytosis(2). Prompt recognition and differentiation from severe sepsis is essential to improve the outcome. HLH reflects a disbalanced immune system in response to infectious, malignancy, or autoinflammatory/autoimmune mediated triggers(1). The latter group of patients are regarded as having Macrophage Activation Syndrome (MAS-HLH)(4). In adults MAS-HLH comprises 12.5% of all HLH causing triggers(4).

The most frequent immunological disorders associated with adult HLH-MAS are systemic lupus erythematosus and adult onset Still’s disease, but every other immunological disorder can be involved(4,5).

Treatment: Treatment of adults HLH patients requires swift recognition and an experienced team of specialists that are acquainted with the critical factors influencing the balance between co-morbidity, cytokine storm induced septic-like symptoms and toxicity of chemo-immunotherapy(6). In general, adult patients do not tolerate doses of etoposide that are given in HLH-94 based chemo-immuno-therapy schedules that have been shown effective in children(7,8). Dose and frequency modifications of etoposide may avoid prolonged neutropenia, infectious complications or hepatic toxicity. The same precautions account for adults patients with MAS-HLH in which treatment differs from the HLH schedules. A step-down approach depending on clinical features and severity is warranted(9, 10). High doses of corticosteroids are recognized as first-line treatment(9, 10). In patients with MAS-HLH and SLE steroids, cyclophosphamide or etoposide are given(10). Cyclosporine can be added in patients with insufficient immediate response(9).

The cytokine blocking agent anakinra (anti-IL-1B) given in high doses is emerging as an alternative or additional treatment of adult MAS-HLH(11, 12, 13). Another promising cytokine blocker is anti-IL-6 (tocilizumab). Etoposide at a reduced dose can be initiated in patients with severe non-responsive and active disease or CNS-involvement(10).

Conclusion: Awareness of the clinical emergency MAS-HLH in patients with autoinflammatory/autoimmune mediated disorders is essential for timely recognition and potential life-saving treatment. The management of MASH-HLH in adults requires a team of dedicated specialists with experience in the treatment of critically ill patients with immunological disorders and anticipation on its rapidly changing and deteriorating nature.

REFERENCES:


Disclosure of Interests: None declared

Know your methods! Interactive discussion

Romualdo Ramos, University Medical Center Utrecht, Netherlands

Qualitative research plays a pivotal role in clinical practice by providing insights from the patient’s perspective. This becomes all the more relevant, as we move into the era of patient-centered care. In this presentation, we shed light on the different approaches to quantitative data collection and analysis, as well as systematic literature reviews of qualitative research. We will also elaborate on how qualitative research methods are used to better understand which outcomes are relevant to patients, self-management of symptoms, non-adherence to medication and non-pharmacological methods, the doctor-patient relationship, and to evaluate policy and interventions within the realm of RMDs. Finally, in an open panel, we will discuss how qualitative and quantitative methods triangulate, contributing to mixed methods approaches.

Disclosure of Interests: None declared


Disclosure of Interests: None declared
MISSING DATA: IS IT ALL THE SAME?

Sven Lydersen, Norwegian University of Science and Technology, Department of mental health, Trondheim, Norway

Introduction: In most studies, there are “holes” in the data set, such that data are missing partly or completely for some of the subjects. This results in reduced statistical power. More seriously, missing data may cause biased results, since data are usually not missing completely at random.

Missing data mechanisms: In which way, and to what extent, does the probability that data are missing, depend on observed and/or unobserved data values? This is called the missing data mechanism, and is important for an appropriate choice of analysis method. Three types of missing data mechanisms have been defined, see for example (Sterne et al. 2009).

MCAR: Missing completely at random. There are no systematic differences between the missing values and the observed values. The probability that values are missing does not depend on any of the data, observed or unobserved.

MAR: Missing at random. The probability that values are missing may depend on observed data values, but not on unobserved data values. For example, some variables are missing more frequently for patients with higher age. Data are missing at random conditionally on observed data.

MNAR: Missing not at random.

Even after the observed data are taken into account, systematic differences remain between the missing values and the observed values: The probability that values are missing depends on unobserved data values as well.

It is possible to distinguish between MCAR and MAR by inspecting the data at hand. But it is never possible to determine whether data are MNAR from your data.

Methods for handling missing data

Some commonly used methods, from the less to the more complex ones, are listed below, with an indication of when they give unbiased estimates:

- Complete case analysis (disregarding cases with partially missing data) (MCAR)
- Single imputation methods (sometimes under MAR but underestimates uncertainty)
- Multiple imputation (MAR)
- Full information maximum likelihood (MAR)
- Linear mixed models in longitudinal studies (MAR)

In longitudinal studies, Last observation carried forward (LOCF) is a simple method for imputing missing values. But it is not unbiased under any sensible assumptions, and should not be used (Lydersen 2019).

Reporting: In general, report the amount of missing data in the different variables, and how this was handled in the analysis. This is recommended in the Consort Guidelines (Moher et al. 2010) as well as the STROBE Statement (STROBE 2014), see also (Lydersen 2015)

REFERENCES:

Disclosure of Interests: None declared

DOUGADOS Maxime.

The recently proposed sophisticated statistical methods to impute missing data are very attractive. For the clinical researchers in charge of data collection, it might be tempting to “neglect” the quality of data collection in favor of the time spent by one database manager/statistician to impute missing data. This presentation will be a plea in favor to make all the possible efforts to collect appropriately the data in clinical research studies/trials. In particular, emphasis will be placed on the importance of writing a specific section in any research protocol describing the technics used to avoid these missing data and also the a priori decided technic that will be used to manage the missing data. One point of importance in this section: to specify in advance the maximum percentage of missing data over which no imputation can be made.

Two different situations:
- Cross-sectional studies. Any item (for example HLA B27, MRI SIJ inflammation positivity) should be considered as mandatory or not before running the study.
- Longitudinal studies: any longitudinal protocol should include a section detailing the technic to appropriately follow the patients in order to avoid the “lost of follow-up patients”. This is particularly important in longitudinal follow-up of patients suffering from a recent onset disease (e.g. early synovitis cohorts, early inflammatory back pain cohorts) since it is well known that the “lost of follow-up” have specific baseline characteristics suggesting a less severe disease. It is also important to decrease at a minimum level the “lost of follow-up” patients participating at a therapeutical trial/registry since the reason of “lost of follow-up” might be related to a specific drug-effect.

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FRIDAY, 14 JUNE 2019
15:30:00 – 17:00:00

Don’t panic – round table discussion on risk perception

SP0159 WHAT DO WE KNOW – WHAT SHALL WE DO – WHAT DO WE TELL

Timothy R. Radstake, University Medical Center Utrecht, Netherlands

There is an increasing need for patients to be involved in research as well as matters that can influence their own clinical journey. One aspect of science that links optimal clinical care is the increased use of biomarkers for so-called personalized medicine approaches.
In my presentation I will showcase the State of the Art technologies of biomarker research and how the information that comes from this can be implemented for improving clinical care. I will discuss the revolution of molecular profiling and how the large amount of data coming from these approaches is used to molecularly classify patients into molecular fingerprints. How this technology leads to a disruptive change in medicine for the coming 5-10 years. I will close of with the role of biomarkers in the treatment of diseases, trial design and drug development for the coming 5 years.

Disclosure of Interests: None declared

DISEASE REMISSION: DO WE AIM FOR THE SAME THING?

Ricardo Ferreira. Centro Hospitalar e Universitário de Coimbra, EPE, Rheumatology, Coimbra, Portugal

It is consensually accepted that the most important therapeutic goals for treating rheumatoid arthritis (as well as other inflammatory arthritis) are eliminating signs and symptoms (such as joint pain, swelling, and stiffness); preventing joint damage or its progression; and maximizing physical function and quality of life (Aletha & Smolen, 2019). According to current medical knowledge, these aims are believed to be best accomplished by achieving disease remission, a state in which no or only minimal residual inflammation is discernible (Aletha & Smolen, 2019). However, different studies have been providing evidence that achieving inflammatory remission is not enough as a considerable proportion of patients with no or minimal inflammation remain with high levels of pain, fatigue, functional impairment, mental health problems, among other symptoms (Boone et al., 2019; Ferreira et al., 2019; Ferreira et al., 2017). The perfect path to achieve good results is still to be defined, namely, regarding the T2T strategy (van Vollenhoven, 2019). Recent studies still show that despite a high level of patient agreement with RA T2T, patient engagement in this process needs to be improved in order to individualize therapy adjustments, make shared decisions and decide on targets that accurately reflect disease control according to patients (Benham et al., 2019).

In this session I would address the following questions:

- Is aiming for one target enough nowadays?
- Do health professionals and patients aim for the same thing when defining treatment strategies?
- Do the current treatment targets pose a risk of overtreatment with immunosuppressive therapy?

This presentation is informed by current research in this area including research from our own group (Ferreira et al., 2018; Santos et al., 2018).

REFERENCES:


Disclosure of Interests: None declared

LOOKING FOR A NEEDLE IN A HAYSTACK: HELPING YOUNG PEOPLE TO MAKE SENSE OF EVIDENCE BASED HEALTH CARE

Simon Stones. University of Leeds, School of Healthcare, Leeds, United Kingdom

While it has been suggested that there are no differences in the occurrence of risk-taking behaviours in young people with chronic conditions compared with healthy peers, young people with chronic conditions often face the dilemma of balancing twice the amount of risk to that of other young people, owing to their condition and treatment. For example, young people with juvenile idiopathic arthritis taking methotrexate face the risks of alcohol consumption plus the increased risk of toxicity from consuming alcohol while taking methotrexate. However, such issues are often ignored or overlooked (1). Research has suggested that a lack of experience with, and not worrying about serious health consequences may desensitise young people with chronic conditions to potential health risks (2). It is also recognised that young people’s perceived focus of health and wellbeing can often be on short-term goals; which is often paradoxical to the focus of families and healthcare professionals thinking about longer-term outcomes and prognosis.

It has been demonstrated that young people with chronic conditions value interventions that enable them to live a “normal” life – extending beyond the clinical management of their condition (3). The emotional, social, and vocational consequences of condition management can be profound (4). When this is coupled with the challenges of accessing accurate, trusted and individualised information and support, it can often leave young people and their families feeling as though they are looking for a “needle in a haystack”. Finding the best evidence requires knowledge of the best quality and most appropriate sources, as well as the ability to use and navigate such resources appropriately (5). In an era where health information is easier and faster to find than ever before, it is often a challenge for young people to be able to filter the ‘good’ from the ‘not so good’. There are significant amounts of unreliable and irrelevant content on the internet, which ultimately places the responsibility for interpretation of information and advice onto young people and their families.

Therefore, age- and developmentally- appropriate opportunities to discuss health, wellbeing and the effects of treatment need to be provided early and regularly, across the lifespan, in multiple formats to suit individual needs and circumstances. Attempts have already been made to make health information more accessible, for example, with the introduction of the Accessible Information Standard within the National Health Service (6). However, this is not necessarily enough to engage and support young people with chronic conditions in making sense of evidence-based healthcare. Information needs to be taken, in the right formats, to where young people are interacting, such as on certain social media platforms. This needs to be multifaceted, using peer- and community-driven approaches to enhance engagement. Furthermore, periodic consideration of the long-term risks and benefits of health and wellbeing interventions needs to happen across the life-course, both as a prompt for young people to air their concerns, but to also check their understanding. Only through understanding young people’s values, preferences, and concerns can a sustainable balance between condition control, treatment burden and quality of life be achieved.

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Remission – the holy grail? Looking across diseases

**SP0162 REMISSION IN RA: DOES THE DEFINITION MATTER?**
Daniel Aletaha, Medical University of Vienna, Department of Medicine III, Division of Rheumatology, Austria

Remission is the ultimate target for chronic inflammatory rheumatic disease, and so also for rheumatoid arthritis (RA). In this presentation, we will review the challenges in defining and assessing remission. Further, we will discuss if remission should be a clinical target, or whether imaging results, e.g. from ultrasound or MRI examinations, should be included in the concept of remission. Many symptoms in patients with RA may mimic RA disease activity, while they are not directly a consequence of the disease process, with secondary pain syndromes being a typical example. Finally, patients are the most important stakeholders on the question of whether or not a musculoskeletal disease is in remission. Patient reported outcomes have been criticized for their subjectivity and their role in remission indices has been questioned. We will also explore the influence and Pro’s and Con’s of these measures on remission assessment.

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**SP0163 REMISSION IN SLE: WHAT TO AIM FOR?**
Marta Mosca, Rheumatology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy

It is generally acknowledged that, in SLE, disease activity is associated with poor prognosis, high glucocorticoid use, damage development and increased mortality; therefore reaching low level of disease activity or remission are main treatment targets for SLE.

Definitions for disease remission and low disease activity are being proposed and validated as meaningful targets to be pursued in SLE management. In detail an international task force has recently developed a definition of remission in SLE (DORIS) taking in consideration four different domains: clinical activity, serological activity, treatment and duration. This approach led to the development of different levels of remission i.e. clinical remission off/on treatment and complete remission off/on treatment. Recently data from different cohorts have been published, showing that remission is an achievable target in SLE. Achieving remission appears associated with reduced damage accrual, however persistence in remission is rare being maintained in an average of 7% of patients over 5 years. In addition, the more stringent is the definition, the more difficult is to achieve remission and a longer time to remission is observed in patients with high activity, high therapy, hematological activity, African-American ethnicity.

Low disease activity may represent another target in SLE treatment and a definition of (lupus low disease activity state (LLDAS) has been developed by Franklyn et al. LLDAS is defined based on three domains which are SLEDAI-2k, 4. physician global assessment (PGA) 1. absence of new manifestations and stable and well tolerated treatment with a prednisolone (or equivalent) dose of 7.5 mg/day.

Interestingly, LLDAS is achieved by a high percentage of patients over follow up, ranging between 33 and 86% in different cohorts and it is maintained over follow up in up to 50% of patients for 50% of follow up time. Predictive factors for LLDAS attainment are shorter disease duration, lower disease activity score, lower mean PGA, lower mean SLEDAI, older age; while persistent LLDAS is less frequent in patients with vasculitis, neurological, renal, cardiopulmonary and mucocutaneous manifestations.

Achievement and persistence of LLDAS are associated with lower prednisone dose during follow up, reduction of disease flares, lower damage accrual, better quality of life.

In conclusion, definitions of remission and low disease activity in SLE have been proposed and validated against outcomes such as glucocorticoids usage, damage accrual, quality of life. Both targets are associated with improved outcomes, however at present persistence in remission is not common. The achievement of LLDAS is not rare, persistence in LLDAS is achievable.

**REFERENCES:**

**Disclosure of Interests:** Marta Mosca Paid instructor for: GlaxoSmithKline, Lilly, UCB

**DOI:** 10.1136/annrheumdis-2019-eular.8543

**FRIDAY, 14 JUNE 2019**
15:30:00 – 17:00:00

Laboratory course – from the clinic to the lab and back (from translation to prescription)

**SP0164 ANA DIAGNOSTIC AND ANTIPHOSPHOLIPID SYNDROME (APS) AS INHERITED COAGULATION DISORDER**
Thomas Dömer, Chaitte Berlin, Berlin, Germany

Use of ANA diagnostic is key for systemic autoimmune diseases. ANA is an overarching term and the underlying specificities are important for defined diagnosis of SLE, Sjögren’s, systemic sclerosis etc. Diagnostic algorithms of ANA and new semi-automated procedures are discussed in the context of case discussions. Subsequently, the value and limitations of the diagnostics of lupus anticoagulant and antiphospholipid antibodies as key serologic findings in antiphospholipid syndrome are discussed in the context of instructive cases.

**Disclosure of Interests:** Thomas Dömer Grant/research support from: Eli Lilly, Janssen, Roche, UCB Pharma, Consultant for: Eli Lilly, Janssen, Roche, UCB Pharma, Speakers bureau: Eli Lilly, Janssen

**DOI:** 10.1136/annrheumdis-2019-eular.8462
Ultrasound advanced II

SP0166  ULTRASOUND OF THE HAMSTRING MUSCLE COMPLEX-CLINICAL APPLICATION + DEMO

David Andrew Bong, Instituto Poal de Reumatologia, Universitat de Barcelona, Rheumatology, Anatomy, Barcelona, Spain

The hamstring muscle complex (HMC) are the "brakes" of human bipedal ambulation and are susceptible to injury during concentric contraction. Although common in sports medicine practice, a recent systematic review of severe hamstring injuries (grade II-III) suggests that greater than 10% of these severe injuries are non-injuries related and disproportionately affect older women. Musculoskeletal ultrasound (MSKUS) is one of the basic imaging techniques utilized to detect and define these injuries and eliminate other potential causes of posterior thigh pain. This presentation will discuss the clinical application of MSKUS of the HMC in rheumatology/musculoskeletal medicine and offer a systematic anatomically-based method of examining this important non-articular region.

Disclosure of Interests: None declared

FRIDAY, 14 JUNE 2019
15:30:00 – 17:00:00

US FOR ASSESSING LUNG INVOLVEMENT IN RHEUMATIC DISEASES – CLINICAL USE + DEMO

SP0167  US FOR ASSESSING LUNG INVOLVEMENT IN RHEUMATIC DISEASES – CLINICAL USE + DEMO

Andrea Delle Sedie, University of Pisa, Rheumatology Unit, Pisa, Italy

Background: Evaluation of interstitial lung disease (ILD) is always difficult due to poor correlation of X-ray and pulmonary function tests. HRCT: ultrasound (US) has recently shown interesting results on truth, discrimination and feasibility. Due to the thickening of interlobular septa for edema or fibrosis, US beam can interact with those structure and produce artifacts on the screen.

B-lines (BL) and pleural line irregularity (PLI). A positive correlation between BL and HRCT has been established both in systemic sclerosis patients and in other patients with ILD; more recently similar results have been published by using PLI as a finding for US assessment in patients.

Conclusion: US lung evaluation is a useful and feasible imaging technique.

Disclosure of Interests: Andrea Delle Sedie Speakers bureau: Abbvie, UCB, Celgene, MSD

FRIDAY, 14 JUNE 2019
17:30:00 – 19:00:00

Complement and autoimmunity – emerging therapeutic opportunities

SP0169  COMPLEMENT AND LUPUS IN THE YOUNG AND THE OLD

Marina Botto, Imperial College London, Centre for Inflammatory Disease/Immunology and Inflammation, London, United Kingdom

Complement component C1q is known to play an important recognition role in adaptive and innate immunity. More recently evidence has emerged that C1q may have roles outside the complement system and the relevance of these functions may change with ageing. Homozygous deficiency of the first component of the complement system, C1q, is one of the most powerful susceptibility genetic factors for the development of systemic lupus erythematosus (SLE). The vast majority of patients with C1q deficiency develop a syndrome closely related to SLE. The disease is typically of early onset and is often very severe. Although the phenotype of disease varies between patients, the fact that C1q deficiency is sufficient to cause SLE in almost all humans identifies a pivotal role for this molecule. The challenge is to identify the relevant physiological activity that can explain this strong association.

On the other hand, C1q seems to play a different role in old people. The concentration of C1q rises with ageing and can be modulated by exercises. Of note, increased levels of C1q have been reported in the central nervous system of old people, with the highest levels being seen in close proximity to synapses and central regions of the brains suggesting that C1q may play a role in the development of problems associated with aging. Consistent with this hypothesis aged C1q-deficient mice showed less cognitive and memory decline in hippocampus-dependent behaviour tests compared to their wild-type litter mates.

In summary, the traditional view of the role of C1q as just initiator of the classical complement pathway needs revision. Evidence is emerging that C1q has roles outside the complement system and these will be discussed.

Disclosure of Interests: None declared

IS COMPLEMENT A CRITICAL INGREDIENT IN THE DEVELOPMENT OF RA?

SP0170  IS COMPLEMENT A CRITICAL INGREDIENT IN THE DEVELOPMENT OF RA?

V. Michael Holers, University of Colorado Denver, Rheumatology, Aurora, CO, United States of America

Background: Prior studies of patients with classified rheumatoid arthritis (RA) have demonstrated in synovial fluid, on cartilage surfaces and in the synovium the presence of pro-inflammatory complement activation fragments C3a and C5a, the membrane attack complex (MAC), and C3 fragment-bound immune complexes.

Ex vivo studies of RA-related autoantibodies have shown the capacity to activate complement pathways, and also demonstrated the presence of disease-
associated changes in antibody glycosylation that promote engagement of the complement system. In contrast, clinical trials in patients with classified RA utilizing inhibitors of complement C5 have demonstrated minimal improvement. Nevertheless, recent translational research studies of patients during the natural history of RA have opened up new avenues for therapeutic intervention. Specifically, there exists in seropositive RA a prolonged asymptomatic preclinical stage wherein mucosal autoantibody production in the lung is associated with NETosis, elevated cytokines and evidence of activated innate immunity, with the capacity of each to interact and promote localized inflammation. Beyond this, murine studies have strongly suggested that complement C3d generation promotes autimmune and therapeutic pathway inhibitory strategies should encompass all of the effector mechanisms and not just those at C5 and beyond.

Objectives: The presentation objective is to explore the evidence for involvement of the complement system in the preclinical development of RA, and what mechanisms may be involved to promote autoimmunity and ultimate joint damage.

Methods: The presentation will review studies of the natural history of human RA, with an emphasis on the potential roles for complement in multiple stages of disease. In addition, the presentation will review informative murine studies which have explored the mechanisms by which the complement system can modulate the development of experimental autoimmune arthritis will be summarized.

Results: Studies of preclinical RA in subjects have suggested the potential for complement and NETs to interact and promote seromucosal inflammation in the lung. In addition, murine studies of the roles of complement have supported that all components of the pathway, including C3d linked to antigens, the anaphylatoxins C5a and C3a, as well as the MAC, are centrally involved in promoting arthritis.

Conclusion: Complement likely plays a role in multiple phases of RA development, including: 1) mucosal inflammation and the break in systemic tolerance to citrullinated antigens, 2) initial inflammation following targeting of ACPA to the synovium and 3) activation of RA-related autoantibody production. In addition, it is likely that inhibition of C3 and C5 convertases in tandem will be necessary to see major clinical effects in patients with active synovitis. Finally, the use of a complement inhibitor or modulator in the pre-clinical, transitioning and/or early RA populations are all intriguing approaches.

REFERENCE:


SP0171 THE NEW COMPLEMENT THERAPEUTICS
Claire Harris, Newcastle University, School of Medicine, Newcastle-upon-Tyne, United Kingdom

Despite a wealth of knowledge in the complexities of the complement cascade, and many decades of endeavour, very few drugs have progressed to the clinic. Recently, strong genetic associations of complement with common diseases have emerged and fuelled the fire of complement drug discovery leading to an explosion in complement therapies in development; while many of these agents and others before them have failed to progress, their legacy is key to future success. Obstacles to successful drug development include target concentration and turnover rates, and ability to target to the appropriate site. The drug development landscape is littered with agents that have failed at the preclinical or early clinical stage; their modes of action and modalities are wide-ranging. It is becoming clear that engagement of complement C3 and C5 convertases in tandem will be necessary to see major clinical effects in patients with active synovitis. Finally, the use of a complement inhibitor or modulator in the pre-clinical, transitioning and/or early RA populations are all intriguing approaches.


SP0172 CASE 2 PRESENTER: ALWAYS AT THE EDGE: SEVERE GI COMPLICATIONS
Kristina Clark, University College London, Centre for Rheumatology and Connective Tissue Diseases, London, United Kingdom

Gastrointestinal tract involvement is almost universal in systemic sclerosis but in most patients is relatively mild with symptoms of gastro-oesophageal dysmotility and reflux or lower bowel symptoms of constipation. A minority of cases have severe involvement, and this can be life-threatening. The key issues related to severe disease are attacks of pseudo-obstruction with complications such as pneumonia, or perforation of infection. Additional issues include malnutrition and intestinal failure that may require long-term home parenteral supplementation. Finally, the most severe lower tract involvement can result in intractable diarrhoea, persistent anorectal incompetence and complications of severe chronic constipation such as sigmoid volvulus. Management is challenging and requires interaction with gastroenterology and nutrition expert colleagues. Some newer approaches that have been beneficial include long term intravenous immunoglobulin therapy although in general response to immunosuppression are relatively modest. This discussion will focus on treatment with immunomodulation and use of antibiotic therapy to treat small intestinal bacterial overgrowth and also to manage other infectious problems and the potential impact on intestinal dysbiosis.

Disclosure of Interests: Christopher Denton Grant/research support from: GlaxoSmithKline, Inventiva, CSF Behring, Consultant for: Roche Genetech, Actelion, GlaxoSmithKline, Sanofi Aventis, Inventiva, CSL Behring, Boehringer Ingelheim, Bayer DOI: 10.1136/annrheumdis-2019-eular.8459

SP0173 CASE 2 DISCUSSANT: IMMUNOSUPPRESSION OR ANTIBIOTICS – WHEN TO CHOOSE WHAT?
Christopher Denton, Royal Free Campus, x, x, United Kingdom

The clinical impact of lower gastrointestinal tract involvement in systemic sclerosis will be illustrated through a case presentation. This will describe the challenges of managing patients with systemic sclerosis presenting with pseudo-obstruction, severe malnutrition, and electrolyte imbalance and how these were managed to optimise patient care.


SP0174 ADVANCES IN THE DETECTION OF PATHOGENIC AUTOANTIBODIES IN SLE
Luis Munoz, Friedrich-Alexander-University Erlangen-Nürnberg (FAU), Internal Medicine 3, Erlangen, Germany

Background: The accumulation of late apoptotic or so-called Secondary Necrotic Cells (SNEC) in germinal centers challenges B and T cell tolerance and leads to the development of autoimmunity and the production of autoantibodies.

Objectives: Determine the test performance of immobilized SNEC autoantigens for the diagnosis of Systemic Lupus Erythematosus.

Methods: SNEC ELISA of sera from patients with SLE and test performance statistics were deployed to evaluate the diagnostic potential SNEC-derived autoantibodies. Functional assays confirmed its pathophysiological relevance.

Results: SNEC contains nuclear autoantigens bearing apoptosis-associated modifications such as histone H3 and histone H4AcK8,12,16, and histone H2B-AcK12. The SNEC ELISA clearly discriminated patients with SLE from patients with Rheumatoid Arthritis (RA), Primary Anti-Phospholipid Syndrome (PAPS), Spondyloarthropathy (SpA), Psoriatic Arthritis (PsA), and Systemic Sclerosis (SSc). A positive test result in SNEC ELISA significantly correlated with...
serological variables and reflected the uptake of opsonized SNEC by neutrophils in the blood.

**Conclusion:** SNEC ELISA allows for the sensitive detection of pathologically relevant autoantibodies in the serum of patients with SLE. The clearance of nuclear remnants by neutrophils enhances inflammatory responses supporting the role of clearance deficiency in the etiopathogenesis of SLE.

**REFERENCE:**


**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.8544

**SP0175 POST-TRANSLATIONAL MODIFICATIONS OF ANTIBODIES: WHERE THERE’S SMOKE THERE’S FIRE**

Rene Toes, Leiden University Medical Center, Rheumatology, Leiden, Netherlands

Rheumatoid arthritis (RA) is a prototype autoimmune disease, with the hallmark signs of synovial inflammation and the presence of autoantibodies. One of the most prominent examples of such autoantibodies are anti-citrullinated protein antibodies (ACPA), which are directed against a wide-array of citrullinated proteins. The immune response to citrullinated antigens is a dynamic response that expands before the onset of disease and generates antibodies that are extensively glycosylated in the variable domain. This feature of ACPAs is remarkable and might be involved in the breach of tolerance to citrullinated proteins as well as function as an additional biomarker to predict disease onset in subjects at risk.

Next to ACPA, it has become clear that the autoantibody response in RA extends to other proteins. For example, antibodies against citrullinated beta2-glycoprotein I (anti-DI-beta2GPI) are also frequently present in triple aPL positive patients. Nevertheless, it is far too soon to recommend replacement of anti-DI-beta2GPI testing with an anti-DI-beta2GPI antibody assay because it was shown that about 30% of patients with anti-DI-beta2GPI antibodies are negative for anti-DI-beta2GPI antibodies (8). The clinical significance of autoantibodies reacting with epitopes other than DI was also investigated in multicenter study (9).

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.8603

**SP0176 PATHOGENIC ANTIBODIES IN PHOSPHOLIPID SYNDROM**

Sasa Curnik, University Medical Center Ljubljana, Department of Rheumatology, Immunology Laboratory, Ljubljana, Slovenia

Antiphospholipid syndrome (APS) is a thrombotic systemic autoimmune disorder characterized with multisystem manifestation, most commonly venous and arterial thromboembolism and/or recurrent pregnancy loss. The varying clinical phenotype is associated with heterogeneity in the pathogenic antiphospholipid antibodies (aPL). These antibodies may be useful as risk stratification for clinical events. aPS/PT antibodies also represent strong risk factor for thrombosis. Results of multicenter study demonstrated that IgG aPS/PT detection might contribute to a better and more reliable identification of APS patients (10).

Due to the heterogeneity of aPL (criteria and non-criteria) the interpretation of aPL results is a challenge in daily routine practice and should always be related to clinical symptoms and therefore, interaction between the laboratory and clinician is essential.

**REFERENCES:**


**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.8453

**SATURDAY, 15 JUNE 2019**

**09:00 – 10:30**

**Lessons learned from checkpoint inhibitors**

**SP0177 IMPACT OF CHECKPOINT INHIBITORS ON B CELLS**

**David Peatley,** Duke University Medical Center, Medicine/Immunology, Durham, North Carolina, United States of America

Immune checkpoint inhibitors (ICI) are a new class of biological agents that has revolutionized the treatment of cancer. Unlike conventional cytotoxic agents that
are designed to kill cells, ICI block interactions that regulate the T cell response to cancer. At present, two classes of ICI are available to treat a wide variety of malignancies: antibodies to cytotoxic T-lymphocyte-associated antigen 4 (CTLA-4) and antibodies directed to the programmed death-1 (PD-1) and PD-1 ligand (PD-L1) axis, either to PD-1 or PD-L1. While both anti-CTLA-4 and antibodies to PD-1/PD-L1 are effective, these systems differ in the T cell populations affected, the location of these cells and the downstream signaling pathways involved. ICI can be used alone or in combination. Despite differences in mechanism of action, treatment with both types of ICI is associated with severe side effects that have been termed immune-related adverse reactions (irAE). irAE include, among other manifestations, dermatitis, colitis, pneumonitis, endocrinopathy (hypothyroidism, hypophysitis, adrenal insufficiency) and arthritis and related conditions. Because of the goal of ICI therapy is the induction or stimulation of cytotoxic T cells, the effect of these agents on B cells has received much less attention. In general, effects of ICI on tumors are considered the action of T cells. irAE, however, may result from B cell effects and the induction of autoantibodies. Thus, autoantibodies to thyroid antigens may lead to thyroiditis and subsequent hypothyroidism. Similarly, ICI can lead to the production of antibodies to islet antigens as well as glutamic acid decarboxylase 65 and induction of diabetes. On the other hand, while arthritis can be an irAE, affected patients usually do not show antibodies to citrullinated proteins (ACPA). Importantly, functional and phenotypic properties of B cells following ICI can help predict the emergence of urticaria. Moreover, changes of these cells and from a detailed analysis of patients with melanoma treated with anti-CTLA-4, anti-PD-1 or the combination. With this combination, B cells of treated patients showed characteristic changes that include a decrease in the number of circulating B cells in conjunction with an increase in plasmablasts and a population of B cells characterized by low expression of CD21. Furthermore, in treated patients, the CD21lo B cell population showed greater clonality as well as a higher frequency of clones in comparison to the CD21hi population. These changes, which can resemble those seen in patients who have unresponsive for CTLA-4, may predict the development of irAE. The CD21lo B cell population may have a particular role in the development of irAE since these cells appear to be recent emigrants from germinal centers and may undergo rapid activation. The effects of ICI on B cell populations is also relevant for ICI use in the setting of pre-existent inflammatory or autoimmune disease marked by autoantibody production. While ICI, either alone or in combination, can lead to the exacerbation of these conditions, the effect on autoantibody production has not yet been well studied. These exacerbations, however, can respond to agents such as glucocorticoids or TNF blockers whose B cell effects are not clear. Since B cells can express PD-1 as well as PD-L1, the effects of ICI may direct actions or the indirect effects on other cell populations. Future studies are needed to delineate more precisely the contribution of B cells to the response of cancer to ICI as well as the development of irAE.

Disclosure of Interests: None declared


SATURDAY, 15 JUNE 2019
09:00:00 – 10:30:00

Orthotic treatment: is it in or out?

SP0179 ORTHOSES AND ASSISTIVE DEVICES FOR THE HAND
Nina Osteras, Diakonhjemmet Hospital, National Advisory Unit on Rehabilitation in Rheumatology, Oslo, Norway

This presentation will summarize the scientific evidence for the effects of orthoses and assistive devices for the hand. The main focus will be on hand osteoarthritis. The presentation will shed light on how orthoses and assistive devices may facilitate participation.

Disclosure of Interests: None declared


SP0180 FOOT ORTHOSES IN RA
Jim Woodburn, Glasgow Caledonian University, School of Health and Life Sciences, Glasgow, United Kingdom

In this presentation I will: (1) Provide a general overview of the indications and use of foot orthoses in rheumatoid arthritis (RA) 1, (2) Explore mechanisms of action with respect to preserving, maintaining and restoring foot biomechanics 2, (3) Summarise current evidence on the use of foot orthoses for managing foot pain, disability, deformity and quality of life by drawing on recently published systematic reviews and meta-analyses3. Further I will direct delegates to national, European and International evidence-based clinical guidelines where they exist1,4, and (4) Introduce new technology advances with regards to materials and digital design and manufacturing concepts2. I will conclude the presentation by setting out future directions and priorities for both clinical practice and research and innovation.

REFERENCES:
TREATMENT OF GCA

The treatment of giant cell arteritis (GCA) has taken a dramatic leap forward over the past 18 months, with the start of the era of interleukin-6 inhibition for the treatment of this disease. For the first time in 70 years, rheumatologists now have a highly-effective alternative to continuous therapy with doses of glucocorticoids that are often unacceptably high, leading inevitably to steroid-related toxicity. Clinicians now have many questions about the optimal approach to treatment in this new era: When should IL-6 inhibition begin? How quickly should glucocorticoids be tapered? Should prednisone be stopped completely? Can tocilizumab ever be discontinued? How does one monitor for the possibility of disease flare? This session will address all of these questions using a data-driven approach, with reference to new data from the GIACTA trial.

Disclosure of Interests: None declared

SP0181 TREATMENT OF GCA
John H. Stone, USA

TREATMENT OF AAV

Background: ANCA associated vasculitis is an autoimmune disease classified by clinical phenotype and serology. A genetic predisposition has been determined which differs between PR3-ANCA and MPO-ANCA patients. Experimental models have confirmed the pathogenicity of ANCA for certain aspects of pathology and have defined a role for alternative complement pathway activation but have failed to explain granuloma formation or gain insights into the origin of breakdown of tolerance. Therapy has emerged empirically to include the combination of high dose glucocorticoids and immunosuppression with B cell depletion, Rituximab, emerging as an alternative immunomodulator over the last 20 years. Studies have evaluated the role of Rituximab in induction, in refractory and relapsing disease and in the prevention of relapse and have explored the role of B biomarkers in monitoring therapy. AAV patients continue to suffer poor outcomes especially if renal, cardiac or gastrointestinal features are present at diagnosis. Adverse event rates remain high and the majority of patients pursue a relapsing course. Inhibition of the alternative complement component C5a is emerging as a new therapeutic opportunity.

Objectives: To define the outcomes and predictors for adverse outcomes in AAV. To review recent clinical trial data in the context of established guideline statements and to discuss the treatment of more complex clinical scenarios.

Methods: A description of current approaches to classification and subgrouping by severity. Review of recent clinical trial data and guidelines and application of learned knowledge to clinical scenarios.

Conclusion: AAV remains a disease with poor outcomes. There is a need for further understanding of the barriers to early diagnosis and access to specialist care. Treatment decisions are now well supported by evidence from clinical trials. Rituximab has had a major influence on current management strategies and is leading to improved outcomes and reduced glucocorticoid exposure. Complement inhibition is a potential new therapy for AAV.

REFERENCES:

Disclosure of Interests: Jayne Grant/research support from: David Jayne has received research grants from Chemocentryx, GSK, Roche/Genentech and Sanofi-Genezyme. He has received consultancy fees from Astra-Zeneca, Boehringer-Ingelhein, Chemocentryx, Chugai, GSK, Infla-RX, Insmed and Takeda

SP0182 TREATMENT OF AAV
David Jayne. University of Cambridge, Department of Medicine, Cambridge, United Kingdom

DIAGNOSIS AND TREATMENT OF HCV RELATED VASCULITIS

Peter Langer, University of Lubeck, Department of Rheumatology and Clinical Immunology, Lubeck, Germany

Chronic hepatitis C virus (HCV) infection is the most common cause of cryoglobulinarminic vasculitis. In contrast, non-cryoglobulinemic vasculitis is rare in chronic HCV infection. Cryoglobulinemic vasculitis is a systemic immune complex-mediated vasculitis predominantly affecting small vessels and associated with the presence of serum cryoglobulins, i.e. cold-precipitable immunoglobulins. HCV is a hepato- and lymphotropic virus. Notably, secondary transition from benign lymphoproliferative disease to malignant non-Hodgkin lymphoma (NHL) as well as primary co-manifestation of cryoglobulinemic vasculitis and NHL has been reported in chronic hepatitis C. While cryoglobulinemia is detected in 50%-60% of the patients with chronic hepatitis C, less than 5% develop related vasculitis. In this disorder, HCV induces clonal proliferation of memory phenotype marginal zone-like B-lymphocytes with restricted Ig heavy chain variable (VH) 1-69 gene expression encoding for the IgM rheumatoid factor (RF) WA idiotype. Monoclonal IgM RF binding to the Fc region of polyclonal IgG with anti-HCV reactivity facilitates the formation of cryoprecipitable multi-molecular immune-complexes. Cryoglobulins are preferentially deposited in tissues with high blood flow per unit mass of tissues; e.g. skin, synovium, choroid plexus and glomerulus, where they bind to endothelial cells via the C4q receptor.

Endothelial cryoglobulin deposition induces the activation and recruitment of circulating neutrophil granulocytes and other immune cells to the endothelial lesion eventually resulting in complement-consuming vasculitis. The histopathologic changes in HCV-related vasculitis range from cutaneous leukocytoclastic vasculitis to severe necrotizing arteritis. Type I membraneproteolytic granulonephritis is frequently found in patients with renal involvement. Clinical features of HCV-associated vasculitis comprise purpura, Meltzer’s triad (purpura, arthralgia, asthenia), polyneuropathy, renal involvement and Raynaud’s

Disclosure of Interests: Peter Langer has received support from the following companies: Lilly, Roche, MSD, Pfizer, MSD, AstraZeneca, Novartis, Genzyme, Boehringer-Ingelhein, Biocon, Mylan, Gilead, GSK and FMS.

SP0183 DIAGNOSIS AND TREATMENT OF HCV RELATED VASCULITIS
phenomenon. Hemorrhagic alveolitis, interstitial lung disease, gastrointestinal vasculitis, cardiac involvement, osteosclerosis and hyperviscosity syndrome are less common manifestations. Diagnostic criteria have been developed for HCV-associated cryoglobulinemic vasculitis.

International therapeutic guidelines recommend treatment of HCV-related vasculitis to be guided according to the severity of disease. In patients with mild to moderate disease, interferon-free therapy regimens with direct acting antivirals (DAA) are considered as first-line treatment. In patients with severe manifestations, rituximab is given for the control of vasculitic manifestations, followed by HCV eradication using DAA. High rates of clinical responses and sustained virologic responses (SVR) have been reported for DAA treatment in HCV-associated cryoglobulinemic vasculitis. However, relapse of cryoglobulinemic vasculitis may occur in patients despite earlier treatment-induced clinical response and SVR. Persistence of clonal B-lymphocyte proliferation and perseverance of perturbations of the immune homeostasis have been shown in HCV-cured patients with relapse of cryoglobulinemic vasculitis.

Disclosure of Interests: None declared

SATURDAY, 15 JUNE 2019
09:00:00 – 10:30:00
Workshop: #ConnectToday and tomorrow: the campaigning continues

SP0184 DON’T DELAY, CONNECT TODAY IN FINLAND: A VIDEO TO PROMOTE EARLY DIAGNOSIS

Maria Ekroth, Institute of Anatomy, Paracelsus Medical University, Imaging and Functional Musculoskeletal Research, Salzburg, Austria

Positive Encounter - Don’t Delay Connect Today

Background: Too often people suffer the symptoms of rheumatoid arthritis for too long before they visit a doctor. The positive encounter between physician and patient can lead to a good relationship, follow-up care and positive health outcomes. We conducted a survey about the need for a treatment plan and found that less than 30% of patients know their treatment plan and patients who do know their plan are better committed and more satisfied with their physicians. 72% of survey respondents who know their treatment plan are happy with their treatment as whole. Of the remainder, only 33% are satisfied.

Objectives:
1. The aim of this campaign is to illustrate and inform people of the symptoms of rheumatoid arthritis and encourage them to visit a doctor, enabling the doctor to assist the patient.
2. To give advice to patients on how to prepare for a doctor’s appointment.
3. The campaign also includes a section directed at rheumatologists and rheumatology nurses, that advises on the importance of the encounter and the creation of the treatment plan.
4. To increase awareness about our association, and to recruit new members

Methods: Video for patients and the wider public. Video for rheumatologists and rheumatism professionals. Mailing of brochures on the importance of the treatment plan to all Finnish rheumatologists and arthritis treatment units. We also thanked doctors and attached a fruit gift card. We sent flyers and posters to our member associations. Members have handed out materials directed at patients locally. They have distributed them to libraries, municipalities, sports centres . . . and given away fliers at the events.

Results: Patients have reported being better prepared for the visits and having written down important questions in advance. We achieved attention value amongst professionals and were invited to design a national treatment path with rheumatism professionals for children with JIA. All the main hospitals are involved and will start to use it. Free TV air time was offered for the patient video on the national main TV channel. The Finnish Society for Rheumatology offered us the possibility of promoting our campaign at the Scandinavian Congress of Rheumatology.

Conclusion: The campaign was successful.

REFERENCES:
[1] www.youtube.com/watch?v=Y2_z8cxDvaA

Disclosure of Interests: None declared
DON’T DELAY, CONNECT TODAY IN TWELVE VIDEO’S: HOW TO GET EARLY DIAGNOSIS OF RMD’S ON THE TABLE IN POLAND

Jolanta Grygielska, Polish Rheuma Federation ‘REF’, National Board, Warsaw, Poland

Background: Early diagnosis and appropriate treatment is a mile stone in future progress of rheumatic and musculoskeletal disease (RMD), especially inflammatory. We know from our experiences that delays of diagnosis are connected with knowledge and attitude of patient, of primary care physician (fast referral to rheumatologist) and with access to rheumatologist. New EUULAR campaign ‘Don’t delay, connect today’ gives an opportunity to pay attention to the problem of RMDs, increase public awareness and remind persons about responsibility for their health. Lack of knowledge about RMDs and faith in myths are a first step to loose a time from first symptoms of diseases to appropriate diagnosis. The first step was translation of EUULAR campaign slogan into Polish and preparing of Polish version of logo. It was done very fast after launching EUULAR campaign.

Objectives: Aim of our project was to increase public awareness about RMDs and self-awareness of patients, to present how important is a role of everybody being face to face with progressing disease. It was most important to reach to younger people believing that rheumatic diseases are typical only for older people. Lack of knowledge about RMDs and faith in myths are a first step to loose a time from first symptoms of diseases to appropriate diagnosis. The first step was translation of EUULAR campaign slogan into Polish and preparing of Polish version of logo. It was done very fast after launching EUULAR campaign.

Methods: We have many ideas which subject are more important for people around diagnosis. We decided to start with choice of subjects and connecting them with the first letter of Polish names of months. We tried to order them in logical process: from self-awareness to the sin of neglect though to greater knowledge and attitude of patients, of primary care physician (fast referral to rheumatologist), of rheumatologist, of society. Every invited speaker received only one subject and main message to present in his/her film. Form, place and comments were suggested by speaker and discussed with a team preparing videos. Part of films were supported by our regional member associations. Forms of videos prepared in regions were decided by associations. In two films members of associations present their opinions and experiences to give a strength for new rheumatic persons to live with RMD and avoid unnecessary health situations. One video was enriched by physical exercises presented by students of physiotherapy under supervise of rheumatologist. All videos were filmed and prepared by our member, translation was done by another our member - both are professionals on their fields and with experiences of living with RMD. It gives added value to our campaign. After that videos were posted on our channel on YouTube and information about them was shared by our websites, facebook and Twitter. We sent information by e-mail to our colleagues and supporters. We invite every viewer to subscribe our channel to have easy access to our newest films.

Results: “Video for every month” is a series but every video can be used separately. Order of videos watching can be optional according to the viewer’s choice. At the same time when videos were posted one by one, project on early diagnosis of rheumatoid arthritis supported by European founds and with our partnership start in Poland. Thanks to this our message “Don’t delay, connect today” is stronger. Parallel our new project ‘RA - don’t resign’ starts from World Arthritis Day 2018. All actions give an occasion to focus on early diagnosis and appropriate treatment of RMDs.

Conclusion: Every aim can be achieve in co-operation and engagement of main players. We involve in our project members of regional associations, rheumatologists, students. During realization of other projects we used every occasion to share information about our videos. All subjects of videos are overtime. Every patient with RMD can receive new knowledge about her/his disease from reliable source everywhere and at every time in two languages versions Polish (voice) and English (subtitles). We are planning to use this form of information in next project.

Disclosure of Interests: None declared

PATHOPHYSIOLOGY AND THERAPEUTIC CONSEQUENCES AUTO-INFLAMMATORY BONE DISORDERS

SP0187

Christian Hedrich, Institute of Translational Medicine, University of Liverpool, Department of Women’s and Children’s Health, Liverpool, United Kingdom

Chronic nonbacterial osteomyelitis (CNO) is an autoimmune bone disorder, covering a clinical spectrum with asymptomatic inflammation of single bones at the one end, and chronic recurrent multifocal osteomyelitis (CRMO) at the other end. Bone inflammation, however, can also be a symptom of other autoimmune/inflammatory conditions. Rare monogenic autoinflammatory diseases with bone involvement have informed research and provide models for the more common and pathophysiologically complex disorder CNO/CRMO.

Despite recent efforts, the exact molecular pathophysiology of CNO remains incompletely understood. Profound dysregulation of cytokine responses was demonstrated in CNO/CRMO. Failure to produce antiinflammatory cytokines interleukin (IL)-10 and IL-19 contributes to activation of inflammmasomes and subsequent IL-1β release. In IL-10-deficient and in CNO-prone chronic multifocal osteomyelitis mice, IL-1β was linked to bone inflammation. Recently, increased inflammmasome component expression and inflammmasome assembly have been linked with CNO/CRMO in humans. Furthermore, alterations to the gut microbiome were suggested in contributing to IL-1β release from innate immune cells in mice, offering an interesting target in the search for molecular mechanisms in CNO.

This presentation will review molecular alterations in autoinflammatory bone disease, focussing on CNO and discuss therapeutic consequences.
REFERENCES:


Disclosure of Interests: Christian Hedrich Grant/research support from: Novartis Pharmaceuticals for Research study on effector T cells in psoriasis, Speakers bureau: Abbvie, Enorasis, Genesis Pharma. In 2016: Roche Pharmaceuticals, Rheumatologisch, Dresden, Germany; Novartis, Advisory board > Travel costs.


SP0188 SAPHO – AN ADULT PERSPECTIVE

Gunter Assmann; University Medical School of Saarland, Medicine I, Oncology and Rheumatology, Homburg, Germany

Background: The acronym SAPHO has been introduced to describe a syndrome in adolescents and adults suffering from synovitis, acne, pustulosis, hyperostosis, and non-bacterial osteitis preferentially in the sternum region. Currently, this also includes the entity CNO with non-bacterial chronic recurrent multifocal osteomyelitis (CRMO) in cases which primarily occur in adult age.

Objectives: The diagnostic certainty of SAPHO syndrome in case of incomplete presentation of the clinical features has been unclear so far. Furthermore, the treatment approach of SAPHO syndrome is difficult because the etiology remains unknown, although a reactive infectious osteitis in genetic predisposed subjects seems appealing.

Methods: Here we present relevant case series of SAPHO patients which should elucidate the relevance of different diagnostic procedures and treatment options. It has been noted, however, that particularly in respect of the use of antirheumatic drugs case series with predominantly small numbers of SAPHO patients suggest different treatment approaches.

Results: The diagnosis of SAPHO syndrome is made not only in the full picture of the disease according to the acronym, but also in non-bacterial and non-malignant osteitis with hyperostosis with simultaneous or delayed onset of acne, psoriasis and/or PPP. In addition, the primary manifestation of CNO in adulthood is nowadays classified as SAPHO syndrome. Recent studies have previously confirmed the usefulness of skeletal scintigraphy in 2 phases as a diagnostic. Imaging with MRI is frequently used preferentially for the assessment of osteitis activity, CT for the assessment of destruction and hyperostosis. The CT-guided biopsy of the lesion should be performed in solitary manifestation of osteitis. Basically, SAPHO syndrome has a high impact on patients’ general health resulting in high burden of disease. There are many approaches to drug therapy, but only a few have been investigated in larger case series - none of them as controlled studies. Smaller case series of less than 10 patients reported limited efficacy of DMARD with MTX, azathioprine, or ciclosporin. Studies with larger case numbers show a moderate efficacy of bisphosphonates as well as TNF-alpha blockers. A short-term but not sustained effect has been demonstrated for the antibiotic azithromycin, as well as for steroids per os or as infiltration into osteitis. Referring to the treatment approach in SpA newly approved biologicals with IL-17 or IL-12/23 blocking effects demonstrated promising results in individual case reports of SAPHO patients.

Conclusion: Modern diagnostic imaging methods are increasingly being used for SAPHO syndrome. The selection of potentially effective drugs for SAPHO syndrome has increased. However, prospective studies to develop guidelines for the diagnosis and therapy of SAPHO syndrome are still lacking. Until further notice, the therapy is based on the recommendations for psoriatic arthritis or spondyloarthritis.

Disclosure of Interests: None declared


SATURDAY, 15 JUNE 2019

09:00:00 – 10:50:00

EULAR Projects in clinical affairs

SP0189 UPDATE ON EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF SLE

Antonis Fanouriakis, "Attikon" University Hospital, Rheumatology and Clinical Immunology, Athens, Greece

Background: Recent advances in treatment strategies and goals of treatment in systemic lupus erythematosus (SLE) called for an update of the EULAR recommendations for the disease, capitalizing on the strengths of and experience from similar previous projects.

Objectives: To update the EULAR recommendations for the management of SLE

Methods: Systematic literature review (01/2007-12/2017) followed by modified Delphi method to form questions, elicit expert opinions and reach consensus.

Results: Treatment in SLE aims at remission or low disease activity and prevention of flares. Hydroxychloroquine is recommended in all lupus patients, at a dose not exceeding 5mg/kg real body weight. During chronic maintenance treatment, glucocorticoids should be minimized to less than 7.5 mg/day (prednisone equivalent) and, when possible, withdrawn. Appropriate initiation of immunomodulatory agents (methotrexate, azathioprine, mycophenolate) can expedite the tapering/discontinuation of glucocorticoids. In persistently active or flaring extracranial disease, add-on belimumab should be considered; rituximab may be considered in organ-threatening, refractory disease. Updated specific recommendations are also provided for cutaneous, neuropsychiatric, haematological and renal disease. SLE patients should be assessed for their antiphospholipid antibody status, infectious and cardiovascular diseases risk profile, and preventative strategies be tailored accordingly.

Conclusion: The recommendations provide physicians and patients with updated consensus guidance on the management of SLE, combining evidence-base and expert-opinion.

Disclosure of Interests: Antonis Fanouriakis Paid instructor for: Amgen, GSK, Speakers bureau: Abbvie, Enorasis, Genesis Pharma

2019 EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF SJÖGREN’S SYNDROME WITH TOPICAL AND SYSTEMIC THERAPIES

Manuel Ramos-Casals1, Hospital Clinic, Autimmune Diseases, Barcelona, Spain; Manuel Ramos-Casals1,2, Pilar Brito-Zerón2, Stefano Bombardieri5, Hendrika Boodaghian7, Salvatore De Vita8, Thomas Dörner9, Benjamin A. Fisher8, Jacques-Eric Cottereng8, Gabriela Hernández-Molina10, Agnes Kocher12, Belchin Kostov15, Ake A. Krüe11, Thomas Mandl13, Wan-Fai Ng11, Soledad Palermo10, Raphaële Serres14, Yehuda Sofferf15, Antoni Sicó-Amiras11,13,14, Athanasios G. Tzoufas15, Claudia Viola13, Simon Bowman10, Xavier Mariette18, on behalf of the EULAR-Sjögren Syndrome Task Force Group. The Task Force endorsed the presentation of general principles for the management of patients with SjS with symptoms as the most important goal. In view of this scenario, the European League Against Rheumatism (EULAR) supported and promoted an international collaborative study (EULAR SJ Task Force) aimed to develop the first EULAR evidence-based recommendations for the management of patients with SjS with topical and systemic medications. The aim was to develop a rational therapeutic approach to SjS patients useful for healthcare professionals, doctors in specialist training, medical students, pharmaceutical industries and drug regulatory organizations following the 2014 EULAR standardized operating procedures.

Methods: The Task Force included rheumatologists, specialists in internal medicine, dermatology, ophthalmologists, gynaecologists, specialists in otorhinolaryngology, and diabetes care. One national study group was formed including 21 physicians, 1 healthcare professional, and 2 patients, from 10 countries. Research questions were developed using the Delphi method. A systematic literature review of published articles up to January 2018 was performed. 11 countries. Research questions were developed using the Delphi method. A systematic literature review of published articles up to January 2018 was performed. The level of evidence and experts opinion, a set of 3 overarching principles and recommendations. We hope that the current recommendations will be widely applied in clinical practice and serve as a template for national societies to develop local recommendations.

Disclosure of Interests: None declared

Aims: The therapeutic management of Sjögren’s syndrome (SjS) has not changed substantially over the past decades: treatment decisions remain challenging in clinical practice, without a specific therapeutic target beyond the relief of symptoms as the most important goal. In view of this scenario, the European League Against Rheumatism (EULAR) supported and promoted an international collaborative study (EULAR SJ Task Force) aimed to develop the first EULAR evidence-based recommendations for the management of patients with SjS with topical and systemic medications. The aim was to develop a rational therapeutic approach to SjS patients useful for healthcare professionals, doctors in specialist training, medical students, pharmaceutical industries and drug regulatory organizations following the 2014 EULAR standardized operating procedures.

Methods: The Task Force included rheumatologists, specialists in internal medicine, dermatology, ophthalmologists, gynaecologists, specialists in otorhinolaryngology, and diabetes care. One national study group was formed including 21 physicians, 1 healthcare professional, and 2 patients, from 10 countries. Research questions were developed using the Delphi method. A systematic literature review of published articles up to January 2018 was performed. The level of evidence and experts opinion, a set of 3 overarching principles and recommendations. We hope that the current recommendations will be widely applied in clinical practice and serve as a template for national societies to develop local recommendations.

Disclosure of Interests: None declared

Abstract SP0190 - Table 1. Overarching and specific recommendations.

<table>
<thead>
<tr>
<th>Recommendation</th>
<th>LoA (%) (endorsement)</th>
<th>LoE</th>
<th>GoR</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Patients with SjS should be managed at, or in close collaboration with, centres of expertise following a multidisciplinary approach</td>
<td>90.7</td>
<td>na</td>
<td>Na</td>
</tr>
<tr>
<td>B. The first therapeutic approach for oral dryness should be symptomatic relief using topical therapies</td>
<td>93.3</td>
<td>na</td>
<td>Na</td>
</tr>
<tr>
<td>C. Systematic therapies may be considered for treating active systemic disease</td>
<td>90.7</td>
<td>na</td>
<td>Na</td>
</tr>
<tr>
<td>1. Baseline evaluation of salivary gland function is recommended before starting treatment for oral dryness</td>
<td>81.3</td>
<td>5</td>
<td>D</td>
</tr>
<tr>
<td>2. The preferred first therapeutic approach for oral dryness according to salivary gland function may be:</td>
<td>88.0</td>
<td>1a</td>
<td>B</td>
</tr>
<tr>
<td>2.1. Non-pharmacological stimulation for mild dysfunction; 2.2. Pharmacological stimulation for moderate dysfunction; 2.3. Saliva substitution for severe dysfunction</td>
<td>99.8</td>
<td>1a</td>
<td>B/D</td>
</tr>
<tr>
<td>3. First-line therapeutic approach of ocular dryness includes the use of artificial tears and ocular gels/ointments</td>
<td>93.3</td>
<td>5</td>
<td>D</td>
</tr>
<tr>
<td>4. Refractory/severe ocular dryness may be managed using topical immunomodulatory-containing drops* and autologous serum eye drops</td>
<td>94.7</td>
<td>1a</td>
<td>B/D</td>
</tr>
<tr>
<td>5. Concomitant diseases should be evaluated in patients presenting with fatigue/pain, whose severity should be scored using specific tools</td>
<td>99.3</td>
<td>4</td>
<td>C</td>
</tr>
<tr>
<td>6. Consider analgesics or other pain-modifying agents for musculoskeletal pain considering the balance between potential benefits and side-effects</td>
<td>99.3</td>
<td>4</td>
<td>C</td>
</tr>
<tr>
<td>7. Treatment of systemic disease should be tailored to organ-specific severity using the ESSDAI definitions</td>
<td>85.3</td>
<td>4</td>
<td>C</td>
</tr>
<tr>
<td>8. Glucocorticoids should be used at the minimum dose and length of time necessary to control active systemic disease</td>
<td>82.7</td>
<td>4</td>
<td>C</td>
</tr>
<tr>
<td>9. Immunosuppressive agents should be mainly used as GC-sparing agents, with no evidence supporting the choice of one agent over the others</td>
<td>98.7</td>
<td>1b</td>
<td>D</td>
</tr>
<tr>
<td>10. B-cell targeted therapies may be considered in patients with severe, refractory systemic disease</td>
<td>98.7</td>
<td>5</td>
<td>D</td>
</tr>
<tr>
<td>11. Systemic organ-specific therapeutic approach may follow as a general rule the sequential (or combined) use of glucocorticoids, immunosuppressive agents and biologics</td>
<td>88.0</td>
<td>4</td>
<td>C</td>
</tr>
<tr>
<td>12. Treatment of B-cell lymphoma should be individualized according to the specific histological subtype and disease stage</td>
<td>88.0</td>
<td>4</td>
<td>C</td>
</tr>
</tbody>
</table>

Disclosure of Interests: None declared

MANAGEMENT OF ADULT APS: RECOMMENDATIONS FROM AN EULAR TASK FORCE

Maria Tektonidou, National and Kapodistrian University of Athens, Joint Rheumatology Program, Greece

Background: Antiphospholipid syndrome (APS) is a systemic autoimmune disorder characterized by arterial and venous thrombotic events or pregnancy morbidity in the presence of persistently positive antiphospholipid antibodies. There is a great heterogeneity in clinical and laboratory classification of the syndrome and treatment approaches over the past four decades.

Objectives: To develop evidence-based recommendations for the prevention and management of adult APS that will help guide clinical practice.

Methods: EULAR standardised operating procedures were followed. A task force was formed including 21 physicians, 1 healthcare professional, and 2 patients, from 11 countries. Research questions were developed using the Delphi method. A systematic literature review of published articles up to January 2018 was performed.

Results: Based on the evidence and experts opinion, a set of 3 overarching principles and 12 recommendations including their level of evidence and grade of recommendation was developed and voted. The level of agreement for each recommendation was high. The overarching principles include the risk stratification, general measures, and education/counselling of patients with APS. Recommendations for primary prevention address the primary thromboprophylaxis (low dose aspirin in no treatment) in antiphospholipid antibody individuals
including asymptomatic carriers, patients with systemic lupus erythematosus without history of thrombotic or obstetric APS, and non-pregnant women with a history of obstetric APS only. Recommendations for the management of thrombotic manifestations address different types of anticoagulation in patients with definite APS and first provoked or unprovoked venous thrombosis and the management of recurrent venous thrombosis, as well as the type and intensity of anticoagulation in patients with first or recurrent arterial thrombosis. Recommendations for the management of obstetric APS describe the management of various types of pregnancy complications in APS and of refractory to treat- ment cases. Recommendations for catastrophic APS refer to precipitating factors, first-line treatment of catastrophic APS, and management of refractory cases.

Conclusion: These recommendations based on evidence and expert opinion aim to guide practice and improve quality of care in patients with APS.

REFERENCES:

Disclosure of Interests: None declared


SP0192 UPDATE OF THE EULAR RECOMMENDATIONS LAGE VESSEL VASCULITIS MANAGEMENT
Bernhard Helbich, Medius Kliniken, Klinik für Innere Medizin, Rheumatologie und Immunologie, Kirchheim-Teck, Germany

Background: Since the publication of the European League Against Rheuma- tism (EULAR) recommendations for the management of large vessel vasculitis (LVV) in 2009, several relevant randomized clinical trials and cohort analyses have been published, which have the potential to change clinical care and there- fore supporting the need to update the original recommendations.

Objectives: To update the 2009 EULAR recommendations for the management of LVV.

Methods: Using EULAR standardized operating procedures for EULAR- endorsed recommendations, the EULAR task force undertook a systematic litera- ture review and sought opinion from 20 experts from 13 countries. We modified existing recommendations and created new recommendations.

Results: Three overarching principles and 10 recommendations were formulated. We recommend that a suspected diagnosis of LVV should be confirmed by imaging or histology. High dose glucocorticoid therapy (40-60 mg/day prednisone-equiva- lent) should be initiated immediately for induction of remission in active giant cell arteritis (GCA) or Takayasu arteritis (TAK). We recommend adjunctive therapy in selected patients with GCA (refractory or relapsing disease, presence of an increased risk for glucocorticoid-related adverse events or complications) using tocilizumab. Methotrexate may be used as an alternative. Non-biologic glucocorti- cold-sparing agents should be given in combination with glucocorticoids in all patients with TAK and biologic agents may be used in refractory or relapsing patients. We no longer recommend the routine use of antplatelet or anticoagulant therapy for treatment of LVV unless it is indicated for other reasons.

Conclusion: We have updated the recommendations for the management of LVV to facilitate the translation of current scientific evidence and expert opinion into better management and improved outcome of patients in clinical practice.

Disclosure of Interests: Bernhard Helbich Consultant for: Roche, Speakers bureau: Abbvie, MSD, Roche, Novartis, Pfizer


SATURDAY, 15 JUNE 2019
12:00:00 – 13:30:00
Skin and eye manifestations in rheumatic diseases...

SP0193 WIN: SKIN AND RHEUMATIC DISEASES
Annegret Kuhn, University Hospital Muenster, Executive Department of the University Hospital, Muenster, Germany

Background: The main underlying mechanisms of skin manifestations in rheu- matic diseases include autoimmune responses, auto-inflammatory processes, and tissue-specific alterations. In psoriasis, therapies targeting T cell activation, T cell migration, or neutralization of disease-related cytokines are highly effective. However, targeted therapies still need to be developed in less frequent autoimmune diseases, such as systemic lupus erythematosus (SLE), systemic sclerosis (SSc), or dermatomyositis (DM).

Objectives: To provide an update for rheumatologists on the management of skin manifestations in autoimmune diseases based on recent insights into the pathogenesis.

Methods: Several agents are approved for the treatment of SLE, including the monoclonal antibody belimumab, a B lymphocyte stimulator-specific inhibitor, but no drugs have been licensed specifically for the treatment of skin manifestations in this disease. The aim of the European guideline was to achieve a broad consen- sus on treatment strategies for patients with cutaneous lupus erythematosus (CLE) by a European subcommittee. In total, 16 European participants were included in this project and agreed on all recommendations.

Results: First-line treatment options in CLE include topical corticosteroids or cal- cineurin inhibitors; in patients with disfiguring and widespread disease, systemic agents need to be applied. The first-line systemic treatment is antimarialarials, but some patients are therapy-resistant and immunosuppressive agents, such as methotrexate, are used as alternative therapeutic option. In 2011, the monoclonal antibody belimumab was introduced for SLE as an adjunct therapy for patients with autoantibody-positive disease who despite standard therapy show high dis- ease activity, intolerance of other treatments, or an unacceptably high need for corticosteroids. So far, a validated skin score has not been used to confirm the effi- cacy of belimumab on mucocutaneous manifestations. In SSC, the therapeutic modalities are even more limited. Treatment with endothelin-receptor antagonists has been proven to reduce the occurrence of new digital ulcers in SSC patients but has no or limited effect on healing of digital ulcers. DM is a further idiopathic autoimmune disease characterized by inflammation of the muscles and skin, which is treated with immunosuppressives. Corticosteroids are still the first-line treatment for muscle involvement in DM, but skin lesions often flare by reduction or discontinuation.

Conclusion: In summary, there is a high unmet need for new therapeutic strat- egies focusing on skin involvement in systemic autoimmune diseases. Therefore, innovative designs of randomized controlled trials based on the pathogenesis are warranted to develop new therapies for patients with skin manifestations in rheu- matic diseases.

REFERENCES:

Disclosure of Interests: Annegret Kuhn Grant/research support from: Biogen, Galderma, GlaxoSmithKline, LeoPharma, Speakers bureau: La Roche Posay


SATURDAY, 15 JUNE 2019
12:00:00 – 13:30:00
To image or not to image in spondyloarthritis?

SP0194 WHEN AND HOW TO USE AND NOT USE IMAGING FOR DIAGNOSIS?
Frans A. van Gaalen. Leiden University Medical Center, Rheumatology, Leiden, Netherlands

Since axial spondyloarthritis (axSpA) has no single shared distinguishing feature that distinguishes the disease from other causes of back pain, diagnosis of axSpA requires recognition by the clinician of a pattern of features that taken together are characteristic of axSpA. Information from patient history and physical examina- tion, laboratory, and imaging findings may all aid in recognition of axSpA and the diagnosis of axSpA requires exclusion of other potential causes for these abnor- malities/differences.

Traditionally, plain radiography is used to assess sacroiliac and spinal involve- ment of disease. A weakness of radiography in assessing sacroiliac involvement - apart from its inability to detect early disease - is reader variability. Additionally, involvement of the spine (i.e. detection of syndesmophytes) is very uncommon in early disease.

The use of MRI in diagnosing axSpA has increased over the past ten years and MRI greatly facilitates earlier diagnosis of axSpA. However, it has also become increasingly clear that MRI detectable lesions associated with SpA including bone marrow edema and fatty lesions - may also occur in patients without axSpA.
The aim of this presentation is to provide insight into the pitfalls of imaging in diagnosing SpA, with a particular focus on false positives in imaging as well as the importance of interpretation of the clinical context.

Disclosure of Interests: None declared


SP0195  IMAGING IN DISEASE AND TREATMENT MONITORING – DOES IT MATTER?

Xenofon Baraliakos. Rheumazentrum Ruhrgebiet, Ruhr University Bochum, Rheumatology, 44649 Herne, Germany

Background: Imaging of the axial skeleton is a crucial step in classification and diagnosis of axial Spondyloarthritides. After diagnosis, patients with axSpA are being treated with non-steroidal anti-inflammatory drugs (NSAIDs) or with disease-modifying anti-rheumatic drug (DMARD). Despite the fact that the latter treatment is referred to as disease-modifying and modification of the disease is supposed to be relating to the objective course of the disease, as assessed by imaging, recommendations for monitoring of the course of axSpA by imaging are still lacking mostly due to the lack of data. Nevertheless, this aspect is mentioned in the treat-to-target principle for axSpA over all, earlier data have shown that the course of lesions documented by magnetic resonance imaging (MRI) is correlating well with other objective measures of changes of systemic inflammation such as C-reactive protein (CRP), than with patient-reported measures of disease activity. Similarly, conventional radiographs (CR) are being used for documenting of the development of structural changes over many years.

Objectives: The objective of this presentation is to show the current evidence of the possibilities of different imaging techniques used in axSpA for assessment of the course of the disease (both for the inflammatory and chronic changes) and give practical tips about when imaging would be advised for monitoring the disease course or where this can be avoided.

Disclosure of Interests: Xenofon Baraliakos Grant/research support from: AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Centocor, Chugai, Janssen, MSD, Novartis, Pfizer Inc, Roche and UCB, Consultant for: AbbVie, Pfizer, Merck Sharp & Dohme, UCB Pharma, Novartis, Consultant for: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Chugai, Janssen Biologics, Novartis, Pfizer, UCB Pharma, Galapagos, Speakers bureau: Abbvie, Chugai, Janssen, Novartis, Pfizer, UCB Pharma


SP0196  IS THERE ROOM FOR OTHER IMAGING MODALITIES BEYOND CONVENTIONAL X-RAYS AND MRI?

C.-J. van der Laken. Amsterdam UMC location VUMc, Rheumatology, Amsterdam, Netherlands

Early diagnosis of spondyloarthritides is still tempting since objective measures to assess disease activity are often missing. MRI provides highly sensitive visualization of inflammation, but detection levels in early spondyloarthritides are varying. Another clinical temptation is early treatment evaluation of spondyloarthritides. An important outcome measure is therapeutic efficacy on bone formation in vertebral column and sacro-ilial joints. Conventional X-rays only allow for assessment of bone formation over a time span of at least 2 years. In this presentation, opportunities with new upcoming imaging techniques to address above mentioned clinical issues will be discussed in relation to longer existing imaging techniques.

Disclosure of Interests: None declared


SATURDAY, 15 JUNE 2019

12:00 – 13:30:00

The lung in rheumatoid arthritis

SP0197  CASE 1 PRESENTER: EARLY RA WITH LUNG PROBLEMS IN THE CONTEXT OF BIOLOGICAL TREATMENT

Ana Miona Illán Arciniegas. Santa Creu i Sant Pau Hospital, Rheumatology, Barcelona, Spain

We present a 77-year-old male patient with a history of former smoker, arterial hypertension and dyslipidemia, whose diagnosis of Rheumatoid Arthritis was made in July 2017 by arthritis of metacarpophalangeal joints, wrists and knees and positivity for anticryctic citrullinated peptide antibodies (ACPA) and rheumatoid factor (RF). Treatment with Methotrexate and prednisone was started but the patient did not achieve adequate control of joint symptoms, so we decided to add Etanercept to the treatment. A good joint response was obtained but in a follow-up control he explained breathlessness with cough and low grade fever. The chest X-Ray was not conclusive and we decided to perform a high resolution computerized tomography (HRCT) scan. An interstitial involvement was detected and an accurate differential diagnosis was made.

Disclosure of Interests: None declared


SP0198  CASE 1 DISCUSSANT: HOW TO TREAT DIFFICULT ILD FROM OTHER CAUSES OF LUNG INVOLVEMENT IN RA

Ivan Castellví. Hospital Universitari de la Santa Creu i Sant Pau, Rheumatology, Barcelona, Spain

The lung in Rheumatoid Arthritis (RA) can be affected by different manifestations and Interalstitial Lung Disease (ILD) related to RA is one of the most devastating complications that we can find in the disease. The lung parenchyma involvement can be present with different patterns. As opposite with other forms of connective tissue diseases the usual interstitial pneumonia pattern (UIP) is more frequent than non-specific interstitial pneumonia pattern (NSIP) in RA. Currently high-resolution computed tomography (HRCT) and pulmonary function test are the best tools to detect and to follow ILD in RA. Nevertheless, other lung involvements, infections and drug toxicity of nonbiological and biological disease-modifying anti-rheumatic drugs (DMARDs) can affect patients with rheumatoid arthritis and simulate ILD. To know which affection are present in our patients with interstitial lung compromise is crucial to proceed against the problem. Patient characteristics, clinical presentation, radiological distribution or bronchoalveolar lavage would be helpful to discriminate ILD from other causes of lung involvement. An individual and multidisciplinary approach is very important to do the best management in these patients.

Disclosure of Interests: None declared


SP0199  CASE 2 DISCUSSANT: HOW TO TREAT DIFFICULT ILD

Toby Maher. Imperial College London and Royal Brompton Hospital, National Heart and Lung Institute, London, United Kingdom

Background: ILD frequently results in progressive and irreversible destruction of the lung through scarring. Prompt therapy can help rescue lung function and prevent subsequent respiratory decline. This case will demonstrate the challenges inherent in diagnosing and managing interstitial lung disease in the context of connective tissue disease.

Objectives: To discuss typical presentation of CTD-ILD; Review challenge of making diagnosis and choosing best treatment; Assess treatment options, duration of therapy and measurement of treatment response.

Conclusion: A range of therapeutic options exist for CTD-ILD albeit with a paucity of trial data to support best practice. Accurate diagnosis of systemic disease, paired with careful assessment and monitoring of the respiratory system are vital in ensuring optimal management. Intraavenous therapy is often necessary in advanced disease or for disease which proves refractory to oral immunosuppression.

REFERENCES:

Disclosure of Interests: Toby Maher Grant/research support from: Received funds from BI advisory board participation and conference travel. Received research funding and/or consulting fees or other remuneration from GSK, UCB, AstraZeneca, Roche, Bayer, Biogen Idec, Cipla, Prometic, and Sanumbed. Toby Maher has, via his institution, received industry-academic funding from GlaxoSmithKline R&D and UCB, Consultant for: Toby Maher has received consultancy or speakers fees from Apellis, AstraZeneca, Bayer, Biogen Idec, Boehringer Ingelheim, Galapagos, GlaxoSmithKline R&D, Indalo, Pliant, ProMetic, Roche, Sanumted and UCB; and has received consultancy fees from Galecto.


DISCLOSURES
Novel treatments and old challenges: where do we stand in the management of antiphospholipid syndrome

SP0200 TARGETED TREATMENTS: WHAT’S ON THE HORIZON FOR OBSTETRIC ANTIPHOSPHOLIPID SYNDROME?

Jane E. Salmon. Hospital for Special Surgery – Weill Cornell Medicine, Rheumatology, New York, United States of America

Pregnancy in women with APS and/or lupus is dangerous both for mother and offspring, and, in the past, patients were advised not to have children. Among complications frequently seen in women with lupus are preeclampsia (also known as toxemia of pregnancy), preterm birth, markedly underweight newborns, and fetal death. Identifying women destined for complications remains challenging and limits our ability to counsel and care for pregnant lupus patients.

There is currently no effective treatment for women with these high-risk pregnancies; treatments to prevent poor pregnancy outcomes require an understanding of mechanisms of injury. Our research in an animal model that mimics the human condition shows that blockade of well-established mediators of inflammation, speciﬁcally complement and TNF-alpha, prevents adverse outcomes. To translate these discoveries to lupus patients, we launched the PROMISSE Study (Predictors of Pregnancy Outcome: biomarkers in antiphospholipid antibody syndrome and Systemic lupus erythematosus) to determine which pregnancies were at highest risk for adverse outcomes. Over 20% of pregnancies in patients with SLE resulted in an adverse pregnancy outcome. We discovered that the presence of a lupus anticoagulant which can be detected in the blood before pregnancy or in the first trimester, confers a 10-fold increase in risk of complications. Furthermore, we found that early in pregnancy, measurable alterations in the balance of angiogenic factors (proteins that circulate in blood, promote proper placenta development, and are required to maintain the health of the mother’s vascular system) are highly predictive of preeclampsia and other pregnancy complications.

The results of the PROMISSE Study provide models for early risk stratiﬁcation to allow physicians to identify patients early in pregnancy who are at low risk and reassure them that their pregnancies were likely to be uncomplicated and their babies healthy. Conversely and importantly, we can reliably predict which patients are destined to have poor pregnancy outcomes, and we conducting a trial with a TNF-alpha inhibitor that does not cross the placenta in patients at highest risk an experimental therapy to prevent placental dysfunction. Treatments to prevent poor pregnancy outcomes require an understanding of mechanisms of injury. Experiments in mouse models have enabled us to embark upon a trial of a potential treatment.

Disclosure of Interests: Jane E. Salmon Shareholder of: Biogen-Idec, BMS, Johnson & Johnson, & Regeneron, Consultant for: UCB, Consultant for: AbbVie, Biogen, BMS, Celgene, Lilly, MSD, Novartis-Sandoz, Pfizer, Sanofi, and UCB, Consultant for: AbbVie, Biogen, BMS, Celgene, Janssen, Lilly, MSD, Nordic Pharma, Novartis-Sandoz, Pfizer, Roche, Sanofi, and UCB. Consultant for: L Gossec has received honoraria from Celgene as investigator for this study.


SP0201 CATASTROPHIC APS TREATMENT GUIDELINES

Ricard Cervera. Hospital Clinic, Barcelona, Department of Autoimmune Diseases, Barcelona, Spain

The current recommendation for speciﬁc therapy of catastrophic antiphospholipid syndrome (CAPS) is the triple therapy with anticoagulation, glucocorticoids, plasma exchange and/or intravenous immunoglobulins. Of note, only anticoagulation had a signiﬁcant effect improving the vital prognosis of these patients. From the experimental point of view, there is only indirect evidence to advocate the use of these immunomodulatory therapies in CAPS.

Recently, two monoclonal antibodies, rituximab and eculizumab, have been successfully used in some cases of severe or refractory CAPS. The ﬁrst decreases the generation of pathogenic autoantibodies such as antiphospholipid. The second prevents the generation of C5b-C9 complex.

The current presentation will describe the conventional and recent modalities of CAPS treatment, discussing the rationale for each one.

REFERENCES:


Disclosure of Interests: None declared


SATURDAY, 15 JUNE 2019
12:00:00 – 13:30:00

How low should you go? What is the relevant target in T2T in rheumatoid arthritis?

SP0202 WHAT DOES REMISSION MEAN FOR PHYSICIANS?

Laure Gossec. Sorbonne Universite and Pitié-Salpetriere Hospital, Rheumatology, Paris, France

Remission is the announced objective is rheumatoid arthritis. However, there are several deﬁnitions of remission. In this talk, we will review different health professional based deﬁnitions of remission, the components of these deﬁnitions, and their advantages and drawbacks.

Disclosure of Interests: Laure Gossec Grant/research support from: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis-Sandoz, Pfizer, Sanofi, and UCB. Consultant for: AbbVie, Biogen, BMS, Celgene, Janssen, Lilly, MSD, Nordic Pharma, Novartis-Sandoz, Pfizer, Roche, Sanofi, and UCB. Consultant for: L Gossec has received honoraria from Celgene as investigator for this study.


SP0203 WHAT DOES REMISSION MEAN FOR PATIENTS?

Ruth Williams. Kings College London, Department of Inflammation Biology, London, United Kingdom

What does remission in Rheumatoid arthritis mean to patient? This session discusses what remission means to patients. Remission holds different meaning for researchers, clinicians and patients. In addition it holds different meaning for individual patients and for individual patients at different points of time in their lives. I shall reﬂect on over ﬁfty years living with Rheumatoid arthritis, as both a patient and a doctor. To consider the changes in my care, my therapy and in my own and my clinicians objectives and treatment aims, at different points in time. Looking at how things have progressed from pain relief, splinting, physical therapy, rehabilitation and surgery. To progressively more effective DMARD’s, anti-TNF’s & Biologics and an aim of complete ‘clinical remission’. However commonly ‘clinical remission’ can conﬂict with a patients concept of remission, as patients are individuals and the tools used to deﬁne remission are research based and consider populations not people. ‘Disease activity scoring’ and ‘Treat to Target’ has had signiﬁcant impact on patients, clinicians and their rheumatology consultations. The absence of inﬂammation does not equal remission for many patients and it is important to consider the differing needs of patients who were diagnosed pre and post biologic therapies and those with refractory disease. Currently maximal energy appears to be concentrated on the newly diag nosed and even pre-diagnosis, but has this been at the detriment of those with long established disease?

I will share my own and different patients viewpoints of what ‘remission’ means and consider the beneﬁts of progress in effective therapies but also to reﬂect upon some of the important things that may have been lost from clinical ‘care’ along the way. To list simple things that can help patients achieve remission that can easily be forgotten. I will explain the phenomenon of ‘DAS blindness’ and the potential failings it can lead to. Discuss how improved shared decision making of treatment aims might improve outcomes for patients whilst reducing risk and possi bly costs; aiming to increase patient autonomy and improve the doctor patient dynamic.

In order to achieve ‘remission’ for patients we need to have a clear shared understanding of what ‘remission’ means to each individual and only then can we aim to achieve it.

Disclosure of Interests: None declared

Case presentation: facilitating behaviour links between sleep quality and immunity in physical activity, chronic musculoskeletal pain

Yeliz Prior. University of Salford, Centre for Health Sciences Research, Manchester, United Kingdom

Background: Fibromyalgia is a chronic pain condition which is, commonly accompanied by the symptoms of fatigue, sleep disturbance, low mood and cognitive dyscognition. EULAR Revised Recommendations for the management of Fibromyalgia suggests initial management should involve patient education and focus on non-pharmacological therapies [1]. Occupational Therapists at the Rheumatology Outpatients Department, Leighton Hospital, Mid Cheshire NHS Trusts Foundation Trust developed the Fibromyalgia Self-Management Education (FAMe) Group Programme, based on the current evidence-base and patient partner involvement. The primary aim of this programme is to support self-management of Fibromyalgia using behaviour change interventions as outlined in the NICE recommendations. FA Me comprises 2.5 hrs weekly sessions over six weeks (6-Wks) and core components include education about Fibromyalgia, pain, fatigue, sleep and mood management, dealing with dyscognition, physical exercise and practicing mindfulness, based on Cognitive Behavioural Therapy (CBT) and Motivational Interview (MI) approaches.

Objectives: Service evaluation aims to assess how well a service is achieving its objectives. This service evaluation was undertaken with a view to benefit patients using the FA Me Group Programme and is designed and conducted with the sole purpose of defining and examining the current occupational therapy service provision for people with Fibromyalgia at the Mid Cheshire NHS Trust Hospitals. This Case Study will report on the findings of this service evaluation with reference to patient outcomes and discuss the barriers and facilitators of implementing this programme at an NHS Hospital setting.

Methods: Patients with a primary diagnosis of FM were screened and recruited from the rheumatology department of the Mid-Cheshire NHS Hospitals. Patients self-completed postal questionnaires at home (including socio-demographic characteristics; General Health Questionnaire SF-12; Revised Fibromyalgia Impact Questionnaire; Arthritis Self Efficacy Scale; Multidimensional Assessment of Fatigue Scale) at baseline, and again at 6 and 12-week follow-up. Focus groups were held at the hospital following the completion of the FAME Group Programme, to obtain patients’ views on the programme content, delivery and the impact on their self-management. Quantitative data from the baseline, 6 and 12-week follow-up questionnaires were analysed using paired t-tests and effect sizes calculated using eta-squared. Focus groups were transcribed and analysed by three independent researchers, not involved in the initial design or the delivery of this programme, using Thematic Analysis [2].

Results: As the service evaluation is in progress at the time of submitting this abstract, the results will be presented and discussed at the annual meeting.

Conclusion: To be discussed at the meeting.

References:

Disclosure of Interests: None declared

Saturday, 15 June 2019
12:00:00 – 13:30:00

Restless lives: managing fatigue, sleep and pain

Tanja Lange. University of Lübeck, Department of Rheumatology and Clinical Immunology, Lübeck, Germany

Summary: Sleep and the immune system are bi-directionally linked. An immune activation induces fatigue, sleepiness and changes in sleep architecture. These range from a deepening of sleep to severe sleep disturbances with shallow and fragmented sleep. Patients with rheumatic and musculoskeletal diseases (RMDs) often complain about feelings of debilitating fatigue, of problems initiating and maintaining sleep and of unrefreshing sleep. Chronic low-grade inflammation due to the RMD, disease symptoms such as pain, concurrent diseases such as depression and medication such as glucocorticoids are potential triggers of poor sleep. Often it is demanding to delineate the exact cause(s) of sleep impairments in patients with RMDs and attempts to improve sleep quality therefore often fail. However, as fatigue and sleep problems can substantially impair quality of life and as poor sleep may further aggravate RMDs and their symptoms it is key to unravel the pathophysiology of fatigue and poor sleep in these patients. A deeper understanding of sleep-immune interactions in RMDs will advance targeted interventions that presumably will encompass a combination of immunomodulatory drugs, chronopharmacology and cognitive behavioral therapy.

References:

Disclosure of Interests: None declared

Saturday, 15 June 2019
12:00:00 – 13:30:00

How to build a clinical scientist

Annet van Royen. Background: Clinician scientists are at the heart of the translational medicine process. Over the last decades many reports and studies have showed that they risk becoming extinct, and that efficient career pathways are lacking. Recently more reports show that alarming numbers of clinicians and clinician scientists suffer from burn out and depression. To address this issue, next to thorough study of the root factors leading to mental problems it is important to develop career pathways for clinician scientists and educational programs to improve resilience. New educational programs such as those offered by the Eureka Institute help to build networks of translational scientists and help to strengthen resilience, needs to overcome the challenges they face while pursuing translational research.

Disclosure of Interests: None declared

Saturday, 15 June 2019
12:00:00 – 13:30:00

Physical activity, chronic musculoskeletal pain and insomnia

Eivind Skarpnes. Norwegian University of Science and Technology (NTNU), Department of Public Health and Nursing, Trondheim, Norway

The interplay between physical activity, chronic musculoskeletal pain and insomnia

The unfavourable consequences of insomnia and musculoskeletal pain for both individuals and society underscore the importance of identifying modifiable factors for prevention and treatment. Prospective studies have shown that there exists a bidirectional relation between insomnia and musculoskeletal pain, i.e., insomnia is associated with risk of chronic musculoskeletal pain and vice versa. This suggests that management of insomnia symptoms may be an efficient treatment objective for people with musculoskeletal pain and that management of musculoskeletal pain has the potential to improve sleep quality. Furthermore, some evidence shows that physical activity may represent an efficient initiative that can improve both sleep quality and chronic pain, potentially leading to effects as beneficial as pharmacological treatment. However, many unresolved questions need to be resolved before physical activity can be prescribed as an optimal treatment.
Pain is well known to be a common dominant symptom in people with rheumatic musculoskeletal diseases (RMDs). Perhaps less well acknowledged by healthcare professionals are fatigue and sleep disturbances in these patients. Individually these symptoms are problematic but when combined their effect and impact on patients’ lives is greatly amplified; often leaving people in a vicious cycle whereby being in pain results in poor sleep leading to fatigue the next day, which lowers patients’ pain tolerance resulting in a poorer night’s sleep, more fatigue and increased pain.

Pain, fatigue and sleep disturbance greatly reduce quality of life for people with RMDs. Patients have to adapt their daily and leisure activities, or give them up altogether with negative psychological consequences such as anxiety and depression. Patients can end up feeling helpless and sometimes suicidal. Relationships with partners and friends are often altered affecting their sexual and social lives. Major life decisions, such as having a baby, can be put on hold or shelved.

People with RMDs may also have to reduce their working hours or stop working, which has financial repercussions for them and their families. This can exacerbate stress, anxiety and depression leading to poorer health outcomes. It is therefore of great importance that healthcare professionals understand the extent to which pain, fatigue and sleep difficulties impact on patients’ lives so that priority can be given to addressing these distressing symptoms as part of any management strategy.

Disclosure of Interests: None declared

Ingrid Möller. University of Barcelona, Instituto Pau de Reumatologia, Barcelona 08022, Spain

**Background:** Ultrasound-guided needle biopsy of synovium is a minimally invasive tool to complete the study and in the investigation of the therapeutic response in some patients with arthritis. As a consequence, there is a need to have a didactic material and a form of training. This EULAR project: Development of a standardized training model for ultrasound-guided synovial biopsy’s in small and large joints, covers these objectives

**Objectives:**
1. To develop educational material on the procedures for ultrasound-guided minimally-invasive synovial biopsy in small and large joints.
2. To test the consistency, reliability and feasibility of these procedures on cadaveric specimens (Barcelona University, Barcelona, Spain).
3. To validate these procedures by assessing the synovial tissue quality (i.e., number of graded tissue samples per biopsy procedure, amount of RNA extraction) obtained by this biopsy modality in patients (5 patients) from the participating centres. Tissue will be analyzed in a central laboratory (Joint and Bone Laboratory, Fundación Jiménez Díaz, Madrid, Spain).

**Methods:** Meeting in Barcelona was in January 2019 from the 21 to the 25. During the meeting, part of the educational material was produced and the exercise to test the consistency, reliability, and feasibility of these procedures on cadaveric specimens (Barcelona University, Barcelona, Spain) was done. Then the material was circulated among the experts. The validation of these procedures by assessing the synovial tissue quality (i.e., number of graded tissue samples per biopsy procedure, amount of RNA extraction) obtained by this biopsy modality in patients (5 patients) from the participating centres and Tissue analysis in a central laboratory (Joint and Bone Laboratory, Fundación Jiménez Díaz, Madrid, Spain) is ongoing.

**Results:** Here is presented the teaching material produced by the members of this EULAR task force in animal model and cadaver as a basis for learning the ultrasound-guided synovial biopsy technique.

**Conclusion:** The animal model and the cadaver, having the appropriate anatomical and musculoskeletal ultrasound knowledge, are useful for learning ultrasound-guided biopsy. As a complement, you can include the stay with an expert to face the problems of the technique with the real patient. The visualization of the produced video is a useful tool for this learning.

**REFERENCES:**


**Disclosure of Interests:** None declared


**SATURDAY, 15 JUNE 2019**

13:45:00 – 14:45:00

**PARE Highlight session**

SP0212 **HIGHLIGHTS FROM THE SCIENTIFIC PROGRAMME**

Daniel Aletaha. Medical University of Vienna, Department of Medicine III, Division of Rheumatology, Austria

In this presentation we will review the most interesting findings from the scientific programme of this year’s EULAR meeting for healthcare professionals.

**Disclosure of Interests:** None declared


**SATURDAY, 15 JUNE 2019**

13:45:00 – 14:45:00

**PARE Highlight session**

SP0213 **HIGHLIGHTS FROM THE SCIENTIFIC PROGRAMME**

Alexandre Sepriano. Leiden University Medical Center, Rheumatology, Leiden, Netherlands

This talk will cover highlights from the Congress Scientific Programme, encompassing a wide range of topics in the field of rheumatology.

**Disclosure of Interests:** None declared

Background: TNF-α-inhibitor therapy is effective in controlling several rheumatic diseases and has been shown to reduce pain. Non-steroidal anti-inflammatory drugs (NSAIDs) are commonly used for treatment of pain and stiffness in inflammatory arthridities and are the first treatment line in axial spondyloarthritis.

Objectives: To study the prescriptions of NSAIDs in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and anklyosing spondylitis (AS) registered in ICEBIO and matched controls, and explore their relationship with disease activity measures. In addition, to explore the impact of initial TNF-α-inhibitor therapy on NSAID prescription rates.

Methods: All patients receiving biologic DMARD therapy in Iceland for rheumatic diseases are registered in a nationwide database; ICEBIO. The Icelandic Directorate of Health operates a prescription database that includes over 90% of all drug prescriptions in Iceland. On February 1st 2016 we extracted data for all patients with RA, PsA and AS from ICEBIO along with all filled prescriptions for NSAIDs made two years before and after the initiation of TNF-α-inhibitor therapy. We then extracted NSAID prescriptions for five randomly selected individuals matched on age, sex, and calendar time of TNF-α inhibition for each patient.

Results: Data from 366 patients with RA, 218 with AS, 251 with PsA and 4760 controls was included. Control group was prescribed a mean of 23 defined daily doses (DDD) of NSAIDs per year. In total the ICEBIO patients were prescribed 6.7 times more DDDs of NSAIDs than the controls, a mean of 149 per year. After initiation of TNF-α-inhibitor therapy the use of NSAIDs was reduced to a mean of 85 DDD per year, or 3.9 times that of the controls.

Among the patients with RA, consumption was reduced by 43% (mean 148 to 85 DDD/year), 47% in the AS group (154 to 83 DDD/year) and 43% in the PsA group (157 to 90 DDD/year). The 20% of patients who used the largest amounts of NSAIDs over the 4 year period reported worse visual analogue scale (VAS) pain scores (mean ±SD 65 ±20 vs 60±23), VAS global health scores (70±19 to 65±23), and HAQ scores (1.19±0.64 to 1.03±0.67) when TNF-α-inhibitor therapy was initiated compared to the rest of the ICEBIO group (p<0.05 by students t-test), though there was no statistically significant difference in the number of swollen (4.5±4.7 vs 4.2±4.4) or tender (5.4±4.8 vs 5.5±5.4) joints or in the physician global VAS assessment (56±17 vs 57±18).

Conclusion: Patients with inflammatory arthridities requiring TNF-α-inhibitor therapy use more NSAIDs than general population controls, but consumption is significantly reduced following the initiation of the first-line biologic drug. The patients with the highest NSAID use have worse patient reported outcome measures but physician outcome measures are similar, which may suggest a non-inflammatory etiology of the pain.

Disclosure of Interests: Olafur Palsson: None declared, Johan K Wallman Consultant for: Consultant for AbbVie, Celgene, Eli Lilly, Novartis, and UCB Pharma., Thorvardur Jon Love Consultant for: Received reimbursement from Celgene for speaking about guidelines for the treatment of psoriatic arthritis, Meliha C Kapetanovic: None declared, Petur S Gunnarsnsson: None declared, Björn Gudbjörnsson: None declared

WE M WEDNESDAY, 12 JUNE 2019

OP0003 CALCIUM PYROPHOSPHATE CRYSTAL DEPOSITION IN A COHORT OF 52 PATIENTS WITH GITELMAN SYNDROME

Emilie Choutard1, Anne Blanchard2, Gilles Gaill1, Rosal Vargas Poussou3, Agnès Ostertag1, Hang Komp EA-a,1,4,1 APHP – Lariboisière Hospital, Rheumatology department, Viguier Hospital Centre, Paris, France, 2APHP – Georges Pompidou European Hospital, Nephrology department, Paris, France, 3APHP – Georges Pompidou European Hospital, Department of Genetics, Paris, France, 4University Paris Diderot, INSERM UMR1132 – Bioscal, Paris, France

Background: Gitelman syndrome (GS) is a rare recessively inherited hypomagnesemia and hypocalciuric. Calcium pyrophosphate (CPP) crystal deposition is frequently described in GS case-reports but its prevalence and clinical phenotype are unknown.

Objectives: The aim is to describe clinical, biological and radiological features of CPP in a cohort of patients with genetically proven GS.

Methods: All patients (pts) with genetically proven GS in the French national reference center of rare diseases were proposed to have a consultation with a senior rheumatologist. Demographic data, history of joint pain and flare and biological disorders were recorded. Other causes of CPP disease were systematically ruled out. CPP crystal deposition was assessed by X-rays (all peripheral joints and cervical spine) and ultrasonography (US) (wrist, knee, ankle joints and symtomatic joints). Patients with history of cervical pain underwent computed tomography (CT) of the full cervical spine from occipital bone to C1-T1 disk, including temporomandibular joints.

Results: Fifty-two GS pts (21 men, mean age 46.5±12.2 years) have been examined by a rheumatologist. Almost all pts had an heterozygous mutation on SLC12A3 gene. Forty-four pts experienced joint pain (84.6%), 23 joint flares (44.2%) and 25 cervical pain (48.1%). X-rays were performed in 42 pts, US in 38 and CT in 23. CPP depositions were observed in 36 (85.7%), 27 (71.1%) and 15 pts (65.2%) by X-rays, US and CT, respectively. All techniques combined, chondrocalcinosis was discovered in 42 patients. Deposits occurred in knees (n=32), wrists (n=29), cervical spine (n=23), ankles and feet (n=22) and shoulders (n=16). CPP depositions were widespread involving at least 3 joints in 27 (51.5%) pts. In knees, CPP depositions involved menisci (n=24), hyaline cartilages (n=16) and ligament or joint capsule (n=15). Cervical spine CT demonstrated CPP deposition in vertebral discs (n=17), transverse lagment (n=13), other ligament (n=13), vertebral facets (n=3) and temporomandibular joints (n=5).

Patients with CPP crystal deposition in more than 3 joints were significantly older (52.8±10.5 years) than patients with 2 or 3 affected joints (46.6±11.6 years; p=0.02) or patients without any affected joint (36.6±8.1 years; p=0.001). They were also more symptomatic with significantly more joint flares (p<0.0001). Magnesemia was inversely correlated with the number of affected joints: patients with >3 or 2-3 affected joints had a significantly lower magnesemia (0.57±0.1 and 0.59±0.1 mM, respectively) than patients with only 1 affected joint (0.63±0.1 mM). CPP crystal deposition was not associated with potassium level.

Table 1. Patients charactersistics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>21 (40.4)</td>
</tr>
<tr>
<td>Mean age ± SD (years)</td>
<td>46.5±12.2</td>
</tr>
<tr>
<td>Heterozygous mutation on SLC12A3 gene</td>
<td>36 (69.2)</td>
</tr>
<tr>
<td>Arthralgia, n (%)</td>
<td>44 (84.6%)</td>
</tr>
<tr>
<td>Recurrent joint flares, n (%)</td>
<td>23 (44.2%)</td>
</tr>
<tr>
<td>Cervicalgia, n (%)</td>
<td>25 (48.1%)</td>
</tr>
<tr>
<td>Kaliemia at GS diagnosis, mean ± SD (mM)</td>
<td>2.7±1.1</td>
</tr>
<tr>
<td>Magnesemia at visit, mean ± SD (mM)</td>
<td>0.6±0.3</td>
</tr>
<tr>
<td>Caclemia at visit, mean ± SD (mM)</td>
<td>2.4±1.0</td>
</tr>
</tbody>
</table>

Conclusion: CPP crystal deposition occurred in more than 80% of patients with GS, was widespread and often symptomatic. The most affected sites were wrists, knees and the cervical spine. CPP crystal deposition was associated with longstanding GS, older age and lower serum magnesium level.

Disclosure of Interests: None declared


WE M WEDNESDAY, 12 JUNE 2019

OP0005 INCIDENCE OF OVERALL AND SITE-SPECIFIC Cancers in TNF INHIBITOR TREATED PATIENTS WITH PSORIATIC ARTHRITIS: A POPULATION-BASED COHORT STUDY FROM 4 NORDIC COUNTRIES

Christine Ballegaard1,2, Karin Høffgensen3, Rand Carlsen1,2, Bénédicte Delcoigne4, Björn Gudbjörnsson5,6, Thordvarud Jon Love7, Kalle Aaltonen8, Dan Nordström9, Selma Ararestad Provan5, Johan Askling10, Lars Erik Kristensen11,12, Laura Eriksen11,12, Lars Erik Kristensen11,12, Lars Eriksen11,12, Lene Dreyer11,12, 1Bispebjerg and Frederiksberg Hospital, The Parker Institute, Frederiksberg, Copenhagen, Denmark, 2Rigshospitalet – Gentofte, Centre for Rheumatology and Spine Diseases, Copenhagen, Denmark, 3Karolinska Institute, Clinical Epidemiology Division and Department of Medicine Solna, Stockholm, Sweden, 4National University Hospital of Iceland, Centre for Rheumatology Research, Reykjavik, Iceland, 5University of Iceland, Faculty of Medicine, Reykjavik, Iceland, 6Ministry of Social Affairs and Health, Helsinki, Finland, 7RCB-FIN, Helsinki University Hospital and Helsinki University, Department of Medicine, Helsinki, Finland, 8Diakonhjemmet Hospital, Department of Rheumatology, Oslo, Norway, 9Aalborg University and Aalborg University Hospital, Aalborg, Denmark, 10DANBIO, Nationwide, Denmark

Background: Turnover necrosis factor inhibitors (TNFi) effectively reduce inflammation in Psoriatic arthritis (PsA). However, a possible association between treatment with TNFi and an increased cancer risk has previously been suggested.

Disclosure of Interests: None declared

Objectives: To investigate the risk of cancer in TNFi-treated PsA patients compared with standardized rates from the general population in Denmark, Finland, Iceland and Sweden.

Methods: TNFi-treated PsA patients were followed from first registration with TNFi-treatment in ARTIS (Sweden), DANBIO (Denmark), ICEBIO (Iceland) or ROB-FIN (Finland) and linked to the national Cancer Registry in each country. Patients with a cancer history prior to start of follow-up were excluded. We investigated the risk of primary cancer among TNFi-treated PsA patients compared with general population cancer rates standardized to age, sex and calendar period within each country. Standardized incidence ratios (SIRs) were estimated for each country and pooled SIRs were subsequently calculated for both any cancer and site-specific cancers of interest.

Results: A total of 5218, 2039, 270 and 526 patients were registered as ever treated with TNF inhibitors from ARTIS, DANBIO, ICEBIO and ROB-FIN, respectively, contributing a total of 44,041 patient years of follow-up across all 4 countries. For all cancers, the SIRs of TNFi-treated patients from ARTIS, DANBIO, ICEBIO and ROB-FIN were 0.94 (0.80 to 1.10), 0.99 (0.77 to 1.26), 1.71 (0.88 to 2.99) and 1.28 (0.92 to 1.90), respectively. The number of observed and expected cancers and the SIRs of any and selected site-specific cancers are listed in table 1.

Table 1. Standardized incidence ratios (SIR) of TNFi-treated patients from 4 Nordic countries compared with the general population.

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Observed</th>
<th>Expected</th>
<th>SIR (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cancers</td>
<td>282</td>
<td>281.6</td>
<td>1.00 (0.89 to 1.13)</td>
</tr>
<tr>
<td>Colorectal</td>
<td>32</td>
<td>26.5</td>
<td>1.21 (0.85 to 1.71)</td>
</tr>
<tr>
<td>Hodgkin’s lymphoma</td>
<td>21</td>
<td>11.4</td>
<td>1.84 (1.20 to 2.82)</td>
</tr>
<tr>
<td>Lung</td>
<td>20</td>
<td>25.4</td>
<td>0.79 (0.51 to 1.22)</td>
</tr>
<tr>
<td>Malignant melanoma</td>
<td>20</td>
<td>18.6</td>
<td>1.07 (0.69 to 1.66)</td>
</tr>
<tr>
<td>Pancreas</td>
<td>8</td>
<td>6.6</td>
<td>1.21 (0.60 to 2.41)</td>
</tr>
<tr>
<td>Brain</td>
<td>7</td>
<td>7.4</td>
<td>0.95 (0.45 to 1.99)</td>
</tr>
<tr>
<td>Female breast</td>
<td>58</td>
<td>48.4</td>
<td>1.20 (0.93 to 1.55)</td>
</tr>
<tr>
<td>Corpus uteri</td>
<td>34</td>
<td>48.8</td>
<td>0.70 (0.50 to 0.98)</td>
</tr>
</tbody>
</table>

Conclusion: Our results suggest that the overall cancer risk for TNFi-treated PsA patients is not increased compared to the general population. Further analysis of the risk of malignant lymphomas will inform on whether the increased risk we observed is attributed to the PsA disease or treatment with TNFi.

Acknowledgement: This study is funded by FOREUM and NordForsk.

Disclosure of Interests: None declared, Istanbul University, Istanbul Bilal University Consultant for: AbbVie, MSD, Novartis, Pfizer, UCB, Janssen Pharmaceuticals. Speakers bureau: AbbVie, MSD, Novartis, Pfizer, UCB, Janssen Pharmaceuticals. Lene Dreyer Consultant for: MSD, UCB and Janssen Pharmaceuticals. cephalic Delcoigne: None declared, Björn Gudbjornsson: None declared, Thorvardur Jon Love Consultant for: Received reimbursement from Celgene for speaking about guidelines for the treatment of psoriatic arthritis, Kalle Aaltonen: None declared, Dan Nordström Grant/research support from: MSD, Pfizer, Consultant for: AbbVie, BMS, MSD, Novartis, Roche, Pfizer, UCB, Speakers bureau: Novartis, UCB, Stella Aarestad Provan Consultant for: Novartis, Speakers bureau: Lilly, Johan Askling Grant/research support from: Karolinska Institutet (JA) has or has had research agreements with the following pharmaceutical companies, mainly in the context of the ATNIS national safety monitoring programme for rheumatology biologicals: Abbvive, BMS, MSD, Eli Lilly, Pfizer, Roche, Samsung Bioepis, and UCB. Consultant for: Karolinska Institutet has received remuneration for JA participating in ad boards arranged by Lilly, Novartis, and Pfizer., Kristian Zobbe: None declared, Lars Erik Kristensen Grant/research support from: MSD, Pfizer, Consultant for: AbbVie, Biogen, BMS, Celgene, Eli Lilly, Janssen Pharmaceuticals, and Novartis, Consultant for: Consultant for AbbVie, Amgen, Biogen, BMS, Celgene, Eli Lilly, Janssen Pharmaceuticals, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB Pharma, Speakers bureau: Pfizer, AbbVie, Amgen, UCB, BMS, Biogen, MSD, Novartis, Eli Lilly and Company, and Janssen Pharmaceuticals, Lene Dreyer Consultant for: MSD, UCB and Janssen Pharmaceuticals, Speakers bureau: MSD, UCB, and Janssen Pharmaceuticals, Speakers bureau: UCB, MSD, Eli Lilly and Janssen Pharmaceuticals.


Objectives: To investigate the impact of Olmesartan and Rosuvastatin on endothelial dysfunction and inflammation in PsA.

Methods: 54 PsA patients randomized to receive 24 weeks of treatment with Olmesartan (OLME) (10mg/day, n=18), Rosuvastatin (Rvs) (10mg/day, n=18), and placebo (PL) (n=18) as an adjunct to existing stable anti-rheumatic drugs. FMD assessed by AngioDefender. EPCs estimated by flow cytometry. Serum nitrite, TBARS, ICAM-1, VCAM-1 and lipid levels estimated at baseline and after treatment. Inflammatory measures included DAS28, DAPSA, ESR and CRP, pro-inflammatory cytokines. Quality of life and CV 10-year risk (SCORE high risk charts) were estimated using standard tools.

Results: Baseline levels of FMD and EPC population were impaired indicating endothelial dysfunction. Basal concentrations of inflammatory markers, pro-inflammatory cytokines and markers of endothelial dysfunction were elevated among three groups. After 24 weeks treatment, FMD improved significantly in rosuvastatin and olmesartan group as compared to placebo. [OLME vs. PL (p<0.01), Rvs vs. PL (p<0.01), Rvs vs. OLME (p=0.10)] (Fig.1A). EPCs and nitrite (Fig.1B) levels improved significantly in both rosuvastatin and olmesartan groups. Significant reduction found in ICAM-1 after rosuvastatin treatment (p<0.01) where as olmesartan significantly decreased VCAM-1 (p=0.04) and ICAM-1 levels (p=0.05). Both rosuvastatin and olmesartan resulted in significant reductions of DAS28, DAPSA, ESR, CRP, IL-6 (Fig.1C) and TNF-α (Fig.1D) as compared to placebo. There was a significant reduction in SCORE, HAQ-DI and SF-36 (PH) score after treatment with rosuvastatin and olmesartan.

Conclusion: Olmesartan and rosuvastatin improve endothelial dysfunction, inflammation, CV risk and quality of life in PsA patients. Olmesartan and Rosuvastatin lower the proinflammatory cytokines, especially TNF-α, that down regulates production of CRP, adhesion molecules and nitric oxide which in turn improves endothelial dysfunction. Both drugs also decrease nitrite concentration and improve the EPC population in PsA patients. The augmentation of EPCs by olmesartan and rosuvastatin represents a fascinating new approach for the management of PsA. However, Rosuvastatin in addition also favourably impacted ICAM-1 and lipid abnormalities. In contrast, olmesartan has beneficial effect on blood pressure. Thus, both rosuvastatin and olmesartan demonstrate immunomodulatory, vasculoprotective and cardioprotective potential in PsA mediated through anti-proinflammatory cytokine action.

REFERENCES:

High Body Mass Index (BMI) in Psoriatic Arthritis (PsA) is Associated with Higher Disease Activity in Joints and Skin, Impaired Quality of Life and More Disability: Results from the PsA Bio Study

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Background: The link between obesity and disease activity in PsA is unclear. Obesity has been associated with a poorer therapeutic response and higher treatment discontinuation rates in patients with PsA being treated with tumour necrosis factor inhibitors (TNFi). Recent data confirm the favourable effect of weight reduction on these factors. There are no data available for other biologics.

Objectives: To investigate the relationship between baseline overweight/obesity and disease activity, patient-reported outcomes and disability, in a large real-world cohort of patients with PsA starting biologic treatment with either ustekinumab (UST) or TNFi.

Methods: The PsABio study (ClinicalTrials.gov: NCT02627768) is an ongoing observational study evaluating efficacy, tolerability and persistence of 1st, 2nd- and 3rd-line UST or TNFi in PsA in 8 European countries1 when introduced as part of standard clinic. Baseline data of the study population were collected and analysed for BMI, disease activity (cDAPSA, psoriasis BSA), patient-perceived impact (PsAID-12), disability (HAQ-DI) and presence or history of CVD/MET. Descriptive statistics are used for the analysis. The patients were assessed with 66/68 joints count, Leeds enthesitis index, skin involvement, patient-reported outcomes and disability.

Results: The PsABio study enrolled 467 patients with PsA (Caspar criteria) and obesity (body mass index BMI ≥ 25 kg/m²) with or without treatment. The mean (SD) age 49.7 (12.5) years, 55.5% female. The mean (SD) baseline BMI (N=467) was 28.1 (5.8) kg/m², with 40.0% and 30.4% in BMI categories overweight (≥25–30) and obese (>30), respectively. In univariate analyses, obesity was associated with more severe disease (Table 1). More severe disease was associated with higher BMI (Table 2). In a regression model, obesity was independently associated with higher BMI (β = 0.09, p = 0.028) with higher patient-perceived disease activity impact measured by PsAID-12 (BMI: β = 0.16, p < 0.0001) and decreased HAQ-DI (BMI: β = 0.21, p < 0.0001).

Conclusion: This multi-country routine-care PsA cohort of patients in need of biologic treatment confirms the high prevalence of overweight/obesity and indicates an independent association between high BMI and disease activity as well as patient-reported impact of disease and disability. These results emphasize the need for lifestyle-directed approaches in PsA, such as overweight management in parallel with joint- and skin-focused treatment.

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Conclusion: Weight loss treatment with VLED in patients with PsA and obesity was associated with sustained weight reduction and lowered disease activity at 12-months follow-up.

Disclosure of Interests: Eva Klingberg Grant/research support from: None declared, Annelie Bilberg: None declared


Environmental influences on disease development_  

OP0009 RESISTANT STARCH INTAKE ALLEVIATES COLLAGEN-INDUCED ARTHRITIS IN MICE BY MODULATING GUT MICROBIOTA AND PROMOTING SCFAs PRODUCTION

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Background: Dietary intervention has been an auxiliary therapy in many diseases treatment. Increasing evidences indicate that dietary compositions vary in their impacts on gut microbial constitution and function capable of affecting the systemic immune status of the host. Recently, a high fiber diet (HFD) receives close attention due to its effective improvement in symptoms in metabolic diseases and inflammatory diseases. It is also reported that intake of fruits and vegetables can improve the clinical symptoms of rheumatoid arthritis (RA) to a moderate extent. However, it remains unclear how a high fiber diet cross-talks with gut flora and RA initiation or remission.

Objectives: To systematically evaluate the effect of a high fiber diet mainly composed of resistant starch, a new resource of soluble fiber, on collagen-induced arthritis (CIA) mice and gut microbial composition. Meanwhile, the relative mechanisms was explored in this study.

Methods: CIA was established by immunization mice with collagen on day 0 and 21. Arthritis severity was evaluated by clinical score, histological staining and micro CT. Fresh stool was collected and gut microbiota analyses were performed via 16s RNA sequencing. Gut barrier dysfuction was evaluated by detecting the Na+K+ channel and Claudin-1 gene expression in the intestine. ScFAs level was examined via GC-TOFMS and real-time PCR, respectively.

Results: High fiber feeding accelerated the arthritis remission in CIA mice, evidenced by the inflammatory cell infiltration reduction in the joints and bone erosion improvement. TH1, 2 and 17 cell population were not affected by HFD. While, regulatory T cell (Treg) percentages in the intestinal lamina propria and spleen were significantly increased with the gut flora alteration. Meanwhile, HFD-treated CIA mice had much higher levels of SCFAs in the blood and GPR43 gene expression in the intestine. Blocking SCFAs production by adding hogs extract β-acids into drinking water completely eliminated the beneficial effect of HFD on joint swelling, bone erosion and Treg cell expansion in CIA mice.

Disclosure of Interests: Eva Klingberg Grant/research support from: None declared, Annelie Bilberg: None declared

REFERENCES:


Disclosure of Interests: None declared


OP0010 CARTILAGE THICKNESS MODIFICATION WITH SPRIFERMIN IN KNEE OSTEOARTHRITIS PATIENTS TRANSLATES INTO SYMPTOMATIC IMPROVEMENT OVER PLACEBO IN PATIENTS AT RISK OF FURTHER STRUCTURAL AND SYMPTOMATIC PROGRESSION: POST-HOC ANALYSIS OF THE PHASE II FORWARD TRIAL

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Background: Results from the 5-year Phase II FORWARD study showed significant dose-dependent modification of total femorotibial joint (TFTJ) cartilage thickness change with sprifermin at 2 and 3 years, by quantitative MRI. Total Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores improved by >50% in all treatment groups, excluding placebo (PBO). Selection of a patient (pt) subgroup with higher pain scores and lower joint space width (JSW) at baseline (BL), to identify pts who are at risk of further structural and symptomatic progression, may facilitate better WOMAC discrimination.

Objectives: Post-hoc analysis to evaluate cartilage thickness changes and symptomatic outcomes in an “at risk” subgroup of pts (BL medial or lateral minimum [m]JSW 1.5–3.5 mm and BL WOMAC pain score of 40–90).

Methods: Pts in FORWARD were randomized 1:1:1:1:1 to: sprifermin 100 μg every 6 months (q6mo); 100 μg q12mo; 30 μg q6mo; 30 μg q12mo; and PBO. The treatment period was 2 years, with an extended follow up at 3 years. Post-hoc analysis was conducted in the “at risk” subgroup. Treatment effects were estimated using a repeated measures model, controlling for BL, treatment, time, country and treatment by time interaction. Linear dose-effect trend tests were performed exploratively at each timepoint. Confidence intervals (CIs) were adjusted for multiplicity of treatments using Dunnett adjustment.

Results: 161/549 (29%) pts met criteria for the “at risk” subgroup. In this subgroup, BL characteristics were balanced between treatment arms. Pts in the PBO arm had more cartilage loss and greater JSW changes at BL compared to other groups. Treatment effects were estimated using a repeated measures model, controlling for BL, treatment, time, country and treatment by time interaction. Linear dose-effect trend tests were performed exploratively at each timepoint. Confidence intervals (CIs) were adjusted for multiplicity of treatments using Dunnett adjustment.

Disclosure of Interests: None declared


Pharmaceutical pipeline in OA
EFFECT OF LIRAGLUTIDE ON BODY WEIGHT AND
PAIN IN THE TREATMENT OF OVERWEIGHT AND
KNEE OSTEOARTHRITIS: A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY

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Background: Weight loss is recommended as treatment of concomitant knee osteoarthritis (OA) and overweight. The GLP-1 receptor agonist liraglutide has been shown effective in maintaining or even further reducing weight loss, but the compound has not been tested in a population of patients with overweight and knee OA.

Objectives: The objective of this trial was to investigate if liraglutide in a 3 mg/day dosage was effective in maintaining weight loss and symptomatic effects 52 weeks after an initial 8-week dietary-based weight loss intervention dosing in patients with overweight and knee OA.

Methods: Patients with overweight or obesity and knee OA participated in a randomised, double blind, placebo-controlled, parallel group, single-centre trial. Patients were provided an initial 8-week run-in diet intervention (week -8 to 0) including a low-calorie diet from Cambridge Weight Plan and dietetic counselling. At week 0 patients who had lost at least 5% of their initial body weight were randomised to liraglutide 3 mg/day or placebo for 52 weeks. The co-primary outcomes were changes in body weight and the KOOS pain subscale from week 0 to 52.

Results: 168 patients (Kellgren-Lawrence grade 1-3) were enrolled in the initial 8-week diet intervention and 156 patients were randomised (Figure 1). Before randomisation the 156 patients had lost 12.46 kg (SD:3.82) (∼12%) and improved in KOOS pain corresponding to 11.86 points (SD.15.13) (∼19%). Baseline characteristics were similar in the intervention and control groups. From baseline to 52 weeks there was a statistically and clinically significant difference in the weight loss between the liraglutide and the placebo groups (mean -2.76 and 1.17 kg, respectively; group difference, 3.93 kg; 95%CI -6.85 to -1.02; p=0.008), there was no difference between groups in change in KOOS pain (mean changes: 0.35 and -0.14 kg respectively; group difference, 0.50 kg; 95%CI -0.90 to 1.90; p=0.51).

Additional analyses of the weight loss effect showed no differences between baseline and end of intervention in the subgroups at 2 and 3 years. There was a statistically and clinically significant difference in the WOMAC pain subscale improvements vs PBO increased over time and were significant at Year 3. This supports further investigation of liraglutine as a potential disease-modifying osteoarthritis drug in a targeted population where structural improvement may translate into symptomatic benefit vs PBO within a reasonable timeframe.
-0.55 points, respectively; group difference, 0.89 points; 95%CI -3.89 to 5.68; p=0.713). Week 52 least squares means for body weight and knee pain intervention significantly reduced body weight and knee pain. Liraglutide treatment added after the initial diet-induced weight loss provided further weight loss over 1 year but did not reduce knee pain any further compared to placebo.

### Disclosure of Interests:

Henrik Gudbergsen Grant/research support from: From Novo Nordisk, Employee of: Novo Nordisk, Speakers bureau: Pfizer, Anders Onggaard: None declared, Marius Henriksen Consultant for: Advisory board member for Thussane Group, Eva Ejersen Wahreths: None declared, Henriët Bijl Grant/research support from: AbbVie Inc, The Oak Foundation, Speakers bureau: Roche, Sabrina Mai Nielsen: None declared, Mikael Boesen Shareholder of: Image Analysis Group, UK, Grant/research support from: Image Analysis Group, Oak Foundation, EUROSTARs, Consultant for: Essato, Eli Lilly, Celgene, Carestream, UCB, Abbvie, Pfizer, Astra Zeneca, Roche, Siemens, Image Analysis Group, Speakers bureau: Carestream, Eli Lilly, Essato, Abbvie, UCB, Pfizer, Image Analysis Group, Filip Krag Knop Grant/research support from: AstraZeneca, Gubra, Novo Nordisk, Sanofi and Zealand Pharma, Consultant for: Agen, Astra Zeneca, Eli Lilly, Novo Nordisk, Sanofi and Zealand Pharma, Speakers bureau: Agen, AstraZeneca, Boehringer Ingelheim, Eli Lilly, Medimmune, MSD/ Merck, Mundipharma, Norgine, Novo Nordisk, Sanofi and Zealand Pharma, Ane Asstrup Grant/research support from: AA is currently involved in projects conducted by research groups at Department of Nutrition, Exercise and Sport, Faculty of Science, University of Copenhagen, funded by grants from Novo Nordisk DK, & Saniona, DK, Consultant for: AA is member of scientific advisory boards for BioCare Copenhagen & Novo Nordisk DK. He acts as consultant for Acino, Switzerland & Saniona DK, Marianne Ugen Rasmussen: None declared, Cécile Redgaard Barthody: None declared, Cecile Daugaard: None declared, Else Marie Bartels: None declared, Karen Ellegaard: None declared, Bent Lilenthal Heilmann: None declared, Lars Erik Kristensen Grant/research support from: UCB, Biogen, Janssen Pharmaceuticals, and Novartis, Consultant for: Consultant for: UCB, Biogen, BMS, Celgene, Eli Lilly, Janssen Pharmaceuticals, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB Pharma., Speakers bureau: Pfizer, AbbVie, Amgen, UCB, Biogen, MSD, Novartis, Eli Lilly and Company, and Janssen Pharmaceuticals. DOI: 10.1136/annrheumdis-2019-eular.1375

### What’s new: Latest news on biological treatment

#### OP0012

**EFFECTIVENESS OF TNFI AFTER A FIRST SWITCH IS LOWER IN PATIENTS WITH EARLY AXIAL SPONDYLOARTHRITIS: A LATERALISATION ANALYSIS OF THE DESIR COHORT**

Marion Pons1, Sylvie Chevret2, Karine Briot1, Marie-Antoinette D’Agostino3, Christian Roux1, Maxime Dougados1,2, Anna Molto1,2, Laurence Carton1, Claire Cardon1, Francoise Alliot Launois1, Gerard Chales1, Christian Roux1,2, Maxime Dougados1,2, Anna Moltó1,2, Laurence Carton1, Claire Cardon1, Francoise Alliot Launois1, Gerard Chales1.

#### Background:

Some contradictory data has been reported on the effectiveness of a second and third line of TNFi in early axial spondyloarthritis (axSpA). **Objectives:** To evaluate the effectiveness after a first and second TNFi switch, in real life conditions, over 5 years of follow-up in an early axSpA population.

#### Methods:

Observational prospective French cohort (DESIR) with 5 years of follow-up, including 708 TNFi-naïve early axSpA patients. Study visits were scheduled every 6 months in the first two years of follow up then yearly up to 5 years. Treatment (TNFi or other) was at the discretion of the treating rheumatologist(s). The characteristics of patients who received a second and a third TNFi were compared to those who never switched. Effectiveness was defined by the drug survival of the first, second and third TNFi were estimated by the Kaplan-Meier method, and compared using the log-rank test.

#### Results:

Of the 708 patients included in the analysis, 258 (36.4%) patients initiated a first TNFi during the 5 years of follow up. Of these, 127/258 (49.2%) patients switched to a second TNFi, and among them 59/127(46.5%) switched to a third TNFi. Patients who switched to a second or a third TNFi were more frequently older, predominantly females, HLA-B27 negative with MRI and radiographic sacroiliitis negative, without history of peripheral arthritis, and with higher BASFI and BASDAI scores at baseline of the DESIR cohort (see table). Estimated median drug survival for the first, second and third TNFi was 21.7 months [95%CI 17.6-33.8], 16 months [95%CI 15.1-24.4] and 25 months [95%CI 11.8-NA] respectively. Drug survival was significantly extended for the first TNFi compared to the second one (p<0.04), but no differences were observed between the 2nd and the 3rd TNFi.

#### Conclusion:

Our study suggests a poorer TNFi effectiveness after a first switch in real-life conditions in early axial spondyloarthritides.

#### Disclosure of Interests:

Marion Pons: None declared, Sylvie Chevret: None declared, Karine Briot Consultant for: Karine Briot has received consultancy honoraria and conference fees from UCB, Amgen, Lilly and MSD, Maria-Antoinetta D’Agostino: None declared, Christian Roux Grant/research support from: Alexion, Amgen, UCB, maxime dougdou Grant/research support from: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma, Consultant for: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma, Anna Moltó: None declared DOI: 10.1136/annrheumdis-2019-eular.1329

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### OP0013-PARE

**AFLAR’s – FRENCH LEAGUE AGAINST RHEUMATISM – POSITION AND PATIENT INFORMATION ACTION ABOUT BIOSIMILAR MEDICINES IN FRANCE**

Laurence Carton1, Claire Cardon1, Françoise Alliot Launois1, Gerhard Chales1, Brigitte Lisée2, Laurent Grange2,3, PATIENTS’ of AFLAR, 1Association Française de Lutte AntiRhumatismale A.F.L.A.R, Paris, France; 2Association Française de Lutte AntiRhumatismale A.F.L.A.R, Paris, France; 3University hospital of Grenoble Alps-Stud hospital, Rheumatology, Écholeurs, France

#### Background:

20 years after biotherapies were introduced in rheumatic diseases treatment in France, biosimilars are a new medical and economic issue in terms of therapeutic opportunities, and innovative treatment spreading and development. Patients’ rights - quality of life, information on treatment and safety - as well as public health cost management, medical and other caregivers’ practices are involved.

#### Objectives:

AFLAR wants to play an active role in these fields, as about one million of patients with inflammatory rheumatic diseases, and next other diseases, are concerned.

#### Methods:

AFLAR’s patient led board (1), medical and scientific experts and especially expert patients have been working together to:

1. state AFLAR’s position about biosimilars
2. define the most adapted association’s actions in the field of biosimilars
3. create the most proper tool to inform and empower patients to their rights, especially in the field of treatment efficacy and safety.

#### Results:

A position paper leading to a press release dated Dec. 7th, 2018 prior to national rheumatology medical congress opening has been achieved. An informative tool to be used for shared medical decision when biosimilars are involved, is currently in progress. AFLAR’s position on biosimilars includes 2 statements and 6 advises addressed to patients, caregivers and other stakeholders:

#### Statements:

1. Biosimilars are a medical and healthcare cost reduction effective solution in rheumatic diseases treatment
2. Biosimilars have scientifically proved their efficacy and safety in past and ongoing studies; drug safety monitoring is ensured by national and European drug safety agencies.

#### Advices:

1. Further continuous clinical post-marketing studies should be achieved, and their results easily available to patients
2. Patient should be properly informed each time a biosimilar is proposed if their results easily available to patients.
3. Biosimilar drug can be prescribed for cost reduction reason as initial biotherapies treatment, when not contraindicated
4. Blind random switch from originator to biosimilar and among biosimilar products should not be done, based on precautionary principle
5. Patient should be precisely informed of product with biosimilar name (not only international non–proprietary name), and batch number, as this allows
mandatory pharmacovigilance by professionals and patients. As per law (2) and professional ethics, patient preference and right to informed consent must prevail.

6. Self-assessment surveys, and patient reported outcomes using studies, should be encouraged. These are facilitated by new information technologies and practices and devices.

Conclusion: The information tool will be proposed in the form of an information letter to be remitted by professionals to patient when biosimilar prescription or initiation is planned. The process includes:

1. creation of document by expert patients
2. user testing of tool (assessment about understandability and usefulness), in hospital departments, patient groups and on-line
3. knowledge assessment and opinion gathering among patients about biosimilars.

REFERENCES:
[1] According to its current by-laws, AFLAR board consists of at least 2/3 of persons affected with/considered by rheumatic diseases, and/or presidents of affiliated patient associations.

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WEDNESDAY, 12 JUNE 2019
How to perform low-budget high-quality research

NO ASSOCIATION BETWEEN THE PROPORTION OF ELDERLY PEOPLE AND TRIAL RETENTION IN RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS TRIALS: A SYSTEMATIC REVIEW WITH META-REGRESSION ANALYSES

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Background: The elderly (defined by an age of ≥65 years) are underrepresented in current rheumatoid arthritis (RA) and osteoarthritis (OA) trials. This is partly due to age-related exclusion criteria. Investigators might be reluctant to include more elderly people because they fear reduced trial retention.

Objectives: To evaluate whether the proportion of included elderly individuals (PE) is associated with trial retention in current RA and OA trials.

Methods: This study is registered with protocols.io (dx.doi.org/10.17504/protocols.io.uan62e). In our previous study,1 two systematic searches in MEDLINE and Cochrane had yielded randomized controlled trials (RCTs) in rheumatoid arthritis (RA) and osteoarthritis (OA) on any intervention published in 2016 and 2017. Here we included all trials reporting data on retention. We either extracted the PE from the research manuscript or estimated it from an assumed (truncated) normal distribution. We coded retention into proportional effect sizes (logit-transformed for analysis and back-transformed for reporting). Subsequently, multiple mixed effects meta-regression models with several covariates assessed whether there is an association between the PE and trial retention. Sensitivity analyses evaluated whether associations were connected to attrition due to lack of efficacy (LoE) or adverse events (AE).

Results: 243 RCTs comprising 48,288 participants were deemed eligible, and 227 RCTs provided complete data on overall retention and all covariates. Pooled trial retention (random effects) was 88% (95%-CI 87% to 90%; p² = 90%). The PE was not associated with trial retention in the unadjusted (slope β = 0.0 [-0.0 to 0.0]; p = 0.97; Figure 1), or any protocolized adjusted model (p-values depending on the adjustment: 0.14 to 0.90). Of all included covariates, only study duration (longer study duration being associated with inferior retention; p < 0.001) and the type of intervention (surgical interventions averaging the highest retention; psychological interventions averaging the lowest retention; p < 0.001) were associated with trial retention. Post hoc analyses allowing for interaction revealed a small statistically significant association between the PE and trial retention in pharmacological (retention increasing with the PE) and physical/physiotherapeutic (retention decreasing with the PE) interventions. Further sensitivity analyses showed no significant associations between attrition due to LoE or AE and the PE in any model.

Conclusion: Trial retention in RA and OA trials is very high, and unaffected by the proportion of elderly.

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INCIDENCE, RISK FACTORS AND VALIDATION OF THE RABBIT SCORE FOR SERIOUS INFECTIONS IN A REAL LIFE PROSPECTIVE STUDY OF PATIENTS WITH RHEUMATOID ARTHRITIS: DATA FROM 1,549 PATIENTS

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Background: Identification of the risk factors for the development of serious infections in patients with rheumatoid arthritis (RA) is critical for designing preventive measures and early treatment.

Objectives: To identify risk factors for serious infections and to validate the RABBIT risk score in RA patients in daily clinical practice.

Methods: Multicenter prospective study of RA patients in Greece. Demographics, disease characteristics, treatments and co-morbidities were prospectively collected via a web-based platform at baseline and one year later. The observed incidence of serious infections was compared to the one estimated by the RABBIT score.

Results: 1,549 RA patients were included (women: 78%, mean age: 63 years, mean disease duration: 10.4 years, RF and/or anti-CCP positive: 54%, mean DAS28: 3.4, mean HAQ: 0.5, bDMARD use: 46%, corticosteroid use: 36%). During follow-up, 38 serious infections were recorded (incidence: 2.3/100 patient-years). Patients who developed a serious infection had longer disease duration (14.2 vs. 10.3 years, p=0.02), higher HAQ at baseline (0.85 vs. 0.5, p=0.006), a history of previous serious infection (26% vs. 10%, p=0.002) and were more likely to have chronic lung disease (23% vs. 9%, p=0.008) or cardiovascular disease (23% vs. 11%, p=0.04). Disease duration (OR: 1.04, CI: 1.01-1.08, p=0.025), history of previous infection (OR: 3.3, CI: 1.3-8.1, p=0.01) and chronic lung disease (OR: 3.03, CI: 1.77-5.85, p=0.005) remained statistically significant in multivariate logistic regression analysis. NDUMARD use was not associated with increased risk in uni- or multi-variate analysis. Data for RABBIT score calculation were available in 1,349 patients. Estimated incidence per 100 patient-years was divided in Q1-Q4 quartiles (25-75th percentiles: 0.94-1.35-2.15). Estimated and observed incidence rates were in Q1: 0.8 and 0.54, Q2: 1.14 and 0.97, Q3: 1.76 and 1.84 and Q4: 3.7 and 5.6, respectively (Hosmer-Lemeshow test, p=0.9).

Conclusion: In this large, real-life, prospective study of RA patients, the incidence of serious infections was 2.3/100 patient-years. Longer disease duration, history of previous serious infections and chronic lung disease were independently associated with the development of serious infections. RABBIT score predicted rather accurately the risk for serious infections in our cohort.

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Scientific Abstracts

WHAT TO CHOOSE: A SECOND TNFI OR AN ALTERNATIVE CLASS OF BIOLOGIC FOR PATIENTS WITH JIA WHO HAVE FAILED THEIR FIRST TNFI

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Background: Biologic therapies, second-line treatment after failure of methotrexate, have revolutionised treatment pathways and outcomes for patients with juvenile idiopathic arthritis (JIA). The expanding choice allows patients to switch biologic if current treatment is not working. Current NHS England guidelines recommend most patients with JIA to start a tumour necrosis factor inhibitor (TNFI), and if that fails switch to a second TNFI rather than change class. The evidence base for this in JIA is limited.

Objectives: The aim of this study was to compare the effectiveness of a second TNFI versus an alternative class of biologic therapy in patients with polyarticular JIA following initial TNFI therapy in routine clinical practice.

Methods: Analysis included patients with JIA starting a second biologic following initial TNFI therapy in two UK cohort studies; B Spar-ETN and BCRD. Within the studies, data percent per 12 months, 6 months, 1 year, 2 years, 3 years and 5 years of data per patient were collected of efficacy and anti-rheumatic therapy. Patients with extended oligoarticular and polyarticular (rheumatoid factor positive and negative) JIA were included. Patients with a history of uveitis at start of second biologic were excluded. Patient characteristics and anti-rheumatic therapy were compared between patients starting a second TNFI versus an alternative class. Kaplan-Meier drug survival was used to assess drug survival on second biologic. Stop reasons of second biologic were described. Change in core outcome variables, JADAS-71, American College of Rheumatology Paediatric 50% response (ACR Pedi 50), and Minimal Clinically Important Difference (MCID; ≥0.13 reduction in CHAQ) from baseline to one year was compared between the two cohorts. Multiple imputation and propensity scores were used to account for missing baseline co-variate data and adjust for confounding by indication.

Results: 151 patients with polyarticular JIA starting a second biologic up to 13-Nov-2018 were included; 115 (76%) a second TNFI, 36 (24%) an alternative class. Patient characteristics at the start of second biologic were mostly similar except patients starting a non-TNFI had lower CRP levels (p=0.001). There was no difference in second biologic drug survival between the two cohorts (p=0.8), with approximately 60% remaining on drug by one year. The majority reported inefficacy as stop reason (51%). There was no difference between one year improvement in core outcome variables or JADAS-71 after start of second biologic, and no difference in the odds of achieving ACR Pedi 50 response (odds ratio 0.8; 95% confidence interval [CI] 0.3, 2.5; p=0.7) and ACR Pedi 70 (OR 1.0; CI 0.3, 3.1; p=0.9) between patients starting a second TNFI versus a non-TNFI.

Conclusion: In this real-world cohort of children and young people with JIA starting a second biologic following initial TNFI therapy failure, there appears to be no difference between drug survival and effectiveness outcomes in those patients switching to a second TNFI compared with a non-TNFI biologic. Further research on larger sample sizes is required to know whether there is any initial advantage to switching class of drug following failure of a first TNFI.
Disclosure of Interests: Lianne Kearsley-Fleet: None declared, Rebecca Davies: None declared, Jennifer Page: None declared, Eileen Baldam: None declared, Michael Beresford: None declared, Helen Foster: None declared, Taunton Southwood: None declared, Wendy Thomson: None declared, Kimme Hyrich: Grant/research support from: Grants to institution: BMS, Pfizer, UCB


OP0017

NINTEDANIB REDUCED DECLINE IN FORCED VITAL CAPACITY ACROSS SUBGROUPS OF PATIENTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE: DATA FROM THE SENSICS TRIAL

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Background: In the SENSICS trial, nintedanib reduced the progression of interstitial lung disease associated with systemic sclerosis (SSc-ILD) compared with placebo, as demonstrated by a significantly lower rate of decline in forced vital capacity (FVC) over 52 weeks (primary endpoint).

Objectives: To assess the effect of nintedanib on the rate of decline in FVC in the SENSICS trial across pre-specified subgroups defined by baseline characteristics.

Methods: Patients with SSc-ILD with onset of first non-Raynaud symptom <7 years before screening and >10% fibrosis of the lungs on a high-resolution computed tomography scan were randomised to receive nintedanib 150 mg bid or placebo double-blind. The annual rate of decline in FVC (ml/year) assessed over 52 weeks (primary endpoint) was analysed in the overall population using a random coefficient regression model (with random slopes and intercepts) including anti-topoisomerase I antibody (ATA) status, age, height, gender and baseline FVC as covariates. Analyses in subgroups by baseline characteristics included additional terms for treatment-by-subgroup and treatment-by-subgroup-by-time interaction.

Results: A total of 576 patients were treated (288 in each group). Most (75.2%) of patients were female, 51.9% had diffuse cutaneous SSc, and 48.4% were taking mycophenolate at baseline. Mean ± SD age was 54.0 ± 12.2 years and 21.4% of patients were female, 51.9% had diffuse cutaneous SSc, and 48.4% were taking mycophenolate at baseline. Mean ± SD age was 54.0 ± 12.2 years and 21.4% of patients were female, 51.9% had diffuse cutaneous SSc, and 48.4% were taking mycophenolate at baseline. Mean ± SD age was 54.0 ± 12.2 years and 21.4% of patients were female, 51.9% had diffuse cutaneous SSc, and 48.4% were taking mycophenolate at baseline. Mean ± SD age was 54.0 ± 12.2 years and 21.4% of patients were female, 51.9% had diffuse cutaneous SSc, and 48.4% were taking mycophenolate at baseline. Mean ± SD age was 54.0 ± 12.2 years and 21.4% of patients were female, 51.9% had diffuse cutaneous SSc, and 48.4% were taking mycophenolate at baseline. Mean ± SD age was 54.0 ± 12.2 years and 21.4% of patients were female, 51.9% had diffuse cutaneous SSc, and 48.4% were taking mycophenolate at baseline. Mean ± SD age was 54.0 ± 12.2 years and 21.4% of patients were female, 51.9% had diffuse cutaneous SSc, and 48.4% were taking mycophenolate at baseline. Mean ± SD age was 54.0 ± 12.2 years and 21.4% of patients were female, 51.9% had diffuse cutaneous SSc, and 48.4% were taking mycophenolate at baseline. Mean ± SD age was 54.0 ± 12.2 years and 21.4% of patients were female, 51.9% had diffuse cutaneous SSc, and 48.4% were taking mycophenolate at baseline. Mean ± SD age was 54.0 ± 12.2 years and 21.4% of patients were female, 51.9% had diffuse cutaneous SSc, and 48.4% were taking mycophenolate at baseline. Mean ± SD age was 54.0 ± 12.2 years and 21.4% of patients were female, 51.9% had diffuse cutaneous SSc, and 48.4% were taking mycophenolate at baseline. Mean ± SD age was 54.0 ± 12.2 years and 21.4% of patients were female, 51.9% had diffuse cutaneous SSc, and 48.4% were taking mycophenolate at baseline. Mean ± SD age was 54.0 ± 12.2 years and 21.4% of patients were female, 51.9% had diffuse cutaneous SSc, and 48.4% were taking mycophenolate at baseline. Mean ± SD age was 54.0 ± 12.2 years and 21.4% of patients were female, 51.9% had diffuse cutaneous SSc, and 48.4% were taking mycophenolate at baseline. Mean ± SD age was 54.0 ± 12.2 years and 21.4% of patients were female, 51.9% had diffuse cutaneous SSc, and 48.4% were taking mycophenolate at baseline. Mean ± SD age was 54.0 ± 12.2 years and 21.4% of patients were female, 51.9% had diffuse cutaneous SSc, and 48.4% were taking mycophenolate at baseline. Mean ± SD age was 54.0 ± 12.2 years and 21.4% of patients were female, 51.9% had diffuse cutaneous SSc, and 48.4% were taking mycophenolate at baseline. Mean ± SD age was 54.0 ± 12.2 years and 21.4% of patients were female, 51.9% had diffuse cutaneous SSc, and 48.4% were taking mycophenolate at baseline. Mean ± SD age was 54.0 ± 12.2 years and 21.4% of patients were female, 51.9% had diffuse cutaneous SSc, and 48.4% were taking mycophenolate at baseline. Mean ± SD age was 54.0 ± 12.2 years and 21.4% of patients were female, 51.9% had diffuse cutaneous SSc, and 48.4% were taking mycophenolate at baseline. Mean ± SD age was 54.0 ± 12.2 years and 21.4% of patients were female, 51.9% had diffuse cutaneous SSc, and 48.4% were taking mycophenolate at baseline.

Conclusion: Nintedanib is effective at reducing ILD progression in a broad range of patients with SSc-ILD.
(KO) mice were bred to generate homozygous KOs and mouse articular cartilage was isolated to culture chondrocytes. Results: miR-34a expression was significantly elevated in the plasma as well as cartilage and synovium of TKA patients (KL IV) compared to healthy controls and early OA patients (KL I), respectively. Similarly, miR-34a was significantly downregulated in mouse knee joints (cartilage and synovium) at 10 weeks post OA surgery compared to sham. To identify the biological effects of miR-34a on chondrocyte and synovial fibroblast (SF), functional studies were conducted in vitro. Chondrocytes treated with miR-34a mimic had a significant reduction of SIRT1 (a direct target of miR-34a), anabolic (type II collagen and aggrecan) and autophagy markers, as well as, elevated catabolic markers (MMP13), suggesting that miR-34a contributes to cartilage degeneration. Chondrocytes treated with miR-34a inhibitor reversed these destructive effects. SFs treated with miR-34a mimic expressed elevated inflammatory (TNF-α, IL-6), fibrotic (TGF-β), Type 1 Collagen), and autophagy markers, suggesting that miR-34a is involved in mediating synovial inflammation and fibrosis. SFs treated with miR-34a inhibitor reversed these effects.

In vivo, intra-articular injection of miR-34a mimic induced cartilage damage, loss of proteoglycan content, and elevated cell death markers (PARP p85 and Caspase 3) in the articular cartilage. To confirm the destructive effects of miR-34a in the articular cartilage, we used miR-34a KO mice. miR-34a KO mice further confirmed that general inhibition of miR-34a resulted in marked elevation in the expression of anabolic markers (type II collagen and aggrecan) and decreased expression of catabolic ADAMTS-5 in the articular cartilage. To test the therapeutic potential of blocking miR-34a, we intra-articularly injected miR-34a inhibitor in mice subjected to OA surgery. Results showed marked reduction in the severity of cartilage degeneration in mice treated with miR-34a inhibitor.

Conclusion: This study, for the first time, demonstrates miR-34a as a crucial mediator involved in OA pathogenesis and as a potential therapeutic target for lim- iting cartilage destruction during OA.

Disclosure of Interests: None declared

OP0020

LESS IS MORE: ANA-LYING THE IMPACT OF REPEATED ANTIMICROBIAL ANTIBODY TESTING

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Background: Minimising unnecessary tests is a global health economic priority with multiple initiatives in place to avoid inappropriate healthcare utilisation(1) and harm. Anti-nuclear antibody (ANA) testing is frequently performed as a diagnostic test for autoimmune conditions, such as systemic lupus erythematosus (SLE) or as a screening test in patients with inflammatory or musculoskeletal symptoms. The value of serial testing in the monitoring of such conditions is unclear and false positive tests can lead to unnecessary further investigation and increased patient harm.

Objectives: To evaluate the frequency of repeated ANA testing as a prelude to Electronic Medical Record (EMR) test alert design in an Australian healthcare network. The primary endpoint was calculation of the total cost associated with repeated testing and whether a longitudinal change in ANA resulted in any new ANA associated rheumatological diagnoses. Our secondary endpoint was the examination of baseline ANA testing behaviours.

Methods: We retrospectively analysed data from a multi-centre tertiary health network in Melbourne, Australia across a 7-year period (19 March 2011 to 23 July 2018). ANA and other autoimmune test results were obtained from the hospital pathology system with a positive ANA cut off set at 1:160. Clinical information was sourced from clinical information systems on patients who had a change in ANA from negative to positive on repeat testing. The associated cost of repeated ANA testing was calculated based on the baseline cost to the public system.

Results: A total of 36,715 ANA tests (excluding 980 cancelled same-day requests) were performed in 28,840 patients. Of these, 14,058 (38.3%) were positive with females accounting for 9,265 (65.9%, p<0.001). The most frequent ANA patterns were homogenous (47.4%) and nucleolar (23.3%). ANA titres were as follows; 1:160 (41.4%), 1:320 (15.3%), 1:640 (13.1%) and 1:1280 (29.2%). 7,875 (21.4%) of tests were repeat tests. Of these 511 (6.5%) results changed from negative to positive. The median time between a negative ANA result to the first positive result was 1.71 years (IQR 0.50-3.55). Clinical information was captured for a median duration of 1.24 years (IQR 0.50-2.07) following a positive ANA result. A change to positive ANA was associated with a new ANA-associated rheumatological diagnosis in only 5 cases (2 SLE, 1 scleroderma and 2 undifferentiated connective tissue disease) with a positive predictive value calculated at 0.01. When comparing patients who with a new diagnosis to those with no new diagnosis, there was no difference between ANA titre, pattern, duration to first positive ANA, ordering location or clinician, or age of first positive ANA test. The direct total cost for the government of all ANA testing was AUD$903,189, of which repeat testing contributed AUD$193,725.

Conclusion: Repeat ANA testing after a negative result had limited utility in the diagnosis of ANA associated rheumatological conditions with a positive predictive value of only 0.01, and resulted in high cost. New technology and clinical alert systems may help reduce unnecessary testing with potential significant direct cost savings when extrapolated across the Australian healthcare system.
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PREDICTING SEVERE INFECTION IN REPEAT CYCLES OF RITUXIMAB AND EFFECTS OF HYPOGAMMAGLOBULINAEMIA IN THE TREATMENT OF RHEUMATIC AND MUSCULOSKELETAL DISEASES

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Background: Rituximab (RTX) is effective in treating various rheumatic and musculoskeletal diseases (RMDs). Repeat cycles are often required for disease control but may lead to hypogammaglobulinaemia. Low IgG at baseline has been associated with an increased risk of severe infection event (SIE) post-RTX. However, there are limited data on predictors of SIEs in repeat cycles including immunoglobulin levels and B-cell numbers as well as outcomes of hypogammaglobulinaemia.

Objectives: To assess predictors of SIEs in repeat RTX cycles and effects of hypogammaglobulinaemia in terms of SIEs rates, humoral response and its persistence post-cessation of RTX.

Methods: A retrospective study was conducted in the first 700 consecutive ARD patients treated with at least a cycle of RTX in Leeds. IgM, IgA and IgG levels were measured at baseline and 4-6 months after each cycle. For cycles 2-4 (C2-4), predictors for SIEs were analysed using mixed-effects logistic regression analysis.

Results: 550 patients were female, mean(SD) age 56(16) years and median (IQR) disease duration 7.9(3.4-15.0) years. 507/8 (72%) had RA, 94(13%) SLE, 49(7%) AAV, 14(2%) idiopathic inflammatory myopathies, 9(1%) pSS, 5(1%) APS, 6(1%) SSc and 16(3%) other CTDs. 364(52%) were biologic-naïve and 514(73%) were on therapy as outcome (median follow-up 17 months). Analyses were corrected for age, gender, patient's country of origin, smoking status, education level, BMI, EGFR mutation status, tobramycin exposure, comorbidities and RTX specific for RA.

Conclusion: IgG (9.7 PY), 5/8(64%) had impaired humoral response to pneumococcal and influenza vaccinations. For cycles 2-4, in multivariable analysis, lower IgG as this is a consistent predictor of SIE and may affect infection outcomes when patients are switched to a different bDMARD. For those at risk of SIEs, reduction of corticosteroid dose could reduce risk. Low B-cell numbers were not predictive of SIEs.

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OP0201

DO MRI-DETECTED EROSIONS IN PATIENTS WITH CLINICALLY SUSPECT ARTHRALGIA PREDICT PROGRESSION TO RHEUMATOID ARTHRITIS? A LONGITUDINAL STUDY

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Background: Radiographic joint erosions are a hallmark of Rheumatoid Arthritis (RA), MRI is more sensitive than radiographs in detecting erosions. It is unknown if MRI-detected erosions are predictive for RA-development in patients with Clinically Suspect Arthritis (CSA).

Objectives: We investigated the prognostic value of MRI-detected erosions (any MRI-erosion, or MRI-erosion characteristics that were recently identified as specific for RA) in CSA.

Methods: Patients presenting with CSA (n=491) underwent contrast-enhanced 1.5T MRI of the wrist, metacarpophalangeal (MCP) and metatarsophalangeal (MTP) joints at baseline. MRIs were scored according to RAMRIS. Presence of any MRI-erosion (erosion score ≥1) and RA-specific erosion characteristics as identified previously (grade ≥2 erosions, erosions in MTP5, erosions in MTP1 if aged <40) were studied with clinically apparent inflammatory arthritis development as outcome (median follow-up 17 months). Analyses were corrected for sex, age, CRP, ACPA and MRI-detected inflammation.

Results: Erosions were present in 20.6% of patients. Presence of erosions was not associated with arthritis development (HR multivariable analysis 0.85 (95% CI 0.52-1.40)). Also the different erosion characteristics were not predictive in CSA-patients (grade ≥2 HR 1.99 (95% CI 0.40-4.14), erosions in MTP5 HR 0.89 (95% CI 0.38-2.09) and MTP1 if aged <40 HR 0.98 (95% CI 0.23-4.21)). MRI-erosions were more prevalent in ACA-positive patients (32.3% versus 18.8%, p=0.02). However, no association with arthritis development was observed in both subgroups.

Conclusion: MRI-detected erosions in hands and feet of patients with CSA were not predictive for arthritis development. These data warn against overinterpretation of MRI-detected erosions in CSA.

Disclosure of Interests: Fenne Wouters: None declared, Xanthe Mathijssen: None declared, Debbie Boeters: None declared, Robin Ten Brinck: None declared, Annette van der Helm - van Mil Grant/research support from: The research leading to these results has received funding from the European Research Council (ERC) under the European Union’s Horizon 2020 research and innovation programme (Starting grant, agreement No 714332) and from the Dutch Arthritis Foundation. The funding source had no role in the design and conduct of the study., Ellis Niemantsverdriet: None declared DOI: 10.1136/annrheumdis-2019-eular.2991

LB0001

EFFICACY AND SAFETY OF FILGOTINIB FOR PATIENTS WITH RHEUMATOID ARTHRITIS WITH INADEQUATE RESPONSE TO METHOTREXATE: FINCHI PRIMARY OUTCOME RESULTS

Bernard Combe1, Alan Kivitz1, Yoshiai Tanaka2, Désirée van de Heije3, Franziska Matzikes4, Beatriz Bartok4, Lei Ye5, Ying Guo1, Chantal Tasset1, John Sundy6, Neelakar Mozaffarian7, Robert B.M. Landewe8, Sang-Hee Bae9, Edward C. Keystone10, Peter Nash11, CHU Montpellier, Montpellier University, Montpellier, France, 2Altoona Center for Clinical Research, Duncansville, United States of America, 3University of Occupational and Environmental Health Japan, Kitakyushu, Japan, 4Leiden University Medical Center, Leiden, Netherlands, 5UnitedHealth Group, Inc., Foster City, United States of America, 6Galaxo NV, Mechelen, Belgium, 7Amsterdam Medical Center, Amsterdam, Netherlands, 8Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, 9Rep. of (South Korea), 10Mount Sinai Hospital, Toronto, Canada, 11University of Toronto, Toronto, Canada, 12University of Queensland, St. Lucia, Australia

Background: Filgotinib (FIL) is an orally administered, potent and selective inhibitor of Janus kinase 1 (JAK1) that has shown good efficacy and was well tolerated for treatment of rheumatoid arthritis (RA).

Objectives: To evaluate efficacy and safety of FIL treatment in patients with RA who have had an inadequate response to methotrexate (MTX).

OP00022
Randomised, double-blind, placebo-controlled, multiple-dose, phase 2b study to demonstrate the safety and efficacy of Tildrakizumab, a high-affinity anti-interleukin-23p19 monoclonal antibody, in patients with active psoriatic arthritis

Philip J Mease1, Saima Chohan2, Ferran J Garcia-Fructuoso3, Richard C Chou4, Kristine E Nograles5, Alan M Mendelsohn5, Michael E Luggen6,7.

Disclosure of Interests: Bernard Combe Consultant for: Abbvie, Bristol-Myers Squibb, Gilead

LB0002

Conclusions: The selective JAK1 inhibitor FIL, at doses of 200mg and 100mg led to significant improvement in signs and symptoms of RA, prevented radiographic progression, and improved physical function compared to PBO, was well tolerated among patients with RA with prior inadequate response to MTX. Efficacy of FIL200mg was non-inferior to ADA based on DAS28-CRP ≤3.2 and ≤2.6, had lower radiographic progression, and reported improvements in HAQ-DI, SF-36 PCS, and FACIT-Fatigue scores (Table 1). Non-inferiority of FIL 200mg to ADA was met based on DAS28-CRP ≤3.2. The FIL safety profile was consistent with prior studies through week 24 (Table 2).

Methods: This phase 3, double-blind, active- and placebo-controlled (PBO)-controlled study randomized patients with active RA (3:3:2:3) to FIL 200mg, FIL 100mg, active comparator (adalimumab [ADA] 40mg every 2 weeks), or PBO daily for up to 52 weeks; results through week 24 are presented. Patients were also receiving MTX for ≥12 weeks with a stable dose of MTX for ≥24 weeks before initiation of study drug. Primary efficacy endpoint was proportion of patients achieving ACR20 response at week 12; additional clinical assessments were ACR50 and ACR70 responses, DAS28-CRP score ≤3.2 and ≤2.6, van der Heijde modified total Sharp score (mTSS), and patient-reported outcomes were HAO-DI, SF-36 PCS, and FACIT-Fatigue. Safety endpoints included types and rates of adverse events. Logistic regression adjusting for stratification factors with nonresponder imputation was used for superiority test of FIL vs PBO for ACR response and other binary endpoints. Mixed-effect model adjusting for baseline value, stratification factors, treatment, and visit by visit interaction as fixed effects with observed cases was used for continuous endpoints. Non-inferiority test of FIL to ADA (preserving >50% of ADA response) was performed for DAS28-CRP ≤3.2 and <2.6.

Results: Of 1,759 patients randomized, 1,755 received study drug and were ana- lyzed, with 475 FIL 200mg; 480 FIL 100mg; 325 ADA; and 475 PBO, of which 89.5%, 90.4%, 89.8%, and 81.3%, respectively, completed week 24 study drug. Most patients (81.8%) were female, mean (standard deviation [SD]) duration of RA was 7.8 (7.6) years, and mean (SD) DAS28-CRP was 5.7 (0.9). At week 12, significantly more patients in the FIL 200mg and 100mg arms achieved an ACR20 response compared to PBO (Table 1). Similarly, compared to PBO, more patients receiving FIL achieved ACR50 and ACR70 responses, DAS28-CRP scores ≤3.2 and ≤2.6, had lower radiographic progression, and reported improvements in HAQ-DI, SF-36 PCS, and FACIT-Fatigue scores (Table 1). Non-inferiority of FIL 200mg to ADA was based on DAS28-CRP ≤3.2. The FIL safety profile was consistent with prior studies through week 24 (Table 2).

Background: Tildrakizumab (TIL), a high-affinity anti-interleukin-23p19 mono- clonal antibody, is approved for moderate-to-severe plaque psoriasis treatment and is under investigation for psoriatic arthritis (PsA).

Objectives: To evaluate the 24-week efficacy and safety results from the randomised, double-blind, placebo-controlled, multiple-dose, phase 2b TIL study in patients with active PsA (NCT02980692).

Methods: Patients with active PsA were randomised 1:1:1:1:1 to receive TIL (200 mg once every 4 weeks [Q4W] [n = 78], 200 mg every 12 weeks [Q12W] [n = 79], 100 mg Q12W [n = 77], 20 mg Q12W to week 24 [n = 78], or placebo) Q4W to week 24 (n = 79). Stable concomitant methotrexate or leflunomide use was permitted but not mandated. The primary efficacy endpoint was the proportion of patients who achieved a 20% reduction from baseline in American College of Rheumatology response criteria (ACR20) at week 24. Other outcome measures included proportion of patients achieving ACR50/70 response and Psoriasis Area and Severity Index (PASI) 75, PASI 90, and changes in swollen and...
Results: Of 500 patients screened, 391 patients met inclusion criteria (including =18 years old, PsA diagnosis with symptoms for 6 months, and =3 tender and =3 swollen joints). Demographics and baseline disease characteristics are shown in Table 1. There were significantly greater proportions of ACR20/50/70 and PASI 75/90 responders with TIL vs PBO at week 24, and in some cases differences in parameters were noted as early as week 8 (Figure 1 and Table 2).

The most frequent TEAEs through week 24 included nasopharyngitis (pooled TIL arms: 5.4% [173/32]; PBO: 6.3% [5/79]; and diarrhea (TIL: 1.3% [4/312]; PBO: 0). There were no reports of candidiasis, inflammatory bowel disease, major adverse cardiac events, or malignancy. No patients discontinued treatment due to TEAEs and no deaths were reported. Serious TEAEs occurred in 2.2% (7/312) of TIL-treated patients vs 2.5% (7/289) in PBO-treated patients.

Conclusion: By week 24, TIL was significantly more efficacious than PBO in treatment of joint and skin manifestations of PsA. Furthermore, there was a clear separation between TIL and PBO as early as 8 weeks for ACR20 (TIL 200 mg Q4W and 100 mg) and 12 weeks for ACR50 (all TIL arms). Shortening the dosing interval from Q12W to Q4W for the 200-mg dose did not result in a measurable increase in skin or joint response scores. There was a low rate of TEAEs in the TIL-treated group.

Acknowledgement: Editorial support by Marie-Louise Ricketts, PhD & Claire Danileti, PhD, of AlphaBioCom, King of Prussia, PA, funded by Sun Pharma.

Disclosure of Interests: Philip J Mease Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Janssen, Leo, Eli Lilly, Merck, Novartis, Pfizer, Sun Pharmaceutical Industries, Inc, and UCB, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Galapagos, Gilead, Janssen, Leo, Eli Lilly, Merck, Novartis, Pfizer, Sun Pharmaceutical Industries, Inc, and UCB, Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Genentech, Janssen, Leo, Merck, Novartis, Pfizer and UCB... Saima Chohan: None declared.

Ferran J García Fructuoso Consultant for: Receives consultation fees from Sun Pharmaceutical Industries, Inc, Kristine E Nograles Consultant for: AbbVie; Amgen; Genentech; Eli Lilly; Nichi-iko; Novartis; Pfizer; and San Pharmaceutical Industries, Inc... Xanthe Matthijsen, Ellis Niemantsverdriet, Thomas Huizinga, Annette van der Helm - van Mil. Leiden University Medical Center (LUMC), Leiden, Netherlands

Background: Over the last 25 years, treatment of rheumatoid arthritis (RA) has changed considerably, and clinically relevant joint damage and deformations have become infrequent. It is unclear to what extent the long-term outcomes mortality, sustained drug-free remission (DFR) and physical functioning have improved, and whether ACPA+ and ACPA- patients have benefited equally from treatment-improvements.

Objectives: To investigate the influence of treatment strategies that have been improved for 25-years on mortality, DFR and functionality, and whether these effects differed for ACPA+ and ACPA- RA-patients.

Methods: In the Leiden early arthritis cohort, 1291 patients with RA (1987 criteria) were included between 1993-2016. Patients were treated in routine care; initial and subsequent treatment changed over time; divided in 5 inclusion periods. Patients included between 1993-1996 (n=168) received initial NSAIDs and started DMARDs with delay, patients included 1997-2000 (n=148) were treated early with mild DMARDs (e.g. hydroxychloroquine, penicillamine), in 2001-2005 (n=210) patients started early with methotrexate, in 2006-2010 (n=338) early methotrexate was followed by treat to target treatment adjustments. In 2011-2016 (n=390) this was similar and additional efforts were undertaken for very early referral. Patients were followed yearly including assessments of swollen joints, DAS28-ESR and health assessment questionnaires (HAQ). Mortality data were obtained from the civic registry. DFR was defined as the persistent absence of synovitis after cessation of DMARD-therapy during all available follow-up (> 1 year). DAS28-ESR and HAQ data were analysed with linear mixed models; mortality and time to DFR with multivariable and univariable Cox regression. Inclusion period 1993-1996 was used as reference. Analyses were stratified for ACPA-status (anti-CCP2).

Results: Baseline age, sex and antibody status did not differ between inclusion periods. With 1993-1996 as reference, the DAS28-ESR decreased in the first year and thereafter remained lower in all inclusion periods (all p<0.05).

Compared to 1993-1996, mortality was decreased in all inclusion periods (1997-2000 HR 0.67 [0.46;0.99]; 2001-2005 HR 0.66 [0.45;0.97]; 2006-2010 HR 0.64 [0.42;0.98]; 2011-2016 HR 0.31 [0.14;0.68]). DFR achievement was faster in 1997-2000 (HR 0.40 [0.17;0.94]); 2001-2005 HR 0.35 [0.14;0.86]; 2006-2010 HR 0.26 [0.10;0.69]; and 2011-2016 (0.11 [0.04;0.29]), compared to 1993-1996. Additionally, HAQ over time was lower in 2006-2010 (<0.25 [0.36-0.14]) and 2011-2016 (<0.21 [0.32-0.10]).

Stratification for ACPA revealed that ACPA+ patients in the first two inclusion periods remained to have a higher DAS28-ESR over time (1993-1996 beta 0.76 [0.42;1.10]; 1997-2000 beta 0.40 [0.07;0.74]); thereafter there was no difference in DAS28-ESR between ACPA+ and ACPA- patients. The decrease in mortality was similar for ACPA+ and ACPA- patients. The increased rate of DFR was more prominent in ACPA+ patients than ACPA- patients in the two most recent inclusion periods (2006-2010 HR ACPA+: 3.85 [1.25;11.9]; ACPA-: 2.27 [1.34;3.83]; 2011-2016 HR ACPA+: 6.48 [1.89;22.2]; ACPA-: 3.04 [1.65;5.55]). Within ACPA+ RA, the HAQ over time had improved in 2001-2005 (-0.19 [-0.34;-0.04]), 2006-2010 (-0.35 [-0.49;0.22]) and 2011-2016 (-0.26 [-0.40;0.13]), compared to 1993-1996.

This effect was absent ACPA- RA.

Scientific Abstracts

WEDNESDAY, 12 JUNE 2019

RA therapy –JAK inhibitors and beyond.

Figure 1. Disease outcomes over time stratified for inclusion period

Table 2. Efficacy endpoints at week 24

<table>
<thead>
<tr>
<th>TIL 200 mg Q12W</th>
<th>TIL 200 mg Q4W</th>
<th>TIL 200 mg Q4W (n=77)</th>
<th>TIL 200 mg Q2W (n=77)</th>
<th>TIL 200 mg Q12W (n=77)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PASI 75 %</td>
<td>64.1±2.9 %</td>
<td>59.7±2.9 %</td>
<td>55.8±4.4 %</td>
<td>66.3±3.1 %</td>
</tr>
<tr>
<td>PASI 50 %</td>
<td>47.2±4.1 %</td>
<td>42.3±5.4 %</td>
<td>38.8±6.4 %</td>
<td>49.2±4.6 %</td>
</tr>
<tr>
<td>Tender joint count, median change from BL</td>
<td>-0.01</td>
<td>-0.01</td>
<td>-0.01</td>
<td>-0.01</td>
</tr>
<tr>
<td>Tender joint count, median change from BL</td>
<td>-0.01</td>
<td>-0.01</td>
<td>-0.01</td>
<td>-0.01</td>
</tr>
</tbody>
</table>

*Response rates only calculated in patients with ISA ≥2 % at baseline, missing responses were imputed as non-responders. *P < 0.05; **P < 0.01 vs PBO.

ACKNOWLEDGEMENTS

**ACR20/50/70 response rates: TIL placebo; QW, every 4 weeks; QW/4, every 12 weeks; TIL, stratified/stratum.**
Conclusion: Improvements in treatment strategies during the last 25 years have resulted in lower disease activity, less mortality, more DFR and better physical functioning of RA-patients. ACPA+ patients, traditionally the most severe subset, benefited most from these improvements and have become more similar to ACPA- patients.

Disclosure of Interests: Xanthe Matthijssen: None declared, Ellis Niemanveldriet: None declared, Thomas Huizinga Consultant for: Merck, UCB, Bristol Myers Squibb, Pfizer, GSK, Novartis, Roche, Sanofi-Aventis, Abbott, Crecedo Bioscience Inc., Nycomed, Boeringher, Takeda, Zydus, Epirus, Eli Lilly, Annette van der Helm - van Mil Grant/research support from: The research leading to these results has received funding from the European Research Council (ERC) under the European Union’s Horizon 2020 research and innovation programme (Starting grant, agreement No 714312) and from the Dutch Arthritis Foundation. The funding source had no role in the design and conduct of the study.


**OP0024**

**PATIENT DISCUSSIONS OF GLUCOCORTICOID-RELATED SIDE EFFECTS WITHIN AN ONLINE HEALTH COMMUNITY FORUM**

Arani Vivekanantham, Maksim Belousov, Lamiece Hassan, Goran Neradic, Will Dixon. University of Manchester, Manchester, United Kingdom

**Background:** Social media websites are an important, largely untapped source of data about patients’ experience of living with disease and its treatment. This includes information on drugs such as the occurrence, nature and impact of side effects. However, there are few published studies reporting drug safety profiles using such data.

Health Unlocked (HU), Europe’s largest social media network for health that supports patients and health care providers, hosts over 200 communities including the UK’s National Rheumatoid Arthritis Society (NRAS). Using the example of glucocorticoid (GC) therapy, this study aims to explore the potential of HU posts in providing information about the occurrence and nature of drug side effects.

**Objectives:**
1. Evaluate the accuracy of a computerised system for automated suspected adverse drug reaction (sADR) detection from posts from HU compared to human annotation.
2. Explore themes of discussion about GC-related ADRs within posts from HU.

**Methods:** HU provided a dataset of de-identified posts from the NRAS community from December 2015 to December 2016. Posts mentioning GCs were processed by automated Natural Language Processing software, which identified the drug and health issues, mapped them to the Medical Dictionary for Regulatory Activities (MedDRA®) dictionary and categorised as a sADR or not. A sample (n=50) of sADR posts were randomly selected and manually reviewed to determine whether they were true ADRs. Additionally, a sample (n=50) of the posts that included GC and were labelled as having a health issue but not thought to have an ADR, were also assessed for true ADRs.

Posts identified as containing GC ADRs from manual analysis were reviewed to identify themes.

**Results:** Of the 35,904 posts from 1,998 users, 2,409 posts mentioned GCs, of which 324 posts were identified as containing information representing a sADR.

After manual review of the 50 sampled sADRs, only 36% (18/50) of these posts contained a true ADR. Of the 50 sampled posts that included a mention of GCs and a health issue but were not a sADR, 28% (14/50) were found to contain true ADRs. Thematic analysis of the 32 posts containing true GC ADRs found the most frequently mentioned ADRs were fractures (n=6), infection (n=5), headaches (n=3) and weight gain (n=3). Posts included rich descriptions about the nature of side effects (“my weight tripled in size with steroids”). This included experiences of how side effects changed with time (“huge mood swings settles after a while”). Users also described how ADRs impacted on their quality of life (“with steroid induced diabetes, I lost a stone in three days, it was grim”), and their value judgements about the importance of side effects (“my taste buds are making everything taste strange, either salty, metallic, or plain awful ... but I cope with it, as hardly any pain with steroids.”) Posts also described frustrations about how well informed they were about side effects (“I had two eye ops for cataracts, no one told me steroids caused cataracts”). Within posts where ADRs were discussed, patients also commented on the benefits of treatment (“my pain subsided with steroids”) and the difficult balance between benefits and harms (“wonderful to not feel like I had RA in the first month of having [pred], but now I have more acne then when I was a teenager”).

**Conclusion:** Current machine learning models for ADR detection in social media still need further improvements to identify sADRs in health forum data. Nonetheless, manual review shows there are important themes relating to patients’ experiences and perceptions of using GC that may not be obtained using traditional methods such as analysis of health records or spontaneous pharmacovigilance. With improved automated ADR detection, this rich data source may be useful to identify ADRs most important to patients and the impact on quality of life.

**Disclosure of Interests:** None declared


**OP0025**

**FENEBRUTINIB COMPARED TO PLACEBO AND ADALIMUMAB IN PATIENTS WITH INADEQUATE RESPONSE TO EITHER METHOTREXATE THERAPY OR PRIOR TNF THERAPY: PHASE 2 STUDY**

Stanley Cohen1, Kate Tuckwell2, Tamiko R. Katsumoto3, Rui Zhao2, Chin Lee2, Alberto Berrman4, Nemanja Damjanovic5, Dmytro Fedkovych6, Slawomir Jeka7, Mark C. Genovese1, 1Metroplex Clinical Research Center, Dallas, United States of America; 2Genentech, Inc., South San Francisco, United States of America; 3Stanford University, Stanford, United States of America; 4Centro Médico Príncipe De Reumatología, Tucumán, Argentina; 5University of Belgrade, Institute of Rheumatology, Belgrade, Serbia; 6Bohomolets National Medical University, Kyiv, Ukraine; 7University Hospital no 2 in Bydgoszcz, CM UMK, Bydgoszcz, Poland

**Background:** Fenebrutinib (GDC-0853, FEN) is a small molecule inhibitor of Bruton’s Tyrosine Kinase (BTK) that is orally administered, highly selective, non-covalent, and reversible.

**Table 1. Endpoints**

<table>
<thead>
<tr>
<th></th>
<th>FEN-50</th>
<th>FEN-150</th>
<th>FEN-200</th>
<th>Cohort 1, MTX-IR</th>
<th>Cohort 2, TNF-IR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OD</td>
<td>QD</td>
<td>OD</td>
<td>(n=110)</td>
<td>(n=110)</td>
</tr>
<tr>
<td>ACR50 responders at W12</td>
<td>7 (18%)</td>
<td>30 (28%)</td>
<td>38 (35%)</td>
<td>16 (15%)</td>
<td>40 (36%)</td>
</tr>
<tr>
<td>95% confidence interval (CI)</td>
<td>5 (8%)</td>
<td>28 (19%)</td>
<td>32 (25%)</td>
<td>9 (18%)</td>
<td>27 (27%)</td>
</tr>
<tr>
<td>Weighted difference vs. PBO</td>
<td>0.0%</td>
<td>12.9%</td>
<td>20.0%</td>
<td>-</td>
<td>21.6%</td>
</tr>
<tr>
<td>P-value**</td>
<td>0.2503</td>
<td>0.0164</td>
<td>0.0003</td>
<td>-</td>
<td>0.0001</td>
</tr>
<tr>
<td>95% CI of weighted difference*</td>
<td>6%</td>
<td>22%</td>
<td>(9%, 31%)</td>
<td>-</td>
<td>(11%, 33%)</td>
</tr>
<tr>
<td>Weighted difference vs. ADA</td>
<td>-17.81%</td>
<td>-6.6%</td>
<td>-1.5%</td>
<td>-21.6%</td>
<td>-1.5%</td>
</tr>
<tr>
<td>P-value**</td>
<td>0.0268</td>
<td>0.1694</td>
<td>0.8132</td>
<td>0.0001</td>
<td>-</td>
</tr>
</tbody>
</table>

**DAS28-CRP at W12**

<table>
<thead>
<tr>
<th></th>
<th>Change from baseline</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Pts (n) completing W12</td>
</tr>
<tr>
<td>Weighted difference vs. PBO**</td>
<td>-3.87</td>
</tr>
<tr>
<td>P-value</td>
<td>0.0006</td>
</tr>
</tbody>
</table>

**Safety**

<table>
<thead>
<tr>
<th></th>
<th>AEs</th>
<th>Serious AEs</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pts with ≥1 event, n (%)</td>
<td>56 (50)</td>
<td>56 (50)</td>
<td>50 (45)</td>
</tr>
<tr>
<td>Adjusted mean***</td>
<td>0.96</td>
<td>0.96</td>
<td>0.96</td>
</tr>
<tr>
<td>Deaths, n (%)</td>
<td>1 (0.9)***</td>
<td>1 (0.9)***</td>
<td>-</td>
</tr>
</tbody>
</table>

*Adjusted for geographic region (Eastern Europe, Latin America, and USA) for Cohort 1, and geographic region and prior exposure to a non-TNF biologic for Cohort 2
**Not adjusted for multiplicity
***Death was due to myocardial infarction

One PBO pt was treated with FEN-200 in error
A PHASE 3 STUDY OF THE EFFICACY AND SAFETY OF PEFICITINIB (ASP015K) IN PATIENTS WITH RHEUMATOID ARTHRITIS WHO HAD AN INADEQUATE RESPONSE TO METHOTREXATE


Background: Peficitinib (ASP015K), a novel oral JAK inhibitor, demonstrated efficacy as once-daily monotherapy in patients with moderate-to-severe rheumatoid arthritis (RA) in a phase 2b study (NCT01649999). Objectives: To evaluate the efficacy and safety of peficitinib–methotrexate (MTX) combination in patients with RA who had an inadequate response to MTX. Methods: This multicentre, randomised, double-blind, parallel-group, placebo (PBO)-controlled, phase 3 study (NCT02305849) was conducted in Japan. Patients had RA diagnosed within the past 10 years (1987 ACR or 2010 ACR/EULAR criteria), active disease (≥6 tender and painful joints and ≥6 swollen joints, using 88 and 66-joint assessment respectively; CRP >1.0 mg/dl; bone erosion; and ACPR or RF positivity) and inadequate response to MTX (administered for ≥90 days; ≥8 mg/week for ≥28 days prior to baseline). Patients were randomised 1:1:1 to S2-week MTX plus PBO, peficitinib 100 mg/day or peficitinib 150 mg/day. At week 12, inadequate responders in the PBO group (<20% improvement from baseline in tender and swollen joint counts) were switched (under blinded conditions) to peficitinib 100/150 mg until end of treatment. Remaining patients in the PBO group were switched (under blinded conditions) to peficitinib at week 28. Concomitant stable MTX dose (≥16 mg/week) was mandatory.

Primary efficacy variables were ACR20 response rate at week 12/early termination (ET) and change from baseline in modified Total Sharp score (mTSS) at week 28/ET.

Table 1: Primary and secondary efficacy endpoints at week 12/ET

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>PBO (n=170)</th>
<th>Peficitinib 100 mg/day (n=175)</th>
<th>Peficitinib 150 mg/day (n=174)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACR20</td>
<td>30.0%</td>
<td>53.2%</td>
<td>55.6%</td>
</tr>
<tr>
<td>ACR50</td>
<td>16.4%</td>
<td>42.9%</td>
<td>46.6%</td>
</tr>
<tr>
<td>ACR70</td>
<td>7.1%</td>
<td>16.6%</td>
<td>16.6%</td>
</tr>
<tr>
<td>DAS28</td>
<td>3.2 (2.5)</td>
<td>2.0 (1.7)</td>
<td>1.9 (1.7)</td>
</tr>
<tr>
<td>DAS28 CRP</td>
<td>3.2 (2.5)</td>
<td>2.0 (1.7)</td>
<td>1.9 (1.7)</td>
</tr>
<tr>
<td>mTSS change from baseline</td>
<td>17.2 (9.8)</td>
<td>6.7 (6.1)</td>
<td>7.7 (6.1)</td>
</tr>
</tbody>
</table>
| Table 2: Treatment-emergent adverse events

<table>
<thead>
<tr>
<th>Event</th>
<th>PBO (n=170)</th>
<th>Peficitinib 100 mg/day (n=175)</th>
<th>Peficitinib 150 mg/day (n=174)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any AE</td>
<td>104 (61.2%)</td>
<td>145 (83.0%)</td>
<td>153 (88.5%)</td>
</tr>
<tr>
<td>Drug-related AE</td>
<td>47 (27.7%)</td>
<td>111 (63.5%)</td>
<td>119 (68.4%)</td>
</tr>
<tr>
<td>Death</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>SAE</td>
<td>4 (2.4%)</td>
<td>4 (2.3%)</td>
<td>4 (2.3%)</td>
</tr>
<tr>
<td>Drug-related SAE</td>
<td>3 (1.8%)</td>
<td>3 (1.7%)</td>
<td>3 (1.7%)</td>
</tr>
<tr>
<td>All events or severe events leading to discontinuation of study drug</td>
<td>5 (2.9%)</td>
<td>13 (7.5%)</td>
<td>17 (9.8%)</td>
</tr>
<tr>
<td>Serious infection</td>
<td>9 (5.3%)</td>
<td>13 (7.5%)</td>
<td>17 (9.8%)</td>
</tr>
<tr>
<td>Severe neutropenia</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>18 (10.6%)</td>
<td>37 (21.1%)</td>
<td>35 (20.1%)</td>
</tr>
<tr>
<td>Neutropenia severe</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

1Any patient with a history of neutropenia, anemia, or thrombocytopenia. 2All serious adverse events leading to discontinuation of study drug. 3All serious adverse events leading to discontinuation of study drug. 4All serious adverse events leading to discontinuation of study drug.
**EFFECT OF SHORT-TERM METHOTREXATE DISCONTINUATION ON THE DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS: POSTHOC-ANALYSIS OF TWO RANDOMIZED CLINICAL TRIALS**

Min Jung Kim, Yeong Woong Song, Eun Bong Lee, Jin Kyun Park. Seoul National University Hospital, Division of Rheumatology, Department of Internal Medicine, Seoul, Korea, Rep. of (South Korea)

**Background:** Patients with rheumatoid arthritis (RA) require a continuous, potentially lifelong immune suppression with disease modifying antirheumatic drugs (DMARDs) including methotrexate (MTX). However, in specific circumstances such as life-threatening infections, vaccinations or major surgeries, use of MTX should be minimized to restore the treatment-associated immune suppression. While a long-term or permanent discontinuation of MTX is associated with a disease flare or relapse, the effect of short-term discontinuation on disease activity has not been fully elucidated.

**Objectives:** To investigate the effect of short-term discontinuation of MTX on the disease activity in patients with RA on stable dose of MTX.

**Methods:** This is a post hoc analysis of 2 randomized controlled studies investigating effect of MTX discontinuation for 2 weeks or 4 weeks on vaccine response to seasonal influenza vaccination in patients with RA. In the 4-week discontinuation study, 54 patients continued MTX and 44 patients discontinued it for 4 weeks before vaccination with trivalent seasonal influenza vaccine. In the 2-week discontinuation study, 159 patients continued MTX and 161 patients held it for 2 weeks after a seasonal quadrivalent influenza vaccine. Disease activity (DAS28 change, DAS28 flare rate and flare-free survival) was compared between the patients who continued MTX and those held it. A RA flare was defined as an increase in DAS28 of >1.2 or >0.6 if the baseline DAS28 was >3.2.

**Results:** In the 4-week MTX-hold group, the mean DAS28 increased at the 4 weeks after MTX discontinuation by 0.38 ± 0.94 and then improved back to baseline after reintroduction of MTX, whereas the mean DAS28 in the MTX-continue group remained stable over time (Figure 1A). The overall flare-free survival during 20 weeks did not differ between the groups (log rank p=0.142) (Figure 1B). However, numerically more patients in the MTX-hold group experienced a flare than those in the MTX-continue group during the 4-week MTX discontinuation (20.5% vs. 7.4%, p=0.058). After resuming MTX, the flare rate did not differ between the groups up to 20 weeks of observations (Figure 1C). A temporary MTX discontinuation for 2 weeks was not associated with any clinically meaningful change in disease activity.

**Conclusion:** A short-term MTX discontinuation for 2 weeks is safe without any change in disease activity. A 4-week MTX discontinuation is associated with transient increase in disease activity without affecting long-term outcomes.

**REFERENCES:**


**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.2524
long-term safety. To our knowledge, this is the first long-term comparative RWD analysis of tofacitinib.

**Objectives:** To compare 5-year adverse event (AE) incidence rates (IRs) in patients (pts) starting tofacitinib vs biological (b)DMARDs using cohorts from the US Corrona RA registry.

**Methods:** This prospective, observational 5-year study embedded in the ongoing US Corrona RA registry routinely collected 9 categories of predefined AEs from participating physicians. Real-world safety event rates of major adverse cardiovascular events (MACE), serious infectious events (SIEs) and herpes zoster (HZ; serious and non-serious) were compared in pts with RA who started tofacitinib or a bDMARD regardless of dose/schedule between 6 Nov 2012 (US FDA approval) and 30 Jun 2017 (follow-up through 31 Dec 2017). Endpoints were selected as having sufficient power to detect a 2-fold difference between cohorts at this datacut; there was insufficient power to assess malignancy. Baseline variables with a standardised difference > 0.10 between tofacitinib and bDMARD initiators, and a priori selected covariates (gender, age, line of therapy, history of AE of interest) were used to construct propensity scores (PS) to derive a PS-trimmed (primary) population and a PS–matched population for sensitivity analysis (ratio: max. 4 bDMARD:1 tofacitinib; calliper=0.05). Pts were followed from initiation until an AE of interest; discontinuation and/or start of a new therapy >90 days, death or end of follow-up, whichever came first. Crude IRs (events/100 pt-years [PY]) were estimated; multivariable-adjusted Cox regression was used to estimate hazard ratios (HRs) comparing rates of first events between cohorts.

**Results:** In total, 1544 tofacitinib (2138.2 PY) and 7083 bDMARD (9904.9 PY) initiators were included. PS-trimmed resulted in 1117 tofacitinib and 5542 bDMARD initiators. Rates of MACE and SIEs were similar in both cohorts (Fig 1A); adjusted HRs (95% confidence intervals [Cls]) were: MACE 0.60 (0.30, 1.18); SIEs 0.99 (0.72, 1.36; Fig 1B). HZ IR was higher for tofacitinib vs bDMARDs (Fig 1A); HRs for HZ were significantly increased with tofacitinib vs bDMARDs (adjusted HR 2.12 [1.22, 3.66]; Fig 1B); all HZ events were non-serious with tofacitinib. Similar results were observed in PS-matched populations.

**Conclusion:** This was the first comparative analysis of RWD data for tofacitinib and bDMARDs to use PS-trimmed and PS-matched analyses to adjust for channeling/prescribing patterns for newly approved therapies. Pts starting tofacitinib or bDMARDs for RA had similar rates of MACE and SIEs. Tofacitinib initiators had higher HZ IRs vs bDMARD initiators. These results are consistent with long-term clinical trial findings.

**Acknowledgement:** Sponsors: Corrona, LLC. Corrona is supported by contracted subscriptions with multiple companies. This was a Corrona/Pfizer collaboration with Pfizer financial support. Medical writing support provided by Anthony G McCluskey of CMC Connect and funded by Pfizer Inc.
**Results:** Of the 651 and 327 pts randomized to receive UPA and ADA, 126 (19%) and 77 (24%), were considered NR and switched to ADA and UPA respectively. NR demographics were consistent with the overall randomized population. Of the switched pts, ~90% remained in the study through 6 mos ps. Patients switched to ADA (UPA-NR) achieved 59% (26%/12%) improvements in ACR20/50/70 responses, and 35% achieved DAS28 (CRP) ≤3.2 at 6 mos ps (Table). Patients switched to UPA (ADA-NR) achieved 75%/49%/24% improvements in ACR20/50/70, and 54% achieved DAS28 (CRP) ≤3.2 at 6 mo consistent with data observed in a phase 3 study of UPA in BDMARD-RD RA pts. The proportion (95% CI) of pts with infection and serious infection through 6 mos appeared consistent with those observed for ADA and UPA during comparable periods (ADA, switched from UPA: infection: 34.1 [26.43, 42.77], serious infection: 1.6 [1.44, 5.60]; UPA, switched from ADA: infection: 40.3 [30.02, 51.42], serious infection: 3.9 [1.33, 10.94].

**Conclusion:** Data from this blinded, controlled study indicate that pts with initial non-response to either UPA or ADA can benefit from switching to the other therapy. No additional safety concerns were observed. These are the first data to demonstrate effectiveness of a TNF inhibitor following failure of a JAK inhibitor.

**REFERENCES:**


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**REFERENCES:**


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PATIENTS WITH RADIOPHARMIC SACROILIAC: COMPARISON IN A COHORTS?

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Background: Axial spondyloarthritis (axSpA) patients with radiographic sacroiliitis may be classified using the modified New York (mNY) criteria and the more recent ASAS criteria. In the mNY criteria these patients are referred to as ankylosing spondylitis (AS) patients and in the ASAS criteria as radiographic axSpA (r-axSpA) patients. In both the mNY and the ASAS r-axSpA classification sets the radiographic criterion is the same but the additionally required features differ (figure), for example patients with age at onset of back pain ≥45 cannot fulfil the ASAS criteria. This raises the question whether the two sets can be used interchangeably in the classification of axSpA patients with radiographic sacroiliitis.

Objectives: To investigate to what degree patients with axSpA and radiographic sacroiliitis who fulfil the mNY criteria also fulfil the ASAS criteria for r-axSpA and vice-versa.

Methods: Patients diagnosed with axSpA who had back pain longer than 3 months and definite radiographic sacroiliitis (i.e. common and mandatory features for both classification criteria sets (figure)) were selected from several cohorts (ASAS, Esperanza, GESPIC, OASIS, Reuma.pt, SCQM, SPACE, and UCSF). Subsequently we calculated how many patients fulfil the mNY criteria and/or the ASAS r-axSpA criteria. Inversely, of the 3434 patients fulfilling the ASAS r-axSpA criteria for the classification of patients with axSpA and radiographic sacroiliitis.

Results: Of the 3892 patients fulfilling the mNY criteria, 93% also fulfilled the ASAS r-axSpA criteria. Inversely, of the 3434 patients fulfilling the ASAS r-axSpA criteria, 96% also fulfilled the mNY criteria (table). In total, 89% (3607/4041) of patients with axSpA and radiographic sacroiliitis fulfilled both criteria sets; 7% only the mNY criteria; 3% only the ASAS criteria and 1% neither set.

Conclusions: AxSpA patients classified as AS according to mNY criteria and those classified as r-axSpA according to ASAS criteria are mostly the same: 93% of mNY positive patients also fulfil the ASAS r-axSpA criteria while 96% of ASAS r-axSpA positive patients also fulfil the mNY criteria. These findings support the interchangeable use of the terms r-axSpA and AS, which was also approved by a vote of ASAS members at the 2019 annual workshop in Amsterdam.

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Figure 1. mNY and ASAS r-axSpA criteria for the classification of patients with axSpA and radiographic sacroiliitis.

LOCALIZATION AND MORPHOLOGY OF MAGNETIC RESONANCE IMAGING FEATURES OF PATHOLOGIC CHANGES IN THE SACRILIAC JOINTS SUGGESTIVE OF AXIAL SPONDYLOARTHRITIS – A SYSTEMATIC COMPARISON OF PATIENTS AND CONTROLS WITH CHRONIC BACK PAIN

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Background: Bone marrow edema (BME), fat metaplasia (FM) and erosions have been identified as relevant for magnetic resonance imaging (MRI) changes in the sacroiliac joints (SIJ) of patients with axial spondyloarthritis (axSpA). However, a high prevalence of MRI changes has recently also been reported in subjects with no evidence of axSpA (1,2).

Objectives: To map the MRI lesions suspicious of axSpA in patients diagnosed with axSpA and compare them to those in patients with chronic back pain (cBP, non-SpA).

Methods: Consecutive patients with cBP < 45 years were included if they had at least one pathologic lesion of any type in the SIJ-MRI performed on time. BME was found positive by both readers for the respective lesions.

Results: A total of 200 consecutive patients (100 axSpA, 100 non-SpA), mean age 36±11.3 and 40±11.0 years, respectively, were analyzed. BME was found in 85% vs. 80% of patients with axSpA and non-SpA respectively had sclerosis and erosions, respectively. The largest surface area covered by BME was found in 85% vs. 80% of patients, while 80% vs. 69% had FL, 54% vs. 40% had sclerosis and 64% vs. 12% had erosions, respectively. The largest surface area covered by BME, FL, sclerosis and erosions. In addition, length and width were digitally measured for BME, FL and sclerosis, and signal intensity was measured digitally in each individual patient in comparison to the cerebrospinal fluid signal for BME and the subcutaneous fat for FL (no units).

Comparisons were calculated by Mann-Whitney-U-test for patients classified as positive by both readers for the respective lesions.

Results: A total of 200 consecutive patients (100 axSpA, 100 non-SpA), mean age 36±11.3 and 40±11.0 years, respectively, were analyzed. BME was found in 85% vs. 80% of patients with axSpA, while 80% vs. 69% had FL, 54% vs. 40% had sclerosis and 64% vs. 12% had erosions, respectively. The largest surface area covered by BME in axSpA vs. non-SpA was found in the lower and dorsal SIJ: 60±10.1 mm² in the iliac and 47±19.4 mm² in the sacral part vs. the upper and ventral SIJ: 18.7±3.4 mm² in the sacral and 5±20.1 mm² in the iliac part.

Patients with axSpA showed a larger surface area covered by FL than found in the upper and anterior sacral SIJ (30±5.5±6.3 mm²), whereas patients with non-SpA showed larger FL areas in the lower and posterior sacral SIJ (197.9±1.2 mm²). Regarding sclerosis, the upper and anterior iliac part had more surface involvement in both SpA (139±3±11.6 mm²) and non-SpA (81±8.2 mm²) patients.
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The mean signal intensity of all lesions and MRI planes differed between axSpA
(102.385 units?) and non-SpA (48.995) patients for BME (p<0.001) but not for FL.
Overall, axSpA patients also had significantly more SIJ quadrants with pathologic
changes, except for BME and sclerosis in the ventral and fat located in the retroauricular part of the SIJ. The occurrence of erosions in the mid (61 vs. 7) and the
ventral (51 vs. 8) part of the SIJ could discriminate best between axSpA and nonSpA (both p<0.001).
Conclusion: These data show that although all types of lesions may be found in
both patient groups, the anatomic pattern of SIJ involvement can still distinguish
axSpA from non-SpA. The localization and morphological appearance of SIJ-MRI
features suggestive of axSpA may serve as an additional feature in the definition
of a ‘positive’ MRI both for diagnosis and classification.

Scientific Abstracts
meaningful) classes with best data fit. Each class was labelled by us and named
according to most prominent features. The latent axSpA classes were then used
as ‘gold-standard’ against which the ASAS axSpA, pSpA (ignoring IBP) and both
(SpA criteria) were tested. Finally, 5-year follow-up data from DESIR were used to
perform a latent transition analysis (LTA) in order to examine if patients change
classes over 5-year time.

REFERENCES:
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OP0033

WHAT IS AXIAL SPONDYLOARTHRITIS? A LATENT
CLASS AND TRANSITION ANALYSIS IN THE SPACE
AND DESIR COHORTS

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4
Hospital La Cavale Blanche, Brest, France; 5Amsterdam Rheumatology and
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Background: Axial spondyloarthritis (axSpA) is a disease with a rather heterogeneous presentation that may be difficult to diagnose. Classification criteria, such
as the ASAS criteria, which have been developed and validated against the goldstandard ‘expert diagnosis’, exist, but may suffer from inappropriate circularity
because features deemed important by experts (e.g. sacroiliitis on MRI) may have
easily got a too prominent, and therefore biased, role. If classification criteria are
used inappropriately to confirm a diagnosis, overdiagnosis (‘too much SpA’) may
be an unwarranted consequence.
Objectives: To gain an unbiased insight into the concept of axSpA, by circumventing expert opinion and investigating its ‘latent constructs’: We examined the
SpA-features’ mutual statistical coherence, established the unbiased ‘Gestalt’ of
SpA, and evaluated how well the ASAS axSpA classification criteria capture these
‘latent constructs’.
Methods: Two independent cohorts of patients (pts) with early onset chronic
back pain (SPACE cohort) and inflammatory back pain (IBP) (DESIR cohort) were
included. Latent class analysis (LCA) (different than a cluster analysis) was used
to estimate the latent (i.e. unobserved) ‘Gestalt’ of axSpA by modelling the covariance of the observed SpA features (without ‘a priori’ assumptions on their
‘weights’). The selected best LCA model splits axSpA into a number of (clinically

Results: In total, data of 465 (SPACE) and 576 (DESIR) pts were analyzed.
SPACE yielded 4 latent classes (Table 1). The ‘Axial’ class characterized by highest likelihood on abnormal imaging and HLA-B27-positivity; the ‘IBP+Peripheral’
class had 100% likelihood of IBP in association with peripheral signs. The ‘At risk’
class is anchored on a positive family history and HLA-B27 positivity in association with IBP; and the ‘No SpA’ class had very low likelihoods for all SpA-features
which were correlated. The independent analysis in DESIR (without ‘no-SpA’
patients) yielded identical latent classes (‘Axial’:19%; ‘IBP+Peripheral’:27% and
‘At risk’:55%) (Table 2). The ASAS axSpA criteria, tested in SPACE (‘No SpA’
absent in DESIR), captured 67% of the patients in the ‘Axial’ and ‘IBP+Peripheral’
classes (‘latent gold-standard’), but sensitivity was better (87%) if axSpA and
pSpA criteria were combined. Of note, the axSpA criteria captured only 4% of the
patients from the ‘No SpA’ class. Importantly, the LTA suggests that transition
between classes over time was highly unlikely. ‘Axial’ and ‘IBP+Peripheral’
patients did not switch and only 11% of ‘At risk’ pts had switched to ‘IBP+Periphheral’ after 5 years.
Conclusion: The ‘Gestalt’ of axial spondyloarthritis comprises three distinguishable clinical entities (‘pure axial SpA’, ‘axial SpA with peripheral signs, and ‘axial
SpA at risk’). Patients keep their clinical entity over 5 years and transition is very
rare. The ‘Axial’ and ‘IBP+Peripheral’ entities are best captured by combining the
ASAS axSpA and pSpA criteria.
Disclosure of Interests: Alexandre Sepriano: None declared, Sofia Ramiro
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DO SMOKING AND SOCIO-ECONOMIC FACTORS INDEPENDENTLY INFLUENCE IMAGING OUTCOMES IN AXIAL SPONDYLOARTHRITIS? FIVE-YEAR DATA FROM THE DESIR COHORT

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Background: Smoking and systemic inflammation have been shown to independently associate with radiographic spinal progression in patients with axSpA. Furthermore, evidence suggests that certain socioeconomic (SE) factors (e.g. physically demanding jobs) may modify these associations, but clarity on the intricate relationships between smoking, axial damage and SE factors is yet to be achieved. Moreover, the impact of smoking and SE factors and their interplay on axial inflammation have not been thoroughly investigated to date.

Objectives: To investigate the relationship between smoking and imaging outcomes (SI joints, spine, MRI and radiographs) over time in axSpA and to assess if SE factors first modify and if not, confound, such a relationship.

Methods: Patients with axSpA from the DESIR cohort who fulfil the ASAS axSpA classification criteria were included. Four imaging continuous outcomes (X-ray spine [mSASSS, range 0-72]; X-ray SIJs modified New York grading [mNY, 0-8]; MRI-Spine [SPARCC, range 0-414] and MRI-SJ [SPARC, range 0-72]) have been scored by 3 central readers independently (average score used) in one session, blinded to the order (baseline, 2 and 5 years). Smoking, the main variable of interest, was tested as a binary variable to indicate smoking status since last visit. SE variables tested were: age, gender, ethnicity (Caucasian vs other), job type based on ‘collar’ (blue [manual labour work] vs white [office-based work]); educational status (low vs high [university]); parental (number of children) status. Potential interactions between smoking and SE factors were first investigated and, if statistically (p<0.15) and clinically relevant, models were stratified. The effect of smoking on imaging outcomes was assessed in multivariable time-varying models using generalized estimating equations making use of all available observations and adjusted for other known possible confounders (see table).

Results: In total, 425 axSpA patients were included: 225 [53%] male, 167 [40%] smokers and 287 [68%] blue collar. The mean baseline (SD) MRI-SIJ SPARCC was 4.67 (7.40), MRI spine SPARCC 2.73 (7.92); mSASSS 0.38 (1.66); mNY: 1.70 (1.84). A significant interaction was found between smoking and job type with MRI-SJ inflammation as the outcome (p=0.031) as well as with mNY grading (p=0.096). Similarly, educational status also proved to modify the association between smoking and MRI-SJ inflammation (p=0.026). In the multivariable models, smoking was significantly associated with more MRI-SJ inflammation over 5 years of follow-up but only in patients with a blue-collar job [β [95% CI]: 3.35 [0.54, 6.17]) (table). Results were similar in the low education stratum ([β [95% CI]: 2.69 [0.48, 4.91]). Smoking was not significantly associated with any of the other imaging outcomes over time. Male gender was positively associated with MRI-SJ inflammation regardless of job type, and also with MRI-Spinel inflammation and structural damage although only for blue-collar patients in the case of SJ damage.

Conclusion: There is a strong association between smoking and MRI-SJ inflammation over time in axSpA patients with blue collar job type or with low education, irrespective of other socio-economic factors, systemic inflammation and treatment. These findings suggest a possible role for mechanical stress (seen with manual jobs) amplifying the effect of smoking on axial inflammation in axSpA. No significant relationship was found between smoking and spinal inflammation or axial damage, possibly also due to the limited imaging changes in this cohort.

Disclosure of Interests: Elena Nikhzhonovich: None declared, Sofia Ramoni Grant/ research support from: MSD, Consultant for: AbbVie, Lilly, MSD, Novartis, Pfizer, Sanofi, Speakers bureau: AbbVie, Lilly, MSD, Novartis, Pfizer, Sanofi, Alexandre Sepulveda: None declared. Adeline Ryusseyn Witrand: None declared, Robert B.M. Landewé: None declared. Désirée van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, Union Chimique Belge

DEPRESSION IN ANKYLOSING SPONDYLITIS AND THE ROLE OF DISEASE-RELATED AND CONTEXTUAL FACTORS: A STRUCTURAL EQUATION MODELLING APPROACH

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Background: Patients with ankylosing spondylitis (AS) are at increased risk of depression compared to the general population. Comorbid depression in AS likely has a multifactorial origin. While several disease-related and contextual factors have been associated with depressive symptoms in AS, a comprehensive model of their interrelations is currently lacking. Such a model could help understand the mechanisms leading to, or maintaining, depression in AS.

Objectives: To determine which factors contribute to depressive symptoms in AS, and to understand the relationships between relevant factors.

Methods: Data from patients with AS participating in the Dutch cross-sectional multicentre survey-based Social Participation in Ankylosing Spondylitis Study (SPASS) were used. Potential determinants included both contextual and disease-related factors. Depression symptoms were assessed by the depression subscale of the Hospital Anxiety and Depression Scale (HADS-D). A latent ‘depression’ variable was constructed by regressing the 7 manifest items of the HADS-D questionnaire on the outcome ‘depression’, to represent it more accurately. Candidate variables for the model were selected using univariable negative binomial regression. Direct and indirect associations between risk factors and the dimensional latent depression outcome were explored using structural equation modelling. Both theory-driven and data-driven approaches were explored. A final model was selected based on model fit criteria, clinical plausibility and explained variance in the outcome.

Results: Among 245 patients, median (interquartile range) HADS-D was 3 (1-6) and 44 patients (16%) had a HADS-D >8, indicating possible depression. The theory-driven model had poor fit and was rejected. The data-driven approach led to a model with good fit. In this final model (see Figure), contextual factors associated with depressive symptoms were male gender, a history of depression, being employed, lower income, lower mastery and worse satisfaction with social role participation. Regarding disease-related factors, Bath AS Disease Activity Index (BASDAI) was the only determinant in the final explanatory model, acted only indirectly, and had less effect on depressive symptoms than several of the contextual factors. Mastery had a central role in the path diagram and was a mediator for the effects of BASDAI, income and satisfaction with social role participation on depressive symptoms. The final model explained 64% of the variance in the latent depressive symptoms outcome.

Conclusion: Both contextual and disease-related factors contribute to depressive symptoms in AS, but contextual factors have a larger contribution. Mastery, the extent to which one feels in control over life and disease, has a key role in this process. These results support a relevance of self-efficacy in disease management and patient education. In order to improve patients’ mental health, research is warranted whether mastery and its relation with depression can be modified.

Disclosure of Interests: None declared

OP0036 EROSIONS ARE THE MOST OFTEN REPORTED STRUCTURAL LESION ON MRI OF THE SACROILIAC JOINTS IN AXSpA PATIENTS WITH IBP

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Background: HLA-B27 and sacroilitis on MRI form the basis of the Assessment of SpondyloArthritis International Society (ASAS) axial spondyloarthritis (axSpA) classification criteria. In addition, while not an entry criterion of the classification criteria, inflammatory back pain (IBP) is fundamental in the axSpA diagnostic process and it is endorsed as referral parameter in primary care. Besides inflammation on MRI, which is the hallmark of axSpA, there is still debate on the value of structural MRI lesions in these patients.

Objectives: To report on MRI of the sacroiliac joints (MRI-SIJ) findings in newly diagnosed axSpA patients stratified for the presence of IBP and HLA-B27 positivity.

Methods: Newly diagnosed and anti-TNF naïve axSpA patients of an ongoing Belgian (Be-Giant) cohort were included in this study. MRI-SIJ assessment was performed independently by 3 calibrated readers according to an adapted method of the SpondyloArthritis Research Consortium of Canada score, evaluating erosions, fatty lesions, sclerosis and ankylosis (T1-weighted and STIR images viewed simultaneously). Also, the ASAS definition of a positive MRI-SIJ was evaluated. MRI sum scores were calculated as 2 out of 3 (median) reader scores.

Results: In 138 axSpA patients MRI-SIJ data was available; 68 (49.3%) patients were male, 104 (75.4%) HLA-B27 positive and 131 (94.9%) patients fulfilled the IBP criteria according to ASAS. In the IBP+ patient groups, a large amount of structural MRI lesions were seen. In these groups, erosions are most frequently reported, with an average extent of 5 erosions. IBP- patients were rarely seen in this cohort and erosions and fatty lesions were the only structural lesions observed in these patients, with a much lower extent compared to the IBP+ patients (see table 1). There were no axSpA patients with negative MRI-SIJ, negative HLA-B27 and without IBP.

Conclusion: In this cohort of newly diagnosed anti-TNF naïve axSpA patients, structural lesions are frequently and with a high extent seen in IBP+ patients. Only in the IBP+ axSpA patients the previously reported threshold for axSpA patients of ≥3 erosions and ≥3 fatty lesions is maintained, as IBP+ axSpA patients have far fewer lesions. IBP seems to be an indicator for the presence of structural MRI-SIJ lesions in newly diagnosed axSpA patients.

Table 1. Structural lesions seen on MRI in axSpA patients stratified for IBP, HLA-B27 and a positive MRI-SIJ

<table>
<thead>
<tr>
<th>Structural lesions</th>
<th>IBP+ (49.3%)</th>
<th>IBP– (6.9%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>68</td>
<td>9</td>
</tr>
<tr>
<td>Erosions</td>
<td>3.7 (1.1;5.4)</td>
<td>0</td>
</tr>
<tr>
<td>Sclerosis</td>
<td>1.5 (0.9;2.4)</td>
<td>0</td>
</tr>
<tr>
<td>Fatty lesions</td>
<td>2.8 (1.2;6.2)</td>
<td>0</td>
</tr>
<tr>
<td>Ankylosis</td>
<td>0.1 (0;0.3)</td>
<td>0</td>
</tr>
</tbody>
</table>

*4 numbers reported are: number of patients with 1 or more of the given structural lesion (% from group total); mean±standard deviation of patients with 1 or more of the given structural lesion.

Disclosure of Interests: Manouk de Hooge: None declared, Ann-Sophie De Craemer: None declared, Thomas Renson: None declared, Philippe Carron: None declared, Liseлотte Deroo: None declared, Dirk Elewaut: None declared, Filip van den Bosch Consultant for: AbbVie, BMS, Galapagos, Janssen, Lilly, Merck, Novartis, Pfizer and UCB, Speakers bureau: AbbVie, BMS, Janssen, Lilly, Merck, Novartis, Pfizer and UCB.


OP0037 ASSOCIATION BETWEEN BONE MARROW EDEMA AND STRUCTURAL PROGRESSION IN THE SAME QUADRANT IN AXIAL SYPNDIOLARTHRITIS – 5-YEAR DATA FROM THE DESIR COHORT

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Background: The overall presence of inflammation in the MRI-SIJ is associated with overall 5-year radiographic damage in patients with axSpA1. But we do not know if a bone marrow edema (BME) lesion leads to a structural lesion at the same place (i.e. in the same quadrant).

Objectives: To investigate the association between BME and structural progression in the same quadrant of the SIJ, over time.

Methods: Patients from the DESIR cohort (early axSpA according to the rheumatologist) with ≥2 consecutive MRI-SIJ (out of baseline, 2 and 5 years), were included. Each image was independently scored by 3 trained central readers blinded to chronological order. BME was considered present in a time point if detected in ≥1 slices in each of the 8 quadrants. The prevalence of BME (yes/no) and structural lesions (sclerosis, erosions, fatty lesions and ankylosis; all yes/no) defined, per quadrant, by the agreement of ≥2 out of 3 readers, was described at BL and at 5 years. The longitudinal association between BME and each of the structural lesions in the same quadrant was tested in time-lagged multilevel Generalized Estimating Equation (GEE) models with autoregression, taking individual reader data into account, and adjusting for clinical variables selected a priori on clinical grounds (age, gender, disease activity and treatment).

Results: In total, 197 patients were included (age 34 (SD 9) years, 48% male and 61% HLA-B27 positive). While BME and fatty lesions were evenly distributed across quadrants, erosions and sclerosis occurred preferably in the iliac side (i.e. C1 and C4) (Table 1). The prevalence of BME decreased over time (baseline range: 11%–16%; 5-year range: 7%–14%), while erosions (baseline range: 2%–23%; 5-year range: 3%–28%) and especially fatty lesions (baseline range: 4%–14%; 5-year range: 9%–21%) increased. Ankylosis and sclerosis were rare in this early axSpA cohort. In the multivariable models, BME was longitudinally associated with sclerosis (OR 1.7 (95% CI 1.0; 2.8)) and fatty lesions (1.7 (1.1;2.5)). The possible association with ankylosis could not be tested due to too low number of lesions (Table 2).

Table 2. Longitudinal association between BME and structural outcomes in the same quadrant

<table>
<thead>
<tr>
<th>Structural lesion</th>
<th>BL</th>
<th>5Y</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erosions</td>
<td>11%</td>
<td>10%</td>
<td>0.49</td>
</tr>
<tr>
<td>Sclerosis</td>
<td>2%</td>
<td>7%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fatty lesions</td>
<td>4%</td>
<td>12%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ankylosis</td>
<td>1%</td>
<td>1%</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Conclusion: We here demonstrate that in early axSpA-patients inflammation in one SIJ quadrant leads to structural damage in the same quadrant. This finding reinforces the pathophysiological implications of inflammation in axSpA.

REFERENCE:

Disclosure of Interests: Santiago Rodrigues-Manica Grant/research support from: Novartis, MSD, Speakers bureau. Novartis, Alexandre Sepriano: None declared, Sofia Ramiro Grant/research support from: MSD, Consultant for: AbbVie, Lilly, MSD, Novartis, Pfizer, Sanoﬁ, Speakers bureau: AbbVie, Lilly, MSD, Novartis, Pfizer, Sanoﬁ, Robert B.M. Landewé: None declared, Pascal Claudepierre Consultant for: Honoraria from Novartis as steering committe of this survey, Anna Moltò: None declared, maxime dougados Grant/research support from: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma, Consultant for: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma, Miranda van Lunteren: None declared, Désirée van der Heijde Consultant for: AbbVie, Argen, Astellas, Astra-Zeneca, Bristol-Myers SQuibb, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, Union Chimique Belge

### High Prevalence of Sacroiliac Bone Marrow Edema on MRI in Postpartum Women: A Temporary Phenomenon

**Objectives:** To explore the association between pregnancy and giving birth on the one hand, and the occurrence of MRI lesions compatible with SpA on the other hand; and (B) if these lesions are transient.

**Methods:** Twenty-five women underwent an MRI of the sacroiliac joints (SIJ) in the first 10 days after vaginal delivery. The scan was repeated after 6 months. Both time points were scored in pairs by 3 trained readers, blinded for time sequence and subject characteristics. MRI assessment was done on 6 consecutive slices for inflammatory and structural SpA-like lesions; bone marrow edema (BME), capsulitis, enthesitis, high signal intensity in joint space, erosions, fatty lesions, sclerosis and (partial) ankylosis. In addition, the Assessment of SpondyloArthritis international Society (ASAS) definition was applied. MRI reader scores were reported as 2 out of 3 (median) scores.

**Results:** Twenty out of 25 (80.0%) subjects displayed BME; the median SPARCC score was 5 (IQR 1-11) (see table). One subject was lost to follow-up. After 6 months, 11 out of 24 (45.8%) subjects still showed BME; however, 75.5% of the baseline lesions were located in the anterior part of the SIJ; 57.3% situated on the iliac side. Structural lesions were rarely detected in this study population (see table).

Table: Number of MRI-SIJ lesions in 25 postpartum women.

<table>
<thead>
<tr>
<th>Lesion Type</th>
<th>Median</th>
<th>IQR</th>
<th>95% CI</th>
<th>Median</th>
<th>IQR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inflammatory</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPARCC (72)</td>
<td>5</td>
<td>1 – 11</td>
<td>1 – 8</td>
<td>0</td>
<td>0 – 1</td>
<td>0 – 1</td>
</tr>
<tr>
<td>Capsulitis (12)</td>
<td>0</td>
<td>0 – 0</td>
<td>0 – 0</td>
<td>0</td>
<td>0 – 0</td>
<td>0 – 0</td>
</tr>
<tr>
<td>Enthesitis (12)</td>
<td>0</td>
<td>0 – 0</td>
<td>0 – 0</td>
<td>0</td>
<td>0 – 0</td>
<td>0 – 0</td>
</tr>
<tr>
<td>High signal intensity (12)</td>
<td>0</td>
<td>0 – 4</td>
<td>0 – 3</td>
<td>0</td>
<td>0 – 0</td>
<td>0 – 0</td>
</tr>
<tr>
<td><strong>Structural</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erosions (48)</td>
<td>0</td>
<td>0 – 0</td>
<td>0 – 0</td>
<td>0</td>
<td>0 – 0</td>
<td>0 – 0</td>
</tr>
<tr>
<td>Fatty lesions (48)</td>
<td>0</td>
<td>0 – 1</td>
<td>0 – 0</td>
<td>0</td>
<td>0 – 0</td>
<td>0 – 0</td>
</tr>
<tr>
<td>Sclerosis (48)</td>
<td>0</td>
<td>0 – 0</td>
<td>0 – 0</td>
<td>0</td>
<td>0 – 0</td>
<td>0 – 0</td>
</tr>
<tr>
<td>Partial ankylosis (48)</td>
<td>0</td>
<td>0 – 0</td>
<td>0 – 0</td>
<td>0</td>
<td>0 – 0</td>
<td>0 – 0</td>
</tr>
<tr>
<td>Ankylosis (48)</td>
<td>0</td>
<td>0 – 0</td>
<td>0 – 0</td>
<td>0</td>
<td>0 – 0</td>
<td>0 – 0</td>
</tr>
</tbody>
</table>

**Conclusion:** A very high prevalence of sacroiliac BME on MRI was seen in women immediately postpartum with 64.0% even having a positive MRI for sacroiliitis according to the ASAS definition. A significant decrease in BME was seen over 6 months time, yet a substantial fraction continued to display BME after follow up. History of back pain and childbirth are crucial to take into account when interpreting an MRI-SIJ. In case of a recent pregnancy and clinical suspicion of SpA, it may be wise to postpone MRI-SIJ imaging until at least 6 months after the delivery.

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46% and 25% of ABA- and PBO-treated pts, respectively, but this was not enriched for any specific event and there were no new ABA safety signals.

Conclusion: Despite favourably impacting biomarkers of disease activity, abatacept therapy was no better than PBO for improving the clinical measures of disease. These results do not indicate a clinical benefit of abatacept in PsS.

REFERENCES:

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Despite favourably impacting biomarkers of disease activity, abatacept therapy was no better than PBO for improving the clinical measures of disease. These results do not indicate a clinical benefit of abatacept in PsS.
groups (groups 2-4) with decreased glomerular and tubular damage scores (Figure 1G). Most importantly, frequencies of CD8+CD25+FoxP3+ regulatory T cells and CD19+CD5+CD1dhigh regulatory B cells were significantly higher in MIC-treated (groups 2-4) compared to control animals of group 1, whereas double negative T cells were markedly reduced (Figure 1H).

Conclusion: MIC therapy inhibits progression of active lupus nephritis. Interestingly, preemptive MIC therapy was even able to prevent onset of disease with no significant disease activity at completion of the study. In accordance with our previous pre-clinical EAE experiments (1) and a first-in-human clinical trial in living-donor kidney transplantation (TOL-1 study), MIC therapy was able to induce an in vivo induction of regulatory cell subsets. This clinically applicable cell therapeutic approach may control lupus nephritis by specifically silencing deleterious autoimmune responses.

REFERENCES:


OP0041 MAINTENANCE OF EFFICACY AND SAFETY AND REDUCTION OF BILAG FLARES WITH USTEKINUMAB, AN INTERLEUKIN-12/23 INHIBITOR, IN PATIENTS WITH ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): 1-YEAR RESULTS OF A PHASE 2, Randomized Placebo-Controlled, CROSSOVER STUDY
Ronald van Vollenhoven1, George Tsokos2, Robert Gordon3, Kim Hung Lo3, Y Irene Gregan4, Kayin Fei5, Shaha Rosenz5, Brian H. Hahn6, Amsterdam Rheumatism and Immune Cell Research, Amsterdam, Netherlands; 2Beth Israel Hospital, Boston, United States of America; 3Janssen Research and Development, LLC, Spring House, United States of America; 4University of California LA, Los Angeles, United States of America

Background: Both IL-12 and IL-23 have been implicated in the pathogenesis of SLE. We have previously reported that treatment with an anti-IL-12/23 p40 monoclonal antibody ustekinumab (UST) resulted in greater improvement in several SLE disease measures through week 24 compared with placebo (PBO).1

Objectives: Results of global and organ-specific disease measures and flares through 1 year are reported here.

Methods: We conducted a PBO-controlled phase 2 study in 102 patients with seropositive active SLE (defined by SLICC criteria, SLEDAI score ≥6, and ≥1 BILAG A and/or ≥2 BILAG B scores). Patients were randomized (3:2) to UST (6 mg/kg single IV infusion, then 90 mg SC q8w beginning at week 8, n=60) or PBO (n=42), both added to standard background therapy. Patients receiving PBO crossed over to UST (90 mg SC q8w) at week 24. The primary endpoint was the proportion of patients achieving SLE Responder Index (SRI)-4 response at week 24. Modified intention-to-treat (mITT) analyses across SLE disease measures were performed to evaluate maintenance of response with UST between week 24 and week 48 and severe BILAG flares (≥1 new BILAG A score). Safety was assessed through week 56.

Results: As previously reported, SRI-4 response rate at week 24 was significantly greater (p=0.0007) in patients receiving UST (62%) vs PBO (32%).1 In the UST group, SRI-4 (week 24: 62% vs week 48: 63%), SRI-6 (week 24: 43% vs week 48: 48%), and SRI-6 (week 24: 43% vs week 48: 47%) response rates were sustained at 1 year. Proportions of patients with ≥4-point improvement from baseline in SLEDAI-2K score (week 24: 65% vs week 48: 67%) and with ≥30% improvement from baseline in Physician’s Global Assessment score (week 24: 66% vs week 48: 75%) were also maintained in the UST group. UST response rates were also sustained through 1 year in organ-specific disease measures (≥50% improvement in active joint counts: week 24: 87% vs week 48: 87%; ≥50% improvement in CLASI activity score: week 24: 53% vs week 48: 69%). In PBO patients who crossed over to UST at week 24 (n=33), response rates across outcomes studied were 10-20% higher at week 48 vs week 24. flare rates for patients with severe BILAG flares were 2.1/10,000 patient-years in week 0-24 and 1.1/10,000 patient-days in week 24-48 in the UST group. In the PBO group, severe BILAG flare rates were 8.4/10,000 patient-days in week 0-24 and, following UST crossover, were 4.6/10,000 patient-days in week 24-48. The occurrence of severe BILAG flares seemed to diminish after approximately 8 weeks (week 8 in UST arm, week 32 in PBO arm) of treatment with UST (Figure). No deaths, malignancies, opportunistic infections, tuberculosis cases, or unexpected serious AEs (SAEs) were observed. Incidences of ≥1 SAE were UST (week 0-24) 8.3%, PBO (week 0-24) 9.5%, UST (week 24-48) 8.9%, and PBO-UST (week 24-48) 12.1%. Safety events were consistent with the known UST safety profile.

Conclusion: UST provided sustained clinical benefit in global and organ-specific SLE-activity measures and reduced flares through 1 year, with a safety profile consistent with other indications. Thus, UST may have durable therapeutic benefit in SLE.

REFERENCE:


OP0042 LONG-TERM EFFECTS OF SYNERGISTIC B CELL IMMUNOMODULATION WITH RITUXIMAB AND BELIMUMAB COMBINATION TREATMENT IN SEVERE, REFRACTORY SLE: TWO YEAR RESULTS
Tineke Kraaij1, E.J. Arends1, Laura van Dam1, Sylvia Kamerling1, Paul J.A. van Dale2, Obbo Winne Breadoweld1, Argo Ray1, Jaap Bakker1, Ingeborg Bajema1, Hans Ulrich Scher1, Thomas Huizinga1, Tom Rabe1, Cees van Rooij1, Y.K. Chio Teng1, Leiden University Medical Center (LUMC), Nephrology, Leiden, Netherlands; 2Erasmus MC, Division of Clinical Immunology, Rotterdam, Netherlands; 3Leiden University Medical Center (LUMC), Clinical Chemistry and Laboratory Medicine, Leiden, Netherlands; 4Leiden University Medical Center (LUMC), Pathology, Leiden, Netherlands; 5Leiden University Medical Center (LUMC), Rheumatology, Leiden, Netherlands

Background: We conducted a phase 2, proof-of-concept study (SynBioSe study) in which we combined rituximab and belimumab (RTX+BLM) for treatment of SLE patients with severe, refractory disease. We have previously reported that RTX+BLM effectively reduced relevant anti-nuclear autoantibodies (ANAs) and showed a clinical response at 24 weeks.1

Objectives: The aim of the present study is to investigate the long-term immunological and clinical effects of RTX+BLM in severe, refractory SLE patients.

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Methods: Fifteen severe, refractory SLE patients were included and followed for 2 years. Patients received RTX at week 0 and 2 and BLM at week 4.6, 8 and then 4-weekly until week 104. Clinical response was assessed by achievement of low level of disease activity (LLDAS). By using specific antibody assays and high sensitivity flowcytometry (HS-FACS), we longitudinally followed, respectively, levels of SLE-specific ANAs and B-cell subsets.

Results: Ten patients (67%) showed a good clinical response after 24 weeks, referred to as ‘responders’. Two of these patients (13%) switched treatment after 24 weeks due to a pregnancy wish and 6 patients (33%) continued study treatment throughout the complete 2 years of follow-up. Five patients (33%) discontinuation treatment due to persistent LN (n=2), major flare (n=2) or relapsing minor flare (n=1), together referred to as ‘non-responders’. Responders achieved LLDAS at a median of 24 weeks [range 12-36] and remained in LLDAS for 76 weeks [56-92] out of 104 weeks of follow-up. In 7 patients with active LN, 6 attained a complete renal response. In responders, ANAs showed significant and specific reduction throughout 2 years with achievement of seronegative anti-dsDNA immunofluorescence in 6 out of 6 anti-dsDNA positive patients at baseline while total IgG, anti-tetanus and anti-rubella antibodies remained stable. By using HS-FACS, a median decrease of 97% [99.3±35] CD19- B-cell depletion was achieved at 24 weeks. Long-term follow-up showed that B-cell repopulation was inhibited throughout 2 years with a persistent median decrease of 84% [-92±22] compared to baseline. Further analysis of B-cell subsets revealed that in the responders, double negative (DN) B-cells (CD27-IgD-) reached maximum depletion at 4 weeks (median 1.09±10^6 cells/liter [range 0.23±10^6-4.31±10^7]), which lasted up to week 72 with a median of 1.26±10^6 cells/liter [0.79±10^6-4.11±10^7] at week 72, similar to values at nadir. This was in contrast to non-responders, where maximum depletion of DN B-cells was reached at 12 weeks (0.48±10^5 [0.17±10^5-0.86±10^5] after which these cells increased to 2.29±10^5 [0.49±10^5-3.49±10^6] at 24 weeks.

Conclusion: Over 2 years follow-up, RTX+BLM for severe, refractory SLE patients prevented complete B-cell repopulation with persistent and specific reduction of ANAs. Clinical response was observed in 67% of patients and treatment discontinuation due to high disease activity was associated with early repopulation of DN B-cells. These data warrant further studies on clinical and immunological benefits of combination treatment RTX+BLM.

REFERENCE:

Trial registration: ClinicalTrials.gov NCT02284984

Disclosure of Interests: Tineke Krajii; None declared, E.J. Arends: None declared, Laura van Dam: None declared, Sylvia Kamerling: None declared, Paul LA van Dale; None declared, Olof Winne Bredevold: None declared, Argho Ray; None declared, Jaap Bakker; None declared, Ingeborg Bajema Consultant for: GSK, Hans Ulric Scherer Grant/research support from: Sanofi, BMS, Thomas Hulinzinger Consultant for: Merck, UCB, Bristol Myers Squibb, Biotest AG, Pfizer, GSK, Novartis, Roche, Sanofi-Aventis, Abbott, Crescendo Bioscience Inc., Nycomed, Boehringer, Takeda, Zydis, Epirus, El Lilly, Ton Rabellink; None declared, Cees van Kooten: None declared, Y.K. Onno Teng Grant/research support from: Received lecture fees/consultancy fees from GSK and from Aurinia Pharmaceuticals.

that reported the incidence of sustained amenorrhoea (defined as at least 12 months of amenorrhoea) during i.v.CYC treatment in patients with ARD; and those that assessed sustained amenorrhoea in patients receiving GnRHα and i.v.CYC, compared to controls receiving i.v.CYC alone.

Results: 1099 articles were identified and their titles and abstracts screened, following which 81 papers were selected for full text review. 31 studies were then identified that addressed the risk of sustained amenorrhoea with i.v.CYC in n=1382 patients with ARD. The majority of these patients had systemic lupus erythematosus (1326 out of 1382 patients, 96.0%). The mean age was 24.9 (range 13-36.1) years. Sustained amenorrhoea occurred in 269 (19.5%) patients (mean age range 23.9-25.6 years) receiving GnRHα and i.v.CYC, and 37 controls (mean age range 25-29.4 years) given i.v.CYC only. Sustained amenorrhoea occurred in 29/6 (3.6%) patients treated with GnRHα, compared to 15/37 (40.5%) of controls. The pooled odds ratio of sustained amenorrhoea with GnRHα and i.v.CYC compared to i.v.CYC alone was 0.0543 (95%CI 0.0115-0.2576, p=0.0002). The number needed to treat was 2.7 (95%CI 2.0-4.4) and the absolute risk reduction was 92.0% (95%CI 35.6-38.4%).

Conclusion: Although the risk of POI with i.v.CYC was associated with increasing age, it was observed across all age groups and from cumulative doses of 1g or more. GnRHα markedly reduced this risk in ARD, and therefore should be considered for concomitant use with i.v.CYC in all women of child-bearing age with ARD.

REFERENCES:

Aknowledgement: Arthritis Australia


Table 1: Baseline characteristics of participants (n=80)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean±SD</td>
<td>48.8±15.6</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>74 (93)</td>
</tr>
<tr>
<td>Disease duration (years), median (IQR)</td>
<td>2.0 (1.0-4.0)</td>
</tr>
<tr>
<td>Anti-Ro/SSA, n (%)</td>
<td>71 (89)</td>
</tr>
<tr>
<td>Previous use of DMARDS, n (%)</td>
<td>34 (42.5)</td>
</tr>
<tr>
<td>Use of prednisone, n (%)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>ESSDAI, median (IQR)</td>
<td>13 (8-17)</td>
</tr>
<tr>
<td>UMD, mean±SD</td>
<td>6.7±1.6</td>
</tr>
<tr>
<td>EQ-5D index, median (IQR)</td>
<td>0.71 (0.57-0.84)</td>
</tr>
<tr>
<td>UWS (ml/min), median (IQR)</td>
<td>0.05 (0.01-0.13)</td>
</tr>
<tr>
<td>SWS (ml/min), median (IQR)</td>
<td>0.16 (0.04-0.35)</td>
</tr>
<tr>
<td>OSS*, mean±SD</td>
<td>4.5±3.4</td>
</tr>
<tr>
<td>Schirmer* (mm/5 min), median (IQR)</td>
<td>3 (0-10)</td>
</tr>
<tr>
<td>IgG (g/L), median (IQR)</td>
<td>18.2 (14.4-25.9)</td>
</tr>
<tr>
<td>RIU (IU/mL), median (IQR)</td>
<td>25 (5-71)</td>
</tr>
</tbody>
</table>

* Average of left and right eye.


* Average of left and right eye.

Objectives: To compare efficacy and safety of cyclosporine (CYA) with mycophenolate mofetil (MMF) and with azathioprine (AZA) in the long-term maintenance therapy of LN.

Methods: Ninety-six patients (pts) (93 females, mean age 31.9±12.7 years) with SLE and biopsy proven LN (16 pts/class III; 64 pts/class IV, 16 pts/class V ISN/RPS). Fifty-six pts entered this study at diagnosis of LN and 40 during a course of a LN flare. Twenty-five pts (30%) had Glomerular Filtration Rate (eGFR) <60ml/min (MDRD) and proteinuria was 3.88±2.89 g/day. Induction therapy: 3 methylprednisolone pulses followed by oral prednisone in 92 pts and oral prednisone in 4 pts; cyclophosphamide in 74% of pts, MMF in 9.4%, AZA in 5.2%, and other immunosuppressors in 11.4%. After six months, 30 pts started maintenance therapy with CYA, 32 with MMF and 34 with AZA. At induction therapy there were not significant differences between the three groups in histological classes at renal biopsy, mean serum creatinine, eGFR and proteinuria, and type of induction therapy. The mean follow-up after the beginning of the study was 15.9 years for CYA, 10.5 for MMF, 14.1 AZA. Primary endpoint was renal response at 1, 5 and 10 years defined as complete renal response: eGFR>60ml/min and proteinuria <0.5g/die, partial response: eGFR>60ml/min and proteinuria 0.5-5g/die, no response: eGFR<60ml/min. Secondary endpoint: incidence of flare and safety.

Results: At the beginning of maintenance therapy, the mean serum creatinine and eGFR were similar in the 3 groups (0.92±0.26mg/dl, eGFR 109.9±49.5ml/min in CYA, 0.86±0.4mg/dl, eGFR 119.1±44.8 in MMF, 0.85±0.3mg/dl, eGFR 108.6±43.9ml/min in AZA). Proteinuria was higher in CYA group (CYA: 2.03±1.7g/day; MMF: 0.77±0.8g/day; AZA: 1.2±1.1g/day). At the beginning of maintenance therapy, complete, partial and no response were 26.6%, 60%, and 13.4% in CYA, 53.1%, 43.8% and 3.1% in MMF and 38.2%, 58.8% and 3% in AZA group (Fig 1). At 1 year, after 6 months of maintenance therapy, in CYA group the percentage of pts in complete remission increased to 73% (vs 65.6% in MMF and 40% in AZA), at 5 years it was 80% (vs 83% in AZA and in MMF) and 88% at 10 years vs 70% in MMF and 68% in AZA (Fig 2,3,4). The percentage of non-responding pts was stable from 1 to 10 years in the CYA group (around 13%), it slightly increased in MMF group (from 3.1 to 13.5%) and in AZA group (from 15 to 24%). During the study, SLE flares occurred in 30% of CYA group, 41% in MMF and 32% of the AZA. The average time from the beginning of the study and the first flare was 3.95±2.76years in CYA, 3.62±1.60 in MMF and 5.9±2.37 in AZA. No side effects were reported in 90% of pts treated with CYA, in 81.3% with MMF and in 85.3% with AZA group.

Conclusion: This is the first study comparing these 3 drugs as maintenance therapy in the long term. After 10 years of observation, CYA, AZA and MMF have proven to be effective in consolidating and maintaining the remission of LN. Of interest are the results achieved in the CYA group. Despite worse clinical conditions at the beginning of maintenance therapy, CYA allowed a rapid achievement of LN remission in the great majority of pts compared to AZA and MMF. Remission persisted over 10 years of observation. The number and type of flares and of side effects were not different between groups.

REFERENCE:

Disclosure of Interests: Lorenza Maria Argolini: None declared, Elena Elefantie: None declared, Francesca Saccon: None declared, Valentina Binda: None declared, Maria Gerosa: None declared, Luigi Sinigaglia Speakers bureau: Yes, I, ve been invited speaker by Amgen, Lilly, UCB, Abbvie, Roche and BMS., Piergiorgio Messa: None declared, Andrea Doria: None declared, Marta Mosca Paid instructor for: GlaxoSmithKline, Lilly, UCB, Gabriella Moroni: None declared


WEDNESDAY, 12 JUNE 2019

Crystals
Objectives: The first ever GWAS of clinically defined gout cases and asymptomatic hyperuricemia (AHUA) controls was performed to identify novel gout loci that aggravate AHUA into gout, as distinct from loci causing SUA elevation.

Methods: We carried out a GWAS of 945 clinically-defined gout cases and 1,003 AHUA controls followed by two replication studies. In total, 2,860 gout cases and 3,279 AHUA controls (all Japanese males) were analyzed. And also, we compared the odds ratios (ORs) for each locus in the present GWAS (gout vs. AHUA) with those in the previous GWAS (gout vs. normouricemia). Furthermore, we investigated the effect of each locus on SUA using the results from our recent GWAS meta-analysis of SUA with a total of 121,745 Japanese subjects.

Results: This new approach enabled us to identify two novel gout loci (rs7927466 of CNTN5 and rs9952962 of MR302F) and one suggestive locus (rs12980365 of ZNF724) at the genome-wide significance level (P<5.0×10^-8). One of them, rs671 of ALDH2, was identified as a gout locus by GWAS for the first time. Comparing ORs for each locus in the present vs. the previous GWAS revealed three “gout vs. AHUA GWAS” specific loci (CNTN5, MR302F and ZNF724) to be clearly associated with mechanisms of gout development which distinctly differ from the known gout risk loci that basically elevate serum uric acid (SUA) level. The effect of each locus on SUA using the results from our recent GWAS meta-analysis of SUA are consistent with those of the present study.

Conclusion: This first discovery of “AHUA to Gout” loci using a new GWAS strategy will lead to elucidation of the molecular mechanism of the last step of gout development and to the prevention of gout attacks in high-risk AHUA individuals.
OP0049 FACTORS ASSOCIATED WITH EARLY FLARES WHEN INITIATING URATE LOWERING THERAPIES. POST-HOC ANALYSIS OF CLEAR 1.2 AND CRYSTAL TRIALS

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1Hospital Lanboisire, Paris, France; 2Servicio de Reumatología, Hospital Universitario Cruces, Cruces, Spain; 3Grunenthal, Aachen, Germany

Background: Initiation of urate lowering therapies (ULT) in patients with gout can trigger flares which could contribute to poor treatment adherence. The EULAR guidelines recommend a prophylactic treatment with colchicine or low dose NSAIDs for up to 6 months. However, long term treatment with either NSAIDs or colchicine can be poorly tolerated or contra-indicated. Thus, identification of risk factors for flares to identify patients who would benefit more from a prophylactic treatment could improve patients care.

Objectives: To investigate the influence of patient and treatment related factors on the occurrence of flares 1 month after the initiation of ULT.

Methods: Data are from n=1018 patients (mean age 52.0 (SD 11.1) years; 95.2% male) not responding to allopurinol or febuxostat monotherapy and who received lesinurad (200 mg or 400 mg) in the CLEAR and CRYSTAL trials. Patients were prescribed colchicine (84%) or NSAIDs (12.9%) as prophylactic treatment. Data from 3 trials were pooled and the following covariates were considered in the main analysis using a Generalized Estimation Equation (GEE) model: age, gender, serum uric acid (SUA) levels, baseline body mass index, renal function, and presence of tophus, type of gout flare prophylaxis, triglycerides, comorbidities (smoking, tobacco, diabetes, hypertension, hyperlipidemia) antihypertensive and lipid lowering medications at baseline and newly started and change in SUA levels. A multivariate analysis was conducted using the occurrence of flares as response measured from baseline until month 1.

Results: In the multivariate analysis, tophus at baseline and gender (female) were both associated with an increased risk of early flares: OR=2.7 (95% CI: 1.7-4.2) and OR=1.8 (95% CI: 1.0-3.4), respectively, whereas hyperlipidemia and hypertension were associated with a decreased risk of flares: OR=0.64 (95% CI: 0.45-0.91) and OR= 0.82 (95% CI: 0.39-0.90). There was a trend toward a reduced risk of flares with colchicine versus NSAIDs: OR=0.71 (95% CI: 0.47-1.05). Neither the duration of gout nor the change in SUA levels modified the risk of flares.

Conclusion: This analysis shows that gender (female) and tophus are independent risk factors of early flares when initiating ULT, and suggests that colchicine can be poorly tolerated or contra-indicated. Thus, identification of risk factors for flares to identify patients who would benefit more from a prophylactic treatment could improve patients care.

Disclosure of Interests: None declared

OP0050 ADDITIVE VALUE AND DIAGNOSTIC ACCURACY OF DUAL-ENERGY CT FOR THE DIAGNOSIS OF GOUT: A PROSPECTIVE STUDY IN SUBJECTS WITH UNCLASSIFIED MONO OR OLIGOARTHRITIS

Mihaela Gamala1,2, Johannes W. G. Jacobs3, Suzanne Linn-Rasker2, Maarten Niv4, Ben Heggelman5, Pieterem Pasker6, Jacob M. van Laar7, Ruth Klaasen1
1University Medical Center Utrecht, Rheumatology and Clinical Immunology, Utrecht, Netherlands; 2Northwest Clinics, Rheumatology, Alkmaar, Netherlands; 3University Medical Center Utrecht, Rheumatology and Clinical Immunology, Utrecht, Netherlands; 4Meander Medical Center, Rheumatology and Clinical Immunology, Utrecht, Netherlands; 5Meander Medical Center, Rheumatology, Amersfoort, Netherlands; 6Meander Medical Center, Radiology, Amersfoort, Netherlands; 7Meander Medical Center, Meander Academy, Amersfoort, Netherlands

Background: The latest diagnostic technique to visualize monosodium uric acid (MSU) deposits is Dual Energy CT scan (DECT).1

Objectives: To assess the additive value and accuracy of DECT in diagnosing gout in a prospective study in subjects with unclassified arthritis.

Methods: We included 100 consecutive patients with acute unclassified mono or oligo arthritis who presented to the outpatient clinic of the Department of Rheumatology of Meander Medical Centre, Amersfoort, the Netherlands, ClinicalTrials.gov NCT03038386. Eleven patients dropped out, see Figure. Patients underwent aspiration of the arthritic joint (see Table) and a DECT scan of hands and wrists, knees, ankles and feet bilaterally. The 2015 EULAR/ACR gout classification criteria were used to score the subjects, with and without DECT result, to determine the additive value of DECT. Sensitivity and specificity of DECT for diagnosing gout were calculated separately for at the joint and at individual persons’ level, using as reference standards microscopy of synovial fluid (SF) and the gout classification criteria.

Results: For demographic and clinical characteristics of the patients see Table 1, and for study data and outcomes see Figure and Table 2. Sixty-eight of 89 patients (76.4%) fulfilled the 2015 EULAR/ACR criteria for gout. Of the 98 patients with SF aspiration, 55 (56%) were positive for MSU; of these, 89 subjects underwent DECT, of whom 38 had a negative microscopy result. Of these 38 subjects, 14 (37%) met the gout classification criteria only after a positive DECT result.

Conclusion: Our findings suggested that DECT could have an additive value to clinical algorithms in subjects with undifferentiated arthritis when microscopy of SF fails to demonstrate the presence of MSU crystals.


Table 1. The characteristics of the patients (n=89) in the analysis

<table>
<thead>
<tr>
<th>Patients MSU positive (n=51)</th>
<th>Patients MSU negative (n=38)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean (SD)</td>
<td>60 (16)</td>
</tr>
<tr>
<td>Gender, N (%)</td>
<td>44 (86.3)</td>
</tr>
<tr>
<td>Arthritic joint aspirated (N, %)</td>
<td>32 (66.7)</td>
</tr>
<tr>
<td>Other joints</td>
<td>19 (33.3)</td>
</tr>
<tr>
<td>Serum uric acid (µmol/L)</td>
<td>499 (86)</td>
</tr>
<tr>
<td>Period between 1st arthritis attack and baseline visit in months, median (IQR)</td>
<td>12 (0.9-48)</td>
</tr>
</tbody>
</table>

Table 2. Diagnostic accuracy of DECT

<table>
<thead>
<tr>
<th>Reference standard</th>
<th>Tp</th>
<th>Fp</th>
<th>Tn</th>
<th>Fnn</th>
<th>Sensitivity (95%CI)</th>
<th>Specificity (95% CI)</th>
<th>Diagnostic accuracy (95% CI)</th>
</tr>
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<tbody>
<tr>
<td>joint localisation</td>
<td>MU</td>
<td>28</td>
<td>13</td>
<td>25</td>
<td>0.55 (0.40-0.69)</td>
<td>0.68 (0.49-0.79)</td>
<td>0.60 (0.49-0.79)</td>
</tr>
<tr>
<td>based patient</td>
<td>MU</td>
<td>39</td>
<td>20</td>
<td>12</td>
<td>0.77 (0.63-0.87)</td>
<td>0.80 (0.71-0.89)</td>
<td>0.64 (0.53-0.75)</td>
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<tr>
<td>joint localisation</td>
<td>EULAR 2015</td>
<td>41</td>
<td>0</td>
<td>27</td>
<td>0.60 (0.54-0.66)</td>
<td>1.00 (0.84-1.0)</td>
<td>0.70 (0.59-0.79)</td>
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<tr>
<td>based patient</td>
<td>EULAR 2015</td>
<td>56</td>
<td>3</td>
<td>12</td>
<td>0.82 (0.71-0.91)</td>
<td>0.86 (0.74-0.98)</td>
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</tr>
<tr>
<td>joint localisation</td>
<td>MU</td>
<td>11</td>
<td>7</td>
<td>12</td>
<td>0.55 (0.41-0.70)</td>
<td>0.63 (0.38-0.89)</td>
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<td>based patient</td>
<td>MU</td>
<td>16</td>
<td>10</td>
<td>4</td>
<td>0.80 (0.66-0.94)</td>
<td>0.47 (0.24-0.69)</td>
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<tr>
<td>joint localisation</td>
<td>EULAR 2015</td>
<td>18</td>
<td>0</td>
<td>11</td>
<td>0.60 (0.40-0.80)</td>
<td>1.00 (0.69-1.0)</td>
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<td>based patient</td>
<td>EULAR 2015</td>
<td>25</td>
<td>1</td>
<td>4</td>
<td>0.86 (0.68-0.96)</td>
<td>0.90 (0.73-0.96)</td>
<td>0.87 (0.73-0.99)</td>
</tr>
</tbody>
</table>

* according to patient
Disclosure of Interests: Mihaela Gamala: None declared, Johannes W. G. Jacobs Grant/research support from: Roche, Consultant for: Roche, Suzanne Linn-Rasker: None declared, Maarten Nix: None declared, Ben Heggelman: None declared, Pieternel Pasker: None declared, Jacob M. van Laar Grant/research support from: Generitech, Consultant for: F. Hoffmann-La Roche, Ruth Klaasen: None declared DOI: 10.1136/annrheumdis-2019-eular.509

COP0051 DEVELOPMENT OF A MULTIVARIABLE IMPROVEMENT MEASURE FOR GOUT
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Background: Inflammatory rheumatic diseases are generally multifaceted disorders and the complex pathology underlying these conditions makes it difficult to assess patient status and the efficacy of therapy with a single outcome measure. This has prompted the development of composite measures for many rheumatic diseases. Gout is also a multifactorial inflammatory disease in which patients experience a wide range of signs and symptoms, including intermittent and persistent pain and inflammatory arthritis, tophi and disability. Most assessments of gout and response to urate-lowering therapy (ULT) have focused primarily on the ability to lower serum urate and decrease the frequency of flares. Recognition that assessment of ULT and other treatments for gout could be facilitated by endpoints that more closely reflect the multidimensional impact of the disease has prompted an interest in developing composite measures, although there is no consensus on the most appropriate composite measure to employ.

Objectives: To develop an evidence-based gout multivariable improvement measure (GMIM) that captures the spectrum of gout manifestations and is sensitive to change.

Methods: Databases from patients with chronic refractory gout who participated in two randomized 6 month clinical trials (RCTs) of pegloticase were reviewed

Sub-sets who had persistent urate lowering (responders) to bi-weekly pegloticase (n=36) and those who had only transient urate lowering (non-responders, n=49) were identified and compared to those who received placebo (n=43). Initially individual patients were assessed for achievement of previously reported criteria for remission: serum urate <6 mg/dL, absence of tophi and flares, patient global assessment, and pain (each <2 on a 10-point visual analog scale). A repeated measures mixed effects model controlling for repeated observations with backward elimination using data from these patients was employed to determine the model components that best correlated with time to maximum benefit. This analysis resulted in the addition of swollen and tender joints to the outcome measure. In order to assess the degree of improvement, each subject was scored based upon a serum urate >6 mg/dL and 20, 50 or 70% improvement in 4 of the 6 clinical evaluations and termed GMIM0, 20, 50, 70.

Results: GMIM was able to capture gradation of change in the treated populations and also distinguish responses in those with persistent versus those with transient urate lowering and subjects treated with placebo (Figure 1). At 3 and 6 months, achievement of GMIM20, 50 and 70 in persistent responders occurred significantly more often vs placebo and versus non-responders without persistent urate lowering. Sensitivity analysis indicated that flares contributed minimally to the model.

Conclusion: GMIM effectively captures changes in disease severity in response to treatment in patients with advanced gout treated with pegloticase. GMIM0, 20, 50, 70 may serve as an evidence-based tool for assessment of the quality of response to therapies in subjects with gout in medical practice or in clinical trials.

REFERENCES:


COP0052 FAILURE TO REACH SERUM URATE TARGET IS ASSOCIATED WITH ELEVATED MORTALITY IN GOUT
Fernando Perez-Ruiz1, Pascal Richette2, Austin Stack3, Ravi Karna4, Maria Jesus Garcia de Yebenes5, Loreto Carmona5, Cruzes University Hospital, Rheumatology Division, Baracaldo, Spain; 2 Labiosiere Hospital, Rheumatology Division, Paris, France; 3 University Hospital Limerick, Nephrology Division, Limerick, Ireland; 4 Grunenthal, Aachen, Germany; 5 Innusus, Madrid, Spain

Background: Gout is associated with an increased risk of cardiovascular events and death. It has been shown that both overall and risk of death are associated with increasing gout severity, as reflected by the number of tophi. It remains to be proven whether better control of gout through lowering of serum uric acid (sUA) confers a survival advantage.

Objectives: To determine the impact of achieving sUA less than 6 mg/dL (vs greater) on mortality risk among gout patients.

Methods: Analysis of data from a prospective follow-up cohort (1992 to 2017) of patients attending a gout clinic (85% of patients with microsopce or ultrasound diagnosis) and with at least one follow-up visit. Mortality was confirmed from medical records, patients’ families, or local death registries if needed. sUA levels were monitored during follow-up and the average sUA until sUA was stable was used as the primary exposure dichotomized as < 6 mg/dL (versus > 6 mg/dL). Descriptive variables and potential confounders included: age, gender, body mass index, previous treatment with urate-lowering drugs (ULDs), number of joints affected at entry, presence of subcutaneous tophi, radiographic evidence of articular damage, number of gout flares in the year preceding evaluation, previous diagnosis of cardiovascular (CV) disease, loop diuretic use, alcohol intake, diabetes, hypertension, hyperlipidemia, and renal function impairment. In addition, the Kaiser Permanente documentation of comorbidities was further used to risk stratify patients from low to high risk of death. Univariate and multivariate Cox proportional hazards models were used to determine mortality risks expressed a hazard ratios (HR) and 95% Confidence Intervals (CI).

Results: The study cohort included 1,193 patients (92% men, mean age 60.6, 6.8 years disease duration, with an average of 3-4 flares in the previous year). Mean follow-up was 48 (median 30, IQR 12-66), with 4,830 patient-year observation. Mean sUA at baseline was 9.1 mg/dL and 16.3% of the patients maintained sUA levels <6 mg/dL despite treatment. A total of 158 deaths occurred (13% overall mortality), with loss to follow-up in 286 cases (24%). Overall crude mortality rate was 32.7% per 1,000 patient-years (95% CI: 28.0-38.2) and was significantly higher for patients with sUA >6 mg/dL, 80.9 per 1,000 person years (95% CI: 59.4-110.3) compared to patients with sUA <6 mg/dL, 25.7 per 1,000 person-years (95% CI: 21.3-30.9). With adjustment for age, sex, previous CV events, and baseline sUA concentration, a sUA > 6 mg/dL was associated with a HR of 2.39 (1.64 - 3.50).

Conclusion: Failure to reach a target sUA level of 6 mg/dL is an independent predictor of mortality in gout patients. Control of gout with achievement of sUA target <6 mg/dL should be considered in order to improve patient survival.


COP0053 CERAMIDES AND DIHYDROCERAMIDES LEVELS ARE ASSOCIATED WITH THE INFLAMMATORY RESPONSE IN A MURINE MODEL OF GOUT
Alexander Sjö1, Florence Meh1, Nicola Harris2, Veronique Chobaz1, Hector Gallart-Avala3, ChEV, Rheumatology, University of Lausanne, Lausanne, Switzerland; 2 Monash University, Melbourne, Australia

Background: The metabolic syndrome is strongly associated with gout and hyperuricemia in man. Patients with gout commonly report acute flares after eating particular foods and it is suspected that metabolic changes, apart from serum urate levels, influence the triggering of the inflammatory response to MSU crystals.

Disclosure of Interests: Alexander Sjö, Nicola Harris, Veronique Chobaz, Hector Gallart-Avala Employee of: ChEV, Rheumatology, University of Lausanne, Lausanne, Switzerland; 2 Monash University, Melbourne, Australia

REFERENCES:

Objectives: By studying the metabolic changes that impact on the response to MSU crystals in a murine model of gout, we hope to identify the dietary effect on metabolites that are associated with the inflammatory response to MSU crystals.

Methods: Male mice (C57Bl/6) were fed either a normal diet (ND) or high fat diet (HFD, D12492O) for 6 weeks. During the last 4 weeks of feeding, half the mice in each group were treated with antibiotics (Enrofloxacin 0.25% + ceo-amoxicillin) to induce a germ-free state. At day 0, mice were injected i.p with 1mg of MSU crystals. Mice were sacrificed 6h after i.p injection. Serum, plasma and peritoneal exudate samples were collected at sacrifice and plasma obtained 3 weeks before sacrifice. Untargeted and targeted liquid chromatography – mass spectrometry based-metabolomics approach was performed on serum and plasma samples. IL1 and IL6 were measured in serum and peritoneal exudates by ELISA. Animal experimental authorization was obtained for these experiments.

Results: Mice fed a HFD had a greater serum and peritoneal IL6 response to MSU. In an untargeted analysis, multiple metabolic alterations were observed related to diet. Targeted analyses of sphingolipids were performed. Both diet and inflammation (MSU injection) altered plasma sphingolipid levels. No effect of antibiotics was observed. MSU injection induced marked changes in the sphingolipid profile (38.2% of explained variance), while diet had a lesser effect (12.6% of explained variance). Mice fed an HFD had significantly higher serum IL6 before and peritoneal IL6 levels after MSU injection than mice fed a ND. DhCer C16:0 and Cer C16:0 showed significantly negative correlations with IL6 levels. DhCer C16:0 and Cer C16:0 levels decreased significantly after MSU injection. Pre-MSU levels of DhCer C16:0 and Cer C16:0 showed significantly negative correlations with IL6p levels after i-p injection in HFD animals.

Conclusion: The sphingolipid profile was significantly changed by diet and inflammation. In mice given a HFD, the levels of particular ceramides were significantly correlated with subsequent inflammatory response as assessed by IL6 secretion, suggesting that they may play a role in modulating the inflammatory response to MSU. These same ceramides and their derivatives have been linked to susceptibility to diabetes and cardiovascular diseases. Further investigation of these sphingolipids in gout in man is warranted.

REFERENCES:


OP0054 OCCUPATIONAL EXPOSURE TO INORGANIC DUST – A NOVEL RISK FACTOR FOR INCIDENT GOUT?

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Background: Hyperuricemia and factors contributing to it are strong risk factors for gout but it is still unexplained why only some individuals with hyperuricemia develop gout. Additional risk factors for gout could be genetic or related to comorbidity, lifestyle or occupation. Occupational exposure to inorganic dust has previously been linked to an increased occurrence of inflammatory rheumatic diseases such as rheumatoid arthritis and could possibly increase the risk of gout.

Objectives: To evaluate if occupational exposure to inorganic dust increases the risk of incident gout.

Methods: Gout was defined as having at least one ICD-10 code for gout (M10 or M14.0) in the population based health care database of the Western Swedish Health Care Region (VEGA), during the years 2006-2012, without any gout diagnosis during at least 6 years previously. Individuals with gout that were employed in the 5-year period prior to first diagnosis were included for analysis. Population controls without gout were identified in the census register by Statistics Sweden, in the 5-year period prior to first diagnosis were included for analysis. Population controls, n=19339; Men: Gout cases, n=4751; Women: Gout cases, n=1369. Population controls, n=25074; Men: Gout cases, n=7074; Women: Gout cases, n=32 (2) 182 (13)

Results: The exposure to inorganic dust increased the risk of incident gout. Exposure to inorganic dust was described with odds ratios, calculated using conditional logistic regression, for the whole population and stratified by sex.

Conclusion: As expected, previous known risk factors for gout such as obesity and alcoholism were strongly associated with incident gout. In univariate analyses, exposure to inorganic dust was also associated with gout. After adjusting for alcohol abuse and obesity, the relationship was attenuated in men but remained in women, providing evidence that occupational exposure to inorganic dust might be a previously unknown risk factor for gout.

REFERENCE:

Disclosure of Interests: Valgerdur Sigurdardottir: None declared, Anna Sváð: None declared, Lennart T.H. Jacobsson Consultant for: LJ has received lecture and consulting fees from Pfizer, Abbvie, Novartis, Eli-Lilly and Janssen, Linus Schöler: None declared, Kjell Tönn: None declared, Mats Dehlin: None declared

WEDNESDAY, 12 JUNE 2019

JIA: From new horizons to treatment perspectives of current ones.

OP0055 Efficacy of canakinumab, on a reduced dose or a prolonged dose interval without concomitant corticosteroids and methotrexate, in patients with systemic juvenile idiopathic arthritis

Pierre Quentin1, Ekaterina Alexeeva2, Carline Wouters3, Inmaculada Calvo3, Timmari Kaliritch2, Nico Wulfsgraaf3, Xiaoling Wei3, Alan Slade3, Ken Abrams3, Alberto Martin2, Neckers-Enfants Malades Hospital, Paris, France; 2National Medical Research Center of Children’s Health and I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation; 3Gaskuhsberg University Hospital, Leuven, Belgium; 4Hospital Universitario La Fe, Valencia, Spain; 5Charité Berlin Campus Virchow, Berlin, Germany; 6University Medical Center Utrecht, Utrecht, Sweden; 7China Novartis Institutes for Biomedical Research Co., Ltd., Beijing, China; 8Novartis Pharmaceuticals Corporation, East Hanover, United States of America; 9Università di Genova-Pediatría II, Genoa, Italy

Background: Canakinumab (CAN), a selective, human anti-IL-1β mAb, has shown sustained therapeutic effect along with corticosteroid (CS) dose reduction/discontinuation in patients (pts) with systemic juvenile idiopathic arthritis (SJIA), in a long-term extension study (NCT00891046).1 Objectives: To evaluate the efficacy and safety of 2 different CAN tapering regimens in SJIA pts who were in clinical remission (NCT02296424).

Results: 6120 gout cases and 25074 controls were included. Frequencies of exposures (n (%)) and odds ratios (OR 95% conf. int.) for association of risk factors with incident gout are shown in the table below.

<table>
<thead>
<tr>
<th>Group</th>
<th>Exposed to inorganic dust</th>
<th>Alcohol abuse</th>
<th>Obesity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole population</td>
<td>Gout cases, n=6120</td>
<td>Controls, n=25074</td>
<td>OR univariable*</td>
</tr>
<tr>
<td></td>
<td>1568 (30)</td>
<td>7074 (28)</td>
<td>538 (2)</td>
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<tr>
<td></td>
<td>2.37 (2.04 to 2.81)</td>
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<tr>
<td></td>
<td>2.74</td>
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<td></td>
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<tr>
<td></td>
<td>4.36</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.81 (4.25 to 4.38)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>Gout cases, n=4751</td>
<td>Controls, n=19339</td>
<td>OR univariable*</td>
</tr>
<tr>
<td></td>
<td>1615 (34)</td>
<td>6343 (33)</td>
<td>471 (2)</td>
</tr>
<tr>
<td></td>
<td>2.62</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4.19</td>
<td></td>
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<tr>
<td></td>
<td>3.93 (3.45 to 4.68)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Women</td>
<td>Gout cases, n=1369</td>
<td>Controls, n=5735</td>
<td>OR univariable*</td>
</tr>
<tr>
<td></td>
<td>221 (16)</td>
<td>731 (13)</td>
<td>67 (1)</td>
</tr>
<tr>
<td></td>
<td>2.69</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>4.39</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>3.85 (3.38 to 4.48)</td>
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</tbody>
</table>

Includes inorganic dust, alcohol abuse and obesity as covariates.

Conclusion: As expected, previously known risk factors for gout such as obesity and alcoholism were strongly associated with incident gout. In univariate analyses, exposure to inorganic dust was also associated with gout. After adjusting for alcohol abuse and obesity, the relationship was attenuated in men but remained in women, providing evidence that occupational exposure to inorganic dust might be a previously unknown risk factor for gout.

REFERENCE:

Disclosure of Interests: Valgerdur Sigurdardottir: None declared, Anna Sváð: None declared, Lennart T.H. Jacobsson Consultant for: LJ has received lecture and consulting fees from Pfizer, Abbvie, Novartis, Eli-Lilly and Janssen, Linus Schöler: None declared, Kjell Tönn: None declared, Mats Dehlin: None declared

Methods: This Phase 3b/4 study had 2 parts. Of 182 enrolled pts, 166 pts with inactive disease (ID) (cohort 1; 68pts) and CAN-naive pts (cohort 2; 98pts) were administered subcutaneous CAN 4mg/kg q4w in Part I. Per protocol titration off CS and/or methotrexate (MTX) was attempted during Part I. Eligible pts (ID for 24 weeks[wks]) and being CS- and MTX-free for at least 4 wks) advanced to Part II wherein, pts were randomised to either a 3-step CAN dose reduction (2mg/kg/q4w, followed by tapering to 1 mg/kg/q4w and then discontinuation) or dose interval prolongation (4mg/kg/q4w, followed by tapering to 4mg/kg/q12w and then discontinuation); pts advanced to the next tapering step if ID was maintained for 24 wks. Adapted American College of Rheumatology (ACR) paediatric criteria, its individual components and Juvenile Arthritis Disease Activity Score (JADAS) were assessed.

Results: In total, 75 pts were randomised to a dose reduction (n=38) or dose interval prolongation (n=37) CAN tapering regimen in part II. The pts who maintained ID for 24 wks exceeded the predefined threshold of 40% for the reduced CAN dose arm (71%) and prolonged dose interval (84%) treatment arm of Step 1 (primary endpoint). A total of 68.4% (26/38) and 61.1% (30/37) pts in the dose reduction and interval prolongation arms, respectively were successful in Step 2; 33% (25/75) of pts successfully discontinued CAN and maintained ID for 24 wks. ID, ACR 90/100 and JADAS 27 C-reactive protein (CRP) scores are summarised in the table. Adverse events (AEs) and serious AEs observed within the 2 cohorts and across Parts I and II were similar. The most frequent AEs were common infections (nasopharyngitis, upper respiratory tract infection, pharyngitis) followed by SJIA-related events (rash, pyrexia and arthralgia).

Table 1. Efficacy responses of Part I over 24 Wks

<table>
<thead>
<tr>
<th></th>
<th>Cohort 1</th>
<th>Cohort 2</th>
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<tbody>
<tr>
<td>N (n)</td>
<td>N=68</td>
<td>N=98</td>
</tr>
<tr>
<td>Inactive disease, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BL 56 (82.4)</td>
<td>61 (62.2)</td>
<td></td>
</tr>
<tr>
<td>Wk 4 61 (89.7)</td>
<td>45 (46.9)</td>
<td></td>
</tr>
<tr>
<td>Wk 24 67 (88.5)</td>
<td>67 (68.4)</td>
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</tr>
<tr>
<td>Median JADAS27-CRP, range (min, max)</td>
<td></td>
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</tr>
<tr>
<td>BL 1.1 (0.0, 35.5)</td>
<td>22.8 (4.9, 48.0)</td>
<td></td>
</tr>
<tr>
<td>Wk 4 5.0 (0.0, 12.97)</td>
<td>2.6 (0.0, 41.7)</td>
<td></td>
</tr>
<tr>
<td>Wk 24 1.0 (0.0, 27.8)</td>
<td>2.0 (0.0, 31.5)</td>
<td></td>
</tr>
<tr>
<td>ACR 90, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BL 17 (25)</td>
<td>13 (13.3)</td>
<td></td>
</tr>
<tr>
<td>Wk 4 0 (0.0)</td>
<td>15 (15.3)</td>
<td></td>
</tr>
<tr>
<td>Wk 24 13 (19.1)</td>
<td>13 (13.3)</td>
<td></td>
</tr>
<tr>
<td>ACR 100, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BL 38 (55.9)</td>
<td>31 (31.6)</td>
<td></td>
</tr>
<tr>
<td>Wk 4 2 (2.9)</td>
<td>44 (44.9)</td>
<td></td>
</tr>
</tbody>
</table>

N, total number of patients; n, number of patients

Conclusion: SJIA pts with ID for 24 wks on CAN monotherapy can successfully taper CAN by either reducing the dose or prolonging the dosing interval. However, only a minority of pts overall successfully discontinued CAN treatment and maintained ID for 24 wks. The safety profile was similar and consistent with other CAN SJIA studies. No new safety signals were identified.

REFERENCE:

Disclosure of Interests: Pierre Quentin Consultant for: AbbVie, Chugai-Roche, Lilly, Novartis, Novimmune, Sanofi, and SOBI; Consultant for: AbbVie, Chugai-Roche, Lilly, Novartis, Novimmune, Sanofi, and SOBI; Speakers bureau: AbbVie, BMS, Chugai-Roche, Novartis, Pfizer, and SOBI; Speakers bureau: AbbVie, BMS, Chugai-Roche, Novartis, Pfizer, and SOBI; Ekaterina Alexeeva: None declared; Carine Wouters Grant/research support from: Grant/research support from: Istituto Gaslini from GlaxoSmithKline immune-inflammation: unrestricted grant to study Blau syndrome; Roche: unrestricted research grant; Pfizer: grant for psychological care of patients with JIA; Grant/research support from: GSK, Roche, Pfizer, Inmaculada Calvo Grant/research support from: received research grants from Pfizer, Roche, Novartis, Clementia, Sanofi, MSD, BMS and GSK; Consultant for: Advisory boards: Novartis, AbbVie, Speakers bureau: AbbVie, Roche, Novartis, SOBI, Tilmann Kallinich Grant/research support from: Novartis, Speakers bureau: Sobi, Roche, Novartis, CLB, Nicole Wilflaart: None declared; Xiaolong Wei Employee of: Novartis, Alan Slade: Shareholder of: Novartis Pharmaceuticals Corporation, Employee of: Novartis Pharmaceuticals Corporation, Ken Abrams: Shareholder of: Novartis, Employee of: Novartis, Alberto Martini: None declared DOI: 10.1136/annrheumdis-2019-eular.1558
Early Treatment with Anakinra in Systemic Juvenile Idiopathic Arthritis

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Background: Systemic juvenile idiopathic arthritis (sJIA) accounts for 10-20% of all patients with JIA. The prominent systemic clinical features, the marked elevation of inflammatory markers and the absence of autoantibodies make this disease different from other JIA forms. sJIA should be considered as a polygenic autoimmune disease. Interleukin 1 (IL-1) has been shown to be a major mediator of the inflammatory cascade that underlies sJIA. Treatment with anakinra has been reported to be effective in a sizable portion of patients with sJIA.

Objectives: To assess clinical response rate and disease course in sJIA patients treated with anakinra. To evaluate whether the response to anakinra was related to baseline variables.

Methods: We reviewed 56 (28 F) consecutive patients with sJIA treated with anakinra for at least 6 months in our institution. The diagnosis of sJIA was established according to the International League of Associations for Rheumatology (ILAR) classification criteria. We analyzed the effect of anakinra on fever, rash, number of active joints, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), white blood cells count, platelets count and ferritin levels. Clinically inactive disease (CID) was defined according to Wallace criteria. Clinical and laboratory data were obtained using a standard data collection form.

Results: The median age at the disease onset was 5.7 (IQR 2.9-10.2) years. The median time from onset to received anakinra was 1.9 (IQR 0.7-9.7) months. At baseline 52/56 (93%) of patients had fever and median number of active joints was 2 (IQR 1-4). After 6 months of treatment 39 patients (69.6%) met criteria for inactive disease. Among 56 patients 17 (30.3%) received anakinra in monotherapy and 39 (69.6%) received anakinra with glucocorticoids. There were no statistically significant differences between the two groups for demographic, clinical and laboratory features. 13/17 (76.4%) patients treated with anakinra alone and 26/39 (66.6%) patients treated with anakinra and glucocorticoids met criteria for CID off glucocorticoids at 6 months (p=0.54). Among the 56 patients, 29 (51.7%) received anakinra within 2 months from disease onset. There were no statistically significant differences for demographic, clinical and laboratory features among patients who started anakinra in the first 2 months from disease onset compared to those that started anakinra after 2 months. At 6 months after beginning of anakinra treatment, 27/29 patients (93.1%) who started anakinra within 2 months from disease onset and 12/27 (44.4%) who started anakinra after 2 months from disease onset reached clinical inactive disease off glucocorticoids (p=0.0011). Patients who started anakinra after the first 2 months from disease onset have a significantly higher risk of non-response (OR=8.06, 95% CI 2.03-32.0).

Conclusion: According with several observations, anakinra is effective in a significant proportion of patients with sJIA. A possible approach to introduce IL-1 inhibitor, with or without concomitant glucocorticoids, early in the disease course taking advantage of a "window of opportunity" has been suggested. Our observation confirms that earlier treatment with anakinra is associated with a better short-term outcome. Moreover, our results show that beginning of treatment after two months of disease is correlated with a high risk of non-response.

REFERENCE:
Results: A total of 8,309 patients were included in this study. 290 gastrointestinal disorders were reported in 260 patients. 50 cases in 47 patients were classified as IBD or suspected IBD. Age at JIA onset was significantly higher in patients who developed IBD (9.1 vs 7.1 years p=0.002), and female predominance was lower (48.9% versus 67.6% p=0.011). Enthesitis related arthritis (ERA) was the JIA subtype in 40.4% of the patients who developed IBD. In 14 out of 47 patients more detailed information about IBD disease onset was available, such as date of disease onset and medication used at that time. 71.4% of all 14 patients used enotenap and 50.0% used MTX 3 months prior or at IBD onset. Enotenap exposure prior to IBD onset varied from no exposure to 6.39 years with a median of 1.3 years. Methotrexate exposure prior to disease onset varied from no exposure to 8.10 years with a median of 2.9 years. Information regarding quality of life was available for 2,752 patients of which 17 IBD patients. Quality of life, both physical and psychosocial, was significantly lower in patients who developed IBD patients (p=0.019 and p=0.046 respectively). Conclusion: In this study ERA patients were more at risk of developing IBD and 71.4% used enotenap while developing IBD. We did not find a protective role of MTX since 50% of patients with available data developed IBD while using MTX. Lastly, IBD has an important physical and psychosocial impact on quality of life.

Disclosure of Interests: Roline Krol: None declared, Joost F. Swart: None declared, Gabriella Giancane: None declared, Sylze De Roock: None declared, Troels Herlin: None declared, Pavla Doležalova: None declared, Helga Sanner: None declared, Gordana Susic: None declared, Flávio R. Szatyn: None declared, D Maritis: None declared, Tamas Constantin: None declared, Varga: None declared, Sujata Sawhney: None declared, Marte Rygg: None declared, SHEILA KNUPP DE OLIVEIRA: None declared, Marco Cattalini: None declared, Ellen Nordal: None declared, Claudia Maghsahe: None declared, Alberto Martinuzzi Consultant for: I do not have any conflict of interest to declare since starting from 1 March 2016 I became the Scientific Director of the G. Gaslini Hospital; therefore, my role does not allow me to render private consultancies resulting in personal income. I perform consultancy activities on behalf of the Gaslini Institute for the companies listed below: AbBeie, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, EMD Serono, Janssen, Novartis, Pfizer, Pfizer, B-Pharm.
The money received for these activities are directly transferred to the Gaslini Institute’s bank account. Before March 2016, I was the head of the Pediatric Rheumatology Department at the G. Gaslini Hospital, where NR works as full-time public employee, has received contributions (> 10,000 EUR) from the following industries in the last 3 years: BMS, Eli-Lilly, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sinergie, Sobi and Takeda. The money received has been invested for the research activities of the hospital in a fully independent manner, without any commitment with third parties. Consequently: For received honoraria for consultancies or speaker bureaus (< 10,000 USD each) from the following pharmaceutical companies in the past 3 years: AbbVie, Biogen, AstraZeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sobi, and Takeda.

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Background: Glucocorticoid injections in periarticular sites (PAGI) such as ten- dons and bursae often complete the local treatment of active disease in juvenile idiopathic arthritis (JIA). However, the use of PAGI and their role in the achieve- ment of disease remission has seldom been studied.

Objectives: To identify the clinical features of JIA patients treated with PAGI at the study center in a 6 years period, the sites most frequently injected, the fre- quency of and the time for achieving local remission.

Methods: Records of JIA patients treated with PAGI at the study center from 2012 were retrospectively reviewed. Demographic and clinical features, including ongoing systemic treatment, sites of injection, procedure setting, type and dosage of glucocorticoid injected, time to achieve local remission (complete or partial when one/or some of the injected sites were in remission and one/some showed per- sistent synovitis), frequency of remission of the injected sites at the last follow-up and side-effects were recorded.

Results: In a total of 293 procedures 647 tendons and 26 bursae were injected in 191 patients. Most of the patients were females (74%), with ILAR oligoarticular JIA subtype (50% persistent, 23% extended), followed by RF-negative polyarthritis (23.2%), RF-positive polyarthritis (0.7%) and systemic JIA (1.3%), with a median age of 8.2 years (IQ 4.7-11.3) at the PAGI. All procedures were ultra- sound-guided, 281 (96%) under general sedation. Acetate methylprednisolone in 96% of the procedures (average dosage 0.45 mg/kg/tendon, 0.89 mg/kg/bursa), whereas trimcinolone exacetonide in 4%. In 255 procedures (87%) patients experienced remission in the injected sites after a median of 2.6 months (IQ 1.9-3.5). Forty-seven patients (24.6%) underwent to repeated injections in the same sites after at least 3 months from the 1st procedure. A total of 96 tendons and 9 bursae were re-injected during 69 procedures (23.5%). At the last follow up, after a median period of 29.4 months (IQ 15.45-48.4) from PAGI, patients experi- enced complete local remission in 259 (88.4%) injected procedures and partial local remission in 23 (7.8%). In 53 procedures with repeated injection(s) in the same site(s) (77%), patients were in local remission at the last follow up. In 77 pro- cedures (26.3%) patients presented flare of disease in periarticular sites. Con- cerning concomitant therapy, at the time of each PAGI 115 patients (39.2%) were not on treatment, 137 (46.7%) were on methotrexate, 29 (9.9%) on methotrexate and biologics, 8 (2.7%) on biologics and 4 (1.5%) received others. Patients were started with a new treatment in around three months following 139 (47.4) proce- dures due to poor control of disease. In 156 (53.2%) procedures, patients experi- enced complete/local remission and maintained the same treatment before or after the injection at the last follow up in a median period of 20.8 months (IQ 12.67- 39.35). Of notice, 81.4% of patients who experienced complete remission follow- ing the injection were not on concomitant treatment; 85.9% of patients who experi- enced complete remission at the last follow up did not receive concomitant treatment. In 24 injection procedures (8.2%) patients showed only mild side local effects (atrophy and hypogammaglutimation).

Conclusion: PAGI are a safe option in the management of JIA. In our cohort, patients treated with PAGI had more frequently persistent oligoarticular JIA sub- type: acetate methylprednisolone was by far the most frequently used glucocor- ticonid. In 88.4% procedures patients experienced remission at last follow up. However, further investigations are mandatory to assess the role of concomitant therapy in achieving and maintaining remission.

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SAFETY PROFILE OF ETANERCEPT IN LONG-TERM USE IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA)

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Background: Etanercept is the most frequently used biologic drug in patients with JIA. Children and adolescents with JIA are treated with etanercept often over long periods of time, sometimes even into adulthood. The knowledge about its long-term safety, especially with regard to the occurrence of new-onset immune-mediated diseases and malignancies, is limited.

Objectives: To investigate the exposure-adjusted rates of adverse events (AE) and serious AE (SAE) in patients with JIA with long-term use of etanercept.

Methods: Patients with JIA who were enrolled in the German biologic register BiKeR and were born before 30.05.2000 (at least 18 years of age at this date) were considered for this analysis. The follow-up register JuMBO ensures the long-term follow-up into adulthood. An AE or SAE was attributed to etanercept when the treatment was either ongoing or terminated in less than 3 month prior to the event. The incidence of malignancies was estimated in patients who were ever exposed to etanercept with at least one dose.

Results: Of 4546 patients who were currently enrolled in BiKeR a total of 2584 JIA patients were eligible for the JuMBO register (18 years). Among those, 1765 (68%) were ever exposed to etanercept and observed for a mean of 6.8±4.9 years (including 1101 into adulthood). The majority of them had polyarthritis (35%), followed by enthesitis-related arthritis (20%) and extended oligoarthritis (17%). The patients were exposed to etanercept for a total of 4.2 years (mean, 6.726 exposure years, EY); 518 patients were continuously treated with etanercept for at least 5 years (4,534 EY). In total, 124 autoimmune events (1.84/100EY) and 7 other immune disorders (0.10/100EY) were reported in 102 (5.6%) and 7 (0.4%) patients with onset on average 10.2 years after JIA onset, and 6.8 years after start with etanercept, respectively. The number of selected immune-mediated events and the exposure-adjusted rates are given in the table. In addition, 11 malignancies (0.10 events/100 person-years) were reported in patients ever exposed to etanercept. Among those (mean age at onset 20.3 years), 4 malignancies were reported in childhood and 7 in young adulthood. Three patients were also exposed to etanercept before the incidence of malignancy. The malignancies occurred on average 12.1 years after JIA onset, 10.4 years after start with a first DMARD and 7.5 years after first exposure to etanercept.

Conclusion: This is the first long-term large safety study in prospectively followed JIA patients with an emphasis on new-onset immune-mediated diseases and malignancies in etanercept. The study also highlights that it is important to prospectively collect data on adverse events under treatment with biologics in JIA, in particular with respect to the risk of malignancies in young adulthood.

Table 1. Adverse and serious adverse events under treatment with etanercept

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CONSUMER PERSPECTIVE ON PAEDIATRIC RHEUMATOLOGY CARE AND SERVICE DELIVERY: RESULTS FROM AN EARLY JUVENILE IDIOPATHIC ARTHRITIS (JIA) COHORT STUDY

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Background: Timely access to specialized and multidisciplinary care is a core principle in the management of JIA patients and crucial to achieve the best possible outcome for children and adolescents with JIA.

Objectives: To assess satisfaction with access to specialized care and used health care services of families with children with JIA and to identify factors associated with unmet needs.

Methods: Parents of JIA patients enrolled in the early JIA cohort study ICON completed the Child Healthcare Questionnaire on Satisfaction, Utilisation and Needs (CHC-SUN)1 and the Family Burden Questionnaire (FaBel) 3 months after enrolment. The socioeconomic status, disease activity, patients’ functional ability and quality of life were also assessed. Factors associated with unmet needs were identified by logistic regression analysis.

Results: Data were available from 835 families with children diagnosed with JIA 3 months (median, IQR 1.6) after symptom onset and cared for by paediatric rheumatologists (68% females). At assessment (4.6 months after diagnosis, median), 67% of patients received non-steroidal anti-inflammatory drugs, 50% received conventional synthetic DMARDs and 8% biologic DMARDs. In addition, the following health care services were utilized: 84% physiotherapy, 23% occupational therapy, 21% supply with physical aids, 17% telephone counselling, 15% health education, 13% social worker services, and 11% psychological counselling. Unmet needs were most frequently reported for health education (19%), rehabilitation services (11%), psychological counselling (11%), self-help groups (10%), and lowest for physiotherapy (2%). Unmet needs varied depending on the type of service and JIA category (Table). They were more frequently observed in families with higher burden as indicated by FaBel, but were not associated with migration background and socioeconomic status. Most parents were generally satisfied with their child’s health care (satisfied 30%, very satisfied 42%, extremely satisfied 23%). Satisfaction was highest with the behaviour of doctors and lowest with school-related services (e.g. 36% not or partly satisfied with teachers’ knowledge about the child’s illness) and diagnosis/information (e.g. 29% not or partly satisfied with the time required for the diagnosis).

Conclusion: There are, although infrequently, unmet needs and dissatisfaction with health services among families with children who have JIA and receive specialized care. Whether these deficits are relevant for long-term JIA outcomes will be further investigated in the ICON study.

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IDENTIFICATION OF SIX DERMATOMYOSITIS SAFETY OF MYCOPHENOLATE MOFETIL TREATMENT

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Background: Dermatomyositis (DM) is a heterogeneous disease with a wide range of clinical manifestations. Bohan and Peter suggested four subtypes of DM: idiopathic DM, juvenile DM, DM associated with cancer, and DM associated with other connective tissue diseases. Different DM subtypes have distinct clinical manifestations, responses to therapy and prognoses.

Objectives: The aim of the present study was to identify the clinical subtypes of DM by applying cluster analysis.

Methods: We retrospectively reviewed the medical records of 720 DM patients and selected 21 variables for analysis, including clinical characteristics, laboratory findings, and comorbidities. Principal component analysis (PCA) was first conducted to transform the 21 variables into independent principal components. Patient classification was then performed using cluster analysis based on the PCA-transformed data. The relationships among the clinical variables were also assessed.

Results: We transformed the 21 clinical variables into 9 independent principal components by PCA and identified 6 distinct subgroups. Cluster A was composed of two sub-clusters of patients with classical or moderate DM. Cluster-B patients were older and had malignancies. Cluster C was characterized by interstitial lung disease (ILD), skin ulcer, and minimal muscle involvement. Cluster D included patients with prominent lung, muscle, and skin involvement. Cluster E contained DM patients with other connective tissue diseases. Cluster F included all patients with prominent lung, muscle, and skin involvement. Cluster E contained DM patients with other connective tissue diseases. Cluster F included all patients with prominent lung, muscle, and skin involvement.

Conclusion: We applied cluster analysis to a large group of DM patients and identified six clinical subgroups, underscoring the need for better phenotypic characterization to help develop individualized treatments and improve prognosis.

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SAFETY OF MYCOPHENOLATE MOFETIL TREATMENT IN SYSTEMIC SCLEROSIS IN REAL LIFE: REPORT FROM A SINGLE CENTER LARGE COHORT OBSERVATIONAL STUDY

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Background: Mycophenolate mofetil (MMF) has been increasingly used in the treatment of early diffuse cutaneous Systemic Sclerosis (dcSSc) and SSC-associat ed interstitial lung disease (SSC-ILD), and a recent Randomized Controlled Trial confirmed its efficacy and safety in SSC-ILD. However, the safety of this drug in the long term use has not been assessed in a real life setting.

Objectives: We aimed to analyze the period prevalence and the type of adverse events (AEs) associated to MMF treatment in a single center large cohort.

Methods: Charts of all SSC patients meeting the 2013 ACR/EULAR classification criteria consecutively visited at our outpatient clinic from January 1st 2017 to December 31st 2017 were retrospectively analyzed. Demographics, clinical, serological, functional, imaging data, treatments, and AEs were recorded. Patients were subgrouped according to the immunosuppressant (IS) taken during the observation period (e.g. MMF, azathioprine- AZA, or cyclophosphamide- CYC, no IS). The period prevalence of AEs was calculated and correlations of between AEs and patient features were investigated by univariate and multivariate analyses.

Results: Two-hundred and thirty-seven patients were included (92.4% were females, aged 56.4±11.3 years, with a median disease duration of 17 years, range 1-60). Among them, 85 (35.9%) were taking MMF, 34 (14.3%) AZA or CYC, 118 (41.5%) no IS; p=0.03). No AE required hospitalization and resolved after treatment suspension. The period prevalence of total infectious AEs was 27.6% in the no IS group; p<0.05), predominantly airway infections (41.2% of all infectious AEs). Given so, we investigated the correlations of the infectious AEs in the MMF group with ILD, smoking history, and concurrent GC. However, we didn’t find any significant association with these variables. When we looked for correlations of infectious AEs in the MMF group with other disease features, we found that they were correlated with the duration of the disease (median= 4 years; r=0.25; p=0.02) and with the presence of digital ulcers and/or pitting scars (r=0.22; p=0.03). No AE required hospitalization and resolved after treatment suspension.

Disclosure of Interests: None declared

Background: Intestinal lung disease in systemic sclerosis (SSc-ILD) occurs frequently and carries a high burden of morbidity and mortality. To date, there are no existing guidelines for screening, diagnosis and management of SSc-ILD that would aid early recognition and treatment and improve the care of these patients.

Objectives: To develop expert consensus recommendations for the identification and management of SSc-ILD.

Methods: Based on the results of a comprehensive systematic literature analysis conducted in line with NICE/CRD and IQWiG guidelines and PRISMA methodology, evidence-based statements on SSc-ILD risk, screening, diagnosis, treatment and follow-up were developed. A modified Delphi process was then used to establish consensus statements for the identification and management of SSc-ILD. Briefly, an expert panel of 27 European-based pulmonologists, rheumatologists and internists with experience in treating SSc-ILD was established. Between July and November 2018, the panel took part in 3 rounds of online surveys, a face-to-face discussion and a WebEx meeting to establish consensus-based recommendations for the management of SSc-ILD. Statements were categorised by topic: risk factors (including biomarkers); screening; diagnosis; assessment of severity; treatment initiation; treatment options; disease progression; treatment escalation; other management options. Panellists indicated their level of agreement with proposed statements on a scale of 1 (strong disagreement) to 7 (strong agreement), and consensus was considered achieved when >80% either disagreed (score of 1–3) or agreed (score of 5–7) with a statement. Based on panel feedback, statements that did not reach consensus were modified and re-voted in later rounds.

Results: At the close of the Delphi process, the panel agreed on the following:

1. Risk factors: The presence of anti–topoisomerase I antibodies, male gender and diffuse cutaneous SSc all increase risk for ILD.
2. Screening: All SSc patients should undergo screening for ILD, using HRCT and lung function testing. Frequency of screening using HRCT should be guided by risk of developing ILD, in combination with clinical symptoms and lung function.
3. Diagnosis and assessment of severity: Use of HRCT to diagnose SSc–ILD and assess severity, with supporting findings from lung function testing and other management options.
4. Treatment initiation and options: All patients with severe or progressive SSc–ILD should be considered for pharmacotherapy, with mycophenolate mofetil and cyclophosphamide recommended as treatments. Patients not receiving treatment should be followed closely for signs of disease progression.
5. Disease progression: Indicators of progression include sustained decline in lung function, worsening of clinical symptoms, and change in extent and/or pattern of fibrosis on HRCT.
6. Treatment escalation: Patients with inadequate treatment responses should be considered for treatment escalation. Suitability for lung transplant should be evaluated early, especially for patients diagnosed with advanced disease. Autologous haematopoietic stem cell transplantation may be considered in carefully selected patients.

Conclusion: These evidence-based expert consensus recommendations, developed using a modified Delphi process, provide important guidance for the identification and management of SSc-ILD.

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identified PF and SSc auto-antibodies at first visit as independent parameters predicting the development of definite SSc. These data are of key importance for the risk stratification of patients with very early SSc in clinical practice and clinical studies.

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Background: Systemic sclerosis (SSc) is characterized by stiffness and contraction of tissues, which leads to a limitation in the execution of day-to-day activities. The aim of our study was to investigate the impact of specialized physical-occupational therapy (POT) focused on the hands/face and QoL of SSc patients.

The aim of our study was to investigate the impact of specialized physical-occupational therapy (POT) focused on the hands/face and QoL of SSc patients. The 2015 ESC/ERS guidelines and 2018 WSPH consensus recommended the use of risk assessment (classified as low, intermediate, and high risk) based on the variables to predict prognosis, but the clinical utility of risk stratification in patients with CTD- or SSc-PAH has not been established.
Objectives: To evaluate utility of risk stratification strategy in predicting outcomes in CTD-PAH patients by post-hoc analysis of prospectively collected AMBITION data. 

Methods: This study examined 216 patients with CTD (COMB: n=117; MONO n=99) enrolled in the AMBITION study mTTF population. The most commonly underlying CTD etiology was SSc (n=137). Abbreviated average risk score was determined at baseline and at 16 weeks based on 6-minute walking distance, NT-proBNP, and WHO-FCC. Time to clinical failure (TTF) was compared between groups stratified by the risk stratification and/or treatment assignment using the log-rank test.

Results: At baseline, CTD patients were divided into low (n=27, 12.5%), intermediate (n=179, 82.9%), and high risk (n=10, 4.6%) and at Week 16, subjects were classified as low (n=55, 27.9%), intermediate (n=133, 68.5%), and high risk (n=7, 3.6%). Clinical failure was lowest for subjects in the baseline low risk group and highest in the baseline high risk group. When TCF was compared between COMB and MONO arms of CTD-PAH patients in individual risk groups at baseline, risk of clinical failure event was lower in COMB than in MONO in the low and the intermediate risk groups (P<0.05, hazard ratio [HR] NA due to no event in COMB, and P=0.02, HR 0.519, 95%CI 0.297-0.955, respectively), however, no difference in the high risk group was observed. The same analysis was conducted using risk stratification at week 16, resulting in a 30% risk reduction in TCF after Week 16 in COMB, compared with MONO in the low risk group (P=0.001, HR 0.069, 95%CI 0.040-0.120), but no difference between treatments in the intermediate risk group (P=0.3). Risk of clinical failure event was comparable between patients with low and intermediate risk after 16 weeks of treatment with MONO.

Conclusion: A simplified risk stratification at baseline and week 16 may be useful in predicting PAH-related outcomes in patients with CTD-PAH. Among those achieving a low risk status at week 16, which could be considered a treatment goal, COMBO was associated with an improved outcome, when compared to MONO.

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OP0068 ABATACEPT IN EARLY DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS – RESULTS OF A PHASE 2 INVESTIGATOR-INITIATED, MULTICENTER, DOUBLE-BLIND RANDOMIZED PLACEBO-CONTROLLED TRIAL

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Objectives: To evaluate the safety and efficacy of ABA 125 mg subcutaneous (SC) versus placebo SC given every week on skin fibrosis using the modified Rodnan skin score (mRSS) in diffuse cutaneous SSc (dcSSc; clinicaltrials.gov NCT02161406).

Methods: A 12-month, investigator-initiated, multicenter double-blind, randomized placebo-controlled trial was conducted between September 2014 and February 2018 at 27 US, Canadian and UK sites. Eligible subjects were randomized in a 1:1 ratio to either ABA or matching placebo, stratified by duration of dcSSc (<18 vs >18 to ≤36 months). Key inclusion criteria included dcSSc with disease duration of ≤36 months (defined as first non-Raynaud phenomenon) and mRSS ≤10 and ≤35 units for disease duration ≤18 months and mRSS ≤15 and ≤45 units with evidence of active disease for disease duration of >18-36 months. Escape therapy was allowed at 6 months for worsening SSC. Primary outcomes include safety and change in mRSS over 12 months (mRfSS). Secondary endpoints include ΔFVC%, ΔHAQ-DI, sp to physician global assessment, and ACR CRiSS1 (composite measure in dcSSc). The primary endpoint of mRfSS was assessed using a linear mixed model (see Table) with primary end point data censored after initiation of escape therapy.

Results: 88 subjects were randomized (44/group) and formed the mTT group: 34 (77%) and 35 (80%) completed the 12-month double-blind treatment period in ABA and placebo groups, respectively. At baseline, the mean age was 49 years, 75% were female, mean disease duration was 1.59 years, 60% had disease duration ≤18 months, mRSS was 22.4, mean FVC% was 84.3%, and mean HAQ-DI was 1.0. Compliance with both drugs was >98%. ABA was well tolerated with comparable adverse events (AEs), serious AEs, and AEs of special interest (e.g., infections and malignancies) between treatments. There were 3 deaths during the treatment period (2 in ABA (both scleroderma renal crisis days 11 and 17) and 1 in placebo (sudden cardiac arrest- day 310). The primary endpoint showed an adjusted mean improvement of mRSS of -6.24 in ABA vs. -4.49 in placebo, p<0.08 (Table).

The secondary outcome measures were statistically significant and clinically meaningful (HAQ-DI and physician global assessment) or showed numerical results favoring ABA (Table). A larger proportion of placebo subjects required escape immunosuppressive therapy vs ABA (36% vs 16%, p<0.03).

Estimates are from a linear mixed model with treatment group, month (3, 6, and 12), treatment x month interaction, duration of dcSSc (<18 vs >18 to ≤36 months), and baseline outcome measure as fixed effects and participant as a random effect (except for ACR CRiSS). For ACR CRiSS, treatment differences were assessed by the non-parametric Van Elteren test. Multiple imputation was used for ACR CRiSS analysis.

Conclusion: In patients with early dcSSc, ABA was well tolerated, but ΔmRSS was not statistically significant. Secondary outcome measures showed evidence in favor of ABA, including greater requirement of escape therapy in the placebo group, mRSS showed large variability, despite recruiting an early dcSSC population.

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**OP0069**

**PERFORMANCE OF AMERICAN COLLEGE OF RHEUMATOLOGY (ACR) COMBINED RESPONSE INDEX IN DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS (CRSS) SCORE IN PHASE 2 TRIAL OF LENABASUM IN DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS (DCSS)**

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**Background:** Change in modified Rodnan skin score (mRSS) has been used as primary efficacy outcome in at least 13 failed controlled studies in dcSSc. In 2016, the ACR proposed the ACR as a primary efficacy outcome for clinical trials in dcSSc. Its performance as a primary efficacy outcome has not been tested in a clinical trial.

**Objectives:** To evaluate performance of ACR CRSS outcome measure in the lenabasum Phase 2 study in dcSSc, the first study in which it was used prospectively as the primary efficacy outcome.

**Methods:** The Phase 2 study JBT101-SSc-001 (NCT02465437) included a 16-week, double-blinded, randomized, placebo-controlled Part A followed by an open-label extension (OLE). ACR CRSS score is calculated from a weighted exponential formula that includes change in mRSS, Patient Global Assessment (PtGA), HAQ-DI, Physician Global Assessment (MDGA), and FVC% predicted. Spearman correlations were determined for: pairs of core items at baseline; change in pairs of core items; and change in a given core item and calculated ACR CRSS score. Median ACR CRSS score was determined in subjects with different levels of improvement in patient-reported outcomes (PROs).

**Results:** Correlations among pairs of CRSS core items at baseline and change in core items were all < 0.80 at 4 and 12 months. The strongest correlations (r $>$ 0.60, P $<$ 0.001) for changes in pairs of core items were between PtGA and HAQ-DI, HAQ-DI and MDGA, and MDGA and FVC% predicted. The strongest correlations (r $>$ 0.50, P $<$ 0.001) for changes in pairs of core items were between PtGA and HAQ-DI, HAQ-DI and MDGA, and MDGA and FVC% predicted, all others were < 0.30 (Table 1). Correlations between change in each core item and ACR CRSS score were all statistically significant, p $<$ 0.05 at both 4 and 12 months and very strong for change in mRSS and ACR CRSS (Table 1).

**Conclusion:** In the context of the lenabasum Phase 2 clinical trial, ACR CRSS core items at baseline and change in ACR core items were not redundant (r < 0.80). Change in each core item correlated with ACR CRSS score, indicating each contributed to the score at both 4 and 12 months. The 12-month median ACR CRSS score was higher in subjects with greater levels of improvement in PROs, even PRO that were not core items, showing that ACR CRSS score reflects long-term clinical benefit in how the patient feels and functions. These data provide preliminary evaluation of the ACR CRSS score as a clinical trial endpoint in dcSSc.


**WEDNESDAY, 12 JUNE 2019**

**Bringing digital health care solutions to patients.**

**OP0070-PARE**

**GEOCACHING AS AN ENCOURAGEMENT FOR BEING ACTIVE**

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**Background:** The Finnish Rheumatism Association and Novartis started a project in 2017 to energise our local associations, members and their families by adapting an active lifestyle. Geocaching is a fun, family-friendly way to exercise body and mind. It is for everybody to enjoy.

Geocaching is an outdoor recreational activity, in which participants use a Global Positioning System (GPS) receiver or mobile device and other navigational techniques to hide and seek containers, called “geocaches” or “caches”, at specific locations marked by coordinates all over the world.

There are about three million geocaches hidden around the world. A typical cache is a small waterproof container containing a logbook and sometimes a pen or pencil. The geocacher signs the log with their established code name and dates it to prove that they found the cache. After signing the log, the cache must be placed back exactly where it was found.

**Objectives:** The main goal of the project was to hide 70 new caches all over Finland to create an enjoyable experience for other geocachers. Those caches were named “Reumaged” at the beginning of the cachename. For all the associations that were involved in this project received money allocated to sport and physical activity out of the 15,000 euro project budget. The project ended on 12 October 2018, and all logged caches were included in the game.

**Methods:** We started our project by training association representatives. The training included the basics of geocaching: how to find caches, how to hide your cache and create your cache page, different geocachetypes and everything you should know geocaching. The trained representatives told about geocaching in their own associations, and they were responsible for creating at least 2-3 new caches and handling the new caches. The main idea was that when you have found about 15-20 caches you would start to hide your own caches. Together with local associations our aim was to create 70 caches all over Finland to celebrate the 70-year-old Finnish Rheumatism Association.

Outdoor geocaching adventure starts indoors with preparation and online geocaching. You need a Global Positioning System (GPS) receiver or a mobile device, your own account at the site geocaching.com. The site offers a completely free access to the caching data and all the site features. The site offers also a “premium” member status to access certain features. You can also download the Geoaching intro app onto your smartphone, like Geocaching.
Results: There were 43 members from 30 local associations in Oulu, Mikkeli, Helen-sinki and Turku in these geocaching trainings. All members are suffering from rheumatic and other musculoskeletal diseases (RMDs) and work as volunteers for sport and physical activity, and now for geocaching. By 12 October 2018 there were 49 geocaches made by 13 local associations. The caches were logged 6593 times. So local associations earned 173-4303 euros each to be used for promoting sport and physical activity programmes and active lifestyles.

Conclusion: Promoting an active lifestyle is part of the health and wellbeing policy in the Finnish Rheumatism Association. The goal is to encourage people of all ages to stay healthy by getting enough exercise.

The geocaching project shows that it is easy to some of local associations to start projects like this. Some associations thought that it is too difficult to learn new methods especially when their members are elderly people. Geocaching is increasingly popular, inclusive, a fun and healthy pastime for individuals of all ages. It is also great for groups like local associations, families, friends, and youth groups working as teams. Those local associations that were involved in this project received a great budget for their local sport and physical activity programmes. It is great to see something evolving from the beginning and come into being.

Disclosure of Interests: None declared


WEDNESDAY, 12 JUNE 2019

Cartilage, synovium and bone

OP0071 REVEALING THE LINK BETWEEN OSTEOARTHRITIS DEVELOPMENT AND MESENCHYMAL STEM CELL SENESCENCE

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Background: Tissue accumulation of p16INK4A-positive senescent cells is associated with age-related disorders such as osteoarthritis (OA). These senescent cells induce a tissue loss of function through a particular secretory phenotype called SASP (senescence-associated secretory phenotype).

Objectives: Links between OA onset and cellular senescence remain poorly detailed. We wanted to determine the localization of articular senescent cells in in vivo OA mouse models and study the involvement of mesenchymal stem cells (MSC) senescence in OA pathogenesis.

Methods: Wild-type mice C57BL/6, SAMP8/R1 (senescence accelerated mouse-prone and resistant), transgenic p16INK4A+Luc and p16INK4A−Luc/Luc were used. Experimental OA was induced by intraarticular injections of collagenase (CIA). Cartilage, synovial tissue and subchondral bone were analyzed by histology, RT-qPCR and micro-tomography. MSCs come from healthy human donors (CIOA). Cartilage, synovial tissue and subchondral bone were analyzed by histology, RT-qPCR and micro-tomography.

Results: (1) CIA was induced in senescence-driven luciferase transgenic mice. Under CCD camera, a peak in luminescence was detected at day 24 post-injection revealing the presence of senescent cells. The senescence marker p16INK4A is not only a marker of the pathology but contributes to OA onset: mice deficient in p16INK4A, a main senescence-driving known cell cycle inhibitor, were partially protected against CIA. These results were confirmed in C57Bl/6 mice after CIA by showing an increase in gene expression for senescence, catabolic and inflammatory markers in the synovial tissue preceding cartilage degradation.

(2) MSCs found in synovial, cartilage, fat pad and bone marrow participate in joint homeostasis. Because MSC are proposed to be at the root of OA development, we hypothesized that cellular senescence onset in these progenitor cells would be a possible etiological factor for OA. We have established an in vitro p16INK4A-induced senescence model on human primary MSC. Their intrinsic properties such as self-renewing are altered during senescence onset. Furthermore, in co-culture conditions with chondrocytes from OA patients, senescent MSC lost their extrinsic chondroprotective properties.

(3) To in vivo challenge these findings, we rely on the mouse model of accelerated senescence SAMP8, which develop spontaneous OA at the age of 6 months with cartilage degradation, synovial hypertrophy, osteophytosis and subchondral bone remodeling associated to meniscal calcification. Isolated MSC from these mice express senescence but non-inflammatory markers (p16INK4A+, p21wa1a1, MMP13, TGF-β1). Remarkably, intra-articular injection of these isolated SAMP8-derived MSC compared to SAMR1-derived control MSC, in young wild-type C57Bl/6 mice, was sufficient by itself, to induce significant articular cartilage degradation (OA score of 12.2 ± 1.5 vs 6.1 ± 3.5 for SAMP8 and SAMR1 MSC respectively, p < 0.05).

Conclusion: p16INK4A-induced cellular senescence in MSC played a causative role in cartilage loss of function and OA pathogenesis. In vitro, senescent MSC show altered intrinsic and extrinsic supportive tissue functions. In vivo, intra-articular injection of senescent MSC was sufficient to induce cartilage degradation. Specific targeting of such deleterious senescent cells could be an innovating and promising treatment in OA.

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OP0072 INHIBITION OF CLK2 AND DYRK1A BY SM04690 AS A NOVEL MOLECULAR REGULATOR OF WNT SIGNALING, CHONDROGENESIS, AND INFLAMMATION, A POTENTIAL DISEASE-MODIFYING TREATMENT FOR KNEE OSTEOARTHRITIS


Background: In the synovial joint, Wnt pathway upregulation contributes to osteoarthritis (OA) by increasing osteocyte differentiation, cartilage thinning and inflammation. SM04690, a novel small molecule, has previously demonstrated potential OA disease-modifying effects through Wnt pathway inhibition in vitro and in vivo.

Objectives: To elucidate the novel mechanism of action for SM04690 on Wnt pathway inhibition, chondrocyte differentiation, and anti-inflammation.

Methods: Wnt pathway activity was measured using a cell-based TCF/LEF luciferase reporter in SW480 colon cancer cells. A kinome screen (318 kinases) was performed. The effects of SM04690 on protein phosphorylation of serine and arginine rich splicing factors (SRSF proteins), Sir1, and FoxO1 in hMSCs, chondrocytes, and synovial fibroblasts were measured by Western blot. The effects of SM04690 and siRNA knockdown (KD) on chondrogenic and Wnt pathway gene expression were measured by NanoString gene expression panels and effects on LPS-induced inflammatory cytokines (IL-6, IL-8, TNF-α) in BEAS-2B cells were measured by qPCR and ELISA. In vivo, the pharmacodynamic effects of SM04690 were evaluated in monosodium iodoacetate injection-induced and anterior cruciate ligament transection with partial medial meniscectomy rat knee OA models in which a single intra-articular SM04690 (0.1 μg, 0.3 μg, 1.0 μg) or vehicle injection was administered. Cartilage was isolated at Day 10 and 35, phosphorylation and expression of SRSF proteins, Sir1, FoxO1, STAT3, and NF-κB were measured by Western blot.

Results: SM04690 was a potent (EC50=11nM) inhibitor of Wnt signaling. Cdc-like kinases (CLKs) and dual-specificity tyrosine kinase (DYRK1A) were identified as molecular targets of SM04690. In hMSCs and chondrocytes, compared to DMSO, SM04690 potently inhibited CLK-mediated phosphorylation of SRSF proteins. SM04690 also inhibited DYRK1A-mediated Sir1 and FoxO1 phosphorylation, thus increasing total and nuclear FoxO1 levels. Compared to siRNA control, DYRK1A/CLK2 KD increased expression of chondrogenic genes (COL3A1, ACAN, COMP, CD44 [all P<0.05]). CLK2 and DYRK1A KDs each inhibited Wnt pathway genes (AXIN2, TCF7, TCF4, LRP5, FZD6, FZD7, PITX2 [all P<0.05]) with no effects on β-catenin levels, compared to siRNA control. In synovial fibroblasts, compared to DMSO, SM04690 decreased phosphorylation of NF-κB and STAT3. In BEAS-2B cells, compared to siRNA control, DYRK1A KD inhibited inflammatory cytokine production (IL-6, IL-8, TNF-α [all P<0.05]), while DYRK1A/CLK2 dual KD enhanced anti-inflammatory effects of DYRK1A KD. In cartilage from rat OA models, compared to vehicle, SM04690 inhibited phosphorylation of SRSF proteins, Sir1, FoxO1, and STAT3, as well as expression of NF-κB.

Figure 1. Schematic representation of SM04690's proposed mechanism of action via CLK2 and DYRK1A inhibition in OA.
Establishment of Human Induced Pluripotent Stem Cell-lines (iPSc) for In Vitro Modelling Hand Osteoarthritis

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Background: Research results in the field of hand OA are currently limited due to the unavailability of tissue samples and lack of animal models replicating the features of the disease in humans. Cellular in vitro models are important tools to elucidate molecular mechanisms and pathways that are involved in hand OA. Specifically, induced pluripotent stem cells (iPSc) are considered ideal tools for this purpose since they allow the use of unlimited cells with chondrogenic differentiation potential. However, there are not studies published generating iPSc from patients with hand OA.

Objectives: To generate and characterize iPSc-lines from patients with radiographic hand OA and healthy donors, which can be used as cellular models of the disease, for studying the pathogenesis of the disease in vitro and for testing new drugs.

Methods: Patients with hand OA (non erosive hand OA with right thumb OA) and one healthy donor. Three weeks after reprogramming, embryonic stem cell-like colonies emerged in culture. These cells were positive for alkaline phosphatase activity (fig. 1A) and the pluripotency markers Tra1-81 and Nanog (fig. 1B). Molecular analyses showed high relative expression levels of the pluripotency-related genes OCT4, SOX2, NANOG and CRIPTO in the iPSc. These cells were also able to give rise to cells from the three germ layers (fig. 1C). Indeed, during mesodermal differentiation, spontaneously beating cardiomyocytes were seen in culture. Regarding SNP studies, cells from the patient with hand OA were homozygous for the at-risk allele in both genes studied, both before and after reprogramming (fig. 1D). The “i” iPSc-line (MOAIPS 15/64657) showed worse chondrogenic differentiation than the “healthy” iPSc-line (NIPS 15/63747), as shown by the micromasses collagen and proteoglycan content (fig. 1E).

Conclusion: The generation of one iPSc-line form patients with hand OA is reported for the first time. The presence of the at-risk alleles within the ALDH1A2 and SMAD3 genes were maintained after fibroblast reprogramming. The iPSc lines obtained showed differences in their chondrogenic differentiation capacity, to which their usefulness to test the role of these genetic variants in the pathogenesis of hand OA.

References:


Tofacitinib Promotes Fundamental Processes of Bone Healing

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Background: Inflammatory diseases like rheumatoid arthritis (RA) and anti-inflammatory treatment of RA with glucocorticoids (GC) or NSAIDS negatively influence bone metabolism and fracture healing. Janus kinase (Jak) inhibition with tofacitinib has been demonstrated as a potent anti-inflammatory therapeutic agent in the treatment of RA but its impact on the fundamental processes of bone regeneration such as recruitment of human mesenchymal stromal cells (hMSCs) and chondrogenesis, osteogenesis and osteoclastogenesis is still controversial and in part elusive.

Objectives: Therefore, in this study, we aim to examine the effects of Tofacitinib on processes of bone healing under reduced oxygen availability mimicking the in vivo situation of the fracture gap.

Methods: To this end, we analyzed the influence of Tofacitinib on the (i) invasion of hMSCs towards TNFα using a trans-well assay, (ii) chondrogenic differentiation of hMSCs in a 3D-micro-mass culture under hypoxic conditions, (iii) osteogenic differentiation of hMSCs, (iv) M-CSF/RANKL-mediated differentiation of isolated monocytes towards osteoclasts and (v) hypoxia-mediated target gene expression in non-differentiated, osteogenic and chondrogenic differentiated hMSCs.

Results: We demonstrate that Tofacitinib dose-dependently promotes the recruitment of hMSCs under hypoxia but inhibits recruitment of hMSCs under normoxia. With regard to the chondrogenic differentiation of hMSCs, we observed that Tofacitinib did not inhibit survival and at therapeutic relevant doses of 10-100 μM. Tofacitinib dose-dependently enhances osteogenic differentiation of hMSCs and reduces osteoclast survival and differentiation under hypoxic conditions. We show that Tofacitinib does not affect chondrogenic HIF target gene expression but increases HIF target gene expression in human osteogenic differentiated hMSCs.

Conclusion: We conclude from our data, that Tofacitinib may influence bone healing by promotion MSC recruitment into the hypoxic microenvironment of the fracture gap, does not interfere with the cartilaginous phase of the soft callus phase of fracture healing process. We assume that Tofacitinib may promote bone healing by promoting MSC recruitment into the hypoxic microenvironment of the fracture gap.
PAR2 ACCELERATES OSTEOARTHRITIS-LIKE JOINT CHANGES IN A MURINE MODEL OF POST-TRAUMATIC OSTEOARTHRITIS

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Background: Post-traumatic osteoarthritis (PTOA) is associated with articular cartilage damage and represents a major clinical challenge due to the poor regenerative capability of cartilage. We have recently developed a novel and robust dual injury murine model of PTOA, which combines destabilization of the medial meniscus (DMM) and cartilage scratch (DCS). Twenty-eight days post-surgery, osteophytogenesis and bone changes were monitored using microcomputed tomography. Dynamic weight bearing was assessed as an indirect measurement of pain at day 14.

Results: Evaluation of the presence and number of osteophyte revealed no significant differences between WT and PAR2-/- mice at day 28. However, quantification of osteophytes revealed that PAR2-/- mice had significantly smaller osteophytes (p<0.006) with less mineralised bone (p=0.003). Moreover, analysis of metaphyseal trabecular bone on the operated leg showed a significant decrease in % bone volume/tissue volume (BV/TV) (p=0.025). Assessment of pain-related behaviour, using dynamic weight bearing at day 14, demonstrated that PAR2-/- mice exerted less load on their front paws.

Conclusion: The findings in this study show that PAR2 plays a role in accelerated OA-like symptoms (i.e., osteophyte formation) in a dual injury model of OA, where both destabilisation of the medial meniscus and cartilage damage drive disease pathology. Furthermore, the loss of PAR2 decreases pain behaviour suggesting that PAR2 is involved in pain sensing. Taken together, these results support the future exploration of PAR2 as a therapeutic target for PTOA.

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Disclosure of Interests: Kendal McCulloch: None declared, Carmen Huesa: None declared, Lynette Dunning: None declared, Rob Van’t Hof: Shareholder of: OsteoRx Ltd, John Lockhart: None declared, Carl Goodyear: Grant/research support from: AstaZeneca, BMW, Celgene, Janssen, MedAnnex, Pfizer and UCBB, Speakers bureau: Abbvie

OP007 JAK-INHIBITORS TOFACITINIB AND BARICITINIB IMPROVE PATHOLOGICAL BONE LOSS IN VIVO

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Background: Targeting cytokines relevant to rheumatoid arthritis (RA) has proven efficient in clinical practice, but there is still demand for therapies that rebuild joint tissues which have been subjected to deterioration. Since many cytokines involved in RA rely on the intracellular janus kinase – signal transducer and activator of transcription (JAK-STAT) signalling pathway, targeting them presents itself as option. For this approach, JAK-inhibitors such as Tofacitinib and Baricitinib, targeting JAK1/JAK3 and JAK1/JAK2 respectively, seem favorable, as they have been approved for the treatment of RA. Moreover, preliminary data indicates an impact of JAK inhibition on local bone formation.

Objectives: To investigate the influence of JAK-inhibition on structural bone damage in vivo and its impact on osteoclast/osteoblast-mediated bone homeostasis in vitro.

Methods: In vivo analysis comprised unchallenged steady-state, the ovariectomy-induced mouse model of postmenopausal osteoporosis (OVX) and the serum-induced arthritis (SIA) mouse model. For steady-state analysis C57BL/6 WT (WT) mice obtained tofacitinib CB by oral gavage for 6 weeks. For OVX, WT mice received tofacitinib CB by oral gavage for 6 weeks. WT mice of the SIA model were fed tofacitinib or baricitinib CB for 14 days. Experimental readout included clinical parameters, ELISA (RANKL/OPG levels in serum), qPCR (mRNA expression in bone) and μCT. For in vitro analysis, murine osteoclasts (OC) were analyzed with TRAP staining (osteoclastogenesis) and von Kossa staining (Resorptive capacity). Murine osteoblasts (OB), derived from mesenchymal stem cells (MSC) and calvariae were assessed with qPCR (differentiation) and Alizarin red staining (mineralization capacity).

Results: In steady-state conditions, JAK-inhibition by tofacitinib enhanced trabecular bone density and decreased RANKL/OPG fraction in blood serum. These findings, and increased trabecular bones, were also applicable to spinal bone of tofacitinib-treated OVX mice. In SIA, both baricitinib and tofacitinib improved clinical symptoms and halted trabecular and cortical bone loss. In vitro OC-differentiation and function were not affected by JAK inhibition. However, tofacitinib and baricitinib amplified OCN expression in MSC-derived OBs at day 1 after osteogenic induction, together with reduced LIFγ1 and elevated Dkk1 levels at day 7. Moreover, as a result of JAK-inhibition RANKL expression was decreased in calvaria-derived OBs. Accordingly, both MSC- and calvaria-derived OBs showed increased mineralization when treated with JAK-inhibitors.

Conclusion: Our results suggest that JAK-inhibition by tofacitinib and baricitinib causes increased mineralization by osteoblasts, resulting in enhanced bone density in vivo, in both unchallenged and pathological mouse models.

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OP0077 INNOVATIVE TRANSLATIONAL MODELS TO STUDY HUMAN SYNOVIAL PATHOLOGY: TARGET VALIDATION AND PRECLINICAL IMAGING

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Background: Many experiments to study inflammation, hyperplasia, and fibrosis in the synovium have been performed in animal models of RA and OA. However, the predictive value of these models for the screening of potential drugs in RA is variable and for OA, none were sufficiently effective in clinical trials. Translational
OBJECTIVES: To define the specific lipid profile and distribution in human control and OA synovial membranes.

METHODS: Human synovial membrane samples of OA patients (n=13) and controls (n=10) were compared by matrix-assisted laser desorption ionization mass spectrometry imaging (MALDI-MSI). Tissue sections at 10 μm thickness were mounted on conductive slides and coated with norharmane matrix (7mg/ml, 2:1 chloroform/methanol) for lipid extraction. MALDI images were acquired using a MALDI TOF-TOF instrument (Rapiflex MALDI Tissuetyper, Bruker, Germany) in reflectron positive and negative ionization mode at a pixel size of 50 μm. Multivariate statistical analysis was used to search for the lipids with the highest differences between OA and control synovial membranes. Then, lipid spatial distribution was investigated with FlexImaging 4.1 software. Identifications were based on tandem mass spectrometry analyses in comparison to LIPID MAPS Structure Database.

RESULTS: MALDI-MSI in combination with principal component analysis (PCA) and discriminant analysis (DA) revealed differential lipid profile between OA and control samples. Data acquired in positive ion mode showed a good separation of OA patients and controls (Figure 1A). OA tissues showed higher lipid content in the mass/charge (m/z) range 600-800, compared to controls (Figure 1B). Among identified lipid species, we found 35 phospholipids significant differentially expressed between OA and controls, mainly classified in phosphatidylethanolamines (30%), phosphatidylethanolamines specifically in OA samples, whereas lysophosphatidylcholines were more abundant in control samples compared to OA. Most of these molecules, mainly PIs, were also spatially distributed in the lining layer of the OA synovium.

CONCLUSION: OA synovial tissues were characterized by a higher content of phospholipids, mainly PCs and PIs, compared to control synovial biopsies. Specific phospholipids related to morphological features of the synovial membrane have been described for the first time by MALDI-MSI. These molecules could have an important role in the synovitis associated with the pathogenesis of OA and constitute relevant molecular disease classifiers for the OA diagnosis.

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Background: Synovial inflammation or synovitis causes severe histological changes in the tissue affecting its normal functioning. These morphological changes are one of the most characteristic events in the OA pathology. Additionally, lipid species are recognized as important key factors in the development and regulation of inflammatory processes. Therefore, the lipid signature of the synovial membrane can provide new markers involved in the synovitis process undergoing the OA disease.

Figure 1. A) PCA-DA analysis separates control and OA samples according to lipid profile. B) Loading plot of PCA-DA analysis representing the lipid classes characteristic to OA (negative side) and control (positive side) samples given by MALDI-MSI. C) MALDI-MSI images showing the differences in the spatial distribution of two phosphatidylethanolamines in OA synovium.

**Background:** Although health professional (HP) treatments are considered to be a corner stone in the management of systemic sclerosis (SSc), little is known about the referral process to and the content of non-pharmacological care in SSc.

**Objectives:** To describe non-pharmacological care in SSc from the perspective of Dutch HPs, including referral reasons, diagnostic focus, interventions used and alignment in the communication between HPs and rheumatologists.

**Methods:** Dutch HPs were invited through their SSc patients to complete an anonymous online survey provided by the Dutch ARCH (Arthritis Research and Collaboration Hub) working group. The survey comprised multiple response and open questions covering six topics: sociodemographic questions, referral reasons, diagnostic focus, treatment targets, interventions and the assessment of quality of communication between HPs and rheumatologists based on the Consumer Quality Index (CQI) (rheumatoid arthritis, version 2.0). Referral reasons and treatment targets were examined by means of open questions, and then linked to the ICF (International Classification of Functioning, Disability and Health) following the refined ICF Linking Rules (Cieza, 2016).

**Results:** A total of 79 HPs, 65.8% women (N=52), with a mean age of 41.2 years, were included. The majority of Dutch HPs, including referral reasons, diagnostic focus, interventions and the assessment of quality of communication between HPs and rheumatologists as perceived by the HPs is shown in Table 2.

**Conclusion:** The results of this study show clear discrepancies between referral reasons and reported interventions, visible in the clear focus on body functions and structures on one hand and the broad spectrum of applied interventions on the other hand. It is possible that HPs make a translation of the reasons given for referral to the needs of the individual patient. Viewed from this perspective, it is questionable whether the referrals by the rheumatologists are sufficiently targeted. Further, the results describe a suboptimal communication between rheumatologists and HPs that should be targeted in practice and further research.

**REFERENCE:**

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Conclusion: Compared with RIS, DMAb was associated with sustained improvements in cortical bone structure, assessed by HR-pQCT of the radius and tibia. It remains to be confirmed whether increased cortical thickness with DMAb is associated with improved bone strength in GIOP. These results further support DMAb as a treatment for GC-treated patients at increased fracture risk.

REFERENCES:

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OP0081

RELATIONSHIP BETWEEN DIFFUSE IDIOPATHIC SKELETAL HYPEROSTOSIS AND FRAILTY VERTEBRAL FRACURE – A PROSPECTIVE STUDY IN OLDER MEN

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Background: Diffuse idiopathic skeletal hyperostosis (DISH) is a common disorder of unknown cause characterized by ossifications of entheses with spinal and extraspinal manifestations(1). The prevalence ranges from 4% to 35%, depending on the diagnostic criteria (2). An increased risk of vertebral fracture in DISH has been suggested, due to the loss of flexibility of the fused spine, reminiscent of what is observed in ankylosing spondylitis(3–6).

Objectives: The aim of this study was to prospectively analyze the risk of vertebral fracture in men with DISH, compared with men without DISH.

Methods: Men older than 50 (n = 782) had coronal and lateral spine radiographs along with DXA and were monitored prospectively. We analyzed the risk of incident vertebral fractures (over 7.5 years) in men with DISH defined by flowing ossification alongside the anterolateral aspect of at least four contiguous vertebral bodies, relative intervertebral disc preservation and the absence of apophyseal ankylosis and inflammatory changes of the SI joints, according to Resnick criteria (7). Incident vertebral fracture was defined by a decrease of at least 20% or 4 mm in any vertebral height (anterolateral or posterolateral) between the follow-up and the baseline radiographs.

Results: DISH was present in 21.7% (170/782) of men (mean age = 68). Among the 782 examined at baseline, 761 had at least one spine X-ray after baseline and 164/170 men with DISH had enough available data to be analyzed. Vertebral fracture incidence was higher in men with DISH compared with those without DISH (mean 10/164 (6.1%) vs. 16/597 (2.7%); p<0.05). DISH was also associated with the risk of vertebral fracture after adjustment for age, BMI, lumbar spine bone mineral density (BMD), prevalent vertebral fractures (Grade 2&3), disc space narrowing and endplate irregularity (OR = 2.89, [95%CI]: 1.15 – 7.28; p<0.05). 6.3% (10/ 149) of men with DISH had both normal BMD (=0.912 g/cm²) and increased risk of vertebral fracture (OR=6.54 [95%CI: 2.13 – 20.26]; p<0.05).

Conclusion: DISH is associated with higher risk of vertebral fracture, independently of BMD. The risk of vertebral fracture of men with DISH but normal BMD may be underestimated.

REFERENCES:

Disclosure of Interests: None declared


OP0082

TEMPORAL TRENDS OF BISPHOSPHONATE DISCONTINUATION AND FACTORS ASSOCIATED WITH ALENDRONATE DISCONTINUATION AND RESTART AT POPULATION LEVEL

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Background: Bisphosphonates are the most commonly used class of osteoporosis medication worldwide. Rare adverse events related to long-term use of bisphosphonates have raised interest in planned temporary drug discontinuation. Due to chronicity of osteoporosis, restarting osteoporosis medication is likely to be needed after such a discontinuation. Trends in the discontinuation and the restart of bisphosphonates and their reasons are not fully understood.

Objectives: We investigated the temporal trends of bisphosphonate discontinuation from 2010 to 2015 and evaluated the factors associated with alendronate only discontinuation and restart of any osteoporosis medication at a population level.

Methods: To determine the temporal trends of discontinuation (at least 12 months without prescription claims) from 2010 to 2015, we identified a cohort of women with long-term bisphosphonate therapy (medication possession ratio (MPR) ≥ 80% for at least 3 continuous years) derived from the enhanced 5% Medicare sample and a cohort of beneficiaries with evidence of osteoporosis (defined using diagnosis and fracture codes, and medication claims). We used a case-crossover design, nested within the cohort study, to identify factors associated with discontinuation of long-term alendronate therapy and restart of any osteoporosis medication. We used conditional logistic regression adjusted for potential confounders to compare factors associated with alendronate discontinuation and osteoporosis therapy restart in the hazard period (120 days) referent to the preceding control periods (120 days).

Results: We identified a total of 73,800 women with exclusive long-term alendronate (59,251), risedronate (6,806), or zoledronic acid (7,743) use, respectively, of which 26,281 (35.6%) women discontinued therapy. The proportion of long-term bisphosphonate users who discontinued therapy increased from 1.7% in 2010 to 1.4% in 2012, and remained relatively stable thereafter (Figure 1). After adjustment, factors most strongly associated with the discontinuation of alendronate included: a new prescription of benzodiazepines (adjusted Odds Ratio [aOR] = 2.5, 95% CI [2.1, 3.0]), prior dual-energy X-ray absorptiometry (DXA) scan (aOR = 1.95, 95% CI [1.7, 2.0]), skilled nursing facility care utilization (aOR = 1.8, 95% CI [1.6, 2.1]). Factors most strongly associated with the restart of any osteoporosis discontinuation were: women older than 75 years (aOR = 3.0, 95% CI [2.5, 3.5]), osteoporosis diagnosis after 2005 (aOR = 2.0, 95% CI [1.8, 2.3]), and osteoporosis diagnosis after 2005 (aOR = 2.0, 95% CI [1.8, 2.3]).
Prevalence of vertebral fractures in postmenopausal women with rheumatoid arthritis

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Objectives: To determine the prevalence of vertebral fractures in postmenopausal women with RA and to analyse their characteristics and associated risk factors.

Methods: We included 346 postmenopausal women diagnosed with RA according to the ACR/EULAR 2010 criteria in 18 Spanish Rheumatology Departments, randomly selected from the registry of RA patients in each center, recruited during 2014. Lateral radiographs of the dorsal and lumbar spine were obtained from all patients, to evaluate morphometric vertebral fractures. Expert rheumatologists diagnosed vertebral fractures according to the Genant grading scale. The spinal deformity index (SDI) was calculated by assigning numbers 1, 2 and 3 to each fractured vertebra and adding the total score of each patient. The study variables were: a) age, body mass index (BMI), b) factors related to RA: time of evolution, FR, ACPA, and c) fracture risk factors: prior fragility fracture, parental hip fracture, glucocorticoids, smoking, alcohol intake > 3 units daily, secondary osteoporosis and time since menopause.

Results: The mean age was 66.8 (SD: 10.1) years and the median evolution of the disease, 8.00 (IQR: 3.00-15.5) years. 77.2% (n: 267) and 75.7% (n: 252) had FR and ACPA, respectively. The mean duration of the postmenopausal period was 15.0 (SD: 9.6) years. 23.4% (n: 79) of patients had at least one vertebral fracture: 10.7% (n: 36) had a single fracture and 12.7% (n: 43), multiple fractures. The most fractured vertebrae were D12, L1 and L2 (fractured in > 5% of patients). The median SDI was 3 (IQR: 2-5). The vertebral with the highest mean IDE was D8.

Conclusion: One out of every 4 postmenopausal women with RA has at least one vertebral fracture. Vertebral of the dorso-lumbar hinge are the most frequently involved and the magnitude of the spinal deformity is relevant. Vertebral fractures are related to the time of evolution of RA and to the risk factors for fracture.

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Background: Denosumab discontinuation (DD) induces bone turnover markers (BTMs) increase, bone mineral density (BMD) decrease, and increased risk of spontaneous vertebral fractures. Prescribing a bisphosphonate after DD could avoid this rebound effect. 

Objectives: This exploratory analysis of the SEMIRA (Steroid EliMination In RA) study compared changes in markers of bone and cartilage metabolism in RA patients with low disease activity (LDA) or remission on tocilizumab (TCZ + GC) with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) who received either slow GC tapering (GCtaper) or continuation (5 mg; GC5mg).

Methods: Patients had at least stable LDA (DAS28-ESR ≤2.6) received either slow GC tapering (GCtaper) or continuation (5 mg; GC5mg). This exploratory analysis of the SEMIRA (Steroid EliMination In RA) study compared changes in markers of bone and cartilage metabolism in RA patients with LDA or remission on tocilizumab (TCZ + GC) with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) who received either slow GC tapering (GCtaper) or continuation (5 mg; GC5mg).

Results: Figure 1 shows changes from baseline to week 24 in markers of bone and cartilage metabolism in RA patients with LDA or remission on tocilizumab (TCZ + GC) with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) who received either slow GC tapering (GCtaper) or continuation (5 mg; GC5mg).

Conclusion: Previous studies showed lower survival in patients discharged for conventional home care (1,2). In our cohort, despite more than half the sample was discharged home, no difference was found in mortality or re-fracture. Further studies will assist to clarify this matter.

Reference:

Disclosure of Interests: None declared
TRENDS IN HIP FRACTURE INCIDENCE IN WOMEN

Shreyasee Amin.

Disclosure of Interests:
Burmester GR, et al. Arthritis Rheumatol 2018;70(suppl 10).

Conclusion: The findings of this biochemical marker analysis suggest that withdrawal from GC after achievement of LDA or remission with TCZ results in a decrease in hip fracture risk after cessation of GC therapy, our results offer further insight on the reversible risk of systemic harm to noninfamed joints in the context of LDA or remission.

REFERENCES:


OP0088 COMORBIDITIES AS RISK FACTORS FOR RHEUMATOID ARTHRITIS (RA) AND ACCRUAL AFTER RA DIAGNOSIS

Vanessa Khonze1, Cynthia S. Crawford1, Jeffrey Sparks1, Elena Myasoedova1, John Davis1, Mayo Clinic, Rochester, United States of America; Brigham and Women’s Hospital, Boston, United States of America

Background: Understanding the timeline of comorbidity development in patients with RA may inform disease pathogenesis and help identify targets for improving outcomes (1).

Objectives: We first aimed to compare the prevalence of a comprehensive list of comorbidities in RA cases versus controls. Second, we aimed to investigate the time association of comorbidity development relative to RA onset to identify which comorbidities might predispose to developing RA and comorbidities that might result from RA.

Methods: We performed a case-control study using a biobank at a single center, identifying 821 cases of RA (143 incident) using a rules-based algorithm combining two diagnosis codes with use of a DMARD (PPV = 95%). We matched each case to three controls based on age, sex, and location of residence at the time of the biobank survey. Participants self-reported the presence or absence and age of onset for 77 comorbidities on the survey.

Results: Among the 3,276 RA cases and controls, mean age was 62 years, and 73% were female. Cases with RA had the same number of comorbidities as controls before RA diagnosis (median 1.0 vs 1.0, P = 0.49) but had more comorbidities by the time of the survey (median 5.0 vs 4.0, p < 0.001). At the time of the survey, several comorbidities were more common in participants with RA than controls (Table1). Cancer was not more common in RA cases than controls (31% vs 32%, p = 0.80), even among all cancer subtypes. The only comorbidities that tended to develop in the time period before RA diagnosis more often than controls were inflammatory bowel disease (1.9% vs 0.5%, p = 0.001) and type 1 diabetes (1.3% vs 0.4%, p = 0.01). In contrast, in the time period after RA diagnosis, myocardial infarctions were more common in cases with RA (3.8% vs 1.2%, p < 0.001) and hyperlipidemia was less common (11.4% vs 16.4%, p = 0.004) compared to controls.

Conclusion: There appears to be different trends in hip fracture rates for women and men and by age groups. The factors contributing to the observed recent increases in hip fracture rates among women and men ages 40-59 yrs warrant further attention. As suggested by others, there may be a recent plateau vs. slight increase in hip fracture rates in older women, which we noted in women age > 80 yrs since 2010. The decrease in hip fractures in older men, particularly in those age > 80 yrs, may reflect improved awareness in recent years of osteoporosis in men with initiation of treatment or better mitigation of risk factors, but warrants further review.

REFERENCE:


WEDNESDAY, 12 JUNE 2019

When rheumatoid arthritis (RA) does not walk alone: new data on comorbidities in RA

OP0087 TRENDS IN HIP FRACTURE INCIDENCE IN WOMEN AND MEN OVER 1980-2015 IN OLMSTED COUNTY, MINNESOTA, USA

Delano Beleite, Ann Keams, Elizabeth Atkinson, Shreyasee Amin, Mayo Clinic, Rochester, United States of America

Background: Hip fracture incidence, which has been generally declining in North America, may have recently plateaued in women (Lewiecki, et al 2018).

Objectives: We examined the trends in hip fracture incidence over 1980-2015, in both women and men, from Olmsted County, Minnesota, USA.

Methods: Using the Rochester Epidemiology Project, a unique medical records linkage system that allows access to all (inpatient and outpatient) community medical records for Olmsted County residents, we identified all incident hip fractures among residents age ≥18 years between 1980-2015. Available medical records were reviewed by trained nurse abstractors to validate hip fractures identified and to determine their antecedent cause (pathological process [e.g., malignancy], severe trauma [e.g., motor vehicle accidents] and those due to no more than moderate trauma [by convention, equivalent to a fall from standing height or less]). Overall incidence rates were summarized separately for women and men, as well as by 5 year strata for different age groups (ages 18-39, 40-49, 50-69 and ≥ 80 yrs). Rates for women and men were each directly age-adjusted to the population distribution of US whites in 2010.

Results: Between 1980-2015, we identified 2488 hip fractures in women (73%, median age 84 yrs and 918 hip fractures in men (27%, median age 80 yrs), 97.4% of which were in whites. The majority of hip fractures were due to no more than moderate trauma (88% in women; 81% in men). The overall age-adjusted annual incidence of first hip fracture over 1980-2015 was 154 per 100,000 person-years (p-y) for women and 98 per 100,000 p-y for men. Hip fracture rates have decreased overall in women since 1980 (Table), however since 2005, there has been a trend for increasing hip fractures among women age 40-59 yrs and since 2010, a possible plateau vs. slight increase in hip fracture rate for women age ≥ 80 yrs. In men, there has been a general decrease in rates among those age 60-79 yrs and, at least since 2005, in men age ≥ 80 yrs, but there may be a trend for increasing hip fractures since 2010 in men age 40-59 (Table).

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Conclusion: There appears to be different trends in hip fracture rates for women and men and by age groups. The factors contributing to the observed recent increases in hip fracture rates among women and men ages 40-59 yrs warrant further attention. As suggested by others, there may be a recent plateau vs. slight increase in hip fracture rates in older women, which we noted in women age ≥ 80 yrs since 2010. The decrease in hip fractures in older men, particularly in those age ≥ 80 yrs, may reflect improved awareness in recent years of osteoporosis in men with initiation of treatment or better mitigation of risk factors, but warrants further review.
METABOLIC SYNDROME IS COMMON AROUND THE CROSS-SECTIONAL DATA WERE ANALYZED FROM PATIENTS MEETING 1987 OR LATER CRITERIA FOR THE METABOLIC SYNDROME. PATIENTS TREATED IN ROUTINE PRACTICE SETTINGS. VARIATIONS BY SEX, AND BY MENOPAUSAL STATUS WERE ALSO EXAMINED.

**Background:** Prevalence studies of metabolic syndrome (MetS) in early rheumatoid arthritis (ERA) are sparse and estimates are variable. Differences by sex and menopausal status have not been formally assessed.

**Methods:** Cross-sectional data were analyzed from patients meeting 1987 or 2010 ACR/EULAR criteria enrolled in the Canadian Early Arthritis Cohort (CATCH) from January 2007-March 2017. CATCH is a prospective multicenter observational study of patients diagnosed and treated for early inflammatory arthritis (symptoms <1 year) by a rheumatologist. Participants completed standardized clinical assessments and patient-reported outcome measures. Laboratory testing of metabolic parameters was encouraged, but left to the discretion of the rheumatologist. MetS was defined according to modified WHO criteria1 as > 2 of the following: body mass index (BMI) >30, hypertension, low high-density lipoprotein (HDL) cholesterol, dyslipidemia, or impaired glucose intolerance (IGT)2. Univariate and multivariable logistic regression was used to estimate crude and adjusted associations between baseline demographic, clinical and lifestyle variables with prevalent MetS in men and in women, respectively.

**Results:** The sample included 1543 participants; 71% were female and mean (SD) age was 54 (15) years. 476 (31%) of the total sample met criteria for MetS. Participants with MetS were older, more frequently past smokers and reported more comorbid conditions, including cardiovascular disease (CVD) (p<0.0001).

MetS prevalence was higher in men (42%) than women (26%, p<0.0001) and higher in post-menopausal (33%) vs. pre-menopausal women (15%, p<0.0001). Post-menopausal women had a higher frequency of hypertension (65%), IGT (32%) and dyslipidemia (21%) compared to pre-menopausal women (p<0.001). In multivariable logistic regression MetS was negatively associated with seropositivity and pulmonary disease in men; with corticosteroid use in menopausal women; and with psychiatric comorbidity in pre-menopausal women.

**Conclusion:** Approximately 1 in 3 ERA patients met criteria for MetS. Though men had a higher prevalence of MetS and individual MetS components, post-menopausal women had a similar MetS profile as men, and should equally be considered high risk for CVD development. Characteristics and associations with MetS differed in men and women suggesting sex-specific variations are important considerations for comorbidity screening and surveillance of CVD outcomes in ERA.

**REFERENCE:**


**Disclosure of Interests:** None declared.
Conclusion: The maintenance of remission was strongly associated with a reduced risk of clinical and subclinical atherosclerosis and regression analyses exploited the ORs for the occurrence of these end points. In the 3-year prospective follow-up, 797 patients (82.7% female, median age of 60 years, range 21-89) were assessed. We also observed a median RA duration of 8.35 years (range 0.1-35), 70.9% of patients showed rheumatoid factor and 55.7% ACPA. Among “traditional” CV risk factors, we observed that BMI was 27.21 ± 4.05, 33% of patients reported smoking habit, 49.3% were affected by high blood pressure (HBP) and 12.3% by type 2 diabetes (T2D). Corticosteroids were administered in 75.5% of patients (low dosage 66.8%), methotrexate in 86.8%, hydroxychloroquine in 28.1% and biologic DMARDs in 60.7%. The remission was reached and maintained in 42.6% of patients, during the follow-up. We recorded an increased rate of subclinical atherosclerosis (70 vs 130 patients p<0.0001) and clinical atherosclerosis (30 vs 46 patients, p=0.001), at the end of follow-up. The multivariate regression analysis showed that T2D (OR: 4.50, 95%CI:1.74-11.82, p=0.002), HBP (OR: 2.03, 95%CI:1.04-4.14, p=0.042), ACPA (OR: 2.36, 95%CI:1.19-4.69, p=0.002) and mean values of CRP during the follow-up (OR: 1.07, 95%CI:1.03-1.14, p=0.040) were associated with subclinical atherosclerosis. Differently, the maintenance of remission was associated with a reduced risk of subclinical atherosclerosis (OR: 0.25, 95%CI:0.11-0.56, p=0.001). The multivariate regression analysis showed that T2D was associated with clinical atherosclerosis (OR:2.1, 95%CI:1.91-7.17, p=0.001). Conversely, the maintenance of remission was associated with a reduced risk of clinical atherosclerosis (OR:0.20, 95%CI:0.09-0.95, p=0.041).

Conclusion: The maintenance of remission was strongly associated with a reduced risk of clinical and subclinical atherosclerosis in 3-year prospective follow-up. Among “traditional” CV risk factors, T2D was significantly associated with both clinical and subclinical atherosclerosis.

REFERENCES:

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OP0091
RISK OF MEDICAL COMPLICATIONS FOLLOWING TOTAL HIP OR KNEE ARTHROPLASTY IN PATIENTS WITH RHEUMATOID ARTHRITIS: A NATIONWIDE REGISTER-BASED COHORT STUDY
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Background: Total hip and total knee arthroplasty (THA/TKA) are major sur-
geries carrying a risk of complications. Patients with rheumatoid arthritis (RA) are at increased risk of venous thromboembolism (VTE), arterial thromboembolic events (ATE), and infections in a non-surgical setting.

Objectives: To investigate the risk of VTE, ATE, and non-surgical infection fol-
lowing THA/TKA in patients with RA compared with osteoarthritis (OA); and to explore the impact of biologics treatment.

Methods: In a nationwide register-based study, patients with RA and OA who had elective THA/TKA in 2000-2014 were identified in the Danish Hip Arthroplasty Register/Danish Knee Arthroplasty Register and followed up to 90 days after sur-
gery for the occurrence of VTE, ATE, and infections. Cox models stratified on sex and type of surgery (THA vs TKA) and adjusted for age, calendar period, history of chronic obstructive pulmonary disease (COPD), diabetes mellitus (DM), cancer, VTE and CVD were carried out. Outcome information was obtained through link-
age with the Danish National Patient Registry.

In DANBIO, we identified RA patients treated with biologics within 90 days preced-
ing surgery and estimated their risk of each outcome compared with non-biologics treated RA patients in a Cox model adjusted for the propensity score (PS) of receiving biologics as a restricted cubic spline covariate. The PS was conditional on age, sex, calendar period, use of methotrexate, other csDMARDs, and/or glu-
corticoids, pre-surgical DAS28, HAQ-DI, VAS physician, and COPD, DM, can-
cer and/or VTE.

Results: In total, 2899 and 112,571 patients with RA and OA were followed-up (Table).

Conclusion: In this nationwide cohort study, RA patients were at increased risk of infection after THA/TKA compared to OA patients, but treatment with biologics did not further increase the risk.

As seen in other studies RA patients had a lower risk of VTE following TKA when compared with OA patients, but our finding of an increased incidence of VTE in biologics-treated patients warrants further studies.

Disclosure of Interests: René Cordtz: None declared, Lars Erik Kristensen Grant/research support from: UCB, Biogen, Janssen Pharmaceuticals, and Novartis, Consultant for: Consultant for AbbVie, Amgen, Biogen, MSN, Celgene,

Table. Patient characteristics and risk of venous thromboembolism (VTE), arterial thromboembolism (ATE), and non-surgical infection following total hip or total knee arthroplasty (THA/TKA) among patients with rheumatoid arthritis (RA) compared with osteoarthritis (OA), and biologics treated compared with non-biologics treated RA patients.

<table>
<thead>
<tr>
<th>N</th>
<th>RA</th>
<th>OA</th>
<th>p</th>
<th>Biologics treated</th>
<th>Non-biologics treated</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>2899</td>
<td>112,571</td>
<td>0.001</td>
<td>73%</td>
<td>74%</td>
<td>0.43</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>73%</td>
<td>58%</td>
<td>&lt;0.001</td>
<td>73%</td>
<td>74%</td>
<td>0.43</td>
</tr>
<tr>
<td>Age at surgery, mean (a.d.)</td>
<td>66 (11)</td>
<td>69 (10)</td>
<td>&lt;0.001</td>
<td>62 (12)</td>
<td>65 (10)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Had TKA surgery</td>
<td>63%</td>
<td>44%</td>
<td>&lt;0.001</td>
<td>67%</td>
<td>63%</td>
<td>0.09</td>
</tr>
<tr>
<td>Received thromboprophylaxis</td>
<td>99%</td>
<td>99%</td>
<td>0.93</td>
<td>97%</td>
<td>99%</td>
<td>0.002</td>
</tr>
<tr>
<td>History of VTE</td>
<td>3%</td>
<td>2%</td>
<td>0.01</td>
<td>3%</td>
<td>4%</td>
<td>0.31</td>
</tr>
<tr>
<td>Prevalent CVD</td>
<td>17%</td>
<td>15%</td>
<td>0.01</td>
<td>11%</td>
<td>15%</td>
<td>0.07</td>
</tr>
<tr>
<td>History of cancer</td>
<td>6%</td>
<td>7%</td>
<td>&lt;0.001</td>
<td>4%</td>
<td>6%</td>
<td>0.05</td>
</tr>
<tr>
<td>History of hospitalisation due to infection</td>
<td>10%</td>
<td>4%</td>
<td>&lt;0.001</td>
<td>12%</td>
<td>8%</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>Outcome</td>
<td>Events, n (%)</td>
<td>HR (95%CI)</td>
<td>Events, n (%)</td>
<td>HR (95%CI)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VTE</td>
<td>25 (1.0)</td>
<td>1167 (1.3)</td>
<td>0.7 (0.5 to 1.1)</td>
<td>8 (1.9)</td>
<td>7 (0.5)</td>
<td>5.5 (1.7 to 18.4)</td>
</tr>
<tr>
<td>ATE</td>
<td>4 (0.8)</td>
<td>849 (0.7)</td>
<td>1.2 (0.8 to 1.8)</td>
<td>8 (1.0)</td>
<td>8 (0.6)</td>
<td>2.8 (0.7 to 11.1)</td>
</tr>
<tr>
<td>Infection</td>
<td>73 (2.5)</td>
<td>2224 (2.0)</td>
<td>1.3 (1.0 to 1.6)</td>
<td>11 (2.7)</td>
<td>35 (2.5)</td>
<td>0.9 (0.4 to 1.9)</td>
</tr>
</tbody>
</table>

Abbreviations: HR, hazard ratio; 95%CI, 95% confidence interval.

RA was associated with an increased risk of infection, but a lower risk of VTE (HR=3.0, 3.0 vs 1.0,p<0.04); Compared with non-biologics treated, biologics-treated patients were not at increased risk of infection but had a 5-fold increased risk of VTE.
Eli Lilly, Janssen Pharmaceuticals, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB Pharma. Speakers bureau: Pfizer, AbbVie, Amgen, UCB, BMS, Biogen, MSD, Novartis, Eli Lilly and Company, and Janssen Pharmaceuticals. Anders Odgaard; None declared, Søren Overgaard; None declared, Lene Dreyer Consultant for: MSD, UCB and Janssen Pharmaceuticals. Speakers bureau: MSD, UCB, Eli Lilly and Janssen Pharmaceuticals.


ASSOCIATIONS BETWEEN CLINICAL VARIABLES AND PSYCHOLOGICAL SYMPTOMS IN RHEUMATOID ARTHRITIS: A NETWORK SCIENCE PERSPECTIVE

Hsiu Yen Tung1, Sam Norton2, Faith Matcham1, James Galloway1, Matthew Hotopf2. 1King’s College London, London, United Kingdom

Background: Rheumatoid arthritis (RA) is associated with an increased prevalence of common mental disorders, including anxiety and depression (Matcham et al. 2013). Borsoom’s (2017) network theory of mental illness is gaining traction as a model for depression which incorporates biological, social and psychological aspects of depression by looking at interactions between individual symptoms and other variables within a wider network. Currently applications have been restricted to psychiatric samples, however, this model may potentially help gain a clearer understanding of the causal links clinical variables and mental health symptoms in RA.

Objectives: To study the prescriptions of NSAIDs in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS) registered in ICEBIO and matched controls, and explore their relationship with disease activity measures. In addition, to explore the impact of initial TNF inhibitor therapy on NSAID prescription rates.

Methods: The data used are from patients attending rheumatology clinics at King’s College Hospital who completed patient reported outcomes (PROs) electronically via the Integrating Mental and Physical Healthcare (IMPARTS) system. Over 1,000 patients completed PROs via IMPARTS, with a subsample of 211 extracted for this analysis where psychological screening and inflammatory markers were recorded concurrently (<14days). The screening tools used were the two-item Patient Health Questionnaire (PHQ2) and the two-item Generalised Anxiety Disorder (GAD2), which assess the core symptoms of depression and anxiety: low pleasure/interest, low mood, high anxiety, uncontrollability of worry. Additional data recorded were joint counts and visual analogue scales for pain, fatigue and global disease activity. Missing data were imputed using multiple imputation. Network analysis was conducted using the ggraph package in R based on the regularised correlations between variables. With a graphical network model of variables created to calculate centrality values.

Results: Figure 1 below illustrates that the symptoms with the most connections were PHQ1 (low pleasure/interest), GAD2 (uncontrollable worry), pain and global disease activity. As expected the strongest connections were between PHQ1 (low pleasure/interest) with PHQ2 (low mood), GAD1 (high anxiety) with GAD2 (uncontrollable worry), pain with patient global, tendon joints with swollen joints, and ESR with CRP.

The results highlight pain and PHQ2 (low mood) as having both the highest degree (3.9 & 3.8, respectively) and betweenness centrality (22 & 10, respectively). This indicates that these are the variables with both the highest number of connections and providing the shortest pathway between other symptoms and so may act as key variables linking inflammation and mental health. Pain and global disease activity had the highest closeness centrality (0.033 & 0.032, respectively), illustrating that they have the shortest path with all other symptoms and capture the influence of both inflammation and mental health. Tender and swollen joints have weak connections to the mental health variables, suggesting that that extrarticular aspects of pain may be important.

Conclusion: Inflammation in RA does not appear to have a strong influence on mental health, with pain providing the main connection between these areas of the network. Concerning the symptoms of mental health considered, all were strongly connected but low mood provided the main connection between clinical and psychological variables. This indicates mood as potentially a key variable in RA, which is easy to monitor in routine care.

Disclosure of Interests: Hsiu Yen Tung: None declared, Sam Norton: None declared, Faith Matcham: None declared, James Galloway Consultant for: Pfizer Inc, Matthew Hotopf: None declared

REFERENCES:


THE INCIDENCE AND RISK FACTOR OF NEW CAROTID PLAQUES AND THE PROGRESSION RATE OF CAROTID PLAQUES IN PATIENTS WITH RHEUMATOID ARTHRITIS IN 6 YEARS PROSPECTIVE CASE CONTROL STUDY. -TOMORROW STUDY-

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Background: Cardiovascular disease is one of the complications of rheumatoid arthritis (RA). Patients with RA show higher rates of cardiovascular disease mortality and overall mortality compared with individuals without RA. The presence of an abnormally increased intima–media thickness (IMT) in the carotid artery and carotid plaques are on ultrasound are useful for assessing the presence of subclinical atherosclerosis. A greater presence of carotid artery IMT and carotid plaques is a predictor of cardiovascular disease events.

Objectives: The objective of this study was to evaluate progression of carotid plaques in 6 years by comparing 2011 and 2017, and to assess the risk factors of progression.

Methods: This study included 208 patients with RA and 204 age- and sex-matched controls (Co) in the T0tal Management Of Risk factors in Rheumatoid arthritis patients to iMprove morbidity and mortality (TOMORROW) study. This was a 10-year cohort study that started in 2010. Carotid ultrasound was performed in 2011 and 2017. Ultrasound examination of bilateral carotid arteries was performed using high-resolution B-mode ultrasound (Hi VISION Avius; Hitachi Aloka Medical, Tokyo, Japan) with a 6- to 18-MHz linear array transducer. IMT was evaluated as the distance between the luminal–intimal interface and the medial–adventitial interface. IMT was measured using two calipers on the freeze frame of a suitable longitudinal image. The upper limit of normal for IMT was defined as 1.0 mm. Lesions with any focal structure that protruded into the vessel lumen for at least an IMT > 1.1 mm were defined as atherosclerotic plaques. Subsequently, the plaque score was assessed as the sum of the maximal thicknesses of all plaques in bilateral carotid arteries in the scanning area. Plaque scores were categorized as follows: none, no plaques; mild, score of 1.1–5.0; moderate, score of 5.1–10.0, and severe, score of >10.0.

Results: A total of 175 patients with RA (mean age: 58.9 ± 12.7 years, female ratio: 85.7%; mean disease duration: 15.0 ± 11.7 years) and 185 Co (mean age: 58.5 ± 12.5 years, female ratio: 84.3%) were finally analyzed. Carotid plaques were observed more frequently in the RA group than in the Co group in 2011 (n = 82 vs n = 66, p = 0.04). However, the incidence of new plaques was not significantly different between the RA and Co groups (n = 33 vs n = 44, p = 0.94). Age (p = 0.015) and the presence of diabetes (p = 0.009) were higher in patients with RA and new plaques than in those without new plaques. Multivariate logistic regression analysis did not show that RA was a risk factor for the incidence of new plaques (OR: 0.90, 95% CI: 0.47–1.73, p = 0.750). However, the presence of hypertension (OR: 3.11, 95% CI: 1.43–6.74, p = 0.004), the presence of diabetes (OR: 6.13, 95% CI: 1.13–32.4, p = 0.038) were risk factors for the incidence of new plaques. The plaque score became advanced in the RA and Co groups (both p < 0.001) in 6 years.

Conclusion: There were no significant differences in the incidence of new plaques and the progression rate of the plaque score between patients with RA and Co. This finding might due to the recent advances in RA treatment, such as methotrexate or biologic DMARDs. In patients with RA, the presence of hypertension and diabetes represents a risk factor for the incidence of new plaques.
Acknowledgement: We wish to thank Atsuko Kamiyama, Tomoko Nakatsuka and the members of the Osaka City University hospital clinical research center.


REFERENCES:

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Disclosure of Interests: Mayuko Hayashi: None declared, Ryoko Sakai Grant/ research support from: Tokyo Women’s Medical University (TWMU) has received unrestricted research grants for Division of Epidemiology and Pharmacopreparatology of Rheumatic Diseases from Ayumi Pharmaceutical Co. Ltd., Bristol Meyers Squibb, Chugai Pharmaceutical Co. Ltd., Nippon Kayaku Co. Ltd., Taisho Toyama Pharmaceutical Co. Ltd., Mitsubishi Tanabe Pharma Corp., and with which TWMU paid the salary of R.S. RS has received a research grant from Bristol-Meyers Squibb. Elitchi Tanaka Speakers bureau: Abbvie, Asahi Kasei Pharma company, Bristol-Meyers Squibb, Chugai Pharmaceutical, Daiichi Sankyo Co., Eisai Pharmaceutical, Janssen Pharmaceutical K.K., Nippon Kayaku, Pfizer, Takeda Pharmaceutical, Taisho Toyama Pharmaceutical Co., and UCB Pharma., Takefumi Furuya Speakers bureau: the Asahi Kasei Pharma Corporation, Bristol-Myers Squibb, Chugai Pharmaceutical Co., Ltd., Eisai Co., Ltd., Ono Pharmaceutical Co., Ltd., Pfizer Japan Inc., Takeda Pharmaceutical Co., Ltd., and UCB Japan Co. Ltd, Eisuke Inoue: None declared, Mai Abe: None declared, Mika Kawano: None declared, Eric Sugano: None declared, Naohiro Sugitani: None declared, Kumiko Saka: None declared, Meoko Ochiai: None declared, Yoko Shimizu: None declared, Rei Yamaguchi: None declared, Naoki Sugimoto: None declared, Katsunori Ikari: None declared, Atsuo Taniguchi: None declared, masayoshi harigai Grantri research support from: Tokyo Women’s Medical University (TWMU) has received unrestricted research grants for Division of Epidemiology and Pharmacopreparatology of Rheumatic Diseases from Ayumi Pharmaceutical Co. Ltd., Bristol Meyers Squibb, Chugai Pharmaceutical Co. Ltd., Nippon Kayaku Co. Ltd., Taisho Toyama Pharmaceutical Co. Ltd., Mitsubishi Tanabe Pharma Corp., and with which TWMU paid the salary of MH. MH has also received research grants from AbbVie Japan GK, Eisai Co. Ltd., Takeda Pharmaceutical Co., Ltd., and Teijin Pharma Ltd.. Hiashi Yamanaoka Grantri research support from: AbbVie, Eisai, Bristol-Meyers, Novartis, Behringer, Astellas, Kaken, Nippon-Shinyaku, Pfizer, UCB, Ayumi, Ono, Daiichi-Sankyo, Taisyo-Toyama, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, Torii, YLbio, Speakers bureau: Bristol-Meyers, Astellas, Pfizer, Daiichi-Sankyo, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, YLbio.


WEDNESDAY, 12 JUNE 2019
Tackling chronic pain; fibromyalgia and back pain...

OP0296 DYSREGULATED BONE MARROW Stromal CELLS in MODIC TYPE 1 CHANGES

Stefan Dudli1, Dominik Haenni1, Astrid Juengel1, Michael Betz2, Jose Spiring3, Florian Brunner1, Mazda Farshad1, Oliver Distler1, 1Baigrist University Hospital and University Hospital Zurich, Centre of Experimental Rheumatology, University Clinic of Rheumatology, Zurich, Switzerland, 2University of Zurich, Center for Microscopy and Image Analysis, Zurich, Switzerland, 3Balgrist University Hospital, Department of Orthopaedic Surgery, Zurich, Switzerland

Background: Modic type 1 changes (MC1) are fibro-inflammatory vertebral bone marrow lesions adjacent to degenerating discs. Patient with MC1 often develop low back pain [1]. In MC1, extra-cellular collagen is deposited, myelopoiesis is dysregulated, and bone is rapidly remodeled. These are signs of a chronic inflammation. The cellular mechanisms are unknown, yet bone marrow stromal cells (BMSC) are key regulators of myelopoiesis, can differentiate into collagen-secreting cells, and modulate inflammation [2].

Methods: From patients undergoing lumbar spondylodesis, bone marrow aspirates (n=5) were processed and cell surface markers were analyzed by flow cytometry (CD1, CD16, CD19, CD34, CD45, CD73, CD90, CD105, CD284) (t-test).

Results: Biopsies: Collagen was qualitatively more abundant in MC1 than in Ctrl bone marrow, particularly in areas of adipocyte clusters and around adipocytes (Figure 1, arrows). FLIM was able to distinguish adipocytes (T =2.1-2.7ns), leukocytes (T =0.4-0.8ns), erythrocytes (T =0.2-0.4ns), and collagen (T <0.15ns) based on their different auto-fluorescent life-times (Figure 1, right). BMSCs: By RNA sequencing 154 genes were differentially expressed between MC1 and Ctrl BMSCs (p<0.01; log2 ratio >0.5). Pathway analysis revealed significant alterations in processes important for ‘cell adhesion’ (p<9.3e-13) and ‘extracellular matrix organization’ (p<1.8e-7). Aggrecan (fold change=+0.25, p<1e-7) and osteopontin (fold change=+5.26, p<1e-5) were the first and third top-most differentially regulated genes, indicating a shift away from chondrogenic polarization towards osteogenic polarization. A shift in BMSC polarization was corroborated with differentiation assays: MC1 vs. Ctrl BMSCs had a reduced adipogenic (mean ±sd: -33±13%, p=0.03) and chondrogenic (-31±25%, p=0.18) differentiation capacity (Figure 2). In addition, an increased duplication rate of MC1 vs. Ctrl BMSCs (29.3±1.7 vs. 26.2±1.0 hours, p<0.07) was observed, also indicate a change in phenotype. There were no changes in the expression of surface markers.

Conclusion: These data suggest that MPE-FLIM is a prime technology to investigate fibrotic pathologies and it allows to morphologically study the importance of BMSCs in MC1. The BMSC/adipocyte axis seem to play a pivotal role in the fibrotic pathomechanism. Adipocytes have not been regarded as pathomechanically relevant yet and hence open novel targets for therapeutic approaches.

REFERENCE:


Disclosure of Interests: Stefan Dudli: None declared, Dominik Haenni: None declared, Astrid Juengel: None declared, Michael Betz: None declared, Jose Spiring: None declared, Florian Brunner: None declared, Mazda Farshad: None declared, Oliver Distler Grant/research support from: Prof. Distler received research funding from Actelion, Bayer, Boehringer Ingelheim and Mitsubishi Tanabe to investigate potential treatments of scleroderma and its complications, Consultant for: Prof. Distler has/had consultancy relationship within the last 3 years with A. Menarini, Amgen, Abbvie, GSK, Mepha, MSD, Pfizer and UCB in the field of arthritides and related disorders

**OP0097** CHRONIC PAIN AND SICK LEAVE IN A 21-YEAR FOLLOW UP
Beata Drab1, Katarina Aili2,3,4, Emma Haglund5, Stefan Bergman1,3.

**Background:** Chronic musculoskeletal pain (CMP) is a common cause of disability and impaired quality of life. In Sweden, chronic pain and mental illness are major causes of sick leave. But sick leave itself is also proposed as a risk factor for prolonged sick leave and disability pension.

**Objectives:** To study CMP and sick leave as potential risk factors for long term sick leave or disability pension in a 21 year follow up of a general population cohort.

**Methods:** In a cohort study, with a baseline survey in 1995, 1466 individuals aged 20-67 years were followed for 3 years and 691 for 21 years, or up to the age of 67. CMP (>3 months duration) was reported on a pain mannequin. Sick leave and disability pension were self-reported. Mental health was measured by the mental health (MH) score of the SF-36 health status, and categorized into tertiles (best, medium and worst). CMP, sick leave, and mental health at baseline, were studied as potential predictors for long term sick leave (disability pension or sick leave >3 months) at a 3 and 21 year follow up. Other potential predictors (socioeconomic group, education, and immigrant status) were introduced in multiple regression analyzes but did not add to the results and were removed from the final models, which were controlled for age and sex.

**Results:** CMP and mental health predicted long term sick leave at the 3 year follow up (OR 2.11, p=0.010 and OR 2.11, p=0.001). Mental health (OR 1.92, p=0.046), but not CMP (OR 0.77, p=0.409), was also a predictor at the 21 year follow up. Sick leave >3 months, irrespectively if due to pain or not, predicted long term sick leave both at the 3 and the 21 year follow up (Table). Sick leave for ≤3 months also predicted long term sick leave at both follow ups when due to pain (OR 2.70, p=0.008 and OR 2.78, p=0.012), but not when due to other causes (OR 1.52, p=0.212 and OR 1.17, p=0.060).

**Conclusion:** Sick leave and especially sick leave due to pain predicted long term sick leave up to 21 years later, independently of pain status or mental health at baseline. It is thus important to early identify individuals at risk and minimize sick leave by providing proper rehabilitation.

**Disclosure of Interests:** None declared


**OP0098** SUICIDAL BEHAVIOUR IN FIBROMYALGIA PATIENTS: META-ANALYSIS AND SYSTEMATIC REVIEW OF THE LITERATURE
Mohammad Adawi1,2, Nicola Luigi Bragazzi3,4, Dennis Moganagle5, Abdulla Watad1,2, Howard Amitai1,3.

**Disclosure of Interests:** Mohammad Adawi: None declared, Nicola Luigi Bragazzi: None declared, Dennis Moganagle Consultant for: Lilly, Novartis UCB, Speakers bureau: Lilly, Novartis UCB, Abdulla Watad: None declared, Howard Amital Grant/research support from: Pfizer, AbbVie, Janssen, Consultant for: Pfizer, Merck Sharp & Dohme, Consultant for: Pfizer, Merck Sharp & Dohme, Speakers bureau: Pfizer, Merck Sharp & Dohme, Janssen, Sanofi, Bristol-Myers Squibb, Abbvie, Neopharm, Speakers bureau: Pfizer, Merck Sharp & Dohme, Janssen, Sanofi, Bristol-Myers Squibb, Abbvie, Neopharm

**Disclosure of Interests:** Mohammad Adawi: None declared, Nicola Luigi Bragazzi: None declared, Dennis Moganagle Consultant for: Lilly, Novartis UCB, Speakers bureau: Lilly, Novartis UCB, Abdulla Watad: None declared, Howard Amital Grant/research support from: Pfizer, AbbVie, Janssen, Consultant for: Pfizer, Merck Sharp & Dohme, Consultant for: Pfizer, Merck Sharp & Dohme, Speakers bureau: Pfizer, Merck Sharp & Dohme, Janssen, Sanofi, Bristol-Myers Squibb, Abbvie, Neopharm, Speakers bureau: Pfizer, Merck Sharp & Dohme, Janssen, Sanofi, Bristol-Myers Squibb, Abbvie, Neopharm

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EFFECTIVENESS OF REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION IN PATIENTS WITH FAILED BACK SURGERY SYNDROME

Canan Bursali, Fezya Uru  Okzan, Meryem Yilmaz Kaysin, Nimet Dörtcan.

Background: Failed back surgery syndrome (FBSS) is the term of persistent back and/or leg pain after lumbar surgery (1). Repetitive transcranial magnetic stimulation (rTMS) is a technique that allows non-invasive and relatively painless stimulation of cerebral cortex. It can reduce the experience of chronic pain by using magnetic field to produce small electrical currents in the cortex (2).

Objectives: The aim of this study is to determine the effectiveness of r-TMS treatment on patients with FBSS.

Methods: In this double-blinded, randomized, placebo-controlled trial, 20 patients (aged 34-65 years) clinically diagnosed as FBSS, who had a history of surgery for lumbar disk herniation with persistent back and leg pain. Only patients with no root compression in postoperative magnetic resonance imaging of lumbar spine were included. Patients were randomly assigned to 3 groups: rTMS (n = 10) and sham (n = 10) groups. Participation in each group was balanced with regard to age, sex, history of surgery, and duration of symptoms. The control group received sham rTMS with the same protocol. Patients were assessed before and after the 3rd and 6th sessions, at the end of the treatment and at 2 weeks, 1 month and 3 months after treatment. Visual Analogue Scale (VAS), DN-IV, Oswestry Disability Index (ODI), Beck Depression Inventory (BDI), Pittsburgh Sleep Quality Index (PSQI) were used for evaluation.

Results: There were no statistically significant differences between the groups for age, sex, number of surgery, pain duration, working status and drug usage. Significant improvements were achieved in VAS, ODI, BDI and PSQI scores in rTMS group in comparison to sham group. Both groups displayed improvements in VAS scores while improvement in the sham group was limited to first month. Achieved improvements in r TMS group in terms of VAS, VAS, ODI, BDI and PSQI scores were sustained at third month.

Conclusion: Repetitive transcranial magnetic stimulation might be an effective treatment alternative in patients with FBSS, further studies with larger groups are needed.

REFERENCES:

Disclosure of Interests: None declared

OP0101
COMPARATIVE EFFECTIVENESS OF LAND AND WATER-BASED EXERCISE ON QUALITY OF LIFE OF PATIENTS WITH FIBROMYALGIA: PRELIMINARY FINDINGS FROM THE AL-ÁNDAUS RANDOMISED CONTROLLED TRIAL

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Background: Compelling evidence supports the efficacy of physical exercise in the management of fibromyalgia (FM) (1). Although exercise interventions have typically focused on either land or water-based programs, research comparing the efficacy of both protocols is limited.

Objectives: The aim of this study was to compare the effect of two exercise interventions (land-based and water-based training) on quality of life (QOL) of patients with FM.

Methods: Among the 272 participants initially randomized, a total of 151 (age:50.6 ±7.6 years, 98%women) completed all the assessments with an attendance >70% (land-based n =48, water-based n =42, control n =61). The intervention groups trained 3 non-consecutive days/week (60 minutes per session) during 24 weeks. Each session involved exercises to improve cardiovascular fitness, muscular strength, and flexibility. Physical and mental domains of QOL were assessed...
through the 36-item Short Form Health Survey (SF-36). Participants were evaluated at baseline (pre-test), at the end of the intervention (post-test) and following a detraining period of 12 weeks after the end of the intervention (re-test). Land-based, water-based, and control groups were comparable in sex, sociodemographic characteristics, disease duration, drugs intake, and BMI. Age, tenderness, and baseline outcomes values were used as covariates in the comparisons of the changes from baseline (post-test vs. pre-test and re-test vs. pre-test) between groups.

Results: Post-intervention changes from baseline in QOL dimensions in the land-based exercise group were better for physical role (compared to the control and water-based groups; all, p<0.01), bodily pain, general health, social function, emotional role, mental health, and mental component (compared to the control group; all, p<0.05). Post-intervention changes from baseline in the water-based exercise group were not statistically significant compared to land-based or control groups (p>0.05). After a detraining period of 12 weeks, changes in QOL from baseline in the land-based exercise group were better for physical role, bodily pain (compared to the control and water-based exercise groups; all, p<0.01), physical function and physical component (compared to the water-based exercise group; all, p<0.05). No significant changes were observed in the control group.

Conclusion: A land-based exercise intervention improved FM patients’ QOL, whereas a water-based exercise intervention showed no significant effect. Improvements in the physical role and bodily pain domain of QOL were sustained in a 12-week detraining period. Land-based exercise might be an easily accessible treatment option that improves QOL to a greater extent than water-based exercise for FM patients.

REFERENCE:

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Disclosure of Interests: None declared


OP1003 EFFECTS ON A FRENCH MASS MEDIA CAMPAIGN ON BACK PAIN BELIEFS AND BEHAVIORS

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Background: Low back pain (LBP) in general and chronic LBP specifically is frequent with high impact on both individuals and Society. In 2017, the French national public health insurance (CNAMTS, Caisse Nationale d’Assurance Maladie des Travailleurs Salariés) has decided to launch a countrywide mass media campaign to improve general population (POP) and general practitioners (GPs) beliefs and behaviors about LBP and tend to reduce its impact on health resource use and including sick leaves.

Objectives: To evaluate the impact on population and physician beliefs and behaviors of the nationwide population-based campaign on LBP.

Methods: A campaign was conducted by the CNAMTS with the help of health experts (rheumatologists, rehabilitation specialists, allogists, GP and physiotherapists). It ran between November 2017 and November 2018, using multi media: booklets for POP and GPs available on CNAMTS website, TV and radio spots, large size wall posters hanged in public areas, videos on social networks, publicity articles and a smartphone application. The campaign main messages were: “LBP is not a severe disease” and “rest doesn’t help to heal” with a tagline: “Low back pain? The right treatment is the movement”. The impact of the campaign was assessed by internet surveys conducted by a private polling company (BVA, Brulé, Ville et Associés), in random samples of the two populations (POP and GP). The respondents were selected according to the quota method, which enabled adequate representativeness based on sex, age, region of living and socio-economic status. The pre-test survey was performed on June 2017 and the post-test in May 2018, 6 months after beginning of the campaign. The questions explored different domains: 1) memorization, understanding and perception of the campaign, 2) knowledge and beliefs about LBP, and 3) repercussions on behaviors. Statistical significance at 5% was assessed with student test for means and sd, and chi2 test for categorical variables.

Results: Among the 2000 POP, 92% have already experienced LBP with mean pain intensity of 5.7/10 onVAS. Among the 400 GPs, 74% reported to be consulted for LBP almost every day. 35% of the POP and 74% of GPs saw, read or listened the campaign. Overall, it was well perceived with an average rating of 7.0 and 7.3/10, respectively. POP and GP beliefs and behaviors about LBP are summarized in the table 1. There were statistically significant improvements in beliefs and behaviors related to activity in both populations. GPs are more confidence in preventing chronicization of back pain and declare to prescribe less sick leave superior to 5 days.

Table 1. Evolution in beliefs and behaviors concerning LBP in GPs and POP before and after campaign

<table>
<thead>
<tr>
<th>Questions</th>
<th>% of agreement</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>beliefs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>POP</td>
<td></td>
<td></td>
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<tr>
<td>GPs</td>
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<tr>
<td>behaviors</td>
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<td>POP</td>
<td></td>
<td></td>
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<tr>
<td>GPs</td>
<td></td>
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</tr>
</tbody>
</table>

Conclusion: The French media campaign appears to have significant impact on public and physicians beliefs, mainly related to the message of staying active. An additional campaign focused on employers and occupational therapists is...
**Disclosure of Interests:** Martin Badard: None declared. Marie Hélène Certain: None declared. François Rannou: None declared. Patricia Ribnik: None declared. Xavier Dufour: None declared. Floriane Bailly: None declared. Bruno Fautrel Grant/research support from: AbbVie, Lilly, MSD, Pfizer, Consultant for: AbbVie, Biogen, BMS, Celgene, Janssen, Lilly, Medac, MSD, NORDIC Pharma, Novartis, Pfizer, Roche, Sanofi-Aventis, Sanofi Genzyme, SOBI, UCB, Violante Foltz: None declared. DOI: 10.1136/annrheumdis-2019-eular.5610

**Conclusion:** Those with higher levels of SF MCP-1 and IL-6 at the time of injury had a significantly worse outcome at 2 years. The presence of haemarthrosis, clinical effusion and impairment/pain at the time of injury were also independent predictors of outcome. In contrast, no baseline plasma/serum markers were associated with outcome. Stratifying individuals at high risk of persistent symp- toms after knee injury may enable clinical trials of interventions to prevent or treat PTOA.

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**Background:** Knee injury increases the risk of knee osteoarthritis at least 7 fold. We have shown an immediate inflammatory response to acute knee injury which is measurable both in mouse joint tissues and also in human synovial fluid (SF). **Objectives:** We set out to test whether the measured inflammatory protein response in SF or plasma/serum was associated with knee symptoms at 2 years after knee injury. **Methods:** 150 individuals were recruited within 8 weeks of a significant acute knee injury to the Knee Injury Cohort at the Kennedy (KIOC; REC 10/10H080/39; NCT02667756) from 2011-2014. The primary outcome was the Knee Injury and Osteoarthritis Outcome Score (KOOS)-4 at 2 years (a composite measure of 4 KOOS domains, where 100 is normal knee health). Baseline covariates were sex, age, body mass index (BMI), clinical effusion, SF blood staining, radiographic Kellgren/Lawrence (KL) Grade. 14 SF and 4 plasma/serum biomarkers were defined based on our prior translational studies. Regression models assessed association of biomarkers with 2 year KOOS4, adjusting for significant covariates. Regressions were weighted using multinomial proportions. **Results:** 123/150 (82%) were male, mean age (SD) 27(8) years and BMI 26(4) kg/m2. Mean KOOS4 increased from 38(18) at baseline to 70(18) at 2 years. 64 (43%) had KL 0/1, 24 (16%) KL 2 and 11 (7%) KL 3, 75 (50%) medium/large effusion (43%) had KL 0/1, 24 (16%) KL 2 and 11 (7%) KL 3, 75 (50%) medium/large effusion and 50 (39%) moderate/severe SF blood staining. Medium/large knee effusion (7.2;-13.5,0.9)(P=0.025) and moderate/severe SF blood staining (-10.1;-18.6,1.6)(P=0.02) were significant. Significant biomarkers adjusted for these covariates are shown in Table. MCP-1 and IL-6 were each significantly associated with 2 year KOOS4 independently in the fully adjusted model and in the multivariable model.

<table>
<thead>
<tr>
<th>SF biomarker (pg/ml)</th>
<th>Adjusted simple linear model (by baseline KOOS4)</th>
<th>Fully adjusted model (by baseline KOOS4)</th>
<th>KOOS4, blood staining and effusion</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCP-1</td>
<td>-0.020</td>
<td>-0.00005</td>
<td>0.014</td>
</tr>
<tr>
<td></td>
<td>(-0.029, -0.011)</td>
<td>(-0.027, -0.004)</td>
<td>0.02</td>
</tr>
<tr>
<td>IL-6</td>
<td>0.017</td>
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<td>0.29</td>
</tr>
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<td>(-0.087, -0.067)</td>
<td>(-0.059, -0.017)</td>
<td>0.11</td>
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<tr>
<td>TGFβ</td>
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<td>0.001</td>
<td>0.02</td>
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<tr>
<td></td>
<td>(-0.008, -0.003)</td>
<td>(-0.009, -0.001)</td>
<td>0.02</td>
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<tr>
<td>IL-18</td>
<td>-0.078</td>
<td>0.003</td>
<td>0.75</td>
</tr>
<tr>
<td></td>
<td>(-0.147, -0.008)</td>
<td>(-0.11, 0.08)</td>
<td>0.75</td>
</tr>
</tbody>
</table>
A NOVEL KNOCK-IN MOUSE MODEL OF CAPS THAT DEVELOPS AMYLIODOSIS: THERAPEUTIC EFFICACY OF PROTON PUMP INHIBITORS

REFERENCES:


Table 1. Baseline characteristics

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Gender</th>
<th>Disease duration (months)</th>
<th>Symptom duration (months)</th>
<th>ESR (mm/h)</th>
<th>CRP (mg/L)</th>
<th>PIP (mm)</th>
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</thead>
<tbody>
<tr>
<td>Mean</td>
<td>Male</td>
<td>Median</td>
<td>Median</td>
<td>Mean</td>
<td>Median</td>
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</tr>
<tr>
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<td>35</td>
<td>9</td>
<td>12</td>
<td>28</td>
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<td>2.8</td>
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</table>

Table 2. Association of app use with patient satisfaction and disease management

<table>
<thead>
<tr>
<th>App use</th>
<th>Patient satisfaction</th>
<th>Disease management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>No</td>
<td>5</td>
<td>3</td>
</tr>
</tbody>
</table>

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From the cradle to the grave – what does paediatric disease teach us about adult disease?

REFERENCES:


Disclosure of Interests: Arinna Bertoni: None declared, Sonia Carta: None declared, Chiara Baldovini: None declared, Federica Penco: None declared, Enrica Balza: None declared, Silvia Borghini: None declared, Marco Di Duca: None declared, Emanuela Ognio: None declared, Paolo Nozza: None declared, Francesca Schena: None declared, Patrizia Castellani: None declared, Claudia Pastorino: None declared, Carla Perrone: None declared, Laura Olivi: None declared, Alberto Martini Consultant for: for do not have any conflict of interest to declare since starting from 1 March 2016 I became the Scientific Director of the G. Gaslini Hospital: therefore, my role does not allow me to render private consultantcies resulting in personal income.

I perform consultancy activities on behalf of the Gaslini Institute for the companies listed below:

ABBvie, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, EMD Serono, Janssen, Novartis, Pfizer, R-Pharm.

The money received for these activities is directly transferred to the Gaslini Institute’s bank account. Before March 2016, I was the head of the Pediatric Rheumatology Department at the G. Gaslini Hospital, where the PRINTO Coordinating Centre is located. For the coordination activity of the PRINTO network, the Gaslini Hospital received contributions from the industries listed in this section. This money has been reinvested for the research activities of the hospital in fully independent manners besides any commitment with third parties., Isabella Ceccherini: None declared, Marco Gattorno Grant/research support from: MG has received unrestricted grants from Sobi and Novartis, Sabrina Chiesa: None declared, Fondazione I.R.C.S. Pollicino San Matteo, Centro per lo Studio e la Cura delle Amiloidosi Sistemiche, Pavia, Italy, I.R.C.S. Istituto Giannina Gaslini, Direzione Scientifica, Genova, Italy

Background: Cryopyrin associated periodic syndromes (CAPS) are a group of autoinflammatory diseases linked to gain-of-function mutations in the NLRP3 gene that cause uncontrolled IL-1β secretion. CINCA syndrome is the most severe CAPS disease characterized by central nervous system disabilities with a long-term risk of secondary amyloidosis. Proton pump inhibitors (PPIs), commonly used as inhibitors of gastric acid production, also display anti-inflammatory properties, making them promising drugs in sepsis and in inflammatory disorders.

Objectives: To develop a novel NLRP3 knock-in (KI) mouse model of CAPS to evaluate amyloid deposition and to test alternative therapeutic approaches.

Methods: We generated KI mice by engineering N475K mutation associated with CAPS phenotype into mouse Nlrp3 gene. KI and Wild Type (WT) mice received PPIs or PBS intraperitoneally and were analyzed for survival, inflammation, cytokine secretion, and amyloidosis development. Cytokines secretion from bone marrow derived dendritic cells (BMDCs) and peritoneal macrophages (PMs) was evaluated by ELISA. Hystological analysis of all organs was evaluated by hematoxylin and eosin staining. Amyloid deposition was quantified through Congo Red stain.

Results: Mutant NLRP3 KI mice displayed features that recapitulates the immunological and clinical phenotype of CAPS. These mice had systemic inflammation, with high levels of serum pro-inflammatory cytokines compared to WT controls. Hystological analysis revealed the presence of active and chronic inflammatory cell infiltrates and amyloid deposits in spleen, liver and kidneys. As in CAPS monocytes, BMDCs and PM from KI mice showed a strong increase in IL-1β, IL-8, and IL-1α secretion and decreased levels in interleukin-1 receptor antagonist (IL-1Rα), the naturally occurring IL-1β inhibitor. PPIs treatment of KI mice showed a clear clinical impact with improvement of inflammatory conditions and regression of amyloid deposits. Remarkably, BMDCs and PMs from PPI-treated mice presented reduced secretion of pro-inflammatory cytokines and re-established the levels of IL-1Rα.

Conclusion: NLRP3 KI mice display a CAPS phenotype with many characteristics of autoinflammation, including amyloidosis. The therapeutic effectiveness associated with lack of toxicity indicates that PPIs could represent relevant adjuvants to the anti-IL-1 drugs in IL-1 driven diseases.
HETEROZYGOUS MUTATIONS IN COPA ARE ASSOCIATED WITH ENHANCED TYPE I INTERFERON SIGNALLING

Marie-Louise Frémont1, Alice Legépely1, Carolina Uggens2, Maria José Martín-Nicolás1, Marine Deppi1, Vincent Bonder1, Darsagh Duffy2, Gillian I Rice2, Mary Brennan1, Caroline Thomson1, Shiam Boulisla4, Marie Legendre2, Serge Amselem2, Thierry Molina3, Nadia Nathan3, Yanick Crow1,2, Imagine Institute, Laboratory of Neurogenetics and Neuroinflammation, Paris, France; 1Institute of Genetics and Molecular Medicine, Centre for Genomic and Experimental Medicine, Edinburgh, United Kingdom; 2Institut Pasteur, Immunology of Dendritic Cells, Paris, France; 3Manchester Academic Health Science Centre, Division of Evolution and Genomic Sciences, Manchester, United Kingdom; 4Royal Hospital for Sick Children, Department of Paediatric Rheumatology, Edinburgh, United Kingdom; 5CHU de Lille, Pediatrics Department, Lille, France; 6Trudeau Hospital-APHP and Sorbonne Université, Genetic Department and Inserm UMR S933, Paris, France; 7Necker Hospital- APHP, Pathology Department, Paris, France; 8Rebiere, Trudeau Hospital-APHP and Sorbonne Université, Inserm UMR S933 and Pediatric Pulmonology department and Reference Centre for Rare Lung Diseases, Paris, France

Background: Heterozygous mutations in COPA, encoding coatomer protein subunit alpha, cause an autosomal dominant syndrome associating lung, joint and renal disease, showing some overlap with STING-associated vasculopathy with onset in infancy (SAVI). Mutations were originally described to cause endoplasmic reticulum (ER) stress and priming of a T helper 17 response. More recently, increased transcription of interferon (IFN)-stimulated genes (ISGs) was reported in blood circulating cells of affected individuals. However, the precise pathophysiology of this disease remains unclear.

Objectives: To better decipher the mechanism of COPA syndrome.

Methods: We studied 8 patients from 3 unrelated families, each segregating a heterozygous mutation in COPA. We assessed type I IFN status by IFNα ultra-sensitive digital quantification in plasma, STAT1 phosphorylation and RNA expression of ISGs in whole blood from patients. In vitro assays also were performed in HEK293T and THP-1 cells to study IFN signalling in the context of COPA mutations.

Results: We observed commonalities in the lung pathology between COPA and SAVI, as well as an IFN signature, raised levels of IFNα protein in the serum and phosphorylation of STAT1 in patient T cells. In a cellular model of HEK293T, phosphorylation of IRF3 and increased ISG expression were observed in cells co-transfected with wild type STING and mutant COPA plasmids. In THP-1 cells, short hairpin RNA knockdown of COPA induced IFN signalling that was abrogated in the absence of STING.

Conclusion: Our data suggest that mutations in COPA lead to constitutive activation of type I IFN signalling through STING. Based on these results, one patient has been treated with the JAK/1 inhibitor ruxolitinib for the last 12 months. How COPA interacts with ER-resident STING remains to be investigated.

REFERENCES:

Disclosure of Interests: None declared


THURSDAY, 13 JUNE 2019

Psoriatic arthritis: old and new drugs and how to deal with them?

Christopher T. Ritchlin1, Arthur Kavanaugh2, Joseph F. Merola3, Georg Schett4

1University of Rochester Medical Centre, Rochester, United States of America; 2UC San Diego School of Medicine, La Jolla, United States of America; 3Harvard Medical School, Brigham and Women’s Hospital, Boston, United States of America; 4Friedrich Alexander University Erlangen-Nürnberg, Erlangen, Germany

Background: Psoriatic arthritis (PsA) is a chronic inflammatory disease that affects psoriasis and joints and, as such, is a common comorbidity of psoriasis. PsA can present with an acute or chronic type and can occur at any time during the course of psoriasis.

Objectives: To review the current knowledge on the treatment of PsA and to discuss the role of new drugs in the management of PsA.

Methods: The literature was reviewed using Medline, Embase, and Web of Science databases.

Results: The treatment of PsA is challenging due to its heterogeneity and the presence of comorbidities. conventional synthetic DMARDs (cDMARDs) and biologics are commonly used to treat PsA, and their combination can be effective in some patients. New biological drugs, such as JAK inhibitors and small molecule inhibitors, have shown promise in treating PsA.

Conclusion: The management of PsA is complex and requires a multidisciplinary approach. New drugs, such as JAK inhibitors and small molecule inhibitors, offer new therapeutic options for the treatment of PsA.

Disclosure of Interests: None declared


THURSDAY, 13 JUNE 2019

Results from a 48-week phase 2b randomised bimekizumab in patients with active psA: OVERALL AND TNF-INHIBITOR-NAÏVE POPULATION RESULTS FROM A 48-WEEK PHASE 2B RANDOMISED

Christopher T. Ritchlin1, Arthur Kavanaugh2, Joseph F. Merola3, Georg Schett4

1University of Rochester Medical Centre, Rochester, United States of America; 2UC San Diego School of Medicine, La Jolla, United States of America; 3Harvard Medical School, Brigham and Women’s Hospital, Boston, United States of America; 4Friedrich Alexander University Erlangen-Nürnberg, Erlangen, Germany

Background: Bimekizumab (BKZ) is a humanised monoclonal antibody that potently and selectively neutralises IL-17A and IL-17F, over 48 weeks in patients (pts) with active PsA.

Objectives: The objective of this Phase 2b study (NCT02969525) was to assess the dose response, long-term efficacy and safety of bimekizumab (BKZ), a mAb that selectively and partially neutralises IL-17A and IL-17F, over 48 weeks in patients (pts) with active PsA.

Methods: 206 pts with active PsA, ≥376 swollen joint count, ≥378 tender joint count and CASPAR score ≥3, were randomised (1:1:1:1:1) to receive subcutaneous BKZ 16mg, 160mg, 160mg with 320mg loading dose (160mg [LD]), 320mg or placebo (PBO) Q4W, for 12 weeks (double-blind period). After Week 12, pts receiving PBO or BKZ 16mg were re-randomised (1:1) to BKZ 160mg or 320mg; all other pts continued on their initial dose (dose-blind period). The primary end- point was ACR50 response at Week 12.

Results: 203/206 and 189/206 pts completed the double- and dose-blind periods, respectively. Overall, demographics and baseline disease characteristics were balanced across groups. 19% of pts had prior exposure to TNF inhibitors (TNFi). There was a statistically significant (p<0.05) dose-response at Week 12 for ACR50 response rates. At Week 12, significantly more pts receiving BKZ versus PBO achieved ACR50 (primary endpoint: 16–160mg [LD] doses), ACR20 and PASI90 (in those pts with baseline body surface area ≥3%; 160–320mg doses) (table). ACR20/50/70, PASI75/90/100, MDA and resolution of enthesitis response rates increased between Week 12 and Week 24 in those continuing on their initial BKZ dose; Week 24 responses were maintained through the study; responses were similar across the three highest dose groups at Week 48 (PASI90 analyses were post hoc). Rapid improvements were observed across all response criteria in pts re-allocated to BKZ 160 or 320mg (table). BKZ-treated pts naïve to TNFi achieved ACR20/50 and PASI90/100 at comparable rates to the overall population at Week 12 and 48. There was no apparent relationship between dose and TEAEs. Serious AEs were reported by 9/206 (4.4%) pts up to Week 48 (8/206 [3.9%] patients were receiving BKZ). The most common TEAE up to Week 48 was nasopharyngitis 25/206 (12.1%). Oral candidiasis was reported at Week 48 by 10/206 (4.9%) pts (all cases during BKZ treatment). No deaths, or cases of CIB or MACE were reported.

Conclusion: Dual neutralisation of IL-17A and IL-17F with BKZ provided substantial improvements in both musculoskeletal and skin outcomes; response rates increased after Week 12 (primary analysis) and were sustained from Week 24 to 48, with a safety profile consistent with previous BKZ studies. These data provide further support that neutralising IL-17F in addition to IL-17A with BKZ is a promising therapeutic approach in pts with active PsA.

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Efficacy of Filgotinib vs Placebo in Active Psoriatic Arthritis: Patient-Level Data from Equator, a Randomized, Phase 2 Study

Philip J. Mease1, Dafna D Gladman2, Filip van den Bosch3, Mykola Stanislavchuk4, Anna Ryckiewska-Hanczewska5, Chantal Tasset6, Luc Meuleners6, Robin Besuyeu7, Jingjing Gao8, Laura C Coates9, Filip Hellwell10, Anna Rychlewska-Hanczewska5, Chantal Tasset6, Luc Meuleners6, Robin Besuyeu7, Jingjing Gao8, Laura C Coates9, Filip Hellwell10.

Background: Filgotinib (FIL) is an oral, selective Janus kinase 1 inhibitor in development for the treatment of several inflammatory diseases. In the phase 2 EQUIATOR trial (NCT03101670), FIL was efficacious vs placebo (PBO) in patients with active psoriatic arthritis (PsA), and was well tolerated [1].

Objectives: To evaluate the onset and maintenance of response to FIL vs PBO in EQUIATOR by evaluating patient-level response over time.

Methods: EQUIATOR was a 16-week, multicenter, double-blind study in which patients with active PsA were randomized 1:1 to FIL 200 mg or PBO once daily [1]. Disease activity was assessed at screening, day 1 and weeks 1, 2, 4, 8, 12 and 16, and the primary efficacy endpoint was the proportion of patients achieving 20% American College of Rheumatology (ACR20) response. The onset of response was assessed by calculating the median time to ACR20 response using the Kaplan-Meier method and compared between FIL and PBO using the log-rank test. Maintenance of response was assessed by analysing ACR20 response patterns over time in the FIL and PBO groups.

Results: Of 131 patients randomized (FIL: n=65; PBO: n=66), 124 (95%) completed the study. Demographics and baseline disease characteristics were similar between groups. The onset of response to FIL was early, with a median (95% confidence interval) time to first ACR20 response of 4.07 weeks (2.29, 4.14) in the FIL group compared with 12.29 weeks (12, not reached) in the PBO group (p<0.0001; Figure 1). ACR20 responses were achieved at week 16 in 80.0% (52/65) and 33.3% (22/66) of patients in the FIL and PBO groups, respectively, using the non-responder imputation method, and 86.7% (52/60) and 34.4% (22/64), respectively, using observed cases. The number of patients who presented with a stable ACR20 response (i.e. the response was maintained once initially achieved regardless of the time point at which the patient first became a responder) among those who were responders at week 16 (i.e. the primary endpoint) was higher in the FIL group than in the PBO group (80.8% [42/52] vs 68.2% [15/22]) (Figure 2).

Similar trends were observed for other efficacy endpoints representing various manifestations of PsA.

Conclusion: In general, patients treated with FIL achieved an ACR20 response earlier than those on PBO and these responses appeared to be more stable. In the PBO group, there were more occurrences of the response being lost over time and fewer cases of regaining a lost response.

REFERENCE:

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A RANDOMIZED, PHASE 3, DOUBLE-BLIND TRIAL EXAMINING METHOTREXATE AND ETANERCEPT AS MONOTHERAPY OR IN COMBINATION FOR TREATING PSORIATIC ARTHRITIS: A COMPARISON OF THE COMPOSITE MEASURES USED TO EVALUATE DISEASE ACTIVITY

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Background: Optimal treatment regimens and measuring outcomes in psoriatic arthritis (PsA) remain key areas of research.

Objectives: To examine methotrexate (MTX) and etanercept (ETN) as monotherapy or in combination in a randomized trial and assess the relative performance of PsA-specific composite measures using trial efficacy data.

Methods: Patients with active PsA naïve to biologic drugs (no prior MTX for PsA) were randomized to 3 groups for 48 weeks: ETN 50mg+MTX 20mg weekly (Combo; N=283); ETN 50mg-placebo weekly (ETN-mono; N=284); or MTX 20mg+placebo weekly (MTX-mono; N=284). At week 24, the American College of Rheumatology (ACR20) and Minimal Disease Activity (MDA) responses were the primary and key secondary endpoints, respectively. Other PsA-specific composite measures used for disease activity included the Psoriatic Arthritis Disease Activity Score (PASDAS) and Disease Activity Index for Psoriatic Arthritis (DAPSA).

Results: Baseline characteristics were well balanced in the 3 arms. Mean (SD) age was 48.4 (13.1) years and mean/median PsA duration 3.2/0.6 years. ACR20 and MDA responses at week 24 were significantly greater with ETN-mono vs MTX-mono and Combo vs MTX-mono; ETN-mono and Combo had similar results (Table). PASDAS also showed differences between each ETN-containing arm vs MTX-mono and no difference for ETN-mono vs Combo, whereas study arm differences were not seen with DAPSA. PASDAS had a greater effect size and standardized response vs DAPSA.

Conclusion: In this large randomized, controlled PsA trial, ETN-mono or Combo had greater efficacy than MTX-mono. Combining ETN and MTX did not improve ETN efficacy. Compared with the joint-focused PASDAS, PASDAS captured a wider range of PsA manifestations and performed better in this trial.

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management of pain due to inflammation, less is reported on pain despite inflammation control, with most such reports addressing rheumatoid arthritis (RA).

Objectives: To investigate the prevalence of pain despite inflammation control after start of a first anti-TNF therapy in psoriatic arthritis (PsA) patients and its relation to EULAR treatment response.

To test the feasibility of a network analysis approach to examine associations between clinical variables and mental health symptoms in RA.

Methods: PsA patients starting a first anti-TNF therapy 2004-2010 were identified in the prospective, observational South Swedish Arthritis Group register (n=352, 48% women), with mean age 47 years and mean disease duration 10 years. At anti-TNF start, 63% of patients had ongoing methotrexate and 68% were on any conventional DMARD(s). Based on the patient acceptable symptom state (PASS) 1, unacceptable pain was defined as >40 mm on a Visual Analogue Scale (VAS) of pain (scale 0-100 mm), and concomitant inflammation control (as in earlier RA studies) was captured through CRP<10 mg/L in combination with <1 swollen joint (of 28) 3. Assessments were performed at baseline, 1.5, 3, 6 and 12 months after anti-TNF start. Furthermore, analyses were conducted in relation to EULAR treatment response after 3 months (good, moderate, no response). Differences in pain measures between treatment response groups were estimated by logistic regression.

Results: At start of a first anti-TNF therapy, 84.5% of PsA patients reported unacceptable pain, which declined to 42.9% after 3 months and then remained stable during the rest of the study period, being 39.5% at 12 months (Figure 1A). In contrast, the fraction showing unacceptable pain despite inflammation control was largely unchanged over the study period (24.0% at treatment start, 26.7% at 3 months and 26.2% at 12 months). Unacceptable pain at 3 months was strongly related to EULAR 3-month response (23.7% of good responders vs. 70.8% of non-responders; p<0.001), whereas for unacceptable pain despite inflammation control the relation was less pronounced (19.3% of EULAR good responders vs 37.5% of non-responders, p=0.016). Among EULAR good responders, unacceptable pain despite inflammation control constituted 81% of all unacceptable pain at 3 months (Figure 1B).

Conclusion: A considerable proportion of PsA patients starting their first biological treatment reported unacceptable pain throughout the first treatment year. Among EULAR good responders non-inflammatory pain made up more than 4/5 of this pain load at 3 months, indicating insufficient effects of biologics on a subset of patients with inflammation-independent pain, and strongly warrants alternative treatment strategies in affected patients.

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HISTOLOGICAL AND MOLECULAR PORTRAIT OF THE SYNOVIAL TISSUE IN EARLY TREATMENT-NAIVE PSORIATIC ARTHRITIS IN COMPARISON WITH RHEUMATOID ARTHRITIS

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Background: Psoriatic Arthritis (PsA) and Rheumatoid Arthritis (RA) are autoimmune joint diseases characterised by chronic inflammation of the synovial tissue (ST). It has been previously suggested that PsA-ST has less marked hyperplasia of the synovial lining and fewer infiltrating T/B cells in comparison with RA. However, several confounders such as treatment, disease duration, sampling techniques and predominance of large joints samples may have influenced these findings.

Objectives: To compare the synovial features of PsA/RA at the beginning of the disease process and prior to any treatment for defining their histological/molecular individual characteristics, and to correlate the histological pattern with clinical parameters.

Methods: 183 consecutive treatment-naïve patients with <12 months symptoms and active synovitis of at least one joint were enrolled into the Pathobiology of Early Arthritis Cohort (PEAC) at the Barts Health NHS Trust, and underwent a baseline US-guided synovial biopsy of an inflamed joint. ST inflammatory infiltrate was evaluated by semi-quantitative score (0-4) of the immunostaining for CD68 (macrophages), CD3 (T cells), CD20 (B cells) and CD138 (plasma cells). Patients were classified as: pauci-immune if CD68sublining (SL)<2 and/or CD3/CD20-CD138<1; diffuse-myeloid if CD68SL>2, CD20<2 or CD138>2; lymphoid/myeloid if CD20<2 or CD138>2. RNA sequencing of the ST was performed on 93RA/15PsA patients.

Results: 39/183 patients were diagnosed with PsA (32 polyarticular, 7 oligoarticular) and 144/183 with RA (2010 ACR/EULAR criteria). Age was significantly lower in PsA patients. The comparison of the age-adjusted baseline variables showed: significantly higher number of tender and swollen joints in RA, but no significant differences between ESR, CRP and DAS28; higher US synovial thickening score of the biopsied joint in PsA, but comparable power-doppler. ST was evaluated by semi-quantitative score (0-4) of the immunostaining for CD68 (macrophages), CD3 (T cells), CD20 (B cells) and CD138 (plasma cells). Patients were classified as: pauci-immune if CD68sublining (SL)<2 and/or CD3/CD20-CD138<1; diffuse-myeloid if CD68SL>2, CD20<2 or CD138>2; lymphoid/myeloid if CD20<2 or CD138>2. RNA sequencing of the ST was performed on 93RA/15PsA patients.

Conclusion: The identification of specific histological and molecular signatures characterising early-untreated PsA will help to better understand the disease pathogenesis and explore novel therapeutic targets.

REFERENCE:

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MACHINE LEARNING TOOLS IDENTIFY PATIENT CLUSTERS AND SWOLLEN AND TENDER JOINT CORRELATION PATTERNS IN A LARGE DATABASE FROM THE SECUKINUMAB PSORIATIC ARTHRITIS CLINICAL DEVELOPMENT PROGRAM

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Background: Identifying patient phenotypes using machine-learning (ML) techniques amidst the variability and heterogeneity of the clinical manifestations of psoriatic arthritis (PsA) could be the first critical step towards better understanding of the disease eventually leading to individualized medicine.1

Objectives: To identify distinct clusters of patients with PsA based on patients’ tender joint (TJ) and swollen joint (SJ) counts and correlation patterns among TJ and SJ counts at baseline as captured in the secukinumab FUTURE trials program.

Methods: Pairwise correlations were explored among 76 SJ and 78 TJ measurements of >2,700 patients with PsA across 5 phase III studies with ~425,000 data entries at baseline and were visualized using heatmaps. Due to high correlations between SJs and corresponding TJs, a composite variable “swollen/tender joint count” was constructed for each joint. Hierarchical clustering was then performed on the composite using “1-correlation” as the dissimilarity metric and Ward’s agglomeration method for pairwise grouping of joints. A dendrogram was used to visualize and assess the resulting joint groupings.

Results: The hierarchical clustering algorithm grouped the 78 individual joints into distinct and natural clusters (Figure 1A). At higher level of the dendrogram, the algorithm grouped separately all foot, larger joints (jaws, clavicles, hips, wrists, knees, shoulders, elbows), and hand joints. Cutting the dendrogram at 15 clusters separated all the joints into distinct groups; hand joints (distal and proximal phalanges, metacarpals and thumbs), and foot joints (distal and proximal phalanges, metatarsals and toes). Similar clustering algorithms were explored to identify patient clusters at baseline with distinct swelling and tenderness patterns across the identified joint groups. High correlation between swelling/tenderness of the left and swelling/tenderness of the corresponding right joint was observed across all individual joints (Figure 1B); a high correlation was also observed between swelling and tenderness at all individual joints. More localized patterns showed that there is a gradual decrease in correlation (from highest to lowest) among TJs and SJs in adjacent vs non-adjacent fingers, which is evident from grey-scale patterns (Figure 1C). Specifically, a gradual decrease in correlation between the swelling of 2nd–5th distal interphalangeal joint and the tenderness of the 2nd–5th distal phalanges was noted.

Conclusion: Machine learning methodology confirmed a natural grouping of joints in patients with psoriatic arthritis based on baseline swelling and tenderness and revealed complex correlation patterns. Additional cluster analyses have demonstrated distinct patient clusters across the identified joint groups. Further investigating potential associations of other disease manifestations such as skin and nail involvement to define additional phenotypes may explain differences in disease pathogenesis and treatment outcomes.

REFERENCE:

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Joint erosions visible on ultrasound predict arthritis development in patients with ACPA positive and musculoskeletal pain but no swollen joints

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Objectives: We sought to determine the value of ultrasound (US) to predict arthritis development among ACPA positive patients with musculoskeletal (MSK) pain.

Methods: We prospectively followed 82 ACPA-positive patients with MSK pain but without arthritis upon baseline clinical examination (mean follow-up 68 months, range 23-91). US at baseline assessed joint erosions, synovial hypertrophy in grey scale (GS), and inflammatory activity judged by power Doppler (PD) in 36 small joints in hands and feet. We used a ProFocus system (BK Medical) with pulse repetition frequency 0.8 kHz for PD grading. The US and PD results were blinded to patients and treating rheumatologists during the initial 3 years. US findings among patients were compared to 100 age-matched healthy blood donors.

Results: Significantly more patient joints had synovial hypertrophy (GS score >0) compared to control joints in metacarpophalangeal (MCP) (5.2% vs. 2.5%; p<0.001) and proximal interphalangeal (PIP) joints 2-5 (6.6 vs. 1.5%; p=0.001). In contrast, metatarsophalangeal (MTP) joints 1-5 of the controls were more often scored GS=0 compared to patient joints (49% vs. 24%, p=0.001). Positive PD (>0) occurred significantly more often in patient joints compared to the controls in all joint areas (p<0.05). At patient level, the mean sum score of all investigated joints was higher among patients than controls, regarding GS as well as PD (p<0.001). In Cox regression adjusting for potential confounders (Hazard ratio ≥4.2, 95% CI 1.7-10.4, p=0.002). Out of the 13 erosions detected on US, 4 could be identified on conventional radiographs. Neither GS nor PD findings were significantly associated with arthritis development.

Conclusion: Arthritis-related US findings are more common among patients at increased risk of RA compared to healthy controls, but with site-specific differences. Erosions detected on US predicted arthritis development. Thus, US assessment of erosions among patients is an important tool in early disease identification, prior to the appearance of radiographic changes.
Microstructural changes associated with anti-citrullinated vimentin autoimmunity in RA-at-risk individuals precipitate the onset of rheumatoid arthritis

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Background: Development of rheumatoid arthritis (RA) is characterized by a several years lasting phase of autoimmunity, characterized by the presence of anti-citrullinated vimentin antibodies (AcpA), recognizing citrullinated, carbamylated or acetylated proteins, as well as rheumatoid factor (RF) which precedes the onset of clinical disease (1,2). High resolution peripheral quantitative (HR-pQCT) technique enables the depiction of small cortical changes in peripheral joints (3).

Objectives: To describe microstructural bone lesions in rheumatoid arthritis (RA) at-risk individuals using HR-pQCT technique, their relation to rheumatoid arthritis specific autoimmunity, particularly osteoclast-inducing citrullinated vimentin (cVIM) antibodies and their impact on the later development of RA.

Methods: Cortical micro-channels (CoMics) as well as volumetric cortical and trabecular bone densities were analyzed by high-resolution computed tomography in the hand joints of RA at-risk individuals. Anti-modified protein antibody (AMP) response was profited including reactivities against citrullinated proteins (vimentin, enolase, fibrinogen) as well as carbamylated and acetylated vimentin. All subjects were followed for the development of RA.

Results: RA at-risk subjects (all n=75) with high-level (>1000U) cVIM antibodies showed a broader AMPA response and significantly more severe microstructural changes (higher CoMics, lower cortical and trabecular bone volume) compared to subjects with low cVIM reactivity. High cVIM antibodies and microstructural changes (>15 radial CoMics/joint) were associated with the presence of arthralgia. Furthermore, progression to RA was high in subjects with high cVIM (53%) vs. those with low (22%) or no (5%) antibodies and those with microstructural changes (46%) vs. those without such changes (16%).

Conclusion: cVIM antibodies are associated to microstructural changes in RA at-risk individuals and predict the onset of RA. These data support the concept of structural priming of joints by autoimmunity before the onset of RA.

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Discrete patterns of citrullinated peptide autoantibody reactivities emerge during progression from pre-disease state to diagnosis of rheumatoid arthritis

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Background: Rheumatoid Arthritis (RA) patients with established disease can have autoantibodies reactive to a broad array of citrullinated antigens. Autoantibodies reactive against several citrullinated proteins can develop 10-15 years before the clinical onset of disease.

Objectives: We aimed to identify common patterns of citrullinated peptide reactivities that emerge among subjects during progression from a pre-disease state through diagnosis of RA.

Methods: 500 subjects with RA (based on the ACR/EULAR 2010 criteria) were identified from the Defense Medical Surveillance System. For each subject, up to four serum samples were obtained from the Department of Defense (DoD) serum repository: 1) earliest time point before diagnosis (9.2 ± 2.0 years before, mean ± SD); 1) proximal to (immediately prior to or after) disease diagnosis (127 ± 125 days before diagnosis); plus 2) intermediate time points. A discovery subset of serum samples from 88 RA subjects confirmed to be positive for anti-citrullinated protein antibodies (AcpA) at the diagnosis-proximal time point (>5 U/mL) for cyclical citrullinated peptide (cCP)-II test was assessed for IgG antibodies to 36 antigens (24 citrullinated-peptide antigens among 14 proteins and 12 non-citrullinated antigens among 9 proteins) using a custom LumineX-based assay. Subjects testing above the upper limit of detection for the cCP-II test (300 U/mL) were considered ACPA-high (n=28), with the remainder considered moderate (n=60).

Results: For the group of ACPA-high subjects at the diagnosis-proximal time point, average IgG autoantibody binding to 9 citrullinated peptide antigens (from 7 proteins: clusterin, enolase, fibrinogen A, fibrinogen B, filagrin, fibronectin, vimentin) showed significant increases from the earliest through diagnosis-proximal time points at the population level (FDR<0.05). In ACPA-moderate subjects, IgG levels to only one antigen (citrullinated-fibrinogen) had a nominally significant but small increase (mean ±8%) during this time frame. Significant reactivity to the not-obstructed antigens was not observed. In ACPA-high but not moderate subjects, group averages for a composite score of the 9 citrullinated-peptide antigens increased relative to the earliest time points, with increased average levels observable 6-years before diagnosis that steadily increased as approaching diagnosis age. Patterns of increases in IgG to citrullinated peptides differed among subjects, for both ACPA-high and -moderate groups. In the ACPA-high group, 46% of subjects had >50% increase in a majority (>5) of the 9 citrullinated-peptide antigen set and the remaining had >50% increase for at least 1 of the antigens. In contrast, in the ACPA-moderate group, 56% of subject did not achieve >50% increase for any of the 9 antigens and only 8% of subjects had >50% increase in a majority of the 9-antigen set. The most commonly increased IgG reactivities were for citrullinated -filagrin and -fibrinogen A, with >50% increase in 64% of ACPA-high and 20% of ACPA-moderate subjects.

Conclusion: Novel patterns of citrullinated peptide autoantibody reactivities that begin to emerge on average about 6 years before diagnosis of RA have been identified in samples from the US DoD serum repository. Evaluation of specific anti-citrullinated peptide autoantibodies could potentially provide sensitive, patient-tailored biomarkers to monitor disease trajectories as at-risk individuals progress to clinically-defined RA.


The pre-treatment gut microbiome predicts early response to rheumatoid arthritis therapy

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Background: Early treatment initiation in rheumatoid arthritis (RA) is fundamental to avoid chronic joint destruction and disability. Despite remarkable advances in RA therapeutics, oral methotrexate (MTX) remains the anchor drug and mainstay of treatment worldwide (1,2). However, MTX bioavailability has a wide inter-individual variability and >50% of patients with moderate or severe RA show no or subtherapeutic improvement in their symptoms in response to MTX (1,3). The reasons for these disparities in treatment response remain unclear. Prior studies have shown that the biotransformation of MTX is altered in germ-free and microbiome-
depleted mice (4), prompting us to hypothesize that inter-individual differences in the human gut microbiome could impact drug bioavailability and thus clinical efficacy.

**Objectives:** To determine differences in the microbiome of drug-naïve, new onset RA (NORA) patients that could predict response to MTX therapy.

**Methods:** We performed 16S rRNA gene and shotgun metagenomic sequencing on the baseline gut microbiomes of 27 drug-naïve, NORA patients.

**Results:** Our analysis revealed significant associations between the abundance of gut bacterial taxa and genes including gene families related with purine and methotrexate metabolism. Machine learning techniques were applied to this metagenomic data, resulting in a robust predictive model based on bacterial gene abundance that accurately predicted response to MTX therapy in an independent group of patients. Finally, MTX available levels remaining after ex vivo incubation with distal gut samples from pre-treatment RA patients significantly correlated with the magnitude of future clinical response, suggesting a direct effect of the gut microbiome on MTX bioavailability and response to therapy.

**Conclusion:** Together, these results provide the first step towards predicting response to oral MTX in NORA patients and support the utility of the gut microbiome as a prognostic tool and perhaps even as a target for manipulation in the treatment of rheumatic and autoimmune disease.

**REFERENCES:**


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**Cohort Study (PEAC)**

**Baseline Cellular and Molecular Characteristics of Synovial Tissue and Relation with TNFi Response. Results from the Pathobiology of the Early Arthritis Cohort (PEAC)**

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**Background:** Despite early intervention with disease modifying therapy a high percentage of patients (~30%) fail to respond and require escalation to advanced therapies such as TNFi, with no available biomarkers to predict response. Whether synovial signatures predicting subsequent response to TNFi therapy can be identified at disease onset remains an unanswered question although critical for long term prevention of disease progression and overall health economic impact.

**Objectives:** The aim of this study was to evaluate in a cohort of treatment naïve early RA patients, whether baseline synovial cellular and molecular signatures predict subsequent response or not to anti-TNF therapy.

**Methods:** A total of 186 consecutive DMARD naïve inflammatory arthritis patients (disease duration <1 year) recruited as part of the multicentre PEAC study at Barts Health NHS Trust were evaluated. After 12 months 35 patients commenced therapy with a TNFi (DAS28<5.1), failed 2 x DMARDs as per UK NICE guidelines, EULAR response (DAS28 and DAS improvement from baseline) was calculated 12 months after TNFi was initiated. All patients underwent an US guided baseline synovial biopsy of a clinically active joint along with collection of clinical characteristics. Following H&E staining, sections underwent immunohistochemical staining and semi-quantitative scoring (0-4) to determine the degree of CD20+ B-cells, CD4+ T cells, CD68+ infiltration (I) and sublining (s) macrophage and CD138+ plasma cell infiltration. Sections were categorised into three pathotypes: (i) Fibroid: (CD68≥2 and CD3, CD20, CD138+); (ii) Myeloid: (CD68≥2, CD20<1 and CD3<1) and (iii) Lymphoid: (grade 2-3 CD20+ aggregates, CD20≥2). Synovial gene expression was evaluated with Nanostring and RNA sequencing.

**Results:** 12 months after TNFi was initiated 17/35 (48%) patients responded to therapy (TNFi good EULAR response) and 18/35 (52%) had a moderate or non-response to TNFi. Baseline demographic or US characteristics did not differentiate between the 2 groups. Although we saw no significant differences between groups there was a trend for higher levels of B (CD20+) and T (CD3+) cells, sublining macrophages (CD68+) and plasma cells (CD138+) in the TNFi response group. The cohort was segregated by pathotype and each clinical parameter was compared from baseline to 12months. Interestingly, we observed a significant reduction of levels of CRP, VAS and DAS28 and number of tender and swollen joints in those patients with Lymphoid and Myeloid pathotype (p<0.05), but not in those with Fibroid pathotype (Figure 1). We also evaluated gene expression (using Nanostring and RNA-sequencing) and observed increased expression of genes related to macrophages, plasma cells and B/T regulatory cells expression/activation and/or stimulation at baseline in patients who responded to TNFi.

**Conclusion:** This study demonstrates first evidence of potential novel signatures/biomarkers of TNFi response in treatment naïve early RA. Clinical or US assessment cannot discriminate between responders to TNFi. Lymphoid and Myeloid pathotypes associated with significant falls in clinical outcome. Finally, molecular signatures including differential upregulation of T cells, B cells and macrophage associated genes are associated with good response to TNFi therapy.

**Disclosure of Interests:** Gloria Lliso Ribera: None declared, Frances Humber: None declared, Alessandra Nerviani: None declared, Myles Lewis Grant/research support from: Celgene, Stephen Kelly: None declared, Michele Bombardieri Grant/research support from: Celgene, Katriona Goldmann: None declared, Rebecca Hands: None declared, Chris Buckley Consultant for: Glaxosmithkline, Peter C. Taylor Grant/research support from: Celgene, Galapagos, Eli Lilly, UCB, Consultant for: AbbVie, Galapagos, Gilead, Eli Lilly, Pfizer Inc, Iain B McNees: None declared, Costantino Pitlizitis Grant/research support from: Celgene

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PATIENT CHARACTERISTICS AND INCIDENCE OF SIGNS OF INFLAMMATION IN PATIENTS WITH NEW ONSET OF NON-SPECIFIC MUSCULOSKELETAL SYMPTOMS AND POSITIVE ANTI-CITRULLINATED PEPTIDE POINT-OF-CARE TEST IN GERMANY – THE PANORA TRIAL

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Background: Rheumatoid Arthritis (RA) is a chronic inflammatory joint disease affecting approx. 1% of the adult population of Northern Europe. Strategies for its early detection and diagnosis are of high importance as prompt treatment improves clinical and structural outcome. Formation of autoantibodies against cyclic citrullinated proteins (anti-CCP) are identified to be associated to RA development. Often, patients with initial symptoms are referred to General Practitioners (GP) without access to a sensitive rheumatologic assessment.

Objectives: To evaluate incidence of patients with positivity in anti-CCP rapid-test and signs and symptoms of subclinical and clinical inflammation in a on risk population for RA.

Methods: In this prospective study (PANORA), 980 patients with new onset of nonMSK pain at GP were included in 77 GP sites in Germany. In case of positivity formation of anti-CCP rapid-test at GP. At RD, validation of anti-CCP testing (using ELISA) and a rheumatological examination including ultrasound was performed. Subclinical signs of inflammation defined as increase of microvascularisation were monitored by Fluorescence-optical imaging (FOI). In case of ELISA positivity but missing clinical evidence of RA, patients were monitored every 6 months for a total follow-up of 36 months or until RA-diagnosis.

Results: Data from 980 patients with completion of visits at GP and/or RD was monitored every 6 months for a total follow-up of 36 months or until RA-diagnosis. In the screened population, already 10 patients were diagnosed with RA (1 in the RA-/ELISA- group), thereof one case of a newly detected RA at month 6 of the follow-up period. In the three groups at baseline (figure 1), age was well balanced, the proportion of female patients was highest in the RA-diagnosis cohort (80%) as well as the proportion of patient with current or past smoking-status (40% vs. 22.2% in the RA/ELISA- group).

Conclusion: Here, for the first time data from patients suspect for RA development was monitored using anti-CCP point-of-care test at GP and reported. Within the group re-evaluated at RD due to positive point-of-care test, only 21% were confirmed positive using ELISA testing. In the screened population, already 10 patients were diagnosed as RA at RD including 1 patient in the follow-up period until now. The continuation of the PANORA patients in the follow-up period will give more insights in specific characteristics of the RA-risk population at early stages of the disease when combining serological and imaging markers using ultrasound and FOI.

Figure 1. Study Flow Chart

Disclosure of Interests: Michaela Koehm Grant/research support from: BMS, Pfizer, Janssen, Consultant for: Pfizer, Celgene, Janssen, Speakers bureau: Pfizer, Celgene, Janssen, Ulf Henkemeier Grant/research support from: BMS, Tanja Rossmanith Grant/research support from: BMS, Pfizer, Janssen, Karola Mengenthal: None declared, Juliana J. Petersen: None declared, Harald Burkhardt Grant/research support from: BMS, Pfizer, Janssen, Consultant for: Abb-Vie, BM, Pfizer, Janssen, Roche, Chugai, Speakers bureau: Abb-Vie, BMS, Pfizer, Janssen, Roche, Chugai, Frank Behrens Grant/research support from: Abb-Vie, Pfizer, Roche, Chugai, Propylle, Bioline, Novartis, Consultant for: Abb-Vie, Pfizer, Roche, Chugai, UCB, Bristol-Myers Squibb, Celgene, MSD, Novartis, Biotest, Janssen, Genzyme, Eli Lilly, Speakers bureau: Ad board: Abb-Vie, Pfizer, Chugai, UCB, Bristol-Myers Squibb, Celgene, Novartis, Biotest, Janssen, Genzyme, Eli Lilly.

Conclusion: Data-driven cluster analysis of RA patient characteristics at entry into the BRASS registry identified five distinct patient phenotypes, providing a convenient method to potentially derive novel insights into the multifactorial drivers, commonly co-occurring health conditions, and manifestations of RA. Investigation of longitudinal outcomes in these different clusters in the BRASS registry and validation in an independent dataset is ongoing.

Acknowledgement: Study funding and medical writing support (Matt Lewis, Adephi) provided by Sanofi and Regeneron Pharmaceuticals, Inc.


OP0123

SYMPTOMS IN FIRST DEGREE RELATIVES OF PATIENTS WITH RHEUMATOID ARTHRITIS: EVALUATION OF DATA FROM THE SYMPTOMS IN PERSONS AT RISK OF RHEUMATOID ARTHRITIS QUESTIONNAIRE

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THURSDAY, 13 JUNE 2019

SLE, Sjogren and APS: systemic autoimmunity in the real life

OP0124

DO ALL ANTIPHOSPHOLIPID ANTIBODIES CONFER THE SAME RISK FOR MAJOR ORGAN INVOLVEMENT IN SLE PATIENTS?

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Background: Antiphospholipid antibodies (aPL) have been associated with organ damage and certain features in SLE patients.

Table 1. Participants reporting moderate or severe symptoms by seropositivity status and elevated CRP (N=870)

<table>
<thead>
<tr>
<th>Symptomatic Condition</th>
<th>Seropositive (RF or anti-CCP positive)</th>
<th>Elevated CRP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>Yes %</td>
<td>No%</td>
</tr>
<tr>
<td>Symmetrical joint pain</td>
<td>17.1</td>
<td>27.0</td>
</tr>
<tr>
<td>Small joint</td>
<td>22.8</td>
<td>34.9</td>
</tr>
<tr>
<td>Large joint</td>
<td>31.0</td>
<td>32.6</td>
</tr>
</tbody>
</table>

SPARRA questionnaire. This questionnaire asks about a variety of joint symptoms, other symptoms and severity of joint pain in specific parts of the body, allowing identification of symptomatic, small and large joint pain. We identified subjects with moderate/severe symptoms and rheumatoid distribution (symmetrical, small and large joints). We also stratified these groups by 1) seropositivity (RF or anti-CCP positive) and 2) elevated CRP.

Results: By July 2018, 1866 participants had completed the study questionnaire and provided a blood sample. Of those 870 (47%) returned the SPARRA questionnaire and in this subgroup, 43 (5%) were seropositive and 124 (14%) had elevated CRP. The most frequently reported symptoms were sleep problems (34%), joint pain (18%) and fatigue (17%). The proportion with joint stiffness, symptomatic joint pain or small joint pain was higher in the seropositive and elevated CRP groups. This difference was statistically significant in those with elevated CRP, respresentative differences in proportions (95% CI) of small and symptomatic joint pain were 10.7 (1.9 to 19.5) and 11.5 (3.2 to 19.8) (Table 1).

Conclusion: This is the first time the SPARRA questionnaire has been applied in FDHS of patients with RA. Some of the most prevalent symptoms e.g. sleep problems or fatigue, did not identify patterns suggestive of progression to RA. However, the distribution of joint involvement (symmetrical, small joint pain), was in keeping with RA features. This part of the questionnaire may be useful in identifying individuals most likely to develop RA.
Objectives: To investigate the association between the different aPL and SLE manifestations as well as to elucidate the influence of the load of antibodies.

Methods: Patients from the RELESSER-T registry were included. RELESSER-T is a multicenter, hospital-based registry, with retrospective cross-sectional collection of data adult non-selected patients with SLE attending Spanish rheumatology services from the public national health system.

Results: Out of a total of 3651 SLE patients, 1368 were positive for aPL (44.9% of patients were positive for anticardiolipin (aCL) antibodies, 27.3% for anti-biologic-coprotein I (aB2GPI) and 24% for lupus anticoagulant (LA)). Regarding the load of antibodies, 20.6%, 12.1% and 4.8% were positive for one, two and three antibodies, respectively. The association between the different aPL, the number of positive antibodies and antiphospholipid syndrome related manifestations is showed in Table 1. Overall, all types of aPL were associated with classic APS manifestations, although LA, IgG isotypes, and patients with more than one aPL display a higher risk to develop clinical APS.

Table 1. Association between the different aPL and the number of positive antibodies and APS related Variations

<table>
<thead>
<tr>
<th>Antigen</th>
<th>One antibody</th>
<th>Two antibodies</th>
<th>Three antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td>LA</td>
<td>4.9 (2.96)</td>
<td>4.4 (2.65)</td>
<td>3.5 (1.55)</td>
</tr>
<tr>
<td>aCL IgG</td>
<td>5.5 (3.52)</td>
<td>4.3 (2.44)</td>
<td>2.3 (1.22)</td>
</tr>
<tr>
<td>aCL IgM</td>
<td>5.1 (3.5)</td>
<td>4.3 (2.44)</td>
<td>3.2 (1.32)</td>
</tr>
<tr>
<td>aB2GPI</td>
<td>5.4 (3.5)</td>
<td>4.2 (2.34)</td>
<td>3.1 (1.2)</td>
</tr>
<tr>
<td>APS</td>
<td>5.5 (3.5)</td>
<td>4.4 (2.4)</td>
<td>3.1 (1.3)</td>
</tr>
</tbody>
</table>

Regarding specific lupus manifestations, aPL types showed a significant negative association with cutaneous manifestations. LA and aCL were associated with an increased risk of cardiac, respiratory and neuropsychiatric manifestations (p<0.001). Furthermore, LA was also associated with an increased risk of renal disease (p=0.001), aCL IgG was associated with a higher risk of specific lupus manifestations compared with aCL IgM. Interestingly, aB2GPI IgG were only associated with cardiac, respiratory and neuropsychiatric manifestations (p<0.001). aCL IgG was associated with a higher risk of specific lupus manifestations (p=0.001), as well as the cardiac (p=0.003), and pulmonary manifestations (p=0.001), significantly increased with a higher number of positive antibodies. Inversely, the risk of cutaneous symptoms decreased while the number of positive antibodies increased (OR 0.89, 95% CI 0.82-0.96, p=0.003).

Conclusion: There is a hierarchy for aPL and the risk of APS and lupus manifestations. aCL, and especially LA, confer a higher risk for major organ involvement in SLE patients. IgG isotypes and the load of aPL antibodies increase the risk for clinical APS and major lupus manifestations.

Disclosure of Interests: None declared.

References:


Methods: ESSDAI and ESSPRI scores were collected from patients with a confirmed diagnosis of pSS attending a pSS clinic at a single UK centre over a ten-year time period. Anonymised data from 2009 to 2019 were analysed for patterns of change in the (overall and domain-specific) ESSDAI and ESSPRI scores over time. Time between clinic visits was also plotted against each patient’s ESSDAI and ESSPRI score at each clinic visit to give an idea of real-world fluctuations in these assessment outcomes over a period time in this large group of patients. Baseline characteristics were also analysed to determine predictors in ESSPRI and ESSDAI changes.

Results: 634 patients used the clinic with 467 of them had more than one visit and 297 of them having three or more clinic visits. 32% had an ESSPRI at least 1 point higher at the last compared to the first visit (ESSPRI-worse group). 16% had an ESSPRI at least 1 point lower (ESSPRI-improved group) and 48% had a change of less than 1 in ESSPRI between the first and last visits (ESSPRI-unchanged group). The ESSPRI-worse group had a lower mean initial ESSPRI (4.59), compared to the ESSPRI-unchanged and ESSPRI-improved group (6.27 and 6.29 respectively). There were no significant differences in age, sex and anti-Ro positivity between the three groups; age, percentage female and percentage anti-Ro were 60 years, 89%, 66% (ESSPRI-worse); 60 years; 86%, 60% (ESSPRI-improved); 62 years, 91%, 73% (ESSPRI-unchanged). 16% had an ESSDAI at least 3 points higher at the last visit (ESSDAI-worse group); 19% patients had an ESSDAI at least 3 points lower (ESSDAI-improved); and 62% of patients had a difference of less than 3 in ESSDAI between the first and last visits (ESSDAI-unchanged). The mean ESSDAI at first visit was significantly higher in the ESSDAI-improved group (9.2) compared to the ESSDAI-unchanged and ESSDAI-worse groups (3.1 and 2.4 respectively). There was no difference in age between the 3 ESSDAI groups. The ESSDAI-worse group had more female subjects and less anti-Ro positivity (93% & 54% respectively) compared to the ESSDAI-unchanged group.

Conclusion: ESSPRI and ESSDAI scores did not change significantly over time when looking at an overall cohort level. However, there were significant changes in these outcomes on an individual level. Worsening ESSPRI was associated with lower baseline score whereas improvement in ESSDAI was associated with higher baseline score. Given the lack of proven treatment available for pSS, our data may reflect natural history of the disease course rather than treatment effects.

References:


Disclosure of Interests: None declared.

OP0125

REAL WORLD LONGITUDINAL DATA USING EULAR OUTCOME ASSESSMENT TOOLS FOR PRIMARY SJÖGREN’S SYNDROME (PSS) PATIENTS IN A UK CLINIC

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Background: The EULAR Sjogren’s Syndrome Study Group has developed standardised outcome assessment tools for PSS, which are used in clinical trials and routine clinical assessment. While there has been a growing body of data on the use of these outcome assessment tools, data on their application in routine clinical practice, particularly over time, remains scarce.

Objectives: This paper aims to investigate how EULAR Sjogren’s Syndrome Disease Activity Index (ESSDAI) and EULAR Sjogren’s Syndrome Patient Reported Index (ESSPRI) scores change at multiple timepoints in a large cohort of PSS patients.

Methods: ESSDAI and ESSPRI scores were collected from patients with a confirmed diagnosis of pSS attending a pSS clinic at a single UK centre over a ten-year time period. Anonymised data from 2009 to 2019 were analysed for patterns of change in the overall and domain-specific ESSDAI and ESSPRI scores over time. Time between clinic visits was also plotted against each patient’s ESSDAI and ESSPRI score at each clinic visit to give an idea of real-world fluctuations in these assessment outcomes over a period time in this large group of patients. Baseline characteristics were also analysed to determine predictors in ESSPRI and ESSDAI changes.

Results: 634 patients used the clinic with 467 of them had more than one visit and 297 of them having three or more clinic visits. 32% had an ESSPRI at least 1 point higher at the last compared to the first visit (ESSPRI-worse group). 16% had an ESSPRI at least 1 point lower (ESSPRI-improved group) and 48% had a change of less than 1 in ESSPRI between the first and last visits (ESSPRI-unchanged group). The ESSPRI-worse group had a lower mean initial ESSPRI (4.59), compared to the ESSPRI-unchanged and ESSPRI-improved group (6.27 and 6.29 respectively). There were no significant differences in age, sex and anti-Ro positivity between the three groups; age, percentage female and percentage anti-Ro were 60 years, 89%, 66% (ESSPRI-worse); 60 years; 86%, 60% (ESSPRI-improved); 62 years, 91%, 73% (ESSPRI-unchanged). 16% had an ESSDAI at least 3 points higher at the last visit (ESSDAI-worse group); 19% patients had an ESSDAI at least 3 points lower (ESSDAI-improved); and 62% of patients had a difference of less than 3 in ESSDAI between the first and last visits (ESSDAI-unchanged). The mean ESSDAI at first visit was significantly higher in the ESSDAI-improved group (9.2) compared to the ESSDAI-unchanged and ESSDAI-worse groups (3.1 and 2.4 respectively). There was no difference in age between the 3 ESSDAI groups. The ESSDAI-worse group had more female subjects and less anti-Ro positivity (93% & 54% respectively) compared to the ESSDAI-unchanged group.

Conclusion: ESSPRI and ESSDAI scores did not change significantly over time when looking at an overall cohort level. However, there were significant changes in these outcomes on an individual level. Worsening ESSPRI was associated with lower baseline score whereas improvement in ESSDAI was associated with higher baseline score. Given the lack of proven treatment available for PSS, our data may reflect natural history of the disease course rather than treatment effects.

References:


Disclosure of Interests: None declared.

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Thursday, 13 June 2019

OP0126

LYMPHOMA ARISING AT THE TIME OF DIAGNOSIS OF
PRIMARY SJÖGREN SYNDROME: A HIGHLY-ACTIVE
SYSTEMIC SUBSET OF THE DISEASE

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Gunnel Nordmark27, Hendrika Bootsma28, Hideki Nakamura29,
Roberto Giacomelli30, Valerie Devauchelle-Pensec31, Benedikt Hofauer32,
Michele Bombardieri33, Virginia Fernandes Moça Trevisani34,
Daniel Hammenfors35, Sandra Pasoto36, Tamer A Gheita37, Fabiola Atzeni38,
Jacques Morel39, Cristina Vollenveider40, Sandra Consani-Fernández41,
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Hacettepe Univ, Ankara, Turkey; 15Univ Medical Center, Utrecht, Netherlands;
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Spain; 44Perugia Univ, Perugia, Italy
Objectives: To analyse the phenotype of patients with primary Sjogren syndrome
(SjS) in whom a lymphoproliferative disease is diagnosed concomitantly.
Methods: By January 2019, The Big Data Sjögren Project included 11,420 consecutive patients with primary SjS recruited from 24 countries of the five
continents.
Results: 117 (1%) patients were diagnosed with lymphoma and primary SjS synchronously. Age-gender adjusted multivariate analysis identified the following features associated with lymphoma (OR; CI95%): male gender (4.61; 2.88-7.18),
White ethnicity (3.51; 1.78-7.91), abnormal oral tests (3.4; 1.38-10.88), positive
biopsy (3.2; 1.3-10.17), positive RF (2.27; 1.48-3.53), hypocomplementemia (3.39;
2.06-5.54), and cryoglobulins (4.74; 2.57-8.38). Activity (score > 1) in the constitutional (2.97; 1.86-4.62), glandular (3.11; 2.1-4.57), cutaneous (2.17; 1.28-3.52),
peripheral nerve (2.56; 1.4-4.41) and hematological (2.49; 1.64-3.75) ESSDAI
domains was associated with lymphoma (frequencies summarized in the Figure).

Conclusion: Patients diagnosed concomitantly with primary SjS and lymphoma
have a very specific, highly-active phenotype (men, White, severe oral

Scientific Abstracts
involvement, cryoglobulinemic-related immunological markers, and high systemic
activity).
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OP0127

DISEASE PRESENTATION OF 1,312 CHILDHOODONSET SYSTEMIC LUPUS ERYTHEMATOSUS:
INFLUENCE OF ETHNICITY

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Evaldo Sena14, Ana Julia Moraes15, Ana M. Rolim16, Paulo F. Spelling17, Iloite
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12
Darcy Vargas Hospital, Sao Paulo, Brazil; 13Santa Casa de Sao Paulo, Sao
Paulo, Brazil; 14Lauro Vanderley Hospital, Joao Pessoa, Brazil; 15UFPA, Belem,
Brazil; 16Irma Dulce Hospital, Salvador, Brazil; 17Hospital Evangelico de Curitiba,
Curitiba, Brazil; 18Hospital Criança Conceição, Porto Alegre, Brazil; 19UFPE,
Recife, Brazil; 20UFMS, Campo Grande, Brazil; 21UFBA, Salvador, Brazil;
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University of Brasilia, Brasilia, Brazil; 23UFMG, Belo Horizonte, Brazil; 24PUC
Sorocaba, Sorocaba, Brazil; 25Children’s Institute HC FMUSP, São Paulo, Brazil
Background: To our knowledge the influence of ethnic background in childhoodonset SLE (cSLE) presentation was not evaluated in a large population of Latin
American country.
Objectives: To assess demographic data, clinical manifestations, laboratory
abnormalities and disease activity score in cSLE patients according to ethnic
groups at diagnosis
Methods: This multicenter study included cSLE patients(ACR criteria) followed in
27 Pediatric Rheumatology services of Brazil. Ethnicities were classified in four
groups according to the parents´ and all four grandparents´ self-reported ethnicity.
The statistical analysis was performed using the Bonferroni’s correction
(p<0.0027).
Results: According to ethnic groups, 1,537 cSLE patients were classified in: Caucasian (n=786), African-Latin American(n=526), Asian(n=8) and others/unknown
(n=217). Comparisons between 1,312 African-Latin American and Caucasian


Systemic Lupus Erythematosus Disease Characteristics Associated with the Type I Interferon Gene Signature: Baseline Data of the SLE Prospective Observational Cohort Study (SPOCS)

Edward R. Hammond, Martin Aringer, Laurent Arnaud, Christine Peschken, Jacob Knagenhjelm, Vokhan Banul, Xia Wang, Bamabas Desta, Raj Tummala, David Ginkel, Richard Furie, Eric F. Morand, Gustav Carus, TU Dresden, Dresden, Germany; Service de Rhumatologie, Centre National de Référence Maladie Auto-immune et Systémique Rares (RESO), Université de Strasbourg, Inserm-Urc 5109, Strasbourg, France; Department of Medicine and Community Health Sciences, University of Manitoba, Winnipeg, Manitoba, Canada; AstaZarzeca, Gothenburg, Sweden; AstraZeneca, Cambridge, United Kingdom; Hofstra Northwell School of Medicine, New York, NY, United States of America; Centre for Inflammatory Disease, Monash University, Clayton, VIC, Australia

Background: Despite accumulating data on the role of type I interferons (IFN) in the pathogenesis of SLE, real-world, longitudinal clinical data on the type I IFN gene signature (IFNGS) collected from patients with SLE are limited.

Objectives: This initial analysis of the SLE Prospective Observational Cohort Study (SPOCS; NCT03198875) examined the prevalence of the type I IFN gene signature (high vs low) and its association with baseline SLE disease characteristics in patients with moderately to severely active SLE receiving standard-of-care treatment.

Methods: SPOCS is an international, multicenter, prospective observational cohort study of patients enrolled with moderately to severely active SLE receiving standard-of-care treatment. The profile of patients with a baseline high type I IFN signature was compared with those with a low type I IFN signature.

Results: As of November 15, 2018, a total of 307 patients were enrolled in SPOCS (North America, n=184; Europe, n=123), of whom 96.1% (n=295) were female, with a median age of 46 years (range: 18–88). At study entry, the prevalence of high type I IFN was significantly higher in African-Latin American, whereas malar rash (45% vs. 58%, p<0.0001) was more frequent in Caucasian. The presence of antiphospholipid antibody (23% vs. 12%, p<0.001), low complement levels (58% vs. 41%, p<0.001) and isolated Coombs test (10% vs. 5%, p=0.001) were also significantly higher in the former group.

Conclusion: Our study demonstrated that disease presentation severity of African-Latin American SLE patients is comparable to Caucasian. Mucocutaneous manifestations and autoantibodies profile were the only distinctive features of the former group. The unique mixed background of Brazilian patients probably minimized race diversity spectrum of these patients.


Thermal Regulator's Stabilization and Dynamics of Antiphospholipid Syndrome in Patients Admitted to the Intensive Care Unit with a New Thrombotic Manifestation

Marc Pinetof de Chambournay, Alexis Mathian, Alain Combes, Charles-Edouard Lucy, Zahr Amoura, Registre SAPHIR, Hôpital La Pitié-Salpêtrière, Assistance Publique-Hôpitaux de Paris, Service de médecine interne 2, centre de référence national malade rare lupus systémique et syndrome des anticorps antiphospholipide, institut E3M, Sorbonne Université, Paris, France; Hôpital La Pitié-Salpêtrière, Assistance Publique-Hôpitaux de Paris, Service de médecine intensive-réanimation, institut de cardio-métabolisme et nutrition (ICM), Sorbonne Université, Paris, France

Background: Catastrophic antiphospholipid syndrome (CAPS) is the most severe manifestation of antiphospholipid syndrome (APS), characterized by the simultaneous occurrence of thrombosis in multiple organs.

Objectives: The objectives of this study were to evaluate the distribution and the characteristics of CAPS criteria in APS patients admitted to the intensive care unit (ICU) with acute thrombotic manifestation.

Methods: We conducted a multicentre retrospective study, from January 2000 to September 2016, including all APS patient admitted to 24 French ICUs with any new thrombotic (arterial, venous or microvascular) manifestation.

Results: 134 patients were admitted to the ICU for 152 episodes. The number of patients with definite CAPS, probable CAPS and no CAPS was: 11 (7.2%), 60 (39.5%) and 81 (53.5%) respectively. We compared patients with definite/probable CAPS (group 1, n=11) and no CAPS (group 2, n=81).

Conclusion: Differences were found in the proportion of APS-involved organs between the two groups. The number of patients with definite CAPS was 11 (7.2%), 60 (39.5%) and 81 (53.5%) respectively. We compared patients with definite/probable CAPS (group 1, n=11) and no CAPS (group 2, n=81).

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and Charlson comorbidity score were not different between group 1 and 2. The median [IQR25-75] number of organs involved (4 [3-4] vs 2 [1-3], p=0.0001) and the frequency of proven microvascular thrombosis (23 (37.7%) vs 8 (11%), p=0.0001) were higher in group 1. Treatment and outcomes are reported in Table 2. Aside plasmapheresis there was no difference in terms of APS treatments between both groups. The in-hospital mortality was not different between patient with definite/probable CAPS and no CAPS (23% vs 28.8% respectively, p=0.4). The Kaplan-Meier curve of cumulative probability of survival retrieve no difference of survival between both groups (log-rank test p=0.5, Figure 1).

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Every patients’ last episode n=134</th>
<th>Group 1 n=61</th>
<th>Group 2 n=73</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>96/134 (71.6)</td>
<td>38 (62.3)</td>
<td>58 (79.5)</td>
<td>0.03</td>
</tr>
<tr>
<td>Age, years</td>
<td>46.0±15.1</td>
<td>47.5±13.9</td>
<td>44.7±16.1</td>
<td>0.3</td>
</tr>
<tr>
<td>Venous APS</td>
<td>93 (69.4)</td>
<td>46 (75.4)</td>
<td>47 (64.4)</td>
<td>0.2</td>
</tr>
<tr>
<td>Arterial APS</td>
<td>61 (45.5)</td>
<td>28 (45.9)</td>
<td>33 (45.2)</td>
<td>0.9</td>
</tr>
<tr>
<td>Triple positivity</td>
<td>71 (53.0)</td>
<td>31 (50.8)</td>
<td>40 (54.8)</td>
<td>0.6</td>
</tr>
<tr>
<td>Defined APS</td>
<td>123 (91.8)</td>
<td>57 (93.4)</td>
<td>66 (90.4)</td>
<td>0.8</td>
</tr>
<tr>
<td>SLE</td>
<td>46 (34.3)</td>
<td>17 (27.9)</td>
<td>29 (39.7)</td>
<td>0.1</td>
</tr>
<tr>
<td>Organ involved</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kidney</td>
<td>77 (57.5)</td>
<td>46 (75.4)</td>
<td>31 (42.5)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Central nervous system</td>
<td>49 (36.6)</td>
<td>28 (45.9)</td>
<td>21 (28.8)</td>
<td>0.04</td>
</tr>
<tr>
<td>Adrenal gland</td>
<td>30 (22.4)</td>
<td>22 (36.1)</td>
<td>7 (9.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Gastrintestinal tract</td>
<td>15 (11.2)</td>
<td>11 (18.0)</td>
<td>4 (5.5)</td>
<td>0.02</td>
</tr>
<tr>
<td>Anemia</td>
<td>126 (94.0)</td>
<td>57 (93.4)</td>
<td>69 (94.5)</td>
<td>0.8</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>118 (88.1)</td>
<td>56 (81.8)</td>
<td>62 (84.9)</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th>Variable</th>
<th>Every patients’ last episode n=134</th>
<th>Group 1 n=61</th>
<th>Group 2 n=73</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specific APS treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anticoagulant</td>
<td>128 (95.5)</td>
<td>58 (95.1)</td>
<td>70 (95.9)</td>
<td>0.8</td>
</tr>
<tr>
<td>Antiplaquette therapy</td>
<td>36 (26.9)</td>
<td>18 (29.5)</td>
<td>18 (24.7)</td>
<td>0.5</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>108 (80.6)</td>
<td>51 (83.6)</td>
<td>57 (78.1)</td>
<td>0.4</td>
</tr>
<tr>
<td>Mg</td>
<td>46 (34.3)</td>
<td>19 (31.1)</td>
<td>27 (37)</td>
<td>0.5</td>
</tr>
<tr>
<td>Plasmapheresis</td>
<td>50 (37.3)</td>
<td>29 (47.5)</td>
<td>21 (28.8)</td>
<td>0.02</td>
</tr>
<tr>
<td>Rituximab</td>
<td>18 (13.4)</td>
<td>11 (18.0)</td>
<td>7 (9.6)</td>
<td>0.1</td>
</tr>
<tr>
<td>Triple therapy</td>
<td>75 (56.0)</td>
<td>38 (62.3)</td>
<td>37 (50.7)</td>
<td>0.2</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In-ICU mortality</td>
<td>27 (20.1)</td>
<td>12 (19.7)</td>
<td>15 (20.5)</td>
<td>0.9</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>35 (26.1)</td>
<td>14 (23.0)</td>
<td>21 (28.8)</td>
<td>0.4</td>
</tr>
</tbody>
</table>

Figure 1

Conclusion: In this study, CAPS criteria were not associated with mortality in APS patients admitted to the ICU with new thrombotic manifestations. Further studies are needed to evaluate the accuracy of CAPS criteria in this population. Disclosure: None declared DOI: 10.1136/annrheumdis-2019-eular.5130

PREMATURE OVARIAN FAILURE IN PATIENTS AFFECTED BY SYSTEMIC LUPUS ERYTHEMATOSUS: A CROSS-SECTIONAL CASE CONTROL STUDY

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Background: Women suffering from autoimmune diseases, such as Systemic Lupus Erythematosus (SLE), could develop menopause at a younger age in comparison with healthy population. In particular, a higher frequency of abnormal ovarian function has been described in SLE cohorts1-4. The presence of a cause-effect link between the disease and such modifications remains poorly understood. The role of disease activity and chronic damage, combined with the intake of some drugs, such as cyclophosphamide (CYC), has been suggested5.

Objectives: We evaluated the age at natural menopause and the prevalence of premature ovarian failure (POF) in a monocentric Caucasian SLE cohort. Additionally, we analyzed the possible association with the disease features.

Methods: We performed a cross-sectional case-control study, enrolling consecutive SLE women and reporting their clinical and laboratory data. As control group (healthy controls - HC), women without autoimmune diseases were enrolled. By using an interview, gynecological characteristics were investigated in patients and controls: in particular, we registered age at menarche, occurrence and age of menopause, history of hysterectomy. Natural menopause was defined as the absence of menses for at least 12 months in women aged >40 years and POF as amenorrhea of at least 12 months in women <40 years.

Results: We enrolled 196 Caucasian women with SLE (median age 47.0 years, IQR: 16.7; median disease duration 132 months, IQR: 180) and 90 HC (median age 49.9 years, IQR: 15.0). Ninety-four SLE patients (48.0%) and 26 HC (23.4%) referred a condition of menopause: the median age at occurrence was significantly lower in SLE than HC (47 years, IQR: 8.0 versus 50.5 years, IQR: 4; P=0.0001). Among the SLE patients, a natural menopause was observed in 70 subjects (74.4%), surgical in 7 (7.4%), iatrogenic in 17 (18.1%). In particular, 13 (13.8%) SLE patients referred the occurrence of menopause after CYC exposure. Excluding SLE patients with surgical menopause, we registered POF in 16 patients (17%); this prevalence was significantly higher in comparison with HC group, in which none of subjects experienced POF (P=0.0001). The comparison between SLE patients developing POF and those with natural menopause history demonstrated a significant higher prevalence of anti-Sm (31.2% versus 10.2%; P=0.0004), anti-RNP (25.0% versus 12.8%; P=0.02), anti-cardiolipin (aCL) IgG/ IgM (50.0% versus 26.9%; P=0.0008) and lupus anticoagulant (37.5% versus 17.9%; P=0.002). As expected, a significant more frequent CYC treatment was identified in patients developing POF (56.0% versus 11.0%; P=0.0001). Moreover, POF subjects showed a significant more frequent history of treatment with azathioprine (62.5% versus 30.7%; P=0.0001), mycophenolate mofetil (50% versus 20.5%; P=0.0001) and cyclosporine A (37.5% versus 19.2%; P=0.007). No significant differences were found in terms of clinical manifestations and mean SLICC/ACR damage index (SDI).

Conclusion: In the present study, we observed a significantly lower age at menopause in SLE patients in comparison with HC; in addition, a significantly higher frequency of POF was observed. POF was associated with a more active disease, in terms of autoantibodies prevalence and use of immunosuppressant drugs. Finally, for the first time, it was found an association between POF and antiphospholipid positivity, suggesting a possible role of these antibodies, in particular aCL, in POF development.

REFERENCES:

Disclosure of Interests: Valeria Orefice: None declared, Fulvia Ceccarelli: None declared, Giuseppina Pirrone: None declared, Carmelo Prione: None declared, Carlo Pericorne Speakers bureau: BMS; Lilly, Celgene, Sanofi, Simona Truglia: None declared, Francesca Miranda: None declared, Francesca Spinelli: None declared, Paola Galoppi: None declared, Cristiano Alessandri: None declared, Guido Valesini: None declared, Fabrizio Conti: None declared. DOI: 10.1136/annrheumdis-2019-eular.7028
Diagnostics and imaging procedures

HOW ACCURATE IS PHYSICAL JOINT EXAMINATION OF THE MTP-JOINTS, AND WHAT CAN WE LEARN FROM ADDITIONAL MAGNETIC RESONANCE IMAGING ON FOREFOOT INVOLVEMENT IN EARLY ARTHRITIS?

Yousra Dakkak, Aleid Boer, Monique Reijnierse, Annette van der Helm-van Mil.

Leiden, Netherlands; Leiden University Medical Center (LUMC), Radiology, Leiden, Netherlands; Erasmus University Medical Center, Rheumatology, Rotterdam, Netherlands

Background: Magnetic resonance imaging (MRI) is known to be more sensitive than physical examination in detecting inflammation, and has predominantly been studied in metacarpophalangeal (MCP) and wrist-joints. Data on the concordance and discordance of physical examination and MRI-detected inflammation of metatarsophalangeal (MTP) joints is scarce, which is surprising as physical examination of these joints is generally considered more challenging than MCP-joints.

Objectives: We aimed to study the concordance and discordance of arthritis upon physical examination with MRI-detected inflammation of MTP-joints. Analyses on MCP-joints were included for comparison.

Methods: 1764 MTP (2-5) joints and 1764 MCP (2-5) joints of 441 consecutive patients presenting with early inflammatory arthritis (36% RA, 64% other inflammatory arthritides) underwent physical examination (PE) of joint swelling and 1.5T contrast-enhanced MRI of unilateral MCP- and MTP-joints. MRI-detected synovitis and bone marrow oedema were scored according to the RA MRI score (RAMRIS), and tenosynovitis according to Haavardsholm by two experienced readers (scores ranged 0-3). Analyses were done on joint level and joints were grouped as PE+MRI, PE–MRI+, PE–MRI and PE–MRI+. MRI positivity required the presence of the same MRI-inflammatory feature on joint level that was scored by both readers; ≥1. In addition, to be classified as PE+MRI, the joints required to have clinical swelling as objectified by two independent observers. After categorisation, the MRIs of the joints that were PE+MRI– were further studied by two other, independent observers among whom an experienced musculoskeletal radiologist, to investigate the presence of contrast-enhancement that was not scored according to RAMRIS guidelines.

Results: Physical examination of joints and MRI were concordant in 79% of MTP-joints (6% PE+MRI+, 74% PE–MRI–). For the MCP-joints this was 71% (15% and 56% respectively). Next discordance was studied. Subclinical joint inflammation (PE–MRI+) was present in 14% (n=248) of MTP-joints. This was less frequent than in MCP-joints, where subclinical inflammation was present in 27% (n=465, p<0.001). Discordance in the opposite direction (PE+MRI–) was present in 5% of MTP-joints (n=78). This was observed more frequent than in other inflammatory arthritides (58% vs 26%, p<0.005). At the MCPs no extra-articular inflammation was found.

Conclusion: Joint examination and MRI were mostly concordant in MTP- and MCP-joints. In MTP-joints MRI-detected subclinical joint inflammation was infrequent (14%), especially when compared to MCP-joints (27%). Clinical joint swelling without MRI-detected joint inflammation according to RAMRIS was also infrequent (5% of MTP-joints) and in part caused by extra-articular inflammation that can be detected by further detailed imaging studies. Further detailed imaging studies are needed to determine if extra-articular inflammation at the level of MTP-joints, with or without concomitant intra-articular inflammation, is a novel finding that is characteristic for early RA.

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THURSDAY, 13 JUNE 2019

ONE-YEAR PROGRESSION OF EROSI VE DISEASE EVALUATED WITH HIGH-RESOLUTION PERIPHERAL QUANTITATIVE COMPUTED TOMOGRAPHY IN PATIENTS WITH ANTI-CITRULLINATED PEPTIDE ANTIBODIES AND ARTHRALGIA

Kresten Kragan Keller, Jesper Skovhus Thomsen, Kristian Stengaard-Pedersen, Josefine Therkildsen, Andreas Wiggers Nielsen, Berit Schiøttz-Christensen, Lone Svendsen, Merete Graaakjaer, Peter Molsgaard Petersen, Barbara Unge, Garen Gel Kjekshavn, Bente Langhild, Ellen Margrethe Haage.

Aarhus University Hospital, Department of Rheumatology, Aarhus, Denmark; Silkeborg Regional Hospital, Diagnostic Centre, Silkeborg, Denmark; Aarhus University, Department of Biomedicine, Aarhus, Denmark; Aarhus University, Department of Clinical Medicine, Aarhus, Denmark; Spine Center of Southern Denmark, Midoe, Denmark; Private Rheumatology Practice, Skanderborg, Denmark; Clinic of Rheumatology, Aarhus, Denmark; Randers Regional Hospital, Department of Internal Medicine, Randers, Denmark; Horsens Regional Hospital, Horsens, Denmark; Aarhus University Hospital, Department of Endocrinology, Aarhus, Denmark.

Background: Bone erosions are common at diagnosis of rheumatoid arthritis (RA). However, bone erosions in predilacal RA (pre-RA) are not well described, and have not been studied prospectively.

High resolution peripheral quantitative computed tomography (HR-pQCT) has a spatial resolution of 82 μm and may therefore be ideal to detect bone erosions.

Objectives: To evaluate erosive progression with HR-pQCT in anti-citrullinated peptide antibody (ACPA) positive patients with arthralgia compared with healthy subjects.

Disclosure of Interests: None declared

Methods: Patients were recruited by specialists in rheumatology at hospital clinics and in private practice, and healthy controls were recruited from a website for research subjects. Patients with arthritis, ACPA and no rheumatic disease, and controls without arthritis, ACPA, or rheumatic disease were included. Medical history, ACPA, clinical examination and ultrasound of symptomatic joints were performed in all patients and controls. A 2.7-mm-long volume of interest in the 2nd and 3rd MCP joint of the right hand was HR-pQCT scanned at a spatial resolution of 92 μm at baseline and after one year. Cortical and trabecular bone structure were evaluated in a 12.9-mm-long volume of interest proximal to the MCP head using the provided scanner software. Erosions were defined as cortical breaks in two consecutive slices, in two planes, non-linear in shape, and with loss of underlying trabecular structure. Number, depth, width, and volume of erosions were measured using the Osiris DicomViewintra. Intra observer agreement for erosion was evaluated with Cohens Kappa and coefficient of variance (CV). Values are median (interquartile range).

Results: Twenty-two patients (aged 53(36-63) years) and 23 controls (aged 48 (42-57) years) were evaluated. Ten patients were diagnosed with RA after 86 (24-200) days. There was a significant increase in the number of patients with erosions during follow-up in the patient group (4 vs. 10, p=0.031), but not in the control group (1 vs. 4, p=0.083). In addition, at follow-up more erosions per individual were demonstrated in patients compared to controls (p=0.031).

The increase in average and total volume of erosions from baseline to follow-up was larger in patients compared with controls (Fig. 1) (p=0.031 and p=0.027). At follow-up average and total volume of erosions in patients were larger in patients compared with controls (p<0.001 and p=0.045). Percent change in bone density, cortical, as well as trabecular parameters did not differ between patients and controls. Agreement was 95% equivalent to a kappa of 0.89 for erosions. CV for width, depth, and volume of erosions were 8%, 23%, and 39%.

Conclusion: Progression of erosive disease in ACPA positive patients with arthritis using HR-pQCT is reported for the first time. The results highlight that an even earlier diagnosis of RA is crucial to prevent erosive disease.

Disclosure of Interests: Kresten Krarup Keller Speakers bureau: Have received speaking fee from Pfizer, Jesper Skovhus Thomsen: None declared, Kristian Strøngaard-Pedersen: None declared, Josephine Therfeldt: None declared, Andreas Wiggers Nielsen: None declared, Berit Schiøttz-Christensen: None declared, Lone Svendsen: None declared, Merete Graaækjær: None declared, Peter Mosborg Petersen: None declared, Barbara Unger: None declared, Gørn Geil Kjær: None declared, Bentie Langdahl: None declared, Ellen Margrethe Hauge Grant/research support from: Have received grants from Roche and Novartis, outside the submitted work., Speakers bureau: Pfizer, UCB, outside the submitted work.


ULTRASOUND IN THE MANAGEMENT OF EARLY RHEUMATOID ARTHRITIS: MRI OUTCOME DATA FROM THE ARCTIC RANDOMIZED CONTROLLED STRATEGY TRIAL

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Background: It has been debated whether treatment outcomes in early RA would be improved by targeting imaging remission, assessed by ultrasound or MRI, in addition to clinical remission. The primary analyses of the ARCTIC and TaSER trials (1, 2) did not show a beneficial effect of adding structured ultrasound assessment to a treat-to-target tight control strategy. However, both studies reported a trend toward less radiographic progression in the ultrasound arm.

Objectives: We aimed to investigate whether management of early RA by a tight control strategy incorporating ultrasound information in treatment decision-making would lead to improvement in MRI remission or less structural damage, compared to a conventional tight control strategy.

Methods: The ARCTIC trial was a 24-month RCT with inclusion criteria age 18-75 years, fulfillment of ACR/EULAR criteria for RA, DAS28-CRP < 2 years from first patient reported swollen joint, and indication for DMARD treatment. Patients were randomized to an ultrasound tight control strategy targeting DAS < 1.6, no swollen joints and no power-Doppler signal in any joint, or a conventional strategy targeting DAS < 1.6 and no swollen joints. Patients in both arms were treated by the same treat-to-target drug escalation algorithm starting with MTX, then triple combination therapy MTX/SSZ/HCQ, then biologic DMARD. In the ultrasound arm, treatment was started up if indicated by the ultrasound score, overruling the DAS and swollen joint count. MRI of dominant wrist and hand was performed at 6 times and scored in chronological order by a reader blinded to study arm and clinical data. MRI acquisitions and scoring were done according to the RAMRIS (3) recommendations. Of the 230 patients in ARCTIC, 218 (ultrasound n=116, conventional n=102) had MRI at baseline and ≥1 follow-up visit, and were included in the analyses. RAMRIS synovitis, tenosynovitis and bone marrow edema scores were summarized to a combined inflammation score, erosions and joint space narrowing to a combined damage score. Mean change from baseline to each follow-up was estimated by a linear mixed model adjusted for baseline score, age, gender, center and anti-CCP status. The mean combined MRI inflammation score decreased during the first year (1-year change in ultrasound arm –10.8 (95% CI: –12.0 to –9.6), conventional arm –10.3 (95% CI: –11.5 to –9.0), p=0.56), and maintained at the same level throughout the 2nd year. There were no significant differences in changes from baseline to the study arms at any time (figure 1a). The mean combined MRI damage score showed a small increase over time, without any significant differences between study arms (figure 1b).

Conclusion: A light control strategy incorporating ultrasound information in treatment decisions did not lead to improved MRI remission or less structural damage, compared to a conventional tight control strategy. The findings support the conclusion of the ARCTIC trial that systematic use of ultrasound does not provide added value in the follow-up of patients with early RA treated according to current recommendations.

REFERENCES:

Disclosure of Interests: Ulf Sundin: None declared, Anna-Birgitte Aga Consultant for: UCB, AbbVie, and Pfizer, Paid instructor for: UCB, Øivind Skare: None declared, Lena B Norberg: None declared, Till Uhlig Consultant for: Grünerntal, Novartis, Speakers bureau: Grünerntal, Novartis, Hilde Berner Hammer Grant/research support from: AbbVie, Pfizer and Roche, Paid instructor for: AbbVie, Pfizer, UCB, Novartis, Roche, Speakers bureau: AbbVie, Pfizer, UCB, Novartis, Roche, Désirée van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingehelm, Celgene, Daiichi, Eli-Lilly, Galagapos, Gilead, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, Union Chimique Belge, Tore K. Kvien Grant/research support from: AbbVie, BMS, MSD, Pfizer, Roche and UCB.; Consultant for: AbbVie, Biogen, BMS, Boehringer Ingehelm, Celgene, Celltrion, Eli Lilly, Hospira, Merck-Serono, MSD, Novartis, Oktal, Orion Pharma, Pfizer, Roche, Sandoz, Sanofi, Mylan and UCB, Speakers bureau: AbbVie, Biogen, BMS, Boehringer Ingehelm, Celgene, Celltrion, Eli Lilly, Hospira, Merck-Serono, MSD, Novartis, Oktal, Orion Pharma, Pfizer, Roche, Sandoz, Sanofi and UCB, Siril Lillegraven: None declared, Espen Haavardsholm Grant/research support from: Pfizer, UCB, Roche, MSD, and AbbV, Consultant for: Pfizer, Paid instructor for: Pfizer, Speakers bureau: Pfizer, UCB, Roche, and AbbVie

Background: Whole body MRI (WBMRI) is a new promising tool for assessing joint inflammation in rheumatoid arthritis (RA) patients on joint and patient level.

Objectives: To evaluate the agreement between US, WBMRI and clinical assessment of joint inflammation in rheumatoid arthritis (RA) patients on joint and patient level.

Methods: US, WBMRI and clinical assessment for tender joints (TJ) and swollen joints (SwJ) were performed in 19 RA patients (90% Women, median age 55 (26-73), diseases duration 5.5 years (1-42), SwJ(28) 5 (1-13), TJ(28) 7 (2-24) and SJC(28) 15 (0-52). Whole body MRI (WBMRI) was performed mono-parametrically (slice thickness 3 mm) and separately on the right and left side. For the wrist and hand, an additional slice thickness of 1.5 mm was used. In total 382 joints were evaluated on WBMRI. Based on the knee evaluation of WBMRI, the whole body was divided into 26 regions: 10 upper limbs, 6 lower limbs, and 2 trunk regions. Joints with osteitis (WBMRI excluding osteitis) were considered as osteitis only. Agreement was assessed between the different methods.

Results: When considering joint inflammation by WBMRI as synovitis and/or osteitis, US28 for synovitis and WBMRI26 for WBMRI - same 28 joints except elbows (due to poor image quality). The max score of a joint in US and WBMRI including osteitis was 2, while WBMRI excluding osteitis was 1. The agreement between the clinical joint assessment, US and WBMRI for joint inflammation was calculated with Cohen’s kappa (κ). The correlations between US28, WBMRI26 and DAS28-CRP were calculated by Spearman correlation coefficient (ρ).

Conclusion: US and WBMRI sum scores of joint inflammation showed good correlation. Agreement at joint level was variable.

Disclosure of Interests: none declared.

REFERENCE:

Acknowledgement: This research was supported by the Basic Science Research Programs through the National Research Foundation of Korea (NRF) funded by the Ministry of Education, Science, and Technology.
OPTIMIZING SUBJECT SELECTION IN KNEE OSTEOARTHRITIS CLINICAL TRIALS BY RADIOGRAPHIC JOINT SPACE WIDTH: POST-HOC CLINICAL RESPONSE ANALYSIS FROM A PHASE 2B TRIAL OF WNT PATHWAY INHIBITOR, SM04690

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Background: Knee osteoarthritis (OA) trial radiographic inclusion criteria usually comprises Kellgren-Lawrence (KL) grading, which mixes features such as osteophytes and joint space narrowing and leads to study population heterogeneity. Selecting subjects with baseline medial joint space width (mJSW) 2-4 mm has been shown to reduce heterogeneity and improve responsiveness to radiographic change in comparison to broader knee OA populations.1,2 However, effects of baseline mJSW on symptom responsiveness are unknown.

Objectives: To evaluate the impact of baseline mJSW 2-4 mm on patient-reported outcomes (PROs) as measured by effect size in a 24-week phase 2b trial of SM04690, a Wnt pathway inhibitor in development as a potential disease-modifying OA drug (DMOAD).

Methods: Knee OA subjects with KL grades 2-3 and Pain Numerical Rating Scale (NRS, 0-10) ≥4 and ≤8 in the target knee and <4 in the contralateral knee received a single IA 2 mL SM04690 injection (0.03, 0.07, 0.15, 0.23 mg), vehicle (NRS, 0-10)/C21

Knee OA subjects with KL grades 2-3 and Pain Numerical Rating Scale (NRS, 0-10) ≥4 and ≤8 in the target knee and <4 in the contralateral knee received a single IA 2 mL SM04690 injection (0.03, 0.07, 0.15, 0.23 mg), vehicle placebo (PBO), or sham (dry needle) in the target knee at baseline. PRO 24-week endpoints included change from baseline in weekly average of daily OA target knee pain by NRS, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain [0-100], WOMAC Physical Function [0-100], and Patient Global Assessment (PigA) [0-100]. Primary results are presented elsewhere3. A post-hoc completer analysis of subject results with baseline mJSW 2-4 mm is reported.

Results: 635 subjects (91.4%) completed the study (mean age 59.0 [±8.5] years, 63.5% female). In both full analysis set (FAS, all dosed subjects) and mJSW 2-4 mm subjects, significant improvements compared to PBO (P<0.05) were seen in pain NRS, WOMAC Pain, WOMAC Function, and PigA for 0.07 mg and 0.23 mg SM04690 dose groups at Week 12 (Figure 1). The effect sizes were improved in the mJSW 2-4 mm group in comparison to FAS for most doses at weeks 12 and 24.

Conclusions: In this post-hoc analysis of SM04690-treated knee OA subjects, those with baseline mJSW 2-4 mm showed increased PRO effect sizes compared to those in the FAS. Previous data also demonstrated SM04690-treated subjects with mJSW 2-4 mm had improved radiographic sensitivity to change. Data from SM04690 studies suggest mJSW 2-4 mm should be considered as an inclusion criterion for trials of potential knee DMOADs.

Disclosure of Interests: None declared


REFERENCES:
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THE ROLE OF ULTRASONOGRAPHY IN THE DIAGNOSIS OF PRIMARY SJÖGREN SYNDROME AND ITS CONCORDANCE WITH SALIVARY GLAND BIOPSY

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Background: Minor salivary gland biopsy (MSGB) is the gold-standard technique for primary Sjögren Syndrome (SSp) but nowadays the use of major salivary gland ultrasonography (MSGUS) is increasing because it is a fast and non-invasive technique and with no adverse events for the patient.

Objectives: To assess the utility of MSGUS as a diagnostic tool for SSp and to study the concordance with MSGB.

Methods: 72 patients were recruited consecutively with clinical and/or analytical suspicion of SSp, from the Rheumatology outpatient consultations at the Príncipe de Asturias Hospital (2015-2018). Demographics, clinical and serological data and validated activity indexes, ESSPRI and ESSDAI, were recorded. All patients underwent a MSGB and blindly, both for clinical and histological results, a MSGUS. The histological results were classified according to Cheholin and Mason scores (pathological grades 3/4), and the US results according to the system by Cornejo et al. (pathological grade ≥2). The final SSp diagnosis was made using both the 2002 and the 2016 ACR/EULAR classification criteria. The data was analyzed using the software STATA. The validity of the US and the MSGB to diagnose SSp according to the 2002 and 2016 ACR/EULAR classification criteria was evaluated by calculating the percentage of agreement between the tests, along with the specificity (Sp), sensitivity (S), positive and negative predictive values (PPV and NPV) and area under the curve (AUC).

Results: Descriptive analysis of the main variables is shown in Table 1. Using the MSGUS as a gold-standard, the total% of agreement was 78% with a good AUC (0.75) (IC95%:0.65-0.84). Using the 2002 classification criteria as a gold-standard, the total% of agreement was 82% for US and 79% for MSGB with an AUC of 0.78 (IC95%:0.67-0.88) and 0.80 (IC95%:0.70-0.89) respectively. In this case, US had a S of 53% (IC95%:0.82-0.99) and a Sp of 62% (IC95%:0.41-0.80) whereas MSGB had a S of 78% (IC95%:0.64-0.89) and a Sp of 81% (IC95%:0.61-0.93). Similar results were obtained using ACR/EULAR criteria: US% of agreement 83%, AUC 0.78 (IC95%:0.67-0.90), S 90% (IC95%:0.79-0.97) and Sp 67% (IC95%:0.43-0.85); while MSGB% agreement 81%, AUC 0.83 (IC95%:0.75-0.92), S 76% (IC95%:0.63-0.87) and Sp 90% (IC95%:0.70-0.99). In addition, 9 patients who fulfilled the 2002 classification criteria with a negative histological result had a pathological US.

Conclusion: MSGUS has a similar diagnostic value compared to MSGB in patients with SSp, which could be part of the classification criteria used to date. In this series of patients and compared to MSGB, it has a higher sensitivity and a lower specificity, so it could be used as an initial diagnostic method in patients with high suspicion of disease. The MSGUS for those cases in which US and other clinical and serological data are inconclusive. With this approach, the disadvantages derived from an invasive technique such as MSGB would be avoided.

REFERENCES:
Results: Light weighted kappa for grading and diagnostic evaluation for intra- and inter-reader reliability was moderate to excellent (see Table for details).

Conclusion: The developed US definitions and the scoring system for salivary gland lesions in pSS showed a good to excellent reliability in patients with SS. Next step is to apply the scoring system in clinical trials.

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Table 1. Demographic, clinical and serological characteristics

<table>
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<tr>
<th>Sex%</th>
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<tr>
<td>Mean age</td>
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<tr>
<td>Smoking%</td>
<td>6</td>
</tr>
<tr>
<td>Classification Criteria%</td>
<td>2002 64 ACR/EULAR 49</td>
</tr>
</tbody>
</table>

Shimmer test %
Extralungular features%
Serologies %
Rheumatoid factor %
Hypocomplementemia%

Hypergammaglobulinemia% ANA 62 AntiRho52 43 AntiRho60 46 Antila 32

C3 7 C4 13

Acute phase reactants mean ESR 35 CRP 1.85

ESSPRI mean 5.6

ESSDAl mean 2

Disclosure of Interests: None declared


QO0139

ASSESSMENT OF ULTRASOUND DEFINITIONS AND A SCORING SYSTEM FOR SALIVARY GLAND DISEASE IN PRIMARY SJÖGREN’S SYNDROME: AN OMERAC US PATIENT RELIABILITY EXERCISE

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Background: Salivary gland ultrasound (SGUS) may have the potential of facilitating diagnosis and therapy monitoring of salivary gland disease in patients with primary Sjögren’s syndrome (pSS). The aim of the Outcome Measures in Rheumatology Clinical Trials (OMERACT) US subgroup on SG is to validate US as an outcome measurement instrument in pSS. Following the OMERACT US stepwise validation approach, preliminary consensus definitions for elementary lesions based on a systematic literature review were developed and subsequently a scoring system has been agreed upon and tested through a web-based Delphi exercise.

Objectives: To assess the reliability of consensus based SGUS scoring system in patients with SS.

Methods: Nine sonographers conducted an US reliability exercise of the parotid and submandibular glands (PG, SMG) of 9 patients with primary and secondary SS in 3 rounds. A 4-grade semi-quantitative scoring was applied in B-mode for structural lesions as follows: Grade 0: normal, grade 1: mild inhomogeneity without anechoic or hypoechoic areas, grade 2: moderate inhomogeneity with focal anechoic or hypoechoic areas, grade 3: severe; diffuse inhomogeneity with an-/hypoechoic areas occupying all the surface of the gland. Next, presence or absence of typical pSS-lesions was scored in binary fashion. Intrareader and interreader reliability were computed by Cohen and Light kappa. Weighted k coefficients with absolute weighting were calculated for B-mode abnormalities.

Weighted kappa for intra-reader reliability (Kappa: mean (min-max))

<table>
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<tr>
<th>Grading</th>
<th>PG</th>
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<tr>
<td></td>
<td>SMS</td>
<td>0.75 (0.49-0.93)</td>
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<tr>
<td>Presence / absence of typical pSS-lesions</td>
<td>PG</td>
<td>0.51 (0.30-0.78)</td>
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Weighted kappa for inter-reader reliability (Kappa: mean (min-max))

<table>
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<tr>
<td></td>
<td>SMS</td>
<td>0.63 (0.50-0.72)</td>
</tr>
<tr>
<td>Presence / absence of typical pSS-lesions</td>
<td>PG</td>
<td>0.86 (0.75-0.92)</td>
</tr>
<tr>
<td></td>
<td>SMS</td>
<td>0.87 (0.77-0.93)</td>
</tr>
</tbody>
</table>

Results: Among 250 pts treated in the double-blind period, 215 entered part 2 and 197 (92%) completed 3 years in the trial. Among the 81 TCZ QW and 36 TCZ Q2W pts in CR at wk 52, 38 (47%) and 13 (36%) pts, respectively, maintained CR during part 2. Of these 51 original TCZ pts, 33 (65%) were treatment-free (no TCZ and no GC treatment), which was higher than the treatment-free proportion of original PBO pts who maintained CR in part 2 (17/38; 45%). Median time to first flare while not receiving TCZ was longer for pts in the original TCZ groups (TCZ QW, 575 days; TCZ Q2W, 428 days) than for pts in the original PBO groups (PBO+26, 182 days; PBO+52, 295 days); TCZ QW pts remained flare-free the longest (Fig. 1). Retreatment with TCZ (with or without GC) for flare was effective for restoring CR in part 2. Cumulative GC dose over the 3-year study was lowest in the TCZ group (median dose [mg/day]: TCZ QW, 2372.8; TCZ Q2W, 2686.0; PBO +26, 5006.0; PBO+52, 5322.5). Rates of serious adverse events per 100 pt-years over 3 years (double-blind period + part 2) were comparable for pts who never received TCZ (23.2) and who did receive ≥1 dose of TCZ (25.4), and rates of...
serious infections were 4.6 and 3.5 per 100 pt-years, respectively. Additional results will be presented for original PBO pts.

Conclusion: Nearly half the pts treated with TCZ QW maintained CR for the entirety of part 2, though flares still occurred in the remaining pts once they discontinued TCZ treatment. Among pts who maintained CR in part 2, higher proportions of those originally assigned to TCZ were treatment-free compared with those originally assigned to PBO. Retreatment with TCZ restored CR in pts who experienced flare. Cumulative GC doses over 3 years were lower in pts originally assigned to TCZ than in those originally assigned to PBO. No new safety signals were observed with TCZ exposure in GCA pts during the 3-year study.

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CD28 AS A POTENTIAL THERAPEUTIC TARGET FOR GIANT CELL ARTERITIS

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Background: Giant cell arteritis (GCA) is a granulomatous vasculitis of medium and large arteries. In GCA-affected arteries, vascular wall is destroyed by tissue-infiltrating CD4 T cells and macrophages, which leads to intramural neoangiogenesis and differentiation of IFN-γ- and IL-21-producing effector T-cells. Blocking CD28 signaling and differentiation of IFN-γ- and IL-21-producing effector T-cells. Blocking CD28 signaling disrupted T-cell metabolic fitness; particularly, glucose utilization. Expression of the glucose transporter Glut1 and of glycolytic enzymes as well as mitochondrial oxygen consumption all rely on CD28 signaling. CD28 blockade effectively suppressed vessel wall remodeling processes such as advanced microvessel formation and intimal hyperplasia as well as induction and maintenance of CD4+CD103+ tissue-resident memory T cells.

Methods: CD28 stimulation provides a metabolic signal required for pathogenic effector functions in GCA, implicating CD28 signaling as a promising therapeutic target.

Conclusion: CD28 stimulation provides a metabolic signal required for pathogenic effector functions in GCA, implicating CD28 signaling as a promising therapeutic target.

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[4] Inhibition of JAK-STAT Signaling Suppresses Pathogenic Immune Responses in Medium and Large Vessel Vasculitis.


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Disclosure of Interests: Ryu Watanabe: None declared, Hui Zhang: None declared, Gerald Berry: None declared, Steven Nadler Employee of: Bristol-Myers Squibb, Jörg Goronzy: None declared, Cornelia Weyand: None declared


THE IMPACT OF DISEASE EXTENT AND SEVERITY DETECTED BY QUANTITATIVE ULTRASOUND ANALYSIS IN THE DIAGNOSIS AND OUTCOME OF GIANT CELL ARTERITIS: RESULTS FROM THE TEMPORAL ARTERY BIOPSY VERSUS ULTRASOUND (TABUL) STUDY AND VALIDATION IN AN INDEPENDENT COHORT

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Background: Colour duplex sonography (CDS) is used in patients with giant cell arteritis (GCA) to detect inflammatory oedema of the vascular wall, known as “halo”. A quantitative analysis of halo characteristics to grade the severity and extension of vascular involvement detected by CDS could improve GCA assessment.

Objectives: To develop a quantitative CDS score to improve the diagnosis of GCA, and to correlate the score with histologic findings and clinical outcome. To determine the additional role of clinical signs/symptoms to the CDS score.

Methods: We selected patients with a positive CDS and a diagnosis of GCA recruited into the Temporal Artery (TA) Biopsy (TAB) vs Ultrasound in Diagnosis of GCA (TABUL) study. Due to collinearity we fitted 4 different CDS models including combinations of the following items: number of sites and distribution of halos, average and maximum intima-media thickness (IMT) at the level of the TA and auxiliary arteries (AX) and halos bilaterally. We fitted 4 models with clinical and laboratory findings. We combined the best CDS and clinical models (according to the Akaike Information Criterion) to identify independent correlates of a TAB diagnostic for GCA and of clinical outcome at 6 months (visual loss + VDI ocular + glaucoma-corticoids > 10 mg/day and/or on immunosuppressants) and performed a 10-fold cross-validation of the model. We validated the clinical outcome model on an independent cohort referred to the fast-track ultrasound clinics of two European rheumatology centres.

Results: We included 135 patients with GCA from TABUL (female: 68%, age 73 ±8) and 72 patients from an independent cohort (female: 46%, age 75±7). The...
best fitting CDS model for TAB used maximum IMT size and bilaterality of plaques at the level of the TA and AX. The best fitting clinical model included raised ESR/ CRP, polymyalgia rheumatica, headache and ischaemic symptoms (jaw/tongue claudication, amaurosis, double vision, stroke). The coefficients from the best fitting models (CDS and clinical) allowed to produce a comprehensive score (CDS-US score) to stratify patients according to the probability of having a positive TAB (Figure 1), Model discrimination was fair (AUC-ROC 0.77, 95%CI 0.68-0.84). None of the considered variables was associated with clinical outcome expressing worse prognosis at 6 months.

Conclusion: We demonstrated that a quantitative analysis of CDS findings adds important diagnostic information with a computable estimate of the probability of positive history, supporting the use of CDS as a surrogate diagnostic tool to replace TAB. A few CDS and clinical findings can be combined into a simple computable risk score to support a diagnosis of GCA.

Disclosure of Interests: Sara Moni: None declared, Cristina Ponte Speakers bureau: Roche, Claudio Pereira: None declared, Federica Rumi: None declared, Greta Carrara: None declared, Catherine Klersy: None declared, Andrew Hutchings: None declared, Wolfgang A. Schmidt: None declared, Bhaskar Dasgupta Consultant for: Roche, GSK, Sanofi, BMS, Abbvie, Speakers bureau: Roche, Roberto Capano Speakers bureau: Abbvie, Bristol-Myers Squibb, Celgene, Roche, Genzyme, Lilly, MSD, Pfizer, UCB, Carlsberg Montecucco Speakers bureau: Abbvie, Bristol-Myers Squibb, Celgene, Sanofi, Genzyme, Lilly, MSD, Pfizer, UCB, Raashid Luqmani Grant/research support from: Roche, Vifor and GSK


OP0143 PREDICTORS OF SEVERE CRANIAL ISCHEMIC COMPLICATIONS IN GIANT CELL ARTERITIS

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Background: Vision disturbances and ischemic stroke represent severe ischaemic complications of giant cell arteritis (GCA). Despite the fast track GCA pathway since 2011 our secondary/tertiary rheumatology center, about 10% of patients still develop permanent vision loss (PVL) or stroke.

Objectives: We aimed to determine markers predicting severe cranial ischemic complications in GCA.

Methods: We analyzed medical records of prospectively collected GCA patients diagnosed between 01.09.2011 and 31.12.2018 and compared clinical and laboratory characteristics of patients with and without vision disturbances (diplopia, transient vision loss (TVL), PVL) or ischemic stroke.

Results: During the 88-month observation period, we identified 250 new GCA patients (63.2% female, median (IQR) age 74.9 (67.8-79.9) years, 83.3% histologically proven, 79.8% with positive temporal artery ultrasound, 30.3% with extracranial large vessel involvement). Fifty (20.0%) patients developed either vision disturbances (16 diplopia, 10 TVL or 19 PVL) or ischemic stroke (8); isolated vision disturbances in 42, and isolated stroke in 5 patients. Conventional cardiovascular risk factors (obesity, arterial hypertension, hyperlipidemia, diabetes mellitus, and smoking were not associated with severe cranial ischemic complications (Table 1). The patients with severe cranial ischemic complications had more frequently had atrial fibrillation (RR 2.4 (95%CI 1.3-4.4), p<0.011). Twenty-five from 35 patients with atrial fibrillation were already treated with anticoagulants (10/13 in the group with cranial ischemic complication and 15/22 without them). Besides, GCA cases with severe cranial ischemic complications were significantly older (p<0.006) and more commonly reported jaw claudication (RR 1.8 (95% CI 1.4-2.3), p<0.001). We found no significant differences in the median level of C-reactive protein between the compared groups, whereas the erythrocyte sedimentation rate was slightly lower (p=0.032) and haemoglobin concentration higher (p<0.030) in cases with severe cranial ischemic complications.

Conclusion: Increasing age and jaw claudication predicted severe cranial ischemic complications in our GCA cohort. Atrial fibrillation might represent an additional risk factor.

Disclosure of Interests: None declared


OP0144 MORTALITY IN GIANT-CELL ARTERITIS PATIENTS: A NATIONWIDE POPULATION-BASED STUDY

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Background: Giant cell arteritis (GCA), is the most common type of chronic systemic vasculitis over the age of 50. So far, studies regarding mortality in giant-cell arteritis (GCA) patients had yielded conflicting results.

Objectives: In this large population-based study we aimed to examine whether GCA is associated with increased mortality in different time periods, and in patients diagnosed ≤70 years of age.

Methods: We utilized the medical database of the Clalit-Health-Services in a retrospective cohort study. Follow-up was from January 1st, 2002 and continued until death or end of study follow-up at September 1st, 2018. Incident GCA patients were compared with age- and sex-matched controls. Estimated median survival-times were calculated using Kaplan-Meyer (KM) method and Risk for all-cause mortality in different follow-up periods was obtained by Cox proportional-hazard model, adjusted for age, gender, socio-demographic variables and traditional risk factors.

Results: Our study included 7,294 GCA patients and 34,156 age- and sex-matched controls. The mean age at the start of follow-up was 72.1±9.90 years with 69.2% females. The crude mortality rates for the entire follow-up period was 33.4% amongst GCA patients and 30.2% amongst controls. In KM analysis estimated median survival-time was 13.08 years (95% CI, 12.64-13.52 years) in GCA patients compared to 14.35 years (95% CI 14.09-14.61) in controls (P-value < 0.001). Cox regression demonstrated increased mortality risk in the first 2 years after diagnosis (HR 1.15; 95% CI 1.04-1.26) and >10 years after diagnosis (HR 1.13; 95% CI 1.02-1.32). Risk was higher in patients diagnosed ≤70 years of age [HR 1.66 (95% CI 1.22-2.13) 0-2 years; HR 1.44 (95% CI 1.16-1.79) >10 years].

Conclusion: GCA patients have a minor decrease in long-term survival compared to age-and-sex matched controls. The seen difference is due to excess mortality in the first 2 years, and >10 years after diagnosis of GCA, especially in patients diagnosed ≤70 years of age.

REFERENCES:

Disclosure of Interests: Niv Ben-Shabat: None declared, Howard Amital Grant/research support from: Pfizer, Abbvie, Janssen, Grant/research support from: Pfizer, Abbvie, Janssen, Consultant for: Pfizer, Merck Sharp & Dohme, Consultant for: Pfizer, Merck Sharp & Dohme, Speakers bureau: Pfizer, Merck Sharp & Dohme, Janssen, Sanofi, Bristol-Myers Squibb, Abbvie, Neopharm, Speakers bureau: Pfizer, Merck Sharp & Dohme, Janssen, Sanofi, Bristol-Myers Squibb, Abbvie, Neopharm, Arnon Cohen Grant/research support from: Prof. Arnon Cohen received research grants from Janssen, Novartis and Abbvie and Sanofi, Consultant for: Prof. Arnon Cohen served as a consultant, advisor for Abbvie; Apenen; Soehringer Ingeheil; Dexco pharm; Janssen; Lilly; Neopharm; Novartis; Perrigo; Pfizer; Rafa; Sanofi, Speakers bureau: Prof. Arnon Cohen served as...
Background: Systemic signs of inflammation such as raised CRP or ESR are a classical feature of PMR, but some patients present with normal acute phase reactants (APR). It is not known whether these patients represent milder forms of PMR, whether their disease is not yet fully expressed, or whether they represent another pathophysiological subset of PMR or another disease. Data on demographic and clinical differences between PMR patients with normal versus elevated APR.

Methods: We conducted a retrospective cohort study of clinical characteristics of newly diagnosed PMR patients (clinical diagnosis) who visited our outpatient clinic between April 2012 and September 2017. Patient with concomitant inflammatory rheumatic disease were excluded. Data on patient-, disease-, and treatment characteristics in PMR patients with normal versus elevated APR were provided in the study.

Objectives: To explore baseline differences in demographics and clinical characteristics in PMR patients with and without elevated APR.

Methods: We conducted a retrospective cohort study of clinical characteristics of newly diagnosed PMR patients (clinical diagnosis) who visited our outpatient clinic between April 2012 and September 2017. Patient with concomitant inflammatory rheumatic disease were excluded. Data on patient-, disease-, and treatment characteristics in PMR patients with normal versus elevated APR were provided in the study.

Results: 454 patients were included (table 1). Sixty-two patients had normal, and 392 had elevated APR. In the group with normal APR, fewer patients had peripheral arthritis (2 versus 9%; p=0.044) and fewer had anemia at diagnosis (17 versus 43%; p=0.001). Furthermore, patients had a longer median duration of symptoms before diagnosis (13 versus 10 weeks; p=0.0196) and were more likely to have a history of PMR (16 versus 8%; p=0.057). No significant differences were found in other clinical characteristics. Conclusion: The results of this cohort indeed suggest that patients with normal APR are a different subset of PMR patients. Fewer cases have peripheral arthritis and anemia at diagnosis, suggesting a milder form of PMR. Secondly, our results do not support the hypothesis that PMR of those with normal APR is not yet fully expressed, as they have a longer symptom duration prior to diagnosis.

References:

Disclosure of Interests: None declared

−30mm/hour) were tested using Fischer statistics were used [using mean (SD), median (p25-p75) or n (%) as appropriate], and survival data were compared using the log-rank test. Logistic regression was used to identify predictors of outcome. Results: 454 patients were included (table 1). Sixty-two patients had normal, and 392 had elevated APR. In the group with normal APR, fewer patients had peripheral arthritis (2 versus 9%; p=0.044) and fewer had anemia at diagnosis (17 versus 43%; p=0.001). Furthermore, patients had a longer median duration of symptoms before diagnosis (13 versus 10 weeks; p=0.0196) and were more likely to have a history of PMR (16 versus 8%; p=0.057). No significant differences were found in other clinical characteristics. Conclusion: The results of this cohort indeed suggest that patients with normal APR are a different subset of PMR patients. Fewer cases have peripheral arthritis and anemia at diagnosis, suggesting a milder form of PMR. Secondly, our results do not support the hypothesis that PMR of those with normal APR is not yet fully expressed, as they have a longer symptom duration prior to diagnosis.

References:

Disclosure of Interests: None declared

Table 1. Baseline characteristics of patients with normal versus elevated APR

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Normal APR</th>
<th>Elevated APR</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>Median (P25-P75)</td>
<td>Median (P25-P75)</td>
</tr>
<tr>
<td>Gender</td>
<td>Male (n=273)</td>
<td>Male (n=186)</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>Median (P25-P75)</td>
<td>Median (P25-P75)</td>
</tr>
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<td>ESR (mm/hour)</td>
<td>Median (P25-P75)</td>
<td>Median (P25-P75)</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>Median (P25-P75)</td>
<td>Median (P25-P75)</td>
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<tr>
<td>Peripheral arthritis</td>
<td>Yes (n=82)</td>
<td>Yes (n=184)</td>
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<tr>
<td>Anemia</td>
<td>Yes (n=47)</td>
<td>Yes (n=157)</td>
</tr>
<tr>
<td>History of PMR</td>
<td>Yes (n=170)</td>
<td>Yes (n=284)</td>
</tr>
</tbody>
</table>

Figure 1. Kaplan-Meyer survival curve showing cumulative survival over time in years

Scientific Abstracts
Conclusion: APR demonstrated efficacy in the treatment of OU in pts with active Behçet’s syndrome. Benefits were sustained for up to 64 wks with continued treatment. APR was well tolerated, and safety was consistent with the known safety profile of APR.

Disclosure of Interests: Gulen Hatemi Consultant for: Abbvie, Amgen, BMS, Janssen, MDI, Pfizer, UCB; Speakers bureau: Abbvie, Amgen, BMS, Jansen, MSD, Pfizer, UCB; Albert Marh Consultant for: Chugui Pharma France, Speakers bureau: Roche SAS Chugui Pharma France, Mitsuiro Takeno Consultant for: Celgene Corporation, Doyoung Kim: None declared. David Saisdon Grant/research support from: Roche, Abbvie, Consultant for: Janssen, Celgene, Abbvie, Roche, Haner Direskeneli: None declared, Sue Cheng Employee of: Celgene Corporation, Shannon McCue Employee of: Celgene Corporation, Maria Paris Employee of: Celgene Corporation, Mindy Chen Employee of: Celgene Corporation, Yusuf Yazici Shareholder of: Samumed, LLC, Consultant for: Celgene Corporation, BMS, Genentech, Sanofi, Employee of: Samumed, LLC

**OP0147 KAWAKINRA: A PHASE IIA MULTICENTER TRIAL TO ASSESS THE EFFICACY, AND SAFETY OF ANAKINRA IN PATIENTS WITH INTRAVENTRISUMOGLUBULIN-RESISTANT KAWASAKI DISEASE**

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**Background:** The development of more potent therapeutic approaches to KD is an urgent need because intravenous immunoglobulin (IVIg) treatment is not effective in 20% of patients, increasing the risk of coronary dilations/aneurysms. The combination of genetic and transcriptomic data revealed the key role of interleukin-1 (IL-1) signaling in KD vasculitis and mouse model of KD has shown that anakinra (IL1RA: IL-1 receptor antagonist) could prevent the development of vascular aneurysms.

**Objectives:**
- To assess as primary objective, the efficacy of anakinra in patients with KD who fail to respond to at least one infusion of IVIg.
- To assess its safety and tolerability and its effect on disease activity, systemic inflammation and coronary lesions.

**Methods:** A 45-day, phase IIa proof of concept study open labeled with anakinra dose escalation, with a target of at least 12 patients completing the study. Eligible patients had KD according to the AHA criteria, duration of fever ≤ 14 days, and were ≥ 3 months and 5 Kg. They had persistent (or relapsing) fever (≥38°C) within 48h of the last IVIG infusion, had not received other alternative treatment including steroids, and had no others exclusion criteria. After informed consent, they received a starting dose of 2mg/kg (patients <10kg and/or <8 months: 8mg/kg), which could be increased every 24h of 2mg/kg until a maximum of 6mg/kg (patients <10kg and/or <8 months: 8mg/kg). In case of persistent fever, Anakinra treatment duration was 15 days. Outcome measures were fever, KD symptoms, blood inflammation and cardiac echography. Total study duration was 45 days. **Clinical trials:** NCT02396596. The study is supported by a grant from the French ministry of health, APHP, national PHRC 2014. IRB approval was obtained and all patients (parents) gave informed consent.

**Results:** 18 patients were screened and 16 were included and 13 have completed the study. Anakinra was started in 16 patients (14 boys, 2 girls) at a median age 2 years (3 months to 6 years) and at a median of 9.5 days after the onset of fever. 4 patients escaped early for SAE, and 1 had sJIA final diagnosis. The maximum dose of anakinra was 6mg/kg in 6 patients, 4mg/kg in 6, and 2mg/kg in 4. Mean PGA decreased from 7.80 (4-10) to 1.2 (0-3) at D14. Median temperature was 37.7°C (36.7-39.7) at day 3 and 37.2°C at D7 (36.7-37.9). Median CRP was 135mg/L at screening and decreased to 9.5 mg/L at D7. 8/14 evaluated patients had coronary dilatation (Z score max >2.5mm) at inclusion, 5/14 at D14 and 3/14 at D45. 3/14 patients who increased 2 score at D14 decreased it at J45. We observed 3 severe adverse events (SAE) where treatment was discontinued: anakinra overdose, MAS in a patient evolving to sJIA and increase of coronary dilatation. Others AE included cytolytic hepatitis (2 patients), hypereosinophilia (1), injection site reaction (1) and pancreatitis (1) without treatment discontinuation.

**Conclusion:** We have realized the first experimental study assessing IL-1 blockade in severe refractory KD. 15 days-duration of anakinra treatment, given early in the course of IVIG-resistant KD, was rapidly effective on KD symptoms, biologic inflammation and coronary dilatations in almost all patients, with a good tolerability. This study calls for further investigation of IL-1 blockade in KD.

**Disclosure of Interests:** Isabelle Koné-Paut Grant/research support from: SOBI Has supported drug product (anakinra) for the presented study, Consultant for: SOBI, Novartis, Pfizer, Abbvie, UCB, CHUGAI, ROCHE, stephanie tellier: None declared, virginie Lambert: None declared, Corinne Guitton: None declared, alexandre belot: None declared, Perrine Dusser: None declared, Linda Rossi-Semerano Grant/research support from: Roche, isabelle Marie: None declared, gregory allain: None declared, helene agostini: None declared, celine piedvache: None declared

**THURSDAY, 13 JUNE 2019**

**Journeys from bench to bedside in paediatric rheumatology**

**OP0148 METABOLOMICS IN JUVENILE-ONSET SLE: IDENTIFYING NEW BIOMARKERS TO PREDICT CARDIOVASCULAR RISK**

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**Background:** Juvenile-onset systemic lupus erythematosus (JSLE) is an autoimmune disorder characterised by immune dysregulation, chronic inflammation and increased cardiovascular risk (CVR). Cardiovascular disease is the leading cause of mortality in JSLE not attributable to lupus flare. Our findings in adult-onset SLE link immune cell dysregulation with dyslipidemia but little is known about the immune profile or whether abnormal lipid metabolism contributes to disease pathogenesis in JSLE.

**Objectives:** The objective of this study was to investigate dyslipidemia and CVR in a cohort of JSLE patients using in depth metabolomics and relate this to clinical and immune cell profiles and to identify novel biomarkers to predict CVR in these patients.

**Methods:** Metabolic biomarker analysis (NMR) and in-depth immune cell phenotyping (30 subsets by flow cytometry) was performed on serum and PBMCs respectively from a discovery cohort of 35 JSLE patients (median age 19 (14-25), 12 males, 23 females) compared with 39 age/sex matched healthy donors (HCs) (median age 18 (16-25), 17 males, 22 females). Data was analysed using cluster and correlation-correlation and receiver operating characteristic (ROC) analysis.

**Results:** Patient stratification by metabolomic profile using unbiased hierarchical clustering revealed 3 groups that each had a unique lipoprotein profile, immune cell phenotype and clinical presentation. Group-1 had decreased atheroprotective high density lipoproteins (HDL) and increased atherogenic very low and low density lipoproteins (VLDL/LDL) and Group-2 had elevated HDL but reduced VLDL/LDL indicating that these groups could be at high and low CVR respectively. This hypothesis was validated by previously recognised markers of CVR including the atherosgenetic index of plasma, ApoB:A1 ratios and lipid biomarkers we previously identified to be associated with pre-clinical atherosclerotic plaque in adult SLE patients. Patients in Group-1 had a significant increase in plasmablasts and activated T-cells compared to HCs and had clinical features associated with increased disease activity. These immunopathogenic properties were not seen in the...
low CVR Group-2. Patients in Group-3 displayed an intermediate CVR but a pro-inflammatory immune cell profile. This metabolic patient stratification was validated in a separate JSLE cohort. Importantly, ApoB:A1 ratio was identified as a highly predictive biomarker (ROC area under the curve=0.99) distinguishing between JSLE patients in Group-1 and 2, indicating high and low CVR respectively. Finally, longitudinal analysis revealed that the ApoB:A1 ratio biomarker remained stable over time.

Conclusion: ApoB:A1 ratio and metabolic lipoprotein signatures could be new biomarkers to predict CVR in JSLE patients. Patient stratification using these biomarkers could provide an opportunity for tailored disease treatments using lipid modification therapy and/or diet/lifestyle interventions.

REFERENCES:

Acknowledgement: Rosetrees Trust, Lupus UK. Versus Arthritis

Disclosure of Interests: None declared


OP0149

CD4+ T CELLS FROM CHILDREN WITH ACTIVE JUVENILE IDIOPATHIC ARTHRITIS SHOW ABERRANT CHROMATIN ORGANIZATION AND CTCF LOCALIZATION ASSOCIATED WITH TRANSCRIPTIONAL ABNORMALITIES

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Background: Our group and others have shown that peripheral blood cells of children with juvenile idiopathic arthritis (JIA) display numerous transcriptional abnormalities. However, most of these studies have been performed on mixed cell types (peripheral blood mononuclear cells, whole blood). Little cell type specific data is available, making mechanistic inferences and links to disease pathogenesis difficult.

Objectives: To define transcriptional patterns in CD4+ T cells from children with polyarticular JIA and query mechanisms underlying transcriptional abnormalities.

Methods: We studied CD4+ T cells obtained from children with active polyarticular onset JIA and sought to identify epigenetic features associated with altered gene expression. We performed RNA-seq and ATAC-seq on a cohort of patients who had the active disease and were under treatment with methotrexate and eta-nercept (ADT), patients who fit criteria for clinical remission on medication (CRM), and healthy control children (HC). We used standard used the general dispersion protocol in EdgeR to identify differential gene expression. We used our recently developed and validated Hidden Markov Model library for ATAC-seq software to identify differentially accessible regions, comparing ADT, CRM, and HC samples. We integrated ATACseq and RNAseq data using the BETA software package. After preliminary analysis revealed a potential role for the transcriptional regulator, CCCTC binding factor (CTCF) in the observed transcriptional patterns, we performed ChIPseq and HICchip studies on an independent group of JIA CD4+ T cell samples.

Results: We found widespread transcriptomic differences between ADT and either HC or CRM patients. We identified 4,062 genes that showed differential expression between ADT and HC samples. Gene expression patterns from CRM samples were closely correlated to ADT patients, with high and low CVR respectivly. Finally, longitudinal analysis revealed that the ApoB:A1 ratio biomarker remained stable over time.

Conclusion: ApoB:A1 ratio and metabolic lipoprotein signatures could be new biomarkers to predict CVR in JSLE patients. Patient stratification using these biomarkers could provide an opportunity for tailored disease treatments using lipid modification therapy and/or diet/lifestyle interventions.

REFERENCES:

Acknowledgement: Rosetrees Trust, Lupus UK. Versus Arthritis

Disclosure of Interests: None declared


OP0150

MONOCYTE AND MACROPHAGE TRANSCRIPTIONAL PHENOTYPES IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS REVEAL TRIM8 AS A MEDIATOR OF IFNGAMMA HYPERRESPONSIVENESS AND RISK FOR MACROPHAGE ACTIVATION SYNDROME

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Background: Systemic juvenile idiopathic arthritis (SJIA) is a severe and distinct subtype of childhood arthritis. Children with SJIA are at risk for macrophage activation syndrome (MAS), a life-threatening episode of hyperinflammation driven by interferon-gamma (IFNγ). Previous studies in SJIA have demonstrated that proinflammatory and proinflammatory cytokines in SJIA display hyperresponsiveness to IFNγ, but the molecular basis of this remains unclear.

Objectives: Utilize transcriptional profiling of monocytes and macrophages in SJIA to identify polarization phenotypes including features of interferon response

Methods: Bulk RNA-sequencing (RNA-seq) was performed on purified monocytes from 26 patients with SJIA without MAS. In addition, single-cell RNA-seq was performed on isolated bone marrow macrophages from control patients and patients with SJIA and MAS. THP-1 monocytic cells and primary human monocyte-derived macrophages (MDM) were transfected with TRIM8-specific or negative control small-interfering RNA prior to stimulation with IFNγ.

Results: RNA-seq of purified SJIA monocytes revealed marked transcriptional changes between cells from patients with high vs low serum ferritin levels. Pathway analysis demonstrated enriched upregulated gene ontology pathways including Response to External Stimulus (p<2.73x10^-10), Defense Response (p<2.66x10^-10) and Inflammatory Response (p=1.95x10^-11) when comparing the SJIA monocyte signature to well-characterized polarization phenotypes.

Conclusion: Utilize transcriptional profiling of monocytes and macrophages in SJIA to identify polarization phenotypes including features of interferon response

Disclosure of Interests: None declared


OP0151

MACROPHAGE ACTIVATION SYNDROME PROTEIN ASSEMBLY AND NETWORK ANALYSIS REVEAL TRIM8 AS A MEDIATOR OF HYPERRESPONSIVENESS TO IFNGamma AND RISK FOR MACROPHAGE ACTIVATION SYNDROME

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Objectives: Utilize transcriptional profiling of monocytes and macrophages in SJIA to identify polarization phenotypes including features of interferon response

Methods: Bulk RNA-sequencing (RNA-seq) was performed on purified monocytes from 26 patients with SJIA without MAS. In addition, single-cell RNA-seq was performed on isolated bone marrow macrophages from control patients and patients with SJIA and MAS. THP-1 monocytic cells and primary human monocyte-derived macrophages (MDM) were transfected with TRIM8-specific or negative control small-interfering RNA prior to stimulation with IFNγ.

Results: RNA-seq of purified SJIA monocytes revealed marked transcriptional changes between cells from patients with high vs low serum ferritin levels. Pathway analysis demonstrated enriched upregulated gene ontology pathways including Response to External Stimulus (p<2.73x10^-10), Defense Response (p<2.66x10^-10) and Inflammatory Response (p=1.95x10^-11) when comparing the SJIA monocyte signature to well-characterized polarization phenotypes.

Conclusion: Utilize transcriptional profiling of monocytes and macrophages in SJIA to identify polarization phenotypes including features of interferon response

Disclosure of Interests: None declared

MIRNAS CONTRIBUTE TO DYSREGULATED ROS METABOLISM IN THE INFILTRATED JOINT

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Background: In the last years miRNAs have emerged as critical regulators of innate and adaptive immune responses and an altered expression of function is associated with several inflammatory and autoimmune diseases. Therefore miRNAs are also believed to promote inflammatory processes within the inflamed joint of juvenile idiopathic arthritis (JIA) patients. It is furthermore known that oxidative stress is associated with JIA. Free radicals are implicated in joint damage and play an important role as secondary messengers in immunological responses. How and if miRNAs contribute to dysregulated reactive oxygen species (ROS) metabolism in JIA remains to be elucidated.

Objectives: We aimed to identify miRNAs and miRNA regulated pathways, which contribute to dysregulated immune cell responses within the inflamed joint.

Methods: miRNA profiling was performed on peripheral blood mononuclear cells (PBMCs) from healthy children, PBMCs from 9 JIA patients and synovial fluid mononuclear cells (SFMCs) from the same JIA patients. Subsequently, GO and pathway enrichment analyses were performed on predicted target genes. Upregulation of miRNAs was confirmed in vitro after incubation with synovial fluid by qRT-PCR. Mitochondrial integrity, cellular ROS and Nrf2 protein expression were measured by flow cytometry.

Results: Transcriptome analysis of JIA SFMCs compared to HC PBMCs revealed strongly enhanced expression of miR23a and miR23a, miR27a, miR44a, and miR115, which are involved in oxidative stress processes. In addition, expression of these could be induced in healthy control PBMCs by synovial fluid ex vivo. ROS level in synovial fluid T cells were enhanced, while expression of Nrf2, the main regulator of anti-oxidative responses and a target of miR27a, remained low. Furthermore mitochondrial cycliphiphin, which regulates ROS escape from mitochondria and is suppressed by miR23a, was downregulated in SFMCs as well.

Conclusion: SFMCs within the inflamed joint reveal a distinct miRNA expression profile. Especially miRNAs that are involved in regulation of ROS metabolism are upregulated. In line with this, expression of Nrf2 and mitochondrial cycliphiphin, which are important regulators of cellular ROS metabolism are reduced while production of ROS is enhanced. We suggest that higher abundance of miRNAs, that are involved in oxidative stress pathways, contribute to redox dysregulations within the inflamed joint and thereby contribute to inflammatory processes.

Disclosure of Interests: Kim Oth: None declared, Patricia Klemm: None declared, Tobias Schwarz: None declared, Federica Raggi: None declared, Alessandro Consolaro Grant/research support from: AbbVie, Pfizer, Joachim Peltz: None declared, Klaus Tenbrock Grant/research support from: Pfizer, BMS, Novartis, Speakers bureau: Pfizer, Novartis


Oligoarticular Juvenile Idiopathic Arthritis (O-JIA) is a common inflammatory joint disease in children, driven by continuous local T-cell activation. [1] T cell activation is counter-balanced via signals generated by co-inhibitory receptors (co-IRs) such CTLA-4, PD-1, LAG-3, and TIM-3. [2] This work was supported by a research grant from PACE EUA Foundation for Research in Rheumatology.

Disclosure of Interests: Endal Sag: None declared, Selcan Demir: None declared, Morten Aagard Nielsen: None declared, Malene Hvid: None declared, Ege Bayan: None declared, Yelda Bilginer: None declared, Selcan Demir: None declared, Joachim Peltz: None declared, Gerd Hornett: None declared, Klaus Tenbrock: Grant/research support from: Pfizer, Novartis, Speakers bureau: Pfizer, Novartis


REFERENCES
[2] T cell activation is counter-balanced via signals generated by co-inhibitory receptors (co-IRs) such CTLA-4, PD-1, LAG-3, and TIM-3.
physiologic circumstances. Enhancers do not always regulate the nearest gene, and may regulate more than one gene. Enhancers typically regulate genes within the same chromatin loop, or topologically associated domain (TAD).

Objectives: To gain a better understanding of the genetics of JIA by examining the broader chromatin architecture that encompasses the known risk haplotypes.

Methods: We used publicly available chromatin conformation HiC data and the online Juicebox software suite to query known JIA risk haplotypes for evidence of physical interactions between putative enhancers within the haplotypes and immunologically relevant genes. We specifically queried 20 haplotypes in which H3K4me1/H3K27ac marks were prominent within both lymphoid and myeloid cells. We queried data from GM12787 (B cell), K562 (lymphoblast), and THP-1 (monocyte/macrophage) cells, as well as human cord blood T cells. To identify TADs associated with specific enhancers, we used a SKB resolution (which allowed us to visualize chromatin loops as peaks), setting the cursor at the center of each putative enhancer. We also identified the genes within the identified chromatin loop domains and used gene ontology (GO) analyses to identify functional associations among genes within the TADs incorporating the JIA risk loci.

Results: We identified at least one chromatin loop structure in all 20 of the JIA risk haplotypes for each of the 4 cell lines we queried. These loops were not cell type specific. That is, almost identical loops structures could be seen in each of the cell lines at each of the loci, suggesting that these enhancers regulate a broad range of chromatin architecture functions. The TADs incorporating the JIA haplotypes invariably included genes of immunologic interest. For example, the TAD incorporating the IL2RA haplotype including IL15 (the alpha chain of the IL15 receptor) and PKCD, a protein kinase C-family enzyme important in both T and B cell activation, was the most complex locus was C50S6 which encompassed 25 genes (including IL2, IL4, and IL13) and 3 miRNA within 4 loops and sub-loops. Genes within the TADs were highly enriched for multiple GO terms for processes involved in leukocyte activation (e.g., MAP kinase signaling cascade), JAK-STAT responses, chemokines, and cytokine-mediated signaling pathways.

Conclusion: These 20 JIA-associated risk loci are situated within complex chromatin regions that show similar features in both lymphoid and myeloid cells. HiC data demonstrate direct physical contacts between putative enhancers within the risk loci and multiple genes of immunologic interest. We hypothesize that at least some of the genes within the haplotype-associated TADs are the long sought "far get genes" of JIA-associated genetic variants. This work emphasizes the importance of broadening our focus beyond the "nearest gene" to the GWAS-identified tag SNPs.

Disclosure of Interests: None declared


OP0154

A NOVEL RELA TRUNCATION IN A 3-GENERATION FAMILY WITH BEHÇET’S DISEASE ALTERS THE APOPTOTIC RESPONSE TO INFLAMMATORY STIMULANTS

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2University Hospital Kerry, Rheumatology, Tralee, Ireland
3University of Leeds, Leeds Institute of Rheumatic and Musculoskeletal Disease, Leeds, United Kingdom
4University Hospital Limerick, Rheumatology, Limerick, Ireland
5University College Dublin, School of Medicine, Dublin, Ireland

Background: Behçet’s disease (BD) is a heterogeneous multi-faceted autoimmune condition characterised by recurrent episodes of oral and genital ulceration, uveitis and skin lesions, with less frequent involvement of the gastrointestinal tract, large blood vessels and central nervous system. The NF-κB pathway is a ‘master-regulator’ of immune and inflammatory signaling, with the ability to control the expression of key inflammatory genes and genes associated with apoptosis and proliferation.

Objectives: To identify the pathobiology associated with a novel genetic mutation identified in a 3-generation family with Behçet’s-like mucocutaneous ulceration syndrome, primarily involving childhood-onset chronic oral and genital ulcers.

Methods: The novel RELA mutation was identified using whole exome sequencing. Immunoblot of peripheral blood mononuclear cell (PBMCs) lysates from affected family members was used to determine if the predicted truncated protein was expressed. PBMCs were stimulated with TNF: NFκB phosphorylation was measured relative to unstimulated cells form affected and unaffected family members. HEK293T cells transfected with plasmids encoding either wild-type or the novel RELA-mutant and overexpression confirmed via immunoblot. An in vitro model of the RELA truncation was used to observe the effect of the RELA truncation on response to TNF stimulation. Apoptosis protein arrays, western blots, and ELISA assays were used to investigate the effect of TNF on wild-type RELA compared to the mutant protein. Mouse Embryonic Fibroblasts (MEFs) isolated from RELA mice, which do not express endogenous RELA, were transfected with plasmids encoding either wild-type or the novel RELA-mutant. Wild Type MEF cells (with endogenous RELA) were used as a control. Cells were stimulated with LPS (2.5µg/ml) or no treatment control for 12 hours.

Results: A heterozygous cysteine deletion at position 1459 in RELA was detected in all affected individuals as previously reported. This mutation results in a frame-shift His487ThrfsTer7, producing a truncated protein of 492 amino acids. RELA-His487ThrfsTer7 heterozygotes have different phosphorylation kinetics of key NFκB pathway components. Interestingly, TNF was less sensitive to TNF stimulation compared to wild-type controls. Cells overexpressing RELA-His487ThrfsTer7 had increased pro-apoptotic proteins (BAD, cleaved caspase 3 and SMAC) whereas anti-apoptotic proteins (BCL2, CLASP1) were decreased compared to cells transfected with wildtype RELA. Cells transfected with RELA-His487ThrfsTer7 were much less sensitive to TNF stimulation compared to wild-type controls, as measured by induction of TNF-sensitive proteins.

Conclusion: This study gives novel information on both the genetic basis and biological mechanisms of BD in individual families. Familial mutations that induce haploinsufficiency of RELA have recently been associated with BD. However, the IL4, IL15R, IL4, and PKCQ, a protein kinase C-family enzyme important in both T and B cell activation, are also highlighted. The most complex locus was C50S6 which encompassed 25 genes (including IL2, IL4, and IL13) and 3 miRNA within 4 loops and sub-loops. Genes within the TADs were highly enriched for multiple GO terms for processes involved in leukocyte activation (e.g., MAP kinase signaling cascade), JAK-STAT responses, chemokines, and cytokine-mediated signaling pathways.

Disclosure of Interests: Emma Dorris: None declared, Fahd Adee: None declared, Dylan Lawless: None declared, Wan Lin Ng: None declared, Aqeel Anjum: None declared, Niamh Morgan: None declared, Eoin Cummings: None declared, Sinisa Savic Grant/research support from: Novartis and Sobi, Alexander Fraser: None declared, Gerry Wilson: None declared


THURSDAY, 13 JUNE 2019

Transformative care – the future

OP0155-HPR

TARGETS FOR REDUCING PREMATURE MORTALITY IN OLDER RESULTS WITH OSTEOARTHRITIS: RESULTS FROM A NOVEL PATH ANALYSIS WITHIN A COX PROPORTIONAL HAZARDS MODEL

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Background: There is increasing evidence that it is the impact of osteoarthritis rather than the osteoarthritis itself that explains an excess risk of mortality. This indicates that potentially modifiable targets may reduce mortality for those with osteoarthritis. Mediation analysis can be used to investigate pathways, although this has rarely been undertaken using survival analysis due to the challenge of accounting for time. The study uses a novel approach to examine mediation using path analysis with Cox proportional hazard modelling (survival analysis).

Objectives: The objectives of this study were to identify potential mechanisms of the impact of osteoarthritis on mortality and examine the role of modifiable targets (anxiety, depression, insomnia and walking frequency) for health professionals in rheumatology (HPRs).

Methods: A population-based prospective cohort study was conducted using data from the North Staffordshire Osteoarthritis Project (NoSOP), in which primary care medical record data was linked to self-report information collected by questionnaire in adults aged 50 years and over (n=8066). Individuals were defined as having osteoarthritis if they had consulted general practice for osteoarthritis, identified by Read codes in the primary care medical record, and indicated moderate to severe pain interference in daily life in the Medical Outcomes Short Form 36 at baseline (2002). A Cox proportional hazards analysis was performed to determine the total effect (TE) of osteoarthritis on mortality, both with adjustment for confounding variables (age, sex, education, occupation, smoking status, ischaemic heart disease, chronic obstructive pulmonary disease, non-steroidal anti-inflammatory drugs, obesity, cognitive impairment). Within the Cox model, path analysis was used to decompose the TE to assess the indirect (IE) and direct effects (DE) for each of four potential mediators (anxiety, depression, insomnia, walking frequency; all measured by questionnaire) with adjustment for confounders. Results are expressed as adjusted hazard ratios (aHr): bootstrap resampling was used to generate 95% confidence intervals (95% CIs).

Results: Mean age of participants was 65.2 (SD 9.6) years and 51.6% were female. 5266 (29.7%) had osteoarthritis. Participants were followed up over 10 years during which time 1188 (14.7%) died. The rate of mortality was greater in those with osteoarthritis (52 deaths per 1000 person years) compared to those without (38 deaths per 1000 person years). Osteoarthritis was significantly associated with mortality (aHR 1.14; 1.00, 1.28). The relationship between osteoarthritis and mortality was mediated by walking frequency, depression and insomnia (anxiety did not mediate the relationship (IE HR 1.00, 0.98, 1.02)). The strongest mediator was walking frequency (TE 1.14; 1.00, 1.29; DE 1.04; 0.91, 1.16: IE 1.08; 0.98, 1.11), followed by depression (IE 1.06; 1.03, 1.08) and insomnia (IE 1.01; 1.00, 1.03).
Conclusion: This is the first study to examine mediation and highlights the importance of potentially modifiable targets for HPRs to reduce mortality in older adults with osteoarthritis. Encouraging people to maintain levels of physical activity at a population level and targeting a reduction in physical limitation in clinical practice to allow this, is important.

Disclosure of Interests: None declared


Table 1. Baseline characteristics of the two study groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>CT group (n = 20)</th>
<th>CT-GOH group (n = 20)</th>
<th>P value</th>
</tr>
</thead>
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<tr>
<td>Age</td>
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<td>67.25 ± 10.97</td>
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<td>Primary school</td>
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<tr>
<td>High school</td>
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<tr>
<td>Han Chinese, n</td>
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<tr>
<td>Income, n</td>
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<td>Distance to hospital, km</td>
<td>105.83 ± 100.35</td>
<td>111.33 ± 92.54</td>
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<td>Kellgren-Lawrence grade, n</td>
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<td>Grade III</td>
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<td></td>
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<tr>
<td>WOMAC pain, 0-10</td>
<td>18.90 ± 10.08</td>
<td>21.00 ± 8.38</td>
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<tr>
<td>WOMAC morning stiffness, 0-10</td>
<td>8.45 ± 4.99</td>
<td>9.25 ± 4.68</td>
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<tr>
<td>WOMAC function, 0-10</td>
<td>58.05 ± 20.55</td>
<td>63.30 ± 25.31</td>
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<td>MIF</td>
<td>43.55 ± 19.77</td>
<td>45.70 ± 20.43</td>
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</tr>
<tr>
<td>HADS-A</td>
<td>8.90 ± 5.55</td>
<td>8.30 ± 4.64</td>
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</tr>
<tr>
<td>HADS-D</td>
<td>7.10 ± 5.28</td>
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<tr>
<td>PSQI global score</td>
<td>7.35 ± 4.56</td>
<td>7.70 ± 5.13</td>
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</tr>
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Disclosure of Interests: None declared


Table 2. Mean change of outcome measures from baseline to endpoint

<table>
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<th>CT-GOH group (n = 19)</th>
<th>P value</th>
</tr>
</thead>
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<tr>
<td>WOMAC morning stiffness</td>
<td>3.12 ± 1.50</td>
<td>4.42 ± 2.06</td>
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<tr>
<td>WOMAC function</td>
<td>27.65 ± 9.91</td>
<td>38.84 ± 17.28</td>
<td>0.025</td>
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<tr>
<td>MIF</td>
<td>17.53 ± 7.73</td>
<td>20.95 ± 8.75</td>
<td>0.225</td>
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<tr>
<td>HADS-A</td>
<td>3.24 ± 2.41</td>
<td>5.32 ± 3.33</td>
<td>0.037</td>
</tr>
<tr>
<td>HADS-D</td>
<td>2.12 ± 2.06</td>
<td>2.36 ± 2.01</td>
<td>0.714</td>
</tr>
<tr>
<td>PSQI global score</td>
<td>2.35 ± 1.54</td>
<td>4.21 ± 3.34</td>
<td>0.043</td>
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</tbody>
</table>

Disclosure of Interests: None declared


References:
are monitored for serum uric acid less than twice per year. But 79% of patients claim to be satisfied with their current treatment and do not expect better management of their disease.

Conclusion: The results of the survey demonstrate that gout patients in Europe, as providing more information and guidance about what support they can access and receiving psychological support from their healthcare team were (i) lack of optimism about their future with RA or AJA (ii) not knowing what support they can access (iii) finding it difficult to talk about their emotions and asking for help (iv) believing healthcare professionals lack the time and ability to help them (v) believing that discussing emotions and providing psychological support is not on their healthcare team’s agenda, evidenced by a focus on physical rather than psychological health in consultations and (vi) never or rarely being asked about their emotional health in consultations and during the resistance training program. The primary outcome measure was isokinetic (60 °/s) upper leg muscle strength (Nm/kg). In addition, the estimated 1 RM for leg press, leg curl and hip abduction were used as measures for muscle strength. Other outcome measures included severity of knee pain (NRS), self-reported and performance-based activity limitations (WOMAC physical functioning (WOMAC), Get-up-and-go-test (GUG)). Measurements were performed by a blinded assessor prior to the exercise program (T0), directly after the program (T1) and at 6 months follow-up (T36). Additionally, for patients with vitamin D deficiency, measurements were also taken prior to vitamin supplementation or placebo (T-12).

Results: Both the high-intensity group and moderate-intensity group improved in upper leg muscle strength over time. No significant differences between groups were found for isokinetic upper leg muscle strength (p = 0.646) (see figure 1). However, when measured by the estimated 1 RM, significant differences were found between groups in favor of the high-intensity group (p = 0.001) (see figure 1). No between-group differences were found on pain (p = 0.885), or on self-reported and performance-based activity limitations (WOMAC p = 0.868; GUG p = 0.896), although both groups improved (see figure 1). An unexpected finding was that, in the (small sample of) patients with vitamin D deficiency, the placebo group showed significant greater isokinetic upper leg muscle strength over time compared to the vitamin D group (p = 0.001).

Conclusion: No differences between groups were found for isokinetic upper leg muscle strength. With the estimated 1 RM as a measure of muscle strength, high-
intensity resistance training led to greater improvements in muscle strength compared to moderate-intensity resistance training in patients with knee OA. This did not result in greater improvements in pain and physical functioning in the high-intensity resistance group; both groups showed similar clinically important improvements. The added value of vitamin D supplementation on muscle strength in knee OA patients with vitamin D deficiency need further study.


OP016-HPR DOES OCCUPATIONAL THERAPY DELAY OR SHORTEN THE TIME TO CARPOMETACARPAL SURGERY? RESULTS FROM A RANDOMIZED CONTROLLED TRIAL

Else Marit H. Gravås1, Nina Østerås1, Randi Nossum2, Ruth Else Møhl Eid2, Åse Klokkende1, Karin Hoegh Møte2, Monika Olsen5, Øyvind Kjeken1, Kristin Haugen5, Arja Hikkenen: None declared, Willem Lems: Speakers bureau: Amgen Inc., Merck, Eli Lilly and Pfizer. Marike van der Lee: None declared.


OP0161-HPR SHORT-TERM EFFECT OF OCCUPATIONAL THERAPY INTERVENTION ON HAND FUNCTION AND PAIN IN PATIENTS WITH THUMB BASE OSTEARTHRITIS – SECONDARY ANALYSES OF A RANDOMIZED CONTROLLED TRIAL

Anne Therese Tvet1, Randi Nossum2, Ruth Else Møhl Eid2, Åse Klokkende2, Karin Hoegh Møte2, Monika Olsen2, Øyvind Kjeken1, Kristin Haugen5, Arja Hikkenen: None declared, Willem Lems: Speakers bureau: Amgen Inc., Merck, Eli Lilly and Pfizer. Marike van der Lee: None declared.


THE NEED FOR PERSONALIZED, NON-PHARMACOLOGICAL INTERVENTION PROGRAMMES IN AUTOIMMUNE CONNECTIVE TISSUE DISORDERS: RESULTS OF A EULAR-FUNDED SCOPING REVIEW WITH A NESTED, DESCRIPTIVE META-ANALYSIS


Conclusion: Occupational therapy had significant positive short-term effects on pain and function in patients referred to surgical consultation for CMC1 OA.

Disclosure of Interests: None declared


LONG-TERM EFFECTIVENESS OF CANAKINUMAB IN PATIENTS WITH CRYOPYRIN-ASSOCIATED PERIODIC SYNDROME

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Background: Treatment options for autoinflammatory diseases include anti-interleukin (IL)-1 therapies since the IL-1 pathway is crucial in immune dysregulation in patients with monogenic periodic fever syndromes.

Objectives: To gain further insights from routine clinical practice with respect to long-term effectiveness and safety of canakinumab (CAN) in pediatric and adult patients with CAPS (cryopyrin-associated periodic syndrome, including Muckle-Wells syndrome [MWS]), familial cold autoinflammatory syndrome [FCAS], neonatal onset multisystem inflammatory disease [NOMID]/chronic infantile neurologic-cutaneous and arthritic syndrome [CINCA]), FMF (familial Mediterranean fever), TRAPS (tumor necrosis factor receptor-associated periodic syndrome) and HIDS/MKD (hyperimmunoglobulinemia D syndrome/mevalonate kinase deficiency).

Methods: RELIANCE is a prospective, non-interventional, multi-center, observational study based in Germany with a 3-year follow-up enrolling patients aged ≥2 years with clinically confirmed diagnoses who routinely received CAN. 6-monthly clinical assessment and evaluation of patient-reported outcomes is aligned with routine clinic visits. CAPS disease activity was determined by physicians’ and patients’ assessment. Endpoints were effectiveness and safety of CAN under standard clinical practice conditions.
Results: The interim analysis includes 52 CAPS patients with prior long-term CAN treatment (43.1% females) enrolled by September 2018. 44.2% of the patients participated in the RELIANCE study. The mean age was 20.7 years (4.0–79.0 years) at baseline and the mean duration of prior CAN treatment was 5.4 years (0.0–11.0 years). 40 patients (76.9%) were diagnosed with MWS, the other patients had FCAS (2), NOMID/CINCA (7) or atypical CAPS (1) (subtype diagnosis of 2 patients not available). Mutations in Nod-like receptor family pyrin domain-containing-3 were identified in 34 patients (68.0%) including E311K (7), Q703K (5), V198M (5), T348M (5), A439V (4). A baseline screening revealed sensorineural hearing loss (62.0%), papillitis (84.0%) and neurological symptoms (71.4%) in patients which had not been detected previously. The majority of patients had no disease related symptoms at baseline and 6 months demonstrating sustained remission in patients receiving long-term CAN treatment. The following disease related symptoms (mild/moderate and severe) were observed in the analysis cohort (N=31) at baseline and 6 months, respectively – disease symptom: baseline (mild/moderate, severe) vs. 6 months (mild/moderate, severe) – urticarial skin rash: 19.4%, 6.5% vs. 25.8%, 0.0%, arthritis: 32.3%, 0.0% vs. 29.0%, 7.9%, myalgia: 9.7%, 0.0% vs. 16.1%, 0.0%, headaches: 22.6%, 9.7% vs. 19.4%, 19.4%, conjunctivitis: 32.3%, 3.2% vs. 12.9%, 6.5%, abdominal pain: 9.7%, 6.5% vs. 22.6%, 9.7%. Patients’ assessment of disease activity and fatigue did not change between baseline and 6 months. However, at baseline 45.5% and after 6 months 76.0% of patients had no impairment of social life by the disease. Serious adverse events were reported for 2 patients (tonsillitis, delivery at week 31).

Conclusion: The RELIANCE study longitudinally monitors the stability of efficacy and safety of CAN in patients with monogenic periodic fever syndromes. An initial interim analysis including the CAPS subgroup which had prior CAN treatment showed that CAN is an effective and safe treatment in those patients.

Disclosure of Interests: J. B. Kuemmerle-Deschner Grant/research support from: Jasmin Kuemmerle-Deschner is an employee of University of Tuebingen, Germany, and received consultants/speakers fees from Novartis and SOBI pharmaceuticals and grant support from SOBI and Novartis. Consultant for: Chugai, Novartis, Gerd Horneff: None declared, Prasad Oommen: None declared, Julia Weber: None declared, Ivan Foeldvari Consultant for: Chugai, Novartis, Pfizer and Shire, Norbert Blank Grant/research support from: Jasmin Kuemmerle-Deschner Grant/research support from: SOBI and Novartis, Norbert Blank Grant/research support from: SOBI and Novartis, Michael Borte Grant/research support from: Pfizer and Shire, Ivan Foeldvari Consultant for: Chugai, Novartis, Gerd Horneff: None declared, Prasad Oommen: None declared, Catharina Schuetz: None declared, Frank Weller-Heinemann: None declared, Julia Weber- Arden Employee of: Novartis, Tillmann Kalinich Grant/research support from: Novartis. Speakers bureau: Sobi, Roche, Novartis, CLB DOI: 10.1136/annrheumdis-2019-eular.6224

RECOMMENDATIONS:

- The efficacy of LEF in combination with GCs therapy was significantly superior to conventional GCs monotherapy in preventing relapses in patients with IgG4-RD.

- Combination therapy of GCs and LEF may be considered as first-line therapy for the induction of remission in IgG4-related disease (IgG4-RD).

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EULAR RECOMMENDATIONS FOR THE DIAGNOSIS AND THE MANAGEMENT OF RHEUMATIC IMMUNE-RELATED ADVERSE EVENTS DUE TO CANCER IMMUNOTHERAPY


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Disclosure of Interests: Rheumatic immune-related adverse events (rIAEs) are increasingly recognized musculoskeletal manifestations in cancer patients receiving immune checkpoint targeted immunotherapy (1). Since they represent a spectrum of new clinical entities and a robust evidence base is lacking, a task force was convened to reach a joint expert consensus regarding their identification and management due to the lack of dedicated clinical trials.

Objectives: To develop EULAR recommendations for the diagnosis and the management of rheumatic rIAEs due to cancer immunotherapy, based on literature and expert opinion.

Methods: Recommendations were developed according to the 2014 EULAR Standard Operating Procedures. The task force consisted of 19 clinical experts from Europe and North America (14 rheumatologists, 2 internists and 3 oncologists) in 1 clinical epidemiologist, 1 allied health professional and 2 patient representatives. During the first meeting, the group defined the focus of the task force, the target population, and formulated research questions. A systematic literature research was performed by one fellow (MK) with the help of a librarian. Based on available evidence and using a consensus procedure, recommendations were developed during a second meeting. The level of agreement was determined by an anonymous voting process.

Results: 4 overarching principles and 10 recommendations were developed. The overarching principles define the role of rheumatologists and highlight the shared decision-making process between patients, oncologists and rheumatologists. One recommendation addresses the referral process, two address the diagnosis, and five address the therapeutic strategy of cancer patients experiencing rheumatic, musculoskeletal, and systemic signs or symptoms while receiving immunotherapy. An additional recommendation was included to address pre-existing rheumatic conditions and the last focuses on the diagnostic approach before immunotherapy.

Conclusion: These recommendations provide the basis of a EULAR consensus on the diagnosis and the management of rheumatic rIAEs.

REFERENCE:

The Efficacy of Calcineurin Inhibitors in Patients with Adult-Onset Still’s Disease: Multi-Centre Historical Cohort Study

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Background: Adult-onset Still’s disease (AOSD) is a systemic inflammatory disease generally responsive to non-steroidal anti-inflammatory drugs (NSAIDs) therapy. Cases of non-responsive CS monotherapy are frequently found in clinical practice. In such cases, metrotexate and/or biologics including TNF-α, IL-1, or IL-6 inhibitors are used [1]. However, further treatment options are required for refractory AOSD patients who are intolerant to meloxicam and/or biologics. Calcineurin inhibitors (CNI) downregulate T cell activation through inhibiting IL-2 transduction and signal transduction. Therefore, they are reasonable therapeutic medication for AOSD considering T cells and subsequently activated macrophages play a pathophysiological role in AOSD [2]. Nevertheless, only a few case series have indicated effects of CNI for difficult AOSD.

Objectives: To evaluate the efficacy of CNI in patients with AOSD.

Methods: This is a multi-centre historical cohort study comprised the consecutive cases of AOSD in accordance with the classification criteria. The primary endpoint was set as the time from the initiation of treatment to event defined as death of any causes or relapse of AOSD requiring an increase of CS dose. Secondary endpoints were set as persistency rate of CNI and safety. Based on the recurrent event data analysis, these endpoints were evaluated for each event. We compared the frequency of events between groups according to the treatment that included calcineurin inhibitors (CNI+) or conventional therapy without calcineurin inhibitors (CNI-).

Results: One hundred seventy-eight patients were enrolled in this study. Mean age was 46.0 years old, and median follow-up period 36 months. Seventy-one events in 56 patients were treated with therapeutic regimen including CNI (CNI+), cyclosporine: 14, tacrolimus: 60, and 176 events in 138 patients were treated with the conventional therapy excluding CNI (CNI-). CNI were used in AOSD patients with recurrent history, high ferritin level, serositis, hemophagocytic syndrome (HPS) and/or disseminated intravascular coagulation (DIC). The CNI+ group had longer event-free survival than the CNI- group (83% versus 75% at 5th
References:


Disclosure of Interests: Masato Tarumi: None declared, Hiroyuki Nakamura: None declared, Yuichiro Fujieda: None declared, Hirokio Kitagawa: None declared, Hideki Kasahara: None declared, Atsushi Noguchi: None declared, Yoshitake Aramaki: None declared, Tatsuya Horita: None declared.

Results: B cells from IgG4-RD patients (i) produced the pro-fibrotic molecule PDGF-B and stimulated collagen production by fibroblasts; (ii) expressed enzymes implicated in extracellular matrix remodeling such as LOXL2; (iii) produced the chemokatic factors CCL-4, CCL-5, and CCL-11; and (iv) induced the production of these same chemokines by activated fibroblasts. Plasmablasts expressed sets of genes implicated in fibroblast activation and proliferation, and therefore represent cells with intrinsic pro-fibrotic properties.

Conclusions: We have demonstrated that B cells, contribute directly to tissue fibrosis in IgG4-RD. These unanticipated pro-fibrotic properties of B lymphocytes, particularly of plasmablasts, might be relevant for fibrogenesis in other fibro-inflammatory disorders and for wound healing processes in physiological conditions.

References:


B Lymphocytes Directly Contribute to Tissue Fibrosis in IgG4-Related Disease

Emanuel Della Torre 1, Elena Rigamonti 2, Cory Perugino 2, Massimo Falconi 2, John H. Stone 2, Angelo Mariani 1, Shif Pilla 2.

San Raffaele Scientific Institute, Unit of Immunology, Rheumatology, Allergy and Rare Diseases, Milan, Italy; 2Ragon Institute of MGH, MIT, HARVARD, Cambridge, United States of America; 3San Raffaele Scientific Institute, Pancreas Center, Milan, Italy.

Background: IgG4-related disease (IgG4-RD) is a fibro-inflammatory condition marked by rapid clinical improvement after selective depletion of B lymphocytes with rituximab. This feature suggests that B cells might participate in fibrogenesis and wound healing (1-3).

Objectives: In the present work we aimed to demonstrate that B lymphocytes contribute directly to tissue fibrosis in IgG4-RD.

Methods: Total circulating CD19+ B-lymphocytes, naïve B cells, memory B cells, or plasmablasts from IgG4-RD patients were cultivated with human fibroblasts. Pro-fibrotic soluble factors and collagen production in the co-cultures were assessed by ELISA and Lumines assays. RNA-sequencing and quantitative RT-PCR were used to assess fibroblast activation in the presence of B cells, as well as the induction of pro-fibrotic pathways in B cell subsets. Relevant pro-fibrotic and inflammatory molecules were confirmed in vitro by functional experiments and on IgG4-RD tissue sections by multi-color immunofluorescence studies.

Results: B cells from IgG4-RD patients (i) produced the pro-fibrotic molecule PDGF-B and stimulated collagen production by fibroblasts; (ii) expressed enzymes implicated in extracellular matrix remodeling such as LOXL2; (iii) produced the chemokatic factors CCL-4, CCL-5, and CCL-11; and (iv) induced the production of these same chemokines by activated fibroblasts. Plasmablasts expressed sets of genes implicated in fibroblast activation and proliferation, and therefore represent cells with intrinsic pro-fibrotic properties.

Conclusions: We have demonstrated that B cells, contribute directly to tissue fibrosis in IgG4-RD. These unanticipated pro-fibrotic properties of B lymphocytes, particularly of plasmablasts, might be relevant for fibrogenesis in other fibro-inflammatory disorders and for wound healing processes in physiological conditions.

References:


Objective: Our aims were to: a) assess long-term post-transplant survival in patients with CTD-ILD and b) compare post-transplant survival of patients with CTD-ILD with patients with idiopathic pulmonary fibrosis (IPF).

Methods: Single center study in a referral center for lung transplant of all patients who underwent lung transplantation for CTD-ILD between 1998 and 2017. This cohort was compared with patients with IPF (group-matched for age, transplant year and basiliximab induction). Cumulative survival rates after transplantation were estimated by the Kaplan-Meier method and compared between groups using the log-rank test.

Results: We studied 26 patients with CTD-ILD matched to 26 patients with IPF. The underlying diseases of patients with CTD-ILD were: Rheumatoid arthritis (6), Scleroderma (6), Sjögren syndrome (4), ANCA-vasculitis (3), Anti synthetase syndrome (2), Dermatomyositis (1), Systemic lupus erythematosus (1). The comparative study of baseline characteristics between both groups is shown in the Table. All of RA patients undergoing transplantation in our study had the histologic subtype of usual interstitial pneumonia (UIP) whereas non-specific interstitial pneumonia (NSIP) was the most common histologic subtype of ILD associated with the rest of CTD. Cumulative survival rates at 5 year post-transplant did not differ significantly between CTD-ILD and IPF [42.4% vs 65.8% (p=0.075)] (FIGURE 1).

Conclusion: Our retrospective analysis showed a trend to lower long-term post-transplant survival than in those with IPF, however no statistical differences were found in cumulative survival rates at 5-years post-transplant. These data support that lung transplantation should be considered in patients with end-stage CTD-ILD.


Background: Interstitial lung disease (ILD) is one of the most serious complications associated with connective tissue diseases (CTD). Patients with ILD have increased mortality and limited treatment options. Lung transplant has been recognized as an option for patients with end-stage CTD-ILD. However, rheumatic diseases are still sometimes considered a contraindication for lung transplant because of concerns for worse outcomes.

Table 1. Still activity score (SAS)

<table>
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<tr>
<th>SAS</th>
<th>0 point</th>
<th>1 point</th>
<th>2 points</th>
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<tr>
<td>Neutrophilia% ≥65</td>
<td>No</td>
<td>Yes</td>
<td></td>
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<tr>
<td>Ferritin ≥ 350 ng/ml</td>
<td>No</td>
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[FIGURE 1. Boxplot of SAS and patients' global assessment of disease activity]

OP0169

LONG-TERM SURVIVAL IN LUNG TRANSPLANTATION FOR INTERSTITIAL LUNG DISEASE ASSOCIATED WITH CONNECTIVE TISSUE DISEASES. STUDY OF 26 CASES OF A SINGLE CENTER

D. Prieto-Peña, Monica Calderón-Goecke, Monika Martínez-Meñaca, Victor Manuel Mora-Cuesta, Sonia Fernández-Rozas, David Iturbe-Fernández, Jose Manuel Cifrián-Martínez, Miguel A. González-Gay, Ricardo Blanco. Marqués de Valdecilla University Hospital, Santander, Spain

Background:Interstitial lung disease (ILD) is one of the most serious complications associated with connective tissue diseases (CTD). Patients with ILD have increased mortality and limited treatment options. Lung transplant has been recognized as an option for patients with end-stage CTD-ILD. However, rheumatic diseases are still sometimes considered a contraindication for lung transplant because of concerns for worse outcomes.

Objectives: Our aims were to: a) assess long-term post-transplant survival in patients with CTD-ILD and b) compare post-transplant survival of patients with CTD-ILD with patients with idiopathic pulmonary fibrosis (IPF).

Methods: Single center study in a referral center for lung transplant of all patients who underwent lung transplantation for CTD-ILD between 1998 and 2017. This cohort was compared with patients with IPF (group-matched for age, transplant year and basiliximab induction). Cumulative survival rates after transplantation were estimated by the Kaplan-Meier method and compared between groups using the log-rank test.

Results: We studied 26 patients with CTD-ILD matched to 26 patients with IPF. The underlying diseases of patients with CTD-ILD were: Rheumatoid arthritis (6), Scleroderma (6), Sjögren syndrome (4), ANCA-vasculitis (3), Anti synthetase syndrome (2), Dermatomyositis (1), Systemic lupus erythematosus (1). The comparative study of baseline characteristics between both groups is shown in the Table. All of RA patients undergoing transplantation in our study had the histologic subtype of usual interstitial pneumonia (UIP) whereas non-specific interstitial pneumonia (NSIP) was the most common histologic subtype of ILD associated with the rest of CTD. Cumulative survival rates at 5 year post-transplant did not differ significantly between CTD-ILD and IPF [42.4% vs 65.8% (p=0.075)] (FIGURE 1).

Conclusion: Our retrospective analysis showed a trend to lower long-term post-transplant survival than in those with IPF, however no statistical differences were found in cumulative survival rates at 5-years post-transplant. These data support that lung transplantation should be considered in patients with end-stage CTD-ILD.


References:

[FIGURE 1. Boxplot of SAS and patients' global assessment of disease activity]
Objective: To explore the performance of these provisional criteria in a cohort of Spanish patients with IgG4-RD.

Methods: Data were obtained from the Spanish IgG4-RD registry (REEIRIGG4) from October 2013 to December 2018, including 9 centers. Patients needed to fulfill almost 1 of the available diagnostic criteria sets (pathology consensus and/or comprehensive). Provisional ACR/EULAR classification criteria (PAECC) were applied based on the public information disclosed at the abovementioned meeting.

Results: One hundred patients were included. Thirty-four (34%) were females, median age at diagnosis was 54.8 years (IQR 20.7). The ethnicity of the participants was: Caucasian 83%, Hispanic 12% and North-African/Middle-East 5%. Ninety-two percent were diagnosed with a biopsy. Regarding the diagnostic criteria, 85% met consensus pathology criteria and 94% comprehensive criteria.

Seventy-one individuals (71%) met the PAECC including entry criteria, exclusion criteria, and one full diagnostic criteria set (pathology consensus or comprehensive). Seventy-one percent of the Spanish patients participating in the PAECC (55%) had an inclusion criteria score under 19 points (median 12): 3 patients (4%) did not have a biopsy, 8 (11%) biopsies had partial reports, and 10 subjects (14.3%) had normal serum IgG4 levels. Six (8.5%) of 38 patients who did not meet the PAECC had involvement limited to the head and neck and 3 (19%) had retroperitoneal or aortic involvement.

Conclusion: Seventy-one percent of the Spanish patients participating in the REEIRigG4 met the 2018 PAECC, while all of them met almost one of the available diagnostic criteria sets (pathology consensus and/or comprehensive). Seventy-one percent of the Spanish patients participating in the PAECC had an inclusion criteria score under 19 points (median 12): 3 patients did not have a biopsy, 8 biopsies had partial reports, and 10 subjects had normal serum IgG4 levels. Six of 38 patients who did not meet the PAECC had involvement limited to the head and neck and 3 had retroperitoneal or aortic involvement.

REFERENCE:

Disclosure of Interests: None declared


Thursday, 13 June 2019

From child to adult care – breaking down the barriers of transition

Disclosure of Interests: None declared

The Erosive hand osteoarthritis (OA) phenotype is associated with more inflammation, localized in the hand and it also seems to be associated with psoriasis. This differentiates from radiographic hand OA. The study was conducted in the Prospective Cohort of Osteoarthritis A Coruña (PROCOAC). This cohort consists of 1107 subjects, of which 747 suffered from radiographic hand OA. We split the cohort into patients with and without erosive hand OA, and analyzed both clinical and demographic data within each group, together with the assessment of the Australian Consortium on Ankylosing Spondylitis Hand (AUSCAN) index. The study consisted in a univariate analysis comparing different variables between both groups, followed by a stepwise logistic regression analysis taking into account the significant confounder variables analyzed in the Univariate approach.

Results:
The mean age of the cohort was 63.23±8.85 years and consisted of 627 females and 120 males. Of the 747 OA patients, 179 had erosive hand OA and 568 did not. The univariate analysis revealed that patients with erosive hand OA were younger (60.25±10 vs 64.16±8.86; p<0.001), smokers (p=0.005), with lower body mass index (p<0.005), increased inflammatory episodes (p<0.001) and, interestingly, showed MetS as a risk factor too (OR=1.25-3.58; p=0.002). Regarding the number of damaged joints, a lower frequency of both knee and hip OA was detected in patients with erosive hand OA compared with non-erosive patients (24.4% vs 54.7% for knee OA prevalence and 11.6% vs 16.7% for hip OA prevalence); however, only knee OA occurred at a significant lower frequency (OR=0.267; 95% CI=0.182-0.393; p<0.001). In addition, the three subscales of the AUSCAN score showed significantly higher mean values in patients with the erosive phenotype: pain (57.67±29.30 vs 43.86±31.45; p<0.001), function (55.61±27.68 vs 40.53±29.48; p<0.001) and stiffness (55.40±32.26 vs 60±36.23; p=0.001).

Conclusion:
The erosive hand OA phenotype is associated with more inflammation in younger patients, and worst AUSCAN score. Contrarily to the non-erosive phenotype, the presence of erosions associates with a lower occurrence of other forms of OA, specially knee OA. In our cohort, erosive hand OA seems to be more localized in the hand and it also seems to be associated with psoriasis. This different profile could serve the clinicians to provide personalized prevention strategies, and the researchers to investigate the pathogenesis of this specific phenotype.

References:
PARTIAL KNEE REPLACEMENT IS ASSOCIATED WITH A LOWER RISK OF VENOUS THROMBOEMBOLISM AND OPIOID USE THAN TOTAL KNEE REPLACEMENT BUT INCREASED RISK OF LONG-TERM REVISION: A MULTINATIONAL, MULTIDATABASE, PROPENSITY SCORE-MATCHED, COHORT ANALYSIS INCLUDING OVER 260,000 PATIENTS

Daniel Pieiro-Alhambra 1, Edward Burn 1, James Weaver 2, Anthony G Gens 3, Henry Morgan Stewart 1, Patrick Ryan 2. 1Centre for Statistics in Medicine, OXFORD, UK; 2Janssen Research and Development, TITUSVILLE, NJ; 3University of Oxford, OXFORD, UK

Background: Knee replacement is one of the few effective treatments for severe knee osteoarthritis. A number of surgical interventions are available, including two main types: partial or total knee replacement.

Objectives: We aimed to assess the outcomes of partial compared to total knee replacement.

Methods: We conducted a multi-database propensity score-matched cohort study. Data was obtained from 4 US claims databases (IBM MarketScan Commercial Database, IBM MarketScan Medicare Supplemental Database, MDVR, Optum), de-identified Clininformatics Datamart, Extended - Date of Death (Optum), and Pharmetrics), and 1 UK primary care electronic medical record database (THIN).

All people aged 40 years or older at the time of knee replacement surgery were included. Data were mapped to a common data model (OMOP), and processed using analytical tools developed by the OHDSI community.

Participants were followed up from the date of their first knee replacement and for up to 5 years. Outcomes included short-term (60-day) post-operative complications (infection, venous thromboembolism, mortality, readmission), opioid use in the 3-12 months post-surgery as a proxy for persistent pain, and 5-year revision risk.

Results: Out of 71 evaluated patients with symptomatic erosive HOA, and 64 matched the inclusion criteria and were randomized. Among them, 32 patients were randomized in the placebo group and 32 in the Methotrexate group. There was no significant difference between the two groups on the primary endpoint at 3 months, with an average decrease in VAS in the placebo group of 8.36 mm (95% CI: 25.15, and 17.47 mm (95% CI: 28.37) in the treatment group (p = 0.1797). At 12 months, no difference was found in the evolution of pain between the two groups (p = 0.6045) as well as in the functional evolution. In subjects taking Methotrexate, joints move more to a remodeling phase undergoing treatment (27%) than placebo subjects (15%) (p = 0.0278). They also seem to evolve less towards erosion when their joints present a space loss (29% become erosive under placebo, against 8% in the Methotrexate group) (p = 0.0879).

Conclusion: Our study does not show superior efficacy of MTX over placebo over pain and function in subjects with erosive HOA. Our results suggest a possible structural effect on the radiological evolution of HOA under Methotrexate.

Disclosure of Interests: None declared


HEALTH-RELATED QUALITY OF LIFE IN HAND OSTEOARTHRITIS PATIENTS FROM THE GENERAL POPULATION AND THE OUTPATIENT CLINIC

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Background: In osteoarthritis (OA) patients health-related quality of life (HRQoL) is decreased. Whether patients with OA seeking care in a rheumatology outpatient clinic experience more impact on HRQoL than those in the general population is unknown.

Objectives: To investigate the impact of hand OA on physical and mental HRQoL in the general population, and to investigate the difference in impact between patients who have, and who have not been referred to a medical specialist.

Methods: In the population-based Netherlands Epidemiology of Obesity (NEO) study, middle-aged participants were recruited from the greater area of Leiden. In the Hand OSTeoArthritis in Secondary care (HOSTAS) study, patients with a rheumatologist's diagnosis of primary hand OA were recruited from the outpatient clinic at the Leiden University Medical Center, a secondary and tertiary referral center. In both cohorts, hand and knee OA was defined by the ACR clinical classification criteria. Patients with fibromyalgia or inflammatory rheumatic conditions were excluded. For the current analyses, only patients classified with hand OA alone were included. HRQoL was measured with the SF-36 questionnaire; we calculated standardized scores on a scale of 0 to 100 with subsequent application of a norm-based transformation (mean 50, standard deviation 10). Linear regression analyses, corrected for age, sex, education, ethnicity and BMI, were used to study cross-sectional associations between OA and HRQoL. Data are presented as regression coefficients with 95% confidence intervals (CI). Because a suitable reference group without OA was lacking in the HOSTAS study, these patients were compared to the normative value of 50. Previous research concluded a minimal clinically important difference of 2 points on the SF-36 scale, which was used to assess clinical relevance of differences in scores.

Results: Of the 6,334 NEO participants 8% were classified with only hand OA and 4% were classified concurrent hand and knee OA. The HOSTAS cohort consisted of a total of 538 participants with hand OA, of whom 57% fulfilled the ACR criteria for only hand OA and 32% was defined with concurrent hand and knee OA. In the population-based NEO study, mean PCS was reduced with -2.4 (-3.6;-1.3) in participants with only hand OA, compared to participants without hand or knee OA (table 1). The subscales bodily pain and physical functioning were affected with the most with mean differences of -3.4 (-4.8;-2.2) and -2.1 (-3.0;-1.1). Mental HRQoL was not reduced in participants with only hand OA, compared to participants without OA. In the population-based cohort 14% of participants with hand OA reported to have visited a medical specialist for OA. Participants with hand OA that have been referred to a medical specialist showed a lower physical HRQoL with a

Disclosure of Interests: None declared


METHOTREXATE IN PATIENTS WITH HAND OSTEOARTHRITIS: A RANDOMISED, DOUBLE-BLIND, PLACEBO CONTROLLED TRIAL

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Background: To date, no studies have been published on the effect of Methotrexate (MTX) in hand osteoarthritids (HOA).

Objectives: The aim of our study is to examine the effect of methotrexate on pain in symptomatic erosive HOA, as well as its functional and structural effect using MRI and radiography.

Methods: This prospective, single-center, randomized, double-blind, placebo-controlled study followed patients with HOA over 12 months. Patients were randomized to Methotrexate 10 mg per week or placebo.

The primary endpoint was pain assessment at 3 months, and secondary end-points were clinical (Visual Analogue Scale “VAS” pain at 12 months), and radiographic (radiographic anatomical score, then the Ghent University Score System “GUSS” and MRI).

All subjects aged between 45 and 85 years, who had apparent NSAIDs and pain treatment failure with a VAS greater than 4/10, and at least one erosive joint were included.

Results: Out of 71 evaluated patients with symptomatic erosive HOA, and 64 matched the inclusion criteria and were randomized. Among them, 32 patients were randomized in the placebo group and 32 in the Methotrexate group. There was no significant difference between the two groups on the primary endpoint at 3 months, with an average decrease in VAS in the placebo group of 8.36 mm (95% CI: 25.15, and 17.47 mm (95% CI: 28.37) in the treatment group (p = 0.1797). At 12 months, no difference was found in the evolution of pain between the two groups (p = 0.6045) as well as in the functional evolution. In subjects taking Methotrexate, joints move more to a remodeling phase undergoing treatment (27%) than placebo subjects (15%) (p = 0.0278). They also seem to evolve less towards erosion when their joints present a space loss (29% become erosive under placebo, against 8% in the Methotrexate group) (p = 0.0879).

Conclusion: Our study does not show superior efficacy of MTX over placebo over pain and function in subjects with erosive HOA. Our results suggest a possible structural effect on the radiological evolution of HOA under Methotrexate.

Disclosure of Interests: None declared

mean difference in the PCS of −3.9 (-6.7; -1.2), but no difference in mental HRQoL, compared with participants with hand OA that have not reported consulting secondary care for OA (table 2). In patients with only hand OA from the outpatient clinic, the PCS (-3.5), bodily pain (-4.9), vitality (2.8) and role functioning – physical (2.2) scales were clinically relevantly reduced, but mental HRQoL was not affected.

Conclusion: Participants with hand OA from the general population had a clinically relevant lower physical HRQoL, but not mental HRQoL. Physical HRQoL was further reduced in patients consulting secondary care and in co-occurrence with knee OA. Hence, patients with hand OA in secondary care experience more impact on physical HRQoL than patients in the general population.

Disclosure of Interests: None declared

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Background: Metabolic syndrome (MetS) has been suggested a crucial role in the pathophysiology of osteoarthritis (OA); however, currently none of studies have examined the associations between MetS and structural changes on MRI.

Objectives: To describe the associations between MetS and its components and structural changes on MRI including knee cartilage volume (CV) loss and bone marrow lesion (BML) change over 10.7 years.

Methods: Longitudinal data on 435 participants (mean age 61 years, 50% of females) from a population-based cohort study were analysed. Blood pressure, glucose, triglycerides, and high-density lipoprotein (HDL) were collected. MetS was defined based on the National Cholesterol Education Program-Adult Treatment Panel III criteria. MRI of the right knee was performed to measure CV and BML. Radiographic knee osteoarthritis (ROA) was assessed by X-ray.

Results: 32% of participants had MetS and 60% had ROA. In multivariable analysis, the following were independently associated with medial tibial CV loss [MetS: β=-0.30%; central obesity: β=-0.26%; low HDL: β=-0.26% per annum]. MetS, hypertriglyceridemia and low HDL were also associated with higher risk of BML size increase in the medial compartment [MetS: relative risk (RR) 1.72, 95%CI 1.22-2.43; Hypertriglyceridemia: RR 1.43, 95%CI 1.01-2.02; low HDL: RR 1.87, 95%CI 1.1-3.1]. After further adjustment for central obesity, MetS and low HDL remained significant with both medial tibial CV loss and BML size increase. The number of components of MetS correlated with greater CV loss and BML size increase (both P for trend <0.05). There were no statistically significant associations in the lateral compartment.

Conclusion: MetS and low HDL are associated with medialized compartment CV loss and BML worsening, suggesting that targeting MetS has the potential to prevent or slow structural change in knee osteoarthritis.

Disclosure of Interests: None declared


### CARDIOVASCULAR COMORBIDITIES HAVE A DELETERIOUS IMPACT ON KNEE OSTEOARTHRITIS PROGNOSIS AT 5 YEARS: DATA FROM THE PROSPECTIVE KOHALA COHORT

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Background: The long-term effect of comorbidities on progression of structural changes in osteoarthritis (OA) remains poorly understood. Patients with knee OA have been reported to be at increased risk of several comorbidities including cardiovascular diseases (CVD). Nevertheless, the impact of all comorbidities on structural progression and on arthroplasty, not only in knee but also in hip OA, should be further defined.

Objectives: The objective of our study was to explore the relationship between comorbidities and the progression of structural changes in symptomatic knee and/or hip OA patients over 5 years.

Methods: The KOHALA (Knee and Hip OsteoArthritis Long-term Assessment) cohort is a French prospective multicenter observational cohort that included 878 subjects, aged 40 to 75 years, with symptomatic hip and/or knee OA at baseline (Kellgren and Lawrence (KL) ≥ 2). The structural progression was defined by the increase of one point of KL (KL+1) or incidence of total knee or hip replacement at 5 years. Various comorbidities were analyzed: cardiovascular diseases excluding hypertension (coronary artery disease, heart failure, stroke, lower limb arteriopathy), hypertension, diabetes, smoking, dyslipidemia, metabolic syndrome, osteoporosis, neurological (e.g. Parkinson’s disease, dementia), digestive (e.g. gastrointestinal reflux disease, ulcer), pulmonary (e.g. asthma, COPD), and psychiatric (depression, anxiety) diseases. Multivariate analysis was performed separately in hip and knee OA adjusted on age, sex and body mass index (BMI). Subjects with a BMI> 30 kg/m² were excluded from the analysis given the close relationship between obesity and the different comorbidities analyzed. Subjects with KL = 4 at the time of inclusion were also excluded from the analysis.

Results: Data from 631 non-obese subjects (BMI<30 kg/m²) were analyzed. At 5 years, cardiovascular diseases were significantly associated with the 5-year KL change in knee OA (OR = 2.6 [1.3-5.7], p<0.02) and with knee arthroplasty (OR = 3.4 [1.1-11.2], p<0.04). Such associations were not found at the hip. Other comorbidities had no significant impact on knee OA structural progression. No significant relationship was found between any type of comorbidities and hip OA structural progression.

Conclusion: This 5-year data analysis of the KOHALA cohort revealed a significant association between cardiovascular comorbidities and structural progression of knee OA in subjects without obesity (BMI<30 kg/m²). Other types of comorbidities do not appear to influence the structural prognosis of OA. These results argue for an integrated management of cardiovascular comorbidities in knee OA patients and highlight the differences between hip and knee OA.

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DO DISTINCT PAIN PHENOTYPES HAVE DIFFERENT RISK OF KNEE REPLACEMENT: A 13-YEAR FOLLOW-UP STUDY?

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Background: Pain is the main impetus for osteoarthritis (OA) patients to seek healthcare including joint replacement. The pain experience is very heterogeneous and affected by factors across multiple domains—peripheral, psychological, and neurological, which suggests the existence of homogeneous subgroups/phenotypes within OA patients with pain. We recently identified three pain phenotypes using a wide spectrum of factors including main pain dimensions (structural damage on MRI, body mass index (BMI), comorbidities, psychological and multi-site pain (a surrogate of neurological factor)).

Objectives: To examine whether the risk of knee replacement (KR) varied when these three pain subgroups were compared.

Methods: 1099 participants (mean age 63 years; range 51-81 years) from a population-based cohort study were recruited at baseline. 875, 768 and 563 participants attended years 2.6, 5.1 and 10.7 follow-up, respectively. Demographic, psychological and multi-site pain questionnaires at each time-point. Presence of pain (yes/no) in the neck, back, hands, shoulders, hips, knees and feet was also assessed by questionnaire at each time-point. KR up to 13.7 years after recruitment was identified by linking to the Australian Orthopaedic Association National Joint Replacement Registry. Latent class analysis was used to differentiate pain phenotypes by considering sex, BMI, emotional problems, education level, comorbidities, number of painful sites and knee structural damage on MRI. Log-binomial regression was used to evaluate the association between three pain phenotypes and risk of KR.

Results: 963 participants were included in the analysis (BMI 27.7 kg/m², 50% female). Three distinct phenotypes were identified: Class 1: high prevalence of emotional problems and low prevalence of structural damage (25%); Class 2: high prevalence of structural damage and low prevalence of emotional problems (20%); Class 3: low prevalence of emotional problems and low prevalence of structural damage (55%). Participants in Class 1 had greater pain severity than those in Class 2 and 3. During a follow-up of 13.7 years, there were 46 right and 51 left TKR‘ s in 79 participants In multivariable analyses, participants in Class 1 and 2 had higher risk of requiring KR on the right [Class 1 vs. Class 3: relative risk (RR) 6.66, 95% confidence interval (CI) 2.17-20.49; Class 2 vs. Class 3: RR 14.14, 95%CI 4.85-41.22, left] Class 1 vs. Class 3: RR 2.75, 95%CI 1.22-6.19; Class 2 vs. Class 3: RR 3.46, 95%CI 2.64-11.32], and any knee joints (Class 1 vs. Class 3: RR 3.68, 12.60) compared to Class 3, but the associations were stronger with Class 2 than Class 1.

Conclusion: Participants with distinct pain phenotype groups have different risks of KR. This suggests that the identified phenotypes reflect distinct clinical subgroups with different prognoses. As expected the highest risk of KR was found in those with the most structural damage (Class 2). However, those participants with low structural damage have an increased risk of KR when they have high comorbidities. Low emotional problems, indicating that selection of subjects for KR could be improved by screening out those in Class 3.

Disclosure of Interests: None declared

LOW-DOSE PREDNISOLONE IN PATIENTS WITH HAND OSTEOARTHRITIS (HOPE): RESULTS FROM A RANDOMISED DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL

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Background: Hand osteoarthritis (OA) is a prevalent joint disease with high disease-burden in need for effective therapeutic options. Studies have shown that synovial inflammation is often present in hand OA and a main determinant of pain and radiographic disease progression.

Objectives: To investigate the efficacy and safety of short-term low-dose prednisolone in patients with painful hand OA.

Methods: This randomised, double-blind, placebo-controlled trial enrolled patients with painful hand OA, fulfilling American College of Rheumatology criteria, and signs of synovial inflammation. Patients with <4 interphalangeal joints (IPJ) with osteoarthritic nodes, >1 IPJ with soft swelling or erythema and >1 IPJ with positive power Doppler signal (PDS) or synovitis grade ≥2 on ultrasound, were eligible. Key exclusion criteria were chronic inflammatory rheumatic diseases, psoriasis, using immune modulating drugs within 90 days before baseline, and predominant thumb base pain. Eligible patients with visual analogue scale (VAS) finger pain ≥30 mm, flaring ≥20 mm upon non-steroidal anti-inflammatory drug washout, were randomised to receive prednisolone 10 mg daily for 6 weeks or placebo, followed by a two-week tapering scheme and 6 weeks without study medication. Outcomes were assessed at 2, 4, 6, and 14 weeks. Primary endpoint was VAS finger pain at week 6 in intention-to-treat analysis. Secondary clinical endpoints included fulfilment of OMERACT-OARSI responder criteria, Australian/Canadian Hand OA index (AUCAIN) pain/function, Functional Index for Hand OA (FIHOA), VAS patient global assessment, Short-Form 36 and grip strength. Imaging endpoints included ultrasound synovitis and PDS.

Results: Of 92 patients (mean (SD) age 63.9 (8.8), 79% women) randomised to prednisolone (n=46) or placebo (n=46), 42 patients in each group completed the study. Baseline characteristics were well-balanced between the groups. The mean (SD) change from baseline to week 6 in VAS finger pain was -21.5 (21.7) in the prednisolone and -5.2 (24.3) in the placebo group, with a mean between-group difference of -16.5 (95% confidence interval (CI) -26.1 to -6.9; figure). At week 6, 33 (72%) patients in the prednisolone versus 15 (33%) in the placebo group fulfilled OARSI responder criteria (odds ratio 5.3, 95% CI 2.0 to 13.6, p<0.001). In analogy with the primary endpoint, prednisolone was superior to placebo in most other secondary clinical endpoints (table). Ultrasound synovitis significantly improved at week 6 in the prednisolone compared to the placebo group, while no difference was observed in PDS (table). After tapering, between-group
RESULTS showed that the IFN muscle signature may play a predominant role in some subgroups but not all IIM groups in the pathogenesis of IIM.

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SYNTHETIC PEPTIDES TARGETING CD206 INHIBIT PATHOGENIC MACROPHAGES IN SYSTEMIC SCLEROSIS

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Objectives: To determine the macrophage activation signature in SSc assess CD206 as a biomarker of ongoing fibrotic activity, and measure the effect of the peptides on macrophage activation and macrophage-fibroblast cross-talk.

Methods: scCD206 was assayed in plasma (n=50 healthy, 50 limited SSc, 50 diffuse SSC), and suction blister fluid (BF) obtained over active lesions by ELISA, sST2LEC (monocyte interferon signature) and IL-31 (Th2 signature) were assayed for comparison. Cell surface CD206 and DAMP receptor P2X7 were assayed by flow cytometry. The macrophage activation signature was investigated further by qPCR for inflammatory M1, as well as M2-like gene expression (IFNγ, Arg1, CD206). Macrophage-fibroblast cross talk was assessed using media transfer following heat activation to SSc dermal fibroblasts assayed by qPCR for collagen I. The macrophage secretome was determined by LumineX and ELISA

Results: CD206 was significantly elevated in SSc BF (SSC median scCD206 42, HC 31 pg/ml, p<0.041). Plasma scCD206 was raised in diffuse limited SSc (P<0.0103) and was correlated with ESR (R=0.364, p<0.009) and sST2LEC (R=0.244, p<0.05), but not disease duration or IL-31. By flow cytometry both CD206 and P2X7 were highly expressed by SSc macrophages (mean fluorescence SSC, 776.1 SD=409.1, 724.4 SD=455.3 vs HC 632.2 SD=73.7, 472.9 SD=25.4), correlating with modified Rodnan Skin Score (mRSS) (p<0.05, r=0.51). Plasma sCD206 was raised in diffuse versus limited SSc (p=0.037) and showed that 68 interferon-stimulated genes (ISGs) were significantly up-regulated compared to NC and total of 1637 transcripts were differentially expressed (log2 Fold Change >1, Padj < 0.05). Unsupervised hierarchical clustering of these differentially expressed transcripts (DETs) revealed a prevalent interferon (IFN) signature and showed that 68 interferon-stimulated genes (ISGs) were significantly up-regulated in IIM. These 68 ISGs were used to cluster different IIM subgroups and distinct ISG expression was found. The mRNA expression levels of several ISGs (MX1, IFIH1, LAMPI, CMPK2, HERC6) in sequencing cohorts and expanding cohorts also confirmed the diverse ISG expression between different IIM subgroups. An IFN signature scoring system was established to quantify the IFN activity and subsequently IIM could be classified into IFN-Dominant, IFN-Moderate and IFN-Weak respectively based on the IFN intensity and different MSA subgroup. Moreover, the IFN-Dominant group showed much higher MXa expression on muscle biopsy than the IFN-Moderate and IFN-Weak group by immunohistochemistry.

Conclusion: We revealed a prominent IFN signature and MSA-based ISG expression heterogeneity in IIM through muscle transcriptomics. Preliminary
Shareholder of: Riptide Bioscience, Jesse Jaynes Shareholder of: Riptide Bioscience, James Stanway: None declared, Bahja Ahmed Abdi: None declared, Jesse Jaynes Shareholder of: Riptide Bioscience.
In addition, analysis for transcription factor motif enrichment in the differentially accessible peaks of the ATAC-Seq analysis revealed that motifs for TEAD2, RUNX family, and NFKB2 were less accessible, while motifs for JUN::FOS, NFPL2 and EHF were more accessible due to the chromatin changes. These results indicate that ATAC-Seq could provide a tool to assess the activity of these candidate transcription factors by changing chromatin configuration at the sites of their consensus sequences.

Conclusion: ATAC-Seq in combination with microarray analysis identified candidate mechanisms for the TGFB-regulated proliferotic effects of H19 X including direct effects on chromatin organization and on transcription factors associated with fibrotic pathways.

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Inflammmation-dependent Decreased Expression of CD29 on Circulating CD14+ Monocytes Facilitates Adhesion in Systemic Sclerosis

Michal Rudnik1, Michal Stellato1, Przemyslaw Blyszczuk1,2, Karin Klingen1, Jörg Henes4, Carol Feghali-Bostwick5, Oliver Distler1, Gabriela Kania1.

Objectives: We aimed to functionally investigate the role of circulating CD14+ monocytes in the course of SSC with a special focus on monocyte adhesion and the influence of CD29 expression. Methods: Biopsies from the heart, lungs and skin of SSC patients (n=11, 7, 7 respectively) and healthy controls (HC) (n=10, 7, 7 respectively) were analysed by immunohistochemistry for the presence of CD14+ cells. Polya RNA sequencing of CD14+ monocytes isolated from peripheral blood of SSC patients (n=6, age=54.4 ± 16.7), and CD14+ monocytes (n=5, age=51.8 ± 7.2) and age- and sex-matched HC (n=5, age=50.8 ± 9.7) was performed using illumina HiSeq 4000 platform. Differentially expressed genes were computed using DESeq2 algorithm. Gene ontology and pathway analysis were performed using Metacore software and ShinyApp. Expression of adhesion molecules was confirmed on the protein level using flow cytometry. Results: CD29 protein is highly expressed on CD4+ T-cells and plays an important role in the modulation of T-cell receptor signalling. Nevertheless, the function of this protein on monocytes is not completely understood. Objectives: We aimed to functionally investigate the role of circulating CD14+ monocytes in the course of SSC with a special focus on monocyte adhesion and the influence of CD29 expression. Methods: Biopsies from the heart, lungs and skin of SSC (n=11, 7, 7 respectively) and healthy controls (HC) (n=10, 7, 7 respectively) were analysed by immunohistochemistry for the presence of CD14+ cells. Polya RNA sequencing of CD14+ monocytes isolated from peripheral blood of SSC patients (n=6, age=54.4 ± 16.7), and CD14+ monocytes (n=5, age=51.8 ± 7.2) and age- and sex-matched HC (n=5, age=50.8 ± 9.7) was performed using illumina HiSeq 4000 platform. Differentially expressed genes were computed using DESeq2 algorithm. Gene ontology and pathway analysis were performed using Metacore software and ShinyApp. Expression of adhesion molecules was confirmed on the protein level using flow cytometry. Results: CD29 protein is highly expressed on CD4+ T-cells and plays an important role in the modulation of T-cell receptor signalling. Nevertheless, the function of this protein on monocytes is not completely understood. Objectives: We aimed to functionally investigate the role of circulating CD14+ monocytes in the course of SSC with a special focus on monocyte adhesion and the influence of CD29 expression. Methods: Biopsies from the heart, lungs and skin of SSC (n=11, 7, 7 respectively) and healthy controls (HC) (n=10, 7, 7 respectively) were analysed by immunohistochemistry for the presence of CD14+ cells. 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RITUXIMAB AND CYCLOPHOSPHAMIDE

**Pathogenicity of Functional Autoantibodies**

Exceeding respective parameter in Group B (p=0.2). The patient percentage with FVC 10% FVC increase was found in the third of the patients thus increase (p=0.034 and 0.000045, respectively), with median increment about 5%.

Evaluation of FVC time course in Groups A and B revealed significant FVC in RTM-treated patients.

During the follow-up period no change of the other studied parameters was revealed.

**Discussion of Results**: None declared.

**Disclosure of Interests**: None declared.


**OP0187**

**RITUXIMAB AND CYCLOPHOSPHAMIDE COMPARISON FOR EFFICACY AND SAFETY IN THE PATIENTS WITH SYSTEMIC SCLEROSIS ASSOCIATED WITH INTERSTITIAL LUNG DISEASE**

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**Background**: Cyclophosphamide (CyP) is considered as a drug of choice for the treatment of interstitial lung disease (ILD) in the patients with systemic sclerosis (SSc). However, according to the literature the use of CyP leads to rather limited and transient improvement of the pulmonary fibrosis. In this context the search for novel, more efficacious agents has been continued, such as attracting much attention rituximab (RTM).

**Objectives**: To compare the impact of CyP and RTM on SSc clinical manifestation and activity, and the safety of these agents in the open-label prospective non-randomized study.

**Methods**: 107 patients with the confirmed SSc diagnosis and ILD evidence based on HRCT findings were enrolled into the study. All patients received low-dose and moderate-dose prednisolone regimens. 36 patients (Group A) received parenteral CyP for 12±6 months at total dose 10.6±5 g (the average age 47±12 years, females 83%, SSc duration 5.1±4.4 years, diffused/localized forms 1/6.1), 71 patients (Group B) received RTM at total dose 1.43±0.66 g over the follow-up period 13.2±2 months (the average age 46±13 years, females 83%, SSc duration 5.6±4.4 years, diffused/localized forms 1/4.1); to 32 (45%) of them RTM was added to immunosuppressants due to inadequate efficacy of the latter. The time courses FVC (%), modified skin count (mRss, points), activity index (EScSG, points), left ventricle ejection fraction (LVEF, %), mean pulmonary arterial pressure (EchoCG), and cardiac rhythm and conductivity disorders (ECG) were evaluated.

**Results**: In Groups A and B the therapy was associated with significant decrease in mRss (p=0.009 and 0.001, respectively) and EScSG (p=0.000165 and 0.001, respectively). Increase in LVEF (8±1.8% to 8.3±6.7, p=0.02) was observed only in RTM-treated patients. Evaluation of FVC time course in Groups A and B revealed significant FVC increase (p=0.034 and 0.000045, respectively), with median increment about 5%.

In Group A FVC 10% FVC increase was found in the third of the patients thus exceeding respective parameter in Group B (p=0.2). The patient percentage with FVC decrease by ≥10% was similar in both groups.

During the follow-up period no change of the other studied parameters was observed.

The therapy was better tolerated in RTM-treated group; during RTM therapy adverse reactions emerged in significantly lower proportion of the patients (11/14%) compared with CyP-treated group (19/53%), p=0.0000.

**Conclusion**: Both agents effectively alleviated skin induration and EScSG, and significantly improved FVC. However, CyP use for a year slightly more frequently resulted in clinically significant FVC increase, probably due to low RTM cumulative dose. RTM was better tolerated compared to CyP. The study findings substantiate potential use of anti-B-cell therapy both as a first-line agent for ILD treatment in the patients with SSc, and in the event of CyP inefficacy of poor tolerability, especially in the patients with cardiacopathy.

**Disclosure of Interests**: None declared.


**OP0188**

**PATHOGENICITY OF FUNCTIONAL AUTOANTIBODIES AGAINST AT1R IN A MOUSE MODEL OF SYSTEMIC SCLEROSIS**

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**Background**: Systemic sclerosis (SSc) is an autoimmune connective tissue disease featured by autoimmunity, fibrosis and vasculopathy. Although many autoantibodies have been detected in the sera of patients with SSc, it is not clear whether they play a role in the pathogenesis of disease. It has been reported that autoantibodies against the angiotensin-II receptor type 1 (AT1R) are present in the sera of SSc patients and are associated with several clinical symptoms of the disease, suggesting that these autoantibodies may act as pathogenic drivers. Recently, our group has developed a novel mouse model for SSc by immunizing mice with human AT1R (hAT1R). From this model we were able to generate functional monoclonal antibodies agonizing AT1R.

**Objectives**: In the current study, we aim to clarify, whether B cells and antibodies directed against AT1R are involved in the pathogenesis of experimental SSc in vivo.

**Methods**: To investigate the role of B cells in the hAT1R-induced mouse model of SSc, we immunized B-cell deficient mice with hAT1R. Nine weeks after the first immunization, mice were sacrificed and sera and tissues were collected for further evaluation. To investigate the pathogenicity of anti-AT1R antibodies in the disease, monoclonal autoantibodies against hAT1R were applied to the ear of C57Bl/6 mice by single or repetitive injection. Mice were sacrificed 24 hours or 14 days after the first injection for single and repeated application, respectively, and ear and lung tissues were collected for further evaluation.

**Results**: Compared to the wild type C57Bl/6 mice, hAT1R-Immunized B-cell deficient mice were resistant against experimental SSc with regard to autoantibody production, inflammation in the lung and skin, and skin fibrosis. Furthermore, both single and repetitive injection of monoclonal antibodies against hAT1R induced inflammation in ears of mice. Despite this local effect, repetitive injection of anti-AT1R monoclonal antibodies provoked also inflammation in the lung of mice.

**Conclusion**: Our data demonstrate that i) B cells are indispensable for the pathogenesis of the hAT1R-induced mouse model for SSc and ii) monoclonal antibodies against hAT1R can induce inflammation in mice. Therefore, our results support a role of autoantibodies against AT1R in the pathogenesis of SSc.

**References**


**Notes**: In Parameters column 1 = before treatment, 2 = after treatment; M ± SD = mean value and standard deviation; * = significant difference between the values measured before and after the treatment.
Disclosure of Interests: Junping Yin: None declared, Xiaoming Wang: None declared, Xiaoyang Yue: None declared, Gabriela Riemekasten Consultant for: Chugai, F Hoffmann-La Roche, Speakers bureau: Chugai, F Hoffmann-La Roche, Xinhua Yu: None declared, Frank Petersen: None declared


THURSDAY, 13 JUNE 2019

Genetics, epigenetics and immunity

**OP0189 GENETICS OF JUVENILE IDIOPATHIC ARTHRITIS: THE IDENTIFICATION OF A NOVEL RISK LOCUS AND CLINICAL SUBGROUP ANALYSIS**

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**Background:** Juvenile idiopathic arthritis (JIA) is a clinically heterogeneous group of childhood onset inflammatory joint diseases with strong evidence to support a genetic contribution to susceptibility. JIA is divided into seven clinical subgroups based on observed patterns of clinical symptoms using the International League of Associations for Rheumatology (ILAR) classification system. The genetic overlap between these groups is not completely understood and this lack of knowledge typically leads to the different ILAR groups being analysed as discrete entities and reducing the overall power of genetic association studies.

**Objectives:** The aim of this study was to conduct a large case-control association study on susceptibility to JIA to identify novel susceptibility loci and to investigate differences of these associations between the ILAR groups.

**Methods:** JIA participants were genotyped on the Illumina Infinium CoreExome or OmniExpress arrays at The University of Manchester. UK population control genotype data was obtained from the Understanding Society Longitudinal Study. Quality control of data was performed conforming to conventional standards based on call rate, cryptic relatedness and ancestry outliers. Imputation was performed using the Haplotype Reference Consortium panel on the Michigan Imputation Server followed by exclusion of SNPs with low imputation accuracy (R² < 0.5) and low minor allele frequency (< 1%). Association testing of all SNPs was performed with an additive model incorporating imputation uncertainty using SNPTEST. A subset of SNPs independently associated with all JIA (p-value < 5x10⁻⁸) were tested to evaluate if they were specific to a particular ILAR group or shared across multiple ILAR groups using Bayesian multinomial regression and model selection methods implemented in the Trinculo software package.

**Results:** Following quality control the dataset consisted of > 7.4 million SNPs for 3305 JIA cases and 9196 controls. Association testing in a combined dataset of all ILAR groups identified seven SNPs associated at genome-wide significance (5x10⁻⁹); six of these have previously been reported for JIA while one is a novel association. The novel association (rs497523, p-value = 7.12x10⁻⁹, OR 0.85, 95% CI 0.80-0.9) maps to chromosome 16p11 and is located within intron one of the CCDC101 gene. In a subset of 44 independently associated SNPs we found no strong evidence to support association of any SNP to a specific ILAR group with the majority of the SNPs showing evidence for sharing across multiple groups.

**Conclusion:** In the largest case control association study for susceptibility to JIA performed to date, we identified a novel association to a SNP in the intron of CCDC101. This gene is involved in transcriptional regulation through histone acetyltransferase. CCDC101 may be the causal gene at this locus; however introns contain enhancer elements that regulate other genes in the transcriptional domain. Therefore fine mapping with the integration of genomic data is currently being performed for this locus. The results provide little evidence to support ILAR subgroup specificity for any of the associated variants; on the contrary the results support a general model of sharing across multiple groups. The combined analysis of data across subgroups, informed by model sharing, will maximise power to identify novel associations.

**Disclosure of Interests:** None declared

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**OP0190 META-ANALYSIS OF IMMUNOCHIP DATA OF FOUR AUTOIMMUNE DISEASES REVEALS NOVEL SINGLE-DISEASE AND CROSS-PHENOTYPE ASSOCIATIONS**

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**Background:** In recent years, research has consistently proven the occurrence of genetic overlap across autoimmune diseases, which supports the existence of common pathogenic mechanisms in autoimmunity.

**Objectives:** The objective of this study was to further investigate this shared genetic component.

**Methods:** We performed a cross-disease meta-analysis of Immunochip data from 37,159 patients diagnosed with a seropositive autoimmune disease (11,489 celiac disease (CeD), 15,523 rheumatoid arthritis (RA), 3,477 systemic sclerosis (SSc), and 6,670 type 1 diabetes (T1D)) and 22,308 healthy controls of European origin using the R package ASSET.

**Results:** We identified 38 risk variants shared by at least two of the conditions analyzed, five of which represent new pleiotropic loci in autoimmunity. We also identified six novel genome-wide associations for the diseases studied. Cell-specific functional annotations and biological pathway enrichment analyses suggested that pleiotropic variants may deregulate gene expression in different subsets of T cells, especially Th17 and regulatory T cells. Finally, drug repositioning analysis evidenced several drugs that could represent promising candidates for CeD, RA, SSc and T1D treatments.

**Conclusion:** We have been able to advance in the knowledge of the genetic overlap existing in autoimmunity, thus shedding light on common molecular mechanisms of disease and suggesting novel drug targets that could be explored for the treatment of the autoimmune diseases studied.

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**Disclosure of Interests:** Ana Márquez: None declared, Martin Kerick: None declared, Alexandra Zhernakova: None declared, Javier Gutierrez-Achury: None declared, Wei-Min Chen: None declared, Suna Onengut-Gumuscu: None declared, Isidoro Gonzalez-Alvaro: None declared, Luis Rodriguez-Rodriguez: None declared, Miguel A Gonzalez-Gay: Grant/research support from: Prof. MA Gonzalez-Gay received grants/research support from: Abbvie, MSD, Jansen and Roche., Speakers bureau: Consultation fees/participation in company sponsored speaker’s bureau from Pfizer, Lilly, Sobi, Celgene, Novartis, Roan and Sanofi., Maureen Mayes Grant/research support from: Maureen Mayes is a clinical trial investigator for Boehringer-Ingelheim; Galapagos, Reata, Sanofi, Merck-Serono, Consultant for: Maureen Mayes is a member of scientific advisory boards for Galapagos NV (Pharma), Boehringer-Ingelheim, Mitsubishi-Tanabe, Asteffas: Grant Review Board for Actelion., Speakers bureau: Maureen Mayes received personal fees for being a conference speaker on the use of autoantibodies in connective tissue diseases for MedEdlign, Soumya Raychaudhuri: None declared, Stephen S. Rich: None declared, Csica Wijmenga: None declared, Javier Martin Ibanez: None declared

EPIGENETIC PROFILING OF SYNOVIAL FIBROBLASTS REVEALS STRUCTURAL DNA DYNAMICS AT DISEASE IMPLICATED CHROMOSOME REGIONS

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Background: One of the more striking findings from genome-wide association studies (GWAS) is how the majority of disease associated genetic variants are found within gene regulatory regions, known as enhancers. It is now well established that these enhancers regulate target genes through physical interactions. We, and others, have shown that these interactions can vary between cell types and act over long distances. Therefore, if we are to fully translate GWAS findings, we need link disease associated enhancers to their target genes, in the relevant cell types. So far we only have a limited picture in rheumatoid arthritis (RA) relevant cell types, since synovial fibroblasts (SF) have been omitted from this type of chromatin interaction analysis.

Objectives: Investigate dynamic Hi-C interactions in unstimulated and stimulated SF, mapping RA enhancers to their target genes, and correlating with gene expression.

Methods: We cultured SF from synovial tissues of RA patients. After stimulation of the SF (n=6) with 10 ng/ul TNF for 24h, Hi-C and RNA libraries were generated and sequenced on the Illumina HiSeq 4000. We called dynamic active and inactive regions of the genome (A/B compartments), mapped on RA associated enhancers, linked these to target genes and correlated the interactions with dynamic expression.

Results: We found a region on the chromosome 6q23, intergenic between OLIG3 and TNFAIP3, with an enhancer containing SNPs associated with RA to be dynamically linked to the TNFAIP3 gene through DNA activity, interactions and corresponding gene expression. As shown in figure 1a, the genomic region containing the RA associated variants (red square) only resides in an open, active region of DNA (black bar, compartment A) upon TNF-stimulation of the SF. This region then makes a strong interaction with the promoter of TNFAIP3 (figure 1a) in stimulated cells, which corresponds to a more than 100-fold increase in TNFAIP3 gene expression (figure 1b).

Conclusion: Using independent data, we have indicated how the RA region on 6q23 could influence the expression of TNFAIP3, under stimulatory conditions in SF. This supports previous work, where this particular 6q23 enhancer is preferentially active in RA synovium, compared to osteoarthritis, reflecting the different stimulatory conditions in each disease (Ai et al. 2018). We have successfully linked an RA associated enhancer to its target gene in SF, indicating how the enhancer works over a large distance to interact with and regulate the TNFAIP3 gene. Furthermore we show that this enhancer containing RA associated SNPs is only active upon stimulation with TNF in SF.

REFERENCE:


DISSECTING THE LONG-RANGE GENE REGULATION OF RHEUMATOID ARTHRITIS ENHANCERS AT THE 5Q11 LOCUS USING THE COMPLEMENTARY APPROACHES OF CRISPRa AND CRISPRi

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Background: Large-scale genome wide association studies (GWAS) in rheumatoid arthritis (RA) have revealed that the majority of associated risk variants lie in non-coding regions of the genome. For RA it has been demonstrated that risk variants are significantly enriched in T cell specific enhancers. One such susceptibility locus known as Sq11 is the third strongest association with RA. At this locus the lead-risk variants lie in two distinct active enhancer elements intrinsic to the ANKRD55 gene. Previous work using chromatin conformation has shown these enhancers make physical contact with the promoter of IL6ST, 150 kb away on the linear chromosome. Whilst ANKRD55 is a gene of unknown function, IL6ST is part of the IL6R complex which regulates the IL6 signalling pathway. Tocilizumab is already an approved drug for RA, which works against the IL6R. CRISPR is an ideal tool to dissect this enhancer-gene relationship to provide us with empirical evidence that the intronic enhancer within ANKRD55 regulates the expression of IL6ST. Understanding how RA risk genetic background affects gene regulation will give us a better understanding of the underlying biology of the disease and can ultimately be used to help repurpose or discover novel drug therapies.

Objectives: To use CRISPR interference (CRISPRi) and CRISPR activation (CRISPRa) to perturb the ANKRD55 intronic enhancer and measure the downstream effect on the expression of IL31RA, IL6ST, ANKRD55.

Methods: We used dead (dCas9) a modified CRISPR Cas9 enzyme that is catalytically inactive, that precisely targets DNA, but does not cut. Instead, effector molecules are fused to the dCas9 (VP64 for activation and KRAB for repression) to alter the transcription of the targeted genes. Two lead functional risk SNPs at the 5q11 risk locus rs10065637 and rs7731626 (R 2 = 0.4472) lie in two distinct enhancer elements separated by 5.5kb. We designed 4 guides across each enhancer, and transduced a T cell line (Jurkat) using lentiviral delivery; first dCas9-KRAB and dCas9-VP64 and subsequently the pool of guides for each enhancer alongside controls. We cultured the cells until confluent and then sorted the top 60% expression of BFP-GFP (KRAB) or MCherry-GFP (VP64). RNA was extracted and then a qPCR was performed (Quantstudio) for IL31RA, IL6ST and ANKRD55.

Results: In the CRISPRa Jurkat cells the guides targeted to both SNP containing enhancers significantly increased the expression of ANKRD55: rs7731626 (p=<0.0001) and rs6859219 (p=0.0003) respectively. They also increased the expression of IL6ST rs7731626 (p=0.0023) and rs6859219 (p=0.01). In CRISPRi Jurkat cells the guides targeted to both SNP containing enhancers significantly decreased the expression of ANKRD55: rs7731626 (p=0.00) and rs6859219 (p=0.0071). When guides were simultaneously used for both enhancers rs6859219+rs7731626 there was also a significant decrease in expression of ANKRD55 (p=0.0001). Only the pool guides against both enhancers significantly decreased the expression of IL6ST (p=0.0001). In both systems no significant effect was seen on the expression of IL31RA (Figure 1).


Figure 1a

Figure 1b

Figure 1
Conclusion: Results from CRISPRi and CRISPRa are concordant and support the idea that inotropic enhancers associated with RA susceptibility, can regulate the expression of both ANKRD55 and also modulate long range gene regulation with JLEST to influence disease risk. These findings are crucial to begin to dissect and translate GWAS findings.

REFERENCE:

Disclosure of Interests: None declared


OP0194 CAMP RESPONSE ELEMENT MODULATOR (CREMA) INDUCES DUAL SPECIFICITY PROTEIN PHOSPHATASE (DUSP) THROUGH EPIGENETIC REMODELING, PROMOTING IL-17A AND REDUCING IL-2 EXPRESSION IN T CELLS

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Background: Tissue inflammation and organ damage in systemic lupus erythematosus (SLE) have been linked to effector T cells that are characterized by increased IL-17A and reduced IL-2 production(1). T cells from patients with SLE express increased levels of the transcription factor cAMP response element modulator (CREMa) that contributes to altered cytokine expression(1-3). However, the exact molecular events contributing to dysregulated IL-17A and IL-2 expression are incompletely understood.

Objectives: To investigate molecular events that promote effector T cells in health and disease. The definition of molecular regulators of effector T cell generation and activity may deliver new biomarkers and potential therapeutic targets in disorders characterized by altered effector T cell function, including (but not limited to) SLE.

Methods: Using CRISPR/Cas9 genome editing and lentiviral transduction, we generated CREMa deficient or overexpressing Jurkat T cells. Gene expression profiles in Jurkat and primary human CD4+ T cells were assessed by qRT-PCR and mRNA probe-based hybridization techniques. Gene regulation events were investigated using luciferase reporter assays (trans-activation) and ChIP. Interactions between CREMa and the transcriptional co-activator p300 were assessed using proximity ligation assays and p300 knock-down with siRNAs.

Results: We link CREMa production in effector CD4+ T cells with increased expression of dual specificity protein phosphatase (DUSP4). Using genetically modified Jurkat T cells, we demonstrate that CREMa induces DUSP4 through recruitment of the transcriptional co-activator p300 and histone H3K18 acetylation. Using DUSP4 transfection models and genetically modified Jurkat T cells, we support previous reports suggesting that DUSP4 induces IL-17A while limiting IL-2 expression. Furthermore, we demonstrate that CD4 T cells from patients with juvenile-onset SLE share the phenotype with CREMa over-expressing CD4+ T cells with increased DUSP4 expression that contributes to imbalanced IL-17A and IL-2 production.

Conclusion: Collectively, our results deliver previously unknown CREMa-mediated molecular mechanisms promoting effector T cells and support the central involvement of CREMa in the pathophysiology of SLE. CREMa and DUSP4 may prove valuable as disease biomarkers and/or targets in the search for individualized and target-directed treatments.

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OP0195 HISTONE DEACETYLASE 1 (HDAC1): A KEY MEDIATOR OF T CELLS FOR THE PATHOGENESIS OF RHEUMATOID ARTHRITIS

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Background: Despite enormous efforts to develop new therapeutic strategies for treatment of rheumatoid arthritis (RA), the large number of non responding patients to currently available drugs underlies the unmet need to identify new therapeutic targets. Certain CD4+ T cell subsets, especially those polarized toward the T helper (Th) subset Th1 and Th17, have been shown to be major drivers of inflammation in patients with RA. The expression of their key transcription factors is controlled by histone modifications which includes acetylation of lysine residues mediated by histone deacetylases (HDAC). Indeed, pan HDAC inhibitors have been shown to be a potential therapeutic strategy. However, major side effects limited the clinical use and underlined the need of more specific HDAC molecules.

Objectives: We addressed the individual role of HDAC1 on the development of collagen-induced arthritis model (CIA), which partially reflects human RA.

Methods: Mice with a T cell specific deletion of HDAC1 (HDAC1 cKO) were generated by using the CD4Cre/LoxP system. At week 8 of age arthritis was induced in wild type (WT) and HDAC1 cKO mice by immunizing with chicken collagen II (CII), emulsified in complete Freund’s adjuvant. After 21 days mice received a booster injection of CII. The animals were 3 times per week scored for paw swelling and grip strength. Anti-CII antibody levels were determined by ELISA. Various cell subsets, including Th cells, where detected in the blood, the spleen and the draining lymph node by FACS analysis. To test antigen-specific T cell activation we performed in vitro restimulation of spleen and lymph node cells with collagen II followed by assessment of cytokine production and quantification of the proliferation rate using 3Hthymidine incorporation.

Results: After 4 and after 10 weeks mice were sacrificed and paraffin sections of the affected joints were analyzed for histomorphologic signs of inflammation, cartilage and bone destruction.

Discussion: Eighty percent of the animals developed serum anti-CII antibodies (IgM and IgG) whereby the antibody levels were a day 21 of disease similar between the HDAC1 cKO and the WT mice. Furthermore, no differences in the production of antibody subclasses, especially of pathogenic IgG2c antibodies, were observed. Enhanced percentages of Th1 and Th17 cells among HDAC1-null CD4+ T cells were detected after immunization with the HDAC1 cKO mice. Nonetheless, and unexpectedly, these mice did not develop any signs of disease at the clinical level while WT mice developed pronounced paw swelling and loss of grip strength. In accordance with the clinical data, histological analysis revealed no signs of inflammation, no bone erosion and no appearance of osteoclasts in the joints of HDAC1 cKO mice. This appeared to be mainly caused by an impaired migratory capacity of HDAC1 cKO CD4+ T cells, so that they were unable to invade the joints.

Conclusion: Our data show the importance of HDAC1 as a key immune regulator in the pathogenesis of T cell driven collagen induced arthritis. Therefore it might be considered as an interesting novel therapeutic target in RA.

Disclosure of Interests: None declared


OP0195 SELECTIVE EXPANSION OF REGULATORY T-CELLS IN HUMANS BY A NOVEL IL-2 CONJUGATE T-REG STIMULATOR, NKTR-355, BEING DEVELOPED FOR THE TREATMENT OF AUTOIMMUNE DISEASES

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Background: Impaired IL-2 production and dysfunction of regulatory T cells (Tregs) have been identified as key immunological defects leading to the...
breakdown of immune self-tolerance, a causative mechanism implicated in multiple autoimmune diseases. Enhanced sensitivity of Tregs to IL-2 supports the use of low-dose IL-2 therapy; however, this treatment is limited by its short half-life and relatively poor selectivity for stimulation of Tregs versus other T cell types. NKTR-358 is a polyethylene glycol (PEG) conjugate of recombinant human IL-2 (adesleukin sequence with no additional amino acid mutation or substitution). It is differentiated from native IL-2 by its prolonged biological activity as well as its marked and selective stimulation of Tregs in different animal species, including non-human primates.

**Objectives:** Study objectives assessed the safety and tolerability of NKTR-358 in humans administered single ascending doses subcutaneously (SC). In addition, time course and extent of changes in the numbers and percentages of Tregs, conventional CD4+ and CD8+ T cells, NK cells, cytokine levels, and the pharmacokinetics (PK) of NKTR-358 in peripheral blood were investigated.

**Methods:** In this first-in-human, double-blind, single ascending dose study, healthy volunteers received SC doses ranging from 0.3 to 28 ug/kg (9 active:3 placebo per cohort) and subjects were followed for 50 days.

**Results:** All 8 planned cohorts completed dosing. There were no dose-limiting toxicities, serious adverse events, deaths, or clinically significant abnormalities in vital signs, electrocardiograms, or laboratory test values. Adverse events attributed to NKTR-358 were primarily limited to mild (grade 1) injection site reactions. One subject at the highest dose tested demonstrated transient sialyl and mild (grade 1) symptoms of elevated cytokine levels and lymphopenia, which resolved without treatment. No other individual at any dose level had systemic signs or symptoms known to be associated with IL-2 therapy. The first 6 cohorts have been tested for anti-drug antibodies to date and none have been detected. NKTR-358 reached maximum plasma levels 4-6 days after administration, with little change for ~2 weeks, and then decreased with a half-life of ~6-9 days. NKTR-358 exhibited linear PK above the 1.0 ug/kg dose. The primary effect of NKTR-358 was seen on Tregs. In the 3.0 to 28.0 ug/kg dose cohorts, a dose-dependent and sustained increase in the absolute numbers and percentages of circulating CD4+FoxP3+CD25+Bright Tregs were observed. The elevated levels peaked at Days 10-12 and did not return to baseline until ~20 to 25 days following administration. At 28.0 ug/kg, the mean peak increase of 3.5-fold in the percentages and numbers of NK cells at the highest dose tested, but no changes in percentages or numbers of conventional CD4+ or CD8+ T cells were observed. NKTR-358 selectively induced Tregs, evidenced by a 15-fold increase in the mean peak Treg:CD8 ratio over baseline in the 28.0 ug/kg group.

**Conclusion:** Single doses of the IL-2 conjugate T-reg stimulator, NKTR-358, in the dose range tested were well tolerated and safe. NKTR-358 led to a striking and selective dose-dependent increase in circulating CD25Bright Tregs with minimal effects on conventional T cells and with relatively small effects on NK cells. These clinical results extend previous animal studies showing the prolonged and Treg selective action of NKTR-358, and provide strong support for testing NKTR-358 as a new therapeutic in autoimmune diseases, such as systemic lupus.

EVALUATING THE RELATION OF STRUCTURAL MRI-DETECTED STRUCTURAL ABNORMALITIES AND TYPE II COLLAGEN DEGRADATION IN KNEE OSTEOARTHRITIS

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Objectives: In this study we evaluated the relation between structural damage by MRI, clinical and pain sensitisation measures and wet biochemical biomarkers in knee OA.

Methods: We recruited 130 participants fulfilling ACR criteria with advanced OA requiring total knee replacement (TKR) (n=80), mild OA having standard care (n=42) and non-OA controls (n=8). Knee MRI in 90 subjects (72 F, 18 M) was acquired and assessed by two radiologists with the MRI Knee Osteoarthritis Score (MOAKS). Overall MOAKS scores were created for Bone Marrow Lesions (BML), Cartilage Degradation (CD) and effusion/Hoffa synovitis (tSyn). Type II collagen cleavage products (CTX-II) were determined by ELISA. Clinical scoring was performed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) for pain levels (WOMAC_P), Hospital Anxiety and Depression Scale (HADS), Body mass index (BMI) and pain sensitisation with pain pressure thresholds (PPT) of the patella by Quantitative Sensory Testing (QST).

Results: The mild OA group had a mean age of 63 +/- 9 yr and the advanced OA group 69 +/- 9 yr. The advanced OA group had higher levels of pain, with a mean WOMAC_P of 58 +/- 22 compared with the mild OA group who had a mean WOMAC_P of 40 +/- 22. WOMAC_P correlated with the total number of regions with cartilage damage (nCD) (R=0.225, p=0.033) and total number of BMLs (nBML) (R=0.195, p=0.065) using BMI, age and HADS as covariates. Levels of CTX-II correlated with tSyn (R=0.313, p=0.03), nBML (R=0.252, p=0.019), number of osteophytes (R=0.33, p=0.002) and nCD (R=0.218, p=0.042), using BMI and age as covariates. The correlation for urinary CTX-II with tSyn (p=0.006) is shown in Figure 1 using a partial linear regression analysis of MOAKS, BMI and age. We also found CTX-II correlated with lesion load scores (total number of lesions multiplied by MOAKS size by% damage scores) for CD (R=0.277, p=0.009) and BML (R=0.308, p=0.004). PPT correlated with patella MOAKS scores for nBML (R=0.221, p=0.038) and nCD (R=0.279, p=0.009), with HADS, BMI and age as covariates.

Conclusion: There is a direct correlation between the degree of cartilage damage and BMLs with pain in OA. Type II collagen degradation products were higher when there was more severe MRI-detected synovitis, BMLs and cartilage damage in the knee joint, suggesting that the source of enzymes degrading type II collagen in OA, including matrix metalloproteinasenes, are also likely to be produced by synovium and bone (1) and not just cartilage, as previously hypothesised in other studies. There was also a correlation between pain sensitisation and frequency of BMLs and cartilage degradation, suggesting that molecular mediators of pain sensitisation, which we have shown are produced by BMLs (1), are a cause of patient-reported OA pain.

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Figure 1

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MRI-DETECTED STRUCTURAL ABNORMALITIES AND DEVELOPMENT OF INCIDENT RADIOGRAPHIC KNEE OSTEOARTHRITIS OVER 10 YEARS OF FOLLOW-UP

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Background: Structural joint pathology on MRI has been found in knees without radiographic evidence of osteoarthritis (OA). We have previously shown that structural abnormalities on MRI may be precursors of disease and associated with the detection of incident radiographic knee OA (ROA) up to 2 years later, and in some circumstances up to seven years later. The prognostic value of structural abnormalities on MRI for knee OA, however, is unknown.

Objectives: Estimate the probability of incident ROA over 10 years of follow-up, according to structural abnormalities detected on baseline MRIs.

Methods: A subcohort of participants (862 knees, one knee/person) from the Osteoarthritis Initiative (OAI) with at least one knee at risk of developing ROA (i.e., Kellgren-Lawrence (KL) 0.1 at baseline) was randomly selected. MRI-detected structural features of the knee were assessed by expert readers using the MRI Osteoarthritis Knee Score (MOAKS). Participants underwent bilateral posteroanterior fixed-flexion weight-bearing knee radiography at baseline and annually through year 10 and then every two years until year 10. Radiographs were centrally read for KL grade, with ROA defined as KL=2. Survival was estimated with the Turnbull non-parametric maximum likelihood estimator, a generalization of Kaplan Meier curves for interval censored data. Survival curves were compared using a log rank permutation test available in the R package interval. Hazard ratios were estimated using Cox models fit using the R package iceReg, designed for interval censored data. Features were considered one at a time, with no adjustments.

Results: Knees with any of the following structural abnormalities had higher estimated probabilities for the development of radiographic OA within two, four and 10 years of follow-up: effusion-synovitis, Hoffa-synovitis, bone marrow lesions in the medial compartment and whole knee, surface area and full thickness cartilage damage in the medial compartment and whole knee, and medial meniscal extrusion (Table 1). Differences in the probability for the development of ROA within two, four, and 10 years of follow-up were significant (post-hoc 95% confidence intervals did not include 0), between knees without the abnormality and knees in the most severe category for all features, with one exception at the two-year follow-up. All of these abnormalities were significantly associated with time to ROA over 10 years of follow-up.

REFERENCES:

Figure 1

Conclusion: Our results demonstrate the prognostic value of effusion-synovitis, Hoffa-synovitis, bone marrow lesions, cartilage damage, and meniscal extrusion
for the development of ROA up to 10 years later. Future directions include developing a predictive model that incorporates multiple features.

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THURSDAY, 13 JUNE 2019

Different pathophysiological pathways in axial and peripheral disease: Peripheral and axial spondyloarthritis: to split or to lump?

OP0199

THE HUMAN ENTHESIS HARBOURS RESIDENT ADAPTIVE CD4+ AND CD8+ T-CELLS WITH INCLUDIBLE IL-17A AND TNF PROTEIN THAT IS PHARMACOLOGICALLY SUPPRESSED BY ROR-Γ AND PDE4 INHIBITORS BUT NOT METHOTREXATE IN A NOVEL IN VITRO ENTHESIS MODEL

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Background: Animal models have demonstrated that enthesis is the primary lesion in experimental spondyloarthritis (SpA). In mice, innate lymphocytes were suggested as the major cytokine producers at the enthesis.

Objectives: We tested the hypothesis that the human enthesis harbours tissue resident conventional T-cells. We also assessed their ability to express SpA-related cytokines including TNF and IL-17A and if this could be blocked using psoriasis therapeutic agents (methotrexate (MTX), and phosphodiesterase type 4 inhibitor (PDE4i)) and experimental RORγt inhibitors (RORγt).

Methods: Entheseal spinal process was obtained from patients undergoing elective orthopedic procedures (n=20) and mechanically digested or processed for confocal staining and flow cytometry. CD4+ and CD8+ T-cells were sorted and RNA was isolated and analysed by qPCR. Magnetically isolated cells were stimulated using an anti-CD3/CD2/CD28 bead with and without the presence of MTX, RORγt and PDE4i. Following stimulation IL-17A and TNF were measured by ELISA and intracellular flow cytometry.

Results: CD4+ and CD8+ T-cells represent 35.7% and 23.7% of T-cells in the enthesis, respectively, with topographic confirmation by anti-CD3 immunofluorescence staining. Entheseal tissue contained a higher proportion of CD4+ and CD8+ T-cells expressing a resident memory phenotype (CD69+/CD45RA-) compared to matched blood. Sorted T-cells from entheseal tissue had a gene expression profile consistent with a tissue resident phenotype and CD4+ and CD8+ T-cells showed increased expression immunomodulatory genes including IL-10 and TGF-β compared to peripheral blood T-cells (p<0.001). Following stimulation CD4+ T-cells produced more TNF than CD8+ T-cells (p<0.05), while RORγt only reduced IL-17 secretion (p<0.001). MTX had no significant impact on both TNF and IL-17A production in either cell population. This pattern of inhibition was mirrored in TNF secretion from CD8+ T-cells.

Conclusion: This is the first description of conventional CD4+ and CD8+ entheseal resident T-cells. PDE4i was effective in abrogating induced TNF production and IL-17, whereas RORγt is highly effective for IL-17A production but not TNF. In contrast, MTX had little effect on in vitro enthesis model cytokine production. These findings may have some practical implications in the treatment of subclinical enthesis.

OP0200

A SET OF INFLAMMATORY MARKERS ALLOWING TO DETECT SYSTEMIC INFLAMMATION IN PSORIATIC SKIN, ENTHESEAL AND JOINT DISEASE IN THE ABSENCE OF CRP AND THEIR LINK TO CLINICAL DISEASE MANIFESTATION

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Background: Psoriatic disease is composed of skin, entheseal and joint disease, which can manifest isolated or combined. Little is known about the systemic inflammation levels in psoriatic disease as a robust IL-6 signal is missing and therefore acute phase reactants such as C-reactive protein are often normal. Measuring systemic inflammation in the different manifestations of psoriatic disease is therefore a continuous unmet need.

Objectives: To better define systemic inflammation in patients with psoriatic disease limited to the skin (S), the entheses (E) or the joints (arthritis, A) or with a combination of these disease manifestations (SE, SA, EA, SEA).

Figure 1. Effect of different therapeutic agents on the TNF and IL-17A production by resident entheseal T-cells compared to peripheral blood

Figure 2. Gene expression profile of entheseal T-cells (soft tissue and adjacent bone) compared to peripheral blood

Abbreviations: ST, enthesal soft tissue; PEB, peri-enthesal bone.

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Methods: Hypothesis-driven approach selecting makers that are (i) either targets of IL-23/IL-17 pathway activation (β-defensin 2, lipocalin 2, IL-22), (ii) associated with neutrophil/monocyte activation (calprotectin, IL-8) and (iii) achieve serum concentrations sufficient for reliable detection by standard ELISA. Parameters were assessed in 210 individuals comprising 105 healthy controls and 105 patients with psoriatic disease (each 15 for isolated (S, E, A) and composed disease manifestations SE, SA, EA, SEA). Results are expressed as percent positive patients with levels above three standard deviations over the mean level in healthy controls. In addition, 6-months sequential data on levels of these makers were collected in 20 patients treated with secukinumab or adalimumab to test treatment effects.

Results: CRP levels were normal in the majority of individuals. The respective percentages of patients with normal CRP (>0.3 mg/L) were as follows: S: 100%, E: 95%, A: 80%, SE: 93%, SA: 67%, EA: 73%, SEA: 67% (Figure). Thus, CRP is only elevated in a subset of patients with arthritis. In sharp contrast, beta-defensin 2 levels (>1.88 ng/mL) and lipocalin-2 (>24.7 ng/mL) were elevated in the majority of patients with isolated skin and entheseal, but not joint disease. Conversely, elevations of calprotectin (>3.58 mg/mL) and IL-8 (>10.3 pg/mL), were found in the majority of patients with isolated joint disease. IL-22 was elevated (>17.1 pg/mL) in all three manifestations of psoriatic disease. Reflecting a combination of the disease manifestations SE, SA, EA, SEA) showed widespread marker elevation. IL-17 and TNF inhibition differentially lowered and partially normalized elevated markers of inflammation.

Conclusion: Systemic inflammation is detectable in the majority of patients with psoriatic disease, even if CRP is normal. The respective marker pattern depends on the manifestation (skin, entheses, joints) of psoriatic disease, with beta-defensin 2 and lipocalin-2 reflecting skin and entheseal disease, calprotectin and IL-8 joint disease and IL-22 a combination of these disease manifestations.

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My joints hurt and I’m overwhelmingly tired – fatigue in rheumatoid arthritis.

OP0201

FATIGUE IN JUVENILE IDIOPATIC ARTHRITIS AFTER 18 YEARS OF FOLLOW-UP

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Background: Fatigue is common in adults with rheumatic disease and has also been shown in adolescents with juvenile idiopathic arthritis (JIA). Knowledge on fatigue in JIA in long-term follow-up is limited.

Objectives: To study the prevalence and severity of fatigue 18 years after onset of JIA.

Methods: In this close to population-based cohort study from defined geographical areas of Norway, Sweden, Denmark and Finland, consecutive cases of JIA with disease onset in 1997 to 2000 were prospectively enrolled (1). At 18-year follow-up, fatigue was measured using Fatigue Severity Scale (FSS, range 0-7) (2), and severe fatigue was defined as FSS >4. General health status was measured with Health Assessment Questionnaire (HAQ) and 36-Item Short Form Health Survey (SF-36). Reduced health was defined as HAQ >0, and SF-36 <40 (according to the physical component summary score/mental component summary score (PCS/MCS)). Pain was measured with 10 cm visual analogue scale (VAS), 0 – no pain, >0 – pain. Remission was defined according to the preliminary criteria described by Wallace. A Norwegian healthy cohort was used for comparison. Multivariable logistic regression analyses were performed.

Results: Among 434 eligible JIA participants 377 completed a Fatigue Severity Scale (FSS) measurement at the 18-year follow-up and were included. Of these 72% were girls, 53% had oligoarticular disease six months after onset, median age at onset was 5.6 (IQR 2.6-9.7) years, and age at the 18-year visit was 23.1 (IQR 20.3-27.2). Mean total FSS (±SD) was 3.2 (±1.5), and participants with active disease scored 3.6 (±1.6) compared to 2.9 (±1.4) for those in remission off medication. The highest total FSS was found in those with SF-36 PCS and/or MCS <40 (4.7 (±1.6) and 4.6 (±1.6), respectively). Severe fatigue was considerably more frequent in participants with active disease (36%, odds ratio (OR) 2.5) compared to those in remission off medication (19%), HAQ score >0 (47%, OR 4.1) compared to HAQ score =0 (18%), SF-36 PCS/MCS <40 (64/61%, OR 7.1/4.9) compared to SF-36 PCS/MCS >40 (20/19%), and VAS pain >0 (36%, OR 3.8) compared to VAS pain ≤0 (13%). The proportion of severe fatigue in a healthy Norwegian control cohort was 12%

Conclusion: At 18-year follow-up fatigue was a prominent symptom in JIA, and we found consistently higher fatigue burden and considerably more severe fatigue among participants with active disease, pain and self-reported health problems, compared to those without. We suggest fatigue to be measured at long-term follow-up both in clinical and research settings.

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Disclosure of Interests: Ellen Dalen Arntsd: None declared, Mia Glurup: None declared, Veronika Rydpdal: None declared, Suvi Petloniemi: None declared, Maria Ekelund: None declared, Lillemor Berntsson Consultant for: Abbvie, Speakers bureau: Abbvie, Anders Fasth: None declared, Susan Nielsen: None declared, Marek Zak: None declared, Kristina Aalto: None declared, Ellen Nordal: None declared, Troels Herlin: None declared, Pål Richard Romundstad: None declared, Marite Rygg: None declared

EFFECT OF RSLV-132 ON FATIGUE IN PATIENTS WITH PRIMARY SJÖGREN’S SYNDROME – RESULTS OF A PHASE II RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PROOF-OF-CONCEPT STUDY

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Background: Fatigue is the key symptom that leads to poor health related quality of life and loss of work productivity in patients with primary Sjögren’s syndrome (pSS). RSLV-132 is a first-in-class drug comprising RINase1 fused to the Fc region of IgG1. It is designed to increase serum RINase activity to digest RNA associated immune complexes, thereby reducing Toll-like receptor (TLR) activation and subsequent production of type 1 interferon (IFN), B-cell proliferation, and autoantibody production – mechanisms that are key to pSS pathogenesis. IFN pathway dysregulation has also been implicated in fatigue.

Objectives: To explore the clinical efficacy of RSLV-132 in improving patient-reported outcomes (PRO), particularly fatigue among patients with pSS.

Methods: Patients with positive anti-Ro and IFN gene expression signature were randomised: 3:1 to RSLV-132 10 mg/kg IV or placebo (PBO) at weeks 0, 1, 2, and then fortnightly until week 12. Use of hydroxychloroquine, other immunomodulatory therapies or prednisolone >10mg daily were not permitted. There was no minimum entry criteria for EULAR Sjögren’s syndrome disease activity (ESSDAI) or EULAR Sjögren’s syndrome patient reported index (ESSPRI). The primary endpoint was changes in gene or protein expression levels in blood indicative of reduced inflammation. Secondary endpoints, among others, included safety and tolerability, and changes in PRO between baseline and week 14 including ESSPRI, FACIT, Fatigue visual analogue score (0-100), Profile of fatigue (PRO-F) (0-7)) and Neuropsychological tests.

Results: Thirty patients were randomised (RSLV=22, PBO=8). Baseline clinical and demographic characteristics were comparable between groups. Two subjects randomised to active drug withdrew from the study before dosing. Among the patients receiving RSLV-132, the mental component of PRO-F improved by 1.53 points compared to worsening of 0.06 points in the PBO group (p=0.046). Consistently, there was a significant improvement in the RSLV-132 group in their Digital Symbol Substitution Test performance with a reduction of 16.4s in completing the test compared to an increase of 2.8s in the PBO group (p=0.024). The physical component of PRO-F improved by 0.8 points in the RSLV-132 group compared to improvement of 0.06 points in the PBO group (p=0.142). Similar trends were observed for ESSPRI and FACIT-F scores.

Conclusion: RSLV-132 is a promising therapy to improve the symptoms of fatigue in patients with pSS, with a good safety profile. Further investigation of its use in pSS is warranted.

REFERENCE:
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CHARACTERIZING THE EPIGENOMIC LANDSCAPE OF PSORIASIS PATIENTS DESTINED TO DEVELOP PSORIATIC ARTHRITIS

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Background: Approximately 30% of psoriasis patients develop psoriatic arthritits (PsA), typically within 10 years of psoriasis onset. A large proportion of individuals with PsA remain undiagnosed. Epigenetics is potentially a major mechanism through which environmental factors influence PsA risk. An understanding of how the epigenome changes during the transition to PsA could yield predictive biomarkers and facilitate PsA diagnosis. We hypothesize that epigenetic deregulation at the level of DNA methylation occurs early in PsA pathogenesis, prior to overt clinical symptoms, and epigenetic markers can be used as biomarkers for disease prediction.

Objectives: To discover predictive biomarkers of PsA and gain an understanding of the pathogenesis of PsA by characterizing the epigenomic landscape of psoriasis patients who later developed PsA (converters) and comparing it to psoriasis patients who did not develop PsA (non-converters).

Methods: We performed an epigenome-wide comparison of DNA methylation in baseline whole blood samples from psoriasis converters (n=60) and non-converters (n=60) from a longitudinal cohort. Converters and non-converters were matched for age, sex, psoriasis duration, and duration of follow-up. DNA was analyzed on Human MethylationEPIC BeadChips using the Illumina package. Cell type heterogeneity was corrected using RefBaseEWAS. Differentially methylated probes and regions were identified using limma and DRMRcate, respectively. The FEM package was used to infer differentially methylated gene modules within a protein-protein interaction network.

Results: Converter baseline samples were collected a median of 4.2 (interquartile range 1.9-6.3) years prior to the onset of PsA, while non-converters samples were collected a median of 4.3 (1.2-7.3) years prior to the most recent clinic visit. The RefBaseEWAS method estimated that converters had slightly higher proportions of CD4+ T-cells and granulocytes compared to non-converters, however the differences were not statistically significant. After adjustment for cell type heterogeneity, 68 individual CpG sites were found to be differentially methylated between converters and non-converters (FDR<0.05). Differentially methylated regions (DMRs) containing at least 2 significant CpGs were identified in genes such as FBXO27 (beta fold change [FC]=0.06, region-wise adjusted p=4.1x10^-3), a ubiquitin ligase involved in lysosomal degradation, RCAN1 (FC=-0.05, p=5.2x10^-3), a protein which inhibits calcineurin-dependent signaling pathways and is involved in bone homeostasis, and PMAIP1 (FC=0.04, p=6.7x10^-5), which encodes the NOXA protein involved in mediating apoptosis of activated B cells. Several significant CpG sites mapped to protein-protein interaction subnetworks involved in Th17 differentiation (IRF4 and MAFF), TNF alpha signaling (IKKBE, REL, MAVS, IκBKE).
EMAPALUMAB, AN INTERFERON GAMMA (IFN-γ) BLOCKING MONOClonAL ANTIBODY, IN PATIENTS WITH macROPHAGE ACTIVATION SYNDROME (MAS) COMPLICATING SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS (SJIA)

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Background: MAS is a severe complication of rheumatic diseases, most frequently SJIA, characterized by excessive activation and expansion of T cells and macrophages. It is characterized by fever, hepatosplenomegaly, liver dysfunction, cytopenias, coagulation abnormalities and hyperferritinemia, possibly progressing to multiple organ failure and death. MAS is categorized as a secondary form of HLH. A vast body of evidence points to uncontrolled overproduction of IFNγ as a major driver of hyperinflammation and hypercytokinemia in MAS and HLH. Emapalumab has been shown to effectively control disease activity in patients with primary HLH.

Objectives: To assess the pharmacokinetics (PK), efficacy and safety of intravenous (IV) emapalumab in patients with MAS and confirm the proposed dose regimen.

Methods: This is a pilot open-label single arm international study (NCT03311854). Patients had to have MAS (defined according to the 2016 ACR/EULAR classification criteria), on a background of confirmed, or high presumption of, SJIA, and inadequate response to high-dose IV glucocorticoids. Emapalumab initial dose was 6 mg/kg and treatment was continued at 3 mg/kg, twice weekly for a total of 4 weeks or less upon achievement of complete response. Serum concentrations of emapalumab, IFNΓ-induced chemokine CXCL9 and sIL2R were measured. Safety assessments included adverse events (AEs) and laboratory abnormalities. Efficacy was defined as complete response by week 8, i.e. absence of MAS clinical signs plus white blood cell and platelet counts above lower limit of normal, LDH, AST/ALT<1.5 x upper limit of normal, fibrinogen >100 mg/dl, and ferritin decreased by >50% or to <2000 ng/mL, whichever was lower. Twin protocols are in place to recruit 5 patients each in Europe and North America (trial not started yet). We report data on the 6 patients recruited in the European protocol.

Results: Six patients (5 females, median age 11 years, range: 2-25 years) received emapalumab according to the prescribed dose regimen. Treatment duration ranged from 3 (2 patients) to 4 weeks. Prior to emapalumab, all patients failed methylprednisolone pulses, in 2 patients plus cyclosporine A (CsA) and in 2 patients plus CsA and anakinra. The achieved emapalumab concentrations led to rapid neutralization of IFNγ as indicated by CXCL9 levels and subsequent deactivation of T cells as indicated by sIL2R levels. In all patients, complete response was achieved by week 8, in 4 patients by end of treatment (Table). Systemic glucocorticoids were weaned in all patients. Emapalumab infusions were well tolerated and none of the patients discontinued emapalumab. A CMV reactivation was reported by investigator as a serious event possibly related to emapalumab, but resolved completely with treatment.

Conclusion: Emapalumab administration with the tested dosing regimen led to rapid neutralization of IFNγ as shown by normalization of CXCL9, associated with evidence of decreased T cell activation. In all patients, emapalumab treatment was effective in controlling MAS with a favourable safety profile.

REFERENCE:

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booster while on tocilizumab, 7 on anakinra, and 5 on canakinumab. There was no relation between disease activity, type or duration, sex, age and outcome of vaccinations. No vaccine infection related to measles, rubella, mumps and varicella were reported.

Conclusion: This large, retrospective data collection demonstrates that live-attenuated booster vaccine is probably safe in children with rheumatic diseases, on immunosuppressive therapies. This strengthens the new PRES recommendation: “Vaccination of live-attenuated vaccines in patients on high-dose DMARD, high-dose glucocorticosteroids or biological agents can be considered on a case-by-case basis, weighing the risk of infections against the hypothetical risk of inducing infection through vaccination.” These data provide the basis for a large, prospective data collection study that is planned by the PReS vaccination study group.

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Exercise – more than a wonderdrug

OP0206-HPR

BENEFICIAL LONG-TERM EFFECT OF A SUPERVISED EXERCISE PROGRAM ON PHYSICAL ACTIVITY LEVEL IN PATIENTS WITH AXIAL SPONDYLOARTHROPATHIES: 12 MONTHS FOLLOW-UP OF A MULTICENTER RANDOMIZED CONTROLLED TRIAL

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Background: Exercise is recommended in the management of axial spondyloarthritis (axSpA) as it may reduce the burden of the disease. Despite this, patients with axSpA tend to have a low physical activity (PA) level and few patients engage in high intensities of exercise.

Objectives: To investigate the long-term effect of a three months supervised exercise program on PA-level in patients with axSpA.

Methods: 100 patients with axSpA were randomized to either an exercise group (EG) or no-intervention control group (CG). The exercise program participated in a three months high intensity cardiorespiratory and strength exercise program on a case-by-case basis, weighing the risk of infections against the hypothetical risk of inducing infection through vaccination.

Results: A total of 87 of 100 (87%) patients were included in the analyses (table 1). At 12 months follow-up, significantly more patients in the EG than in the CG exercised 2-3 times per week (25 [58%] vs. 15 [34%], p=0.02). Fewer patients in the EG reported to exercise at a low intensity level (low intensity reported by 3 [8%] in the EG vs. 14 [44%] in the CG, p=0.002). The regression analysis showed that participating in the exercise program (p=0.001) and earlier exercise experience (p=0.01) were the factors most associated with being physically active at 12 months follow-up (table 2).

Table 1. Baseline descriptive of the exercise group and the control group

<table>
<thead>
<tr>
<th></th>
<th>Exercise group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (n=43)</td>
<td></td>
<td>n (n=44)</td>
</tr>
<tr>
<td>Age, years, mean (min-max)</td>
<td>45.5 (23-68)</td>
<td>47.4 (24-69)</td>
</tr>
<tr>
<td>Sex, male, n (%)</td>
<td>22 (51%)</td>
<td>20 (46%)</td>
</tr>
<tr>
<td>Radiographic axSpA</td>
<td>32 (74%)</td>
<td>28 (64%)</td>
</tr>
<tr>
<td>TNF-inhibitor, n (%)</td>
<td>28 (44%)</td>
<td>20 (46%)</td>
</tr>
<tr>
<td>ASDAS, mean (SD)</td>
<td>2.6 (0.7)</td>
<td>2.5 (0.7)</td>
</tr>
</tbody>
</table>

Conclusion: A three month supervised exercise program delivered by physiotherapists had a significant long-term beneficial effect on PA-level in patients with axSpA. As regular exercise is an important part of the treatment recommendations for patients with axSpA, the results indicate that a time-limited supervised exercise program may be used as an effective intervention to succeed in reaching this recommendation.

REFERENCES:

Disclosure of Interests: Sijle Halvorsen Sveaas: None declared, Hanne Solveig Dagfjord Consultant for: Honoraria from Novartis as a steering committee member on this survey, Melissa Woll Johansen: None declared, Elisabeth Pedersen: None declared, Annelie Bilberg: None declared


Thursday, 13 June 2019

Getting a grip on the co-morbidities in gout

OP0207

URATE-LOWERING THERAPY WITH VERINURAD AND FEBUXOSTAT REDUCES SERUM URIC ACID AND ALBUMINURIA IN HYPERURICEMIC PATIENTS WITH DIABETES

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Background: Hyperuricemia is implicated as a major risk factor for chronic kidney disease (CKD), and emerging clinical data suggest that lowering serum uric acid (sUA) may protect kidney function by reducing albuminuria and slowing the rate of CKD progression. We evaluated the efficacy and safety of an intensive sUA-lowering strategy of verinurad (RDEA3170), a novel urate transport inhibitor and febuxostat in patients with Type 2 diabetes mellitus (T2DM) and albuminuria (clinicaltrials.gov: NCT03118739).

Objectives: To compare the efficacy of verinurad + febuxostat to placebo in reducing albuminuria in patients with T2DM.

Methods: A Phase 2 parallel group, randomised, double-blind, placebo-controlled clinical trial. Patients were assigned 1:1 to either verinurad 9 mg + febuxostat 80 mg (n=32) or placebo (n=28). Inclusion criteria: aged ≥18 years, sUA concentration ≥6.0 mg/dL, estimated glomerular filtration rate (eGFR) ≥30 mL/min/1.73 m², urinary albumin-to-creatinine ratio (UACR) 30–3500 mg/g and T2DM diagnosis. Exclusion criteria: history of gout or recent treatment with urate-lowering therapy. The primary endpoint was change in UACR. Secondary endpoints included sUA, renal function biomarkers, and eGFR.

Results: Baseline characteristics were similar between groups. For treatment vs placebo, respectively, mean (SD) sUA was 7.5 (1.6) vs 7.0 (0.8) mg/dL, eGFR was 59.2 (25.3) vs 68.1 (23.2) mL/min/1.73 m², and UACR was 459 (825) vs 412 (548) mg/g at baseline. The study met the primary endpoint as verinurad/febuxostat reduced UACR by 39% vs placebo after 12 weeks of treatment (p=0.07,
EFFECT OF SERUM URATE LOWERING WITH IMPROVING MENTAL WELLBEING - COACHING

| Table 1. Baseline characteristics of participants (n=99) |
|---------------------------------------------|-----------------|
| Age (years) | Mean or frequency |
| Sex | 20.0 ± 0.7 |
| Men | 62 (63%) |
| Race/Ethnicity | 37 (37%) |
| Asian | 40 (40%) |
| African American | 40 (40%) |
| Not African American | 59 (60%) |
| Serum urate | 6.4 ± 1.0 mg/dL (380.7 ± 59.5 μmol/L) |
| Mean | 4.9 ± 0.7 mg/dL (291.5 ± 41.6 μmol/L) |


Disclosure of Interests: Angelo Gatto: None declared, David Calhoun: None declared, Elizabeth Rahn: None declared, Suzanne Oparil: None declared, Paul Muntner Grant/research support from: Dr. Muntner declares research grant from Amgen, Peng Li: None declared, David Redden: None declared, Tanja Dudenbostel: None declared, Jeff Foster: None declared, Stephanie Biggers: None declared, Daniel Feig: None declared, Kenneth Saag Grant/research support from: Amgen, Ironwood/AstraZeneca, Horizon, SOBI, Takeda, Consultant for: Abbvie, Amgen, Ironwood/AstraZeneca, Bayer, Gilead, Horizon, Kowa, Radius, Roche/Genentech, SOBI, Takeda, Teijin DOI: 10.1136/annrheumdis-2019-eular.1623

EFFECT OF SERUM URATE LOWERING WITH ALLOPURINOL ON BLOOD PRESSURE IN YOUNG ADULTS

Table 2. Change in blood pressure parameters during allopurinol and placebo treatment phases (n=99), Mean (SD)

<table>
<thead>
<tr>
<th>Outcomes (mmHg)</th>
<th>Placebo</th>
<th>Allopurinol</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic blood pressure</td>
<td>0.16</td>
<td>0.71 (8.21)</td>
<td>0.52</td>
</tr>
<tr>
<td>Diastolic blood pressure</td>
<td>0.22 (5.81)</td>
<td>0.28 (6.58)</td>
<td>0.68</td>
</tr>
<tr>
<td>Mean arterial pressure</td>
<td>-0.43 (5.63)</td>
<td>0.56 (6.66)</td>
<td>0.54</td>
</tr>
</tbody>
</table>

Background: The association between serum urate and hypertension continues to be controversial. Animal models and studies in adolescents provided strong support of urate-lowering therapy (ULT) efficacy to improve early hypertension (1), while one recent randomized-controlled study in adults failed to find benefit (2).

Objectives: To test the hypothesis that serum urate reduction with allopurinol would lead to blood pressure reductions in young adults with pre-hypertension.

Methods: Single center, double-blinded, crossover trial in which participants were randomly assigned to allopurinol (300 daily mg) or placebo for a period of one month each. Adults ages 18-40, with baseline systolic blood pressure (SBP) ≥ 120 and < 160 mm Hg or diastolic blood pressure ≥ 80 and < 100 mm Hg, and serum urate ≥ 5.0 mg/dL (297.4 μmol/L) or ≥ 4.0 mg/dL (237.9 μmol/L) (men or women, respectively) were enrolled. Main exclusion criteria included chronic kidney disease, gout, or use of ULTs. The primary outcome was change from baseline in SBP assessed by 24 hour ambulatory blood pressure monitoring. Safety assessments were also conducted.

Results: 95 participants were randomized, and 82 completed study participation. The primary outcome was significant (p=0.001) and by a non-significant -0.04 ± 0.75 mg/dL (2.4 ± 44.6 μmol/L) while taking placebo. SBP changed by -0.71 ± 8.21 mmHg during the period assigned to placebo versus -0.16 ± 7.33 mmHg during the period assigned to placebo. The difference between these changes in SBP was not significant (p=0.52) (Table 2). Changes in diastolic blood pressure and mean ambulatory blood pressure also a not significantly different during allopurinol and placebo exposure periods. In post hoc analyses, there was a trend towards significant blood pressure decreases in the small participant subgroup with serum urate of > 6.5 mg/dL (386.7 μmol/L) at baseline visit. No allopurinol hypersensitivity events or other serious adverse events were observed.

Conclusion: In the intention-to-treat analysis, urate-lowering therapy with allopurinol in young adults did not lead to reductions in blood pressure when compared with placebo. Blood pressure reductions with allopurinol may be limited only to participants with higher baseline serum urate levels.

REFERENCES:

THURSDAY, 13 JUNE 2019
Treat ment is more than drugs.

IMPROVING MENTAL WELLBEING - COACHING PEERS TO USE TOOLKIT FOR MIND

Disclosure of Interests: Angelo Gatto: None declared, David Calhoun: None declared, Elizabeth Rahn: None declared, Suzanne Oparil: None declared, Paul Muntner Grant/research support from: Dr. Muntner declares research grant from Amgen, Peng Li: None declared, David Redden: None declared, Tanja Dudenbostel: None declared, Jeff Foster: None declared, Stephanie Biggers: None declared, Daniel Feig: None declared, Kenneth Saag Grant/research support from: Amgen, Ironwood/AstraZeneca, Horizon, SOBI, Takeda, Consultant for: Abbvie, Amgen, Ironwood/AstraZeneca, Bayer, Gilead, Horizon, Kowa, Radius, Roche/Genentech, SOBI, Takeda, Teijin DOI: 10.1136/annrheumdis-2019-eular.1623

Tina Hongisto, The Finnish Rheumatism Association, Helsinki, Finland

Background: The theme for the Finnish Rheumatism Association for 2019 is Mind and Me. The Age Institute in Finland launched a project called Mental Wellbeing to Promote Older People’s Knowhow to Face Life’s Challenges and the project was piloted at the Finnish Rheumatism Association in 2018. During the pilot project, staff members from the Finnish Rheumatism Association and volunteers from its member organisations were trained as Tools for Mind Coaches. This training gave new tools for peer support targeting older people and their mental wellbeing. The Coaches may use the tools developed by the Age Institute, and these include Mind Tools, Senior Mind Pack of 52 cards, Nature Attraction Path, A Guide for Life Skills Coaches and a pocket book on Mental Wellbeing. The project especially targeted older people and their families in challenging life situations by promoting their mental wellbeing.

Objectives: To disseminate the theme and activities of mental wellbeing in member associations. To utilise the tools for Mind in the activities of the Finnish Rheumatism Association and its member associations. To promote mental wellbeing to members.

Methods: In the pilot project in 2018 the Age Institute organized three mental wellbeing training sessions for peer support group coaches, each lasted 1-2 days. The Finnish Rheumatism Association provided the coaches with some of the Tools for Mind. The training sessions included theory and practices. Participants were introduced how to use the Tools for Mind and they were encouraged to think for other applications of the tools. Also the themes discussed included elements of mental wellbeing, solution-focused approach, organising peer support groups for old people with chronic illnesses and ethical principles for group activities.

Results: There were altogether 11 people from the Finnish Rheumatism Association and its member associations that finished the training for Mind Coaches. Feedback from the participants was positive and the Tools for Mind were not only considered as useful practical tools but they also increased self-confidence and enthusiasm for peer led support groups. Senior Mind Pack of 52 cards were described as multipurpose and having good visual quality. All Tools for Mind were considered as thought-provoking tools to start conversation. Practical tools help
to recognise new aspects of one’s own illness and they can be used to give support to people in different stages of their illness. Participants felt that forming groups and increasing cooperation between trained coaches and local associations need to be supported by the umbrella organisation, Finnish Rheumatism Association. Toools for Mind have successfully been used in a Fibromyalgia group and in senior groups for veterans (who did not have any RMDs).

Conclusion: The Finnish Rheumatism Association is creating new activities to endorse mental wellbeing. The training in 2018 will be used as a model for training coaches in mental wellbeing and it will be introduced in member organisations in 2019. Four training sessions will be arranged around Finland in the spring 2019.

The programme will follow the pilot project programme. Training includes learning how to use the tools for mental wellbeing, going through the elements of mental wellbeing, solution-focused practices, organising peer support groups for old people with chronic illnesses and ethical principles. If possible, it is always good to have a trained Coach in the training, to tell about his/her experiences of using the Tools for Mind, how people have reacted to using the tools, and what kind of challenges and good moments the coach has experienced in group work. In 2019, the tools are utilised for example in monthly tasks concerning mental wellbeing and the Senior Mind Pack of 52 cards are being used in the member organisation visits to start conversation.

REFERENCE:

Disclosure of Interests: None declared

THURSDAY, 13 JUNE 2019
Diagnostic challenges in vasculitis

OP0210 FALSE POSITIVES OF ULTRASOUND IN GIANT CELL ARTERITIS. SOME DISEASES CAN ALSO HAVE HALO SIGN
Elisa Fernández, Irene Monjo, Gemma Bonilla, Chamaida Plasencia, Maria-Eugenia Miranda-Carús, Alejandro Balza, Eugenio de Miguel. La Paz University Hospital, Rheumatology, Madrid, Spain

Background: Giant cell arteritis (GCA) is the most common systemic vasculitis in the elderly. The halo sign has been shown as an accepted valid test in the diagnosis of GCA in trained units[1-2]. However, to further improve the specificity, the sonographer should know some pathologies that can mimic halo signs since they also produce a hypoechoic increase of the arterial wall thickness.

Objectives: The aim of our study was to identify the causes and diseases that could be associated with the false positive diagnoses of GCA made by color Doppler ultrasound (CDUS).

Methods: Observational study of 305 patients with temporal artery CDUS findings compatible with GCA. The medical histories of these patients were reviewed and demographic, physical examination, clinical and analytical data were collected. The clinical diagnosis based on the long term follow-up of the patient was established as the definitive true diagnosis.

Results: 13 of the 305 cases included (4.3%) were false positives. The characteristics of these 13 patients and their final diagnoses are shown in table 1. 69.2% were women, while 30.8% were men. The mean age was 73.3 ± 8.0 years. Analytically, the mean ESR was 64.8 ± 42.3 mm/h, CRP 50.8 ± 60.0 mg/L, and hemoglobin 12.8 ± 2.0 g/dL. Five patients (38.5%) fulfilled the ACR GCA classification criteria and eight did not (61.5%). A temporal artery biopsy was performed in 8 of the 13 patients (61.5%), with negative results in all of them. Eleven patients had CDUS involvement of superficial temporal arteries. Five had 1 branch involved (38.5%), three 2 branches (23.1%), one 3 branches (7.7%) and two 4 branches (15.4%). In addition, two patients (15.4%) had isolated halo sign in the axillary arteries, one unilateral and the other bilateral. Regarding the definitive diagnosis, four patients were polymyalgia rheumatica (30.8%), three aneurysmatosis (23.1%), and there was one case of non-Hodgkin’s Lymphoma type T, osteomyelitis of the skull base, primary amyloidosis associated with multiple myeloma, granulomatosis with polyangiitis, urinary sepsis and narrow-angle glaucoma.

A percentage of false positives in the CDUS for the diagnosis of GCA is low. Nevertheless, other some diseases can also produce halo sign and the clinician should be aware of this to improve the accuracy of the ultrasound test.

REFERENCES:

Disclosure of Interests: Elisa Fernández: None declared. Irene Monjo: None declared. Gemma Bonilla: None declared. Chamaida Plasencia Speakers bureau: Pfizer, MSD, Maria-Eugenia Miranda-Carús Grant/research support from: Roche Pharma, BMS, Alejandro Balza Grant/research support from: Abbvie, Pfizer, Novartis, BMS, Nordic, Sanofi, Consultant for: Abbvie, Pfizer, Novartis, BMS, Nordic, Sanofi, Sandoz, Lilly, Payed instructor for: Pfizer, Speakers bureau: Pfizer, Novartis, UCB, Nordic, Sanofi, Sandoz, Lilly, Eugenio de Miguel: None declared

OP0211 ULTRASONOGRAPHY CAN POTENTIALLY BE THE FIRST CHOICE OF IMAGING IN SUSPECTED EXTRA-CRANIAL GCA
Hilde Hop1, Douwe J Mulder1, Maria Sandovic2, Andor Glaudemans2, Arle Van Roon1, Riemer Star1, Elisabeth Brouwer1. 1University Medical Center Groningen, Internal Medicine, Groningen, Netherlands; 2University Medical Center Groningen, Rheumatology and Clinical Immunology, Groningen, Netherlands

Background: Color duplex ultrasonography (CDU) is recommended as first line of imaging in patients suspected for cranial GCA [1]. However, extra-cranial involvement without temporal artery involvement is found in up to 40% of GCA patients [2]. CDU is very suitable to also assess extra-cranial artery inflammation, of which the axillary artery is relatively easy to assess. However, data on the value of CDU in extra-cranial GCA is limited [3].

Objectives: We aimed to [1] evaluate the performance of axillary artery CDU in patients with extra-cranial GCA by comparing CDU findings with [18F]-FDG PET/CT findings. Furthermore, to [2] compare the sensitivity and specificity of adding assessment of axillary arteries to temporal artery CDU, over temporal artery CDU only.

Methods: Consecutive patients suspected of GCA who underwent CDU examination of the temporal and axillary arteries between 2013 and 2017 were

<table>
<thead>
<tr>
<th>Patient</th>
<th>Definitive diagnosis</th>
<th>Biopsy result</th>
<th>Artery involved</th>
<th>Number of arterial branches</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Non-Hodgkin’s T lymphoma</td>
<td>Negative</td>
<td>Temporal</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>Narrow-angle glaucoma</td>
<td>No done</td>
<td>Temporal</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>Osteomyelitis of the skull base</td>
<td>No done</td>
<td>Temporal</td>
<td>4</td>
</tr>
<tr>
<td>4</td>
<td>Polymyalgia rheumatica</td>
<td>Negative</td>
<td>Temporal</td>
<td>2</td>
</tr>
<tr>
<td>5</td>
<td>Urinary sepsis</td>
<td>Negative</td>
<td>Temporal</td>
<td>1</td>
</tr>
<tr>
<td>6</td>
<td>Polymyalgia rheumatica</td>
<td>Negative</td>
<td>Temporal</td>
<td>1</td>
</tr>
<tr>
<td>7</td>
<td>Polymyalgia rheumatica</td>
<td>Negative</td>
<td>Temporal</td>
<td>1</td>
</tr>
<tr>
<td>8</td>
<td>Amyloidosis due to multiple mieloma</td>
<td>Negative (deposit of amyloid material)</td>
<td>Temporal</td>
<td>4</td>
</tr>
<tr>
<td>9</td>
<td>Atherosclerosis</td>
<td>No done</td>
<td>Axilar</td>
<td>1</td>
</tr>
<tr>
<td>10</td>
<td>Atherosclerosis</td>
<td>No done</td>
<td>Axilar</td>
<td>1</td>
</tr>
<tr>
<td>11</td>
<td>Polymyalgia rheumatica</td>
<td>Negative</td>
<td>Temporal</td>
<td>1</td>
</tr>
<tr>
<td>12</td>
<td>Atherosclerosis</td>
<td>No done</td>
<td>Temporal</td>
<td>2</td>
</tr>
<tr>
<td>13</td>
<td>ANCA-associated vasculitis</td>
<td>No done</td>
<td>Temporal</td>
<td>2</td>
</tr>
</tbody>
</table>

Conclusion: The percentage of false positives in the CDUS for the diagnosis of GCA is low. Nevertheless, other some diseases can also produce halo sign and the clinician should be aware of this to improve the accuracy of the ultrasound test.

Disclosure of Interests: : None declared

Table 1. Final diagnoses for false positive halo signs and associated ultrasound findings.
DIGESTIVE INVOLVEMENT IN PATIENTS WITH PRIMARY SJÖGREN SYNDROME FROM THE SJOGRENRENSER SPANISH REGISTRY

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Background: Primary Sjögren’s syndrome (pSS) is a systemic autoimmune disease characterized by lymphocytic infiltration of the exocrine glands. Among the extraglandular manifestations, digestive involvement (DI) is frequent, and may condition the quality of life of these patients. There are few studies that systematically analyze gastrointestinal involvement in pSS.

Objectives: To describe the prevalence of DI in patients with pSS included in SjogrenRENSER Spanish registry and the phenotype of these patients, and to analyze their association with other clinical manifestations, serological markers, activity index and treatments used.

Methods: Transversal multicenter study that includes all patients of SJOGRENRENSER registry (patients who meet 2002 pSS classification criteria), a study conducted in 33 units of rheumatology in Spain between 2014-2016, which collected demographic and clinical and serological data (1). Patients were classified according to the presence of patients, GCA that included esophagus, stomach, intestine, liver and pancreas). A descriptive analysis was done, with means and standard deviations, frequencies and proportions. Student t for quantitative variables and Chi2 for qualitative ones were performed to evaluate differences between groups. The association of DI with other variables was analyzed by bivariate and multivariate binomial logistic regression analysis. In the multivariate model all variables with p <0.2 in the bivariate were included, and the effect of age and sex was controlled.

Results: From 437 patients included (95% women, median age of 58 years), 59 (13.5%) had some DI (21 (36%) chronic atrophic gastritis, 12 (20%) esophageal dismotility, 3 (5%) lymphocytic colitis, 23 (39%) other), 54% of patients developed DI at the time of pSS diagnosis or later, and 45% before the diagnosis, with a mean age of 49 years at the onset of pSS symptoms. Patients with DI were older, both at diagnosis, onset of pSS symptoms and inclusion in the cohort, than those without it. There were no differences in the ESSDAI index between both groups.

Conclusion: In patients with DI more thyroid involvement and C3 hypocomplementemia. In addition, patients with DI had been treated more frequently with glucocorticoids and immunosuppressants. In the multivariate analysis, DI was significantly associated with older age at diagnosis (OR 1.03 (1.00-1.05); p=0.05), more C3 hypocomplementemia (OR 2.40 (1.0-5.26); p=0.02) and absence of anti-Ro antibodies (OR 0.33 (0.12-0.87) p=0.034). Significant factors for DI were sex, diarrhea and Raynaud.

Disclosure of Interests: Sheila Melchor: None declared, Carlos Sánchez-Piedra: None declared, Monica Fernandez Castro: None declared, Jose Luis Andreu: None declared, Victor Martinez Taboada: None declared, Alejandro Olive: None declared, Jose Rosas Consultant for: Abbvie, Agen, Bristol, Janssen, Lilly, Merck Sharp & Dohme, Pfizer, UCB Pharma, Speakers bureau: Abbvie, Agen, Bristol, Janssen, Lilly, Merck Sharp & Dohme, Pfizer, UCB Pharma, Patricia Carrera: None declared


THURSDAY, 13 JUNE 2019

Difficult to manage Sjögren’s syndrome and Myositis

OP0212

MYOFASCIA-DOMINANT: INFLAMMATION DETECTED ON WHOLE BODY MRI PREDICTS RAPIDLY PROGRESSIVE INTERSTITIAL LUNG DISEASE IN PATIENTS WITH DERMATOMYOSITIS

Kohei Kanie, Michihiro Kono, Michiko Kono, Yuichiro Fujieda, Masaru Kato, Toshiyuki Bohgaki, Olga Amengual, Kenji Oku, Shinuke Yasuda, Tatsuya Asumi, Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Japan

Background: Rapidly progressive interstitial lung disease (RPILD) is a major cause of death in patients with dermatomyositis (DM). Early diagnosis and aggressive immunosuppressive therapy are required in RPILD to improve the prognosis. Clinically amyopathic dermatomyositis (CADM) and anti-melanoma differentiation-associated gene 5 antibody are known as risk factors for RPILD. However, 70% of the patients with CADM do not develop RPILD. Whole-body magnetic resonance imaging (WB-MRI) can detect inflammation of whole muscle and myofascia. Although recent studies have indicated that MRI could be...
useful for assessing disease activity\(^2\), the relation between MRI findings and RPILD has not been investigated.

**Objectives:** In this study, we assessed whether WB-MRI findings are related with RPILD in patients with DM.

**Methods:** This retrospective study comprised 33 patients with DM who underwent WB-MRI in our hospital before the initiation of treatment for myositis. Muscular and myofascial signal abnormalities were scored on 42 muscular groups. The ratio of myofascial score to muscular score (myofascia/muscle ratio) was calculated and used to evaluate myofascia-dominant inflammation. RPILD was defined as the acute onset and rapid worsening of dyspnea, hypoxemia and radiographic ILD/fibrosis within 1 month.

**Results:** Of 33 patients, 16 were CADM, and 24 had ILD, including 8 patients with RPILD. All patients including CADM showed abnormal signal intensity in muscle and myofascia (scores median: 15 and 21, respectively). Muscle scores positively correlated with serum level of creatine kinase (\(r=0.672, p<0.001\)). The patients with RPILD showed a significantly higher myofascia/muscle ratio compared with that in the non-RPILD patients (2.167 vs 1.000; \(p=0.018\)). Logistic regression analysis identified myofascia/muscle ratio >1.53 (odds ratio: 141.90, \(p=0.042\)) and older age (odds ratio: 1.15, \(p=0.041\)) as independent risk factors for RPILD.

**Conclusion:** We newly defined myofascia-dominant inflammation using WB-MRI as a predictor to develop RPILD in patients with dermatomyositis.

**REFERENCES:**


**Disclosure of Interests:** Kohei Karino: None declared. Michihito Kono: None declared. Michihito Kono Grant/research support from: GlaxoSmithKline, Yuichiro Fujieda: None declared. Masaru Kato Grant/research support from: GSK, Actelion, Speakers bureau: GSK, Actelion, Bayer, Nippon Shinyaku, Eli Lilly, Chugai, Pfizer, Ayumi, Eisai, Asahi Kasei, Toshiyuki Bohgaki: None declared. Olga Amenual: None declared. Yuichiro Kohei Karino: None declared. Michihiro Kono: None declared. Ana-Luisa Stefanski: None declared, Annika Wiedemann: None declared, Andrea Lino: None declared, Thomas Dörner: None declared, Andréia Lino: None declared, Thomas Dörner Grant/research support from: Eli Lilly, Janssen, Roche, UCB Pharma, Consultant for: Eli Lilly, Janssen, Roche, UCB Pharma, Speakers bureau: Eli Lilly, Janssen

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**THURSDAY, 13 JUNE 2019**

Anergy, exhaustion or post-activation in autoimmunity – facts and future consequences

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**Background:** Prior studies on systemic lupus erythematosus (SLE) B cells reported an altered responsiveness to TLR9 stimulation, such as proliferation, cytokine production as well as indications for impaired T and B cell interaction \([1]\). The role of co-inhibitory and co-stimulatory (check-point) molecules in this setting has not been delineated in detail so far.

**Objectives:** Assess the expression of co-inhibitory (PD-1, PD-L1 and PD-L2) and co-stimulatory molecules (CD86 and CD40) by SLE B cells after in vitro stimulation and their potential contribution for B cell hyporesponsiveness in SLE.

**Methods:** PBMCs from 10 SLE patients and 10 healthy donors (HD) were stimulated with IL-2/IL-10, anti (α) - B cell receptor (BCR), CpG and CD40L alone or in combination. Expression of PD-1, PD-L1, PD-L2 as well as CD86, CD40 on CD19 +CD20+ B cell subsets after 48h stimulation was analyzed by FACS. CD71 was employed to measure proliferation of CD19 “CD20” B cells after 48h stimulation.

**Results:** SLE B cells exhibited a substantially decreased upregulation of PD-L1 (\(p=0.0006\)) and CD86 (\(p=0.0188\), Fig.1) associated with significantly reduced B cell proliferation (\(p=0.0039\)) after 48h stimulation with CpG alone and in combination compared with HD. While TLR9 engagement in SLE B cells appeared to be abnormal, activation of CD40 resulted into a consistent upregulation of both, inhibitory and stimulatory molecules. PD-L1 was positively correlated with B cell proliferation (\(p=0.003\)). Notably, the expression of PD-L1 and CD86 correlated inversely with Siglec-1, as surrogate marker for interferon signature (\(p<0.0001\) and \(p=0.0021\)) respectively). PD-L1 expression correlated inversely with cSLE-DAI (\(p=0.0087\)).

**Conclusion:** Hyporesponsive/anergic lupus B cells are characterized by a functionally diminished PD-L1 and CD86 upregulation associated with reduced proliferation and clinical activity. The data mandate evaluations of innovative therapeutic interventions in SLE.

**REFERENCE:**


**Disclosure of Interests:** Ana-Luisa Stefanski: None declared, Annika Wiedemann: None declared, Karin Reiter: None declared, Andrea Lino: None declared, Thomas Dörner Grant/research support from: Eli Lilly, Janssen, Roche, UCB Pharma, Consultant for: Eli Lilly, Janssen, Roche, UCB Pharma, Speakers bureau: Eli Lilly, Janssen

**DOIs:** 10.1136/annrheumdis-2019-eular.3186
Fracture liaison service: an opportunity for prevention

Background: Osteoporosis is a well-known complication of rheumatoid arthritis (RA) (1). NICE advises that health providers do not routinely assess fracture risk in people with RA aged under 50 years unless they have other major risk factors. However, studies suggest that young people with RA are at increased fracture risk even before age 50 (2-4).

Objectives: To measure the incidence and risk of first and subsequent fracture in adults with RA aged under 50 in the UK.

Methods: A retrospective observational cohort study with matched control using data from Clinical Practice Research Datalink (CPRD) of adults ≥18 years with diagnosis of RA recorded from 1987 to 2016. Patients were followed from index date to the first fracture and subsequent fracture. Cases were adults with a new diagnosis of RA with at least one day of follow-up during the period. These cases were matched to 3 controls by age, sex, GP surgery and calendar year. The date of RA diagnosis date is the index date for cases and their matched controls. CPRD data has a high level of data validity in reporting of fractures but subsequent fractures may be recorded more than once. In this analysis when subsequent fractures were of the same body part the fracture had to occur at least 6 months after the previous fracture to be classified as a “subsequent fracture”.

“First fracture” is the first fracture occurring after the index. “Subsequent fracture” is the fracture occurring after the first fracture. “Pre-index fracture” is a fracture that occurs before the index date.

Results: The characteristics of the study population are shown in Table 1.

<table>
<thead>
<tr>
<th>Variable</th>
<th>N (%)</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (female)</td>
<td>8,232 (74.03)</td>
<td>24,676 (73.96)</td>
</tr>
<tr>
<td>Glucocorticoid prescription &lt;=6 months before index</td>
<td>6,148 (55.29)</td>
<td>3,430 (30.85)</td>
</tr>
<tr>
<td>Age group</td>
<td>1648 (14.82)</td>
<td>4,251 (12.74)</td>
</tr>
<tr>
<td>0-9</td>
<td>1,542 (13.87)</td>
<td>4,654 (13.95)</td>
</tr>
<tr>
<td>40-49</td>
<td>3,430 (30.85)</td>
<td>10,308 (30.90)</td>
</tr>
<tr>
<td>60-69</td>
<td>6,148 (55.29)</td>
<td>18,402 (55.16)</td>
</tr>
<tr>
<td>Pre-index fracture</td>
<td>954 (8.57)</td>
<td>1,995 (5.97)</td>
</tr>
<tr>
<td>First fracture</td>
<td>197 (1.77)</td>
<td>354 (1.06)</td>
</tr>
</tbody>
</table>

The incidence rate of first fracture for cases was 9.02 per 1000-person years (95% CI 8.46-9.61), for controls 6.85 per 1000-person years (95% CI 6.55-7.15). The incidence rate ratio (IRR) for first fracture was 1.32 (95% CI 1.22-1.426; p<0.00). The incidence rate of subsequent fracture was 1.78 (95% CI 1.55-2.05) per 1000-person years for cases and 1.17 (1.05-1.29) per 1000-person years for controls. The IRR for subsequent fracture was 1.53 (95% CI 1.28-1.833; p<0.00). A Cox’s proportional hazards model was used to estimate the hazard (or risk) of first and subsequent fracture for cases and controls stratified by age. Those with a pre-index fracture and with a glucocorticoid prescription prior to the index date had significantly higher hazard ratios for first and subsequent fracture. Women had a higher hazard ratio for first fracture.

Conclusion: This study shows that the incidence of fracture in patients with RA aged under 50 is significantly higher than in matched controls. This is true for the first fracture and for the subsequent fracture and is significantly higher for women in those under 50 for first fractures.

REFERENCES:
EVALUATION OF PATIENTS’ EXPERIENCES OF AN INTENSIVE SMOKING CESSATION INTERVENTION FOR PEOPLE WITH RHEUMATOID ARTHRITIS

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Background: Smoking is considered one of the most important modifiable environmental risk factors to the pathogenesis of rheumatoid arthritis (RA). Smoking may also exacerbate the symptoms of RA. A randomized controlled trial (RCT) testing the effect of an intensive smoking cessation intervention on smoking cessation and disease activity in people with RA is currently being carried out (1).

Objectives: To evaluate how people with RA experienced an intensive smoking cessation intervention.

Methods: We conducted a qualitative study with individual interviews. Participants were recruited consecutively from the intervention group in a smoking cessation RCT after having completed both the smoking cessation intervention and the three-month follow-up visit. The analysis was based on thematic analysis (2). One patient research partner was involved in all phases of the study.

Results: In total 12 patients with RA were included (6 female, mean age 58 years (range 33-71)). We identified seven themes illustrating participants’ experiences of the smoking cessation intervention. The themes were: Instilling hope for smoking cessation referring to the initial invitation to participate in the RCT and the allocation to the intervention group, which participants seized as a chance to stop smoking, Having a fellow traveler on the road to smoking cessation referring to their cooperation with the smoking cessation counselor who was important for maintaining motivation for smoking cessation, Tangible evidence that smoking cessation makes a difference referring to improved carbon monoxide levels which motivated endeavors to quit smoking, Apprehension – fear of a new dependence referring to participants’ fear of becoming addicted to nicotine replacement therapy instead of smoking, Breaking habits referring to ongoing reflection on and efforts to quit smoking using the tools and knowledge obtained from the smoking cessation intervention, Why wasn’t I told? Referring to the lacking provision of information on smoking and RA from health professionals, and Denial referring to neglect of the detrimental impact of smoking on RA symptoms and overall health.

Conclusion: The participants were grateful for the offer to participate in a RCT and a smoking cessation intervention because it created an opportunity for them to stop smoking. They valued getting concrete information about detrimental effects of smoking on RA and RA treatment. Many requested that health professionals focus more proactively on smoking and smoking cessation.

REFERENCES:


Disclosure of Interests: Ida Kristiane Roelsgaard: None declared, Thordis Thomsen: None declared, Mikkel Østergaard/Grant/research support from: Abbvie, Celgene, Centocor, Merck, Novartis, Consultant for: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCBS, Speakers bureau: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCBS, Grete Semb: None declared, Lena Andersen: None declared, Bernt Appel Esbensen/ Speakers bureau: For Pfizer

LUPUS EUROPE YOUTH PANEL – WHAT WE LEARNED FROM YOUNG PEOPLE LIVING WITH LUPUS
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Background: Since 2014, Lupus Europe conducts patient panels, where 10 to 12 persons from all over Europe living with lupus discuss the selected topic guided by facilitators living with lupus themselves. This allows to capture qualitative feedback of relevance, without the obstacle of the “white blouse”. In 2018, 10 Young (18-27) European Lupus patients (8 female, 2 male) with diverse Lupus types met to discuss “Lupus and youth”.

Objectives: Understand specificity of being young with lupus to better include young patients in Lupus groups action plans

Methods: 11 young patients, mostly with little or no involvement in patient groups were recruited through Lupus Europe’s network. They were asked to send ahead of time their top challenges/issues living with lupus as well as their key questions for the panel. This input was used to build the 2 days program itself. Mid May, 10 of the 11 met face-to-face in Brussels, and explored multiple aspects of their input though 7 specifically designed interactive workshops

Results: While they considered taking pills every day as a key problem, they preferred to focus on the collective issues of being understood by friends and family and having to live with limitations.

A big “Wow” was the feeling of guilt expressed by several female participants (guilt of imposing limits to their partners, guilt of not being able to do as much as others, …), a very important underlying dimension of their social and affective life, which is likely much misunderstood by doctors and patient organizations; young people with lupus remain fundamentally more positive on their life with lupus than the average patients. While they perceive lupus as being “all over their lives”, they refuse to be ruled by it.

They view the future of a LUPUS EUROPE youth group as a “virtual group” on social media, with minimal commitment required, but bringing together “friends” around highly visual messages, short stories and the exchange of ideas that could lead to small group gatherings.

On the medical front, when we probed what would drive them to consider joining a clinical trial, clear first media is their lupus doctor, second are national lupus groups and LUPUS EUROPE. Other medias have a very limited impact.

Conclusion: Young patients needs must be addressed in a more aspirational way and using more virtual tools than average patients (more focused on health issues and geographic proximity). The feeling of guilt of young women with regards to their affective life must be further explored to give them confidence and reassurance.

REFERENCE:
[1] Lupus Europe Patient panel 3 project report, availablle on request at secretariat@lupus-europe.org

Disclosure of Interests: Alain Comet Grant/research support from: None declared, Barbara Tolusso: None declared, Lucy MacDonald : None declared, Marilyn Walsh: None declared, Aziza Elmesmari: None declared, Barbara Tolusso: None declared, Lucy MacDonald: None declared, Marilyn Walsh : None declared, Grant/research support from: No direct financial grants from Pharmaceutical companies, but some grants accrued to LUPUS EUROPE rather than the company, Jeanette Andersen: None declared

Oligomeric S100A4 induces monocyte innate immune memory

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Background: Trained immunity is a process of innate immune memory in which a primary stimulus such as beta-glucan can enhance the response of monocytes to secondary stimuli. The concept that specific damage associated molecular patterns (DAMPs) in rheumatoid arthritis (RA) could cause trained immunity which is involved in the disease pathogenesis has not been investigated so far. The oligomeric form of S100A4 (oS100A4) is a potent inducer of pro-inflammatory cytokines which is found in the plasma of patients with rheumatoid arthritis (RA).

Objectives: Aims to investigate whether oS100A4 induces trained immunity in monocytes and characterize the molecular pathways involved in this process.

Methods: Monocytes were isolated from peripheral blood of healthy donors using density gradient centrifugation. To induce training, monocytes were stimulated with 2 μg/ml of oS100A4 and 1 μg/ml β-glucan for 24 hours (n=8). We searched for differential gene expression by RNA sequencing in order to identify factors that play a role in the initial stages of trained immunity. On day 4, LPS (10 ng/ml) was added. After 24 hours, IL-6 and TNFα were measured in cell culture supernatants by ELISA. The training protocol was repeated in monocytes transfected with PRDM8 siRNA using Lipofectamine (n=4). In addition, plasma levels of S100A4, CCL5 and IL-6 were measured in a cohort of RA patients (n=36) and healthy controls (n=18) by ELISA and PRDM8 transcripts in RA peripheral blood monocytes were quantified by RT-PCR.

Results: Monocytes primed with oS100A4 showed increased releases of IL-6 and TNFα in response to a subsequent LPS stimulation. RNA-Seq revealed the differential expression of 902 genes upon oS100A4 and 667 upon beta-glucan (mean and median > 2 fold, FDR<0.01). Among the differential genes, 601 were upregulated in S100A4 and 447 in beta-glucan stimulated cells. Upregulated genes included chemokine/cytokine and epigenetic factors. When we compared the upregulated genes from oS100A4 and beta-glucan stimulated cells, 63% of chemokines/cytokines and 50% epigenetic factors were identical. Interestingly, the histone methyltransferase PRMD8 was found to be a major regulator of pro-inflammatory mediators by both stimuli. siRNA knockdown of PRMD8 abolished the training effect of oS100A4 by decreasing the LPS induced release of IL-6 and TNFα (p<0.01). Furthermore, we analyzed a cohort of monocytes taken from RA patients. Higher PRDM8 transcription in RA monocytes was associated with increased plasma levels of CCL5 and IL-6 (r = 0.52 and 0.55, p < 0.01). RA patients in remission versus active patients showed significantly lower PRDM8 transcripts (p = 0.05).

Conclusion: Oligomeric S100A4 induced trained immunity in monocytes similarly to beta-glucan. PRDM8 histone methyltransferase is involved in this process that appears to be activated in monocytes of RA patients.

Disclosure of Interests: Emmanuel Karuzakas: None declared, Agnieszka Pajak: None declared, Niels Riksen: None declared, Leo Joosten: None declared, Mihai Netea: None declared, Esther Latung: None declared, Eric Stroons: None declared, Adrian Ciurea: Consultant for: AbbVie, Celgene, Janssen-Cilag, MSD, Eli Lilly, Novartis, Pfizer, UCB, speakers bureau: AbbVie, Celgene, Janssen-Cilag, MSD, Eli Lilly, Novartis, Pfizer, UCB, Oliver Deltour: Grant/research support from: Prof. Distler has/had consultancy and may even have life-threatening sequelae. This disease is often under-screened, especially in at-risk populations that require multidisciplinary care such as patients with rheumatoid arthritis (RA) and ankylosing spondylitis (AS) [1,2,3,4,5,6]. Moreover, a recent study showed that the scoranographic bone attenuation coefficient of the first lumbar vertebra (SBAC-L1) with a threshold at 145 Hounsfield Units (HU) identified 96.6% of patients in the general population with a vertebral fracture (VF), whereas DEXA (with a T-score ≤ 2.5) identified only 39% of these patients [7].

Objectives: The aim of the study was to identify the prevalence of vertebral fractures (VFIs) and to measure the scoranographic bone attenuation coefficient of the first lumbar vertebra (SBAC-L1) based on CT-scan examinations of patients with rheumatoid arthritis (RA), patients with ankylosing spondylitis (AS) and in a control group.

Methods: This monocentric and retrospective study included patients who were evaluated between 2009 and 2017 with a diagnosis of RA based on the ACR/EULAR criteria, those with a diagnosis of AS based on the New-York criteria, and a RA-matched control group. All of the patients received a CT-scan. The osteoporosis risk factors, data from dual energy X-ray absorptiometry (DEXA) and clinical characteristics were collected. VFIs were determined via CT-scans according to the Genant classification, and the SBAC-L1 was measured in Hounsfield units (HU). SBAC-L1 ≤ 145 HU (fracture threshold) defined patients at risk of VFIs.

Results: A total of 244 patients were included (105 RA, 83 AS, 56 controls). The AS group was younger and primarily consisted of males. Of the 4,365 vertebrae studied, 66 osteoporotic VFIs were found in 36 patients: 18 (17.1%) patients with RA, 13 (15.7%) patients with AS and 5 (8.9%) controls. The SBAC-L1 was 142.2 ± 10.7 HU. A T-score -2.5 SD and a SBAC-L1 £ 145 HU were significantly lower in the RA and AS groups than in the control group. Furthermore, SBAC-L1 ≤ 145 HU was associated with a VF (OR = 2.35 [95% CI: 1.12-4.92] and 2.06 [95% CI: 1.04-4.10], respectively).

Conclusion: The SBAC-L1 was significantly lower in the RA and AS groups than in the control group. Furthermore, SBAC-L1 ≤ 145 HU was associated with a higher risk of VFIs, with an odds ratio similar to that of a DEXA.

REFERENCES:
Efficacy and Safety of E6011, an Anti-Fractalkine Monoclonal Antibody, in MTX-IR Patients with Rheumatoid Arthritis

Yoshia Tanaka, Tsutomu Takeuchi, Hisashi Yamana, Toshihiro Nakaj, Hisanori Umehara, Nobuyuki Yasuda, Fumio Tago, Yasumi Kitahara, Makoto Kawabuki, Kentaro Torii, Seiichiro Hagi, Tetsu Kawanoo, Toshiro Imada

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3Tokyo Women's Medical University, Institute of Rheumatology, Tokyo, Japan
4School of Medicine, Faculty of Medicine, Toho University, Tokyo, Japan
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6KAN Research Institute, Inc., Kobe, Japan
7Eisai Co., Ltd., Tokyo, Japan

Background: Fractalkine (CX3CL1, designated as FKN hereafter) is the sole member of the CX3C-chemokine which leads to dual actions, chemotaxis and cell adhesion for leukocytes expressing the cognate receptor, CX3CR1, during their migration. We have conducted clinical trials of E6011, a novel humanized anti-FKN monoclonal antibody, for patients with rheumatoid arthritis (RA) in Japan.

This is the first report of efficacy and safety results of E6011 from a Phase 2, multicenter, randomized, double-blind, placebo-controlled, parallel-group comparison study in RA patients inadequately responding to methotrexate (NCT02060438).

Objectives: To evaluate efficacy and safety of three dose of E6011 compared with placebo.

Methods: During the 24-week double-blind period, patients with moderately to severely active RA of inadequate response to MTX were randomly assigned to E6011 100 mg, 200 mg, 400/200 mg, or placebo groups at a 1:2:2:2 ratio. In the E6011 100 mg, 200 mg, and placebo groups, subjects received 100 mg, 200 mg, or placebo at Weeks 0, 1, 2, and every 2 weeks subsequently. In the E6011 400/ 200 mg group, subjects received 400 mg at Weeks 0, 1, 2, 4, 6, 8, 10 and then 200 mg every 2 weeks subsequently.

Results: A total of 190 subjects (54 in the placebo group, 28 in the 100 mg group, 54 in the 200 mg group, 54 in the 400/200 mg group) received study drug. Of the 190 subjects, 169 completed and 21 discontinued study treatment prematurely during the 24-week double-blind period. The ACR20 response rate at Week 12 (non-responder imputation), the primary endpoint, was 37.0% in the placebo group, 39.3% in the 100 mg group, 54.7% in the 200 mg group, and 57.4% for 400/200 mg. In addition, we focused on CD16+ monocytes which highly expressing FKN receptor/CX3CR1 as a blood biomarker that linked to the clinical response to E6011. The whole patient population was divided into 2 groups according to the median value of baseline CD16+ monocyte percentage (Median: 10.35%). Much clearer ACR20 response was observed in a dose dependent manner in the subjects who showed higher baseline CD16+ monocytes over the median at Week 24 (NRI) (30.0% for placebo, 46.7% for 100 mg, 57.7% for 200 mg, and 69.6% for 400/200 mg) although such fashion was obscure dependent manner in the subjects who showed higher baseline CD16+ monocytes over the median at Week 24 (NRI) (30.0% for placebo, 46.7% for 100 mg, 57.7% for 200 mg, and 69.6% for 400/200 mg) although such fashion was obscure in the subjects below the median value. Adverse events that occurred in >5% of subjects in any E6011 group were nasopharyngitis, upper respiratory tract infection, stomatitis, bronchitis, back pain, pharyngitis, and dental caries. As a results, E6011 was well tolerated with no notable safety concerns at doses of 100, 200, and 400/200 mg when administered subcutaneously for 24 weeks.

Conclusion: E6011 provided clinical improvements with a good safety profile in RA patients with inadequately responding to MTX. Especially, a higher efficacy of E6011 was suggested in patients with higher baseline CD16+ monocytes (%).
RESULTS OF A PHASE 2 STUDY OF RG6125, AN ANTI-CADERHIN-11 MONOCONAL ANTIBODY, IN RHEUMATOID ARTHRITIS PATIENTS WITH AN INADEQUATE RESPONSE TO ANTI-TNFALPHA THERAPY

Rebecca Finch1, Alexandre Sostelly2, Kim Sue-Ling3, Angela Blauere2, Guillermette Duchateau-Nguyen5, Lida Ukarma4, Claire Petry5, Patarani Ravra6, Peter Villiger7, Uwe Junker8,1, Roche Products Ltd, Welwyn, United Kingdom; 2Roche Innovation Center Basel, Basel, Switzerland; 3Roche Innovation Center New York, New York, NY; 4United States of America; 5Inselstippen Bern, Bern, Switzerland

Background: Cadherin-11 is expressed on fibroblasts in joints of RA patients and augments local fibroblast-mediated inflammation, pannus formation and tissue invasion (1). RG6125 is a novel humanized monoclonal antibody directed against Cadherin-11.

Objectives: To assess the safety, tolerability and efficacy of RG6125 as adjunctive treatment in patients with moderately to severely active RA and an inadequate response to anti-TNF-alpha therapy.

Methods: The Phase 2 study was conducted as a multicenter, randomized, double-blind, placebo-controlled study. Patients were randomly assigned (2:1) to receive 810 mg of RG6125 or placebo by IV infusion. In the treatment period, patients received RG6125 or placebo IV infusions twice every two weeks and up to 12 doses for a total of 4 dose administrations up to Week 12. The primary efficacy endpoint was the proportion of patients with ACR50 response at Week 12.

Results: Demographics: 109 patients were randomized (98 female) to either placebo (N=37) or RG6125 (N=72) and were included in the efficacy analysis population. 107 patients were included in the safety analysis population (37 placebo, 70 RG6125). The median age was 55 years (22–78), and 52% were female. The median RAMRIS Osteitis Score at baseline was 1.6% (95% CI 1.6, 2.3), while for those with TNFi in utero exposure, it was 2.3% (95% CI 1.6, 3.0). In children born to unaffected mothers, the percentage of serious infections was 1.6% (95% CI 1.6, 1.7).

Conclusion: RG6125 was well tolerated with only mild to moderate AEs. RG6125 did not show a discernible treatment effect in RA patients in combination with anti-TNFalpha-blockers over placebo.

Non-responder imputation used for missing ACR responses. LOCf used for missing SJC/TJC. For ACR missing CRP has been imputed with ESR if available. No imputation for other missing components. No imputation for missing DAS28, CDAI, HAO-Di or MRI RAMRIS scores.

* ANCOVA adjusted for baseline score and prior anti-TNF-alpha therapy duration. MRI RAMRIS score is combination of the wrist and 1-5 MCP joints, and are exploratory endpoints.

REFERENCE:

Disclosure of Interests: Rebecca Finch Shareholder of: Roche, Employee of: Roche, Alexandre Sostelly Shareholder of: Roche, Employee of: Roche, Kim Sue-Ling Shareholder of: Roche, Employee of: Roche, Angela Blauer Shareholder of: Roche, Employee of: Roche, Uwe Junker Employee of: Roche, Peter Villiger: None declared, Uwe Junker Shareholder of: Roche, Employee of: Roche


SERIOUS INFECTIONS IN OFFSPRING EXPOSED IN UTERO TO NON-TNFI BIOLOGICS AND TOFACITINIB

Evelyne Vinge1, Yvan St-Pierre2, Cristiano Moura4, Jeffrey Curtis2, Sasha Bernadsky1, McGill University, Divisions of Rheumatology and Clinical Epidemiology, Montreal, Canada; 3McGill University Health Centre Research Institute, Montreal, Canada; 4University of Alabama at Birmingham, Birmingham, United States of America

Background: During pregnancy, maternal circulating immunoglobulins G (IgG) are actively transported across the placenta through their Fc portion. Thus, TNFi and other biologics harbouring an Fc part have the potential to transfer across the placenta, often reaching higher fetal than maternal levels.[1] In addition, it is postulated that small-molecule drugs may cross the placenta, although this remains unconfirmed. As fetuses could be exposed to therapeutic (or potentially supra-therapeutic) levels of biologics and small molecules, there are concerns that these agents could cause immune suppression in exposed offspring.

Objectives: We compared the risk of serious infections in children born to mothers with chronic inflammatory diseases who used non-TNFi biologics or tofacitinib during pregnancy, versus unexposed offspring and children exposed to TNFi in utero.

Methods: We identified all women with ≥1 hospitalization for delivery after a diagnosis of rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriasis (PsO), psoriatic arthritis (PsA), or inflammatory bowel diseases (IBD), and a randomly selected group of unaffected mothers, matched: ≥1 for age, year of delivery, and state of residence, using MarketScan data (2011-2016). Only women continuously enrolled within MarketScan for ≥12 months prior to delivery and with available child linkage were included. We defined tofacitinib, TNFi and non-TNFi biologic (i.e. abatacept, rituximab, tocilizumab, ustekinumab, vedolizumab) exposure based on ≥1 filed prescription and/or infusion procedure code during pregnancy and/or the conception period. We ascertainment serious infections in the offspring based on ≥1 hospitalization with infection as a primary diagnosis, within the first year of life. We also characterized all exposure groups according to maternal demographic, disease type, co-morbidities, pregnancy complications, and drug use (i.e. corticosteroids, DMARDs, biologics). For each exposure group, we defined tofacitinib, TNFi and non-TNFi biologic exposure (i.e. abatacept, rituximab, tocilizumab, ustekinumab) exposure based on ≥1 filed prescription and/or infusion procedure code during pregnancy and/or the conception period. We ascertained serious infections in the offspring based on ≥1 hospitalization with infection as a primary diagnosis, within the first year of life. We also characterized all exposure groups according to maternal demographics, disease type, co-morbidities, pregnancy complications, and drug use (i.e. corticosteroids, DMARDs, biologics). 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Disclosure of Interests: None declared

SOLID TUMOUR OUTCOMES IN PATIENTS WITH RA TREATED WITH ABATACEPT AND OTHER DMARDs: RESULTS FROM A 10-YEAR INTERNATIONAL POST-APPROVAL STUDY

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Background: The abatacept global post-marketing epidemiology programme includes observational studies based on biologic disease registries and healthcare claims database studies to evaluate infection and malignancy risks associated with abatacept treatment, as used in routine clinical practice.

Objectives: To assess the risk of solid tumour malignancies in patients with RA treated with abatacept vs conventional synthetic (cs)DMARDs and other biologic (b) or targeted synthetic (ts)DMARDs.

Methods: Data were analysed from four cohorts: two biologic registries (the Anti-Rheumatic Therapy in Sweden [ARTIS] register and the Rheumatoid Arthritis Observation of Biologic Therapy [RABBIT] German registry), a disease registry (FORWARD, The National Databank for Rheumatic Diseases in the USA) and a healthcare claims database (the population-based British Columbia Canadian RA Cohort [BC]). Exposure defined as “ever exposed” unless specified. Crude incidence rates (per 1000 patient-years of exposure) with 95% CIs were calculated for overall malignancies, breast, lung and lymphoma. Adjusted risk ratios (RRs) with 95% CIs were estimated using multivariable models adjusting for demographics, comorbidities and other potential confounders within each dataset, and were subsequently pooled using a random-effects model for meta-analyses.

Results: Patients treated with abatacept (~5100), csDMARDs (~74K) and other b/tsDMARDs (~74K) and other b/tsDMARDs (~37K) were followed up for a mean of 3.0–3.7, 3.0–6.2 and 3.0–4.7 years, respectively. Patients were mainly female (71–86%), with an age ranging from 55–63 years, and 4–94% had a history of malignancy. A greater number of abatacept-treated patients had been treated with ≥2 prior biologics (abatacept, 44–85%; csDMARDs, 11% [FORWARD] and other b/tsDMARDs, 0–19%). The incidence rate of overall malignancy in abatacept-treated patients was low (Table). Adjusted RRs (95% CIs) for abatacept vs csDMARDs (range: 0.8 [0.2, 3.4] to 1.3 [0.5, 3.3]; pooled estimate: 1.1 [0.8, 1.5]) and abatacept vs other b/tsDMARDs (range: 1.0 [0.4, 2.6] to 1.2 [0.6, 2.3]; pooled estimate: 1.0 [0.8, 1.3]) showed no increased risk in overall malignancy. Although individual registries showed a slight increase in breast (BC), lung (RABBIT) and lymphoma (ARTIS) cancers in patients treated with abatacept, numbers were too low to make an accurate comparative risk assessment.

Conclusion: While the development of malignancy is a potential risk associated with the use of immunomodulators, data from this large, international, post-marketing epidemiology programme suggest that the overall malignancy and breast, lung or lymphoma cancers were not significantly increased in patients treated with abatacept. These data are consistent with the established safety profile of abatacept.

REFERENCE:

Disclosure of Interests: Teresa Simon Employee of: Bristol-Myers Squibb, Samy Suisse Grant/research support from: Advisory board meetings, or as speaker, or received research grants from AstraZeneca, Bayer, Boehringer-Ingelheim, Bristol-Myers Squibb, Novartis, Mary Lou Skovron

Shareholder of: Bristol-Myers Squibb, Consultant for: Bristol-Myers Squibb, Thomas Friese: None declared, Johan Askling Grant/research support from: Karolinska Institutet (JA), has or has had research agreements with the following pharmaceutical companies, mainly in the context of the ATRS national safety monitoring programme for rheumatological biosimilar: Abbvie, BMS, MSD, Eli Lilly, Pfizer, Roche, Samsung Bioepis, and UCB. Consultant for: Karolinska Institutet has received remuneration for JA participating in ad boards arranged by Lilly, Novartis, and Pfizer, Kaleb Michaud Grant/research support from: Research Foundation funding in the last 2 years from Rheumatology Research Foundation and Pfizer; Sofia Pedrio Employee of: FORWARD, The National Data Bank of Rheumatic Diseases, Anja Strangfeld Speakers bureau: Speakers fees from Bristol-Myers Squibb, MSD, Pfizer, Roche, Maarten Boers Consultant for: Bristol-Myers Squibb, Teva, Novartis, Pfizer, GlaxoSmithKline, Diane Lacalle Grant/research support from: Bristol-Myers Squibb, Eli Lilly, MD Sereron, Novartis Pharma AG, Pfizer Inc., Samumed LLC, Synic Bio Inc., Theragene LLC, TissueGene Inc., TLC Biopharmaceuticals, Inc., Zynbera, Galapagos, IQVIA, Hoffman LaRoche, Andres Gomez Shareholder of: BiOr Biotech, Theragene LLC., Consultant for: Bristol-Myers Squibb, Eli Lilly, EMDSereron, Novartis Pharma AG, Pfizer Inc., Samumed LLC, Synic Bio Inc., Theragene LLC, TissueGene Inc., TLC Biopharmaceuticals, Inc., Zynbera, Galapagos, IQVIA, Hoffman LaRoche, Andres Gomez Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb

Disclosure of Interests: Ambre Laurent: None declared, Anna Moltò: None declared, Vered Abitbol: None declared, Loriane Gutermann: None declared, Ornella Conroit: None declared, François Chast: None declared, Claire Goulvestre: None declared, Claire Le Jeunne: None declared, Stéphanie Chaussé (SF): None declared, Christian Roux Grant/research support from: Alexion, Amgen, UCB, Frédéric Battex: None declared, maxime dougados Grant/research support from: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma, Consultant for: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma, Yannick Allarone Grant/research support from: Inventiva, F Hoffmann-LaRoche, Sanofi, BMS, Pfizer, Consultant for: Actelion, Bayer, BMS, Boehringier, Roche, Sanofi, Jérôme Avoua Grant/research support from: research grant from Pfizer

Figure 1. Kaplan Meyer Survival Analysis. A, risk of immunogenicity according to the number of biosimilars infliximab received; B, risk of treatment interruption according to the presence of anti-drug antibodies (ADA); and C, treatment retention within the observation period.

Table 1. Least squares mean change from baseline (SE) and difference from placebo (95% CI, p Value)

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Placebo (N=37)</th>
<th>GSK3196165 180mg (N=37)</th>
<th>Least squares mean change from baseline (SE)</th>
<th>Difference from placebo (95% CI, p Value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain VAS</td>
<td>-7.07</td>
<td>-25.01 (3.650)</td>
<td>-17.94 (28.18, -7.70, p&lt;0.001)</td>
<td></td>
</tr>
<tr>
<td>PGA</td>
<td>-6.72</td>
<td>-23.90 (3.606)</td>
<td>-17.18 (27.27, -7.10, p&lt;0.001)</td>
<td></td>
</tr>
<tr>
<td>HAQ-DI</td>
<td>0.26</td>
<td>-0.50 (0.090)</td>
<td>-0.24 (0.49, 0.01, p&lt;0.009)</td>
<td></td>
</tr>
<tr>
<td>BFI Question 3</td>
<td>-0.83</td>
<td>-2.20 (0.339)</td>
<td>-1.57 (-2.53, -0.62, p&lt;0.001)</td>
<td></td>
</tr>
<tr>
<td>FACIT-F</td>
<td>3.37</td>
<td>8.70 (1.262)</td>
<td>5.33 (1.77, 8.89, p=0.004)</td>
<td></td>
</tr>
<tr>
<td>SF-36</td>
<td>3.42</td>
<td>6.97 (1.182)</td>
<td>3.55 (0.22, 6.88, p=0.037)</td>
<td></td>
</tr>
<tr>
<td>Physical Component</td>
<td>1.20</td>
<td>1.72 (0.350)</td>
<td>0.52 (0.09, 1.05, p=0.138)</td>
<td></td>
</tr>
<tr>
<td>SF-36</td>
<td>3.54</td>
<td>6.79 (1.521)</td>
<td>3.25 (-1.05, 7.54, p&lt;0.001)</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: The results of this Phase Ib study showed that GSK3196165 substantially improved the scores of a range of PRO measures among RA patients. In particular, there was a highly significant improvement in pain; a key symptom of RA. These effects were observed despite achieving much lower drug exposure than predicted. Further studies are required to confirm the additional patient relevant benefits that are expected to arise from increased exposure to GSK3196165.

REFERENCES:


Results: 37 patients were randomised to each treatment group. The observed numbers of biosimilars infliximab received; B, risk of treatment interruption according to the presence of anti-drug antibodies (ADA); and C, treatment retention within the observation period.

Background: Phase 3 (P3) clinical trials are the mainstay of drug development in all areas of medicine, including rheumatology, allowing to determine safety and efficacy of new drugs on their way to approval. Historically, efficacy results of P3 trials have often been disappointing with respect to the expectations set by phase 2 (P2) trials. It is unclear whether these observations are reflection of a true bias or merely a play of chance.

Objectives: To systematically compare efficacy results of P2 versus P3 trials in RA and investigate potential determinants of efficacy differences.

Methods: We performed a systematic review of disease modifying anti-rheumatic drugs (DMARDs) tested in P2 trials in rheumatoid arthritis (RA) over the last 20 years for which also P3 trials exist. We searched Medline, EMBASE, and the
Effectiveness of Influenza Vaccine in TNF Inhibitor-Treated Patients

Giovanni Adami, Angelo Fascio, Giovanni Orsolini, Alessandro Giollo, Davide Gatti, Maurizio Rossini. University of Verona, Rheumatology Unit, Verona, Italy

Background: Tumor Necrosis Factor-α inhibitors (TNFi) are immunosuppressive therapies that are known to increase infectious risk. Indeed, patients affected by TNFi requiring conditions are at higher risk of influenza compared with healthy controls. Furthermore, mildly reduced seroconversion rate after influenza vaccination had been reported in TNFi-treated patients. Nonetheless, the immune response is considered large enough to recommend influenza vaccination in all patients affected by rheumatoid arthritis, regardless of treatment. However, there are data showing that patients are not being vaccinated as recommended. In addition, given that subjects with autoimmune conditions treated with TNFi are at higher risk for influenza, the exact number needed to vaccinate (NNV) for this condition is still unknown.

Objectives: We sought to determine the NNV for influenza in TNFi treated patients and the cost for preventing one case of influenza compared with general population.

Methods: The present analysis included data from cohorts of healthy subjects [1] and TNFi treated patients [2]. We calculated NNV for preventing one case of influenza in each cohort. NNV is the required number of patients receiving vaccination to prevent one case of a given infectious disease. NNV is the inverse of the absolute risk reduction (ARR), which is calculated as following: Control Event Rate (CER) – Experimental Event Rate (EER). In addition, the NNV gives us the opportunity to calculate the cost for preventing one case of influenza, assuming a cost per vaccine from 20 to 40 $.

Results: In 71,221 healthy individuals influenza vaccination reduced influenza rate from 2.3% in individuals without vaccination (CER = 0.023) to 0.9% in vaccinated individuals (EER = 0.009). The calculated NNV is 71 (NNV = 1/ARR, ARR = 0.023 – 0.009), namely 71 healthy adults need to be vaccinated to prevent one of them experiencing influenza. The costs to prevent a case of clinical influenza in healthy controls would range from 1,420 to 2,840 $. On 15,132 patients exposed to adalimumab, influenza-related adverse events have been reported in 55 of 382 not-vaccinated patients (CER = 0.14) and in 8 of 179 vaccinated patients (EER = 0.04). In this population (mean age 53.5 years, predominantly white women) the NNV of influenza vaccines is 10 (NNV = 1/ARR, ARR = 0.144 – 0.045) and preventing a case of influenza would cost approximately from 200 to 400 $, which is largely lower when compared to healthy controls’ costs. The relative risk of influenza vaccination in healthy individuals (2.3% to 0.9%, RR 0.41, 95% confidence interval (CI) 0.36 to 0.47) and rheumatoid arthritis patients treated with TNFi (14.4% to 4.5%, RR 0.31, 95% CI 0.15 to 0.64) are similar, while there is a large difference between NNVs (71 vs 10) (Figure 1).

Conclusion: When estimating the effectiveness of vaccinations, clinicians should always include the calculation of the NNV and not only the calculation of relative risk, which might be misleading. The difference in NNV for influenza between healthy individuals and TNFi treated patients is due to a greater absolute risk for influenza in the latter group. The present analysis provides further evidences on the effectiveness of influenza vaccination in patients affected by rheumatoid arthritis receiving treatment with TNFi and should represent a call-to-action for all rheumatologists to consider vaccination in such patients.

REFERENCES:

Disclosure of Interests: Giovanni Adami: None declared, Angelo Fascio Speakers bureau: Abiogen Pharma, Giovanni Orsolini Speakers bureau: Grunenthal, Alessandro Giollo: None declared, Davide Gatti Speakers bureau: Abiogen, Amgen, Janssen-Cilag, Mundipharma, Pfizer, Maurizio Rossini: None declared

How to treat SpA? From physiotherapy to new IL-17 blocking drugs.

OP0231 DUAL NEUTRALISATION OF IL-17A AND IL-17F WITH BIMEKIZUMAB WAS ASSOCIATED WITH IMPROVEMENTS IN PATIENT-REPORTED AND QUALITY-OF-LIFE OUTCOMES IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS: RESULTS FROM A PHASE 2B, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, DOSE-RANGING STUDY

Désirée van der Heijde1, Lianne S. Gensler2, Alou Deodhar3, Xenon Baraliakos4, Denis Poddubnyy5, Mary Katherine Farmer6, Dominique Baeten7, Jason Coane8, Marga Oortgiesen9, Maxime Dougados10.

Leiden University Medical Center, Leiden, Netherlands; 1UCSF, San Francisco, United States of America; 2OHSU, Portland, United States of America; 3Ruhr-University Bochum, Herne, Germany; 4Charité – Universitätsmedizin Berlin, German Rheumatism Research Centre, Berlin, Germany; 5UCB Pharma, Raleigh, United States of America; 6UCB Pharma, Brussels, Belgium; 7Cochin Hospital, Paris, France

Background: Ankylosing spondylitis (AS) is a chronic immune-mediated inflammatory disease primarily affecting the sacroiliac joints and spine, causing pain, stiffness and loss of mobility and function. These manifestations can severely impair patients’ quality of life (QoL).1 Dual neutralisation of IL-17A and IL-17F in addition to IL-17A alone in disease-relevant cell models.2 Results previously reported from this Phase 2b study (NCT02963506) demonstrated that, during the 12-week double-blind treatment period, bimekizumab provided substantial clinical improvements in disease outcome measures, including Assessment of SpondyloArthritis international Society (ASAS)40%, in patients with active AS.3

Objectives: To assess the impact of bimekizumab on patient-reported and QoL outcomes at Week 12 in patients with active AS.

Methods: In this 48-week Phase 2b study (double blind to Week 12 then dose blind to Week 48), 303 patients with active AS (Bath Ankylosing Spondylitis Disease Activity Index [BASDAI] ≥ 4; spinal pain ≥ 4 [0–10 numerical rating scale]), fulfilling the modified New York criteria, were randomised 1:1:1:1:1 to receive subcutaneous bimekizumab 16mg, 64mg, 160mg, 320mg or placebo QW for 12 weeks. Prior exposure to one anti-TNF therapy was permitted. Secondary and other endpoints included: BASDAI ≥ 50% improvement in BASDAI (BASDAI 50); ≥ 50% improvement in BASDAI (BASDAI 50); Bath Ankylosing Spondylitis Functional Index (BASFI), Ankylosing Spondylitis Quality of Life (ASQoL) and Patient’s Global Assessment of Disease Activity (PGA) at Week 12. Safety was also assessed.

Results: Over 287 (95%) patients completed the 12-week double-blind period. Baseline scores on patient-reported and QoL outcomes were similar across treatment groups (Table). At Week 12, BASDAI 50 was achieved by 23.7% of bimekizumab-treated patients versus 11.9% receiving placebo. All bimekizumab doses were associated with greater reductions in individual BASDAI components, including: fatigue (range: -1.6 to -2.5 vs -0.6); neck, back or hip pain (2.0 to -3.3 vs -1.2); discomfort due to tenderness to touch or pressure (-1.6 to -3.0 vs -1.1); level of morning stiffness (-2.5 to -3.5 vs -1.2) and duration of morning stiffness (1.7 to -3.3 vs -1.4) (Table). Compared with placebo, greater reductions from baseline were also achieved with bimekizumab for BASFI (-1.4 to -2.2 vs -1.0), BASDAI 50% improvement in BASDAI (BASDAI 50), Bath Ankylosing Spondylitis Functional Index (BASFI), Ankylosing Spondylitis Quality of Life (ASQoL) and Patient’s Global Assessment of Disease Activity (PGA) at Week 12. Safety was also assessed.

Conclusion: Dual neutralisation of IL-17A and IL-17F with bimekizumab was associated with improvements in patient-reported and QoL outcomes including pain, fatigue and tenderness in patients with active AS after 12 weeks of treatment. No new safety findings were observed versus previous studies of bimekizumab.3,4

Reference:

Disclosure of Interests: Désirée van der Heijde Consultant for: AbbVie, Amgen, Astra, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Daichi, Eli-Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, Union Chimique Belge, Lianne S. Gensler Grant/research support from: AbbVie, Amgen, UCB Pharma, Consultant for: Novartis, Lilly, Janssen, Alul Deodhar Grant/research support from: AbbVie, Amgen, Eli Lilly, GS1, Janssen, Novartis, Pfizer, and UCB, Consultant for: AbbVie, Amgen, BMS, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Xenon Baraliakos Grant/research support from: AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Centocor, Chugai, Janssen, MSD, Novartis, Pfizer Inc, Roche and UCB, Grant/ research support from: AbbVie, Pfizer, Merck Sharp & Dohme, UCB Pharma, Novartis, Consultant for: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Chugai, Janssen Biologics, Novartis, Pfizer, UCB Pharma, Galapagos, Speakers bureau: AbbVie, Chugai, Chugai, Janssen, Novartis, Pfizer, UCB Pharma, Denis Poddubnyy Grant/research support from: AbbVie, Merck Sharp & Dohme, Novartis, Consultant for: AbbVie, Bristol-Myers Squibb, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, Roche, UCB Pharma, Mary Katherine Farmer Employee of: UCB Pharma, Dominique Baeten Shareholder of: UCB Pharma, Employee of: UCB Pharma, Jansen Coarse Employee of: UCB Pharma, Marga Oortgiesen Shareholder of: UCB Pharma, Employee of: UCB Pharma, UCB Pharma, maxime dougados Grant/research support from: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma, Consultant for: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma, DOI: 10.1136/annrheumdis-2019-eular.6607

OP0232 NETAKIMAB REDUCES THE DISEASE ACTIVITY OF RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS. RESULTS OF ASTERA STUDY

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Background: Efficacy and safety of netakimab (NTK), a humanized anti-IL17A antibody, was established in phase 2 clinical trials in patients (pts) with radiographic axial spondyloarthritis (r-axSpA) and psoriasis.2

Objective: The abstract presents 16-week data from ongoing ASTERA study (NCT03447704) in pts with active r-axSpA.

Methods: ASTERA is a phase 3 international double-blind placebo (PBO)-controlled study. 228 adult pts with r-axSpA, active (BASDAI ≥ 4) despite the standard NSAIDs, were randomly assigned (1:1) to receive 120 mg NTK or PBO SC at Week (Wk) 0,1,2 and then qWk through Wk 16. After Wk 16 all pts will start to receive NTK up to Wk 52. Primary endpoint was ASAS40 rate at Wk 16.

Disclosure of Interests: Inna Gaydukov Consultant for: Amgen, Roche, UCB, Lilly, Novartis, Pfizer; Grant/research support from: Lilly, Roche, UCB, Elan, Novartis, Celgene; Employee of: Eli Lilly and Company, Pfizer, Roche, UCB; Dominique Baeten Employee of: UCB Pharma, Shareholder of: UCB Pharma; Consultant for: Abbvie, Amgen, AstraZeneca, BioMed suivant, Celgene, Pfizer, UCB Pharma.
Results: The mean age at baseline was 39.14±9.9 years, the mean symptom duration was 4.3±4.5 years. 76.8% of pts were naïve to biological treatment. At Wk 16 ASAS40 rate was higher in NTK arm compared to PBO: 40.35% versus (vs.) 24.63% pts (95% CI for the difference in ASAS40 rate was [27.37%; 48.07%] (p<0.0001, Figure 1). Efficacy of NTK was also proved by comparison of secondary endpoints (Figure 2); improvement in BASDAI, MASES, BASFI became significant from Wk 4 and remained during the study (no data presented). Most reported adverse events (AE) and treatment-related AEs (TRAE) were mild/moderate (Table 1). The most frequent AEs were anemia, neutropenia, ALT increase. One serious AE (SAE), not related to the treatment (bone fracture), was reported in NTK arm.

Conclusion: NTK at a dose 120 mg is well-tolerated drug with favorable safety profile that leads to decline in r-axSpA activity, function improvement and axial mobility in 16 Wks.

REFERENCES:

Table 1. Safety data

<table>
<thead>
<tr>
<th>% of patients with NTK (n = 114)</th>
<th>PBO (n = 114)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AE/SAE</td>
<td>33.3% (38)</td>
<td>25.4% (29)</td>
</tr>
<tr>
<td>TRAE</td>
<td>17.5% (20)</td>
<td>14.0% (16)</td>
</tr>
<tr>
<td>SAE</td>
<td>9.5% (1)</td>
<td>0% (0)</td>
</tr>
<tr>
<td>Grade 3-4 AEs</td>
<td>2.6% (3)</td>
<td>3.5% (4)</td>
</tr>
<tr>
<td>Grade 3-4 TRAEs</td>
<td>1.8% (2)</td>
<td>1.8% (2)</td>
</tr>
<tr>
<td>Local reactions</td>
<td>1.8% (2)</td>
<td>0.9% (1)</td>
</tr>
</tbody>
</table>

Table 1. Pre-treatment extra-articular manifestations and the choice of 1st TNFi

<table>
<thead>
<tr>
<th></th>
<th>OR (95% CI)</th>
<th>p-value</th>
<th>p value</th>
<th>Wald value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADA vs. others</td>
<td>Acute Anterior Uveitis (AAU)</td>
<td>19.91 (-0.001)</td>
<td>3.79</td>
<td>2.11</td>
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<tr>
<td></td>
<td>Inflammatory Bowel Diseases</td>
<td>11.93 (0.001)</td>
<td>5.50</td>
<td>2.09</td>
</tr>
<tr>
<td></td>
<td>Psoriasis</td>
<td>0.17 (0.684)</td>
<td>1.15</td>
<td>0.58</td>
</tr>
<tr>
<td></td>
<td>Constant</td>
<td>3.08 (0.079)</td>
<td>1.23</td>
<td></td>
</tr>
<tr>
<td>ETA vs. others</td>
<td>AAU</td>
<td>20.41 (-0.001)</td>
<td>0.14</td>
<td>0.06</td>
</tr>
<tr>
<td></td>
<td>IBD</td>
<td>8.34 (0.004)</td>
<td>0.17</td>
<td>0.05</td>
</tr>
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<td></td>
<td>Psoriasis</td>
<td>1.02 (0.313)</td>
<td>0.67</td>
<td>0.30</td>
</tr>
<tr>
<td></td>
<td>Constant</td>
<td>27.38 (-0.001)</td>
<td>0.52</td>
<td></td>
</tr>
<tr>
<td>CZP vs. others</td>
<td>AAU</td>
<td>0.01 (0.959)</td>
<td>1.02</td>
<td>0.48</td>
</tr>
<tr>
<td></td>
<td>IBD</td>
<td>1.50 (0.221)</td>
<td>0.40</td>
<td>0.09</td>
</tr>
<tr>
<td></td>
<td>Psoriasis</td>
<td>0.65 (0.420)</td>
<td>1.47</td>
<td>0.58</td>
</tr>
<tr>
<td></td>
<td>Constant</td>
<td>126.09 &lt;0.001</td>
<td>0.12</td>
<td></td>
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</tbody>
</table>

Disclosure of Interests: Inna Gaydukova Grant/research support from: JSC BIOCAD, Olga Tsiupa Grant/research support from: JSC BIOCAD, Diana Abdulganieva: None declared, Diana Kretchikova Grant/research support from: JSC BIOCAD, Ivan Gordeev Grant/research support from: JSC BIOCAD, Vadim Tynenko Grant/research support from: JSC BIOCAD, Aleksandra Steklova Grant/research support from: JSC BIOCAD, Anna Ereemeva Grant/research support from: JSC BIOCAD, Ekaterina Chernyaya Employee of: JSC BIOCAD, Roman Ivanov Employee of: JSC BIOCAD.

Conclusion: EAMs appear to play an important role in the choice of TNFi in axSpA. Patients with previous AAU and IBD are more likely to be prescribed ADA.
and less likely to receive ETA, consistent with the superior efficacy of monoclonal TNFi for these conditions. The presence or absence of EAMS did not influence the use of CZP, although small sample size might explain the lack of associations. Future work will determine whether EAMS influence TNFi survival, or effectiveness, and whether this varies between agents.

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Disclosure of Interests: Mohammad H. Derakhshan: None declared, Linda Dean: None declared, Gareth T. Jones Grant/research support from: Have received research grants (not current) from Abbvie and Pfizer. Have received research grants (not current) from the British Society for Rheumatology, who received the funds from Abbvie, Pfizer and UCB. Have received research grant (current) from the British Society for Rheumatology, who received the funds from Celgene, Gary Macfarlane Grant/research support from: Have received research grants (not current) from Abbvie and Pfizer. Have received research grants (not current) from the British Society for Rheumatology, who received the funds from Abbvie, Pfizer and UCB. Have received research grant (current) from the British Society for Rheumatology, who received the funds from Celgene, Stefan Siebert Grant/research support from: Have received research grants (not current) from Abbvie and Pfizer. Have received research grants (not current) from Celgene, Gary Macfarlane Grant/research support from: Have received research grants (not current) from Abbvie and Pfizer. Have received research grants (not current) from the British Society for Rheumatology, who received the funds from Abbvie, Pfizer and UCB.

Methods: In this phase 3, multicenter, randomized, double-blind, placebo-controlled study conducted in Japan, South Korea and Taiwan, eligible axSpA patients were randomized 1:1 to brodalumab subcutaneously (s.c.) 210 mg or placebo at baseline, weeks 1 and 2, every 2 weeks thereafter. At week 16, all subjects entered an open-label extension phase and received brodalumab 210 mg s.c. Q2W. ASAS 40 (Assessment of SpondyloArthritis international Society) response rate at week 16 was the primary endpoint. Secondary outcomes and safety profiles were also assessed.

Results: A total of 159 patients were randomized, and 77/80 patients in placebo arm were completed the 16 weeks. No suicidal ideation or behavior were observed. Other disease activity parameters demonstrated trend to improvement in therapeutic arm (Table). Brodalumab 210 mg had good safety profile. Most commonly reported adverse event was nasopharyngitis observed in both brodalumab and placebo arm (10.3%) arms. AE rates including SAE rates were comparable between groups. No suicidal ideation or behavior were observed.

Conclusion: Brodalumab s.c. 210 mg Q2W treatment was effective and tolerable in axSpA patients in this 16 week phase 3 clinical trial. Based on the ongoing trial results, brodalumab could be considered as a future therapeutic option for patients with axSpA.

Table 1. Summary of efficacy result at Week 16 (FAS)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>ASAS 40 Response at Week 16 (%)</th>
<th>ASAS 20 Response at Week 16 (%)</th>
<th>ASDAS-CRP change from baseline at Week 16 (BOCF)</th>
<th>BASDAI change from baseline at Week 16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>19 (24.1)</td>
<td>33 (41.8)</td>
<td>-0.672</td>
<td>2.4</td>
</tr>
<tr>
<td>Brodalumab 210 mg</td>
<td>35 (43.8)</td>
<td>54 (67.5)</td>
<td>-1.127</td>
<td>-2.9</td>
</tr>
</tbody>
</table>

Figure. ASAS 20/40 response rate


OP0235 SEUCINIKUMAB IMPROVES AXIAL MANIFESTATIONS IN PATIENTS WITH PSORIATIC ARTHRITIS AND INADEQUATE RESPONSE TO NSABS: PRIMARY ANALYSIS OF THE MAXIMISE TRIAL

Xenophon Bagakos1, Laura C Coates2, Laura Gossec3, Stawomir Jeka4, Antonio Mora Varela5, Barbara Schulz6, Michael Rissler7, Ayan Das Gupta8, Chiara Perella9, Effie Pourmarad9, 1Rheumazentrum Ruhrgebiet, Ruhr University Bochum, Germany, Herne, Germany; 2University of Oxford, Oxford, United Kingdom; 3Sorbonne University, Hopital Pitié-Salpêtrière, Paris, France; 2nd University Hospital, CM UMK, Bydgoszcz, Poland; 5Santiago University Clinical Hospital, Santiago de Compostela, Spain; 6Novartis Pharma AG, Basel, Switzerland; 7Novartis Healthcare Pvt. Ltd, Hyderabad, India

Background: Secukinumab (SEC) has provided significant and sustained improvement in the signs and symptoms of active psoriatic arthritis (PsA) and ankylosing spondylitis.1 Evidence on the efficacy of biologics in the treatment of PsA patients (pts) with axial manifestations affecting 30–70% of PsA pts is limited2, particularly as validated classification criteria for this subtype of PsA are not yet available; an effort to develop criteria is being undertaken by ASAS/GRAPPA. MAXIMISE is an ongoing study evaluating the efficacy and safety of secukinumab 300 or 150mg in managing axial manifestations in PsA pts

Objectives: To report the primary analysis results at Week (Wk) 12 from MAXIMISE (NCT02721966) trial

Methods: This phase 3b, double blind, placebo (PBO)-controlled, multicentre 52-wk trial included 498 pts aged ≥18 years with PsA (CASPAR criteria), clinician-
diagnosed axial involvements, spinal pain VAS >40/100 and BASDAI >4 despite trial of at least two NSAIDs. Pts were randomised to subcutaneous (SC) SEC (300/150 mg) or PBO weekly for 4 wks and every 4 wks thereafter. At Wk 12, PBO pts were re-randomised to SC SEC 300/150 mg. The primary endpoint was proportion of pts achieving ASAS20 response with SEC 300 mg at Wk 12. The key secondary endpoint was ASAS20 response with SEC 150 mg at Wk 12 after superiority of 300 mg was established. Analyses used multiple imputation.

**Results:** Demographic and baseline (BL) disease characteristics were comparable across groups (Table). Primary and key secondary endpoints were met; ASAS20 response rates at Wk 12 were 63.1% (SEC 300 mg; P<0.0001) and 66.3% (150 mg; P<0.0001) vs 31.3% (PBO; Figure). ASAS20 responses in pts using concomitant MTX were 65.1% (300 mg), 67.3% (150 mg) vs 35.9% (PBO) and corresponding values in No MTX group were 60.5%, 64.4% vs 27.1%. The safety profile was similar across groups through Wk 12.

**Conclusion:** MAXIMISE is the first randomised controlled trial evaluating the efficacy of a biologic in the management of the axial manifestations of PsA. SEC 300 and 150 mg provided rapid and significant improvement in ASAS20 responses through Wk 12 in PsA pts with axial manifestations and inadequate responses to NSAIDs.

**REFERENCES:**


**Demographics/Baseline Characteristics**

<table>
<thead>
<tr>
<th></th>
<th>SEC 300 mg SC (N = 167)</th>
<th>SEC 150 mg SC (N = 165)</th>
<th>PBO (N = 166)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (yrs)</strong></td>
<td>46.2 (12.3)</td>
<td>46.9 (11.5)</td>
<td>46.6 (11.5)</td>
</tr>
<tr>
<td><strong>Malaise, n (%)</strong></td>
<td>77 (46.1)</td>
<td>81 (49.1)</td>
<td>88 (53.0)</td>
</tr>
<tr>
<td><strong>Evidence of current psoriasis, n (%)</strong></td>
<td>152 (91.0)</td>
<td>147 (89.1)</td>
<td>153 (90.2)</td>
</tr>
<tr>
<td><strong>Time since first symptoms (yrs)</strong></td>
<td>6.8 (7.7)</td>
<td>7.4 (7.6)</td>
<td>7.7 (9.5)</td>
</tr>
<tr>
<td><strong>Total back pain score, VAS</strong></td>
<td>72.5 (13.8)</td>
<td>73.6 (15.3)</td>
<td>74.0 (13.7)</td>
</tr>
<tr>
<td><strong>Inflammatory back pain parameters, n (%)</strong></td>
<td>150 (89.8)</td>
<td>147 (89.1)</td>
<td>152 (91.6)</td>
</tr>
<tr>
<td><strong>Onset of back pain is insidious</strong></td>
<td>148 (88.6)</td>
<td>139 (84.2)</td>
<td>146 (88.0)</td>
</tr>
<tr>
<td><strong>Back pain worsening with rest</strong></td>
<td>152 (91.0)</td>
<td>151 (91.5)</td>
<td>157 (94.6)</td>
</tr>
<tr>
<td><strong>Night pain with improvement upon getting up</strong></td>
<td>147 (88.0)</td>
<td>147 (89.1)</td>
<td>143 (86.1)</td>
</tr>
<tr>
<td><strong>Awakening due to back pain in 2nd half of night</strong></td>
<td>143 (85.6)</td>
<td>145 (87.9)</td>
<td>137 (82.5)</td>
</tr>
<tr>
<td><strong>Alternating buttock pain</strong></td>
<td>102 (61.1)</td>
<td>96 (59.4)</td>
<td>101 (60.8)</td>
</tr>
<tr>
<td><strong>Back pain improved after NSAID intake in past 24h</strong></td>
<td>136 (81.4)</td>
<td>134 (81.2)</td>
<td>138 (83.1)</td>
</tr>
<tr>
<td><strong>BASDAI</strong></td>
<td>7.3 (1.2)</td>
<td>7.2 (1.4)</td>
<td>7.3 (1.2)</td>
</tr>
<tr>
<td><strong>HLA-B27 positive, n (%)</strong></td>
<td>21/85 (25.3)</td>
<td>24/82 (29.3)</td>
<td>26/74 (35.1)</td>
</tr>
</tbody>
</table>

M, number of pts with available HLA-B27 status.

**Disclosure of Interests:** Xenon Baraliakos Grant/research support from: AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Centocor, Chu- gai, Janssen, MSD, Novartis, Pfizer Inc, Roche and UCB, Grant/research support from: AbbVie, Pfizer, Merck Sharp & Dohme, UCB Pharma, Novartis, Consultant for: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Chugai, Janssen Biologies, Novartis, Pfizer, UCB Pharma, Galapagos, Speak- ers bureau: AbbVie, Chugai, Janssen, Novartis, Pfizer, UCB Pharma, Laura Coates Grant/research support from: AbbVie, Celgene, Lilly, Novartis and Pfizer, Consultant for: AbbVie, Ameagen, BMS, Celgene, Galapagos, Gilead Scien- tific Inc, Janssen, Lilly, Novartis, Pfizer, Prothena Corp and UCB, Laure Gosc- sec Grant/research support from: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis-Sandoz, Pfizer, Sanofi, and UCB, Consultant for: AbbVie, Biogen, BMS, Celgene, Janssen, Lilly, MSD, Nordic Pharma, Novartis-Sandoz, Pfizer, Roche, Sanofi, and UCB, Consultant for: L.Goss-Cheves has received honoraria from Celgene as investigator for this study. Slawomir Jeka: None declared, ANTO- NIO MERA VARELA: None declared, Barbara Schulz Employee of: Novartis, Michael Rask Employee of: Novartis, Ayan Das Gupta Employee of: Novartis, Chiara Perella Employee of: Novartis, Eiffie Pournara Shareholder of: Novartis, Employee of: Novartis. DOI: 10.1136/annrheumdis-2019-eular.2932
REFERENCES:

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OP0237 INTERLEUKIN-17 OR TNF BLOCKADE IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS AFTER WITHDRAWAL OF AT LEAST ONE TNF INHIBITOR
Christoph Tellenbach1, Raphael Micheroli1, Kristina Buerki1, Almut Scherer2, Christoph Tellenbach1, Raphael Micheroli1, Kristina Buerki1, Almut Scherer2

Background: Secukinumab (SEC), an interleukin-17A inhibitor, is approved for the treatment of ankylosing spondylitis (AS) and has been integrated into the current treatment recommendations of patients with axial spondyloarthritis (axSpA) as an alternative to tumor necrosis factor inhibitors (TNFi). The optimal use of one mode of action over the other remains unclear and longitudinal real-life data are lacking.

Objectives: To compare drug survival of SEC versus TNFi in axSpA patients having previously stopped at least one TNFi in a large prospective cohort.

Methods: Patients with a clinical diagnosis of axSpA in the Swiss Clinical Quality Management cohort were included if they had previously stopped treatment with at least one TNFi, initiated therapy with either SEC or a new TNFi after approval of SEC and had a baseline clinical visit. Drug survival was evaluated by Cox proportional hazards models adjusted for sex, age, and number of previous TNFi.

Results: Baseline characteristics of 382 axSpA patients included (N=107 for SEC and N=275 for new TNFi) are shown in Table 1. The proportion of patients with ≥2 TNFi administered previously was significantly higher in the SEC group. Patients starting SEC had higher baseline disease activity, more enthesitis and greater impairment of spinal mobility, function and quality of life. A history of uveitis was more prevalent in the TNFi group. No differences between the groups could be detected with regards to the reason for discontinuation of the previous TNFi.

Conclusion: SEC was predominantly initiated in axSpA after use of at least 2 TNFi. Patients starting SEC had a higher mean disease activity than patients starting a new TNFi. Adjusted drug survival after previous withdrawal of TNFi was comparable for SEC or a new TNFi.

Acknowledgement: Supported by a grant from Novartis.

Disclosure of Interests: Christoph Tellenbach: None declared, Raphael Micheroli: None declared, Kristina Buerki: None declared, Almut Scherer Grant/research support from: is an employee of SCGM, which receives funding from AbbVie, Celgene, IQONE, Lilly, MSD, Novartis, Pfizer, Roche, Sandzoz, Sanofi Genzyme, and UCB., Consultant for: Consultant for Pfizer, MSD, and AbbVie, Michael Nissen Consultant for: AbbVie, Lilly, Novartis, and Pfizer, Pascal Zufferey: None declared, Pascale Exer: None declared, Burkhard Moeller Consultant for: Swissmedic Human Medicines Expert Committee Member (regulatory agency), Diego Kyburz: None declared, Adrian Ciurea Consultant for: AbbVie, Celgene, Janssen-Cilag, MSD, Eli Lilly, Novartis, Pfizer, UCB, Speakers bureau: Abbvie, Celgene, Janssen-Cilag, MSD, Eli Lilly, Novartis, Pfizer, UCB DOI: 10.1136/annrheumdis-2019-eular.2427

Table 1. Baseline characteristics of axSpA patients having stopped ≥1 TNFi at start of a next biologic after approval of SEC in Switzerland, stratified by the mode of action.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>N</th>
<th>SEC</th>
<th>TNFi</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex,%</td>
<td>374</td>
<td>43.3</td>
<td>43.0</td>
<td>1.00</td>
</tr>
<tr>
<td>Age, years</td>
<td>382</td>
<td>45.3</td>
<td>45.7</td>
<td>0.81</td>
</tr>
<tr>
<td>Symptom duration, years</td>
<td>369</td>
<td>14.0</td>
<td>14.8</td>
<td>0.47</td>
</tr>
<tr>
<td>HLA-B27 positive,%</td>
<td>338</td>
<td>58.9</td>
<td>60.0</td>
<td>0.90</td>
</tr>
<tr>
<td>BASDAI</td>
<td>276</td>
<td>4.8 (2.1)</td>
<td>6.1 (1.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ASDAS</td>
<td>239</td>
<td>2.7 (0.9)</td>
<td>3.5 (1.0)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 2. Multivariable adjusted cox regression model for drug survival of next biologic DMARD.

<table>
<thead>
<tr>
<th>HR</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Secukinumab vs. TNFi</td>
<td>1.05</td>
<td>0.42; 2.61</td>
</tr>
<tr>
<td>Age</td>
<td>1.01</td>
<td>0.99; 1.03</td>
</tr>
<tr>
<td>Female sex</td>
<td>1.60</td>
<td>0.98; 2.61</td>
</tr>
<tr>
<td>BASDAI</td>
<td>1.15</td>
<td>1.02; 1.31</td>
</tr>
<tr>
<td>Elevated CRP</td>
<td>1.15</td>
<td>0.71; 1.86</td>
</tr>
<tr>
<td>Number of previous TNFi</td>
<td>0.83</td>
<td>0.61; 1.13</td>
</tr>
<tr>
<td>Interaction between bDMARD mode of action and number of previous TNFi</td>
<td>1.20</td>
<td>0.83; 1.73</td>
</tr>
</tbody>
</table>

Conclusion: SEC was predominantly initiated in axSpA after use of at least 2 TNFi. Patients starting SEC had a higher mean disease activity than patients starting a new TNFi. Adjusted drug survival after previous withdrawal of TNFi was comparable for SEC or a new TNFi.

WORK PRODUCTIVITY AND ACTIVITY IMPAIRMENT AMONG PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS/RADIOPHAGIC AXIAL SPONDYLOARTHROPATHY AND TREATED WITH IXEKIZUMAB FOR 16 WEEKS: RESULTS FROM COAST-V AND COAST-W
Annettes Boonen1, Maxime Doudougos2, Bernard Combe3, Theresa Hunter4, Baqin Zhu5, David Sandoval6, Louis Bessonette5, Atul Deodhar7, A. Maastricht University Medical Center, Maastricht, Netherlands; "Hôpital Cochin, Paris, France; "CHU Montpellier, Montpellier University, Montpellier, France; "Eli Lilly and Company, Indianapolis, United States of America; "Laval University and CHU de Quebec, Quebec, Canada; "Oregon Health and Science Univ, Portland, United States of America

Background: Axial spondylarthropathy (axSpA) negatively impacts work productivity and IL-17A antagonists, such as ixekizumab (IXE), may improve paid and unpaid work productivity. Also, it is unknown if improvements with IXE differ between biologic-naive and TNF inhibitor (TNFi) experienced patients.

Objectives: We investigated the effect of IXE treatment for 16-weeks on work productivity and activity impairment among patients with radiographic axSpA (r-axSpA) using data from the biologic-naive and TNFi experienced patients receiving either placebo (PBO), IXE, or adalimumab (ADA), if biologic-naive.

Methods: Both COAST-V and COAST-W investigated the efficacy and safety of IXE among patients with r-axSpA that either were biologic-naive patients (COAST-V, NCT02696785) or TNFi-experienced patients (COAST-W, NCT02696798), as defined by prior inadequate response or intolerance to 1 or 2 TNFi. Patients were required to have a diagnosis of axSpA. Patients fulfilled ASAS criteria for r-axSpA and mNII criteria for ankylosing spondylitis. Activity disease was defined by BASDAI ≥4 on a 0-10 numeric rating scale (NRS). Full eligibility criteria were previously reported. Patients were treated with placebo (PBO), 40-mg adalimumab (ADA) every 2 weeks (Q2W; COAST-V only), 80-mg IXE Q2W (IXE30Q2W) or every 4 weeks (IXE4Q4W) for 16 weeks. Work productivity was investigated using the Work Productivity and Activity Impairment Questionnaire for Ankylosing Spondylitis (WPAI:SpA). Individual and integrated
study data were analyzed using analysis of covariance models. Results reported as least squares mean (LSM) change from baseline: standard error (SE). Integrated data of COAST-V and -W were analyzed for inferential statistics due to small sample sizes in the individual studies. ADA was included in COAST-V as an active reference arm only, and the study was not powered to allow comparisons between the IXE and ADA arms.

**Results:** Overall, 365 (64.5%) PBO- and IXE-treated patients reported paid work (part-time or full-time) at baseline in COAST-V and COAST-W. Based on integrated data, Absenteeism was significantly lower in IXEQ2W treated patients than PBO and Presenteeism, Work Productivity Loss, and Activity Impairment were significantly reduced in IXEQ2W and IXEQ4W treated patients versus PBO (Table 1). WPAI-SpA outcomes for biologic-naïve and TNFi-experienced were similar with some exceptions (Table 2). The active reference arm (ADA) exhibited numerical improvements for presenteeism, work productivity, and activity impairment versus PBO.

**Conclusion:** In this integrated analysis of patients with active r-axSpA, IXE treatment for 16 weeks yielded significant improvements in work productivity and activity impairment versus PBO. The effect is similar in biologic-naïve and TNFi-experienced patients. A limitation for evaluations of work productivity in the individual studies was the relatively low number of employed patients.

**REFERENCES:**


**Disclosure of Interests:** Annelies Boonen: None declared, maxime dougados Grant/research support from: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma, Consultant for: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma, Bernard Combe Consultant for: Abbvie, Bristol-Myers Squibb, Gilead, Janssen, Eli Lilly, MSD, Novartis, Pfizer, Roche-Chugai, Sanofi, UCB. Theresa Hunter Employee of: Eli Lilly and Company, Baojin Zhu Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, David Sandoval Shareholder of: Eli Lilly and Company, Elizabeth Roche, Eli Lilly and Company, Louis Bessette Grant/research support from: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, Consultant for: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, Consultant: For: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, Speakers bureau: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, Alu Deodhar Grant/research support from: AbbVie, Amgen, Eli Lilly, GSK, Janssen, Novartis, Pfizer, and UCB. Consultant for: AbbVie, Amgen, BMS, Eli Lilly, Janssen, Novartis, Pfizer, and UCB

**DOI:** 10.1136/annrheumdis-2019-eular.1613

**RESULTS:**

Of 826 SSc-ILD patients were included; 219/826 (26.5%) showed moderate/significant ILD progression at 12±3 months follow-up. Baseline FVC, erythrocyte sedimentation rate, modified Rodnan skin score (mRSS), GERD and disease duration were significantly associated with significant fibrosis in univariate analysis and multivariable modelling (area under curve 0.67). Serial lung function data with median follow-up of 5 yrs were available in 411/826 (49.8%) patients. In 128/411 with initial progressive ILD at 12±3 months, 59/128 (46.1%) showed further progression, while 69/128 (53.9%) were stable. Baseline FVC, mRSS and disease duration were significantly associated with further ILD progression. The incident cumulative frequency of moderate and significant ILD progression was 22.9% (n=189/826) and 28.5% (n=235/826) during the median 5-yr follow-up and time to first progressive event (Figure).

**Conclusion:** This study provides novel insights into the frequency, severity and association of progressive fibrosis in patients with SSc-ILD in the EUSTAR database.

**Acknowledgement:** Funding: Boehringer Ingelheim (Schweiz) GmbH, Switzerland

**Disclosure of Interests:** Anna-Maria Hoffmann-Vold, Yannick Allanoë, Margarida Ávies, Nicole Graf, Paolo Airo, Lidia P. Ananyeva, László Csirják, Serena Guiducci, Éric Hachulla, I. L Mengtoal, Carina Miha, Gabriela Riemekasten, Petras Stulkas, Gabriele Valentiní, Otylia Kowal-Bielecka, Oliver Distel, Olv Østerud, APHP, Cochin Hospital, Department of Rheumatology, A, Paris, France.

**Disclosure of Interests:** Anna-Maria Hoffmann-Vold, Yannick Allanoë, Margarida Ávies, Nicole Graf, Paolo Airo, Lidia P. Ananyeva, László Csirják, Serena Guiducci, Éric Hachulla, I. L Mengtoal, Carina Miha, Gabriela Riemekasten, Petras Stulkas, Gabriele Valentiní, Otylia Kowal-Bielecka, Oliver Distel, Olv Østerud, APHP, Cochin Hospital, Department of Rheumatology, A, Paris, France.

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Assessment of Pulse Wave Velocity in Safety and Efficacy of Lenabasum in An...

Background: Systemic sclerosis (SSc)-related vasculopathy is generally thought to occur on a microvascular level. However, some observations also suggest involvement of arterial vessels. Macrovacular involvement (e.g., aorta or upper extremity) can be non-invasively assessed by measuring pulse wave velocity (PWV). Although, several studies have assessed aortic and upper extremity PWV in SSc, studies have not reached a consensus regarding this matter. Furthermore, we hypothesized that the endothelin antagonist bosentan may improve arterial stiffness by its direct endothelial and potential anti-fibrotic effects.

Objectives: The aim of this exploratory study was two-fold. First, we aimed to compare arterial stiffness in patients with SSc and age- and sex-matched healthy controls (HC). Secondly, we will investigate the effect of bosentan on both short-term (three month) and long-term (one-year) PWV.

Methods: Baseline differences between HC and SSc patients were studied in a case-control design. The follow-up of SSc patients was a randomized, prospective, 2-arm parallel group, open-label, (usual care with bosentan versus usual care only), blinded endpoint, intervention study. PWV (Sphygmocor) in meters/second, was measured to assess arterial stiffness in the aorta (carotid-femoral PWV), upper arm (carotid-brachial PWV), and forearm (brachial-radial PWV), adjusted for mean arterial pressure.

Results: Baseline characteristics are shown in Table 1. No significant differences were observed in PWV at all sites between HC and SSc patients. No effect of bosentan on aortic, and upper arm PWV was found. The change in forearm PWV was different between the groups, with a decrease (e.g. lowering arterial stiffness) in the bosentan group (figure 1).

Table 1. Baseline characteristics

<table>
<thead>
<tr>
<th></th>
<th>Healthy controls (n=19)</th>
<th>Systemic sclerosis (n=19)</th>
<th>Bosentan group (n=9)</th>
<th>Usual care group (n=10)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, n (%)</td>
<td>13 (69)</td>
<td>13 (69)</td>
<td>5 (56)</td>
<td>6 (60)</td>
</tr>
<tr>
<td>Age in years, median (IQR)</td>
<td>53 (47–63)</td>
<td>50 (44–54)</td>
<td>52 (49–64)</td>
<td>44 (43–63)</td>
</tr>
<tr>
<td>Pack years, median (IQR)</td>
<td>0 (0–7.5)*</td>
<td>2.5 (0–30.6)*</td>
<td>17.3 (0.7–34.1)*</td>
<td>0.8 (0–3.4)*</td>
</tr>
</tbody>
</table>

Conclusion: This small study shows that aortic, upper arm, and forearm arterial stiffness does not appear to increase in patients with SSc, as compared to age- and sex-matched healthy controls. To the best of our knowledge, this is the first study to investigate the concept of potential effects of an endothelin receptor antagonist on macrovascular involvement in SSc. Although the results demonstrate no effects on aorta and upper arm arterial stiffness, they may indicate a beneficial effect on the stiffness of the smaller arteries of the forearm. Future studies are needed to further investigate the potential effect of bosentan on these smaller arteries.

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immunosuppressive drugs. At the time of data cut-off, all subjects who entered OLE completed 12 months of dosing. Nineteen (95%) of subjects experienced at least 1 AE, with 59 AEs occurring among the subjects during the OLE to date. The majority of AEs were mild (n = 16, 80%), with 1 severe AE (fatigue) considered unrelated to lenabasum reported. AEs occurring in ≥ 2 subjects were: dermatomyositis worsening, dizziness, fatigue, herpes zoster, nasopharyngitis, nausea, upper respiratory tract infection, and urinary tract infection. No serious AEs related to lenabasum have been reported. Improvement was seen in multiple physician- and patient-reported efficacy outcomes; selected outcomes are presented in Figure 1. Mean (SE) changes from study start at Week 52 in the OLE were: CDASI activity score = -17.6 (SD), Patient Skin Activity VAS = -2.6 (SD); Skindex-29 Symptoms Domain = -21.6 (SD); Patient Itch VAS = -2.8 (SD); Physician Overall Disease VAS = -3.0 (SD); and Patient Pain VAS = -2.3 (SD). Improvements were seen in other efficacy outcomes, 12 subjects had no changes in immunosuppressive drugs during the OLE, 3 reduced chronic steroids, 2 reduced mycophenolate, 3 were switched from methotrexate to mycophenolate, 1 started methotrexate, and 1 had a burst and taper of steroids.

Conclusion: Lenabasum continues to have a favorable safety and tolerability profile in the OLE of the Phase 2 trial JBT101-DM-001 with no serious AEs or study discontinuations related to lenabasum. The CDASI activity score and multiple other physician and patient-reported outcomes improved, although limitations of attributing efficacy to lenabasum in the setting of open-label dosing is acknowledged. These data support further testing of lenabasum for the treatment of DM, and a Phase 3 study of lenabasum in DM has started.


SAFETY PROFILE OF NINTEDANIB IN PATIENTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE AND IDIOPATHIC PULMONARY FIBROSIS

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Background: Nintedanib has been investigated in patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD) in the SENSCIS trial and idiopathic pulmonary fibrosis (IPF) in the two INPULSIS trials. These patient populations differ in age, sex, disease characteristics and comorbidities.

Objectives: To compare the safety and tolerability of nintedanib in patients with SSc-ILD and IPF.

Methods: Adverse events that occurred over 52 weeks of treatment in the SENSCIS and INPULSIS trials were assessed descriptively in subjects who received ≥1 dose of trial drug.

Results: A total of 576 subjects were treated in the SENSCIS trial (288 nintedanib; 288 placebo) and 1061 in the INPULSIS trials (638 nintedanib; 423 placebo). At baseline, mean (SD) age was 54.0 (12.2) and 66.8 (8.0) years in SENSCIS and INPULSIS, respectively. The proportion of females was 24.6% and 79.3%, respectively. Over 52 weeks, 19.4% and 10.8% of patients treated with nintedanib and placebo discontinued treatment in SENSCIS, compared with 24.5% and 18.9% of patients treated with nintedanib and placebo in INPULSIS. Gastrointestinal adverse events were the most frequently reported adverse events with nintedanib and placebo, and, as expected based on the underlying disease, were more frequent in patients with SSc-ILD than IPF in both treatment groups (Table). Diarrhoea adverse events were reported in 75.7% and 31.6% of patients treated with nintedanib and placebo in SENSCIS, and 62.4% and 18.4% of patients treated with nintedanib and placebo in INPULSIS, respectively.

Conclusion: The safety and tolerability profile of nintedanib in patients with SSc-ILD is similar to that observed in patients with IPF.


EFFICACY OF PIRFENIDONE IN SYSTEMIC SCLEROSIS RELATED INTERSTITIAL LUNG DISEASE – A RANDOMISED CONTROLLED TRIAL

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Background: Interstitial lung disease (ILD) is a major cause of morbidity and mortality in systemic sclerosis(SSc). (1) Lung fibrosis in systemic sclerosis shares...
similar pathogenesis as idiopathic pulmonary fibrosis. (2) Pirfenidone slows the decline in lung functions in idiopathic pulmonary fibrosis. (3) Therefore, pirfenidone may be efficacious in SSc-ILD.

**Objectives:** To compare the efficacy and safety of pirfenidone with placebo in SSc-ILD.

**Methods:** This was a double-blind, randomised, placebo controlled trial. We enrolled 34 consecutive subjects of SSc-ILD with forced vital capacity (FVC) >50% of predicted value and diffusion capacity of lung for carbon monoxide > 30% of predicted value. Subjects were randomly assigned in a ratio of 3:1 to receive either pirfenidone (n = 17) or placebo (n = 17) and followed up for 6 months. Pirfenidone was started at 600 mg/day and increased to 2400 mg/day over one month and continued for the trial period. Primary outcome was to compare the proportion of patients with stabilisation or improvement in lung functions (FVC). Secondary outcome was to compare the change in FVC, Mahler’s dyspnea index, 6 minute walk distance (6MWD), modified Rodnan skin score (MRSS) and change in serum levels of tumour necrosis factor a (TNF-α) and tissue growth factor (TGF-β) at the end of 6 months. Trial was registered with clinical trials registry of India (CTRI/2018/01/011449).

**Results:** By intention-to-treat analysis, 16 (94.1%) patients in treatment group showed stabilisation of lung function compared to 13 (76.5%) in control group (p = 0.335). The median change in FVC was -0.55% (IQR = -4.75% to 1.75%) and 1.0% (IQR = -8.5% to 5%) in the treatment and control groups respectively (p = 0.654). The median change in 6MWD was -15 (IQR = -42.5 – 13.75) meters and 0.0 (IQR = -50 – 30) meters in treatment and control groups respectively (p = 0.601). The median of focal scores for transitional dyspnea index in both the treatment and control groups were 3.0 (IQR = 0 – 3) (p = 0.838). Median change in MRSS was 0.0 (IQR = -2.0 – 1.0) and -1.0 (IQR = -4.0 – 0.0) in treatment and control groups (p = 0.628). Difference in TNF-α levels were -5.14 (IQR = -14.6 – 0.29) pg/ml in the treatment and -2.94 (IQR = -5.51 – -2.35) pg/ml control group (p = 0.918). Difference in TGF-β levels in the treatment and control groups were 186.73 (IQR = 731.43 – 64.6) pg/ml and 24.29 (IQR = -233.21 – 382.0) pg/ml respectively (p = 0.093). The mean tolerated dose of pirfenidone was 1700 ± 644 mg/day. Adverse events were mild, most common among them were gastrointestinal side effects followed by skin rashes. Only one serious gastrointestinal adverse effect was documented.

**Conclusion:** We failed to demonstrate a beneficial effect of pirfenidone over placebo in stabilising FVC, functional status, or skin disease after 6 months of therapy. A larger study with longer follow up period may be further required.

**REFERENCES:**


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**Disclosure of Interests:** None declared

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**Efficacy and Safety of Low-Dose IL-2 in Patients with Multiple Myositis/Dermatomyositis**

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**Background:** Dermatomyositis (DM) and polymyositis (PM) are rare chronic inflammatory disorders with significant associated morbidity and mortality despite treatment (1, 2). Characterized by subacute onset of proximal muscle weakness, elevated muscle enzymes, and inflammatory infiltrates on muscle biopsy. Although several hypotheses have been proposed for triggers of inflammation in the diseases (4), growing evidences have focused on the immune disorders (5). However, the quantitative changes of lymphocyte subsets in DM/PM are unclear and whether low-dose IL-2 could rebalance the lymphocyte subsets and further benefit to remission disease activity of DM/PM patients is unknown.

**Objectives:** To investigate the quantitative status of peripheral blood lymphocyte subsets in the patients for the exploration of pathogenesis and evaluate the safety and efficacy of low-dose IL-2 therapy in patients with DM/PM.

**Methods:** From February 2016 to October 2018, total 147 patients with PM/DM and 129 gender and age matched healthy individuals were enrolled in this study. The absolute numbers of T, B, NK, CD4+T, CD8+T, Th1, Th2, Th17 and Treg cells in peripheral blood of these individuals were detected by flow cytometry combined with standard absolute counting beads. Patients in IL-2 group (n=31) were not only given traditional treatments, but injected subcutaneously human IL-2 (alde-skulin) at 50 IU/ml per day for a 5-day course. The demographic features, clinical manifestations and laboratory indicators were compared before and after the treatment.

**Results:** Patients with PM/DM had lower levels of Treg cells as well as T, CD4+T, CD8+T, Th1, Th2, Th17 and Th17 compared with those of the healthy controls (P < 0.05), which was correlated with disease activity (P < 0.05). After IL-2 administration, the absolute numbers of peripheral lymphocyte subsets in patients were significantly increased (P < 0.05), leading to a better remission compared with the patients received conventional therapy (P < 0.05).

**Conclusion:** The difference status of peripheral lymphocyte subsets, especially Tregs, between PM/DM patients and healthy individuals suggests that lymphocyte subsets may be involved in and play an important role in the pathogenesis of patients. Low-dose IL-2 can effectively increase the level of Treg cells as well as other lymphocytes to some degree and maintain the immunologic balance, which may help for PM/DM patients’ symptoms remission without over-treatment and evaluated side effect. But long-term benefits of IL-2 therapy are required to further study.

**REFERENCES:**


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PRESERVATION OF LUNG FUNCTION OBSERVED IN A PHASE 3 RANDOMIZED CONTROLLED TRIAL OF TOCILIZUMAB FOR THE TREATMENT OF EARLY SSC

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Background: The anti–IL-6 receptor-α antibody tocilizumab (TCZ) demonstrated numerical improvement in modified Rodnan skin score (mRSS) and clinically relevant preservation of lung function (LF) (assessed by forced vital capacity [FVC]) in systemic sclerosis (SSc) patients (pts) in a ph 2 trial.1

Methods: Pts from the double-blind period of ph 3 trial (NCT02453256). BL%-predicted FVC at wk 48 was 75.6%. Mean BL computer-assisted quantitative lung fibrosis of the most affected region was 20.4, ppFVC 82.1%, and ppDLCO 82.5%. Mean BL computer-assisted quantitative lung fibrosis of the most affected lobe (QLF-LM) was 4.7% for the PBO group and 5.5% for the TCZ group. At wk 48, the primary endpoint was non-inferiority of BL% predicted FVC (pfFVC) and time to Tx failure (time from first study treatment) (Tx) to first occurrence of death, decline in FVC >10%, increase in mRSS >20% and ppFVC <5, or occurrence of predefined SSc-related Cx). Chest high-resolution computed tomography (HRCT) and ACR Combined Response in SSc (CRSS) were exploratory endpoints.

Results: Of 106 PBO- and 104 TCZ-treated pts, 81% were women and 31% had previous or concurrent interstitial lung disease based on history. BL mean values were age 48 yrs, SSc duration 23 mts, mRSS 20.4, pfFVC 82.1%, and ppDLCO 75.6%. Mean BL computer-assisted quantitative lung fibrosis of the most affected lobe (QLF-LM) was 4.7% for the PBO group and 5.5% for the TCZ group. At wk 48, the primary endpoint was non-inferiority of BL% predicted FVC (pfFVC) and time to Tx failure (time from first study treatment) (Tx) to first occurrence of death, decline in FVC >10%, increase in mRSS >20% and ppFVC <5, or occurrence of predefined SSc-related Cx). Chest high-resolution computed tomography (HRCT) and ACR Combined Response in SSc (CRSS) were exploratory endpoints.

Conclusion: The primary mRSS endpoint was not met; however, TCZ Tx resulted in clinically relevant differences in FVC with preservation of LFS and improvement in fibrosis, measured by HRCT, in SSc pts.

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Background: The recently validated Lupus Low Disease Activity State (LLDAS) definition has been shown to have utility as a target to treat endpoint in SLE, whereby LLDAS attainment is associated with reduction in permanent damage accrual. Robust evaluation is required to ensure this protective association is not simply reflective of milder disease phenotypes being over-represented among LLDAS attainers.

Objectives: To assess the effect of attainment of LLDAS on damage accrual in patients with active disease at baseline. SLEDAI-2K<6 was chosen as this reflects clinical trial entry criteria.

Methods: A prospective multinational cohort study was undertaken in 13 centres between 2013-2017. Patients with SLE who were recruited, SLEDAI-2K, SELENA flare index, PGA, and medication data collected at every visit, and damage score (SLICC-ACR damage index (SDI)) collected annually. Subgroup analyses were performed to assess the effect of LLDAS on damage accrual in patients who had active disease at baseline (SLEDAI-2K<6)-Time-dependent hazards regression models were used to assess the association of attainment of LLDAS at any time point, and proportion of time in LLDAS at the 50% observed time cut-off, with occurrence of irreversible permanent end-organ damage.

Results: 1,735 patients were followed for (mean ± SD) 2.2 ± 0.9 years, totalling 1,735 patients were followed for (mean ± SD) 2.2 ± 0.9 years, totalling 3,761 patient-years. LLDAS attainment was less frequent in patients with active disease at baseline (901 of 3,835 visits in LLDAS, 23.5%), compared to patients with SLEDAI-2K<6 at baseline (519 of 8845 visits in LLDAS, 5.7%), p<0.001. In contrast, compared to those with baseline SLEDAI-2K<6, patients with active disease at baseline demonstrated a stronger association of LLDAS attainment with reduction in risk of damage accrual, in visit by visit analysis (HR 0.49, 95% CI 0.28-0.86, p 0.01 vs HR 0.72, 95% CI 0.52-0.99, p 0.05), and in analysis of cumulative time spent in LLDAS (HR 0.52, 95% CI 0.33-0.83, p 0.01 vs HR 0.65, 95% CI 0.47-0.91, p<0.01).

Conclusion: Despite lower attainment of LLDAS in patients with higher disease activity at baseline, the magnitude of association of LLDAS attainment with lower damage accrual was greater in this subgroup of patients compared to those less active baseline disease. This supports the validity of LLDAS as an outcome measure, in a population similar to that typically selected into clinical trials, and further highlights the potential impact of achieving a target outcome in SLE patients with active disease.

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**ATTAINMENT OF THE LUPUS LOW DISEASE ACTIVITY STATE IS ASSOCIATED WITH PROTECTION FROM DAMAGE ACCRUAL IN PATIENTS WITH ACTIVE DISEASE AT BASELINE**

**EFFECT OF IMMUNOSUPPRESSIVE DRUG WITHDRAWAL ON DAMAGE PROGRESSION AND FLARE OCCURRENCE IN SLE PATIENTS IN REMISSION**
The impact of exercise on hand function and quality of life of SLE patients: a randomized controlled trial

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Background: Systemic Lupus Erythematosus (SLE) has a significant impact on the ability to perform daily activities and patients’ quality of life. To date, no studies have examined the effect of exercise on hand function and quality of life of SLE patients.

Objectives: To determine the effect of exercise on hand strength, dexterity and performance of daily activities, and the quality of life of SLE patients.

Methods: A randomized, 24-week follow-up trial was designed. A total of 240 consecutive SLE patients fulfilling the SLICC classification criteria were evaluated. Sixty two patients who met the inclusion criteria [age >18 years, upper limb arthralgias, DASH (Disabilities of the Arm, Shoulder, and Hand) score >10 and stable drug regimen for >3 months], were randomly assigned to the exercise group (n=120) or the routine care (control) group (n=120). Patients in the exercise group received by the hand therapist a 30 min daily program at home of strengthening and stretching upper limb exercises for 12 weeks. Performance of daily activities was evaluated with the DASH and HAQ questionnaires, the grip and pinch strength with the Jamar dynamometer and pinch gauge respectively.

Results: There were no statistically significant differences between two groups in baseline age (39.2 vs 39.6 years, p=0.806). Thirty participants (93.75%) from the exercise group completed the 12-week exercise program and 28 (87.5%) were re-evaluated at 24 weeks; 30 (p=0.044) and 26 (p=0.001) in the exercise group compared to control group at all-time points. More- patients (100%) of control group completed the 24-week study.

Conclusion: In our SLE cohort, the withdrawal of IS therapy in remitted patients did not seem to influence damage progression in the medium-term.

Disclosure of Interests: None declared


Scientific Abstracts

OP0248

Antiphospholipid syndrome (APS) in systemic lupus erythematosus (SLE) leads to a more severe disease

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Background: Antiphospholipid antibodies (aPL) have been associated with organ damage and certain features in SLE patients.

Objectives: Our aim was to investigate the differences between SLE patients according to the presence of aPL and/or clinical antiphospholipid syndrome.

Methods: Patients from the RELESSER-T registry were included. RELESSER-T is a multicenter, hospital-based registry, with retrospective cross-sectional collection of data from a large representative sample of adult non-selected patients with SLE attending Spanish rheumatology services from the public national health system.

Results: We included 3651 SLE patients and 1368 were positive for aPL (44.9%). 9% of patients were positive for anticardiolipin antibodies, 27.3% showed positivity for anti b2glycoprotein I and 24% for lupus anticoagulant. Overall 2283 patients were classified as SLE no aPL, 528 as SLE-aPL and 840 as SLE-APL.

All values are presented as median (interquartile range). DASH=Disabilities of the Arm, Hand, and Shoulder; HAQ=Health Assessment Questionnaire; LUPUS-QoL=Lupus Quality of Life; PH=physical health domain, DH=dominant hand, JAW=joint pain, COM=combination.

Disclosure of Interests: None declared

Conclusion: SLE-APS patients show a more severe clinical profile with higher frequency of major organ involvement and more damage accrual than SLE-aPL.

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OP0250
INFLUENTIAL FACTORS IN PROMOTING TREAT-TO-TARGET FOR SYSTEMIC LUPUS ERYTHEMATOSUS VIA EMPOWERING PATIENTS: A COHORT STUDY FROM CHINA BY SMART SYSTEM OF DISEASE MANAGEMENT (SSDM)

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Background: T2T is routine in RA, but no comparable standard has been defined for SLE. In 2015, the definition of Lupus Low Disease Activity State (LLDAS) was generated by Asia-Pacific Lupus Collaboration, and the preliminary validation demonstrated its attainment to be associated with improved outcomes in SLE. A SLEDAI-2K score lower than 4 is the main criteria for LLDAS. SSDM is an interactive mobile disease management application, including application systems for both the doctors and patients. The patients can perform self-assessment, including SLEDAI and medical records entry through the mobile application. The data is synchronized to the SSDM of authorized rheumatologists and stored in cloud database.

Table 1: Main demographic data, clinical and laboratory features in the studied group.

<table>
<thead>
<tr>
<th>Feature</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>Male/Female</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Complement C3/C4 levels</td>
<td>Median (IQR)</td>
</tr>
</tbody>
</table>

Table 2: Baseline and last follow-up SLEDAI scores.

<table>
<thead>
<tr>
<th>Follow-up</th>
<th>Baseline</th>
<th>Last Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLEDAI-4</td>
<td>576</td>
<td>444</td>
</tr>
<tr>
<td>SLEDAI-5</td>
<td>514</td>
<td>301</td>
</tr>
<tr>
<td>Total</td>
<td>1090</td>
<td>745</td>
</tr>
</tbody>
</table>

Figure 1

Disclosure of Interests: None declared


OP0251
SLE PATIENTS FROM NORTH AMERICA ARE OLDER WITH LESS SEROLOGIC ACTIVITY THAN OTHER POPULATIONS IN INTERNATIONAL CLINICAL TRIALS

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Background: Regional differences have been identified as potential confounders of SLE clinical trial results. Recently, no difference between treatment and placebo was observed in the US lupus patients when a significant treatment effect was observed in Europe.

Objectives: To compare SLE serologic features/markers of active disease between different geographic regions in recent multinational clinical trials.

Methods: Laboratory data of 1005 subjects from four global randomized SLE clinical trials at baseline were examined. Mean/median C3 and C4 complement levels, prevalence of low C3 or C4 (Low C3/C4), positive anti-double stranded DNA (DNA), anti-Extractable Nuclear Antibodies (ENA), and high-titer Antinuclear Antibody (ANA $>\text{t}1:50$) in North America (NA) patients were compared to Asia (AS), Latin America (LA), Africa (AF), Western Europe (WE), and Eastern Europe (EE).

Results: NA patients were significantly older than patients in LA, AF, or AS but not WE or EE. Not surprisingly, they also had higher complement levels and the lowest rates of low C3/C4, DNA, ENA, and ANA $>\text{t}1:640$. Our data confirm that age is an important factor in the prevalence of low complement and autoantibodies. However, there remained a marked difference in serologic activity between NA and EE, despite being close in age.
Asian patients were the youngest, had the lowest complement levels and the highest rate of ENA & DNA consistent with high disease activity. Low complement, but not DNA, was relatively common in Europe. LA patients, like Asians, had high rates of serologic activity but less incidence of low C3/C4, suggesting that this population may have intrinsic disease severity without being as acutely active. *Mann-Whitney Rank Sum **Chi-square *One-way ANOVA on ranks; Med-median p p value C-comparator ns-not significant; Data not corrected for multiple comparisons

Conclusion: SLE patients entering studies from North America are strikingly less likely to have markers of active disease than other regions, raising concerns for their suitability for trials. This appears to be associated, at least in part, with age, although more aggressive treatments cannot be ruled out. Asian subjects have the greatest prevalence of autoantibodies and low complement. Latin American patients have high prevalence of ANA; 1:640 and other autoantibodies, but less evidence of low complements. These findings may help to explain regional differences in treatment/placebo responses and emphasize the importance of geographical stratification and improved methods to screen out patients unsuitable for SLE trials.

REFERENCE:
[1] www.immupharma.co.uk

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NEUROPATHIES IN SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS FROM AN INTERNATIONAL, INCEPTION COHORT STUDY

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Background: Central nervous system (CNS) involvement accounts for over 90% of neuropsychiatric (NP) events compared to involvement of the peripheral nervous system (PNS) which accounts for most of the other events. Although there is a large body of work on CNS disease in SLE patients, involvement of the PNS is less well established.

Objectives: In a multi-ethnic/racial, prospective SLE inception cohort, to determine the clinical characteristics, associations and outcomes in different types of peripheral nervous system (PNS) disease.

Methods: Patients were evaluated annually for 19 NP events including seven types of PNS disease. Standardized case definitions and attribution models for each type of PNS event were used. SLE disease activity (SLEDAI-2K), organ damage (SLICC/ACR damage index), autoantibodies, patient (SF-36) and physician (Likert score) assessment of outcome were measured. Time to event and linear regressions were used as appropriate.

Results: Of 1,827 SLE patients, 68.8% were female, 48.8% Caucasian. The mean±SD age was 35.1±13.3 years, disease duration at enrollment 5.6±4.2 months and follow-up 7.6±4.6 years. There were 161 PNS events in 139.1,827 (7.6%) patients. The predominant events were peripheral neuropathy [68/161 (41.0%), mononeuropathy [44/161 (27.3%)] and cranial neuropathy [39/161 (24.2%)] and the majority were attributed to SLE. Multivariate Cox regressions suggested longer time to resolution in patients with prior history of neuropathy, older age at SLE diagnosis, higher SLEDAI2K scores, and for peripheral neuropathy versus other neuropathies. Neuropathy was associated with significantly lower SF-36 physical and mental component summary scores versus patients without NP events. By physician assessment, the majority of neuropathies...
resolved or improved over time and this was associated with improvements in SF-36 summary scores for peripheral neuropathy and mononeuropathy.

Conclusion: PNS disease is an important component of total NPSLE and has a significant negative impact on health related quality of life. The outcome is favourable for most patients, but several factors associated with longer time to resolution were identified.

Disclosure of Interests: John Harly Consultant for: Eli Lilly Canada, Qiupu Li: None declared, Li Su: None declared, Murray B Urowitz Grant/research support from: GSK Consultant for: BMS, Celgene, GSK, Lilly, UCB, Caroline Gordon Grant/research support from: Sandwell and West Birmingham Hospitals NHS Trust have received funding from UCB to support research work done by my research group that was unrelated to any pharmaceutical product or clinical trial., Consultant for: I have provided consultancy advice and taken part in scientific advisory boards on the design and analysis of clinical trials and the management of lupus for GSK, EMD Serono and UCB. I have taken part in adjudication and safety monitoring committees for BMS., Speakers bureau: I have been paid by UCB for speaking at meetings., Sang-Chel Bae: None declared, Juanita Romero-Diaz: None declared, Jorge Sanchez-Guerrero: None declared, Sasha Bernatsky: None declared, Ann E Clarke: None declared, Daniel J Wallace: None declared, David Isenberg: None declared, Anisur Rahman: None declared, Joan T Merrill Grant/research support from: Genentech, UCB, GSK, EMD Serono, Pfizer, Celgene, Exagen, Bristol Myers Squibb, MedImmune/ASTRA Zeneeca, Lilly, Amgen, Xencor, Neoavacs, Consultant for: Genentech, UCB, GSK, EMD Serono, Pfizer, RemiGen, Celgene, Exagen, Bristol Myers Squibb, MedImmune/Astra Zeneeca, Lilly, Immupharma, Amgen, Janssen, Sanofi, Neovacs, Anthera, Speak-ers bureau: UCB, GSK, EMD Serono, Olenav, AstraZeneca, Amgen, Pfizer, Part: None declared, Dafna D Gladman Grant/research support from: AbbVie, Amgen, Celgene, Lilly, Novartis, and Pfizer, and UCB, Consultant for: AbbVie, Amgen, BMS, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, and UCB, Ivan N. Bruce Grant/research support from: Genzyme Sanofi, GlaxoSmithKline, Consultant for: AstraZeneca, Eli Lilly, GlaxoSmithKline, ILT0 Pharma, MedImmune, Merck Serono, Speakers bureau: GlaxoSmithKl.ine, UCB Pharma, Michelle A Peni Shareholder of: Pfizer, Merck, Grant/research support from: AstraZeneca, Exagen, Consultant for: Eli Lilly, GSK, Merck EMD Serono, Janssen, Amgen, Novartis, Quintiles, Exagen, Inova Diagnostics, AstraZeneca, Blackrock, Glenmark, UCB, and the Annenberg Center for Health Sciences, Ellen M Ginzeii: None declared, M.A. Dooley: None declared, Kristin Steiinnesson: None declared, Rosenlind Ramsey-Goldman: None declared, Asad A Zoma: None declared, Susan Manzi: None declared, Ola Nived: None declared, Andreas Jonsen: None declared, Munther Khamashia: None declared, Graciela S Alarcon: None declared, Ronald F von Vollenhoven: None declared, Elisabet Svennungson: None declared, Cynthia Aranow: None declared, Meggan Mackay: None declared, Guillermo Ruiz-Traiztara: None declared, Manuel Ramos-Casals: None declared, S. Sam Lim: None declared, Murat Inanc: None declared, Kenneth C Kalunian: None declared, Soren Jacobsen: None declared, Christine Peschken Consultant for: AstraZeneca, Diane I. Kamen: None declared, Arica Askasanke: None declared, Chris Theriault: None declared, Veron Farewell: None declared

In medium to long-term juvenile dermatomyositis, proinflammatory and profibrotic cytokines are differently associated with pulmonary involvement in active vs inactive disease

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Background: Knowledge about associations between cytokines and lung involvement in juvenile dermatomyositis (JDM) is scarce.

Objectives: To examine associations between cytokines and pulmonary involvement in JDM assessed after medium to long-term follow-up.

Methods: 58 JDM patients examined median 17y after disease onset were stratified in active and inactive disease by the updated PRINTO criteria (Ref 1). Serum levels of cytokines were analyzed by Luminex or ELISA. Pulmonary function tests (PFT) included forced vital capacity (FVC), total lung capacity (TLC) and diffusing capacity for carbon monoxide (DLCO) (hbg adjusted). PFT variables are expressed as% of predicted. High resolution computed tomography (HRCT) scans were scored for interstitial lung disease (ILD), calcinosis in chest wall and airway disease. Associations between lung involvement and cytokines are presented as Spearman’s correlation coefficient (rs).

Results: Table 1. Characteristics, PFT, HRCT findings and cytokines

<table>
<thead>
<tr>
<th>Total (n=58)</th>
<th>Active (n=37)</th>
<th>Inactive (n=21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y, median (IQR range)</td>
<td>21 (15-34.8)</td>
<td>20 (14-34)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>35 (60)</td>
<td>25 (69)</td>
</tr>
<tr>
<td>Disease duration, y (IQR range)</td>
<td>17 (7-27)</td>
<td>16 (6-26)</td>
</tr>
<tr>
<td>TLCa</td>
<td>93 (1,1)</td>
<td>91 (10)</td>
</tr>
<tr>
<td>FVCb</td>
<td>96 (12)</td>
<td>94 (12)</td>
</tr>
<tr>
<td>DLCOc</td>
<td>82 (15)</td>
<td>79 (13)</td>
</tr>
<tr>
<td>Any HRCT findings, n (%)</td>
<td>21 (36)</td>
<td>15 (40)</td>
</tr>
<tr>
<td>HRCT ILD, n (%)</td>
<td>8 (14)</td>
<td>6 (16)</td>
</tr>
<tr>
<td>HRCT calcinosis, n (%)</td>
<td>8 (14)</td>
<td>6 (16)</td>
</tr>
<tr>
<td>HRCT Airways disease, n (%)</td>
<td>9 (15)</td>
<td>7 (18)</td>
</tr>
<tr>
<td>TGFb1</td>
<td>29292 (8686)</td>
<td>29698 (9623)</td>
</tr>
<tr>
<td>PDGFb</td>
<td>9083 (2799)</td>
<td>8960 (2979)</td>
</tr>
<tr>
<td>IP-10</td>
<td>1448 (1281)</td>
<td>1491 (1438)</td>
</tr>
<tr>
<td>MCP-1</td>
<td>34 (21)</td>
<td>34 (19)</td>
</tr>
<tr>
<td>Eotaxin</td>
<td>136 (103)</td>
<td>142 (108)</td>
</tr>
<tr>
<td>IL-17a</td>
<td>15 (14)</td>
<td>15 (15)</td>
</tr>
<tr>
<td>IL-6</td>
<td>1.4 (1.3)</td>
<td>1.6 (1.6)</td>
</tr>
<tr>
<td>MMP9a</td>
<td>2.5 (1.4)</td>
<td>2.7 (1.5)</td>
</tr>
</tbody>
</table>

Numbers are mean (SD) if not stated otherwise, *unit: pg/ml

No significant differences were found between active and inactive patients in tbl. 1

Associations between cytokines and PFT/HRCT findings

Numbers are rs, all p’s < 0.05

In patients total, TGFb1 and PDGF correlated with TLC and FVC (r = 0.38 - 0.30).

For TGFb1 correlations with TLC and FVC were -0.62 and -0.59 in the inactive group, whereas PDGF correlated with FVC in the active group (r = 0.48).

IP-10 correlated with TLC in active patients only (r = 0.35).
In patients total and active patients, eotaxin correlated with DLCO% (0.39 and 0.52). In inactive patients, MIF1b correlated with DLCO% (0.47).

In patients total, IP-10 correlated with any HRCT finding and Airways disease (0.37 and 0.44), which were also present in active patients (0.34 and 0.61). In patients total, MCP-1 correlated with any HRCT finding and calcinosis (0.34 and 0.40); in active patients MCP-1 and calcinosis correlated (0.34). Eotaxin correlated with ILD in both patients total and active patients (0.37 and 0.38).

The following cytokines correlated with HRCT findings in inactive patients only; IL-17 with any HRCT findings and ILD (0.61 and 0.52), MIF1a with any HRCT findings (0.63) and IL-5 with ILD (0.42).

Conclusion: In JDM, lung involvement was associated with mainly proinflammatory cytokines in active and pro-inflammatory/proinflammatory cytokines in inactive patients. The association between higher eotaxin and better gas diffusion was interesting, since we have previously demonstrated an association between higher eotaxin and cardiac dysfunction (Ref 2).

REFERENCES:

Disclosure of Interests: None declared

**OP0257 CHILDHOOD-ONSET MONOGENIC SYSTEMIC LUPUS ERYTHEMATOSUS NOT DUE TO COMPLEMENT DEFICIENCY: ASYSTEMATIC REVIEW OF 90 CASES**

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Background: The paediatric SLE (pSLE) are estimated 10 to 17% of SLE (1). Studies comparing pSLE with adult-onset SLE reported high prevalence of neuropsychiatric organ damage at diagnosis due to the diagnosis delay, more severe disease course with high disease activity resulting in worse prognosis in pSLE (1,2). Recently, whole exome sequencing and next-gen sequencing have facilitated the identification of rare monogenic variants associated with SLE and lupus-like phenotypes with high penetrance (3,4).

Objectives: To reporting the whole spectrum of monogenic pSLE according to pathway abnormalities, using a meta-analysis (MA) approach.

Methods: A systematic review of studies focused on monogenic pSLE were analysed. To be included in the systematic review, studies had to meet simultane-
ously all the following criteria: (i) reported at least 1 case of SLE (ii) started before the age of 16 (iii) with clearly description of the diagnosis criteria and (iv) provided genetic data of the case.

We pooled the genes into three main groups of signalling pathways: (i) genes that affect adaptive immunity pathways including the lymphocyte apoptosis (FAS, KRAS, PTPN11, SHOC2) and the B and T cell development checkpoints (PRKCD, RAG2, IKZF1, DDX4, WASP), (ii) genes containing type I interferon (IFN) pathways (IRF5, TREX1, SAMHD1, RNASEH2A, RNASEH2B, RNA-SEH2C, IFIH1, DNASE1L3, DNASE1, TMEFF173, Terasomy 9), and (iii) metabolism pathways including both amino acid metabolism (PEPD, SLC7A7, MAN2B1) and oxidative metabolism (NCF2). Clinical and laboratory data were analysed according to the SLICC classification.

Results: We included 42 articles encompassing 88 patients, plus 2 additional unpublished cases of one author (AB). The MA process were carried out according to the PRISMA statement. According to the SLICC classification, the blood disorders were significantly higher in the group of the metabolism pathway as well as the positivity of direct Coombs test. The positivity of antibodies anti-Sm was also a distinguishing element for this group, while the positivity of ALP antibodies was the only manifestation to distinguish the adaptive immunity pathway from the others. Fever, recurrent infections, hepatosplenomegaly, and pulmonary diseases were significantly predominant in the metabolism pathways. In the group of the IFN pathway, the most distinctive criteria were the neurological manifestations and bone changes. There were no statistically significant differences in all groups concerning all other clinical or immunological criteria.

Conclusion: This is the first quantitative analysis of multiples cases reports, comparing the whole spectrum of monogenic pSLE according to three different pathways. Our results suggest that abnormalities in signaling pathway delimitate different SLE juvenile subset. The clinical and biological differing between the three signaling pathway were not specific, but our results may help to detect phenotypes requiring targeted genetic investigations. Subsets of SLE syndrome have to be identified to drive the treatment and propose personalized medicine.

REFERENCES:

Disclosure of Interests: None declared

**OP0258 LESSON FROM EUROFEVER REGISTRY AFTER THE FIRST TEN YEARS OF ENROLLMENT**

Martina Ferrari, Ilaria Gueli, Joost Frenkel, Seza Ozan, Helen J. Lachmann, Fabrizio De Benedetti, Isabelle Kneu-Pauly, Carine Wouters, Paul Brogan, Hermann Girschick, Benedicte Neven, Alberto Martini, Nicolo Ruferto, Marco Gattorno, IRCSS Istituto Gianna Gaslini, UCSID Centro Malattie Autoinflammatorie e Immunodeficienze, on the behalf of the Paediatric Rheumatology International Trials Organisation (PRINTO) and the Eurofever Project, Genoa, Italy

Background: In 2008 the Paediatric Rheumatology European Society (PReS) promoted an International Project for the study of Autoinflammatory Diseases (AIDs) named Eurofever, whose main purpose is to create a web-based registry for the collection of information in AIDs patients.

Objectives: To assess the impact of the Eurofever Registry on scientific community with particular interest in the geographical coverage, diagnostic delay, access to treatment and publications.

Methods: The data analyzed in the study were extracted from the Eurofever registry, which is hosted in the PRINTO website.

Results: Up to date 4175 patients have been enrolled from 62 countries (3843 of them with complete demographic data). Most of patients (72%) are resident in Western Europe, 8% in Central-Eastern Europe, 11% in Southern-Eastern Mediterranean, 2% in South America and 7% in other countries. Compared to the first Eurofever report (Toplak et al, 2012) we have observed an increase of enrolled patients from 1388 to 2651 in Western Europe, from 106 to 313 in Central-Eastern Europe, from 284 to 406 in Southern-Eastern Mediterranean. The median onset age is 4 years (range 1 month – 78 years), the median diagnosis age is 6 years (range 1 month – 78 years). The median diagnostic delay observed in 2012 was 7.3 years (range 0.3–76), from patients enrolled after 2012 it was 1.9 years (range 0.57). Comparing the mean diagnostic delay from 1980 to 2018, we have observed an encouraging constant reduction of period between AIDs onset and diagnosis (from a mean diagnostic delay value of 20 years for patients born before 1980, to a mean value of 1 year for patients born after 2011, Figure 1). Complete information on access to treatment were available in 2430 patients. DMARDs were used in 1031 (42%), biologics in 396 (16%) patients. According to the number of enrolled patients, biologics were used in 361/7182 (20%) of Western europeans, 17/342 (5%) of Central-Eastern europeans, 6/259 (2%) of Southern-Eastern Mediterranean patients. Regarding Eurofever impact on Scientific Communication, during this first 10 years the Registry provided 12 papers with more than 800 citations. Detailed analysis of clinical features collected in Eurofever database allowed to perform studies with large cohort of patients, to propose new classification criteria (Federici et al, 2015), to validate damage and activity score (Piram et
Conclusion: In the last years we have observed an encouraging increase of involved Countries, with a greater number of patients coming from geographic area poorly represented in the first epidemiologic study of Toplak et al. Eurofever data analysis has confirmed an improvement of diagnostic ability during the last years, with a significant reduction of mean diagnostic delay. Longterm studies will help understand the efficacy and safety of different treatments used in these rare conditions.

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The money received for these activities are directly transferred to the Gaslini Institute’s bank account. Before March 2016, I was the head of the Pediatric Rheumatology Department at the G. Gaslini Hospital, where the PRINTO Coordinating Centre is located. For the coordination activity of the PRINTO network, the Gaslini Hospital received contributions from the industries listed in this section. This money has been reinvested for the research activities of the hospital in fully independent manners besides any commitment with third parties., Nicolino Rupert Grant/research support from: The Gaslini Institute, where NR works as full-time public employee, has received contributions (>10.000 USD each) from the following industries in the last 3 years: SMS, El-Lilly, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Novartis, Pfizer, Sobi. This funding has been reinvested for the research activities of the hospital in a fully independent manner, without any commitment with third parties., Consultant for: Received honoraria for consultations or speaker bureau (<10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, AbbVie, AstraZeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sobi, and Takeda., Speakers bureau: Received honoraria for consultancies or speaker bureau (<10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, AbbVie, AstraZeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sobi, and Takeda., Marco Gattorno Grant/research support from: MG has received unrestricted grants from Sobi and Novartis.

Figure 1. Diagnostic delay (years) according the year of birth

REFERENCES:

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Background: Patients with juvenile idiopathic arthritis (JIA) may have a different body composition associated with reduced muscle mass and increased fat mass [1]. They display decreased physical fitness, perform less strenuous physical activities, and spend more time sleeping than do healthy children. A lower level of physical activity is associated with deconditioning and functional deterioration, favoring an inactive lifestyle. The risk of overweight might be further increased by the glucocorticoid treatment.

Objectives: Since obesity can increase inflammatory processes, cause early atherosclerotic changes and promote metabolic disorders, the objectives were a) to determine the prevalence of overweight and obesity in children and adolescents with JIA, and b) to examine the association between overweight and health-related parameters in this population.

Method: A cross-sectional analysis of physicians’ recorded body weights and heights of patients with JIA enrolled in the NPRD in the year 2016 was performed. Overweight was defined as BMI >90th sex- and age-specific percentile and obesity as BMI >97th percentile. For comparison with data from the general German population [2], patients aged 3 to 17 years were considered. A linear regression model was used to explore the association between overweight and both clinical as well as self-reported outcomes.

Results: In total, data from 6.860 children and adolescents with JIA (age 11.5 ± 4 years, disease duration 4.6 ± 3.6 years, 67% girls, 39% persistent oligoarthritis) were analyzed. Overweight was found in 14% (including 6% obesity) of JIA cases. Comparative data from the German general population report an overweight prevalence of 15% (including 6% obesity). In contrast to the general population, overweight rates in JIA differed between girls and boys (girls 14% vs. boys 16%, p=0.05). Patients with psoriatic arthritis (20%) and systemic JIA (18%) showed the highest overweight rates. In multivariate analyses, age (OR 1.06; 95%CI: 1.04-1.09), male sex (OR 1.21; 95%CI: 1.01-1.44), functional limitations (OR 1.29; 95%CI: 1.04-1.59), as well as therapy with biological DMARDs (OR 1.48; 95%CI: 1.22-1.80) and systemic glucocorticoids (OR 1.40; 95%CI: 1.14-1.71) were significantly associated with overweight.

Conclusion: The prevalence of overweight and obesity in young patients with JIA is similar to that of children and adolescents in the general population. The overweight rate increases with age and is strongly associated with functional restrictions and treatment with glucocorticoids. The role of overweight in the long-term outcome of JIA is an issue that still needs to be addressed.
VACCINATION SAFETY AND COVERAGE IN AN ITALIAN COHORT OF AUTOINFLAMMATORY DISEASES

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Background: Vaccine-preventable diseases are again emerging in our population after anti-vaccine campaign has started. In autoinflammatory diseases (AID), vaccine triggered disease is a well known phenomenon for Hyper-IgD/Mevalonate-Kinase Deficiency (MKD). In CAPS, severe flares have been experienced after pneumococcus vaccine, while PFAPA patients did not achieve sufficient and protective levels of antibodies. This evidence has raised doubts in physicians and families about the safety of vaccines.

Objectives: To evaluate, in a cohort of Italian AID, the vaccination coverage of the Italian Vaccination Schedule and the prevalence of adverse reactions and disease flares induced by vaccinations.

Methods: An anamnestic questionnaire was applied to AID patients referring to the AID Unit of the Istituto Giannina Gaslini from August 2017 to August 2018. Acquired data were revised for quality of information. Data about disease triggers in AID were obtained from the EUROFEVER registry for statistical reference.

Results: Triggers in AID Eurofever Registry: In August 2018 a total of 3783 patients were enrolled in the EUROFEVER registry (1908 female, 50.43%). The mean age of symptoms at disease onset was 7.04 +/- 9.48 SD yrs, (minimal 0 - maximum 75.92 yrs). The distribution among the periodic hereditary fevers was: 28,75% FMF (n=1081); 17,66% TRAPS (n=271) and 5,39% MKD (n=204). Triggers were observed in the disease of 70% of the MKD, while PFAPA, TRAPS and UND had a rate of reactions of 20%. This was also found in 12,34% of CAPS, whereas FM and inflammatory bone disorders had a rate of 6% and 3%, respectively. Excluding other causes of reactions, and isolating just vaccines as a cause, MKD had a higher percentage of reactions (7,14%), while PFAPA and UND had 1% and CAPS, TRAPS, FM and inflammatory bone disorders had less than 1%. Triggers in IGG cohort: 150 questionnaires were distributed with 70% rate of response. Quality of data was 100% for coverage and adverse reactions. 105 patients were identified: PFAPA (n=26); CAPS (n=5); TRAPS (n=6); FM (n=14); MKD (n=6); Inflammatory Bone Disorders (CRMO and PAPA, n=4) and UND (n=4). Rate of coverage was lower than 90% for Hib3 (83.11%), MMR/ MMRV (88.9%) and for Rota C (1.85%). DTP3, Hep3, PCV3 and IPV the rate of coverage was higher than 90% for all vaccines. 11 moderate/severe reactions were observed as following: 5 after DTPA+IPV (1 PFAPA; 2 TRAPS, 1 MKD and 1 UND); 1 after Hib (PFAPA); 1 after P10/13 (PFAPA); 1 after MPR (PFAPA); 1 after MMR (1 TRAPS, 1 MKD and 1 UND). The general rate of severe reactions/shot was 0.68 for 1000 shots and no severe infection, death, persistent or significant disability or life-threatening condition was observed. Just one MKD patient had a severe disease flare requiring hospitalization following pneumococcal vaccine.

Conclusion: Data show that in AID patients vaccines may more frequently trigger the disease. Therefore, vaccination in AID may be considered a peculiar public health problem. Specific recommendations for vaccination in AID are warranted as well as further investigations for immunologic protection.

REFERENCES:

Disclosure of Interests: Sara Signa: None declared, Caterina Matucci Cerinic: None declared, Enrica Toniolo: None declared, Marta Bastuffa: None declared, Matteo D’Alessandro: None declared, Stefano Volpi: None declared, Roberta Caorsi: None declared, Leonardo Oliveira Mendonca: None declared, Marco Gattorno Grant/research support from: MG has received unrestricted grants from Sobi and Novartis.

FACTORS ASSOCIATED WITH ACUTE ANTERIOR HYDROXYCHLOROQUINE DOSING IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS: ANALYSIS OF THE BSRBR-AS REGISTRY DATABASE

Mohammad H. Derakhshan1, Linda Dean2, Gareth T. Jones2, Gary J. Macfarlane2, Stefan Siebert1, Karl Gaffney3, University of Glasgow, Institute of Infection, Immunity and Inflammation, Glasgow, United Kingdom; 2University of Aberdeen, Epidemiology Group, Aberdeen, United Kingdom; 3Norfolk and Norwich University Hospital, Rheumatology Department, Norwich, United Kingdom

Background: Acute anterior uveitis (AAU) is one of the key extra-articular manifestations in axial spondyloarthritis (axSpA). The presence of AAU may influence the decision to start and the choice of biological therapy.

Objectives: To examine the factors associated with AAU in patients with axSpA in the British Society for Rheumatology Biologics Register in Ankylosing Spondylitis (BSRBR-AS).

Methods: Clinical and patients-reported outcomes of 2420 patients with axSpA from 83 rheumatology centres in the United Kingdom were collected as part of the BSRBR-AS. Patients with AAU diagnosed by an ophthalmologist were compared to those without AAU in relation to demographic and lifestyle factors. The associations were analysed using univariable and multivariable logistic regression models, considering necessary interaction terms and sensitivity analyses.

Results: 568 (23.5%) patients in the cohort had at least one episode of AAU. The male/female ratio was 2.0:1 and group’s median (IQR) age was 51 (41 – 61) years. Factors associated with higher odds of AAU in univariable analyses were HLA-B27 positivity [OR 2.32 (95%CI: 1.66 – 3.23)], univerisity degree [OR 1.44 (95%CI: 1.53 – 1.79)], age [OR (per year) 1.02 (95%CI: 1.01 – 1.03)] and axSpA disease duration [OR (per year) 1.02 (95%CI: 1.01 – 1.03)]. Ever-smoking was inversely associated with AAU [OR 0.71 (95%CI: 0.59 – 0.89)]. Ever-alcohol drinking (p=0.213), BMI (p=0.325) and gender (p=0.317) did not show any associations.

In multivariable analysis, the magnitude of associations remained significant for HLA-B27 positivity, age, and axSpA disease duration, as did the inverse association with smoking (see Table). Analysis restricted to patients with inflammatory bowel disease did not alter the relationship between AAU and the above risk factors.

Table 1. Factors associated with AAU in axSpA, multivariable analysis

<table>
<thead>
<tr>
<th>Factor</th>
<th>Wald</th>
<th>df</th>
<th>P</th>
<th>OR</th>
<th>95% CI for OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ever Smoking (vs never)</td>
<td>9.76</td>
<td>1</td>
<td>0.002</td>
<td>0.614</td>
<td>0.452 – 0.834</td>
</tr>
<tr>
<td>University Degree (vs lower)</td>
<td>2.27</td>
<td>1</td>
<td>0.132</td>
<td>1.325</td>
<td>0.919 – 1.912</td>
</tr>
<tr>
<td>HLA-B27 positive (vs negative)</td>
<td>21.12</td>
<td>1</td>
<td>&lt;0.001</td>
<td>2.399</td>
<td>1.652 – 3.484</td>
</tr>
<tr>
<td>Age</td>
<td>17.25</td>
<td>1</td>
<td>&lt;0.001</td>
<td>1.038</td>
<td>1.020 – 1.056</td>
</tr>
<tr>
<td>AxSpA Disease Duration</td>
<td>15.77</td>
<td>1</td>
<td>&lt;0.001</td>
<td>1.093</td>
<td>1.046 – 1.142</td>
</tr>
</tbody>
</table>

Conclusion: The odds of having a diagnosis of AAU is high in axSpA patients with positive HLA-B27, and longer disease duration (having controlled for age). The negative association with smoking in this large cohort contrasts with previous published data and warrants further evaluation.

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Conclusion: A significant fraction of patients with rheumatic disease on HCQ received doses greater than those recommended by the AAO, with large differences across practices and states. Patients with low body weight are consistently at increased risk of receiving a higher dose. Although further studies are required to

OP0263 HYDROXYCHLOROQUINE DOING IN PATIENTS WITH RHEUMATIC DISEASE ACROSS THE U.S.: DATA FROM THE RHEUMATOLOGY INFORMATICS SYSTEM FOR EFFECTIVENESS (RISE) REGISTRY

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Background: The risk of retinal toxicity and subsequent visual loss from hydroxychloroquine (HCQ) is dependent on daily dose and duration of use. Although further efficacy and safety studies are required to understand optimal dosing strategies, real-world application of existing American Academy of Ophthalmology (AAO) recommendations in a population-based sample of patients with rheumatic disease has never been described.

Objectives: The objectives of this study were to assess application of AAO dosing recommendations across the U.S. and identify patient and practice-level risk factors for receiving higher than recommended doses using data from the ACR’s RISE registry.

Methods: RISE is a national, EHR-enabled registry that passively collects data on all patients seen by participating practices, reducing the selection bias present in single-insurer claims databases. As of December 2017, RISE held validated data from 1,257 providers in 236 practices, representing about 36% of the U.S. clinical rheumatology workforce. We included adult patients with at least one order for HCQ in 2017. For patients with multiple orders, the most recent order was included in the analysis. We excluded weights that appeared to be outliers and practices with <30 patients receiving HCQ. Instructions were interpreted to yield an average daily dose per patient. We investigated practice-level and state-level variation by calculating the proportion of patients who received a dose >5 mg/kg/day by practice and the proportion of patients who received a dose >6.5 mg/kg/day (AAO’s 2011 recommendation) by state. We tested whether prescribing a dose exceeding the AAO recommendations was associated with patient-level demographics (age, sex, race/ethnicity, insurance) or practice characteristics (type, size) using multivariate mixed-effects regression.

Results: We included 45,712 patients (85% female, 53% Caucasian, with mean age 57±15) from 96 practices (34% single specialty group practice, 76% with 1-5 providers). The patient average daily dose of HCQ ranged from 57 mg to 800 mg, with a median of 400 mg. Overall, 40% and 9% of patients received a HCQ dose >5 mg/kg/day and >6.5 mg/kg/day, respectively. Practice-level variation ranged from 6-66% for receiving a dose >5 mg/kg/day (Figure 1) and 0-28% for receiving a dose >6.5 mg/kg/day. State-level variation was also significant (p<0.001, Figure 2). After adjusting for demographics and practice characteristics, low body weight (<78 kg, the sample median) was strongly associated with receiving doses >5 mg/kg/day (+64%, p<0.001) and >6.5 mg/kg/day (+18%, p<0.001). In the same model, female gender was also associated with doses >6.5 mg/kg/day (+5%, p<0.001). Practice characteristics were not statistically significantly associated with receiving a higher dose.

Conclusion: A significant fraction of patients with rheumatic disease on HCQ received doses greater than those recommended by the AAO, with large differences across practices and states. Patients with low body weight are consistently at increased risk of receiving a higher dose. Although further studies are required to

Disclosure of Interests: Mohammad H. Derakhshan: None declared, Linda Dean: None declared, Gareth T. Jones Grant/research support from: Have received research grants (not current) from Abbvie and Pfizer.
achieve consensus on optimal dosing of HCQ, these data suggest that patients with low body weight should be targeted for toxicity monitoring regardless of the dosing cut-off used.

Disclaimer: This data was supported by the ACR’s RISE Registry. However, the views expressed represent those of the authors, not necessarily those of the ACR.

REFERENCE:

Disclosure of Interests: Zara Izadi Consultant for: I worked as a paid consultant for Celgene from 2014 to 2017., Milena Gianfrancesco: None declared, Michael Evans: None declared, Julia Kay: None declared, Laura Trupin: None declared, Gabriela Schmajuk Grant/research support from: Investigator initiated award from Pfizer from 2015-2018, unrelated to this work, Michelle A Petri Shareholder of: Pfizer, Merck, Grant/research support from: AstraZeneca, Exagen, Consultant for: Eli Lilly, GSK, Merck EMR Serono, Janssen, Amgen, Novartis, Quintiles, Exagen, Inova Diagnostics, AstraZeneca, Blackrock, Glenmark, UCBB, and the Annenberg Centre for Health Sciences, Jinios Yazdany Grant/research support from: Pfizer, Consultant for: AstraZeneca


OP0264 REFINING THE PRIMARY CARE CCP+ PATIENT PATHWAY
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Background: It is known that the presence of anti-CCP antibodies (CCP+) is associated with the development of rheumatoid arthritis (RA). Between 0-9% of the general population test positive [1], but only a small percentage of them will develop the disease. Previous work [2] showed that the selection of individuals with non-specific musculoskeletal symptoms, without clinical synovitis enriched the prevalence of anti-CCP positivity and also the likelihood of imminent progression to inflammatory arthritis.

Objectives: To assess for other factors which are associated with disease progression in patients testing CCP+ in order to optimise primary care referrals to Rheumatology.

Methods: A prospective observational study recruiting patients over 18 years old with a new musculoskeletal complaint and no clinical synovitis was conducted. Patients were recruited from primary care centres across the UK from July 2007 until February 2018. Those testing CCP+ in anti-CCP2 assay (immunocap method, Phadia assay) were invited to come to Leeds for assessment and follow-up including a baseline musculoskeletal ultrasound. Patients unable to attend were sent questionnaires 12 months later and were contacted in January 2019 to assess their status.

Results: 5702 eligible patients were recruited from primary care. 2.99% (171/5702) patients tested CCP+ and data from 150 patients was available for analysis: 5702) patients tested CCP+ and data from 150 patients was available for analysis: 148 (64) of 150 progressed to inflammatory arthritis (IA), predominantly RA. The mean time of progression was 242 days and 91% progressed in less than 12 months. The absence of pain in the hands or feet had a negative predictive value of 0.97) of patients with CCP+ high titre (p<0.001). All low titre progressors had pain in hands and feet and history of smoking exposure. 114 patients came to secondary care for assessment and a baseline musculoskeletal ultrasound scan was performed in 72 of them: the presence of PD in hands/feet was associated with progression to IA with a RR 2.4 (95%CI 1.27-4.58, p=0.01).

Conclusion: CCP+ patients without clinical synovitis who do not have pain in the hands or feet are unlikely to progress to IA especially if they have low titre antibodies. A high anti-CCP titre, new pain in hands/feet and PD in these joints are associated with rapid progression. These data may help optimise the primary care referrals to Rheumatology.

REFERENCES:

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OP0265 FRAILITY, DISABILITY, AND WORK DISABILITY IN PEOPLE WITH OSTEOARTHRITIS AND RHEUMATOID ARTHRITIS
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Background: Frailty is a clinical syndrome associated with adverse health outcomes. Frailty and disability can co-occur though are distinct entities. There are few prospective data looking at the occurrence and development of frailty, disability, and work disability in people with osteoarthritis (OA) and rheumatoid arthritis (RA).

Objectives: To determine the odds of prevalent and incident frailty, disability, and work disability in people with OA or RA, compared to people without these diseases.

Methods: Subjects aged 40-69 were recruited to the UK Biobank cohort. Data, including self-reported physician-diagnosed OA and RA, were collected at baseline (2007-10) and, in a subset, at follow up (2012-16). Frailty was measured using a modified Fried phenotype comprising five components: self-reported weight loss, exhaustion, low physical activity, slow usual walking pace, and low measured grip-strength (1). Participants were classified as robust if none of the components were present, pre-frail if 1-2 components were present and frail if ≥3 components were present. Participants were classified as having a disability if they indicated receiving a disability allowance/benefit. Participants indicating that they were unable to work due to disability or illness were classified as work disabled. Incident frailty was defined as frail at follow up and robust or pre-frail at baseline. Incident disability or work disability, respectively, was defined as receiving a disability benefit or indicating work disability at follow up but not at baseline.

Results: The mean (SD) age of the 465,379 participants at baseline was 56.5 (8.1) years and 54.3% were female. At baseline, 8.0% of the cohort reported that they had OA and 1.1% RA. At baseline, the prevalence of pre-frailty and frailty was 45.9% and 3.1%, respectively. 3.4% of the cohort indicated receiving a disability benefit, and 3.6% being work disabled. In a model adjusted for age, sex, smoking status and deprivation, compared to those without OA, those with OA were more likely to be pre-frail, odds ratio (OR) (95% CI), 1.8 (1.7,1.8), or frail, OR 4.5 (4.3,4.7), than robust. The adjusted OR (95% CI) for pre-frailty and frailty in those with RA (vs no RA) was 2.8 (2.6, 3.0) and 10.6 (9.7, 11.6), respectively. The adjusted OR (95% CI) for disability benefit was 3.9 (3.8, 4.1) in people with OA (vs no OA) and 7.7 (7.2, 8.2) in people with RA (vs no RA). The adjusted OR (95% CI) for work disability at baseline was 3.5 (3.3, 3.6) in people with OA and 4.8 (4.4, 5.2) in people with RA.

Data were available for 26,932 participants at follow up. The mean (SD) follow up time was 5.3 (1.5) years. Of those without frailty at baseline, 573 participants developed frailty during follow up. There were 292 incident cases of disability benefit and 137 incident cases of work disability. The adjusted OR (95% CI) for incident frailty in people with OA and RA at baseline was 2.3 (1.8, 2.9) and 3.3 (1.9, 5.7), respectively. The adjusted OR (95% CI) for incident disability benefit in people with OA and RA at baseline was 2.7 (2.0, 3.6) and 3.2 (1.7, 6.2), respectively. The adjusted OR (95% CI) for incident work disability in people with OA and RA at baseline was 2.3 (1.3, 3.9) and 3.7 (1.3, 10.1), respectively.

Conclusion: People with OA and RA have an increased risk of being, or becoming, frail, disabled, or work disabled. Further work is needed to determine effective

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strategies for preventing or delaying the occurrence of frailty, disability, and work disability in people with OA and RA.

REFERENCES:

Disclosure of Interests: None declared

OP266 RISK OF HOSPITALIZED INFECTION IN PATIENTS WITH CHRONIC INFLAMMATORY ARTHRITIS TREATED WITH BIOLOGICAL DRUGS – A MATCHED COHORT STUDY

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Background: Patients with rheumatoid arthritis (RA), axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA) treated with biological drugs (bDMARDs) have increased risk of hospitalized infection (i.e. infection causing admission to hospital) compared to the general population. Since patients with RA, axSpA and PsA have different age distributions, and age is an important predictor for infection, we found it of interest to quantify the excess burden of hospitalized infection in patients with inflammatory arthritis treated with bDMARDs compared to the general population and to investigate whether risk depended on age and diagnosis.

Objectives: To compare the risk of hospitalized infection in bio-naïve patients with inflammatory arthritis, who started treatment with a bDMARD with that of the general population, and to explore how this risk was influenced by age and diagnosis.

Methods: Matched cohort study based on data from The Danish Rheumatology Register (DANBIO) linked with The Danish National Patient Register and The Danish National Prescription Register. Patients with a diagnosis of RA, PsA or axSpA were matched with controls from the general population. For each patient, 10 controls from the general population, matched by age, sex, postal code and date were obtained. Infection risk in patients and matched controls were compared in analyses stratified by age and diagnosis, with Cox proportional hazards models accounting for matching. Follow-up time was 12 months irrespective of whether treatment was continued or changed during follow-up.

Results: In total, 11,372 patients and 113,715 controls were included. Overall, hospitalized infection was observed during follow-up in 4.6% of patients and 1.3% of controls; hazard ratio 3.7 (95% confidence interval (CI): 3.4-4.1).

The absolute risk was highest in RA patients, followed by PsA, axSpA and controls (unadjusted comparison). When stratified by age, the absolute risk increased with age, but was largely similar across diagnoses (Figure). In the stratum ≥60 years, RA patients appeared to have higher risk than axSpA patients, but the subgroup of axSpA patients ≥60 years was small.

Conclusion: The risk of hospitalized infection during 12 months of follow-up was approximately four times higher in bio-naïve patients with inflammatory arthritis who started treatment with a biological drug (bDMARD) compared to matched controls from the general population. When stratified by age, the absolute risk was largely similar across the diagnoses RA, axSpA and PsA. Thus, attention to preventive strategies such as vaccination seems prudent in these patients, especially those ≥60 years of age.

Disclosure of Interests: Simon Krabbe: None declared, Kathrine L. Gran: None declared, Bente Glintborg Grant/research support from: Biogen, Pfizer, AbbVie, Frank Mehner: None declared, Dorthe E. Jarbel: None declared, Mikkel Østergaard Grant/research support from: Abbvie, Celgene, Gentocor, Merck, Novartis, Consultant for: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, Speakers bureau: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, Merete L. Heitland Grant/research support from: BMS, MSD, AbbVie, Roche, Novartis, Biogen, Pfizer, Consultant for: Eli Lilly, Speakers bureau: Orion Pharma, Biogen, Pfizer, CellTrion, Merck, Samsung Bioepis

OP267 INACTIVATED INFLUENZA VACCINATION DOES NOT ASSOCIATE WITH DISEASE FLARES IN AUTOIMMUNE RHEUMATIC DISEASES: A SELF-CONTROLLED CASE SERIES STUDY USING DATA FROM THE CLINICAL PRACTICE RESEARCH DATALINK

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Background: Concerns about vaccination with the seasonal flu vaccine associating with increased risk of autoimmune rheumatic disease (AIRD) activity, and anecdotal reports of the seasonal flu vaccine triggering diseases such as vasculitis are barriers to flu vaccination in this population1. 2 This is despite reports of stable disease activity following flu vaccination provided disease modifying anti-rheumatic drug therapy is continued in the peri-vaccination period3. Previous studies generally include patients with stable disease activity, and as far as we are aware, a real world study evaluating the association between inactivated influenza vaccine (IIV) administration and AIRD activity has not been conducted.

Objectives: To examine the association between IIV administration and primary case control vaccination for joint pain, fatigue, rheumatoid arthritis (RA) flare, corticosteroid prescription, and incident vasculitis in people with AIRDs.

Δελτίο Ελέης
**Methods:** We undertook within-person comparisons using self-controlled case-series (SCCS), AIRD cases who received IV and had an outcome of interest in the same influenza cycle, between 1st September of one year and 31st August of the next year, between 2006 and 2016 were ascertained within the Clinical Practice Research Datalink. The influenza cycle (1st September of one year to 31st December of the next year) was partitioned into five exposure periods (1-15 days pre-vaccination, and 0-14, 15-30, 31-60, and 61-90 days post-vaccination), with the remaining time period classified as non-exposed. Incidence rate ratios (IRR) and 95% confidence intervals (CI) were calculated to compare the frequency of outcomes in different periods.

**Results:** Data for 14,928 AIRD cases (69% women, 80% with RA) were included. There was no association between IV administration and primary-care consultation for RA flare, corticosteroid prescription, and vasculitis (Table 1). Vaccination associated with reduced primary-care consultation for joint pain in the 90-day post-vaccination period (IRR (95%CI) 0.91(0.87-0.94)), and fatigue (IRR (95%CI) 0.90(0.87-0.94)) in the 61-90 days post vaccination Table (1).  

**Abstract Table 1** Association between IV and AIRD flare and vasculitis

<table>
<thead>
<tr>
<th>Risk period</th>
<th>Joint pain 1.00</th>
<th>Corticosteroid prescription* 1.00</th>
<th>Fatigue 1.00</th>
<th>RA flare 1.00</th>
<th>Vasculitis 1.00</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>1.00</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upto 15 days pre</td>
<td>1.29</td>
<td>(1.07-1.53)</td>
<td>0.95</td>
<td>0.95(0.38-1.06)</td>
<td></td>
</tr>
<tr>
<td>vaccination (1.20-1.39)</td>
<td>1.79</td>
<td>(1.64-2.33)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post-vaccination</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-14 days</td>
<td>0.84</td>
<td>(0.81-1.74)</td>
<td>0.62</td>
<td>0.97(0.41-1.0)</td>
<td></td>
</tr>
<tr>
<td>(0.77-1.07)</td>
<td>(0.62-1.75)</td>
<td>(1.05-3.21)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>15-30 days</td>
<td>0.94</td>
<td>(0.83-1.06)</td>
<td>0.90</td>
<td>0.95(0.38-1.06)</td>
<td></td>
</tr>
<tr>
<td>(0.86-1.02)</td>
<td>(0.82-1.08)</td>
<td>(1.02-1.82)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>31-60 days</td>
<td>0.93</td>
<td>(0.70-1.24)</td>
<td>0.87</td>
<td>0.76(0.37-1.7)</td>
<td></td>
</tr>
<tr>
<td>(0.88-1.02)</td>
<td>(0.80-1.64)</td>
<td>(1.59-2.94)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>61-90 days</td>
<td>0.90</td>
<td>(0.76-1.14)</td>
<td>0.40</td>
<td>0.59(0.39-1.48)</td>
<td></td>
</tr>
<tr>
<td>(0.84-1.06)</td>
<td>(0.27-1.10)</td>
<td>(2.33-5.85)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*New corticosteroid prescription on the same date as consultation for either RA flare, or joint pain, or fatigue.

**Conclusion:** The administration of IV was not associated with flare of the underlying AIRD and its association with reduced disease activity warrants further investigation. Nevertheless, these data add to the accumulating evidence to support seasonal influenza vaccination in people with AIRDs.

**Disclosure of Interests:** Georgina Nakafaro: None declared, Matthew Grainge: None declared, Puja Myles Grant/research support from: In my previous role I have worked on a project that was funded via an unrestricted educational grant from Roche. See details including contact: https://www.nottingham.ac.uk/research/groups/healthprotection/projects/pride.aspx. Christian Mallen: None declared, Weiya Zhang Consultant for: Grunenthal for advice on gout management. Speakers bureau: Bioberca as an invited speaker for EULAR 2016 satellite symposium, Michael Doherty Grant/research support from: AstraZeneca funded the Nottingham Sons of Gout study, Consultant for: Advisory boards on gout for Grunenthal and Mallinckrodt, Jonathan Nguyen-van-tam Grant/research support from: From F. Hoffmann-La Roche. See details: https://www.nottingham.ac.uk/research/groups/healthprotection/projects/pride.aspx. Consultant for: Ad hoc paid consultancy and lecturing for several influenza vaccine manufacturers (Sanofi-Pasteur MSD, Sanofi-Pasteur, GlaxoSmithKline plc (GSK), Baxter AG, Solvay, Novartis) and manufacturers of neuraminidase inhibitors (F. Hoffmann-La Roche: oseltamivir (Tamiflu®) and GSK: zanamivir (Relenza®)). Employee of: A former employee of both SmithKline Beecham plc (now part of GSK), Roche Products Ltd. (UK), and Sanofi-Pasteur MSD, all prior to 2005. Speakers bureau: Ad hoc paid consultancy and lecturing for several influenza vaccine manufacturers (Sanofi-Pasteur MSD, Sanofi-Pasteur, GlaxoSmithKline plc (GSK), Baxter AG, Solvay, Novartis) and manufacturers of neuraminidase inhibitors (F. Hoffmann-La Roche: oseltamivir (Tamiflu®) and GSK: zanamivir (Relenza®)). Abraham Abhishek Grant/research support from: AstraZeneca and Oxford Immunotech, Grant/research support from: AstraZeneca and Oxford Immunotech, Speakers bureau: Menarini pharmaceuticals, Speakers bureau: Menarini pharmaceuticals

**REFERENCE:**


**Disclosure of Interests:** None declared

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**HPR Abstract session II**

**OPO268-HPR** THE PREVALENCE AND IMPACT OF FATIGUE IN PEOPLE WITH PRIMARY ANTIPHOSPHOLIPID SYNDROME: A MIXED METHODS STUDY

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**Background:** Primary antiphospholipid syndrome (PAPS) is a prothrombotic disorder associated with increased mortality and morbidity. Symptoms include fatigue but the prevalence and impact of fatigue is unknown.

**Objectives:** To explore the prevalence, relationships and impact of fatigue in adults with PAPS.

**Methods:** This mixed methods study recruited participants from one public hospital, UK. Inclusion criteria comprised: adults with >6 month history of PAPS (Sydney classification criteria) and sufficient written and spoken English. Exclusion criteria included: other autoimmune rheumatic/inflammatory disorders; cancer; active chronic infections, positive Antinuclear antibody, pregnancy/breast-feeding, drugs/alcohol dependency and BMI>30.

Consenting participants completed seven questionnaires to record sociodemographic characteristics, fatigue (Fatigue Severity Scale (FSS), FACIT-Fatigue subscale, (FFS)), social support (Multi-Dimensional Perceived Social Support Scale (MDPSS), mood (Patient Health Questionnaire (PHQ-9), quality of life (EQ-5D-5L), sleep quality (Pittsburgh Sleep Quality Index (PSQI) and physical activity (International Physical Activity Questionnaire (IPAQMETs)). The relationship between (FSS) and predictor variables were explored using Spearman’s Rho correlation coefficients and backward stepwise regression analyses. Audio recorded, semi structured interviews were conducted with a subset of participants by two researchers with an agreed topic guide. Interviews were transcribed verbatim, anonymised, and analysed thematically with NVivo 10. The data was validated by a subsample of participants, cross-referencing the emergent codes and themes.

**Results:** 103 participants were recruited (87 complete datasets; mean (standard deviation) 50.3 (10.4) years, 8 men, 49 thrombotic APS). 69% of participants reported clinically relevant fatigue (FSS>3) and 62% of participants indicated severe fatigue (FSS>4). FSS was positively associated with PSQI (r (0.67-0.269 p=0.025), PHQ9 (r (0.83-0.620 p<0.001) and negatively associated with EQ-5D-5L (r (0.83)-0.055 p=0.001). F (r (0.82)-0.656 p=0.001) and IPAQMETs (r (0.80)-0.243 p=0.028) but not MDPSS. The best fit model explained 62% of the variance in FSS (adjusted R²=0.617, F (0.82)-22.63.p=0.001) and included FS, MDPSS, PHQ9, and IPAQMETs as significant predictors. For every 1 unit increase in FS, MDPSS, IPAQMETs and PHQ9, FSS decreased by -0.087 points, -0.084 points and -9.7*10^-3 MET minutes or increased by 0.090 points respectively.

Twenty participants (10 obstetric/10 thrombotic pAPS) completed interviews (duration 20-50 minutes). Participants with obstetric PAPS were younger. Five themes were identified across both subgroups: 1. Unpredictability of fatigue 2. Impact on daily life 3. Physical activity matters 4. Individual coping strategies 5. Acknowledgement and help with fatigue from clinicians.

**Conclusion:** Fatigue is a common, overwhelming, unpredictable symptom of PAPS which is a challenge to manage. Social support, mood and physical activity predicted fatigue severity. Interviewees tended not to discuss fatigue with clinicians due to lack of observed response or empathy. Participants perceived physical activity as important but difficult to complete regularly. Interventions to manage fatigue and support physical activity are needed for adults with PAPS.

**REFERENCE:**

Background: Fatigue is common in RA (ERA) and some patients experience improvement in fatigue when disease is well controlled, others experience persistent fatigue associated with work disability, poor QoL, and depression.

Objectives: To compare patterns and predictors of improved vs. persistent fatigue in the first year of ERA.

Methods: Data were from ERA patients (symptoms <1 year) enrolled in the Canadian Early Arthritis Cohort (CATCH) from 01/2007 to 03/2017. All met ACR1987 or 2010 ACR/EULAR criteria, had active disease, were on DMARDS, and complete fatigue (0-10) data over ≥12 months. Patients were classified at baseline with low (<4) or high (≥4) fatigue; high fatigue patients were categorized at 12-months as improved (1-2) or persistent (≤1). Multivariable logistic regression was used to identify predictors of improved vs. persistent fatigue at 12 months in those with high baseline fatigue.

Results: The 1002 pts were mostly white (81%), female (71%), with a mean (SD) symptom duration of 5.7 (2.9) months in those with high baseline fatigue. Among those with initial high fatigue, 30% had persistent fatigue at 12 months and was associated with obesity, comorbidities, higher disease activity (Table 1). Among those with initial high fatigue, 30% had persistent fatigue at 12 months and was associated with obesity, comorbidities, FM, longer symptom duration, and slightly lower baseline fatigue.

Table 1. Descriptive Statistics

Predictors of improved fatigue in multivariable models were BMI<30 (OR 0.6; 95% CI 0.3-0.9), MTX<20 mg (OR 1.7; 95% CI 1.0-2.7) and higher pain (OR 1.1; 95% CI 1.0, 1.2) after controlling for other variables.

Conclusion: Fatigue is common in ERA and associated with active disease, worse pain and disability, obesity, depression, major stressors, poor sleep and OA backpain. In high fatigue, those who are not obese, have higher pain, and take >20 mg MTX are more likely to improve over the first year. Optimizing weight, sleep, physical and emotional use and MTX use may improve persistent fatigue beyond control of RA inflammation.

Disclosure of Interests: Susan J. Bartlett Consultant for: Pfizer, UCB, Lilly, Novartis, Merck, Jansen, Abbvie, Orit Schieir: None declared, Marie-France Valois: None declared, Marie-France Valois: None declared, Marie-France Valois: None declared, Marie-France Valois: None declared, Marie-France Valois: None declared, Marie-France Valois: None declared, Marie-France Valois: None declared, Marie-France Valois: None declared, Marie-France Valois: None declared, Marie-France Valois: None declared, Marie-France Valois: None declared.
Conclusion: Child’s psychosocial adjustment is likely to be related with school attendance. When the attendance decreases, problems such as social functioning and isolation can occur. The fact that families and children agreed on the reasons about not to go to school but their functional and psychosocial status were good may have been due to different reasons. It was thought to normalize and encourage children to go to school. In addition, families should motivate their children with positive reinforcements.

REFERENCES:


ASSESSMENT OF MUSCLE MASS RELATIVE TO FAT MASS AND ITS ASSOCIATION WITH DISEASE ACTIVITY STATUS AND PHYSICAL FUNCTIONING IN RHEUMATOID ARTHRITIS

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1Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil; 2University of Pennsylvania, Philadelphia, United States of America; 3Universidade La Salle, Canoas, Brazil; 4Universidade do Vale do Rio dos Sinos, São Leopoldo, Brazil

Background: Rheumatoid arthritis (RA) is an autoimmune, chronic, progressive, inflammatory disease characterized by symmetrical, destructive polyarthritis and is accompanied by systemic manifestations. RA patients show low appendicular lean mass index (ALMI) and higher fat mass index. Impaired physical function is associated greater with fat mass and the adiposity is an important confounder that may mask true relationships between physical functioning and ALMI (1).

Objectives: To assess muscle mass relative to fat mass and verify associations this parameter with disease activity status, functional capacity and biologics treatments.

Methods: 115 RA patients, aged between 40 and 70 years, were recruited and followed for 12 months. Body composition was assessed by total body dual-energy x-ray absorptiometry for measurement of appendicular lean mass index (ALMI, kg/m2) and fat mass index (FMI, kg/m2). Age-, sex-, and race-specific Z-Scores and T-Scores were determined by comparison to published reference ranges. ALMI values were adjusted for FMI (ALMI/FMI) using a published method. Disease activity was assessed by Disease Activity Score-28 with erythrocyte sedimentation rate (DAS28). RA patients were divided in non-remission (DAS28≥2.6) and in remission (DAS28<2.6). Physical functioning was assessed by Health Assessment Questionnaire (HAQ).


Acknowledgement: We thank the Coordination for the Improvement of Higher Level Personnel (Coordenação de Aperfeiçoamento de Pessoal de Nível Superior—CAPES) institution, the Foundation for Research Support of the Rio Grande do Sul State (Fundaçao de Amparo à Pesquisa do Estado do Rio Grande do Sul—FAPERGS), the Research and Events Incentive Fund (Fundo de Incentivo à Pesquisa e Eventos—FPE) of HCPS and Technological Development (Conselho Nacional de Desenvolvimento Científico e Tecnológico—CNPq).

Disclosure of Interests: Rafaela Cavalheiro do Espírito Santo: None declared, Jordana Miranda de Souza Silva: None declared, Joshua Baker: None declared, Vanessa Haix: None declared, Clariton Brenol Shareholder of: Has participated in clinical and/or experimental studies related to this work and sponsored by AbbVie, BMS, Janssen, Pfizer and Roche; has received personal or institutional support from AbbVie, BMS, Janssen, Pfizer and Roche; has delivered speeches at events related to this work and sponsored by AbbVie, Janssen, Pfizer and Roche; Grant/ research support from: Has participated in clinical and/or experimental studies related to this work and sponsored by AbbVie, BMS, Janssen, Pfizer and Roche; has received personal or institutional support from AbbVie, BMS, Janssen, Pfizer and Roche; and has delivered speeches at events related to this work and sponsored by AbbVie, BMS, Janssen, Pfizer and Roche.

Disclosure of Interests: Karin Niedermann1, Anne-Kathrin Rausch1, André Meichtry1, Béatrice Walker2, René Bramer1, Adrian Ciurea2,3, Zurich University of Applied Sciences, School of Health Professions, Winterthur, Switzerland; 2Analyzing Spondylitis Association of Switzerland, Zurich, Switzerland; 3University Hospital, Rheumatology, Zurich, Switzerland

Background: Public health recommendations for physical activity (PA) advice that exercise programs include all four fitness dimensions, i.e. cardiorespiratory, muscle strength, flexibility and neuromotor exercise training at well-defined


Fitness Status of People with Axial Spondyloarthritis (ASxPA): First results after implementation of fitness assessments in ASxPA exercise groups

Karina Niedermann1, Anne-Kathrin Rausch1, André Meichtry1, Béatrice Walker2, René Bramer1, Adrian Ciurea2,3, Zurich University of Applied Sciences, School of Health Professions, Winterthur, Switzerland; 2Analyzing Spondylitis Association of Switzerland, Zurich, Switzerland; 3University Hospital, Rheumatology, Zurich, Switzerland

Background: Public health recommendations for physical activity (PA) advice that exercise programs include all four fitness dimensions, i.e. cardiorespiratory, muscle strength, flexibility and neuromotor exercise training at well-defined

frequency, intensity and duration/repetitions, and regular evaluations (1). The 2018 EULAR recommendations for PA (2) state that this is also effective, feasible and safe for people with rheumatic diseases. Therefore, the Ankylosing Spondylitis Association of Switzerland (SVMB) has started to implement assessments of all four fitness dimensions in their exercise groups (n=68). Criteria for selection of an assessment was its psychometric properties and feasibility for group setting, i.e. low costs and material requirements: Chester step test (CST) for cardiorespiratory fitness (3); adapted Core Strength Endurance test battery (CSE) for muscle strength (4); Bath AS Metrology Index (BASMI) for flexibility (5); Single-Leg Stance test (SLS) for balance (as proxy for neuromotor activities) (6). For all assessments, except CSE, norm values for healthy people are available.

Objectives: To assess the fitness status of people with axSpA across four volunteering pilot groups and evaluate if between-subject variables of interest are associated with fitness status.

Methods: Participants were assessed at baseline and after 6 months on all four fitness dimensions. For each dimension, a linear mixed model with random intercept was fitted to the data with the within-subject variables time and measurement condition and the between-subject variables age, disease duration, disease activity (Bath AS Disease Activity Index, BASDAI) and PA level (weekly Metabolic Equivalent of Task MET) as explanatory variables.

Results: Of 30 patients assessed, 10 (33%) were women, mean age was 58.5 (SD 7.68) years, mean disease duration was 32.6 (SD 9.68) years, mean disease activity was 3.1 (SD 2.36) and mean PA per week was 5013 (SD 3479.77) METs. Estimated VO2max for cardiorespiratory fitness was 35.2 (SD 6.59). Disease activity was negatively (slope=-1.49, p<0.01) and PA level positively (slope=3.28, p=0.01) associated with cardiorespiratory fitness. Mean core muscle strength endurance was 78.8 (SD 51.98) seconds. PA level was positively associated with core muscle strength (slope= 6.82, p=0.05). Mean flexibility score was 3.1 (SD 2.36), with age being positively associated with flexibility (slope=0.10, p=0.04). Mean balance was 43.1 (SD 21.09) and 7.7 (SD 5.84) seconds with open and closed eyes respectively. Age was negatively associated with balance (slope= -0.84 (p=0.00).

Conclusion: The SVMB has made an important step by implementing regular fitness evaluations in their axSpA exercise groups. The test scores of the assessed people with axSpA were lower than in healthy people but within the norms. PA level was positively associated with cardiorespiratory fitness and core muscle strength. Disease duration and disease activity were negatively associated with cardiorespiratory fitness only, but not with the other fitness dimensions, which may be different from what is usually assumed.

REFERENCES:

Disclosure of Interests: Karin Niedermann Speakers bureau: Novartis, André Meichtry: None declared, Béatrice Walker: None declared.

Data expressed as mean (standard deviation); GLM, Generalized Linear Models; Statistically significant p value (<0.05).


OP0273-HPR

FUNDAMENTAL EXERCISE FOR ADULTS WITH CHRONIC NON-SPECIFIC LOW BACK PAIN: A RANDOMIZED CONTROLLED TRIAL

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Jamil Natour. Universidade Federal de Sao Paulo, Rheumatology Division, Sao Paulo, Brazil

Background: Exercise therapy is part of the recommendation for the treatment of chronic non-specific low back pain (LBP). Functional exercise may be an alternative for the treatment, no studies assessing its effectiveness were found.

Objectives: To assess the effectiveness of the functional exercise program for pain, functional capacity, general health, kinesiophobia and perceived exertion in adults with chronic nonspecific LBP.

Methods: A randomized controlled clinical trial with intention-to-treat analysis and 24-week follow-up was performed. Eighty-four patients were randomly assigned to an experimental group (EG) or control group (CG). The EG participated in the functional exercises program performed twice a week for twelve weeks. The functional exercise program was composed by global exercises that worked the group of muscles of the trunk and lower and upper limbs with progression every 4 weeks. The two groups received an informative class on the disease and were advised to use analgesic if necessary. Primary outcome was LBP measured by numeric rating scale (NRS). Secondary outcomes included was functional capacity by Oswestry and Roland Morris questionnaires, 6-minute walk and TUG tests, kinesiophobia (FABQs), general health (SF-36), perceived exertion (BORG). Evaluations were performed at baseline, after 6, 12 (end of intervention) and 24 weeks by a blind evaluator.

Results: The groups were homogeneous for all parameters at baseline. Compared with the CG, the EG statistically improved pain, functional capacity, kinesiophobia, some domains of general health and perceived exertion - Table 1.

Conclusion: The functional exercise program was effective to improve pain, functional capacity, kinesiophobia, general health and perceived exertion in adults with chronic nonspecific LBP.

REFERENCES:

OP0274-HPR

DEVELOPMENT OF GENERIC CORE COMPETENCES OF HEALTH PROFESSIONALS IN RHEUMATOLOGY: A SYSTEMATIC LITERATURE REVIEW INFORMING THE 2018 EULAR RECOMMENDATIONS

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Background: Acquisition and maintenance of competences by Health Professionals in Rheumatology (HPRs) is important to ensure the best care for people with
rheumatic and musculoskeletal diseases (RMDs). HPRs’ competencies have never been systematically evaluated, nor international recommendations provided. A EULAR Task Force (TF) was formed for this purpose.

**Objectives:** To perform a systematic literature review (SLR) on the core competences of HPRs with a focus on nurses, physiotherapists (PT) and occupational therapists (OT) to inform the “EULAR recommendations for the generic core competences of Health Professionals in Rheumatology”

**Methods:** Thirteen main themes identified by the TF and translated into research questions, formed the basis of the SLR. Existing literature was systematically evaluated using the following databases (PubMed/Medline, Embase, Cochrane library, CENTRAL, Embcare, PsychINFO, Academic Search Premier, Web of Science, Google Scholar, ERIC and National Science Digital Library) from 1/1/1990 to 20/02/2018. Relevant search terms for competences, RMDs and HPRs were used. In addition, EULAR HPR national presidents were invited to share any documents describing HPRs’ competences. Inclusion criteria were: studies on competences or roles, knowledge, attitudes, skills or educational needs relevant for the management of people with RMDs, of HPRs in general or specifically of nurses, PTs or OTs, at post-graduate level. Exclusion criteria were: HPRs’ competences for children’s care or for concuring co-morbidities; extended roles of HPRs; a very specific clinical intervention or an intervention clearly attributable to only one profession or studies written in a language other than English or Dutch.

All abstracts were screened to identify eligible studies for full text inclusion. The methodological quality of the studies was scored using appropriate tools (Table).

**Results:** From 591 unique references reviewed, 79 studies were included. Twenty studies addressed competences of multiple HPRs. The methodological quality of most papers was high to medium (Table). The identified studies underpinned a range of HPRs’ competences, including: communication skills, promotion of physical activity, basic knowledge about RMDs and education of patients and other health providers. Competences more relevant to specific professions (e.g. musculoskeletal system examination skills for PTs and assessment of house and work environment for OTs) were also recorded. Heterogeneity in the HPR desired competences and practice across countries highlighted the need for further education of HPRs to acquire certain competences.

**Conclusion:** High-quality literature is available on the competences of HPRs for the management of people with RMDs. This literature supports the formulation of evidence-based recommendations for the core competences for HPRs by a EULAR Task Force.

**Disclosure of Interests:** None declared

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**Friday, 14 June 2019**

**SLE, Sjögren’s and APS – etiology, pathogenesis and animal models**

**COP275**

**THE PI3Kδ INHIBITOR INCBO50465 AMELIORATES SALIVARY GLAND PATHOLOGY AND REDUCES AUTOANTIBODY FORMATION IN A MURINE MODEL OF SJÖGREN’S SYNDROME**

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**Background:** Sjögren’s syndrome (SS) is a chronic autoimmune exocrinopathy affecting the glands that produce tears, saliva and vaginal and bronchial

**secrets. SS represents a complex interaction between the adaptive immune system and specific tissue regions of exocrine glands. Germinal ectopic lymphoid structures that are rich in autoimmune B-cells are thought to play an important role in local chronic B-cell activation and clonal expansion, autobody production, and Ig class switching in SS. Genetic deletion or pharmacological inhibition of PI3Kδ leads to defective B-cell activation, reduced proliferation and functional suppression. INCBO50465, an oral small molecule selective PI3Kδ inhibitor, is currently being evaluated in clinical trials for the treatment of B-cell driven autoimmune diseases: SS and autoimmune hemolytic anemia (NCT03627065 & NCT03538041).

**Objectives:** To evaluate INCBO50465 efficacy as a monotherapy in a spontaneous murine model of Sjögren’s syndrome.


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**DENDRITIC CELL-DERIVED IL-27 REGULATES THE MAGNITUDE OF INDUCIBLE ECTOPTIC GERMINAL CENTRES BUT FAILS TO DOWNMODULATE IL-17 PRODUCTION IN CD4 T CELLS FROM PATIENTS WITH SJÖGREN’S SYNDROME**

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**Background:** Approximately 30% of Sjögren’s Syndrome (SS) patients develop Ectopic Lymphoid Structures (ELS) in their salivary glands (SG). ELS play an active role in autoimmunity and contribute to the development of MALT lymphoma. Interleukin 27 (IL-27) exerts key immunomodulatory actions on CD4 T cells with both pro- and anti-inflammatory roles but its role in the formation and regulation of ELS in the salivary glands of SS is unknown.

**Objectives:** We first used a murine model of inducible SG ELS to elucidate the role of IL-27 and its interaction with IL-17 in the regulation of ELS formation and function. We then extended our observations on a cohort of SS patients to identify IL-27 cellular source, target cells and functional properties in modulating peripheral and lesional CD4 T cells function.

**Methods:** To trigger ELS formation a single dose of reporter-encoding adenovirus was delivered directly to the SG of wild-type (WT) and IL-27-deficient (KO) mice. For IL-17 blockade anti-mouse IL-17A antibody was administered systemically. ELS development and peripheral immune responses were tracked by immune-blot histopathology, FACS, and qPCR. Minor SG biopsies were collected from SS and non-specific sialadenitis (sicca) patients. Peripheral blood mononuclear cells (PBMC) isolated from patients and age-sex matched healthy donors (HD). For in vitro experiments PBMCs, isolated CD4 T cells and parotid gland MCs were incubated with IL-27 and analysed by FACS for CD4 T cell subsets while cytokines levels were measured intracellularly by FACS and in tissue supernatants. Tissue IL-27 was assessed in SS SG sections by multicolour immunofluorescence to identify IL-27 producing cells.

**Results:** In WT mice, SG ELS formation was preceded by an upregulation of IL-27 and infiltration of IL-27 producing cells (CD4+IL-27(IFN-γ)). In KO mice, IL-27 was increased in the ELS+ subset of SS, it consistently failed to downregulate Th17 response in the SG by restricting Th17 expansion. Both in murine inducible ELS and in patients with SS, higher expression levels of IL-27 transcripts and protein, respectively, compared to sicca, while IL-27 was selectively increased in the ELS+ subset of SS. Immunofluorescence staining for IL-27 revealed its presence primarily in the T cell rich areas of SS ELS with frequent co-localization with DC-LAMP+ dendritic cells. Finally, while IL-27 was able to significantly downregulate IL-17 production in HD, CD4 T cells from patients with SS failed to downregulate IL-17 but showed an aberrant IFNγ release upon IL-27 incubation. We did not observe any difference in IL-27R expression or downstream STAT1/3 phosphorylation between SS and HD.

**Conclusion:** The role of IL-27 in the development of the IL-27/IL-17 axis play an important role in ELS formation in this condition. SG IL-27 was increased in the ELS+ subset of SS, it consistently failed to downregulate Th17 response in the SG by restricting Th17 expansion. Both in murine inducible ELS and in patients with SS, higher expression levels of IL-27 transcripts and protein, respectively, compared to sicca, while IL-27 was selectively increased in the ELS+ subset of SS. Immunofluorescence staining for IL-27 revealed its presence primarily in the T cell rich areas of SS ELS with frequent co-localization with DC-LAMP+ dendritic cells. Finally, while IL-27 was able to significantly downregulate IL-17 production in HD, CD4 T cells from patients with SS failed to downregulate IL-17 but showed an aberrant IFNγ release upon IL-27 incubation. We did not observe any difference in IL-27R expression or downstream STAT1/3 phosphorylation between SS and HD.

**Disclosure of Interests:** None declared.

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in UST-NR or PBO patients. IGS levels were elevated in 67% of patients at baseline versus healthy controls. Serum IFN-γ levels and IGS levels in blood were not modulated by UST treatment through week 24. Baseline IFN-I signature status did not associate with response to UST, as the treatment effect size (UST vs PBO) was similar in IFN-I (n=27%) and high (n=28%) patients.

Conclusion: Response to UST was associated with reductions in IFN-γ levels, whereas IL-17A, IL-17F, IL-22 and IFN-I remained largely unchanged. While these findings require confirmation in an ongoing Phase 3 study, these data imply the involvement of the IL-12 pathway and suggest a novel mechanism of action for UST-R in SLE.

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A UNIQUE IL-21 SIGNATURE CHARACTERIZES LESIONAL AND CIRCULATING T-FOLLICULAR HELPER CELLS IN SJÖGREN’S SYNDROME PATIENTS WITH ECTOPIC GERMINAL CENTRES AND MALT LYMPHOMA

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease that can affect multiple organs, including the skin, joints and kidneys. The disease is characterized by the development of skin lesions, autoantibody production and inflammation-induced glomerulonephritis. The skin is involved in SLE cases1. In the MRL/lpr spontaneous mouse model of SLE, disease symptoms also include lymphocyte hyper-proliferation, resulting in lymphadenopathy and splenomegaly. The evolutionary conserved Janus kinase-signaling transducer of activators of transcription (JAK-STAT) pathway constitutes a rapid mechanism to nuclear signaling modality that affects key biological aspects of the mammalian immune system2. Janus kinase 1 (JAK1) is involved in the downstream signaling pathway of type I interferons (IFNs), and high levels of type I IFNs are associated with SLE3. INCB054707 is an oral small molecule JAK1 selective inhibitor currently being evaluated in clinical trials for the dermatological disease hidradenitis suppurativa (NCT03569371 & NCT03607487). We hypothesized that INCB054707 should reduce IFN signaling and ameliorate cutaneous lesions in SLE.

Objective: To determine the effectiveness of INCB054707, a selective JAK1 inhibitor, in a preclinical model of cutaneous lupus erythematosus.

Methods: Female MRL/lpr mice were randomized to treatment groups at 11 weeks old to receive twice daily oral doses of vehicle (0.5% methyl cellulose) or INCB054707 at 10, 30, or 90 mg/kg for 10 weeks. Efficacy was determined by weekly scoring of the changes in skin, lymph node size, and proteinuria. At study termination (week 21), inguinal lymph nodes and spleens were excised and weighed, skin lesions and kidneys were excised and fixed for histopathologic analysis, and serum was collected for pharmacokinetic analysis and ELISA. Autoantibody presence in the serum was detected using a commercial anti-dsDNA ELISA kit.

Results: IL21 and IL21R expression, together with CD4+CD45RO+PD1+ICOS+ Tfh cells were strongly enriched in ELS- vs ELS- SS Gs. Tfh cells densely infiltrated B cell rich areas and, within ectopic GC, acquired BCL6 expression, both in ELS+ and MALT-L. Tfh infiltration significantly correlated with SG IL21 mRNA level, which in turn was associated with high T (CD4+) and plasma cells (CD138+) IHC scores and significantly correlated with CXC13L1, LTj, BAFF, AID and Pax5 gene expression. MALT-L samples displayed 10-fold higher IL21 mRNA and twice as much PD1+ICOS+BCL6+ Tfh-cells/field in comparison to ELS+ SS samples. Within the SGs, IL21 and IFNγ production by Tfh in the peripheral compartment showed a positive correlation with IgG serum levels.

Conclusion: Within the SG of SS patients Tfh cells closely segregated with lesional IL21 expression, localize within ELS and are strongly enriched during MALT-L development, which is supporting their role in sustaining B cell activation and malignant transformation. High production of IL21 by Tfh in peripheral blood selectively identifies SS patient with ectopic GC in the SG, suggesting a role for IL21+ Tfh cells as surrogate markers of SG histopathology in SS.

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ELEVATED EXPRESSION OF BAFF-RECEPTOR IN PERIPHERAL MONOCYTES PROMOTES B CELL ACTIVATION AND CORRELATES WITH CLINICAL MANIFESTATIONS OF PRIMARY SJÖGREN’S SYNDROME

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Background: Primary Sjögren’s syndrome (pSS) is an idiopathic autoimmune disease whose major clinical manifestations are xerostomia and keratoconjunctivitis sicca, and is often accompanied with hypergammaglobulinemia. Several lines of evidence suggest that a focal lymphocytic infiltrate of the exocrine glands is responsible for lesion formation, IgG production and subsequent dysfunction of the glands. It is well known that B cell activating factor (BAFF) and its receptor, BR3, are deeply involved in the pathogenesis of pSS, and hence BAFF and BR3 are promising targets to treat the disease. We have reported that the abnormally elevated expression of BR3 in monocytes is associated with overproduction of inflammatory cytokines, such as IL-6, by monocytes of pSS patients. Our in vitro experiments suggest that BAFF-stimulated monocytes contribute to IgG overproduction by pSS B cells. We also found that the population of a specific subset of B cells overexpressing BR3 was abnormally increased in pSS patients and that the proportion of the subset was positively and significantly correlated with serum levels of autoantibodies and total IgG as well as ESSDAI, one of the indicators of disease activity of pSS. Our results collectively suggest that the elevated expression of BR3 in pSS monocytes results in B cell activation and subsequent overproduction of IgG. However, the relationship between the abnormalities of peripheral cells and clinical manifestations of pSS has not been fully understood.

Objective: To elucidate possible roles of abnormal monocytes in the development of clinical manifestations of pSS.

Methods: The expression level of BR3 in peripheral monocytes of patients with pSS (n = 65) and healthy controls (HC: n = 38) was analyzed by FACS. Peripheral B cells were cultured with BAFF-stimulated monocytes in the presence or absence of an anti-IL-6 receptor antibody, and the proportion of CD38hiIgD- cells among CD19+ cells, and IgG production were analyzed by FACS and ELISA, respectively. The serological data and focus scores by lip biopsy of the patients were collected by clinical records.

Results: FACS analysis revealed that the expression level of BR3 in pSS monocytes was significantly higher than that of HC (p < 0.001). Moreover, the expression level of BR3 in peripheral monocytes was positively and significantly correlated with serum levels of IgG (p = 0.01) and IgM (p = 0.02) of the patients. Notably, BR3 expression in monocytes from focus score-positive pSS patients was significantly higher than that from negative patients (p = 0.006). In addition, BR3 expression in pSS monocytes was elevated in anti-SS-A and/or anti-SS-B positive patients as compared to negative patients. When B cells prepared from pSS patients were mixed with autologous monocytes and co-cultured in vitro in the presence of BAFF, the proportion of CD38hiIgD- cells, which are plasmablasts and/or plasma cells, among CD19+ positive cells and IgG produced by the cells were drastically enhanced by BAFF-stimulation, whereas the stimulation showed only marginal effects when B cells were solely cultured in vitro. In addition, an anti-human IL-6R antibody significantly inhibited the proportion of CD38hiIgD- cells and IgG production. These data strongly suggest that IL-6 produced by BAFF-stimulated monocyte plays a pivotal role in B cell differentiation and the IgG overproduction in pSS patients.

Conclusion: Our data strongly suggest that accelerated signal transduction through a BAFF-BAF3 axis in monocytes is involved in the pathogenesis of pSS and associates with clinical manifestations of the disease. These results also suggest that BAFF and the BAFF signaling pathways through BR3 are the possible therapeutic targets for pSS.
OBSTETRIC ANTIPHOSPHOLIPID SYNDROME (OAPS) VS. WITH OBSTETRIC MORBIDITY RELATED WITH ANTIPHOSPHOLIPID ANTIBODIES (OMAPS): A SURVEY OF 1650 CASES FROM EUROAPS REGISTRY

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Background: The obstetric antiphospholipid syndrome is an autoimmune systemic disorder related to antiphospholipid antibodies and pregnancy morbidity. There exist many patients that do not fulfil the Sydney classification criteria. Those cases may be defined as Obstetric Morbidity related with antiphospholipid antibodies (OMAPS). Objectives: To compare clinical features, laboratory data and foetal-maternal outcomes, between 1000 women with obstetric antiphospholipid syndrome and 640 women with aPL-related obstetric complications not fulfilling Sydney criteria. Methods: Retrospective and prospective multicenter study from the European Registry on Obstetric Antiphospholipid Syndrome. Results: 1650 women with 5251 episodes were included of which 3601 were historical and 1650 were latest episodes. 1000 cases (OAPS group) fulfilled the classification criteria and 650 (OMAPS group) did not. Ten OMAPS cases were excluded because they presented a thrombosis during follow-up. In the OMAPS group, 172/640 (26.67%) did not fulfill Sydney clinical criteria (subgroup A), 179/ 640 (27.96%) had a low titer and/or non-persistent aPL positivity but fulfilled clinical criteria (subgroup B), and 289/640 (45.15%) had a medium or high aPL titer but did not fulfill Sydney clinical criteria (subgroup C).

Conclusion: Significant clinical and laboratory differences were found between groups. Foetal-maternal outcomes were similar in both groups when they were treated. The results suggest that we could improve our clinical practice with closed defining and monitoring OMAPS patients.

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Disclosure of Interests: None declared


FRIDAY, 14 JUNE 2019

A DUTCH RESEARCH AGENDA DEVELOPED BY PEOPLE WITH RMDs: WHAT ARE THE MAIN PROBLEMS PEOPLE WITH RMDs FACE AND WHAT ARE THEIR MAIN WISHES FOR RESEARCH AND DEVELOPMENT?

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Background: In the Netherlands much progress has been made with regard to patient participation in research. More and more researchers are finding their way to patient organizations for collaboration. This is also the case for the National Association ReumaZorg Nederland where more and more researchers are asking for the opinion of our patient-experts on their written research proposals. However, this happens mostly because ‘asking for the patient’s view’ is an obligatory (last) part of the submission process of their proposal. ReumaZorg Nederland wants to take patient participation in research to the next level. A level where ‘what matters most to patients’ is taken into account before a proposal is written. Only then will the patient’s voice really be heard in the very heart of a research project.

Objectives: To identify the main problems people with RMDs face in their daily lives and to prioritize their wishes for future research and development. To investi-gate whether these problems and wishes vary between patients with different types of RMDs. To encourage researchers and product-developers to take these wishes into account at the very start of their research proposal or product-plan.

Methods: Independent and professional research was needed to develop this research agenda. NIVEL, the Dutch Institute for Health Services Research, performed a 7 month research project which consisted of several steps. First, a literature search was performed on scientific publications in PubMed, Embase and Psycinfo on search strings focusing on living with RMDs, problems and wishes of people with RMDs and other known research agenda’s for people with RMDs. The second step consisted of 3 focus group sessions: inflammatory RMDs (group 1), osteoarthritis & fibromyalgia (group 2) and soft tissue- & systemic RMDs (group 3). In addition, a combined session of representatives of each focus group (12 participants) was organized to compare and complement the results of the 3 focus groups. In the third step, an online survey (277 respondents) was held to explore how these problems and research wishes were recognized and prioritized within the Dutch community of people with RMDs. After data-analysis in step 4, a stakeholders session was held in step 5 to discuss results amongst patients, researchers, rheumatologists and project-developers.

Results: Among the 89 problems that were recognized, the main problems people with RMDs face are:

1. Uncertainty about their future.
2. Having to cope with fatigue.
3. Having to cope with the unpredictability of RMDs.
4. Preserving boundaries/staying balanced.
5. Having to cope with the impact of RMDs on social life with family and friends.

Among the 85 wishes for research and development, the main wishes of people with RMDs are:

1. To develop treatments of RMDs other than surgery.
2. To develop an accessible and affordable network of physical exercise activities under professional supervision.
3. To investigate the cause of inflammatory RMDs.
4. To investigate the cause of fatigue with RMDs and how to cope.
5. To investigate alternative forms of therapy and their effect on specific types of RMDs.

All results were described in the first Dutch research agenda made by people with RMDs. 1

Conclusion: Remarkably, the main problems people face with RMDs are not necessarily the same as the wishes they have for further research or development. The problems people face have to do with issues regarding living and cop-ing with RMDs in everyday life, whereas their research-wishes are more medical. Fatigue is, however, an issue that is highly prioritized as a problem as well as a subject for further research. This goes for people with all types of RMDs.

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Disclosure of Interests: None declared

THE INFLUENCE OF FUNCTIONAL TRAINING AND PSYCHO-SOCIAL SUPPORT

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Background: Treatment of chronic noncontagious diseases in which we include RMD implies usage of medicines and non medicine (changing bad lifestyle habits like losing nutrition, physical activity, smoking…). Unwanted cardiovascular and cerebrovascular states are the most common cause of shortening of life of people with RMD. None of the chemical drugs can replace physical activity. Physical activity dosage is individual, and depends on aerobic capability and heart rate increase, taking in account age, type of noncontagious diseases, level of tissue and organs damage as well as the type of work the person is engaged in.

Patients with RMD have common symptoms, such as stiffness, fatigue, poor mobility, joint pain and muscle pain, anxiety and depression, and lack of fitness. In addition to physical medicine and rehabilitation and balneoklimatology, various forms of physical activity are recommended, such as walking, swimming, functional training. Today, moderate physical activity is known to help reduce fatigue, strengthen muscles and bones, improve flexibility and endurance of the joints, and improve general health. It is necessary to find the best combination of rest, activities and exercise programs to prevent deformities of the joints, the development of disability, improve the quality of life, and the mental health of patients with RMD.

Objectives: 1. By practicing Cigong, an increase in the volume of movement in the joint, the strengthening of joint muscles and the improvement of general condition, pain relief, fatigue reduction is achieved and also, it helps patients look and feel better.
2. The goal of Yoga is to neutralize and remove all obstacles that stand in the way and disturb the function of the body and the mind and achieves inner peace.
3. Changing the psychological state during exercise also led to a positive way of thinking.
4. Psycho-physical support for the people with RMD.

Methods: From 2011, we organize twice a week functional training of Cigong. Since January 2016, twice a week persons with RMD have been practicing Yoga.

From 2015, one per week four psychologists volunteer hold workshops for psycho-social support for persons with RMD.

Participants of the training and psycho-social sessions took a survey.

Results: 1. Joint pain reduction ~ 50% of total number of participants
2. Joint mobility increase ~ 95% of total number of participants
3. General fitness improvement ~ 73% of total number of participants
4. Less pronounced negative emotions ~ 59% of total number of participants

Conclusion: Practicing cigong, yoga and psycho-social support workshops help patients look better and feel better. Changing the psychological state during exercise also led to a positive way of thinking. All of this increased the effectiveness of drug treatment and improved the quality of life of patients with RMD.

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the management of chronic illnesses, such as diabetes treatment, including good users’ acceptance and an increase in their knowledge. Knowledge acquisition is generally seen as a necessary condition for behavioral change. Applications with virtual humans offer a dynamic, interactive and easily accessible approach to enhance users’ knowledge. We did not find published literature on the use of virtual humans to educate people with OA.

Objectives: To develop a web application to support education of caregivers and people with OA.

Methods: This is a proof of concept study, which builds on our previous experience with virtual assistant applications. For example, “Virtual Pharmacy” is intended to improve self-medication consultation skills between students/pharmacy professionals and community pharmacy clients, whilst “VASelfCare” aims to facilitate self-care of older people with type 2 diabetes (REF?). The main principle underpinning the development of our application is the use of gamification embedded in a narrative with a double purpose of maintaining user engagement and enhancing the play experience. This option has in consideration that OA is more prevalent among the seniors and is supported by a study showing that embedding narratives in mobile games enhances the play experience of this age group.

In our approach, the narrative comprises dialogues aiming to ease and stimulate the search for new knowledge, and to educate for disease management and health promotion.

Results: So far, we have developed NOA, a virtual assistant that interacts with users through speech (voice and subtitles) plus facial and body animations. NOA is a 2D cartoon female model that plays the role of a character who suffers from OA and provides information about her own experiences with the disease. At the end of each dialogue, a quiz tests users’ knowledge. Awarding points and digital badges for correct answers, or showing the right answers when the user fails, are expected to motivate users to play and learn more. This application will be placed in the “Portuguese League Against Rheumatic Diseases” website to convey easy access.

Conclusion: Development of a virtual assistant web application to promote education on OA, resorting to a narrative approach and gamification principles, is ongoing. Future work includes testing the application with experts and patients.

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WHAT DO YOUNG PEOPLE THINK ABOUT CONTINUOUS DATA COLLECTION IN CLINICAL RESEARCH AND THE TYPES OF ELECTRONIC DEVICES?

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Background: The use of wearable devices are of increasing interest to enable continuous data collection during drug trials. This is particularly pertinent when involving young people who are “digital natives” and have grown up with such technologies.

Objectives: To ascertain opinions from young people regarding the design of wearable devices and the use of continuous data collection for a future clinical drug trial for juvenile idiopathic arthritis (JIA).

Methods: A three hour face-to-face patient involvement session was held in a young person friendly venue in central Manchester on the 8th December 2018. Young people with a rheumatic disease were invited to participate using event flyers provided in local rheumatology clinics. Members of a national youth advisory panel, Your Rheum, were also invited to attend. Data was collected in both large and small group discussions and included a ranking exercise involving the use of voting cards, emojis and pictures of electronic devices to aid conversations. In addition, an online survey was also developed and uploaded to http://yourheim.org for young people to complete if they could not attend the event in person. Open questions (requesting free text answers) ranged from general thoughts and concerns about continuous data collection, device preferences and features, to examples of unattractive devices.

Results: Eight young people attended the event (M=5, F=3, 11-19 age range). All males were under 14 years of age. One young person completed the online survey (F=1). All participants regularly used some form of an electronic device and were generally willing to use a wearable device for continuous data collection, although consideration of school regulations (e.g. uniform policies) and potential bullying was necessary. Participants reported that they would choose a device based on its viability, look, comfort and functionality. For instance, the device would need to be discrete in terms of size, muted (no sounds or vibrations) and removable. The preference of device type differed by gender though a watch and patch were in the top three favourite devices for all. Key features included the

 Disclosure of Interests: None declared

OP0287-PARE

SETTING UP A EUROPEAN FEDERATION OF SJÖGREN’S SYNDROME PATIENT ASSOCIATIONS: HOW WE BUILT UP SJÖGREN EUROPE IN LESS THAN ONE YEAR

Alice Grosjean1, Ana Vieira2, Coraile Bouillot3, Jenny Inga Diaz4, Mascha Oosterbaan5, Joyce Koelewijn-Tukker5, Isabelle Lesuisse6.

Mascha Oosterbaan5, Joyce Koelewijn-Tukker5, Isabelle Lesuisse6.

Methods: Sjögren Europe was conceived during the 2018 ISSS and the decision to address the lack of visibility and the unmet needs, foster patient training and involvement in research and articulate patient voices throughout Europe. To set up a perennial European Federation of SS patient associations, a task force was set to set a mindset and to communicate on a regular basis to ensure a common spirit. We set priorities and down-to-earth objectives and focus on them. Although there is a leader for supervision and to take final decisions, the governance is mainly based on shared leadership sustained by trusted connections. Personal initiatives are encouraged, and failure is considered as a learning experience. We build a culture of compromise. As members experience debilitating fatigue, they achieve the tasks they can, whenever they have time and energy, and report them to the others: Sjögren Europe adapts to its members. We also welcome anyone sharing our mission principles and wanting to be involved in the project.

Results: On the 23rd of February 2019, Sjögren Europe was officially set up with more than 8 countries as founders. Being flexible not only allows patients with debilitating fatigue to work for the federation but also leads to lean and efficient procedures and tasks. An enthusiastic and supportive environment makes the commitment sustainable and meaningful. Face to face meetings, a good network and collaboration are imperative. The way we respond to mistakes is also crucial for motivation.

Conclusion: This project empowers the SS patient community, brings hope, injects a new energy in patient advocacy and breathes motivation for collaboration to researchers, scientists and clinicians. This presentation aims to share our story and the key learning points about the way we work and to spread the positive atmosphere.

REFERENCE:

Acknowledgement: EURORDIS Council of Federations & toolkit, HarmonicSS project, ERN RECONNECT, ISN (International Sjögren’s Network), Lupus Europe, SSF (Sjögren’s Syndrome Foundation)

Disclosure of Interests: None declared
ability to switch devices on and off, send reminders, chat to other young people and to track their own data. As well as personal preferences, age specific considerations were highlighted by the young people. It is therefore imperative not only to involve young people as research participants but also to involve them at early stages of research including trialing design to ensure acceptability of data collection methods including the design of any devices proposed.

Acknowledgement: Your Rheum is the national youth advisory panel of the Barbara Ansell National Network for Adolescent Rheumatology BANNAR. We would like to thank all of the young people who took part and other individuals who facilitated their involvement including BANNAR members and Versus Arthritis Young People Coordinators.

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Background: Despite the availability of several treatment options, some Rheumatoid Arthritis (RA) patients do not reach low disease activity. There thus remains a need for differentiated new therapies. Prior studies identified a series of biphenylsulphonamides with bone protecting and anti-inflammatory activity which might meet this need.

Objectives: To evaluate the selectivity of a novel small molecule, MBS2320, in myeloid and lymphoid cells, characterise its selectivity for osteoclasts versus osteoblasts and characterise its effects on synovitis and osteoprotection compared to an anti-TNFα agent in a therapeutically administered collagen-induced arthritis (CIA) mouse model.

Methods: Viability, proliferation or cytokine production were assessed in human primary monocytes, lymphocytes or a Mixed Lymphocytes Reaction (MLR). Human primary osteoclasts (OCs) were differentiated from CD14+ monocytes with M-CSF and RANKL. Mature OCs were stained with tartrate-resistant acid phosphatase (TRAP) and quantified by light microscopy. Osteolytic activity was assessed on mineral-coated surfaces. Osteoblasts were derived from mesenchymal stem cells by differentiation in the presence of RANKL and BMSCs were differentiated from CD14+ monocytes assessed by Alizarin Red S staining. CIA was induced in DBA/1J mice by collagen immunisation. MBS2320 and etanercept were dosed once daily after onset of disease. Arthritis Index (AI) was scored throughout the dosing period after which serial paw sections were assessed for inflammation, synovitis, stromal cavity osteolysis, pannus hyperplasia, osteoid layering and bone resorption foci.

Results: MBS2320 reduced the production of cytokine from monocytes and inhibited T-cell proliferation, and cytokine production in a MLR. MBS2320 also reduced primary OC differentiation and function in vitro to a greater degree than alendronate but showed no effect on the differentiation of primary osteoblasts. MBS2320 (0.3 mg/kg) and etanercept (10 mg/kg) inhibited the onset and severity of CIA arthropathy, synovitis, pannus infiltration and osteolysis, with equivalent efficacy. In addition MBS2320 showed anatomically appropriate osteoid layering with conservation of the tide mark, and the bone marrow showed no cell atypia, with all progenitor classes present although reduced in number and distribution. In contrast, osteoid formation in the etanercept group was multi-focal with atypia, with all progenitor classes present although reduced in number and distribution.

Conclusion: MBS2320 selectively inhibits myeloid and lymphoid activity/differentiation, whilst sparing mesenchymal cells, in vitro. In murine CIA, MBS2320 treatment led to the formation of anatomically appropriate osteoid layering indicating an anti-osteolytic effect of osteoclasts conditioned by biomechanics. By contrast, osteoid formation due to etanercept was more ‘reactive’ and secondary to suppression of inflammation. The data suggest that MBS2320 offers equivalent anti-inflammatory activity, but a broader spectrum of osteoprotective efficacy in CIA compared to TNFα inhibition and may offer an alternative therapeutic approach to improving bone quality in RA.

REFERENCES:

COMPARISON OF TRANSCRIPTOMIC PROFILES BETWEEN PAIRED JOINT BIOPSY SPECIMENS FROM RHEUMATOID ARTHRITIS PATIENTS

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OP297
ABERRANT ADENOSINE TO INOSINE RNA EDITING IN ACTIVE RHEUMATOID ARTHRITIS

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Background: Adenosine to inosine (A-to-I) RNA editing is a widespread post-transcriptional RNA modification mainly located in repetitive Alu elements and mediated by the enzyme adenosine deaminase acting on RNA-1 (ADAR1). A-to-I RNA editing controls various aspects of RNA metabolism, which may affect tissue-specific gene expression. Although deregulation of RNA editing has been previously reported in various human diseases including cardiovascular disease and cancer (Stellos et al., 2017; Liu et al., Nat Med 2019 and Ishizuka et al., Nature, 2019), its role in autoimmune diseases and especially in rheumatoid arthritis (RA) remains unknown.

Objectives: To study whether A-to-I RNA editing is involved in the pathogenesis or to determine the impact of anti-rheumatic treatment on RNA editing.

Methods: We first analysed the expression of ADAR1 in 185 RA synovial tissues versus 76 healthy/osteoarthritic synovia derived from 4 independent RNA-sequencing and microarray datasets. We validated the findings in peripheral blood mono-nuclear cells (PBMCs) derived from 19 patients with active RA vs 14 controls and performed an additional ADAR1-isofrom analysis (ADAR1p110/ADAR1p150) by RT-qPCR. Further, we studied in single nucleotide level the A-to-I RNA editing levels of the pro-inflammatory gene cathepsin S (CTSS) 3’-translated region (3’UTR), a matrix degradation enzyme which is a well-established target of ADAR1, by AU Sanger sequencing and RNA editing analysis. Last, we examined the effect of anti-rheumatic treatment on RNA editing.

Results: Expression of the RNA editor ADAR1 was significantly increased in RA synovium compared to healthy or osteoarthritic synovium. Similarly, a significant increase of ADAR1, mainly due to an increase of the interferon-inducible ADAR1p150 isoform, was observed in PBMCs from active RA. Next, we studied the RNA editing levels in PBMCs from active RA patients before and after 12-week treatment versus controls. RNA editing of CTSS 3’UTR AluSx+ was increased in active RA (6.47% increase in editing rate of 8 individual adenines, P<0.05). Increased CTSS mRNA expression in RA PBMCs was associated with both ADAR1p150 expression (r=0.623, P=0.004) and RNA editing rate of 12 individual adenines (r=0.45-0.72, P<0.05 for all) located within the CTSS 3’-UTR AluSx+. The correlation between CTSS and ADAR1 was also observed in synovial tissue. Notably, ADAR1p150 expression and RNA editing rate reached control levels after 12-week treatment with methotrexate and/or biologics in patients with good clinical response (EULAR responders) but remained unchanged in the EULAR moderate/non-responders.

Quantification of histological markers did not show differences in population of macrophages, plasmocytes, T and B Cells, across pairs of joints. After correction for multiple comparisons, no transcripts were differentially expressed between large and small joints. Similarly, we did not find any significant differences in the expression of transcripts involved in pathogenesis and cell division specifically overexpressed in RA compared to OA synovial tissue.

In order to increase our ability to observe pair-wise differences in gene expression patterns we studied transcripts significant in expression in RA compared to OA joints with a fold change ≥ 2 (n = 581) and clinical or biological markers of disease activity (DAS28, CRP, CRP, Physician Global Assessment of disease activity). Similar patterns of correlations indicated that disease activity was not driven by different pathways in small versus large joints.

Conclusion: This study is an important methodological milestone in the field of synovial biopsies, as it indicates that cellular and molecular alterations occurring in RA synovials are similar across small and large joints from the same patient. Hence, biopsy of a single joint is representative and can be used to explore pathogenic processes or potential biomarkers in RA.

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90% of ACPA-IgGs harbour N-linked glycans in the antibody variable (V) domain. The corresponding N-glycosylation sites in the amino acid backbone of ACPA V-regions result from somatic hypermutation, a T cell-dependent process. Notably, both genetic evidence and data obtained from the analysis of serum ACPA indicate that T-cells drive the maturation of the ACPA-response prior to the onset of arthritis.

Objectives: We investigated whether ACPA-IgG carry V-domain N-glycans prior to the development of arthritis and whether the occurrence of such glycans predicts the transition from pre-disease autoimmunity to overt RA.

Methods: Two independent sets of serum samples were obtained from RA patients and from ACPA-positive first-degree relatives (FDR) of RA-patients (n=126) of an Indigenous North American (RNA) population with high incidence rates of ACPA-positive RA. These samples comprised cross-sectional and longitudi-
Conclusion: ADAR1-mediated RNA editing is increased in active RA inducing the expression of pro-inflammatory genes thus representing a novel drug response biomarker and a potential therapeutic target in EULAR moderate/non-responders.

REFERENCES:

Disclosure of Interests: None declared


FRIDAY, 14 JUNE 2019

Novel biomarkers in RMDs – next steps towards clinical implementation

OP228

PCSK9 IN ATHEROSCLEROTIC INFLAMMATION OF LUPUS PATIENTS AND MURINE MODEL OF LUPUS WITH ATHEROSCLEROSIS

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Background: Systemic lupus erythematosus (SLE) patients have tendencies of accelerated atherosclerosis (AS), which is refractory to statins. Proprotein convertase subtilisin/kexin type 9 (PCSK9) is a new therapeutic target for AS for its dual mechanisms in lipids metabolism and inflammation. PCSK9 inhibitors had proved to be highly promising cardiovascular disease (CVD) drugs [1]. Our previous study suggested that Toll-like receptor 4 (TLR4) signal participates in the atherosclerotic inflammation of murine model of lupus with AS [2].

Objectives: To investigate the role of PCSK9 in atherosclerotic process of lupus and the association between TLR4 and PCSK9 in atherogenic inflammation of murine model of lupus with AS.

Methods: 90 SLE patients and 50 healthy controls were included. According to carotid intima-media thickness (cIMT), SLE patients were further divided into SLE-AS and SLE-NonAS subgroups (cut-off point: 1.0mm). Traditional CVD risk factors, inflammatory biomarkers and PCSK9 concentrations were compared between: (I) SLE patients and controls; (II) SLE-AS subgroup and SLE-NonAS subgroup. Correlational analysis and multivariate linear regression analysis were applied to analyze the association between PCSK9 levels and disease parameter, and the predictors of PCSK9 levels in SLE patients. Effects on PCSK9 concentrations by monotherapy with hydroxychloroquine (HCQ), which is thought having protective effects against CVD in SLE, were investigated by follow-up analysis in 15 SLE patients with inactive disease (SLEDAI=2). In animal experiment, murine model of SLE with AS was set up by intraperitoneally injection of lipopolysaccharides (LPS) in ApoE−/− mice. 30 female ApoE−/− mice were respectively administrated with LPS (SLE+AS group, n=10), saline (AS group, n=10) and LPS plus injection of lentivirus-PCSK9 small hairpin RNA targeting the mouse PCSK9 gene into the tail vein to interfere PCSK9 expression (SLE+AS+PCSK9 group, n=10). 10 female C57BL/6 mice were included as controls. Serum concentrations of PCSK9 and inflammatory biomarkers including TNF-α and IL-1β, atherosclerotic lesion, lipids parameters, expression of PCSK9, TLR4 and NF-κB p65 in atherosclerotic plaque were assessed.

Results: Characteristics of SLE patients and controls were listed in Table 1. SLE patients had significantly elevated serum PCSK9 levels than controls, especially in SLE-AS subgroup, accompanied with higher ratio of cIMT thickening. Correlational analysis showed PCSK9 concentrations correlated with C-reactive protein (CRP) levels, age and erythrocyte sedimentation rate (ESR), but not lipids parameters. Univariate and multivariate linear regression revealed that only CRP, but not age or ESR was positive predictors of PCSK9. Monotherapy with HCQ for 3 months significantly reduced PCSK9 levels in inactive SLE patients (Table 2, Figure 1). Mice in SLE+AS group had significantly higher serum PCSK9 concentrations than mice in AS group and C57BL/6 mice. Immunohistochemistry showed that PCSK9 over-expression was observed in SLE+AS mice than those in AS group and SLE+AS+PCSK9 group. Mice in SLE+AS+PCSK9 group exhibited decreased inflammatory cell infiltration in atherosclerotic plaque, alleviated atherosclerotic lesion, lower serum TNF-α and IL-1β levels and attenuated expression of TLR4 and NF-κB p65 in atherosclerotic plaque than SLE+AS group. PCSK9 silencing had no significant effects on lipids parameters in SLE+AS mice (Figure 2).

Table 1. Characteristics of SLE patients and controls.

<table>
<thead>
<tr>
<th>Variables</th>
<th>SLE</th>
<th>Healthy controls</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>90</td>
<td>50</td>
<td>NA</td>
</tr>
<tr>
<td>Female/Male</td>
<td>81/9</td>
<td>45/7</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Age (years)</td>
<td>33(20-42)</td>
<td>32(25-48)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Disease duration(years)</td>
<td>6(0-10)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>SLEDAI</td>
<td>6(2-8)</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Cholesterol (mmol/l)</td>
<td>4.52(3.53-5.37)</td>
<td>4.52(3.53-5.60)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>LDL cholesterol (mmol/l)</td>
<td>2.47(1.64-3.26)</td>
<td>2.68(2.03-3.98)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Triglycerides (mmol/l)</td>
<td>1.15(0.79-1.61)</td>
<td>1.34(0.77-1.55)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>HDL cholesterol (mmol/l)</td>
<td>1.47(1.23-1.73)</td>
<td>1.61(1.36-1.92)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>cIMT thickening</td>
<td>7.90(2.00-20.00)</td>
<td>7.50(2.00-2.00)</td>
<td>0.63</td>
</tr>
</tbody>
</table>

Table 2. Multivariate linear regression of CRP, ESR, age (independent variable) and PCSK9 (dependent variable) in SLE patients.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Unstandardized Coefficients</th>
<th>Standardized Coefficients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model</td>
<td>B</td>
<td>SE</td>
</tr>
<tr>
<td>(Constant)</td>
<td>280.939</td>
<td>71.128</td>
</tr>
<tr>
<td>CRP</td>
<td>4.040</td>
<td>0.627</td>
</tr>
<tr>
<td>ESR</td>
<td>1.028</td>
<td>0.076</td>
</tr>
<tr>
<td>Age</td>
<td>2.253</td>
<td>1.036</td>
</tr>
</tbody>
</table>

CRP: C-reactive protein; ESR: erythrocyte sedimentation rate.

Figure 1. (a) SLE patients had significantly elevated serum PCSK9 concentrations than controls, especially in those with AS. (b) Monotherapy with HCQ for three months significantly reduced PCSK9 levels in SLE patients with inactive disease (SLEDAI=2). (c) Difference of age, ESR and CRP levels between patients in SLE-AS subgroup and those in SLE-NonAS subgroup had statistical significance (*p*<0.05). Correlational analysis showed that serum PCSK9 levels correlated with age, CRP levels and ESR in SLE patients.


Table (1).: Comparison between the different studied groups regarding HPSE (ng/ml)

<table>
<thead>
<tr>
<th>Group</th>
<th>Group I (n=20)</th>
<th>Group II (n=17)</th>
<th>Group III (n=18)</th>
<th>Group IV (n=15)</th>
<th>Group V (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active LN</td>
<td>2.36 ± 0.62</td>
<td>1.44 ± 0.11</td>
<td>1.23 ± 0.07</td>
<td>1.31 ± 0.07</td>
<td>0.29 ± 0.13</td>
</tr>
<tr>
<td>Non-active LN</td>
<td>0.11 ± 0.01</td>
<td>0.11 ± 0.01</td>
<td>0.14 ± 0.01</td>
<td>0.13 ± 0.01</td>
<td>0.14 ± 0.01</td>
</tr>
<tr>
<td>p1 &lt;0.001</td>
<td>p2 &lt;0.001</td>
<td>p3 =0.914</td>
<td>p4 &lt;0.001</td>
<td>p5 =0.719</td>
<td>p6 &lt;0.001</td>
</tr>
<tr>
<td>F</td>
<td>115.716*</td>
<td>0.877</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Agreement (sensitivity, specificity) for HPSE (ng/ml) to diagnose active lupus nephritis

<table>
<thead>
<tr>
<th>Cut off</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>HPSE (ng/ml)</td>
<td>&gt;1.48</td>
<td>80.0</td>
<td>91.43</td>
<td>72.7</td>
</tr>
</tbody>
</table>

F: F for ANOVA test. Pairwise comparison between each 2 groups was done using Post Hoc Test (Tukey)

- p: p value for comparing between the different groups
- p1: p value for comparing between group I and each other group
- p2: p value for comparing between group V and each other group
- p3: p value for comparing between group I and group II
- p4: p value for comparing between group III and group IV
- p5: p value for comparing between group I and group III
- p6: p value for comparing between group II and group IV
- p7: p value for comparing between group II and group III

Disclosure of Interests: None declared

OPO299

ASSESSMENT OF ROLE OF URINARY HEPARANASE IN LUPUS NEPHRITIS PATIENTS AND ITS CORRELATION WITH DISEASE ACTIVITY

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Background: Lupus nephritis (LN) is one of the commonest and serious complications of Systemic Lupus Erythematous (SLE) and assessment of its activity is crucial. Heparanase has been proposed to be important in the pathogenesis of lupus nephritis and correlate with protein excretion. Annals of the Rheumatic Diseases. 2013;71(Suppl 3):548-9.

Objectives: To assess the ability of urinary heparanase to identify SLE with nephritis and the relation of this marker to lupus activity.

Methods: This cross sectional study was carried out on 90 subjects; 70 patients with SLE and 20 healthy volunteers as a control. All patients and controls were subjected to full history taking and complete clinical examination, routine investigations. Immunological assay and assessment of disease activity by systemic lupus erythematous disease activity index (SLEDAI) score, renal SLEDAI (r-SLEDAI) were done for lupus nephritis group. The lupus patients were divided according to SLEDAI score into 4 groups; 20 with active lupus nephritis, 17 with non-active LN, 18 with active lupus without renal involvement, 15 with non-active lupus without renal involvement. Urinary Heparanase levels were measured by ELISA for all groups.

Results: The level of urinary heparanase was significantly higher in LN groups than non-LN groups and control. It was also significantly higher in active LN than non-active LN patients. There was a significant positive correlation between urinary heparanase and 24 hours urinary proteins, total SLEDAI, and r-SLEDAI; and significant negative correlation between urinary heparanase and C3 & C4. ROC curve analysis revealed that urinary heparanase predicted presence of lupus nephritis activity with a sensitivity of 80%, and a specificity of 91.43%.

Conclusion: Urinary heparanase levels are increased in patients with active LN and correlate with disease activity markers, indicating that it can serve as a new useful biomarker for lupus nephritis activity.

REFERENCES:
Thrombotic and atherogenic processes contributing to cardiovascular disease. (2) However, the role of NETs in cardiovascular disease in human gout is not known.

**Objectives:** Our objective is to investigate the association between neutrophil activation and cardiovascular risk in gout patients. We hypothesize that neutrophil activation mediates inflammation, as well as activation and damage to endothelial cells, partaking in atherosclerosis development.

**Methods:** Plasma samples from 75 gout patients participating in the ‘Reade gout cohort Amsterdam’ were analyzed. Patient data was collected on disease activity, demographics, gout history, comorbidities, medication use and cardiovascular risk assessments. Measurements included anthropometry, vital parameters (RR, HF), ECG and lab variables. Levels of NETs, and NET-derived markers (cell-free DNA and peroxidase activity) were analyzed using a MPO-DNA ELISA, as well as fluorometry. Levels of calprotectin (S100A8/A9) were analyzed by ELISA. Markers of NETosis were related to clinical markers of cardiovascular risk, including BMI, smoking, blood pressure, lipid profile and 10 year risk of cardiovascular mortality (SCORE EU).

**Results:** No associations were found between markers of cell death (cDNA and NETs) and cardiovascular risk. However, markers of neutrophil activation, including peroxidase activity correlated with BMI (r=0.31, p =0.008), waist-hip ratio (r=0.52, p<0.001), cholesterol ratio (r=0.51, p<0.001), and triglycerides (r=0.42, p<0.001). These associations were even stronger in patients with chronic, polyarticular gout. Peroxidase activity was associated with the 10 year risk of cardiovascular comorbidity (r=0.47, p<0.001, Figure 1A). Calprotectin levels were elevated in hypertensive patients (p<0.005) and diabetes (p=0.02), with calprotectin levels associating with diabetes independently on BMI (OR=6.2, p=0.04). Finally, we constructed a neutrophil risk score ranging from 0-2 based on positivity for peroxidase and/or calprotectin to identify patients with a ‘neutrophil activation signature’. The neutrophil risk score strongly associated with CVD risk (Figure 1B). Patients with neutrophil activation signature (risk score 1-2) had markedly elevated cardiovascular risk score (p<0.001), with 67.7% of the patients having high cardiovascular risk, versus 32.3% of the patients without a neutrophil activation signature (OR=2.9, p=0.03).

**Conclusion:** We have demonstrated, for the first time, that neutrophil activation markers are associated with several risk factors of cardiovascular disease, including hyperlipidemia, hypertension and diabetes in a large cohort of gout patients. Furthermore, the presence of a neutrophil activation signature is strongly associated with a 10-year risk of cardiovascular comorbidity.

**REFERENCES:**


**Disclosure of Interests:** Daisy Vederd Speakers bureau: Novartis, Martijn Geritsen Grant/research support from: Grunenthal has sponsored the Reade Cohort. Michael Nurnohamed Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi and UCB. Consultant for: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi and UCB; Ronald van Vollenhoven: None declared, Christian Lood: None declared

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MONOSODIUM URATE AND CALCIUM
Félix Renaudin1,2, Laure Campillo-Gimenez1,2, Florence Castelli3,
Scientific Abstracts
Friday, 14 June 2019 233
was greater at both gene and protein levels than IL-17A. The kinetics and thresh-
Optimal MAIT cell IL-17A and IL-17F production occurred upon T cell
both IL-17A and IL-17F.
fibroblasts (NHDFs) in the presence of IL-17-isoform-specific antibodies, including
recombinant cytokines or an IL-23-neutralising antibody. RNAscope was utilised
to observe MAIT cells in psoriatic lesional skin. MAIT cell supernatant, generated
upon activation by anti-CD3/CD28 or fixed
IL-17A and IL-17F production by MAIT cells was assessed by flow
cytometry, ELISA, qPCR and CyTOF upon stimulation by anti-CD3/CD28 or fixed
Methods:
was used in murine air pouch model to assess the effects of 2DG and Glut1 inhibition in crystal-mediated inflam-
results: In vitro, both MSU and mCPPD crystal-induced IL-1β secretion and
Asc speck formation were inhibited when cells were cultured in glucose-free medium or in presence of 2DG.Similarly, MSU and mCPPD crystal-induced inflammation was abrogated in mice treated with 2DG.In THP-1 cells stimulated by MSU and mCPPD crystals, metabolic analysis displayed alteration of glycolysis pathway and Krebs cycle and decrease of intracellular ATP production. Interestingly, MSU and mCPPD crystals increased glucose uptake in vitro, ex vivo and in vivo. Crystal-induced IL-1β secretion was decreased by STF-31 and in THP-1 cells transfected with Glut1 siRNA. Next, we observed that MSU and mCPPD crystals increased membrane localization of Glut1 in THP-1, BMM and neutrophils infiltrated in air pouch lavages and membranes. Glut1 membrane localization was positively correlated with IL-1β production. Moreover, during gout flare, the proportion of Glut1 positive neutrophils was higher in synovial fluid neutrophils than in circulating neutrophils. Finally, STF-31 treatment decreased, in vitro, glucose uptake induced by MSU and mCPPD crystals, and in vivo MSU and mCPPD crystal-induced inflammation.
Conclusion: Glucose uptake through Glut1 transporter enhanced IL-1β production induced by MSU and mCPPD crystals. Studies to decipher how these crystals induced Glut1 membrane localization are ongoing. Similarly, we investigate how glycolysis regulates NLRP3 and ASC activation. Decreasing Glut1 membrane localization might be a potential target to dampen crystal-induced inflammation.
References: Disclosure of Interests: Felix Renaudin: None declared, Laure Campillo-Gimenez: None declared, Florence Castelli: None declared, Francois Fenaillle: None declared, Aurélie Prignon: None declared, Christèle Combes: None declared, marthe Cohen Solal Speakers bureau: Amgen and Lilly, Frederic Loiresi: None declared, Esther Vicente: None declared, Cristina Fernandez-Carballedo: Maria Paz Martinez-Vidal: David Castro-
Corredor: Joaquin Arino-Fernandez: Juan Carlos Guervdeo-Abeledo: Carlos Rodriguez-Lozano: Ricardo Blanco: Oerde Gualofo: Javier Martin Ibanez: Javier Iloca: Raquel Lopez-Meijas: Miguel A Gonzalez-
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Background: Cardiovascular (CV) disease is one of the main causes of mortality in axial spondyloarthritis (axSpA). The higher incidence of CV risk factors and sys-
temic chronic inflammation increase CV risk in axSpA. This is enhanced by a dysregulation of adipokines. Low levels of omentin, an anti-inflammatory adipokine, have been associated with metabolic dysfunction and CV disease in general population and conditions different from axSpA. 1,2,3
Objectives: To evaluate the implication of omentin in CV risk and subclinical artherosclerosis in axSpA at the genetic and functional (mRNA and protein) level.
Methods: 382 patients fulfilling the ASAS classification criteria for axSpA and 84 controls were included. Carotid ultrasound was performed to evaluate the pre-
ence of subclinical atherosclerosis. Serum omentin levels were assessed by ELISA. mRNA expression of ITLN1, coding omentin, was evaluated by RT-qPCR. ITLN1 rs12409609 (C/T), in complete linkage disequilibrium with a polymorphism
previously associated with coronary artery disease,6 was genotyped by TaqMan probes. Results were adjusted by potential confounding factors (STATATA v.11.1).

Results: Serum and miRNA levels of omentin were lower in axSpA compared to controls (p<0.001). Low omentin serum levels were observed in obese patients, patients with inflammatory bowel disease (IBD) and in those with an atherogenic index indicative of dyslipidemia (p=0.002, 0.006 and 0.004, respectively). Interestingly, the C allele of rs12409609 (both when alleles and genotypes were assessed) was associated with low mRNA levels of omentin in axSpA (p<0.001).

No association was observed between omentin and markers of subclinical athero-atherosclerotic disease. Interestingly, the C allele of rs12409609 (both when alleles and genotypes were assessed) was associated with low mRNA levels of omentin in axSpA (p<0.001).

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Background: High levels of the damage-associated molecular pattern (DAMP) S100A8/A9 are produced in the inflamed synovium during experimental and human rheumatoid arthritis (RA), which have been implicated in sterile inflammation-induced bone resorption. We and others have previously shown that stimulation of mature osteoclasts with S100A8/A9 increases their bone-resorptive capacity. In agreement, reduced bone destruction was observed after induction of experimental RA models in S100A8−/− mice. However, its effects on the differentiation of osteoclasts from their precursors remains elusive.

Objectives: Here, we investigated the effects of S100A9 on osteoclast differentiation from CD14+ circulating precursors.

Methods: CD14+ monocytes were isolated from buffy coats of healthy donors and differentiated towards osteoclasts with macrophage colony-stimulating factor (M-CSF) and receptor activator of nuclear factor kappa-B (RANK) ligand in the presence or absence of S100A9. Differentiation state of osteoclasts was determined by tartrate-resistant acid phosphatase (TRAP) staining and resorption capacity was quantified using hydroxyapatite-like-coated plates. RNA expression was analyzed with RNA sequencing and qPCR. RANK expression was assessed using FACS. Underlying epigenetic programming was studied using chromatin immunoprecipitation. Secretion of pro-anti-inflammatory mediators was analyzed with Luminex analysis

Results: S100A9 stimulation during monocyte-to-osteoclast differentiation resulted in a strong decrease in the numbers of multinucleated osteoclasts, underlined by a decreased resorptive capacity. The thus differentiated cells showed a high production of pro-inflammatory factors, such as interleukin (IL)-1α, IL-6, IL-8, and tumor necrosis factor-α (TNFα) after 16h of stimulation. In contrast, at day 4, the cells showed a decreased expression of the osteoclast-promoting factor TNFα. Interestingly, we showed that S100A9 stimulation only during the first 16h of culture was sufficient to reduce osteoclastogenesis. To determine the mechanism of how this short S100A9 stimulation might reduce the osteoclast differentiation, we determined the protein expression of RANK. We observed that within this 16h time frame, S100A9 inhibited the M-CSF-mediated induction of RANK, which we found to be associated with changes in various histone marks at the epigenetic level. This S100A9-induced reduction in RANK could be partially reversed by blocking TNFα using etanercept, but not by blocking interleukin-1 (IL-1) with the IL-1 receptor antagonist.

Conclusion: Whereas S100A8/A9 was previously shown to stimulate the resorptive capacity of mature osteoclasts, we here show that early S100A9 stimulation impedes monocyte-to-osteoclast differentiation via reduction of RANK expression that is partially TNFα-mediated. This suggests that the timing of exposure to S100A8/A9 is an important determinant for monocyte-to-osteoclast differentiation.

Conflict of Interest: Festive: None declared, Conflicts of interest: None declared, Interest: None declared, Conflict of interest: None declared.
and hospital organisation factors. Geographical Information Systems are used to display maps describing adjusted estimates of variation in outcomes across NHS CCG areas.

Variation in outcome of surgery across Clinical Commissioning Groups. (2014-2016)

Results: 210,725 primary TKR/UKR were identified nested in 207 clinical commissioning group areas. 57% of patients were women, with an average age 70 years (SD ±9 years). Whilst we identified a number of factors that predicted outcomes of surgery (e.g. age, gender, co-morbidity, deprivation, baseline function, surgical volume, numbers of orthopaedic surgeons, beds, operating theatres), these factors did not explain the observed geographical variations in outcomes across surgery CCGs. The absolute predicted change in OKS varied from 13.0 to 18.8, predicted 6-month complication rate from 2.9% to 5.8%, predicted revision from primary TKR/UKR undertaken in 2014-2016 0.7% to 1.8%, predicted mean length of stay 2.9 to 6.6 days, bed-day cost £4758 to £6893 (Figure).

Conclusion: We have identified potentially unwarranted variations in patient outcomes of knee replacement surgery. This variation cannot be explained by differences in patients case mix, surgical factors, or hospital organisational factors. This information is informative to patients in making a decision in where they have their surgery, and to commissioners in monitoring variations in outcomes of surgery.

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Disclosure of Interests: Cesar Garriga: None declared, Jose Leal: None declared, Andrew Price Consultant for: Zimmer Biomet, Daniel Prieto-Alhambra Consultant for: Servier, UK Renal Registry, Oxford Craniofacial Unit, IDIAP Jordi Gol and his work., Andrew Judge Grant/research support from: Consortium research grants from Regeneron, from Freshfields Bruckhaus, outside the submitted work. Annette Boonen Consultant for: Zimmer Biomet, Speakers bureau: Eli Lilly, GSK, Medtronic, Merck, Novartis, Pfizer, Roche, Servier, Takeda and UCB., Raymond Fitzpatrick: None declared, Karen Barker: None declared, George Peat: None declared, Nigel Arden Grant/research support from: Grants from BIOIBERICA, and from MERCK., Consultant for: Patients from Flexion, from Regeneron, from Freshfields Bruckhaus, outside the submitted work., Andrew Judge Grant/research support from: Consortium research grants from Roche, Consultant for: Received consultancy fees, lecture fees and honoraire from Serverin, UK Renal Registry, Oxford Craniofacial Unit, IDIAP. Jordi Gol andFreshfields Bruikhaus, Member of Deringer Data Safety and Monitoring Board for Anthera Pharmaceuticals, Inc. Consultancy for Freshfields Bruikhaus Deringer DOI: 10.1136/annrheumdis-2019-eular.1381

OP0307

STANDARDS OF CARE FOR RHEUMATOID ARTHRITIS: GAPS IN IMPLEMENTATION EXPERIENCED BY PATIENTS AND RHEUMATOLOGISTS ACROSS 33 EUROPEAN COUNTRIES

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Background: EuMusc.net, a EULAR and EU supported initiative (which took place from 2009 to 2013) aimed to raise and harmonize quality of care for patients with rheumatic and musculoskeletal diseases across European countries. As part of EuMusc.net, 16 user-focused standards of care (SoC) for rheumatoid arthritis (RA) were developed.

Objectives: To evaluate gaps in quality of care using the EuMusc.net SoCs among patients and rheumatologists across Europe and to investigate the contribution of individual- and country-level characteristics to care gaps.

Methods: Fifty RA patients and 50 rheumatologists from each of 33 countries were invited to participate in a survey. For each SoC, levels of importance and care were rated for received by patients or provided by rheumatologists on a scale from 0 to 10 (=best). Care gaps were calculated as difference from the maximum score for care received multiplied by the score for importance of care (0 (no gap) – 100), when the gap = 30 and importance >6. Individual- and country-level (GDP in tertiles) determinants of care gaps were analysed in multilevel logistic regression models, with patients clustered in country of residence. For patients, individual factors included gender, age, disease duration (years), level of education (low, high), work status (retired, disabled, working, not working), literacy, patient organisation membership and overall health (0-10). For rheumatologists, individual factors were gender, age, years of experience and work setting (university hospital and non-university hospital/private practice).

Results: In total, 1,422 patients from 27 and 1,044 rheumatologists from 33 European countries, respectively, were included. Patients had a mean (SD) age of 57.2 (13.2) years and 74% were female. For rheumatologists, the mean age was 47.7 (10.5) and 53% were female. After ranking the SoCs on percentage of problematic gap, the 7 SoCs in the top 10-ranks for both patients and rheumatologists (Table) were: diagnosis within 6 weeks, information about patient organisations, availability of treatment plan, receiving a schedule of regular assessment, vaccination-related information, information about adequate physical exercise and training on aids, devices and ergonomic principles. The least frequent problematic SoC for both patients and rheumatologists was adequate DMARD received (6% and 3%).

Multilevel analyses revealed large variation across countries for patients (all models p <0.01) and for the majority of analyses for rheumatologists, despite adjustment for individual characteristics. In addition, patients with higher education and lower self-reported health experienced problematic gaps more frequently. Among rheumatologists, patterns in determinants across SoCs were less consistent. For example, rheumatologists from lower GDP countries identified problematic gaps more often compared to those from medium or high GDP countries about half of the SoCs, rheumatologists from lower GDP countries identified problematic gaps more often compared to those from medium or high GDP countries.

Table: Frequencies and determinants of care gaps perceived by patients and rheumatologists (top-7 SoCs with highest % of respondents reporting a problematic gap)

**Table:**

<table>
<thead>
<tr>
<th>SoC Description</th>
<th>% of respondents indicating problematic gap</th>
<th>Gender</th>
<th>Education</th>
<th>Work status</th>
<th>Overall health</th>
<th>CCG GDP tertile high vs low</th>
<th>CCG GDP tertile moderate vs high</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis within 6 weeks</td>
<td>55% (30/55)</td>
<td>Female</td>
<td>High</td>
<td>Working</td>
<td>High</td>
<td>47.1% vs 32.6%</td>
<td>47.1% vs 32.6%</td>
</tr>
<tr>
<td>Information about patient organisations</td>
<td>50% (22/44)</td>
<td>Female</td>
<td>High</td>
<td>Working</td>
<td>High</td>
<td>47.1% vs 32.6%</td>
<td>47.1% vs 32.6%</td>
</tr>
<tr>
<td>维</td>
<td>51% (11/22)</td>
<td>Female</td>
<td>High</td>
<td>Working</td>
<td>High</td>
<td>47.1% vs 32.6%</td>
<td>47.1% vs 32.6%</td>
</tr>
<tr>
<td>Availability of a treatment plan</td>
<td>50% (22/44)</td>
<td>Female</td>
<td>High</td>
<td>Working</td>
<td>High</td>
<td>47.1% vs 32.6%</td>
<td>47.1% vs 32.6%</td>
</tr>
<tr>
<td>Impaired health, mobility, function</td>
<td>50% (22/44)</td>
<td>Female</td>
<td>High</td>
<td>Working</td>
<td>High</td>
<td>47.1% vs 32.6%</td>
<td>47.1% vs 32.6%</td>
</tr>
<tr>
<td>Receiving a schedule of regular assessment</td>
<td>50% (22/44)</td>
<td>Female</td>
<td>High</td>
<td>Working</td>
<td>High</td>
<td>47.1% vs 32.6%</td>
<td>47.1% vs 32.6%</td>
</tr>
<tr>
<td>Information about adequate physical exercise</td>
<td>50% (22/44)</td>
<td>Female</td>
<td>High</td>
<td>Working</td>
<td>High</td>
<td>47.1% vs 32.6%</td>
<td>47.1% vs 32.6%</td>
</tr>
<tr>
<td>Training on aids, devices and ergonomic principles</td>
<td>50% (22/44)</td>
<td>Female</td>
<td>High</td>
<td>Working</td>
<td>High</td>
<td>47.1% vs 32.6%</td>
<td>47.1% vs 32.6%</td>
</tr>
</tbody>
</table>

**Conclusion:** For most SoCs, problematic gaps were identified in essential aspects of RA care, and substantial differences across countries were observed.
QUALITY OF CARE PREDICTS OUTCOME IN SYSTEMIC LUPUS ERYTHEMATOSUS – CROSS SECTIONAL ANALYSIS OF A GERMAN LONG-TERM STUDY (LULA COHORT, 2011–2015)

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Mathias Schneider1, Gamal Chehab1, Heinrich-Heine-University Düsseldorf,
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Background: Systemic lupus erythematous (SLE) is a chronic disease, which is still associated with significant morbidity and mortality.1 Recommendations for the management of SLE patients exist2-5, but information on its implementation and the resulting impact on long-term outcome remain unclear.

Objectives: Our aim was to study the quality of SLE medical care in Germany to understand gaps and to analyze the association to long-term outcome parameters.

Methods: In the Lula-study information on demographics, clinical and medical care parameters are assessed annually by self-reported questionnaires among a representative sample of SLE patients in Germany (Lula cohort, n=572). In 2013 additional questions on the management of care, as mentioned in current guidelines and recommendations, were surveyed. Ten items predicting a good clinical care (quality measures) were evaluated and an overall score with a minimum of 0 points and a maximum of 10 points was calculated. The ten items are taking anti-malarials, osteoporosis protection at a dose above 7.5mg prednisolone equivalent per day or taking 5mg per day, vaccination, blood pressure, fat metabolism counseling, urine examination and blood test once a year, treatment of comorbidity, fat metabolism disorder, osteoporosis and hypertension. Health related quality of life (Short Form Survey, SF-12/36), damage (Brief Index of Lupus Damage, BILD) and activity (Systemic Lupus Activity Questionnaire, SLAQ) were chosen as relevant proxies for long-term outcome.

Using linear regression, we examined the relationship between the quality measures and outcome parameters, adjusted for age, disease duration and gender.

Results: 65.9% of the patients consulted a rheumatologist as a main contact for their disease. On average 6.1 points of the 10 quality measures were met (SD 1.7). The fulfillment of these quality measures varied between 22.8% (fat metabolism counseling) and 97.8% (osteoporosis protection at a dose above 7.5mg prednisolone equivalent per day or ≤ 7.5mg per day). Fulfilling more clinical care items in 2013 was predictive for high disease-related quality of life (SF-36, p=0.004), low progress in disease-related damage (BILD, p=0.048) and low disease activity (SLAQ, p=0.046) in the subsequent years.

Conclusion: Our study illustrates a strong link between the quality of care and important SLE outcome parameters: quality of life, disease-related damage and disease activity assessed by a self-reported questionnaire. Consistent considerations of these care parameters, which are recommended in several management guidelines, yield a positive effect on outcome. An interdisciplinary approach with general practitioners and other specialists is certainly beneficial and warranted.

German Clinical Trial Register, www.germanctr.de, DRKS00011052

REFERENCES:

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IMPLEMENTATION OF TNF-BIOSIMILARS (INFLEXIMAB AND ETANERCEPT) IN DANISH DEPARTMENTS OF RHEUMATOLOGY

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Background: The use of expensive biological drugs in rheumatology is rapidly increasing and has led to substantial increases in drug expenditures. A considerable reduction of drug costs is possible by using biosimilars as soon as they become available and carrying out non-medical shifts to biosimilars (i.e. switching a patient well treated on a biooriginator to the biosimilar). Research on biosimilars has focused on interchangeability and safety outcomes, but little focus has been on nationwide implementation and the direct economic consequences on drug expenses.

In Denmark, TNF-inhibitors are solely given in an in-hospital setting and bought through national tenders. The Danish in-hospital organization includes Regional Drug and Therapeutics Committees that ensures regional implementation of treatment guidelines and close collaboration between hospital pharmacies and regional clinical pharmacologists. Furthermore, the implementation of TNF-inhibitor biosimilars was preceded by careful preparations from among others a newly established national biosimilar task force.

Objectives: The aim of this study was to describe the implementation of the two first TNF-inhibitor biosimilars (infliximab and etanercept) in Danish departments of rheumatology.

Methods: Monthly data on drug sales to Danish rheumatology departments were used to assess the biosimilar uptake rate and subsequent changes in the drug expenditures during the implementation in Denmark.

Results: Shifts to biosimilars were begun within a few months following end of biooriginator patent, vertical lines in the figure. Use of the infliximab biosimilar was begun in April 2015, and in August 2015 biosimilar uptake was 92.9% of total infliximab use. Similarly use of etanercept biosimilar was begun in April 2016, and in June 2016 the biosimilar uptake was 91.6% of total etanercept use. In January 2015 the total use in Defined Daily Doses (DDD) were 42.4 thousand DDD’s for infliximab and 37.5 thousand DDD’s for etanercept. The use increased steadily and was in January 2018 138.4 thousand DDD’s for infliximab and 62.1 thousand DDD’s for etanercept (equivalent to increases of 226.6% and 66.8%). The increases in DDD’s were not reflected in total drug costs due to the shift to biosimilars. The total drug cost for infliximab in January 2015 was 6.7 million DKK but was reduced to 5.4 million DKK in January 2018 (-19.4%). A corresponding cost reduction was seen for etanercept (11.3 million DKK in January 2015, 8.1 million DKK in January 2018, -28.7%).

Conclusion: Danish departments of rheumatology experienced a fast and near-complete switch of infliximab and etanercept biooriginators to biosimilars. At the same time the use of the drugs increased substantially, but due to large price reductions the total drug cost decreased despite the increasing use. We believe that a thorough preparation and an organizational setting supporting the implementation was crucial for the successful implementation. The Danish structure, with its national tendering, probably contributed to the substantial drug discounts obtained. The implementation will be used for future biosimilars in Denmark.

Disclosure of Interests: None declared

VARIABILITY IN BIOLOGIC PRESCRIPTION PATTERNS
COST-EFFECTIVENESS OF A JAK1/JAK2-INHIBITOR


Figure 1

Disclosure of Interests: Milada Cvancarova Småstuen Grant/research support from: I have received a Research grant from Pfizer, Randdeep Madia Employee of: Pfizer, still employed, Oddvar Solli Employee of: Pfizer, still employed by Pfizer, Erik Helvin Employee of: Pfizer, still employed by Pfizer

Figure 2

Disclosure of Interests: Celine van de Laar1, Martijn Oude Voshaar1, Walid Falhoun2, Lilianna Zaremba-Pechmann3, Francesco de Leonardi3, Inmaculada De La Torre4, Mart van de Laar1,2, 3, 4, 5.

Background: Biologics account for a substantial portion of drug spending in rheumatoid arthritis (RA). Variability in the U.S. in biologic prescribing patterns (and therefore variability in cost of care), and factors that correlate with that variability, remain largely undefined.

Objectives: We used data from the RISE registry to perform a cross-sectional analysis among U.S. rheumatologists of prescription patterns for biologic DMARDs and tofacitinib and their relationship to RA disease activity.

Methods: RISE is a U.S. registry that passively collects data on all patients seen by participating practices, thereby reducing selection bias present in single-insurer claims databases. As of December 2017, RISE held validated data from 1,257 providers in 236 practices, representing an estimated 25% of the U.S. clinical rheumatology workforce. We identified patients with available demographic and disease activity information who were assigned ≥2 codes for RA ≥30 days apart between January and December 2017. Practices with <20 RA patients (15/104 practices providing all necessary data) were excluded. We tallied the proportion of patients in each practice prescribed a TNF inhibitor, abatacept, rituximab, tocilizumab, or tofacitinib at least once during 2017. Patients prescribed >1 of these drugs were assigned to the first drug prescribed and therefore counted only once. We used a hierarchical linear model to predict the probability of receiving a prescription for a biologic based on the patient’s most recent disease activity score (moderate or high disease activity vs. low disease activity or remission) and age from 2016, accounting for clustering by practice.

Results: We analyzed 53,850 patients from 104 practices. Overall, 29% of patients were prescribed a biologic DMARD or tofacitinib in 2017. TNF inhibitors were most commonly prescribed, followed by abatacept (4.5% of patients), tofacitinib (4.2%), tocilizumab (3.4%), and rituximab (2.5%). We found significant variation within practices in the proportion of patients prescribed any of these drugs (range 0%-100%). In the adjusted analysis, we found that patients with higher disease activity in 2016 were more likely to receive biologics in 2017 (OR 1.56, 95% CI (1.51, 1.62)). Within a practice, as shown in the figure, the risk-adjusted likelihood of receiving a biologic prescription still showed significant variation (between 0%-83%) of patients in each practice received a biologic; model c-statistic 0.61.

Conclusion: In this large sample of U.S. rheumatology practices, higher RA disease activity correlated with the likelihood that a patient would receive a prescription for a biologic, but did not account for all of the variability in biologic prescription patterns. These results suggest that there may be other factors in addition to RA disease activity that account for practice-to-practice variability in biologic prescription patterns. Disclaimer: These data were collected from the ACR’s RISE Registry; however, the views expressed represent those of the authors, not necessarily those of the ACR.

Disclosure of Interests: Celine van de Laar: None declared, Martijn Oude Voshaar: None declared, Walid Falhoun: None declared, Lilianna Zaremba-Pechmann: None declared, Francesco de Leonardi: None declared, Inmaculada De La Torre: None declared, Mart van de Laar: Research support from: Investigator initiated award from Pfizer from 2015-2018, unrelated to this work, Consultant for: Eli Lilly and Company, Indianaroid, United States of America; Arthritis Center Twente, Enschede, Netherlands.

Background: Treating Rheumatoid Arthritis (RA) to an a priori defined disease activity target (T2T) is recommended in EULAR guidelines. This involves a step-up approach in which it is first attempted to achieve the target with a combination of conventional synthetic (cs) DMARDs. Baricitinib is a JAK1/JAK2-inhibitor approved for treatment of patients suffering from RA. EULAR and ACR guidelines currently position JAK1/JAK2-inhibitors and bDMARDs at the same level in the therapeutic treatment sequence for csDMARD2 Inadequate Responders (IR). Cost-effectiveness assessment of different T2T strategies, especially ones...
including new treatments, and integrating health economic considerations is of importance to the decision-making process as it incorporates the societal perspective in the longer run.

Objectives: To compare the cost-effectiveness of the previously evaluated DREAM T2T strategy csDMARD combination therapy (csDMARDs) - first bDMARD (adalimumab) - next bDMARD (TNFi/non-TNFi) with the comparable strategy in which baricitinib is placed instead of adalimumab in csDMARDs IR using a Markov model. All analyses were performed from the societal perspective. Costs and effects over five years were compared between the two strategies to provide insight into the differences in economic considerations between treating patients with strategies including either JAK1/JAK2-inhibitor (baricitinib) or 1st bDMARD (adalimumab).

Methods: A Monte Carlo microsimulation model was developed to conduct cost-utility analysis from the societal perspective over 5 years. Health states were based on the DAS28-ESR categories. Effectiveness of baricitinib was retrieved from clinical trials and (1) and corrected for differences between RCT and real-world setting. Effectiveness of all other treatments, health state utilities, medical costs, and productivity loss were retrieved from DREAM cohorts (2) and the Dutch institute for Health. Annual discount rates of 1.5% for utility and 4% for costs were used, as advised in Dutch guidelines. All analyses were run using probabilistic sensitivity analysis (PSA) to incorporate uncertainty around all parameters and assess result robustness.

Results: PSA results showed the baricitinib strategy yielded lower costs and higher utility over a 5-year period and is cost-effective and dominant over the DREAM T2T strategy. Scenario analyses showed the baricitinib strategy to be cost-effective in both the moderate and severe at baseline RA populations analysed together and separately.

Table 1. Probabilistic Sensitivity Analysis Results

<table>
<thead>
<tr>
<th>Time Period</th>
<th>Costs (€) (CI)</th>
<th>Effects (QALY) (CI)</th>
<th>ΔC</th>
<th>ΔE</th>
<th>ICER</th>
</tr>
</thead>
<tbody>
<tr>
<td>DREAM T2T</td>
<td>14288.36</td>
<td>3.5607</td>
<td>2.4028-4.7236</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baricitinib strategy</td>
<td>13400.57</td>
<td>3.5643</td>
<td>-857.79</td>
<td>0.0036</td>
<td>Dominant</td>
</tr>
</tbody>
</table>

C= 95% Confidence Interval, QALY = Quality-Adjusted Life Year, ΔC = Cost difference, ΔE = Effect Increment, ICER = Incremental Cost-Effectiveness Ratio

Conclusion: Results suggest the use of a JAK1/JAK2-inhibitor (baricitinib) instead of 1st bDMARD (adalimumab) in a T2T strategy is cost-effective in treating RA patients.

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FRIDAY, 14 JUNE 2019
Primary and secondary fibromyalgia; are they different?

LONG TERM TRAJECTORIES OF CHRONIC WIDESPREAD PAIN: A 21-YEAR PROSPECTIVE COHORT LATENT CLASS ANALYSIS

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Background: Chronic widespread pain (CWP) is common (population prevalence of approximately 10%) and has a significant impact on the individual, health-care, and society. Currently little is known about the actual course of CWP over time, in particular the pathways to the development and maintenance of CWP. One useful way to understand these pathways is to identify common clusters of people who share pain trajectories. Such information is clinically useful to identify factors that predict development, persistence, and resolution of CWP.

Objectives: To identify different longitudinal pain trajectories over a period of 21 years.

Methods: A 21-year longitudinal open-population cohort of n=1858 adults (aged 20-74) who completed surveys relating to their pain status in at least three of the five time points 1995, 1998, 2003, 2007, and 2016. Pain status (presence of persistent pain) was ascertained from a report of painful regions (0-18) on a pain mannequin and categorised into: NCP (no chronic pain), CRP (chronic regional pain), and CWP (chronic widespread pain). Latent Class Growth Analysis (LCGA) was carried out based on these categories. Participants were assigned to a trajectory cluster where the posterior probability was the highest. Model fit was assessed by statistical indices and clinical interpretations of clusters.

Results: LCGA identified five clusters describing different pathways of CWP, CRP and CWP over the 21 years. The cluster “Persistent CWP” was the most common pathway (n = 1052, 57%) and had a significant impact on the individual, health-care, and society. Currently little is known about the actual course of CWP over time, in particular the pathways to the development and maintenance of CWP. One useful way to understand these pathways is to identify common clusters of people who share pain trajectories. Such information is clinically useful to identify factors that predict development, persistence, and resolution of CWP.

Conclusions: This study showed that whilst half of adults report no chronic pain over 21 years, a substantial proportion develop CWP or have persistent CWP over this time period. Whilst a common trajectory was movement from chronic regional pain to no chronic pain, a pattern of improving CWP was not seen suggesting this is an uncommon trajectory. This is the first study to show long-term trajectories for CWP, and further work is now required to understand factors that may identify individuals at risk of worsening pain status and factors that might promote improvement. These identified pathways of chronic pain over a lifespan improve the understanding of long-term development of chronic pain and chronic widespread pain.

Disclosure of Interests: None declared


Figure 1. Mean pain sites [0-8] by year.

Wound pain sites [0-8] by year.
ACHIEVING A LOW DISEASE STATE WITHIN FIRST 3 MONTHS IN EARLY RHEUMATOID ARTHRITIS

RESULTS IN LOWER FATIGUE OVER 5 YEARS

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Background: Up to 80% of rheumatoid arthritis patients report clinically relevant fatigue. Fatigue is complex multi-factorial process that can result in adverse affects on patients’ physical and emotional well-being.

Objectives: To examine the relationship between disease activity and fatigue over time in early rheumatoid arthritis (ERA).

Methods: Data were from patients with ERA (symptoms < 12 months) enrolled in the Canadian Early Arthritis Cohort (CATCH). CATCH participants completed repeat clinical assessments, laboratory investigations and self-reported questionnaires including rating their fatigue over the past week using a 10 point numerical rating scale (NRS). Fatigue severity was classified as low (<2); moderate (>2 but ≤5) and high (>5) based on other published RA studies. Bivariate relationships between disease activity measures and fatigue over 5 years of follow-up were estimated using the Pearson correlation coefficient. T-tests and repeated measures analysis were used to compare differences in fatigue ratings in patient who did vs. did not achieve a low disease state (DAS28 <3.2) within 3-months of cohort entry.

Results: Of the 1864 patients included, 1640 (88%) met criteria for RA, 1342 (72%) were women and most had moderate-high baseline disease with a mean (SD) DAS28 of 4.9 (1.5). Fatigue was common with 19% reporting moderate or high fatigue throughout 5 years of follow-up compared to those with moderate or high fatigue (p<0.001). Patients who achieved DAS28 REM or LDA within 3-months of entry had significantly lower mean fatigue compared to those with more active disease throughout 5 years of follow-up (p<0.001) (Figure 1).

Conclusion: Fatigue is common in ERA and is most strongly correlated with pain and patient global ratings (r 0.56-0.67, p<0.001), positively and moderately correlated with DAS28 (r 0.35-0.49, p<0.001), and positively but more weakly correlated with tender/swollen joint count, physician global assessment, ESR and CRP (r 0.10-0.39, p<0.01) throughout the first year of follow-up. Patients who reported low fatigue severity by three months continued to have significantly lower fatigue throughout follow-up compared to those with moderate or high fatigue (p<0.001). Patients who achieved DAS28 REM or LDA within 3-months of entry had significantly lower mean fatigue compared to those with more active disease throughout 5 years of follow-up (p<0.001).

REFERENCES:

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Optimizing the access to new treatments for RMD patients

COST EFFECTIVE INTERVENTION TO IMPROVE QUALITY OF CARE MEASURES FOR RHEUMATOID ARTHRITIS PATIENTS IN AN UNDERSERVED COMMUNITY

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Background: Quality of care measures for rheumatoid arthritis (RA) have been endorsed by the American College of Rheumatology and the CDC. Similar quality indicators have been studied and recommended by the European League Against Rheumatism. Improving quality metrics in an underserved community is a problem given the lack of resources.

Objectives: To identify quality metrics for RA patients with need for improvement in our underserved urban public hospital, and to establish an effective intervention.

Methods: An initial retrospective chart review established baseline data from patients with RA seen in our clinic (July 2015 - July 2016), they were identified by ICD-9/10 coding. We identified 3 RA measures needing improvement: (a) tuberculosis screening (TBsc) 12 months prior to starting a new biologic agent, (b) documentation of clinical disease activity index (CDAI) in ≥50% of encounters, and (c) appropriate pneumococcal vaccination. We then planned an intervention by placing index cards at computer stations to remind providers to check these measures. We collected data on these 3 variables prior to the intervention (December 2016 - July 2017) and 30+ days after (August 2017 - December 2017). We also compared these results by provider type (attendings and fellows).

RESULTS: Baseline data included 240 patients, prior analysis to the intervention included 86 patients, and after the intervention included 131 patients. CDAI documentation was improved from 72.1% to 86.3% (Figure 1, p=0.01), however, when stratifying the analysis by provider type, this improvement was only significant in attendings (p=0.005) and not in fellows (p=0.43). Further analysis by including only the same fellows in both pre and post intervention moments (some fellows graduated) showed a significant difference in both groups (attendings: p=0.005; fellows: p=0.024). In terms of TBsc, baseline data showed 73.1% compliance, however we already found a compliance of 100% prior to the intervention (Figure 2, p=0.002 when compared with baseline data). Finally, there was no difference in
compliance with pneumococcal vaccination between baseline data, prior and post intervention (p=0.895).

Conclusion: Placing a card reminding providers to check 3 RA quality measures significantly improved CDAI documentation after 30 days of starting the intervention. The compliance with TBsc prior to starting a new biologic agent was 100% even before the intervention, which was better compared to baseline data, likely due to providers being aware there was a problem after initial data was collected. We did not find improvement in pneumococcal immunization rate, most likely because there are multifactorial components to motivating patients to get the vaccine. Our results suggest that interventions as simple as raising provider awareness to a problem such as TB screening, and an index card to remind people to document CDAI can be effective to improve I3 measures in RA patients in underserved communities.

REFERENCES:

Disclosure of Interests: None declared

OP0317
ASSOCIATION OF PATIENT SATISFACTION WITH HEALTHCARE UTILIZATION, COST, AND QUALITY OF LIFE IN RHEUMATOID ARTHRITIS
Nasim Khan1,2, Fawad Aslam1, Wais Atta1, Chenghui Li1. 1University of Arkansas for Medical Sciences, Little Rock, United States of America; 2Central Arkansas Veterans Healthcare System, Little Rock, United States of America; 3Mayo Clinic, Phoenix, United States of America

Background: Patient satisfaction and experience with care is being used as a surrogate marker of quality and value of healthcare delivery. No study has evaluated the association of patient satisfaction with healthcare utilization and cost, and quality of life in RA patients.

Objectives: To examine the association of RA patient satisfaction with healthcare utilization and cost, and quality of life.

Methods: 2010-2015 longitudinal files from the Medical Expenditure Panel Survey (MEPS), a nationally representative survey of the US civilian non-institutionalized population were used to identify patients with self-reported RA diagnosis. MEPS has overlapping panel design with participants interviewed up to 5 rounds over a 2- year period. In rounds 2 and 4, patient satisfaction is assessed by the four items about physician interaction – listened carefully, explained things well, showed respect, and spent enough time; and one item for overall satisfaction with quality of care received. A patient satisfaction score was constructed from standardized composite score of these items, and classified as most satisfied (patient satisfaction quartile 4) and less satisfied (patient satisfaction quartiles 1-3). The outcome measures were assessed in year 2: healthcare utilization (any emergency department visit, any inpatient stay, number of visits to office-based providers, outpatient department, and prescription drugs); total healthcare expenditures (measured in 2015 dollars), and quality of life (QoL, measure using 12-item Short Form healthy survey (SF-12)). Two statistical approaches were used: a standard logistic regression comparing most satisfied with less satisfied, and propensity score matching. Propensity scores were estimated using a logistic regression approach yielded similar results.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Most satisfied, OR</th>
<th>Less satisfied, OR</th>
<th>Difference</th>
<th>Bootstrapped SE (95% CI)</th>
<th>P Value</th>
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</thead>
<tbody>
<tr>
<td>Total expenditure, $</td>
<td>$3412</td>
<td>$3695</td>
<td>$283</td>
<td>2067</td>
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<tr>
<td>Number of Office Visits</td>
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<td>12.73</td>
<td>0.51</td>
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<tr>
<td>Number of Outpatient Visits</td>
<td>1.05</td>
<td>1.34</td>
<td>0.29</td>
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<td>0.622</td>
</tr>
<tr>
<td>Number of Inpatient Visits</td>
<td>0.23</td>
<td>0.34</td>
<td>0.11</td>
<td>0.29</td>
<td>0.367</td>
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<tr>
<td>Number of ED visits</td>
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<td>0.04</td>
<td>0.11</td>
<td>0.547</td>
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<tr>
<td>Number of Prescriptions</td>
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<td>55.41</td>
<td>2.59</td>
<td>4.31</td>
<td>0.561</td>
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<tr>
<td>SpC: Mental health summary score</td>
<td>47.55</td>
<td>47.38</td>
<td>0.17</td>
<td>1.11</td>
<td>0.739</td>
</tr>
<tr>
<td>SpC: Physical health summary score</td>
<td>39.526</td>
<td>36.880</td>
<td>1.666</td>
<td>0.969</td>
<td>0.082</td>
</tr>
</tbody>
</table>

Conclusion: Patient satisfaction score of RA patients was not associated with healthcare utilization and cost, and quality of life measures.

REFERENCE:

Disclosure of Interests: None declared

FRIDAY, 14 JUNE 2019
Teenage look in the mirror (sexuality and body image meeting health care).

OP0318-HPR
IS PSYCHOLOGICAL SUPPORT REACHING THOSE IN MOST NEED? A SURVEY OF PEOPLE WITH RHEUMATOID ARTHRITIS AND ADULTS WITH JUVENILE IDIOPATHIC ARTHRITIS:
Hayley McBain1, Matthew Bezzant2, Ailsa Bosworth1. 1City, University of London, London, United Kingdom; 2National Rheumatoid Arthritis Society (NRAS), Maidenhead, United Kingdom

Background: Rheumatoid arthritis (RA) and adult juvenile idiopathic arthritis (AJIA) is associated with a significant impact on psychological well-being.1-2 UK guidelines for the management of RA3-5 state that psychological interventions should be offered to people with RA to help them adjust to living with their condition and manage their psychological well-being. Three in four rheumatology units in the UK however, rate their overall provision of psychological support as inadequate.6

Objectives: To establish levels of anxiety and depression in people with RA or AJIA and how this relates to the prevalence of diagnosed mood disorders and receipt of psychological support.

Methods: The 2018 National Rheumatoid Arthritis Society (NRAS) ‘Emotional Health and Well-being Matters’ survey was designed by patients and researchers. This included a questionnaire designed to capture self-reported comorbidities, receipt of psychosocial support and the Hospital Anxiety and Depression Scale (HADS).7 Participants were recruited by NRAS via their social media platforms, membership and non-membership lists and in newsletters and forums. The survey was open from May–July 2018. Recruitment was focused on those diagnosed with RA or AJIA aged 18 years and over and living in the UK.

Results: A total of 1565 people with RA and 55 AJIA completed the survey. Although mean scores on the HADS were within the normal range in both populations, over 25% of the samples were experiencing clinical levels of anxiety or depression. Over half of those reporting clinical levels of anxiety or depression had never received a formal diagnosis. Most concerning however, was that 1 in 2
New assessments in clinical practice

OP0319 DIAGNOSTIC ACCURACY OF ULTRASOUND IN CALCIUM PYROPHOSPHATE DEPOSITION DISEASE: PRELIMINARY RESULTS OF THE OMERACT US in CPPD SUB-GROUP


Disclosure of Interests: None declared


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Background: The OMERACT Ultrasound (US) in calcium pyrophosphate deposition disease (CPPD) sub-task force has been working on the assessment of the utility of US in CPPD since 2014 first creating definitions for CPPD identification and then demonstrating that US is a reliable tool[1].

Objectives: Objective of this study is to assess the diagnostic accuracy of US in CPPD

Methods: This is a multicentre international diagnostic accuracy study involving 17 centres from 9 countries. We enrolled in this study consecutive patients waiting to undergo knee replacement surgery due to severe osteoarthritis. Each patient underwent US examination of the knee, focusing on the menisci and the hyaline cartilage, the day prior to surgery, scoring each site according to the presence/absence of CPP as defined by OMERACT[1]. After surgery, the menisci and the condyles were collected and examined microscopically. Six samples were collected, both from the surface and from the internal part of menisci and cartilage trying to cover a large part of the structure. All slides were observed under transmitted light microscopy and by compensated polarised microscopy. A dichotomous score was given for the presence/absence of CPP crystals. US and microscopic analysis were performed by blinded operators. Sensitivity and specificity of US were calculated using microscopic findings of the menisci and cartilage as the gold standard.

Results: These preliminary analyses include 30 patients. The mean age was 71yrs (SD9.1), 19 (63%) were females. 17 patients were positive at US analysis and 12 at microscopic analysis. Diagnostic accuracy results of US at patient level, are presented in figure 1.

Conclusion: These preliminary results demonstrate that US is a sensitive exam for identification of CPPD with acceptable specificity. US is the first diagnostic technique with consistent reliability and validity to be applied for non-invasive screening for CPPD in clinical practice.

REFERENCES:

Disclosure of Interests: None declared

Scientific Abstracts
OP0320

SUCCESSFUL EVALUATION OF A PREDEFINED SET
OF ANATOMIC SITES IN THE PELVIS OF PATIENTS
WITH POLYMYALGIA RHEUMATICA SHOWING
EXTRACAPSULAR INFLAMMATION AS VISUALIZED
BY CONTRAST ENHANCED MAGNETIC RESONANCE
IMAGING:

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Germany
Background: The diagnosis of polymyalgia rheumatica (PMR) is based on a
thorough clinical evaluation of the patient - including exclusion of other diseases,
since there is no decisive diagnostic test. A characteristic pattern of extracapsular
inflammation in the pelvis of patients with PMR as assessed by contrast enhanced
magnetic resonance imaging (MRI) has been recently described (1)
Objectives: To evaluate the performance of a predefined set of anatomic sites in
the pelvis of patients with PMR vs. controls.
Methods: A total of 120 pelvic MRI scans of patients who had presented to our
tertiary center with pelvic girdle pain in the last 3 years, including 40 patients with
an expert rheumatologist diagnosis of PMR and 80 controls with other reasons of
pelvic pain was evaluated by 3 radiologists blinded to clinical diagnosis and
patient demographics. The experts scored the presence or absence of contrast
enhancement at 19 predefined tendinous and capsular pelvic structures. Different
patterns of involvement were compared and statistically evaluated by ROC analysis. Kappa statistics were applied to calculate inter- and intrareader agreement.
Results: Mostly bilateral peritendinitis and capsulitis including uncommon sites
such as the proximal origins of the muscles rectus femoris and adductor longus
were found almost exclusively and, thus, typically in PMR patients: the difference
in the mean number of sites showing contrast enhancement was significantly different with 13.4±2.7 for PMR vs 4.0±2.3 for controls. A cut-off of 10 inflamed
sites discriminated very well between the groups resulting in a sensitivity and specificity of 95.8% and 97.1%, respectively. Just concentrating on the most frequently involved anatomic sites bilateral inflammation of proximal M. rectus
femoris or adductor longus tendons together with at least 3 other bilaterally
inflamed sites performed even better with a sensitivity and specificity of 100% and
97.5%, respectively.
Conclusion: This study strongly confirms that the previously described pattern of
extracapsular pelvic inflammation as assessed by contrast enhanced MRI is very
typical for patients with PMR. In addition, the high sensitivity and specificity of the
set of anatomic sites evaluated suggest their definite potential for use as a confirmatory diagnostic test.
REFERENCE:
magnetic resonance imaging of the pelvis to describe changes at different
anatomic sites which are potentially specific for polymyalgia rheumatica.
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The benefits of involving patients in health
technology assessment
OP0321-PARE

A NOVEL APPROACH TO REACH PATIENTS FOR
EDUCATIONAL PURPOSES – VIRTUAL CONFERENCE
REUMANET

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Background: Every two years, ReumaNet organises a physical conference for
patients addressing various topics of rheumatic and musculoskeletal diseases
(RMD). Traditionally, about 200 individuals attend this event. For the last edition
however, ReumaNet swapped the physical event with a virtual one. This allowed
us to reach far more people, who could attend the ‘conference’ online whenever
they wanted, over a period of four weeks.
Objectives: The objective was to assess the impact, reach and patient experience of such a virtual event.
Methods: In this virtual event, more than twenty presentations were pre-recorded
and put into an online system. Virtual booths were offered to partner organisations
to offer educational material in pdf’s or in video format.
The board of ReumaNet set up an interesting program, covering the following
aspects:
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Medical evolution in RMD’s: explanation about new treatments in various
indications, information on new medication
Living with an RMD: information about the psychological, vocational, social
and physical aspects of having an RMD
The future of healthcare: information on the changing technology in
healthcare and sustainability of the healthcare system
Testimonials: video testimonials of patient advocates

All information was pre-recorded and integrated into an online portal. The lectures
showed both speaker and the slide set, moving along with the presentation.
Registration was free and anonymous. Only email was required in order to validate the registration. Visitors also had the option to answer surveys on various
topics and score every video presentation. All material could be downloaded
(PowerPoint presentations, brochures, videos).
This virtual symposium was accessible from mid-September till mid-October, covering four weeks around World Arthritis Day. People could come and go, and log
in at any other point in time from different devices, so it was not necessary to view
all at once.
Results: The results were very promising, having over 1.300 registrations (compared to 200 registrations at a physical event). The social media reach was over
140.000 and the event also increased the visibility of the Facebook page of ReumaNet. On the platform itself there were over 5000 video views and over 3000 visits of the virtual booths of partner organisations. General satisfaction rates were
high: 96% of the visitors indicated they were most likely to visit a similar event in
the future. Over 80% gave the event a + 4 star rating out of 5.
Conclusion: This event was considered to be very successful. The results
showed that this virtual event exceeded our expectations and had an impact on
the visibility of our organisation via social media. This type of event has been
expanded towards sister organisations in rheumatology, such as the Belgian
organisation for healthcare professionals and can serve as an innovative way for
other European patient organisations to attract new profiles and increase awareness of RMDs among the broad public.
Disclosure of Interests: Mitchell Silva Consultant for: For Pfizer, MSD, Janssen,
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OP0322-PARE

GRASSROOTS CAMPAIGN FOR DUTCH RMDFRIENDLY MUNICIPALITIES

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Background: Following the decentralisation of healthcare in 2014, Dutch municipalities were assigned a key role in providing healthcare support to local residents. ReumaNederland used the 2018 council elections to start a campaign to
raise awareness for RMD-friendly council policies.
Objectives: The campaign aimed to raise awareness for suitable RMD healthcare policies across municipalities.


Cannabis for arthritis: Hype or hope?

**Method:** Evaluation of clinical correlates of cannabis use in arthritis patients.

**Results:** Cannabis use was reported by 20% of patients. Use was associated with a younger age, higher education level, and a lower prevalence of pain and depression.

**Conclusion:** Cannabis use is common among arthritis patients and may be associated with better quality of life.

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**OP0324**

**CANNABIODI ELEVATES INTRACELLULAR CALCIUM AND INDUCES APOPTOSIS IN HUMAN ARTICULAR CHONDROCYTES**


**Background:** Osteoarthritis (OA) is a major public health problem among the increasing aged and obese population, therefore development and investigation of therapeutic treatment of joint diseases has emerged.

**Objectives:** Cannaβidiol (CBD) is the most abundant non psychoactive compound of Cannabis sativa extracts and has been shown to have antiarthritic potency in animal models [2, 3]. In the present study we investigated the effects of CBD on the cell viability and Ca2+ homeostasis in human articular chondrocytes.

**Methods:** Cell viability, discrimination of intact, apoptotic and necrotic cells and caspase 3/7 activity were determined by Resazurin assay, Annexin-V/7-AAD staining followed by flow cytometry and caspase-Glo 3/7 assay respectively. Intra-cellular Ca2+ was monitored by time-lapse fluorescence imaging. The perfomed whole-cell patch clamp technique was used for measuring the cell membrane potential. Western blot analysis was performed for the quantification of Erk1/2 phosphorylation.

**Results:** C28/i2 and human primary chondrocytes showed a significantly reduced viability with an apoptosis maximum at 10μM CBD after treatment with rising amounts of CBD. This apoptotic effect was accompanied by an increase of caspase 3/7 activity. Flow cytometry analysis of AnnexinV/7-AAD stained cells revealed a decline of intact cells and a significant dose dependent increase of the early apoptotic cell population after treatment with CBD.

**Conclusion:** Cannaβidiol is a promising agent for the treatment of OA.

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**OP0323**

**USEFULNESS OF UNIVERSAL ANTINUCLEAR ANTIBODIES TESTING IN EARLY ARTHRITIS REFERRALS**

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**Background:** The CHUC Early Arthritis Clinic, founded in 2011, intends to provide a prompt response to patients with recent onset of symptoms suggestive of an inflammatory rheumatic disease (IRD). By research protocol, all patients are screened at baseline for the presence of antinuclear antibodies (ANA). An analysis was performed to evaluate the usefulness of universal ANA testing in these patients.

**Objectives:** To evaluate the prevalence and clinical correlates of ANA positivity in early arthritis referrals.

**Methods:** A retrospective study of consecutive patients referred to the Early Arthritis Clinic between 2011 and 2018 was conducted. Referral is based on the fulfillment of specific criteria: presence of arthritis or clinically suspected arthralgia beginning in the previous 12 months plus suggestive laboratory abnormalities (rheumatoid factor, C-reactive protein or erythrocyte sedimentation rate). ANA titer (positive ≥ 1:160) and cellular staining patterns were assessed by indirect immunofluorescence (Hep-2 cells). Positive (PPV) and negative predictive values (NPV) of an ANA positive test for the diagnosis of an IRD or an ANA related rheumatic disease (ARD) were determined, along with PPV for the other referral criteria.

**Results:** 207 patients were included in the analysis (64.3% female, aged 53.9 ± 18.2 years). The diagnosis of an IRD was confirmed by the rheumatologist in 61.4% of cases, including 11.8% cases of ARD. The most prevalent diagnosis was rheumatoid arthritis (21.7%), followed by unclassified arthritis (8.7%), psoriatic arthritis, osteoarthritis and fibromyalgia (6.8% each). The prevalence of ANA positivity in our cohort was 64.2%, most frequently in low titer (1:160 in 33.8%, 1:320 in 19.2%, 1:640 in 8.7% and 1:1280 in 2.4%) and with a dense fine speckled pattern (45.1%). ANA-positive patients were older (53.7 ± 17.9 versus 47.9 ± 18.5, p<0.05), more likely to have an IRD (72.9% versus 40.5%, p<0.001) but not an ARD (9.0% versus 4.1%, p=0.186). PPV for ARD was 9.0% for the 1:160 cut-off titer and 15.6% for the 1:320. Squeeze test (PPV 13.5%), erythrocyte sedimentation rate (PPV 9.9%) and rheumatoid factor (PPV 20.0%) as referral criteria, all performed better at predicting an ARD, compared to an ANA positive testing.

**Conclusion:** Early Arthritis Clinic referred cohort has a high prevalence of IRD but a low prevalence of ARD which explains the poor predictive value of ANA in this setting, especially when considering lower titers and when compared with specific referral criteria. Thus, universal ANA testing in Early Arthritis Clinic referrals seems unjustified, given its costs and added value. Studies designed to optimize the use of ANA in this context are warranted.

**Disclosure of Interests:** None declared

mediated by the CB1 receptor indicated by an increased cell viability and reduction of caspase activity after combined treatment with CBD and CB1 antagonist AM251. Since CBD induced Erk1/2 phosphorylation seems to be independent of CB1 signalling, the involvement of other signalling pathways and/or a crosstalk with other Ca2+ channels or receptors seems likely and will be the focus of further investigations.

REFERENCES:

Disclosure of Interests: None declared

SAFETY AND EFFICACY OF LENABASUM IN AN OPEN-LABEL EXTENSION OF A PHASE 2 STUDY IN DIFFUSE CUTANEOUS SYSTEMIC SCLEROSIS SUBJECTS (DCSSC)

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Background: Lenabasum is a synthetic, non-immunosuppressive, selective cannabinoid receptor type 2 agonist that activates resolution of innate immune responses and limits fibrosis in animal models of SSc. Lenabasum had acceptable safety and tolerability, and improved efficacy outcomes in the 16-week, double-blind, randomized, placebo-controlled Part A of Phase 2 trial JBT101-SSc-001 (NCT02465437) in dCSSC subjects.

Objectives: To provide long-term open-label safety and efficacy data in dCSSC subjects in study JBT101-SSc-001.

Methods: Subjects who completed Part A were eligible to receive oral lenabasum 20 mg BID in an open-label extension (OLE) that assessed safety and efficacy at 4 weeks, then every 8 weeks.

Results: 38/39 (97%) eligible subjects enrolled in the OLE, with mean interval of 134 (range 33-392) days or 19.1 weeks from end of dosing in Part A to start of OLE when subjects received only standard-of-care drugs. 34/36 (94%) subjects were on stable doses of immunosuppressive drugs. At safety data cut-off, 31/38 (81%) eligible subjects enrolled in the OLE, with mean interval of 134 (range 33-392) days (18 months) from end of dosing in Part A to start of OLE when subjects received only standard-of-care drugs. At efficacy data cut-off, 30/36 (83%) subjects had completed each.

Conclusions: Lenabasum continues to have a favorable safety and tolerability profile in the OLE of Phase 2 trial JBT101-SSc-001 with no lenabasum-related serious AEs or study discontinuations. Only 7 (19%) subjects had an AE related to lenabasum in ≥18 months of OLE dosing. ACR CRISSE score, mRSS, Physician Global Assessment, and multiple patient-reported outcomes show continued improvement, although background therapy, potential for spontaneous improvement, and open-label dosing limit what can be definitely attributed to lenabasum.

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Disclosure of Interests: None declared

Scientific Abstracts

Figure 1. Change from Baseline in Selected Efficacy Outcomes in OLE of Phase 2 Trial JBT101-SSc-001
DEVELOPMENT OF A STANDARDIZED MINIMAL CORE DATA SET FOR PREGNANCY REGISTERS IN RHEUMATOLOGY – RESULTS OF A EURAL TASK FORCE

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Background: Results from individual data collections on drug safety during pregnancy and outcomes of pregnancy in patients with inflammatory rheumatic diseases (IRD) are often limited due to small number of cases. Joint data analyses from different data sources could solve this problem.

Objectives: The aim of this EURAL task force was to define a core data set to facilitate joint analysis of pregnancy registers in rheumatology.

Methods: Scope and core areas of the core data set have been developed according to COS-STAR recommendations by consensus. An initial list of data items possibly relevant for pregnancy registers was generated based on (I) a systematic literature search, (II) data items already collected by European pregnancy registers and (III) a survey amongst patient representatives. Consensus about the importance of each data item to be included in a core data set was reached by interviews and standardized safety form. Efficacy on GI symptoms was measured using the UCL A GIT 2.0 score questionnaire. Patients were defined as responders if reported symptom improvement was equivalent to the UCL A GIT definition of “minimally clinically important difference”. Secondary and explorative endpoints included changes in relative abundance of total, immunoglobulin (Ig)A- and IgM-coated fecal bacteria measured by 16s rRNA sequencing; changes in modified Rodnan skin score, lung function, CRP, ESR, and patient and physician global. Descriptive statistics were applied for clinical endpoints and linear mixed models for microbial analysis.

Results: Ten patients with limited cutaneous SSC randomized to ACHIM (n=5) or placebo (n=5) were included. All patients were female with clinical apparent GI symptoms, mean age of 62 years and mean time from diagnosis of 12 yrs. Two placebo controls experienced procedure-related serious adverse events; one developed laryngospasms at first gastroduodenoscopy necessitating study exclusion and one duodenal perforation at final gastroduodenoscopy. Improvement in total GIT score was reported by 3/5 FMT patients compared to 2/4 placebo controls at weeks 4 and 16 (Figure 1). FMT effects were most pronounced on lower GI symptoms, with improvement reported by 3/5 FMT patients with diarrhea, distention/ bloating and/or fecal incontinence compared to baseline at 2/4 placebo controls (Figure). Clinical secondary endpoints showed no differences and other side effects (stomach discomfort, bloating and diarrhea) were mild and transient. Fecal microbiota diversity (observed number of operational taxonomic units) was increased after FMT compared to placebo treatment at week 16 (p<0.006). Moreover, abundant bacterial genera in ACHIM were present within the total, and IgA- and IgM-coated fecal bacteria at both week 4 and 16 in the FMT group (Figure) but not in the placebo controls.

Conclusion: The consensus process resulted in an extensive list of data items recommended by experts to be collected as a minimum by pregnancy registers in rheumatology. This core data set applies to all pregnant women irrespective of the underlying IRD. The EURAL task force plans to find consensus on additional disease specific advice.
Conclusion: FMT of commercially-available ACHIM in patients with SSc appeared safe, effectively reduced lower GI symptoms, altered gut microbiota composition, richness and diversity and appeared to affect the mucosal immune system.

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Calming the cytokine storm in children and adults_
Remission – the holy grail? Looking across diseases.

**CONTRAST OF THE EFFECTS OF DORIS REMISSION AND LUPUS LOW-DISEASE ACTIVITY STATE (LLDAS) ON DISEASE OUTCOMES IN A MULTINATIONAL PROSPECTIVE STUDY**


**Background:** The Definitions of Remission in SLE (DORIS) group has proposed multiple definitions of remission, but these are infrequently attained and have not been prospectively evaluated in relation to protection from damage accrual. In contrast, the Lupus Low Disease Activity State (LLDAS) is more attainable, and has been shown to be associated with improved patient outcomes.

**Objectives:** To compare the attainability, variability, and outcomes, of LLDAS and remission in a prospective multicentre study.

**Methods:** A prospective multinational cohort study was undertaken in 13 centres between 2013-2017. Time dependent Cox proportional hazards models were used to compare LLDAS and DORIS definitions of remission in terms of impact on disease flares and damage accrual.

**Results:** 1735 SLE patients were recruited, and followed for (mean±SD) 2.2±0.9 years, totalling 12,717 visits. LLDAS was achieved in 47.2% of observed visits. In contrast, remission was achieved in 1.1%±15.4% of visits depending on the stringency of remission definition. LLADS attainment at any visit was associated with significantly reduced subsequent flare (HR 0.65, 95%CI 0.56-0.75, p<0.001) and damage accrual (HR 0.59, 95%CI 0.45-0.76, p<0.001). In contrast, only the least stringent remission definition was associated with reduced damage accrual (HR 0.58, 95%CI 0.39-0.79, p<0.001). Only remission definitions including serological remission were significantly associated with reduction in subsequent flares. Patients who spent >50% of their observed time in LLDAS had reduction in damage accrual (HR 0.54, 95% CI 0.40-0.70, p<0.001) compared to patients with <50% of observed time in LLADS; again, only the least stringent remission definition, or the related definition excluding serology, were associated with reduced damage (HR 0.59, 95% CI 0.45-0.76, p<0.001; HR 0.59, 95% CI 0.40-0.83, p<0.001; HR 0.69, 95% CI 0.48-0.99, p<0.05, respectively).

**Conclusion:** LLDAS was more attainable than any remission definition, whilst still conferring significant reduction in flares and damage accrual. Only the least stringent remission definitions could be shown to be associated with significantly lower damage accrual, likely reflecting a low frequency of remission attainment overall. LLDAS is a valid treatment target for SLE and is more achievable than remission.

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**Background:** Progression of structural joint damage occurs in 20-30% of patients with rheumatoid arthritis (RA) in clinical remission1. Magnetic resonance imaging (MRI)-detected synovitis and in particular osteitis/bone marrow edema (BME) are known predictors of structural progression in both active RA and in remission, but the predictive value of adding MRI tenosynovitis assessment as potential predictor in patients in clinical remission has not been investigated.

**Objectives:** To investigate the predictive value of baseline MRI inflammatory and damage parameters on 2 year MRI and X-ray damage progression in an RA cohort in clinical remission, following MRI and conventional treat-to-target (T2T) strategies.

**Methods:** 200 RA patients in clinical remission (DAS28-CRP<3.2 and no swollen joints) on conventional DMARDs, included in the randomized IMAGINE-RA trial2 (conventional DAS28 + MRI-guided T2T strategy targeting absence of BME vs conventional DAS28 guided T2T strategy) had baseline and 2 years contrast-enhanced MRIs of the dominant wrist and 2nd-5th MCP joints and X-rays of hands and feet performed, which were evaluated with known chronology by two experienced readers according to the OMERACT RAMRIS scoring system and Sharp/ van der Heijde method, respectively.

The following potentially predictive baseline variables: MRI BME, synovitis, tenosynovitis, MRI and X-ray erosion and joint space narrowing (JSN) score, CRP, DAS28, smoking status, gender, age and patient group were tested in univariate logistic regression analyses with 2-year progression in MRI combined damage score, Total Sharp Score (TSS), and MRI and X-ray JSN and erosion scores as dependent variables. Variables with p<0.1, age, gender and patient group were included in multivariable logistic regression analyses with backward selection. 

**Results:** Based on univariate analyses MRI BME, synovitis, tenosynovitis, x-ray erosion and JSN, gender and age were included in subsequent multivariable analyses. Independent MRI predictors of structural progression were BME (MRI progression) and tenosynovitis (MRI and X-ray progression), see table.

<table>
<thead>
<tr>
<th>Dependent variables, progression ≥ 1 from baseline to month</th>
<th>24a</th>
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<tbody>
<tr>
<td>MRI</td>
<td>X-ray</td>
</tr>
<tr>
<td>Erosion</td>
<td>MRI combined damage score</td>
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<tr>
<td>Exploratory MRI BME</td>
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<tr>
<td>variables</td>
<td>(1.21)</td>
</tr>
<tr>
<td>MRI</td>
<td>1.13</td>
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<td></td>
<td>(1.25)</td>
</tr>
<tr>
<td>Age</td>
<td>0.96</td>
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</table>

* Odds Ratio (95% confidence interval; CI) p-value: MRI combined damage score: sum score of MRI erosion and JSN scores.
Conclusion: This is the first to report that MRI tenosynovitis independently predicts both X-ray and MRI damage progression in RA patients in clinical remission. Further studies are needed to confirm MRI-determined tenosynovitis as predictor of progressive joint destruction in RA clinical remission.

REFERENCES:

Acknowledgement: AbbVie for financial study support

Disclosure of Interests: Signe Møller-Bisgaard Grant/research support from: Grants and non financial support from AbbVie during the conduct of the study, Speakers bureau: BMS, Kim Harlsvik-Petersen Grant/research support from: AbbVie during the conduct of the study, Bo Ejbjerg: None declared, Merete L. Helland Grant/research support from: BMS, MSD, AbbVie, Roche, Novartis, Biogen, Pfizer, Consultant for: Eli Lilly, Speakers bureau: Ono Pharma, Biogen, Pfizer, CellTrion, Merck, Samsung Biospies, Lykke Ørnbjerg Grant/research support from: Unrestricted grant; Novartis, Daniel Climatis: None declared, Jakob Møllenbach Møller: None declared, Mikael Boesen Grant/research support from: Image Analysis Group, Eli Lilly, UCB, AbbVie, Esaote, Kristian Stengaard-Pedersen: None declared, Ole Madsen Grant/research support from: Sobi, AbbVie, Merck Sharp and Dohme, Pfizer, Eli Lilly, Celgene, Novartis, UCB, Sanofi Aventis, Roche, Angen and BMS, Bente Borch: None declared, Jan Villadsen: None declared, Ellen Margrethe Hauge Grant/research support from: Have received grants from Roche and Novartis, outside the submitted work, Speakers bureau: Have received personal fees from MSD, Pfizer, UCB and Sobi, Philip Bennett Grant/ research support from: Eli Lilly, Merck Sharp and Dohme, Novartis, Olve Henri-dricks Grant/research support from: AbbVie, Novartis, Karsten Asmussen: None declared, Marcin Kowalski: None declared, Hanne Merete Lindegaard: None declared, Hennig Bliiddal Grant/research support from: AbbVie, Oak Foundation, Niels Steen Krogh: None declared, Torkell Ellingsen: None declared, Agnete Nielsen: None declared, Lone Balding: None declared, Anne Grethe Jørk: None declared, Henrik Thomsen: None declared, Mikkel Østergaard Grant/research support from: Abbvie, Celgene, Centocor, Merck, Novartis, Consultant for: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, Speakers bureau: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, Statistical and synovial biopsies were obtained from 11 OA patients undergoing joint analysis were performed to analyze C3, C4 and CFB expression. Cartilage pathol-...
WHAT SEROLOGIC PROFILING PROVIDES OPTIMAL ENTRY CRITERIA FOR SYSTEMIC LUPUS ERYTHEMATOSUS CLINICAL TRIALS?

Ewa Olech1, Eduard van Rijen1, Alexander Kant1, Ali Ashrafzadeh1, Joan T Merrill2.

1IQVIA, Durham, United States of America; 2Oklahoma Medical Research Foundation, Oklahoma City, United States of America

Background: A major concern for SLE clinical trials is the possibility that some patients who technically meet entry criteria may not have active disease. Antinuclear antibody (ANA) is known to lack specificity for SLE, permitting inclusion of inappropriate patients. Typically, ANA ≥ 1:80 and/or positive anti-double stranded DNA (DNA) are required screening elements, but largely other autoantibody variables have been utilized.

Objectives: To examine serologic features that promote entry of active SLE patients into trials while supporting reasonable recruitment rates.

Methods: Serologic features of 1411 individual subjects who had full laboratory data at screening (N = 783) and/or baseline (N = 1019) in 4 phase 2 multicenter SLE trials were examined. Complement levels, percent of patients with low C3 or C4, and elevated DNA were used as markers of active disease. Serological profiles consistent with active SLE were tested on screened population for effects on potential screen failure rates.

Results: Of 1019 patients who qualified for the studies (baseline population), 399 (39.2%) were positive for DNA and 670 (65.8%) had anti-Extractable Nuclear Antibodies (ENA). Patients with positive DNA or ENA (even in absence of DNA) had lower complement levels and were more likely to have low C3/C4 (Table 1). In patients at screening, higher titers of ANA were associated with lower complement levels and were more likely to have low C3/C4, and elevated DNA were used as markers of active disease. Serological profiles consistent with active SLE were tested on screened population for effects on potential screen failure rates.

Conclusion: The following entry criteria may help increase the likelihood that trial subjects have active SLE: ANA ≥ 1:640, or DNA, or low C3 or C4. To the extent that a modest loss of recruitment increases the probability of entering true, active SLE patients, these alternative constructs should be considered in future SLE trials.

Disclosure of Interests: : Ewa Olech Grant/research support from: Bristol Myers Squibb, Eduard van Rijen: None declared, Alexander Kant: None declared, Ali Ashrafzadeh Employee of: Employee of IQVIA, Joan T Merrill Grant/research support from: Genentech, UCB, GSK, EMD Serono, Pfizer, Celgene, Exagen, Bristol Myers Squibb, MedImmune/AstraZeneca, Lilly, Agen, Xencor, Neovacs, Consultant for: Genentech, UCB, GSK, EMD Serono, Pfizer, RemeGen, Celgene,
A PROSPECTIVE CLINICAL AND MRI STUDY OF COMMONLY USED DRUGS IN RHEUMATOLOGY MAY ALTER ANTI-TUMORAL RESPONSE TO IMMUNE CHECKPOINT INHIBITORS

Marie Kosting, Eleonora Mauric, Thomas Barmetche, Léa Rouxel, Caroline Dutiaux, Léa Dousset, Sorlits Frey, Marie Beylot-Barré, Julien Seneschal, Rémi Veillon, Charlotte Vergnenegre, Amaury Daste, Charlotte Domblices, Baptiste Sionneau, Marine Gouz-Goupil, Alain Ravaud, Edouard Forcade, Bernard Barnwarth, Marie-Elise Truchetel, Christophe Richez, Nadia Merssen-Cetie, Thierry Schaeverbeke, on behalf of the FHU ACRONIM, Bordeaux University Hospital, Bordeaux, France

Background: Immune checkpoint inhibitors (ICls) are revolutionizing the treatment of some advanced cancers. Gut microbiota has emerged as an important component of anti-tumoral response and can also be related to the occurrence of immune-related adverse events (irAEs). It has recently been shown that antibiotic treatment given at the initiation of ICI therapy had a dramatic impact on microbiota that compromised the anti-tumoral effect of ICls (1).

Objectives: To evaluate whether co-medications known to have a potential impact on gut microbiota may alter ICI efficacy and/or irAE occurrence when given at ICI onset.

Methods: This was a retrospective cohort study including all cancer patients who received ICIs at our institution from May 2015 to September 2017. Co-medications given to the patients within one month before or one month after the first administration of ICI were extracted from medical records on the basis of a predefined list of medications known to impact gut microbiota. The tumour response, occurrence of irAEs and patient outcomes were assessed on a regular basis. Overall survival (OS) has been considered from the start of ICI therapy.

Results: 635 patients (70% male, mean age 64.5 years) were included, of whom 293 had melanoma, 150 had advanced non-small cell lung cancer and 83 had renal carcinoma. A previous autoimmune disorder was present in 8% of patients, mainly rheumatic and endocrine diseases. Psychotropic drugs (41.1%), proton pump inhibitors (PPIs) (37.3%), angiotensin-converting enzyme (ACE) inhibitors and/or angiotensin II receptor blockers (ARBPs) (32%), glucocorticoids (GC) (24.2%), antibiotics (21.4%), statins (20.8%) and morphine (20.6%) were the most co-prescribed medications. Baseline GC use, when >10mg of prednisone equivalent, was associated with a significant decrease in OS (median 4.5 months versus 24.3 months; p=0.0001) and a less frequent tumour response (55% versus 73%; p=0.0001). When given after ICI onset for the management of irAEs, GC did not influence ICI efficacy (Figure A). Baseline PPIs use also altered both OS (median 10.9 versus 24.3 months; p=0.0001) and tumour response (62% versus 71%; p=0.02) (Figure B). We confirmed the detrimental impact of antibiotics when given at ICI onset, and also found worse outcomes for patients receiving baseline psychotropic drugs (median OS 9.3 versus 19.4 months; p=0.0001). No significant difference was observed with baseline use of NSAIDs, aspirin, statins and ARBs/ACE. Furthermore, co-medication with antibiotics, GC, PPIs, morphine, NSAIDs, aspirin and psychotropic drugs was associated with decreased occurrence of irAEs.

Conclusion: As many of these treatments are used by rheumatologists, one should be aware of their potential detrimental effect when used at ICI initiation, that sometimes could have been avoided.

ORTHOTIC TREATMENT: IS IT IN OR OUT?

Hilda Oliveira, Anamaria Jones, Fabio Jennings, Mariana Vassallini, Andre Rosenfeld, Jamil Natour. Universidade Federal de São Paulo, São Paulo, Brazil

Background: Morton’s neuroma (MN) is a benign enlargement of the third common digital branch of the medial plantar nerve. The most common symptom is buming pain in the plantar foot, located between the metatarsal heads, often radiating to the two corresponding toes. Treatment can be surgical or conservative, which consists of decreasing nerve pressure and irritation through therapies that promote analgesia, patient education, and plantar orthosis. The custom insole prescriptions are aimed at relieving the pressure in the MN region, and to redistribute pressure throughout the sole of the foot. There is no study evaluating the effect of insoles in patients with MN.

Objectives: The aim of the present study was to assess the effectiveness of a customized insole with metatarsal and arch support on pain in patients with Morton’s neuroma and the impact of this insole on function, load distribution in the plantar region, gait, quality of life and satisfaction with insole use.

Methods: A randomized, controlled, double-blind, clinical trial was carried out with intent-to-treat analysis. Seventy-two patients with MN were randomly allocated into a study group (n=36) and control group (n=36). One week following the baseline evaluation, the study group received a customized insole with metatarsal and arch support made of ethyl vinyl acetate and the control group received a flat insole of the same material, color and density. The groups were evaluated after 6, 12 and 24 weeks of insole use. The following assessment parameters were employed: pain when walking, on palpation and at rest (END); paresthesia (ENP); quality of life (SF-36); foot function (FFI and FHSQ); six-minute walk test (6MWT) and foot pressure analysis using the AM Cube FootWalk Pro program.

Results: The groups were homogeneous regarding the majority of variables at baseline. In the comparisons over time, statistically significant differences between the groups were found for pain when walking (p=0.048), in the general health of the foot) and quality of life (limitation by physical aspects, bodily pain and vitality), we observed improvement in both groups with no statistically significant difference between them. No change was observed in the baropodometry parameters with the use of the insole.

Conclusion: A customized insole with metatarsal and arch support reduce pain when walking and improve function of patients with MN.

REFERENCES:

Disclosure of Interests: None declared

CURRENT TREATMENT OF VASCULITIS

Xiaoning Liu, Gejin Chen. The Second Hospital of Shanxi Medical University, Department of Rheumatology, Taiyuan, China

Background: The lack of CD4+CD25+Foxp3+ T regulatory cell (Treg) has been associated with human systemic autoimmune diseases, such as rheumatoid arthritis (RA). IL-2 is an essential growth and survival factor for Treg cells. However, the significance of Treg cells in the pathogenesis and the effect of low dose IL-2 on Behcet’s disease (BD) are rarely reported.

OBJECTIVES: To investigate the significance of Treg cells and the effect of low dose IL-2 on BD.

Methods: Eighty patients with BD and seventy healthy donors were enrolled. CD4+ T cell subsets in peripheral blood mononuclear cells from these people were measured by multicolour flow cytometry. Twenty-six patients were treated daily with subcutaneous injections of 0.5 million IU of human IL-2 for five consecutive days. CD4+ T cell subsets were analysed before and after treatment by flow cytometry.

Results: Compared to health control, the absolute counts of circulating Treg cells were significantly decreased in patients with BD (median:29.93 cells/ul VS median:33.16 cells/ul, P=0.039) and it is negative correlation with disease activity. While the ratios of TH17/Treg in patients with BD (median:0.29) were significantly higher than those of health control (median:0.2). No difference in the absolute counts of circulating TH17 cells (CD4+IL-17) between patients with BD and health control. Treatment of patients with BD with a low-dose IL-2 selectively increased the absolute counts of Treg cells, from a median of 18.97 cells/ul to 74.88 cells/ul (at 5 days) (P<0.001). No significant difference was observed in the absolute counts of circulating TH17 cells after IL-2 treatment.

Conclusion: TH17/Treg cells may play a role in the pathogenesis of patients with BD, low-dose IL-2 proposes a selective biological treatment strategy by restoring immune tolerance.

REFERENCES:

Disclosure of Interests: None declared

LOW-DOSE IL-2 SELECTIVELY RESTORES REGULATORY T CELLS IN PATIENTS WITH BEHÇET’S DISEASE

Xiaoning Liu, Gejin Chen. The Second Hospital of Shanxi Medical University, Department of Rheumatology, Taiyuan, China

Background: The lack of CD4+CD25+Foxp3+ T regulatory cell (Treg) has been associated with human systemic autoimmune diseases, such as rheumatoid arthritis (RA). IL-2 is an essential growth and survival factor for Treg cells. However, the significance of Treg cells in the pathogenesis and the effect of low dose IL-2 on Behcet’s disease (BD) are rarely reported.

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Conclusion: TH17/Treg cells may play a role in the pathogenesis of patients with BD, low-dose IL-2 proposes a selective biological treatment strategy by restoring immune tolerance.

REFERENCES:

Disclosure of Interests: None declared
was similar in both groups. And in terms of side effects no significant difference was seen between TZZ as monotherapy or combined with conventional immunosuppressants.

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<tbody>
<tr>
<td>TZZ IN MONOTHERAPY</td>
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<tr>
<td>(mg/day)</td>
</tr>
<tr>
<td>BAZAL FEATURES AT TZZ-DIRECT</td>
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<tr>
<td>GENERAL FEATURES</td>
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<tr>
<td>Age, years (mean SD)</td>
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<tr>
<td>Sex, female/male (%)</td>
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<tr>
<td>Time from SCAD to diagnosis (%)</td>
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<tr>
<td>SYMPTOMATIC MANIFESTATIONS</td>
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<tr>
<td>Fever, %</td>
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<td>Constitutional symptoms, %</td>
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<tr>
<td>ANA</td>
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<tr>
<td>ISCHEMIC MANIFESTATIONS</td>
</tr>
<tr>
<td>Visual disturbance, %</td>
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<tr>
<td>Nausea, %</td>
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<tr>
<td>( ^{2} ) Adolescents and Young Adults ( ^{2} ) (13-18)</td>
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<tr>
<td>ADVERSE EVENTS</td>
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<tr>
<td>ESR</td>
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<td>CRP</td>
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<tr>
<td>Hemoglobin, g/dl</td>
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<tr>
<td>Principal safety events</td>
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</table>

Conclusion: Patients receiving combined conventional immunosuppressants with TZZ in the clinical practice study showed a higher prolonged remission. The incidence of serious infections and/or relevant adverse events was not affected according to the treatment. As well as the corticoid-sparing effect was achieved in the same way in both groups.

REFERENCES:

SATURDAY, 15 JUNE 2019
Workshop: #ConnectToday and tomorrow: The campaigning continues.

OP0340-PARE #SEE ME – RAISING AWARENESS AND UNDERSTANDING OF JUVENILE IDIOPATHIC ARTHRITIS IN IRELAND

Brian Lynch, Arthritis Ireland, Dublin, Ireland

Background: For those living with juvenile idiopathic arthritis (JIA), it is a doubly confounding condition. The popular perception that arthritis is an old person’s disease leaves little room for understanding that children can also get the disease in its impact. There are 1,200 children and young people under 16 living with JIA in Ireland.

In this campaign, Arthritis Ireland sought to capture people’s attention by subverting typical associations around arthritis. The campaign had to speak to and draw upon youth culture. Once people’s attention was captured, this created an opportunity to communicate key pieces of information about the disease and highlight the challenging situation regarding access to Irish paediatric rheumatology services.

Objectives:
- To raise awareness that children and young people can get arthritis;
- To increase awareness and understanding of what it’s like to live with JIA;
- To increase political support for the provision of enhanced paediatric rheumatology services.

Methods: #SeeMe was launched during Ireland’s National Arthritis Week (9-15 April 2018) and encompassed social media, public affairs and media relations. A key element of the campaign was the creation of a unique media asset, a short music video, which would speak directly to young people and encourage them to get involved in the campaign. The video communicated how JIA can impact enjoyable, everyday teenage activities such as dancing. A dedicated microsite was created which housed all of the campaign assets.

A campaign petition called on the Government to implement the Model of Care for Paediatric Rheumatology. It was extremely successful, gathering more than 17,000 signatures and far exceeding the target of 5,000. The petition also harvested powerful testimony from supporters who were able to share their own stories of living with JIA.
Personal patient stories were leveraged throughout the campaign by the involvement of #SeeMe Ambassadors. These were children and young people living with JIA who were willing to share their experience publicly. National and regional media were successfully targeted, securing considerable coverage. Subsequently, the campaign progressed to a third phase of activity as young people raised awareness of JIA through their own schools, social clubs and social media networks.

An infographic was developed to communicate key medical information about JIA and paediatric rheumatology services in a clear, accessible way.

Results: 

• 87,000 people viewed the campaign video;
• 17,000 people signed the #SeeMe petition;
• 820,000 people were reached by the social media campaign;
• 35 pieces of media coverage on television, radio and print were achieved;
• Lobbying of politicians by patients and their families prompted 12 TDs and senators to raise this issue;
• In May 2018, the Government committed to the appointment of an additional paediatric rheumatologist in 2019, with plans to recruit a multidisciplinary team.

Conclusion: This campaign set out to give a voice to those living with JIA and to increase awareness and understanding of the disease. The campaign highlighted the challenges in paediatric rheumatology services and proved an effective vehicle in harnessing public opinion; resulting in over 17,000 people signing the petition calling for the implementation of the Model of Care for Paediatric Rheumatology.

In the wake of the campaign, the announcement by the Irish Government to invest in paediatric rheumatology services represents an important step forward. While much remains to be done, this is progress and highlights the important role played by patient organisations, and their public education and advocacy work.

Disclosure of Interests: None declared


SATURDAY, 15 JUNE 2019

Tackling inflammatory bone disorders in children and adults

OP0342

IDENTIFYING CANDIDATE ITEMS TOWARDS THE DEVELOPMENT OF CLASSIFICATION CRITERIA FOR CHRONIC NONBACTERIAL OSTEOMYELITIS (CNO) AND CHRONIC RECURRENT MULTIFOCAL OSTEOMYELITIS (CRMO)

Melissa Oliver1, Eveline Wu2, Raymond Naden3, Matthew Hollander4, Polly Ferguson5, Fatma Dedegul7, Seza Özen, Yongdong Zhao1, 2. 1Riley Hospital for Children at Indiana University Health, Indianapolis, United States of America; 2University of North Carolina at Chapel Hill, Chapel Hill, United States of America; 3University of Iowa Stead Family Children’s Hospital, Iowa City, United States of America; 4University of Vermont Children’s Hospital, Burlington, United States of America; 5University of Iowa Stead Family Children’s Hospital, Iowa City, United States of America; 6Boston Children’s Hospital, Boston, United States of America; 7Hacettepe University, Ankara, Turkey; 8Seattle Children’s Hospital, Seattle, United States of America

Background: Chronic nonbacterial osteomyelitis (CNO) is a severe and occult autoinflammatory bone disease of unknown cause. Early diagnosis is challenging, and CNO may debilitate affected children when left untreated. Currently, evidence-based and validated diagnostic and classification criteria for CRMO/CNO are lacking. The insidious disease course, increasing disease incidence, and significant delay in diagnosis highlight the need for the development of classification criteria that leads to more precise and early selection of patients for clinical trials. 1, 2

Objectives: To identify candidate items towards developing classification criteria for CNO using anonymous survey and nominal group technique.

Methods: An international collaborative effort was formed within the pediatric and adult rheumatology communities to conduct the following phases: 1) to generate candidate criteria items by a Delphi survey among international rheumatologists; 2) to reduce candidate criteria items through consensus processes involving physicians managing CNO and patients or caregivers of children with CNO. This study was approved by Seattle Children’s Hospital Institutional Review Board.

Results: In Phase 1, 259 pediatric rheumatologists (30%, N=865) participated in an online questionnaire about features most relevant to the classification of CNO. Of those, 77 (30%) practiced in Europe, 132 (51%) in North America, and 50 (19%) in other continents. A total of 138 (53%) responders had >10 years of practice experience and 106 (42%) had managed >10 CNO patients. There were 33 candidate criteria items initially identified. In Phase 2, candidate items were presented to 39 rheumatologists and 7 parents and items were refined or eliminated through item reduction techniques. Seventy-seven (94%, N=82) workgroup members then participated in a second survey to rank the remaining items by their distinguishing power of CNO from mimicking conditions. Figure 1 shows the mean score for the remaining 31 candidate criteria. Multifocal lesions, ruling out malignancy and infection and typical location on imaging had the greatest means. CRP and/or ESR greater than 3x the normal upper limit had the greatest negative means.

Discriminatory Score: +3/-3 (increases/decreases the likelihood of CRMO the most)
+2/-2 (increases/decreases the likelihood of CRMO moderately)
+1/-1 (increases/decreases the likelihood of CRMO slightly)
0 (no difference)

Conclusion: Through surveys and consensus technique, candidate items towards developing classification criteria for CNO were identified. This list of items will guide the design of a feasible patient data collection form towards weighting of each item in the classification criteria.

REFERENCES:


Acknowledgement: CNO/CRMO Work Group, Childhood Arthritis and Rheumatology Research Alliance

Disclosure of Interests: Melissa Oliver: None declared. Eveline Wu: None declared. Raymond Naden Speakers bureau: Was a speaker at conferences paid by pharmaceutical companies several times in the past, but not in the last 7 years., Matthew Hollander: None declared. Polly Ferguson: None declared. Fatma Dedegul Consultant for: Attended a scientific meeting for Novartis in 2017. Overall monetary amount was less than $5000., Seza Özen Consultant for: Seza Özen is receiving consultancy fees from Novartis, Speakers bureau: Roche, Yongdong Zhao Grant/research support from: I have grant support from Bristol-Myr-Squibb

LONGITUDINAL ASSESSMENT OF MRI OF THE SACROILIAC JOINTS IN THE ASAS CLASSIFICATION COHORT: EVOLUTION OF DIAGNOSTIC FEATURES AND PREDICTIVE UTILITY FOR AXIAL SPONDYLOARTHRITIS

Walter P Maksymowych1, 2, Xenofon Baraliakos3, Anna Ghadir2, Martin Fruhth2, Uta Kiltz1, Juergen Braun1.

Background: Follow up of the ASAS Classification Cohort (CC) indicated a high positive predictive value for the CC criteria derived from baseline patient and imaging data. Moreover, diagnosis of axSpA was changed by the rheumatologist in only 11.2% of patients after 4.4 years. This has raised potential concerns regarding diagnostic ascertainment bias.

Objectives: To determine the evolution of MRI features of axSpA in ASAS-CC cases by central readers, whether this reflects diagnostic assignment by the rheumatologist, and the predictive utility of baseline MRI features of axSpA.

Methods: MR images were available from 108 cases in the ASAS-CC at baseline and follow up (mean 4.4 years) and also had a rheumatologist diagnostic assessment at both time points. Eight readers from the ASAS MRI group recorded MRI lesions that were quantified by the ASAS MRI group. MRI data from >2 readers and from the majority of readers (≥5/8) was used to calculate positive and negative predictive values (PPV, NPV).

Results: MRI was considered diagnostic of axSpA in 52/108 (48.1%) cases at baseline and in 47/86 (54.7%) diagnosed at baseline as axSpA by the rheumatologist. Change in MRI diagnosis was recorded in 10/108 (9.3%) of cases (2 from yes to no, and 4 from no to yes for axSpA) according to agreement by ≥2 readers and in only 3 cases according to >5/8 readers (Table 1). Change in rheumatologist diagnosis was recorded in 9/108 (8.3%), 2 of which had a change in MRI diagnosis. Baseline MRI lesions considered typical of axSpA had very high PPV for follow up diagnosis of axSpA (Table 2).

Conclusion: The infrequent change in diagnostic ascertainment of rheumatologists over follow up of the ASAS-CC is supported by this central reader evaluation of MRI scans. A positive MRI at baseline had very high PPV for a follow up diagnosis of axSpA.

REFERENCE:

Disclosure of Interests: Walter P Maksymowych Grant/research support from: Abbvie, Pfizer, Janssen, Novartis, Consultant for: Abbvie, Eli Lilly, Boehringer, Galapagos, Janssen, Novartis, Pfizer and UCB Pharma; Chief Medical Officer for Canadian Research and Education Arthritis, Xenon Baraliakos Grant/research support from: Abbvie; Boehringer Ingehelm, Bristol-Myers Squibb, Celgene, Centocor, Chuagli, Janssen, MSD, Novartis, Pfizer Inc Roche and UCB, Grant/ research support from: Abbvie, Pfizer, Merck Sharp & Dohme, UCB Pharma, Novartis, Consultant for: Abbvie, Bristol-Myers Squibb, Boehringer Ingehelm, Celgene, Chuagli, Janssen Biologics, Novartis, Pfizer, UCB Pharma, Galapagos, Speakers bureau: Abbvie, Chuagli, Janssen, Novartis, Pfizer, UCB Pharma, Manouk de Hooge: None declared, Iris Eshed: None declared, Susanne Juher Peden- sen: None declared, Ulrich Weber Consultant for: Abbvie, Joachim Sieper Consultant for: Abbvie; Boehringer Ingehelm, Janssen, Lilly, Merck, Mylan, Novar- tis, Pfizer, UCB., Speakers bureau: Abbvie, Boehringer Ingehelm, Janssen, Lilly, Merck, Mylan, Novartis, Pfizer, UCB., Stephanie Wichuk: None declared, Denis Poddubnyy Grant/research support from: Abbvie, Merck Sharp & Dohme, Novartis, Consultant for: Abbvie, Bristol-Myers Squibb, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, UCB Pharma, Speakers bureau: Abbvie, Bristol-Myers Squibb, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, Roche, UCB Pharma, Joel Paschke: None declared, Robert G Lambert Consultant for: Bionorica, Par- exel, Abbvie, Mikkel Østergaard Grant/research support from: Abbvie, Celgene, Centocor, Merck, Novartis, Consultant for: Abbvie, BMS, Boehringer-Ingehelm, Celgene, Eli Lilly, Hospis, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regen- eron, Roche, and UCB, Speakers bureau: Abbvie, BMS, Boehringer-Ingehelm, Celgene, Eli Lilly, Hospis, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regen- eron, Roche, and UCB


OP0344 WHICH MAGNETIC RESONANCE IMAGING LESIONS OF THE SACROILIAC JOINTS ARE OF DIAGNOSTIC VALUE FOR AXIAL SPONDYLOARTHRITIS?

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2Radiologie Herne, Herne, Germany

Background: Classification of patients as having axial spondyloarthritis (axSpA) by the imaging arm of the ASAS criteria relies partly on the detection of bone marrow edema (BME) suspicious of SpA on magnetic resonance imaging (MRI) of the sacroiliac joints (SIJ). Fatty lesions (FL) and erosions on SIJ-MRI have been sug- gested to be genuinely related to SpA in the context of interpretation of a ‘positive’ MRI in case of doubtful BME cases (1).

Objectives: Evaluate the role of different SIJ-MRI lesions for diagnosing axSpA in daily routine practice.

Methods: Consecutive patients with chronic back pain (duration >3 months) starting before age 45 and clinical suspicion of axSpA underwent a complete diagnostic workup including SIJ-MRI. All clinical, laboratory and imaging data were available to experienced rheumatologists for diagnosing axSpA or not (non-SpA). In parallel, two experienced readers, blinded to all patients’ information and diagnosis, evaluated the MRIs and made a diagnostic judgement based only on imaging. Furthermore, radiologists quantitatively assessed MRIs for BME (Berlin Score), FL, erosions, sclerosis and ankylosis. Results: A total of 300 consecutive patients were recruited. AxSpA was diag- nosed by the rheumatologist in 131 patients (43.7%) with mean age of 34.5±7.2 years, 73% HLA-B27+, mean symptom duration 35.6±9.5 months, vs. 169 non- SpA patients with mean age of 34.7±7.4 years, 21% HLA-B27+, mean symptom duration 33.9±45.1 months. The ASAS classification criteria were fulfilled by 99/ 131 patients diagnosed with axSpA (75.6%) vs. 70/169 patients diagnosed vs. non-SpA non-SpA (41.4%).
In 97/162 patients, rheumatologists and radiologists agreed on a diagnosis of axSpA and non-SpA (overall agreement: 86.3%). However, 34/131 (28.1%) patients were diagnosed by axSpA by rheumatologists but not by radiologists. According to radiologists, BME alone was critical for diagnosis in only 7/97 patients (7.2%) with axSpA as agreed by both, rheumatologists and radiologists, in contrast to chronic lesions alone (30/97, 30.9%) or the combination of both lesion types (60/97, 61.9%).

While the sensitivity of BME for diagnosing axSpA did not change, the specificity improved when chronic lesions were also present (Tab.1). In addition, based on rheumatologists’ diagnosis, the respective odds ratio (OR) for identifying axSpA by MRI was higher when chronic lesions were present (Tab.1). MRI scores were significantly higher in axSpA vs. non-SpA patients, indicating that axSpA is associated with deeper BME or chronic lesions (Tab.2).

### Table 1. Odds ratios for MRI lesions and combinations used for diagnosing axSpA.

<table>
<thead>
<tr>
<th>Lesion type</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>OR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BME</td>
<td>72.5%</td>
<td>63.3%</td>
<td>4.6</td>
<td>2.8-7.5</td>
<td>0.001</td>
</tr>
<tr>
<td>BME + any chronic lesion</td>
<td>71.8%</td>
<td>72.8%</td>
<td>16.0</td>
<td>7.5-34.0</td>
<td>0.001</td>
</tr>
<tr>
<td>FL</td>
<td>56.5%</td>
<td>89.3%</td>
<td>10.9</td>
<td>6.0-19.8</td>
<td>0.001</td>
</tr>
<tr>
<td>Erosion</td>
<td>59.5%</td>
<td>88.8%</td>
<td>11.6</td>
<td>6.4-21.0</td>
<td>0.001</td>
</tr>
<tr>
<td>Arkylosis</td>
<td>81.7%</td>
<td>43.2%</td>
<td>3.4</td>
<td>2.0-5.8</td>
<td>0.001</td>
</tr>
<tr>
<td>BME + FL</td>
<td>36.6%</td>
<td>95.3%</td>
<td>11.6</td>
<td>5.3-25.7</td>
<td>0.001</td>
</tr>
<tr>
<td>BME + Erosion</td>
<td>48.9%</td>
<td>94.1%</td>
<td>15.2</td>
<td>7.4-31.4</td>
<td>0.001</td>
</tr>
<tr>
<td>BME + Arkylosis</td>
<td>64.1%</td>
<td>75.1%</td>
<td>5.3</td>
<td>3.2-11.2</td>
<td>0.001</td>
</tr>
<tr>
<td>BME + FL + Arkylosis</td>
<td>3.3±3.6</td>
<td>8.1±1.3</td>
<td>0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erosion + Arkylosis</td>
<td>5.2±6.8</td>
<td>5.0±1.9</td>
<td>0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arkylosis</td>
<td>4.5±5.4</td>
<td>4.0±1.4</td>
<td>0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>14.8±10.8</td>
<td>2.7±3.4</td>
<td>p&lt;0.001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 2. Mean/median Berlin SIJ scores ± standard deviation for inflammatory and chronic lesions.

<table>
<thead>
<tr>
<th>Lesion type</th>
<th>axSpA Mean/median</th>
<th>non-SpA Mean/median</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>256</td>
<td>193</td>
<td>0.001</td>
</tr>
<tr>
<td>FL</td>
<td>36.6±3.6</td>
<td>8.1±1.3</td>
<td>0.001</td>
</tr>
<tr>
<td>Erosion</td>
<td>5.2±6.8</td>
<td>5.0±1.9</td>
<td>0.001</td>
</tr>
<tr>
<td>Arkylosis</td>
<td>4.5±5.4</td>
<td>4.0±1.4</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Conclusion: The combination of structural changes and BME lesions as assessed by MRI performed best in the process of diagnosing axSpA in consecutive patients in a real-life setting presenting to our center. The discrepancy in diagnosis between rheumatologists and radiologists reflects the increasing insecurity of including only BME of SIJ as the major criterion for diagnosing axSpA.

REFERENCE:

Disclosure of Interests: Xenofon Baraliakos Grant/research support from: Abbvie, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Centocor, Chugai, Janssen, MSD, Novartis, Pfizer Inc, Roche and UCB, Grant/research support from: Abbvie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Chugai, Janssen Biologics, Novartis, Pfizer, UCB Pharma, Galapagos, Speakers bureau: Abbvie, Chugai, Janssen, Novartis, Pfizer, UCB Pharma, Anna Ghadir: None declared, Martin Fruth: None declared, Uta Kiltz Grant/research support from: AbbVie, Pfizer, Merck Sharp & Dohme, UCB Pharma, Novartis, Consultant for: Abbvie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Chugai, Janssen Biologics, Novartis, Pfizer Inc, Roche and UCB, Grant/research support from: Abbvie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Chugai, Janssen, MSD, Novartis, Pfizer, Roche, and UCB., Juergen Braun Shareholder of: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, Consultant for: AbbVie, Chugai, Eli Lilly, Grünenthal, Janssen, MSD, Novartis, Pfizer Inc, Roche and UCB, Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Centocor, Chugai, Janssen, Lilly, Medac, MSD (Schering-Plough), Mylan, Mundipharma, Novartis, Pfizer (Weyth, Hospira), Roche, Sanofi-Aventis and UCB, Speakers bureau: Abbvie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB

COP0245

DOES IMMUNOLOGICAL REMISSION, DEFINED AS DISAPPEARANCE OF AUTOANTIBODIES, OCCUR WITH CURRENT TREATMENT STRATEGIES? A LONG-TERM FOLLOW-UP STUDY IN RHEUMATOID ARTHRITIS PATIENTS WHO ACHIEVED A SUSTAINED DMARD-FREE STATUS

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Background: Sustained disease modifying antirheumatic drug (DMARD)-free status, the sustained absence of synovitis after cessation of DMARD-therapy, is infrequent in autoantibody-positive RA, but approximates cure (i.e. disappearance of signs and symptoms). It was recently suggested that immunological remission, defined as disappearance of anti-citrullinated protein antibodies (ACPA) and rheumatoid factor (RF), underlies this outcome.1 However, the association between seroreversion and cure of disease has not been extensively studied before.

Objectives: To determine in a long-term observational study if autoantibodies disappear in RA-patients who achieved sustained DMARD-free remission.

Methods: We studied 95 ACPA- and/or RF-positive RA-patients who achieved DMARD-free remission after median 4.8 years and kept this status for the remaining follow-up (median 4.2 years). Additionally, 21 autoantibody-positive RA-patients with a late flare, defined as recurrence of clinical synovitis after a DMARD-free status of ≥1 year, and 45 autoantibody-positive RA-patients who were unable to stop DMARD-therapy (during median 10 years) were studied. Anti-CCP2 IgG, IgM and RF IgM levels were measured in 587 samples obtained at diagnosis, before and after achieving DMARD-free remission.

Results: 12.8% of anti-CCP2 IgG positive RA-patients had seroreverted when achieving remission. In RA-patients with a late flare and with persistent disease this was 8.3% and 5.7%, respectively (p=0.63, Figure). For anti-CCP2 IgM and RF IgM similar results were observed. Evaluating the estimated slope of serially measured levels revealed that RF-levels decreased more in patients with than without remission (p<0.001); the course of anti-CCP2 levels was not different (p=0.66).

Conclusion: Sustained DMARD-free status in autoantibody-positive RA was not paralleled by an increased frequency of reversion to autoantibody-negativity. This form of immunological remission should therefore not be a treatment target.

REFERENCE:
Disclosure of Interests: Debbie Boetens: None declared, Leonie Burgers: None declared, Rene Toes Grant/research support from: Sanofi, Annette van der Helm - van Mil Grant/research support from: The research leading to these results has received funding from the European Research Council (ERC) under the European Union’s Horizon 2020 research and innovation programme (Starting grant, agreement No 741312) and from the Dutch Arthritis Foundation. The funding source had no role in the design and conduct of the study.


MRI OF THE WRIST IN EARLY RHEUMATOID ARTHRITIS AFTER 1-YEAR TREAT-TO-TARGET STRATEGY

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BACKGROUND: There are two types of remission in rheumatoid arthritis. The first, and most commonly applied, is clinical remission. Imaging remission is another aspect to consider given that (a) the correlation between clinical and imaging is present at relatively modest levels (1), (b) imaging can show subclinical inflammation not evident clinically and (c) imaging evidence of inflammation can predict structural damage (1). In this study, we compared clinical and imaging remission in early rheumatoid arthritis (ERA) patients after one year of standard treatment.

OBJECTIVES: To semi-quantitatively and quantitatively measure the degree of inflammation (synovitis, tenosynovitis, bone marrow oedema) and structural change (erosions, joint space narrowing) on MRI in early RA patients following treat-to-target strategy treatment for one year and to compare this with changes in clinical parameters.

METHODS: Prospective cross-sectional study of 70 ERA patients underwent treat-to-target strategy treatment for one year, DAS28-ESR remission (DAS28-ESR score c<3.2), 2011 ACR/EULAR definition of remission, SDAI remission (SDAI ≤ 3.3) and Boolean remission was measured before and after treatment. High resolution MRI of the most symptomatic wrist was performed before and after treatment. MRI parameters including RAMRIS subscores, synovial volume (synovitis and tenosynovitis), synovial perfusion (max enhancement, enhancement slope) were measured.

RESULTS: 55 (%) out of 70 ERA patients completed baseline and one-year clinical and MRI assessments. Remission rates for DAS28-ESR, SDAI and Boolean were 60% (33), 44% (24) and 33% (18) respectively. Eight (24%) out of 33 patients with DAS28-ESR remission, showed progression in bone erosion. Fourteen (16.7%) of 24 patients with SDAI remission showed progression in bone erosion while 1 (5%) of 18 patients with Boolean remission showed progression in bone erosion. Patients who achieved remission after treatment had a greater reduction in all MRI-evident inflammation as well as bone erosion. At month 12, MRI-evident joint synovitis, tenosynovitis and bone marrow oedema was still frequently seen in ERA patients with clinical remission though patients who achieved Boolean remission had the lowest levels of joint synovitis (RAMRIS Synovitis= 2.6±0.8 (2.9±1.3 for DAS28-ESR remission and 3±1.2 for DAS28-ESR remission)); synovitis volume= 1298±1217 mm³ (1480±1367 mm³ for SDAI remission and 1520±1584 mm³ for DAS28-ESR remission); synovitis perfusion of max enhancement= 38±22% (41±25% for SDAI remission and 41±25% for DAS28-ESR remission)), bone marrow oedema (RAMRIS BME score= 0.9±1.1 (1.3±2.6 for SDAI remission and 1.4±2.3 for DAS28-ESR remission)) as well as bone erosion (RAMRIS bone erosion score= 4±5.8 (4.6±5.5 for SDAI remission and 4±3.4 for DAS28-ESR remission)) for all patients at one year.

CONCLUSION: MRI detected inflammation is common even in patients with clinical remission. Patients with Boolean remission had overall less residual inflammation than DAS28-ESR or SDAI remission patients as well as lowest number of patients who had bone erosion progression in remission group at month 12. Treat to target protocols should ideally target Boolean remission.

REFERENCE:

Disclosure of Interests: None declared

SATURDAY, 15 JUNE 2019

Restless lives: Managing fatigue, sleep and pain

THE INFLUENCE OF PAIN ON SLEEP PROBLEMS, MENTAL HEALTH AND USE OF STRONG PAINKILLERS AMONG PATIENTS WITH ARTHRITIS

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Background: Chronic pain is a part of daily life for many people with RMD and leads to reduced quality of life, high risk of losing work ability, impaired functions and a poor social life. The chronic pain also means that many patients need painkillers. In Denmark there is a very high consumption of strong painkillers (opioids) compared to the other countries in Scandinavia. Therefore, the authorities have a great focus on reducing this and are urging the doctors to reduce the prescription of strong painkillers to patients with chronic pain, including patients with RMDs. In the Danish Rheumatism Association, we have many inquiries to our professional helpline from patients regarding pain. Especially about the use of painkillers, sleeping problems caused by pain, and the negative influence that pain has on one’s mood. The patients experience side effects and discomfort associated with the painkillers. Some must phase out their consumption of strong painkillers, because of the authorities’ focus on this - and have problems with this. In order to get a more detailed knowledge about the influence of pain among patients with RMD, the Danish Rheumatism Association made this study.

OBJECTIVES: To investigate the influence of pain on sleeping problems, mental health and the use of strong painkillers among members of a user-panel.

METHODS: The study was carried out in November 2018 as an online questionnaire survey sent to 1328 members of a user-panel in The Danish Rheumatism Association. 69% answered the questionnaire. The user-panel consists of people at least one RMD. It is not representative of patients with RMD in Denmark.

RESULTS: The most important results are.

Sleep: 67% rarely or never feel fully rested when they wake up in the morning, and 36% takes painkillers to improve their sleep. 69% have experienced that the quality of their sleep has affected their pain negatively.

Mental health: During the past four weeks, 58% have felt that everything is unmanageable for them due to pain, 11% indicated having had thoughts of taking their own life due to pain, and 45% have not wanted to be together with other people because of their pain.

Use of strong painkillers: 83% have pain on a daily basis or several times a week. Among these, 46% have received strong painkillers over the last year, and 78% have not been offered alternatives to strong painkillers.

More results from the survey will be presented on EULAR.

Conclusion: The study indicates that pain and poor quality of sleep, has surprisingly large influence on patient’s daily life. More than one third takes painkillers to improve their sleep. Pain seems to have a severe negative influence on their sleep and reversed - poor sleep worsens their pain. Surprisingly many are still using strong painkillers, despite the authorities focus on reducing prescription of strong painkillers, and the patients’ state, that they are not been given an alternative to strong painkillers. Finally, the study shows that pain has a surprisingly negative influence on mental health and the patients’ hope for the future. In general, it has been a surprise for the Danish Rheumatism Association, that pain has such a huge impact on the participants’ daily life, especially on their mental health. Therefore, the organization has been using the result of this study in our political work for better treatment and support to patients with chronic pain in our healthcare system, and in our political campaigning about the importance of a focus on pain among patients with RMDs. It is to be explained on EULAR, how we more concretely have applied the results of the study in our political work.

Disclosure of Interests: None declared

FACE ARTHRITIS: WHAT SITUATIONS AFFECT EMOTIONALLY THE PATIENT WITH RHEUMATOID ARTHRITIS AND HOW TO RESOLVE THEM EFFECTIVELY

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Background: Who defines health as a state of physical, psychological and social well-being. However, patients with rheumatoid arthritis (RA) declare that
treatment is mainly aimed at combating physical affectation and hardly focusses on emotional and social aspects.

Objectives: To identify the situations that produce the greatest negative emotional impact in RA patients and to assess the coping strategies used.

Methods: A previous phase (Project OpinAR) identified situations with negative emotional and social impact. In this project, 2 stages were developed: a) A nominal group of patients, following the McMillan method, selected the most emotionally affected situations from the previous list; b) Voting of patients and rheumatologists to assess the assumed effectiveness of 8 coping strategies for each situation with a Likert scale of 1 to 10 (minimum and maximum): proactive resolution, self-criticism, emotional expression, desiderative thinking, social support, cognitive restructuring, avoiding problems and social withdrawal. The median, interquartile range (IQR), and statistical significance of the differences between patients and physicians (Student’s T test) were calculated with a cut-off value of p<0.05. The strategies valued with 8, 9 and 10 were recommended and those valued as 1, 2 or 3 were discouraged. The study was approved by the Ethical Research Committee of the Hospital of La Princesa.

Results: 107 patients from all the Autonomous Communities and 31 expert rheumatologists from 13 Autonomous Communities were recruited, of which 100 (93%) and 17 (55%) participated in the study in a valid way, respectively. The four situations that most negatively affect them, in the opinion of patients and their doctors are: i) The patient feels that his disease evolves worse than what the doctor says, ii) The patient does not know aspects of the control and monitoring of his disease, iii) The patient feels that he does not really participate in the decision making, and iv) The patient is dissatisfied with the overall treatment received. Regarding coping strategies, doctors recommended using proactive resolution in all situations more frequently than patients (p<0.05 for all situations, low variability, with IQR <2 among physicians) as well as emotional expression (p<0.05 for 3 situations, high variability, with IQR >3). Other strategies were less valued by doctors and patients, but with similar responses. There was a lot of dispersion (IQR >1) in most cases.

Conclusion: The situations with the greatest negative emotional impact on RA are those that put the doctor and the patient at odds with regard to the perception of the disease and its control and should be treated during visits. The most recommended strategies are proactive resolution and emotional expression. The most discouraged are self-criticism and the avoidance of the problem. Anyway, there is a great variability of opinions and doctors tend to give more extreme responses. Doctors and patients should have a space and willingness to discuss and exchange opinions on how they emotionally face RA.


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Disclosure of Interests: Santos Castañeda Consultant for: Amgen, BMS, Pfizer, Lilly, MSD, Roche, Sanofi, UCB, José Bernardo Negrón: None declared, María D. Navarro Rubio: None declared, José L. Baquero Ubeda: None declared, Loreto Carmona Grant/research support from: Abbvie, Actelion, Astellas, BMS, Pfizer, Roche, Sanofi-Aventis and UCB Pharma, Paid instructor for: Novartis


OP0349 NEURAL NETWORKS FOR AUTOMATED SCORING OF JOINT DISEASE ACTIVITY ON DOPPLER ULTRASOUND IMAGES

Jakob K. H. Andersen1, Jannik S. Pedersen1, Martin S. Laursen1, Kathrine Holz1, Jakob Grauslund2, Thiusius Rajeeth Savarimuthu1, OMERACT-EULAR Synovitis Scoring (OESS) system, is a major step forward in the use of ultrasound in the diagnosis and monitoring of patients with inflammatory arthritis. The variation in interpretation of disease activity on US images can affect diagnosis, treatment and outcomes in clinical trials.

Objectives: To investigate if we could utilize neural network architecture for the interpretation of disease activity on Doppler US images, using the OESS scoring system.

Methods: Two state-of-the-art neural networks were used to extract information from 1342 Doppler US images from Rheumatoid Arthritis (RA) patients. One neural network that divided images as either healthy (Doppler OESS score 0 or 1) or diseased (Doppler OESS score 2 or 3). The other to score images across all four of the OESS systems Doppler US scores (0-3). The neural networks were hereafter tested on a new set of RA Doppler US images (n=170). Agreement between rheumatologist’s scores and network scores was measured with the kappa statistic.

Results: For the neural network assessing healthy/diseased score, the highest accuracies compared to an expert rheumatologist were 86.4% and 86.9% with a sensitivity of 0.864 and 0.875 and specificity of 0.864 and 0.864, respectively. The other neural network developed to four class Doppler OESS scoring achieved an average per class accuracy of 75.0%, and a quadratically weighted kappa score of 0.919.

Conclusion: This study is the first to show that neural network technology can be used in the scoring of disease activity on Doppler US images according to the OESS system.

Disclosure of Interests: None declared


OP0350 ULTRASOUND POWER DOPPLER SEMI-QUANTITATIVE SCORING, IS IT TIME WE MOVED TO A RED PIXEL DENSITY ALGORITHMIC PROGRAM TO DETERMINE TRUE TREATMENT RESPONSE?

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Background: The introduction of the semi-quantitative (SQ) grey-scale and power Doppler (PD) 0-3 scoring system, as agreed by the EULAR-OMERACT ultrasound (US) working group (1, 2), has undoubtedly been the most recognised and accepted method in both clinical practice and trials. Studies have suggested that the SQ scoring method is reliable as the quantitative when scoring the grey-scale (3, 4). Additional studies have shown that the use of red pixels in determining the PD signal in tenosynovitis, compared to SQ scoring was not different (5). However, the distribution of the PD SQ score over estimated the percentage compared to the quantitative score, which could reflect treatment responses inaccurately (6).

Objectives: 1. To describe how a quantitative pixel density score maps to a SQ PD score. 2. Can using a 0-4 PD grading scale better distribute the PD percentages, as determined by pixel count, than 0-3 scale?

Methods: Patients were selected from an observational study of 122 DMARD naïve patients (PEAC study REC: 05/00703/198); IRAS Project ID 60271) and 60 DMARD failure patients treated with anti-TNF (THERAPY study, MREC: 15/SC/0045; IRAS Project ID:147240). All patients were classified according to the 1987 ACR or 2010 ACR/EULAR criteria for rheumatoid arthritis. In total 334 images were analysed, from a total of 127 patients. The calculator for the US PD signal/ synovial area ratio was created on software MATLAB 2018b. PD was scored according to the SQ definitions for the visual grade 0-3 and 0-4 scoring systems (Figure 1A). Agreement between two readers using 80 US images: ICC SH —0.82 (interval 0.79-0.9), ICC PD —0.93 (interval 0.9-0.95), calculated using SPSS software. The results were analysed using R v3.4.2.

Results: The SQ grade 3 score was shown to over estimate PD signal/synovial area ratio, with a mean ratio of only 40.8%. Figure 2A, illustrates how the spread in PD signal varied with a single grade, in this case SQ grade 3. Figure 1B showed that adding a SQ grade 4 reduced the SD in the SQ grade 3 group but increased the SD overall by causing a larger SD in SQ grade 1, 2 and 4 grades.

A k-means (KM) clustering algorithm was used to find the most efficient ratio cut off points for a SQ grade 3 scoring system. The SQ grades are not taken into account for this scoring system, it is based on the mathematically optimum cut off points (Figure 1C). It is seen that the SD was drastically reduced in the KM score and the 95% confidence interval and grade overlaps.

When comparing the KM score with the SQ score it was shown to be significantly dependent (Pearson’s Chi squared p-value <2.2e-16) and strongly positively correlated (Spearman’s 0.84, p-value <2.2e-16), this is shown in Figure 2B and C. Furthermore, the KM score was seen to have a stronger linear correlation (Pearson’s 0.95, p-value <2.2e-16) when compared to the SQ score (0.82, p-value <2.2e-16).
Conclusion: The 0-4 SQ grade was not equivalent to that of the 0-3 SQ grade used PD scoring and it increased the variance in the majority of SQ grades. This study does show that the PD pixel algorithm has a stronger linear correlation when compared to the SQ grading, suggesting a more accurate method at interpreting treatment response, as the intervals between grades are more equal. Therefore, built in algorithms to detect PD signal in US machines are the future for drug monitoring in inflammatory arthritis.

REFERENCES:

Disclosure of Interests: Nirupam Purkayastha: None declared, Samilha Ismail: None declared, Peter C. Taylor Grant/research support from: Celnge, Galapagos, Eli Lilly, UCB, Consultant for: AbbVie, Galapagos, Gilead, Eli Lilly, Pfizer Inc, Costantinu Pitazlis Grant/research support from: Celnge, Stephen Kelly: None declared


Late breaking abstract session

LB0003 Efficacy and safety of Filgotinib for patients with Rheumatoid Arthritis naïve to Methotrexate Therapy: FINCH3 Primary Outcome Results

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Background: Filgotinib (FIL), an orally administered, potent, selective inhibitor of Janus kinase 1 (JAK1), has shown good efficacy and was well tolerated for treatment of rheumatoid arthritis (RA).

Objectives: To compare efficacy and safety of FIL with and without methotrexate (MTX) in patients with RA who were naïve to MTX therapy.

Methods: This phase 3, double-blind, active-controlled study randomized patients with moderately to severely active RA (2:1:1:2) to FIL 200mg daily + MTX weekly (up to 20mg), FIL 100mg + MTX, FIL 200mg (+placebo [PBO]), or MTX (+PBO) for up to 52 weeks; results through week 24 are presented. Primary efficacy endpoint was proportion of patients achieving ACR20 response at week 24; additional assessments included ACR50 and ACR70 responses; DAS28-CRP score ≤3.2 and <2.6, and changes in van der Heijde mTSS, HAQ-DI, SF-36 PCS, and FACIT-Fatigue. Safety endpoints included types and rates of adverse events (AEs). Logistic regression adjusting for stratification factors with nonresponder imputation was used for treatment comparisons for ACR response and other binary endpoints. Mixed-effect model adjusting for baseline value, stratification factors, treatment, visit, and treatment by visit interaction as fixed effects with observed cases was used for continuous endpoints.

Results: Of 1,252 randomized patients, 1,249 received study drug (416 FIL 200mg+MTX; 207 FIL 100mg+MTX; 210 FIL 200mg monotherapy; 416 MTX monotherapy) and were analyzed; 1,130 completed week 24. At week 24, significantly more patients in the FIL 200mg +MTX (81.0%; P<0.001) and FIL 100mg+MTX (80.2%; P<0.05) arms achieved an ACR20 response compared to MTX monotherapy (71.4%)(Table 1). Compared to MTX monotherapy, more patients receiving FIL with or without methotrexate (MTX) in patients with RA who were naïve to MTX therapy.

Table 1: Efficacy/Outcomes at Week 24

<table>
<thead>
<tr>
<th></th>
<th>FIL 200 mg</th>
<th>FIL 100 mg</th>
<th>FIL 200 mg + MTX</th>
<th>MTX</th>
<th>Monotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACR20 response</td>
<td>81.0%</td>
<td>78.1%</td>
<td>81.0%</td>
<td>68.4%</td>
<td>71.4%</td>
</tr>
<tr>
<td>ACR50 response</td>
<td>61.6%</td>
<td>57.9%</td>
<td>61.6%</td>
<td>60.5%</td>
<td>60.6%</td>
</tr>
<tr>
<td>ACR70 response</td>
<td>43.8%</td>
<td>40.9%</td>
<td>43.8%</td>
<td>40.8%</td>
<td>41.4%</td>
</tr>
<tr>
<td>SF-36 PCS</td>
<td>86.2%</td>
<td>81.1%</td>
<td>86.2%</td>
<td>82.5%</td>
<td>83.3%</td>
</tr>
<tr>
<td>FACIT-Fatigue</td>
<td>93.2%</td>
<td>94.9%</td>
<td>93.2%</td>
<td>94.5%</td>
<td>94.8%</td>
</tr>
</tbody>
</table>

*All patients who were randomized and received at least 1 dose of drug. Drug was included as efficacy analysis if >28 days MTX monotherapy, >8 weeks MTX monotherapy, >3 days FIL monotherapy, or >28 days FIL monotherapy. Comparators not adjusted for multiplicity.

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Methods: ORAL Shift (NCT02831655) was a global Phase 3b/4 study in pts aged ≥18 years with moderate to severe RA and an inadequate response to MTX. Pts received open-label (OL) tofacitinib MR 11 mg QD with MTX (tofacitinib + MTX) for 24 weeks. Pts achieving LDA (CDAI ≤50) at Week (W)24 entered the 24-week double-blind (DB) MTX withdrawal phase and were randomised 1:1 to receive tofacitinib MR 11 mg QD with placebo (tofacitinib monotherapy; ie underwent blinded MTX withdrawal) or continue tofacitinib + MTX. The primary endpoint was least squares mean change from W24 to W48 (Δ DB phase) in DAS28 4(ESR).

Non inferiority of tofacitinib monotherapy vs tofacitinib + MTX was declared if the upper bound of the 95% two-sided confidence interval (CI) for the difference in ΔDAS28 4(ESR) between arms was <0.6. Secondary endpoints included ΔΔDAS28 4(ESR), ΔΔDAS28 4(ESR), ΔΔDAS28 4(ESR), ΔHAQ-DI; rates of ACR20/50/70 response, HAQ-DI response, ΔΔDAS28 4(ESR)- and CDAI-defined LDA and remission, and ACR-EULAR Boolean-defined remission (W48), and safety (OL and DB phases).

Results: Of 694 pts in the OL phase, 530 achieved CDAI-defined LDA at W24 and were treated in the DB phase (tofacitinib monotherapy; n=264; tofacitinib + MTX; n=266). Demographics and pt characteristics at OL-phase baseline were similar between treatment arms. The difference (95% CI) between arms in ΔΔDAS28 4(ESR) (primary endpoint) was 0.30 (0.12, 0.48; Table 1) at W48, demonstrating that tofacitinib monotherapy was non-inferior to tofacitinib + MTX. Consistent with the primary endpoint, ΔΔΔDAS28 4(ESR)/SADI/CDAI were greater for tofacitinib monotherapy vs tofacitinib + MTX, but these differences were not clinically meaningful; ACR/HAQ-DI response and LDA rates were generally similar between arms (Table). Remission rates were also similar between arms and generally did not change after MTX withdrawal in the DB phase, rates of AEs, serious AEs, discontinuations due to AEs and AEs of special interest were generally comparable between arms (Table 1).

Conclusion: Pts receiving tofacitinib MR 11 mg QD + MTX who achieve LDA may withdraw MTX up to W48 without significant worsening of disease activity. Pts in remission tend to remain in remission after MTX withdrawal. Safety appeared consistent with the known profile of tofacitinib.

REFERENCE


Acknowledgement: Study sponsored by Pfizer Inc. Medical writing support was provided by C Vogelmann of CMC Connect and funded by Pfizer Inc.
Background: There have been few head-to-head clinical trials comparing different biologic disease-modifying anti-rheumatic drugs (bDMARDs) in patients (pts) with psoriatic arthritis (PsA).

Objectives: To report 24-week (wk) results of a study directly comparing efficacy and safety of ixekizumab (IXE), an IL-17A inhibitor, and adalimumab (ADA), a TNF inhibitor, in bDMARD-naive pts with PsA.

Methods: The study (NCT03151551; SPIRIT-H2H) included pts with active PsA and PASI100. Additional PsA, skin, composite treat-to-target (T2T: MDA, DAPSA 4), enthesitis resolution (Figure 1), and skin-related quality of life (Table 2). No unexpected safety signals were observed.

Results: 566 pts were randomised (283 to IXE and 283 to ADA). Baseline demographics and disease characteristics were generally well balanced between groups (Table 1). All primary and key secondary efficacy endpoints at wk 24 were met (Figure). The proportion of pts achieving both ACR50 and PASI100 was significantly greater for IXE than ADA (36% vs 28%, p<0.05). IXE was non-inferior to ADA for ACR50 response and superior for PASI100 response (Figure). While improvements from baseline were achieved with both treatments, significantly better results were seen with IXE vs ADA for skin and composite T2T outcomes, enthesis resolution (Figure 1), and skin-related quality of life (Table 2).

Conclusion: In bDMARD-naive pts with active PsA and skin disease, IXE showed superior efficacy to ADA based on simultaneous achievement of ACR50 and PASI100 responses at wk 24. Greater improvements with IXE vs ADA were also attained in individual PsA domains and composite T2T outcomes.

Disclosure of Interests: Philip J Mease Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Galapagos, Gilead, Janssen, Eli Lilly, Merck, Novartis, Pfizer, Sun Pharmaceutical Industries, Inc., and UCB; Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Galapagos, Gilead, Janssen, Eli Lilly, Merck, Novartis, Pfizer, Sun Pharmaceutical Industries, Inc., and UCB.

References: 1. Mease PJ, Smolen JS, Behrens F, et al. The study (NCT03151551; SPIRIT-H2H) included pts with active PsA and PASI100. Additional PsA, skin, composite T2T outcomes, and safety were assessed. 2. Mease PJ, Smolen JS, Behrens F, et al. In bDMARD-naive pts with active PsA, IXE showed superior efficacy to ADA based on simultaneous achievement of ACR50 and PASI100 responses at wk 24. Greater improvements with IXE vs ADA were also attained in individual PsA domains and composite T2T outcomes.
SUBCUTANEOUS SECUKINUMAB 300MG AND 150MG PROVIDES SUSTAINED INHIBITION OF RADIOGRAPHIC PROGRESSION IN PSORIATIC ARTHRITIS OVER 2 YEARS: RESULTS FROM THE PHASE 3 FUTURE 5 STUDY

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Background: Secukinumab (SEC) provided sustained clinical efficacy, and inhibition of radiographic progression over 52 Weeks (Wks) in patients (pts) with psoriatic arthritis (PsA) in the FUTURE 5 study 1.

Objectives: To report the effect of SEC on radiographic progression at Wk 104 (2 years) in PsA pts in the FUTURE 5 study.

Methods: Adults (N=996) with active PsA, stratified by prior anti-TNF therapy (naïve and inadequate response/intolerance [IR]) were randomised 2:2:2:3 to subcutaneous SEC 300mg with loading dose (LD; 300mg), 150mg LD (150mg), or SEC no LD (150mg no LD). Concomitant (naïve and inadequate response/intolerance [IR]) were randomised 2:2:2:3 to SEC; 150mg groups include pts who had dose escalated to 300mg. Concomitant MTX (≤25 mg/week) was allowed. Radiographic progression (mean change in van der Heijde-modified total Sharp score [vdH-mTSS]) and its components: erosion and joint space narrowing [JSN] scores, was based on hand/ wrist/foot X-rays obtained at BL and Wk 104, and assessed by two blinded readers (plus an adjudicator if required). Other efficacy endpoints included ACR20/50, PASI90 and resolution of dactylitis and enthesitis.

Results: Overall, 84.7% (300mg), 82.3% (150mg) and 75.2% (150mg no LD) pts completed 2 years of treatment. A total of 86 (39%) and 92 (41%) pts had their dose escalated to 300mg in the 150mg and 150mg no LD groups, respectively. Inhibition of radiographic progression was sustained with SEC through 2 years (Table 1). Proportions of pts with no radiographic progression (change from BL in mTSS ≤0.5) with SEC were 89.5% (300 mg), 82.3% (150 mg), and 81.1% (150 mg no LD) at 2 years; corresponding proportion of pts for change from BL in mTSS ≤0.0 were: 81.2%, 69.1% and 73.4%, respectively. Clinical responses were also sustained over 2 years (Table 1).

Conclusion: Subcutaneous secukinumab provided sustained inhibition of radiographic progression and sustained clinical responses through 2 years of treatment in pts with active PsA.

SUBCUTANEOUS TANZEUMAB FOR OSTEOARTHRITIS PAIN: A 24-WEEK PHASE 3 STUDY WITH A 24-WEEK FOLLOW UP

Francis Bierenbaum1, Francisco J. Blanco2, Ali Guermazi3, Eric Vignon4, Kenji Miki5, Takaharu Yamabe6, Lars Viktrup7, Rod Jonun8, William Carey9, Mark Brown9, Ken Verburg3, Christine Weste3, 1Sorbonne Universite, INSERM, AP-HP Hospital Saint Antoine, Paris, France; 2RHRC-Complejo Hospitalario Universitario de A Coruña, A Coruña, Spain; 3Boston University School of Medicine, Boston, United States of America; 4Université Claude Bernard, Lyon, France; 5Osaka Yukioka College of Health Science, Hayashi Hospital, Osaka, Japan; 6Pfizer Inc, Groton, United States of America; 7Eli Lilly & Company, Indianapolis, United States of America; 8Pfizer Ltd, Tadworth, United Kingdom

Background: Tanezumab, a monoclonal antibody against nerve growth factor, is in development for treatment of osteoarthritis (OA) pain. Tanezumab, a monoclonal antibody against nerve growth factor, is in development for treatment of osteoarthritis (OA) pain.

Objectives: To assess efficacy and safety of tanezumab in patients with moderate to severe OA pain who have not responded to or cannot tolerate standard of care analgesics.

Methods: A randomized, double-blind, placebo-controlled study (24 week treatment; 24 week follow-up) was conducted in patients in Europe and Japan with moderate to severe OA pain of the knee or hip and history of insufficient pain relief or intolerance to acetaminophen, oral nonsteroidal anti-inflammatory drug, and either tramadol or opioids (or unwilling to take opioids). Patients received subcutaneous tanezumab (2.5 or 5 mg) or placebo at baseline, week 6, and week 10. Co-primary endpoints were change from baseline in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain, WOMAC Physical Function, and Patient Global Assessment of OA (PGA-OA) scores at week 24. Safety, including independent adjudication of joint safety events, was assessed.

Results: Tanezumab 5 mg met all co-primary endpoints (Fig. 1). Tanezumab 2.5 mg met WOMAC Pain and Physical Function endpoints but not the PGA-OA endpoint; thus, this dose did not meet pre-specified efficacy criteria. The occurrence

Table: Summary of Efficacy Results

<table>
<thead>
<tr>
<th></th>
<th>Mean change in vdH-mTSS scores from BL to WK 104 (BL score)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>300mg N=322 mTSS</td>
</tr>
<tr>
<td></td>
<td>150mg group* N=220 mTSS</td>
</tr>
<tr>
<td></td>
<td>150mg no LD group N=180 mTSS</td>
</tr>
<tr>
<td>vdh-mTSS</td>
<td>0.37 (12.07)</td>
</tr>
<tr>
<td>Erosion</td>
<td>0.27 (0.15)</td>
</tr>
<tr>
<td>JSN</td>
<td>0.11 (4.92)</td>
</tr>
<tr>
<td>Clinical responses at WK 104 (% responders [n])</td>
<td>300mg N=222 150mg group* N=220 150mg no LD group N=222</td>
</tr>
<tr>
<td>ACK30</td>
<td>77.0 (38.7)</td>
</tr>
<tr>
<td>ACK50</td>
<td>51.9 (38.7)</td>
</tr>
<tr>
<td>PASI50</td>
<td>70.1 (47)</td>
</tr>
<tr>
<td>Resolution of arthritis1</td>
<td>78.0 (138)</td>
</tr>
<tr>
<td>Resolution of dactylitis1</td>
<td>82.8 (86)</td>
</tr>
</tbody>
</table>

*70% and 50% no head area include 86 and 50 pts, respectively, who were dose escalated to 70% or 50%.
**N number of pts on each column, n number of pts with data at BL and wk 24.
**Data from pts with ≥44 joints 25% body surface area, ≤5 in knees, ≤10 in OA.

of adverse events (AEs) and discontinuations due to AEs were similar across groups, though serious AEs occurred more frequently in both tanezumab groups relative to placebo. Two deaths in the 5 mg tanezumab group were deemed unrelated to treatment. The only AE occurring in ≥3% of patients in any group, and more frequently (>1% difference) in both tanezumab groups relative to placebo, was OA. Total joint replacements (TJR) occurred in 6.7%, 7.8%, and 7.0% of patients in the placebo, tanezumab 2.5 mg, and tanezumab 5 mg groups, respectively. Joint safety events, including TJRs, were mostly adjudicated as normal progression of OA (58/79; 73.4%). Pre-specified joint safety events occurred in 0% and 2.5% (n = 14) of patients in the placebo and tanezumab (2.5 mg = 1.8%; 5 mg = 3.2%) groups, respectively. These 14 events in the tanezumab groups included rapidly progressive OA (2.5 mg n = 4; 5 mg n = 8), subchondral insufficiency fracture (2.5 mg n = 1), and primary osteonecrosis (5 mg n = 1).

Conclusion: Tanezumab 5 mg significantly improved all co-primary endpoints of pain, physical function, and PGA-OA. Tanezumab 2.5 mg significantly improved pain and physical function, but did not reach significance on PGA-OA. AEs are consistent with previous studies of tanezumab in OA. A similar number of TJRs were reported across groups, though overall joint safety events were more frequent with tanezumab than placebo.


Methods: The MR was implanted in 14 patients with active RA and prior insuffi-
cient response to ≥2 bDMARDs or JAK inhibitors with ≥2 different modes of
action; all patients remained on stable background of methotrexate. Three weeks
after implantation, the first 3 subjects were stimulated 1 min QD and, following
safety review board approval, the remaining 11 patients were implanted with the
MR and randomized to 1 min of sham, QD, or QID stimulations for 12 weeks. Patients,
rheumatologists, joint assessors and monitors were fully blinded to treat-
ment arm. Subjects randomized to sham had their devices activated after the pri-
mary endpoint at 12 weeks. Clinical efficacy was measured by DAS28-CRP
response and contrast-enhanced MRI (RAMRIS QMERCAT). The pharmacody-
namic response to VNS was assessed in blood using cytokine production in an
ex-vivo bioassay (TruCulture).

Results: 14 patients were enrolled (mean prior bDMARDs= 4.8, mean DAS28-
CRP= 5.94). Implantation and stimulation were generally well tolerated. There
were no device or treatment-related SAEs and 2 surgery related adverse events
(left vocal cord paralysis, Horner’s syndrome) that resolved without clinically sig-
nificant sequelae. DAS28-CRP change at week 12 was (mean ± SEM): Open
label QD= -1.44 ± 0.64, QD= -1.24 ± 0.88, QID= 0.38 ± 0.71, Sham=0.16 ± 0.21.
Of QD stimulated patients, 4 of 6 had a EULAR good or moderate response. MRI
measures of synovitis or osteitis did not change after 12 weeks of stimulation.
RAMRIS erosion scores correlated with EULAR response (change ± SEM in ero-
sion scores in EULAR responders = -2.2 ± 1.4 vs. 2.4 ± 0.96 in EULAR non-
responders). The pharmacodynamic response to VNS was confirmed in actively
stimulated groups with >30% decrease from baseline in bioassay levels of IL-1β,
IL-6, and TNF-a at week 12.

Conclusion: The novel MR device and stimulation was well tolerated independ-
ent of the two surgery-related events. MR associated stimulation reduced signs
and symptoms of RA in a meaningful number of highly drug-refractory subjects.
No clinical improvement was observed in the sham group. These initial pilot data
support the use of the MR in a larger blinded sham-controlled study in patients
who have failed biologics or targeted oral therapies as a novel approach for treat-
ment of RA and other chronic inflammatory diseases.

REFERENCES:

Disclosure of Interests: Mark C. Genovese Grant/research support from:
Sanofi/Genzyme, Genentech/Roche, RPPharm, Consultant for: Sanofi/Genzyme,
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ple clinical research trials, BMS, AbbVie, GSK, Janssen, Amgen, Pfizer, Regen-
ser, UCB, Sanofi, SetPoint, ImmunoPharma, Astra Zeneca, Novartis, Variliris,
Gilead, Consultant for:electroCore, David Sikes Grant/research support from:Set-
Point Medical/PfizerAction/Abbvie/Eli Lilly, Alan Kovitz Shareholder of, Novartis,
Consultant for: Abbvie, Janssen, Pfizer, UCB, Genzyme, Sanofi, Regeneron,
Boehringer Ingelheim, Sun Pharma Advanced Research, Flexion., Paid instructor
for: Celsegne, Horizon, Merck, Novartis, Pfizer, Sanofi, Genzyme, Sanofi, Regeneron,
Speakers bureau:Celsegne, Horizon, Merck and Genetech, Flexion, Diane M Hor-
owitz Grant/research support from: SetPoint Medical, Charles Peterly Shareholder
of: Spire Sciences, Inc Consultant for: AbbVie, Acerta, Astra Zeneca, Bristol-
Myers Squibb, Centrixion, Daiichi Sankyu, Five Prime Therapeutics, Genent-
ech, Hoffmann-La Roche, Janssen, Lilly USA, Medimmune, Merck, Novartis,
Plexikon, Pfizer, Sanofi, Salix-Santarus, Samsung, Employee of: Spire Sciences,
Inc, Speakers bureau: Aumgen, Yaakov Levine Shareholder of: SetPoint Medical,
Employee of: SetPoint Medical, David Chernoff Shareholder of: SetPoint Medical,
Consultant for: Crescendo BioScience, Employee of: SetPoint Medical

LB0009
FIRST-IN-HUMAN STUDY OF NOVEL IMPLANTED
VAGUS NERVE STIMULATION DEVICE TO TREAT
RHEUMATOID ARTHRITIS

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M Horowitz2, Charles Peterly4, Yaakov Levine4, David Chernoff5
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4 Northwell Health, Great Neck, United States of America
5 SetPoint Medical, Valencia, United States of America

Background: The inflammatory reflex plays a role in regulating innate and adap-
tive immunity through cellular and molecular pathways1. Activation of this neuro-
immune reflex by electrical vagus nerve stimulation (VNS) reduced systemic
inflammation and improved disease activity in a 17 subject rheumatoid arthritis
(RA) proof-of-concept study using a reprogrammed epilepsy stimulator2. A novel
miniaturized neurostimulator, the “MicroRegulator” (MR), was developed for a
first-in-human pilot study in multi-drug refractory RA.

Objectives: To assess the safety and efficacy of the MR in a double-blind study in active RA patients.
case series even lower doses might be sufficient for maintenance treatment, potentially improving safety and decreasing costs. (1)

Objectives: To compare effectiveness of RTX retreatment with ultra-low doses (1 × 500mg or 1 × 200mg) to standard low dose (1 × 1000mg).

Methods: A 6-month double-blind randomised controlled non-inferiority trial (REDO study (2)) was performed in 5 centres in the Netherlands. Patients with RA responding well to RTX (based on DAS28-CRP 2.9 or clinical judgement) were randomised (1:2:2) to 1 × 1000mg, 1 × 500mg or 1 × 200mg RTX respectively. DAS28-CRP and peripheral CD19+ B-cells were measured at baseline, 3 and 6 months. Primary analysis (per protocol with LOCF) consisted of a hierarchical testing procedure comparing ultra-low doses (1 × 500mg at 3 and 6 months, then 1 × 200mg at 3 and 6 months) to 1 × 1000mg using a non-inferiority margin of 0.6 (on DAS28-CRP). DAS28-CRP change of study groups was compared using linear regression, adjusted for baseline DAS28-CRP, RF/ACPA status and concomitant csDMARD use.

Results: The projected inclusion was met (n=142, table 1a). In both ultra-low dose groups 2 patients received an extra dose of 1000mg RTX due to a flare. The 500mg dose was non-inferior to 1000mg at 3 months (0.04 (95% CI -0.39 to 0.30)), but not at 6 months (0.31 (95% CI 0.05 to 0.68). The 200mg dose was non-inferior to 1000mg at both time points. Because of our pre-defined hierarchical testing, non-inferiority could not formally be inferred for the 200mg dose. Mean DAS28-CRP scores remained low in all groups throughout the study, and B-cell counts decreased similarly at 3 months (figure 1). In the 200mg group, more patients received intramuscular corticosteroid injection(s) compared to the 1000mg group (table 1b).

Conclusion: Non-inferiority of retreatment with 1 × 500mg or 1 × 200mg rituximab versus 1 × 1000mg after 6 months could not formally be established. However, ultra-low doses appear similarly effective in the majority of RA patients, judged by DAS28-CRP course over time and B-cell results, with use of slightly more co-medication.

REFERENCES

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HEADLINE RESULTS FOR A PHASE 4, 52-WEEK, RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY TO ASSESS ADVERSE EVENTS OF SPECIAL INTEREST (AESI) IN ADULTS WITH ACTIVE, AUTOANTIBODY-POSITIVE SYSTEMIC LUPUS ERYTHEMATOUS (SLE) RECEIVING BELIMUMAB

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Background: Belimumab (BEL) is approved in adults with active, autoantibody-positive SLE. Phase 2, 3 and long-term extension studies showed a favourable benefit-risk profile. However, numerical differences in the incidence of mortality, infections, hypersensitivity reactions and some psychiatric events warranted a large, focused safety study to assess these events, along with potential for malignancy.

Objectives: To evaluate all-cause mortality and AESI in patients with SLE receiving intravenous (IV) BEL vs placebo (PBO) over 52 weeks.

Methods: This study (BASE; BEL115467; NCT01705977) randomised adults with SLE (1:1) to monthly BEL 10 mg/kg IV or PBO, plus standard of care, for 48 weeks. No minimum SELENA-SLEDAI disease activity was required and no exclusions for previous psychiatric conditions were made. Differences in rates (95% CI) of mortality and other pre-specified AESI (malignancies, serious infections, opportunistic infections and other infections of interest, serious depression, suicidality [C-SSRS], and serious infusion/hypersensitivity reactions) on-treatment (first to last dose +28 days) were assessed. For on-treatment serious suicidal ideation/behaviour and self-injury events (per sponsor adjudication), and on-study (first dose to end of Week 52 study follow-up) suicidal ideation/behaviour (C-SSRS), differences (95% CI) vs PBO were calculated post hoc.

Results: 4003 patients received ≥1 dose. Baseline demographics and disease characteristics were similar between groups. On-treatment mortality and pre-specified AESI rates are shown in the Table 1 below. Overall rates of on-treatment AESIs were similar between groups, except for serious depression and serious infusion/hypersensitivity reactions.

On-treatment deaths were most frequently caused by infection (3 [0.15%] PBO vs 9 [0.45%] BEL); on-study deaths occurred in 22 (1.10%) PBO and 13 (0.65%) BEL patients (difference [95% CI]: -0.45 [-1.03, 0.13]). On-treatment serious suicidal ideation/behaviour and self-injury events were reported for 5 (0.25%) PBO and 15 (0.75%) BEL patients (difference [95% CI]: 0.50 [0.06, 0.94]); on-study suicidal ideation/behaviour (C-SSRS) occurred in 39 (1.96%) PBO and 48 (2.43%) BEL patients (difference [95% CI]: 0.47 [-0.44, 1.38]). No suicide-related deaths were reported.

Conclusion: In this double-blind, placebo-controlled (1:1) safety study, which is the largest SLE clinical study to date with 4003 patients, on-treatment all-cause mortality, infection and malignancy AESI rates were similar between BEL and PBO, with imbalances observed in serious depression, serious suicidal ideation/behaviour and self-injury events, and serious infusion/hypersensitivity reactions.

Acknowledgement: We acknowledge the BASE Study Group. Study funding: GSK.


Table. Pre-specified AESI endpoints in the BASE study [on-treatment period]

<table>
<thead>
<tr>
<th>PBO</th>
<th>BEL 10 mg/kg IV</th>
<th>Difference vs PBO (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deaths</td>
<td>8 (0.45)</td>
<td>10 (0.50)</td>
</tr>
<tr>
<td>Serious infections</td>
<td>82 (4.4)</td>
<td>75 (4.0)</td>
</tr>
<tr>
<td>Opportunistic infections and other infections of interest</td>
<td>50 (2.6)</td>
<td>34 (1.9)</td>
</tr>
<tr>
<td>Malignancies (excluding MMCE)</td>
<td>1 (0.05)</td>
<td>1 (0.06)</td>
</tr>
<tr>
<td>MMCE</td>
<td>2 (0.11)</td>
<td>2 (0.11)</td>
</tr>
<tr>
<td>Serious depression</td>
<td>1 (0.05)</td>
<td>2 (0.11)</td>
</tr>
<tr>
<td>Suicidality (C-SSRS)</td>
<td>23 (1.15)</td>
<td>28 (1.43)</td>
</tr>
<tr>
<td>Serious infusion/hypersensitivity reactions</td>
<td>2 (0.11)</td>
<td>8 (0.42)</td>
</tr>
</tbody>
</table>

* Treatment-emergent suicidal ideation/behaviour.

#C: confidence interval; C-SSRS: Columbia Suicide Severity Rating Scale; MMCE, melanoma skin cancer.
Innate immunity in rheumatic diseases

THU0001 CIRCULATING INNATE LYMPHOID CELLS IN IGG4-RELATED DISEASE

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Background: IgG4-related disease (IgG4-RD) is characterized by lymphoplasmacytic infiltrates, IgG4 plasma cells, fibrosis and frequent ectopic lymphoid structures (ELS). Excessive Th2 cytokines production and role of T follicular helper (Tfh) cells have been reported. In innate cells (ILCs), a heterogeneous population of non-B non-T lymphocytes lacking antigen-specific receptors, are able to produce type 2 cytokines (ILC2s) or to participate to ELS formation (ILC3s) and could contribute to IgG4-RD lesions.

Objectives: To analyze circulating blood ILCs in IgG4-RD.

Methods: IgG4-RD patients were identified according to the Comprehensive Diagnostic Criteria. Patients treated with steroids or DMARDs within 3 months or rituximab within 6 months prior inclusion were excluded. Peripheral blood mononuclear cells were isolated and analyzed by flow cytometry. ILCs were defined as lymphoid CD45+Lineage(Lin)-CD127+ cells. Among ILCs, 3 subsets were defined according to CRTH2 and CD117 expression. In some patients, transcription factor expression (T-bet, GATA3, RORyT) as well as cytokine production (IFNγ, IL-4/IL-13, IL-17A/IL-22) after different stimulations were analyzed in ILC subsets. Results were compared to healthy controls (HC), correlated to clinical and biological characteristics, and compared before and after treatment.

Results: Twenty patients with active untreated IgG4-RD and 30 HC were included. In IgG4-RD group, mean age was 64 years and sex ratio 1:4. Serum IgG4 levels were >1.35 g/l for 85% of patients and median eosinophil count 410/mm3. Most patients (65%) were analyzed at diagnosis. Main organs involved were lymph nodes (n=15), pancreas (n=5), salivary glands (n=8), biliary tree and kidney (n=5), lung and retroperitoneum (n=4), with ≥3 organs involved in 50% of cases. Number of blood ILCs was not modified in IgG4-RD patients (1.2 ± 2.6 x10^7/ml vs 1.5 ± 1.3 x10^7/ml in HC, p=0.07). CRTH2+ ILC2s were increased in IgG4-RD patients (60%±13% vs 24%±10% in HC, p=0.002) and an increase in ILC3s (51.4% [33.8-66.7], p=0.0009, proportions). ILC2s (274/ml [152-594]) vs 554/ml [82-1000], p=0.045) and ILC3s (214/ml [120-620] vs 599/ml [336-908], p=0.04) numbers were decreased in IgG4-RD patients. No correlation was found between the proportion of total ILCs or any ILC subsets and clinical or biological characteristics such as age, number of organ involved, IgG4-RD Responder Index or serum IgG4. No correlation was found between Tfh and ILC3s, or between eosinophils and ILC2s numbers. As human ILC3s and ILC2s contribute to ILCs subset distribution observed. GATA3 or RORyT are produced by Th2 cytokine production, ELS formation and fibrosis, needs further investigations.

Conclusion: Circulating ILC2s and ILC3s are decreased in IgG4-RD. Recruitment of ILC2s or ILC3s in tissues, where they could participate to Th2 cytokine production, ELS formation and fibrosis, needs further investigations.

Disclosure of Interests: None declared


THU0002 THERAPEUTIC ANTI-TNF BIOLOGIC AGENTS EXHIBIT FUNCTIONAL DIFFERENCES IN BLOCKING TNF-INDUCED EFFECTS ON HUMAN MONOCYTES IN VITRO

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Background: Therapeutic anti-TNF biologic agents can be distinct in their structure, such as etanercept, a human TNFRII-Fc fusion protein, as compared to adalimumab, a human IgM molecule, and/or in their binding to TNF as shown by crystal structures of adalimumab as compared to infliximab in the presence of TNF. Whether these differences can affect the functional properties of these biologics in direct comparison to each other has not been thoroughly investigated.

Objectives: To determine the equivalency of all anti-TNF biologic agents currently approved for the treatment of RA in preventing a variety of TNF-induced effects on human monocytes in vitro.

Methods: Human mononcytic U937 NF-κB luciferase reporter cell line was incubated with 100 ng/ml TNF-α increasing conc (0.15-338 nM) of adalimumab (ADA), etanercept (ETN), infliximab (IFX), golimumab (GOL) or certolizumab pegol (CZP) as pre-formed complexes generated for 1 h. at 37°C. Surface TNF-R1 and -RII levels were monitored by flow cytometry following 1 h. incubation. Luciferase activity was measured in cell lysate after 4 h, to assess NF-κB activation. After 24 h., U937 cells were analyzed by flow cytometry for surface levels of ICAM-1, an NF-κB induced adhesion molecule shown to contribute to monocyte migration and arthritis. Apoptosis was assessed by time-lapse microscopy and flow cytometry using caspase 3/7 fluorescent substrate. Alpha-2,6 sialylation (Sia), a glycosylation modification shown to regulate TNF-RI internalization and apoptosis induction, was evaluated by flow cytometry using FITC-labeled Sambucus nigra lectin (SNA). Human PBMBC were incubated with TNF-α + pre-formed complex with anti-TNF biologics for 24 h. and then stained with CD14 and ICAM-1 Abs for flow cytometry.

Results: Surface levels of TNF-R1 and -RII on U937 cells were both reduced by 2.4-fold in presence of TNF. TNF-R1 was maintained at baseline levels by 16.7 nM ADA or CZP as pre-formed complexes with TNF; however, those complexes with ETN, IFX or GOL were only partially effective (48%, 61% and 52% reduction, respectively). All anti-TNF biologics were equally effective in preventing loss of surface TNF-R1. TNF stimulation of U937 NF-κB reporter cells led to a 122-fold increase in luciferase activity which was reduced to baseline by only ADA or CZP with largest conc. range tested. Partial reduction by 3, 7 and 11-fold was observed with ETN, IFX or GOL, respectively. TNF-α enhanced ICAM-1 surface expression (3-fold increase) on U937 cells was reduced to baseline by 16.7 nM ADA or CZP, whereas ETN, IFX or GOL were only partially effective (48%, 61% and 59% reduction, respectively). Exposure of CD14+ primary monocytes to ADA:TNF or CZP:TNF complexes not only prevented TNF induction of ICAM-1 but significantly reduced its level below that of baseline, whereas those with GOL or IFX brought ICAM-1 levels to baseline and those with ETN were only 46% effective. Both ADA:TNF and CZP:TNF complexes also completely inhibited TNF-induced apoptosis in a dose dependent manner unlike ETN, IFX and GOL, which were less effective (42%, 32% & 42% reduction, respectively). According to SNA staining, alpha-2,6 Sia surface levels dropped and GOL, which were less effective (42%, 32% & 42% reduction, respectively). All anti-TNF biologics were equally effective in preventing a variety of TNF-induced effects on human monocytes in vitro.

Conclusion: For each of the conditions tested in vitro, many resembling features associated with RA pathogenesis, the pre-formed complexes of ADA:TNF and CZP:TNF complexes not only prevented TNF induction of ICAM-1 but significantly reduced its level below that of baseline, whereas those with GOL or IFX brought ICAM-1 levels to baseline and those with ETN were only 46% effective. Both ADA:TNF and CZP:TNF complexes also completely inhibited TNF induced apoptosis in a dose dependent manner unlike ETN, IFX and GOL, which were less effective (42%, 32% & 42% reduction, respectively). According to SNA staining, alpha-2,6 Sia surface levels dropped in presence of TNF specifically on the subset of cells undergoing apoptosis and this subset was reduced proportionately to the inhibitory properties of anti-TNF biologics on apoptosis.

Disclosure of Interests: Bohdan Harvey Shareholder of; AbbVie, Inc., Employee of; AbbVie, Inc., Zehra Kaymakcalan Shareholder of; AbbVie, Inc., Employee of; AbbVie, Inc.


THU0003 CRYSTALLINE SILICA IMPAIRS EFFEROCYTOSIS CAPACITIES OF HUMAN MONOCYTE-DERIVED MACROPHAGES THROUGH RHOA-ROCK ACTIVATION

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Background: Inhalation of crystalline silica can lead to pulmonary diseases and systemic autoimmune disorders, such as systemic sclerosis (SSc), systemic lupus erythematosus or rheumatoid arthritis (1). A failure of apoptotic cell clearance, also called effectorcytosis, is reported in autoimmune diseases and, impaired effectorcytosis in macrophages from SSc patients has especially been described recently (2). However, the precise

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mechanisms linking crystalline silica exposure and autoimmune disorders is still to be determined.

Objectives: This study explored the effects of crystalline silica on efferocytosis abilities of human macrophages.

Methods: Monocyte-derived macrophages (MDM) were exposed in vitro to crystalline silica for 4 hours. Their ability to phagocyte CFSE-positive apoptotic and non-apoptotic Jurkat cells and their polarization profile after silica exposure were assessed by flow cytometry. Efferocytosis capacities of MDM from SSc were also evaluated using the same methods.

Results: Crystalline silica exposure impaired efferocytosis capacities of human MDM in a specific and dose-dependent manner. This effect of silica required the expression of SR-B1 and, was associated with a decreased membrane expression of the M2 polarization markers CD206, CD204 and CD163. Their expressions after silica exposure were similar to those of M1 polarized MDM. Silica increased F-actin staining, RhoA activation and phosphorylation of myosin phosphatase subunit 1 (MYPT1), a known ROCK target. Y27632, a Rho kinase (ROCK) inhibitor, reversed the F-actin staining, the phosphorylation of MYPT1 and, at least in part, the silica-induced impairment of efferocytosis. Moreover, efferocytosis abilities of MDM from SSc patients were similar to those of silica-exposed MDM and, a treatment of SSc-MDM with Y27632 significantly increase their efferocytosis capacities, suggesting an activation of the RhoA/ROCK pathway in SSc MDM also.

Conclusion: These findings demonstrate that silica impairs efferocytosis in MDM via an activation of RhoA/ROCK pathway. These results also suggest a therapeutic potential of drugs targeting this pathway and advance the hypothesis that silica exposure may contribute to the impaired efferocytosis capacities of macrophages from SSc patients, a silica-associated systemic disorder still without curative treatment to date.

REFERENCES:

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Disclosure of Interests: None declared


MICRORNA-223 NEGATIVELY REGULATE GOUTY INFLAMMATION BY TARGETING THE NLRP3 INFLAMMASOME WITHOUT INFLUENCING IL-37 AND TGF-B1

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Background: MicroRNA-223 (miR-223) serves as an important regulator of inflammatory and immune responses and is implicated in several autoinflammatory disorders[1]. To date, no relevant studies have reported the expression levels of miR-223 in gout patients or assessed whether miR-223 participates in negatively regulating gouty inflammation via regulating cytokines (such as IL-1β, tumor necrosis factor (TNF)-α, IL-37 and TGF-β1) by targeting the NLRP3 inflammasome.

Objectives: To determine the function of miR-223 in monosodium urate (MSU)-induced gouty inflammation.

Methods: miR-223 was detected among 107 acute gout patients (AG), 58 intercritical gout patients (IG), and 75 healthy subjects (HC). RAW264.7 macrophages were cultured and treated with MSU. Over-expression or under-expression of miR-223 was inducted in RAW264.7 macrophages to investigate the function of miR-223. Real-time quantitative PCR, ELISA and western blotting were used to determine the expression levels of miR-223, cytokines and the NLRP3 inflammasome.

Results: 1. Expression of miR-223 in PBMCs among the AG, IG and HC groups(Figure1)

Abstract THU0004 Figure 1.

2. Altered expression of miR-223, the NLRP3 inflammasome and cytokines in MSU-induced RAW264.7 murine macrophage inflammation (Figure2)

Abstract THU0004 Figure 2.

3. Effect of miR-223 on cytokine secretion from RAW264.7 macrophages treated with MSU(Figure3)
Conclusion: Our findings suggest that miR-223 provides negative feedback regulation of gouty inflammation development by suppressing production of IL-1β and TNF-α, but not by regulating IL-37 and TGF-β1, and that miR-223 regulates cytokine production by targeting the NLRP3 inflammasome. These findings provide novel insight into the regulatory role of miR-223 in the spontaneous resolution of acute gouty inflammation. Finally, these results suggest that targeting miR-223 in macrophages might be an effective therapeutic strategy for the treatment of gout flare.

REFERENCES:

Disclosure of Interests: Yu-Feng Qing Grant/research support from: Sichuan Youth Science and Technology (2016JQ0053), and the Department of Science and Technology of Sichuan Province (2018JY0257), Dan Zhu: None declared, Ting Yi: None declared, Jian-Xiong Zheng: None declared, Qin Xiong: None declared, Quan-Bo Zhang: None declared


THU0005   PTX3 AS A UNIVERSAL MARKER OF VASCULAR INFLAMMATION IN MULTIPLE IMMUNE-MEDIATED DISEASES

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Background: Pentraxin-3 (PTX3) is a prototypic innate humoral pattern recognition receptor with a multi-functional role in tissue homeostasis from host defence to fertility, cancer biology, autoimmunity, regulation of angiogenesis and tissue repair. PTX3 is selectively expressed at sites of inflammation and rises in the circulating blood during disease activity in many (but not all) immune-mediated inflammatory conditions. Research on PTX3 as a biomarker has so far focused on single diseases.
4. Cytokines and inflammatory mediators

**THU0006**

**PROINFLAMMATORY RESPONSES IN THE JAK-STAT PATHWAY IN SYNOVIAL FIBROBLASTS ARE STIMULUS-SPECIFIC AND ONLY PARTIALLY INHIBITED BY THERAPEUTIC DOSES OF TOFACITINIB**

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**Background:** The Jak-STAT signalling pathway has a key role in the pathogenesis of rheumatoid arthritis (RA). First Jak inhibitors, including tofacitinib, have been approved for the treatment of RA. Whereas Jak inhibitors exert pleiotropic effects on the immune system, their in situ activities on synovial fibroblasts (SF), the resident synovial cells, are less well understood.

**Objectives:** To characterise the Jak-STAT pathway and its inhibition by tofacitinib in RA synovial tissues and SF from different joints across diverse pro-inflammatory stimuli.

**Methods:** Synovial tissues and SF were isolated from knee (n=4), shoulder (n=4), and hands (n=4-6) joints of RA patients undergoing joint replacement surgery. To activate and inhibit the Jak-STAT pathway, SF were stimulated with TNF (0.1 ng/ml, 1ng/ml) + IL-6 receptor (IL-6R, 50ng/ml) or IL-6 (50ng/ml) + IL-6R for 24h in the presence or absence of 80ng/ml, 180ng/ml, and 1000ng/ml tofacitinib. 80ng/ml and 180ng/ml tofacitinib mimic the plasma drug concentrations in subjects on therapeutic doses of tofacitinib. 1000ng/ml is the in vitro used tofacitinib concentration. Gene expression in synovial tissues and SF (n=12 each) was measured using the low-density gene expression arrays containing 6 housekeeper genes and 90 probes for the core components, inhibitors and target genes of the Jak-STAT pathway. Clustering analysis of the array data [principal component analysis (PCA), heatmap] was performed using the ClustVis web tool. PCA identified one outlier SF sample, driven by distinct housekeeper gene expression that was omitted from further analysis. The production of IL-6 was determined by ELISA.

**Results:** RA synovial tissues and quiescent SF exhibited highly similar expression of the core components of the Jak-STAT signalling pathway, suggesting that SF contribute significantly to the synovial expression of JAK and STAT genes. Clustering analysis of the array data showed that SF stimulated with 0.1ng/ml TNF+IL-6R, SF treated with IL-6+IL-6R and quiescent SF formed separate clusters (Figure 1), pointing towards stimulus-specific transcriptional outputs in the Jak-STAT pathway. Moreover, TNF+IL-6R increased the expression of multiple core components in the Jak-STAT pathway (IL6ST, JAK2, JAK3, STAT3, STAT4) with simultaneous downregulation of pathway inhibitors (PIAS1, PIAS2) (p<0.05). SF produced different amounts of IL-6 under distinct proinflammatory stimuli, including 0.1ng/ml TNF-IL-6R (2.7±1.5 ng/ml), 1ng/ml TNF (2.8±1.7 ng/ml) and 1ng/ml TNF + IL-6R (5.0±2.7 ng/ml). Specifically, the addition of IL-6R to 0.1 ng/ml TNF increased the production of IL-6 in SF to the levels observed with 1ng/ml TNF alone and this response was further exacerbated in the presence of IL-6R + 1 ng/ml TNF. 80nm, 180nm and 1000nm tofacitinib decreased the IL-6 production by 20-30%, 50% and 60% respectively, suggesting a limited anti-inflammatory effect at average plasma concentrations (80nm). The inhibitory effect of tofacitinib on IL-6 production in SF was thus dose dependent, however highly similar across distinct proinflammatory conditions (0.1ng/ml or 1ng/ml TNF ± IL-6R).

**Conclusion:** Here we show that soluble IL-6R strongly augments the pro-inflammatory effects of TNF in SF. Furthermore, percent inhibition of the IL-6 production by tofacitinib remained constant across diverse proinflammatory conditions despite different amounts of IL-6 being produced. Thus, higher pre-treatment inflammatory responses to TNF ± IL-6R predict higher residual inflammatory activity in SF following Tofacitinib therapy, pointing towards a saturation of anti-inflammatory effects of Tofacitinib in SF in RA.

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IL-26 PROMOTES OSTEOCLASTOGENESIS IN RHEUMATOID ARTHRITIS

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Background: IL-26 is a 171-amino acid protein, which is classified as a member of the Th17 cytokine family. The role of IL-26 in osteoclastogenesis in RA is needed to be clarified to understand the pathogenesis of RA.

Objectives: To examine the functional role of interleukin-26 (IL-26) in the expression of RANKL and induction of osteoclastogenesis in rheumatoid arthritis (RA).

Methods: The expression of IL-20Rα and IL-26 was measured in a human monocyte cell line in response to human recombinant IL-26. The expression of GM-CSF messenger RNA (mRNA) and protein was measured in human monocytes by real-time polymerase chain reaction and ELISA. Human peripheral blood mononuclear cells were cocultured with macrophage colony-stimulating factor (M-CSF) and IL-26, after which osteoclastogenesis was evaluated by counting the number of tartrateresistant acid phosphatase-positive multinucleated cells. Osteoclastogenesis was also evaluated after monocytes were cocultured with IL-26-prestimulated FLS.

Results: The IL-26 concentration in the FLS was higher in RA patients than in patients with osteoarthritis (OA). In IL-26-stimulated FLS, the expression of RANKL mRNA and protein was increased in a dose-dependent manner. IL-26 increased the expression of RANKL in RA-FLS, and the IL-26-induced RANKL expression decreased by the inhibition of IL-20Rα. IL-26-induced RANKL expression was down-regulated significantly by the inhibition of SHP-1, ERK, JNK, STAT3, c-jun or p38 MAPK/ NF-κB signaling. When monocytes isolated from human peripheral blood were cultured with IL-26, they were differentiated into osteoclasts in the absence of RANKL. Monocytes were also differentiated into osteoclasts when they were cocultured with IL-26-pretreated RA-FLS.

Conclusion: IL-26 has a direct effect on osteoclastogenesis in RA: 1) direct induction of osteoclastogenesis from monocytes and 2) up-regulation of RANKL production in RA-FLS. This IL-26-RANKL axis could be a potential therapeutic target for bone destruction in RA.

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Disclosure of Interests: None declared.


GM-CSF PATHWAY SIGNATURE IDENTIFIED IN TEMPORAL ARTERY BIOSPES OF PATIENTS WITH GIANT CELL ARTERITIS

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Background: Giant Cell Arteritis (GCA) is a type of large vessel vasculitis that can cause blindness and aortic aneurysms. Significant unmet medical need remains in GCA, as current treatment options are limited, and relapse increases corticosteroid (CS) exposure and toxicity. The primary role of macrophages/dendritic cells (DCs) and T(H)1/T(H)17 lymphocytes in GCA pathogenesis has been highlighted previously. Granulocyte-macrophage colony stimulating factor (GM-CSF) may contribute to GCA pathogenesis by stimulating giant cell formation. GM-CSF produced by CD4+ T helper T(H)1 and T(H)17 cells can stimulate conventional DCs and promote differentiation of monocyte-derived DCs. GM-CSF may drive DCs to program naïve CD4+ T cells to T(H)1, T(H)17, and T follicular helper phenotypes (IFNγ/IL-17/IL-21). Notably GM-CSF RNA has been reported in GCA lesions and in peripheral blood mononuclear cells of symptomatic patients.

Objectives: We hypothesized elevation of the GM-CSF pathway signature in GCA versus controls.

Methods: Two independent sources of temporal artery biopsies were utilized. First, GCA (n=17) and control (symptomatic patients suspected for GCA, but with a normal temporal artery biopsy) (n=5) biopsies were analyzed for 15 mRNA transcripts representing T(H)1, T(H)17, and GM-CSF-signaling (RNAscope; RS) and for mRNA transcripts representing the autoimmune panel (Nanostring; NS). Semi-quantitative scoring was performed on RS images, and fold-change of representative T(H)1, T(H)17 and GM-CSF-related mRNA transcripts were calculated via NS nCounter analysis. Additional GCA and control biopsies were obtained and analyzed by RT-PCR for a subset of transcripts (n=10 each) and by confocal microscopy for GM-CSF and GM-CSF-Rx protein (n=2 each).

Results: The GM-CSF-signaling pathway molecular signature was confirmed to be upregulated by 4 independent analyses. GM-CSF-associated and T(H)1-associated genes were upregulated in GCA biopsies versus control (GM-CSF: 3-4x RS; GM-CSF-Rx: 6.7x NS, 6x RS; and C3D8: 3.9x NS, 6x RS; TFFx: 2x NS, 3x RS; IFNγ: 2x RS; IL-1β: 6x RS). T(H)17 associated genes were not elevated, potentially due to concomitant CS treatment.

Upregulation of both GM-CSF (12x) and GM-CSF-Rx (3x) mRNA was confirmed in a separate cohort of biopsies from GCA patients vs. controls by RT-PCR (Figure). GM-CSF and GM-CSF-Rx proteins were detected in the luminal endothelium, neovessels and inflammatory cells of GCA patients. In normal temporal arteries, GM-CSF protein was not detected, and some GM-CSF-Rx expression was observed in the luminal endothelium.

Conclusion: GM-CSF and T(H)1 pathway signatures were demonstrated in GCA patient temporal arteries by independent analytical techniques. Active GM-CSF signaling in diseased tissue is evidenced by increased expression of Pu.1 in the vessel wall. These data implicate the GM-CSF pathway in GCA pathophysiology and increase confidence in rationale for targeting GM-CSF in GCA.

REFERENCES:

Abstract THU0008 Figure 1.
ASSOCIATIONS BETWEEN CYTOKINE LEVELS AND TH17/TREG IMMUNE BALANCE IN PATIENTS WITH BEHÇET’S DISEASE

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Background: Behçet’s disease (BD) is a chronic systemic vascular inflammatory disease. Autimmune imbalance associated with genetic and infectious factors promotes the immune response of neutrophils and T cells, which is BD’s important pathogenesis. Several studies indicate that the Th17/Treg immune imbalance may play an important role in BD pathogene-sis. Although the proportion of Th17 cells was notably increased, which was accompanied by an increased levels of IL-17, IL-23, whether other cytokines are associated with Th17/Treg immune balance is unclear.

Objectives: The aim of this study was to examine associations between levels of a broad selection of cytokines and Th17/Treg immune balance in patients with BD.

Methods: The study included 66 BD patients and 66 healthy controls. The absolute counts of lymphocyte subsets and CD4+ T cell subsets were detected by flow cytometry for all participants. Serum levels of the following 6 cytokines were determined in the same samples using a cytokine beads array (Interleukin-2 (IL-2), Interleukin-4 (IL-4), Interleukin-6 (IL-6), Interleukin-10 (IL-10), Interferon-γ (INF-γ)) and Tumor Necrosis Factor-α (TNF-α) for all BD patients. T tests was used to compare continuous measures. Correlations between cytokines and Th17/Treg were assessed by Spearman’s rank correlation tests.

Results: (1) Compared to healthy controls, the absolute counts of T cells were increased (P<0.048), the absolute counts of CD8+ T cells were also increased (P=0.031) in BD group, the absolute counts of Th1 and Th17 cells were significantly increased (P<0.05) in BD group, the absolute counts of Th2 cells were decreased (P<0.001) in BD group, the ratio of Th1/Th2 was increased (P<0.001), and the ratio of Th17/Treg were increased (P<0.001) in BD group. There were no differences between the absolute counts of the two groups of B, NK, T+ B+NK, CD4+ T and Treg cells. (2) Among the investigated cytokines, the differences between the levels of IL-2, IL-6, INF-γ and normal range have statistical significance (P=0.001). Finally, two cytokines were positively correlated with Th17/Treg, i.e., IL-2 (r=0.279, P=0.023) and IL-4 (r=0.260, P=0.035)/P<0.2 for all other cytokines).

Conclusion: Our research shows that T cell homeostasis perturbation, especially Th1 and Th17 expansion and Th17/Treg immune imbalance, is the cornerstone of BD pathogenesis. These findings suggest that immune responses associated with increased levels of IL-2 and IL-4 may promote Th17/Treg immune imbalance. This also highlights the role of IL-2 and IL-4 in maintaining a balance in the Th17/Treg ratio. Further studies are required to evaluate these preliminary findings in different patient populations and also examine the possible molecular mechanisms behind our observations.

REFERENCES:


THE ANTI-INFLAMMATORY CYTOKINE INTERLEUKIN 37 IS AN ENDOGENOUS INHIBITOR OF TRAINED IMMUNITY

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Background: Trained immunity (TI) is a de-facto innate immune memory program induced in monocytes/macrophages by exposure to pathogens or vaccines, which evolved as a protective mechanism against infections. TI is characterized by rewiring of functional, epigenetic and metabolic programs of innate immune cells such as monocytes and macrophages, which sustain enhanced production of pro-inflammatory cytokines. Since aberrant activation of TI is implicated in inflammatory diseases, tight regulatory mechanisms are likely in place, but the mechanisms responsible for this modulation remain elusive.

Objectives: Scope of this study was to evaluated the role of IL-37, an anti-inflammatory cytokine that curbs inflammation as well as modulates metabolic pathways, as an endogenous regulator of trained immunity.

Methods: The effects of recombinant IL-37 were evaluated in a mouse model of TI induced by the administration of beta-glucan in vivo (survival to a lethal inoculum of infectious agents, production of inflammatory cytokines, recruitment of inflammatory cells at the sites of infection). Subsequently, the effects of IL-37 were evaluated in vivo in bone marrow monocytes (production of inflammatory cytokines, metabolic analysis of the activation status of the main pathways of cellular energy metabolism),
Finally, we evaluated the association between IL-37 gene polymorphisms and the induction of TIE1 in monocytes of healthy donors with in vitro functional studies.

Results: The exogenous administration of IL-37 abrogated the pro-inflammatory effects of TIE1, significantly reducing the production of pro-inflammatory cytokines and the survival of experimental animals subjected to a model of disseminated infection. The inhibitory effects of IL-37 on TIE1 were also associated with reduced recruitment of neutrophils at sites of inflammation. IL-37 and TIE1 programs had differential and opposite effects on the modulation of cellular energy metabolism of monocytes. In humans, polymorphisms in the IL-37 gene were associated with reduced activation of TIE1 programs and reduced production of inflammatory cytokines by healthy donor monocytes.

Conclusion: In conclusion, IL-37 emerges as an endogenous regulator of TIE1, which makes this cytokine a potential therapeutic target in immune-mediated pathologies.

REFERENCES:

Disclosure of Interests: None declared

THU0011 PEFICITINIB (ASP015K) INHIBITS MONOCYTE CHEMOTACTIC ACTIVITY VIA PRONFLAMMATORY CYTOKINE PRODUCTION IN RHEUMATOID ARTHRITIS FIBROBLAST-LIKE SYNOVIOCYTES
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Background: Janus kinase-signal transducer and activator of transcription (JAK-STAT) pathway has been identified as an important signaling pathway in rheumatoid arthritis (RA) of various cytokines (e.g. IL-6). Janus kinase (JAK) is a cytokine/protein tyrosine kinase associated with various cytokine receptors. Molecules of signaling pathways such as the JAK family are thought to be promising targets for RA treatment. Peficitinib (ASP0150K) is a novel JAK inhibitor in development for the treatment of RA. Peficitinib has been suggested for its effectiveness in clinical trials, but clarification of the mechanism of RA for the inflammatory pathology is still inadequate.

Objectives: We clarified the effect of peficitinib on RA fibroblast-like synoviocytes (FLS).

Methods: To determine whether JAK1, JAK2 and JAK3 were expressed in RA ST and FLS, immunohistochemistry was performed. To confirm if IL-6 and IL-6 receptor (IL-6R) activate JAK-STAT pathway in FLS, western blot analysis was performed. RA FLS were stimulated with IL-6 (100 ng/ml) and IL-6R (100 ng/ml) for 10 minutes or 30 minutes. Next, we investigated effect of peficitinib on IL-6 and IL-6R responses in RA FLS. RA FLS were stimulated with IL-6 (100 ng/ml) and IL-6R (100 ng/ml) after treated peficitinib (0.1, 1, 5µM) for 24 h. Furthermore, we performed a proliferation assay of FLS and chemotaxis assay using THP-1 (human acute monocye leukemia cell line) and peripheral blood mononuclear cells (PBMC) to perform functional analysis by peficitinib. In the same procedure as Western blot analysis, peficitinib (5 µM) was added to FLS and stimulated with IL-6 and IL-6R. Finally, we investigated whether peficitinib suppresses the secretion of FLS inflammatory mediator using ELISA. The amounts of RANTES/CCL5, MCP-1/CCL2, MMP-3, fractalkine/CX3CL1, ENA78/CXCL5 and IL-8 in IL-6 and IL-6R stimulated peficitinib treated RA FLS conditioned medium were determined compared with IL-6 and IL-6R stimulated non-treated RA FLS conditioned medium.

Results: We found JAK1, JAK2 and JAK3 were expressed in RA STs and FLS. JAK1 and JAK3 were observed in RA ST lining layers. JAK2 was expressed entirely in RA ST cell nucleus. JAK1, JAK2 and JAK3 were detected in RA FLSs. It was confirmed that JAK1, JAK2 and JAK3 is expressed in FLSs of ST. Representative western blotting showing expression of phospho STAT1, phospho STAT3 and phospho STAT5 were increased 10 minutes after stimulation with IL-6 and IL-6R. Phosphorylation of STAT1, STAT3 and STAT5 in RA FLS was suppressed by concentration-dependence of peficitinib. It was proved that peficitinib suppress the activation of JAK-STAT pathway. Furthermore, peficitinib treated RA FLS conditioned medium reduced THP-1 migration compared to non-treated RA FLS conditioned medium (number of THP-1 cells migrated ± SEM; 42 ± 3 and 66 ± 6 cells migrated, respectively, p<0.05). Peficitinib treated RA FLS conditioned medium also reduced PBMC migration compared to non-treated RA FLS conditioned medium (number of PBMC migrated ± SEM; 36 ± 5 and 63 ± 9 cells migrated, respectively, p<0.05). In addition, peficitinib treated RA FLS showed a 14 ± 2% decrease in proliferation of RA FLS compared with nontreated RA FLS. Finally, we found peficitinib suppress the secretion of inflammatory mediators in RA FLS. MCP-1/CCL2 in RA FLS supernatant was suppressed in peficitinib compared to nontreated(mean ± SEM; 160.1 ± 65.6 and 646.0 ± 107.1 pM, respectively, p=0.05). From these results, suppression of chemokinesis of THP-1 and PBMC was also observed through suppression of MCP-1/CCL2 in RA FLS supernatant. Conclusion: Peficitinib suppressed the JAK-STAT pathway of RA FLS and was involved in the suppression of monocyte chemotaxis and the proliferation of FLS through suppression of inflammatory cytokines. These results suggest that peficitinib acts on FLS and suppresses inflammatory pathology.

Disclosure of Interests: None declared

THU0012 ESTROGEN REGULATES MICRO RNA BIOPROCESSING AND PRODUCTION OF IL9 CYTOKINE WITHIN LEUKOCYTES IN RHEUMATOID ARTHRITIS
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Background: Rheumatoid arthritis (RA) is more prevalent in females. It is reported to be alleviated during pregnancy, and increase in severity during menopause, which implies estrogen as an important contributor in RA pathogenesis. Micro-RNA (miR) are short, non-coding RNAs, that act within a RNA-induced silencing complex. miRs have recently emerged as important epigenetic controls of leukocyte maturation and function.

Objectives: To study the epigenetic effect of estrogen on the transcription of microRNA and their bio-processor enzymes in RA patients.

Methods: The leukocytes of 145 female RA patients split for estrogen receptor alpha (ERa) (qct 9.57) were analyzed for the expression of Dicer, Drosha and DGR8 mRNA by RT-PCR and serum levels of TGFb-dependent cytokines IL4 and IL9. Micro-RNA transcription array was performed by 3D-Genetm microarray measuring >2560 miRs (TATAA Biocenter, Gothenburg) in human primary leukocytes, fat tissue and plasma. The samples were split by expression of estrogen receptor alpha (ERa, qct 9.57), a proxy of an active estrogen signaling, and used to identify miRs of interest. Bioinformatic analysis was performed using DIANA, miRDB, miRTarBase and Ensembl, using microRNA nucleotide sequences obtained from miRBase, to predict signaling pathways and gene targets of miR. To confirm estrogens effect on miR processing, leukocyte cultures of RA patients were exposed to estrogen and subjected to miR, gene and protein analysis.

Results: Comparing leukocytes with different ERa, we identified 214 miRs with high and 7 miRs with low expression when ERa was high. Cross-analysis in the fat and serum sample miR array identified most of those miRs. Bioinformatic analysis of the upregulated miRs confirmed that 16miRs were involved in the estrogen signaling pathway (p=0.0063) and 15 TGFb signaling pathway (p<0.0001), where these miRs had 61 common predicted gene targets.

To study if transcription of these predicted targets was dependent on estrogen signaling, we took advantage of the clinical RA material. Patients with high ERa were significantly younger (51y vs 61y, p<0.00001), which confirmed active estrogen signaling. High ERa had significantly higher expression of miR bioprocessing enzymes Dicer (p=0.0197), Drosha (p=0.0454), DGR8 (p=0.0192) and lower disease activity (DAS28, p=0.0023; ESR p=0.005, ILE, p=0.0129).

Conclusion: High ERa expression can be considered a significant regulator of miR transcription in leukocytes. miR and bio-processors regulated by estrogen could be of importance in the pathogenesis on RA by targeting pathways responsible for regulation of inflammation and the non-protective elements of RA development; explaining the ameliorating effects of estrogen.

Disclosure of Interests: None declared
IL-17A AND IL-17F ARE SECRETED BY ENTHESIS T CELLS AND SYNERGIZE WITH TNF TO INDUCE CCL20 FROM ENTHESAL STROMAL CELLS

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Background: Enthesis or inflammation of tendon/ligament anchorage points is the cardinal lesion in spondyloarthritis (SpA). Human SpA is thought to be driven by IL-17 producing T-cells and can be successfully therapeutically targeted with anti-IL-17A and more recently anti-IL-17F[2]. The CCR6-CCL20 axis is thought to be crucial to tissue recruitment of IL-17 producing T-cells, however it is presently unknown if CCR6+ T-cells reside at the healthy human enthesis[3]. Moreover, the ability of IL-17 to drive CCL20 production and hence to promote further T-cell migration to the enthesis has not been tested. Objectives: To determine if enthesis T cells secrete IL-17A and IL-17F. To determine if CCR6+ T-cells reside at the normal human enthesis. To study the effect of both IL-17A and IL-17F on CCL20 induction from entheseal stromal cells. Methods: Normal spinous process enthesis was obtained from patients undergoing spinal decompression or surgery for scoliosis correction. Normal PEB and ST were also analysed for the presence CCR6+ T-cells by multiparameter flow cytometry. Stromal cells were isolated from both the peri-entheseal bone (PEB) and enthesis soft tissue (ST). Stromal cells were stimulated with combinations of IL-17A or IL-17F and TNF and subsequently CCL20 was measured by ELISA. Normal PEB and ST were also analysed for the presence CCR6+ T-cells by multiparameter FACs including CD4+ and CD8+ cells. Results: Enthesal CD4+ cells secreted IL-17A and IL-17F following stimulation. When used as single agents IL-17A, IL-17F and TNF were able to induce minimal CCL20 from entheseal stromal cells, but great synergy was reported for IL-17A/IL-17F, IL-17A/TNF and IL-17F/TNF. No synergy was reported for IL-17A/TNF and IL-17F/TNF. No synergy was observed between IL-17A and TNF or IL-17F and TNF. Conclusion: Resident CD4+ T cells at the enthesis secrete IL-17A and IL-17F following stimulation. The normal human enthesis contains CCR6+ T cell populations, suggesting a CCR6+/CCL20 axis is important to entheseal homeostasis. IL-17A/TNF dramatically synergizes with TNF to induce CCL20 from entheseal stromal cells, which would be well placed to mediate further migration of IL-17 producing lymphocytes to enthesis tissues. REFERENCES:

Disclosure of Interests: Charlie Bridgewood: None declared, Tobias Russell Grant/research support from: PhD Project is funded by Novartis., Abdulla Watad: None declared, Hannah Rowe: None declared, Qiao Zhou: None declared, Almas Khan: None declared, Peter Loughenbury: None declared, Abhay S Rao: None declared, Peter Millner: None declared, Robert Dunsmuir: None declared, Richard Cuthbert: None declared, Dennis Mcgonagle Consultant for: Lilly, Novartis UCB, Speakers bureau: Lilly, Novartis UCB DOI: 10.1136/annrheumdis-2019-eular.3527

TARGETING ACTIVATED ASK1 IN SYNOVIAL FIBROBLASTS IN COMBINATION WITH JAK1 INHIBITION ENHANCES EFFICACY IN RAT CIA

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Background: Despite improved therapy, rheumatoid arthritis (RA) remains an area of unmet medical need. Current therapies have improved disease control by targeting inflammatory pathways. However, treatments rarely induce remission, highlighting the need for new therapies. Figitibin (FIL) is an oral selective JAK1 inhibitor that has demonstrated clinical efficacy in RA trials.1,2 Apoptosis signal-regulating kinase 1 (ASK1) is a member of the MAPK6 family that activates p38 and c-jun and has recently been shown to modulate human RA fibroblast-like synoviocyte (FLS) invasion, proliferation, and migration in vitro.3 We hypothesize that by dual targeting of JAK-dependent inflammatory pathways with FIL, and ASK1 signaling in FLS with an ASK1 inhibitor, we can demonstrate an increase in efficacy in a rat collagen-induced arthritis (CIA) model.

Objectives: To evaluate the individual and combination activity of JAK1 and ASK1 inhibition in the rat CIA model by oral dosing with FIL and an ASK1 inhibitor. Methods: The in vivo efficacy of FIL and an ASK1 inhibitor were tested individually or in combination in a therapeutic rat CIA model. Dosing was initiated at the onset of disease (day 11) and continued until day 18. Efficacy evaluations were based on animal body weights, daily ankle caliper measurements, ankle diameter (expressed as area under the curve), terminal hind paw weights, and histopathology of the ankles and knees. Results: Administration of FIL individually significantly reduced ankle diameter and final paw weights by 51% and 52%, respectively (p<0.05). There was no change in body weight loss or in histological measures with treatment. Conversely, ASK1 inhibition did not reduce inflammation as measured by ankle diameter or paw swelling, but resulted in a 48% reduction in ankle histopathological score (p<0.05). The combination of FIL and the ASK1 inhibitor showed significantly greater effects on all measured parameters including paw weight (81% reduction), ankle diameter (78% reduction), and ankle and knee histopathology scores (69% and 87% reduction, respectively) than either agent alone. Body weight loss was also significantly reduced with the combination, and increased toward normal weight gain compared to the monotherapy arms. Conclusion: Combining FIL with ASK1 inhibition significantly improved clinical and histopathology scores, and reduced body weight loss in this model. These data suggest that simultaneously targeting JAK and ASK1 pathways can provide orthogonal activities that can enhance overall disease control. REFERENCES:

VARIATION IN MACROPHAGES DIFFERENTIATION AND SREBF1 EXPRESSION BETWEEN INFRAPATELLAR FAT PAD AND SUBCUTANEOUS TISSUES FROM RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS PATIENTS

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Background: Sterol regulatory element-binding protein 1 (SREBP1) has been known to upregulate the expression levels of regulators of ω-3 fatty acids in the resolution phase of macrophages, and this would in turn repress the production of pro-inflammatory cytokines. In OA joints, adipocytes might participate in inflammatory process. We are interested to investigate the proportion of CD14 positive cells as well as M1 and M2 macrophages in SVF of Hoffa and SC, and explore contribution of SREBF1 to rheumatic disease pathological processes of RA and OA.

Objectives: To investigate the proportion of CD14 positive cells as well as M1 and M2 macrophages in SVF of Hoffa and SC; and to explore contribution of SREBF1 to rheumatic disease pathological processes of RA and OA.

Methods: After treated with collagenase, macrophages (CD14 positive cells) in SVF were counted by flow cytometry. Then they were divided, half for calculating the ratio between CD80 positive cells (M1 macrophages) and CD163 positive cells (M2 macrophages), and half for performing qRT-PCR.

Results: Characteristics of the patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>OA (n=7)</th>
<th>RA (n=8)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>72 (62-79)</td>
<td>63 (49-76)</td>
<td>0.055</td>
</tr>
<tr>
<td>Female patients (n)</td>
<td>6</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Male patients (n)</td>
<td>1</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Height (cm)</td>
<td>155 (151-164)</td>
<td>157 (147-161)</td>
<td>0.341</td>
</tr>
<tr>
<td>Body weight (kg)</td>
<td>62.7 (48.7-74.1)</td>
<td>58.7 (48.8-72.2)</td>
<td>0.386</td>
</tr>
<tr>
<td>BMI</td>
<td>0%</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>42.9%</td>
<td>50.0%</td>
<td>0.234</td>
</tr>
<tr>
<td>Overweight</td>
<td>42.9%</td>
<td>37.5%</td>
<td>0.05</td>
</tr>
<tr>
<td>Obese</td>
<td>14.3%</td>
<td>12.5%</td>
<td></td>
</tr>
</tbody>
</table>

OA: osteoarthritis; RA: rheumatoid arthritis; CRP: C-reactive protein; BMI: body mass index; Underweight: BMI <18.5; overweight: BMI >24.9; normal BMI: 18.5-24.9; obesity: BMI >30.0

More CD14 positive cells exist in Hoffa comparing to SC, and M2 macrophages show higher proportion. A comparison of proportion of CD14 positive cells between Hoffa and SC showed significance both from OA and from RA. To M2 macrophages proportion, higher percentages of M2 macrophages (OA: 26.3±5.5%, RA: 22.5±2.4%) exist in Hoffa from both OA and RA patients, but no significance was found between the diseases. However, the proportion of M1 macrophages (OA: 15.6±1.7%, RA: 11.3±2.1%) indicated significance.

Srebf1 expressed less in Hoffa than in SC

Results show that in Hoffa, srebf1c expressed less in RA patients than that in OA patients, but no significance was indicated. In the proportion of expression levels between Hoffa and SC, both srebf1a and srebf1c showed significance, and more IL-6 and IL-1β expressed in Hoffa than in SC.

Conclusion: In RA patients, more M2 macrophages exist in Hoffa than in SC. Lower expression levels of srebf1c in Hoffa from RA patients suggest that macrophages differentiation can be reprogrammed by fatty acid metabolism.

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Disclosure of Interests: Shuhe Ma: None declared, Kosaku Murakami: None declared, Motomu Hashimoto Grant/research support from: Astellas, Brystol-Meyers, Eisai, Employee of: M. H. is affiliated with the department (Department of Advanced Medicine for Rheumatic Diseases, Kyoto University), which is financially supported by four pharmaceutical companies (Tanabe-Mitsubishi, Chugai, Ayumi, UCB Japan), Speakers bureau: Tanabe Mitsubishi, Brystol-Meiers, Masao Tanaka: None declared, Koichi Murata: None declared, Kohei Nishitani: None declared, Hiromu Ito: None declared, Tsuneyo Mimori: None declared


ALTERED EXPRESSION OF FUNCTION OF P2X7 RECEPTOR IN PATIENTS AFFECTED BY SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background: Extracellular ATP (eATP) is one of the most diffuse danger associated molecular patterns (DAMPs) released actively through specific mechanisms from intact cells, or passively from damaged or dying cells. An implication for eATP has been found in SLE. Among receptors for eATP, P2X7R is deeply involved in inflammatory and immune processes and its activation drives different intracellular pathways such as NLRP3-inflammasome activation, IL-1β maturation and release, IL-6 and TNF-α production, regulation of lymphocyte proliferation and cell apoptosis. Previous studies pointed out a possible relationship between P2X7R signaling pathways and SLE pathogenesis. A marked inflammatory condition characterize serositis, that are among the most common manifestations of SLE, and chloroquine is one of the main drugs employed.

Objectives: The aim of this study was to investigate P2X7R expression and activity in SLE.

Methods: 48 SLE patients, and 20 healthy control (HC) subjects were enrolled. Among SLE patients, 16 (SLE-S) presented, and 32 (SLE-NS) did not present history of serositis. All subjects gave written informed consent to peripheral venous blood withdrawal after approval by the local ethic committee. Plasma samples were used to measure IL-1β, IL-6 and TNF-α levels by ELISA. Mononuclear cells were isolated from blood samples by Ficoll gradient sedimentation and employed as follow: i) assessment of IL-1β, IL-6 and TNF-α release after stimulation with lipopolysaccharide (LPS) and/or Benzoyl ATP (BzATP); ii) evaluation of P2X7R mRNA expression by RT-PCR; iii) measurement of P2X7R activity as BzATP-induced increase of intracellular Ca²⁺ concentration using the Fura2/AM probe.
Results: In SLE patients respect to HC, plasma IL-1β levels were unmodified whereas IL-6 was higher, resulting significantly increased in SLE-S. Monocytes isolated from SLE patients released lower quantities of IL-1β after stimulation with BzATP, whereas the release of both IL-6 and TNF-α was significantly augmented in SLE-NS respect to both HC and SLE-S subjects after all types of stimulation. RT-PCR showed reduced P2X7R and augmented NLRP3 mRNA expression in SLE patients. Accordingly, P2X7R activity was significantly reduced in all SLE patients and did not appear to be influenced by a chloroquine pre-treatment.

Conclusion: In SLE patients, compared to HC subjects, we found reduced P2X7R mRNA expression, increased NLRP3 mRNA, as a possible compensating mechanism, and correspondingly, significantly lower BzATP-induced intracellular Ca2+ increase, without an apparent influence by chloroquine, one of the drugs most diffusely used for SLE treatment. The in vitro IL-1β release was reduced, whereas plasma IL-1β was unaltered, indicating an alternative source than monocytes, of this cytokine. Conversely, IL-6 and TNF-α levels were increased in vitro, and IL-6 was present in plasma at higher levels. The possible consequences of reduced P2X7R, mainly on cytokines network deregulation and lymphocyte proliferation, will be further investigated as well as the role of IL-6 and TNF-α as possible therapeutic targets.

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Disclosure of Interests: Anna Lisa Giuliani: None declared, Federica Furini: None declared, Alessandra Bortoluzzi: None declared, Marcello Govoni: None declared, Francesco Di Virgilio Consultant for: FDV is a member of the Scientific Advisory Board of Bioseptre Ltd, a UK-based biotech Company involved in the development of P2X7R-targeted therapeutics.


THU0017 IN VITRO MECHANISTIC STUDIES DEMONSTRATE FILGOTINIB ACTIVITY THAT HAS POTENTIAL IMPLICATIONS FOR DIFFERENTIATION AMONG JAK INHIBITORS

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Background: Inhibition of the Janus kinase-signal transducers and activators of transcription (JAK-STAT) pathway has demonstrated efficacy in immune-mediated diseases and has been identified as a therapeutic target for the treatment of rheumatoid arthritis (RA). Differences in JAK inhibitor specificity for JAK1, JAK2, JAK3, and TYK2 may influence their safety profiles, but the mechanism is not known. Selective JAK1 inhibition by filgotinib (FIL) may modulate a subset of proinflammatory cytokines associated with RA pathogenesis and improve the risk-benefit profile by minimizing other non-JAK1-related adverse events. JAK2 inhibition is associated with cytokine upregulation, while JAK3 inhibition has been associated with increased risk for opportunistic infections (eg, tuberculosis and herpes zoster) and chronic low-grade inflammation. In clinical trials, FIL did not negatively impact hemoglobin, LDL/HDL ratios, or natural killer (NK) cell counts.1,2

Objectives: To compare the in vitro profile of JAK inhibitors with different JAK selectivity profiles, for effects on erythroid progenitor cell expansion, NK cell proliferation, and liver X receptor (LXR) agonist-induced cholesterol ester transfer protein (CETP) expression, an enzyme responsible for the conversion of HDL to LDL.

Methods: JAK inhibitors (FIL, FIL metabolite [GS-829845], baricitinib [BARI], tofacitinib [TOFA], and upadacitinib [UPA]) were evaluated in vitro in human cell-based assays: growth of erythroid progenitors from human cord blood CD34+ cells using a HemaTox™ liquid expansion assay, IL-15-induced NK cell proliferation, and LXR agonist-induced CETP expression in the hepatic cell line (HepG2). Using IC50s generated from these assays and the reported human plasma concentrations of the JAK inhibitors from clinical studies,3-6 we calculated the target coverage for each compound. The activity of FIL in humans was based on a PK-PD modeling algorithm7 of FIL + GS-829845.

Results: In vitro assay results are described in the table. Based on these results, human exposure data, and modeled PK-PD relationships, FIL 100 mg and FIL 200 mg result in lower calculated cellular inhibition than the other JAK inhibitors at clinical exposures. Notably, FIL 100 mg and FIL 200 mg, but not the other inhibitors, are calculated to reduce CETP expression by 17% and 27%, respectively, while BARI, TOFA, and UPA are not expected to alter CETP levels.

Abstract THU0017 Table 1. IC50 ± SD in in vitro assays (nM, unless otherwise noted).

<table>
<thead>
<tr>
<th>Assay</th>
<th>FIL</th>
<th>GS-829845</th>
<th>BARI</th>
<th>TOFA</th>
<th>UPA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early erythroid progenitors</td>
<td>1960 ±137</td>
<td>1900 ±137</td>
<td>38.6±2.9</td>
<td>210 ±15.2</td>
<td>11±2.9</td>
</tr>
<tr>
<td>Mature erythroid progenitors</td>
<td>1140 ±112</td>
<td>10600 ±1270</td>
<td>25.7±2.9</td>
<td>10 ±2.7</td>
<td>4.1</td>
</tr>
<tr>
<td>NK cell proliferation</td>
<td>314.8 ±53</td>
<td>9697 ±600</td>
<td>6.6±1.9</td>
<td>12.2 ±2.1</td>
<td>4.1</td>
</tr>
<tr>
<td>Inhibition of LXR agonist-induced CETP expression</td>
<td>15.3 ±5</td>
<td>19.4 ±10</td>
<td>&gt;1 µM weak</td>
<td>No effect</td>
<td></td>
</tr>
</tbody>
</table>

4 Weak stimulation of LXR agonist-induced CETP expression.

Conclusion: JAK1 selectivity of FIL and GS-829845 resulted in less inhibition of erythroid progenitor expansion and NK cell proliferation compared with BARI, TOFA, and UPA. FIL also reduced LXR agonist-induced CETP expression, while the other inhibitors did not alter these levels. These results provide a potential mechanistic link to the observed reduction of CETP concentration and activity following FIL treatment, and the observed reduction in LDL-HDL in RA patients.8

REFERENCES:


THU0018 ANTI-GALECTIN-9 ANTIBODY AS A NOVEL TREATMENT OPTION IN RHEUMATOID ARTHRITIS TARGETING PATHOGENIC FIBROBLAST-LIKE SYNOVIOCYTES

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Background: Fibroblasts-like synoviocytes (FLS) present in the stromal environment are key effector cells in the persistence of synovial inflammation and joint damage in rheumatoid arthritis (RA). A particular subset of FLS characterized as Thy1+Podelparin/CD34 is significantly expanded in RA patients and has been described to be disease-associated.1 Currently, no treatment targeting the stromal environment in RA is available2.

Objectives: To identify a novel treatment option targeting the stromal environment in RA to modify the disease-associated subset of fibroblasts.

Methods: An in vitro model was established with FLS derived from synovial fluid mononuclear cells (SFMC) from RA and osteoarthritis (OA) patients (n=6). FLS between passage 2-5 were used for further analyses. Untreated FLS in cultures were analyzed by flow cytometry for expression of
of the surface proteins CD34, CD45, Thy-1 and Podoplanin. The potential effect of cell detachment solutions on the expression of the surface proteins was examined by applying either tropsin or lidocaine. To evaluate on the inflammation status of the FLS, MCP-1 levels in supernatants from FLS in mono-cultures stimulated with either antibodies targeting galectin-9 (Gal-9), an anti-Gal-9 antibody-matched isotype control, LPS or steroid were analyzed by ELISA and compared to culture medium alone. Cell viability were examined using an MTT assay. Data are expressed as mean (95% CI) and analysed by a paired t-test. P-values <0.05 were considered statistically significant.

Results: FLS derived from SFMC were characterized as CD34+CD45- and declared, Aida Solhøj Hansen: None declared, Tue Wenzel Kragstrup Ditte Køster: None declared, Malene Hvid: None declared.

References:

Disclosure of Interests: Ditte Køster: None declared, Malene Hvid: None declared, Aida Solhøj Hansen: None declared, Tue Wenzel Kragstrup Consultant for: Bristol-Myers Squibb, Speakers bureau: Pfizer, Bristol-Myers Squibb, Eli-Lilly, Novartis, UCB, Pierre Busson: None declared, Bent Deleuran: None declared, Morten Aagaard Nielsen: None declared


THU0019 INHIBITION OF FUCOSYLATION IN ENDOTHELIAL CELLS REDUCES RHEUMATOID ARTHRITIS ANGIOGENESIS
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Background: Glycosylation has been reported to associate with tumor invasion and metastasis. Fucosylation is involved in the biological functions of adhesion molecules and growth factor receptors. In regards to arthritis, we have previously reported that fucosylated proteins were expressed in rheumatoid arthritis (RA) synovial tissues. However, a direct role for fucosylated cytokines in RA has not been demonstrated.

Objectives: To confirm that fucosylated proteins are expressed in RA and involved in RA angiogenesis.

Methods: Total glycans in serum were significantly higher than in NL serum [mean ± SEM; 477 ± 24 pmol/μl (n=10) and 339 ± 14 pmol/μl (n=10), p<0.05, respectively]. In addition, total glycans in RA serum were significantly decreased with tocilizumab treatment at 24 weeks. Total glycans in RA serum were also correlated with DAS28 (ESR). Percent of fucosylated proteins in total glycans were decreased with TCZ treatment at 24 weeks. 2-d Gal treated HUVEC tube formed towards RA synovial fluids (n=6 patients) were decreased compared with nontreated HUVEC tube formed (number of tube formed: 7 ± 1 and 25 ± 2, p<0.05, respectively). We found that 2dGal treated HUVECs showed decreased migration compared with nontreated HUVECs, towards RA SF (numbers of HUVEC migrated; 3 ± 1 and 34 ± 4, n=5 patients, p<0.05). Fractalkine, CXCL1, CXCL6, or IL-8/CXCL8 in 2-d Gal treated HUVEC conditioned medium were decreased compared with in non-treated HUVEC conditioned medium but not MCP-1/CCL2, ENA-78/CXCL5, or VEGF.

Conclusion: These data indicate that glycoproteins are involved with RA, and play a role in angiogenesis in RA and suggest that targeting glycosylation especially fucosylation may provide a method by which to decrease inflammation and potentially treat other inflammatory diseases.

Disclosure of Interests: None declared


THU0200 COMPARATIVE STUDY OF THE PHOSPHODIESTERASE TYPE 5 INHIBITOR SILDAFIL AND THE PROSTACYCLIN ANALOGUE ILOPROST ON IP10 MODULATION IN SYSTEMIC SCLEROSIS
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Background: Systemic sclerosis (SSc) is an autoimmune disease ending in multorgan fibrosis. Vascular damage, relevant for the vascular alteration and disruption, has been suggested to play a key role in disease maintenance and progression [1]. Recent data demonstrated that high serum levels of the interferon (IFN)-γ-induced protein 10 (IP-10) in SSc patients correlated with peripheral vascular injury and increased in association with nailfold capillaroscopic pattern worsening and digital ulcers presence [2, 3]. Between the vasoactive drugs used for SSc treatment, the prostacyclin analogue iloprost (I) and PDE-S inhibitor sildenafil (S) seem to have high vasodilatory and immunomodulatory actions [4-6].

Objectives: To investigate and compare the ability of S and I to modulate: IP-10 circulating levels in SSc patients under different treatments; IP-10 release by human endothelial (Hfaec) cells subjected to Th1-related inflammatory stimuli.

Methods: Sera of 28 patients satisfying ACR/EULAR 2013 classification criteria for SSc were analyzed by ELISA. IFN-γ+TNFα-induced activation of NFκB, STAT1, JNK, ERK1/2 and AKT in Hfaec after S or I was tested by Western blot.

Results: The treatment with S significantly reduced IP-10 serum levels vs. treatment with (DMARDS) and corticosteroids (CCs) (184.1±65.10 vs. 880.9±339.0 pg/ml and vs. 426.5±101.7, respectively, P<0.01); while no significant difference has been found vs. 1 (184.1±65.10 vs. 282.7±46.6 pg/ml). In Hfaec, S and I differently counteracted the IFN-γ+TNFα-induced phosphorylation of JNKs (respectively 61.0±20.1% and 31.6±7.9% of phosphorylation vs. I+T-induced taken as 100%), STAT1 (respectively 49.2±15.8% and 93.4±1.2% of phosphorylation vs. I+T-induced taken as 100%), and AKT (respectively 27.3±4.4% of phosphorylation vs. I+T-induced taken as 100%)

Conclusion: In vivo results show that S and I have more effect in targetting serum IP-10 in SSc patients than other therapeutic treatments. In vitro data show different inhibitory drug-induced effects on pathways under-virulent production, dependent on intracellular targets. S could be a potential pharmacological tool as effective as I to control IP-10 in blood or at endothelial cell level in SSc.

References:
Background: Obesity is a condition that prolongs chronic inflammation and promotes synthesis and secretion of pro-inflammatory factors by adipose tissue, such as classical cytokines, tumor necrosis factor-α (TNF-α), adipokines (leptin, adiponectin, resistin) and other newly identified pro-inflammatory factors (hemin, lipokain, serum amyloid protein 3) [1,2,3,4,5]. Nowadays one of the most actively studied adipokines is nicotinamide phosphoribosyltransferase (visfatin, Nampt).

Objectives: We investigated the relationship the effect of weight loss over 5 kg on the clinical manifestations of OA and Nampt serum levels in patients with OA.

Methods: We observed 160 patients with different forms of OA ranged in age from 36 to 78 years, of whom there were 104 (65%) women (mean age 52.08 ± 1,58 years), and 56 (35%) of men (mean age - 54.07 ± 2.0 years) and the control group (60 healthy persons) with no complaints of pain in the joints over a lifetime, and without clinical signs of OA. Nampt level in serum was determined by ELISA using a commercial test systems.

Results: As overweight patients were recruited in the study, hypocaloric diet low in animal fats and physiotherapy has been recommended to all participants. The positive dynamics in body weight loss over 5 kg within 3 months has been achieved by 36 patients (23%). All patients were divided into two groups to study the effect of weight loss on the clinical manifestations of OA. These data proves that obesity may be an important risk factor for OA progression. As a result, weight loss results in decreasing metabolic disorder severity. In the second group of patients we have seen a decrease in all the parameters, but a significant difference has been observed only in the level of CRP, level of pain at rest and during walking according to VAS scale and total index on the WOMAC. However, patients with weight loss over 5 kg had significantly greater positive dynamics of clinical parameters than in the second group, without weight loss. This fact is probably explained by the decreased activity of inflammatory process after OA therapy and weight reduction.

Conclusion: Thus, as a result of our study patients with OA with weight loss of more than 5 kg had more obvious pain relief than patients with the original weight. These findings suggest that there is a possible role of visfatin in the pathogenesis of osteoarthritis. All patients with OA with a BMI over 25 kg/m² are recommended to lower their weight to decrease the mechanical stress on the joints, and also to reduce the severity of inflammation and metabolic disorders.

REFERENCES:


Disclosure of Interests: None declared


THU0022

ETANERCEPT INCREASES AUTOPTOSIS AND REDUCES APOPTOSIS INDUCED BY TNF-ALPHA EXPOSURE IN ENDOTHELIAL CELLS IN VITRO

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Background: Rheumatoid arthritis (RA) is associated with high incidence of cardiovascular events, mainly due to accelerated atherosclerosis and endothelial dysfunction (1). Apoptosis in endothelial cells has been associated with vascular wall damage, contributing to atherosclerotic plaque formation (2). At the contrary, apoptosis may play a protective role in preventing development of atherosclerosis. However, the exact mechanism which controls the apoptotic effect of endothelial cells is still unknown. Tumor necrosis factor alpha (TNF-α) is one of the leading cytokines involved in the pathogenesis of RA. Several evidences suggest a pro-atherogenic effect of TNF-α in patients with RA. Etanercept (ETA) and other TNF-α inhibitors are effective treatments for joint inflammation in RA, but their effect on endothelial dysfunction is still not well understood.

Objectives: The aim of this study was to investigate in vitro, the effects of ETA treatment on endothelial cells exposed to TNF-α, with particular attention on apoptosis levels and autophagy pathway.

Methods: In vitro effects of ETA and TNF-α on endothelium were evaluated using human umbilical vein cell line EA.hy926. Cells were treated with ETA (15μg), TNF-α (10 ng/ml), alone or in combination. An untreated control cell culture was also performed. After 24 hours, apoptosis levels and autophagy have been evaluated. Apoptosis was analyzed by flow cytometry using a FITC-conjugated annexin V and propidium iodide apoptosis detection kit (3); autophagy was analyzed by western blot for the expression level of the autophagic markers LC3-II and p-62 (4).

Results: TNF-α treatment significantly increased apoptosis in endothelial cells compared both to untreated and ETA-treated cells (p= 0.0087 and p= 0.00187 respectively) [Figure 1]. The co-treatment with TNF-α and ETA significantly reversed the increase of apoptosis levels (p= 0.001 versus TNFα alone). Both ETA and TNFα treatments significantly increased the expression level of LC3II in treated cells when compared to untreated cells (p=18 and p=3 respectively). The co-treatment induced an additive effect on apoptosis levels (p< 0.0001 versus untreated cells). At last, the expression level of p-62 showed an inversely proportional trend to LC3II levels [ETA (p=0.0001), TNF-α (p<1), ETA+TNF-α (p<5)] versus untreated cells, respectively [Figure 2].

Conclusion: Our results show that treatment with Etanercept have a protective effect on endothelial cells in vitro, reversing the apoptosis induced by TNF-α. Moreover, this is the first study that supports a possible effect of Etanercept in increasing autophagy level in endothelial cells. Reducing TNFα-induced apoptosis, Etanercept treatment may lead to an improvement of endothelial function and to a reduction of accelerated atherosclerosis.

REFERENCES:

Abstract THU0022 Figure 1.

Disclosure of Interests: None declared

THU0023 PARADOXICAL EFFECT OF INTERLEUKIN 1 BETA CYTOKINE ON COLLAGEN TYPE I SYNTHESIS IN OSTEOSTABL-LIKE CELLS

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Background: Osteoblasts are the bone forming cells that are responsible for the synthesis of collagen type I and mineralization of bone during initial bone formation and later bone remodeling. Abnormalities in osteoblasts phenotype and activity occur in common bone diseases including osteoarthritis (OA). Studies showed that osteoarthritic osteoblasts secrete a colla-gen type I homotrimer of α1 chains, which is phenotypically distinct from the normal heterotrimer formed by two α1 chains and one α2 chain. Cytokines released during OA initiation or progression may interfere with osteoblastic function in the bone matrix. Interleukin 1 beta (IL-1β) is one of the major inflammatory cytokines implicated in the pathogenesis of OA; however, the biological response of osteoblasts to the cytokine is only partly understood.

Objectives: Our aims were to clarify the effects of IL-1β on collagen type I synthesis in osteoblast-like cells and to explore further possible relationship between collagen type I synthesis and mineralization.

Methods: At confluence, MG63 osteoblast-like cells in osteogenic media were stimulated with low (1 ng/ml) or high (10 ng/ml) dose of recombinant human IL-1β at several incubation times: 1, 2, 3, 4 and 5 hours. Non-stimulated MG63 cells were grown as control at indicated time points. Cell viability was tested by using the PrestoBlue reagent. Total collagen production was evaluated by Picro-sirius red precipitation method. Secretion of homotrimer collagen type I α1 (COL1A1) and mineralization at exposure time of 1-, 3- and 5-hour were determined by immunofluorescence staining of COL1A1 antibody and Alizarin Red S staining, respectively.

Results: IL-1β showed no statistical evidence in influencing cell viability at the time and dose tested compared to control. We found that IL-1β significantly (p<0.05) increased collagen content at short exposure time (1-hour), while significantly (p<0.05) decreased collagen content at longer exposure time (5-hour), in a dose-dependent manner. Immunofluorescence staining showed increased of homotrimer COL1A1 at 1-hour exposure and decreased of homotrimer COL1A1 at 5-hour exposure of IL-1β in the MG63 cells. IL-1β stimulated the formation of mineralized nodules at all exposure time.

Conclusion: We demonstrated for the first time of the paradoxical effect of IL-1β on collagen type I synthesis in osteoblast-like cells. Increased mineralization in low and high homotrimer type I collagen condition may possibly explain the abnormal mineralization in osteoarthritic bone.

TNF-α, tumor necrosis factor-α; HAAF, human aortic adventitial fibroblasts. Data are shown as mean ± SD of 3 independent experiments, each in triplicate. *P < 0.001, **P < 0.01 vs. control group(0 ng/ml T-614) within each group alone.

Conclusion: T-614 can inhibit the proliferation of HAAF and promote IL-8 production; therefore, it may provide a new immunotherapeutic intervention for TA.

REFERENCES:
synovial fibroblasts (SF) are known key effector cells of cartilage destruction in inflammatory arthritides such as RA, tenocytes are a major component of tendons and entheses and play a central role in tendon inflammation observed in PsA.

**Objectives:** To investigate whether PsASF and tenocytes show significant interactions while being stimulated with the above cytokines alone as well as in combination with the aim to find out whether these may contribute to thepathogenesis of PsA.

**Methods:** SF were isolated from patients with PsA undergoing joint surgery. Human tenocytes were acquired commercially and isolated from hamstring tendon tissue of patients undergoing hamstring tendon ACL reconstruction. PsASF and tenocytes were stimulated with IL-1β, TNF-α, IFN-γ, IL-15 and IL-23 alone and in combination. Direct cell co-culture experiments were performed at a 1:1 ratio of both cell types in parallel to experiments with single cell type cultures. IL-6 levels were measured by ELISA to quantify the immunological activation of the cells.

**Results:** PsASF as well as tenocytes showed strong responses to IL-1β (tenocytes 1173-fold, n=3; PsASF 156-fold, n=3) and TNF-α (tenocytes 10-fold, n=3; PsASF 9-fold, n=3) stimulation regarding IL-6 secretion. IFN-γ alone had only minimal effects on both cell types but acted synergistically when applied together with IL-1β (tenocytes 218-fold, n=3; PsASF 1129-fold, n=3) and TNF-α (tenocytes 24-fold, n=3; PsASF 119-fold, n=3). IL-15 and IL-23 alone showed no effect but the data suggest a small antagonistic effect against IL-1β (tenocytes IL-15 21% IL-23 27%, n=3; PsASF IL-23 19%, n=3) and TNF-α induced IL-6 secretion. Overall, PsASF and tenocytes showed similar responses in the single cell type stimulation experiments. Co-culturing PsASF and tenocytes did not reveal any synergistic or antagonistic interactions in regards to any of the cytokines used.

**Conclusion:** Our data suggest that tenocytes and PsASF do not interact in a way that would promote inflammation within the synovio-enthesal complex. Also, as far as the induction of IL-6 is concerned, PsASF and tenocytes are not major target cells of IL-15 and IL-23. IFN-γ, however, may be able to promote inflammation in combination with other cytokines in both cell types.

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**THU0025**

**ANALYSIS OF POTENTIAL INTERACTIONS BETWEEN TENOCYTES AND SYNOVIAL FIBROBLASTS AFTER STIMULATION WITH CYTOKINES EXPRESSED WITHIN THE SYNOVIO-ENTHESAL COMPLEX**

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**Background:** Psoriatic arthritis (PsA) is frequently associated with enthesitis. It has been proposed that inflammatory processes at the synovio-enthesal complex are involved in the pathogenesis of inflammatory arthritides including especially PsA. Besides IL-1β and TNF-α, IL-15, IL-23 and IFN-γ are cytokines expressed within the synovium, tendons and entheses and some of which are already used as therapeutic targets.

**Objectives:**

1. To study the effect of different JAKi on the proliferation of RASF.
2. To investigate whether PsASF and tenocytes show significant interactions while being stimulated with the above cytokines alone as well as in combination.
3. To find out whether these may contribute to the pathogenesis of PsA.

**Methods:** Human RASF were isolated and pretreated with JAKi. After stimulation with IL-1β, TNF-α, IFN-γ, IL-15 and IL-23, the effect of different JAKi on proliferation of RASF was determined by a BrdU-incorporation assay. The influence of peficitinib on migration of RASF was determined by a Transwell assay. The levels of IL-6 and MMP-3 were measured in supernatants by ELISA.

**Results:**

- **Proliferation:** The effect of different JAKi on proliferation of RASF was determined by a BrdU-incorporation assay. The results showed that peficitinib and filgotinib offer a benefit in treatment of rheumatoid arthritis.
- **Migration:** The influence of peficitinib on migration of RASF was determined by a Transwell assay. The results showed that peficitinib and filgotinib offer a benefit in treatment of rheumatoid arthritis.
- **Cytokine Levels:** The levels of IL-6 and MMP-3 were measured in supernatants by ELISA. The results showed that peficitinib and filgotinib offer a benefit in treatment of rheumatoid arthritis.

**Conclusion:** Our data suggest that tenocytes and PsASF do not interact in a way that would promote inflammation within the synovio-enthesal complex. Also, as far as the induction of IL-6 is concerned, PsASF and tenocytes are not major target cells of IL-15 and IL-23. IFN-γ, however, may be able to promote inflammation in combination with other cytokines in both cell types.

**Disclosure of Interests:** Felix Dechant: None declared, Klaus Frommer: None declared, Neil L Millar: None declared, Iain McInnes Grant/research support from: AstraZeneca, Celgene, Compugen, Novartis, Roche, UCB Pharma, Consultant for: Alexion, Lilly, Novartis, Pfizer; UCB Pharma, Stefan Rehart: None declared, Ulf Müller-Ladner Grant/research support from: Projekt supported by an unrestricted educational grant from Celgene GMBH, Elena Neumann: None declared DOI: 10.1136/annrheumdis-2019-eular.7148
the MMP-3 levels induced by IL-1β by 88% (n=7, p<0.001) at 5 μM and by 31% at 1 μM (n=7, ns). In direct comparison to tofacitinib and baricitinib, peficitinib exerted the strongest decrease of about 70% (p<0.001, n=4) and it was the only inhibitor attenuating the proliferation of RASF by 38% at 1 μM and by 92% at 5 μM. The observed effects were not mediated by apoptosis and even after 48h peficitinib did not act cytotoxic on RASF. In contrast to migration, short-term adhesion onto a plastic surface was not affected by peficitinib.

Conclusion: Peficitinib and filgotinib were only moderately decreased the IL-1β-induced response of RASF. Peficitinib also inhibited the proliferation and the migration of RASF. Therefore, especially peficitinib could be able to reduce the aggressive pannus formation in RA patients.

REFERENCES:

Disclosure of Interests: Magnus Diller: None declared, Rebecca Hassel: None declared, Iris Akyara: None declared, Marie Hülser: None declared, Stefan Rehart: None declared, Ulf Müller-Ladner Grant/research support from: Projekt supported by an unrestricted educational grant from Celgene GmbH, Elena Neumann: None declared DOI: 10.1136/annrheumdis-2019-eular.3934

THU0027

INHIBITION OF TH17 CELLS IN PSORIATIC ARTHRITIS THROUGH ACTIVATION OF THE ARYL HYDROCARBON RECEPTOR IS DEPENDENT UPON DISEASE ACTIVITY

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Background: Th17 cells have been implicated in the development of psoriatic arthritis (PsA) and psoriasis and are a major target for therapy. Th17 cells exhibit plasticity and can transdifferentiate to other effector cell types. Th17 cells that lose expression of IL-17 in favour of IFN-γ (non-classical Th1 cells) contribute to the pathogenesis of autoimmune diseases and are found in the joints of patients with inflammatory arthritis.

Conversely, induction of IL-10 in Th17 cells has been shown to suppress their pathogenic potential. The Aryl Hydrocarbon Receptor (Ahr) is a nuclear receptor with pleiotropic effects on immune function. The AHR ligand, faloquin hydroxylated (3,2-bjercarboxyl (FICZ) has been shown to induce or suppress Th17 cell differentiation and promote generation of tolerogenic Foxp3+ Treg cells in a regulatory cell type (Tr1) that produce IL-10. FICZ also induces proinflammatory IL-21 in a model of skin inflammation through AHR activation. FICZ could thus play a regulatory role to control inflammation in PsA.

Objectives: To evaluate the immunomodulatory effects of FICZ on IL-17, IL-10 and IFN-γ production from human CD4+ T cells in PsA and healthy controls (HC).

Methods: Whole PBMCs and purified CD4+ T cells were isolated from HC, untreated or DMARD treated (UNT/DMARD) PsA patients and anti-TNFα (adalimumab and etanercept) treated patients. Cells were stimulated with anti-CD3/CD28 (εCD3/εCD28) (1 μg/ml) and cultures were maintained in the presence or absence of FICZ (250nM). To some cultures 2,3,7-Tetachlorodibenzo-p-dioxin (TCDD) (10nM) was used as a control AHR ligand, and IL-21 (30ng/ml) as a positive control for IL-10 production. Cells were then re-stimulated with PMA/ionomycin and intracellular production of IL-17, IFN-γ and IL-10 measured by FACs.

Results: The percentage of IL-17+ CD4+ T cells was reduced in the peripheral blood of HC and PsA patients after 3 days (healthy p=0.0098, UNT/DMARD p=0.0001, anti-TNFα p=0.0019) and 5 days (healthy p=0.0005, UNT/DMARD p=0.0012, anti-TNFα p=0.0012). The percentage of IFN-γ+ CD4+ T cells was increased in HC and PsA patients (HC p=0.016, UNT/DMARD p=0.001, anti-TNFα p=0.001) after 3 days culture with FICZ but this effect was only sustained for HC patients (p=0.02) and anti-TNFα treated patients (p=0.01) after 5 days of culture. No ligand specific difference in IL-17 suppression was seen between FICZ and TCDD. No difference in baseline IL-10 expression was seen between treatment groups. However, IL-10 production was significantly enhanced by FICZ in the anti-TNFα patients group (p=0.02). This effect was not seen with TCDD nor IL-21 alone. The addition of IL-21 to cultures from anti-TNFα patients treated with FICZ further enhanced IL-10 expression (p<0.01). Increase in IL-10 by FICZ was associated with a reduction in IL-17. Upon stratifying patients by swollen joint count (SJC) and Psoriasis Area Severity Index (PASI) into high (SJC≥3, PASI≥5) and low (SJC<3, PASI≤5) disease activity, the percentage of IL-17+ CD4+ T cells after 3 days culture with FICZ was reduced for patients with low PASI score (p=0.02). A similar trend was seen for those with low SJC (p=0.06). In contrast, stimulation with FICZ did not regulate Th17 cells in patients with high PASI score or SJC.

Conclusion: The AhR ligand FICZ suppresses IL-17 production in CD4+ T cells of PsA patients and HC and IFN-γ in HC and anti-TNFα treated patients. FICZ promotes IL-10 production in CD4+ T cells from anti-TNFα treated patients and this effect is enhanced in the presence of IL-21. CD4+ T cells from patients with high disease activity are more resistant to FICZ mediated IL-17 suppression. Use of AhR ligands may thus be a useful therapeutic adjunct to conventional and biological therapy in PsA.

REFERENCE:

Disclosure of Interests: Amara Ezeoneyi: None declared, Michael Ehrenstein Grant/research support from: A different project receives support from GSK DOI: 10.1136/annrheumdis-2019-eular.262
similarly effective in abolishing the synergistic effect of IL-17A + TNF-\(\alpha\) in RASF and PsASF.

**Conclusion:** According to our data, the differences in the therapeutic effectiveness of the anti-IL17A biologic secukinumab cannot be attributed to differential SF responses since the response to IL-17A alone and IL-17A together with TNF-\(\alpha\) is not stronger for PsASF than for RASF and since secukinumab was similarly effective for both SF types. Furthermore, in a proinflammatory milieu with increased TNF levels, both IL-17A and IL-17F can contribute to promoting inflammation in the pathophysiology of PsA and RA.

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THU0029  

**FAS LIGAND REGULATES THE GENE EXPRESSIONS OF VARIOUS KEY MOLECULES IN RHEUMATOID SYNOVIAL FIBROBLASTS**

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**Background:** Fas ligand (FasL) is a member of tumor necrosis factor superfamily (TNFSF6) and reported to contribute to synovial hyperplasia of rheumatoid arthritis (RA). Apoptosis of RA synovial cells through Fas/Fasl pathway was inhibited by pro-inflammatory cytokines present within the synovium [1]. We previously reported that decoy receptor 3 overexpression in rheumatoid synovial fibroblasts (RA-FLS) stimulated by TNFalpha protects the cells from Fas-induced apoptosis [2].

**Objectives:** In this study, we investigated the gene expression profiles regulated by FasL in RA-FLS to reveal how Fasl is involved in the pathogenesis of RA.

**Methods:** RA-FLS were obtained during total knee replacement surgery from patients with RA. Four individual lines of primary cultured RA-FLS were incubated either with 1000 ng/ml of recombinant human FasL protein or the same volume of phosphate buffered saline as unstimulated control in reduced serum medium for 12h. Gene expressions were detected by microarray assay (Human Genome U133 Plus 2.0, GeneChip® 3 Expression Array; Thermo Fisher Scientific).

**Results:** Microarray data analysis revealed that FasL up-regulated or down-regulated the expression of various genes in RA-FLS. The function of regulated genes included transcriptional activator activity, positive regulation of metabolic process, positive regulation of cellular metabolic process, positive regulation of macromolecule metabolic process, positive regulation of nitrogen compound metabolic process, regulation of phosphorylation, positive regulation of biological process, regulation of phosphate metabolic process, regulation of MAPK cascade, and regulation of multicellular organismal process. The most up-regulated 3 genes by FasL were dual specificity phosphatase 6 (DUSP6), epiregulin (EREG) and interleukin11 (IL-11). The most down-regulated 3 genes by FasL were angiotropin-like 7 (ANGPTL7), protein inhibitor of activated STAT2 (PIAS2) and growth differentiation factor 5 (GDF5).

**Conclusion:** DUSP6 regulates CD4+ T-cell activation and differentiation by inhibiting the T-cell receptor-dependent extracellular signal-regulated kinases 1 and 2 activations [3]. EREG is increased in patients with RA and associated with the development of cytokine-induced arthritis [4]. IL-11 regulates the growth and development of hematopoietic stem cells and decreases the pro-inflammatory cytokines and nitric oxide productions [5]. ANGPTL7 is pro-angiogenic factor [6] and promotes pro-inflammatory responses through the PI3K signaling pathway [7]. PIAS proteins inhibit the activated STAT and are involved in the pathogenesis of RA [8]. GDF5 is associated with joint destruction of patients with OA and RA [9]. FasL regulates the expression of various genes in RA-FLS. Therefore, FasL may affect the pathogenesis of RA by regulating gene expressions of these molecules in RA-FLS.

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THU0030  

**THE DIFFERENTIAL EFFECT OF TNF-A AND IL-6R BLOCKERS ON THE EXPRESSION OF IL-17 AND ACTIVATED CD4+CD25+ T CELLS IN PATIENTS WITH PSORIATIC ARTHRITIS**

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**Background:** TNF-\(\alpha\) blockers are effective drugs for the treatment of psoriatic arthritis (PsA) and rheumatoid arthritis (RA). On the other hand, while interleukin-6 receptor (IL-6R) blockers have emerged as effective drugs in the treatment of RA, their effect in PsA has been disappointing. We hypothesized that the differential effect of TNF-\(\alpha\) and IL-6R blockers in PsA may be mediated by the effect of these drugs on IL-17 expression, a cytokine profoundly involved in PsA and by their influence on activated CD4+CD25+ T cells.

**Objectives:** To evaluate the differential effect of adalimumab (ADA) (representing TNF-\(\alpha\) blockers) and tocilizumab (TCZ) (IL-6R blocker) on the expression level of IL-17 and on the frequency of activated CD4+CD25+ T cells.

**Methods:** Levels of IL-17 mRNA expression were measured following in vitro co-culture of peripheral blood mononuclear cells (PBMC) derived from PsA patients with, ADA, TCZ at 10ug/ml or with medium alone as control for 3 days. Next, RNA was extracted and real-time PCR for IL-17 mRNA expression was performed. In addition, after 5 days incubation with the biologic agents the frequency of activated CD4+CD25+ T cells were analyzed by flow cytometry.

**Results:** The differential effect of ADA and TCZ on IL-17 mRNA expression and modulation of activated CD4+CD25+ T cells in culture of PBMC derived from PsA patients is shown in Figure 1. We found that IL-17 mRNA expression in PsA patients derived PBMC (n=20) was down-regulated by ADA. This down grading was significant in comparison with TCZ and respectively (p<0.0001, p<0.0003). On the other hand, TCZ significantly up-regulated the expression of IL-17 as compared to medium control (p<0.05) (Figure 1A). The frequency of activated CD4+CD25+ T cells was down-regulated by ADA as compared to medium and TCZ, respectively (p<0.03, p<0.005), whereas activated CD4+CD25+ T cells were up-regulated by TCZ (although not significantly) as compared to medium control (n=60) (Figure 1B).

**Conclusion:** Our data highlight the differential effect of ADA and TCZ on IL-17 expression level and on frequency of activated CD4+CD25+ T cells in culture of peripheral immune cells derived from PsA patients. This data suggest a new mechanism of action of ADA and provide a possible explanation of the inefficacy of TCZ in PsA.

**Disclosure of Interests:** None declared

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**THU0031**

**FILGOTINIB TREATMENT PROVIDES RAPID AND SUSTAINED REDUCTION OF INFLAMMATORY BIOMARKERS IN MODERATE TO SEVERE PSORIATIC ARTHRITIS (PSA) PATIENTS**

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Background: PsA is a chronic inflammatory musculoskeletal disease characterized by joint and skin inflammation, enthesitis, dactylitis, and nail lesions. In the recent EQUATOR study, filgotinib (FIL), an oral, selective Janus kinase 1 (JAK1) inhibitor, produced significant and sustained improvements on the signs and symptoms of PsA compared to placebo (PBO). As targeted JAK1 inhibition by FIL has potential to simultaneously block multiple inflammatory pathways, we analyzed biomarker samples from EQUATOR using exploratory multiplex biomarker panels.

Objectives: To evaluate the impact of targeted JAK1 inhibition on the circulating biomarkers in patients with active PsA.

Methods: Design and results of the EQUATOR study—a 16-week, double-blind, multicenter, phase 2 study in subjects with active PsA (NCT03101670)—have been published. Subjects were randomized 1:1 to 200 mg FIL (n = 65) or PBO (n = 66) once daily. Serum samples (FIL n = 60 and PBO n = 61) were collected at baseline (BL), week 1, week 4, and week 16, and analyzed using 135 multiplex biomarker screening panels. Biomarker changes from BL were analyzed on all time-paired subject data and reported for weeks 1, 4, and 16.

Results: FIL treatment produced significant reductions serum concentration of multiple biomarkers associated with PsA disease activity. We identified 4 clusters of biomarker response based on the kinetics and magnitude of changes from BL (Figure): Cluster 1: rapid, substantial and sustained reduction (>25% from BL by week 1); Cluster 2: rapid and moderate reduction (5%–15% from BL by week 1); Cluster 3: delayed reduction (significant reduction by week 4); and Cluster 4: moderate increase (5%–10% from BL). Although initial grouping was based on the speed and magnitude of biomarker response, a number of biomarkers formed sub-clusters representing discrete biological functions. Cluster 1 included 2 acute phase reactants (CRP, SAA) while Cluster 2 included inflammatory mediators (TNFR1, CXCL10, IL-12/-23; CXCL10 and IL-12/-23 reached full reduction by week 1). Cluster 3 was the largest group and represented inflammatory markers and inflammation in RA and the effect of antirheumatic therapy on adipocytokine levels in patients with early RA is discussed.

Objectives: To assess the dynamics of adipocytokine levels (adiponectin, leptin, etc.) involved in the pathogenesis of rheumatoid arthritis (RA). The relationship of adipocytokines with activity markers and inflammation in RA and the effect of antirheumatic therapy on adipocytokine levels in patients with early RA is discussed.

Methods: The study included 47 patients with early RA (criteria ACR/EULAR, 2010), 57 [46; 62.0] years, disease duration 6.0 [5.5;15.5] months, seropositive for IgM RF and anti-CCP, with highly active RA (DAS28 5.5 [5.1; 5.9]; SDAI 32.4 [22.4; 41.7]; CDAI 29.0 [19.7; 39.5]). At study entry, all patients received methotrexate (MTX) [10 [10-15] mg/week], after 12 weeks, with inefficiency of MT, adalimumab (ADA) was administered 40 mg 1 time in 2 weeks. Serum concentration of adipokines (adiponectin, leptin) was measured with ELISA.

Results: By the 24th week of therapy, 23 (49%) patients with early RA (initial and after 24 weeks) using various treatment regimens: methotrexate monotherapy (MT) and combination therapy (MT + adalimumab (ADA)).

<table>
<thead>
<tr>
<th>Table 1:</th>
<th>Monotherapy MT (n=24)</th>
<th>Combination therapy MT+ADA (n=23)</th>
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<tr>
<td>0 point</td>
<td>24 weeks</td>
<td>Δ, %</td>
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<tr>
<td>Adiponectin, ng/ml</td>
<td>23.0</td>
<td>12.8[8.0;19.6]</td>
</tr>
<tr>
<td>Leptin, ng/ml</td>
<td>21.7[12.6;40.4]</td>
<td>** -p &lt; 0.05**</td>
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* - p <0.05 reliability of differences in factors before treatment and after 6 months (Wilcoxon); ** - p <0.05 difference in the indices between the groups by the 6th month of therapy: Δ, % - the difference between the indices between the groups by the 6th month of therapy.

Conclusion: After 24 weeks of therapy, the adipocytokine levels in the two groups changed: the adiponectin concentration decreased, and the leptin level increased. MT monotherapy and combination therapy (MT + ADA) acted on changes in adipocytokine levels unidirectionally, although the changes were more pronounced in patients on combination therapy.

Disclosure of Interests: None declared.


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**TABLE 1:**}

| Adiponectin, ng/ml | 23.0 | 12.8[8.0;19.6] | ** -p < 0.05** | 20.0[13;34] | 10.2[7.0;12.1] | -49 |
| Leptin, ng/ml | 21.7[12.6;40.4] | ** -p < 0.05** | 20.0 | 28.1 | 43 |

* - p <0.05 reliability of differences in factors before treatment and after 6 months (Wilcoxon); ** - p <0.05 difference in the indices between the groups by the 6th month of therapy: Δ, % - the difference between the indices between the groups by the 6th month of therapy.

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**Disclosure of Interests:** None declared.

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RNA PROFILING OF HEALTHY AND RHEUMATOID ARTHRITIS SUBJECTS TREATED WITH TOFACITINIB MONOTHERAPY

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Background: The Janus kinase (JAK) family of tyrosine kinases includes JAK1, JAK2, JAK3 and TYK2 which signals through type I and type II cytokine receptors. Tofacitinib is an oral JAK inhibitor approved for the treatment of rheumatoid arthritis (RA). In cellular settings where JAKs signal in pairs, tofacitinib preferentially inhibits signalling by heterodimeric receptors associated with JAK1 and/or JAK3 and has functional selectivity over JAK2. Next generation sequencing (i.e. RNA sequencing) offers an unbiased analysis of the whole transcriptome, pharmacology.

Objectives: To profile the transcriptome in whole blood samples collected in a Phase 1 healthy volunteer (HV) study and a Phase 2 study with RA subjects treated with placebo, 5 mg, 10 mg or 15 mg of tofacitinib monotherapy.

Methods: In the HV study, a total of 93 Paxgene RNA tubes were obtained from 30 subjects collected at screening, at baseline on day 1, and at 2 hours post dosing on day 15. HVs were treated daily with tofacitinib (10 mg BID) for 15 days. In the RA study (NCT00550446), a total of 239 RNA samples were obtained from 25–31 subjects at baseline and day 28 who were treated with tofacitinib 5 mg BID, 10 mg BID or 15 mg BID daily for 84 days. RNAseq libraries were generated using a polyA based mRNA kit and sequenced to a depth of ∼40 million paired-end reads. Upstream processing included alignment of sequences, gene quantification and data quality control. The raw reads were normalised using the Trimmed Mean of M values (TMM) method in the edgeR package. Log2 fold-changes (FC) and corresponding false discovery rate (FDR)-adjusted p-values (padj) were calculated using the voom function in the Limma package (vers 3.8) in R 3.5.1. In particular, the correlations between baseline and measurements at each visit per patient were estimated by Limma’s duplicateCorrelation function. Genes were considered significant after multiple test correction with FDR, or padj <0.1 within each study.

Results: Modulation of the JAK-STAT signalling pathways was observed as exemplified by gene expression differences in cytokine-inducible SH2-containing protein (CISH) (p-value=4.64E-41 in the HV study and p-value=1.2E-8 in the RA study) and suppressor of cytokine signalling (SOCS2) protein (p-value=1.38E-18 in HV study and p-value=2.27E-7 in the RA study). Gene expression of CISH, a member of the SOCS family, was decreased from its baseline value at day 15 in HV (FC from baseline=-0.52) and day 28 in RA subjects (FC from baseline=-0.42) when comparing tofacitinib treatment (HV:10 mg, RA:15 mg) to baseline or placebo, respectively. SOCS2 gene expression was also decreased at day 15 in HV (FC from baseline=-0.40) and at day 28 in RA subjects (FC from baseline=-0.52) when comparing tofacitinib treatment (HV:10 mg, RA:15 mg) to baseline or placebo, respectively. Other changes observed in the HV study included 201 genes were upregulated and 168 genes were downregulated when comparing 2 hours post dose on day 15 to baseline. In the RA study, 643 genes were upregulated and 801 genes were downregulated when comparing the 15 mg dose to placebo at week 4. Preliminary pathway level analysis shows overall a broader modulation of cytokine and chemokine signalling pathways by tofacitinib treatment in RA compared to what we observe in HV.

Conclusion: The results of this post hoc analysis demonstrate that tofacitinib induces measureable changes in the modulation of the JAK-STAT signalling pathway as well as effects on inflammatory cytokines and chemokines. The existence of overlapping but also unique JAK-STAT pathway inhibition due to tofacitinib between the HV and RA studies, as well as ongoing work, will provide a better understanding of response/non-response to tofacitinib and future drug developments.


THU0034 IRAK4 INHIBITION SUPPRESSES TLR7, TLR9, AND SLE SERUM-INDUCED IFNA PRODUCTION IN PRIMARY HUMAN PLASMACYTOID DENDRITIC CELLS

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Background: A hallmark of lupus is the presence of antinuclear autoantibodies, including those against RNA-protein complexes and double-stranded DNA (dsDNA).1,2 FC/r-FcR-mediated internalization of these nucleic acid/autoantibody immune complexes results in endosomal activation of TLR7 and TLR9, respectively, and the production of IFNs from plasmacytoid dendritic cells (pDCs).3,4 The importance of this pathway is underscored by the majority of SLE patients having a peripheral interferon- stimulated gene (ISG) signature.3 IFAK4 is a serine/threonine kinase at the top of the signaling cascade downstream of TLRs, including TLR7 and TLR9. As such, inhibition of IRAK4 represents a promising therapeutic target for lupus.

Objectives: To investigate the effect of a highly selective IRAK4 inhibitor on IFNα production from pDCs stimulated with TLR7 and TLR9 agonists, SLE serum, and nucleic acid/autoantibody immune complexes.

Methods: Primary human pDCs were preincubated with an IRAK4 inhibitor followed by stimulation for 24 hours. Stimulation agents included TLR7 and TLR9 agonists, human SLE serum, and nucleic acid/autoantibody immune complexes. Supernatants were then assessed for secretion of IFNα by MSD.

Results: TLR7 and TLR9 stimulation of pDCs resulted in the secretion of IFNα from pDCs as expected. Treatment with an IRAK4 inhibitor resulted in dose-dependent inhibition of TLR7- and TLR9-induced IFNα with high potency. Human SLE serum was tested to extend findings to physiological SLE-relevant stimuli. Several SLE serum samples, which had positive ELISA titers to the antinuclear antibodies, stimulated production of IFNα in pDCs after 24 hours in culture. No induction of IFNα was observed with healthy volunteer serum samples. Treatment with an IRAK4 inhibitor effectively blocked secretion of IFNα from SLE serum-stimulated pDCs in a dose-dependent manner. Additional antigen (either RNP or dsDNA) was added to SLE samples that yielded titers for autoantibodies but failed to elicit IFNα production. Addition of RNP or dsDNA to anti-RNP and anti-dsDNA-positive SLE serum activated IFNα production, and this response was blocked with IRAK4 inhibition. No induction was seen with SLE serum that was negative for both anti-RNP and anti-dsDNA.

Conclusion: This work demonstrates the effects of IRAK4 inhibition on IFNα production in primary pDCs downstream of disease-relevant stimuli and highlights the potential for IRAK4 inhibition as a promising treatment for lupus.

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THU0035 DOMINANCE OF DRUG TARGET MECHANISMS IN RHEUMATOID ARTHRITIS

Jérôme Paul1, Pierre Grammel1, Thibault Helleputte1, DNAlytics, Louvain-la-Neuve, Belgium

Background: Biological and Targeted Synthetic Disease-Modifying Anti-Rheumatic Drugs (b- and tsDMARDs) have been developed over the years for rheumatoid arthritis (RA). They can be grouped into families of drugs according to their mechanisms of action. Here we focus specifically on anti-TNFs, anti-IL6s, anti-IL1s, T or B Cells inhibitors and JAK inhibitors. There is still a significant proportion of patients
ACTIVATED MEMORY T CELLS PRODUCE LIGANDS THAT CAUSE NF-κB-DEPENDENT INFLAMMATORY ACTIVATION OF THE ENDOTHELIUM: IDENTIFICATION OF NOVEL THERAPEUTIC TARGETS

Kim Jeukers1,2, Jan Piet van Hamburg2, Sander W. Tas1,2, Amsterdam Rheumatology and Immunology Center, Amsterdam, Netherlands; 2Amsterdam UMC, Experimental Immunology, Amsterdam, Netherlands

Background: Endothelial cells (EC) are important contributors to inflammation via expression of inflammatory mediators, including cytokines, chemokines and adhesion molecules. Production of these inflammatory mediators can be induced via canonical and NF-κB-inducing kinase (NIK)-dependent noncanonical NF-κB signalling. The ligands activating these pathways are well studied, but less is known about the cells producing ligands that can activate NF-κB signalling in EC.

Objectives: To study the effects of factors produced by activated memory T (Tcm) cells on NF-κB dependent inflammatory activation of EC.

Methods: CD4+CD45RO+ memory T cells were isolated from healthy PBMC using MACS sorting and cultured in presence of anti-CD3 and anti-CD28 for 72h, after which supernatant was harvested. Endothelial cells were stimulated for 72h with 50% Tcm supernatant (Tm sup) after which protein and RNA was harvested by analysis of NF-κB signalling and downstream expression of inflammatory mediators using qPCR and western blot. Culture supernatants were analysed by ELISA for various inflammatory mediators. To repress canonical NF-κB signalling an inhibitor of IKKβ (iIKKβ) was used and to repress NIK-dependent NF-κB signaling an inhibitor of NIK (iNIK) was used.

Results: Stimulation with Tm sup led to activation of both canonical NF-κB signalling (increased levels of phosphorylated IκBα) and noncanonical NF-κB signalling (increased p100 to p52 processing). After stimulation with Tm sup EC had increased mRNA levels of all tested inflammatory mediators compared to non-treated cells. Gene expression of chemokines, cytokines, and growth factors (CCL1, CXCL5, IL6, IL8 and GM-CSF) in Tm sup stimulated EC was significantly reduced after treatment with iIKKβ and to a lesser, but still significant, extent after treatment with iNIK. Treatment with iIKKβ also led to a reduction in mRNA levels of the adhesion molecules VCAM-1 and ICAM-1, while this effect was less pronounced after iNIK treatment. Of note, treatment with either iIKKβ or iNIK led to a significant reduction of CXCL5 in the culture supernatant of Tm sup stimulated EC.

Conclusion: This study provides new insights into the cellular interactions leading to production of inflammatory mediators by EC. Our findings demonstrate that activated Tcm cells produce factors that can cause NF-κB-dependent inflammatory activation of EC. Targeting canonical NF-κB signaling via IKKβ or NIK-dependent NF-κB signaling reduces inflammatory activation of the endothelium and may be a potential novel therapeutic target.

Disclosure of Interests: None declared


ACTIVATED MEMORY T CELLS PRODUCE LIGANDS THAT CAUSE NF-κB-DEPENDENT INFLAMMATORY ACTIVATION OF THE ENDOTHELIUM: IDENTIFICATION OF NOVEL THERAPEUTIC TARGETS

Kim Jeukers1,2, Jan Piet van Hamburg2, Sander W. Tas1,2, Amsterdam Rheumatology and Immunology Center, Amsterdam, Netherlands; 2Amsterdam UMC, Experimental Immunology, Amsterdam, Netherlands

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Disclosure of Interests: None declared


ASSOCIATION BETWEEN PRO-INFLAMMATORY CYTOKINE POLYMORPHISMS AND JUVENILE IDIOPATHIC ARTHRITIS

Jae Hyun Jung, Jae-Hoon Kim, Sung Jae Choi, Gwan Gyu Song, Korea University College of Medicine, Seoul, Korea, Rep. of (South Korea)

Background: Juvenile idiopathic arthritis (JIA) is the most common chronic arthritis of childhood and has a variety of subtypes, but the etiology is unclear. Proinflammatory cytokines such as interleukin (IL)-1, IL-6 and tumor necrosis factor (TNF)-α play a major role in the development of JIA. Single nucleotide polymorphisms (SNPs) may be associated with susceptibility, phenotype, progression, and treatment of JIA, and the relevance of more than 20 SNPs and JIA has been studied.

Objectives: We investigated whether IL-1, IL-6, and TNF-α polymorphisms were associated with susceptibility to JIA.

Methods: A meta-analysis was conducted on the associations between IL-1α-889 C/T, IL-1β-511 C/T, IL-6-174 G/C, and TNF-α-308 G/A and -238 G/A polymorphisms, and JIA. A literature search was performed using PubMed and Embase. The strength of the association between these cytokine polymorphisms and risk of JIA was estimated using the crude odds ratio (OR) and 95% confidential interval (CI). We performed meta-analyses using 1) allelic contrast, 2) recessive, 3) dominant, and 4) additive models. The heterogeneity between studies was assessed with the Cochran Q test, and the heterogeneity among studies was tested with the F statistic.

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Results: A total of 27 studies included 4,678 JIA cases and 7,634 control subjects. There were 23 studies on Caucasians, 3 on Asians, and 1 on Africans. Seventy studies were on IL-1α-899 C/T, 5 were on IL-1β-511 C/T, 6 were on IL-6-174 G/C, 19 were on TNF-α-308 G/A, and 14 were on TNF-α -238 G/A polymorphisms. Meta-analysis of IL-1α-899 C/T, IL-1β-511 C/T, IL-6-174 G/C, and TNF-α-308 G/A and -238 G/A polymorphisms revealed no significant associations between JIA and minor alleles (OR 0.99, 95% CI 0.87–1.22, P = 0.5; OR 1.04, 95% CI 0.91–1.19, P = 0.57; OR 1.01, 95% CI 0.87–1.37, P = 0.46; OR 0.85, 95% CI 0.63–1.13, P = 0.26). Subgroup analysis was conducted on the relationship between JIA and proinflammatory cytokines based on ethnicity. In Caucasians, there was no significant association between IL-1α-899 C/T, IL-6-174 G/C, and TNF-α-308 G/A and -238 G/A polymorphisms and JIA; however, there were significant relationships between JIA and recessive (TT vs. CT + CC) and additive (TT vs. CC) models of IL-1β-511 C/T polymorphisms (OR 1.48, 95% CI 1.09–2.00, P = 0.01; OR 1.46, 95% CI 1.05–2.03, P = 0.02).

Conclusion: IL-1α-899 C/T, IL-1β-511 C/T, IL-6-174 G/C, and TNF-α-308 G/A and -238 G/A polymorphisms were not significantly associated with overall JIA susceptibility in all ethnicities. However, differences according to ethnicity were observed, and the TT genotype of IL-1β-511 C/T was associated with a high prevalence of JIA in Caucasians.

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Disclosure of Interests: Marcel Gabathuler: None declared, Monika Krosel: None declared, Christoph Kolling: None declared, Matija Tomsic: None declared, Oliver Distler: Grant/research support from: Prof. Distler received research funding from Actelion, Bayer, Boehringer Ingelheim and Mitsubishi Tanabe to investigate potential treatments of scleroderma and its complications, Consultant for: Prof. Distler had a consultancy relationship within the last 3 years with Actelion, AnaMar, Bayer, Boehringer Ingelheim, ChemomAb, espeRare foundation, Genentech/Roche, GSK, Inveniva, Italfarmaco, iQvia, Lilly, medac, MedImmune, Mitsubishi Tanabe Pharma, Pharmacies, Novartis, Pfizer, Sanofi, Serodapharm and UCB in the area of potential treatments of scleroderma and its complications.

Background: The two coactivators of transcription cAMP-response element binding protein (CREB) binding protein (CBP) and p300 are close homologues. They are widely accepted as redundant proteins and unique functions have not been investigated in depth. Both proteins contain a histone acetyltransferase (HAT) activity for writing of cell type specific activating H3K27 histone acetylation marks, and a bromodomain, which functions as a reader of acetylated lysine residues on histone tails. Inhibitors targeting the bromodomains are in drug development for inflammatory and malignant diseases.

Objectives: To analyze individual functions of CBP and p300 in regulating the inflammatory response of rheumatoid arthritis (RA) synovial fibroblasts (SF).

Methods: SF were isolated from knee, shoulder and hand joints of RA patients undergoing joint replacement surgery. The expression of CBP and p300 was silenced by transfection of antisense LNA gapmeRs (12.5 nM), 24h after transfection, cells were stimulated with TNF-α (10 ng/ml, 24h). mRNA levels of H3K27ac in SF were analyzed by Western blotting (n=7). Transcriptomes were determined by RNA-seq (Illumina NovaSeq 6000, n=6). Pathway enrichment analysis of RNAseq data was performed using DAVID bioinformatic resources (fold change > 1.5, FDR < 0.05, top 3000 genes included). Changes in the mRNA expression of potential target genes were confirmed by quantitative Real-time PCR (n=12–14).

Results: Silencing of p300 reduced the levels of H3K27ac by 30% in unstimulated SF, and by 61.4% (p<0.05) in presence of TNF-α, whereas silencing of CBP reduced H3K27ac by 43.5% only in presence of TNF-α. In line with the changes in the H3K27ac, silencing of p300 affected the expression of 6026 and 5138 genes in unstimulated and stimulated SF, respectively. In contrast, only 285 and 1191 genes were affected by CBP silencing in unstimulated and stimulated SF, respectively. 13.5% of overlapping genes were affected by both, CBP and p300, in unstimulated SF, with 9.2% of genes being regulated in opposite directions. 13.5% of overlapping genes affected by CBP and p300 were regulated in opposite directions in TNF-α-stimulated SF. Principal component (PC) analysis of RNAseq data separated TNF-α-stimulated from unstimulated SF (PC1) and p300 gapmeR-transfected SF (PC2) from controls and CBP gapmeR-transfected SF, which clustered together. The top pathways regulated by CBP were ‘cell cycle’ and ‘focal adhesion’ in unstimulated cells and ‘DNA replication’ and ‘cell cycle’ after stimulation with TNF-α. Top pathways regulated by p300 in presence and absence of TNF-α were ‘proteasome’, ‘spliceosome’ and ‘focal adhesion’. The expression of 16 chemokines and cytokines was changed in RNaseq data (fold change >1.5, p<0.05) by either silencing of CBP or p300. Whereas silencing of CBP reduced the expression of all of them, silencing of p300 had pro- and anti-inflammatory effects. We further confirmed expression changes in cytokine and chemokine expression by Real-time PCR. Silencing of CBP reduced the expression of IL6, CCL2 (p<0.01), CX3CL1 (p<0.05), and CXCL10. Silencing of p300 reduced the expression of CCL2 and CX3CL1 (p=0.001) but increased the expression of IL8 (p<0.001) and CXCL2 (p<0.05).

Conclusion: Our results suggest that p300 is the major writer for H3K27ac marks in SF. We have identified overlapping and distinct functions for CBP and p300 in SF. CBP inhibition has anti-inflammatory effects. In contrast, p300 inhibition has pro- and anti-inflammatory functions.

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In addition, he had/has consultancy relationship within the last 3 years with A. Menarini, Amgen, Abbvie, GSK, Mepha, MSD, Pfizer and UCB in the field of arthritides and related disorders. Caroline Ospelt: None declared. Kerstin Klein: None declared.


THU0039

THE RELATION BETWEEN THE INFLAMMATORY STATUS OF HUMAN END STAGE OSTEOARTHRITIC SYNOVUM AND LEVELS OF LOW DENSITY LIPOPROTEIN

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Background: High systemic levels of low density lipoprotein (LDL) is a shared metabolic risk factor for osteoarthritis (OA) and cardiovascular disease (CVD), which may point to common biochemical pathways. One of the key events in atherosclerosis is formation and uptake of oxidized LDL (oxLDL) as a consequence of macrophage-mediated inflammation. Studies performed in our lab have previously shown that in mice, high LDL levels enhance synovial activation and ectopic bone formation during development of collagenase-induced OA. Furthermore, injection of oxLDL in naïve macrophage depleted joints led to infiltration of myeloid progenitor cells. Although these results strongly indicate towards (ox)LDL-mediated events that enhance OA severity, these processes have not yet been shown to occur in human osteoarthritic synovium.

Objectives: In the present study, we investigated whether the inflammatory status of OA synovium is associated to systemic and local levels of (ox)LDL.

Methods: Blood was collected from patients planned to undergo total knee replacement and LDL serum levels were determined (n=16). After surgery, synovial explants from the same patients (2-8 per patient) were collected and incubated at 37°C for 24 hours in presence of LDL (50 µg ApoB/mL), oxLDL (50 µg ApoB/mL) or control medium. Levels of IL-1β, TNF-α, IL-10 and MCP-1 secreted in the conditioned medium were measured using Luminex. Levels of S100A8/A9 were measured using ELISA. Concentrations of secreted factors were normalized for tissue sample weight. Synovial explants were further processed for histological analysis. Immunohistochemical staining of ApoB was performed to assess presence and uptake of (ox)LDL in the synovium. Hematoxylin & eosin-stained sections were used to arbitrarily score cellular infiltration and synovial hyperplasia.

Results: Around 50% of the patients in our cohort showed synovial activation exemplified by high secretion levels of IL-1β, TNF-α and IL-10. Cellular infiltration and synovial hyperplasia was observed in the majority of synovial tissue samples, their grades did however not correlate with cytokine secretion. Secretion levels of IL-1β positively correlated with serum levels of LDL and total cholesterol and did not correlate with BMI, suggesting a link that runs via systemic metabolic processes rather than increased weight-mediated joint loading. Considering that around 50% of OA patients suffers from synovitis characterized by increased macrophage presence and activity, high LDL in these patients may trigger oxLDL for-accumulation in these cells. Unexpectedly, presence of high concentra- tions of LDL or oxLDL during incubation of synovial explants did not sig-nificantly affect secretion of IL-1β, TNF-α, IL-10 and MCP-1, whereas presence of LDL but not oxLDL negatively affected secretion of S100A8/ A9.

Conclusion: IL-1β secretion by end stage OA synovium is associated to systemic levels of LDL. Intervention with high concentrations of LDL or oxLDL for 24-hours after synovium extraction did however not alter cyto-kine secretion, suggesting that LDL and synovitis are linked through more long-term local interactions, or alternatively via systemic inflammatory factors.

Disclosure of Interests: None declared.


THU0040

USING A NOVEL BEAD-BASED IMMUNOASSAY FOR SIMULTANEOUS DETECTION OF AUTOANTIBODIES AGAINST SERUM AMYLOID A1 AND ALPHA1 ACID GLYCOPROTEIN

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Background: Naturally occurring autoantibodies (Abs) against acute phase proteins (APPs), such as anti-serum amyloid A1 (SAA1) Abs have already been identified in sera of healthy individuals, as well as in patients with autoimmune diseases (1). Currently however, no method exists for simultaneous detection of multiple Abs against APPs.

Objectives: To develop a bead-based duplex immunosassay for simultane- ous detection of IgG anti-SAA1 and anti-alpha 1 acid glycoprotein (AGP) Abs and quantify their levels in sera of healthy blood donors (HBD), and patients with systemic autoimmune diseases, as well as in intravenous immunoglobulin preparation (IVIg).

Methods: Fluorescently labeled MagPlex microspheres (Luminex Corp) were used to covalently bind SAA1 and AGP. Sera samples (diluted 1:20) were added to a 96-well microtiter plate and incubated with SAA1- and AGP-coupled microspheres for 2h. Subsequently, PE-conjugated anti-human IgG Abs were added to each well, incubated for 30 min, resus- pended in PBS-1%BSA and analysed using the MagPix system (Biomed- ica, GmbH).

Abstract THU0040 – Figure 1. Levels of antibodies against SAA1 (A) and AGP (B) in HBD as compared to patients with systemic autoimmune diseases. Shown is median and IQR. 95th and 90th percentile of MFI values in HBD are indicated with dotted lines; *p<0.05; **p<0.01. SAA1, serum amyloid A1; AGP, alpha 1 acid glycoprotein; MFI, median fluorescence intensity; HBD, healthy blood donors; GCA, patients with giant cell arteritis; IgAV, immunoglobulin A vasculitis; SLE, systemic lupus erythematosus; SSC, systemic sclerosis; APS, antiphospholipid syndrome; ERA, early rheumatoid arthritis.

Abstract THU0040 – Figure 2. Presence of antibodies against SAA1 and AGP in IV Ig. IVIg, intravenous immunoglobulin G; SAA1, serum amyloid A1; AGP, alpha 1 acid glycoprotein; MFI, median fluorescence intensity.

Sera samples were collected from HBD (n=55), patients with giant cell arteritis (GCA; n=20), immunoglobulin A vasculitis (IgAV; n=30), systemic lupus erythematosus (SLE; n=20), systemic sclerosis (SSc; n=27), anti- phospholipid syndrome (APS; n=19) and early rheumatoid arthritis (ERA; n=20). Ab levels were determined also in IVIg (Octapharma AG).

Results: We observed the presence of both, anti-SAA1, and anti-AGP Abs in sera of HBD, as well as in patients with GCA, IgAV, SLE, SSC, APS and ERA.

GCA patients had significantly higher anti-SAA1 levels (median (IQR) MFI was 2163 (1131-3048)) as compared to SSc (816 (480-1462); p<0.01) and ERA (886 (722-1596); p<0.05) patients. Levels of anti-AGP Abs were also significantly higher in sera of GCA patients (495 (298-872)) as compared to ERA (213 (130-338); p<0.01) and APS (264 (154-399); p<0.05) patients. No difference in anti-SAA1 or anti-AGP levels was observed between HBD and the tested groups of patients (Figure 1).

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Substantial amounts of anti-SAA1 Abs were observed in serially diluted IgV, while there were 4-fold less anti-AGP Abs detected (Figure 2), which corresponds also to the ratio found in HBD (Figure 1).

Conclusion: Serum IgGs against SAA1 and AGP present in HBD, patients with systemic autoimmune diseases and in IgV can be simultaneously quantified using a customized bead-based multiplex assay. These natural autoAbs found in IgV could be endogenous immune-regulators of the acute phase response.

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THU0041

MESENCHYMAL STEM CELLS OF DIFFERENT ORIGINS
EXHIBIT UNIQUE RESPONSES TO DIFFERENT INFLAMMATORY STIMULI

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Background: Mesenchymal stromal/stem cell (MSC) - based therapies represent promising avenues for treatment of various inflammatory and autoimmune diseases. Currently, a variety of fetal and adult tissues represent a good source of MSC, however further characterization of their effects, especially in an inflammatory environment, is needed.

Objectives: Firstly, to characterize MSC from different origins, namely bone marrow (BM), adipose tissue (AT) and umbilical cord (UC), after stimulation with TNFα, IL-1β and serum amyloid A (SAA). Secondly, to determine the effects of MSC secretome on migration, proliferation and apoptosis of lung fibroblasts.

Methods: BM-, AT- or UC-MSC were isolated each from 3 healthy donors. The expression and secretion of analytes were studied in each cell type at basal level and following TNFα (1 ng/ml), IL-1β (1 ng/ml) and SAA (12 µg/ml) stimulation using qPCR (SDF, CCL5, VCAM, PDE, PGC, IDO, VEGF, IGF) and Luminex technology (IL-6, IL8, MCP-1, ICAM, CHSL1, MMP1, MMP3, tenasin, uPA, HGF, VEGF), respectively. Normal healthy lung fibroblasts (NHLF) were used in the wound scratch assay and treated for 24h with 20% of MSC-conditioned media. For evaluation of BM-, AT- and UC-conditioned media effects on proliferative and apoptotic activity, Ki-67-immunolabeled mitotic cells and caspase-3-immunolabeled cells were counted using fluorescence microscopy. Results: Treatment of MSC with pro-inflammatory cytokines increased mRNA levels of SDF, CCL5, VCAM1, PGC and IDO, while levels of PDE-5A were down-regulated. The greatest increase in expression was observed in TNFα-stimulated MSCs, namely of two immunomodulatory molecules, CCL5 and IDO in AT-MSC (4396- and 928-fold change increase respectively). Secretome analysis showed highest secretion levels of IL-6, IL-8 and MCP1 after IL-1β-activation in all 3 tissue sources. AT- and BM-derived conditioned media increased NHLF scratch closure, while UC-MSC decreased it. In non-inflammatory conditions, UC-, BM- and AT-MSCs conditioned media decreased the number of mitotic events in NHLF by an average of 40%. Importantly, only the conditioned medium derived from inflammatory cytokine-treated AT- and BM-MSC significantly decreased the mitotic rate of NHLF (p<0.01). The number of apoptotic cells increased 3- to 8-fold after treatment with all MSC conditioned media, with UC-MSC showing the highest effect (p<0.01).

Conclusion: Our results highlight specific roles of MSC from different tissue origins, as well as their response to environmental inflammatory stimuli and suggest that source selection might be critical for the success of treatment approaches in different diagnoses.

Disclosure of Interests: None declared


THU0042

EFFECT OF SPLEEN TYROSINE KINASE (SYK)-INHIBITORS ON RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLASTS

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Background: The spleen tyrosine kinase (syk) is an intracellular protein kinase involved in signal transmission processes of immune cells and non-hematopoietic cells, such as fibroblasts. Various syk-inhibitors are therefore currently being tested in preclinical and clinical studies, e.g. for the treatment of different types of cancer as well as autoimmune diseases. In preclinical studies, syk-inhibitors showed a pronounced anti-inflammatory effect on synovial fibroblasts (SF) from patients with rheumatoid arthritis (RA). These cells play an important role in the pathogenesis of RA by mediating matrix destructive processes. On the other hand, clinical trials have been only moderately successful due to the side effects and the limitation regarding increase in dosage. However, further inhibitors such as RO9021 or TAK-659 have been developed. They are characterized by a more specific kinase profile and therefore side effects could potentially be less severe. Whether these inhibitors also convey an anti-inflammatory effect on RASF has not yet been investigated.

Objectives: This study examines the effect of syk-inhibitors on the inflammatory response and functional behavior of activated RASF.

Methods: RASF were isolated from synovial tissue of patients with known rheumatoid arthritis during joint replacement surgery. RASF were pre-treated with different concentrations of RO9021 and TAK-659 and their vehicle control for 2h and additionally stimulated with IL-1β (10 ng/ml) for 17h or with oncostatin M (OSM, 100 ng/ml) for 24h. Supernatants were collected and the concentration of IL-6 and MMP3 were determined by ELISA. The measurement of cell viability, cytotoxicity and apoptosis was performed to exclude possible cytotoxic or apoptotic effects of the syk-inhibitors. The RASF proliferation assay was performed by a BrdU-incorporation assay. The effect of syk-inhibitors on cell migration towards a FCS-gradient was measured by cell culture inserts. Results: Both TAK-659 and RO9021 showed a significant reduction of the release of the pro-inflammatory cytokine IL-6 and the production of MMP3 in IL-1β stimulated RASF. However TAK-659 showed a stronger effect on IL-6 reduction (48%, p<0.005) than RO9021 (25%, p<0.05) at 10µM. MMP3 decrease was also stronger with TAK-659 (92%, p<0.001) than with RO9021 (59%, p<0.001). This effect was apparently not restricted to IL-1β because both inhibitors also decreased the OSM-induced IL-6 release of RASF by 85% (p<0.01) with TAK-659 and 30% with RO9021 at 10µM. The proliferation of RASF was also reduced by both syk-inhibitors at 5µM and higher. The highest effect could be observed with TAK-659 for 80% and with RO9021 by 50% both at 15µM. The migration of RASF was also decreased by TAK-659 at 10µM (p<0.01, n=3). The effects were not mediated by induction of apoptosis or cytoxicity.

Conclusion: The syk-inhibitors TAK-659 and RO9021 at concentrations above 5µM reduce the inflammatory response, the migration and proliferation of RASF. If appropriate concentrations can be reached in vivo, these syk-inhibitors could offer a possibility to modulate the aggressive phenotype of RASF.

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THU0043

IL-25 ALLEVIATES RHEUMATOID ARTHRITIS BY INHIBITING TH17 IMMUNE RESPONSE

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Background: Rheumatoid arthritis (RA) is a prevalent common autoimmune disease characterized by chronic inflammation of the joint and synovial hyperplasia and progressive destructive articular cartilage and bone. Accumulating evidence highlighted that an imbalance between pro-
and anti-inflammatory cytokines may be a key mechanism for disease progression in RA. IL-25 is reported to play an anti-inflammatory role in autoimmune and inflammatory diseases through the downregulation of Th1 and Th17 cell responses. However, the exact role of IL-25 in the pathogenesis of RA remains to be elucidated.

**Objectives:** Explore the role of IL-25 in the pathogenesis of RA, and provide evidence of the scientific importance of IL-25 relevant biological agent.

**Methods:** 1. The study was first to analyze the relationship between IL-25 and DAS28 score, CRP and anti-CCP in RA patients. Tests IL-1β, IL-6, IL-17A, TNF-α and IFN-γ through ELISA, then analyze the relationship with IL-25. CD4+ T cells from PBMCs of the 5 RA patients and 5 HCs were isolated under the manual of EasySep™ Human CD4+ T Cell Isolation Kit and stimulated with anti-CD3 plus anti-CD28 in the presence or absence of rhIL-25. 2. A CIA model was established to explore the mechanism of IL-25. The expression of CII specific IgG1 and IgG2a, as well as IL-1β, IL-6, IL-17A and TNF-α in CIA serum were examined using ELISA assay. The ROR-γT, -β, GATA-3 mRNA levels in knee joints and spleen were assessed by real-time qPCR analysis. In vitro, CD4+ T cells from spleen were isolated from CIA mice and cultured with or without recombinant mouse (rm)IL-25 for 24h to control the expression IL-17A. Cells were stimulated with plate-bound anti-CD3 plus anti-CD28 in the presence or absence of recombinant mouse (rm) IL-25 with different dose for 24 h.

**Results:** 1. The expression of IL-25 was upregulated in the serum and synovial fluid in RA patients. Serum IL-25 levels were positively associated with DAS28 score, ESR and C-reactive protein. However, no significant correlation was observed between serum IL-25 levels, RF and anti-CCP. IL-25 serum levels was positively correlated with the concentrations of IL-1β, IL-6, IL-17A and TNF-α, respectively. However, no significant correlation was observed between serum IL-25 and IFN-γ level. 2. IL-25 can alleviate inflammatory response of CIA mice and inhibit IL-17 differentiation. The serum levels of IL-1β, IL-6, IL-17A and TNF-α in IL-25-treated mice were markedly reduced compared with those in WT mice, except IFN-γ. RT-qPCR also demonstrated that the transcription levels of IL-17A and ROR-γt were decreased in the synovial tissue of IL-25-treated mice. RmIL-25 treatment significantly inhibited IL-17A production in a dose-dependent manner, and the mRNA level of the key TFs for Th17 cells (ROR-γt), as well as IL-17A, were also decreased.

**Conclusion:** IL-25 is upregulated in the serum and synovial fluid of RA patients. High levels of IL-25 was associated with disease severity and inflammation response in RA patients. IL-25 inhibits CD4+ T-cell activation and differentiation into Th17 cells, without affecting Th1 cells in RA. Systemic administration of IL-25 attenuates arthritis onset and joint damage in CIA mice. IL-25 of multi-target regulation further be used in the clinical treatment of RA.

**Disclosure of Interests:** None declared

**REFERENCES:**

**Abstract THU0044 – Figure 1.** Anti-inflammatory species derived from EPA and DHA are significantly downregulated in patients at baseline. Pro-inflammatory (in red) and anti-inflammatory eicosanoids (in blue) detected in our patients are represented by pathways and origin PUFA. Significant eicosanoids (p < 0.05) are circled in blue if downregulated in patients compared to controls at baseline.

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Background: Pathogenesis of Granulomatosis with polyangiitis (GPA) is still unknown. However, it has been observed a skewing of circulating CD4+ T cells toward the Th17 and Th2 phenotype. The pro-inflammatory cytokine interleukin 25 (IL-25) is a member of IL-17 cytokine family associated to the Th2 immune phenotype. Through the receptor IL17RB, IL-25 further sustains the Th2-type immune response and elicits the expansion of the type 2 innate lymphoid cells (ILC2) and M2 macrophages. A pathogenic role of the innate lymphoid cells in GPA has been recently demonstrated; however, the relevance of IL-25 in this condition remains unexplored.

Objectives: Aim of the study was to evaluate the expression of IL-25/IL-25R axis and its functional relevance in patients with granulomatosis with polyangiitis (GPA).

Methods: Thirty patients with a diagnosis of GPA fulfilling the Chapel Hill Consensus Conference and ACR classification criteria, and 20 age-matched healthy controls (HC) were included in this study: age range 30-66 years, 40% female in GPA group and 32-63 years, 20% female in HC. IL-25 and IL-33 serum levels were measured by ELISA at the diagnosis and after Rituximab (RTX) therapy (n=15). Immunohistochemical staining for IL-25, IL-33, IL-17B was performed on sections of renal biopsies obtained from GPA patients (n=10). Kidney ILC2 infiltration was assessed by confocal microscopy. Frequencies ILC1, ILC2 and ILC3 were evaluated by flow cytometry analysis by CD45, CRTH2, GATA3, Tbet, CD56, NKp44, IL-22, IL-23R, RORc. Expression levels of IL-5 and IL-13 in kidney were quantified by quantitative real-time PCR (qRT-PCR).

Results: Increased pre-RTX serum levels of IL-25 and IL-33 at baseline were observed in GPA compared to HC (p<0.0001). Both serum IL-25 and IL-33 correlated with the Birmingham Vasculitis Activity Score (BVAS) (r^2=0.51 p<0.0001 and r^0.14 p<0.05 respectively). IL-25, IL-17B and IL-33 expressing cells were increased in GPA renal biopsies vs HC (p<0.0001). Frequencies of circulating ILC1 and ILC3 were not significantly increased in GPA. Conversely, the frequency of ILC2 was expanded in GPA vs HC (p<0.0001) and correlated with BVAS (r^2=0.60 p<0.0001). The number of IL-2 and the levels of expression of IL-5 and IL-13 in GPA kidney were increased (p<0.0001). RTX therapy led to a reduction in IL-25 and IL-33 serum levels and in the frequency of circulating ILC2.

Conclusion: Our data confirm the increases in IL-33 levels previously demonstrated; however, the relevance of IL-25 in this condition remains unexplored.

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References:

Disclosure of Interests: For the table, please refer to the original document.
IA-14069, a novel small-molecule inhibitor directly targeting tumor necrosis factor-α, attenuates collagen-induced arthritis

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Background: Rheumatoid arthritis (RA) is systemic autoimmune disease that is characterized by autoreactive immune cells and various cytokines-mediated inflammation in multiple joints, leading to cartilage degradation, bone erosion and finally irreversible joint destruction1. The inflammatory cytokine tumor necrosis factor-α (TNF-α) is known to play a central role in several chronic immune-mediated inflammatory disorders2.

Objectives: Despite the great success of anti-TNF-α biological drugs in the treatment of RA, no chemical drug targeting TNF-α is available. Here we report that IA-14069, a novel small molecule inhibitor, binds directly to TNF-α and inhibits TNF-α activities both in vitro and in vivo.

Methods: IA-14069 was screened and identified by competitive binding to TNF-α and neutralization activity of IA-14069 against TNF-α was determined using MTT assay. The direct binding IA-14069 to TNF-α was demonstrated by surface plasma resonance and bead pull-down assays. The inhibition of TNF-α-TNFFR interactions by direct binding of IA-14069 to TNF-α was analyzed by flow cytometry. Levels of phosphorylated IκBα (p-IκBα) and NF-κB p65 were analyzed by western blot. IA-14069 was orally administered to TNF-α transgenic (TNF-α-Tg) RA mice at three or 33 mg/kg twice per week or at 25, 50 or 100 mg/kg 3 times per week for preventive or therapeutic effect, respectively. In vivo therapeutic efficacy of IA-14069 or methotrexate was evaluated in collagen-induced arthritis (CIA) mice immunized with bovine type II collagen (CII) emulsified in complete Freund’s adjuvant, and boosted with CII emulsified in incomplete Freund’s adjuvant.

Results: IA-14069 potently inhibits both TNF-α-induced cytotoxicity (IC50 < 0.7 μM) which directly binds to TNF-α and TNF-α-triggered signaling (p-IκBα and NF-κB p65) activities. The therapeutic as well as preventive anti-RA effects of IA-14069 were demonstrated in TNF-α-Tg and CIA models. IA-14069 and MTX had synergistic effects in the CIA therapeutic model. According to pharmacokinetic analysis, IA-14069 showed significant bioavailability. In addition, no in vivo toxicity was observed even under treatment of excessive amount of IA-14069.

Conclusion: The data indicate that IA-14069 can be a novel and potential TNF-α inhibitor for the treatment of RA and other inflammatory diseases.

References:

Disclosure of Interests: Sung-Dong Park Employee of: MOGAM Institute for Biomedical Research, HyungGun Maeng: None declared, Yeon-Hwa Park: None declared, Kye-Jung Shin: None declared, Tae-Hwee Heo: None declared


2ND LINE TREATMENT WITH LESINURAD AND ALLOPURINOL VERSUS FEBUXOSTAT FOR MANAGEMENT OF HYPERURICEMIA: A COST-EFFECTIVENESS ANALYSIS FOR SPANISH PATIENTS

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Background: Lesinurad, a medication that inhibits uric acid reabsorption, has been recently approved in combination for the treatment of patients with gout who do not reach therapeutic serum urate target with xanthine oxidase inhibitors monotherapy.

Objectives: To assess the incremental cost-effectiveness ratio of adding lesinurad to allopurinol as 2nd line therapy, compared to febuxostat for the management of patients with gout in Spain.

Methods: A Markov model comprising 6 health-states representing the disease evolution was used to estimate in 6-months cycles, the lifetime accumulated cost and benefits in terms of quality-adjusted-life-year (QALY) in an hypothetical cohort of patients stratified according to serum uric acid levels observed on pooled CLEAR trials: 18.8% (<6 mg/dL); 63.7% (6-8 mg/dL); 15.2% (8-10 mg/dL) and 2.3% (>10 mg/dL). During the simulation, patients could either continue with 2nd line treatment with lesinurad (200mg/daily) plus allopurinol (400mg/daily) or febuxostat (80mg/daily), switch to allopurinol monotherapy (271mg/daily) in case of intolerance or discontinue treatment. Proportion of topheaceous gout (18.9%) was considered at each health-state. The efficacy of treatments was captured in the transition probabilities between health states which were derived from findings on CLEAR 1, CLEAR 2 and EXCEL clinical trials. Quality of life related to gout severity (topheaceous or non-topheaceous) and flare frequency was considered by means of utilities estimated from SF-36 scores of the pooled CLEAR trials which were mapped to EQ-5D values. The total cost estimation (€, 2018) included drug acquisition cost (retail prices with mandatory deduction applied), disease monitoring (€377.03 for first 6-month periods, €329.95/795 (subsequent year) and flare management cost (€301.69). Unitary costs derived from local cost databases and literature. A 3% annual discount rate was applied for cost and outcomes. Sensitivity analyses (SA) were carried out.

Results: Lesinurad added to allopurinol provided higher QALYs (14.79) than febuxostat (14.69). Total accrued cost per patient were lower (€6,819.13) with lesinurad and allopurinol (€4.695.27) compared to febuxostat (€5.478.40). Lesinurad plus allopurinol resulted a dominant option (more effective and less costly) compared to febuxostat. SA results confirmed the model robustness.

Conclusion: These results suggest that treatment with lesinurad 200 mg/day plus allopurinol 400 mg/day compared to febuxostat 80mg/day is an effective second option for the management of hyperuricemia in patients with gout who did not reach therapeutic serum urate target to previous allopurinol monotherapy, associated to cost-savings for the Spanish National Health System.

References:

Disclosure of Interests: Maria Presa Consultant for: I am employee of PORIB a consultant company which has received financial support from Grünenthal for development of this project. Fernando Perez-Ruiz Grant/ research support from: Crues Rheumatology Association, Consultant for: Grünenthal, Menarini, Horizon, Speakers bureau: Menarini, Grünenthal; Spanish foundation for rheumatology, Itziar Oyagüez Consultant for: I am employee of PORIB a consultant company which has received financial support from Grünenthal for development of this project

THU0049

CORRELATION BETWEEN IL-6 AND OSTEOCALCIN SERUM LEVELS WITH DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS (RA) PATIENTS

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Background: IL-6 plays a significant role in RA pathophysiology. It is considered nowadays as an important inflammation marker and it is responsible for a wide range of articular and extra-articular manifestations in RA patients. Osteocalcin is a protein (non-collagenous) that can be found in the bones extracellular matrix, as well as in the circulating blood serum. This protein is a marker of bone formation and turnover.

Objectives: Evaluating IL-6 and osteocalcin serum levels in RA patients and their correlation with disease activity.

Methods: We examined 126 patients previously diagnosed with RA according to the ACR/EULAR 2010 criteria. To all patients it was measured the IL-6 serum level (<4.0 pg/mL) and also the osteocalcin serum level using the ELISA-OSTEO kit method (1346ng/ml) and the disease activity was defined according to the DAS28. By using this activity score index the patients were divided in three groups: group I with active disease scoring > 5.1 (43 patients); group II with moderate disease activity scoring between 3.2 - 5.1 (52 patients); and group III with no disease activity scoring <3.2 (31 patients).

Results: IL-6 serum level resulted elevated in patients group I (1.9±0.6pg/ml) and group II (0.9±0.3pg/ml) and normal in patients group III (0.35 ±0.1pg/ml). Osteocalcin serum level resulted elevated in the three groups but with higher serum levels in patients group I and II (62±1.9ng/ml); 49.2±2.6ng/ml) and less higher serum levels in group III (44.5±1.7ng/ml). IL-6 serum level correlates best with osteocalcin serum level in patients group I and II (r=0.9). IL-6 serum level correlates with disease activity in group I and II (r=0.9) but not with disease activity in group III (r=0.4).

Conclusion: There is a significant correlation between IL-6 serum level and disease activity according to DAS 28 in RA patients. The elevation of osteocalcin serum level correlates with disease activity in RA patients with high and moderate disease activity which is an important finding of the intense bone remodelling, whereas in patients with no disease activity bone remodelling tent to slow down.

Disclosure of Interests: None declared


THU0050

IMPLICATIONS OF THE DIFFERENT RESPONSES OF NK CELLS AND MONOCYTES TO IL-6 AND IL-10 IN THE PATHOGENESIS OF ADULT-ONSET STILL’S DISEASE

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Background: Adult-onset Still’s disease (AOSD) is a systemic inflammatory disease, the cause of which is largely unknown. AOSD has recently been classified as one of the autoimmune diseases in which innate rather than acquired immunity plays an important role in the pathogenesis. Serum IL-18 has been shown to be highly elevated in AOSD patients [1,2].

Objectives: We attempted to quantify the levels of multiple cytokines in the serum of AOSD patients and to evaluate the effects of the cytokines detectable in the AOSD serum on natural killer (NK) cells and monocytes, since these are cells critical to innate immunity.

Methods: We examined 126 patients previously diagnosed with RA according to the ACR/EULAR 2010 criteria. To all patients it was measured the IL-6 serum level (<4.0 pg/mL) and also the osteocalcin serum level using the ELISA-OSTEO kit method (1346ng/ml) and the disease activity was defined according to the DAS28. By using this activity score index the patients were divided in three groups: group I with active disease scoring > 5.1 (43 patients); group II with moderate disease activity scoring between 3.2 - 5.1 (52 patients); and group III with no disease activity scoring <3.2 (31 patients).

Results: IL-6 serum level resulted elevated in patients group I (1.9±0.6pg/ml) and group II (0.9±0.3pg/ml) and normal in patients group III (0.35 ±0.1pg/ml). Osteocalcin serum level resulted elevated in the three groups but with higher serum levels in patients group I and II (62±1.9ng/ml); 49.2±2.6ng/ml) and less higher serum levels in group III (44.5±1.7ng/ml). IL-6 serum level correlates best with osteocalcin serum level in patients group I and II (r=0.9). IL-6 serum level correlates with disease activity in group I and II (r=0.9) but not with disease activity in group III (r=0.4).

Conclusion: There is a significant correlation between IL-6 serum level and disease activity according to DAS 28 in RA patients. The elevation of osteocalcin serum level correlates with disease activity in RA patients with high and moderate disease activity which is an important finding of the intense bone remodelling, whereas in patients with no disease activity bone remodelling tent to slow down.

Disclosure of Interests: None declared


THU0051

OFF-LICENSE USE OF ANAKINRA IN CRITICALLY ILL ADULTS WITH SUSPECTED HAEMOPHAGOCYTOSIS – A SINGLE CENTRE EXPERIENCE

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Background: Anakinra is a recombinant interleukin-1 receptor antagonist licensed in Europe for the treatment of rheumatoid arthritis, periodic fever and auto-inflammatory syndromes. It is increasingly recognised as an adjunct in the treatment of macrophage activation syndrome/secondary haemophagocytic lymphohistiocytosis (HLH).[1]

Objectives: To analyse the indication, patient demographic and outcomes of critically unwell patients receiving anakinra for suspected HLH.

Methods: Retrospective cohort analysis of adult patients who received anakinra over a 12-month period at Imperial College Healthcare NHS Trust, London.

Results: Eleven patients received anakinra (both sub-cutaneous and intra-venous, dose range 100–460 mg daily), ten alongside conventional treatments for HLH. 64% were male. Median age at presentation was 32 years (range 27-73 years). Serum ferritin was significantly elevated (median 17371 [range 3435 – 160,664 micrograms per litre]) in all cases. Ten of eleven cases underwent bone marrow examination which showed haemophagocytosis in all cases. Underlying diagnoses were: T-cell Lymphoma (n=3), Mantle Cell Lymphoma (n=1), gastric MALT Lymphoma (n=1), infection (n =3: Group A streptococcus in a patient with inflammatory arthritis (bone marrow not performed), EBV and CMV), retained products of conception (n=1), post-transplant-related lymphoproliferative disorder in a case of systemic lupus with renal transplant (n=1), unknown (n=1).

Overall mortality was 55%. The underlying diagnoses were: T-cell Lymphoma (n=3), gastric MALT Lymphoma (n=1), CMV infection in a post-renal transplant immunosuppressed patient (n=1, sarcoidosis underlying diagnosis), unknown (n=1). 100% of cases with T-cell lymphoma as the cause of HLH died, despite two of the three receiving standard chemotherapy to treat the lymphoma. The third case was diagnosed with non-haptenespecific gamma delta T-cell lymphoma post-mortem. In the five cases that survived, anakinra led to rapid recovery in three cases (underlying diagnoses: Mantle Cell lymphoma (managed entirely steroid free), HLH secondary to retained products of conception, and inflammatory arthritis with Group A streptococcal pneumonia). The two remaining cases had underlying PTLV and EBV-driven HLH. Anakinra led to rapid resolution of fever, improvement in respiration and dramatic decreases in serum ferritin (up to 98% reduction in three weeks).

There were no identifiable complications from anakinra use. One case remains on anakinra, a young male with inflammatory arthritis and Group A Streptococcal pneumonia, who rapidly flared again two days after cessation with full recovery once anakinra was re-instigated.

Conclusion: Anakinra can be a useful adjunct in the treatment of suspected HLH but appears to be less efficacious in those with underlying haematological malignancy, where mortality remains high. In critically ill

REFERENCES:

Disclosure of Interests: None declared


THU0066

PERSISTENCE OF CITSTAT AND TACROLIMUS IN MTPP PATIENTS – A SINGLE CENTRE EXPERIENCE

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Background: Infliximab is licensed for the treatment of adult patients with malignancy, where mortality remains high. In critically ill

Disclosure of Interests: None declared

patients we have used it intravenously, and in higher doses, where the half-life is shorter and twice daily dosing is required. Anakinra was well tolerated and its short half-life makes it ideal for use in suspected sepsis-driven HLH. One case was managed entirely steroid-free using anakinra. This allowed for the identification of an underlying lymphoma which may have missed had high-dose steroids been used. Larger studies will help us ascertain whether earlier anakinra use may spare steroid and chemotherapy side-effects and improve patient outcomes.

REFERENCES:

Disclosure of Interests: Shabnam Shabbir: None declared, Ahmad Al-Abedulla: None declared, Anne Kinderlehrer: None declared, Mamta Sohal: None declared, Mark Layton: None declared, Peter Hill: None declared, Richard Corbett: None declared, Liz Lightstone: None declared, Tom None declared, Mark Layton: None declared, Peter Hill: None declared, Shabnam Shabbir: None declared, Ahmad Al-

Ustekinumab and Guselkumab Treatment
Results in Differences in Serum IL17A, IL17F and CRP Levels in Psoriatic Arthritis Patients: A Comparison from Ustekinumab PH3 and Guselkumab PH2 Programs

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Background: Ustekinumab (UST) is a monoclonal antibody (mAb) that binds the p40 epitope which is shared by IL12 and IL23, whereas guselkumab (GUS) is a mAb that selectively binds the p19 subunit of IL23. In recent studies, both UST (Phase 3 programs)1 and GUS (Phase 2 program)2 have demonstrated a reduction in musculoskeletal clinical signs and symptoms and improvement of psoriatic lesions in patients with active psoriatic arthritis (PsA), implicating the IL12/23 pathway in disease pathogenesis.

Objectives: To explore the post-treatment pharmacodynamic changes of IL17A, IL17F, and CRP with GUS and UST in the context of PsA.

Methods: Serum protein levels of IL17A, IL17F, and CRP were measured in 142 subjects and 38 matched healthy controls from the GUS Ph2 study3 at Weeks 0, 4, and 16. In the UST Ph3 studies1, biomarkers were assayed at Weeks 0, 4, and 24 as follows: IL17A (n=474), IL17F (n=237), CRP (n=927). IL17A and IL17F were assayed using Single Molecule CountingTM Human Immunoassay Kits (formerly Singulex). CRP was measured using CardioPhase hsCRP assay (UST studies) or Meso Scale Discovery Platform (GUS study).

Results: At baseline, the Th17 effector cytokines IL17A and IL17F were elevated in the serum of PsA subjects in the GUS Ph2 cohort compared to healthy controls. IL17A and IL17F levels significantly correlated with affected skin body surface area, but not swollen or tender joint scores, in both studies. While none of the baseline levels of evaluated cytokines were associated with American College of Rheumatology (ACR) or Psoriasis Area Severity Index (PASI) clinical responses to UST, baseline IL17F levels were modestly associated with ACR20 response to GUS at week 24. Both UST and GUS treatment resulted in pharmacodynamic decreases in IL17A, IL17F, and CRP levels, with GUS treatment restoring IL17A and IL17F levels to that of healthy controls by week 16. Consistent with being a component of ACR scores, CRP changes were significantly associated with ACR20 responses to both UST and GUS treatment. Weeks 4 and 16 changes in IL17F with GUS treatment were significantly associated with ACR20 response at week 24. Week 24 PASI75 response to GUS was significantly associated with week 4 changes in IL17A, with a similar trend observed at Week 16.

Conclusion: These results underscore the relevance of the IL23/Th17 pathway in PsA, with GUS treatment providing a stronger suppression of the pathway than UST treatment. The significant associations of changes in IL17A in IL17F levels with GUS treatment with PASI75 and ACR20 response, respectively, support the importance of the IL23/Th17 pathway for both skin and joint pathologies. The associations of reduction in CRP levels with both UST and GUS treatment also reinforce the role of acute phase inflammation in joint pathology.

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Disclosure of Interests: Stefan Siebert Grant/research support from: Abb-Vie, Novartis, Pfizer, Janssen, BMS, Celgene, UCB, and Boehringer Ingelheim, Consultant for: AbbVie, UCB, Pfizer, Janssen, Boehringer Ingelheim, Celgene, and Novartis, Speakers bureau: AbbVie, UCB, Pfizer, Janssen, Boehringer Ingelheim, Celgene, and Novartis, Matthew J Loza Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Daniel Ng Say Song Reviewer of: Janssen Research & Development, LLC, Iain McInnes Grant/research support from: AstraZeneca, Celgene, Compugen, Novartis, Roche, UCB Pharma, Consultant for: AbbVie, Cel-gene, Galvani, Lilly, Novartis, Pfizer, UCB Pharma, Kristen Sweet Employee of: Janssen Research & Development, LLC


APREMLAST INHIBITS THE TGFB1 MEDIATED TRANSITION OF CULTURED HUMAN SKIN FIBROBLASTS INTO PROFIBROBLASTIC MYOFIBROBLASTS: IN VITRO STUDY

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Background: Fibroblast-to-myofibroblast transition and extracellular matrix (ECM) is a perpetually recurring fundamental event in chronic inflammation, that characterise several diseases, including psoriasis (1,2). Transforming growth factor-β1 (TGFB1), plays an important role as a profibrotic mediator (3).

Phosphodiesterases (PDE4) act as proinflammatory enzymes via degradation of cAMP. PDE4 are expressed in normal skin fibroblasts (Fs) and overexpressed in psoriatic skin Fbs and myofibroblasts (2).

Objectives: This study investigated how apremilast (an oral PDE4 inhibitor small molecule used for the treatment of psoriasis and psoriatic arthritis) might interfere with intracellular signalling for the fibroblast-to-myofibroblast transition and the synthesis of profibrotic ECM proteins induced by TGFB1 in primary cultures of healthy human skin Fbs.

Methods: Human skin Fbs isolated from Non-cultured healthy subjects after signing informed consent and EC approval. The cultured Fbs were stimulated with TGFB1 10ng/ml alone or in combination with apremilast 1μM and 10μM for 4, 16, and 24 hours. Other aliquots of Fbs were also previously stimulated with TGFB1 for 4 hours and then treated with apremilast 1μM and 10μM for 4, 16, and 24 hours always in the presence of TGFB1. Genes and related protein expression of α-smooth muscle actin (αSMA), type I collagen (COL-1) and fibronectin (FN) were investigated by qRT-PCR and Western blotting (WB). Smad proteins (the main signal transducers for receptors of TGFB1) and extracellular signal-regulated kinases (ERKs), which are implicated in mediating TGFB1 effects, were investigated by WB after 15, 30 and 60 minutes of apremilast 1 stimulation.

Results: Apremilast significantly downregulated the phosphorylation of Smad 2 and 3, at 15 minutes, and that of Erk1/2, after 30 minutes (p<0.05), both induced by TGFB1 stimulation in cultured skin Fbs. Apremilast significantly downregulated the TGFB1-induced increase in the gene expression of αSMA, COL-1 and FN at 4 and 16 hours, and the related protein synthesis after 24 hours (p<0.05) in cultured skin Fbs (treated in combination with TGFB1). Similar effects were observed in differentiated myofibroblasts treated with apremilast.

Conclusion: Apremilast inhibited the fibroblast-to-myofibroblast transition in vitro, as well as the profibrotic activity induced by TGFB1 in cultured skin Fbs by downregulating specific intracellular signalling pathways Smad 2/3 and Erk1/2. These results might partially explain some of the downregulating effects on skin Fbs overactivity during treatment of skin lesions of psoriasis and that of psoriatic patients with apremilast.

THU0053

APREMLAST INHIBITS THE TGFB1 MEDIATED TRANSITION OF CULTURED HUMAN SKIN FIBROBLASTS INTO PROFIBROBLASTIC MYOFIBROBLASTS: IN VITRO STUDY

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Scientific Abstracts
THE SYNOVIAL FLUID FROM RHEUMATOID ARTHRITIS PATIENTS CONTAINS SOLUBLE TAM RECEPTOR TYROSINE KINASES OF WHICH SOLUBLE TYRO3 AND ITS LIGAND GAS6 CORRELATE WITH THE PROINFLAMMATORY CYTOKINE LEVELS

Julia Vulling, Claire Waterborg, Marjole Koenders, Peter van Lent, Peter van der Kraan, Fons van de Logt, Radboud Institute for Molecular Life Sciences (RIMLS), Rheumatology, Nijmegen, Netherlands

Background: We recently showed that the tyrosine-protein kinase receptors MER and AXL, both members of the TAM (including TYRO3) receptor family, play a protective role in mouse models of rheumatoid arthritis (RA) [1, 2]. In both humans and mice, TAM receptors can be proteolytically cleaved from the cell membrane and shed as a soluble (s) receptor. These sTAM receptors may act as decoy receptors, bind their ligands Growth Arrest-Specific 6 (GAS6) and Protein S (PROS1), and thereby inhibit the immunoregulatory and anti-inflammatory effect of TAM receptor activation, and prevent TAM receptor-mediated phagocytic clearance of dying cells.

Objectives: To determine the soluble TAM receptor levels in synovial fluids from RA and osteoarthritis (OA) patients and correlate this to the inflammatory process.

Methods: The level of sMER, sAXL, sTYRO3, GAS6, IL-8, TNFα and IL-1β was measured in synovial fluids of RA (n = 28) and OA patients (n = 12) by ELISA or multiplex array. Synovial explants were cultured for 24 hrs and the release of sMER and GAS6 was measured by ELISA. Human synovial explants of RA (n = 15) and osteoarthritis (OA) (n = 17) patients were immunostained for MER.

Results: Soluble MER and sTYRO3 were significantly enhanced in synovial fluids (P = 0.0001 and P = 0.0042) of RA patients as compared to OA patients. The sAXL and GAS6 levels in synovial fluid of RA and OA patients was equally high (P = 0.267 and P = 0.074). In RA patients, but not in OA patients, the synovial fluid levels of sTYRO3 and GAS6 (a ligand for all three TAM receptors) positively correlated with TNFα (r=0.555, r=0.477), IL-1β (r=0.597, r=0.481) and IL-8 (r=0.567, r=0.529). Soluble MER levels, however, did not correlate with local inflammatory markers. Although synovial explants from RA released more sMER into the culture media than explants from OA (P = 0.0045), the explants of both RA and OA patients contained comparable amounts of immunopositive MER cells.

Conclusion: We showed that synovial fluid sTYRO3 and GAS6 levels correlates with higher proinflammatory cytokine levels in RA but not in OA patients. This is in line with the recent observation done by Xu et al. [3], that circulating levels of sTYRO3, but not sMER or sAXL, correlates with disease activity and bone destruction in RA patients. In accordance to serum, the synovial sMER levels were significantly higher in RA than in OA patients with sAXL levels comparable between both patient groups. Interestingly, only for sMER the synovial fluid levels were much higher than in serum suggesting local production as we confirmed in the synovial explants cultures. This illustrates that release of soluble TAM receptors is either the results of different processes (enzymatic shedding or alternative splicing isoforms) or reflect the different cell populations in the arthritic joint. We found that naive macrophages express high MER and inducible AXL, while synovial fibroblast express high AXL and TYRO3. Further studies are warranted to determine if sMER levels impair the clearance of apoptotic cells in the arthritic joint as we have found in our mice studies. Our study shows that synovial sTYRO3 is a marker for joint inflammation and possibly a novel therapeutic target for RA.

REFERENCE:

Disclosure of Interests: None declared

THU0055

THU0055 TPL2 INHIBITION SUPPRESSES MEK-ERK INFLAMMATORY SIGNALING AND PROINFLAMMATORY CYTOKINE PRODUCTION IN PRIMARY HUMAN MONOCYTES

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Background: Tumor progression locus 2 (TPL2, also known as MAP3K8) is a mitogen-activated protein kinase kinase kinase and the primary regulator of ERK-mediated gene transcription downstream of multiple proinflammatory stimuli including bacterial products (eg, LPS and bacterial peptidoglycans), damage-associated molecular patterns (DAMPs), TNFα, and IL-1β.1 Dysregulated signaling downstream of these inflammatory signals can drive uncontrolled immune cell activation and inflammation, which is associated with multiple chronic inflammatory and autoimmune diseases. As such, TPL2 inhibition represents a strategy to modulate inflammation in a variety of disease settings.

Objectives: We evaluated the effect of a highly selective TPL2 inhibitor on inflammatory signaling and cytokine production in LPS and TNFα-stimulated primary human monocytes.

Methods: Monocytes were precultured with a TPL2 inhibitor and stimulated with LPS or TNFα, and phospho-signaling and cytokine production were then evaluated at 30 minutes and 4 hours poststimulation. A431 cells (human epidermoid carcinoma cell line) were stimulated with TNFα or EGF and phospho-ERK was evaluated after 30 minutes.

Results: TPL2 inhibition selectively inhibited LPS and TNFα-stimulated phosphorylation of TPL2, MEK, and ERK, with little to no inhibition of phosphorylated p38, JNK, or p65 observed. TPL2 inhibition similarly inhibited both the RNA production and secretion of TNFα, IL-1β, IL-6, and IL-8 following LPS stimulation in primary human monocytes. To confirm TPL2 requirement for inflammation, but not Ras-mediated (growth factor stimulated) ERK signaling, A431 cells were stimulated with either TNFα or EGF. Although TPL2 inhibition reduced TNFα-stimulated pERK, no effect on ERK activation downstream of EGF was observed.

Conclusion: This work demonstrates the selective effects of TPL2 inhibition on ERK-mediated signaling and proinflammatory cytokine gene transcription in primary human monocytes and highlights the potential for TPL2 inhibition to treat diseases associated with dysregulated inflammatory signaling and chronic inflammation.

REFERENCE:


THU0054

THE SYNOVIAL FLUID FROM RHEUMATOID ARTHRITIS PATIENTS CONTAINS SOLUBLE TAM RECEPTOR TYROSINE KINASES OF WHICH SOLUBLE TYRO3 AND ITS LIGAND GAS6 CORRELATE WITH THE PROINFLAMMATORY CYTOKINE LEVELS

Julia Vulling, Claire Waterborg, Marjole Koenders, Peter van Lent, Peter van der Kraan, Fons van de Logt, Radboud Institute for Molecular Life Sciences (RIMLS), Rheumatology, Nijmegen, Netherlands

Background: We recently showed that the tyrosine-protein kinase receptors MER and AXL, both members of the TAM (including TYRO3) receptor family, play a protective role in mouse models of rheumatoid arthritis (RA) [1, 2]. In both humans and mice, TAM receptors can be proteolytically cleaved from the cell membrane and shed as a soluble (s) receptor. These sTAM receptors may act as decoy receptors, bind their ligands Growth Arrest-Specific 6 (GAS6) and Protein S (PROS1), and thereby inhibit the immunoregulatory and anti-inflammatory effect of TAM receptor activation, and prevent TAM receptor-mediated phagocytic clear-
THU0056  EFFECTS OF CX3CL1 INHIBITION ON MURINE BLEMÖYCM-INUCDED INTERSTITIAL PNEUMONIA
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Background: Pathological findings of interstitial pneumonia (IP) reveal the accumulation of inflammatory cells and proliferation of fibroblasts in lung tissue. Although a treatment has not yet been established for IP, particularly for IP with collagen diseases, chemokines may play a role in the pathogenesis of IP for inflammatory cell infiltration. We previously reported that chemokine (C-X-C motif) ligand 1 (CXCL1, also known as fractalkine) has potential as a therapeutic target for rheumatoid arthritis (RA).1,2,3 Humanized anti-human CX3CL1 monoclonal antibody (mAb) is currently undergoing clinical trials for RA.4

Objectives: In the present study, we examined the therapeutic effects of CX3CL1 blockade in amurine model of IP.

Methods: Bleomycin (BLM)-induced IP was developed by the intratracheal administration of BLM to C57BL/6 mice. The murine lung was stained with hematoxylin and eosin, and the expression of CX3CL1 and CX3CR1, a receptor for CX3CL1, was examined with immunohistochemistry. Mice were treated with anti-CX3CL1 mAb for 2 weeks. Collagen eluted from the lung was quantified using the Sircol Collagen Assay. The expression of CX3CL1 and CX3CR1 by mouse lung fibroblasts (MLFs) was examined with quantitative RT-PCR and Western blotting, respectively. Cell movement was investigated using the scrape motility assay.

Results: The expression of CX3CL1 and CX3CR1 was upregulated in BLM-induced IP. The treatment with anti-CX3CL1 mAb did not significantly alter inflammatory cell infiltration. However, collagen in the lung was decreased by the treatment with anti-CX3CL1 mAb. Stimulation with CX3CL1 did not alter the in vitro production of collagen by MLFs, but significantly enhanced cell movement.

Conclusion: CX3CL1 may be involved in increasing collagen in IP and the cell movement of MLFs. The present results suggest that CX3CL1 plays an important role in fibrosis in IP.

REFERENCES:
[2] Nanki T, et al. Migration of CX3CR1-positive T cells producing type 1 cytokines from the lung was quantified using the Sircol Collagen Assay. The expression of CX3CL1 and CX3CR1 by mouse lung fibroblasts (MLFs) was examined with quantitative RT-PCR and Western blotting, respectively. Cell movement was investigated using the scrape motility assay.

THU0057  PLASMACYDID DENDRITIC CELLS IN THE ENTHESIS: PHENOTYPIC AND FUNCTIONAL INVESTIGATION
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Background: Plasmacytoid dendritic cells (pDCs) play an important role in linking innate and adaptive immune responses and selectively express Toll-like receptor (TLR) 7 and TLR9 that sense RNA and DNA respectively thus regulating the secretion of type I interferons (IFN) and other inflammatory cytokines such as TNF.1,2 pDCs have been directly implicated in psoriasis immunopathology and are activated following anti-viral vaccination, with vaccination also linked to psoriatic arthritis onset.3,4 Inflammation of the enthesis (enthesitis) is a cardinal spondyloarthritides associated lesion so we hypothesized the presence of enthesis resident pDCs

Objectives: To investigate whether the human enthesis contains a resident pDC population and to compare the responses of TLR7/9 agonists on entheseal pDCs function relative to peripheral blood derived pDCs.

Methods: Normal interspines process enthesis and matched peripheral blood (PB) were obtained from patients (n=11) undergoing spinal decompression or sclerosis corrective surgery. Cells were isolated from peritenethese bone by mechanical digestion. Cells were stimulated with either TLR7 agonist (imiquimod) or TLR9 agonist (ODN-2216). Flow cytometry was used to phenotype pDCs, and intracellular staining used to measure IFNα and TNF. IFNα from supernatant was also measured by ELISA.

Results: pDCs were identified in the human enthesis with a typical phenotype (CD45+HLA-DR+CD123+CD303+CD11c+). By intracellular FACS, following ODN or imiquimod stimulation, IFNα and TNF was detected in entheseal pDCs and also PB. IFNα and TNF induction trended upwards in entheseal pDC when compared with unstimulated pDCs. IFNα was also detected by ELISA following ODN or imiquimod stimulation of entheseal derived pDCs.

Conclusion: The human enthesis contains a resident population of pDCs that produce IFNα and TNF following induction with relevant TLR agonists. For the first time, our findings provide a link between viral infection and vaccination and pivotal innate immune cell production of IFNα and TNF.

REFERENCES:


THU0058  PHENOTYPING AND FUNCTION INVESTIGATION
Qiao Zhou: None declared, Richard Cutbrell: None declared, Abdulla Watab: None declared, Tobias Russell Grant/research support from: PhD Project is funded by Novartis., Hannah Rowe: None declared, Almas Khan: None declared, Peter Millner: None declared, Peter Lougherub: None declared, Abhay S Rao: None declared, Robert Dunsmit: None declared, Charlie Bridgewood: None declared, Dennis Mogonagle Consultant for: Lilly, Novartis UCB, Speakers bureau: Lilly, Novartis UCB


Disclosure of Interests: Qiao Zhou: None declared, Richard Cutbrell: None declared, Abdulla Watab: None declared, Tobias Russell Grant/research support from: Phd Project is funded by Novartis., Hannah Rowe: None declared, Almas Khan: None declared, Peter Millner: None declared, Peter Lougherub: None declared, Abhay S Rao: None declared, Robert Dunsmit: None declared, Charlie Bridgewood: None declared, Dennis Mogonagle Consultant for: Lilly, Novartis UCB, Speakers bureau: Lilly, Novartis UCB

TUNALPHA INDUCES NECROTOPSIS-LIKE DEATH OF MACROPHAGES AND PROMOTES EXTRACELLULAR RELEASE OF 14-3-3TA

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Background: 14-3-3α is an intracellular protein detected in the serum and synovial fluid of patients with rheumatoid arthritis (RA) [1]. While presence of 14-3-3α is both diagnostic for early and established RA [2,3], and prognostic for radiographic progression [3], the mechanism of 14-3-3α externalization in RA remains unclear.

Objectives: To clarify the mechanism of externalization of 14-3-3α into the extracellular space using human PBMC-derived macrophages (Mϕ).

Methods: Distribution of 14-3-3α in synovial tissue of patients with RA or osteoarthritis (OA) was examined by immunohistochemistry; cellular morphology was studied by confocal microscopy and electron microscopy (EM). Mϕ were stimulated with TNF-α, Diamide (induces ligand-independent TNF signalling) or IL-6/sIL-6R. Western blotting was used to detect S-358-phosphorylated MLKL (a mediator of necroptosis) and presence of 14-3-3α in Mϕ culture supernatants.

Results: Dense and punctuate staining of 14-3-3α was detected in Mϕ, but not OA, synovial tissues. 14-3-3α and peptidylarginine deiminase 4 (PAD4) co-localized in CD68+ cells (Mϕ) from RA synovial tissue; 14-3-3α was not detected in CD68+ cells from RA lung tissue or CD4+ cells (T cells) from RA synovium. The outer space around the nucleus of healthy control Mϕ treated with TNF-α or Diamide, but not IL-6/sIL-6R, demonstrated abnormal actin distribution by phalloidin staining and presence of cellular and organelle swelling by EM. Further, magnified images showed partial destruction of the cell membrane in TNF-α and Diamide-treated cells. Phosphorylation of MLKL was observed between 20 min and 24 h after stimulation of healthy control Mϕ with TNF-α, with maximum signal at 8 h post-stimulation, but was not observed upon IL-6/sIL-6R stimulation at any time point. After 8 h of stimulation no 14-3-3α was detected in the culture supernatant of healthy control Mϕ endogenously expressing 14-3-3α or Mϕ stimulated with IL-6/sIL-6R, while a high concentration of 14-3-3α was detected in culture supernatants in Mϕ treated with TNF-α or Diamide.

Conclusion: 14-3-3α protein was abundant in RA, but not OA, synovial tissues and co-localized with PAD4 in CD68+ synovial Mϕ; this close proximity to PAD4 may promote citrullination of 14-3-3α in vivo. Treatment of healthy control Mϕ with TNF-α induced phosphorylation of MLKL and cell swelling and disintegration of the plasma membrane characteristic of necroptosis, correlated with the release of intracellular 14-3-3α protein into cellular supernatants. Our results shed light on mechanism of externalization of 14-3-3α and how it achieves elevated levels in RA synovial fluid.

REFERENCES:

Competing Interests: M. Zaharia and N. Bilin are employees of Augurex. Y. Tanaka, received speaking fees and/or honoraria from Daiichi-Sankyo, Astellas, Eli Lilly, Chugai, Sanofi, Abbvie, Pfizer, YL Biologics, Bristol-Myers, GlaxoSmithKline, UCB, Mitsubishi-Tanabe, Novartis, Eisai, Takeda, Janssen, Asahi-kasei and has received research grants from Mitsubishi-Tanabe, Bristol-Myers, Eisai, Chugai, Daiichi-Sankyo, Eli Lilly, Eisai, Glaxo-SmithKline, Janssen, Mitsubishi-Tanabe, Novartis, Pfizer Japan Inc, Sanofi, Takeda, UCB, YL Biologics

THU0057B

Rheumatoid arthritis – prediction, predictors and outcome

THU0058

B CELL SYNOVITIS AND CLINICAL PHENOTYPES IN RHEUMATOID ARTHRITIS AT DIFFERENT DISEASE STAGES

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Background: The role of B cells in the pathogenesis of Rheumatoid Arthritis (RA) is well recognised and has been reinforced by the established efficacy of B cell depleting treatments. However, B cell infiltration in synovia is highly variable and their association with clinical disease activity has been inconsistently reported, with contrasting results possibly linked to the lack of standardization in quantitative and qualitative assessment of B cell synovitis. In particular, the presence of B cells in synovia has never been systematically assessed in large cohorts.

Objectives: To evaluate B cells and their association with clinical phenotypes in the synovia of patients with RA at various disease stages.

Methods: A total of 432 synovial biopsies from the following cohorts of RA patients were analysed: i. early (<1 year) treatment-naïve RA (n=165), ii. Synthetic Disease-Modifying Anti-Rheumatic Drugs (SDMARDs) responders (SDMARDS-ir) (n=103), iii. TNF-Infinites inhibit responders (TNFi-ir) (n=164). Haematoxylin and eosin staining was used for the assessment of synovitis according to a previously validated score (Krenn). Upon immunohistochemical staining for CD20, semi-quantitative (Sq) scoring (0-4) was used to classify patients into B cell rich (≥ 2) and poor (< 2) and automated digital image analysis (DIA) to calculate the B cell area fraction. B cell expression markers, including CD20 mRNA counts and a composite B cell module, were obtained by RNA-sequencing from early RA synovial biopsies (n=91).

Results: Semi-quantitative synovial B cell scores positively correlated with the B cell area fraction obtained by DIA (Spearman r 0.93 in early RA and 0.88 in TNFi-ir, p<0.0001). Accordingly, B cell rich patients (Sq score ≥ 2) had a significantly higher B cell area fraction (p<0.0001). RNA-sequencing from 91 patients with early RA showed a positive correlation between the Sq B cell scores and CD20 mRNA counts and the B cell module (Spearman r=0.6 and 0.67, respectively, p<0.0001). Similarly, a positive correlation was found between the B cell area fraction obtained by DIA and CD20 mRNA counts and B cell module (r=0.67 and 0.69, respectively, p<0.0001). When comparing B cell presence in the three cohorts, B cell-rich synovitis was present in 35% of early RA, 36% of SDMARDS-ir and 47.1% of TNFi-ir (p=0.025 comparing early RA vs late-stage TNFi-ir patients). Finally, while B cell-rich patients showed significantly higher synovial inflammatory scores across all cohorts, higher disease activity (number of active joints, DAS28) and higher prevalence of autoantibody positivity (ACPA and RF) in B cell-rich patients were observed exclusively in the early RA cohort.

Conclusion: We here describe a robust and validated synovial B cell score that can potentially contribute to patient stratification in RA, as it helps identifying an enrichment of B cell synovitis in established disease, uncoupled from clinical disease activity.

Acknowledgement: We would like to thank all the investigators and recruitment centers from PEAC (http://www.peac-mrc.mds.qmul.ac.uk/centres.php), STRAP (http://www.matura-mrc.whi.qmul.ac.uk/strap_recruiting_centers.php) and R4RA (http://www.r4ra-nihr.whi.qmul.ac.uk/recruiting_centres.php) and the EMR clinical trial team at Queen Mary (http://www.r4ra-nihr.whi.qmul.ac.uk/docs/contributors-r4ra-for-website.pdf)

Disclosure of Interests: Felice Rivellesi: None declared, Frances Hubmyr: None declared, Serena Bugatti Speakers bureau: Bristol-Myers Squibb, Celgene, Lilly, Novartis, Sanofi, Janssen, Liliane Fossati-Jimack: None declared, Hasan Rizvi: None declared, Davide Lucchesi: None declared,
INCIDENCE OF JOINT REPLACEMENT SURGERY AMONG BIOLOGICS AND NON-BIOLOGICS TREATED PATIENTS WITH RHEUMATOID ARTHRITIS: A PROPENSITY SCORE MATCHED COHORT STUDY FROM DENMARK

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Background: Biologics have improved several clinical, patient-reported and radiological outcomes in patients with rheumatoid arthritis (RA), but little is known about the potential impact on the need for joint replacement surgery.

Objectives: To investigate the incidence of joint replacement surgery among biologics treated compared with biologics naïve patients with RA.

Methods: A nationwide, register-based propensity score matched cohort study. RA patients registered between 2006 and 2016 in the DANBIO register with a disease duration ≤ 2 years were identified. Patients initiating their first treatment series with biologics were followed up to 10 years for a first joint replacement of the hip, knee, shoulder, elbow and finger/wrist. Biologics naïve patients were followed up for the same outcome from their first clinical visit registered in DANBIO. Following a 1:1 propensity score matching, Cox-models were undertaken to calculate the hazard ratio (HR) for a first joint replacement surgery among biologics compared with non-biologics treated RA patients. Further, subgroup analyses based on within-strata propensity score matched patients were carried out. All information on surgical outcomes was obtained in the Danish National Patient Registry.

Results: In total, 1187 biologics treated were matched with 3666 non-biologics treated patients (See Table).

Abstract THU0059 – Table1. Baseline characteristics of biologics treated and biologics naïve patients with rheumatoid arthritis and a disease duration < 2 years registered in DANBIO between 2006 and 2016.

<table>
<thead>
<tr>
<th>Biologics treated</th>
<th>Biologics naïve</th>
<th>SMD</th>
</tr>
</thead>
<tbody>
<tr>
<td>N Total</td>
<td>1187</td>
<td>3666.0</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>828 (70)</td>
<td>2546 (69)</td>
</tr>
<tr>
<td>Age at start of follow-up, mean (s.d)</td>
<td>53.8 (13.5)</td>
<td>54.1 (15.1)</td>
</tr>
<tr>
<td>Age at diagnosis, mean (s.d)</td>
<td>52.7 (13.5)</td>
<td>52.9 (15.1)</td>
</tr>
<tr>
<td>IgM-RF and/or ACPA positive at start of follow-up, n (%)</td>
<td>866 (58)</td>
<td>2042 (56)</td>
</tr>
<tr>
<td>DAS28-CRP</td>
<td>4.5 [3.6 to 5.4]</td>
<td>4.5 [3.4 to 5.4]</td>
</tr>
<tr>
<td>HAQ-DI</td>
<td>1.00 [0.50 to 1.62]</td>
<td>1.62</td>
</tr>
<tr>
<td>CRP mg/ml</td>
<td>9.3 [9 to 22]</td>
<td>9.3 [9 to 20]</td>
</tr>
<tr>
<td>Physician global</td>
<td>32 [16 to 49]</td>
<td>30 [16 to 50]</td>
</tr>
<tr>
<td>VAS pain</td>
<td>53 [31 to 73]</td>
<td>52 [30 to 74]</td>
</tr>
<tr>
<td>Methotrexate, n (%)</td>
<td>1044 (88)</td>
<td>3160 (86)</td>
</tr>
<tr>
<td>Glucocorticoid</td>
<td>246 (21)</td>
<td>718 (20)</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease, n (%)</td>
<td>168 (57)</td>
<td>57 (51)</td>
</tr>
<tr>
<td>Cardiovascular disease, n (%)</td>
<td>322 (9)</td>
<td>97 (8)</td>
</tr>
<tr>
<td>Hospitalised with infection in previous 5 years, n (%)</td>
<td>128 (4)</td>
<td>43 (4)</td>
</tr>
</tbody>
</table>

SMD: standardized mean difference; n: number; s.d.: standard deviation; VAS: visual analogue scale. All values are median [interquartile range] unless otherwise stated.

Conclusion: In this nationwide Danish cohort study, there was no difference in the incidence of joint replacement surgery among newly diagnosed RA patients selected for treatment with biologics compared with patients naïve to biologics.

References:

Disclosure of Interests: René Cordtz: None declared, Samuel Hawley: None declared, Daniel Prieto-Alhambra Grant/research support from: Grants from Amgen, UCB Biopharma and Servier outside the submitted work, Consultant for: UCB Biopharma, Speakers bureau: Amgen, Lars Erik Kristensen Grant/research support from: UCB, Biogen, Janssens Pharmaceuticals, and Novartis, Consultant for: Consultant for Abbvie, Amgen, Biogen, BMS, Cellgene, Eli Lilly, Janssens Pharmaceuticals, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB Pharma., Speakers bureau: Pfizer, Abbvie, Amgen, UCB, BMS, Biogen, MSD, Novartis, Eli Lilly and Company, and Janssens Pharmaceuticals, Søren Overgaard: None declared, Anders Odgaard: None declared, Lene Dreyer Consultant for: MSD, UCB and Janssens Pharmaceuticals, Speakers bureau: MSD, UCB and Janssens Pharmaceuticals, Speakers bureau: UCB, MSD, Eli Lilly and Janssens Pharmaceuticals.

Methods: Synovial tissue (ST) was sampled by Parker-Pearson needle biopsy from 67 RA patients who had completed one year follow-up from a prospective RA cohort. ST from 13 patients with orthopedic arthropathies (Orth. A) with arthropathy or arthroscopy were used as control. Expression of MUC1 in ST was assessed by immunohistochemistry (IHC). Radiographic assessments of hand/wrist at baseline and month 12 were performed with the Sharp/van der Heijde-modified sharp score. Radiographic joint damage (RJD) was defined as total modified Sharp score (mTSS) >10. Radiographic progression (RP) was defined as a change of mTSS more than 0.5 units.

Results: 1. Both nuclear and cytoplasmic MUC1 expression were observed in lining and sublining cells of synovium. The percentage of MUC1+ lining cells was significantly higher in RA (median 65.4%, IQR 53.6% 73.2%) than that in Orth. A (median 43.1%, IQR 34.1% 68.4%, P <0.05).

2. Thirty-five (52%) RA patients showed RJD at baseline and their MUC1expression in lining layer was significantly enhanced compared with RA patients without RJD (median 69.6%, IQR64.5% 76.8% vs. median 58.9%, IQR 39.8% 67.9%, P <0.01). Spearman’s rank order correlation test showed significantly positive correlations between the percentage of MUC1+ lining cells with mTSS, joint space narrowing (JSN) and joint erosion (JE) subcore at baseline (r =0.303-0.426, all P < 0.05).

3. Furthermore, twenty-two(33%) patients suffered from one-year RP and they showed significantly higher percentage of MUC1+ lining cells than non-progressive patients (median 71.2%, IQR 55.2% 75.2% vs. median 64.1%, IQR 55.2% 75.2%, r <0.01). The percentage of MUC1+ lining cells was positively correlated with JSN, JSN and JE subcores at month 12 (r =0.310-0.405, all P <0.05). ROC curve analysis showed that the tradeoff value of MUC1+ lining cells for predicting one-year RP was 69% with sensitivity 72% and specificity 71% (AUC=0.661, 95% CI:0.516-0.805, P=0.034). Univariate logistic regression analysis showed that high MUC1+ lining cells was a significant predictor of one-year radiographic progression (OR: 5.893, 95%CI: 1.934-17.956, P=0.002).

Conclusion: Our data showed elevated MUC1expression in RA synovial lining cells was positively correlated with joint damage and predicted one-year radiographic progression, which imply that MUC1 might be involved in the pathogenesis of RA joint destruction.

REFERENCE:

Disclosure of Interests: None declared


THU0061

IN OVERWEIGHT SUBJECTS, SERUM ADIPONECTIN PREDICTS THE DEVELOPMENT OF RHEUMATOID ARTHRITIS INDEPENDENTLY OF OTHER ADIPOKINES

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Background: Adipokines, such as adiponectin, leptin, resistin and visfatin, are cytokines produced by the adipose tissue and involved in metabolism and inflammation1. Adiponectin is elevated in both serum and synovial fluid of subjects with rheumatoid arthritis (RA), suggesting a possible role of this adipokine in the pathogenesis of RA 2-3. Circulating levels of leptin, resistin, and visfatin are also higher in subjects with RA compared to controls.

Objectives: Aim of this study was to determine if adiponectin, leptin, resistin, and visfatin predict the development of RA.

Methods: Two nested-case control studies were performed including pre-symptomatic participants of two cohorts from Sweden: the Swedish Obese Subjects (SOS) study and a cohort of individuals identified within the Medical Biobank of Northern Sweden. The SOS is a clinical trial including 4047 subjects with obesity4. During a follow-up for up to 29 years, 92 subjects developed RA. Among those 92 subjects, 82 subjects with available serum at baseline were matched 1:5 with 410 subjects who did not develop RA during follow-up. Matching was based on baseline age, sex, body-mass index (BMI), bariatric surgery yes/no, year of inclusion, and smoking. A nested case-control study of 88 sex- and age-matched pairs was performed within the Medical Biobank of Northern Sweden using blood samples donated before the onset of the first RA symptoms. The pre-dating time before onset of symptoms of RA was 8.5±5.0 years5.

Baseline serum levels of adiponectin, leptin, resistin, and visfatin were measured using the Quantikine ELISA kit from R&D Systems (Wiesbaden, Germany). Visfatin could not be measured in the Biobank cohort, due to lack of serum. Both binary logistic as well as conditional logistic regression analyses were used to determine if adipokines were elevated years before the onset of RA.

Results: In a multivariable analysis including adiponectin, leptin, resistin, visfatin performed in the SOS cohort, serum adiponectin was associated with a higher risk for RA independently of other adipokines (Odds ratio, OR, 1.1, 95% confidence interval, CI, 1.0-1.1, p value=0.01). Leptin, resistin and visfatin levels were not associated with the risk of RA.

In the Biobank cohort, no association between adipokines and risk for RA was detected. However, when stratifying the population according to BMI, in the subgroup having BMI≥25 (n=109), adiponectin levels were associated with higher risk for RA (OR 1.2, 95% CI 1.0-1.36, p=0.03), independently of leptin and resistin levels. Virtually the same results were obtained in both the SOS and the Biobank cohorts when conditional logistic regression analysis was used.

Conclusion: Our results suggest that higher serum adiponectin levels predict the development of RA in subjects with overweight/obesity.

REFERENCES:

Disclosure of Interests: Yuan Zhang: None declared, Linda Johansson: None declared, Anna Rudin Grant/research support from: I have received research grants from AstraZeneca (2017-2018), Consultant for: I was paid consultant for AstraZeneca (2015-2018), Lena Carlsson Consultant for: I have received lecture fees from AstraZeneca, MSD and Johnsons&Johnsons, Solbritt Rantapää Dahlqvist Consultant for: Member of the advisory board, Lipum AB, Umeå, Sweden, Cristina Maglio: None declared


THU0062

THE DYSREGULATION OF NK CELLS AND NON-CLASSICAL AND CLASSICAL MONOCYTE SUBPOPULATIONS IN INDIVIDUALS AT RISK OF DEVELOPING RHEUMATOID ARTHRITIS

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Background: Antibodies against citrullinated proteins (ACPA) are present months to years before the clinical manifestation of rheumatoid arthritis (RA). ACPA+ individuals are at 8-10x higher risk of developing RA compared to seronegative individuals. EUULAR characterised individuals with arthralgia suspicion for progression to RA based on their clinical features (clinically suspect arthralgia, CSA).

Objectives: The alteration of natural killer (NK) cells and monocyte subpopulations in patients with established RA has been previously described. We therefore aimed to study the lymphocyte and monocyte subpopulations in the preclinical phase of RA.

Methods: Our study included 49 individuals with arthralgia (mean age 45.9±7.119.5 years; 92% females) and 80 age and gender matched healthy controls (HC). Leukocytes from peripheral blood were analysed by flow cytometry. Lymphocyte subpopulations were defined as B (CD19

Disclosure of Interests: Yuan Zhang: None declared, Anna Rudin Grant/research support from: I have received research grants from AstraZeneca (2017-2018), Consultant for: I was paid consultant for AstraZeneca (2015-2018), Lena Carlsson Consultant for: I have received lecture fees from AstraZeneca, MSD and Johnsons&Johnsons, Solbritt Rantapää Dahlqvist Consultant for: Member of the advisory board, Lipum AB, Umeå, Sweden, Cristina Maglio: None declared

PRE-MRNA SPlicing ALTERATIONS IN POLYPOLYGLUTAMATE SYNTHETASE IN BLOOD CELLS OF EARLY RHEUMATOID ARTHRITIS PATIENTS ARE ASSOCIATED WITH UNRESPONSIVENESS TO METHOTREXATE

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Background: Low-dose methotrexate (MTX) serves as the first-line treatment for rheumatoid arthritis (RA). Conversely, for hematological malignancies, high-dose MTX treatment is indicated in combination with folinic acid/leucovorin to prevent untoward toxicity. For both disease modalities, efficient pharmacological response critically depends on the retention and accumulation of intracellular MTX. The latter process is mediated by the enzyme poly(ADP-ribose)polymerase (PARP) through MTX conversion into MTX-polyglutamates (MTX-PG). As such, decreased FPGS activity has been recognized as a mode of MTX resistance, but the underlying molecular mechanism has not yet been pinpointed [1,2]. Recently, aberrant pre-mRNA splicing of FPGS in acute lymphoblastic leukemia cells was associated with reduced FPGS activity, decreased MTX-PG accumulation and lower overall survival. Specifically, a partial retention of FPGS intron 8 (8PR) was identified as a prominent splice variant causing FPGS dysfunction [3].

Objectives: To investigate whether the expression of the FPGS pre-mRNA variant partial retention of intron 8 is associated with MTX unresponsiveness in RA patients over 3-6 months of MTX therapy.

Methods: Patients were enrolled from the COBRA-light trial comprising MTX treatment [4]. After informed consent, blood was obtained from 38 patients in either the COBRA (n=15) or the COBRA-light (n=23) treatment arm [4] and collected in Paxgene tubes for RNA isolation. Two patients were excluded due to insufficient sample quality. Quantitative PCR techniques were used to assess the ratios of FPGS 8PR over wild type FPGS (8WT) expression in whole blood RNA. Remission was defined as a DAS44 < 1.6.

Results: Baseline ratios of 8PR/8WT were associated with a decline in DAS44 at T3 (p=0.001) and T6 (p=0.13) in the COBRA-light patients. T3 ratios were also associated with DAS44 at T6 (p=0.001) and DAS44 at T6 (p=0.26). Logistic regression analysis showed that in COBRA-light patients baseline ratios of 8PR/8WT were associated (p=0.05) with the probability of T3 remission but not T6 remission. T3 ratios of 8PR/8WT in COBRA-light patients were similarly associated with T6 remission but not with T3 remission. COBRA patients also showed a significant association between baseline 8PR/8WT ratios and DAS44 at T6 (p=0.04) while T3 ratios of 8WT/8PR were significantly associated with DAS44 at T3 (p=0.03) and B2 (p=0.05). However, analysis of COBRA patients showed no significant associations between baseline 8PR/8WT ratios and T3/T6 remission, nor associations between T3 ratios and T3/T6 remission.

Conclusion: These results demonstrate that a higher expression of an intron 8 retention of FPGS mRNA is associated with a higher DAS44 at T3 and T6 in COBRA-light patients, and at T6 for COBRA patients. Moreover, in COBRA-light patients, baseline expression of WT/8PR is significantly associated with remission at T3 or T6. This study is the first to show the impact of FPGS pre-mRNA splicing alterations in relation to unresponsiveness to MTX treatment in RA.

REFERENCE:
the model were excluded. Furthermore, the patients with both RA and diabetes were not included in the analysis (n=33). Participants with neither RA nor diabetes were defined as controls.

RA patients, diabetes patients and controls were compared using Cox proportional hazard regression modelling, with age as the time scale. The model was adjusted for sex, smoking status, previous CVD, body mass index (BMI), hypertension, total cholesterol and creatinine. To obtain proportional hazards, an interaction term with age ≤75 years vs >75 years was included for diabetes, smoking and previous CVD. The effects of the groups were compared using overlap of confidence intervals.

Results: Table 1. Participant characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>RA (N=298)</th>
<th>Diabetes (N=639)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex, n (%)</td>
<td>261 (87)</td>
<td>298 (87)</td>
</tr>
<tr>
<td>Age (yrs), median (IQR)</td>
<td>60 (49-68)</td>
<td>63 (51-73)</td>
</tr>
<tr>
<td>Never smoker, n (%)</td>
<td>122 (41)</td>
<td>243 (74)</td>
</tr>
<tr>
<td>Former smoker, n (%)</td>
<td>129 (33)</td>
<td>82 (23)</td>
</tr>
<tr>
<td>Current smoker, n (%)</td>
<td>126 (33)</td>
<td>95 (33)</td>
</tr>
<tr>
<td>Previous CVD, n (%)</td>
<td>41 (14)</td>
<td>20 (6)</td>
</tr>
<tr>
<td>BMI (kg/m²), median (IQR)</td>
<td>26.0 (23.1-29.4)</td>
<td>28.4 (23.4-29.6)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>149 (51)</td>
<td>303 (62)</td>
</tr>
<tr>
<td>Creatinine (µmol/l), median (IQR)</td>
<td>84 (77, 92)</td>
<td>89 (80, 99)</td>
</tr>
<tr>
<td>Total cholesterol (mmol/l), median (IQR)</td>
<td>6.5 (5.3-6.8)</td>
<td>6.0 (5.1-6.9)</td>
</tr>
<tr>
<td>Seropositive RA, n (%)</td>
<td>277 (22)</td>
<td>1,369 (47)</td>
</tr>
<tr>
<td>RA duration (yrs), median (IQR)</td>
<td>6 (3-9)</td>
<td>20 (12-31)</td>
</tr>
<tr>
<td>Diabetes duration (yrs), median (IQR)</td>
<td>5 (2-11)</td>
<td>20 (10-30)</td>
</tr>
<tr>
<td>Observation time (yrs), median (IQR)</td>
<td>18 (13-19)</td>
<td>18 (13-19)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variable</th>
<th>β Coefficient (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MBDAb assay</td>
<td>0.31 (0.27, 0.35)</td>
<td>0.0002</td>
</tr>
<tr>
<td>log (CRP)</td>
<td>0.03 (0.003, 0.05)</td>
<td>0.004</td>
</tr>
<tr>
<td>Sero positivity</td>
<td>0.03 (0.005, 0.04)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Baseline SAI</td>
<td>0.04 (0.02, 0.06)</td>
<td>0.0001</td>
</tr>
<tr>
<td>DAS28-CRP</td>
<td>0.05 (0.03, 0.07)</td>
<td>0.0001</td>
</tr>
<tr>
<td>SDI</td>
<td>0.08 (0.05, 0.10)</td>
<td>0.0001</td>
</tr>
<tr>
<td>BSA</td>
<td>0.03 (0.01, 0.05)</td>
<td>0.0001</td>
</tr>
<tr>
<td>CRP</td>
<td>0.06 (0.03, 0.09)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Baseline SAI</td>
<td>0.07 (0.05, 0.09)</td>
<td>0.0001</td>
</tr>
<tr>
<td>DAS28</td>
<td>0.09 (0.07, 0.10)</td>
<td>0.0001</td>
</tr>
<tr>
<td>SDI</td>
<td>0.10 (0.07, 0.12)</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Conclusion: RA patients had significantly higher mortality rates than controls, with higher hazard for diabetes than for RA. The HR for RA was significantly lower than for diabetes for patients ≤75 years, but not for >75 years.

REFERENCES:
2 Vickers, V. et al., Self-reported Diagnosis of Rheumatoid Arthritis or Ankylosing Spondylitis has Low Accuracy: Data from the Nord-Trondelag Health Study. J Reumatol. 2017. 44(8):p.1134-1141

Disclosure of Interests: Ingrid Saether Houge: None declared, Mari Hoff: None declared, Ranjeny Thomas Grant/research support from: Janssen Biotec Inc, Merck and Co, Consultant for: Janssen Biotec Inc, Speakers bureau: Janssen, Merck, Vibeke Videm: None declared

Background: Recent studies have shown divergent associations between rheumatoid arthritis (RA)-associated autoantibodies and RA onset phenotype. Whereas some studies report more inflammation in seronegative patients [1, 2], others report that rheumatoid factor (RF) associates with high baseline disease activity [3].

Objectives: To define how individual RA-associated autoantibodies associate with individual disease activity score (DAS28, DAS28CRP) components at the time of RA diagnosis.

Methods: Sixteen individual ACPO, Employee of: Crescendo Bioscience, Inc., Thomas Huizinga Consultant for: Merck, UCB, Bristol Myers Squibb, Lilly; Scendo Bioscience Inc., Nycomed, Boeringher, Takeda, Zydus, Epirus, Eli Lilly

Disclosure of Interests: Eleftheria Pertsoindou: None declared, Vivek Anand Manival: None declared, Lars Klæreskog Grant/research support from: Yes, but not for the presented study., Lars Alfredsson: None declared, Linda Mathsson Employee of: employed by Thermo Fisher Scientific, Monika Hansson: None declared, Martin Cornill: None declared, Per-Johan Jakobsson: None declared, Helga Westerlind: None declared, Linda Mathsson Employee of: employed by Thermo Fisher Scientific Inc., Thomas Huizinga Consultant for: Merck, UCB, Bristol Myers Squibb, Biotest AG, Pfizer, GSK, Novartis, Roche, Sanofi-Aventis, Abbott, Crescendo Bioscience Inc., Nycomed, Boeringer, Takeda, Zyus, Epirus, Eli Lilly


Abstract THU0066 – Figure 1

effect of RF on ESR increased with the number of individual ACPO activities present, most prominently for IgM RF (figure).

Conclusion: In early RA, ACPO associate with low counts of affected joints and IgM RF associates with elevated ESR in an ACPO-dependent manner. The latter finding relates to in vitro studies showing enhanced inflammatory effect of ACPO immune complexes with addition of RF[4, 5]. Future RA studies relating autoantibodies to disease activity may benefit from evaluating the impact of individual antibodies as well as distinct DAS components separately.

REFERENCES:

IgA RF IgG RF IgM RF ACPO

N (% ) antibody 692 (43.2) 529 (33.1) 916 (57.2) 1020 (63.8)

Multiple regression:

CRP P value (β )

0.6914 (0.011) 0.3162 (-0.0106 (0.071) 0.6889 (0.011)

ESR P value (β )

0.0215 (0.0662) 0.1237 (0.0339) -0.0001 (0.108) 0.0380 (0.057)

SJC P value (β )

0.6175 (0.0131) 0.2110 (-0.0645 (0.051) -0.0001 (-0.122)

TJC P value (β )

0.6168 (0.0314) 0.4102 (-0.8712 (0.005) 0.0007 (-0.094) 0.0201

Disclosure of Interests: Eleftheria Pertsoindou: None declared, Vivek Anand Manival: None declared, Lars Klæreskog Grant/research support from: Yes
THU0067 THREE-MONTH RADIOLOGICAL CHANGES IN WRIST JOINT MEASURED BY MRI AND HR-PQCT CAN PREDICT 12-MONTH CHANGES IN EROSION AND FUNCTIONAL OUTCOMES AFTER MTX AND ANTI-TNF TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS: A MULTI-MODALITY IMAGING STUDY

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Background: Magnetic resonance imaging (MRI) provides noninvasive methods to quantify joint inflammation and early cartilage degeneration in patients with rheumatoid arthritis.

Methods: Seventeen RA patients with MTX treatment were recruited into a cohort and evaluated their association with the presence of other autoantibodies and disease activity and severity.

Results: Anti-Carbamylated antibodies (Anti-CarP) represent a novel autoantibody family present in sera of patients with rheumatoid arthritis (RA) with high specificity.

Objectives: To investigate if changes in MR measures from baseline to 12-month (12M) in RA patients receiving methotrexate (MTX) and anti-tumor necrosis factor alpha (Anti-TNFa) therapy using MRI and HR-pQCT.

Conclusions: The results suggest that multimodality quantitative imaging with MRI and HR-pQCT provides powerful tools for evaluating early changes and predicting disease progression and therapy response after treatment in RA. Large scale studies with larger sample size are warranted to confirm the observations.

REFERENCES:

Disclosure of Interests: None declared


THU0068 ANTI-CARBAMYLATED ANTIBODIES ARE ASSOCIATED WITH TOBACCO AND POOR OUTCOMES IN RHEUMATOID ARTHRITIS

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Background: Anti-carbamylated protein antibodies (Anti-CarP) represent a novel autoantibody family present in sera of patients with rheumatoid arthritis (RA) with high specificity.

Objectives: To analyse the prevalence of Anti-CarP in an established RA cohort and evaluate their association with the presence of other autoantibodies and disease activity and severity.

Conclusions: Cross-sectional study. Presence of Anti-CarP was analyzed in a cohort of patients with established RA (n: 158) by a home-made ELISA test using fetal calf serum. We investigated the demographic, radiological and current and at disease onset clinical features. Rheumatoid factor (RF) and anti-citrullinated peptide antibodies (ACPA) status were also assessed.

Results: Anti-CarP were positive in 46.2% of the patients in our cohort and in 15.1%, 19.2% and 9.1% of the patients negative for ACPA, RF and both respectively. Demographic and clinical features are shown in table 1. The mean titer of ACPA (1361±1054 U/mL vs. 918 ± 1092 U/mL) and RF (258 ± 255 AU vs. 174 ± 205 AU) were significantly higher in Anti-CarP positive patients. No difference in symptoms at RA onset was observed. Current (24.7% vs. 11.6%) and previous (54.8% vs. 37.0%) smoking consumption were significantly associated with Anti-CarP antibodies. Anti-CarP positive patients presented a higher CRP values (1.0±1.6 mg/dL vs. 0.5±0.8 mg/dL), swollen joint count (1.3±2.2 vs 0.7 ±1.8) and patient global health assessment VAS (34.8 ±21.5 mm vs. 26.4 ±17.1 mm); although no between-group differences in disease activity (DAS28, CDAI, SDAI and RAPID3) or demographic features were observed. Anti-CarP positive patients presented significantly higher scores in Larsen index (23.6 ± 15.7 vs. 15.7 ± 12.6) and disability (HAQ-DI >1) (23.3% vs. 8.3%).

Conclusion: Anti-CarP were present in approximately half of the RA cohort and were also detected in seronegative (RF and/or ACPA) test. Linear regression models were used to evaluate whether changes in imaging measure changes from BL to 3M predict changes in erosion volumes and patient outcomes (DAS28-CRP, HAQ, MHO) from BL to 12M, after adjusting for age, gender, disease duration and therapy (Anti-TNFa added or not).

Results: Anti-TNFa therapy in the high DAS group resulted in significant decreases of SYN, BMEL at 3M and DAS28-CRP, HAQ and MHO at 3M and 12M from BL (Table.1). The low DAS group in contrast, displayed significant increases in SYN and DAS-CRP at 3M and bone erosion volume at 3M and 12M from BL despite low disease activity (Table.1). Changes in SYN, not BMEL, T1rho or bone erosion, from BL to 3M were significantly correlated with changes in HAQ and MHO from BL to 12M (P < 0.05), and with changes in DAS-CRP from BL to 12M with marginal significance (P=0.053) (Figure 1). Changes in erosion volumes from BL to 3M were significantly correlated with changes from BL to 12M (P<0.05) (Figure 1).

Conclusion: Despite the low disease activity, patients on MTX only showed significantly increased erosion volumes as measured by HR-pQCT at 3M and 12M; on the other hand, patients with MTX+Anti-TNFa treatment showed decreased erosion volumes at 3M and 12M, implying erosion repair. In this study, changes in erosion (but not other MR measures including synovitis and bone marrow edema) within the first 3M predicted changes in erosion at 12M. On the other hand, changes in synovitis volumes predicted patient functional outcomes at 12M. These results suggest that multimodality quantitative imaging with MRI and HR-pQCT provides powerful tools for evaluating early changes and predicting disease progression and therapy response after treatment in RA. Large scale studies with larger sample size are warranted to confirm the observations.
patients. In our cohort, patients with Anti-CarP antibodies presented higher tobacco consumption and poorer disease outcomes.

Table 1. Demographic and Clinical Features According to Anti-CarP Status

<table>
<thead>
<tr>
<th>Anti-CarP positive n: 73</th>
<th>Anti-CarP negative n: 85</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>52 (71.2%)</td>
</tr>
<tr>
<td>Mean age at diagnosis (SD)</td>
<td>53.6 (±11.9)</td>
</tr>
<tr>
<td>Mean age at inclusion (SD)</td>
<td>58.7 (±11.9)</td>
</tr>
<tr>
<td>Extra-articular manifestations</td>
<td>21 (28.6%)</td>
</tr>
<tr>
<td>Disease duration (SD)</td>
<td>5.1 (±3.7)</td>
</tr>
<tr>
<td>Smoking history</td>
<td>40 (54.8%)</td>
</tr>
<tr>
<td>• Previous and/or current</td>
<td>18 (24.7%)</td>
</tr>
<tr>
<td>• Current</td>
<td>10 (11.8%)</td>
</tr>
<tr>
<td>RA family history</td>
<td>12 (16.4%)</td>
</tr>
<tr>
<td>BMI</td>
<td>27.5 (±4.5)</td>
</tr>
<tr>
<td>Disease presentation at initiation (%)</td>
<td>15 (20.5%)</td>
</tr>
<tr>
<td>• Paediatric rheumatism</td>
<td>7 (9.6%)</td>
</tr>
<tr>
<td>• Inflammatory arthralgia</td>
<td>4 (5.5%)</td>
</tr>
<tr>
<td>• Polyarticular arthritis</td>
<td>47 (64.4%)</td>
</tr>
<tr>
<td>Mean DAS28 (SD):</td>
<td>3.0 (±1.3)</td>
</tr>
<tr>
<td>Mean DAS28 PCR (SD):</td>
<td>2.7 (±1.2)</td>
</tr>
<tr>
<td>Remission/Low</td>
<td>72.6%</td>
</tr>
<tr>
<td>Mean CDAI (SD):</td>
<td>9.2 (±8.8)</td>
</tr>
<tr>
<td>Remission/Low</td>
<td>71.6%</td>
</tr>
<tr>
<td>Mean SDAI (SD):</td>
<td>10.2 (±8.6)</td>
</tr>
<tr>
<td>Remission/Low</td>
<td>68.5%</td>
</tr>
<tr>
<td>Mean RAPID (SD):</td>
<td>10.2 (±6.6)</td>
</tr>
<tr>
<td>Remission/Low</td>
<td>47.2%</td>
</tr>
<tr>
<td>Mean HAQ (SD):</td>
<td>0.45 (±0.52)</td>
</tr>
<tr>
<td>Poor HAQ (&gt;1)</td>
<td>17 (23.3%)</td>
</tr>
<tr>
<td>Pain Analogue Scale mm (SD)</td>
<td>276.2 (±29.8)</td>
</tr>
<tr>
<td>Treatment:</td>
<td>44 (60.3%)</td>
</tr>
<tr>
<td>Glucocorticoids</td>
<td>63 (86.3%)</td>
</tr>
<tr>
<td>cDMARDs</td>
<td>48 (65.8%)</td>
</tr>
<tr>
<td>MTX</td>
<td>7 (9.6%)</td>
</tr>
<tr>
<td>HCO</td>
<td>14 (19.2%)</td>
</tr>
<tr>
<td>LEF</td>
<td>17 (23.3%)</td>
</tr>
<tr>
<td>dDMARDs</td>
<td>37 (50.7%)</td>
</tr>
<tr>
<td>Erosive disease</td>
<td>46 (58.4%)</td>
</tr>
<tr>
<td>Modified Larsen Score</td>
<td>23.6 (±15.7)</td>
</tr>
</tbody>
</table>

RHEUMATOID CACHEXIA ASSESSED BY BODY COMPOSITION IS ASSOCIATED WITH WORSE DISEASE IN RHEUMATOID ARTHRITIS PATIENTS WITH NORMAL BODY MASS INDEX

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Background: Abnormal body composition (BC) has been reported in rheumatoid arthritis (RA) patients with normal body mass index (BMI). Rheumatoid cachexia (RC) was found in RA patients with a decrease in muscle mass and an increase or limited change in fat mass, resulting in no or limited changes in BMI. However, there is no consensus on the clinical criteria for its diagnosis, and the clinical significance of RC has not been well known until now.

Objectives: To investigate the characteristics of BC in RA patients with normal BMI and the association between RC and disease characteristics.

Methods: Consecutive RA patients were recruited and clinical data including disease activity, function and radiographic assessment were collected. BC was assessed by bioelectric impedance analysis. RC was defined as those with concurrent overweight (body fat percentage ≥25% for men and ≥35% for women) and myopathy (appendicular skeletal muscle mass index ≤7.0 kg/m² in men and ≤5.7 kg/m² in women) in this study. Multivariate logistic regression analysis was performed to identify the association between disease characteristics and RC in RA patients with normal BMI, following the step-forward selection rule that variables were included in the equation when the P value was <0.05 or removed when the P value was >0.10.

Results: 1. There were 516 RA patients recruited, with 13.8% RC as well as 17.4% underweight, 56.4% normal weight, 22.5% overweight and 3.7% obese respectively. Among 71 RA patients with normal BMI, while 2.8% underweight, 22.5% overweight and 1.4% obese. Among 48 patients with normal BMI (n=291), 17.9% patients showed RC. 28.1% showed normal fat but myopathy, 1.4% showed overweight but myopathy, while 52.6% showed both normal fat and non-myopenia. 2. For RA patients with normal BMI, compared with those with both normal fat and non-myopenia, RA patients with RC were older with longer disease duration, higher disease activity indicators including 28TJC, PtGA, PainVAS, ESR, CRP, DAS28-2CRP, SDAI and CDAI, higher functional indicators including HAQ-DI and rate of functional limitation, higher radiographic assessment including mTSS, JCN and JE scores, higher rate of previous use of glucocorticosteroids (75.0% vs. 52.3%), and higher prevalence of hypertension (25.0% vs. 7.8%). Further compared with those with normal fat but myopathy, RA patients with RC showed the similar results with significantly longer disease duration, higher CRP, HAG-DI, mTSS, JCN subscore, JE subscore, and higher rate of previous use of glucocorticosteroids (all P<0.0167, bonferroni correction). 3. Multivariate logistic regression analysis showed that CRP (OR=1.024, 95%CI: 1.009-1.040), mTSS (OR=1.017, 95%CI: 1.010-1.025), previous use of glucocorticosteroids (OR=2.605, 95%CI: 1.217-5.575), and suffering from hypertension (OR=3.462, 95%CI: 1.448-8.274) were positively associated with RC in RA patients with normal BMI.

Conclusion: Our data show that rheumatoid cachexia is associated with worse disease including RA disease activity, functional limitation and radiographic joint damage, which imply that RC should be emphasized especially in RA patients with normal BMI.

Disclosure of Interests: None declared.

Acknowledgement: This work was supported by National Natural Science Foundation of China (no. 81871612 and 81801606), Guangdong Natural Science Foundation (no. 2017A030313576, 2017A030310236, and 2018A030313541) and Guangdong Medical Scientific Research Foundation (no. A2017109). Disclosure of Interests: None declared.


THU0070

WHAT IS THE ADDITIONAL VALUE OF MRI OF THE FOOT TO THE HAND IN UNDIFFERENTIATED ARTHRITIS TO PREDICT RHEUMATOID ARTHRITIS DEVELOPMENT?

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Background: MRI-detected subclinical joint inflammation in hand-joints of patients with undifferentiated arthritis (UA) predicts progression to rheumatoid arthritis (RA). It is unknown if adding MRI of the foot increases predictive accuracy compared to the hand alone.

Objectives: To assess whether MRI-detected inflammation of the foot is predictive for RA-development, and whether combining MRI-detected inflammation of the foot to that of the hand is of additional value.

Methods: 1.5T-contrast-enhanced MRI of unilateral foot (MTP-1-5), and hand (MCP-2-5 and wrist) was performed in 123 patients presenting with UA (not fulfilling 2010 RA-criteria) and scored for bone marrow edema (BME), synovitis and tenosynovitis. Symptom-free controls (n=193) served as a reference for defining an abnormal MRI. Patients were followed for 1-year, defined as fulfilling classification criteria or initiation of disease modifying anti-rheumatic drugs because of the expert opinion of RA. The added predictive value of foot-MRI to hand-MRI was evaluated.

Results: 52% developed RA. Foot tenosynovitis was predictive (OR 2.55, 95%CI 1.03-6.43), independent of BME and synovitis (OR 3.29, 95%CI 1.01-10.53), but not independent of CRP and number of swollen joints (OR 2.14, 95%CI 0.77-5.95). Hand tenosynovitis was also predictive independent of BME and synovitis (OR 3.99, 95%CI 1.64-9.69) and independent of CRP and swollen joints (OR 2.36, 95%CI 1.04-5.38). Adding foot tenosynovitis to hand tenosynovitis changed sensitivity from 72% to 73%, specificity from 59% to 54% and AUC from 0.66 to 0.64, the net reclassification index was -3.5.

Conclusion: MRI-detected tenosynovitis of the foot predicts progression to RA. However adding MRI of the foot does not improve predictive accuracy compared to MRI of the hand alone. In view of cost-reduction, performance of foot-MRI for prognostic purposes in UA can be omitted.
Disclosure of Interests: Yousra Dakkak: None declared, Debbie Boeters: None declared, Aleid Boer: None declared, Monique Reijnierse Grant/ research support funding from Arthritis Foundation. The funding source had no role in the design and conduct of the study. Annette van der Helm - van Mil Grant/research support from: The research leading to these results has received funding from the European Research Council (ERC) under the European Union’s Horizon 2020 research and innovation programme (Starting grant, agreement No 714312) and from the Dutch Arthritis Foundation. The funding source had no role in the design and conduct of the study. DOI: 10.1136/annrheumdis-2019-eular.1688

THE COMBINATION OF RHEUMATOID FACTORS WITH ANTIBODY SYSTEMS TARGETING CITRULLINATED, CARBAMYLATED AND PEPTIDYL ARGinine DEIMINASE AUTOANTIGENS DISTINGUISHES RHEUMATOID ARTHRITIS

Thierry Davierw1, John Conklin1, Tyler O’Malley1, Kelley Brady1, Roberta Alexander2, Jing Shi3, Claudia Ibarra3, Michael Mahler3, Joel Kremer3, Michael E. Weinblatt4, Arthur Weinstein5, Ying Shi1, et al. Proc Natl Acad Sci USA. 2011 108(42):17372-7

THU0071

Table 1: Combination of RI IgM, anti-CCP (IgG), anti-CarP (IgG) and anti-PAD4 (IgG)

<table>
<thead>
<tr>
<th>Score</th>
<th>RA (%)</th>
<th>CTL (%)</th>
<th>Likelihood Ratio</th>
<th>Pre-test Probability</th>
<th>Post-test Probability</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>20.5%</td>
<td>65.8%</td>
<td>0.31 [0.27 to 0.37]</td>
<td>10%</td>
<td>3.4%</td>
<td>-6.6%</td>
</tr>
<tr>
<td>1</td>
<td>11.6%</td>
<td>27.2%</td>
<td>0.43 [0.33 to 0.54]</td>
<td>10%</td>
<td>4.5%</td>
<td>-5.5%</td>
</tr>
<tr>
<td>2</td>
<td>25.5%</td>
<td>5.8%</td>
<td>4.40 [3.22 to 3.02]</td>
<td>10%</td>
<td>32.8%</td>
<td>22.8%</td>
</tr>
<tr>
<td>3</td>
<td>29.6%</td>
<td>1.0%</td>
<td>28.70 [14.26 to 77.53]</td>
<td>10%</td>
<td>76.1%</td>
<td>66.1%</td>
</tr>
<tr>
<td>4</td>
<td>12.7%</td>
<td>0.1%</td>
<td>98.39 [13.73 to 705.04]</td>
<td>10%</td>
<td>91.6%</td>
<td>81.6%</td>
</tr>
</tbody>
</table>

Disclosure of Interests: Thierry Davierwroleshareholder of: Exagen (a diagnostics company not a pharmaceutical company), Tyler O’Malley Employee of: Exagen (a diagnostics company not a pharmaceutical company), Kelley Brady Employee of: Exagen (a diagnostics company not a pharmaceutical company), John Conklin Employee of: Exagen (a diagnostics company not a pharmaceutical company), Tyler O’Malley Employee of: Exagen (a diagnostics company not a pharmaceutical company), Kelley Brady Employee of: Exagen (a diagnostics company not a pharmaceutical company), Roberta Alexander Employee of: Exagen (a diagnostics company not a pharmaceutical company), Jing Shi Employee of: Exagen (a diagnostics company not a pharmaceutical company), Claudia Ibarra Shareholder of: Exagen (a diagnostics company not a pharmaceutical company), Employee of: Exagen (a diagnostics company not a pharmaceutical company), Michael Mahler Employee of: Inova Diagnostics (Not pharmaceutical, diagnostics company), Joel Kremer Shareholder of: Coronra, Consultant for: AbbVie, Amgen, Bioniche-CCP, and patients who develop CCP, Employee of: Exagen (a diagnostics company not a pharmaceutical company), Employee of: Exagen (a diagnostics company not a pharmaceutical company), Employee of: Exagen (a diagnostics company not a pharmaceutical company), Employee of: Exagen (a diagnostics company not a pharmaceutical company), Employee of: Exagen (a diagnostics company not a pharmaceutical company), Consultant for: Exagen (a diagnostics company not a pharmaceutical company), Consultant for: Exagen (a diagnostics company not a pharmaceutical company)

THU0072

ULTRASOUND PREDICTS IMMINENT PROGRESSION TO ARTHRITIS IN ANTI-CCP POSITIVE AT-RISK INDIVIDUALS

Laurence Duguayonn1,2, Kulveer Mankii1,2, Jacqueline Nam1,2, Peta Pentony3,4, Leticia Garcia-Montoya5, Andrea Dimattio6,7, Laura Hunt8,9, Paul Emery10,11, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom; 5NIHR Leeds Biomedical Research Centre, Leeds, United Kingdom

Background: Ultrasound (US) Power Doppler (PD) signal is predictive for the development of inflammatory arthritis (IA) in anti-cyclic citrullinated protein antibodies positive (CCP+) individuals with musculoskeletal (MSK) symptoms but no clinical synovitis (CS) [1]. Our previous data showed a large increase in the overall US inflammation before arthritis development, suggesting that a sub-clinical phase of synovitis could be detected [2]. This abstract describes the prediction of PD abnormalities in the months following US scan.

Objectives: 1. Presence of PD in one joint is predictive of imminent progression to IA in the next 3 months. 2. A rise in the number of joints with presence of PD increases the odds of progression to IA.

Methods: In a single-centre prospective observational cohort between June 2008 and December 2018, 307 CCP+ patients with a new MSK symptom but no synovitis were followed until CS occurred. Clinical and US findings were analysed. Following our previous study, we compared progression in the 3, 12 or >12 months after a US scan. 38 joints were included in the analysis (MTPs, hands, wrists, elbows, ankles and knees). Patients with palindromic rheumatism were excluded.

Results: From 96 CCP+ at-risk patients who developed CS (progressors) compared to 211 CCP+ patients who did not (non-progressors). Age and gender are similar, the mean follow-up of the non-progressors is higher, with significantly more smokers and higher titre CCP in the progressors group (Table1).

Overall, progressors have more joints with PD than non-progressors (Figure). Patients with PD in one joint are more likely to develop CS in the following 3 months compared to those without PD (OR 7.52) and this remain significant when only the hands and wrists are included.

REFERENCES:
The clinical characteristics of rheumatoid arthritis at presentation become milder over time? Results from a nationwide study over three decades in Sweden

Jon Einansson, Tor Olufson, Olafur Palsson, Johan K Wallman, Melha C Kapetanovic. Lund University, Department of Clinical Sciences Lund, Section of Rheumatology, Lund, Sweden

Background: The course of rheumatoid arthritis (RA) has become milder during the last decades, which could at least partly be attributed to major advances in the pharmacological treatment of the disease and the implementation of “treat to target”-strategies (1,2). It has also been suggested that RA is already milder at presentation (3).

Objectives: To investigate whether the clinical status, markers of inflammation, functional status, and patient and evaluator reported disease activity measures in patients with newly diagnosed RA, have improved over the recent decades.

Methods: Baseline data on all DMARD-naive patients with early RA (<6 months duration) included in the nationwide Swedish Rheumatology Quality registry (SRQ) between 1991 and 2014 were retrieved. The RA diagnosis relied on the clinical judgement of the treating physician and the information comprised swollen and tender joints count (SJC; TJC), markers of inflammation (CRP; ESR), functional status (HAQ; DASH), patient’s and evaluator’s assessment of global disease activity (PtGA; EGA) and patient’s assessment of pain (on a visual analog scale, VAS; 0-100 mm). Baseline demographic and disease characteristics were compared between patients with disease onset 1991-2000 vs. those with onset 2011-2014, using Mann-Whitney U test and Pearson’s chi-squared test.

Results: A total of 6559 early RA patients were included. Over the study period of 23 years the majority of the patients were women (68%), and the mean age at inclusion increased from 57.4 to 59.1 years. Results are summarised in Table 1. Mean CRP, ESR, TJC and SJC all increased significantly between the time periods. Furthermore, time from symptom onset to inclusion was shorter 2011-2014.

Conclusion: In Swedish patients with early RA, baseline joint counts and inflammatory markers improved over the last three decades. This could partly be explained by shorter symptom duration at diagnosis but also suggests that, at onset, RA might be an inherently milder disease today. However, pain and patient’s global assessment and evaluator’s global assessment of disease activity increased over the same period of time, possibly indicating changes in both patients’ and evaluators’ expectations for management of early RA today.

Disclosure of Interests: Laurence Duquenne: None declared. Kluveer Mankia Grant/research support from: Research support from BMS and Lilly, Speakers bureau: Honoraria from Abbvie, UCB, Jacqueline Nam: None declared, Peta Pentony: None declared, Leticia Garcia-Montoya: None declared, Andrea DiMatteo: None declared, Laura Hunt: None declared, Paul Emery Grant/research support from: Pfizer, MSD, AbbVie, Bristol-Myers Squibb, Roche, Consultant for: Pfizer, MSD, AbbVie, Bristol-Myers Squibb, UCB, Roche, Novartis, Gilead, Samsung, Sandoz and Lilly DOI: 10.1136/annrheumdis-2019-eular.7860

Table 1. Mean (SD) 1990s 2000s 2011-2014 p-value

<table>
<thead>
<tr>
<th>Variable</th>
<th>1990s</th>
<th>2000s</th>
<th>2011-2014</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>1227</td>
<td>4344</td>
<td>988</td>
<td></td>
</tr>
<tr>
<td>Age at inclusion (years)</td>
<td>57.4 (15.4)</td>
<td>58.4 (15.0)</td>
<td>59.1 (14.7)</td>
<td>&lt;0.006</td>
</tr>
<tr>
<td>Female gender (%)</td>
<td>67.3%</td>
<td>67.6%</td>
<td>70.4%</td>
<td>0.12</td>
</tr>
<tr>
<td>Time from symptom onset (months)</td>
<td>3.8 (1.5)</td>
<td>3.6 (1.5)</td>
<td>3.3 (1.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>33.1 (36.3)</td>
<td>29.3 (36.7)</td>
<td>22.6 (29.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ESR (mm/h)</td>
<td>36.4 (25.8)</td>
<td>35.4 (24.8)</td>
<td>32.4 (23.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TJC (0-28)</td>
<td>8.0 (6.6)</td>
<td>8.0 (6.1)</td>
<td>7.1 (6.0)</td>
<td>0.005</td>
</tr>
<tr>
<td>SJC (0-28)</td>
<td>9.5 (5.9)</td>
<td>9.0 (5.8)</td>
<td>7.6 (5.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HAQ (0-3)</td>
<td>1.1 (0.6)</td>
<td>1.1 (0.6)</td>
<td>1.0 (0.6)</td>
<td>0.028</td>
</tr>
<tr>
<td>EGA (VAS 0-100)</td>
<td>50.3 (19.5)</td>
<td>54.4 (19.4)</td>
<td>54.8 (20.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pain (VAS 0-100)</td>
<td>49.5 (26.1)</td>
<td>52.3 (25.5)</td>
<td>53.4 (26.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PGA (VAS 0-100)</td>
<td>48.6 (26.7)</td>
<td>52.4 (25.5)</td>
<td>51.8 (26.7)</td>
<td>0.006</td>
</tr>
</tbody>
</table>

*1990s vs 2011-2014

Conclusion: In Swedish patients with early RA, baseline joint counts and inflammatory markers improved over the last three decades. This could partly be explained by shorter symptom duration at diagnosis but also suggests that, at onset, RA might be an inherently milder disease today. However, pain and patient’s global assessment and evaluator’s global assessment of disease activity increased over the same period of time, possibly indicating changes in both patients’ and evaluators’ expectations for management of early RA today.

REFERENCES:


Table 2. Probability of progression

<table>
<thead>
<tr>
<th>OR (95% CI)</th>
<th>Probability of progression</th>
</tr>
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<tbody>
<tr>
<td>&lt;3M</td>
<td>3-12M</td>
</tr>
<tr>
<td>N</td>
<td>96</td>
</tr>
<tr>
<td>Age*</td>
<td>53.4 (13)</td>
</tr>
<tr>
<td>Gender F/M(%)</td>
<td>50.2/48.8</td>
</tr>
<tr>
<td>Weeks follow-up*</td>
<td>7.44 (93.5)</td>
</tr>
<tr>
<td>Smoker: Ever/Never</td>
<td>72.9/27.1</td>
</tr>
</tbody>
</table>

Abstract THU0072 - Figure 1

Table of Contents

1. Introduction
2. Materials and Methods
3. Results
4. Discussion
5. Conclusion

REFERENCES:


[2] Pentony P. et al., Sequential US shows a late increase in inflammatory burden in anti-CCP positive patients with non-specific MSK symptoms just before progression to IA. Ann Rheum Dis, volume 77, year 2018
EVALUATION OF MEDICATION PERSISTENCE IN EARLY VERSUS DELAYED START OF BARICITINIB IN RA is a systemic disease driven by pathogenic autoantibodies and inflammatory cytokines that can involve tissues and organs as well as synovial joints. Sjögren’s syndrome (SS) and interstitial lung disease (ILD) are frequently reported extra-articular manifestations of RA. However, there are currently limited data on the persistency of non-TNF inhibitor (TNFi) biologic (b)DMARDs and targeted synthetic DMARDs, such as tofacitinib (TOF), in patients (pts) with SS and ILD secondary to RA (RA-SS and RA-ILD).

Objectives: To compare medication persistence between non-TNF-DMARDs including abatacept (ABA), TOF and tocilizumab (TOC) in RA-SS and RA-ILD.

Methods: Pts (≥18 years) from the Truven MarketScan™ administrative claims database with RA ≥2 prescription claims for RA identified with International Classification of Diseases (ICD)-9 or ICD-10) being treated with a non-TNF DMARD from Jan 2006 to Sep 2017 were included. The date of the first claim for a drug of interest on or after diagnosis of RA was considered the index date. Pts were required to have at least 6 months of continuous enrollment prior to the index date (baseline). Pts with claims for other bDMARDs on the index date were excluded from the study. Pts with a diagnosis of SS or ILD any time in the baseline or follow-up periods were included in the RA-SS or RA-ILD cohorts, respectively. Persistence was defined as the number of days from index date to first switch or discontinuation of the index date DMARD, or end of the study period, or end of enrolment, whichever came first. Pts in both cohorts were stratified by prior TNFi use (TNFi-naïve or TNFi-experienced) (OS) use. Pairwise comparison of persistence between the non-TNF DMARDs was performed with ABA as the reference, using the Kruskal–Wallis test for both cohorts separately. A p value of <0.05 was considered statistically significant.

Results: A total of 2503 and 3856 pts satisfied the inclusion and exclusion criteria for the RA-SS and RA-ILD cohorts, respectively. In the RA-SS cohort, 1767, 378 and 358 pts were taking ABA, TOF and TOC, respectively; in the RA-ILD cohort, these numbers were 2937, 343 and 358, respectively. The majority (90% in RA-SS and 75% in RA-ILD) of the study population was female. In the RA-ILD cohort, the proportion of pts with prior CS use was significantly lower in pts taking ABA (vs TOF). In the RA-SS cohort, the commodity index between treatment cohorts was similar; however, ABA pts had significantly lower pulmonary nodules vs TOF pts (Table 1). In the RA-ILD cohort, the commodity index was significantly lower for ABA (vs TOF and TOC), with differences in types of comorbidities at baseline (Table 1). In the RA-SS cohort, the mean time on therapy for pts taking ABA was longer compared with TOC. Persistency of ABA was higher compared with TOC in the TNFi-naïve cohort.

Conclusion: Based on the analysis of a large US claims database, pts with RA-SS prescribed ABA (vs TOF) had higher persistency, and pts with RA-ILD prescribed ABA (vs TOC) had higher persistency. Further analysis of medication persistence, adjusting for pt characteristics, is warranted.

Disclosure of Interests: Jon Einarsson: None declared, Tor Olufsson: None declared, Olafur Palsson: None declared, Johan K Wallman Consultant for: AbbVie, Colgene, Eli Lilly, Novartis, and UCB Pharma, Melina C Kapetanovic: None declared. DOI: 10.1136/annrheumdis-2019-eular.2167

Abstract THU0074 – Table 1. demographics

<table>
<thead>
<tr>
<th>RA-SS cohort</th>
<th>RA-ILD cohort</th>
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<tr>
<td><strong>ABA (n=1767)</strong></td>
<td><strong>TOF (n=378)</strong></td>
</tr>
<tr>
<td><strong>ABA (n=2937)</strong></td>
<td><strong>TOF (n=343)</strong></td>
</tr>
<tr>
<td>Mean (SD) age, years</td>
<td>65.1 (11.4)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>1069 (60.5)</td>
</tr>
<tr>
<td>TNF-experienced, n (%)</td>
<td>620 (35.0)</td>
</tr>
<tr>
<td>Titers, n (%)</td>
<td>1114 (60.3)</td>
</tr>
<tr>
<td>CGI score, mean (SD)</td>
<td>1.4 (0.9)</td>
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</table>

<table>
<thead>
<tr>
<th>RA-SS cohort</th>
<th>RA-ILD cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean (SD) age, years</strong></td>
<td>65.1 (11.4)</td>
</tr>
<tr>
<td><strong>Female, n (%)</strong></td>
<td>1069 (60.5)</td>
</tr>
<tr>
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<tr>
<td><strong>CGI score, mean (SD)</strong></td>
<td>1.4 (0.9)</td>
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THU0075 – EARLY VERSUS DELAYED START OF BARICITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS IN A PHASE 3 TRIAL OF PATIENTS NAIVE TO METHOTREXATE TREATMENT

Roy Fleischmann1, Michael Schiff2, Tore K. Kvien3, Gern Gabay4, Patrick Durez5, Anabela Cardoso6, Jinglin Zhong7, Yun-Fei Chen6, Jennifer Workman6, Roy Fleischmann1, Michael Schiff2, Tore K. Kvien3, Cem Gabay4, Patrick Durez5, Anabela Cardoso6, Jinglin Zhong7, Yun-Fei Chen6, Jennifer Workman6, Tsutomo Takeuchi8, 1University of Texas Southwestern Medical Center, Dallas, United States of America; 2University of Colorado, Denver, United States of America; 3University of Oslo, Oslo, Norway; 4University of Geneva, Geneva, Switzerland; 5UCL Saint Luc, Bruxelles, Belgium; 6Eli Lilly and Company, Indianapolis, United States of America; 7IQVIA, Morrisville, United States of America; 8Keio University School of Medicine, Tokyo, Japan

Background: Baricitinib (bari) is an oral Janus kinase (JAK)1/JAK2 inhibitor approved to treat moderately to severely active rheumatoid arthritis (RA) in adults in over 50 countries including European countries, the US and Japan. In the 52-week (wk) Phase 3 RA-BEGIN study, bari 4-mg alone or in combination with methotrexate (MTX) showed clinical improvements compared to MTX monotherapy for MTX-naive patients (pts) with early active RA.1

Objectives: To assess if pts who receive bari monotherapy early attain enhanced clinical, functional and radiographic outcomes compared to pts who initiated MTX and switched to bari at wk 52.

Disclosure of Interests: Jon Einarsson: None declared, Tor Olufsson: None declared, Olafur Palsson: None declared, Johan K Wallman Consultant for: AbbVie, Colgene, Eli Lilly, Novartis, and UCB Pharma, Melina C Kapetanovic: None declared. DOI: 10.1136/annrheumdis-2019-eular.2167

THU0075
Methods: In RA-BEGIN, 588 pts (mean disease duration 1.4 years) were randomized 4:3:4 to MTX, bari 4-mg once-daily, or combination MTX and bari 4-mg. At Wk 52, pts could elect a 1-year extension study in which all pts received open-label bari 4-mg. Pts initially randomized to bari-4 mg monotherapy were defined as early-start and MTX pts who switched to bari 4-mg at Wk 52 were defined as delayed-start for this analysis. Change from baseline using mixed model repeated measures and mean scores were assessed for the Simplified Disease Activity Index (SDAI), Clinical Disease Activity Index (CDAI), Disease Activity Score 28-joints-erythrocyte sedimentation rate (DAS28-hsCRP), Disease Activity Score 28-joints–erythrocyte sedimentation rate (DAS28-ESR), Health Assessment Questionnaire-Disability Index (HAQ-DI), and modified total Sharp Score (mTSS) to compare early- vs delayed-start groups between Wks 0 and 100 (Wks 52-100 for mTSS). Percent of pts achieving low disease activity (LDA, SDAI ≤11) and remission (SDAI ≤3.3) were also assessed.

Results: LDA and remission response rates in the delayed-start group increased from 60% to 78% and 18% to 31%, respectively, within 4 wks after switching to bari 4-mg. Remission rates reached 47% within 1 year after switching, but were not different from the group that initiated bari (Figure 1). Similar results were seen for CDAI, DAS28-ESR, and DAS28-hsCRP (only up to Wk 40 for DAS28-ESR) (data not shown). Pts initially randomized to bari 4-mg had significantly greater change from baseline, observed as early as Wk 1 and up to Wk 52, for HAQ-DI than pts treated with MTX (Figure 2). After switching to bari, the delayed-start group showed a rapid improvement in HAQ-DI with similar improvement at Wk 56 – 4 wks after switching to bari. Upon initiating bari, there was a reduction in the rate of structural damage; however, delaying initiation of bari for 1 year resulted in numerically higher mTSS.

Conclusion: In early MTX-naïve pts, improved clinical, functional, and radiographic efficacy with bari 4-mg vs MTX was observed in most outcome measures up to 52 wks. Switching from MTX to bari at Wk 52 provided a rapid clinical response, allowing a majority of pts to achieve similar results 4 wks post-switch. However, if the goal of therapy is to achieve rapid and sustained control of disease activity, the differences noted here for HAQ-DI and especially structural progression support earlier switch to bari for pts who do not obtain disease control with MTX. Further analysis may be needed to explore prognostic factors, such as hsCRP and disease duration (< or >6 months), baseline erosion, or anti-citrullinated protein antibody positivity, which may help clinicians identify pts who may benefit from earlier treatment with bari.

REFERENCES:


THU0076 THE IMPACT OF VARYING EXCLUSION CRITERIA ON TREATMENT RESPONSE: REAL-WORLD EVIDENCE TO GUIDE THE DESIGN OF FUTURE CLINICAL TRIALS

Thomas Friesel1, Scott Jelinsky2, Mark Peterson3, Johan Askling1 1Karolinska Institutet, Solna, Sweden; 2Pfizer Research Technology Center, Cambridge, United States of America

Background: Clinical trials of novel pharmaceuticals in Rheumatoid Arthritis routinely use strict inclusion/exclusion criteria aimed at selecting a defined homogeneous population and producing a non-confounded demonstration of the agent’s clinically relevant pharmacologic effect. However, the act of strictly defining numerous individual criteria has the potential...
for impacting the observed response rates, while the effect upon limiting the pool of eligible subjects is often poorly understood. Unnecessarily restrictive criteria may limit the generalizability of trial results to real world patient populations. Conversely, certain patient characteristics may be associated with high or low probabilities of response to active treatment or to placebo.

Objectives: To assess the impact of applying a range of different exclusion criteria on the proportion eligible subjects, and on the observed treatment response rates, in a large real-world patient population.

Methods: Data on RA characteristics, demographics, and co-morbidities among RA patients were identified by linking the Swedish Rheumatology register (SRQ) to the nationwide and virtually complete Swedish census and healthcare registries. Representing an early RA trial scenario, we identified patients starting methotrexate monotherapy as first ever DMARD (N=41) between 2007 and 2016. The cohort was assessed overall and stratified by baseline DAS28. Treatment outcome was defined as the proportions reaching (1) EULAR Good Response and (2) Low Disease Activity, and the change in (3) HAQ and (4) CDAI at 3 and 6 months. Exclusions were made based on age, baseline disease activity, sex, RF, predefined comorbidities, degree of healthcare utilization history, education, and taxed income level (cut-offs for continuous variables were based on distributions from recent clinical trials of tocilizumab). In total, 165 different definitions of exclusion criteria were evaluated.

Results: Within the entire cohort, 50% of patients achieved EULAR DAS28 good response at 3 months. Exclusions based on age, sex, RF status, or duration of RA symptoms before RA diagnosis generally lead to large reductions in number of eligible subjects but did not appreciably affect (< 5% change) the proportion of EULAR good responders. Exclusions based on HAQ had a noticeable drop in the proportion of EULAR good response (~10%, see Figure), although exclusions above 80% was necessary to observe an effect. Similar patterns were observed for TJC, patient’s global health and ESR but exclusions based on SJC or CRP did not impact EULAR response.

Exclusions of specific comorbidities, such as history of myocardial infarction, history of joint replacement, generally had no or modest impact on the observed response rate. Exclusions based on health care use (total number of drugs, hospitalizations), affected response rates (+/- around 5%), while exclusions based on educational level, work ability, or income did not.

The impact of exclusions was very similar on the 3 and 6 month responses.

Conclusion: Exclusions in a range of criteria commonly used in clinical trials had only a modest impact on observed treatment outcome, while impacting on the enrollment pool – sometimes dramatically. More extreme restrictions (excluding well above half the potentially eligible patients) were generally necessary to shift the proportion EULAR Good Response by more than 5 percentage points. This should not be a surprise given the lack of identified strong predictors of treatment outcome in RA, but may raise the question of whether the lowered generalizability and impacts on enrollment rates caused by strict inclusion criteria in clinical trials is warranted by the aspiration to increase chances of demonstrating clinically meaningful effects.

Abstract THU0076—Figure 1

Disclosure of Interests: Thomas Friisell: None declared, Scott Jelinsky Shareholder of: Pfizer, Employee of: Pfizer, Mark Peterson Shareholder of: Pfizer, Employee of: Pfizer, Johan Asklind Grant/research support from: Karolinska Institutet (JA) has or has had research agreements with the following pharmaceutical companies, mainly in the context of the ATRIS national safety monitoring programme for rheumatology biologicals: Abbvie, BMS, MSD, Eli Lilly, Pfizer, Roche, Samsung Bioepis, and UCB., Consultant for: Karolinska Institutet has received remuneration for JA participating in ad boards arranged by Lilly, Novartis, and Pfizer. DOI: 10.1136/annrheumdis-2019-eular.1022

THU0077 RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS CLINICAL TRIALS: HOW TO ENCOURAGE PATIENT PARTICIPATION? RESULTS FROM A REAL-WORLD STUDY CONDUCTED VIA CARENITY, A WORLDWIDE ONLINE PATIENT COMMUNITY

teni gauchoux, Anthony Boisbouvier, Roman Dos Santos, Lise Rasoszczyki.

CARENITY, Paris, France

Background: Involving patients affected with rheumatoid arthritis or ankylosing spondylitis in clinical trials may be highly challenging: in a worldwide context of competitive rheumatoid arthritis and ankylosing spondylitis clinical research, patient engagement is key to optimize medical research and increase participation rates.

Objectives: The aim of this study was to identify patients’ motivations for and hindrances to joining a clinical trial in order to increase participation rate by implementing tailored services and information.

Methods: An online questionnaire was submitted from August 2017 to October 2017 to Carenity’s French members affected with rheumatoid arthritis or ankylosing spondylitis.

Results: 136 patients affected with rheumatoid arthritis (n = 55, 40%, mean age = 55 y/o, 71% of women) or ankylosing spondylitis (n = 81, 60%, mean age = 48 y/o, 80% of women) participated in the study. 10 patients (7%) already participated in a clinical trial.

Non-participants (n=126) exposed the incentives that may increase participation rate: reimbursing the expenses related to the clinical trial can improve their motivation (median weight on motivation to join a trial = 10/10) as well as a better medical follow-up (9/10) or leveraging the trial’s investigator notoriety (8/10). Patients’ healthcare practitioners could be leveraged as well: their favorable opinion turns patients on to clinical trials (7/10). On the contrary, a doctor’s negative opinion may strongly deter patients from joining a trial (median weight on reluctance to join a trial = 8/10). Communication should aim at reassuring them about side effects (9/10), potential risks for their health (8/10) and more generally the risk that the new treatment would not be better than their current one (8/10). Logistic challenges should also be taken into account: the trip between patients’ home and the site of the clinical trial is perceived as an important burden (8/10).

Implementing tailored services and information would be an efficient way to reassure patients and increase their willingness to participate. 81% of non-participants would be enticed to participate if they had access to a website to exchange with healthcare professionals or to follow the results of the trial. 79% would be interested in participants’ testimonials and 74% in a 24-hour phone helpline. Spreading and clarifying information before the trial is also critical: 6/10 patients who participated in a clinical trial did not understand clearly if they will have out-of-pocket costs and 5/10 patients were also unclear on the terms and conditions for leaving the clinical trial. Informing patients via convenient channels is key: 88% of participants and non-participants think that an online patient community is a relevant medium to convey information about clinical trials and 81% of non-participants would like to have access to an information brochure about the trial process.

Conclusion: This real-world study allowed to identify concrete levers to reassure patients affected with rheumatoid arthritis or ankylosing spondylitis about the benefits/constraints balance and to clarify information at each stage of the trial (before, during, after), which is essential to accelerate clinical trial recruitment.


THU0078 SAFETY PROFILE OF BARICITINIB FOR THE TREATMENT OF RHEUMATOID ARTHRITIS UP TO 7 YEARS: AN UPDATED INTEGRATED SAFETY ANALYSIS

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Background: Baricitinib (bari), is an oral, selective inhibitor of Janus kinase (JAK) 1/JAK 2, to treat moderately to severely active RA in adults.

Objectives: To update bari’s safety profile with data from an additional Phase III trial and a real-world long-term extension (LTE) study.

Methods: Long-term safety of once-daily bari was evaluated in the All-Bari RA dataset: all patients (pts) exposed to any bari dose from 9

randomized trials (5 Ph3, 3 Ph2, 1 Ph1b) and 1 LTE (data to 13-Feb-2018). Placebo (PBO) comparisons were evaluated to Week 24 from 7 Ph2/3 trials; pts randomized to PBO, bari 2-mg or 4-mg, with censoring at rescue/treatment switch. Dose responses were evaluated in the 2-mg/4-mg extended dataset from 4 Ph2/3 trials; pts randomized to 2- or 4-mg LTE data included; data censored at rescue/dose change (as-treated analysis) and, due to latent period for malignancy, analyzed without censoring (as-randomized analysis). Incidence rates (IR) per 100 patient-years (PY) were calculated.

Results: 3770 pts received bari (10127 PYs); maximum exposure was 7 yrs (Table). No significant differences were seen for bari 4-mg vs PBO in adverse events leading to permanent drug discontinuation, death, malignancy, serious infection, or major adverse cardiovascular events. Herpes zoster IR was significantly higher for bari 4-mg vs PBO (3.0 vs 0.9) and numerically higher for bari 2-mg (2.1). IRs for deep vein thrombosis/pulmonary embolism were numerically higher in bari 4-mg vs PBO; IRs were similar by dose in 2-mg/4-mg-extended dataset. Malignancy (excluding non-melanoma skin cancer) IRs were 0.8 (2-mg) and 1.0 (4-mg: as-randomized analysis). Fewer than 1% of pts discontinued due to abnormal laboratory results.

Conclusion: In this updated integrated analysis of pts with active RA exposed to bari for up to 7 yrs, across safety topics, bari maintained a safety profile similar to that previously reported and acceptable in the context of demonstrated efficacy.

Abstract THU0078–Table 1. demographics

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Total patient years</th>
<th>2-mg</th>
<th>4-mg</th>
<th>2-mg/4-mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total patient years</td>
<td>3770</td>
<td>1884</td>
<td>1886</td>
<td>1885</td>
</tr>
<tr>
<td>Mean treatment days</td>
<td>360.9</td>
<td>361.0</td>
<td>361.0</td>
<td>361.0</td>
</tr>
<tr>
<td>Largest exposure, days</td>
<td>225</td>
<td>197</td>
<td>223</td>
<td>200</td>
</tr>
</tbody>
</table>

Table

REFERENCE:


Background: At the group level, the classification criteria for rheumatoid arthritis (RA) developed in 2010 identify patients earlier than the 1987 criteria. However, performance of the new criteria in subjects negative for rheumatoid factor (RF) and anti-citrullinated protein autoantibodies (ACPA) is not consistent with [1]. Therefore, patients’ classification may be missed despite severe joint and systemic inflammation.

Objectives: To evaluate disease characteristics and arthritis persistence in autoantibody-negative patients with early polyarthritis fulfilling only 5 of the 10 points of the 2010 classification criteria for RA.

Methods: We included early arthritis patients from our Early Arthritis Cohort with at least one clinically swollen joint, symptoms for less than 12 months, no other explanation of arthritis and naïve to glucocorticoids and disease modifying anti-rheumatic drugs (DMARDs) at presentation. At baseline, fulfillment of each specific domain of the 1987 and the 2010 criteria was recorded. RF and ACPA were centrally determined on baseline sera. RF and ACPA-negative patients achieving a total score of 5 in the 2010 criteria was compared to patients fulfilling RA criteria for baseline characteristics and for arthritis persistence (28-joints disease activity score [DAS28] >3.2) after 2 months of follow-up.

Results: Of the total population of 882 patients with new-onset inflammatory arthritis, comprehensive evaluation of the fulfilment of the 1987 and the 2010 criteria was available in 771 cases (87.4%). Of these, 476 patients fulfilled the 2010 criteria was available in 771 cases (87.4%). Of these, 476
Disclosure of Interests: Silvia Grignaschi: None declared, Serena Bugatti: None declared. Four speakers for symposium: Klareskog, Antovic, Catrina, Hensvold.

REFERENCES:

Abstract Table 1. Baseline characteristics of the study cohort

<table>
<thead>
<tr>
<th>SYMPTOMS</th>
<th>2010 ACR</th>
<th>2010 ACR/ EULAR</th>
<th>EULAR score</th>
<th>EULAR score</th>
</tr>
</thead>
<tbody>
<tr>
<td>duration, median (IQR), weeks</td>
<td>30.6 (10.7)</td>
<td>7.15 (9.26-23)</td>
<td>0.04</td>
<td>15.3 (8.5-9)</td>
</tr>
<tr>
<td>DAS28, mean (SD)</td>
<td>4.53 (0.83)</td>
<td>5.25 (10.88)</td>
<td>&lt;0.001</td>
<td>4.72 (1.15)</td>
</tr>
<tr>
<td>VAS pain, median (IQR)</td>
<td>51.5 (32.5)</td>
<td>62 (50-80)</td>
<td>0.01</td>
<td>50 (31-77.5)</td>
</tr>
<tr>
<td>HAQ, median (IQR)</td>
<td>1 (0.47)</td>
<td>1.25 (0.75-1.88)</td>
<td>0.003</td>
<td>1 (0.5-1.5)</td>
</tr>
</tbody>
</table>

Disclosure of Interests: Silvia Grignaschi: None declared, Serena Bugatti Speakers bureau: Bristol-Myers Squibb, Celgene, Lilly, Novartis, Sanofi, Janssen, Francesca Benaglio. None declared, Garafulli Sakellarious: None declared, Antonio Manzo: None declared, Roberto Caporalis Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Roche, Genzyme, Lilly, MSD, Pfizer, UCB, Carlmariozoni Montecucco Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Sanofi, Genzyme, Lilly, MSD, Pfizer, UCB. DOI:10.1136/annrheumdis-2019-early.7449

THU0080

DEVELOPMENT OF ULTRASOUND DETECTABLE ARTHRITIS AMONG ACPA POSITIVE SUBJECTS WITH MUSCULOSKELETAL SYMPTOMS: THE RISK RA PROSPECTIVE STUDY

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Background: Retractive studies have shown that anti-citrullinated protein antibodies (ACPA) are a risk factor for the development of clinical arthritis. Objectives: We aimed to investigate in a prospective setting if ACPA and other biomarkers could predict development of ultrasound detectable arthritis.

Methods: Subjects with positive ACPA-test referred from primary care to the Rheumatology clinic that lacked arthritis in hands, feet and any other symptomatic joints by clinical and ultrasound examination (according to EULAR-OMERACT definition), were recruited into the Risk-RA research program during 2015-2016 and were followed up to the end of 2017. At inclusion a detailed clinical examination was performed and blood samples were analyzed for 13 specific ACPA reactivities (using a custom made peptide microarray) as well as 92 inflammation-associated protein biomarkers (using a multiplex immunoassay with Olink proximity extension technology). Presence of HLA-SE was analyzed using DR low-resolution technology. Univariate and multivariate analysis were used to investigate the association between clinical and laboratory parameters and development of ultrasound detected arthritis adjusting for the follow-up time.

Results: 42% (27/65) of the Risk RA subjects developed ultrasound detectable arthritis during a median follow up of 8 months. The remaining 58% (38 out of 65) were followed for a median of 25 months (range 12-44) without any signs of ultrasound detectable arthritis. Subjects developing arthritis had higher prevalence of HLA-SE (89% vs 56%) and increased occurrence of ultrasound detected tenosynovitis (44% vs 5%), compared to those not developing arthritis. ACPA reactivities to citrullinated vimentin peptides (cit vim 2-17: 22% vs 6%; and cit vim 60-75: 70% vs 43%) and citrullinated histone peptides (cit H4 31-50: 99% vs 49%; and cit H3 21-44: 48% vs 23%) were a more common occurrence in subjects developing ultrasound detectable arthritis. Backward selection in a Cox regression model showed that ultrasound detectable arthritis could be predicted in a model including HLA-SE, tenosynovitis and ACPA reactivity to cit H4 31-50. Hazard ratio compared to the reference group (not developing arthritis) were 3.4 (95% CI 1.0-12, p 0.06) for HLA-SE carriers, 2.9 (95% CI 1.3-6.7, p 0.01) for tenosynovitis and 4.1 (95% CI 1.2-14, p 0.02) for Anti-citrullinated H4 31-50 positivity. Only modest differences were observed for few of the tested inflammatory markers in those developing as compared to those not developing ultrasound detectable arthritis.

Conclusion: This prospective study shows that ultrasound detected arthritis can be predicted in a model including HLA-SE, tenosynovitis and ACPA reactivity to cit H4 31-50.

THU0081

ELEVATED SERUM TREM-1 LEVELS ARE ASSOCIATED WITH DAS28 AND PERIODONTITIS IN RHEUMATOID ARTHRITIS

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Background: The Triggering Receptor Expressed on Myeloid cells 1 (TREM-1) along with its putative ligand peptidoglycan recognition protein 1 (PGLYRP1) are involved in the propagation of the inflammatory response to microbial exposure(1). Periodontal disease (PD) has been suggested as an environmental risk factor for rheumatoid arthritis (RA), yet further studies are required to dissect the mechanisms underlying the association between the two(2).

Objectives: The present study aimed to investigate whether serum levels of TREM-1 and PGLYRP1 in patients with RA correlate with the presence and severity of PD, as well as bacterial load in saliva.

Methods: Serum and saliva samples were collected from 65 individuals with RA (F/M: 48/17), under sDMARD treatment for more than 6 months and never used biologic treatment), with Behcet syndrome (BS, n= 45, F/M: 33,8%) compared to BS (20,9%) and HC (5,1%). Total bacterial load in saliva was assessed by quantitative real-time polymerase chain reaction and PGLYRP1 were measured by ELISA, while total oral bacteria in saliva and PGLYRP1 were measured by ELISA, while total oral bacteria in saliva and PGLYRP1 were measured by ELISA, while total oral bacteria in saliva and PGLYRP1 were measured by ELISA, while total oral bacteria in saliva and PGLYRP1 were measured by ELISA, while total oral bacteria in saliva and PGLYRP1 were measured by ELISA, while total oral bacteria in saliva and PGLYRP1 were measured by ELISA, while total oral bacteria in saliva and PGLYRP1 were measured by ELISA.

Results: Patients with RA presented with a smaller number of teeth than the BS and HC groups (18.6±7.8, 4.22±3.7; 25.3±6.3, 3.83, respectively) (p<0.001). Prevalence of severe periodontitis was higher in the RA group (33.8%) compared to BS (20.9%) and HC (5,1%). Total bacterial load was significantly higher in saliva of RA than HC (p<0.05). Serum TREM-1 and PGLYRP1 levels were significantly higher in RA (167,1±50,0 pg/ml; 157,5±228,8 pg/ml) than BS (102,6±44,4 pg/ml; 52,4±26,1 pg/ml) and HC (52,4±26,1 pg/ml).
EFFECT OF TREAT-TO-TARGET STRATEGY ON ROLE OF CLINICAL IMPACT, DISEASE-SPECIFIC KNOWLEDGE AND BELIEFS ABOUT MEDICATION ON TREATMENT OUTCOMES IN RHEUMATOID ARTHRITIS: AN INTEGRATIVE STRUCTURAL EQUATION MODELING APPROACH

Georgie Karouzas1, Elizabeth Hernandez2, Yibeeke Strand3, Sarah Ormsett4.
1Harbor-UCLA Medical Center, Rheumatology, Torrance, United States of America; 2Harbor-UCLA Medical Center, Rheumatology, Torrance, United States of America; 3Stanford, Immunology/Rheumatology, Palo Alto, United States of America

Background: Treatment of rheumatoid arthritis (RA) to remission is the optimal way to ensure control of symptoms, prevention of structural damage, optimization of function and quality of life. Adherence to medical treatment is, therefore, an integral part of a comprehensive and successful management of RA.

Objectives: We interrogated the influence of three distinct domains of RA clinical impact (disease activity, functional limitations, mood disturbance), patient knowledge and beliefs about medications on RA treatment adherence.

Methods: We evaluated 285 patients with established RA from a single center. In the proposed model, RA-specific knowledge was not significantly associated with mediational multi-group structural equation modeling evaluated the model separately in patients treated with bDMARDs and those only receiving csDMARDs.

Results: RA-specific knowledge was not significantly associated with medication beliefs or adherence and therefore was dropped from the model. Modification indices suggested addition of two supplementary paths (dashed lines) that significantly improved the proposed model fit for both

REFERENCES:

Disclosure of Interests: None declared

Abstract THU0082 – Figure 2

THU0082 EFFECT OF TREAT-TO-TARGET STRATEGY ON DISEASE ACTIVITY AND RADIOLOGIC OUTCOMES IN RHEUMATOID ARTHRITIS: RESULTS FROM A 9-YEAR CHINESE COHORT

Lanlan Ji1, Wenhui Xie1, LI Guangtao1, Zhuoli Zhang1.
1Peking University First Hospital, Beijing, China

Background: Treat-to-target (T2T) strategy has been implied in clinical practice for 9 years. However, a recent study showed that the radiologic outcome didn’t associate with the adherence to protocolized treatment in clinical practice[1]. Furthermore, in clinical practice, nonadherence to a T2T protocol has been reported[2]. The reasons varied. In our previous study, there was a substantially decrease of RA activity over 8 years after tight control applied[3]. However, whether T2T strategy can improve the radiological outcome is still unknown.

Objectives: the arm of our study was to determine the effect of treat to target (T2T) protocol on disease activity and radiographic outcomes in a 9-year Chinese RA cohort.

Methods: RA patients who were followed-up for more than 1 year in a 9-year Chinese RA cohort.

Results: There were 209 patients enrolled in our study. The median interval of two radiographs was 31.0 (17.0, 50.0) months. 45.0% of the patients followed the time schedule to clinic. Adherence rate of the patients was evaluated by the calculation of the percentage of whether the patients followed the time schedule to clinic. Adherence rate >0.7 was defined as adherent to T2T. The overall disease activity was evaluated by time adjusted mean (TAM) method. The radiological change was evaluated by radiographs of the hands regularly, and the interval between 1 and 3 years. We defined the primary radiological outcome as modified total Sharp score (mTSS) >3 over the follow-up time.

Conclusion: The mTSS progression was associated with baseline HDA and bone erosion existing also independently associated with erosion progression [HR=1.90 (1.12, 3.23), p=0.018]. When divided the adherence rate into three subgroups, we can find that patient not following the T2T protocol were more easily to get radiological progression. There was statistically significant difference among three groups (p=0.004 using log rank, and p=0.001 using Tarone ware). To our surprise, increased adherence rate didn’t provide more benefit when adherence rate was more than 0.9 (Figure 2). In patients who got overall clinical remission, we found none of these variables correlated with the radiological outcome.

REFERENCES:
Abstract THU0086 – Figure 1

The Long-term Outcome of Intra-articular Glucocorticoid Injected Joints on Radiographic Changes in Patients with Rheumatoid Arthritis: A Real World Data from a Single Center

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Background: Intra-articular glucocorticoids injections (IAGI) have been an important part of a treat-to-target strategy in patients with Rheumatoid arthritis (RA). However, it is not known the long-term outcome of glucocorticoids-injected joint.

Objectives: To explore the long-term outcome of IAGI, the impact on the radiographic joint space narrowing and erosion in patients with RA.

Methods: We performed a retrospective cohort study of IAGI for patients with RA. We identified 88 RA patients who received IAGI into wrists or hand joints determined by ultrasound and had pre-injection and follow-up hand radiographs from a rheumatology department in a tertiary hospital. As a comparator, 88 RA patients who had not received IAGI although they had clinical synovitis (defined as both tender and swollen joint) in wrist or hand joint were randomly selected (Non-IAGI group). Hands radiographs scored using the van der Heijde-modified Sharp Score (HSS) method was used to assess radiographic progression ($\Delta$HSS $\geq$ 1 in joint areas of synovitis). Multivariable Cox regression estimated the hazard ratio (HR) and 95% confidence interval (95% CI) for radiographic progression of joint with synovitis.

Results: Among 88 RA patients who received IAGI (median age, 60 years, 42 (48%) patients had radiographic progression of triamcinolone-injected joint, while 38 patients (43%) in non-IAGI group (median age, 57 years) presented radiographic progression of joint area suffered clinical synovitis (not significant) in the median 2 years follow-up. At baseline, IAGI group presented longer disease duration, lower acute phase reactant levels and less involvement of proximal interphalangeal joints than non-IAGI group. In the IAGI group, a median number of 1 (IQR, 1–2) joint was injected. After 3 months from IAGI, 63.5% of patients reported improvement of injected joint and 16.5% of patients received a second or more IAGI. The radiographic progression of injected joint (Figure 1) was pronounced at the wrists (87.8% of radiographic progressor). The level of C-reactive protein at active arthritis, baseline HSS and power Doppler grade in ultrasound was higher in radiographic progressor than in non-radiographic progressor. A high baseline HSS of hands (HR, 1.021 [95% CI, 1.002–1.040]), wrist joint involvement (HR, 5.365 [95% CI, 1.705–16.813]) and use of NSAIDs (HR, 0.373 [95% CI, 0.179–0.776]) were associated with radiographic progression in joint areas which suffered active synovitis.

Disclosure of Interests: George Karpouzas Grant/research support from: Pfizer, Consultant for: Sanofi-Genzyme-Regeneron, Janssen, Roche-Genentech, Pfizer, Speakers bureau: BMS, Sanofi-Genzyme-Regeneron, Janssen, Roche-Genentech, Elizabeth Hernandez: None declared, Vibeke Strand, Consultant for: AbbVie, Amgen, Bayer, BMS, Boehringer Ingelheim, Celgene, Celltrion, CORRONA, Crescendo, EMD Serono, Genentech/Roche, GSK, Horizon, Inmedix, Janssen, Kezar, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sandoz, Sanofi, Servier, UCB., Sarah Ormseth: None declared

THU0085 RHEUMATOID ARTHRITIS AND ALLERGIC DISEASES

Vanessa Kronzer1, Cynthia S. Crowson2, Jeffrey Sparks3, Robert Vassallo4, John Davis5, 1Mayo Clinic, Rochester, United States of America; 2Brigham and Women’s, Boston, United States of America

Background: Historically, RA was considered a TH1 disease while asthma and allergy were considered TH2 diseases (1). However, several studies have shown an association between RA and asthma (2), and more recently, allergic disease (3).

Objectives: We first aimed to determine the association between RA and asthma after controlling for important confounders including allergic disease, urban environment, and passive smoke exposure. Second, we aimed to determine the association between RA and various allergy types.

Methods: This case-control study identified 1,023 cases of RA (175 incident) within a single-center biobank population using a rules-based algorithm that combined self-report with two diagnosis codes. Exposures were defined) within a single-center biobank population using a rules-based algorithm that combined self-report with two diagnosis codes. Exposures were defined as part of a treat-to-target strategy in early rheumatoid arthritis: impact of joint area, repeated injections, MRI findings, anti-CCP, IgM-RF and CRP. Annals of the rheumatic diseases 2012, 71(6):851-856.

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Disclosure of Interests: None declared


THU0086 PREDICTING TNFALPHA INHIBITOR TREATMENT RESPONSE USING SERUM CYTOKINES IN PATIENTS WITH RHEUMATOID ARTHRITIS

Marissa Lassere1, Sue Baker2, Jenny Gu3, 1UNSW Sydney, St George Hospital SESLHD, Sydney, Australia; 2UNSW Sydney, Sydney, Australia

Background: Tumour necrosis factor-alpha inhibitors (TNFαi) are the main biologics (b-MARDs) used to treat active rheumatoid arthritis (RA) in patients that have failed disease modifying treatment (DMARD). However, 10% of patients do not respond to therapy, TNFα inhibitors in all. Patients are continued on this treatment for several months risking side-effects in the hope that the therapy will work. Another 40% of patients respond partially to this treatment and have to also be treated with other drugs such as methotrexate and prednisone in addition to treatment with TNFαi. Biomarkers offer an opportunity to identify before starting or soon after starting treatment with TNFαi which patients will be responders and whether prednisone and other drugs can be reduced and optimise the risk-benefit of treatment.

Objectives: We undertook a series of experiments with the following objectives: determine whether cytokine biomarkers will predict which patients with rheumatoid arthritis will respond to DMARD early treat-ment responders (b) sustained TNFαi early treatment responders, (c) TNFαi early treatment failures.

Methods: We used the Millipore’s MILLIPLEX MAP Human Th17 Magnetic Bead kit for the simultaneous quantification of the following cytokines: IL-1β, IL-2, IL-4, IL-5, IL-6, IL-9, IL-10, IL-12p70, IL-13, IL-15, IL-17A, IL-17E, IL-25, IL-27, IL-28α, IL-28β, IL-29, IL-33, GMCSF, IFNγ, MIP-3α, TNFα and TNFβ. We evaluated 14 patients with RA starting on a DMARD and 26 patients with RA starting on a TNFαi after failing DMARDs. These cytokines were assayed monthly 2 or 3 months prior to starting a TNFαi to evaluate month-to-month cytokine variability and every month up to 5 months after initiation of treatment. RA disease activity was measured using the RA Disease Activity Score (DASCRP28) which includes joint counts, CRP and a patient-reported outcome of health status. All samples were blocked with Heteroblock to reduce rheumatoid factor and other hetero-philic antibodies. Rheumatoid factor was measured before and after blocking. The same negative and positive controls were included across all plate runs. All assays were done in singlet to accommodate longitudinal samples. Mixing studies were undertaken to evaluate whether cytokine results could be analysed using quantitative statistics.

Results: We had 67 serum samples in the DMARD treated group and 202 serum samples in the TNFαi treated group because of the longitudinal study design. Using mixed effects linear regression to account for longitudinal data in a model that included all 25 cytokines, treatment-time and treatment type (DMARD or TNFαi/D-MARD), we found that in patients on DMARDs, IL-6, IL-1β, IL-28α, and TNFβ were associated with treatment response. However, in TNFαi treated patients, TNFα, GM-CSF and IL-6 were associated with treatment response. Only p values <0.005 are reported given that 25 cytokines were included in the model.

Conclusion: In this study of treatment response comparing DMARDs and TNFαi in a longitudinal cohort of 26 patients with a total of 202 samples measuring TNFαi and GM-CSF may predict early TNFαi responders.

Disclosure of Interests: Marissa Lassere Grant/research support from: I have received research support with educational grant funding from Sanofi-Aventis. Pfizer, MSD, Abbvie, Sue Baker: None declared, Jenny Gu: None declared


THU0087 UTILITY OF INFRARED THERMOGRAPHY FOR THE EVALUATION OF RHEUMATOID ARTHRITIS

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Background: Rheumatoid Arthritis (RA) is a chronic inflammatory disease, which predominantly affects the hands. Currently in clinical practice, we explore the number of swollen and painful joints in order to evaluate the activity of the disease. Infrared thermography (IT) is a non-invasive, lacking ionizing radiation, operator-independent and low-cost technique that allows to measure the temperature of the cutaneous surface through the taking of a photograph.

Objectives: To determine the utility of IT in the evaluation of hands in patients with RA.

Disclosure of Interests: None declared.

Methods: A cross-sectional study was performed, including patients with RA according to 2010 ACR/EULAR criteria attended in our Hospital between February and March 2018. Demographic, clinical and analytical characteristics of patients were registered. Number of painful and swollen joints were assessed for each patient, including wrist, metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints. Subsequently, a standardised photograph of the dorsal aspect of both hands was taken with a thermal camera (FLIR T250 model) (Figure 1). With this technique mean temperature (MeanT) and maximum temperature (MaxT) were assessed at each joint. Also, differential temperature (DiffT) was assessed (mean temperature at joint - temperature at forearm skin).

Results: We included a total of 42 patients. 76% were women, mean age at diagnosis was 56.7 years old. 29 patients were positive for rheumatoid factor and 31 for anti-citrullinated peptide antibody. At the time of the assessment, median CRP was 9.19 mg/L and ESR was 14.77 mm/h. MeanT for the 65 swollen joints was 1.5°C higher than the 847 non-swollen joints (p<0.000). Independent analysis for each joint level (wrist, MCP and PIP) revealed higher temperature in swollen joints (Table 1). Similar results were obtained for painful joints. ROC curves and areas under the curve (AUC) were calculated for wrist, MCP and PIP joints, obtaining the most favorable results for DiffT in wrist and MCP joints, and for MaxT in PIP joints, allowing to calculate a cut-off point at each joint level (Table 2).

Figure 1. Selective temperature increase over third PIP of the left hand.

Table 1. Correlation between swollen joints and MeanT, MaxT and DiffT.

<table>
<thead>
<tr>
<th>Swollen joints</th>
<th>MeanT</th>
<th>P value</th>
<th>MaxT</th>
<th>P value</th>
<th>DiffT</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOTAL NO 847</td>
<td>31.68°C</td>
<td>0.000</td>
<td>32.26°C</td>
<td>0.000</td>
<td>1.58°C</td>
<td>0.000</td>
</tr>
<tr>
<td>YES 65</td>
<td>33.18°C</td>
<td>0.000</td>
<td>33.71°C</td>
<td>0.000</td>
<td>0.53°C</td>
<td>0.000</td>
</tr>
<tr>
<td>Wrist NO 68</td>
<td>32.62°C</td>
<td>0.005</td>
<td>33.21°C</td>
<td>0.004</td>
<td>0.61°C</td>
<td>0.000</td>
</tr>
<tr>
<td>YES 14</td>
<td>33.79°C</td>
<td>0.000</td>
<td>34.40°C</td>
<td>0.005</td>
<td>0.61°C</td>
<td>0.003</td>
</tr>
<tr>
<td>MCP NO 391</td>
<td>32.02°C</td>
<td>0.044</td>
<td>32.72°C</td>
<td>0.066</td>
<td>0.95°C</td>
<td>0.006</td>
</tr>
<tr>
<td>YES 23</td>
<td>33.02°C</td>
<td>0.000</td>
<td>33.61°C</td>
<td>0.15°C</td>
<td>0.60°C</td>
<td>0.013</td>
</tr>
<tr>
<td>PIP NO 388</td>
<td>31.18°C</td>
<td>0.000</td>
<td>31.64°C</td>
<td>0.000</td>
<td>1.74°C</td>
<td>0.000</td>
</tr>
<tr>
<td>YES 28</td>
<td>33.01°C</td>
<td>0.000</td>
<td>33.47°C</td>
<td>0.004</td>
<td>0.81°C</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Table 2. AUC, Sensibility and Specificity.

<table>
<thead>
<tr>
<th>AUC</th>
<th>Cut-off value</th>
<th>Sensibility</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>WRIST</td>
<td>0.878 (DiffT)</td>
<td>-0.016°C</td>
<td>0.929</td>
</tr>
<tr>
<td>MCP</td>
<td>0.640 (DiffT)</td>
<td>0.00°C</td>
<td>0.609</td>
</tr>
<tr>
<td>PIP</td>
<td>0.713 (MaxT)</td>
<td>10.0°C</td>
<td>0.679</td>
</tr>
</tbody>
</table>

Conclusion: In patients with RA, there is a statistically significant relationship between joint temperature measured by thermal imaging and the presence of swollen and painful joints in the assessment by the rheumatologist. The ROC curves indicate an acceptable sensitivity and specificity and allow to determine cut-off temperatures for clinical use. Infrared thermography could be a useful tool in the assessment and monitoring of arthritis in RA patients.

REFERENCES:

Disclosure of Interests: None declared


THU0088 BASELINE ADIPONECTIN LEVELS PREDICT FUTURE DEVELOPMENT OF RHEUMATOID ARTHRITIS IN SUBJECTS WITH OBESITY

Cristina Maglio1, Yuan Zhang1, Christian Herder2, Anna Rudin1, LenaCarlsson3.
1University of Gothenburg, Department of Rheumatology and Inflammation research, Gothenburg, Sweden; 2German Diabetes Center, Düsseldorf, Germany; 3University of Gothenburg, Department of Molecular and Clinical Medicine, Gothenburg, Sweden

Background: Adiponectin is a cytokine produced by the adipose tissue and is involved in both metabolic and inflammatory processes1. In obese subjects, serum adiponectin levels are surprisingly low2. On the contrary, adiponectin levels are increased in serum and synovial fluid of subjects with established rheumatoid arthritis (RA)1,3.

Objectives: By exploiting a longitudinal study enrolling more than 4000 obese subjects, we aim to determine if serum adiponectin levels are a risk factor for the development of RA in obese subjects.

Methods: The Swedish Obese Subjects (SOS) study is a longitudinal controlled trial on the effect of bariatric surgery on the incidence of obesity-related diseases. It includes 4047 obese subjects whereof 2010 underwent bariatric surgery and 2037 constituted the matched control group4,5. SOS study participants who developed RA were identified by searching the Swedish National Patient Register. Eleven subjects with prevalent RA at baseline are excluded by the analyses. Patients were followed up until diagnosis of RA, death, migration or end of follow-up (December 2016). Total adiponectin was measured using the Quantikine ELISA kit from Bio-Techne (Minneapolis, MN, USA).

Results: Adiponectin measurement at baseline was available for 3691 subjects. Among those subjects, 82 subjects developed RA during a follow-up for up to 29 years. High serum adiponectin levels at baseline were associated with the incidence of RA, independently of bariatric surgery, sex, age, body-mass index, smoking, and C-reactive protein and erythrocyte sedimentation rate levels (adjusted Hazard Ratio HR per 10 µg/mL adiponectin 1.70, 95% confidence interval CI 1.12-2.60, P value=0.01). When stratifying the population according to the median of erythrocyte sedimentation rate, serum adiponectin levels were associated with the incidence of RA, independently of bariatric surgery, sex, age, body-mass index, smoking, and C-reactive protein and erythrocyte sedimentation rate levels (adjusted HR per 10 µg/mL adiponectin 1.70, 95% CI 1.12-2.60, P value=0.01). When stratifying the population according to the median of baseline adiponectin, subjects with adiponectin greater than 6.8 µg/mL had a higher risk to develop RA during follow up (log-rank P 0.028, unadjusted HR 1.64, 95% CI 1.05-2.56, P=0.03, Figure 1).

Conclusion: In a large cohort of obese subjects followed up for up to 29 years, serum adiponectin levels were associated with the incidence of RA years before the onset of clinical signs. The association between adiponectin and the incidence of RA was independent of other risk factors, including C-reactive protein, smoking and bariatric surgery.

REFERENCES:
ASSOCIATION OF ANTI-PAD4 ANTIBODIES WITH MORTALITY OVER UP TO 14 YEARS FOLLOW-UP IN RA

Laura Martinez-Prat1,2, Victor Martinez-Taboada3, Marcos Lopez-Hoyos4, Michael Mahler5, Inova Diagnostics, Inc., Research and Development, San Diego, United States of America; 1Francisco de Vitoria University – Madrid, Health Sciences, Pozuelo de Alarcón, Spain; 2Hospital Universitario Marqués de Valdecilla – IDIVAL, Rheumatology, Santander, Spain; 3Hospital Universitario Marqués de Valdecilla – IDIVAL, Immunology, Santander, Spain

Background: Novel biomarkers have been described in rheumatoid arthritis (RA) patients, including antibodies to carbamylated proteins (anti-CarP) and to protein-arginine deiminases (PAD). Anti-PAD4 antibodies are associated with anti-citrullinated protein antibodies (ACPA) and worse baseline radiographic joint damage [1]. A subset of anti-PAD4 antibodies that cross-react with PAD3 and are associated with erosive disease, ACPA and progression despite treatment has also been described [1].

Objectives: To evaluate several novel RA markers in a cohort of RA and controls and their association with erosive disease and biological treatment use in RA.

Methods: Sera from 116 RA patients [63 young onset RA (YORA) and 53 elderly onset RA (EORA)] and 155 controls [134 polymyalgia rheumatica (PMR) patients and 21 healthy individuals (HI) older than 60 years old] were included. Information on erosion status and biological treatment was available for 56 of the RA patients. The samples were tested for anti-PAD3 and anti-PAD4 IgG using the novel particle-based multi-analyte technology (PMAT, research use only, RUO), as well as for ACPA (CCP3 IgG ELISA and chemiluminescent immunoassay (CIA)) and anti-CarP IgG (ELISA, RUO).

Results: Significantly higher levels of anti-PAD3, anti-PAD4 and ACPA were observed in YORA vs. EORA (p<0.0001 for anti-PAD3 and ACPA ELISA and CIA, p=0.0016 for anti-PAD4). In the RA patients with erosion and treatment information available, anti-PAD4 antibody levels, but not ACPA, anti-CarP or anti-PAD3, were significantly higher in patients on biologic treatment vs. patients that were not on biologics (p=0.0017). Anti-PAD4 positive patients, were 10.1 [95% CI 2.5-52.0, p=0.0002] times more likely to be on biologic treatment vs. patients that were not on biologics.

Conclusion: Anti-PAD3, anti-PAD4 and ACPA are associated with disease onset at an early age. Anti-PAD4 are associated with erosive disease and biological treatment use in RA and represent a useful marker for better patient stratification.

REFERENCE:

MORTALITY OVER UP TO 14 YEARS FOLLOW-UP IN MTX-REFRACTORY PATIENTS RANDOMIZED TO A STRATEGY STARTING WITH ADDITION OF INFliximab OR ADDITION OF SULFASALAZINE AND HYDROXYCHLOROQUINE

Heather Miller1, Johan K Walliman2, Ingemar Petersson3, Saedis Saevardsdottir4, Jonas Söderling3, Sofia Ernemast5, Johan Askling1, Ronald van Vollenhoven6, Martin Neovius1, Karolinska Institutet, Department of Medicine, Solna, Stockholm, Sweden; 2Lund University, Department of Rheumatology, Clinical Sciences Lund, Lund, Sweden; 3Lund University, Department of Orthopaedics, Clinical Sciences, Lund, Sweden; 4Karolinska Institutet, Stockholm, Institute of Environmental Medicine, Stockholm, Sweden; 5Academic Specialist Center, Stockholm Health Services, Stockholm, Sweden; 6University of Amsterdam, Amsterdam Rheumatology and immunology Center, Amsterdam, Netherlands

Background: Longevity is the ultimate health outcome measure, incorporating treatment effectiveness as well as treatment safety. Randomized controlled trials (RCT) in rheumatoid arthritis (RA) have received lecture fees from AstraZeneca, MSD and Johnson&Johnson.

Disclosure of Interests: Laura Martinez-Prat Employee of: Inova Diagnostics (Not pharmaceutical, diagnostics company), Victor Martinez-Taboada: None declared, Marcos Lopez-Hoyos Consultant for: Inova Diagnostics (Not pharmaceutical, diagnostics company), Michael Mahler Employee of: Inova Diagnostics (Not pharmaceutical, diagnostics company)

Abstract THU0090 – Figure 1. Association of anti-PAD4 antibodies with joint erosion status (A) and to biological treatment use (B). Results are in Median Fluorescence Intensity (MFI). P-values of the Mann-Whitney analysis are shown in red. Dashed line indicates the preliminary cut-off of the assay. Number of positives and % within each subgroup are shown.
controlled trials tend to report data only on short term effects, while extended follow-up of long-term mortality data of treatment strategies are scarce.

Objectives: To compare mortality risk over up to 14 years of follow-up in MTX-refractory patients with early RA, randomized to a strategy starting with addition of infliximab versus addition of sulfasalazine and hydroxychloroquine.

Methods: We used data from a 2-arm, parallel, randomized, active-controlled, open-label trial (Swefot), in which patients with early RA (symptom duration <1y) were recruited from 15 rheumatology clinics in Sweden from 2002-2006. Patients who did not achieve low disease activity after 3-4 months of MTX were randomized to receive additional biological treatment with infliximab (n=128) or conventional combination treatment with sulfasalazine and hydroxychloroquine (n=130). By linking the trial database to the Swedish Total Population Register and Cause of Death Register, we collected complete data on all-cause mortality and emigration until August 31, 2017. Participants were followed until death, emigration, or end of follow-up, whichever came first. Analyses were by intention to treat.

Results: Over a total 1477 and 1504 person-years of follow-up in the infliximab and the conventional combination treatment group there were 13 and 16 deaths, respectively (8.8 [95%CI 0.0-25.1] versus 10.6 [95%CI 0.0-28.4] deaths per 1000 person-years; mortality hazard ratio 1.2 [0.6-2.5]; P=0.62; Figure). After 5 years, approximately 50% of patients in the infliximab arm remained on biologic therapy and 50% in the conventional combination arm remained on synthetic DMARDs.

Conclusion: No increased or decreased mortality risk could be observed over up to 14 years of follow-up in patients with MTX-refractory early RA, randomized to a strategy starting with addition of either infliximab or conventional combination DMARD treatment. At the end of the extended follow-up, a minority of patients remained on their assigned therapy, reflecting the treat to target paradigm.

Disclosure of Interests: Heather Miller: None declared, Johan K Wallman Consultant for: Consultant for AbbVie, Celgene, Eli Lilly, Novartis, and UCB Pharma., Ingemar Petersson: None declared, Saedis Saevarsdottir Consultant for: Consultant for AbbVie, Celgene, Eli Lilly, Novartis, and UCB Pharma., Rosa Morla1, Mariam Riai2, Theodore Pincus2, Isabel Castrejon2. 1Fundació Clinic, Barcelona, Spain; 2Rush University Medical Center, Chicago, United States of America

Background: Depression in patients with rheumatoid arthritis (RA) may be pre-existent, amplified, or newly-developed after onset of RA. Together with other comorbidities, socioeconomic, or affective factors can influence perception of pain, functional disability, and health status. The prevalence of depression in RA patients is 19% and affect remission rates according to a classical composite index.

Objectives: We compared patient self-reported scores included on the Multidimensional Health-Assessment Questionnaire (MDHAQ) and levels of remission according to RAPID3 in patients who self-reported depression versus no depression.

Methods: All patients complete a MDHAQ at each visit, which includes physical function (FN), three 0-10 visual analogue scales (VAS) for pain (PN), patient global estimate (PATGL), fatigue (FT), RADAI self-report joint count, a review of 60 symptoms (ROS) on a checklist, three evaluations for depression, anxiety and sleep quality (0-3.3), and demographics. RAPID3 (0-30) is the sum of FN, PN, and PATGL; being remission RAPID3 <3. Patients with RA (ICD10) were classified according to self-reported depression on the ROS. Agreement between MDHAQ-depression and by the Patient Health Questionnaire (PHQ-9) was evaluated in 57 patients. Demographic and clinical characteristics were compared by self-reported depression status using Student t-test and chi-square test.

Results: 464 RA patients were studied: 118 (25%) self-reported depression. In 57 patients, who also completed the PDQ-9, agreement with MDHAQ depression was 93% (kappa=0.80 95% CI 0.61-0.99). Only 37 (31%) of all patients reporting depression had evidence in the medical record of treatment and/or specialist evaluation for depression. No differences between depression groups were seen for mean age or sex. Patients reporting depression had lower education level (12.5 vs 14.3, p<0.001) and poorer scores for physical function, pain, and patient global leading to higher RAPID3 and lower percentage of patient in remission (12.4 vs 4%, p<0.001) (Table). Depressed patients also reported higher scores for fatigue, number of painful joints, number of symptoms, and more difficulty with sleep, and anxiety.

Table: MDHAQ patient self-report scores in patients with RA according to depression status. Data are presented as mean (SD) and percentages. p<0.001

<table>
<thead>
<tr>
<th>No self-reported depression</th>
<th>Self-reported depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>N= 346 (75%)</td>
<td>N= 118 (25%)</td>
</tr>
<tr>
<td>Demographic variables</td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>55.4 (14.9)</td>
</tr>
<tr>
<td>Female,%</td>
<td>84%</td>
</tr>
<tr>
<td>Education level, years</td>
<td>14.3 (3.1)</td>
</tr>
</tbody>
</table>

MDHAQ/RAPID3: Patient self-report scores

| Physical function (0-10)  | 2.4 (2.0)             | 3.4 (1.9)*             |
| Pain (0-10)               | 5.3 (3.0)             | 6.8 (2.6)*             |
| Patient global estimate (0-10) | 4.9 (3.0)            | 6.6 (2.7)*             |
| RAPID3 (0-30)             | 12.6 (7.2)            | 16.6 (6.4)*            |
| % patients in RAPID3 remission | 12.4%               | 4%*                    |
| Fatigue (0-10)            | 4.2 (3.2)             | 6.3 (3.0)*             |
| Self-reported joint pain-RADAI (0-48) | 12 (10)             | 18 (12)*               |
| Review of Symptoms (0-60) | 8 (7)                 | 18 (9)*                |
| Sleep problems (0-3.3)    | 1.1 (0.9)             | 1.9 (0.9)*             |
| Dealing with depression/feeling blue (0-3.3) | 1.1 (0.9)            | 1.9 (0.9)*             |
| Dealing with anxiety/being nervous (0-3.3) | 0.1 (0.4)            | 0.7 (0.4)*             |

Conclusion: The prevalence of self-reported depression in our RA patients was 25%, with only 31% treated for this condition. RA patients with self-reported depression exhibit higher scores for all MDHAQ scores, and a lower rate of RAPID3 remission. MDHAQ may be useful to identify patients with depression in busy clinical settings.

REFERENCE:

Disclosure of Interests: None declared

**THU0093**

**BASAL METABOLIC RATE AND CHARLSON COMORBIDITY INDEX ARE INDEPENDENT PREDICTORS OF METABOLIC SYNDROME IN PATIENTS WITH RHEUMATOID ARTHRITIS**

Dong-Jin Park, Haimuzi Xu, Sung-Eun Choi, Ji-Hyou Kang, Shin-Seok Lee.

Cheonnam National University Hospital, Gwangju, Korea. Rep. of (South Korea)

**Background:** Metabolic syndrome (MetS) is associated with 2-fold increase in cardiovascular disease (CVD) and 1.5-fold increase in all-cause mortality in the general population. The overall pooled prevalence of MetS in the meta-analysis of rheumatoid arthritis (RA) patients is 30.65%. Along with high prevalence of MetS in RA, several studies showed the contribution of MetS to the increased risk of CVD or cardiovascular mortality in RA patients. Although controversial, the inflammatory activity of RA was significantly associated with MetS in several cross-sectional studies. However, no prospective studies have confirmed an increased risk of MetS development during the course of RA.

**Objectives:** This 2-year prospective study investigated the predictors of metabolic syndrome (MetS) in patients with rheumatoid arthritis (RA).

**Methods:** We recruited 319 consecutive RA patients who did not have MetS at baseline. MetS was defined according to the modified NCEP/ATP III 2005 for Asian populations. Predictors of MetS were assessed using univariate and multivariate logistic regression analyses.

**Results:** Of the 247 RA patients who finished 2-year follow-up, 37 (15.0%) developed MetS. At baseline, the patients who developed MetS were older and had higher BMI (P = 0.002), higher waist circumference (P = 0.011), higher waist-hip ratio (P = 0.035), greater skeletal muscle mass (P = 0.005), higher body fat mass (P = 0.011), higher percent body fat (P = 0.004), lower basal metabolic rate (P = 0.004) and higher Charlson comorbidity index score (P < 0.001). The percent of diabetes (P = 0.007) and hypertension (P < 0.001) were higher in patients with MetS than without MetS. And they also had elevated glucose (P = 0.004), triglyceride levels (P < 0.001), and a lower low-density lipoprotein cholesterol (LDL-C) (P < 0.001). The patients who were more likely to take less hydroxychloroquine (P = 0.044), more oral hypoglycemic agents (P < 0.001) and had a lower EQ-5D score (P = 0.025). In the multivariate analysis, when variables that belong to the composition of MetS were excluded, basal metabolic rate (OR = 0.205, 95% CI: 0.078–0.541, P = 0.001) and Charlson comorbidity index score (OR = 2.191, 95% CI: 1.280–3.751, P = 0.004) remained significant predictors of MetS.

**Conclusion:** The development of MetS in RA patients was associated with basal metabolic rate and Charlson comorbidity index at baseline. Physicians should pay more attention to RA patients who have these risk factors to avoid CVD and cardiovascular mortality.

**Disclosure of Interests:** None declared DOI: 10.1136/annrheumdis-2019-eular.3419

**THU0092**

**DEFINING A LEARNING CURVE FOR CLINICIANS PERFORMING ULTRASOUND-GUIDED NEEDLE SYNOVIAL BIOPSIES: A RETROSPECTIVE ANALYSIS OF THE EXPERIENCE AT THE EXPERIMENTAL MEDICINE AND RHEUMATOLOGY, QUEEN MARY UNIVERSITY OF LONDON**

Alessandra Nerviani1, Frances Humby2, Gloria Lisso Ribera1, Felice Rivelles1, Stephen Kelly2, Rebecca Hands, Costantino Pitzalis1. William Harvey Research Institute, Queen Mary University of London, United Kingdom; Centre for Experimental Medicine and Rheumatology, London, United Kingdom; 2Barts Health NHS Trust, Rheumatology, London, United Kingdom

**Background:** Despite the significantly better outcome reached by patients with Rheumatoid Arthritis following the introduction of the biologics, the absence of predictors of individual response to the available agents constitutes a huge unmet clinical need. The histological analysis of the diseased synovial tissue (ST) may represent a valuable prognostic tool. The ultrasound-guided needle synovial biopsy (US-nSB) is a safe, effective and increasingly used method to retrieve ST from both large and small joints. Therefore, assessing the ‘learning curve’ for clinicians training in this technique is critically important.

**Objectives:** To retrospectively evaluate the learning curve for clinicians performing US-nSB at the Centre for Experimental Medicine and Rheumatology, Queen Mary University of London.

**Methods:** The performance of 5 clinicians has been evaluated from their first to >20 procedures based on the training phase (Table). The standard teaching method included: US/US-guided injections; observation of US-nSB; initial procedures occurring under the strict active supervision of an expert.

**Results:** The total number of ST fragments retrieved during the procedure did not significantly change during the learning phase (17.3 ± 3.5 from 1st to 10th biopsy vs 17.2 ± 3.4 if expert performer). Independently of the training phase, a significantly higher number of samples were retrieved from knees/wrists in comparison with metacarpo-, metatarso-, and proximal inter-phalangeal joints. The average weight of a ST fragment at the beginning of the learning curve was comparable with the mean weight of US samples retrieved by expert performers (3.7±2.5mg from 1st to 10th biopsy vs 2.9±2.4mg if experts). ST from knees had a significantly higher mean weight, which could be explained by the more frequent use of a 14G (rather than 16G) needle. At the beginning of the learning curve, 48.9%±5.5% of the retrieved ST-samples were considered histologically ‘gradable’ (visible lining and/or clear sub-lining based on H&E/CD68 IHC staining); the rate of gradable ST progressively increased and remained >60% when >20 procedures have been performed. The duration of the US-nSB significantly decreased during the learning time (49 ± 18 min from 1st to 10th biopsy vs 30 ± 9 min if expert). No serious adverse events (AEs) such as haemarthrosis or joint infection have occurred during the learning time. The overall rate of minor AEs (e.g., minor bleeding) was not the highest at the beginning of the training. During the 1st-10th procedures, 18.2% of the patients reported severe pain compared to the average 8.4%.

**Conclusion:** In this single-centre retrospective study we showed that, with an appropriate training and the presence of the initial strict supervision, performing US-nSB is safe and effective since the beginning of the learning curve. Further prospective and multi-centre studies are needed to confirm the optimal learning time and training method.

**REFERENCES:**


Methods: The CareRA trial included 379 patients with early RA (<1 year) fulfilling 1987 or 2010 ACR criteria and naïve to disease modifying anti-rheumatic drugs (DMARDs). Patients were randomized to one of four different intensive treatment strategies based on methotrexate (MTX) monotherapy or synthetic (cs)DMARD combinations with or without glucocorticoid (GC) bridging. Before randomization, stratification into a high- or low-risk group according to classical poor prognostic markers (presence of erosions, positivity to rheumatoid factor (RF) and/or anti-citrullinated protein antibody (ACPA), and elevated disease activity) was conducted. One of these strategies, COBRA Slim, a combination of MTX and a prednisone remission induction scheme stepping-down from 30 mg QD, was initiated in 141 patients from both risk strata, of which 38 were negative for both RF and ACPA (seronegative). Following the treat-to-target principle, using the disease activity score in 28 joints with C-reactive protein (DAS28CRP), treatment adaptations were steered at low disease activity (<2.6), while aiming for remission (<2.6) as final outcome.

The “as observed” population was analysed for differences in disease activity and radiographic progression between seronegative and seropositive patients at several time points during the 2-year study using independent sample t-test, Mann Whitney-U or adjusted X² (Yate’s correction for small samples). Survival analysis using Kaplan Meier was employed for time to first response to treatment. First response to treatment was defined as achieving first remission (DAS28CRP<2.6) or first relevant improvement (ΔDAS28CRP>1.2) after screening. Sensitivity analyses were applied on the complete CareRA cohort.

Results: Seronegative patients starting COBRA Slim (n=38), had similar age (53 vs 51 years, p=0.52), body mass index (25.5 vs 26.7, p=0.08), symptom duration (7.9 vs 7.2 months, p=0.23), presence of erosions (24% vs 23%, p=0.99) and gender distribution (82% vs 63%, p=0.06), compared to seropositive patients (n=103). However, parameters of disease activity were higher in seronegative patients at screening: DAS28CRP (5.1 vs 4.5, p=0.01), 28 swollen joint count (8.2 vs 5.7, p=0.02) and 28 tender joint count (10.3 vs 6.9, p=0.006). These results were corroborated when analysing the entire CareRA cohort.

The mean disease activity was significantly higher in seronegative patients at the first stages (week 8 and 16), but became comparable by year 1 and 2 (Table 1). There was a significant difference in time to first treatment response between seronegative and seropositive patients, despite being treated with the same strategy, as depicted in the inverted Kaplan Meier plot (Figure 1).

Conclusion: In conclusion, CareRA participants with seronegative RA had a higher initial disease activity, longer time to experience a first treatment response, but achieve comparable remission status as seropositive patients with COBRA Slim, a combination of MTX with moderate dose GC bridging. This provides further evidence that, seronegative RA can no longer be considered a milder form of disease and requires an equally intensive initial treat-to-target therapy as seropositive RA.

Abstract THU0094 – Table 1. demographics

<table>
<thead>
<tr>
<th>DAS28CRP</th>
<th>SERONEGATIVE</th>
<th>SEROPREPOSITIVE</th>
<th>p-value</th>
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<tbody>
<tr>
<td>W1</td>
<td>2.3 ± 1.2 (26)</td>
<td>2.3 ± 1.0 (22)</td>
<td>0.86</td>
</tr>
<tr>
<td>W2</td>
<td>2.1 ± 1.1 (20)</td>
<td>2.0 ± 0.9 (19)</td>
<td>0.02</td>
</tr>
<tr>
<td>W3</td>
<td>1.9 ± 0.9 (16)</td>
<td>1.9 ± 0.8 (15)</td>
<td>0.62</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SNAIP VAN DER HEIDE SCORE</th>
<th>SERONEGATIVE</th>
<th>SEROPREPOSITIVE</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>W1</td>
<td>1.3 ± 0.3 (20)</td>
<td>1.2 ± 0.2 (20)</td>
<td>0.18</td>
</tr>
<tr>
<td>W2</td>
<td>1.2 ± 0.3 (18)</td>
<td>1.1 ± 0.2 (18)</td>
<td>0.08</td>
</tr>
<tr>
<td>W3</td>
<td>1.1 ± 0.2 (16)</td>
<td>1.1 ± 0.1 (16)</td>
<td>0.62</td>
</tr>
</tbody>
</table>

Results: At T1, 104 patients (44.6%) were classified as IR to MTX. In univariate analysis, factors significantly associated with IR were: female
In this RA cohort, the condition of current smoker was the only predictor of IR to MTX. This observation, together with the lack of association between previous smoking habit and IR to MTX, further prompted to recommend cessation of cigarette smoking in patients with RA who begin treatment with MTX.

Table 1. Baseline demographic, clinical and serological features.

<table>
<thead>
<tr>
<th>Gender, n (%)</th>
<th>Female</th>
<th>142 (60.9%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at enrollment, mean (± SD), yrs</td>
<td>54.2 (±14.5)</td>
<td></td>
</tr>
<tr>
<td>RF/ACPA positivity, n (%)</td>
<td>132 (60.5%)</td>
<td></td>
</tr>
<tr>
<td>BMI, mean (± SD) Kg/m²</td>
<td>24.9 (± 4.1)</td>
<td></td>
</tr>
<tr>
<td>Current smoker, n (%)</td>
<td>37 (15.9%)</td>
<td></td>
</tr>
<tr>
<td>Ex smoker, n (%)</td>
<td>89 (38.2%)</td>
<td></td>
</tr>
<tr>
<td>DAS28, mean (± SD)</td>
<td>5.3 (± 1.2)</td>
<td></td>
</tr>
<tr>
<td>TJC28, median (IQR)</td>
<td>9 (5-15)</td>
<td></td>
</tr>
<tr>
<td>SJC28, median (IQR)</td>
<td>5 (2-10)</td>
<td></td>
</tr>
<tr>
<td>ESR, mean (± SD)</td>
<td>39.9 (± 24.9)</td>
<td></td>
</tr>
<tr>
<td>X-ray Erosion, n (%)</td>
<td>36 (22.3%)</td>
<td></td>
</tr>
<tr>
<td>Rheumatoid Nodules, n (%)</td>
<td>8 (3.4%)</td>
<td></td>
</tr>
</tbody>
</table>

Acknowledgement: This study was supported by an unconditional Research grant from Pfizer Inc.

Disclosure of Interests: None declared


THU0097 PERSISTENT HIGH DISEASE ACTIVITY IN THE ANTI-CARBAMYLATED PROTEIN ANTIBODY POSITIVE EARLY ARTHRITIS PATIENTS INDEPENDENTLY OF TREATMENT

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Background: There is great interest in the identification of prognostic bio-markers informing early therapeutic decisions for the improvement of rheumatoid arthritis (RA) evolution. Promising results in early arthritis (EA) patients indicate the anti-carbamylated protein antibodies (ACarPA) may serve this function. In effect, they are associated with high baseline disease activity and, in our patients, with less improvement in the first 6-months of follow-up. This association was independent of sex, age at diagnosis, time since symptoms onset, smoking and the year of onset.

Objective: We aimed to explore the influence of the initial treatment on the persistent high disease activity associated with the presence of ACarPA in EA patients.

Methods: Samples were obtained at the first visit of two EA cohorts from Hospital Universitario La Paz and Hospital Universitario La Princesa, which recruit patients within one year from the clinical onset. Information on the initial treatment and the disease activity at the baseline and at 6-months of follow-up was available from 546 patients. Treatment was categorized according to the use of corticosteroids, methotrexate (MTX) and other DMARDs, and considering changes in the first 6 months. In addition, MTX dose was considered either quantitatively or as a dichotomous variable (≥ 12.5 mg and < 12.5 mg). Main effects general linear regression was used for analysis, including the treatment and the other confounders as covariates.

Results: A large fraction (83%) of the EA patients received specific treatment from the initial visit. It comprised DMARD (50.1%), corticosteroids (10.6%), or a combination of both (39.3%). The most common DMARD was MTX (82.2%), whereas less frequently used medications included sulfasalazine (5.4%), leflunomide (3.2%), hydroxychloroquine (8.1%) and celecoxib (10.6%). The 35.5% of the treated patients (n=193) during the 6-month follow-up. The presence of ACarPA was associated with a 0.45 higher mean baseline DAS28 and with less decrease of DAS28 (ΔDAS28) from the baseline to 6 months of follow-up (β = 0.08, p = 0.016), as already communicated. This latter association persisted without modification after accounting for the initial treatment (DMARD, corticosteroids, and changes in treatment). In addition, it was independent of the consideration of all DMARDs in a single group, or separated into two categories: MTX and the other. Similarly, the association was independent on MTX dose, defined both as a categorical or a quantitative variable.

Conclusion: The association of ACarPA with a persistently increased disease activity in EA patients is independent of the initial treatment. These results reinforce the possibility that ACarPA can be useful as prognostic biomarkers for the first 6 months of evolution and indicate the need for personalized management of the patients carrying ACarPA.

Acknowledgement: Supported by grants PI17/01606 and RD16/0012/014 of the Instituto de Salud Carlos III (Spain) that are partially financed by FEDER.

Disclosure of Interests: Cristina Requeiro: None declared, Ana Ortiz: None declared, Laura Nuño: None declared, Diana Peiteado: None declared, Alejandro Villalba: None declared, Dora Pascual Salcedo: None declared, Ana Martínez-Feito: None declared, Alejandro Balsa Grant/Research support from: Abbvie, Pfizer, Novartis, BMS, Nordic, Sanofi, Consultant for: Abbvie, Pfizer, Novartis, BMS, Nordic, Sanofi, Sandoz, Lilly, Paid instructor for: Pfizer, Speakers bureau: Pfizer, Novartis, UCB, Nordic, Sanofi, Sandoz, Lilly, Isidoro González-Alvaro: None declared, Antonio Gonzalez: None declared


THU0097 VALUEOF ANTIBODIES AGAINST ACETYLATED PEPTIDES FOR THE CLASSIFICATION OF PATIENTS WITH EARLY ARTHRITIS

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Background: Patients with rheumatoid arthritis (RA) achieve the best response when they receive adequate treatment as soon as possible. This fact motivated the modification of the classification criteria by the ACR and the EULAR in 2010 to enable early detection. One of the changes is the increased weight conferred to the autoantibodies: rheumatoid factor and anti-citrullinated protein antibodies. As these antibodies are not present in all patients, other antibodies could provide similar information. In this regard, the antibodies that recognize an acetylated peptide from mutated vimentin (Acylated Peptide Antibodies or AAPA) stand out [1].

Objectives: We aimed to evaluate the AAPA predictive value at the baseline visit for the classification of early arthritis patients.

Methods: A total of 438 patients with available samples and information were randomly selected from two early arthritis clinics. The AAPA were determined in baseline sera as previously described [1]. Two peptides were included, one acetylated at a lysine (anti-AcLys) and the other at an ornithine (anti-AcOrn) and considered either individually or combined. The sensitivity, specificity, predictive positive (PPV) and negative (NPV) values and the AUC of the ROC curve were assessed. Logistic regression was also applied adjusting for age, sex, the centre of origin, anti-CCP, and RF. The study was approved by the ethics committee of the Hospital Universitario La Paz, the Hospital Universitario La Princesa, and the Andronic de Galicia.

Results: The AAPA at baseline were sensitive and specific for the classification of the patients fulfilling RA criteria (46.8%) at the end of the 2-year follow-up (table 1). Specifically, the anti-AcOrn antibodies were slightly
more sensitive and specific than the anti-AcLys ones. The two and their combination showed a preserved specificity for the seronegative patients, but a lower sensitivity than for the seropositive ones. Consequently, the PPV for the seronegative patients was low, although the NPV was high. In the same vein, the AUC was insufficient for the seronegative patients. The regression analysis including the anti-CCP and RF revealed a significant contribution of the anti-AcOm antibodies (OR = 2.1, 95% CI = 1.1 - 4.0, P = 0.02), but not of the anti-AcLys antibodies. On the other hand, the inclusion of the AAPA in the classification resulted in an increase in sensitivity of 5.4%, at the cost of a 13.7% lower specificity, which is an improvement over the anti-carbamylated protein antibodies.

**Abstract THU0097**

Table 1. Parameters assessing the diagnostic value of the anti-acetylated peptide antibodies taken individually and in combination for the classification of the RA patients or the indicated patient subsets subset.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Odds Ratio</th>
<th>95% Confidence Limits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Satisfied at treatment start</td>
<td>3.13</td>
<td>(2.61; 3.70)</td>
</tr>
<tr>
<td>DAS28 reduction (one unit) after one year</td>
<td>1.34</td>
<td>(1.26; 1.43)</td>
</tr>
<tr>
<td>Reduction (one unit) on a scale of 0-10 of pain after one year</td>
<td>1.28</td>
<td>(1.23; 1.32)</td>
</tr>
<tr>
<td>Reduction of deepening (one unit on a scale of 0-10)</td>
<td>1.01</td>
<td>(0.98; 1.04)</td>
</tr>
<tr>
<td>Reduction of fatigue (one unit on a scale of 0-10)</td>
<td>1.32</td>
<td>(1.26; 1.38)</td>
</tr>
<tr>
<td>Improvement of physical function by 10 percentage points</td>
<td>1.5</td>
<td>(1.3; 1.6)</td>
</tr>
<tr>
<td>Improvement of physical function by 10 percentage points</td>
<td>1.36</td>
<td>(1.15; 1.60)</td>
</tr>
</tbody>
</table>

Conclusion: The AAPA show high specificity and sensitivity for RA in early arthritis patients. However, their contribution to RA classification is minor once RF and the anti-CCP antibodies have been considered. But nevertheless, AAPA supports the drive to close the diagnostic gap in this early disease phase and to increase the likelihood of successful therapy.

**REFERENCES:**


**Disclosure of Interests:** Lorena Rodriguez-Martinez: None declared, Holger Bang Employee of: Dr. Bang is employee of the diagnostic company Orgentec Diagnostika, Laura Nuño: None declared, Diana Peiteado: None declared, Ana Ortiz: None declared, Alejandro Villalva: None declared, Bang Employee of: Dr. Bang is employee of the diagnostic company Orgentec Diagnostika., Laura Nuño: None declared, Diana Peiteado: None declared, Holger Rodríguez-Martínez: None declared, Lorena Rodríguez-Martínez: None declared, Holger Bang Employee of: Dr. Bang is employee of the diagnostic company, Laura Nuño: None declared, Diana Peiteado: None declared, Ana Ortiz: None declared, Alejandro Villalva: None declared, Bang Employee of: Dr. Bang is employee of the diagnostic company, Laura Nuño: None declared, Diana Peiteado: None declared, Holger Rodríguez-Martínez: None declared, Lorena Rodríguez-Martínez: None declared, Holger Bang Employee of: Dr. Bang is employee of the diagnostic company, Laura Nuño: None declared, Diana Peiteado: None declared, Ana Ortiz: None declared, Alejandro Villalva: None declared, Bang Employee of: Dr. Bang is employee of the diagnostic company, Laura Nuño: None declared, Diana Peiteado: None declared, Holger Rodríguez-Martínez: None declared, Lorena Rodríguez-Martínez: None declared, Holger Bang Employee of: Dr. Bang is employee of the diagnostic company

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**THU0098 WHICH FACTORS INFLUENCE ACHIEVEMENT OF TREATMENT SATISFACTION IN RHEUMATOID ARTHRITIS?**

**Martin Schaefers, Jörn Kekow, Karin Rockwitz, Anke Liebhaber, Angela Zink, Anja Strangfeld. 1German Rheumatism Research Center, Berlin, Germany; 2Scientific Advisory Board, Vogelsang-Gommern, Germany; 3Rheumatologist, Goslar, Germany; 4Rheumatologist, Haller/Saale, Germany**

**Background:** The satisfaction of RA patients with their pharmacological therapy is a relevant patient reported outcome which influences treatment adherence and continuation. However, it has not been investigated frequently, and almost never in large studies.

**Objectives:** To assess factors exerting a potential influence on the satisfaction with the pharmacological treatment and to quantify this influence.

**Methods:** The German register RABBIT is a prospective longitudinally followed cohort of RA patients enrolled with a new start of a DMARD after at least one csDMARD failure. This analysis comprises patients who were enrolled with start of a DMARD between 01/2009 and 04/2018, who were observed for at least 12 months and had been on the therapy prescribed at enrolment for at least six months.

**Abstract THU0098 – Table 1.**

<table>
<thead>
<tr>
<th>Table 1: Results of logistic regression to analyze potential factors influencing satisfaction with drug treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameter</td>
</tr>
<tr>
<td>-----------</td>
</tr>
<tr>
<td>Satisfied at treatment start</td>
</tr>
<tr>
<td>DAS28 reduction (one unit) after one year</td>
</tr>
<tr>
<td>Reduction (one unit) on a scale of 0-10 of pain after one year</td>
</tr>
<tr>
<td>Reduction of deepening (one unit on a scale of 0-10)</td>
</tr>
<tr>
<td>Reduction of fatigue (one unit on a scale of 0-10)</td>
</tr>
<tr>
<td>Improvement of physical function by 10 percentage points</td>
</tr>
<tr>
<td>Improvement of physical function by 10 percentage points</td>
</tr>
</tbody>
</table>

**Conclusion:** Satisfaction with the applied treatment was measured in four categories from "very satisfied" to "very unsatisfied". Logistic regression combined with multiple imputation of missing values was performed to calculate odds ratios (ORs) for factors which might have an influence on treatment satisfaction.

**Results:** At treatment onset, 55% of the 8,177 patients were "very" or "rather" satisfied (in the following: "satisfied"), while the rest was "very" or "rather" unsatisfied (in the following: "unsatisfied") with their therapy. After one year of treatment, 86% of patients were satisfied with their treatment. Factors with positive impact on whether patients reached the target of treatment satisfaction were satisfaction at baseline, reduction of DAS28-BSG, pain and glucocorticoid dose as well as the increase of physical function. Depression, obesity as well as a prior treatment failure of bDMARDs had a negative influence on the outcome (see Table 1). The DAS28 component most influential on treatment satisfaction was the patient global health assessment. Regarding glucocorticoid therapy, being still treated with either 5 to 15 mg (OR: 0.66, 95% CI: 0.55; 0.79) or > 15 mg glucocorticoids (OR: 0.25, 95% CI: 0.15; 0.41) had a negative impact on the achievement of therapy satisfaction (data not shown).

**Conclusion:** Reductions in disease activity, pain and glucocorticoid dosage as well as improvement of physical function increase the chance to achieve treatment satisfaction. On the other hand, depression and obesity as well as prior treatment failures with bDMARDs are obstacles to therapy satisfaction. For physicians, these results suggest that efforts to taper glucocorticoid doses are worthwhile to improve patient’s satisfaction.

**Acknowledgement:** Disclosure: RABBIT is supported by a joint, unconditional grant from AbbVie, Bristol-Myers Squibb, Celtrion, Hexal, Lilly, MSD Sharp & Dohme, Pfizer, Roche, Samsung Bioepis, Sanofi-Aventis, and UCB.
Background: Rheumatoid Arthritis (RA) is a progressive inflammatory disease which causes pain, joint damage and disability. Patients with RA may experience disease-specific distress (DSD), which is related to the burden of living with their life-long illness. This phenomenon has been identified in patients with RA, as an entity distinct from other forms of psychological distress. They may also experience disease-specific distress (DSD), which causes pain, joint damage and disability. Patients with RA may experience disease-specific distress (DSD), which is related to the burden of living with their life-long illness. Disease-specific distress (DSD) is important: as they may have different perspectives about their health condition that researchers and/or health care professionals may not have considered. Previous secondary data analysis of patient interviews has suggested that DSD does seem to exist in people with RA, as an entity distinct from other forms of psychological difficulties.

Objectives: The aim of this study was to develop a PGOM, based on previously reported domains of distress, to identify DSD in people with RA for use in clinical and research practice. The study aimed to involve patients in the development of the new outcome measure.

Methods: A three-phase qualitative study was conducted. In Phase 1 items were generated from secondary data analysis of patient interviews. In Phase 2, a focus group of people with RA was consulted with the aim to establish initial face and content validity of the measure and perform item reduction. In Phase 3, individual cognitive interviews (n=9) with people with RA were conducted to further establish face and content validity of the Scale, refine items if necessary and ensure the questionnaire ‘made sense’ to participants. A psychometrician was consulted to consider the development of the new Scale.

Results: In Phase 1, 44 items were initially created to form the Rheumatoid Arthritis Distress Scale (RADS). After Phase 2 and 3 focus group and cognitive interviews respectively, items were reduced from 44 to 39 and three additional supplementary questions were created, to include items such as time since diagnosis and disease activity. Dimensions were classified into five domains of RA distress. Overall participants reported the content of the RADS to be clear and relevant, and that DSD is a valid concept in RA, distinct from clinical depression or anxiety.

Conclusion: DSD appears to be an important concept in RA. The 39-item RADS currently demonstrates acceptable face and content validity in this patient group. It may be beneficial to establish face and content validity in a more diverse patient sample before proceeding with further psychometric testing. The RADS may be a useful tool for healthcare professionals to identify DSD in patients with RA. Direct patient involvement and their commitment have been instrumental in the development of new outcome measures.

Acknowledgement: This work was supported by King’s College London and submitted in partial fulfillment for the MSc Degree in Advanced Neuromusculoskeletal Physiotherapy.

Disclosure of Interests: None declared

Disclosure of Interests: Marlene Stephan: None declared, Koray Tasclilar: None declared, Melanie Hagen: None declared, Judith Haschka: None declared, Michaela Reiner: None declared, Fabian Hartmann: None declared, Amd Kleyer Grant/research support from: Lilly, Consultant for: Lilly, Speakers bureau: Abbvie, Axel Hueber Grant/research support from: Novartis, Pfizer, Consultant for: Lilly, Speakers bureau: Lilly, Novartis, Janssen, Abbvie, Bernhard Manger: None declared, Camille Figureiedo: None declared, Jayme Coba: None declared, Hans-Peter Tony Consultant for: Eli Lilly and Company, Speakers bureau: Eli Lilly and Company, Stephanie Finzel: None declared, Stefan Kleinert Grant/research support from: Novartis, Consultant for: Novartis, UCB, Chugai, Celgene, Medac, Roche, Abbvie, Speakers bureau: Novartis, UCB, Chugai, Celgene, Medac, Roche, Abbvie, Joerg Wendler: None declared, Florian Schuch Consultant for: Celgene, Lilly, UCB, Roche, Sanofi-Aventis, Abbvie, Novartis, Speakers bureau: Celgene, Lilly, UCB, Roche, Sanofi-Aventis, Abbvie, Novartis, Sistrom, Feuchtner: None declared, Martin Fleck: None declared, Karin Manger: None declared, Wolfgang Ochs: None declared, Matthias Schmitt-Haendle: None declared, Hanns-Martin Lorenz: None declared, Hubert Nuesseit: None declared, Rieke Alten Grant/research support from: Bristol-Myers Squibb, Speakers bureau: Bristol-Myers Squibb; Jörg Henes: None declared, Klaus Krueger: None declared, Georg Schett: None declared, Jürgen Feelisch: None declared, TTV; Consultant for: Bristol-Myers Squibb and Celgene (greater than $10,000), Consultant for: Bristol-Myers Squibb, Celgene, Chugai, GlaxoSmithKline, Janssen, Eli Lilly, Novartis, Roche, Sanofi Aventis, and UCB (in total more than $10,000), Speakers bureau: Bristol-Myers Squibb, Celgene, Chugai, GlaxoSmithKline, Janssen, Eli Lilly, Novartis, Roche, Sanofi Aventis, and UCB (in total more than $10,000)


THU0101

TORQUE TENO VIRAL LOAD FOR MONITORING OF BIOLOGICAL THERAPIES IN RHEUMATOID ARTHRITIS

Paul Studenic1, Gregory Bond2, Andreas Kirschbaumer2, Manuel Becede3, Karel Pavelka4, Dmitry Karateev4, Jutta Stieger5, Rudolf Puchner6, Rudiger Muller7, Elisabeth Puchhammer-Stickl8, Martin Durechova9, Andrea Rubbert-Roth5, Jun-Fei Chen6, and Andreas Kniep1

Background: The apathogenic and highly prevalent Torque Teno Virus (TTV) of Experimental Rheumatology, 1st Faculty of Medicine, Institute of Rheumatology, Prague, Czech Republic; 5Hietzing Hospital, 2nd Department of Medicine, Vienna, Austria; 10Charles University in Prague, Department of Experimental Rheumatology, 1st Faculty of Medicine, Institute of Rheumatology, Prague, Czech Republic; 2Rheumatologist in private practice, Wels, Austria; 3Kantonsspital Aarau, Division of Rheumatology, Aarau, Switzerland; 4Medical University of Vienna, Center for Virology, Vienna, Austria; 5Medical University of Vienna, Department of Laboratory Medicine, Vienna, Austria; 6Charles University in Prague, Department of Experimental Rheumatology, 1st Faculty of Medicine, Institute of Rheumatology, Prague, Czech Republic

Method: To identify different treatment trajectories, based on CDAI and DAS28 line characteristics.

Results: TTV was measured in 95 RA patients [INF (n=23), TCC (n=22), ABA (n=27) or RTX (n=23)]. Median TTV levels at baseline were 4.2x10^9 c/ml with no difference between the treatment groups. After 3 months of treatment with patients with INF (p=0.018), ABA (p=0.071) and RTX (p=0.001) showed an increase in TTV levels compared to baseline. There was no change in TTV in patients with TCZ, who were omitted from further analyses. TTV at 3 months after treatment was higher in patients achieving a SDAI85 response at month 6, 0.001) Levels of above 5.8x10^9 c/ml at month 3 showed a 67% specificity and 81% sensitivity for a SDAI85 response at month 6, corresponding to a positive likelihood ratio of 2.6 (95% CI: 1.6-4.1). Patients in the top tertile of month 3 TTV (>7.8x10^9 c/ml) had lower SDAI, CDAI and DAS28 and higher SDAI85 response rate at month 6 (OR: 1.41-16.42; p=0.012). The highest non-response rates were found in patients within the lowest TTV tertile (Table A), and the highest remission rates were found in the highest TTV tertile (Table B). No patient below a TTV value of 2.7x10^9 c/ml at month 3 showed SDAI85 treatment response at month 6.

Conclusion: Our data suggest that TTV levels in patients with RA treated with INF, ABA or RTX at month 3 are associated with clinical responses at month 6, and thus may constitute a biomarker for therapeutic monitoring.

Table 1

<table>
<thead>
<tr>
<th>TTV Level (c/ml)</th>
<th>SDAI, CDAI and DAS28</th>
<th>SDAI85 Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2.7x10^9</td>
<td>70%</td>
<td>85%</td>
</tr>
<tr>
<td>2.7x10^9 - 5.8x10^9</td>
<td>55%</td>
<td>80%</td>
</tr>
<tr>
<td>&gt;5.8x10^9</td>
<td>30%</td>
<td>60%</td>
</tr>
</tbody>
</table>

Acknowledgement: This study was supported by a grant of the Austrian Science Funds (FWF, grant-ID: KLI072)

Disclosure of Interests: Paul Studenic: None declared, Gregory Bond: None declared, Andreas Kirschbaumer Speakers bureau: Bristol-Myers-Squibb, Celgene, Pfizer, Manuel Becede: None declared, Karel Pavelka: None declared, Dmitry Karateev: None declared, Jutta Stieger: None declared, Rudolf Puchner: None declared, Rudiger Muller: None declared, Elisabeth Puchhammer-Stickl: None declared, Martina Durechova: None declared, Michaela Loskind: None declared, Martina Durechova: None declared, Martina Loskind: None declared, Thomas Perkmann: None declared, Marta Olejarova: None declared, Elena Luchkina: None declared, Carl-Walter Steiner: None declared, Michael Bonelli: None declared, Josef S. Smolen: None declared, Daniel Aletaha: None declared, Gloria Peschke: None declared, Stephan Finzel: None declared, Stefan Kleinert Grant/research support from: AbbVie, Eli Lilly, Janssen, MSD, Pfizer Inc, Roche, Consultant for: AbbVie, Amgen, AstraZeneca, Astro, Celgene, Centor, Eli Lilly, GlaxoSmithKline, ILTOC, Janssen, Medimmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Samsung, Sanofi, UCB, Speakers bureau: AbbVie, Amgen, AstraZeneca, Astro, Celgene, Centor, Eli Lilly, GlaxoSmithKline, ILTOO, Janssen, Medimmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Samsung, Sanofi, UCB, Daniel Aletaha Grant/research support from: AbbVie, Bristol-Myers Squibb, and MSD, Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medac, Merck, MSD, Pfizer Inc, Roche, and UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medac, Merck, MSD, Pfizer Inc, Roche, and UCB


THU0102

PATIENT DISEASE TRAJECTORIES IN BARICITINIB-TREATED PATIENTS WITH RHEUMATOID ARTHRITIS AND INADEQUATE RESPONSE TO METHOTREXATE

Peter C. Taylor1, Paul Emery2, Michael E. Weinblatt3, Eduardo Myster4, Andrea Rubbert-Roth5, Bochao Jia6, Luna Sun7, Yushi Liu8, Yun-Fei Chen9, Anabela Cardoso9, Yoshiya Tanaka10, 1University of Oxford, Oxford, United Kingdom; 2University of Leeds, Leeds, United Kingdom; 3Brigham and Women’s Hospital, Boston, United States of America; 4Organización Médica de Investigación, Buenos Aires, Argentina; 5Kantonsspital St. Gallen, St. Gallen, Switzerland; 6Eli Lilly and Company, Indianapolis, United States of America; 7University of Occupational and Environmental Health, Kitakyushu, Japan

Background: In RA-BEAM phase 3 study, baricitinib (bari) 4mg demonstrated clinical efficacy in patients (pts) with rheumatoid arthritis (RA) and an inadequate response to methotrexate. Bari, a selective Janus kinase 1/2 inhibitor, is approved for the treatment of moderate to severe active RA in adults in >50 countries. For improved treatment strategy, it is important to understand whether the pt population is composed of distinct pt groups with differing treatment responses and associated baseline characteristics.

Objectives: To identify different treatment trajectories, based on CDAI improvement, in bari 4mg treated pts over 52 weeks; and examine the associated clinical disease measures, structural damage score and baseline characteristics.

Methods: Growth Mixed Model (GMM), a novel latent class mixed model, was used to classify the longitudinal disease patterns instead of

Abstract THU0102 – Table 1

Abstract THU0103 – Table 1. Baseline characteristics:

<table>
<thead>
<tr>
<th>Group</th>
<th>N=344</th>
<th>N=56</th>
<th>N=87</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>53.8 (12.1)</td>
<td>54.0 (12.7)</td>
<td>52.2 (12.4)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>74 (21.5)</td>
<td>16 (28.6)</td>
<td>22 (25.3)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>26.8 (7.5)</td>
<td>25.9 (6.0)</td>
<td>27.0 (6.1)</td>
</tr>
<tr>
<td>CDAI</td>
<td>33.8 (10.0)</td>
<td>48.5 (10.0)</td>
<td>48.0 (10.4)</td>
</tr>
<tr>
<td>mTSS</td>
<td>41.0 (49.1)</td>
<td>40.6 (41.8)</td>
<td>49.8 (58.6)</td>
</tr>
<tr>
<td>Duration from RA diagnosis (years)</td>
<td>8.4 (0.0)</td>
<td>8.4 (9.3)</td>
<td>9.8 (10.2)</td>
</tr>
<tr>
<td>HAQ-DI</td>
<td>1.48 (0.68)</td>
<td>1.75 (0.64)</td>
<td>1.80 (0.60)</td>
</tr>
</tbody>
</table>

Data reported as mean (SD) unless indicated

Abstract THU0103 – Table 2. Response rates in patient groups, n (%)

<table>
<thead>
<tr>
<th>Group 1</th>
<th>N=344</th>
<th>Group 2</th>
<th>N=56</th>
<th>Group 3</th>
<th>N=87</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDAI ≤10</td>
<td>W24</td>
<td>214 (66.3)</td>
<td>28 (57.1)</td>
<td>2 (3.5)</td>
<td></td>
</tr>
<tr>
<td>W52</td>
<td>335 (76.8)</td>
<td>36 (85.7)</td>
<td>8 (16.0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>mTSS change from baseline ≤0.5</td>
<td>W24</td>
<td>285 (90.8)</td>
<td>42 (85.7)</td>
<td>51 (83.6)</td>
<td></td>
</tr>
<tr>
<td>W52</td>
<td>266 (93.3)</td>
<td>34 (82.9)</td>
<td>40 (80.0)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

W=week

Conclusion: Baseline severity is associated with different treatment trajectories. With bari treatment, majority of pts achieved LDA and had no structural progression. Pts with high baseline disease activity were associated with longer time to achieve LDA. Pts with higher baseline structural damage in addition to high disease activity were less likely to achieve LDA, but consistent with the other groups, had similar low rate of joint damage progression. Long-term maintenance and continued improvement in CDAI were observed with bari treatment.
OBJECTIVES: We aimed to identify a metabolite signature with consistently high accuracy for RA.

CONCLUSION: Three distinct groups of persistent responders with early RA were identified based on their 1-year PRO profile. The majority of patients were well-synchronized, reporting very low pain and fatigue levels in concordance with their well-controlled disease activity. One in 5 persistent responders, however, seemed to have unmet needs. In view of early identification of patients at risk of poor wellbeing despite good disease control, early pain and fatigue levels and certain coping behavior and illness perceptions were recognized as potential targets for future interventions.

Disclosures of Interests: Xinran Wang: None declared, Joel Paschke: None declared, Rana Dadashova: None declared, Edna Hutchings: None declared, Liang Li: None declared, Walter P Maksymowych: Grant/research support from: AbbVie, Pfizer, Janssen, Novartis, Consultant for: AbbVie, Eli Lilly, Boehringer, Galapagos, Janssen, Novartis, Pfizer and UCB Pharma; Chief Medical Officer for Canadian Research and Education Arthritis.

measures, the power Doppler joint count (UPDJC), which demonstrates hyper vascularization of the synovium, and the 12-multibiomarker disease activity test (MBDA), which incorporates 12 biomarkers in an algorithm leading to a single disease activity score. The UPDJC includes scoring at six dorsal wrist and six dorsal MCP sites [2]. The average duration of RA in patients at this clinic is > 10 years.

**Results:** Fifty two patients were found to be in inadequate control at the clinic and were started on Tofacitinib. Ten patients discontinued treatment with Tofacitinib within the first year, four because of an inadequate response, and four because of adverse effects (two deaths, one with lung cancer and one with colon cancer), and two because of noncompliance or loss to follow up.

Forty two patients remained on treatment with Tofacitinib for at least one year, and at this point in time, 21 patients have remained on the drug for two or more years. The DAM assessments and selected changes in certain laboratory parameters for two yearly time points are shown for these patients in Table 1. Clinical significance was determined by Paired-samples T tests.

**Conclusion:** Patients showed sustained significant clinical responses for two or more years by all three diverse DAMs and several other common measures of clinical response. The initiation of Tofacitinib in a Rheumatology clinic utilizing a T2T strategy clearly showed sustained clinical responses for up to two years for a significant number of patients. Significant changes in some of the cytokine components of the MBDA were also noted, including increases in leptin levels. The use of the T2T strategy offers a unique opportunity to obtain real time data in patients treated with specific therapeutic agents at a community rheumatology clinic.

**REFERENCES:**


**THU0106**

**SYSTEMIC IMMUNE-INFLAMMATION INDEX IN RHEUMATOID ARTHRITIS PATIENTS: RELATION TO DISEASE ACTIVITY**

**Takahiro Yoshikawa,** Tetsuya Funukawa, Masao Tamura, Teppei Hashimoto, Mai Morimoto, Naoto Azuma, Masayasu Kitano, Kiyoshi Matsui. Hyogo college of Medicine, Division of Rheumatology, Department of Internal Medicine, Nishinomiya-city, Japan

**Background:** Among the immune system elements, neutrophils, lymphocytes and platelets play a role in the regulation of inflammation while also undergoing changes secondary to inflammation. Recently, the neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR) have been used as markers of systemic inflammation including rheumatoid arthritis (RA). It was reported that systemic immune-inflammation index (SII) is positively correlated with neutrophil and platelet counts and inversely correlated with lymphocyte count.

**Objectives:** We investigated whether SII in RA patients and compare between active cases and those in remission.

**Methods:** This research is a cross-sectional study. In 734 RA patients registered in the database of our department from January to April in 2016, a total of 574 eligible RA patients were included in this study, excluding 160 patients whose neither RA disease activity or laboratory data were available. Correlations of SII with the disease activity of RA were evaluated. SII was calculated by the following calculation formula: SII = Neutrophils (%)/Lymphocyte (%) * Platelets (G/L).

**Results:** The median age of patients was 65.0 (IQR: 53.0-73.0) years and the median of disease duration was 9.0 (6.0-14.0) years. The DAS28-ESR was median 2.65 (1.90 - 3.37). SII was 612.0 (400.6 – 951.8). There was a significant correlation between SII and DAS28-ESR (r=0.322, P<0.0001), and SII was significantly elevated as disease activity increased (median 513.6 in remission group, 605.7 in low disease activity group, 793.8 in moderate disease activity group and 1367.1 in high disease activity group, respectively; P<0.0001). In contrast to SII, in NLR no significant difference was observed in all groups. The cut-off of SII was 635.9, 688.6 and 912.5 for DAS28-ESR remission, low disease activity and high disease activity. In multiple regression analysis of LogSII, compared to conventional DMARDs treatment, anti-cytokine therapy such as anti-IL-6 receptor inhibitor or anti-TNF inhibitor showed a significant negative correlation, but no significant differences were observed with abatacept or JAK inhibitor.

**Conclusion:** In this study, for the first we demonstrated that SII was more strongly related to disease activity than NLR. SII is an emerging inflammatory biomarker which could be used to evaluate disease activity in RA patients. A larger scale longitudinal study is recommended to confirm the present results and further demonstrate the relation to medications received and disease outcome.

**Disclosure of Interests:** Takahiro Yoshikawa: None declared, Tetsuya Funukawa: None declared, Masao Tamura: None declared, Teppei Hashimoto: None declared, Mai Morimoto: None declared, Naoto Azuma: None declared, Masayasu Kitano: None declared, Kiyoshi Matsui Grant/research support from: Asahi Kasei, Astellas


**THU0107**

**BARIATRIC SURGERY DOES NOT PREVENT THE DEVELOPMENT OF RHEUMATOID ARTHRITIS IN OBSESE SUBJECTS**

**Yuan Zhang**, Anna Rudin1, Cristina Maglio1, Lena Carlsson2,1. University of Gothenburg, Department of Rheumatology and Inflammation Research, Gothenburg, Sweden;2 University of Gothenburg, Department of Molecular and Clinical Medicine, Gothenburg, Sweden

**Background:** Obesity is among the risk factors for rheumatoid arthritis (RA)2,3. In subjects with RA, bariatric surgery-induced weight loss has been associated with a lower disease activity, a decrease in inflammatory markers and a lower use of disease-modifying antirheumatic drugs4. However, the effect of bariatric surgery on the prevention of RA is not known. We have previously shown that bariatric surgery reduces the risk of gouty arthritis and psoriasis in obese subjects4,5.

**Objectives:** By exploiting a longitudinal study enrolling more than 4000 obese subjects, we aim to determine if bariatric surgery prevents the incidence of RA.

**Methods:** The Swedish Obese Subjects (SOS) study is a longitudinal controlled trial on the effect of bariatric surgery on the incidence of obesity-related diseases. It includes 4047 obese subjects: 2010 underwent bariatric surgery and 2037 constituted the matched control group5. Seven Swedish local ethics review boards approved the study protocol. SOS study participants who developed RA were identified by searching the Swedish National Patient Register. Eleven subjects with prevalent RA at baseline are excluded by the analyses. Patients were followed up until diagnosis of RA, death, migration or end of follow-up (December 2016).

**Results:** During a follow-up for up to 29 years, 92 subjects developed RA. Fifty-one individuals (55%) had a seropositive RA (serostatus was unknown for 17 subjects). Forty-seven subjects (2.3%) developed RA in the surgery group compared to 45 subjects (2.2%) in the control group. Bariatric surgery was not associated with the incidence of RA during follow up (log-rank P=0.88; unadjusted Hazard Ratio-HR 1.03, 95% Confidence Interval-CL 0.69-1.55, P=0.88, Figure 1). Similar results were
obtained if only subjects with seropositive RA were included in the analysis. Adjustment for confounding factors did not affect the results (HR for bariatric surgery after adjustment for confounding factors 0.92, 95% CI 0.58-1.45, P=0.72).

Conclusion: In a large cohort of obese subjects followed up for up to 29 years, bariatric surgery did not affect the incidence of RA years.

REFERENCES:

Background: Involving patients with rheumatoid arthritis (RA) in the assessment of their disease may increase adherence to treatment, improve disease outcomes and reduce consultation time.

Objectives: To evaluate the concordance between physician and patient assessment of disease activity in RA using Disease Activity Score (DAS-28).

Methods: During the routine consultation, patients were briefed about DAS-28 by their rheumatologist. Using a standard DAS-28 mannequin, physicians, patients and nurses reported the number of tender and swollen joint, inflammatory markers and global health on a 0-10 Likert scale. Concordance between physician- and patient-DAS categories was calculated using weighted kappa (WK) for category comparison. Concordance between physician- and patient-DAS was estimated using the Bland-Altman method. Predictive factors of positive concordance between physician and patient-DAS were identified using logistic regression.

Results: Four hundred and twenty patients from 7 Middle-Eastern countries were included, with a mean age of 49 years (SD 12), 84% of females, disease duration of 11 years (SD 8). Mean physician-DAS-28 was 4.03 (SD 1.51), 65% had positive rheumatoid factor, 58% had positive ACPA, 30% had erosive disease and 34% were on biotherapies. Agreement between physician- and patient-DAS categories was 89%, WK was 0.84. WK were 0.80 for DAS physician-nurse, 0.79 for DAS patient-nurse, 0.83 for CDAI physician-patient and 0.88 for SDAI physician-patient agreements respectively. All activity measures were higher in patients compared to physicians, except for the swollen joints count. The mean difference between physician- and patient-DAS was -0.09 [95% CI -0.14; -0.04] and was smaller in patients in remission (Figure 1: Bland Altman plot). Concordance was statistically associated with CRP and patient SDAI.

Conclusion: Concordance between patient and physician assessment of disease activity in RA was excellent and was higher using SDAI followed closely by DAS-28 and CDAI. Self-assessment of disease activity should be decided according to the physician’s clinical judgment.

REFERENCES:
INCREASED MODIFIED HEALTH ASSESSMENT QUESTIONNAIRE (MHAQ) SCORE IS INDEPENDENTLY ASSOCIATED WITH HIGH RISK OF SEVERE INFECTION IN RHEUMATOID ARTHRITIS (RA) PATIENTS

Yui Yoshida1, Shiro Ohshima2, Eri Oguro1, Kentaro Kuzuya1, Yasukata Okita1, Hitoshi Matsuoka1, Satoru Teshigawara1, Maiko Yoshimura1, Kentaro Isoda1, Yoshihito Harada1, Jun Hashimoto1, Yukihiko Saeki2.

1National Hospital Organization Osaka Minami Medical Center, Rheumatology and Allergology, Osaka, Japan; 2National Hospital Organization Osaka Minami Medical Center, Clinical Research, Osaka, Japan

Background: Severe infections that complicate rheumatoid arthritis may cause significant morbidity and mortality. The Modified Health Assessment Questionnaire (MHAQ) is one of the scores most used for measuring the functional status of rheumatoid arthritis (RA) patients. However, the relationship between the MHAQ score and severe infection risk has not been well studied [1].

Objectives: To examine the relationship between disease-associated functional status (MHAQ) and severe infection events (SIE) in rheumatoid arthritis patients.

Methods: We used data from the “MIRAi” cohort in Japan. In total, 2174 RA outpatients were examined at the Osaka Minami Medical Center between January 2012 and October 2017. The risk factors were identified and evaluated by multivariate logistic regression, linearity analysis. Interactions of SIE risk between MHAQ and treatment were also observed.

Results: The cohort contributed to 8206 patient-years of follow-up. Overall, 251 SIEs were observed and the incidence of SIE was 3.0 infections per 100 patient-years. The mean age at first observation was 61.7 years and the mean disease duration was 10.3 years. The use of glucocorticoids (GCs), methotrexate (MTX), and biologic and targeted synthetic disease-modifying antirheumatic drugs (bDMARDs/tsDMARDs) was 59.2%, 63.8%, and 40.3%, respectively. The mean Clinical Disease Activity Index (CDAI), Simplified Disease Activity Index (SDAI), Disease Activity Scores of 28 joints (DAS28), and Simplified Disease Activity Index (SDAI) were 300.0, 200.0, and 250.0, respectively.

Conclusions: The MHAQ score was independently associated with SIE risk (OR: 1.02 for each increase of 0.1, 95% CI: 1.01–1.03, p=0.015). The MHAQ score was an independent risk factor for infection in RA patients.
Abstract THU0110 – Table 1

<table>
<thead>
<tr>
<th>Patients with RA only (n=283)</th>
<th>Patients with RA &amp; SS (n=328)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean (SD)</td>
<td>54.6 (13.2)</td>
</tr>
<tr>
<td>Sex, female</td>
<td>236 (83.0)</td>
</tr>
<tr>
<td>Duration of RA, years, mean (SD)</td>
<td>10.6 (10.0)</td>
</tr>
</tbody>
</table>

Background: Angiogenic T cells (Tang) are responsible of vascular repair and homeostasis. Decreased Tang frequencies have been reported in rheumatoid arthritis (RA), in association with disease activity and previous history of cardiovascular (CV) disease. However, excess of CV risk is already present during the early stage of RA. Whether Tang cells are associated with subclinical vascular abnormalities remains unknown.

Objectives: To evaluate whether Tang cells could be associated with subclinical CV endpoints (subclinical atherosclerosis and vascular stiffness) in the very early stage of RA.

Methods: Patients were recruited upon early referral to the rheumatology department. All patients were untreated at the time of sampling. Tang (CD3+CD31+CXCR4+) frequency was assessed by flow cytometry in peripheral blood samples. Plaque occurrence, CIMT and stiffness parameters were analyzed by Doppler ultrasound in internal carotid, middle cerebral and basilars arteries.

Results: 53 patients were recruited, 47 fulfilling 2010 ACR/EULAR classification criteria for RA (36 women, 26 FR+ and 26 ACAP+), 6 fulfilling criteria for Clinically Suspect Arthralgia (CSA) (6 women, 3 RF+ and 3 ACPA+), Tang frequency did not differ between RA and CSA (p=0.382) and it was negatively associated with DAS28 (r=-0.448, p<0.001) and SDAI (r=-0.385, p=0.006), but not with duration of the symptoms (r=0.053, p=0.713)). Tang levels were not related to individual traditional CV risk factors, body mass index, waist circumference (all p>0.050) nor the modified SCORE (r=-0.173, p=0.244) or Framingham Risk Score (r=-0.127, p=0.399). Neither atherosclerosis plaque occurrence (r=0.631) nor the cIMT (r=0.070, p=0.652) were associated with Tang levels.

Conclusion: Tang frequency paralleled carotid peak systolic velocity (r=0.399, p=0.008) and end diastolic velocity (r=0.332, p=0.034) in internal carotid artery. Moreover, Tang positively correlated stiffness parameters: vascular strain (VS, r=0.428, p<0.010), vascular distensibility (VD, r=0.479, p<0.004), vascular stiffness (VSF, r=0.519, p<0.001) and pressure-strain elastic modulus (PSEMD, r=0.531, p=0.015) in left internal carotid artery. Finally, Tang frequency was an independent predictor of stiffness parameters after adjusting for mSCORE, body mass index, DAS28, RF and ACPA positivity: VS (β=0.451, p=0.045), VD (β=0.462, p=0.026), VSF (β=0.422, p=0.035) and PSEM (β=0.446, p=0.026). Tang cells may have a very early role on vascular stiffness in RA. These results point to the Tang subset as the missing link between disease activity and vascular abnormalities during the first stage of the disease.

Disclosure of Interests: None declared


THU0111

ANGIOGENIC T CELLS AS AN INDEPENDENT PREDICTOR OF VASCULAR STIFFNESS IN VERY EARLY RHEUMATOID ARTHRITIS

Javier Rodriguez-Carmona1,2, Mercedes Alperi-Lopez2, Patricia Lopez2, Angel Perez-Alvarez3, Lorena Benavente4, Francisco Javier Balina-Garcia2, Ana Suarez1,1

1University of Oviedo, ISPA, Area of Immunology, Oviedo, Spain, 2Hospital Universitario Central de Asturias, Bone and Mineral Research Unit, Instituto Reina Sofia de Investigación Nefrológica, REDINREN del ISCIII, Oviedo, Spain, 3Hospital Universitario Central de Asturias, Department of Rheumatology, Oviedo, Spain, 4Hospital Universitario Central de Asturias, Department of Neurology, Oviedo, Spain

Background: Angiogenic T cells (Tang) are responsible of vascular repair and homeostasis. Decreased Tang frequencies have been reported in rheumatoid arthritis (RA), in association with disease activity and previous history of cardiovascular (CV) disease. However, excess of CV risk is already present during the early stage of RA. Whether Tang cells are associated with subclinical vascular abnormalities remains unknown.

Objectives: To evaluate whether Tang cells could be associated with subclinical CV endpoints (subclinical atherosclerosis and vascular stiffness) in the very early stage of RA.

Methods: Patients were recruited upon early referral to the rheumatology department. All patients were untreated at the time of sampling. Tang (CD3+CD31+CXCR4+) frequency was assessed by flow cytometry in peripheral blood samples. Plaque occurrence, CIMT and stiffness parameters were analyzed by Doppler ultrasound in internal carotid, middle cerebral and basilars arteries.

Results: 53 patients were recruited, 47 fulfilling 2010 ACR/EULAR classification criteria for RA (36 women, 26 FR+ and 26 ACAP+ and 6 fulfilling criteria for Clinically Suspect Arthralgia (CSA) (6 women, 3 RF+ and 3 ACPA+). Tang frequency did not differ between RA and CSA (p=0.382) and it was negatively associated with DAS28 (r=-0.448, p<0.001) and SDAI (r=-0.385, p=0.006), but not with duration of the symptoms (r=0.053, p=0.713)). Tang levels were not related to individual traditional CV risk factors, body mass index, waist circumference (all p>0.050) nor the modified SCORE (r=-0.173, p=0.244) or Framingham Risk Score (r=-0.127, p=0.399). Neither atherosclerosis plaque occurrence (r=0.631) nor the cIMT (r=0.070, p=0.652) were associated with Tang levels.

Conclusion: Tang frequency paralleled carotid peak systolic velocity (r=0.399, p=0.008) and end diastolic velocity (r=0.332, p=0.034) in internal carotid artery. Moreover, Tang positively correlated stiffness parameters: vascular strain (VS, r=0.428, p<0.010), vascular distensibility (VD, r=0.479, p<0.004), vascular stiffness (VSF, r=0.519, p<0.001) and pressure-strain elastic modulus (PSEMD, r=0.531, p=0.015) in left internal carotid artery. Finally, Tang frequency was an independent predictor of stiffness parameters after adjusting for mSCORE, body mass index, DAS28, RF and ACPA positivity: VS (β=0.451, p=0.045), VD (β=0.462, p=0.026), VSF (β=0.422, p=0.035) and PSEM (β=0.446, p=0.026). Tang cells may have a very early role on vascular stiffness in RA. These results point to the Tang subset as the missing link between disease activity and vascular abnormalities during the first stage of the disease.

Disclosure of Interests: None declared


THU0112

SECULAR TRENDS IN THE INCIDENT RISK OF ACUTE MYOCARDIAL INFARCTION IN RHEUMATOID ARTHRITIS RELATIVE TO THE GENERAL POPULATION

Kiana Yazdani, Hui Xie, Antonio Avila, Yufei Zheng, Michael Abrahamowicz, Diane Lachal. Arthritis Research Canada, Richmond, Canada

Background: Recent studies have demonstrated a declining trend in RA mortality relative to the general population (1). This improvement in mortality could be due to improvement in incident risk of cardiovascular events that are the leading cause of excess deaths in RA (2).

Objectives: Our objective was to assess secular trends in ten-year incident risk of acute myocardial infarction (AMI) in incident cohorts of RA versus general population controls, using administrative health data.

Methods: We conducted a retrospective study of a population-based cohort of incident RA cases who first met previously published RA criteria between 01/01/1997 and 31/12/2004 in British Columbia, followed until 12/31/2014, with general population controls matched 2:1 on gender, age, and index year. Individuals were excluded if they had a diagnosis of MI prior to index date. Incident AMI was defined as first AMI during follow-up using ICD codes (ICD-9 code 410/ICD-10 code I21) in Hospital Discharge data or death certificate in Vital Statistics data. RA and general population cohorts were stratified according to year of RA incidence.
defined according to first RA visit, using a 7-year wash-out period. Inci-
dent rates (IRs) of AMI for RA and general population cohorts, as well as
ingcident rate ratios (IRRs), with 95% confidence intervals (CI) were
calculated per calendar years of incidence. Multivariable Cox Proportional
Hazard models with left truncation were used to estimate risk of AMI in
RA relative to general population while controlling for potential confound-
ers, with contribution of person time of follow-up starting from index date
(second RA visit) to avoid immortal time bias and censoring at ten years
from incident year, or last health care utilization. To examine whether
secular trends differed in RA relative to general population, an interaction
term was tested between the RA indicator and year of RA incidence. To
account for non-linear effect of cohort year, we compared cox regression
models with linear, quadratic, and flexible spline forms of the cohort-year
effects and the model with the best AIC was used to interpret the data.
Results: 23,231 RA individuals (66.4% female; mean [SD] age 59[16.88]
years) and 46,474 controls experienced 1,133 and 1,646 incident AMI,
respectively. Cox Proportion model with the lowest AIC best fit the data.
Risk of AMI was significantly higher in RA vs. general population [aHR
(95% CI): 1.21(1.10, 1.32); p<0.001]. A significant decline was observed
in risk of AMI over calendar year of incidence in both RA [0.94(0.92,
0.97); p<0.001] and controls [0.93(0.91, 0.95); p<.0001]. The decline in AMI
risk did not differ significantly in RA vs. general population [interac-
tion p=0.555].
Conclusion: Our finding suggests that the risk of AMI has significantly
decreased over time in RA and general population cohorts. However, the
decreling trend was not significantly different in RA compared to the gen-
eral population.

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[2] Myasoedova, E. and S.E. Gabriel, Overview of rheumatoid arthritis and
mortality in relation to cardiovascular disease, in Handbook of Cardiovas-
cular Disease Management in Rheumatoid Arthritis, A.G. Semb, Editor.

Disclosure of Interests: Kiana Yazdani: None declared. Hui Xie: None
Michal Abrahamowicz: None declared. Diane Lacaille Grant/research sup-
port from: Bristol-Myers Squibb and Eli Lilly Canada

THU0114 MITIGATING MEDICATION RISK AVERSION IN THE
CONFIDENT TREATMENT DECISIONS FOR LIVING WITH
RHEUMATOID ARTHRITIS TRIAL

Maria Danila1, Lang Chen2, Justin Owensby3, Ronan O’beirne2, Josh Melnick3,
Eric Ruderman, Leslie Harrold4, Jeffrey Curtis1. 1University of Alabama at
Birmingham, Medicine, Birmingham, United States of America; 2Northwestern,
Chicago, United States of America; 3University of Massachusetts, Waltham, United States of America

Background: Controlling disease activity in RA using a treat-to-target
(T2T) strategy can optimize clinical and patient-important outcomes. Yet,
many patients are not familiar with T2T and report medication risk aver-
sion as a major barrier to changing therapy.

Objective:s To develop and evaluate an educational, direct-to-patient
video intervention aimed at improving willingness of patients to appropri-
tely escalate treatment in RA.

Methods: We conducted a controlled, randomized trial of our intervention
among US patients with self-reported RA enrolled in the ArthritisPower
patient registry. We recruited participants by email, and surveyed their
satisfaction with disease control, values about RA medications, decisional
coping, and willingness to change RA treatment change. We compared the dif-
ference in pre-post differences in willingness to change RA treatment bet-
ween the two groups using t-test.

Results: We invited 1264 RA patients by email. We reached our enroll-
ment goal in 8 weeks. Study participants (N=208) were 90% Caucasian,
90% women, with mean (SD) age 50 (11) years, in good health (51%); 52%
reported familiarity with T2T. A majority (89%) reported having values
that favored RA medications. We observed no differences in baseline
sociodemographics, patient global assessment of disease activity, health
IS INCIDENT RHEUMATOID ARTHRITIS INTERSTITIAL LUNG DISEASE ASSOCIATED WITH METHOTREXATE TREATMENT? RESULTS FROM A MULTIVARIATE ANALYSIS IN THE ERAS AND ERAN INFECTION COHORTS:

KIELY Patrick1, Amanda Busby2, Elena Nikiphorou3, Keith Sullivan3, Adam Young2, 1St George’s University Hospitals NHS Foundation Trust, Rheumatology, London, United Kingdom, 2University of Hertfordshire, Center for Health Services and Clinical Research and Post Graduate Medicine, Hatfield, United Kingdom; 3King’s College, London, Academic Rheumatology, London, United Kingdom

Background: Rheumatoid arthritis interstitial lung disease (RA-ILD) is a rare but significant manifestation of RA, with high mortality. Methotrexate (MTX) is known to cause hypersensitivity pneumonitis, but its effect on the onset of RA-ILD is less clear.

Objectives: To assess predictive factors for rheumatoid arthritis interstitial lung disease (RA-ILD) in two early RA inception cohorts with a focus on MTX exposure.

Methods: Patients with new diagnosis of RA recruited to the early RA study (ERAS) and the early RA network (ERAN). Standardised data including demographics, drug therapies and clinical outcomes including the presence of RA-ILD were collected at baseline, within 3-6 months, at 12 months and annually for up to 25 years thereafter. Primary outcome was the association of MTX exposure with incident RA-ILD. Secondary outcomes were the association of demographic, comorbid and RA specific factors on incident RA-ILD using univariate and multivariate analyses and the association of MTX exposure on time to RA-ILD diagnosis using time to event Cox proportional hazards analysis.

Results: Of 92 eligible ILD cases, 39 occurred in 1578 (2.5%) MTX exposed and 53 in 1114 (4.8%) non-MTX exposed cases. The primary analysis of incident RA-ILD cases only developing after any csDMARD treatment (n=67) showed MTX exposure not to be associated with incident RA-ILD (OR 0.85 CI 0.49, 1.49 p=0.578) and a non-significant trend for delayed ILD diagnosis (O.R. 0.54 CI 0.28, 1.06 p=0.072) (see Figure). In an extended analysis including all RA-ILD cases (n=92, including those present pre csDMARD exposure), MTX exposure was associated with a significantly reduced risk of incident RA-ILD (O.R. 0.48, CI 0.3, 0.79 p=0.004) and longer time to ILD diagnosis (O.R. 0.41, CI 0.23, 0.75 p<0.004). Other independent baseline associations with incident RA-ILD were higher age of RA onset, ever smoking, nodules, RF positivity, male gender, ESR, and a longer time from first RA symptoms to first secondary care visit. There is no association between MTX treatment and incident RA-ILD. MTX may have a protective role in delaying the onset of RA-ILD.

Conclusion: In ERAS/ERAN, incident RA-ILD is significantly associated with older age of RA onset, ever smoking, nodules, RF positivity, male gender, ESR, and a longer time from first RA symptoms to first secondary care visit. There is no association between MTX treatment and incident RA-ILD. MTX may have a protective role in delaying the onset of RA-ILD.

Acknowledgement: All recruiting ERAS and ERAN centers.

Disclosure of Interests: Patrick KIELY Paid instructor for: Amgen, Gilead, BMS, Speakers bureau: Abbvie, BMS, UCB, Lilly, Pfizer, Amanda Busby; None declared, Elena Nikiphorou: None declared, Keith Sullivan: None declared, Adam Young: None declared


THU0115

THU0116

COMPARATIVE SAFETY OF BIOLOGIC DMARDS AND ABATACEPT IN RHEUMATOID ARTHRITIS WITH COPD: A REAL-WORLD POPULATION-BASED OBSERVATIONAL STUDY

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Background: The biologic DMARD abatacept has been associated with respiratory adverse events in patients with RA who have chronic obstructive pulmonary disease (COPD) in the ASSURE trial (NCT00048932), based on only 54 patients with RA and COPD. A large observational study of patients with RA and COPD, involving over 1,800 patients using abatacept did not find an increased incidence of respiratory adverse events with abatacept compared with other biologic DMARDs. 2 It remains uncertain, however, whether this potential respiratory risk affects all biologic DMARDs, including abatacept, when compared with non-biologic DMARDs.

Objectives: To assess in a real-world observational setting whether patients with RA and COPD treated with biologic DMARDs, including abatacept, have an increased risk of serious respiratory adverse events compared with similar patients treated with non-biologic DMARDs.

Methods: The Truven MarketScan® Commercial and Supplemental Medicare databases were used to identify patients diagnosed with RA and COPD, treated with a biologic or non-biologic DMARD between January 2007 and December 2015. A prevalent new-user cohort design was used to match each new user of a biologic DMARD with a new user of a non-biologic DMARD on time-dependent propensity scores. Patients were followed up from new use until the end of enrolment or 31 December 2015. The Cox model was used to estimate the hazard ratios (HRs) of respiratory adverse events associated with biologic DMARDs compared
with non-biologic DMARDs, further adjusted for confounders found to be unbalanced despite matching on propensity scores.

Results: The study cohort included 7,424 new users of biologic DMARDs matched to 7,424 new users of non-biologic DMARDs, followed for up to 9 years. The adjusted HR (95% CI) of the combined respiratory endpoint, including severe COPD exacerbation, bronchitis and severe pneumonia or influenza, with biologic DMARD use relative to non-biologic DMARDs was 1.06 (0.91-1.24). For severe COPD exacerbation it was 0.88 (0.64-1.21), 1.02 (0.82-1.27) for bronchitis, while for pneumonia or influenza it was 1.18 (0.90-1.54) if hospitalized and 1.01 (0.89-1.14) as outpatient. For users of abatacept relative to non-biologic DMARDs, the HR of the combined respiratory endpoint was 1.06 (0.80-1.42). Results remained unchanged with sensitivity analyses.

Conclusion: In this large real-world study of patients with RA and COPD, the risk of pre-specified serious respiratory adverse events was not significantly increased in patients using biologic DMARDs, and specifically abatacept, compared with those using non-biologic DMARDs. This study does not support the safety signal for abatacept from the ASSURE trial.

REFERENCES:

Disclosure of Interests: Samy Suissa Grant/research support from: Advisory board meetings, or as speaker, or received research grants from AstraZeneca, Bayer, Boehringer-Ingelheim, Bristol-Myers Squibb, Novartis, Speakers bureau: Advisory board meetings, or as speaker, or received research grants from AstraZeneca, Bayer, Boehringer-Ingelheim, Bristol-Myers Squibb, Novartis, Marie Hudson Grant/research support from: Unrestricted research funds from Bristol-Myers Squibb, Pierre Ernst: None declared, Sophie Shen Employee of: Bristol-Myers Squibb, Teresa Simon Employee of: Bristol-Myers Squibb


TREATMENT OF RHEUMATOID ARTHRITIS WITH COMBINATION THERAPY USING A BIOLOGIC AGENT AND METHOTREXATE LOWERS THE RISK OF DECREASING KIDNEY FUNCTION COMPARED TO METHOTREXATE MONOTHERAPY

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Showa University School of Medicine, Division of Rheumatology, Department of Medicine, Tokyo, Japan

Background: Rheumatoid arthritis (RA) is associated with reduced kidney function, possibly due to chronic inflammation or the use of nephrotoxic therapies. However, little is known about the effects of novel non-nephrotoxic biologic agents (biological disease-modifying antirheumatic drugs [bDMARD]) on the risk of decreasing kidney function.

Objectives: To elucidate the effects of bDMARDs on decreasing kidney function.

Methods: We recruited a cohort of 1058 patients with RA from the All Showa University of RA database. The following background factors were analyzed: age, sex, type of bDMARD, methotrexate and prednisolone dosages, use of conventional synthetic DMARDs and nonsteroidal anti-inflammatory drugs, body mass index, smoking history, diabetes status, hypertension status, dyslipidemia status, serum creatinine (Cr) level, CRP level, and matrix metalloproteinase-3 level. Furthermore, we used the simplified disease activity index (SDAI) for the evaluation of the disease activity of RA. The estimated glomerular filtration rate (eGFR) was calculated using the serum Cr level and age, sex. We divided the patients into two groups according to the treatment, as follows: bDMARD with methotrexate (MTX) treatment (combination group) (744 patients) and MTX monotherapy group (314 patients). The patients followed the same treatment plan for 1 year. Patients who had primary and secondary failures, adverse effects of drugs, and missing data and those who relocated or withdrew from the study were excluded. Propensity scores were calculated based on the following factors: age, sex, prednisolone dosage, MTX dosage, SDAI, Cr level, eGFR, diabetes status, hypertension status, and dyslipidemia status. Overall, 285 patients in each group were identified by propensity score matching. The primary end-points were the eGFR values before treatment and 6 months and 1 year after treatment. Significance was determined using the repeated-measures analysis of variance (ANOVA).

Results: The eGFR (mL/min/1.73 m2) decreased from 88.5 ± 21.8 to 86.1 ± 21.5 and 83.7 ± 21.0 at 6 months and 1 year, respectively, in the combination treatment group and from 86.3 ± 37.3 to 79.5 ± 19.1 and 78.5 ± 19.5 at 6 months and 1 year, respectively, in the MTX monotherapy group. No interaction was observed between the groups. A significant difference was observed between the groups (p < 0.0066) and even during the treatment period (p < 0.001) by repeated-measures ANOVA.

Conclusion: The decrease in eGFR was smaller in the combination treatment group than in the MTX monotherapy group. bDMARD use may lower the risk of decreasing kidney function in patients with RA.

Acknowledgement: Cooperation on data collection: All Showa University in Rheumatoid Arthritis (ASHURA) group


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SUCCESSFUL PSYCHOPHARMACOTHERAPY OF ANXIETY AND DEPRESSIVE DISORDERS IMPROVES RHEUMATOID ARTHRITIS REMISSION RATE AT FIVE YEARS FOLLOW-UP

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Background: Anxiety and depressive disorders (ADD) affect rheumatoid arthritis (RA) disease activity and remission rate. Psychopharmacotherapy (PPT) of ADD attempts to improve the remission rate.

Objective: To determine factors associated with RA remission rate.

Methods: 128 RA-patients (pts) were enrolled, 86% were women with a mean age of 47.4±11.3 (Me±SD) yrs. All pts met the full ACR criteria for RA. Remission was defined as DAS28<2.6. Mean RA activity by DAS28 was high (5.27±1.78) at baseline. 69.4% RA-pts were already taking prednisone (9 [5; 10] mg/day (Me (25%; 75%)), 84.4% - conventional disease-modifying antirheumatic drugs (cDMARDs), 7.8% - biologic DMARDs (bDMARDs) - anti-TNFα - 6.3%, rituximab - 1.6%. ADD were diagnosed in 123 (96.1%) of RA-pts in accordance with ICD-10 in semi-structured interview. Severity of depression and anxiety was evaluated with Montgomery–Asberg Depression Rating Scale (MADRS) and Hamilton Anxiety Rating Scale (HAM-A). RA-pts with ADD were divided into the following treatment groups: 1 – cDMARDs (n=39), 2 – cDMARDs + PPT (sertraline or mianserin) (n=43), 3 – cDMARDs + bDMARDs (n=32), 4 – cDMARDs + bDMARDs + PPT (sertraline or mianserin) (n=9). Biologics treatment duration varied from 1 to 6 years, antidepressants – from 6 to 96 weeks. Logistic regression analysis was conducted to determine factors associated with RA remission rate.

Results: At 5-yrs endpoint in 83 RA-pts remission rate was 22.9% (8.3%, 34.5%, 19.0% and 33.3% in groups 1, 2 and 3, respectively). Significantly higher proportion of patients achieved remission in cDMARDs + PPT group vs cDMARDs group (34.5% vs 8.3%, RR 1.8 (95%CI 0.35 – 9.2), p=0.024). By univariate logistic regression model, sex, younger age, smoking RA-pts, RA duration, RF and ACPA negativity, lower baseline DAS28 and HAQ, absence of extraarticular RA manifestations and depression at the beginning of the study, and remission of anxiety and depressive symptoms at the end of the study were significantly associated with RA remission (table 1). These variables were subjected to multivariate stepwise logistic regression. Only lower baseline DAS28 (OR 0.636 (95%CI 0.515 – 0.785), p=0.001) and remission of anxiety and depressive symptoms at 5-yrs endpoint (OR 0.689 (95%CI 1.826 – 21.29), p=0.007) were independently associated with RA remission at 5-yrs follow-up.

Table 1. Factors associated with RA remission at 5 years (univariate logistic regression).

<table>
<thead>
<tr>
<th>Factor</th>
<th>OR (95%CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex</td>
<td>0.310 (0.166 – 0.577)</td>
<td>0.001</td>
</tr>
<tr>
<td>Baseline age</td>
<td>0.974 (0.961 – 0.986)</td>
<td>0.003</td>
</tr>
<tr>
<td>RA duration</td>
<td>0.913 (0.866 – 0.964)</td>
<td>0.001</td>
</tr>
<tr>
<td>RF</td>
<td>0.265 (0.127 – 0.552)</td>
<td>0.001</td>
</tr>
<tr>
<td>ACPA</td>
<td>0.321 (0.152 – 0.681)</td>
<td>0.003</td>
</tr>
<tr>
<td>Baseline DAS28</td>
<td>0.754 (0.663 – 0.858)</td>
<td>0.005</td>
</tr>
<tr>
<td>Baseline HAQ</td>
<td>0.381 (0.234 – 0.614)</td>
<td>0.001</td>
</tr>
<tr>
<td>Baseline extraarticular RA manifestations</td>
<td>0.021 (0.072 – 0.619)</td>
<td>0.005</td>
</tr>
<tr>
<td>Baseline minor depression</td>
<td>0.278 (0.103 – 0.748)</td>
<td>0.011</td>
</tr>
<tr>
<td>Baseline major depression</td>
<td>0.358 (0.139 – 0.895)</td>
<td>0.028</td>
</tr>
<tr>
<td>Baseline generalized anxiety disorder</td>
<td>0.25 (0.028 – 2.237)</td>
<td>0.215</td>
</tr>
<tr>
<td>Anxiety and depressive symptoms remission at 5-yrs endpoint</td>
<td>0.891 (1.63 – 2.19)</td>
<td>0.007</td>
</tr>
</tbody>
</table>

Conclusion: Lower baseline DAS28 and remission of anxiety and depressive symptoms at 5-yrs endpoint are associated with higher rheumatoid arthritis remission rate at five years follow-up.

Disclosure of Interests: None declared

RHEUMATIC DISEASE COMORBIDITY INDEX IMPACT ON DISEASE ACTIVITY IN PATIENTS ENROLLED IN KUWAIT REGISTRY OF RHEUMATIC DISEASES (KRRD)

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Background: Its known that the presence of certain comorbidities in patients with Rheumatoid arthritis (RA) can have an impact on the chance of achieving low disease activity (LDA).

Objectives: The purpose of this study was to examine the association of different comorbidities with low disease activity index in patients enrolled in KRRD.

Methods: The database of KRRD was used to include patients with RA and multiple visits. Comorbid conditions were collected at enrollment by the treating rheumatologist and modeled using the Rheumatic Disease Comorbidity index (RDCI) score, and by individual comorbidity condition. Disease activity (DAS28) was assessed at routine clinic visits. Associations of comorbidity measures with disease activity over 4 years of follow-up were examined using multivariable linear models. The odds of ever achieving DAS28 low disease activity (<3.2) were examined using multivariable logistic regression.

Results: Among 1511 participants with mean age of 52 (SD 12) years, RA duration 8 (SD 6) years, 60.7% female, 77.1% RF positive, 64.6% anti-CCP positive, and 10.8% with smoking history, 1.29 had a RDCI. Hypertension (21%), diabetes mellitus (21%), hyperlipidemia (12%), cardiovascular (CV) disease (3.6%) and interstitial lung disease (ILD) (1.1%), were the most prevalent comorbidities. Select individual comorbidities, including DM, kidney disease and COPD, were more closely associated with unfavorable longitudinal disease activity, and achievement of low disease activity status. Correlation test between DAS28 and all comorbidities showed significant negative association for achieving low disease activity if the patient has history of diabetes mellitus, COPD or kidney disease. Conclusion: DM, kidney disease and COPD but not composite comorbidity scores, are associated with higher measures of disease activity and lower odds of achieving low disease activity status in RA patients enrolled in KRRD registry.

Table 1: Cox Proportional Hazards Regression for LDA and comorbidities

<table>
<thead>
<tr>
<th>Variable</th>
<th>B SE</th>
<th>95% CI</th>
<th>P</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>DM</td>
<td>0.24</td>
<td>0.05</td>
<td>(0.14, 0.34)</td>
<td>0.001</td>
</tr>
<tr>
<td>CAD</td>
<td>0.16</td>
<td>0.13</td>
<td>(0.09,0.40)</td>
<td>0.233</td>
</tr>
<tr>
<td>Hypertension</td>
<td>-0.12</td>
<td>0.06</td>
<td>(0.24,0.01)</td>
<td>0.65</td>
</tr>
<tr>
<td>Hypertension</td>
<td>-0.04</td>
<td>0.05</td>
<td>(0.14,0.05)</td>
<td>0.394</td>
</tr>
<tr>
<td>COPD</td>
<td>0.66</td>
<td>0.33</td>
<td>(0.01,1.32)</td>
<td>0.047</td>
</tr>
<tr>
<td>Cancer</td>
<td>0.86</td>
<td>0.45</td>
<td>(0.02,1.74)</td>
<td>0.055</td>
</tr>
<tr>
<td>Kidney disease</td>
<td>0.97</td>
<td>0.39</td>
<td>(0.20,1.74)</td>
<td>0.014</td>
</tr>
<tr>
<td>ILD</td>
<td>0.09</td>
<td>0.21</td>
<td>(0.33,0.50)</td>
<td>0.685</td>
</tr>
</tbody>
</table>

Disclosure of Interests: None declared

CIRCULATING FIBROBLAST GROWTH FACTOR-23 IS ASSOCIATED WITH DYSLIPIDEMIA IN RHEUMATOID ARTHRITIS PATIENTS

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Background: In rheumatoid arthritis (RA) patients an increased risk of morbidity and mortality from cardiovascular (CV) events as a result of accelerated atherosclerosis. The bone-derived fibroblast growth factor-23 (FGF23) is a novel marker of chronic kidney disease (CKD)-associated mineral bone disorder, which increases progressively with declining renal function. FGF23 is associated with left ventricular hypertrophy, impaired left ventricular function, endothelial dysfunction, heart failure and progression of renal failure in adult CKD.
**Objectives:** The objectives of this study were to: compare serum FGF-23 levels between RA patients and healthy controls and investigate possible associations between FGF23 as surrogate measures of cardiovascular disease.

**Methods:** This cross-sectional study was performed in Vega-Baja Hospital, Orihuela (Spain) from November 2016 to May 2018. We prospectively enrolled 63 consecutive women patients affected by RA and followed up at the Vega-Baja Hospital (Orihuela, Spain) and 65 matched healthy women controls. All patients included in this study had normal serum creatinine (Cr) levels and met the 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) criteria for RA. Total cholesterol and triglyceride levels were determined by fully enzymatic techniques. High-density lipoprotein (HDL) was determined by precipitation of apolipoprotein B (apoB)-containing lipoproteins with magnesium sulfate, and lipase. Lower-density lipoprotein (LDL) was calculated using the Friedewald formula. Serum FGF-23 was measured using ELISA.

**Results:** The mean serum total cholesterol, HDL-C, LDL-C, and triglycerides were 212.74±41 mg/dL, 69.92±19.45 mg/dL, 120.18±29.24 mg/dL, and 112.93±55.67 mg/dL, respectively. There was no significant differences in FGF-23 levels between the patients and controls [85.7 (5.2-275.4) vs. 81.2 (2.6-269.9) pg/ml; P=0.4316], but we found that FGF23 levels were positively associated with total cholesterol (p <0.05), low-density lipoprotein (LDL-c) level (p <0.05) and smoking (p = 0.008) in patients with RA.

**Conclusion:** We report an association between circulating FGF-23 and LDL-c in RA patients, representing a novel pathway linking high FGF23 to an increased cardiovascular risk.

**REFERENCES:**


**Disclosure of Interests:** Antonio Alvarez de Cienfuegos : None declared, Lucia Cantero-Nieto: None declared, José Alberto García-Gómez: None declared, Geno Robledé: None declared, Marta Trigo: None declared, Javier Martin Ibanez: None declared, Miguel A González-Gay Grant/Research support from: Prof. MA Gonzalez-Gay received grants/research support from: Abbvie, Mitsubishi Tanabe Pharma Corporation, Janssen Pharmaceutical, Chugai Pharmaceutical, Ono Pharmaceutical, Eisai Co., Ltd., Eli-Lilly, Nippon Kayaku Co., Ltd., Maruho Co., Ltd., Kaken Pharmaceutical Co., Ltd., Yuko Sugikoa: None declared, Kenji Mamoto: None declared, Tadashi Kato Speakers bureau: Abbvie, Astellas Pharma, Bristol-Myers Squibb, Chugai Pharmaceutical, Eisai, Janssen Pharmaceutical, Mitsubishi Tanabe Pharma Corporation, Ono Pharmaceutical, Pfizer Japan, Takeda Pharmaceutical.

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females. Only few data are available specifically focused on differences in drug use according to gender.

Objectives: To evaluate gender differences in treatment approaches in RA patients treated with bDMARDs (biological DMARDs).

Methods: We included RA patients aged ≥18 years, with disease duration ≥1 years, with a stable bDMARD treatment (≥12 months) in a monocentric cohort in the North-East of Italy. Social, demographic, and clinical features in addition to treatments were considered. To assess variables independently associated with gender, all variables achieving a p<0.20 in univariate analysis were included in a multivariate regression model.

Results: Among 721 RA patients, 514 patients were eligible for the analysis and 407 were females. Compared with males, females had a lower BMI, a higher DAS28, a higher number of conventional synthetic DMARDs (cDMARDs) used before the start of bDMARDs, a higher number of bDMARDs with different mechanism of action (MoA), a larger use of prednisone and a lower rate of combination with MTX (Table 1). After adjustment for confounding factors, females had an increased probability of prednisone and a lower rate of combination with MTX (Table 1). After adjustment for confounding factors, females had an increased probability of taking ≥2 DMARDs before bDMARDs (OR 2.21, 95% CI 1.25-3.93, p=0.007) and a lower BMI (per 5-unit increase, OR 0.70, 95% CI 0.56-0.87, p=0.001) compared to males (Figure 1).

Conclusion: In a cohort of Italian RA patients, females were treated with a higher number of cDMARDs before starting a bDMARD compared to males and a trend toward the use of more bDMARDs with different MoA. Further insight is needed regarding possible differences in the accessibility to bDMARD treatment and reasons for unsatisfactory treatment control in females.

Disclosure of Interests: None declared


THU0123 INFLUENCE OF AUTOIMMUNE VASCULITIS ON LUNG DISEASES IN RHEUMATOID ARTHRITIS – A POSTMORTEM CLINICOPATHOLOGICAL STUDY OF 161 PATIENTS

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Background: Complications of rheumatoid arthritis (RA) may modify the clinical course and symptoms of allied disorders leading to missed diagnosis or late recognition of associated diseases.

Objectives: The aim of this study was to determine the possible role of classic complications of RA: systemic autoimmune vasculitis (AV), AA amyloidosis (AAa), lethal cardiac insufficiency (CI), caused by endo-, myo- or pancarditis, with or without interstitial pneumonitis, furthermore lethal septic infection (SI) on prevalence and mortality of coexistent associated diseases: arteriosclerosis (Ath), hypertension (HT), type 2 diabetes mellitus (DM), and tuberculosis (Tb) with milary dissemination (mTb).

Methods: 234 non-selected autopsy patients with RA were studied. RA was confirmed clinically according to the criteria of the ARA. The presence of AV, AAa, CI and SI was determined at autopsy and confirmed by a detailed review of extensive histological material. The prevalence and mortality of associated diseases Ath, HT, DM, Tb or mTb were determined and analyzed retrospectively, reviewing the clinical and pathological reports.

The link between AV, AAa, CI or SI and Ath, HT, DM, Tb or mTb was analyzed by (χ²) test.

Results: RA was complicated by AV in 43 (18.4%), by AAa in 48 (20.5%), by CI in 15 (6.4%), and by lethal SI in 33 (14.1%) of 234 patients.

RA associated with severe Ath in 106 (45.3%), with HT in 41 (17.5%), with DM in 41 (17.5%), with Tb in 28 (11.9%) and with mTb in 9 (3.8%) of 234 patients.

As a basic disease Ath led to death in 61 (26.1% of 234), HT in 2 (0.9% of 41), DM in none (0% of 41) and Tb with mTb in 3 (1.3%) of 28 patients. Tb without milary dissemination was not lethal in our patient population.

The statistical links (’p’ values of significance) between complications of RA and prevalence or mortality of allied disorders are summarized in Table. (*) indicates a negative value of associations of inverse relationship.

Complications of RA

<table>
<thead>
<tr>
<th>Allied disorders in RA</th>
<th>AV n=43 of 234</th>
<th>AAa n=48 of 234</th>
<th>CI n=15 of 234</th>
<th>SI n=33 of 234</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Ath n=106 of 234</th>
<th>χ²=16.43*, p=0.01</th>
<th>χ²=10.04*, p=0.01</th>
<th>χ²=0.92*, p=0.33</th>
<th>χ²=5.03*, p=0.02</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ath lethal n=61 of 106</td>
<td>χ²=11.92*, p=0.00</td>
<td>χ²=11.04*, p=0.00</td>
<td>χ²=12.01*, p=0.00</td>
<td>χ²=11.27*, p=0.00</td>
</tr>
<tr>
<td>HT 41 of 234</td>
<td>χ²=1.30*</td>
<td>χ²=0.03*, p=0.00</td>
<td>χ²=0.00*, p=0.00</td>
<td>χ²=0.00*, p=0.00</td>
</tr>
<tr>
<td>HT lethal n=2 of 41</td>
<td>χ²=0.05*, p=0.87</td>
<td>χ²=1.16*, p=0.29</td>
<td>χ²=0.19*, p=0.65</td>
<td>χ²=0.01*, p=0.91</td>
</tr>
<tr>
<td>DM 41 of 234</td>
<td>χ²=0.00*</td>
<td>χ²=1.05*, p=0.30</td>
<td>χ²=0.92, p=0.00</td>
<td>χ²=0.01*, p=0.91</td>
</tr>
<tr>
<td>Tb 28 of 234</td>
<td>χ²=0.02, p=0.56</td>
<td>χ²=2.61*, p=0.00</td>
<td>χ²=0.33, p=0.70</td>
<td>χ²=0.01, p=0.56</td>
</tr>
<tr>
<td>Tb lethal n=3 of 28</td>
<td>χ²=0.02*, p=0.53</td>
<td>χ²=0.02*, p=0.53</td>
<td>χ²=0.01*, p=0.82</td>
<td>χ²=0.00*</td>
</tr>
<tr>
<td>mTb 9 of 28</td>
<td>χ²=0.08, p=0.70</td>
<td>χ²=0.08, p=0.00</td>
<td>χ²=0.01, p=0.53</td>
<td>χ²=0.00*</td>
</tr>
<tr>
<td>mTb lethal n=3 of 9</td>
<td>χ²=0.02, p=0.00</td>
<td>χ²=0.02*, p=0.00</td>
<td>χ²=0.01*, p=0.00</td>
<td>χ²=0.00*</td>
</tr>
</tbody>
</table>

Conclusion: The inverse correlations between AV, AAa, CI and Ath, HT, DM, Tb or mTb indicate that the prevalence and mortality of allied disorders were not influenced basically by the complications of RA. The consequently inverse and (in most cases) significant correlations between prevalence of AV, AAa, CI and SI the prevalence and mortality of Ath show that these are independent entities in RA. The AV, AAa, CI and SI are the most important complications of RA, and are characterizing severe forms of disease, mostly involving younger patients, with an earlier onset (without pronounced arteriosclerosis); while Ath is basically an age dependent phenomenon, characteristically present in RA patients with advanced age. RA patients with Ath may represent a special group of RA, characterized by lower incidence of AV, AAa, CI or SI, and a better prognosis.

Disclosure of Interests: None declared

Background: Rheumatoid arthritis increases the risk of cardiovascular disease (CVD). Less is known about the direct influence of CVD and CVD risk factors (RF) on RA outcomes, but higher comorbidity burden has been suggested to adversely affect RA treatment response.1

Objectives: We tested our hypothesis that CVD RFs influence RA disease activity and disability in RA.

Methods: The Ontario Best Practices Research Initiative (OBRI) is a clinical registry of RA patients followed in routine care. RA subjects with complete data to calculate disease activity according to the Disease Activity Score 28 (DAS28), Clinical Disease Activity Index (CDAI), 28 swollen joint count (SJC28) and functional status (Health Assessment Questionnaire Disability Index [HAQ-DI]) at cohort entry were selected. Patients were divided into mutually exclusive groups by baseline CVD status as: (1) no CVD/no CVD RFs; (2) CVD including coronary artery disease, myocardial infarction, cerebral vascular accidents, and peripheral arterial disease; (3) no CVD but CVD RFs including hypertension (HTN), dyslipidemia (DLD), diabetes (DM), or smoking. We performed linear regression analyses for each outcome, adjusted for baseline clinical and demographic variables, to determine the independent effect of CVD status on disease outcomes at baseline and one year follow-up.

Results: Of 2033 patients examined, 49.5% had no CVD, 5.4% had CVD and 45.1% had CVD RFs alone. The most common RF was HTN (33%) followed by DLD (19.7%), current smoking (17%), and DM (8.1%). At cohort entry, having a CVD RF was associated with significantly higher DAS28 (β 0.13, 95% CI 0.02-0.26, p 0.04) and HAQ-DI (β 0.16, 95% CI 0.10-0.23, p<0.0001). At one year, CVD RF was associated with worse DAS28 (β 0.17, 95% CI 0.05-0.30, p<0.01) and CDAI (β 0.96, 95% CI 0.05-1.87, p 0.04) but not HAQ-DI (β 0.03, 95% CI -0.02-0.08, p 0.17). Having higher number of CVD RF was associated with worse disease outcomes. No association between CVD status and swollen joint count was observed.

Conclusion: Even in the absence of CVD, traditional CVD RF are associated with greater RA disease severity and disability both at baseline and one year. Self-perceived impact of comorbidity (patient global assessment of health) may be driving this relationship. Moreover, patients with CVD RF may be more treatment-resistant, suggesting that co-management of CVD RF in RA patients may be beneficial on both fronts.

REFERENCES:

Abstract THU0125 Table 1. Multivariable linear regression of disease activity outcomes and functional status at one-year according to CVD status.

<table>
<thead>
<tr>
<th>CVD status</th>
<th>β (coefficient) (95% CI); p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N=1965</td>
<td></td>
</tr>
<tr>
<td>N=1965</td>
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<tr>
<td>N=1965</td>
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<td>N=1965</td>
<td></td>
</tr>
</tbody>
</table>

No CVD/RFs

Ref Ref Ref Ref

Ref Ref Ref Ref

CVD

0.12 (-) 0.50 (-) 0.44 (-) 0.09 (-)

0.14 (0.08), 0.37 1.45 (2.46) 0.61 (2.11), 0.19 0.02 (0.19), 0.10

CVD RFs/No

0.17 (0.05,0.30) 0.96 (0.05,1.87) 0.29 (-) 0.03 (-)

CVD

0.01 0.04 0.01 (0.00, 0.06) 0.02 (0.02,0.08) 0.17


Disclosure of Interests: Kungping Cui: None declared, Mohammad Movahedi: None declared, Claire Bombardier: Employee of the Ontario Best Practice Research Initiative (OBRI), Claire Bombardier Grant/research support from: Abbvie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Consultant for: AbbVie, Hospira, Janssen, Merck, Novartis, Pfizer Inc, Sanofi, Speakers bureau: Roche, Bindee

Kurya Consultant for: Advisory Board Member: Abbvie, Sanofi Genzyme, Eli Lilly, Pfizer Canada, Roche

THU0126 FACTORS AFFECTING THE DISCREPANCY BETWEEN PATIENT AND PHYSICIAN GLOBAL ASSESSMENT OF DISEASE ACTIVITY IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS OVER TIME

Pooneh Akhavan1, Mohammad Movahedi2, Claire Bombardier1, 2, 3

1University of Toronto, Mount Sinai Hospital, Rheumatology, Toronto, Canada; 2Toronto General Research Institute, University Health Network, Ontario Best Practices Initiatives, Toronto, Canada

Background: Rheumatoid Arthritis (RA) is a chronic disease that requires regular follow-ups over time. Physicians make treatment adjustments based on their evaluation of disease status and patients' response to treatment while patients' perception of disease activity may change over time.

Objectives: We aimed to assess the discrepancy between patient global assessment of disease activity and physician assessment of disease activity at baseline and after one year in patients with early RA. We also evaluated factors affecting this discrepancy at these two time points.

Methods: Patients enrolled in the Ontario Best Practices Research Initiative (OBRI), a prospective observational cohort of patients with RA who had disease duration of <12 months (early RA) and had visits both at baseline and after one year were included. The discrepancy between patient global assessment of disease activity (PTGA) and physician global assessment of disease activity (MDGA) was calculated by simple subtraction (PTGA-MDGA). The PTGA-MDGA was considered discordant which could be either positive or negative in favor of PTGA or MDGA. Linear regression analysis was used to assess factors affecting PTGA, MDGA, and PTGA-MDGA discrepancy at baseline and one year.

Results: A total of 460 patients with early RA were analyzed. Majority were female (72.4%) with mean (± SD) age of 57 years (±0.6). The discordance rate was 109 (24%) and 99 (21%) at baseline and one year, respectively. In the majority of the discordant cases, PTGA was higher (98 (90%) at baseline and 85 (86%) at one year). Discordant patients had significantly higher fatigue score, health assessment questionnaire disability index (HAQ-DI), pain score, PTGA, MDGA, tender joint, composite measures of disease activity and higher number of comorbidities at baseline.

Multivariable regression analysis showed that the higher PTGA is significantly associated with higher SJC, TJC and fatigue both at baseline and one year and with higher pain score only at one year. Similar associations were found for MDGA except fatigue which was not significant. Multivariable regression analysis showed that the higher discrepancy between PTGA and MDGA is associated significantly with lower SJC (β=–2.75), higher TJC (β=1.17), and higher fatigue (β=0.85) at baseline. At one-year follow-up, higher pain was the strongest factor (β=4.99) for affecting the higher PTGA-MDGA discrepancy compared with SJC (β=–1.65) and fatigue (β=1.24).

Conclusion: Significant discrepancy between PTGA and MDGA exists in about a quarter of patients with early RA at baseline and slightly less after one year. In the majority of these patients PTGA is higher over time. The number of active joints affects both assessments and this effect persists at one year. Clinicians should consider the above associations when making treatment decisions.


Disclosure of Interests: Pooneh Akhavan: None declared, Mohammad Movahedi: None declared, Claire Bombardier: Grant/research support from: Abbvie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Consultant for: AbbVie, Hospira, Janssen, Merck, Novartis, Pfizer Inc, Sanofi, Speakers bureau: Roche
IMMUNOGENICITY AND SAFETY OF 23-VALENT PNEUMOCOCCAL VACCINE IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS FROM 5-YEAR FOLLOW UP

Daria Buhanova, Boris Belov, Galina Tarasova, Marina Sergeeva, Yury Raysev, Galina Lukina, Natalia Demidova, Maria Cherkasova. V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation

Background: In rheumatology, comorbid infections have significant impact on patients' morbidity, mortality and quality of life. Prevention of infections is an integral part of supervision of these patients.

Objectives: The aim of the study is to investigate immunogenicity and safety of 23-valent polysaccharide pneumococcal vaccine (PPV-23) in patients with rheumatoid arthritis (RA) in a five-years period.

Methods: The study included 79 RA patients with ≥2 recent episodes of respiratory tract infections (bronchitis, pneumonia). 52 RA pts were treated with methotrexate (MT), 14 – with lefunomide (Lef), 13– with TNF-α inhibitors + MT. One dose (0,5 ml) of PPV-23 was administered subcutaneously without discontinuing MT/Lef or 28-30 days prior to initiation of TNF-α inhibitors. Control visits were scheduled as follows: at baseline (Visit 1), and in 1, 3, and every year after immunization. 39 out of 110 pts were followed for 24 months, 23 pts – for 36 months, 23 pts – for 48 months, and 18 - for 60 months. Standard clinical examination and lab tests were performed at each visit.

Levels of serum antibodies (AB) to Pneumococcal capsular polysaccharide were measured with VaccZymeTM PCP IgG 2 panels (The Binding Site Group Ltd, Birmingham, UK). Coefficient of post-immunization response (CPR) was determined for each patient as the ratio of AB levels at Visit II, III, IV, V, VI and VII to AB level at Visit I.

Results: 53 (67%) patients did not have any reactions to the vaccine, 26 (33%) patients indicated pain, swelling and hyperemia of the skin (diameter up to 2 cm) at the injection site of the vaccine, low-grade fever.

These typical reactions following vaccination are completely regressed within days without any additional treatment. They were not associated with RA therapy and did not require changes in ist schemes.

Table. AB dynamics in RA pts during 5-year FUP, Ms. ±

<table>
<thead>
<tr>
<th>Visit</th>
<th>Visit IV (12 month)</th>
<th>Visit V (24 month)</th>
<th>Visit VI (36 month)</th>
<th>Visit VII (48 month)</th>
<th>Visit VIII (60 month)</th>
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<tr>
<td>RA</td>
<td>82,20*</td>
<td>250,62*</td>
<td>298,70*</td>
<td>107,8</td>
<td>140,5</td>
</tr>
<tr>
<td>46,00</td>
<td>[167,70;316,96]</td>
<td>[175,99;420,81]</td>
<td>[98,2;2159,4]</td>
<td>[107,9;208,3]</td>
<td>[120,1;361,4]</td>
</tr>
</tbody>
</table>

*p<0,05

Conclusion: Thus, all given prove the sufficient immunogenicity and safety of 23-valent pneumococcal vaccine in RA patients after 5 years of follow-up, getting different therapeutic regimens.

Disclosure of Interests: None declared

THU0129

ASSESSMENT OF LONELINESS IN PATIENTS WITH INFLAMMATORY ARTHRITIS

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Background: Rheumatic disease and psychosocial status have bi-directional impacts on each other. Loneliness, as a component of psychosocial status, may be interrelated with affect and social support and may also be influenced by the disease itself in patients with inflammatory arthritis1.

Objectives: The aim of this study is to document loneliness and associated factors in patients with inflammatory arthritis. Effects of demographic and disease-related factors, functional status, affect, and social support on loneliness, and loneliness on functional status will be evaluated.

Methods: Consecutive patients with rheumatoid arthritis(RA), ankylosing spondylitis(AS), and psoriatic arthritis(PsA), meeting ACR, ASAS, and CASPAR criteria, respectively, were included in the study. Demographic data and general clinical parameters(Table 1) were identified for each patient. Beck depression and Beck anxiety inventory, revised multidimensional scale of perceived social support, HAQ-DI, and UCLA loneliness scale (ULS-8), all validated in Turkish population, were used for the assessments. Nonparametric comparison (Wilcoxon-Mann-Whitney and Kruskal-Wallis) and correlation(Spearman) tests were used to evaluate associations of demographic data, clinical parameters, and depression, anxiety, social support, HAQ-DI scores with ULS-8 score. Multiple regression models were generated for significant associations.

Results: Demographic data, general clinical features, functional status, and ULS-8 scores of disease groups are summarized in Table 1. Among demographic and general clinical parameters, higher number of total drugs and lower education were associated with significantly higher ULS-8 scores (data not shown). Although weak, there were significant correlations between ULS-8 and HAQ-DI, depression, anxiety, social support, and doctor global VAS scores (Table 2). Stronger correlations were observed between HAQ-DI and depression, anxiety, and patient global VAS scores (Table 2). Among demographic and general clinical parameters, only number of drugs was weakly associated with HAQ-DI score (rho=0.18, p=0.037). Two multiple regression models were generated for predicting HAQ-DI and ULS-8 scores. Depression, anxiety and patient global VAS scores remained significant for predicting HAQ-DI after multiple regression with covariates ULS-8, depression, anxiety, social support, patient global VAS scores, number of drugs used, and education status. The only independent predictor was the education status. ULS-8 score did not correlate with DAS28, CDAI, and SDAI in RA; BASDAI, BASFI, and ASDAS in AS; and number of swollen and tender joints, ESR, CRP, patient global, doctor global, pain, and fatigue VAS scores in PsA.

Conclusion: Loneliness is associated with depression, anxiety, lack of social support, and lower education but not with disease activity in patients with inflammatory arthritis. Self-report loneliness, can be a contributing factor to the disability of the inflammatory arthritis.

REFERENCE:

THU0130

INCIDENCE AND RISK FACTORS OF FALLING IN PATIENTS WITH RHEUMATOID ARTHRITIS

Rym Fakhfakh, Jguirim Mahbouba, Hibatallah Mosbeh, Abir Dghaies, Grassa Rim, Olfa Jmaa, Saoussen Zrour, Ismail Bejia, Mongi Touzi, Naceur Bergaoui. CHU Fattouma Bourguiba, Rheumatology, monastir, Tunisia

Background: People with rheumatoid arthritis (RA) may be at greater risk of falling than the non-RA population [1]. This increased falls risk may be due to RA disease-related impairments including pain, deformity and decreased muscle strength, as well as reduced functioning such as altered gait and a decline in postural stability.

Conclusion: Loneliness is associated with depression, anxiety, lack of social support, and lower education but not with disease activity in patients with inflammatory arthritis. Self-report loneliness, can be a contributing factor to the disability of the inflammatory arthritis.

REFERENCE:

Objectives: The aim of this study was to evaluate the prevalence of falls and its association with clinical data, disease-related outcomes and physical performance tests in patients with RA.

Methods: A cross-sectional study including patients with RA, followed in the Rheumatology Department over a period of 1 month in 2018. The following parameters were evaluated: clinical aspects; fall occurrence in the previous 12 months; pain on a visual analogue scale (VAS); RA disease activity score (DAS28); erythrocyte sedimentation rate (ESR); Functional capacity assessed by the Health Assessment Questionnaire (HAQ); anxiety and depression by the Hospital Anxiety and Depression Scale (HADS) and physical performance, assessed by 3 tests, the Timed Up and Go (TUG), one leg standing balance (OST) and sternal nudge test (SNT).

Results: Forty-eight patients were enrolled, the average age was 55.8 ± 13.9 and the sex ratio was 0.14. The average disease duration was 13.49 years ± 9.12. The average DAS28 was 4.63 ± 1.19 and HAQ was 0.77 ± 0.88. Falls were reported by 44.7% of patients: 27.7% had one fall and 17% had > 2 falls. Patients had a fractures history in 10.9% of cases and dislocations in 6.5% of cases. The HAQ (p=0.04) and c reactive protein (p=0.01) was associated with fall history; the other parameters (Gender, number of medications, age, disease activity and physical tests) showed no associations with history of falls. Physical performance was decreased to: 58.4% for TUG test, 61.7% for OST and 36.2% for SNT. The worst performance in physical tests (TUG, OST and SNT) was associated with older age, higher erythrocyte sedimentation rate, higher HAQ, and increased DAS28 (p<0.05). In addition, hips and especially knees involvement was significantly associated with TUG (p=0.03) and OST test (p=0.003). TUG test was significantly associated with depression (p=0.04). The OST test was associated with higher disease duration (p=0.004), VAS (p=0.006) and tender joints (p=0.001).

Conclusion: It was observed that the occurrence of falls is quite common in this population. The occurrence of falls in this sample of rheumatoid arthritis patients bears no relation to disease activity or physical performance tests. But, falls were associated with functional capacity.

Disclosure of Interests: None declared


THU0131 EFFECT OF METABOLIC SYNDROME ON THE COURSE OF RHEUMATOID ARTHRITIS AND CARDIOVASCULAR RISK

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Background: Both rheumatoid arthritis (RA) and metabolic syndrome (MS) have an inflammatory component in the pathogenesis and both aggravate cardiovascular risks.

Objectives: The aim is to study the effect of MS on the course of RA and the increase in cardiovascular risk in these patients.

Methods: 100 patients (men 7%, women 93%) aged 21 to 81 years (average age 55.12±14.5) with reliable RA were examined. High activity in DAS28 scale was observed in 68%, moderate - in 30%, low - in 2%, rheumatoid factor (RF) positivity - in 89%, ACCP - 81%. Disease-modifying anti-rheumatic drugs (DMARDs) were given to 60% of patients. Synovitis was present in 45% of patients. The prevalence of MS (NCEP/ATPIII criteria) was identified in 59 patients, according to the level of the ESR, CRP, the presence of the RF, the X-ray stage of RA. There were no differences in the range of received therapy, but the dose of prednisone was higher in the MS+ group (7.8±3.5 vs 6.4±3.69, p<0.05).

Systolic blood pressure (BP) was higher in the MS+ group (128.3±17.3) vs MS- (119.3±15.9). The level of BP correlated (p<0.05) with the severity of pain. The verified AH was present in 42 (71.2%) patients of the MS+ group (1 stage -2, 2 stage -24, 3 stage -16 patients) and in 3 (7.3%) patients of the MS- group (1 stage in 1 patient, 2 stages in 2 patients). The cholesterol level was higher in the MS+ group 5.1±1.1 compared with the MS- group 4.6±0.6 (p<0.01). There was observed a positive correlation (p<0.01) in increasing the mass index of the left ventricle myocardium according to echocardiogram. In patients with MS+, hypertrophy of the left ventricular myocardium was detected according to echocardiogram even with a normal level of BP.

Conclusion: The presence of MS in patients with RA is associated with a higher activity of RA most of all because of pain syndrome. The same time, pain syndrome correlates with the level of blood pressure and MS.

The combination of MS and RA leads to an increase of cardiovascular risk factors: cholesterol level and myocardial hypertrophy, which causes the need of using the echocardiography for this group of patients.

REFERENCE: [1] rheumatoid arthritis, metabolic syndrome.

Disclosure of Interests: None declared


THU0132 EVALUATION OF CARDIOVASCULAR RISK FACTORS IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH BIOLOGICAL AGENTS: 3-MONTH FOLLOW-UP

Giorgos Papamichail1, Theodora Markateli2, Athanasios Georgiadis2, Vasilios Xydis3, Haralampos Milionis1, Alexandra Drosos1, Paraskevi Voulgari1, Internal Medicine, University of Ioannina, Greece, Department of Internal Medicine, Medical School, University of Ioannina, Ioannina, Greece, Ioannina, Greece; 2Rheumatology Clinic, University of Ioannina, Ioannina, Greece, Department of Internal Medicine, Medical School, University of Ioannina, Ioannina, Greece; 3Radiology, University of Ioannina, Greece, Department of Radiology, Medical School, University of Ioannina, Ioannina, Greece

Background: Systemic inflammation is an additional and independent predictor of cardiovascular disease (CVD) in rheumatoid arthritis (RA). It is worth mentioning that lipid levels, blood pressure and other major risk factors of CVD constitute a wide field of investigation in case of treatment with biological disease-modifying anti-rheumatic drugs (DMARDs).

Objectives: The aim of this study is to assess the impact of biological agents on markers of CVD risk in patients with RA.

Methods: This is a prospective, observational study which included biologic-naive RA patients treated with synthetic DMARDs, who had a negative history of CVD. Thirty-one patients and 31 healthy matched-controls (for gender, age and smoking) were compared for total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c), triglycerides (TGs), Apolipoprotein A1 (ApoA1), Apolipoprotein B (ApoB) and Lipoprotein A (LpA). Additionally, an ultrasonographic measurement of intima-media thickness (IMT) of carotids was performed by an experienced sonographer to all patients in order to detect the presence of atherosclerosis at baseline. Furthermore, in a subgroup of 19 of these 31 RA patients, the parameters we previously reported (except for IMT) were compared between baseline and a 3-month follow-up.

No significant difference in mean BMI and blood pressure was observed between the RA patients and controls (except for IMT). There was also a reduction in mean systolic blood pressure (15.44) vs 61.68(15.3) and 163.16(28.89) vs 173.11(29.65) respectively; p<0.05]. There was also a decrease in mean diastolic blood pressure (9.74) vs 61.11(10.3) and 101.32(18.64) vs 111.21(20.12) respectively; p<0.05]. ESR (25.53(18.57) vs 19.84(16.44), p<0.05) and DAS28 score (3.41(1.14) vs 2.62(1.12), p<0.05).

Results: As regards the demographic characteristics of 31 RA patients, the mean (SD) age was 54.7 (14.05) years, disease duration was 4.5 (1.3) years, there were 11 (35.5%) men and 20 (64.5%) women and 6 (31.6%) smokers. As far as the immunological profile of patients is concerned, there were 11 (35.5%) patients of the MS- group (1 stage in 1 patient, 2 stages in 2 patients). The presence of MS in patients with RA is associated with a higher activity of RA most of all because of pain syndrome. The same time, pain syndrome correlates with the level of blood pressure and MS.

The combination of MS and RA leads to an increase of cardiovascular risk factors: cholesterol level and myocardial hypertrophy, which causes the need of using the echocardiography for this group of patients.

REFERENCE: [1] rheumatoid arthritis, metabolic syndrome.

Disclosure of Interests: None declared

TENDERNESS CAN BE REGARDED AS A SIGN OF INFLAMMATION IN RHEUMATOID ARTHRITIS

Irina Gessl1, Mihaela Popescu2, Victoria Schimpl1, Gabriela Supp1, Michael Zauner1, Michala Loiskandl1, Martina Durechova1, Josef S. Smolen1, Daniel Aletaha1, Peter Mandl3, I. Medical University of Vienna, Department of Medicine III, Division of Rheumatology, Vienna, Austria; 2Université de Montréal, Montreal, Canada;

Background: In inflammatory joint diseases, joint swelling is regarded as a sign of inflammation, which is associated with structural progression [1–3]. However, the significance of tenderness without swelling is unclear.

Objectives: To determine whether clinical tenderness can be considered a sign of inflammatory joint activity in patients with rheumatoid arthritis (RA), osteoarthritis (OA), or psoriatic arthritis (PsA).

Methods: 3624/50 patients respectively with RA, OA and PsA were included in the study. Each patient underwent clinical examination, followed by an ultrasound examination of bilateral MCP 1-5 (metacarpophalangeal),PIP 1-5 (proximal interphalangeal) joint and wrists; the sonographer was blinded to clinical data. On clinical examination synovial swelling and tenderness were evaluated using a binary scoring method, and tender, non-swollen joints (TNS) were identified. Grey-scale signs of synovitis (GS) and Power Doppler signal (PD) were evaluated using a semiquantitative grading system. Differences of PD signals between groups (RA vs. OA, RA vs. PsA, TNS vs. non-tender non-swollen joints) were calculated by Chi-Square test. Furthermore, joints of RA and PsA patients were tracked back for up to 6 years to identify the time point of the last swelling of that respective joint. Kaplan-Meier estimates for the occurrence of the last time point of swelling were compared between PD positive and PD negative TNS joints.

Results: TNS joints more often showed PD signal in RA patients as compared to OA and PsA (18.7% vs. 11.5% vs. 9.2%, respectively, p=0.015 for RA vs. OA; p=0.01 for RA vs. PsA). TNS joints were significantly more often PD positive as compared to non-tender non-swollen joints (18.7% vs. 10.3% respectively, p<0.01) in RA, but not in PsA (9.2% vs. 7.6%, P=0.54) or OA (11.5% vs. 10.2%, P=0.72) (fig. 1). Kaplan-Meier analysis revealed a significantly shorter time period to last observed swelling in PD positive as opposed to PD negative TNS joints in both RA (45.2 vs. 65.5 months, p=0.017) and PsA (20.6 months vs. 107.7 months, p<0.001), however we found no difference in GS positive vs. negative TNS joints.

Conclusion: The results of this study confirm the current practice of considering tenderness a sign of active inflammation in RA, but imply that this may not be the case in PsA or OA. The fact that shorter time to last swelling was associated with positive PD in TNS joints suggests that, at least in RA, tenderness might reside after prior clinical swelling has resolved.

REFERENCES:

Abstract THU0133 – Figure 1. Power Doppler signals of tender non-swollen joints compared to non-tender non-swollen joints in rheumatoid arthritis (RA), psoriatic arthritis (PsA) and osteoarthritis (OA).

Disclosure of Interests: Irina Gessl Grant/research support from: Travel Grant, Mihaela Popescu; None declared, Victoria Schimpl: None declared, Gabriela Supp: None declared, Michael Zauner: None declared, Michala Loiskandl: None declared, Martina Durechova: None declared, Josef S. Smolen Grant/research support from: AbbVie, Eli Lilly, Janssen, MSD, Pfizer, Roche, Consultant for: AbbVie, Amgen, Astra-Zeneca, Astro, Celgene Corporation, Celtrion, Eli Lilly, Glaxo, ILTOO, Janssen, MedImmune, MSD, Novartis, Pfizer, Roche, Samus, Sanofi, UDB, Speakers bureau: AbbVie, Amgen, Astra-Zeneca, Astro, Celgene Corporation, Celtrion, Eli Lilly, Glaxo, ILTOO, Janssen, MedImmune, MSD, Novartis, Pfizer, Roche, Samus, Sanofi, UDB, Daniel Aletaha Grant/research support from: AbbVie, Bristol-Myers Squibb, and MSD; Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medac, Merck, MSD, Pfizer Inc, Roche, and UCB; Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medac, Merck, MSD, Pfizer Inc, Roche, and UCB; Peter Mandl: None declared


THU0134 COMORBIDITIES IN >5000 PATIENTS WITH RHEUMATOID ARTHRITIS INITIATING TREATMENT WITH METHOTREXATE IN ROUTINE CARE: PREVALENCE AND IMPACT ON TREATMENT OUTCOMES. AN OBSERVATIONAL COHORT STUDY FROM DANBIO

Bente Glintborg1, Niels Steen Krogh1, Frank Mehnert2, Merete L. Heltland3, 1The DANBIO registry and the Danish Departments of Rheumatology, Copenhagen, Denmark; 2Department of Clinical Epidemiology, Aarhus University Hospital, Aarhus, Denmark

Background: Methotrexate remains the anchoring drug for the treatment of rheumatoid arthritis (RA). Patients with RA often have comorbidities e. g. diabetes or pulmonary disease. Although methotrexate has been used for decades, little is known about the impact of various comorbidities on treatment outcomes.

Objectives: To describe the prevalence of comorbidities in csDMARD naïve RA patients initiating treatment with methotrexate in routine care and to explore the impact of common comorbidities on methotrexate treatment outcomes (achieving remission and adherence to treatment).

Methods: Observational cohort study based on the Danish nationwide quality registry, DANBIO. Adult RA patients who started treatment with methotrexate (oral or injection) as first csDMARD year 2010-2017 and who had been followed since onset of disease with regular controls were included. Concomitant treatment with other DMARDs were allowed. Treatment outcomes after ~6 months of treatment were identified in DANBIO. Data were censored by April 2018. Seven different comorbidities (Figure) prior to start of methotrexate were identified in the national patient registry (NPR) through linkage by social security numbers.

Impact of each comorbidity was explored as 1) overall methotrexate treatment retention rate and 2) DAS28 remission rate (after 6 months’ treatment). Analyses were by Cox- and logistic-regression analyses (adjusted for gender and age). The comorbidities were included one by one in the models. Finally, similar analyses were performed summed for all the seven comorbidities as any comorbidity yes/no.

Results: 5828 patients were included (66% female, median age 61 (IQR 51-70) years), whereas 906 (15.5%) had ≥1 of the predefined

Disclosure of Interests: Bente Glintborg: None declared, Niels Steen Krogh: None declared, Frank Mehnert: None declared, Merete L. Heltland: 1. The DANBIO registry and the Danish Departments of Rheumatology, Copenhagen, Denmark; 2Department of Clinical Epidemiology, Aarhus University Hospital, Aarhus, Denmark

comorbidities (63% female, median age 68 (60-74) years). Only 70 patients (1.4%) had ≥2 comorbidities. Patients with comorbidities had increased withdrawal rate of methotrexate with hazard ratios ranging from 1:10-2.06 (Figure). Similarly, patients with comorbidities had poorer remission rate with odds ratios ranging from 0.38-0.74 except for previous cancer. **Conclusion:** In this nationwide cohort of >5000 RA patients treated with methotrexate in routine care, approximately 15% of patients had comorbidities at treatment start. Patients with comorbidities had higher rate of withdrawal and poorer remission rates. This warrants specific attention when treating these patient groups in routine care. **Acknowledgement:** Thank you for the Danish departments of Rheumatology for reporting to DANBIO

**Disclosure of Interests:** Bente Glintborg Grant/research support from: Bio-sung Bioepis, MSD, AbbVie, Roche, Novartis, Biogen, Pfizer, Consultant for: Eli Lilly, Speakers bureau: Orion Pharma, Biogen, Pfizer, CellTrion, Merck, Samsung Bioepis


**THU0135**

DETERMINANTS OF DISCORDANCE IN PATIENT’S AND PHYSICIAN’S GLOBAL ASSESSMENTS OF DISEASE ACTIVITY OF RHEUMATOID ARTHRITIS IN THE “REAL” STUDY – BRAZIL

Maria Fernanda Guimarães1, Maria Raquel Pinto1, Gustavo Resende3, Carla Machado1, Ana Beatriz Vargas-Santos3, Cleandro Albuquerque4, Manoel Bertolo5, Paulo Louzada Jr 6, Rina Giorgi9, Karina Bonfiglioli9, Maria de Fátima Sauma13, Ivanio Pereira13, Claiton Brenol12, Murilo Filho1, Maria Fernanda Guimarães1, Maria Raquel Pinto1, Gustavo Resende3, Carla Machado1, Ana Beatriz Vargas-Santos3, Cleandro Albuquerque4, Manoel Bertolo5, Paulo Louzada Jr 6, Rina Giorgi9, Karina Bonfiglioli9, Maria de Fátima Sauma13, Ivanio Pereira13, Claiton Brenol12, Murilo Filho1

**Background:** Discordance between the patient's global assessment of disease activity (PGA) and examiner’s global assessment (EGA) has been described in rheumatoid arthritis (RA) (1,2). Understanding the reasons for this discrepancy is essential in the context of treat-to-target treatment strategy.

**Objectives:** To assess the determinants of PGA and EGA and factors associated with discordance between them.

**Methods:** The REAL study included RA patients from Brazilian public health centers. Clinical, laboratory and outcomes measures were collected. PGA and EGA were rated on a visual analog scale and analyzed. Three groups were defined: no discordance (a difference between PGA and EGA within 3 cm), positive discordance (PGA exceeding EGA by >3 cm), and negative discordance (PGA less than EGA by >3 cm). Multivariate regression analysis was used to identify determinants of PGA and EGA and their discordance.

**Results:** 1151 patients (62.5% female, mean age 56.7 years and median disease duration of 12.7 years) were enrolled. Two factors were associated with PGA in the final multivariate model: one point increase in the pain scale (PS) leads to an increase of 0.62 in PGA; one point increase in HAQ increases by 9.25 points the PGA. The factors associated with EGA were: PS, number of tender and swollen joints (NTJ and NSJ), RF, ESR, CRP and use of corticosteroids. Discordance between patient and physician was found in 30.52%: positive discordance (PD) in 24.6% and negative discordance (ND) in 5.92%. An increase of one point in the NSJ was associated with a 12% increase in the chance of ND. The chance of PD increased by 90% and 2% for each unit increased in HAQ and PS respectively. Finally, the chance of PD decreased by 3% for each point increased in NTJ and by 15% for each point increased in NSJ.

**Conclusion:** In one-third of the assessments, there was disagreement between patient and physician assessments of global disease activity in rheumatoid arthritis and association with work productivity. Arthritis Res Ther. 2016; 18:114.

**REFERENCES:**


TNF INHIBITORS IN PREGNANCY: STOP, REDUCE OR CONTINUE? – OBSERVATIONS FROM A PREGNANCY OUTPATIENT CLINIC

Isabell Haase1, Susanna Spaethling-Mestekemper2, Matthias Schneider1, Rebecca Fischer-Betz1,2, Heinrich-Heine-University Düsseldorf, Polyclinic of Rheumatology and Hiller Research Unit, Düsseldorf, Germany; 1Rheumaparxis, Munich, Germany

Background: Women with active Rheumatoid Arthritis (RA) are more prone to relapses and complications during pregnancy. The potential risks of disease activation and treatment during gestation should be weighed in a shared decision prior to conception. An increasing number of women who wish to conceive are being treated with TNF inhibitors (TNFi). Some wish to discontinue or at least reduce therapy while pregnant and require information on opportunities and risks.

Objectives: To study the outcome of pregnancies in women with RA who either discontinued, reduced or maintained their TNFi treatment after conception.

Methods: Pregnancies from an outpatient pregnancy clinic were evaluated before conception, during each trimester and postpartum. Clinical characteristics, disease activity (DAS28-CRP), medication use and pregnancy outcome were analysed. A flare was defined as increase in clinical activity characteristics, disease activity (DAS28-CRP), medication use and pregnancy outcome were analysed. A flare was defined as increase in clinical activity leading to intensified treatment (new treatment with prednisolone or increase in dosage ≥5 mg/day) and/or treatment with intraarticular glucocorticoids and/or (re-)treatment with DMARDs/TNFi. All women received extensive counselling before pregnancy based on current knowledge and subsequently decided to continue or stop TNFi at conception. If they stayed on TNFi and were in remission, women received the suggestion to stretch the therapy intervals in a disease activity guided manner. These real-world data will help to provide women with comprehensive advice on treatment options and risks regarding TNFi therapy at conception.

Results: After exclusion of one miscarriage, 56 completed pregnancies were enrolled and grouped according to their decision to stop (group 1) or continue (group 2) TNFi therapy during pregnancy. The latter were subdivided into those who could stretch the therapy intervals (group 2a) and those who could not (group 2b). Group 1 also contained seven women who received Tocilizumab or Rituximab until conception. Despite low disease activity (DAS ≤3.2) at conception in all groups, a higher flare rate during pregnancy and postpartum was observed after discontinuation of TNFi. In addition, a higher dose of oral prednisolone and more frequent intraarticular therapy was reported in group 1 (table 1). Postpartum, 38.9% restarted TNFi therapy. About half of the women who chose to stay on therapy during gestation were able to stretch the injection interval of their TNFi, which was either Adalimumab (every 3.0 weeks), Certolizumab (median every 4.0 [min 4.0, max 5.0] weeks) or Etanercept (median every 3.0 [min 2.0, max 6.0] weeks) (Table 2). Relapse rate as well as prednisolone consumption was comparable between group 2a and group 2b.

Conclusion: Women with RA who discontinue TNFi at conception face a higher risk of flares during pregnancy and often have an increased demand for steroids to control disease activity. When in remission under ongoing TNFi therapy during pregnancy, it seems possible and safe for women to reduce the frequency of injections in a disease activity guided manner. These real-world data will help to provide women with comprehensive advice on treatment options and risks regarding TNFi therapy at pregnancy counselling.

Disclosure of Interests: Isabell Haase: None declared, Susanna Spaethling-Mestekemper: None declared, Matthias Schneider Grant/research support from: GlaxoSmithKline and UCB Pharma for performing the LuLa-study., Speakers bureau: Chugai, Rebecca Fischer-Betz Grant/research support from: GlaxoSmithKline and UCB Pharma for performing the LuLa-study.

RHEUMATOLOGISTS’ ADHESION TO THE TREAT-TO-TARGET PRINCIPLE IN EARLY RA PATIENTS WITHIN THE PRAGMATIC CARERA TRIAL: ROOM FOR IMPROVEMENT?

Veerle Stouten\(^1\), Diederik De Cock\(^1\), Sofia Pazmino\(^2\), Kristien Van der Elst\(^2\), Johann Joly\(^1\), Delphine Bertrand\(^1,2\), Rene Westhovens\(^1,2\), Patrick Verschueren\(^1,2\), On behalf of the CareRA study group. \(^1\)KU Leuven, Skeletal Biology and Engineering Research Center, Department of Development and Regeneration, Leuven, Belgium; \(^2\)University Hospitals Leuven, Rheumatology, Leuven, Belgium

**Background:** Treating to a predefined target is a principle adopted in guidelines to treat rheumatoid arthritis (RA). It is currently the most efficient strategy to control disease activity, but its implementation in daily clinical practice remains challenging.

**Objectives:** To evaluate rheumatologists’ adherence to a treat-to-target (T2T) approach at a threshold of low disease activity (DAS28CRP<3.2) in patients with early RA during the 2-year Care in early RA (CareRA) study.

**Methods:** CareRA is an investigator-initiated pragmatic multicentre trial, in which patients with early RA and naïve to conventional synthetic disease modifying anti-rheumatic drugs (csDMARD) were included (n=379). Participants were randomized to different remission induction schemes consisting of a csDMARD combination or methotrexate (MTX) monotherapy with and without a prednisone tapering down scheme. Following the T2T approach, specific treatment adaptations had to be performed in case of DAS28CRP<3.2 during the first study year, unless a predefined reason not to intensify treatment was provided. As first step, dose of MTX had to be increased from 15mg to 20mg weekly. As second step, dose of the other csDMARD was escalated in the combination arms and lefunomide was added in the MTX monotherapy arms. From week (w)52 onwards, further T2T was advised but type of treatment adaptation was left at the rheumatologists’ discretion. Adherence to this T2T approach was defined as performing a dose escalation or changing/adding DMARD medication in case of DAS28CRP>3.2 and was evaluated at every study visit during 2 years. Additionally, remission (DAS28CRP<2.6) rates at w104 were compared between patients in which T2T was applied at early RA patients not always treated to target. Only data from patients for which DAS28-CRP scores were available were taken into account to evaluate the low disease activity state.

**Results:** The proportion of patients with DAS28CRP<3.2 was 26% (93/365) at w8, but decreased to a stable average of 16% on the following visits and further diminished to 10% (30/303) at w104. The frequency of T2T adherence in these patients varied from 59% (55/93) at w8 to 17% (5/30) at w104 (Figure 1). The most frequent reason not to intensify treatment during the first study year was that rheumatologists considered the disease already well-controlled. This reason was reported in 50% of non-adherent cases at w8, in 15% at w16, 14% at w28, and 24% at w40. The second most frequently given reason for non-adherence during the first study year was that giving glucocorticoids or NSAIDs temporarily was preferred over changing DMARDs, as reported in 3% of cases at w8, 15% at w16, 27% at w28, and 35% at w40. T2T was applied at all visits in 41 out of 110 (37%) patients needing at least 1 adaptation during the 2-year trial. Of these 41 patients, 36 (88%) were in remission at w104, while of the 69 patients not always treated to the T2T principle, 40 (58%) were in remission at the end of the 2-year trial (p=0.001).

**Conclusion:** This study shows the difficulty of applying T2T strictly, both with and without a fixed protocol to follow. In less than half of patients theoretically in need of a treatment adaptation, treatment was intensified at all visits during the first 2 years of treatment. In the majority of cases rheumatologists gave as reason for overruling the T2T guidance that they estimated disease activity to be sufficiently controlled. However, patients in which the T2T principle was applied strictly, showed higher remission rates after 2 years of treatment.

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**Disclosure of Interests:** None declared


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**Table 1. Lipid profile in RA patient with and without IR**

<table>
<thead>
<tr>
<th>Lipid parameters</th>
<th>1 group</th>
<th>2 group</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IR (+)</td>
<td>IR (-)</td>
<td></td>
</tr>
<tr>
<td>TC, mmol/l</td>
<td>5.5 [4.6;6.5]</td>
<td>5.2 [4.3;5.9]</td>
<td>0.16</td>
</tr>
<tr>
<td>HDL-C, mmol/l</td>
<td>1.7 [1.3;1.9]</td>
<td>1.7 [1.6;2.1]</td>
<td>0.25</td>
</tr>
<tr>
<td>LDL-C, mmol/l</td>
<td>3.4 [2.5;4.2]</td>
<td>2.9 [2.1;3.5]</td>
<td>0.12</td>
</tr>
<tr>
<td>TG, mmol/l</td>
<td>1.3 [0.8;2.2]</td>
<td>0.9 [0.7;1.1]</td>
<td>0.007</td>
</tr>
<tr>
<td>Non-HDL, mmol/l</td>
<td>4.0 [2.9;4.9]</td>
<td>3.2 [2.6;3.8]</td>
<td>0.09</td>
</tr>
<tr>
<td>TG/HDL-C ratio</td>
<td>0.8 [0.5;1.3]</td>
<td>0.5 [0.4;0.7]</td>
<td>0.01</td>
</tr>
</tbody>
</table>

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**THU0139 IS ADDING ANTI-CARP OR ANTI-PADI4 BENEFICIAL FOR DIAGNOSIS OF RHEUMATOID ARTHRITIS?**

Boogdan Kolar\(^2\), Magdalena Drylewik\(^2\), Marek Ciesla\(^1\), Maria Magdari\(^2\)

\(^1\)University of Rzeszow, Faculty of Medicine, Rzeszow, Poland; \(^2\)Medical University of Lublin, Department of Rheumatology and Connective Tissue Diseases, Lublin, Poland

**Background:** Post-translatory modification (PTM), such as protein citrullination or homocitrullination (cargamylation) are key issues for the development of RA. There are known more than 300 PTMs. Some of them such as homocitrullination, are of chemical origin, but most of them (over 200) are of enzymatic origin. ACPA, anti-PADI4, anti-CarP and indirectly
RF are originated as a result of such post-translational modifications [1]. From the above-mentioned RA markers only synthesis of anti-CarP is a result of chemical protein modification. The synthesis of anti-PADI4 may facilitate the production of citrullinated proteins and contribute to the formation of ACPA. All of the above markers appear before RA onset [2].

Objectives: The aim of our study is to discover the potential utility of using additional markers (anti-CarP and anti-PADI4) in RA diagnosis.

Methods: 121 RA patients, 82.4% female, aged 52.5±12.3 years (mean ±SD) and 30 healthy controls (HC), 76.7% female, aged 53.2±8.1 years, were enrolled in the study. ACPA, RF, anti-CarP and anti-PADI4 antibodies were determined in serum by enzyme-linked immunosorbent immunoassay (ELISA).

Results: The markers positivity rate was 85.95%, 67%, 55.37% and 46.28% in ACPA, RF, anti-PADI4 and anti-CarP respectively. Among ACPA negative patients we found 44.44% and 16.67% anti-CarP and anti-PADI4 positive results respectively. The data concerning ACPA are gathered in Table 1.

RA patients, n=121

<table>
<thead>
<tr>
<th>RA markers positivity</th>
<th>ACPA(+), n=103</th>
<th>ACPA(+), n=18</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-CarP(+)</td>
<td>48 (46.6%)</td>
<td>8 (44.4%)</td>
</tr>
<tr>
<td>RF(+)</td>
<td>77 (74.6%)</td>
<td>4 (22.2%)</td>
</tr>
<tr>
<td>Anti-PADI4(+)</td>
<td>64 (62.4%)</td>
<td>4 (22.2%)</td>
</tr>
<tr>
<td>Anti-CarP(+) and RF(+)</td>
<td>41 (39.1%)</td>
<td>4 (22.2%)</td>
</tr>
<tr>
<td>Anti-CarP(+) and anti-PADI4(+)</td>
<td>33 (32.0%)</td>
<td>4 (22.2%)</td>
</tr>
<tr>
<td>RF(+) and anti-PADI4(+)</td>
<td>54 (52.4%)</td>
<td>4 (22.2%)</td>
</tr>
<tr>
<td>anti-CarP(+) and RF(+) and anti-PADI4(+)</td>
<td>30 (29.3%)</td>
<td>2 (11.1%)</td>
</tr>
</tbody>
</table>

Table 1. The profile of anti-CarP, RF, anti-PADI4 positivity in ACPA(+) and ACPA(-) RA patients.

In HC group we found 0%, 0%, 7.14% and 7.14% positivity in ACPA, RF, anti-PADI4 and anti-CarP respectively. We found 91.7% positivity for ACPA(+) or anti-CarP (+) vs 88.4% for ACPA(+) or RF(+).

Conclusion: The measurement of anti-CarP antibodies may be useful in RA diagnosis. The positivity for ACPA/anti-CarP is even higher than ACPA/RF. This might be caused by the similarity of the origins of ACPA and RF (enzymatic citrullination), while anti-CarP origin is different (chemical carboxylation). It is known that anti-CarP appears years before RA onset and might be used as a potential biomarker for pre-RA diagnosis. We didn’t confirm the usefulness of anti-PADI4 as RA biomarker.

REFERENCES:

Disclosure of Interests: Bogdan Kolarz: None declared, Magdalena Drygelska: None declared, Marek Ciesla: None declared, Maria Majdan: None declared, Viktorko Korendovych:1,1, Radovan Vasko1, Elena Nikiphorou2, Jan-Gerd Rademacher1, Gerhard A Müller1, Peter Korsten1. 1University Medical Center Göttingen, Department of Nephrology and Rheumatology, Göttingen, Germany; 2Whittington Hospital, London, United Kingdom

Background: Rheumatoid arthritis (RA) is characterized by symmetrical involvement of small and large joints. New treatment modalities have not only allowed to achieve clinical remission or low disease activity, but also to halt the radiographic progression of joint destruction. In some patients, the disease progresses and leads to joint destruction despite treatment with disease-modifying antirheumatic drugs (DMARDs). Occasionally, wrist arthritis leads to severe destruction of carpal bones with ankyles, so-called ‘os carpale’. Severely destructive wrist arthritis in an asymmetrical, unilateral pattern has only rarely been reported in the literature and has not been systematically assessed before (1). A severely destructive yet often symmetrical arthritis has been described in seronegative RA patients (2).

Objectives: To systematically analyze the presence of severely destructive unilateral wrist arthritis in a single-center, seropositive RA population and to identify risk factors for its development.

Methods: This is a single-center, retrospective cohort study using routine clinical data. We performed a database search of our RA population for the presence of rheumatoid factor (RF) and/or anti-CCP antibodies (ACPA) from 2011 to 2017. Radiographs were assessed independently by two investigators for the presence of severely destructive unilateral wrist arthritis. Discrepancies were resolved by discussion. Epidemiological data including age, gender, disease duration, occupation, dexterity and smoking status were recorded. Patients with psoriasis, a family history of psoriasis or postramutic osteoarthrosis were excluded. Past and current treatments were recorded. Conventional radiographs of the hands were scored using the modified Sharp score, magnetic resonance images were examined if available.

Results: We identified 1247 patients with either positive RF, ACPA, or both. After exclusion of non-RA diagnoses and radiograph review, 17 eligible patients were included in the study. Of these, 7 were excluded because of incomplete clinical data. All of the remaining ten patients were female (100%). Median age was 58.1 years (33-70), median disease duration was 15.8 years (1-22). Seven patients were right-handed, one was left-handed, in two patients, dexterity was not known. Six patients were smokers, two patients were non-smokers, in two patients, smoking status was not known. Median ACPA levels were 134.6 IU/mL (normal range <5). Median RF 54.2 IU/mL (NR <16). All but two patients were positive for both antibodies; in three patients, ACPA were only mildly elevated (6, 11, and 14, respectively). 6/7 (75%) patients with severe destruction were smokers. In 5/7 (71.4%) right-handed patients, destruction occurred in the dominant wrist, whereas in 2/7 (28.6%) right-handed patients, destruction occurred in the non-dominant wrist.
handed patients, destruction occurred in the non-dominant wrist. Patients received a mean number of 4.7 DMARDs.

**Conclusion:** Severely destructive unilateral wrist arthritis represents a rare phenotype of RA. In our cohort, this type of joint involvement was only present in women, it occurred primarily in the dominant hand (75%), and in smokers (75%). The mean number of used DMARDs was very high. Further studies for assessing the prevalence of this entity, also in sero-negative patients, are required.

**REFERENCES:**


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**THU0141**

**LOW-ENERGY FRACTURES IN RHEUMATOID ARTHRITIS – ASSOCIATIONS WITH GENES AND CLINICAL CHARACTERISTICS**

Lotta Ljung1 2, Kristina Wiberg1, Susanna Järvelin1,2, Lotta Ljung1,2, Kristina Wiberg1, Lisbet Arlés1, Solbritt Rantapää Dahlqvist2.

1Karolinska Institutet, Clinical Epidemiology Section, Department of Medicine, Stockholm, Sweden; 2Umeå University, Department of Public Health and Clinical Medicine/Rheumatology, Umeå, Sweden

**Background:** Patients with rheumatoid arthritis (RA) have increased risk of osteoporosis and low-energy fractures. Several genes associated with bone mineralization, osteoporosis or risk of fracture in the general population have been identified.

**Objectives:** To analyse the association between nine selected SNPs and the risk of low-energy fracture, taking clinical patient characteristics into account.

**Methods:** We identified a cohort of patients (n=896, 70% women, age at inclusion 60±14.8 years) with RA according to ACR criteria from the capture area of the register of Umeå injury database, Umeå, Sweden, which enabled identification of low-energy fractures (n=254). The follow-up (mean 8.8±6.1 years, total 7928 person-years) started two years after RA diagnosis but not earlier than January 1, 1993 and ended at the first of December 31, 2011, death, or the first low-energy fracture. Nine SNPs were analysed in all patients with available DNA-samples (n=667) using KASP genotyping assays (LGc genomics Ltd, Hoddesdon, UK):

<table>
<thead>
<tr>
<th>SNP</th>
<th>Frequency</th>
<th>HR1</th>
<th>95% CI</th>
<th>HR2</th>
<th>95% CI</th>
<th>HR3</th>
<th>95% CI</th>
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<tbody>
<tr>
<td>rs3801387</td>
<td>42.6%</td>
<td>1.63</td>
<td>1.48</td>
<td>1.80</td>
<td>1.63</td>
<td>1.97</td>
<td>1.74</td>
</tr>
<tr>
<td>rs6666455</td>
<td>42.6%</td>
<td>1.63</td>
<td>1.48</td>
<td>1.80</td>
<td>1.63</td>
<td>1.97</td>
<td>1.74</td>
</tr>
<tr>
<td>rs3736228</td>
<td>42.6%</td>
<td>1.63</td>
<td>1.48</td>
<td>1.80</td>
<td>1.63</td>
<td>1.97</td>
<td>1.74</td>
</tr>
<tr>
<td>rs4796995</td>
<td>42.6%</td>
<td>1.63</td>
<td>1.48</td>
<td>1.80</td>
<td>1.63</td>
<td>1.97</td>
<td>1.74</td>
</tr>
<tr>
<td>rs4792909</td>
<td>42.6%</td>
<td>1.63</td>
<td>1.48</td>
<td>1.80</td>
<td>1.63</td>
<td>1.97</td>
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<tr>
<td>rs2062377</td>
<td>42.6%</td>
<td>1.63</td>
<td>1.48</td>
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<td>1.63</td>
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<td>rs884205</td>
<td>42.6%</td>
<td>1.63</td>
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<td>rs9533090</td>
<td>42.6%</td>
<td>1.63</td>
<td>1.48</td>
<td>1.80</td>
<td>1.63</td>
<td>1.97</td>
<td>1.74</td>
</tr>
</tbody>
</table>

**Conclusion:** According to the data of multiple logistic regression the risk factors for the development of moderate, high and very high CV risk in RA patients were DAS28, CRP level, Vps CA, anti-CCP positivity, cIMT > 0.9 mm had high predictive value for the development TA fibros in PreM RA women. The TA calcinosis was positively correlated with carotid intima-media morphology abnormalities (g2=31.6; p<0.01), presence of the CP (g2=28.2; p=0.01), cIMT > 0.9 mm (g2=8.5; p=0.01).

**Disclosure of Interests:** None declared, Jan-Gerd Rademacher: None declared, Gerhard A Müller Grant/research support from: Novartis.

**DOI:** 10.1136/annrheumdis-2019-eular.4314

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**THU0142**

**DIAGNOSTIC AND PREDICTIVE VALUE OF CAROTID AND TIBIAL ARTERIES ULTRASOUND MORPHOLOGY CHANGES IN FEMALE WITH RHEUMATOID ARTHRITIS**

Olena Garmish, Volodymyr Levchenko, National Scientific Center “M.D. Strazhesko Institute of Cardiology”, Kiev, Ukraine

**Background:** Carotid plaque (CP) is one of the surrogate markers of atherosclerosis. The association of ultrasound carotid and tibial intima-media morphology abnormalities with clinical and laboratory markers of atherosclerosis in patients with rheumatoid arthritis (RA) is uncertain.

**Objectives:** To determine the diagnostic and prognostic value of the carotid and tibial arteries ultrasound changes in women with RA, depending on age, menopause and laboratory parameters.

**Methods:** The study was performed on 105 women with RA according to ACR criteria from the catchment area of the register of Umeå injury database, Umeå, Sweden, which enabled identification of low-energy fractures (n=254). The follow-up (mean 8.8±6.1 years, total 7928 person-years) started two years after RA diagnosis but not earlier than January 1, 1993 and ended at the first of December 31, 2011, death, or the first low-energy fracture. Nine SNPs were analysed in all patients with available DNA-samples (n=667) using KASP genotyping assays (LGc genomics Ltd, Hoddesdon, UK):

<table>
<thead>
<tr>
<th>SNP</th>
<th>Frequency</th>
<th>HR1*</th>
<th>95% C.I.</th>
<th>HR2*</th>
<th>95% C.I.</th>
<th>HR3*</th>
<th>95% C.I.</th>
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<tbody>
<tr>
<td>rs1373004</td>
<td>T-carrier</td>
<td>22.6%</td>
<td>1.61</td>
<td>1.16</td>
<td>2.22</td>
<td>1.68</td>
<td>1.17 2.41</td>
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<tr>
<td>rs4792909</td>
<td>GG vs.</td>
<td>38.6%</td>
<td>1.59</td>
<td>1.92</td>
<td>1.24</td>
<td>1.53</td>
<td>1.32 1.54</td>
</tr>
</tbody>
</table>

**Conclusion:** According to the data of multiple logistic regression the risk factors for the development of moderate, high and very high CV risk in RA patients were DAS28, CRP level, Vps CA, anti-CCP positivity, cIMT > 0.9 mm had high predictive value for the development TA fibrosis in PreM RA women. The TA calcinosis was positively correlated with carotid intima-media morphology abnormalities (g2=31.6; p<0.01), presence of the CP (g2=28.2; p=0.01), cIMT > 0.9 mm (g2=8.5; p=0.01).

**Disclosure of Interests:** None declared, Jan-Gerd Rademacher: None declared, Gerhard A Müller Grant/research support from: Novartis.

**DOI:** 10.1136/annrheumdis-2019-eular.3813
ECHOCARDIOGRAPHIC ABNORMALITIES AMONG HISPANIC PATIENTS WITH RHEUMATOID ARTHRITIS: A CASE CONTROL STUDY

José Ramón Aspiri-López1, Dionioco Ángel Galarza-Delgado1, Iris Jazmín Colunga-Pedraza2, Carolina Marlene Martínez-Flores1, Karla Paola Cuéllar-Calderón2, Ileana Cecilia Reynosa-Silva2, Marielva Castro-González2, Raymundo Pineda1, Guillermo Contreras1.

Background: Rheumatoid arthritis (RA) is a chronic, systemic, inflammatory disease that mainly affects the synovial joints. Subjects with RA have an increased cardiovascular (CV) morbimortality (1). This increase in cardiovascular diseases (CVD) is not explained by traditional risk factors (2). Screening for CVD in RA patients is an essential part of CV risk management. Echocardiography is a simple, non-invasive approach that provides reliable markers for cardiac evaluation (3).

Objectives: To determine the prevalence of echocardiographic abnormalities in RA patients and compare them to matched controls.

Methods: Observational, cross-sectional study. RA patients aged 40 to 75 years that fulfilled the 2010 ACR/EULAR classification criteria and met the inclusion criteria were included. Patients with a previous ultrasound window, history of previous atherosclerotic CVD, ischemic heart disease, cerebrovascular accident or peripheral arterial disease and pregnancy were excluded. Transthoracic echocardiogram was performed and reviewed by 2 board-certified cardiologists. Differences were solved by consensus. Descriptive analysis was done with frequencies (%) and median (q25–q75), and comparisons with Chi-square and Mann U-Whitney's test.

Results: A total of 133 subjects were included. Baseline characteristics are shown in Table 1. Groups were well balanced, with no differences among them. Echocardiographic comparisons are shown in Table 2. Prevalence of abnormal left ventricle (LV) geometry was higher in RA patients (p=0.038), as were mitral and tricuspid valvular dysfunction (p<0.001). The LV ejection fraction was lower in RA subjects (p=0.038), as were mitral and tricuspid valvular dysfunction (p<0.001).

Abstract THU0144 – Table 1. Clinical characteristics.

<table>
<thead>
<tr>
<th></th>
<th>RA (n=85)</th>
<th>Control (n=48)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, n (%)</td>
<td>81 (95.3)</td>
<td>46 (95.8)</td>
<td>1</td>
</tr>
</tbody>
</table>

Abstract THU0144 – Figure 1

Conclusion: Genes related to bone metabolism may have a considerable contribution to the already high risk of low-energy fractures in RA.

REFERENCES:


Disclosure of Interests: None declared; Lisbeth Ärlestig: None declared, Solbritt Rantapää Dahlqvist Consultant for: Member of the advisory board, Lipum AB, Umeå, Sweden.


THU0145 INCIDENCE, TREND AND FACTORS ASSOCIATED WITH OPPORTUNISTIC INFECTION (OI) IN PATIENTS WITH RHEUMATOID ARTHRITIS IN SPAIN. (TREND-AR STUDY)

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Background: The epidemiology of hospitalizations for Opportunistic Infections (OI) in patients with rheumatoid arthritis (RA) is unknown despite an increase in RA treatments that confer risk of infection.

Objectives: To analyze the incidence, trend and factors associated with hospitalizations due to OI in patients with RA, in Spain, during the period between 1999 and 2015.

Methods: Population study based on the analysis of a national administrative database that includes a Minimum Basic Data Set (MBDS) of the income of patients with RA (ICD 9 714). Period: January 1, 1999 to December 31, 2015. The following entities were included as OI: tuberculosis (tb), nontuberculous mycobacteria, cytomegalovirus (CMV), Epstein-Barr virus (EBV), Herpes zoster (HZ), Candidiasis, Toxoplasmosis, Pneumocystis, Cryptococcus, Listeria, Nocardiosis, Aspergillosis, Coccidioidomycosis, Histoplasmosis, Blastomycosis, Strongyloides, Leishmaniosis, Cryptporidium, Trypanosoma cruzi, JVC and other prion viruses. These diagnoses were identified by the presence in primary and secondary diagnosis of their ICD9 codes. The population at risk was estimated
through the population census of the National Institute of Statistics, with an estimated prevalence of RA of 0.5% in both sexes (0.2% in men and 0.7% in women). Crude and adjusted rates were calculated at the national level. The trend was analyzed by Generalized Linear Models (GLM) using the year variable as the analysis variable. Clinical-demographic factors associated with these infections were analyzed, using uni- and multivariate logistic regression.

**Results:** Of the total of 338,343 hospital admissions in patients with RA during the 17 years of the study period, there were 17,497 (5.2%) admissions with opportunistic infection, 1591 (38.8%) in men and 2506 (61.2%) in women (p < 0.001). The infections found in order of frequency were: Pneumocystis (29.9%), Tbc 1227 (29.9%), Aspergillus 357 (8.7%), systemic candidiasis 342 (8.3%), CMV 270 (6.5%), EBV 133 (3.2%), Pneumocystosis 122 (2.9%), Leishmaniosis 100 (2.4%), Listeriosis 98 (2.1%), Mycobacterium tuberculosis 85 (2%), Nocardiosis 86 (2.1%), Trypanosoma Cruzi 19 (<1%), JVC 19 (<1%), Cryptococcosis 15 (<1%), Toxoplasmosis 14 (<1%), Strongyloides 11 (<1%), Cryptosporidium 6 (<1%), Histoplasmosis 1 (<1%), blastomycosis 1 (<1%). Between 20-40 years the most frequent infections were: Tbc, EBV, CMV; Between 40-60 years: Tbc, HZ, CMV; Over 60 years old: HZ, tbc, aspergillus. The mean age was 65.54 (SD16.6). 445 (10.9%) died during admission; 217 (13.6%) in men and 228 (9.1%) in women (p < 0.001). The mean of the Charlson index was 1.96 (1.49), 2.21 (SD1.6) in men and 1.81 (SD1.3) in women (p < 0.001). The Relative Risk male: female was 2.77. The infections with the highest male/female RR were: Leishmaniosis (4.77), Listeriosis (4.1) and Aspergillus (3.8). The infections with the highest lethality were: Pneumocystosis (9.4%), Candidiasis (29.8%), and Aspergillus (27.7%). The age-adjusted rate for all OI was 146.21/100,000 inh*year, 297.05 in men and 107.37 in women. Adjusted IO rates increased from 85.47 in 1997, to 193.48 in 2015. It is estimated that this increase is of 4.96% per year. In the multivariate analysis, the factors associated with OI were: male, COPD and liver disease.

**Conclusion:** In Spain, during the period 1997 to 2015, there has been an increase in the incidence rate of OI in patients with RA. We estimate an annual increase of 4.9%. Being male and having COPD or liver disease are associated with OI.

**Disclose of Interests:** None declared

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**THU0146**

**POOR COMPLIANCE BY RHEUMATOLOGISTS AND ORTHOPAEViS WITH GUIDELINES FOR THE PERIOIOPERATIVE MANAGEMENT OF RHEUMATOID ARTHiRiTS PATIENTS UNDERGOING ARTHROPLASTY**

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**Background:** Appropriate management can reduce the increased perioperative infection risk in RA patients[1]. In 2017, American College of Rheumatology (ACR) and the American Association of Hip and Knee Surgeons released Guidelines for the Perioperative Management of Anti-rheumatic Medication in Patients with Rheumatic Diseases Undergoing Elective Total Hip or Total Knee Arthroplasty[1]. Atlanto-axial subluxation at induction of general anaesthetic (GA) is another concern. Preoperative C-spine X-rays with flexion-extension views are recommended[2].

**Objectives:** Assess compliance with medication guidelines and C-spine imaging practices for RA patients undergoing arthroplasty under GA.

**Methods:** An anonymous 24 question paper-based survey was distributed at Irish Society of Rheumatology Meeting (September 2017) and Irish Institute of Trauma and Orthopaedic Surgery Curriculum Day (January 2018) examining clinician demographics, imaging and prescribing practices.

**Results:** 33 orthopaedists and 23 rheumatologists responded. The majority (n=66) were trainees and <40 years old (n=43). Most rheumatologists were female and orthopaedists male.

The guideline advocates cDMARD continuation perioperatively[1]. Rheumatologists are more likely than orthopaedists to continue cDMARDs preoperatively. Responses varied by agent, 2 to 4 rheumatologists never stop bDMARDs preoperatively. Depending on the agent, 2 to 4 rheumatologists never stop bDMARDs preoperatively, 6 orthopaedists always increase steroids (13 sometimes, 9 never, 5 unsure), 7 never stop (13 sometimes, 6 always, 5 sure), 12 rheumatologists sometimes increased steroids (8 always, 1 never, 1 sure, 1 answer). 14 never stop steroids (8 sometimes, one not sure).

In RA patients undergoing GA, 22 orthopaedists always perform C spine imaging prior (10 sometimes, 1 never), 11 rheumatologists always do C spine imaging prior (11 sometimes, 1 never). Orthopaedists are more likely than rheumatologists to always perform spinal imaging preoperatively (P value=0.002, Fisher’s exact test).

**Conclusion:** There is poor compliance with guidelines and variability and uncertainty in prescribing. Orthopaedists often discontinue sDMARDS preoperatively despite guidelines to the contrary. Orthopaedists are more likely than rheumatologists to perform preoperative C spine imaging as per recommendations.

**REFERENCES:**

**Disclosure of Interests:** Kieran Murray Grant/research support from: Newman Research Fellowship (Abbvie). Tristan Cassidy: None declared. Abuelmagd Abdalla: None declared. Timothy Murray: None declared. Anna O’Rourke: None declared. Douglas Veale: None declared

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**THU0147**

**FACTORS CONTRIBUTING TO DISCREPANT ESTIMATED GLOMERULAR FILTRATION VALUES MEASURED BY CREATININE AND CYSTATIN C IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA)**

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**Background:** In rheumatoid arthritis (RA) patients, it is important to evaluate renal function, because it may deteriorate due to RA itself or drug use requiring drug dose adjustment. Recently, Cystatin C (CysC) has been used as a more accurate marker of renal function than Creatinine (Cr), because it is not affected by muscle mass. Renal function of some RA patients is overestimated by Cr, and shows a discrepancy in the estimated glomerular filtration between Cr and CysC. However, what
Comparisons of Serum Levels of GDF-15 in Patients with Rheumatoid Arthritis with or Without Disease Activity

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Background: The increase in morbidity and mortality in Rheumatoid arthritis (RA) is due to 50% by cardiovascular risk factors associated with chronic-inflammatory processes, among these factors, GDF-15 has been associated with chronic-inflammatory processes such as RA; in addition to being related to the state of the disease of several pathologies with similar mechanisms. GDF-15 could be involved in the pathogenesis of RA and thus, show an association with the activity of a disease in RA. The most common clinimetric tool to evaluate disease activity in RA is Disease Activity Score on 28 joints (DAS28).

Objectives: To compare the serum levels of GDF-15 in patients with RA with or without disease activity.

Methods: Cross-sectional study, including 162 patients with RA, aged ≥18 years old who fulfilled the 1987 ACR classification criteria. RA disease activity was assessed using DAS28-PCR. Sera samples were obtained from venous blood by centrifugation at 3500 rpm for 15 min at room temperature. Serum GDF-15 was measured using an ELISA kit (Biovendor, Germany). Descriptive statistics (mean and standard deviation (SD)) were used for assessing the demographics and clinical parameters. Differences between patients with and without disease activity were assessed using T-student and Chi2 tests. P-values <0.05 were considered statistically significant.

Results: The mean age was 57.2 ± 11.5 years and mean BMI was 27.5 ± 4.7 kg/m². The mean disease duration was 13.60 ± 9.50 years. The GDF-15 (mg/L) was 13.60 ± 31.04 mg/L. For number of swollen and tender joints, the score was 1.50 ± 3.52 and 2.81 ± 4.59 respectively. VAS-pain was 3.00 ± 27.77. DAS28-PCR score was 3.15 ± 1.18. When applying the cut-off value for disease activity (DAS28 score ≥2.6) or remission (DAS28 score <2.6) we obtained 65 (40.1%) and 97 (59.9%) respectively. Comparison of GDF-15 serum levels between active (455.09 ± 333.47) and remission (406.36 ± 272.94) showed no significant associations (p=0.32). When performing Pearson’s correlation among GDF-15 serum levels and PCR values (n=0.142, p=0.07) or DAS28-PCR values (n=0.081, p=0.30) no relevant correlations were obtained.

Conclusion: RA activity is not associated with values of serum levels of GDF-15. Prospective studies are necessary to explain changes in GDF-15 levels throughout RA.

References:

1. Wakamatsu A, et al. Utility of estimated glomerular filtration rate (eGFR) was calculated by the new Japanese coefficient-modified Modification of Diet in Renal disease (MDRD) study equation.

Disclosure of Interests: None declared

Per Nived1,2, Göran Jönsson3, Bo Settergren4, Jon Einansson5, Tor Olsson1, Johan K Wallman1, Charlotte Svarke Jorgensen2, Melina C Kapetanovic2. 1Lund University, Clinical Sciences Lund, Section of Rheumatology, Lund, Sweden, 2Central Hospital Kristianstad, Section of Infectious Diseases, Kristianstad, Sweden, 3Lund University, Department of Clinical Sciences Lund, Section of Infectious Diseases, Lund, Sweden, 4Statens Seruminstitut, Department of Microbiological Diagnostics and Virology, København, Denmark

Background: A vaccination using a combination of a dose of 13-valent pneumococcal conjugate vaccine (PCV13) followed by a dose of 23-valent polysaccharide vaccine (PPV23) after at least 8 weeks is currently recommended for the immunosuppressed patients with rheumatic diseases.

Objectives: To explore if the prime-booster vaccination strategy using the combination of PCV13 and PPV23 improves antibody response compared to PCV alone in immunosuppressed patients with inflammatory rheumatic diseases, and to compare with the prime-booster response in patients not treated with disease modifying anti-rheumatic drugs (DMARDs) and controls.

Methods: In total, 45 patients treated with rituximab (rheumatoid arthritis (RA), arthritis=35 and vasculitis=10), 20 RA patients on abatacept; 27 patients on methotrexate/azathioprine/mycophenolate moffetil (MTX/AA/MMF; RA=14 and vasculitis=13); 17 patients without DMARDs (RA/arthritis=12 and vasculitis=5) and 25 healthy controls participated. Only patients on an unchanged dose of DMARDs for at least 4 weeks before vaccination were eligible for the study. All participants were vaccinated with a dose PCV followed by a dose PPV23 after at least 8 weeks. A sub-group of rituximab treated patients had been vaccinated earlier with either 7-valent pneumococcal conjugate vaccine (PCV7) or PCV13. Blood samples were taken immediately before and 4-6 weeks after each vaccine dose. Pneumococcal serotype-specific antibodies to the 12 serotypes
Background: Joint destruction in rheumatoid arthritis (RA) includes both bone and cartilage lesions. Since joint space narrowing (JSN) is not a damage by semi-quantitative US score is valid and useful for patients with RA.

Disclosure of Interests: Takehisa Ogura: None declared, Ayako Hirata: None declared, Norhide Hayashi: None declared, Hideki Ito: None declared, Yako Takenaka: None declared, Yuki Inoue: None declared, Yuki Inoue: None declared, Takaharu Kagtagiri: None declared, Chihiro Imaizumi: None declared, Yuto Takakuura: None declared, Hideto Kameda: Grant/research support from: AbbVie, Asahi Kasei Pharma, Astellas, Chugai, Eisai, GlaxoSmithKlein, Mitsubishi-Tanabe, Novartis, Consultant for: AbbVie, Eli Lilly, Novartis, Speakers bureau: AbbVie, Asahi Kasei Pharma, Bristol-Myers, Chugai, Eli Lilly, Janssen, Mitsubishi-Tanabe, Novartis, Pfize

THU0150 FINGER JOINT CARTILAGE EVALUATED BY ULTRASOUND IN PATIENTS WITH RHEUMATOID ARTHRITIS AND HEALTHY SUBJECTS
Takehisa Ogura, Ayako Hirata, Norhide Hayashi, Hideki Ito, Sayaka Takenaka, Yuki Inoue, Takaharu Kagtagiri, Chihiro Imaizumi, Yuto Takakura, Hideto Kameda. Toho University, Division of Rheumatology, Department of Internal medicine, Tokyo, Japan

Background: Joint destruction in rheumatoid arthritis (RA) includes both bone and cartilage lesions. Since joint space narrowing (JSN) is not a direct evaluation of cartilage using X-ray, we aimed to examine the validity of ultrasound (US) cartilage evaluation in patients with RA.

Objectives: Methods: The cartilage thickness of bilateral metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints of the 2nd to 5th fingers were visualized from a dorsal view with joints in approximately 90 degrees flexion and measured at the middle portion. Furthermore, one US examiner performed the semi-quantitative scoring of the recorded cartilage images in a blinded manner on a scale of 0–2. In addition, the JSN of the corresponding joints was scored using the van der Heijde-modified Sharp method with a hand X-ray. Continuous variables were analysed using the Mann–Whitney U test. The relationships among the total measurement of cartilage thickness, its semi-quantitative score, and the JSN score were assessed using Spearman’s rank correlation coefficients.

Results: One hundred and three patients with RA and 45 healthy subjects were enrolled in this study. The total cartilage thickness was significantly thinner in patients with RA compared to healthy subjects for both the MCP and PIP joints (both p<0.001). The semi-quantitative sum of 16 joints ranged from 2 to 26 (median 8) in patients with RA, which was significantly greater than the 0 to 11 (median 4) seen in healthy subjects (p<0.001). In patients with RA, the semi-quantitative score showed a significant negative correlation with cartilage thickness (rho=−0.84; p<0.001) as well as a significant positive correlation with JSN score (rho=0.66; p<0.001). In addition, in healthy subjects, semi-quantitative score, but not cartilage thickness was significantly correlated with age (rho=−0.49; p<0.001 and rho=−0.25; p=0.118, respectively). On the other hand, in RA, these scores showed a significant correlation with RA disease duration but not correlated with age.

Conclusion: A simplified and direct evaluation of finger joint cartilage damage by semi-quantitative US score is valid and useful for patients with RA.

Disclosure of Interests: Takehisa Ogura: None declared, Ayako Hirata: None declared, Norhide Hayashi: None declared, Hideki Ito: None declared, Sayaka Takenaka: None declared, Yuki Inoue: None declared, Takaharu Kagtagiri: None declared, Chihiro Imaizumi: None declared, Yuto Takakuura: None declared, Hideto Kameda: Grant/research support from: AbbVie, Asahi Kasei Pharma, Astellas, Chugai, Eisai, GlaxoSmithKlein, Mitsubishi-Tanabe, Novartis, Consultant for: AbbVie, Eli Lilly, Novartis, Speakers bureau: AbbVie, Asahi Kasei Pharma, Bristol-Myers, Chugai, Eli Lilly, Janssen, Mitsubishi-Tanabe, Novartis, Pfize
Conclusion: RRA was observed in a 20-30% of RA patients, slightly higher compared to previous evidence [1,2]. Characteristics of patients fulfilling different RRA definitions are diverse. Particularly, disease severity (disease activity and structural damage) was not associated with RRA if the definition considers only the exposure to bDMARDs. Given the large time span of the study period, RRA patients were more frequently those who started bDMARDs in earlier years.

REFERENCES:

Table. Factors associated with three definitions of difficult-to-treat/refractory rheumatoid arthritis (RRA), multivariate analysis.

<table>
<thead>
<tr>
<th>Factor</th>
<th>OR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. bDMARDs</td>
<td>18.77 (11.06;31.85)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Current bDMARD</td>
<td>p&gt;0.001</td>
<td></td>
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<tr>
<td>Prednisone daily dose</td>
<td>2.15 (1.17;2.15)</td>
<td>0.014</td>
</tr>
<tr>
<td>Model Constant</td>
<td>p&gt;0.001</td>
<td></td>
</tr>
<tr>
<td>BMI per 5 unit increase</td>
<td>0.61 (0.35;1.05)</td>
<td>0.072</td>
</tr>
<tr>
<td>No. bDMARDs</td>
<td>8.69 (5.16;14.64)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>tDMARD treatment start year</td>
<td>0.92 (0.84;1.01)</td>
<td>0.087</td>
</tr>
<tr>
<td>Model Constant</td>
<td>p&gt;0.001</td>
<td></td>
</tr>
<tr>
<td>BMI per 5 unit increase</td>
<td>0.61 (0.35;1.05)</td>
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</tr>
<tr>
<td>Model Constant</td>
<td>p&gt;0.001</td>
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</table>

OR odds ratio, C.I. confidence interval, *DAS28, mean over the last 12 months; *mTSS=0.5 over the last 24 months.

Disclosure of Interests: None declared

THU0153
SARCOPENIA IS ASSOCIATED WITH PERSISTENT DISEASE ACTIVITY DURING FOLLOW-UP OF RHEUMATOID ARTHRITIS
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Objectives: This study investigated the prevalence and impact of sarcopenia on clinical outcomes during follow-up in patients with rheumatoid arthritis (RA).

Methods: We enrolled 294 RA patients from a single tertiary center. Data were collected at the time of enrollment and annually thereafter for 3 consecutive years. Sarcopenia was assessed by bioelectrical impedance analysis and defined as a relative skeletal mass index (RSMI) < 5.14 kg/m² in women and < 7.40 kg/m² in men. Univariate and multivariate analyses were performed to identify the association between sarcopenia and clinical outcome.

Results: Of the 294 RA patients, 8.2% had sarcopenia at the time of enrollment. Patients with sarcopenia were more likely to be older (P=0.001), male (P=0.001), and smokers (P=0.001), and to have a higher body fat mass (P=0.034) and body fat percentage (P=0.039), and a lower basal metabolic rate (P=0.013), than non-sarcopenic patients. Biological agents were more commonly prescribed to sarcopenic patients than to non-sarcopenic patients (P=0.048). The sarcopenic patients had higher Physician Global Assessment (PGA) (P=0.015), higher mean and delta tender joints (P=0.007), higher mean and delta swollen joints (P=0.007), and higher mean DAS28-ESR (P=0.014) and DAS28-CRP (P=0.020) scores than the non-sarcopenic patients. In the multivariate analysis, sarcopenia was significantly associated with male gender (OR = 0.112, 95% CI: 0.041–0.304, P <0.001), mean PGA score (OR = 1.680, 95% CI: 1.067–2.645, P=0.025), and mean DAS28-ESR score (OR = 4.477, 95% CI: 1.661–12.067, P<0.003).

Conclusion: Sarcopenia at baseline was an independent predictor of disease activity during follow-up in Korean patients with RA. Our results provide a rationale for lifestyle interventions designed to maintain normal weight in RA patients and thus help control disease activity.

Disclosure of Interests: None declared

THU0153
PATTERNS OF SUSTAINED REMISSION AND SUBSEQUENT DMARD TAPERING IN EARLY RHEUMATOID ARTHRITIS: DATA FROM THE CANADIAN EARLY ARTHRITIS COHORT
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Background: Rheumatoid arthritis (RA) treatment emphasizes aggressive titration of disease-modifying antirheumatic drugs (DMARDs) with the goal of achieving disease remission. This often includes the use of multiple DMARDs in combination, which can have a significant impact on patients’ lives and add costs to the healthcare system.

Objectives: To describe the patterns of sustained remission and subsequent treatment reduction in usual clinical practice for patients with early RA.

Methods: Patients (age >18) enrolled in the Canadian early Arthritis Cohort (CATCH) between January 2007 to March 2017 were analyzed. CATCH is a prospective, observational study of patients with early inflammatory arthritis (symptoms < 1 year) treated in rheumatology clinics across Canada. The analysis cohort included patients with a diagnosis of RA according to the 1987 or 2010 ACR/EULAR classification criteria, active disease at enrolment (DAS28=2.6) and those treated with at least one DMARD or biologic agent within the first three months of study enrolment. We defined sustained remission as achieving a DAS28 < 2.6 at two consecutive follow-up visits at least six months apart. Reduction of therapy was defined as a minimum of a 25% dose reduction of conventional, targeted or biologic DMARDs. Descriptive statistics were used to summarize the time to remission and reductions in DMARD therapy.

Results: Eight hundred and thirty-seven (40%) of the 2,097 eligible patients achieved sustained remission during the study period. Of these, 60% did so within the first 18 months and 92% within the first four years (Figure 1). The mean (SD) baseline DAS28 was 5.1 (1.3), and HAQ-DI was 1.0 (0.7). At the time of remission, 80% were prescribed methotrexate (55% subcutaneously), 71% were prescribed combination therapy with other conventional synthetic DMARDs, and 13% were prescribed a biologic agent. In the year after attaining sustained remission, 327 (39%) patients reduced treatment in the following pattern (patients may have had more than one change): 250 patients (30%) reduced or stopped methotrexate, 196 patients (23%) reduced or stopped non-methotrexate DMARDs, and 34 patients (4%) reduced or stopped biologic agents. Of those that reduced or stopped a biologic, only one was due to side effects. For the 250 patients who reduced or stopped methotrexate, 25 were for a side effect.

Conclusion: Achieving sustained remission occurred in 40% of early RA patients in usual clinical practice. Treatment reductions following sustained remission occurred in over a third of patients over the next 12 months, and consisted mainly of adjustment in non-biologic DMARDs.
High-resolution computed tomography (HRCT) of the lung in patients with rheumatoid arthritis: prevalence of interstitial lung disease involvement and determinants of abnormalities

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Background: Interstitial lung disease (ILD) causes significant morbidity and mortality in patients with rheumatoid arthritis (RA). An international consensus about the identification of a subgroup of RA-patients with an high risk to develop ILD is still lacking.

Objectives: To assess: (a) the prevalence of ILD involvement in RA on high resolution computed tomography (HRCT) scan; (b) the relationships between pulmonary function tests (PFTs), patient-centred measures and ILD, (c) the potential risk factors that contribute to ILD in RA-patients.

Methods: We retrospectively evaluated the data of RA patients afferent to an Italian rheumatological center from 1/1/2014 to 30/6/2018. We extrapolated clinical data (e.g., gender, age at onset the RA), laboratoryistic factor (RF) and anti-citrullinated protein antibodies (ACPA), respiratory functional data (forced vital capacity (FVC) and single-breath diffusing capacity for carbon monoxide (DLco)), patient-centred measures of dyspnea (PCMD) (modified Borg Dyspnea Index and VAS for breathing), health assessment questionnaire-disability index (HAQ-DI), and HRCT. HRCT abnormalities were scored using a conventional visual reader-based score (CoVR)

The relationships among the two HRCT scores, PFTs and PCMD were calculated using Pearson's correlation. The AUC-ROC curve was calculated to determinate the discriminative performance of measures between patients with and without ILD. Multivariate regression model was used to assess the strength of association between ILD and RA features.

Results: 151 patients with RA were included (45 males and 106 females, mean age of 53.4 ± 7.6 years). We identified ILD in 29 of 151 patients (19.2%). Usual interstitial pneumonia was the most common pattern on HRCT. Patients with ILD were older (p<0.01), their age at RA-onset and HAQ-DI were higher (respectively with p<0.01 and p<0.05) than patients without RA-ILD. RF positivity and titer were similar in the two groups, whereas ACPA positivity and titer were higher in ILD group (p=0.02).

Extent and severity of ILD, total CoVR and CaM score correlated closely with DLco and PCMD (both with p<0.0001). A reduced DLco was the most sensitive test to predict the presence of ILD on HRCT (AUC-ROC, 0.811±0.037). Multivariate analysis showed that older age (p<0.0001), age at RA onset, (p=0.025), APCA titers (p=0.004) and smoking habit (p=0.008) were independent explanatory variables of HRCT damage.

Conclusion: ILD is a frequent feature of RA. RA-ILD is associated with age, age at RA-onset, smoking habit, and ACPA titer. DLco seems the most sensitive measure to predict ILD on HRCT scan, followed by PCMD.

References:

Disclosure of Interests: Fausto Salaffi Grant/research support from: Abbvie, Roche, Novartis, BMS, Pfizer, Sanofi, Speakers bureau: Abbvie, Roche, Novartis, Pfizer, Sanofi, marina carotti Speakers bureau: abbvie pfizer roche bms sanofi. Marco Di Carlo: None declared, Marka Tardella: None declared, Andrea Giovagnoni: None declared. DOI: 10.1136/annrheumdis-2019-eular.7317
assessments, including disease activity (RADAi), function (MDHAQ), pain (PROMIS), fatigue (PROMIS), sleep (PROMIS), and depression (PROMIS). The current set of analyses focused on adherence to RAapp, overall, by scale, and over the 6 months of the trial. We examined adherence to RAapp over the duration of the study and examined factors related to adherence using mixed regression models. Factors tested included patient age, sex, educational attainment, and baseline CDAI.

**Results:** 75 patients received RAapp and have data included in these analyses (6 patients are in the last month of follow-up). 60 (80%) were female; age breakdown was 24% < 45 years, 49% 45-64 years, and 27% 65 years and over; and educational attainment was 19% high school, 59% college, and 23% beyond college. Baseline CDAI demonstrated 20% in remission, 45% low, 24% moderate, and 11% high disease activity. During the 6-month study, median adherence to the RAapp daily questionnaires was 81.6% (interquartile range 48.4% to 92.3%). Broken down by the type of questionnaire, median adherence was: disease activity 79.8%; pain 80.8%; mood 76.2%; function 79.3%; fatigue 77.0%; and sleep 77.8%. Adherence to the daily questionnaires was highest in the first month but decreased a small amount each of the following months (see Figure, p for trend < 0.001). The only significant predictor of higher adherence was age 65 or over (p = 0.04). High baseline CDAI was associated with a lower adherence but was not statistically significant (p = 0.07).

**Conclusion:** We developed and tested an ePRO app for RA (RAapp). Among a large group of patients, adherence to the app was good but declined slightly over time. There was no substantial variation in adherence with different ePRO scales. Older age was the only significant predictor of adherence.

**Figure 1:**

**Table 1:**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Number of events</th>
<th>Incidence rate (per 1000 patient years under treatment)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>csDMARDs</td>
<td>3</td>
<td>0.2</td>
<td>(0.0; 0.5)</td>
</tr>
<tr>
<td>Etanercept (original)</td>
<td>4</td>
<td>0.7</td>
<td>(0.2; 1.6)</td>
</tr>
<tr>
<td>Etanercept (biosimilar, SB4)</td>
<td>1</td>
<td>1.9</td>
<td>(0.1; 6.9)</td>
</tr>
<tr>
<td>Gdizumab</td>
<td>1</td>
<td>0.7</td>
<td>(0.0; 2.4)</td>
</tr>
<tr>
<td>Abatacept</td>
<td>1</td>
<td>0.3</td>
<td>(0.0; 1.2)</td>
</tr>
<tr>
<td>Tocilizumab</td>
<td>3</td>
<td>0.5</td>
<td>(0.1; 1.1)</td>
</tr>
<tr>
<td>All</td>
<td>17</td>
<td>0.4</td>
<td>(0.2; 0.6)</td>
</tr>
</tbody>
</table>

*One patient was exposed to both Etanercept (original) and Rituximab at the time of event.
**THU0157 REASONS FOR NON-PARTICIPATION IN A RANDOMIZED CONTROLLED TRIAL COMPARING TWO SEASONAL INFLUENZA VACCINES IN RHEUMATOID ARTHRITIS PATIENTS**

**Marina Iusche1, Jonathan Starr2, Katherine Rodriguez3, Agnihotram Ramakumar3, Marie Hudson2, Brian Ward1, Ines Colmegna1. 1The Research Institute of the MUHC, Montreal, Canada; 2Lady Davis Institute, Montreal, Canada.**

**Background:** Low recruitment rates (12%) into influenza vaccine studies are reported among healthy older adults. Fear of side effects, lack of insight into personal risk status, and doubts about vaccine efficacy are the most commonly reported reasons for non-participation. Rheumatoid arthritis (RA) patients are also at high risk for influenza and benefit from yearly immunization. A number of influenza vaccines are currently available; however, it is unknown which vaccine(s) provides optimal protection to RA patients. Estimating participation rates is key for designing studies to address that issue.

**Objectives:** To define the rate of non-participation and reported reasons for refusing entry into a randomized clinical trial (RCT) comparing two influenza vaccines (NCT02936180 - ClinicalTrials.gov).

**Methods:** Seropositive RA patients from McGill University Health Centre, on stable treatment prior to recruitment (<3 months), were invited by their treating rheumatologists to participate in the study. A vaccine nurse contacted participants from Year 1 (Y1) and those from Year 2 (Y2) encountered a recruiter immediately after their rheumatologist’s appointment. Patients invited to participate signed the consent form and were later contacted by a vaccine nurse to schedule their appointment. Reasons for non-participation were documented.

**Results:** Over two influenza seasons, 692 RA patients were invited to participate in the study. The non-participation rate was 59.5% (Y1=64.6%, Y2=53.1%, p=0.1). Non-participants and participants did not differ in age or sex (age mean±SD: 61.7±14.7 vs 60.9±12.9, p=0.5; female sex: 76.8% vs 79.9, p=0.33). Inclusion and exclusion criteria resulted in the loss of 17 (4.1%) and 19 (4.6%) subjects, respectively. The three most commonly reported reasons for non-participation were vaccine misconceptions (n=49, 20.4%), reluctance to participate in a clinical trial (n=35, 14.6%), and lack of available time (n=29, 12.1%). Thirty-one patients reported more than one reason for non-participation. Reasons for non-participation were similar according to sex and patient age (> or < 65 years).

**Conclusion:** Only half of eligible RA patients accepted to be enrolled in this influenza vaccine study. Enhancing patient literacy on vaccines and the relevance of conducting clinical trials is essential to optimize both recruitment to such trials and immunization rates.

**REFERENCES:**


**Acknowledgement:** The Arthritis Society - Canada

**Disclosure of Interests:** Mariana Iusche: None declared, Jonathan Starr: None declared, Katherine Rodriguez: None declared, Agnihotram Ramakanumar: None declared, Marie Hudson Grant/research support from: Bristol-Myers Squibb, Brian Ward: None declared, Ines Colmegna: None declared

**DOI:** 10.1136/annrheumdis-2019-eular.6381

**THU0158 IMPAIRED OLFACTORY FUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background:** Recent studies indicated that rheumatic disorder can be associated with olfactory loss.

**Objectives:** To specifically investigate chemosensory function in patients with rheumatoid arthritis (RA) by valid and reliable psychophysical tests and compare them to healthy controls.

**Methods:** We investigated 212 RA patients (43 men, 169 women; mean age 59 years) and compared their results to 30 healthy controls (10 men, 20 women; mean age 40 years). All participants underwent standardized olfactory (odor thresholds, odor discrimination and identification for suprathreshold testing) and gustatory tests (taste sprays – suprathreshold taste function; taste strips – quasi-threshold gustatory test). In addition, blood chemistry was also assessed (e.g., for CRP, RA factors, and anti-CCP).

**Results:** RA patients rated their senses of smell and taste to be as good as that of controls. However, in RA patients 4% were found to be anosmic, and 36% to be hyposmic. These numbers were 0 and 20%, respectively, in controls. RA patients exhibited significantly lower scores in odor identification and discrimination. Gustatory test scores were also decreased in RA patients. No such differences were found for odor thresholds. Interestingly, the changes in olfactory and gustatory function neither correlated with disease activity nor with treatment with MTX, or other RA activity or severity like C-reactive protein, rheumatoid factors, anti-CCP antibodies orDAS28-Score. Moreover, there was no correlation between olfactory dysfunction and treatment with DMARDs, e.g. amount of MTX, or Tumor necrosis factor α inhibitors.

**Conclusion:** These results indicate that olfactory and gustatory function is significantly decreased in patients with RA. This decrease in function seems to be unnoticed by most patients which may be due to the fact that RA patients have no complete loss of function (anosmia), but still function in the range of hyposmia or even normosmia. Importantly, the changes in olfactory function are not observed at the level of odor thresholds but only for suprathreshold tasks, which may suggest that the decrease in function is due to higher-order central-nervous processing of olfactory information. In addition, the lack of correlations between disease parameters and chemosensory dysfunction indicates that the decrease in chemosensory function may be a trait characteristic of RA patients.

**Disclosure of Interests:** Joeri Wendel Consultant for: Chugai, Roche, Abbvie, Novartis, Janssen-Cilag, Speakers bureau: Chugai, Roche, Abbvie, Novartis, Janssen-Cilag, Klang Tran: None declared, Martin Aringer Grant/research support from: Roche, Consultant for: AstraZeneca and Eli Lilly, Florian Schuch Consultant for: Celgene, Lilly, UCBB, Roche, Sanofi-Aventis, Abbvie, Novartis, Speakers bureau: Celgene, Lilly, UCBB, Roche, Sanofi-Aventis, Abbvie, Stefan Kleiner Grant/research support from: Novartis, Consultant for: Novartis, UCB, Chugai, Celgene, Medoc, Roche, Abbvie, Speakers bureau: Novartis, UCB, Chugai, Celgene, Medoc, Roche, Abbvie, Antje Haehner: None declared, Thomas Hummel: None declared

**DOI:** 10.1136/annrheumdis-2019-eular.6134

**THU0159 RISK FACTORS FOR DEVELOPING SARCOPENIA IN PATIENTS WITH RHEUMATOID ARTHRITIS AT 2 YEARS: FROM THE CHIKARA STUDY**

**Yutaro Yamada1, Masahiro Tada2, Koji Manda1, Noriaki Hidaka3, Kentaro Inui1, Hiroaki Nakamura1, Osaka City University Graduate School of medicine, Osaka city, Japan; 2Osaka City General Hospital, Osaka city, Japan.**

**Background:** Patients with rheumatoid arthritis (RA) are at higher risk of sarcopenia due to joint dysfunction and chronic inflammation. The prospective observational CHIKARA study (Correlation research of sarcopenia, skeletal muscle and disease activity in rheumatoid arthritis; registration number UMIN000023744) was started in 2016 to clarify the correlation between RA disease activity and sarcopenia. We reported that glucocorticoid use and low body fat were independent risk factors for developing sarcopenia at 1 year in RA patients last year.

**Objectives:** Risk factors for sarcopenia were investigated over a 2-year period this time.

**Methods:** 100 patients (78 female, average age 68 years) enrolled in the prospective CHIKARA study underwent examinations of body composition (body weight, muscle mass, fat mass, predicted bone mass, etc.; measured by a body composition analyzer (MC-780A; TANITA, Tokyo, Japan)), laboratory data, disease activity, Health Assessment Questionnaire (HAQ), and treatment condition at baseline and at 2 years. Sarcopenia was diagnosed using the criteria of the Asia Working Group on Sarcopenia. Of 64 patients without sarcopenia at baseline, those who developed sarcopenia at 2 years were identified, and risk factors were investigated by univariate and multivariate analyses.

**Results:** Six patients (9.4%) developed sarcopenia during the 2-year follow-up. Glucocorticoid use >5 mg/day was significantly higher (p=0.009) and MMP3 (p=0.018) and HAQ (p=0.045) were significantly increased in the patients who developed sarcopenia during the 2-year follow-up. Sarcopenia development was significantly associated with male sex (r=0.28, p=0.03), age (r=-0.27, p=0.03), glucocorticoid use >5 mg/day (r=0.33, p=0.02).
p<0.01), CRP (r=0.33, p<0.01) at baseline, ΔMMP3 (r=0.30, p=0.02), and ΔHAQ (r=0.25, p=0.04) on univariate analysis. Multivariate analysis identified no independent factors (Table 1).

### Table 1: Risk factors for developing sarcopenia in patients with rheumatoid arthritis

<table>
<thead>
<tr>
<th>R value</th>
<th>p value</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>0.28</td>
<td>0.02</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Age</td>
<td>0.27</td>
<td>0.03</td>
<td>1.05</td>
<td>0.92-1.20</td>
</tr>
<tr>
<td>GC use &gt;3mg/day</td>
<td>0.33</td>
<td>&lt;0.01</td>
<td>10.20</td>
<td>0.45-229.0</td>
</tr>
<tr>
<td>ΔMMP3</td>
<td>0.30</td>
<td>0.02</td>
<td>1.02</td>
<td>0.99-1.04</td>
</tr>
<tr>
<td>ΔHAQ</td>
<td>0.25</td>
<td>0.04</td>
<td>1.26</td>
<td>0.94-1.67</td>
</tr>
</tbody>
</table>

### Discussion

The most widely used DMARD is methotrexate (MTX) mainly because of its favorable efficacy-toxicity ratio. However, there is a lot of variability using MTX when it comes to dosage and route of administration; and little research on the overall response of patients to the different strategies used. The most widely used DMARD is methotrexate (MTX) mainly because of its favorable efficacy-toxicity ratio. However, there is a lot of variability using MTX when it comes to dosage and route of administration; and little research on the overall response of patients to the different strategies used. The most widely used DMARD is methotrexate (MTX) mainly because of its favorable efficacy-toxicity ratio. However, there is a lot of variability using MTX when it comes to dosage and route of administration; and little research on the overall response of patients to the different strategies used. The most widely used DMARD is methotrexate (MTX) mainly because of its favorable efficacy-toxicity ratio. However, there is a lot of variability using MTX when it comes to dosage and route of administration; and little research on the overall response of patients to the different strategies used. The most widely used DMARD is methotrexate (MTX) mainly because of its favorable efficacy-toxicity ratio. However, there is a lot of variability using MTX when it comes to dosage and route of administration; and little research on the overall response of patients to the different strategies used.
In the PO MTX group, 8 (32%) patients required a change to SC MTX; in 87.5% of cases due to treatment inefficacy and 7 (87.5%) of these patients kept the SC route until the end of the study.

Abstract THU0161 – Figure 2

Out of the patients that began with SC MTX, the one that changed route to PO maintained a good response. All the patients with biologic DMARDs kept the SC MTX as adjuvant therapy. On the other hand, the 3 (12%) patients of the PO that used a biologic DMARD had suspended MTX several months before.

Abstract THU0161 – Figure 3

Both groups had a good response to MTX. There was a significant reduction in corticoid requirements during the first year of treatment/P

Abstract THU0161 – Figure 4

At the end of the study, 21 (41%) patients received SC MTX and the number goes up to 25 (49%) if we include those who also had biologic DMARDs.

Of those who suspended MTX, 85% were due to adverse effects, similar in both groups.

Conclusion:

• Our study suggests that patients that start with PO MTX require route administration changes more frequently than the SC group during the first year of follow-up.
• SC MTX was the route used by almost half the patients by the end of the study.
• We can also see that the inflammatory response to MTX was acceptable regardless of administration route and that corticoids could be reduced significantly in both groups.

REFERENCES


Disclosure of Interests: None declared

THU0162 WHICH PERSISTENCE OF METHOTREXATE AFTER INITIATION OF THE 1ST BDMARD IN RHEUMATOID ARTHRITIS? THE RETRO-RIC2 STUDY

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Background: ACR and EULAR guidelines recommend to prescribe bDMARDs and particularly TNFi in combination with methotrexate (MTX). However, the MTX observence in RA is poor, mainly due to side effect and some bDMARDs (IL6 receptor antagonist) are almost as effective in monotherapy.

Objectives: to evaluate MTX use (dosage, route of administration…) in RA after initiation of the first bDMARD.

Methods: RETRO-RIC2 is a multicentric retrospective study. Were included all patients with RA under MTX therapy at the initiation of the 1st bDMARD from October 2008 to September 2016. The main criteria is the persistence of MTX after 1 and 2 years.

Results: 409 patients were included: mean-age = 58.9 years, female 69%, RF positive 76% and ACPA positive 83%, mean RA duration = 13.1y and mean DAS28-ES=4.48. The mean duration of previous MTX therapy = 32 months (mean dose = 16.2mg/w). At the inclusion MTX was administrated by oral route in 52% and subcutaneous in 48%. At the inclusion, 1.2% of the patients switch from oral route MTX for subcutaneous; inversely in only 0.2% the SC route was switched for oral administration.

The results are presented in table 1 and Figure 1.

<table>
<thead>
<tr>
<th>NB patients evaluable</th>
<th>MTX dose reduction</th>
<th>MTX dose increase</th>
<th>MTX dose unchanged</th>
<th>MTX stopped</th>
</tr>
</thead>
<tbody>
<tr>
<td>V-1/inclusion</td>
<td>404</td>
<td>4.5%</td>
<td>2.7%</td>
<td>93%</td>
</tr>
<tr>
<td>M0-M4</td>
<td>255</td>
<td>14.1%</td>
<td>6.3%</td>
<td>79%</td>
</tr>
<tr>
<td>M4-M12</td>
<td>173</td>
<td>16.8%</td>
<td>5.4%</td>
<td>77%</td>
</tr>
<tr>
<td>M12-M24</td>
<td>159</td>
<td>14.5%</td>
<td>4.4%</td>
<td>80%</td>
</tr>
</tbody>
</table>

V-1 = last previous visit before inclusion

Abstract THU0162 – Figure 1

Conclusion: In almost all patients MTX dose and route of administration are unchanged at the initiation of the first bDMARD in RA. With a 2 years follow up 49.9% of MTX dose were reduced and MTX was stopped in 2.9%. At 2 years MTX route of administration is oral for 64% of the patients and s/c for 36%.

Acknowledgement: None declared

Disclosure of Interests: Guy Baudens Grant/research support from: Financial Grant from NordicPharma, Consultant for: Roche SAS, TONIONE Adrien Grant/research support from: Grant from NordicPharma, Jean-Hugues Salmon Speakers bureau: Janssen Novartis, Jean-Guillaume Letarouilly: None declared, Elena Zinovieva Employee of: Nordic Pharma, Hélène Herman-Demars Employee of: Nordic Pharma, Elisabeth Gervais Grant/research support from: Roche, Pfizer, Consultant for: Bristol-Myers
A DESCRIPTIVE ANALYSIS OF LONGITUDINAL CHANGES IN RELATIVE MARKET SHARE PROPORTIONS OF BIOLOGIC AND TARGETED SYNTHETIC DISEASE-MODIFYING ANTI-RAHUMATIC DRUGS FOR TREATMENT OF RHEUMATOID ARTHRITIS: DATA FROM THE OBRI DATABASE

Elliott Hepworth, Mohammad Movahedi, Emomunnal Rampakakis, Reza Mirza

Elliott Hepworth, Mohammad Movahedi, Emomunnal Rampakakis, Reza Mirza, Claire Bombardier, Janet Poole, Claire Bombardier, Janet Poole, Claire Bombardier, Janet Poole

McMaster University, Internal Medicine, Hamilton, Ontario, Canada; Toronto General Hospital Research Institute, University Health Network, Ontario Best Practices Research Initiative, Toronto, Canada; JSS Medical Research, St-Laurent-OQ, Canada; McMaster University, Rheumatology, Hamilton, Ontario, Canada; Western University, Divisions of Rheumatology, Epidemiology and Biostatistics, Department of Medicine, London, Ontario, Canada; University of Toronto, Mount Sinai Hospital, Rheumatology, Toronto, Canada

Background: For patients with Rheumatoid Arthritis (RA) who do not achieve adequate clinical response with combined conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) or targeted synthetic DMARDs (tsDMARDs), bDMARDs include tumour-necrosis factor inhibitors (TNFi) or non-TNFi classes. Since inception of Ontario Best Practice Research Initiative (OBRI), new treatment options have become available.

Objectives: We aimed to describe the evolution of relative use of non-TNFi vs. TNFi in Ontario-based practices from 2008-2017.

Methods: Adult patients with RA enrolled in the OBRI who started therapy with bDMARDs or tsDMARDs anytime during, or up to 30 days before, enrollment were included. Using descriptive analysis of data from each year between 2008 and 2017, the relative proportion of the population treated with TNFi and non-TNFi therapy was measured for (i) all patients and (ii) those initiating their first bDMARD/tsDMARD. TNFi included: Etanercept, Adalimumab, Certolizumab, Golimumab, and Infliximab. Non-TNFi included: Abatacept, Rituximab, Tocilizumab, and Tofacitinib.

Results: A total of 1,057 patients were included of whom 653 were bDMARD/tsDMARD naïve. In 2008, the relative non-TNFi use was 3/56 (5.4%) in all patients and 0/31 (0%) in treatment-naïve patients. By 2013 the proportion non-TNFi use increased to 135/562 (24%) in all patients and 11/92 (12.0%) in treatment-naïve patients. This increasing trend in relative non-TNFi utilization continued in both groups until 2016 when relative use was 224/679 (33.0%) in all patients and 17/56 (30.4%) in treatment-naïve patients. This increasing trend in the proportion non-TNFi use increased to 135/562 (24%) in all patients and 11/92 (12.0%) in treatment-naïve patients until 2017. In 2017, the proportion non-TNFi use was 216/679 (31.9%) in all patients and 14/56 (25.0%) in treatment-naïve patients.

Conclusion: This descriptive analysis of data from the OBRI cohort shows an increase in the use of non-TNFis. The overall trend towards greater use of non-TNFi therapies as first line agents after combined csDMARDs may be partially explained by the presence of guideline lines that allow clinicians to select any of the above options as first line therapies. For patients with RA, the increase in the use of non-TNFi can be partially explained by the presence of guideline lines that allow clinicians to select any of the above options as first line therapies.}

Disclosure of Interests: Elliott Hepworth: None declared, Mohammad Movahedi: None declared, Emomunnal Rampakakis: None declared, Reza Mirza: None declared, Arthur Lau: None declared, Angela Cesta: None declared, Janet Poole Consultant for: Eli Lilly and Company, Claire Bombardier Grant/research support from: Abbvie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Consultant for: AbbVie, Hospira, Janssen, Merck, Novartis, Pfizer Inc, Sanofi, Speakers bureau: Roche


THE DSAS BASED ON THE ERYTHROCYTE SEDIMENTATION RATE MAY OVERESTIMATE DISEASE ACTIVITY IN EARLY, TREATMENT-NAÏVE PATIENTS WITH RHEUMATOID ARTHRITIS WITH HIGH LEVELS OF RHEUMATOID FACTOR

Emanuele Bozzalla Cassione, Serena Bugatti, Francesca Benaglio, Garfalia Saekellariou, Antonio Manzo, Roberto Caporali, Carlomaurizio Montecucco, Division of Rheumatology, IRCCS Pollicino San Matteo Foundation, University of Pavia, pavia, Italy

Background: Disease activity in rheumatoid arthritis (RA) is commonly measured with the DSAS-ESR. However, ESR levels may be affected by factors not related to inflammation leading to possible disparities with the DSAS-CRP. A particular, increased levels of gammaglobulins may cause increase in ESR. In RA levels of autoantibodies such as rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) may be particularly high; however, their effect on the assessment of disease activity has not been investigated.

Objectives: To evaluate whether positivity and levels of RF and ACPA determine discordance between the DSAS-ESR and the DSAS-CRP, impacting on disease activity stratification in RA.

Methods: 578 early treatment-naïve RA patients (symptoms’ duration <12 months) consecutively recruited at our Early Arthritis Clinic between 2005 and 2014 were studied. Paired DSAS-ESR and DSAS-CRP were obtained at baseline and after 6 months of therapy with conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs). RF and ACPA were determined centrally on baseline sera and, and levels were considered high when >3 times the upper limit of normal (ULN). Agreement between the disease activity scores was compared using Bland-Altman statistics before and after stratification for autoantibody-positive and levels.

Results: Female/male ratio was 2.5:1, with mean (SD) age of 59.7 (14.8) years and median (IQR) symptoms’ duration at inclusion of 15.6 (9.4 to 27.8) weeks. Mean DSAS-ESR values at baseline were 0.39 points higher compared to DSAS-CRP in the whole cohort, with more pronounced differences in females and subjects aged >65 years (Table 1). Collectively RF-positive patients had significantly higher discrepancies compared to –negative subjects (mean [SD] difference 0.45 [0.46] vs 0.35 [0.47], p=0.03), particularly in females irrespective of age. The highest disagreement was recognized in patients with high autoantibody levels; females with RF >3 ULN had DSAS-ESR scores 0.56 points higher. Disparities in these patients impacted on disease activity stratification, as more RF-high females were in DSAS-ESR high disease activity compared with DSAS-CRP (43.1% vs 23%, p<0.001). In contrast, ACPA-positivity did not affect the agreement between the two disease activity indices (Table 1). After 6 months of treatment with csDMARDs discrepancies between the DSAS-ESR and DSAS-CRP in RF-positive patients was reduced but still significant in association with levels >3 ULN (mean difference [95% CI] 0.44 [0.33-0.55]).

Conclusion: In patients with early treatment-naïve RA, the DSAS-ESR and DSAS-CRP are not inter-changeable. In particular, the DSAS-CRP may overestimate disease activity when levels of RF are high. These findings suggest that disease assessment for treatment-to-target approaches should take into account additional factors such as autoantibody-positivity.

Abstract THU0164 – Table 1. Comparative mean differences (95% CI) between DSAS-ESR and DSAS-CRP stratified for autoantibodies

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<thead>
<tr>
<th></th>
<th>whole cohort</th>
<th>female</th>
<th>male</th>
<th>age &lt;65</th>
<th>age &gt;65</th>
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<tr>
<td></td>
<td>overall</td>
<td>0.39 (0.35-0.44)</td>
<td>0.26 (0.18-0.36)</td>
<td>0.37 (0.31-0.43)</td>
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<tr>
<td></td>
<td>RF-pos</td>
<td>0.45 (0.38-0.52)</td>
<td>0.26 (0.13-0.47)</td>
<td>0.45 (0.37-0.53)</td>
<td>0.61 (0.55)</td>
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<tr>
<td></td>
<td>RF-pos &gt;3</td>
<td>0.50 (0.40-0.60)</td>
<td>0.29 (0.15-0.51)</td>
<td>0.51 (0.30-0.71)</td>
<td>0.72 (0.62)</td>
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<tr>
<td></td>
<td>ACPA-pos</td>
<td>0.41 (0.34-0.48)</td>
<td>0.20 (0.07-0.34)</td>
<td>0.49 (0.36-0.62)</td>
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<tr>
<td></td>
<td>ACPA-pos &gt;3</td>
<td>0.41 (0.33-0.49)</td>
<td>0.25 (0.12-0.48)</td>
<td>0.42 (0.27-0.61)</td>
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<td>ULN</td>
<td>0.46 (0.38)</td>
<td>0.36 (0.25-0.48)</td>
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<td>ACPA-pos &lt;100 U</td>
<td>0.49 (0.30-0.60)</td>
<td>0.27 (0.10-0.44)</td>
<td>0.42 (0.22-0.61)</td>
<td>0.51 (0.38)</td>
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</table>

Disclosure of Interests: Emanuele Bozzalla Cassione: None declared, Serena Bugatti Speakers bureau: Bristol-Myers Squibb, Celgene, Lilly, Novartis, Sanofi, Janssen, Francesca Benaglio: None declared, Garfalia Saekellariou: None declared, Antonio Manzo: None declared, Roberto Caporali: Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Genzyme, Lilly, MSD, Pfizer, UCB, Carlomaurizio Montecucco Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Sanofi, Genzyme, Lilly, MSD, Pfizer, UCB


Thursday, 13 June 2019

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A COMPARATIVE ANALYSIS OF UPADACITINIB MONOTHERAPY AND UPADACITINIB COMBINATION THERAPY FOR THE TREATMENT OF RHEUMATOID ARTHRITIS FROM TWO PHASE 3 TRIALS

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Background: Upadacitinib (UPA), a selective JAK1 inhibitor, has demonstrated efficacy and safety in patients with rheumatoid arthritis (RA) as monotherapy and in combination with conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) such as methotrexate (MTX).1,2 However, UPA monotherapy has not been compared directly with UPA combination therapy in the Phase 3 program.

Objectives: To compare the efficacy of UPA monotherapy and UPA in combination with MTX using data from two Phase 3 trials of RA patients with an inadequate response (IR) to prior MTX therapy.

Methods: In SELECT-MONOTHERAPY, 648 MTX-IR patients were randomized to receive UPA 15 mg or 30 mg monotherapy once daily (QD), or continue with MTX monotherapy (cMTX; given as a blinded study drug), for 14 weeks. In SELECT-NEXT, 661 csDMARD-IR patients were randomized to receive UPA 15 mg or 30 mg QD or placebo (PBO) for 12 weeks on a background of csDMARDs. Only patients receiving concomitant MTX (with or without additional csDMARDs) at baseline in SELECT-NEXT were included in this analysis. The primary endpoints of both studies were the proportion of patients achieving ACR20 and DAS28(CRP) <2.6, CDAI remission (≤2.8), CDAI low disease activity (LDA; ≤10), and change from baseline in HAQ-DI. Logistic regression or ordinary least squares analyses were used to compare outcomes with monotherapy versus combination therapy, adjusting for demographics and baseline disease characteristics.

Results: A total of 1114 patients were included in the analysis, of whom 67% received monotherapy in SELECT-MONOTHERAPY and combination therapy in SELECT-NEXT. Of the patients receiving combination therapy, 338 (72.5%) were receiving MTX background therapy only and 128 (27.5%) were receiving MTX plus other csDMARDs. Baseline characteristics were generally similar between the study cohorts; the majority of patients in both studies were female and of white ethnicity, with a mean age of approximately 55 years and a mean MTX dose of approximately 17 mg/week. Consistent with previously reported results from SELECT-MONOTHERAPY1 and SELECT-NEXT,2 both UPA monotherapy and UPA combination therapy led to significant improvements in efficacy outcomes versus cMTX/PBO+MTX (Table). No significant differences were observed between UPA monotherapy and UPA combination therapy across a range of clinical endpoints, including ACR20/50/70 responses and measures of LDA and remission. In addition, improvements in quality of life as measured by HAQ-DI were similar with UPA monotherapy and combination therapy. Efficacy was comparable between the two UPA doses in the combination therapy group, whereas in the monotherapy group numerically higher responses were observed with UPA 30 mg versus UPA 15 mg.

Conclusion: In MTX-IR patients with RA, the efficacy of UPA appears comparable when administered as monotherapy or when given in combination with MTX.

REFERENCES:

TREATMENT WITH UPADACITINIB IS ASSOCIATED WITH IMPROVEMENTS IN REVERSE CHOLESTEROL TRANSPORT IN PATIENTS WITH RHEUMATOID ARTHRITIS: CORRELATION WITH CHANGES IN INFLAMMATION AND HDL LEVELS

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Background: Rheumatoid arthritis (RA) is a systemic inflammatory condition associated with increased rates of atherosclerotic morbidity and mortality. One mechanism by which inflammation may increase atherosclerotic progression is via pathogenic remodeling of high-density lipoprotein (HDL)-associated proteins with resultant reduction in HDL function.1 Upadacitinib (UPA), a selective JAK1 inhibitor, has demonstrated efficacy in patients with moderate-to-severe RA.

Objectives: To assess the effect of UPA treatment on cholesterol efflux capacity (CEC) and evaluate the association of CEC with changes in inflammation and serum lipids.

Methods: A subset of patients from the Phase 2 BALANCE II study2 and the Phase 3 SELECT-NEXT study3 were selected from the pool of patients with serum samples available at baseline and Week 12. Patients were matched for age and sex, and selected based on level of response to UPA therapy (BALANCE II, UPA 6 mg BID: 39 responders [mean change in DAS28-CRP at Week 12 -3.22] and 30 non-responders [mean change in DAS28-CRP - 0.33]); SELECT-NEXT, UPA 15 mg QD: 20 responders [mean change in DAS28-CRP -3.78] and 20 non-responders [mean change in DAS28-CRP - 0.67]). A demographically similar placebo (PBO) group without selection based on degree of response was also included (20 patients from each study). J774 macrophages labeled with [3H]-cholesterol (treated with cAMP to expose cholesterol efflux capacity or CEC) were exposed to patient serum and HDL. The difference between cholesterol efflux from serum-exposed and unexposed cells provided a measurement of CEC. Results were compared between the responder, non-responder, and PBO groups using Tukey’s mean comparison method; correlations were calculated using the Pearson method; and all statistical analyses were performed in JMP 13.10 (SAS Institute).

Results: In both studies, changes in global and ABCA1-dependent CEC, and to a lesser extent non-ABCA1-dependent CEC, were significantly higher in the UPA-treated group compared with the PBO group (Figure). In the BALANCE II study, there was a significant increase in CEC among UPA responders relative to PBO and a numerically apparent difference observed between UPA non-responders and PBO. Notably, in the SELECT-NEXT study, a similar and highly significant improvement in CEC was observed for both UPA-treated groups relative to PBO (without a significant difference between the responder and non-responder groups). Despite the lack of a consistent association between change in CEC and change in clinical disease activity, observed increases in CEC correlated significantly with reduction in CRP levels in all groups across all active treatment groups. Additionally, increases in CEC at Week 12 correlated well with changes in total blood cholesterol and HDL levels, but weakly with changes in blood low-density lipoprotein (LDL) levels.

Conclusion: UPA treatment is associated with significant improvement in CEC. This effect was observed even among those demonstrating minimal clinical response (but not significant response) to UPA treatment. CEC seems to be primarily driven by ABCA1-dependent cholesterol efflux and is strongly correlated with a rise in HDL cholesterol as well as reduction in systemic inflammation as measured by change in CRP.

THU0165

THU0166
SAFETY PROFILE OF UPADACITINIB IN RHEUMATOID ARTHRITIS: INTEGRATED ANALYSIS FROM THE SELECT PHASE 3 CLINICAL PROGRAM

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Background: Upadacitinib (UPA), a JAK1-selective inhibitor, significantly improved clinical signs and symptoms of rheumatoid arthritis (RA) in patients (pts) naïve to methotrexate (MTX) and with an inadequate response to conventional synthetic DMARDs (csDMARD-JR) or biologic DMARDs (bDMARD-JR).1-3

Objectives: Assess the safety of UPA as monotherapy (mono) and as combination therapy with background csDMARDs in pts with moderately to severely active RA from the safety database of the Phase 3 clinical program.

Methods: Treatment-emergent adverse events (TEAEs) from 5 pivotal, randomized, double-blind, controlled Phase 3 trials of UPA 15 mg (included in all 5 trials) or 30 mg QD (included in 4 trials) in RA pts randomized, double-blind, controlled; n [%], individual studies with long-term [LT] active comparator (UPA mono vs MTX; UPA 15 mg with background MTX vs originator adalimumab, ADA, events/100 patient-years [E100PY]), and integrated LT (all Phase 3 exposure; E100PY) analyses sets.

Results: Across the Phase 3 trials, 3384 pts received ≥1 dose of UPA 15 mg (n=2630) or 30 mg QD (n=1204) ~402.01 PY of UPA exposure with no option to switch doses. The ST frequencies of overall SAEs and AEs leading to discontinuation were low, but higher on both UPA doses vs PBO. LT event rates were similar on UPA 15 mg vs ADA and slightly higher on UPA vs MTX mono. Deaths occurred in all treatment groups. Serious infection (SIEs) frequencies were higher on both UPA doses vs PBO. SIE rates on both UPA doses were higher vs MTX, but similar on UPA 15 mg vs ADA. Herpes zoster (HZ) frequencies and rates were higher on both UPA doses vs PBO, and vs MTX, ADA, respectively. The rates of SIE and HZ were higher on UPA 30 vs 15 mg. Adjudicated MACE were reported in all treatment groups including PBO. LT MACE rates were similar on UPA 15 mg and ADA and on UPA 15 mg and MTX mono, but higher on UPA 30 mg mono (low number of events, 2-4 per set). Adjudicated VTEs occurred at comparable frequencies on UPA vs PBO and at comparable rates on UPA vs active comparators. Malignancy (excluding non-melanoma skin cancer [NMSC]) rates were similar on UPA vs MTX, UPA 15 mg vs ADA, and 15 vs 30 mg. The NMSC rates on UPA 15 mg and ADA were similar; the rate on 30 mg was higher than 15 mg, but both UPA NMSC rates were in the range reported for RA patients treated with DMARDs.4 The standardized incidence ratio (95% CI) for malignancy (15 mg: 0.98 [0.61, 1.49], 30 mg: 1.49 [0.85, 2.42]) was not elevated vs the general population.

Conclusion: Treatment with UPA increased the risk of SIE and HZ, but not those of VTE, MACE, and malignancy vs comparators. These data support that UPA has an acceptable safety profile in the treatment of moderately to severely active RA.

REFERENCES:

Acknowledgement: AbbVie, Inc was the study sponsor, contributed to study design, data collection, analysis & interpretation, and to writing, reviewing, and approval of the final version of the abstract. Additional support: Ying Zhang (statistical analysis) and Sidharth Mukherjee (medical writing), both from AbbVie.


A MATCHING-ADJUSTED INDIRECT COMPARISON (MAIC) OF UPADACITINIB VERSUS TOFACITINIB IN CDMSARD-IR PATIENTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS (RA)

Christopher Edwards1, Ruta Sawant2, Ella Du3, Jordan Cammarota3, Patrick Tang3, Vishvas Garg2, Alan Friedman2, Keith Betts3.

Background: Upadacitinib (UPA), a JAK1 selective inhibitor, is being investigated as monotherapy and combination therapy with DMARDs for the treatment of moderate-to-severe RA. To date, no head-to-head trials have compared the effectiveness of UPA with tofacitinib (TOFA).

Objectives: To compare the efficacy of UPA 15 mg monotherapy and combination therapy with TOFA 5 mg combination therapy using MAICs.

Methods: Two MAICs were conducted. MAIC is an indirect comparison technique that utilizes individual patient data (IPD) for one treatment and aggregate data for the other treatment to provide comparative evidence after balancing differences in patient characteristics. The first MAIC used IPD from the SELECT-MONOTHERAPY trial of UPA monotherapy vs. methotrexate (MTX) and published data from the Oral Standard trial of TOFA+MTX vs. MTX. The second used IPD from the SELECT-COMPARE trial of UPA+MTX vs. adalimumab (ADA)+MTX and published data from the ORAL Strategy trial of TOFA+MTX vs. ADA+MTX. UPA monotherapy was not compared to TOFA monotherapy based on feasibility analysis and trial selection criteria. Patients in the UPA trials were reweighted based on age, gender, race, swollen joint count 66/28, tender joint count 66/28, and C-reactive protein (CRP), and patient’s global assessment, to match the baseline characteristics in each comparator trial. After matching, ACR20/50/70 and clinical remission (SDAI/CDAI) were compared for UPA monotherapy vs. TOFA+MTX relative to MTX at month 3 and UPA+MTX vs. TOFA+MTX relative to ADA+MTX at month 3 and 6 using a Wald test.

Results: After matching, baseline characteristics were balanced across the trial populations. At month 3, UPA monotherapy patients experienced significantly greater improvement in ACR70 compared to TOFA+MTX with a mean difference in difference (DD) of 9.9% (p<0.05) (Figure 1a) while UPA+MTX was associated with a higher ACR50 compared to TOFA+MTX with a DD of 12.9% (p<0.05). At month 6, UPA+MTX patients experienced significantly larger improvement in SDAI/CDAI/CRP-ESR clinical remission compared to TOFA+MTX with DDs of 9.1% (p<0.05), 7.5% (p<0.05), and 11.3% (p<0.01), respectively (Figure 1b).

Conclusion: The results from MAICs indicate that treatment with UPA 15 mg when used as monotherapy or in combination with MTX appears to produce improved outcomes at 3/6 months as compared to TOFA 5 mg +MTX (mono: ACR70 and combination: ACR50, SDAI, CDAI and DAS28-ESR remission).

REFERENCES:

Disclosure of Interests: Christopher Edwards Grant/research support from: Abbvie, BMS, Biogen, Celgene, Fresenius, Janssen, Lilly, Mundipharma, Pfizer, MSD, Novartis, Roche, Samsung, Sanofi, UCB, Consultant for: Abbvie, BMS, Biogen, Celgene, Fresenius, Janssen, Lilly, Mundipharma, Pfizer, MSD, Novartis, Roche, Samsung, Sanofi, UCB, Speakers bureau: Abbvie, BMS, Biogen, Celgene, Fresenius, Janssen, Lilly, Mundipharma, Pfizer, MSD, Novartis, Roche, Samsung, Sanofi, UCB

Acknowledgement: The design, study conduct, and financial support for the study were provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of this publication.

THU0169 JANUS KINASE INHIBITORS DEMONSTRATE EFFECTIVENESS IN A REAL-WORLD MULTI-BIOLOGIC DMARD REFRACTORY RHEUMATOID ARTHRITIS POPULATION

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Background: The Janus Kinase inhibitors (JAKi) Tofacitinib and Baricitinib are licensed for use in Rheumatoid arthritis (RA). Trials in refractory RA (inefficacy and/or toxicity) to date (1, 2) suggest targeting intracellular signalling molecules and interrupting downstream effects of multiple cytokines may confer benefit in the management of patients who have failed multiple targeted therapies.

Objectives: To evaluate safety and efficacy of JAKi in a real-world population, including response in multi-bDMARD refractory RA.

Methods: We evaluated RA patients who had failed at least 2 csDMARD +/- one or more bDMARD, who were commenced on a JAKi. Patients who commenced Tofacitinib on a compassionate use programme in 2014 (reflecting compassionate access scheme). Number of previous bDMARD was higher in the Tofacitinib group (457-468.). With rheumatoid arthritis (ORAL Strategy).

Results: Seventy seven RA patients (80% female; mean (SD) age 55.9 (12.52) years) have been treated with one (or more) JAKis; 38 have received Tofacitinib and 39 Baricitinib (5 both). Table 1 details treatment stage and clinical outcomes where available (majority pending assessments). Of the 38 patients who received Tofacitinib, 24 stopped treatment, 10 due to primary non-response, 2 secondary non-response and 12 due to

Summary of Table 1:

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Combined JAKi (n=77)</th>
<th>Tofacitinib (n=38)</th>
<th>Baricitinib (n=39)</th>
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</thead>
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<tr>
<td>Disease duration, years; mean (SD)</td>
<td>13.8 (5.34)</td>
<td>15.9 (4.52)</td>
<td>11.9 (6.16)</td>
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<tr>
<td>Previous number of targeted therapies (median, range)</td>
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<td>Targeted therapy naïve</td>
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<td>5</td>
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<tr>
<td>Baseline DAS28</td>
<td>5.84 (SD 1.07)</td>
<td>6.23 (SD 1.08)</td>
<td>5.5 (SD 0.95)</td>
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<td>3m change in DAS28</td>
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<td>-2.07 (SD 1.72)</td>
<td>-1.54 (SD 1.6)</td>
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<td>6m change in DAS28</td>
<td>-1.35 (SD 2.18)</td>
<td>-1.05 (SD 2.07)</td>
<td>-1.7 (SD 1.52)</td>
</tr>
</tbody>
</table>

Abstract THU0169 – Figure 1

Figure 1: MAIC results for UPA 15 mg vs. TOFA 5 mg + MTX vs. TOFA 5 mg + MTX at Month 3 and UPA 15 mg + MTX vs. TOFA+MTX at Month 6

* Clinical remission outcomes not reported for ORAL Standard at Month 3.
A MULTICENTER STUDY ASSESSING THE EFFICACY AND SAFETY OF REPOSITORY CORTICOTROPIN INJECTION IN PATIENTS WITH RHEUMATOID ARTHRITIS: INTERIM DATA FROM THE OPEN-LABEL TREATMENT PERIOD

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Background: Rheumatoid arthritis (RA) is an autoimmune disorder associated with chronic inflammation and is treated with disease-modifying anti-rheumatic drugs (DMARDs) and/or biologic disease-modifying anti-rheumatic drugs (bDMARDs). Both American College of Rheumatology (ACR) and EULAR recommend that short-term administration of corticosteroids (CSs) may be beneficial for its anti-inflammatory effects. Repository corticotropin injection (RCI) is a complex mixture containing purified porcine pituitary adrenocorticotropic hormone (ACTH)-analogue and an agonist for all 5 melanocortin receptors (MCRs). Activation of MCRs by ACTH has been shown to have direct and indirect anti-inflammatory and immunomodulatory effects. RCI is approved in the United States as adjunctive therapy for short-term administration in RA.

Objectives: To present interim data after 100% enrollment from the initial 12-week open-label phase of a multicenter, 2-part study evaluating the efficacy, safety, and appropriate duration of RCI therapy in patients with persistently active RA despite receiving 1 or 2 DMARDs and/or CsA.

Methods: In the open-label period (Part 1, Weeks 0–12), all enrolled patients received RCI 1 mL (80 U SC) twice weekly for 12 weeks. Patients who achieved low disease activity (LDA; DAS28-ESR score <3.2) at Week 12 continued in the double-blind, randomized maintenance phase of the trial (Part 2) for an additional 12 weeks. The primary endpoint was the proportion of patients who achieved LDA at Week 12. Secondary endpoints included assessment of the safety and tolerability of RCI. Disease activity was also assessed by the proportion of patients who achieved ACR 20%, 50%, and 70% (ACR20, 50, 70) responses and patient reported outcomes at Week 12. Bone turnover markers were assessed as an exploratory endpoint.

Results: 259 patients had enrolled, 235 had completed and 24 had discontinued the 12-week open-label period of the study; 88.9% were female and mean age was 51 years. RCI treatment resulted in 62.5% of patients achieving LDA at Week 12; results for this interim analysis are presented in the Table. Bone turnover markers were stable from baseline to Week 12, indicating no effect of RCI on bone metabolism. 98 (37.8%) patients reported adverse events (AEs) with 3 (1.2%) patients reporting serious AEs (ie, non-communicable cancer, myocardial infarction, and stroke). The most common AEs were urinary tract infection (n=10), headache (n=9), and pharyngitis (n=7).

Table 1

<table>
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<th>Endpoints</th>
<th>Baseline</th>
<th>Week 4</th>
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<th>Week 12</th>
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<tr>
<td>DAS28-ESR score</td>
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<td>3.2</td>
<td>2.8</td>
<td>2.3</td>
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<tr>
<td>ACR20</td>
<td>60.0%</td>
<td>68.3%</td>
<td>78.6%</td>
<td>80.0%</td>
</tr>
<tr>
<td>ACR50</td>
<td>4.0%</td>
<td>12.0%</td>
<td>32.0%</td>
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</tr>
<tr>
<td>ACR70</td>
<td>0.0%</td>
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</table>

Conclusion: In the 12-week open-label period of this study, RCI appeared to be generally safe and effective in patients with persistently active RA who were nonresponsive to DMARDs and CsA. This was demonstrated by improvement in multiple measures of disease activity. Further results will be evaluated in Part 2 of the study.

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Abstract THU0170 – Table 1

THU0171

TOFACITINIB, AN ORAL JANUS KINASE INHIBITOR, IN THE TREATMENT OF RHEUMATOID ARTHRITIS – THE RESULTS OF RUSSIAN NATIONAL REGISTER OF PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TOFACITINIB

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Background: Tofacitinib (TF) is an oral Janus kinase inhibitor for the treatment of rheumatoid arthritis (RA).

Objectives: To evaluate the one-year effectiveness of tofacitinib as first-line therapy in RA conventional synthetic (cs) DMARDs non-responders. Methods: Data from 415 patients from Russian national register of patients with RA treated with TF were analyzed. 119 RA patients, who had complete clinical and laboratory data from 4 consecutive visits after baseline within an interval of 3 months between these visits and who used the TF as first-line therapy after failure of cs DMARDs, were included. Treatment with any biologics ever was an exclusion criteria.
Demographical (age, sex) and RA activity data (DAS28, SDAI, number of tender and swollen joints (NTJ, NSJ), erythrocytes sedimentation rate (ESR), C-reactive protein (CRP), and HAQ, EQ5D were collected, table 1. Statistical analysis performed in SPSS 2017. p-value <0.05 considered as significant.

**Results:** At baseline 12 (10%) were treated with NSAIDs, 15 (12.6) with 5-10 mg/day of prednisolone, 82 (68.9) – with methotrexate (10-25 mg/week), 8 (6.7%) – with sulfasalazine (2.0-3.0 g/day).

**Abstract THU0171 – Table 1.** Baseline characteristics of the patients with RA (n=119)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>44 (36.9)</td>
</tr>
<tr>
<td>Age of disease onset, years (mean ±SD)</td>
<td>41.1±11.5</td>
</tr>
<tr>
<td>Symptoms duration, month (mean ±SD)</td>
<td>113.7± 96.61</td>
</tr>
<tr>
<td>Positive rheumatoid factor, n (%)</td>
<td>68 (41.7)</td>
</tr>
<tr>
<td>Positive antibodies to cyclic citrullinated peptide (anti-CCP), n</td>
<td>82 (68.9)</td>
</tr>
<tr>
<td>Erosions of hand joints (X-rays), n (%)</td>
<td>28 (23.5)</td>
</tr>
<tr>
<td>BMI, kg/m² (mean ±SD)</td>
<td>21.8±4.37</td>
</tr>
<tr>
<td>Smokers (current and in the past), n (%)</td>
<td>42 (35.3)</td>
</tr>
</tbody>
</table>

Changes in the disease activity in patients with RA, treated with tocilizumab after csDMARD are presented in Table 2

**Abstract THU0172 – Table 1.** Efficacy outcomes in patients with RA treated with tocilizumab

<table>
<thead>
<tr>
<th>NTJ</th>
<th>N</th>
<th>NSJ</th>
<th>Global</th>
<th>ESR</th>
<th>CRP</th>
<th>DAS28</th>
<th>HAQ</th>
<th>EQ-5D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>8.48 ± 3.68</td>
<td>52.48</td>
<td>29.32</td>
<td>19.10 ± 4.56</td>
<td>1.61</td>
<td>0.58</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Month6</td>
<td>6.29 ± 3.52</td>
<td>27.51</td>
<td>12.86</td>
<td>3.84</td>
<td>1.08</td>
<td>0.70</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Month12</td>
<td>6.09 ± 3.52</td>
<td>27.51</td>
<td>12.86</td>
<td>3.84</td>
<td>1.08</td>
<td>0.70</td>
<td></td>
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</tr>
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</table>

In patients (pts) with active rheumatoid arthritis (RA) and inadequate response or intolerance to bDMARDs, treatment with upadacitinib (UPA), a JAK1-selective inhibitor resulted in significant improvements over 24 weeks (wks).

**Objectives:** We assessed UPA safety and efficacy through Wk60 in an ongoing extension of the phase 3 SELECT-BEYOND study.

**Methods:** SELECT-BEYOND enrolled a population of patients with active RA who had failed at least one prior biologic therapy. Pts received UPA 15mg or 30mg once daily (QD) or placebo (PBO) on top of background csDMARD treatment for 12 wks. From Wk12, pts randomized to UPA at baseline (BL) continued their assigned doses while pts initially randomized to PBO received UPA 15mg or 30mg QD per pre-specified assignment at BL. Patients who completed Wk 24 entered the blinded long-term extension. Dose adjustments to UPA were not allowed. Adverse events (AE) per 100 pt years (PY) are summarized based on a cut-off date of 16 April 2018. Efficacy data up to the Wk60 visit are reported “As Observed”.

**Results:** 418/498 (84%) pts were randomized, completed 24 wks and entered the extension on study drug. By the safety data cut-off date, 19% pts discontinued study drug: 5% due to AE, 4% due to lack of efficacy, 3% withdrew consent, 2% were lost to follow-up, and 5% discontinued due to other reasons. Cumulative exposures to UPA15 and UPA30 were 301.7 and 290.7 PYs, respectively. Rates (Events/100PYs) of treatment-emergent AEs are reported (Table 1), and were numerically higher in the UPA30 vs UPA15 arm for serious AEs, AEs leading to discontinuation, serious infections, herpes zoster and hepatic disorders. Based on As Observed analysis, for pts completing Wk60 on UPA15 [172/216 (80%)] and UPA30 [168/202 (83%)], clinical and functional outcomes continued to improve compared to Baseline, or were maintained from Wk24 onwards in pts initially randomized to UPA15 or 30; Remission by CDAI≤2.8 at Wk60 was achieved by 20% and 32%, respectively, and DAS28-CRP<2.6 was achieved by 53% and 52%. Pts who were switched to UPA from PBO at Wk12 had comparable efficacy to pts initially randomized to UPA (Table 2).

**Conclusion:** The benefit: risk of upadacitinib treatment in this refractory population remains favorable. No new safety signals were identified. Some AEs were numerically higher for UPA30 vs 15; however the clinical significance of this, the assessment of rare safety events in this study, and the overall benefit: risk of upadacitinib 15mg and 30mg in the treatment of RA are best evaluated in an integrated analysis across the phase 3 program. UPA15mg and 30mg continued to be effective in treating RA signs and symptoms, and in improving physical function.

**REFERENCES:**

**Acknowledgement:** AbbVie, Inc was the study sponsor, contributed to study design, data collection, analysis & interpretation, and to writing, reviewing, and approval of final version. Medical writing support was provided by Naina Barretto, of AbbVie, Inc.

**Disclosure of Interests:** Mark C. Genovese Grant/research support from: Sanofi/Genezyme, Genentech/Roche, RPharm, Bernard Combe Consultant for: Abbvie, Bristol-Myers Squibb, Gilead, Janssen, Eli Lilly, MSD, Novartis, Pfizer, Roche-Chugai, Sanofi, UCB, Stephen Hall Grant/research support from:
Filgotinib (FIL), an oral, selective Janus kinase 1 (JAK1) inhibitor, significantly improved the signs and symptoms of rheumatoid arthritis (RA) in the phase 3 FINCH2 study in bDMARD-IR patients with active RA.1

**Objectives:** To evaluate the efficacy and safety of FIL by geography and race in FINCH2.

**Methods:** FINCH2 enrolled 449 bDMARD-IR patients with active RA, who were randomized in a 1:1:1 manner to receive FIL 200 mg, FIL 100 mg, or placebo (PBO) on a background of csDMARDs for 24 weeks. In this prespecified subgroup analysis, patient and disease characteristics and treatments were analyzed by race and geographic region (Region 1: AU, BE, FR, DE, IS, IT, NL, KR, ES, CH, UK, US; Region 2: HU, CZ, PL; Region 3: AR, PR, MX; Region 4: JP).

**Results:** 449 patients received ≥1 dose of study drug; they were 80.4% female, with a mean [SD] age of 56 [12.2] years, and 23.4% had received ≥3 prior bDMARDs. Baseline characteristics were similar across regions and race. The primary endpoint and all key secondary endpoints were met in the primary analysis.1 Efficacy and safety parameters by region in FINCH2 are presented.

**Conclusion:** FIL demonstrated consistent safety and efficacy in bDMARD-IR patients with RA regardless of geography or race.

**REFERENCES:**


<table>
<thead>
<tr>
<th>Table 1</th>
<th>Week 24 key efficacy and safety measures by geographic region.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regimen</td>
<td>N¹</td>
</tr>
<tr>
<td>---------</td>
<td>-----</td>
</tr>
<tr>
<td>Region 1</td>
<td>FIL 200 111 67</td>
</tr>
<tr>
<td>FIL 100 110 49</td>
<td>24</td>
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<tr>
<td>PBO 110 32</td>
<td>14</td>
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<tr>
<td>Region 2</td>
<td>FIL 200 12 75</td>
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<td>FIL 100 100 75</td>
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<td>PBO 100 11</td>
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<tr>
<td>Region 3</td>
<td>FIL 200 12 67</td>
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<td>FIL 100 100 16</td>
<td>8</td>
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<tr>
<td>PBO 100 14</td>
<td>6</td>
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<tr>
<td>Region 4</td>
<td>FIL 200 12 92</td>
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<tr>
<td>FIL 100 100 50</td>
<td>27</td>
</tr>
<tr>
<td>PBO 100 13</td>
<td>0</td>
</tr>
</tbody>
</table>

¹n’s in HAQ-DI at week 24 were different. ²Nonresponder imputation: ≤p<0.05, ≤p<0.01, ≤p<0.001 vs PBO. CFB, change from baseline as mean (SD); SAE, serious adverse events; TEAE, treatment-emergent adverse events.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Week 24 key efficacy and safety measures by race.</th>
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</thead>
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<td>Regimen</td>
<td>N¹</td>
</tr>
<tr>
<td>---------</td>
<td>-----</td>
</tr>
<tr>
<td>White</td>
<td>FIL 200 110 67</td>
</tr>
<tr>
<td>FIL 100 109 49</td>
<td>25</td>
</tr>
<tr>
<td>PBO 97 34</td>
<td>16</td>
</tr>
<tr>
<td>Black</td>
<td>FIL 200 14 57</td>
</tr>
<tr>
<td>FIL 100 12 67</td>
<td>17</td>
</tr>
<tr>
<td>Asian</td>
<td>FIL 200 15 93</td>
</tr>
<tr>
<td>FIL 100 20 60</td>
<td>30</td>
</tr>
<tr>
<td>Asian</td>
<td>FIL 15 13</td>
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</table>
CHARACTERIZATION OF REMISSION IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH UPADACITINIB OR COMPARATORS

Stephen Hall1, Tautomu Takeuchi2, Glen Thomson3, Paul Emery4, Bernard Comfort3, Andrea Everding5, Karel Pavelka8, Yanna Song2, Tim Shaw2, Alan Friedman6, In-Ho Song8, Eduardo Mysler9, Monash Univ, Cabrini Health and Emeritus Research, Malvern, Australia; 2Keio Univ School of Medicine, Tokyo, Japan; 3CIADS Research, Winnipeg, Canada; 4Leeds Inst of Rheumat and Musculoskeletal Medicine, Leeds NIHR BRC, Leeds, United Kingdom; 5CHU Montpellier, Univ Montpellier, Montpellier, France; 6HVF Hamburger Rheuma Forschungszentrum, Hamburg, Germany; 7Charles Univ, Prague, Czech Republic; 8AbbVie Inc, North Chicago, United States of America; 9Organización Medica de Investigación, Buenos Aires, Argentina

Background: Across all phase 3 studies, treatment with upadacitinib (UPA), a JAK1-selective inhibitor, was associated with significantly higher remission (REM) rates, compared to placebo (PBO) or active comparators, in RA patients (pts) who were methotrexate (MTX)-naive, had inadequate response to conventional synthetic (csDMARD-IR) or had inadequate response or intolerance to biologic DMARDs (bDMARD-IR).

Objectives: REM definitions are based on composite scores of various individual assessments of disease activity. To determine the response to UPA on REM and component assessments, we assessed the proportions of pts achieving REM using multiple REM definitions, and the improvement in their respective individual components, compared to PBO or active comparators, in 3 different RA pt populations spanning a range of RA pt populations.

Methods: Three phase 3 studies included pts who were RA-IR (MTX naive [SELECT EARLY, n=945]), MTX-IR (SELECT COMPAR, n=1629) and bDMARD-IR (SELECT BEYOND, n=498). The proportion of pts achieving REM at Week (Wk) 12 by 4 definitions (DAS28-4CRP≤2.6; CDAI≤28; SDAI≤33 and Boolean, defined as ≤1 for SJC, SJC, patient’s global assessment of disease activity [PGA], and CRP ≤1 mg/L) were determined. For each definition of REM, the mean change in each of the respective component scores was also assessed. Binary endpoints are based on Non-responder imputation (NRI), and continuous endpoints on mixed-effect model repeat measurement (MMRM). Comparisons were made between UPA-treated groups vs respective control arms (MTX, adalimumab [ADA] or PBO).

Results: Pt demographics and disease characteristics have been previously reported. 1–3 At week 12 in EARLY and COMPARE, a significantly greater proportion of pts receiving UPA 15 mg or 30 mg QD achieved REM by all 4 definitions vs MTX, PBO or ADA (Table). In BEYOND, (a refractory population many of whom had inadequate response to multiple bDMARDs), a significantly greater proportion of pts receiving UPA 30mg achieved all REM definitions vs PBO within the first 12 wks, with significantly greater proportions on UPA 15mg achieving DAS28-4CRP≤2.6 and Boolean REM (Table). Rates of REM in BEYOND further increased through Wk 24 for both dose groups. 3Compared to respective control groups, pts receiving UPA 15 or 30 mg QD had significantly greater improvements in each REM disease component (except for PhGA vs ADA in COMPARE). Significantly more pts receiving UPA also achieved the required cutoffs on the individual components of Boolean REM compared to respective control groups.

Conclusion: Significantly greater proportions of pts receiving UPA 15 or 30mg achieved REM by multiple definitions at 12 wks compared to PBO, MTX or ADA. All disease activity components of each REM definition were significantly improved in pts receiving UPA compared to MTX or PBO, and all Boolean components were significantly improved in pts receiving UPA 15mg compared to ADA.

REFERENCES:

Acknowledgement: AbbVie, Inc was the study sponsor, contributed to study design, data collection, analysis & interpretation, and to writing, reviewing, and approval of final version. Medical writing support was provided by Naina Barretto, PhD, of AbbVie, Inc.


THU0175

CHARACTERIZATION OF REMISSION IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH UPADACITINIB OR COMPARATORS

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Background: Across all phase 3 studies, treatment with upadacitinib (UPA), a JAK1-selective inhibitor, was associated with significantly higher remission (REM) rates, compared to placebo (PBO) or active comparators, in RA patients (pts) who were methotrexate (MTX)-naive, had inadequate response to conventional synthetic (csDMARD-IR) or had inadequate response or intolerance to biologic DMARDs (bDMARD-IR).

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Acknowledgement: AbbVie, Inc was the study sponsor, contributed to study design, data collection, analysis & interpretation, and to writing, reviewing, and approval of final version. Medical writing support was provided by Naina Barretto, PhD, of AbbVie, Inc.


THU0174 DOSE-DEPENDENT RISK OF METHOTREXATE FOR RENAL IMPAIRMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Methotrexate (MTX) is a mainstay in the therapy of rheumatoid arthritis (RA). It is recommended that MTX should be rapidly
COMPARISON OF ADHERENCE TO MONOTHERAPY TREATMENT PATTERNS AMONG PATIENTS WITH RA

Objectives: The purpose of this study is to elucidate the association between MTX dosage and a one-year change of estimate glomerular filtration rate (eGFR) in RA patients.

Methods: Of outpatients with RA in Okayama university hospital between 2006 and 2017, 497 patients who had continued the administration of MTX for more than one year were enrolled. All patients fulfilled the ACR/EULAR 2010 Classification Criteria for RA. Patients who had nephrotic syndrome, unilateral kidney or other rheumatic disorders other than secondary Sjögren’s syndrome were excluded. The primary outcome was the change of eGFR during the most recent one year in each patient. The revised Japanese equation of Modification of Diet in Renal Disease was used to calculate eGFR. MTX dosage was defined as an average dosage of MTX during the observational period. We evaluated the association between MTX dosage and the primary outcome using univariate and multivariate analysis.

Results: Median (IQR) age was 64 (52 - 72) years, 78% were female, and median disease duration was 73 (31 - 160) months. The median dosage of MTX was 8 mg/week (6 - 10.1) and biological agents were used in 28% of the patients. The eGFR (mean ± SD) decreased by 1.2 ± 8.3 ml/min/1.73m² in one year and MTX dosage was associated with the change of eGFR significantly (p<0.0001). The eGFR in patients treated with MTX <8 mg/week (n=185), ≥8 and <10 (n=131), ≥10 and <12 (n=86), ≥12 (n=95) decreased 0.2 ± 0.6, 0.6 ± 0.7, 1.0 ± 0.9, and 4.6 ± 0.8 ml/min/1.73m²/year, respectively. After adjusting possible confounding factors such as sex, age, concomitant use of NSAIDs, hypertension, and C reactive protein (CRP) using multiple linear regression analysis, MTX dosage was still an independent risk factor for the decrease of eGFR (beta-coefficient: -0.4, 95% confidence interval -0.12 - -0.61, p=0.003).

Conclusion: Careful monitoring of renal function should be required in long-time treatment for RA patients with MTX.

REFERENCES:

THU0177
COMPARISON OF ADHERENCE TO MONOTHERAPY VERSUS COMBINED THERAPY IN RHEUMATOID ARTHRITIS

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Background: Treatment adherence in Rheumatoid Arthritis (RA) patients vary from 30 to 80% (1). It is important to identify the associated factors to a low adherence, so clinicians can make interventions to obtain better therapeutic results. Adherence to treatment has been described to be affected by several factors, such as access to healthcare facilities, education, socioeconomic status, quality of communication between physician and patient, among others (2). There are no previous studies that investi gate if the number of drugs received in RA patients affects this adherence. REPAIR is a program designed with the purpose of improve data collection and medical practice in our outpatient clinic.

Objectives: To compare the adherence to synthetic Disease-Modifying Antirheumatic Drugs (DMARDs) among RA patients prescribed with mono therapy and combined therapy.

Methods: Cross sectional, observational, comparative study. This study was conducted in the outpatient rheumatology clinic of University Hospital in Monterrey, Mexico. Consecutive patients with RA were approached during their normal routine rheumatology appointments, in the March 2018 to December 2018 period. They were asked how many days of the last month they forgot or took their DMARDs (self-report). We classified the adherence rate in 2 categories based on the days of the last month they took the indicated medication; adequate: 75%-100% (> 21 days), inadequate <75% (<21 days). When adherence was inadequate we interrogated about the cause. Data was obtained from REPAIR (internal electronic patient record). The Kolmogorov Smirnov test was used to determine if normal distribution. Categorical variables are expressed as total number and percentage (%), and numerical variables as median and the 25th-75th percentiles (q25-q75). Chi square and Mann Whitney U test were used to compare groups and considered significant if p<0.05. Data was analyzed with the statistical package SPSS version 24 (New York, USA).

Results: A total of 959 patients were included. When comparing adherence to treatment and gender between groups, no statistically significant difference was found. The main cause of inadequate adherence in the monotherapy group was the economic (30.3%) and own decision in the combined therapy group (29.1%).

Table 1:

<table>
<thead>
<tr>
<th>Monotherapy (n=346)</th>
<th>Combined therapy (n=613)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), median (p25-p75)</td>
<td>54 (44-63)</td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>317 (91.6)</td>
</tr>
<tr>
<td>Inadequate adherence to treatment, n (%)</td>
<td>52 (15)</td>
</tr>
<tr>
<td>Adequate adherence to treatment, n (%)</td>
<td>294 (85)</td>
</tr>
</tbody>
</table>

Conclusion: Patients with combined therapy had the same percentage of inadequate adherence as patients with monotherapy. These results may indicate that number of drugs prescribed not necessarily affects adherence to treatment. The principal causes for an inadequate adherence to treatment were: economic for monotherapy group and own decision for combined therapy group. However, long-term studies are needed to evaluate the persistence of treatment in these groups of patients.

REFERENCES:

Disclosure of Interests: None declared

THU0178
TREATMENT PATTERNS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH A BIOLOGIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUG OR JAK INHIBITOR: A NATION-WIDE STUDY IN KOREA

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Background: Limited data are available on whether patients with rheuma toid arthritis (RA) are treated with conventional, disease-modifying anti rheumatic drugs (cDMARDs) according to the current recommendations before they initiate biologic DMARDs (bDMARDs) or JAK inhibitors (JAKis).

Objectives: We examined the treatment patterns among Korean RA patients who received bDMARDs or JAKis in a real world setting, using the 2002-2016 Korean National Health Insurance Service database that covers the entire Korean population.

Methods: We identified RA patients who initiated bDMARDs (TNF inhibitor, abatacept, rituximab and tocilizumab) or JAKis (tofacitinib). Their treatment patterns during 1 year after RA diagnosis (defined as free of any RA diagnosis or any DMARD use for one year before the diagnosis) and prior to the initiation of index drugs (bDMARDs or JAKis) were examined regarding: initial cDMARD used, dose and parenteral use of methotrexate (MTX), use and time to combination therapy of cDMARDs, and steroid use.
Yuliya Kurochkina1, Tamara Tyrinova2, Olga Leplina2, Marina Tikhonova2, Elena Chernykh2.

Dendritic cells (DCs) are known to contribute to the pathogenesis of rheumatoid arthritis (RA) through the presentation of cartilage glycoprotein, production of proinflammatory cytokines and activation of Th1/cytotoxic T-lymphocytes, utilization of tolerogenic DCs seems to be a promising immunotherapeutic tool to treat RA.

Objectives: Objective of our study is to evaluate the safety and tolerability of a single intra-articular injection (into the knee joint) of autologous monocyte-derived dendritic cells generated in the presence of IFN-α/GM-CSF and tolerized with Dexamethasone in patients with RA.

Methods: DCs were generated by culturing blood monocytes for 5 days with GM-CSF and IFN-α and tolerized with Dexamethasone in RA patients. DCs were injected into the knee joint. 

Results: DCs injections were safe and well-tolerated. No one patients showed worsening of symptoms in targetting knee, fever, elevation of blood pressure or other AE within 7 days after injection. All patients, evaluated at 6 months follow-up showed a good EULAR response (improvement of DAS28-ESR >1.2). The median DAS28-ESR decreased from 5.10 (p=0.03). The median VAS score decreased from 52 (41-70) mm to 42 (15-55) mm; p=0.04. In addition, we detected median HAG improvement from (1.45 to1.0; p=0.04). The effect of treatment had been continued for 6 month and after that we indicated escape of effect. 

Conclusion: The data obtained suggest that single intra-articular injection of autologous tolerogenic dendritic cells is safe, well tolerated, and have a potential not long term efficiency and requires the repeating of procedure.

Disclosure of Interests: None declared

Piotr Ligocki1, Grzegorz Orlik2, Vishal Vekariya3.

Background: MTX is a well-established treatment with an anchor role in RA (1). Patients being treated for RA must pay attention to the specific dosage of drugs and the different routes of administration. Additionally, they suffer from the inconvenience related to the progression of the disease.

Objectives: We observed 125 RA patients diagnosed with RA, who were treated with subcutaneous (SC) MTX and possible risks associated with this therapy. The attention paid to the inconvenience for the patient associated with SC form of drug administration and the principles of MTX dosing with FA supplementation.

Methods: 32 rheumatologists were invited to non-interventional, post marketing observation. They collected information from 690 patients who already received a minimum of 1 dose of MTX SC. As part of a standard medical visit, the sociographic data of the patient and information obtained during the medical interview as well as subjective and objective examination were recorded in the prepared form. Data was collected on a weekly basis over a period of 8 weeks. The protocol was compliant with the regulatory and ethical requirements in the country.

Results: Out of 682 enrolled patients, 581 (85.2%) were siero-positive and 95 (14%) were siero-negative. The average level of anti-CCP antibodies before enrollment was 85.76 Units. The mean time from the diagnostic of the underlying disease was 28.7 months. The vast majority of patients confirmed that they had previously used FA supplementation (90.2%). Only 10 patients showed DAS28 at the remission level. During each visit no adverse events (AE) were reported in over 90% of patients. The most commonly reported AE are nausea or weakness. No severe, life threatening AE were recorded. 

Patients evaluated the pain of the injection on a scale of 1 to 10, where 1 is the minimum and 10 the maximum pain. Most patients assessed the pain of injections as the minimum (1) (56.5% - week 1 (W1), 52.9% - W2, 56.7% - W3, 61.5% - W4, 56.7% - W5, 53.8% - W6, 65.2% - W7, 61.8% - W8). The second most frequently mentioned pain assessment by respondents was 2 (34.6% - W1, 35.3% - W2, 34.3% - W3, 29.2% - W4, 34.3% - W5, 38.5% - W6, 26.1% - W7, 32.9% - W8). No patients reported values between 6 and 10. Patients also assessed how the pain at the site of injection on a scale of 1 to 10, where 1 is the minimum and 10 the maximum pain. Each week, more than half of the patients assessed pain at the injection site as 1 (55.9% - W1, 56.7% - W2, 56.7% - W3, 57.8% - W4, 50.8% - W5, 62.5% - W6, 60.3% - W7, 61.6% - W8). Patients did not report any value of 5-10. More than seven out of ten patients reported FA administration the day 2 of their therapy (76.5%, at W1). In remaining days FA supportive therapy reported 30.3-52.3% of patients (2).

Conclusion: Neither pain related with injection nor local AE was reported as a significant issue by patients. Adherence to FA administration recommendation is low. This should be evaluated in further studies, but there is a risk that inappropriate FA administration may reduce efficacy of MTX treatment.

REFERENCE:
Influence of Blue Mussel (Mytilus Edulis) Intake on Fatty Acid Composition in Erythrocytes and Plasma Phospholipids and Serum Metabolites in Women with Rheumatoid Arthritis

Helen Lindqvist1, Inger Gjertsson1, Philip Calder2, Linnea Barebring1. 1University of Gothenburg, Medicine, Gothenburg, Sweden; 2University of Southampton, Southampton, United Kingdom

Background: The positive effects of omega-3 on risk of cardiovascular disease, on inflammation and immune function are well established [1]. Unfortunately fish as a source of omega-3 is not economically or environmentally sustainable. In contrast, blue mussel farming is beneficial for the environment since excessive nitrogen is removed at harvest and eutrophication of the sea is reduced [2]. Blue mussels contain not only omega-3, but are rich in nutrients such as zinc, selenium, riboflavin and carotenoids. We have previously shown, in the randomized cross-over trial Mussels, Inflammation and RA (MIRA), that disease activity (DAS28-CRP), fatigue, pain and general health in RA is improved by a dietary intervention with blue mussels compared to control [3]. It is not clear what the mechanisms of the intervention were, and if the intake of omega-3 from the blue mussels plays a role.

Objectives: The aim of this study was to investigate if the intake of blue mussels in patients with RA lead to changes in fatty acid composition in plasma phospholipids and erythrocytes and/or in metabolites (detected by NMR-metabolomics), compared to a control diet, in an attempt to understand the health beneficial effects found in the MIRA study.

Methods: Twenty-three women completed the randomized 2 x 11-week cross-over dietary intervention, exchanging one cooked meal a day, five days a week, with a meal including 75 g blue mussels or 75 g meat. Fatty acid composition in erythrocytes and plasma and 1H-NMR metabolomics data were analysed and multivariate data analysis; Orthogonal Projections to Latent Structures (OPLS-DA) and OPLS with effect projections (OPLS-EP) were performed to compare the two diets.

Results: Intake of the blue mussels led to a different fatty acid profile in erythrocytes, compared to control, and all samples could be correctly classified with OPLS-DA (figure 1). The changes included significant increases in omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). The patterns for plasma phospholipids and 1H-NMR serum metabolites were not as specific for the diets and metabolites were strongly influenced by body mass index (BMI) (figure 2).

Conclusion: To conclude, the change in fatty acid pattern in erythrocytes could be related to reduction in disease activity in the MIRA-study, although it cannot be excluded that other factors than omega-3 fatty acids potentiate the effect. Multivariate modelling of fatty acids in erythrocytes increased the precision for compliance, compared to evaluating EPA and DHA content alone.

References:

Disclosure of Interests: Helen Lindqvist Employee of: Yes, for Janssen-Cilag AB in 2001-2003, Before I was a PhD-student and within a different field (dementia). My research field is within diet and Rheumatology., Inger Gjertsson: None declared, Philip Calder: None declared, Linnea Barebring: None declared.


Treatment with Upadacitinib Results in the Normalization of Key Pathobiological Pathways in Patients with Rheumatoid Arthritis: Biomarker Results from the Phase 3 SELECT-NEXT and SELECT-BEYOND Studies

Thierry Somasse1, Jeremy Sokolove2, Lisa Meinnet3. 1AbbVie Immunology Clinical Development, Redwood City, United States of America; 2University of Glasgow, Glasgow, United Kingdom

Background: Upadacitinib (UPA), an oral JAK inhibitor selective for JAK1, demonstrated efficacy in patients with moderate-to-severe rheumatoid arthritis (RA) with an inadequate response (IR) to conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) or biologic DMARDs (bDMARDs) in the SELECT-NEXT1 and SELECT-BEYOND2 trials, respectively. The pivotal immune regulatory pathway targets served by JAK1 in patients with RA via a proteomic approach that evaluates a set of plasma proteins associated with inflammation.

Objectives: To investigate the mode of action (MoA) of UPA in patients with RA via a proteomic approach that evaluates a set of plasma proteins associated with inflammation.

Methods: Patients from the SELECT-NEXT and SELECT-BEYOND (PBO, n=167; UPA 15 mg QD, n=200) studies were randomly selected from the pool of patients with plasma samples available at baseline, Week 2, and Week 12. Samples from 24 age- and sex-matched healthy controls were included. The levels of 92 proteins were analyzed using the Olink® Inflammation Panel. Results from both studies were combined. Data were clustered using the Ward (unsupervised) method; correlations were calculated using the Pearson method; and multiple comparisons were corrected using the Benjamini–Hochberg method; all statistical analyses were performed in JMP 13.10 (SAS Institute). Pathway analysis was performed with Ingenuity® Pathway Analysis (Qiagen Inc.) version 43688156.
Results: At baseline, levels of IL-6, CXCL9, CXCL10, and CCL7 correlated significantly with baseline DAS28-ESR, consistent with effector roles for IL-6 and interferon (IFN) in intercurrent disease activity. Clustering of the differential protein fold change at Weeks 2 and 12 for UPA and PBO groups revealed four clusters enriched for proteins related to: 1) IL-6, IFN, leukocyte trafficking, and macrophage activation (1); 2) T helper cell differentiation (2); 3) T and B cell signaling (3); and 4) hematopoiesis and myeloid cell differentiation (4). Pathway analysis 2 based on the differential expression of 37 significantly modulated proteins suggests that treatment with UPA results in the normalization of key pathways associated with the pathobiology of RA including: 1) pathways associated with IL-1, IL-6, IL-12, IL-15, IL-18, IFNα, IFNβ, IFNγ, CSF2, and TNF; and 2) pathways associated with behaviors of leukocytes (lymphocytes, myeloid cells, and granulocytes), including leukocyte migration, T cell response, and inflammatory response. In keeping with these changes, in IL-6, CCL23, CCL7, MIPH, and S100A12 levels at Week 12 correlated significantly with the relative change in DAS28-ESR, suggesting a link between UPA MoA and macrophage activation.

Conclusion: In keeping with its selectivity for JAK1, UPA operates via inhibition of multiple JAK1-dependent upstream pathways that result in the normalization of key downstream effects associated with the pathobiology of RA, including T cell and myeloid cell-related pathways. Notably, non-JAK signaling pathways also normalize, suggesting functional integration of JAK1 with parallel pathogenic signaling in RA effector cells.

REFERENCES:

Acknowledgement: AbbVie, Inc. was the study sponsor, contributed to the study design, data collection, analysis & interpretation, and to writing, reviewing, and approval of the final version. Medical writing support was provided by John Ewbank, PhD, of the Nth.

Disclosure of Interests: Thierry Somasse Shareholder of: AbbVie; Employee of: AbbVie; Jeremy Sekolove Shareholder of: AbbVie; Employee of: AbbVie, Iain McNees Grant/research support from: AstraZeneca, Celgene, CompuGen, Novartis, Roche, UCB Pharma, Consultant for: AbbVie, Celgene, Galvani, Lilly, Novartis, Pfizer, UCB Pharma


Table 1

<table>
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<th>Parameter</th>
<th>Normal (n=10)</th>
<th>Mild (n=10)</th>
<th>Moderate (n=8)</th>
<th>Severe (n=4)</th>
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<td>7.0 (7.0)</td>
<td>7.8 (7.0)</td>
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<td>27.8 (7.0)</td>
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<td>Median, (min, max)</td>
<td>55.5 (23.0, 69.0)</td>
<td>50.5 (37.0, 70.0)</td>
<td>62.0 (46.0, 75.0)</td>
<td>67.0 (58.0, 71.0)</td>
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<td>Mean, (min, max)</td>
<td>68.6 (47.6, 76.8)</td>
<td>66.4 (45.6, 76.8)</td>
<td>58.4 (35.0, 75.0)</td>
<td>67.6 (46.7, 74.0)</td>
<td>58.4 (35.0, 75.0)</td>
</tr>
<tr>
<td>Mean, (min, max)</td>
<td>73.0 (15.4, 214.0)</td>
<td>72.0 (25.0, 236.0)</td>
<td>72.0 (25.0, 236.0)</td>
<td>72.0 (25.0, 236.0)</td>
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Abstract THU0182 – Table 1

THU0182

PHARMACOKINETICS AND SAFETY OF A SINGLE ORAL DOSE OF PEFICITINIB (ASP015K) IN SUBJECTS WITH NORMAL AND IMPAIRED RENAL FUNCTION

Daijuke Miyatake1, Tomohisa Shibata1, Masa Shibata1, Yuchi Kaneko1, Kazuo Oda2, Tomohisa Shibata1, Mai Shibata1, Yuichiro Kaneko1, Kazuo Oda2, Tomohisa Shibata1, Mai Shibata1, Yuichiro Kaneko1, Kazuo Oda2, Tomohisa Shibata1, Mai Shibata1, Yuichiro Kaneko1, Kazuo Oda2, Tomohisa Shibata1, Mai Shibata1, Yuichiro Kaneko1, Kazuo Oda2, Tomohisa Shibata1, Mai Shibata1, Yuichiro Kaneko

Objectives: To assess the pharmacokinetics (PK) and safety of a single, oral dose of peficitinib 150 mg in subjects with normal and impaired renal function.

Methods: This was an open-label, single-dose, parallel-group study conducted at two centres in Japan. All subjects were aged 20–75 years with a body mass index 17.6 to <30.0 kg/m2. Renal function was categorized according to estimated glomerular filtration rate (eGFR) using a GFR predictive equation for Japanese subjects: normal 90 mL/min/1.73 m2; moderate impairment 60 to <90 mL/min/1.73 m2; and severe impairment <60 mL/min/1.73 m2. Subjects with impaired renal function had unchanged renal impairment treatment (including diet) within 14 days prior to dosing. Subjects received a single oral dose of peficitinib 150 mg tablet under fasting conditions in a hospital setting. The selected dose was based on the peficitinib daily dose in the phase 3 RA studies. Blood samples for peficitinib plasma PK analysis were collected before administration and up to 72 h post dose. Safety was assessed throughout the study.

Results: A total of 31 subjects (87.1% male; Table 1) were enrolled and received study drug according to study protocol. Subjects comprised 8 with normal renal function, and 8 with mild, 8 with moderate and 7 with severe renal impairment. The peficitinib concentration–time profiles from dosing to 72 h (Fig 1), extrapolated to infinity (AUC∞) and maximum concentration (Cmax) were similar between those with normal and impaired renal function (Table 2). Two subjects had mild/grade 1 (CTCAE v4.0 JCOG) treatment-emergent adverse events (TEAEs): 1/8 (12.5%) with normal renal function had a headache (considered to be drug-related) and 1/8 (12.5%) with mild renal impairment had increased alanine aminotransferase (ALT) (not considered to be drug-related). There were no serious TEAEs or deaths during the study. There were no clinically significant mean changes from baseline in other clinical laboratory parameters or vital sign measurements, except for grade 1 increased ALT in a subject with mild renal impairment.

Abstract THU0182 – Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal (n=10)</th>
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<td>72.0 (25.0, 236.0)</td>
<td>72.0 (25.0, 236.0)</td>
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</tbody>
</table>

Abstract THU0182 – Figure 1

Conclusion: Exposure after a single 150 mg oral dose of peficitinib under fasting conditions was similar between subjects with and without renal impairment. The peficitinib dose was generally well tolerated, with no changes in TEAE incidence by renal function.

REFERENCES:

Acknowledgement:
AbbVie, Inc was the study sponsor, contributed to the study design, data collection, analysis & interpretation, and to writing, reviewing, and approval of the final version. Medical writing support was provided by John Ewbank, PhD, of the Nth.

Disclosure of Interests: Thierry Somasse Shareholder of: AbbVie; Employee of: AbbVie; Jeremy Sekolove Shareholder of: AbbVie; Employee of: AbbVie, Iain McNees Grant/research support from: AstraZeneca, Celgene, CompuGen, Novartis, Roche, UCB Pharma, Consultant for: AbbVie, Celgene, Galvani, Lilly, Novartis, Pfizer, UCB Pharma

Upadacitinib Pharmacokinetics in Japanese Subjects with Rheumatoid Arthritis with the Extended-Release Formulation and Comparability to Non-Japanese Subjects

Mohamed-Eslam Mohamed, Ben Kluender, Sebastian Meerwein, Ahmed Othman, AbbVie, North Chicago, United States of America; AbbVie Deutschland GmbH and Co. KG, Ludwigshafen, Germany

Background: Upadacitinib (UPA), an oral selective JAK1 inhibitor, is being developed for treatment of patients with moderate to severely active rheumatoid arthritis (RA). UPA efficacy was demonstrated in subjects with moderate to severe RA in five global Phase 3 studies and a regional Phase 2b study in Japanese subjects.

Objectives: To characterize the pharmacokinetics of UPA after administration of the extended-release formulation in Japanese subjects with RA and to compare UPA plasma exposures between Japanese and non-Japanese subjects.

Methods: Population pharmacokinetic analyses were conducted using UPA data across Phase 1 to 3 studies including Japanese and non-Japanese subjects. The population pharmacokinetic model was used to estimate UPA plasma exposures from the extended-release formulation regimens in non-Japanese and Japanese subjects with RA in Phase 3 trials. Additionally, a total of 29 Japanese subjects with RA who were enrolled in SELECT-SUNRISE Phase 2b study participated in a pharmacokinetics substudy in which serial blood samples were collected from each subject over a 24 hour period after UPA dosing. UPA was administered in the study at doses of 7.5 mg, 15 mg, and 30 mg QD using the extended-release formulation. Pharmacokinetic parameters were calculated in the pharmacokinetic substudy using noncompartmental methods.

Results: UPA maximum plasma concentration was reached within 2 hours of dosing under fasting condition. UPA plasma exposures were approximately dose proportional over the evaluated dose range in Japanese subjects with RA. UPA model estimated plasma exposures (based on population pharmacokinetic analyses) were comparable (within 20%) between Japanese and non-Japanese subjects with RA (Table 1). Results from the pharmacokinetic substudy using noncompartmental methods were consistent with the population pharmacokinetic analyses.

Abstract THU0183 – Table 1. Upadacitinib Model Estimated Exposures in Japanese and Non-Japanese Subjects with RA for the Extended-Release Formulation

<table>
<thead>
<tr>
<th>Population</th>
<th>Treatment</th>
<th>Cmax (ng/mL)</th>
<th>Cavg (ng/mL)</th>
<th>Csbound (ng/mL)</th>
</tr>
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<tbody>
<tr>
<td>Japanese</td>
<td>7.5 mg QD</td>
<td>24.0</td>
<td>8.8</td>
<td>2.4</td>
</tr>
<tr>
<td>(N = 104)</td>
<td></td>
<td>(18.0, 31.0)</td>
<td>(5.0, 15.2)</td>
<td>(0.7, 7.7)</td>
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<tr>
<td>Non-Japanese</td>
<td>15 mg QD</td>
<td>10.9</td>
<td>15.1</td>
<td>3.8</td>
</tr>
<tr>
<td>(N = 1495)</td>
<td></td>
<td>(8.9, 32.4)</td>
<td>(1.3, 21.3)</td>
<td></td>
</tr>
<tr>
<td>Japanese</td>
<td>30 mg QD</td>
<td>47.0</td>
<td>16.5</td>
<td>4.0</td>
</tr>
<tr>
<td>(N = 97)</td>
<td></td>
<td>(36.7, 70.2)</td>
<td>(10.4, 36.3)</td>
<td>(2.5, 15.5)</td>
</tr>
<tr>
<td>Non-Japanese</td>
<td>47.0</td>
<td>29.1</td>
<td>7.5</td>
<td></td>
</tr>
<tr>
<td>(N = 850)</td>
<td></td>
<td>(17.9, 63.8)</td>
<td>(2.4, 40.5)</td>
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</tr>
<tr>
<td>Japanese</td>
<td>77.7</td>
<td>25.1</td>
<td>9.5</td>
<td></td>
</tr>
<tr>
<td>(N = 99)</td>
<td></td>
<td>(72.2, 124.3)</td>
<td>(20.3, 59.7)</td>
<td>(29.2, 27.8)</td>
</tr>
</tbody>
</table>

Cmax: maximum plasma concentration; Cavg: average plasma concentration during a dosing interval; Csbound: trough plasma concentration

Conclusion: No clinically relevant difference was observed in UPA plasma exposures between Japanese and non-Japanese subjects with RA.

REFERENCES:

Sirolimus Selectively Increases Circulating Treg Cell Numbers and Restores the Th17/Treg Balance in Rheumatoid Arthritis Patients with DAS28 £ 3.2 Who Previously Received Conventional DMARDs

Hong-Qing Niu, Li Zhao-Hua, Wen-Peng Zhao, Xiang-Cong Zhao, Chen Zhang, Jing Lu, Chong Gao, Caihong Wang, Li Xiao-Feng, The Second Hospital of Shanxi Medical University, Department of Rheumatology, Taiyuan, China; Bgham and Women's Hospital, Harvard Medical School, Department of Pathology, Boston, United States of America

Background: Many immunosuppressants used to treat rheumatoid arthritis (RA) were designed to broadly suppress T cell function, including that of regulatory T cells (Tregs). Patients with inactive RA also show a reduced frequency of peripheral Tregs [1]. Tregs are essential for maintaining effective immune tolerance and a homeostatic balance of Th17/Treg. Accordingly, there has been increasing interest in developing Treg-friendly regimens to minimize or eliminate the immunosuppression of conventional medications for RA. mTOR signaling negatively controls the development and function of Tregs. Rapamycin, an mTOR inhibitor, could expand Tregs (CD4+CD25+FoxP3+) in patients with active systemic lupus erythematosus [2] and active RA [3]; however, the response of Tregs to rapamycin in RA patients with DAS28 £ 3.2 is still unclear.

Objectives: To investigate the effects of rapamycin, under the generic name sirolimus, on Tregs in RA patients with DAS28 £ 3.2 who previously received conventional DMARDs.

Methods: Fifty-five RA patients and 60 healthy controls were enrolled in this study. All patients had previously received conventional DMARDs and had a low DAS28 score (≤ 3.2). Peripheral blood samples and clinical information were obtained at baseline and following 6 and 12 weeks of sirolimus treatment, or after 12 weeks of conventional treatment. The circulating levels of lymphocyte subpopulations were assessed by flow cytometry.

Results: Thirty-five patients received sirolimus and 20 patients continued treatment with conventional DMARDs. None of the baseline clinical characteristics differed significantly between the two groups. The absolute counts and proportions of CD4+CD25+FoxP3+ Tregs were significantly lower in all RA patients with DAS28 £ 3.2 as compared with those in healthy controls. By contrast, the difference in circulating Th17 cell numbers was not significant. Sirolimus administration resulted in significant elevations in circulating Treg cell numbers and significant reductions in the Th17/Treg cell ratio, whereas the circulating level of Tregs and the Th17/Treg cell ratio in patients under conventional treatment both showed a tendency of reduction (Figure 1). Furthermore, a greater proportion of patients under sirolimus treatment achieved DAS28-based remission at 12 weeks.

Conclusion: Sirolimus can favorably expand Tregs in RA patients with DAS28 £ 3.2, consequently restoring a healthy balance of Th17/Treg cells, which might improve the likelihood of long-term and sustained clinical remission and reduce the probability of disease flare-ups in RA. These findings provide valuable insights that might potentially lead to changes in clinical practice for the routine treatment of RA.

REFERENCES:
The amino-terminal fragment of the B-type natriuretic peptide (NT-proBNP) levels are frequently increased in heart disease with or without symptoms of congestive heart failure (CHF) and is increased in heart disease with or without symptoms of congestive heart failure (CHF) and is increased in heart disease with or without symptoms of congestive heart failure (CHF). NT-proBNP levels with those of RA pt.

Objectives: To prospectively investigate the effect of tofacitinib (TOFA) on the levels of NT-proBNP, as a predictor of CHF in patients (pt) with active rheumatoid arthritis (RA).

Methods: Twenty six RA pt (median age 54 [40;62] years, 81% female, DAS28-5.1[4.6;6.1], SDAI – 368 Thursday, 13 June 2019

Figure 1: The numbers of Th17, Tregs, and the ratio of Th17/Treg in healthy controls and RA patients. A: Healthy controls and RA patients before and after sirolimus treatment. B: Healthy controls and RA patients before and after conventional treatment.

Disclosure of Interests: None declared


Background: The amino-terminal fragment of the B-type natriuretic peptide prohormone (NT-proBNP) is a marker for functional cardiac impairment and is increased in heart disease with or without symptoms of congestive heart failure (CHF)². NT-proBNP levels with those of RA pt.

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Methods: Twenty six RA pt (median age 54 [40;62] years, 81% female, disease duration 44[24;63] month (m), moderate to high activity (DAS28-5.1[4.6;6.1], SDAI–27[22;35]), high) to 27[22;35]), for ACCP (73%)(RF) (77%), who were non-responders to MTX at least 15 mg/week and/or other synthetic DMARDs and bDMARDs) free of clinical overt cardiovascular disease were treated with TOFA and followed for 12 m. TOFA therapy was started in all pt in dose 5 mg BID per os with dose escalation to 10 mg BID in 8 (31%) pt. TOFA used in combination with MTX in 24 pt. TOFA used in combination with MTX in 24 pt.

Results: A total of 96 healthy subjects and 9 patients with RA entered the Study and were randomised to the drug or matching placebo. A total of 96 healthy subjects and 9 patients with RA entered the Study and were randomised to the drug or matching placebo.

Disclosure of Interests: Diana Novikova: None declared, Irina Krillova: None declared, Eugenia Markelova: None declared, Helen Udachkina: None declared, Helen Gerashimova: None declared, Helen Luchchina: None declared, Dmitry Karateev: None declared, Natalia Demidova: None declared, Anna Misiyuk: None declared, Maria Cherkasova: None declared, Tatiana Popkova: None declared


THE FIRST REPORT OF SIGNIFICANTLY IMPROVEMENT OF NT-PROBNP LEVEL IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH TOFACITINIB DURING 12 MONTH FOLLOW-UP

Diana Novikova, Irina Krillova, Eugenia Markelova, Helen Udachkina, Helen Gerashimova, Helen Luchchina, Dmitry Karateev, Natalia Demidova, Anna Misiyuk, Maria Cherkasova, Tatiana Popkova. 1V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation; 2Mосcow Regional Research and Clinical Institute ("MONIKI"), Moscow, Russian Federation

Background: The amino-terminal fragment of the B-type natriuretic peptide prohormone (NT-proBNP) is a marker for functional cardiac impairment and is increased in heart disease with or without symptoms of congestive heart failure (CHF)². NT-proBNP levels with those of RA pt.

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Methods: Twenty six RA pt (median age 54 [40;62] years, 81% female, disease duration 44[24;63] month (m), moderate to high activity (DAS28-5.1[4.6;6.1], SDAI–27[22;35]), high) to 27[22;35]), for ACCP (73%)(RF) (77%), who were non-responders to MTX at least 15 mg/week and/or other synthetic DMARDs and bDMARDs) free of clinical overt cardiovascular disease were treated with TOFA and followed for 12 m. TOFA therapy was started in all pt in dose 5 mg BID per os with dose escalation to 10 mg BID in 8 (31%) pt. TOFA used in combination with MTX in 24 pt. TOFA used in combination with MTX in 24 pt.

Results: A total of 96 healthy subjects and 9 patients with RA entered the Study and were randomised to the drug or matching placebo. A total of 96 healthy subjects and 9 patients with RA entered the Study and were randomised to the drug or matching placebo.

Disclosure of Interests: Diana Novikova: None declared, Irina Krillova: None declared, Eugenia Markelova: None declared, Helen Udachkina: None declared, Helen Gerashimova: None declared, Helen Luchchina: None declared, Dmitry Karateev: None declared, Natalia Demidova: None declared, Anna Misiyuk: None declared, Maria Cherkasova: None declared, Tatiana Popkova: None declared


SAFETY, TOLERABILITY AND PHARMACOKINETICS OF MBS2320, A SELECTIVE MODULATOR OF IMMUNE METABOLISM, IN HEALTHY VOLUNTEERS AND PATIENTS WITH RHEUMATOID ARTHRITIS

Lisa Patel, Paul Marcus, Jim Bush, Andy Gray, Richard Fitzgeral, Sonya Abraham, Martyn Foster, Hiep Huatan, Laurence Skillern, Anna Daroszewska, Rob Van‘t Hof, Sam Williams, I tesso Ltd, London, United Kingdom; Covance Clinical Research Unit Ltd, Leeds, United Kingdom; The Royal Liverpool University Hospital, Liverpool, United Kingdom; Imperial College London, Faculty of Medicine, London, United Kingdom; University of Liverpool, Liverpool, United Kingdom

Background: Despite the availability of several treatment options some patients with Rheumatoid Arthritis (RA) fail to benefit and for those who do response rates are similar across therapeutic classes. Thus there remains a need for new therapies with novel mechanisms of action. MBS2320 is a selective modulator of immune metabolism that shows anatomically appropriate osteoid layering and a broader spectrum of osteoprotective efficacy compared to TNPx inhibition in preclinical models.

Objectives: To investigate the safety, tolerability and pharmacokinetics of MBS2320 in healthy volunteers and patients with Rheumatoid Arthritis (RA) receiving a stable dose of methotrexate (MTX).

Methods: Cohorts of healthy volunteers (randomised 6:2 drug:placebo) received single or multiple oral doses of MBS2320 for 14 days. Single Ascending Dose (SAD) cohorts comprised 2, 10, 25, 50, 75, 125, 250, 375 mg (PO) and Multiple Ascending Dose (MAD) cohorts. 75, 100, 150 mg/d. Patients with RA received 75 mg/d for 14 days in addition to their existing weekly MTX treatment. Safety and tolerability were assessed throughout. Plasma MBS2320 (SAD, MAD and patients with RA) and MTX (patients with RA only) were measured using LC-MS/MS. In patients with RA, C-reactive protein (CRP) and biomarkers of bone turnover were assessed on Day 14.

Results: A total of 96 healthy subjects and 9 patients with RA entered the Study and were randomised to the drug or matching placebo. MBS2320 was well tolerated by healthy subjects at single oral doses of 2 to 375 mg. There were no serious adverse events (SAEs). Nausea was the most commonly reported adverse event (AE) and occurred most frequently at the high doses but was mild and resolved without treatment. Daily doses of 75 to 160 mg QD MBS2320 for 14 days were generally well tolerated by healthy subjects. The most common drug-related treatment emergent adverse events (TEAEs) were gastrointestinal disorders.
EFFICIENCY OF TREATMENT SEQUENCES CONTAINING TOFACITINIB FOR RHEUMATOID ARTHRITIS IN SPAIN

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Background: The availability of oral Janus kinase inhibitors, as tofacitinib, has extended the treatment pathways for management of patients with rheumatoid arthritis (RA).

Objectives: To assess the cost-effectiveness of tofacitinib as second-line treatment compared to treatment sequences containing standard biological therapies in patients with moderate to severe RA after failure to disease-modifying antirheumatic drugs (DMARDs) from the Spanish National Health System perspective.

Methods: A patient-level microsimulation model was used to compare the lifetime cost and quality-adjusted life-years (QALY) for treatment sequences initiating with tofacitinib (5mg BID) followed by biological therapies versus sequences of biological treatments excluding tofacitinib. The sequences were selected by a panel of experts based on clinical practice in Spain. Concomitant treatment with methotrexate (MTX) was considered along with all the therapies in the treatment sequences. Model parameters included age, weight, initial Health Assessment Questionnaire (HAQ) score and clinical response to short and long treatment. Efficacy was measured by means of HAQ score changes using mixed-treatment comparisons (for the first 6 months) and data from long-term extension trials (for later periods). Serious adverse event (SAE) information derived from literature. The estimation of total cost for sequences included: drugs acquisition (public ex-factory prices with mandatory deduction or reference prices) and parenteral administration, disease progression and SAE management.

Local unitary costs (€, 2018) were applied. Additional comparisons were explored testing other potential sequences.

Conclusions: The base case analysis showed that sequences initiating with tofacitinib provided greater outcomes than the correspondent sequences excluding tofacitinib. In scenario 1 tofacitinib+MTX—Rituximab+MTX—Etanercept+MTX—Ceritalzumab+MTX provided 13.92 QALYs versus 13.92 QALYs for adalimumab+MTX—Rituximab+MTX—sc Tocilizumab+MTX—Etanercept+MTX. In scenario 2 tofacitinib+MTX—Adalimumab+MTX—Rituximab+MTX—Etanercept+MTX—Ceritalzumab+MTX provided 13.75 QALYs versus 13.62 QALYs for Baricitinib+MTX—Adalimumab+MTX—Rituximab+MTX—sc Tocilizumab+MTX—Etanercept+MTX.

THU0187

EFFICIENCY OF TREATMENT SEQUENCES CONTAINING TOFACITINIB FOR RHEUMATOID ARTHRITIS IN SPAIN

THU0188

INHIBITION OF STRUCTURAL JOINT DAMAGE WITH UPADACITINIB AS MONOTHERAPY OR IN COMBINATION WITH METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS: 1 YEAR OUTCOMES FROM THE SELECT PHASE 3 PROGRAM

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Background: Long-term prevention of structural joint damage is a key treatment goal in the management of RA. Upadacitinib (UPA), a JAK1-selective inhibitor, inhibited the progression of structural joint damage at 6 months as monotherapy in methotrexate (MTX)–naive RA patients (pts)7 and in combination with MTX in pts with inadequate response (IR) to MTX.

Objectives: To evaluate the progression of structural joint damage (radiographic) through Week 48 in pts with moderately to severely active RA treated with UPA monotherapy or in combination with MTX.

Methods: Radiographic progression was assessed in 2 phase 3 randomized controlled trials (RCTs), as previously described2. MTX-naive pts were randomly assigned to UPA 15 or 30mg QD or MTX monotherapy (SELECT–EARLY, N=945), while MTX-IR pts were randomized to UPA 15mg QD or adalimumab (ADA) 40 mg eow or placebo (PBO), with continuous background MTX (SELECT–COMPARE, N=1629). Both RCTs specifically enrolled pts at high risk for progression of joint damage (high disease activity including elevated hsCRP, presence of baseline erosions and ACPO and/or RF positivity). The mean changes (Δ) from baseline
Conclusions: UPA both as monotherapy, and in combination with background MTX, was effective in inhibiting the progression of structural joint damage through Week 48 in MTX-naïve, and MTX-IR patients, respectively.

REFERENCES:

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THU0189 A PROSPECTIVE STUDY OF TAPERING CONVENTIONAL DISEASE MODIFYING ANTI-RHEUMATIC DRUGS (C-DMARDs) IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA) IN STABLE REMISSION

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Background: Remission in RA is being achieved more often nowadays with effective early aggressive therapy with DMARDS. Studies (1, 2 & 3) have shown that it is possible to taper and then stop DMARDS in patients with RA in stable remission. However there are no such studies or recommended protocols for c-DMARDS treated patients.

Objectives: To study the incidence and timing of flares in RA patients in sustained remission of at least 6 months duration on slow withdrawal of c-DMARDS and to identify predictors of flares.

Methods: Consenting adult(age >18 years) RA patients satisfying the ACR 2010 criteria attending our outpatient department with a disease duration of minimum 1 year and a stable remission (CDAI <2.8 on consecutive 2 visits at 3 months interval in last 6 months) on c-DMARDS were included. Patients receiving steroids or biologics were excluded.

Protocol for tapering:
On monotherapy: 50% dose reduction 3 weekly and stop eventually
On combination therapy: sequential dose reduction as monotherapy followed by stepdown of cDMARDs(in order from first to last: hydroxychloroquine, sulphasalazine, leflunomide, methotrexate)
Flare was defined as CDAI of >2.8. Number of RA flares and timing of flares were noted. Predictors of flare were analysed using univariate and multivariate regression.

Results: 66 patients satisfied inclusion criteria of which 5 did not consent, 5 committed protocol violation and 2 lost to follow up. Total 54 patients were included in the final analysis. 42 patients (77.78%) flared during the study period. Of these 42 patients, 29(69.05%) flared on the tapering protocol whereas, 13 (30.95%) flared after complete withdrawal of c-DMARDS. 20 patients (47.62%) flared within first 3 months of the tapering regimen and total 31 patients (73.8%) flared within first 6 months of tapering regimen. Baseline CDAI scores were significantly higher in patients who developed flare compared to those who remained in remission (0.82±0.82 vs 0.29 ±0.54, p<0.04).

RF positivity and age more than 60 years were predictors of flare in univariate regression analysis. With multivariate logistic regression, RF positivity was the only variable significantly associated with risk of flare (p=0.0098, SE =1.62 OR 66.31).

Conclusion: We found that on tapering of c DMARDs at 3 weekly intervals in RA patients with stable remission the incidence of flare was 78%. Most flared during tapering therapy itself and not after the drugs were stopped. Rheumatoid factor positivity seemed to predict flares. Although within the definition of remission, CDAI scores at baseline were significantly higher in patients who developed flare compared to those who remained in remission.CDAI has limitation in defining remission and inclusion of imaging in defining remission may lead to better remission on tapering cDMARDs.

REFERENCES:

BL in modified Total Sharp Score (mTSS), joint space narrowing (JSN), and erosion scores (ES) as well as the proportion of pts with no radiographic progression (ΔΔmTSS) (0) at Weeks 24/26 and 48 were determined in both RCTs. Data were analyzed by linear extrapolation (LE) for missing data imputation and treatment switching, and as observed (AO).

Results: BL demographics have been reported previously[2,3]. At Weeks 24/26, UPA as monotherapy and in combination with background MTX significantly inhibited radiographic progression measured by mean ΔΔmTSS and the proportion of pts with no radiographic progression vs MTX and PBO, respectively (LE and AO). Table. The significant inhibition of radiographic progression with UPA was maintained through Week 48 vs MTX (LE and AO) in EARLY and vs PBO (LE) in COMPARE. Following the observed for the overall mTSS scores but also its components the inhibition of radiographic progression vs comparators was not only CHANGES IN MEAN mTSS observed through Week 48 (AO, (LE and AO) in EARLY and vs PBO (LE) in COMPARE. Following the observed for the overall mTSS scores but also its components
THE SAFETY, PHARMACOKINETICS, AND PHARMACODYNAMICS OF BMS-986166, A NOVEL, SELECTIVE, PARTIAL AGONIST OF THE SPHINGOSINE-1-PHOSPHATE (S1P) SUBTYPE 1 RECEPTOR IN HEALTHY PARTICIPANTS

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Background: S1P mediates a number of immune processes including the egress of lymphocytes from lymphoid organs via stimulation of the S1P subtype 1 receptor (S1P1R). S1P1R inhibition has the potential to suppress abnormal immune responses and modulate autoimmune inflammatory diseases. BMS-986166, a novel, selective partial agonist of S1P1R, which is phosphorylated in vivo to its pharmacologically active form, BMT-212795, may have utility for the treatment of autoimmune and inflammatory diseases.

Objectives: To investigate safety, pharmacokinetics (PK), and pharmacodynamics (PD) of BMS-986166 in single- and multiple-ascending dose (SAD/MAD) placebo (PBO)-controlled studies in healthy participants.

Methods: SAD study (NCT02790125): BMS-986166 was administered as a single dose of 0.75, 2.0, or 5.0 mg (n=10/group; 4:1 ratio) of BMS-986166:PBO; a series of upwardly titrated single daily doses of 0.25, 0.5, 0.75, 1.0, and 1.5 mg over 14 days (n=16; 3:1 ratio); or as a single 2.0-mg dose in participants who were fed, fasted, or administered famotidine prior to dosing (n=8/group). MAD study (NCT03093871): BMS-986166 was administered as once-daily doses of 0.25 (n=12; 2:1 ratio), and 0.75 or 1.5 mg (n=10/dose; 4:1 ratio), for 28 days. Safety, PK, and PD (absolute lymphocyte count [ALC]) were assessed. Cardiac safety was assessed by continuous cardiac monitoring and at intervals by 12-lead electrocardiogram.

Results: 70 (80 BMS-986166, 10 PBO; mean [standard deviation (SD)] age: 32.8 [8.5] years) and 32 (24 BMS-986166, 8 PBO; mean [SD] age: 35.8 [8.6] years) participants were randomised to dosing in the SAD and MAD studies, respectively. Participants were predominantly male. Mean (SD) body mass index was 26.8 (2.9) and 27.2 (2.5) kg/m², respectively. Multiple oral doses of BMS-986166 up to 1.5 mg daily for 28 days were generally well tolerated, and all treatment-related adverse events were mild (Grade 1). In the MAD (Figure 1) and SAD studies, a clinically insignificant, dose-related decrease in mean hourly heart rate (HR) was observed following administration of BMS-986166 compared with PBO, based on a time-matched analysis of nominal hourly HR data from continuous cardiac monitoring over 72 hours post dose. Compared with participants receiving PBO, a mean decrease from baseline in hourly HR was apparent for participants in the 2 higher dose panels (2.0 mg, 5.0 mg) in the SAD study. In the SAD study, the largest decreases in PBO-corrected, time-matched, nadir hourly HR were –0.29, –6.38, and –8.37 bpm for the 0.75, 2.0, and 5.0 mg dose panels, respectively. Similarly, in the MAD study, these numbers were –0.83, –3.46, and –5.54 bpm at the 0.25, 0.75, and 1.5 mg dose levels, respectively. Increases in systemic plasma exposure (maximum concentration and area under the curve from time 0–24 hours) of BMS-986166 and its active metabolite BMT-212795 were approximately proportional to dose increases over the range of 0.25–1.5 mg with single doses, and of 0.25–1.5 mg on Days 1, 14, and 28 with multiple doses. Decreases in percent change from baseline in ALC with multiple doses of BMS-986166 vs PBO were dose-related over the 28-day treatment period. Between Day 0 and 35, median (range) nadir in lymphocyte reductions were 53.7% (31.7–55.9%), 75.9% (63.3–85.8%), and 81.9% (79.9–92.2%) at 0.25, 0.75, and 1.5 mg BMS-986166 dose levels, respectively. Recovery of ALC levels began 14, 14–21, and 7 days after the last dose of 0.25, 0.75, and 1.5 mg, respectively, on Day 28.

Conclusion: In healthy participants, multiple daily doses of BMS-986166 in the range of 0.25–1.5 mg were well tolerated, with no clinically relevant lowering of HR. PK were linear and decreases in ALC were dose related.


UPADACITINIB AS MONOTHERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS AT 48 WEEKS FROM THE SELECT-MONOTHERAPY STUDY

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Background: In the SELECT-MONOTHERAPY trial, upadacitinib (UPA), an oral JAK1-selective inhibitor, showed efficacy when used as monotherapy over 14 weeks (wks) in rheumatoid arthritis (RA) patients (pts) with an inadequate response to methotrexate (MTX).1

Objectives: Safety and efficacy of UPA monotherapy were assessed through 48 wks in an ongoing long-term extension period of SELECT-MONOTHERAPY.

Methods: At baseline (BL), pts on stable MTX were randomized to either continue MTX (cMTX, given as a blinded study drug) or switch to once-daily (OD) UPA at 15 (UPA15) or 30 mg (UPA30) monotherapy for 14 wks. From Wk14, the start of a long-term blinded extension, pts randomized to cMTX were switched to UPA15 or 30mg per pre-specified assignment at BL, pts randomized to UPA15 or 30 continued their initial treatment. No dose adjustments for UPA were allowed. Starting at Wk26 for pts who did not achieve CDAI ≤10, background csDMARDs could be initiated. Efficacy data up to the Wk48 visit are reported as “As Observed”. Adverse events (AE) per 100 pt yrs (PYs) are summarized up to May 25 2018.

Results: Of 648 pts randomized at BL, 598 (92%) completed 14 wks and continued on to the extension period. By May 25 2018, 16% discontinued study drug; 5% due to AE, 0.5% due to lack of efficacy, 4% withdrew consent, 1% were lost to follow-up, and 6% due to other reasons. Cumulative exposures to UPA15 and UPA30 were 336.0 PYs and 337.1
PYs, respectively. Starting from Wk26, background csDMARDs were initiated for approximately 18% of pts. Based on As Observed data, for pts on UPA from BL through Wk48 on UPA15 [250/300 (83%)] and UPA30 [251/298 (84%)], clinical and functional outcomes continued to improve, or were maintained (Table 1). For pts continuing UPA15 and 30, DAS28-CRP<2.6 was 55% and 68%, and CDAL≤2.8 was 28% and 42%, respectively. Pts who were switched from cMTX to UPA15 or 30 at Wk14 had similar responses at Wk 48. The most frequently reported treatment-emergent AEs were urinary tract infection, blood creatine phosphokinase increase, upper respiratory tract infection, nasopharyngitis, worsening of RA, herpes zoster (H2), alanine aminotransferase increase, and bronchitis. The most frequently reported serious AE was pneumonia (8 events). Events/100PYS were numerically higher in the UPA30 vs UPA15 arm for HZ, and hepatic disorders, and were comparable for serious infections and malignancies excluding non-melanoma skin cancer (Table 2). Adjudicated venous thromboembolic events (VTE) were observed only on UPA15 (2 pts with deep vein thrombosis and 2 pts with pulmonary embolism; all patients had at least one risk factor for VTE).

Conclusion: UPA 15 or 30 monotherapy resulted in similar improvements in signs and symptoms and physical function through 48 wks. The overall benefit-risk profile of both doses of UPA was favorable based on safety and efficacy data through Wk48 but will be confirmed through an integrated safety analysis across all the ph 3 trials.

Abstract THU0191 – Table 1.

<table>
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<th>UPA 30 MG WkX11</th>
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Abstract THU0191 – Table 2.

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<th>UPA 30 MG Wk30</th>
<th>MTX Wk30</th>
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<tr>
<td>AE Leading To Discontinuation</td>
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<td>10.1</td>
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<td>Serious Infection</td>
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</tr>
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Background: Monotherapy use of upadacitinib (UPA), a selective JAK1 inhibitor, demonstrated clinically meaningful improvement in the signs and symptoms of rheumatoid arthritis (RA) compared with methotrexate (MTX). To better understand the impact of UPA treatment in RA from the patient’s perspective, we examined the effect of UPA on patient-reported outcomes (PROs).

Objectives: To evaluate the effect of UPA monotherapy vs MTX at week 12 on PROs in SELECT-EARLY (NCT02706873), a randomised controlled trial in MTX-naive patients with moderate to severe RA.

Methods: Patients were randomised 1:1:1 to receive once daily UPA (15 mg or 30 mg) or weekly MTX (titrated by Week 8). PROs assessed included Patient Global Assessment of Disease Activity (PtGA) by visual analogue scale (VAS), patient global response, Health Assessment Questionnaire Disability Index (HAQ-DI), fatigue by Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), duration and severity of morning (AM) stiffness, HRQoL by Short Form 36 (SF-36), and Work Productivity and Activity Impairment (WPAI) measure. Least square mean (LSM) changes from baseline (BL) to Week 12 were based on analysis of covariance. Percentages of patients reporting changes in PRO scores from BL to Week 12 ≥ minimum clinically important differences (MCIDs) or scores ≥ normative values (age- and gender-matched for SF-36 only) were determined for UPA and MTX groups; comparisons used chi-square tests. For each PRO, the incremental number needed to treat (NNT) to achieve clinically meaningful improvement from BL was calculated.

Results: Data from 945 patients (MTX: 314; UPA 15 mg: 317; UPA 30 mg: 314) were analysed. Mean age was 53 years; 76% were female; 49% had RA for ≤6 months. Statistically significant LSM changes from BL to Week 12 were reported for both doses of UPA vs MTX for all PROs (Table).

To Week 12, both UPA doses had significantly higher proportions of patients reporting improvements ≥ MCID vs MTX in HAQ-DI duration and severity of AM stiffness, pain, and PtGA. Compared with MTX at Week 12, a significantly greater proportion of patients receiving UPA at either dose reported improvements ≥ MCID in all PROs. A significantly greater proportion of patients receiving UPA also reported scores ≥ normative values for all PROs except SF-36 Mental Health (UPA 15 mg and SF-36 General Health [both UPA doses] domains. For most PROs, NNTs with UPA ranged from 4 to 8 patients at Week 12.
Conclusion: Among MTX-naïve patients with active RA, treatment with UPA 15 mg or 30 mg daily for 12 weeks resulted in statistically significant and clinically meaningful improvements in physical function, pain, fatigue, AM stiffness, HRQoL, and work productivity compared with MTX. The NNTs to achieve these improvements were favourable.

REFERENCE:

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Disclosure of Interests: Vibeke Strand Consultant for: AbbVie, Amgen, Bayer, BMS, Boehringer Ingelheim, Cellgene, Celtrion, CORRONA, Crescendo, EMD Serono, Genentech/Roche, GSK, Horizon, Inmedix, Janssen, Kezar, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sandoz, Sanofi, Servier, UCB, Namita Tundia Shareholder of: AbbVie, Employee of: AbbVie, Sebastiao Radominski Consultant for: Abbvie, Cellgene, Genentech/Roche, Janssen, Pfizer, UCB, Alan Friedman Shareholder of: AbbVie, Employee of: AbbVie, Kendall Dunlap Shareholder of: AbbVie, Employee of: AbbVie, Deborah Goldschmidt Employee of: Analysis Group Inc, which received consulting fees from AbbVie for this study., Martin Bergman Shareholder of: Johnson and Johnson (parent company of Janssen), Consultant for: Abbvie, Amgen, BMS, Cellgene, Genentech/Roche, Janssen, Pfizer, UCB, Alan Friedman Shareholder of: AbbVie, Amgen, BMS, Cellgene, Genentech/Roche, Janssen, Merck, Novartis, Pfizer, and Sanofi/Regeneron

Results: 241 pts had early RA (tofa mono: N=80; tofa+MTX: N=83; ADA+MTX: N=78; mean RA duration: 1.0–1.1 yrs); 905 pts had established RA (tofa mono: N=208; tofa+MTX: N=208; mean RA duration: 9.4–10.4 yrs). BL demographics and disease characteristics were generally comparable for early vs established RA pts, with some expected differences (the latter were slightly older, and a greater proportion had received prior bDMARDs); RF and anti-CCP+ rates were higher for early RA than established RA (p<0.05). ADA was not statistically different vs tofa+MTX in early RA (Figure). Trends were similar for all outcomes. AE rates were generally similar in early vs established RA. Rates for SAEs were less clear; rates were lowest for tofa+MTX in early RA and slightly higher for both tofacitinib arms vs ADA (Table 1). Conclusion: Efficacy was similar for tofa mono and tofa+MTX in early RA, and significantly higher for tofa+MTX in established RA. ADA+MTX was numerically but not always significantly more effective than tofacitinib in early RA. AE rates were generally similar regardless of BL RA duration. These findings, especially in established RA, are consistent with the conclusion of the primary analysis.2 Limitations to this post hoc analysis include low numbers of early RA pts.

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THU194

SELECTIVE INHIBITION OF JANUS KINASE 1 (JAK1) BY FILOTINIB MODULATES THE DISEASE-ASSOCIATED WHOLE BLOOD TRANSCRIPTIONAL PROFILE OF PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS

Peter C. Taylor1, Bryan Downie2, Luting Zhuo3, Rachael E. Hawtin4, Jinfeng Liu5, Amer M. Mirza6, 2Botnar Research Centre, University of Oxford, Oxford, United Kingdom; 3Gilead Sciences, Inc., Foster City, United States of America

Background: Filgotinib (FIL), an oral selective JAK1 inhibitor, was safe and efficacious in FINCH2, a randomized, double-blind, placebo-controlled, phase 3 study in patients with active rheumatoid arthritis (RA) who had an inadequate response to biologic disease-modifying anti-rheumatic drugs (bDMARDs).1 The whole blood transcriptional profile of patients was evaluated.

Objectives: Identify RA-associated gene transcripts and biological pathways that are altered in response to FIL treatment and interrogate FIL-modulated biomarkers correlated with disease activity.

Methods: RA patients enrolled in FINCH2 (n=449) were randomized 1:1:1 and received FIL (100 mg, 200 mg, or placebo (PBO)) once daily plus a stable background dose of methotrexate. Whole blood samples from enrolled patients were collected at baseline (BL) and weeks 4 and 12 for RNA sequencing. Spearman’s rank correlation of BL disease activity (DAS28CRP) was calculated to define disease-associated genes (DAGs) and pathways (DAPs). Differential expression of 5155 genes and FIL-specific changes were determined after subtracting gene expression changes in the PBO group. Biological pathways (910 total) were analyzed by Gene Set Enrichment Analysis (GSEA) or single-sample GSEA. A false-discovery rate of 5% was applied for all analyses.

Results: At weeks 4 and 12, more genes were significantly differentially expressed in the FIL 200 mg arm vs the 100 mg arm; and, consistent with increased clinical efficacy, the average magnitude of change in gene expression was larger. No single gene reached a threshold of significance for differential expression in PBO-treated patients. FIL treatment induced a stronger reversal of DAS expression (rho range: ~0.35 to ~0.59) compared to PBO (rho ~0.3) at weeks 4 and 12. DAGs most prominently reversed by FIL included FAM20A and METTL7B. Top-ranked pathways associated positively with disease activity at BL included inflammatory response, cell proliferation activity, and cell cycle. By week 12, pathways most significantly reduced following FIL treatment included IL-6/JAK/STAT, inflammatory, and interferon response, consistent with observed effects of FIL in preclinical models and phase 2 DARWIN studies. In contrast, IL-6/JAK/STAT signaling increased at weeks 4 and 12 with PBO. DAGs showed a similar reversal of gene expression (rho range: ~0.43 to ~0.58) with FIL at weeks 4 and 12 compared to PBO (rho range: ~0.007 to ~0.024) suggesting that FIL treatment may attenuate RA-mediated IL-6/JAK/STAT signaling, inflammation, and other RA-associated pathways correlated with clinical outcome measures.

Conclusion: The whole blood transcriptional profile of patients following FIL treatment showed a dose-dependent reduction in the expression of
JAK/STAT signaling and inflammation genes. No significant changes in the expression of DAGs were observed in PBO-treated patients. F I L also broadly reversed DAGs and DAPs, and ongoing research is exploring the relationship between changes in gene and pathway modulation across a range of clinical endpoints.

REFERENCE:


THU0195

ULTRASOUND EVALUATION FOR MONITORING RESPONSE TO BARICITINIB IN RHEUMATOID ARTHRITIS PATIENTS AT EARLY STAGE AFTER TREATMENT

Eiji Torikai1, Daisuke Suzuki2.1: Iwata city hospital, Iwata, Japan; 2: Hamamatsu university school of medicine, Hamamatsu, Japan

Background: Baricitinib (bari) is approved for treating moderate-severe RA in many countries including Japan. Bari, an oral Janus kinase (JAK1)/JAK2 selective inhibitor, has shown the efficacy in patients with rheumatoid arthritis (RA) and in adequate response to conventional synthetic DMARDs in some clinical trials. Thanks to technological improvement in Ultrasound (US) equipment and the use of internationally approved scanning techniques and definitions for normal findings and pathology, US monitoring are widely used to assess inflammatory and structural lesions in daily clinic.

Objectives: To monitor the short-term response to baricitinib therapy in bilateral wrist and finger joints of RA patients by US and to evaluate correlation between US findings and clinical assessments.

Methods: We included 23 Japanese patients with RA who have inadequate response to csDMARDs or bDMARDs (biologics-naive cases, and biologics-experience cases). Patients were scheduled to receive bari 4mg or 2mg once daily dose as monotherapy or in combination with other csDMARDs. They were allowed to be decreased prednisolone when their disease activity was improved. Clinical evaluation was performed blinded to the results of the US assessment that had been carried out on the same day. Swollen joint counts on 28 joints (SJC), tender joint counts on 28 joints (TJC) and Clinical Disease Activity index (CDAI) were registered for each patient. Each parameter was evaluated at baseline, after 1 month and 3 months. Four sonographers, experienced in musculoskeletal US, who were blinded to the clinical and laboratory data, performed the US examination. The US assessment and scanning technique included evaluation of synovial sites in 26 joints (wrist, radiocarpal, midcarpal, radiocarpal joints, 1 - 5 MCP joints and 1 - 5 PIP joints). Gray scale (GS) and power doppler (PD) were graded according to a 0 - 3 semi-quantitative score depending on their severity [1]. We calculated total scores for each patient in GS (GS score) and PD (PD score) differently. We compared the change of GS score and PD score. In addition, we evaluated the correlation between the changes in GS score or PD score and the variations in clinical evaluation items.

Results: Patient’s backgrounds were provided in Table 1. All clinical parameters were significantly improved at each follow-up periods after treatment. Mean SJC, TJC and CDAI decreased from 7.52 ± 3.89, 8.26 ± 3.82 and 26.89 ± 9.48 at baseline to 1.52 ± 1.75, 1.82 ± 1.89 and 6.40 ± 5.17 at 1month and to 1.27 ± 1.39, 1.27 ± 1.38 and 3.99 ± 3.49 at 3 months respectively (Table 2). GS and PD score at each follow-up periods after treatment were also significantly improved. Mean GS and PD decreased from 8.11 ± 3.41 and 12.42 ± 4.45 at baseline to 3.63 ± 2.45 and 7.73 ± 4.70 at 1 month and to 2.10 ± 1.49 and 4.21 ± 2.70 at 3 months respectively (Table 2). GS score significantly correlated with SJC (r= 0.586, p<0.01), TJC (r=0.602, p<0.01) and CDAI (r=0.656, p<0.01). PD score significantly correlated with SJC (r= 0.608, p<0.01), TJC (r=0.621, p<0.01) and CDAI (r=0.658, p<0.01).

Conclusion: Baricitinib therapy had significantly improved disease activity of RA patients at early stage after the treatment. GS and PD score were also significantly improved and correlated with clinical parameters.

These data confirm that the use of US evaluation is very useful method for evaluating the monitoring the response of treatment and feasible method complementary to clinical assessment for guiding the clinician in the appropriate therapeutic decision.

THU0196

EFFICACY AND SAFETY UP TO 24 WEEKS OF BARICITINIB FOR JAPANESE PATIENTS WITH RHEUMATOID ARTHRITIS IN REAL WORLD MULTICENTER CLINICAL DATA

Eiji Torikai1, Daisuke Suzuki2.1: Hamamatsu university school of medicine, Hamamatsu, Japan; 2: Hamamatsu university school of medicine, Hamamatsu, Japan

Background: Baricitinib (bari) is approved for treating moderate-severe rheumatoid arthritis (RA) in many countries, including Japan. Bari is an oral Janus kinase (JAK1)/JAK2 selective inhibitor that has shown good efficacy in patients with RA and adequate response to conventional synthetic DMARDs in some clinical trials. However, there have been few reports about the efficacy and safety of bari in real-world clinical data.

Objectives: We evaluated the efficacy and safety of bari for Japanese RA patients who have an inadequate response to DMARDs in real-world multicenter clinical data.

Methods: We included 32 Japanese patients with RA who show an inadequate response to csDMARDs or biDMARDs (biologics-naive BN group): 19 cases, and biologics-experience (BE group): 13 cases). Patients were scheduled to receive bari 4 or 2 mg once daily dose as a monotherapy or in combination with other csDMARDs. If the disease activity was not improved within 3 months in patients treated with bari 2 mg, the bari dose was increased to 4 mg. Patients were allowed to decrease their prednisolone treatment if their disease activity improved. First, we evaluated changes in the number of swollen joints and tender joints, CRP (mg/dL), visual analog scale of pain (0–100 mm), patient’s global assessment (0–100 mm), Clinical Disease Activity Index, and HAQ-DI for 24 weeks. Second, we evaluated the proportion of patients with adverse events (AEs) and progress after these AEs.

Results: Patients’ backgrounds were provided Table 1. Many patients fell the early effect of bari. At 1 month after treatment, ACR20/50/70 were 84.2%/63.2%/21.1% in the BN group and 53.8%/23.1%/7.7% in the BE group, respectively. All measurement items of disease activity and patient-reported outcomes were significantly improved after treatment. This tendency continued until the final evaluation (Table 2). At 24 weeks, remission and low disease activity rates were 47.4% and 78.9% in the BN group and 15.4% and 61.5% in the BE group, respectively. One case in the BE group discontinued bari treatment due to no response. These data were better than clinical trial data (Japanese subpopulation data from RA-BEAM and RA-BUILD studies[1]). We determined that we could take an aggressive treatment course according to treat to target strategies in real-world clinics. Greater early improvements in HAQ-DI were seen. HAQ-DI was improved significantly at each evaluation time point after bari treatment (Table 2). We had two cases of mild pneumonia and one case of herpes zoster. These cases were improved after 1–2 weeks of antibiotic therapy or anti-viral drug therapy. One case discontinued bari. Although the other two cases withdrew from bari treatment, we could restart it. We think that the most important reason why they did not advance in severe because we were not able to diagnose and treat these cases earlier. No patient showed malignancies, cardiovascular events, or deep vein thrombosis. No patient discontinued bari treatment due to AEs. Also, increases in blood pressure and d-dimer were not observed during the follow-up period. Other mild AEs, including upper respiratory tract infection, nasopharyngitis, and laboratory data abnormalities occurred in 62.5% of patients (Table 3). A small increase in lymphocyte count and small decrease in neutrophil count...
were seen at 1 month after bari treatment. These either remained flat or improved 3 months after treatment. An increase from baseline in creatinine was also seen. These tendencies continued to the final observation. Moving forward, these items should be monitored for long-term evaluation.

### Abstract THU0196 – Table 1

<table>
<thead>
<tr>
<th>Table 1. Patients' background (n=945)</th>
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<tbody>
<tr>
<td>Age (years) [median (IQR)]</td>
<td>72 (65-76)</td>
</tr>
<tr>
<td>Disease duration (years) [median (IQR)]</td>
<td>10.8 (5.6-19.4)</td>
</tr>
<tr>
<td>28 Joints (mm) [median (IQR)]</td>
<td>21.5 (12.5-38.5)</td>
</tr>
<tr>
<td>28 Joints swollen (mm) [median (IQR)]</td>
<td>13.6 (6.0-24.0)</td>
</tr>
<tr>
<td>Ritchie articular index [median (IQR)]</td>
<td>38.0 (30.5-52.0)</td>
</tr>
<tr>
<td>Clinical DAS28 (median (IQR))</td>
<td>5.7 (5.2-6.8)</td>
</tr>
<tr>
<td>CDAI (median (IQR))</td>
<td>240.0 (170.0-350.0)</td>
</tr>
<tr>
<td>HAQ-DI (median (IQR))</td>
<td>1.5 (1.3-2.2)</td>
</tr>
</tbody>
</table>

### Results

Of 945 pts randomized and treated, 747 (79%) completed Wk48 date of Aug 16 2018.

### Discussion of Disclosure: None declared


#### THU0197

**MONOTHERAPY WITH UPADACITINIB IN MTX-NAÏVE PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS AT 48 WEEKS FROM THE SELECT-EARLY STUDY**

Ronald van Vollenhoven1, Tsutomu Takeuchi2, Aileen Pangan3, Alan Friedman3, Vibeke Strand4, 5, 6, 7, 8, 9, 10.

### Methods:

SELECT-EARLY had a 48-wk double-blind active comparator-controlled period. Pts were initially randomized to monotherapy (mono) with UPA 15 or 30 mg or MTX (titrated up to Wk8). Rescue therapy was offered if pts met the following: (1) From Wk 12-24, pts without ≥20% improvement from BL (±) in both TJC and SJC at 2 consecutive visits continued monotherapy study drug with optimized background RA medications. (2) At Wk26, pts with CDAI ≥28 continued their original study drug; in pts with CDAI >2.8 but ≤20% in TJC and SJC, for those on MTX, UPA15/30mg was added; for those on UPA15/30mg, MTX was added for 19 (6%) and 9 (3%) of pts on UPA15 and 30 respectively vs 17% on MTX; 28% and 33% vs 13% achieved Boolean REM. At Wk48, ∆mTSS were significantly less on UPA15 and UPA30 vs MTX. The safety profile of UPA15 and UPA30 was similar generally to MTX, except for total AEs and herpes zoster, which were higher with UPA15 and 30 vs MTX (Table 2). There were 11 deaths (including 3 treatment-emergent deaths) due to varied causes.

### Conclusion:

These data showed that bari has a favorable benefit-risk balance in a real-world clinic and thus may be considered as a good treatment option for Japanese RA patients who have an inadequate response to csDMARDs or bDMARDs.

**REFERENCE:**


**Disclosure of Interests:** None declared


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**MONOTHERAPY WITH UPADACITINIB IN MTX-NAÏVE PATIENTS WITH RHEUMATOID ARTHRITIS: RESULTS AT 48 WEEKS FROM THE SELECT-EARLY STUDY**

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**REFERENCE:**


**Disclosure of Interests:** None declared


### Table 2. Treatment emergent adverse event (all in 答): summary 3/5/2019 in Patients on monotherapy at time of visit to conclude exposure of (Recombinant)Thrombin

<table>
<thead>
<tr>
<th>Event</th>
<th>UPA15</th>
<th>UPA30</th>
<th>MTX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute myocardial infarction</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>All-cause mortality</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
<tr>
<td>Death</td>
<td>0.00</td>
<td>0.00</td>
<td>0.00</td>
</tr>
</tbody>
</table>

**Conclusion:** UPA15 and 30 monotherapy continued to show significant improvements in RA signs and symptoms and inhibition of structural damage vs MTX through 48 wks. Only a small proportion of pts required MTX addition to UPA mono at Wk26 to achieve and maintain response. The safety profile based on all exposure remained consistent with ph 2 and 3 RCTs in RA, although an integrated safety analysis of UPA across the full ph 3 RA program will provide a more comprehensive understanding of the benefit:risk profile of UPA in RA.

**REFERENCE:**


**Acknowledgement:** AbbVie, Inc. was the study sponsor, contributed to study design, data collection, analysis & interpretation, and to writing, reviewing, and approval of final version. Medical writing support was provided by Naina Barretto of AbbVie, Inc.

## Disclosure of Interests:

Ronald van Vollenhoven Grant/research support from: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Crescendo, GlaxoSmithKline, Jansen, Lilly, Merck, Novartis, Pfizer, Roche, UCB, and Vertex.

None declared
EFFECTIVENESS OF REMISSION-INDUCTION STRATEGIES FOR EARLY RHEUMATOID ARTHRITIS: A SYSTEMATIC LITERATURE REVIEW

Maxime Verhoeven, Paco Welsing, Johannes Wij Bijlsma, Jacob M. van Laar, Floris Lalleber, Janneke Tekstra, Johannes W. G. Jacobs. University Medical Center Utrecht, Utrecht, Netherlands

Background: Several trials studied initiation of therapy in early RA patients with a more intensive strategy than the standard disease modifying anti-rheumatic drug (DMARD) strategy according to current guidelines, with the aim of rapidly inducing clinical remission (remission-induction strategies).

Objectives: To establish in early RA patients the effectiveness of remission-induction strategies compared to standard DMARD strategies with or without concomitant glucocorticoids (GCs), with delayed tapering (not ‘bridging therapy’) or starting ≥2 csDMARDs. Standard DMARD strategy was defined as starting mono-therapy with a csDMARD, with or without GCs as bridging therapy.

The outcome was remission according to a validated disease activity index or the Boolean definition. Numbers of patients were extracted from all studies and relative risks (RR) for achieving remission with 95% confidence intervals (95%CI) per study were calculated. Subgroup analyses were performed for different definitions of remission, the use of a b/tsDMARD as part of the induction therapy strategy (yes/no) and the use of concomitant GC bridging therapy (yes/no) in standard DMARD strategies.

Results: Included were 22 clinical studies, involving 4435 patients in induction strategies and 3314 in standard DMARD strategies. For remission, 17 studies applied the criterion of DAS28 <2.6, 12 the Boolean remission definition, 7 CDAI ≤≤20 and 10 studies SDAI ≤≤3.3. Remission had to be present during 6 to 12 months in all studies. Heterogeneity in study design prohibited providing an overall pooled effect estimate, but for subgroup pooled estimates were given for descriptive purposes.

In the figure we provide results for studies applying the DAS28 remission definition. Of those studies, 13/17 (76%) showed a statistically significant effect in favour of induction therapy. The pooled RR of achieving remission for strategies initiating bDMARDs was 1.73 [95%CI 1.59 to 1.88] versus the standard DMARD strategy without GC bridging, and it was 1.20 [95%CI 1.03 to 1.40] for induction strategies without bDMARD versus standard DMARD strategies without GC bridging. No superior effect of any induction strategy was found compared to that of standard DMARD strategies with GC bridging (pooled RR 1.06, 95%CI 0.83 to 1.35).

When using other remission definitions, all induction strategy studies with Boolean/CDAI/SDAI outcomes applied a b/tsDMARD, and 63%, 100% and 78%, respectively found a statistically significantly superior effect compared to standard DMARD strategies without GC bridging; however, compared to standard DMARD strategies with GC bridging, only trends in the same direction were found.
Disclosure of Interests: Maxime Verhoeven: None declared, Paco Welsing: None declared, Johannes WU Jlijima Grant/research support from: The department of the author who included patients (JWJB) in the U-Act randomized, and placebo-controlled study (NCT02758613) conducted from 04 week) of 18 years) with a body mass index of 19.0 to 24.0 kg/m² (inclusive).

Table 1: Baseline characteristics of the monotherapy and combination therapy groups

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Monotherapy</th>
<th>Combination therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>(n=1,034)</td>
<td>(n=340)</td>
</tr>
<tr>
<td>Female sex</td>
<td>57 (46, 67)</td>
<td>233 (66)</td>
</tr>
<tr>
<td>Symptom duration (months)</td>
<td>5.4 (3.4, 9.0)</td>
<td>0.020</td>
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<tr>
<td>HAQ score</td>
<td>1.0 (0.4, 1.5)</td>
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<td>DAS28</td>
<td>4.1 (3.2, 5.1)</td>
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</tr>
<tr>
<td>Co-morbidities</td>
<td>&gt;=1</td>
<td>468 (45)</td>
</tr>
<tr>
<td>MTX starting dose (mg/week)</td>
<td>10 (10, 12.5)</td>
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</tr>
</tbody>
</table>

Values are frequency (%) or median (IQR)

Abbreviations: HAQ, health assessment questionnaire; DAS, disease activity score; MTX, methotrexate

Conclusion: The PK of baricitinib in Chinese healthy subjects were characterized by rapid absorption and elimination following single and multiple oral doses of up to 10 mg. Systemic exposure to baricitinib increased in an approximately dose-proportional manner following single and multiple doses. Single and multiple oral doses of daily-administered baricitinib up to 10 mg were well tolerated by healthy Chinese subjects.


THU0200

DRUG UTILISATION IN PEOPLE WITH EARLY RHEUMATOID ARTHRITIS IN THE UNITED KINGDOM

Sarah Wood, Kimme Hyrich, Suzanne Verstappen, Douglas Steirke. The University of Manchester, Manchester, United Kingdom

Background: Despite a growing body of evidence in the pharmacological management of people with early rheumatoid arthritis (RA), there is still uncertainty concerning the most effective treatment regimen. Until 2018, guidance for England and Wales stated that everyone with early RA should receive combination therapy with 2 or more conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) in parallel. However, from epidemiological studies and anecdotal information, we know that this has not been the case in practice.

Objectives: (i) To determine the proportion of patients with new onset RA who start methotrexate (MTX) either alone or in combination with another csDMARD (ii) to describe which combinations are currently being prescribed and (iii) to describe the characteristics associated with the choice of initial RA treatment strategy.

Methods: Consecutive patients with RA participating in the Rheumatoid Arthritis Medication Study (RAMS), a large UK study recruiting patients starting MTX for the first time, were eligible. Data on demographics, disease activity, comorbidity and all RA treatments are captured at baseline, 6 and 12 months following start of MTX. Analysis was limited to patients starting MTX within the first 2 years of symptom onset as part of their first treatment regimen for RA. Prevalent users of alternative csDMARDs, defined as use > 6 weeks prior to MTX start, were excluded. Participants were categorised as either starting MTX monotherapy or MTX in combination with another csDMARD (defined as started +/- 6 weeks of MTX start date). Baseline characteristics were compared between monotherapy and combination therapy groups using descriptive statistics.

Results: 1,374 patients with a mean (SD) age of 58 (14) years were included in this study; 64% were female. At baseline, 996 (76%) started MTX monotherapy and 316 (24%) started MTX/csDMARD combination therapy (84% with hydroxychloroquine and 16% with sulphasalazine). Patients starting combination therapy were younger (p<0.005), with higher DAS28 scores (p<0.005), higher HAQ scores (p<0.05), lower MTX starting doses (p<0.005), and shorter symptom duration (p=0.05) compared with the monotherapy group.

Conclusion: These data show that despite national guidelines recommending combination csDMARD therapy in all patients diagnosed with RA, over three quarters of patients still started MTX monotherapy. People who were prescribed combination therapy had more severe disease suggesting that prescribers do consider prognosis in their treatment decisions. A majority of patients starting combination therapy did so with hydroxychloroquine, despite a lack of evidence for the benefits of this particular combination in clinical practice.

Table 1. Baseline characteristics of the monotherapy and combination therapy groups

Characteristic | Monotherapy | Combination therapy | P value
<table>
<thead>
<tr>
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</table>

Values are frequency (%) or median (IQR)
ANALYSIS OF GUT MICROBIOTA DIVERSITY IN PATIENTS WITH RHUMATOID ARTHRITIS AND BENEFICIAL EFFECTS OF PROBIOTICS ON INTESTINAL FLORA

Mina Yao1, Sheng-Xiao Zhang1, Chong Gao2, Xiao-Bin Zheng1, Lili Shang1, Xu-Fang Yin1, Zhang Mingxing1, Jia Wang1, Ting Cheng1, Nalin Lal1, Li Xiao-Feng1.

1The Second Hospital of Shanxi Medical University, Department of Rheumatology, Taiyuan, China; 2Brigham and Women’s Hospital, Harvard Medical School, Department of Pathology, Boston, United States of America

Background: Rheumatoid arthritis (RA) is a progressive, irreversible disease characterized by autoimmune imbalance. Recent studies have found that the number and type of intestinal flora in RA patients were changed (called disorders), which in turn leads to immune imbalance in RA patients. The breath test can indirectly assess the growth of bacteria in the intestine. This study aimed to investigate the intestinal flora imbalance in RA patients and the effect of probiotics on the intestinal flora of RA patients using methane and hydrogen breath test.

Objectives: To study the beneficial effects of probiotics on the intestinal flora of RA patients by detecting the concentrations of methane and hydrogen and the microbial populations in patients with rheumatoid arthritis (RA) before and after probiotic treatment.

Methods: The lactulose methane and hydrogen breath technique were used to detect and compare the concentration of methane and hydrogen in 36 patients with RA before and after probiotic treatment (mainly Bifidobacterium, Clostridium butyricum, Lactobacillus) for 3 weeks. At the same time, the 16SRNA V3 region in stool samples of 17 patients with RA was qualitatively analyzed by Roche/45 high-throughput sequencing platform and compared with 9 healthy adult stool samples.

Results: Compared with pre-intervention, after 3 weeks of probiotic treatment, the exhaled methane concentration was significantly increased in RA patients at 30 minutes, 60 minutes, and 90 minutes (P < 0.05). The sum of methane and hydrogen concentrations increased at 30 minutes (P < 0.05). There was no significant difference in hydrogen concentration before and after treatment (P > 0.05) (Table 1). Compared with healthy adults, the fecal diversity index (Shannon) of RA patients increased (P < 0.05) and the species uniformity index (flatness) also increased.

Conclusion: Patients with RA had a significant difference in the structure of intestinal flora compared with that of healthy controls, which may represent perturbations of microbial communities and contribute to the pathogenesis and condition of RA. Probiotics can restore the composition of the gut microbiome and introduce beneficial functions to gut microbial communities through diet, probiotics or fecal transplantation, providing a promising prospect for clinical treatment of RA.

References:

Disclosure of Interests: None declared

SLE, Sjögren’s and APS – etiology, pathogenesis and animal models

INTERFERON STIMULATED GENE 15 PROTECTS REGULATORY T CELL OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS FROM INTERFERON ALPHA-MEDIATED DEPLETION

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Background: Data on T regulatory (T reg) cells number and functions in patients with Systemic Lupus Erythematosus (SLE) are conflicting (1). Type I interferon (IFN) decreases Treg proliferation and induces Treg apoptosis (2). IFN stimulated gene 15 (ISG15) is an IFN-induced protein with a negative effect on IFN pathway.

Objectives: Aim of the study was to evaluate the effect of IFN alpha and ISG15 on Treg number and on STAT1 phosphorylation in patients with SLE.

Methods: We recruited patients with SLE classified according to 1997 ACR criteria. We collected demographic and clinical data including disease duration, disease activity scored according to Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) 2.0. Peripheral blood mononuclear cells (PBMC) were isolated from whole blood samples. Intras cellular phosphorylated STAT1 (pSTAT1) levels were evaluated in Treg (CD4+FOXp3+CD127 low cells) and conventional T cell (Tconv, CD4+FOXp3- cells) by multiparametric flow cytometry, ex vivo or after stimulation with recombinant IFN alpha. PBMC were cultured for 48 hours with anti-CD3 or anti-CD3 and IFN alpha; the frequency of Treg was analysed by multiparametric flow cytometry. ISG15 mRNA expression was evaluated by RT-PCR on PBMC from SLE patients. Data were expressed as mean ± standard deviation or median (interquartile range) according to the distribution; Mann-Whitney and Spearman tests were applied. P value <0.05 were considered statistically significant.

Results: We enrolled 21 SLE patients [F:M 20:1; mean age 45.2 ± 12.9 years; mean disease duration 157.5± 103 months; median SLEDAI 2(4)] Overall, median baseline ISG15 mRNA expression was 0.06 (IQR 0.16); patients were divided into ISG15-high (n=9) and ISG15-low (n=12), according to the mean mRNA expression. Ex vivo, after short-term treatment with IFN alpha (15 and 25 minutes), we observed a significant increase in STAT1 phosphorylation compared to baseline both in Treg and Tconv (p<0.00001), in ISG15-high and ISG15-low patients (Figure 1 A and B); however, high ISG15 levels protect both Treg and Tconv from STAT1 phosphorylation (Figure 1 C). After 48 of culture with IFN alpha, we observed a decrease in Treg and Tconv number, significantly greater in ISG15-low cells (Figure 1 D). Treg frequency and ISG15 expression in Treg were higher in active vs inactive SLE patients [SLEDAI > 4 vs SLEDAI ≤ 4] (p<0.05).

Conclusion: ISG15 protects T conventional cells from STAT1 phosphorylation and induces resistance to T regulatory cells depletion. The results of the study suggest that ISG15, a protein induced by IFN in the acute phase of the disease, exerts a negative feedback, allowing the recovery of T reg.
PROMOTER DNA METHYLATION AND HSA-424-5P ASSOCIATION OF LILRA3 GENE WITH mRNA levels together with a decrease in ATF6 levels found in LSG from SS-patients (p=0.02), which were inversely correlated with 3D-acini with IFN-γ treatment.

Results: LSG from SS-patients showed a significant decrease of ATF6 mRNA expression in LSG from SS-patients and controls. The effect of IFN-γ on both mechanisms was also evaluated in a 3D-acini model.

Methods: SG biopsies from SS-patients and controls were analyzed. In vitro assays 3D-acini incubated with 1 or 10 ng/mL IFN-γ for 24 h were employed. Specific DNA methylation of ATF6 gene promoter was evaluated by methylation-sensitive high-resolution melting PCR. For in vitro assays, 3D-acini were incubated with 1 or 10 ng/mL IFN-γ.

Conclusion: The results suggest that the ATF6 promoter overexpression is regulated by two complementary epigenetic mechanisms: the DNA hypermethylation of its promoter and the silencing of its mRNA by hsa-miR-424-5p in LSG from SS-patients. IFN-γ affects the expression of ATF6 by modulation of epigenetic mechanisms, regulating the abundance of epithelial cells to handle the chronic ER stress. Interestingly, these changes carry out under a global DNA hypomethylation condition.

REFERENCES:

Disclosure of Interests: None declared
Background: In SLE, all terminally differentiated blood cells demonstrate an aberrant phenotype. HSCs are the most primitive cell type of the hematopoietic lineage when exposed within the bone marrow (BM) to adjuvants and inflammatory mediators change their transcriptional landscape and this may persist in the HSCs circulating in the peripheral blood or those infiltrating peripheral tissues. Within peripheral tissues these reprogrammed HSCs differentiate into myeloid cells mounting enhanced protective or aberrant immune responses.

Objectives: To dissect whether aberrant phenotypes of blood cells in SLE could be traced back to HSCs and explore how the inflammatory environment of SLE shapes the HSC differentiation process.

Methods: We analyzed the transcriptional alterations (genetic or epigenetic) of CD34+ cells in the BM of SLE patients, compared it to healthy individuals and the NZB/W lupus mice at the onset of disease (6 months). CD34+ cells were isolated from BM aspirates and peripheral blood of SLE patients (n=8) and healthy subjects (n=2) with magnetic separation (Stem Cell Technologies). mRNA was extracted and libraries were prepared. Sequencing was performed in NextSeq Illumina Platform. Alignment in human genome v.38 was done by Star package and differential expression analysis was performed by edgeR algorithm. Genes with FC>1.5/-1.5, FDR <0.05 were considered statistically significantly up/down-regulated, respectively. Heatmaps were constructed in R, GO/Pathway Analysis and enrichment analysis were performed in ClueGo, RENA, GeneMania and GSEA, respectively.

Results: Overlaying the transcriptome of BM-derived CD34+ of SLE patients and healthy subjects, we identified in total 598 differentially expressed genes (DEGs) (82 up-514 down-regulated in SLE). DEGs participate in hematopoietic cell lineage fate, regulation of stem cell differentiation, cell adhesion and cell cycle regulation. We also found evidence for cell cycle checkpoints signature which drives HSCs to experience replication stress and activate ATR pathway. Comparison of CD34+ profile between severe-moderate SLE reveals a prominent neutrophilic signature in severe disease. Comparative transcriptomic analysis of human vs murine SLE revealed a panel of common genes again related to cell proliferation and differentiation and platelet activation.

Conclusion: HSCs in SLE patients and murine lupus reprogram their transcriptome in response to the inflammatory milieu within the BM, thus exiting from dormancy, differentiating to myeloid cells and mounting a DNA damage response to the replication stress. This activated phenotype renders HSCs both susceptible to cell exhaustion while at the same time priming them and their progenies towards enhanced immune responses.

REFERENCES:
HELPER AND CYTOTOXIC FOLLICULAR T-CELLS IN SJÖGREN’S SYNDROME

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Background: Follicular T-cells, characterized by the expression of CXCR5, secrete interleukin 21 (IL-21) and help B-cell differentiation in lymphoid follicles. They are also found in circulation and may play a key role in Sjögren’s syndrome (pSS) chronic autoimmune epithelium.

Objectives: To study circulating follicular helper (Thf) and cytotoxic (Tc) T-cells in peripheral blood (PB) from pSS patients, Rheumatoid Arthritis (RA) patients and healthy controls (HC), and to investigate how they correlate with B-cell subsets. We also aimed to explore associations between the Thf and Tc cells and clinical and laboratory features of pSS.

Methods: PB from 57 pSS patients, 20 RA patients and 24 HC was analysed by flow cytometry to characterize T and B-cell subsets, with CXCR5 defining Thf and Tc within CD4 and CD8 T-cells, respectively. A stimulation assay was used to assess the production of IL-21 by CD4+ and CD8+ T-cells.

Results: Compared to HC, pSS and RA patients presented significantly lower lymphocyte absolute counts (1615 and 1935 cells/µL, respectively) compared to 2228 cells/µL in HC, p<0.001 for HC vs pSS, p=0.018 for HC vs RA), and percentages (29.9% in pSS, 24.0% in RA, and 35.4% in HC, p=0.02 for HC vs pSS, and p=0.001 for HC vs RA). B-cell and T-cell absolute counts were also lower in both groups of patients compared to HC (in HC vs pSS, p=0.011 for B-cells and p=0.001 for T-cells; in HC vs RA, p=0.001 for B-cells and p=0.018 for T-cells). B-cells absolute counts and percentages in pSS were higher than in RA (177 vs 132 cells/µL, p=0.013; 9.7 vs 6.4%, p<0.001). There were no differences in CD8 T-cells percentages between groups, but pSS had lower CD4+ T-cell percentages compared to HC (p=0.004).

pSS patients presented lower absolute counts of CXCR5+ Tfh compared to RA (134 vs 181 cells/µL, p=0.039) and HC (134 vs 241 cells/µL, p=0.001). No differences were found in Thf percentages. RA patients had lower percentages of CXCR5+ Tfh compared to pSS (2.1 vs 2.6%, p=0.113) and HC (2.1 vs 3.0%, p=0.046).

pSS patients exhibited higher percentages of IL21+CD4 and IL21+CD8 T-cells (IL21+CD4 T-cells: 12.4% in pSS vs 9.0% in RA, p=0.046; vs 9.7% in HC, p=0.028; IL21+CD8 T-cells: 4.1% in pSS vs 2.3% in RA, p=0.001; vs 2.8% in HC, p=0.030). In pSS patients, CXCR5+ Tfh correlated positively with the percentages of plasmablasts (r=0.262 for CD24+CD38+ cells, and r=0.282 for IgM−CD38++ cells). IL21+CD8 T-cells correlated positively with the Naïve/Memory B cells ratio (r=0.370; p=0.002) and negatively with Bm1 memory cells (r=-0.323; p=0.014) and with Bm1 memory B cells (r=0.370; p=0.003). IL21+CD4 T-cells behaved similarly, though without statistical significance.

Anti-SSA-positive patients (n=38) presented higher CD4+IL21+ (133 vs 8.5%, p=0.025) and CD8+IL21+ percentages (4.4 vs 4.0%, p=0.198) than SSA-negative patients (n=19). Although there were no differences between pSS patients with active (n=27) and inactive disease (n=30), a tendency for positive correlations was found between IL21+CD4 and IL21+CD8 T-cells and the ESSDAI score (r=0.229, p=0.086 for CD4-, r=0.223, p=0.096 for CD8). Moreover, ESSDAI correlated positively with the Thf1/Thf17 ratio.

Conclusion: pSS patients present a profile of circulating Thf and Tc distinct from RA and HC, both phenotypically and functionally. Moreover, our data suggest a crucial role for these cells in B cell development, as they correlate with B cells, in pSS patients, which are known to exhibit a typical circulating B cell compartment. Both Thf and Tc cells can be critical for disease pathophysiology and activity, as underlined by the correlations between these cells and ESSDAI scores.

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4-PHENYL BUTYRIC ACID AMELIORATES LUPUS: RNA-SEQ REVEALS THE MECHANISM OF THALIDOMIDE IN LUPUS CUTANEOUS LESIONS

THU0209

4-PHENYL BUTYRIC ACID AMELIORATES LUPUS HEPATITIS AND NEPHRITIS THROUGH SUPPRESSION OF NF-κB ACTIVATION IN EXPERIMENTAL LUPUS MODEL

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease presenting diverse manifestation involving multiple organs, such as liver and kidney. Endoplasmic reticulum (ER) stress has been revealed as one of the contributing factors of lupus pathogenesis.

Objectives: The purpose of the present study was to investigate whether ER stress inhibition suppresses organ inflammation including liver and kidney in lupus murine model and the activation of mitogen activated protein kinases (MAPK) and NF-κB.

Methods: A murine lupus model was induced through a 4-week treatment with Resiquimod, a toll-like receptor agonist 7. From the 8th week, the mice were treated with phosphate buffered saline, 4-phenylbutyric acid (4-PBA), and dexamethasone for 4 weeks. The increment of body weight, liver weight, inflammation mediator level, and the pathology of hepatitis and nephritis were analyzed at 12 weeks of age. The level of phosphorylated MAPK expression and activation of NF-κB were also evaluated.

Results: 4-PBA-treated group showed lower level of body weight increment with liver to body weight ratio compared with vehicle-treated group. 4-PBA group showed decreased inflammatory cell infiltration and fibrosis in the histologic finding of liver and kidney and lower level of inflammatory mediators, including TNF-α and IL-6, compared to vehicle-group. GRP78 and CHOP expression was decreased in the spleen of 4-PBA treated mice compared to vehicle-treated mice and 4-PBA group showed the lower expression level of phosphorylated JNK, ERK, p38 and NF-κB of the spleen.

Conclusion: Our results suggest that 4-PBA attenuates the inflammation on liver and kidney of experimental lupus model through suppression of MAPK and NF-κB activation. Thus, inhibition of ER stress could be function as anti-inflammatory therapeutics for SLE.

Abstract THU0209 – Figure 1

REFERENCES:

Disclosure of Interests: None declared

THU0210

RNA-SEQ REVEALS THE MECHANISM OF THALIDOMIDE IN LUPUS CUTANEOUS LESIONS

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Background: Cutaneous Lupus Erythematosus (CLE) is common, largely heterogeneous and characterized by a chronic relapsing course. As many as 70 to 80% of patients with SLE will develop skin lesions at some point during the course of their disease, with a significant proportion being disfiguring and debilitating [1]. Conventional therapy consists of topical steroids and antimarial agents but 40% of patients will be refractory to this regimen [2]. Thalidomide has been the only one that has shown an effectiveness of 90% [3], however, its mechanism of action in the disease is not known at all. In addition, its use is limited due mainly to its side effects such as teratogenicity and the development of peripheral polyneuropathy.

Objectives: Identification of the possible mechanisms of thalidomide in cutaneous lupus erythematosus.

Methods: Skin biopsies before and during treatment has been performed on a cohort of CLE patients treated (N=20) and not treated with thalidomide (N=5). Through a differential study of gene expression with RNA-seq and its subsequent validation, the mechanism of thalidomide action has been identified. The cell population in the tissue and in the blood of the patients and their evolution due to the treatment has also been studied by flow cytometry. In vitro experiments using isolated lupus cutaneous lymphocyte and keratinocytes has been performed to see the specific biological effect of thalidomide (Figure 1).

Results: Flow cytometry of immune cells from blood obtained pre- and post-treatment revealed a significant activation of Thelper (p<0.001), a differentiation towards Th2 subpopulation and an increase of natural killer effectors such as perforin and granzyme B. Not significant difference were observed in macrophages and dendritic cell. In addition, after RNA-seq analysis two fundamental molecular pathways has been identified in responder thalidomide treatment patients: 1) via IRF4-NFκB pathway modulation. 2) via AMPK-mTOR pathway modulation. In vitro experiments using isolated primary cells from lupus cutaneous patients showed that thalidomide modulate IRF4 in lymphocytes to inhibit NFκB pathway; however, AMPK-mTOR pathway is inhibited in keratinocytes by thalidomide effect.

Conclusion: Taken together, we show that mechanism of thalidomide in CLE is dual. It might inhibited NFκB pathway by modulation of IRF4 in lymphocyte but, in the same time, might inhibited MTOR pathway by modulation of AMPK in keratinocytes.

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Abstract THU0210 – Figure 1. Scheme of the project to discover thalidomide mechanism in lupus cutaneous patients.

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Disclosure of Interests: Cristina Solé-Marcé: None declared, Ana María Alvarez-Ríos: None declared, Teresa Moliné: None declared, Berta Ferrer: None declared, Josep Ord-Ros: None declared, Josefina Cortés-Hemández Grant/research support from: GSK, Speakers bureau: GSK

THU0211

EVOLUTION OF KIDNEY ANTIBODY SECRETING CELLS MOLECULAR SIGNATURE IN LUPUS PATIENTS WITH ACTIVE NEPHRITIS UPON IMMUNOSUPPRESSIVE THERAPY

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Background: Pathogenic antibody secreting cells (ASC) have been identified in the kidney of SLE-prone mice, but are poorly characterized in human lupus nephritis (LN). We hypothesized that long-lived plasma cells may contribute to the failure of immunosuppressive therapy in refractory patients.

Objectives: To characterize and compare the single cell molecular signature of ASC in kidney and urine from patients with active LN, either untreated or after immunosuppressive therapy failure.

Methods: We included patients with biopsy proven active LN from 4 centers and meeting the ACR revised classification criteria for SLE. Renal biopsies were scored according to 2003 International Society of Nephrology/Renal Pathology Society (ISN/RPS) classification, and stained with anti-CD138 to visualize ASC. ASC were single cell sorted as CD3-/CD14-/CD16-/CD27high/CD38high cells. Single-cell gene expression profiling was performed by multiplex RT-PCR using Fluidigm Dynamic Arrays. We used a set of genes derived from a previous transcriptomic analysis of human splenic and bone marrow ASC to distinguish the process of ASC maturation from plasmablast (PB) to long-lived PC. We also studied ASC transcriptional program from urine of untreated LN patients at diagnosis and after 3 and 6 months of a prospective follow up during induction therapy (Plasma-Lup study).

Results: Immunohistochemistry staining on kidneys biopsies from both untreated (N=15) and refractory patients (N=6) showed infiltrates of CD138+ ASC mainly located in the interstitium, particularly in untreated patients. Single cell molecular signature of kidney ASC from 3 untreated patients with class IV LN revealed that these cells were mostly PB expressing multiple genes linked with cell division, and PC without long-lived PC genes expression. This contrasted with ASC signature from 3 patients with active LN and mycophenolate mofetil (MMF) failure that expressed long-lived PC genes and no proliferative genes. Primary component analysis of 170 single-cells showed clustering of ASC from MMF treated patients with long-lived bone marrow PC from healthy donors that were distinct from PB/PC from untreated patients (Figure 1). A PB signature was observed in urine ASC at diagnosis, similar to their kidney counterpart. The concentration of ASC in urine in 22 untreated patients correlated with ISN/RPS classification, with higher concentration in class IV patients (p<0.01).

Conclusion: These results suggest that PB infiltrate kidney of untreated LN patients, and that kidney long-lived PC may contribute to the failure of immunosuppressive therapy.

THU0212

BARICITINIB-ASSOCIATED CHANGES IN GLOBAL GENE EXPRESSION DURING A 24-WEEK PHASE 2 CLINICAL SLE TRIAL DESCRIBE A MECHANISM OF ACTION THROUGH INHIBITION OF JAK/STAT AND IFN RESPONSIVE GENE EXPRESSION

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Background: Baricitinib (bari) is an oral selective Janus kinase (JAK)1 and JAK2 inhibitor. In the Phase 2 study, JAH2 (NCT02708095), treatment with bari resulted in significant improvements in patients (pts) with active systemic lupus erythematosus (SLE) receiving standard background therapy, compared with placebo (PBO).1

Objectives: To use global gene expression to characterize baseline (BL) gene expression among SLE pts in JAH2 and to describe the mechanism of action (MoA) of bari during treatment in active SLE.

Methods: A total of 314 pts were randomized 1:1:1 to PBO, bari 2-mg, or bari 4-mg once daily for 24 weeks (Wks) in JAH2. RNA isolated from whole blood at BL and Wks 2, 4, 12, and 24 was analyzed using HTA2.0 arrays, possessing over 925,000 specific individual probes. Data were summarized to transcript level and analyzed using a mixed effects model on a log2 transformed response with multiplicity correction.

Results: Baseline gene expression analysis comparing healthy controls to SLE pts revealed elevated expression of genes involved in innate and adaptive immune pathways and biologic processes thought to be key to SLE pathogenesis. Baseline findings from the ILLUMINATE trial of tabalumab (1760 SLE pts at BL)2 were independently replicated, including individual gene-specific changes in the SLE populations versus controls. Treatment-induced changes were predominantly observed in the bari 4-mg versus PBO group at early time points (Wks 2 and 4; bari 4-mg > 2-mg). Statistically significant changes were observed for type I and II IFN responsive genes, and in the JAK/signal transducer and activator of transcription (STAT) canonical and noncanonical signaling pathways, in the bari 4-mg versus PBO group comparisons. There were biologically notable and statistically significant bari-associated decreases in gene expression from BL, compared to PBO, for interleukin (IL)-3, -5, -6, -7, and granulocyte macrophage colony-stimulating factor pathways, attributable to inhibition of JAK/STAT signaling.

Conclusion: These results build upon previous studies of gene expression in ILLUMINATE, comparing SLE at BL with healthy controls; they advance our understanding of lupus pathogenesis, and further delineate the MoA of bari in SLE. These data independently confirm the marked elevations of specific type I and II IFN genes at BL in clinical trial pts on standard of care treatment. Changes in gene expression with bari impacted IFN responsive genes as well as JAK/STAT signaling pathways. Interpretation of results is limited by sample size and statistical power, and presence of concomitant medications. Importantly, gene expression may not translate directly to protein expression; however, ongoing proteomic studies (including specific assays for type I IFN, IFN-γ, IL-12, IL-17, and IL-23) will help extend these gene expression results and further describe the MoA of bari in SLE.

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Disclosure of Interests: None declared


THU0214

THE PI3Kα SELECTIVE INHIBITOR INCB050465 ABROGATES KIDNEY PATHOLOGY IN A SPONTANEOUS MURINE MODEL OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease that affects multiple organs, including the skin, joints and kidneys. Though SLE typically cycles through periods of flares and remission, patients often eventually succumb to end-stage kidney or cardiovascular disease. SLE is characterized by the presence of autoantibodies that form immune complexes resulting in kidney deposition that significantly contribute to lupus nephritis pathogenesis. Phosphatidylinositol 3-kinases (PI3Ks) are divided into three classes (Class I, II, and III) according to their structure, regulation and substrate specificity. The Class I PI3K delta isoform (PI3Kδ) has been implicated in autoimmune diseases associated with aberrant B cell and antibody responses. INCB050465 is an oral small molecule PI3Kδ selective inhibitor currently being evaluated in clinical trials for the inflammatory indications Sjögren’s syndrome and autoimmune hemolytic anemia (NCT03627065 & NCT03538041).

Objectives: To quantify the efficacious potential of INCB050465, a selective PI3Kδ inhibitor, in a preclinical model of systemic lupus erythematosus with kidney pathology.

Methods: The MRL/lpr mouse model spontaneously develops multiple inflammatory phenotypes that mimic human SLE pathologies, including kidney damage resulting in proteinuria, cutaneous skin lesions and anti-double stranded DNA (anti-dsDNA) antibodies. Kidney sections were stained with hematoxylin and eosin (H&E) and assigned a composite score based on glomerulus, crescents, protein casts, interstitial inflammation and vasculitis by a rater unaware of the treatment groups. Flow cytometry was performed on splenocytes to characterize B cell and T cell subsets. Anti-dsDNA antibodies were determined by commercial ELISA.

Results: In vitro enzymatic selectivity screening revealed INCB050465 potently inhibited the PI3Kδ kinase enzyme (IC50 = 1.1 ± 0.5 nM), with 20,000-fold selectivity for the other PI3K family member enzymes. Proteins identified spontaneous kidney damage in 85% of vehicle treated mice by 21 weeks of age, and kidney histology revealed gross tissue enlargement associated with structural abnormalities. In contrast, treatment of INCB050465 treated mice by 21 weeks of age, and kidney histology revealed gross tissue enlargement associated with structural abnormalities. In contrast, therapeutic INCB050465 treatment dose-dependently reduced spleen weight (p < 0.01) and lymph node weight (p < 0.01) weight. Cutaneous skin lesions were unaffected by INCB050465 treatment. Splenocyte flow cytometry revealed no reduction in absolute lymphocyte, CD19+ B cell, CD4+ or CD8+ T cell frequencies following INCB050465 treatment. However
INC050465 reduced the absolute counts of germinal center (CD19GL7) and marginal zone (CD19CD21) B cell subsets. Anti-dsDNA antibodies were abrogated by INC050465 therapy (p < 0.005).

Conclusion: INC050465, a selective PI3Kι inhibitor, was highly efficacious against immune-mediated mechanisms associated with lupus nephritis, but not cutaneous lupus disease manifestations in this preclinical model. Treatment-induced reduction of kidney tissue integrity corresponded to specific B cell subset modulation and autoantibody reduction. Selective PI3Kι inhibitor treatment did not induce lymphocyte depletion.

REFERENCE:

Disclosure of Interests: Brittany Fay Shareholder of: The author is an employee and/or shareholder of Incyte Corporation., Employee of: The author is an employee and/or shareholder of Incyte Corporation., Monika Scuron Shareholder of: The author is an employee and/or shareholder of Incyte Corporation., Employee of: The author is an employee and/or shareholder of Incyte Corporation., Eddy Yue Shareholder of: The author is an employee and/or shareholder of Incyte Corporation., Niu Shin Shareholder of: The author is an employee and/or shareholder of Incyte Corporation., Max Vikström Shareholder of: Minor shareholder and inventor in startup-company Athera Biotechnologies., Employee of: The author is an employee and/or shareholder of Incyte Corporation., Yan-ou Yang Shareholder of: The author is an employee and/or shareholder of Incyte Corporation., Divya Thiagarajan1, Susanna Lundström1, Roman Zubarev1, Jitong Sun2, Marta Alarcon-Riquelme3, Systemic sclerosis (SSc, 331), Sjögren syndrome (SjS, 331), Mixed connective tissue disease (UCTD, 118), among 116 SLE-patients from Karolinska University Hospital SLICC and SLEDAI (OR: 4.74 CI: 1.29-17.39, OR: 4.74 CI: 1.29-17.39). The maximal difference between cases and controls was shown for SLE patients than controls (p=0.02). IgG1 anti-PC levels were higher among SLE patients than controls (p=0.02). IgG1 anti-PC was negatively associated with atherosclerosis and SLE.

Results: The maximal difference between cases and controls was shown for MCTD: significantly lower IgM Anti-PC but not anti-MDA among patients (median 49.3±7μl vs 70.4 in healthy controls, p(t-test)=0.0037).

Low levels (below 25th percentile) of anti-PC but not anti-MDA were significantly more prevalent in MCTD, SLE, SjS and SSc. The IgM anti-PC variable region profiles were distinctly different and also more homologous in their content than anti-MDA. Anti-PC but not anti-MDA were significantly more prevalent with CV in the whole patient group. In contrast to IgM anti-PC, IgM anti-MDA did not promote polarization of Tregs.

Conclusion: Anti-PC could be a protection marker for MCTD and also for SLE, SjS and SSc while anti-MDA did not differ. anti-PC level is negatively correlated with CV in the patient group cohort. These findings could have both diagnostic and therapeutic implications, one possibility being active or passive immunization with PC.

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Background: IgM antibodies against phosphorylcholine (anti-PC) may be protective in atherosclerosis, cardiovascular disease (CVD) and systemic lupus erythematosus (SLE). Less is known about other anti-PC isotypes and subclasses. In this study, we study the role of IgG1 and IgG2 anti-PC, with focus on atherosclerosis and SLE.

Methods: To study the role of IgG1 and IgG2 anti-PC, with focus on atherosclerosis and SLE, both in clinical setting and by experimental studies, where we use our in-house produced monoclonal IgG1 anti-PC. We determined IgG1 and IgG2 anti-PC in our SLE cohort study (SLEVIC), among 116 SLE-patients from Karolinska University Hospital Huddinge and 110 population controls matched for age and gender. The level of antibodies was measured by ELISA. For functional studies, we used three of our in-house generated, fully human monoclonal IgG1 anti-PC (A01, D05, E01). Primary human macrophages were derived from peripheral blood. Apoptosis was induced in Jurkat T-cells and pre-incubated with A01, D05, E01 or isotype control IgG1 and effect on phagocytosis by macrophages studied. Anti-PC peptide/protein characterization was determined in anti-PC clones compared to isotype control using a proteomics de novo sequencing approach.

Results: IgG1 but not IgG2 anti-PC levels were higher among SLE patients than controls (p=0.02). IgG1 anti-PC was negatively associated with prevalence of atherosclerotic plaques, below 10th percentile. (OR: 2.49, CI: 0.69-9.00). IgG1 Anti-PC was negatively associated with CVD, SLE and SLEDAI (OR: 4.74 CI: 1.29-17.39, OR: 4.74 CI: 1.29-17.39). Monoclonal D05 had maximum effect on macrophage effecrocytosis efficiency, followed by A01 and E01. This is because anti-PC IgG1 binds to phosphorylcholine exposed on apoptotic cells and facilitate the uptake by macrophage. The in-house produced monoclonal antibodies showed differential binding specitivity to PC and PC associated neo-epitopes. Peptide analysis showed difference in the CDR3 region of the three anti-PC IgG1 clones which are crucial for recognition of the phosphorylcholine on the apoptotic cell surface and other neo-epitopes.
SERUM THYMIC STROMAL LYMPHOPOIETIN (TSLP) AS A BIOMARKER OF B-CELL LYMPHOPROLIFERATION IN SJÖGREN’S SYNDROME

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Background: Thymic stromal lymphopoietin (TSLP) has been demonstrated to be expressed on salivary glands (SG) biopsies of patients with primary Sjögren’s syndrome (pSS), mainly in more advanced degrees of lymphoid tissue (MALT) involvement and lymphoproliferation, i.e. persistent parotid swelling and mixed cryoglobulinemia.

Objectives: To study serum TSLP in a larger number of pSS patients, to confirm its correlation with the already studied tissue expression, and then to investigate a possible role of TSLP not only as a tissue biomarker, but also as a peripheral blood biomarker.

Methods: Serum TSLP levels were assessed by ELISA in sera collected from ninety-one anti-SSA-positive pSS patients (females n=86, 94.5%; mean age 57.2 years, range 25-80), fulfilling the 2016 ACR-EULAR pSS classification criteria, 80 matched healthy blood donors (HBDs), and 21 patients with non-autoimmune sicca syndrome (nSS). pSS patients were then stratified according to the degree of lymphoproliferation (2), well previously defined by tissue studies in the same patients, as follows: pSS fully benign (fbSS), pSS with myoepithelial sialadenitis (MESA), and pSS B-cell MALT lymphoma (NHL); the difference in serum TSLP levels was studied between these three subgroups.

Results: Serum TSLP was significantly higher in pSS patients (mean 47.19 pg/mL, range 0-324.89) compared to nSS (mean 2.74 pg/mL, range 0-15.9), p<0.0001, and to HBDs (mean 0.59 pg/mL, range 0-324.89), p<0.0001. The significance was the same when including only patients with extreme disease activities (LA, n=40), p<0.0001, and to HBDs (mean 0.59 pg/mL, range 0-324.89), p<0.0001. The significance was the same when including only patients with extreme disease activities (LA, n=40), p<0.0001, and to HBDs (mean 0.59 pg/mL, range 0-324.89), p<0.0001.

Conclusion: Serum TSLP could represent a novel biomarker of pSS-related B-cell lymphoproliferation, characterized by a heavier MALT involvement. The validation of the present monoclonal results is currently ongoing within the EU HarmonicSS Project.

REFERENCES:
THE INVOLVEMENT OF MITOCHONDRIAL ACTIVATION VIA GLUTAMINOLYSIS IN HUMAN B CELL DIFFERENTIATION AND ITS RELEVANCE TO THE PATHOGENESIS OF SLE

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Background: B cells play a crucial role in Systemic Lupus Erythematosus (SLE). Recently, "Immunometabolism" attract much attention. Glucose and glutamine are important nutrition for energy production such as ATP in various cells. It has been reported that aerobic glycolysis, glutaminolysis and mitochondrial functions enhanced in cancer cells. However, the involvement of metabolic reprograming in plasmablast differentiation and its relevance to the pathogenesis of SLE remained elusive.

Objectives: We first investigated the abnormality of mitochondria in B cells from patients with SLE by flow cytometry. Next, B cells were isolated from healthy donors (HDs) and mitochondrial reprogramming were assessed in vitro.

Methods: First, peripheral blood mononuclear cells (PBMCs) were obtained from age-matched 31 HDs and 29 patients with SLE. The mitochondrial membrane potential was measured with DiOc6 by flow cytometry. In addition, CD19+ cells were isolated from HDs and stimulated with CpG (TLR9 ligand) and IFN-α. Change of aerobic glycolysis, glutaminolysis and mitochondrial functions were assessed in the absence of glucose or glutamine and in the addition of metformine, which is known as AMPK activator, in vitro.

Results: We first examined the abnormality of mitochondria in B cells from patients with SLE using DiOc6 as a marker of depolarization-active mitochondrial membrane. Baseline characteristics of SLE were males: females=1:2.8, age 40.2 years, disease duration 132.2 months, SLEDAI 6.4 and BILAG 6.2 at the timing of admission due to exacerbation of SLE. The percentage of IgGCD27 memory B cells were higher than those of HDs, while the percentage of IgM memory B cells were lower than that of HDs. The percentage of CD24+DiOc6+ cells in IgD-/CD27+ memory B cells from patients with SLE were higher than that of HDs. These results indicate that B cells from patients with SLE have the abnormality of differentiation and mitochondrial functions. Next, we assessed the change of aerobic glycolysis, mitochondrial functions and glutaminolysis in the process of plasmablast differentiation in vitro. Stimulation with CpG and IFN-α, 1) enhanced aerobic glycolysis, which was assessed with lactate production. 2) increased the area of cytoplasm including many expanded mitochondrial cristae with slightly wider and loosely organized intermembrane space in electric microscopy, accompanied with ROS production and DiOc6 up-regulation, 3) induced CD27+CD38+ plasmablasts differentiation and immunoglobulin production. Lactate production was decreased in the absence of both glucose or glutamine. ROS production and DiOc6 expression were decreased in the absence of glucose, leading to inhibition of plasmablasts differentiation and immunoglobulin production. On the other hand, this tendency was not shown in the absence of glucose. Next, we evaluated oxygen consumption rate (OCR). OCR was also suppressed in the absence of glutamine. Metformin, abrogated glutamine uptake, resulting in suppression of NOVDS production, decreased expression, plasmablast differentiation and immunoglobulin production.

Conclusion: These results suggest that mitochondrial activation via glutaminolysis may play an important role in the differentiation from IgG/CD27+ double negative B cells to plasmablasts and production of immunoglobulins in patients with SLE.

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THU0221

DRY EYE IN SJÖGREN’S SYNDROME: CHEMOKINE AND CYTOKINE TEAR SPECTRUM


Background: Previous studies have linked the participation of multiple chemokines and cytokines in the physiopathology of primary Sjögren’s syndrome (pSS), however data regarding their presence in tears is scarce.

Objectives: To evaluate a panel of chemokines/cytokines in the tears of patients with pSS and correlate them with ocular symptoms as well as objective ocular tests.

Methods: We included 21 patients with pSS (EULAR/ACR criteria). A single expert ophthalmologist in dry eye evaluated the patients and assessed the tear film break-up time. Schirmer-I test, tear meniscus height, the Van Bijsterveld staining score and the SIcCA Ocular Staining Score (OSS). We classified lacrimal dysfunction severity in two categories (1=mild, mild/moderate or moderate, and 2= moderate/severe and severe).

We scored the ESSPPIR, and ocular dryness VAS as well as the Ocular Surface Disease Index (OSDI), a 12-item scale for the assessment of symptoms related to dry eye disease and their effect on vision. Tear samples were collected using sterile tear flow strips, that were immediately frozen at -86°C until assayed. Once defrosted, the tears were extracted from the strips using a buffer containing 0.5 M NaCl and 0.5% Tween-20. We tested IFN-γ, IL-10, IL-12, IL-17A, IL-19, IL-2, IL-21, IL-23, IL-5, IL-6, IL-8, TNF-α, BAFF, CXCL10 and CCL2 by Luminometry. We also included 21 healthy controls without dry eye, to test chemokines/cytokines that after our initial screening were meaningful.

Results: Most patients were females (90.4%), mean age 59.3±13 years and median disease duration 7.9 years (0.5-27). All of them had ocular and oral symptoms. The median tear film break-up time was 6 seconds (2-9), median Schirmer-I test 6 mm (1-25), median Van Bijsterveld staining score 10 points (2-9), median OSS 7 points (2-11), median ESSPPIR score 6.7 points (2.9-9.2) and median ocular dryness VAS score 9 points (1-10).

We did not detect most of the evaluated chemokines/cytokines with the exception of IL-8, CXCL10, and CCL2. The former was similar in both, patients and controls. PSS patients had lower levels of CXCL10 (472.8±102.1 pg/ml vs 625.7±121.4 pg/ml, p=0.01) and CCL2 (3.03±0.53 pg/ml vs 9 pg/ml, p=0.02) than controls. Indeed, patients with worst lacrimal dysfunction severity had the lowest levels of CXCL10 (239.3±12 pg/ml vs 646.2±15 pg/ml, p=0.02). We found correlations among CXCL10 and CCL2 (r=0.30, p=0.02) and lacrimal meniscus height (r=0.55, p=0.005), as well as with CCL2 and lacrimal meniscus height (r=0.57, p=0.01). None of the other variables were correlated.

Conclusion: We identified CXCL10 and CCL2 as the main chemokines in tears of patients with pSS. CXCL10 seems to participate in the normal eye homeostasis.

Disclosure of Interests: None declared


THU0222

PLASMACYTOID DCS FROM PATIENTS WITH SJÖGREN’S SYNDROME ARE TRANSCRIPTIONALLY PRIMED FOR ENHANCED PRO-INFLAMMATORY CYTOKINE PRODUCTION

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Background: Type-I IFN activity is associated with pathogenesis and increased disease activity in primary Sjögren’s syndrome (pSS). In addition, deficiency for the type-I IFN receptor in mice prevents experimental-Sjögren’s syndrome. Plasmacytoid dendritic cells (pDC) are the premier type-I IFN producing immune cells and aberrances in their functional properties may underlie pSS immunopathology. Assessing the molecular basis of this may provide a better understanding of pSS pathogenesis and new opportunities for therapeutic intervention.

Objectives: To delineate the dysregulation of pSS pDCs using RNA-sequencing and compare their transcriptional profile to pDCs obtained from patients with non-Sjögren’s sicca (nSS) and healthy controls (HC).

Methods: All pSS patients met the classification criteria. nSS patients presented with dryness complaints without a known cause, did not have any genetically relevant autoimmune disease including pSS as evaluated by an experienced rheumatologist, and did not fulfill the classification criteria. pSS (n=25), nSS (n=20), and HC (n=17) donors were included in two independent cohorts (n=31 each). Circulating BDCA-4 expressing pDCs were isolated and RNA-sequencing was performed, after which data-driven networks and modular analysis were used to identify signatures of consistently differentially-expressed genes. pSS and HC pDCs were cultured in the presence of endosomal TLR ligands, after which gene expression and secreted cytokine levels were measured.

Results: We identified signatures of consistently co-expressed and differentially expressed genes that indicated transcriptional activation in patient pDCs, which was remarkably reproducible in two independent cohorts. These included a type-I IFN-associated signature, a ribosomal protein signature, and a transcriptional machinery signature. Corroborating the transcriptomic profile, stimulated pSS pDCs produced higher levels of type-I interferon upon in vitro stimulation. nSS patients formed an intermediate group in which some patients were molecularly similar to pSS patients. Finally, we developed a discriminative classifier on the basis of the identified transcriptional profiles that discriminated pSS patients from HC with 100% sensitivity and 80% specificity, and identified a group of pSS-like patients within the nSS group.

Conclusion: Circulating pSS pDCs exhibit a transcriptional signature similar to activated pDCs and are primed for enhanced production of pro-inflammatory cytokines, including type-I IFN. Our data provide in-depth characterization of the aberrant regulation of pSS pDCs and substantiate their perceived role in the immunopathology of pSS and other type-I interferon-associated autoimmune diseases.

Disclosure of Interests: None declared


THU0223

CHRONIC ADRENERGIC STIMULATION OF MINOR SALIVARY GLANDS OF PATIENTS WITH PRIMARY SJÖGREN’S DRIVES ER STRESS AND ACTIVATION OF THE UNFOLDED PROTEIN RESPONSE

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Background: Sjögren’s syndrome (SS) is a common autoimmune disease in which the main targets of immune injury are specific secretory epithelia, such as salivary and lacrimal glands. Stress appears to play a significant role in the initiation and exacerbation of SS.

Objectives: The aim of the present study was to investigate whether chronic stress plays a role in triggering endoplasmic reticulum (ER) stress in salivary gland epithelial cells from SS patients.

Methods: Minor salivary gland biopsy specimens were obtained from six SS patients and six control patients with sicca symptoms not fulfilling AECG criteria [1]. The expression and cellular localization of β1-, β2- and α1-adrenoceptors and the levels of cAMP were measured by immunofluorescence. The morphology of the ER was evaluated in situ by Transmission Electron Microscopy (TEM). Primary salivary gland epithelial cell lines (SGEC) derived from minor salivary gland biopsies, were established by the explant out-growth technique [2] and were treated with epinephrine and norepinephrine. The protein levels of the ER stress markers GRP78/Bip and C/EBP homologous protein (CHOP) were determined by immunoblot analysis.

Results: In situ immunofluorescence staining revealed increased expression of β1-, β2- and α1-adrenoceptors as well as cAMP levels in tissues derived from SS patients compared to controls. TEM evaluation of salivary tissues from SS subjects revealed extensive dilation of the ER lumen compared to controls. Treatment of SGEC with epinephrine and norepinephrine did not influence cell survival (cell viability assay). To mimic chronic stress in vitro, epinephrine was applied for 10 days on SGEC. It was found that 20μM Epinephrine induced severe ER stress on SGEC, as attested by increased expression ofGRP78/Bip and CHOP, after 3 and 6 days of treatment. The expression of ER stress markers returned to basal levels after 10 days of treatment.

Disclosure of Interests: None declared
Conclusion: Our data revealed that adrenergic receptors are differentially expressed by salivary epithelium of SS patients compared to control tissues. This finding was further substantiated by the increased levels of cAMP, indicating a profound sympathetic stimulation of this secretory tissue. The dilated ER lumen of the salivary gland epithelial cells from SS patients confirmed the occurrence of ER stress. Moreover, the finding that catecholamines induce severe ER stress in vitro in SGEC under conditions resembling chronic stress suggests a causative relationship between sympathetic tone and ER stress. Deciphering the role of chronic stress in ER machinery will provide important insights that may lead to novel therapeutic targets for SS.

REFERENCES:

Disclosure of Interests: None declared

THU0224

THE HEPATITIS VIRUS PRESI PROTEIN RETARDS THE ONSET OF LUPUS-LIKE GLOMERULONEPHRITIS IN NZB/W F1 MICE

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Background: Infection can trigger autoimmunity but the nature of the pathogen could enhance or inhibit the onset of the disease. In this study we tested the tolerogenic effect of the surface Hepatitis B Virus capsid protein preS1 in a lupus mouse model.

Objectives: To evaluate the effect of administration of Hepatitis B virus preS1 subunit to NZB/WF1 mice

Methods: Mice (10 each group) were injected with a total volume of 200μl of 32.5 μg PreS1 in 200μl PBS (group 1), 200μl PBS (group 2), 3 times at 11th, 14th and 17th weeks of age. Urine samples were collected weekly to evaluate proteinuria by reactive strips. Blood samples were collected before every injection, at 22th and 26th weeks, and at death to evaluate levels of anti-C1q and anti-dsDNA by home-made ELISA tests. Tissues were harvested for histological analyses. Proteinuria free and survival rates were analyzed by Kaplan-Meier method using Mantel-Cox test for comparisons. Neurocognitive functions were evaluated with Staircase, Y-Maze and Forced Swim Test.

Results: Anti-dsDNA and Anti-C1q levels (ODxSD) were significantly higher in PBS than in preS1 treated mice (Figure 1). Mean proteinuria levels (mg/dl±SD) were higher in PBS than in preS1 treated mice. Proteinuria free survival rate (300 mg/dl) was lower in group 2 than group 1 (p=0.016; Figure 2). Also survival rate was significantly lower in PBS than in preS1 treated mice. Severe segmental and focal glomerulonephritis in both groups with large cellular infiltration in the glomeruli and extramedullary hematopoiesis in the spleen and liver. Notably, in salivary glands, severe acute inflammation was observed in group 1 and chronic inflammation in group 2.

Conclusion: HBV capsid protein preS1 causes a delay in the onset of lupus-like glomerulonephritis and ameliorates behavioral disorders in NZW/B1 F1 mice. This peptide seems to induce a tolerizing rather than a pathogenic effect in these autoimmune prone mice models.

Disclosure of Interests: None declared

THU0225

THE MOLECULAR PROFILING OF MONOCYTES FROM PATIENTS WITH PRIMARY ANTIPHOSPHOLIPID SYNDROME IDENTIFIES SEVERAL NETWORKS RELATED TO THEIR ATHEROTHROMBOTIC STATUS.

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Objectives: 1. To characterize the miRNAs and microRNAs transcriptomes of monocytes, key immune cells in the atherothrombotic pathology of Antiphospholipid Syndrome patients (APS). 2. To evaluate the role of antiphospholipid antibodies (aPL) in the regulation of these processes. 3. To identify and characterize circulating microRNAs secreted by activated monocytes.

Methods: Monocytes from peripheral blood of 40 APS patients and 40 healthy donors were purified by negative immunomagnetic selection. Gene expression microarray (Nanostring) were performed on purified RNA. Functional expression microarray (Agilent G4112F platform) and nCounter microRNA expression array (Nanostring) were performed on purified RNA. Functional categorization of altered genes and miRNAs was made using IPA software, and miRNA-mRNA interaction networks showing inverse correlation expression were identified. Genes and miRNAs integrating the networks were validated in the whole APS cohort by RT-PCR, as well as on a set of thrombotic non-autoimmune patients. Predicted miRNA-mRNA interactions were tested by microRNA transfection experiments. In parallel, a miRNA array in the plasma of those patients was performed, and common deregulated miRNAs between monocytes and plasma were identified. Monocytes isolated from HD were treated in vitro with purified aPLs and the altered gene/miRNA expression induced in monocytes was evaluated. Moreover, the effects of aPLs on the secretion of common deregulated microRNAs in the supernatant of cultured cells were evaluated. 390 Thursday, 13 June 2019

Results: Anti-dsDNA and Anti-C1q levels (ODxSD) were significantly higher in PBS than in preS1 treated mice (Figure 1). Mean proteinuria levels (mg/dl±SD) were higher in PBS than in preS1 treated mice. Proteinuria free survival rate (300 mg/dl) was lower in group 2 than group 1 (p=0.033). Memory deficits (p<0.01) and anxiety-like behavior was pronounced in PBS treated mice. Severe segmental and focal glomerulonephritis in both groups with large proliferation of mesangial and endothelial cells and Russell bodies were found by histological analysis. Mouse treated with preS1 had more chronic inflammation in the kidneys and extramedullary hematopoiesis in the spleen and liver. Notably, in salivary glands, severe acute inflammation was observed in group 1 and chronic inflammation in group 2.

Conclusion: HBV capsid protein preS1 causes a delay in the onset of lupus-like glomerulonephritis and ameliorates behavioral disorders in NZW/B1 F1 mice. This peptide seems to induce a tolerizing rather than a pathogenic effect in these autoimmune prone mice models.

Disclosure of Interests: None declared

Abstract THU0224 – Figure 2

Abstract THU0225 – Figure 1
occurrence and type of thrombotic events, obstetric complications and presence of atheroma plaques were demonstrated. Transfection studies further confirmed the relationship between specific miRNAs and their identified target genes. In vitro studies demonstrated the specific modulation of several genes/miRNAs by aPLs. Furthermore, those autoantibodies promoted the increase in several secreted miRNAs, found simultaneously altered in plasma and monocytes, and deeply involved in the development of inflammation and cardiovascular disease.

Conclusion: 1. Gene and microRNA expression profiles allowed the identification of relevant genes and pathways altered in monocytes and plasma of APS patients, associated with the pathogenesis of the disease and modulated, at least partially, by aPLs. 2. Specific microRNA-miRNA regulatory networks control the biological processes and factors related to the CV pathology in APS. 3. aPL antibodies induce the secretion by monocytes of specific microRNAs that might act as messengers in the bloodstream to propagate their deleterious effects.

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THU0227

DOES THE PRESENCE OF CLASSIC AND NOVEL ANTIPHOSPHOLIPID ANTIBODIES INFLUENCE THE RISK OF THROMBOSIS DEVELOPMENT IN PATIENTS WITH UTERINE MALIGNANCIES?

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Background: Patients with uterine malignancies (UM) are at a higher risk of venous thromboembolism (VTE) than the general population. The malignancy itself, the treatment modalities including medication, surgery and also increased levels of leukocytes, platelets, and tissue factor-positi-ve microvesicles contribute to the risk of developing VTE.

Objectives: Several authors have shown that the antiphospholipid antibodies (aPLs) can be detected in peripheral blood of patients (pts) with malignancies. However, whether or not the aPLs could induce thrombosis in pts with UM is not yet known. The aim of our study was to determine whether the presence of aPLs in patients with uterine malignancies is associated with higher VTE risk than in pts with non-cancer gynecological disorders (NCGD).

Methods: The study involved 151 female pts scheduled for gynecological surgery divided into two groups: Group I with UM (70 pts) confirmed by histopathological examination after surgery; group II with non-cancer gynecological disorders (NCGD) (81pts).

The presence of aPLs was detected in patients' serum before surgery using the commercially available test aPL-immunodot assay Anti-Phospholipid 10 Dot, for the qualitative detection of IgG or IgM antibodies. The statistical data analysis was performed using Statistica v13.0.

The following aPLs were assessed in the study groups: IgM and IgG of a- cardiolipin; a- phosphatidyl acid; a- phosphatidylcholine; a- phosphatidylethanolamine; a- phosphatidylglycerol; a- phosphatidylinositol; a- phosphatidylyserine; a- annexin V; a- 9 2-GP I and a-prothrombin.

Results: The VTE occurred significantly more frequently in pts with UM, compared to pts with NCGD. In UM group VTE was diagnosed before surgery in 9/70 (12.9%) pts; in NCGD group VTE was diagnosed in 3/81 (3.7%) pts, p=0.0001. We have obtained positive test results for classic and novel aPLs significantly more frequently in group I pts with UM (mainly a-9 2-GP I IgM and IgG; a-prothrombin IgM, a- annexin V IgM) than in group II NCGD pts. The positive test for classic or novel aPLs was detected in 17/70 pts with UM (24,3%) and in 6/81 pts with NCGD (7.4%). The differences were statistically significant (p=0.003). All pts with thrombosis in group I (9 pts UM) were positive for at least 3 aPLs (a-9 2-GP I IgM and IgG; a-prothrombin IgM, a- annexin V IgM).

Conclusion: The classic and novel aPLs are found more frequently in pts with uterine malignancies than in pts with non-cancer gynecological disorders. The higher risk of thrombosis is connected with malignancy and the presence of classic and novel aPLs.

The better understanding of the relationships between thrombosis in cancer patients and its immunological determinants (presence of aPLs) may lead to reducing the morbidity and mortality associated with thrombosis in cancer and non-cancer gynecological disorders. We suggest that aPLs could be a novel biomarker of thrombosis risk in gynecological malignancies.

Disclosure of Interests: Andrzej Majdan: None declared, Magdalena Dryglewiska: None declared, Jan Kotarski: None declared, Maria Majdan Speake: Bureau: MSD, UCB, Abbvie, Roche


THU0227

BIOLOGICAL MONITORING OF REMISSION IN SYSTEMIC LUPUS ERYTHEMATOSUS: ABNORMAL SERUM INTERFERON-ALPHA LEVELS PREDICT RELAPSE

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Background: Remission and relapses prevention are the main objectives of the treatment of Systemic Lupus Erythematosus (SLE). Interferon alpha (IFNα) is a key cytokine in SLE, but its usefulness for the definition of remission and for the prediction of flare has not been validated in clinical practice.

Objectives: To study the association between serum IFNα level, remission and risk of relapse.

Methods: 502 SLE patients were assessed for serum IFNα level using a biological functional assay(1). Remission was defined by the absence of clinical manifestation of lupus activity (clinical SELENA-SLEDAI = 0) and a prednisone intake ≤ 5 mg/day(2). Patients in remission were subsequently followed for one year. The SELENA-SLEDAI Flare Index was used to identify SLE flare. Uni- and multivariable analyses were performed to define disease parameters associated with serum IFNα positivity in patients in remission at baseline. Survival curve analysis, log-rank tests and Hazard Ratios (HR) were calculated to evaluate the risk of flare depending on IFNα, dsDNA Abs and C3 levels at baseline.

Disclosure of Interests: None declared.
Results: 345 samples were obtained from patients in remission. 28.6% of the patients in clinical remission on treatment (requiring clinical SELENA-SLEDAI = 0, no positive anti-dsDNA antibodies nor C3 decrease and prednisone intake 1 – 5 mg/day) had an abnormal serum IFNα level, compared to 6.5% of the patients in complete remission on treatment (requiring clinical SELENA-SLEDAI = 0, no anti-dsDNA antibodies and/or C3 decrease and prednisone intake 1 – 5 mg/day). In patients in remission, high serum IFNα levels at baseline were associated in multivariable analysis with the positivity of anti-dsDNA Abs (HR 3.4 [95%CI 1.6-7.2]), p<0.0001) and anti-RNP Abs (HR 3.2 [95%CI 1.5-6.8], p<0.0002). In patients in remission, high serum IFNα level at baseline was a significant and independent risk factor of lupus flare (HR=4.8 [95%CI 2.3-9.7], p<0.0001). Low C3 was also associated with the risk of relapse with a HR=3.2 [95%CI 1.4-7.0], p=0.005, but positive anti-dsDNA Abs was not (HR=1.8 [95%CI 0.9-3.6], p=0.1).

Conclusion: A large number of SLE patients in remission display abnormal levels of serum IFNα. Abnormal levels of serum IFNα in patients in remission were significantly associated with positive anti-dsDNA and anti-RNP Abs and were an independent predictive biomarker of lupus flare in the following year. Adding serum IFNα to the routine laboratory assessments perform in patient in remission could help clinicians to identify a subgroup of SLE patient clinically in remission but serologically active and at higher risk of relapse.

REFERENCES:


THU0228
EXPRESSON OF APOBEC FAMILY MEMBERS AS AMPLIREGULIN ATTENUATES LUPUS NEPHRITIS VIA SUPPRESSION OF PRO-INFLAMMATORY T-CELL FUNCTIONS IN AN ANIMAL MODEL OF SLE

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Background: Amhregulin (AREG) is a member of the epidermal growth factor (EGF) family and plays a role in development, tissue homeostasis and tumorigenesis. Recently, however, AREG has also emerged as novel player in immunity. Interestingly, AREG expression was shown to be one of the most highly upregulated transcripts in peripheral blood leukocytes of patients with systemic lupus erythematosus (SLE) [1]. The functional role of AREG in SLE, and inflammation in general, remains unclear to date and both, pro- and anti-inflammatory functions have been postulated [2, 3].

Objectives: Our aim was to investigate the role of AREG in the mouse model of pristane induced lupus (PIL) with particular focus on lupus nephritis (LN). We further wanted to identify target cells and mechanisms by which AREG exerts its immunomodulatory effects.

Methods: PIL was induced in AREG knock-out (KO) mice and wild type controls. Animals were sacrificed at pre-specified time points. Renal histology, immune complex deposition, leukocyte influx and mRNA expression levels were analyzed. Furthermore, broad in vivo and in vitro analyses of renal pro- and anti-inflammatory cytokine productions were carried out.

Results: Renal AREG mRNA expression significantly increased during development of LN, indicating functional relevance. Indeed, lupus nephritis was significantly aggravated in AREG-KO mice both at early (9 months) and later (12 months) stages after PIL induction. In line with this, we noted increased mRNA expression of immune- and renal-cytokines of pro-inflammatory leukocytes (CD3+ T-cells, macrophages and neutrophils). In addition, we found the CD4+ T-cells of AREG-KO mice to have a more pro-inflammatory phenotype with significantly increased production of pro-inflammatory cytokines (IFNγ and IL-17A) both in ex-vivo culture, as well as FACS-analyses of nephritic kidneys. Mechanistically, we found that AREG treatment of spleen cell cultures potently suppressed cytokine production. More detailed mRNA expression by further in vitro studies indicated, that AREG can directly suppress cytokine production by effecting CD4+ T-cells as well as enhance the suppressive capacity of Foxp3+ regulatory T-cells (Treg).

Conclusion: These data show that AREG has a protective role on development of LN induced by pristane, which might be therapeutically exploited. Our results further suggest, that direct effects on CD4+ Teffector cells, as well as indirect effects via Tregs, are two mechanisms by which AREG exerts its protective role.

REFERENCES:
TNF-ALPHA PROMOTER POLYMORPHISMS (G-308A AND G-238A) ARE ASSOCIATED WITH SUSCEPTIBILITY TO SLE: A HOSPITAL-BASED CASE-CONTROL INVESTIGATION

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Background: Tumour necrosis factor-α (TNF-α) is a proinflammatory cytokine associated with various autoimmune disorders.1 High levels of TNF-α has been reported in systemic lupus erythematosus (SLE)2. Two functional common polymorphisms (G-238A and G-308A) at promoter region of TNF-α gene have been linked to SLE susceptibility in different populations.3,4

Objectives: To investigate association of TNF-α (G-238A and G-308A) polymorphisms with susceptibility/resistance to SLE.

Methods: A total of 102 female SLE patients and 112 age and sex matched healthy controls were enrolled in the study. Patients were examined in detail, physical findings recorded and SLEDAI 2K calculated to assess disease severity. TNF-α polymorphisms (G-238A & G-308A) were typed by polymerase chain reaction and restriction length polymorphism (PCR-RFLP), Plasma level of TNF-α was quantified by ELISA. Statistical analysis was carried using GRAPH PAD PRISM 7.01.

Results: Mean age of SLE patients and healthy controls was 27.84±8.83 and 29.56±5.48 years, respectively. At the time of enrolment, mean disease duration of patients was 2.07±1.13 years. The mean SLEDAI 2K of patients was 16.07±7.56. The prevalence of heterozygous mutant and minor allele of TNF-α (G-238A) polymorphisms were significantly higher in SLE patients compared to healthy controls (GA: P=0.04, OR=2.16; A: P=0.02, OR: 2.09). Furthermore, heterozygous (GA) and minor allele (A) of TNF-α (G-238A) polymorphism were associated with susceptibility to lupus nephritis (GA: P=0.02, OR=2.89; A: P=0.001, OR: 2.92). SLE patients displayed higher levels of plasma TNF-α compared to healthy controls. Although the prevalence of heterozygous mutant and minor allele of TNF-α (G-308A) polymorphism was higher in SLE patients, it was not statistically significant. TNF-α (G-238A and G-308A) variants were associated with higher plasma TNF-α in both SLE patients and healthy control. However, no significant association was observed on distribution of TNF-α polymorphisms (G-238A and G-308A) with severity of disease activity of SLE patients.

Conclusion: The results of the present study demonstrate that TNF-α (G-238A) variant is associated with higher plasma TNF-α level and increased susceptibility to development of SLE and lupus nephritis.

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THU0232 GELSEolin a New Biomarker of Disease Activity in SLE Patients Associated With HDL-C

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Background: Recent proteomics techniques have demonstrated that high-density lipoprotein (HDL) associated proteins are involved in functions related to systemic inflammatory and immune responses in several pathological conditions, including autoimmune diseases. HDL undergoes structural and functional modifications in systemic lupus erythematosus (SLE) patients.

Objectives: To identify potential biomarkers of disease activity analyzing the proteome of HDL particles from SLE patients in clinical remission and when they develop a flare compared to a healthy control group.

Methods: Quantitative proteomic analyses of purified HDL were performed using Tandem Mass Tag (TMT) isobaric tag-labeling and nanoLC-Orbitrap (nLC-MS/MS) from 9 SLE patients in clinical remission when they developed a flare and from 9 healthy controls (9-9-9). We verified the identified proteins by Western blot and ELISA in a cohort of 104 SLE women patients, 46 healthy women and 14 SLE patients when developed a flare.

Results: A total of 83 proteins associated with HDL were identified. We found 17 proteins with a significant fold-change (>1.1) compared with their levels in control patients. In lupus patients experiencing a flare compared with those in remission, we identified 4 proteins with a significant fold-change (C4, Indian Hedgehog protein, S100A8 and gelsolin). Plasma gelsolin (pGSN) levels were decreased in the 104 SLE patients (176.02 (74.9) mcg/l) compared with the control group (217.13(86.7)mcg/l); p <0.005 and when they developed a clinical flare (104.84(41.7)mcg/l); p = 0002). pGSN levels were associated with HDL-c levels (r =−0.316, p<0.001). Antimalarial treated patients showed significant higher levels of pGSN (214.56(88.94)mcg/l respect 170.39(66.38) mcg/l); p = 0.017.

Conclusion: The proteome cargo from HDL differentiates SLE patients from healthy controls. HDL from SLE patients carries proteins that are involved in the activation of the immune system. Decreased pGSN are associated with clinical disease activity in SLE patients. Antimalarial treatment and HDL-c are associated with higher levels of pGSN in SLE patients. pGSN is a potential biomarker of disease activity in SLE patients.

Disclosure of Interests: None declared

THU0233 DIFFERENTIAL METHYLATION OF IL8 AND TISSUE FACTOR PROMOTER IN ANTIIPHOSPHOLIPID SYNDROME

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Background: Antiphospholipid syndrome (APS) is an autoimmune thrombophilia characterized by recurrent thromboembolism and/or pregnancy morbidity in the presence of Antiphospholipid antibodies mainly anti-β2glycoprotein 1 (anti-β2GPI), which lead to monocyte and endothelial cell activation and subsequent tissue factor and proinflammatory cytokine expression such us IL-6 and IL-8 (1). Epigenetics describes changes in gene expression without alterations in the genomic sequence. Methylation of DNA at CpG islands by adding a methyl group to the nucleotide cytosine, is one of main epigenetic mechanisms. Internal medicine department.

Objectives: To explore the possible differential methylation of IL8 and Tissue Factor (F3)gene promoters, which are critical for the pathophysiology of APS.

Methods: Whole blood and serum were isolated from 27 APS patients and 25 healthy donors (nDs). Human umbilical vein endothelial cells (HUVECs) and peripheral blood monocytes were isolated from 3 HDs. Anti-β2GPI IgG was isolated and pooled from 8 APS patients.HUVECs and monocytes were stimulated with a mixture of IgG, β2GPI and CXCL4. Then mRNA was isolated and qPCR was performed for the assessment of IL8 and tissue factor (F3)gene expression. Whole blood DNA from APS patients and HDS and DNA from the in vitro experiments was isolated and bisulfite treated. The methylation of Cpg in the
The association between demyelinating diseases and autoimmune rheumatic disease (SARD) was investigated. The objective was to characterize the clinical profile of patients with SARD and to describe the frequency of antiphospholipid and antinuclear antibodies.

**Background:**
- Multiple sclerosis (MS) and neuromyelitis optica (NMO) are demyelinating processes of the central nervous system (CNS) that can mimic multiple sclerosis (MS).
- The presence of inflammatory arthralgias, Raynaud phenomenon, and neurological symptoms is common in patients with SARD.

**Methods:**
1. The study was a retrospective observational study of patients referred to the Demyelinating Diseases Unit of the Rheumatology Department of the Universitary of Canarias, Neurology, San Cristobal de la Laguna, Spain.
2. Patients were assessed jointly by the Demyelinating Diseases Unit and the rheumatology service.
3. The study included patients with demyelinating processes of the CNS.

**Results:**
- A total of 561 patients were evaluated.
- Of these, 32 patients had MS, 4 had NMO, and 32 had other SARD.
- The most common neurological symptoms were hyperintense injuries in T2, in brain and/or the spinal cord.
- These patients were characterized by a high frequency of reumatic antibody positivity in MS.

**Conclusion:**
- The study highlights the importance of considering SARD in the differential diagnosis of MS.
- Further research is needed to understand the pathophysiological mechanisms underlying the association between demyelinating diseases and SARD.

**Disclosure of Interests:**
- None declared.

**References:**

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**THU0234**

**ASSOCIATION BETWEEN DEMYELINATING DISEASE AND AUTOIMMUNE RHEUMATIC DISEASE: A MULTIDISCIPLINARY EVALUATION**

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**Background:**
- The association between demyelinating diseases and autoimmune rheumatic disease (SARD) is not well understood.
- The aim of this study was to evaluate the association between demyelinating diseases and SARD.

**Methods:**
- A retrospective observational study of patients with demyelinating diseases and SARD was conducted.
- Patients were classified into three groups: MS, NMO, and other SARD.

**Results:**
- A total of 561 patients were evaluated.
- The most common neurological symptoms were hyperintense injuries in T2, in brain and/or the spinal cord.
- These patients were characterized by a high frequency of reumatic antibody positivity in MS.

**Conclusion:**
- The study highlights the importance of considering SARD in the differential diagnosis of MS.
- Further research is needed to understand the pathophysiological mechanisms underlying the association between demyelinating diseases and SARD.

**Disclosure of Interests:**
- None declared.

**References:**
Results: The density of Ikaros and Aiolos positive cells was significantly higher in the SGs of ELS positive SS patients compared to NSCs. As shown in Table 1, the density of Ikaros and Aiolos positive cells in the SGs of SS patients significantly correlated with B and T cell semiquantitative scores and the number of lymphocytic foci. Ikaros positive cell density also correlated with IgG levels and disease activity measured by ESSDAI. Accordingly, SS patients with high expression of Ikaros (>10 Ikaros+ cells/mm², n=11/23) had significantly higher ESSDAI (p=0.023) and higher prevalence of ANA positivity (p=0.019). In vitro experiments confirmed that Ikaros+ cells synthesize more B and T cell mediators and that Ikaros overexpression in vitro stimulates cell growth and proliferation as marker to discriminate active LN [4]. To the best of our knowledge, this is the first screening of miRNAs in urinary exosomes from LN patients to study their role as predictors of response to therapy. 


Methods: Urinary exosomes were isolated and characterized from lupus patients (N=14) during flare and post-treatment time. Patients were divided between responder and non-responder and urinary exosomal miRNA screening analysis was performed according their clinical response. To validate initial results, a new cohort of LN patients were used (N=44).

Results: In the screening, 25 miRNAs were significantly different in comparative group analysis. High levels of miR-31, miR-107 and miR-135b-5p were confirmed to be related with responder patients. We found that miR-135b has the best profile to distinguish the two groups (AUC=0.783 (95% confidence interval [CI], 0.640 - 0.926), cut-off <0.0884 with 77.8% sensitivity and 71.4% specificity). Renal tissue samples from responder patients showed miR-31, miR-107 and miR-135b-5p to be highly expressed compared with non-responders. All miRNAs were predominantly localized in the tubular cells. Stimulated tubular renal cells displayed the higher expression levels of exosome-derived miR-miRNA screening and their delivery cell target (Figure 1).

Background: We previously revealed a role for EZH2 in inducing pro-inflammatory genetic changes in lupus CD4+ T cells.

Inhibitory effect of EZH2 on lupus-like disease in MRL/lpr mice

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Objectives: To determine if inhibiting EZH2 ameliorates lupus-like disease in MRL/lpr mice.

Methods: EZH2 expression levels in multiple cell types in lupus patients were evaluated using flow cytometry and mRNA expression data. Inhibition of EZH2 in MRL/lpr mice was achieved by DZNep intraperitoneal administration using a preventative and a therapeutic treatment model. Effects of DZNep on animal survival, anti-dsDNA antibody production, proteinuria, renal histopathology, cytokine production, and T and B cell numbers and percentages were assessed.

Results: EZH2 expression levels were increased in whole blood, neutrophils, monocytes, B cells, and CD4+ T cells in lupus patients. In MRL/lpr mice, inhibiting EZH2 with DZNep treatment before or after disease onset improved survival and significantly reduced anti-dsDNA antibody production. DZNep-treated mice displayed a significant reduction in renal involvement, splenomegaly, and lymphadenopathy. Lymphoproliferation and numbers of double-negative T cells were significantly reduced in DZNep treated mice. Concentrations of circulating cytokines and chemokines, including TNF, IFN-γ, CCL2, RANTES/CCL5, IL-10, KC/CXCL1, IL-12, IL-1p40 and MIP-1β/CCL4 were decreased in DZNep treated mice.

Conclusion: Inhibition of EZH2 ameliorates lupus-like disease in MRL/lpr mice, suggesting that EZH2 inhibitors may be repurposed as a novel therapeutic option in lupus patients.

Disclosure of Interests: None declared


THU0235

INHIBITION OF EZH2 AMELIORATES LUPUS-LIKE DISEASE IN MRL/LPR MICE

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Objectives: To determine if inhibiting EZH2 ameliorates lupus-like disease in MRL/lpr mice.

Methods: EZH2 expression levels in multiple cell types in lupus patients were evaluated using flow cytometry and mRNA expression data. Inhibition of EZH2 in MRL/lpr mice was achieved by DZNep intraperitoneal administration using a preventative and a therapeutic treatment model. Effects of DZNep on animal survival, anti-dsDNA antibody production, proteinuria, renal histopathology, cytokine production, and T and B cell numbers and percentages were assessed.

Results: EZH2 expression levels were increased in whole blood, neutrophils, monocytes, B cells, and CD4+ T cells in lupus patients. In MRL/lpr mice, inhibiting EZH2 with DZNep treatment before or after disease onset improved survival and significantly reduced anti-dsDNA antibody production. DZNep-treated mice displayed a significant reduction in renal involvement, splenomegaly, and lymphadenopathy. Lymphoproliferation and numbers of double-negative T cells were significantly reduced in DZNep treated mice. Concentrations of circulating cytokines and chemokines, including TNF, IFN-γ, CCL2, RANTES/CCL5, IL-10, KC/CXCL1, IL-12, IL-1p40 and MIP-1β/CCL4 were decreased in DZNep treated mice.

Conclusion: Inhibition of EZH2 ameliorates lupus-like disease in MRL/lpr mice, suggesting that EZH2 inhibitors may be repurposed as a novel therapeutic option in lupus patients.

Disclosure of Interests: None declared


THU0236

URINARY EXOSOMAL MIR-31, MIR-107 AND MIR-135B-5P FROM TUBULAR RENAL CELLS AS RESPONDER BIOMARKER IN LUPUS NEPHRITIS

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Background: Lupus nephritis (LN), occurring in 40–75% of patients with systemic lupus erythematosus (SLE), continues to be one of the most severe forms of lupus with an unpredictable course. Conventional clinical parameters are not sensitive or specific enough for detecting ongoing disease activity, early relapse, disease progression or response to therapy [1]. Exosomal-derived urinary miRNAs can accurately reflect renal dysfunction and structural damage making them good biomarkers for diagnosis and prognosis [2]. In LN, urinary exosomal miR-29c expression levels have been identified as predictor of early fibrosis [3] and miR-146a upregulation as marker to discriminate active LN [4]. To the best of our knowledge, this is the first screening of miRNAs in urinary exosomes from LN patients to study their role as predictors of response to therapy.


Methods: Urinary exosomes were isolated and characterized from lupus patients (N=14) during flare and post-treatment time. Patients were divided between responder and non-responder and urinary exosomal miRNA screening analysis was performed according their clinical response. To validate initial results, a new cohort of LN patients were used (N=44).

Results: In the screening, 25 miRNAs were significantly different in comparative group analysis. High levels of miR-31, miR-107 and miR-135b-5p were confirmed to be related with responder patients. We found that miR-135b has the best profile to distinguish the two groups (AUC=0.783 (95% confidence interval [CI], 0.640 - 0.926), cut-off <0.0884 with 77.8% sensitivity and 71.4% specificity). Renal tissue samples from responder patients showed miR-31, miR-107 and miR-135b-5p to be highly expressed compared with non-responders. All miRNAs were predominantly localized in the tubular cells. Stimulated tubular renal cells displayed the higher expression levels of exosome-derived miR-31, miR-107 and miR-135b-5p when compared with endothelial or mesangial cells (p<0.0001). Nevertheless, urinary exosomes from non-responder patient’s internalization was only 50% by mesangial cells compared to 90% from responders.

Conclusion: These results indicated that levels of urinary exosomal miRNAs produced by tubular cells might have a renal recovery role in mesangial cells and be used as new biomarkers of lupus nephritis outcome.

REFERENCES:
MUSCLE ARCHITECTURE IN PATIENTS WITH SJÖGREN’S SYNDROME

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Background: Although fatigue and skeletal muscle involvement is not rare in Sjögren’s Syndrome (SS) patients, there is not much data about the macroscopic structure of the skeletal muscle.

Objectives: 1) To investigate if ultrasonographic muscle architecture and muscle strength differed in SS patients 2) To investigate if these changes correlated with disease activity, fatigue, anxiety and depression.

Methods: Assuming 2.4 mm mean difference and 2.5 mm SD of thickness at vastus lateralis muscle with 80% power and 5% significance 19 SS patients and 19 healthy controls (HCs) were recruited (1). Disease activity was measured by EULAR Sjögren Disease Activity Index (ESSDAI), anxiety and depression were assessed with the Hospital Anxiety and Depression Scale (HADS), fatigue with Multidimensional Assessment Questionnaire (HAQ). A single rheumatologist, blind to the participants’ group assignment, performed the ultrasonographic evaluation using a multi-frequency linear probe. Thickness of bilateral quadriceps femoris, gastrocnemius and soleus muscles, pennation angle and fascicle length were measured. Isokinetic knee and ankle muscle strength tests were performed at 60-180°/s and 30-120°/s respectively by a calibrated isokinetic testing machine.

Results: Patients with SS scored higher than HCs for depression, anxiety, quality of life and fatigue (p<0.0001). At dominant leg, pennation angle of vastus medialis muscle was significantly lower in SS group than HCs (10.26±3.63 SD deg vs 14.15±3.63 SD deg, p=0.049). At non-dominant leg, pennation angle of gastrocnemius medialis muscle was significantly higher in SS group than HCs (22.89±4.82 SD vs 19.15±4.68 SD deg, p=0.006). In addition, fascicle length of gastrocnemius medialis muscle was significantly shorter in SS group than HCs (42.26±10.33 SD mm vs 49.25±8.27 SD mm, p=0.036). Peak torque/body weight of knee and ankle muscles in SS group did not differ from that of HCs. However, in SS group, at dominant leg, ESSDAI was negatively correlated with knee extension strength at velocities 60°/s (r=-0.492, p=0.033), ankle plantar flexion strength at 30°/s velocity (r=-0.730, p=0.001). Similarly at non-dominant leg, ESSDAI was negatively correlated with knee extension strength at velocities 60°/s and 180°/s (r=-0.572, p=0.010, r=-0.617, p=0.05 respectively), knee flexion strength at 60°/s velocity (r=-0.492, p=0.033), ankle plantar flexion strength at 30°/s (r=0.508, p=0.026 respectively) and ankle plantar flexion strength at 30°/s velocity (r=0.506, p=0.027). Fatigue was negatively correlated with ankle plantar flexion strength at 120°/s velocity (r=-0.484, p=0.036) at dominant leg, knee extension strength at 180°/s (r=-0.521, p=0.022) knee flexion at 60°/s velocity (r=0.585, p=0.011) at non-dominant leg. There was no correlation between anxiety, depression and muscle strength.

Conclusion: Patients with SS have some minor structural changes on ultrasonographic evaluation. Although there was no difference in isokinetic muscle strength measurements between groups, knee strength and endurance had a moderate negative correlation with disease activity in SS patients.

REFERENCE:


THU0238 CLINICAL Efficacy of Leflunomide/Hydroxychloroquine Combination Therapy in Primary Sjögren’s Syndrome IS Predicted by Serum Proteome Biomarkers – Results from Repurpss-I

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Background: Despite major efforts to treat primary Sjögren’s syndrome (pSS) advances in pSS treatment remain disappointing. Treatment strategies effective in other immunological conditions lack an effect in pSS. Hence, there is a huge unmet need in finding an effective treatment, let alone to have the ability to predict who responds to what treatment.

Methods: Clinically active (European SS disease activity index ESSDAI score ≥5) pSS patients (n=29) were randomized to receive LEF 20 mg daily and HCQ 200 mg twice daily or placebo/placebo (2 verum:1 placebo) for 24 weeks. Clinical and safety outcomes were assessed at baseline, 8, 16 and 24 weeks. Clinical response was defined by a decrease in ESSDAI of ≥3 points at 24 weeks. In addition, at baseline 386 proteins involved in inflammation, immune response, metabolism and cardio-metabolism were measured in serum of all patients using the Olink platform (for panels, see Olink website).

Results: Overall, LEF/HCQ was safe and well-tolerated and significantly reduced ESSDAI scores, the primary endpoint (p<0.0001). Furthermore, LEF/HCQ treatment was associated with improvement of oral dryness, ESSPRI, Physician’s and Patient’s Global Assessment, serum IgG, IgM rheumatoid factor, C3 and C4 levels (all at least p<0.05), which was not observed in the placebo group. Clinical response was observed in 11 out of 21 patients receiving treatment, providing a unique opportunity to examine biomarkers to predict response. However, except for C3 levels, clinical markers at baseline were not significantly different between responders and non-responders, underscoring the challenges in prediction of therapy response. Olink proteomic analysis revealed 43 significantly differentially expressed proteins between responders and non-responders. Unsupervised hierarchical clustering using the most differentially-expressed analytes (p-value based) demonstrated distinct serum proteomes in responders vs. non-responders. Using multidimensional scaling, based on all measured analytes, a high degree of dissimilarity of responders and non-responders was observed. Next a random forest machine-learning model was established to identify the proteins that best predict response to treatment using the baseline serum proteome. The results were validated using 500 leave-7-out iterations. The highest mean accuracy (84%) was achieved using a set of 16 differentially expressed analytes, indicating a 96% chance to robustly predict responders and a 74% chance to correctly identify non-responders.

Conclusion: We demonstrated a clinical response in pSS patients treated with the combination of leflunomide and hydroxychloroquine. Strikingly, a set of 16 circulating proteins predicts response to therapy with clinically meaningful accuracy. Given the exciting but preliminary nature of these observations a follow-up RCT aimed at replication of these results is warranted.

REFERENCE:

IDENTIFICATION OF BIOMARKERS AND IMMUNE PATHWAYS FOR PERSONALIZED DRUG TARGETING IN PATIENTS WITH NEWLY DIAGNOSED PRIMARY SJÖGREN’S SYNDROME

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Background: Patients with primary Sjögren’s syndrome (pSS) present with heterogeneous clinical symptoms and immune dysregulation. How immune dysregulation in SS arises is poorly understood, which hampers development of effective therapies. Identification of key immune pathways contributing to pSS pathogenesis is essential for successful drug development.

Objectives: To identify early systemic biomarkers and dysregulated immune pathways in newly diagnosed pSS patients by multidimensional immuno-profiling.

Methods: We included 40 newly diagnosed pSS patients (39 female; mean age 51±14 years) and 20 age- and sex-matched non-SS sicca patients (19 female; mean age 50±13 years). All pSS patients fulfilled ACR-EULAR criteria. Serum and peripheral blood mononuclear cells (PBMC) were collected and cryopreserved. PBMCs were thawed for immunophenotyping by flow cytometry and RNA isolation. RNA sequencing was performed using TruSeq Stranded Total RNA Library Prep Gold (Illumina), following manufacturer’s recommendations, and RNAseq libraries were sequenced on a HiSeq2500 system. Additionally, serum proteomics and immunosequencing were performed for pro-inflammatory cytokines in serum were performed.

Results: Interferon (IFN) type I signaling pathways were at the top of enriched pathways in PBMCs from pSS patients, compared with non-SS sicca controls (adjusted p<0.05). Additionally, the gene signature of IgD+CD27-CD16+CD5- (double negative 2; DN2) B cells was significantly upregulated in pSS patients (adj. p<0.05). Immunophenotyping analysis showed increased frequencies of CD4+ pDCs (p=0.004), intermediate monocytes (p<0.008), ICOs+ memory CD4+ T cells (p<0.001), cTfh cells (p<0.001), and cTfr cells (p<0.001) in pSS patients. Memory B cells were significantly decreased in pSS patients (p<0.001). Serum proteomics showed that the top proteins up-regulated in pSS patients were immunoglobulin subunits. The top of up-regulated pathways involved IFN signaling (adj. p<0.05), similar to RNAseq data. Consistently, immunosequencing showed increased levels of CXCL10 in serum and MxA in whole blood of pSS patients, compared with non-SS sicca controls (p<0.009 and p=0.001, respectively). Blood MxA protein levels correlated significantly with the IFN signature score in PBMCs (R=0.8; p<0.0001). The top cell-related biomarkers described above, the frequency of memory B cells, and MxA levels correlated significantly with EULAR Sjögren’s disease activity index (ESSDAI) scores, whereas the frequency of CD4+ pDCs, intermediate monocytes, and serum CXCL10 levels did not correlate with these scores. When a correction for multiple testing was applied, only cTfr cells correlated significantly with ESSDAI scores (R=0.6; p=0.002).

Conclusion: Newly diagnosed patients with pSS show co-activation of the IFN type I and B cell activation pathways, compared to non-SS sicca controls. At the same time, CD4+ T cell subsets critical for B cell function are activated, which can enhance B cell activation and plasma cell dysregulation. Personalized treatment based on the activity of each pathway in individual patients could potentially increase the efficacy of such treatments.

Acknowledgement: Part of this work was funded by NIH grant RFA-DE-06-004


THU0240 GENE EXPRESSION SIGNATURES ARE RELATED TO SPECIFIC SUBSETS OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is a heterogeneous, lifelong autoimmune disease, with a more severe phenotype in children compared to adult-onset SLE [1]. To date, approved drugs are by far not effective enough and have significant side effects, especially due to the use of prednisone. Although profiling of the blood transcriptome revealed a prevalent IFN type I signature in SLE, blocking the IFN pathway only showed efficacy in a subset of adult-onset SLE patients. Recent studies revealed that other gene signatures like IFN type I-II (M5.12), B cell, plasmablast and neutrophil signatures are important in SLE as well and some could be linked to specific clinical phenotypes [2, 3]. Assessment of these novel gene signatures in SLE may help to distinguish specific disease phenotypes and guide treatment choices in the future.

Objectives: To determine and compare the expression of the IFN-, B cell-, plasmablast- and neutrophil signatures in pediatric and adult SLE patients.

Methods: The IFN-I-, M5.12-, neutrophil-, B cell- and plasmablast signatures were measured using real-time quantitative PCR expression on whole blood RNA samples. To identify correlated groups of genes and reduce data complexity, the expression of a selection of genes identified by blood transcriptional profiling was tested and subsequently added to a principle component analysis to obtain a limited set of genes (2-5 per signature), that reliably represent a specific signature.

These signatures were analyzed in three separate pilot cohorts of healthy controls (n=12), pediatric- (n=22; average disease duration=0.9 years) and adult SLE patients (n=38; average disease duration=17.4 years).

Results: IFN-I signature was significantly higher in SLE patients compared to healthy controls (p=0.001), M5.12 (p=0.005) and the B cell (p=0.001) signature showed a significant difference between the pediatric and adult cohort while there was no difference between the neutrophil- and plasmablast signatures in the two patient groups. Interestingly, the B cell gene signature, correlated with age (p=0.001, r = -0.49) and disease duration (p=0.001, r = -0.42). In addition, the possible correlation between the IFN-I signature and the other signatures was investigated. While the IFN-I signature in both adults and children showed a significant positive correlation to the M5.12- (p=0.001, r = 0.97; p=0.006, r = 0.61) and plasmablast (p=0.03, r=0.37; p=0.0037, r=0.62) signature expression, only adult patients had a significant positive correlation of the IFN-I signature to the neutrophil signature (p=0.001, r=0.55).

Conclusion: In this pilot study we found significant differences in gene expression signatures between pediatric and adult SLE patients. Additionally, age and disease duration were significantly correlated to the B cell gene signature. These findings indicate differences in transcriptional profiles in specific subsets of SLE patients which could have therapeutic consequences.

REFERENCES:

Disclosure of Interests: M. Javad Wahadat: None declared, Noortje Groot: None declared, C.G. van Helden-Meeuwen: None declared, Iris LA Bodewes: None declared, Eriska Huijsjer: None declared, Sylvia Kamphuis: None declared, Marjan Vensers: None declared, Ashok Donkre: None declared, Roche received financial support from: MAV.
LUPUS PROGRESSION IS PREVENTED BY TREATMENT WITH VERDINEXOR, AN INHIBITOR OF THE NUCLEAR EXPORT-PROTEIN EXPORTIN-1, BY LIMITING GERMINAL CENTER FORMATION AND DEVELOPMENT OF AUTOREACTIVE ANTIBODY SECRETING CELLS

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Background: Systemic lupus erythematosus (SLE) is a complex autoimmune disease characterized by simultaneous activation of the innate and adaptive arms of the immune system. Recently the nuclear export protein exportin 1 (XPO1) has emerged as an inflammatory target for the treatment of SLE and other autoimmune disorders. Selective Inhibitor of Nuclear Export (SINE) compounds are potent, orally available and well-tolerated XPO1 inhibitors. SINE compounds inhibit the nuclear export of over 220 apoptotic and anti-inflammatory effects, particularly in dampening the NF-kB pathway underlies verdinexor’s ability to control the formation of germinal centers and limit the numbers of autoreactive antibody secreting cells (ASC) in a NZB/NZW F1 murine model of SLE.

Methods: To evaluate the minimal efficacious dose of SINE compounds in a preclinical recovery model of SLE, cohorts of lupus-prone mice with established disease (elevated anti-dsDNA antibody titer and proteinuria) were dosed with SINE compound or vehicle for eight weeks, at which time treatment groups were stratified, and escalating administration schedules (both dose and frequency) of verdinexor were examined for their ability to control recurrent disease. We used flow cytometry to enumerate dsDNA antibody-secreting cells (ASC) in the spleen and bone marrow and immunofluorescence to visualize germinal centers (GC) in spleen.

Results: We found that following induction therapy, treatment with verdinexor significantly maintained disease inhibition effectively at 7.5mg/kg administered weekly. Concomitantly, we observed significantly decreased levels of GC B cells, plasma cells and plasmablast levels in the bone marrow and the spleen 4 weeks after treatment groups were stratified. The potent effect of SINE compound monotherapy on GC and auto-reactive ASC showed that a pronounced elimination of GC and auto-reactive ASC was achieved after 4 weeks of treatment in all treatment groups. We found the effect of verdinexor treatment necessary to maintain disease inhibition after induction therapy.

Conclusions: We found that following induction therapy, treatment with verdinexor significantly maintained disease inhibition effectively at 7.5mg/kg administered weekly. Concomitantly, we observed significantly decreased levels of GC B cells, plasma cells and plasmablast levels in the bone marrow and the spleen 4 weeks after treatment groups were stratified. The potent effect of SINE compound monotherapy on GC and auto-reactive ASC showed that a pronounced elimination of GC and auto-reactive ASC was achieved after 4 weeks of treatment in all treatment groups. We found the effect of verdinexor treatment necessary to maintain disease inhibition after induction therapy.

OBJECTIVE: To examine the ability of verdinexor to control the formation of germinal centers and limit the numbers of autoreactive antibody secreting cells (ASC) in a NZB/NZW F1 murine model of SLE.

THU0242

MIR-326 OVEREXPRESSIN IN T CELLS BREAKS TH17/ TREG BALANCE IN MRL/LPR MICE

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease involving multiple organs leading to tissue damage1. T lymphocytes have been recognized as key contributors to disease pathogenesis2. Inflammatory Th17 subsets promote inflammation, while defects in regulatory T cells (Tregs) lead to uncontrolled immune responses3. Emerging data suggest that single miR species can profoundly alter the phenotype and outcome of immune responses in SLE4.

Objectives: We describe a role for miR-326 in driving deregulation of Th17/Treg balance in lupus mouse and highlight therapeutic advances of miR-326.

Methods: 3 groups of female MRL/lpr mice were injected with lentivirus-miR-326 (LV-326) or lentivirus-miR-326 specific inhibitor (LV-sponge) to increase or inhibit miR-326 expression, respectively, and lentivirus-negative (LV-ctrl) as control, 10 mice per group. The percentage of Th17 cells and Tregs in spleen CD4+ T cells and kidney were detected by flow cytometry. The levels of serum cytokine (IL-17A, IFN-γ, TGF-β) were detected by CBA. Urinary collections (24 h) were collected and assessed for albumin using ELISA. Immunohistochemistry labeled kidney IL-17A and TGF-β expression. Differences between groups were analyzed by SPSS 22.

Results: Day 7 analysis of differentiation of Th17 cells and Tregs in spleen after injection of lentivirus showed an increased percentage of Th17 in LV-326 mice, while reduction of percentage of Tregs in these mice. Testing the serum cytokines revealed that the significantly increased levels of IL-17A and IFN-γ in LV-326 mice, and decreased in LV-sponge mice, no different has been found in TGF-β between the groups. Moreover, LV-326 mice showed higher levels of 24h urinary albumin than LV-sponge and LV-ctrl mice in day 7 after injection of lentivirus. The lentivirus-miR-326 injection promoted the infiltration of Th17 cells and simultaneously increased the expression of IL-17A in kidney, no different has been found of TGF-β.

Conclusions: Our data reveal that miR-326 overexpression increased the differentiation of Th17 cells and decreased the differentiation of Tregs, and accelerated the renal injury in MRL/lpr mice. These suggest that miR-326 may play a catalytic role in the development of lupus-like changes in lupus model mouse by breaks Th17/Treg balance.

REFERENCES:

Disclosure of Interests: None declared


THU0243

ROLE OF METHIONINE AND ITS TRANSPORTER CD98 IN HUMAN B CELL DIFFERENTIATION AND THE RELEVANCE TO PATHOLOGICAL PROCESSES OF SLE

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Background: B cells play an important role in systemic lupus erythematosus (SLE). Several research protocols have focused in recent years on the topic of immunometabolism. Activation of immunocompetent cells depends on rapid synthesis of cell structure components and biomolecules, which requires enormous amounts of energy, nucleic acids and lipids. Amino acids are important ingredients of many metabolic processes. Moreover, the role of amino acids in plasmablast differentiation and their relevance to the pathogenesis of SLE remain elusive.

Objectives: To determine the role of essential amino acids in human B cell differentiation and relevance to the pathogenesis of SLE.

Methods: In the in vitro arm of the study, purified CD19+ B cells from healthy donors were cultured with TLR7/9 ligand (LOX or CpG), IFN-α and B cell receptor (BCR) cross-linking, in the presence or absence of amino acids. We determined 1) the types of amino acids that are important for PB differentiation, 2) the amino acid transporters that are important for PB differentiation, 3) the main signaling pathway(s) involved in the presence of amino acids, 4) the transcriptional factors used in the presence of amino acids. In the clinical arm of the study, peripheral blood mononuclear cells (PBMCs) were obtained from 24 patients with RA, 35 patients with SLE, and 28 age-matched healthy controls, and
subjected to flow cytometric analysis to determine the expression of amino acids-related markers.

Results: 1) Stimulation with the combination of BCR, IFN-α and TLR7/9 ligand induced PB differentiation accompanied by uptake of amino acids. PB differentiation was abrogated in the absence of essential amino acid methionine, and to a lesser extent leucine, but not in non-essential amino acid cystine. 2) LAT1 and CD98 are known amino acid transporters. Stimulation with BCR, IFN-α and TLR7/9 ligand induced CD98 expression but suppressed LAT1 expression. CD98 expression was higher in CD27<sup>−</sup>CD38<sup>+</sup> PB than in CD27<sup>+</sup>CD38<sup>−</sup> non-PB. 3) Previous studies reported that amino acids were perceived by the sensor, leading to mTORC1 phosphorylation. However, the mechanism by which amino acids activate other intracellular signaling pathways in B cells remains elusive. We found that methionine facilitated both the BCR and mTORC1 signals. In addition, the two signals synergistically induced EZH2 expression, which is involved in the epigenetic regulation as a transcriptional factor for histone modification via induction of H3K27me3, in the presence of methionine. 4) Methionine induced EZH2 expression, leading to suppression of BACH2, induction of BLIMP1, XBP1 and PB differentiation. These results indicate that EZH2 is a critical factor for PB differentiation in the presence of methionine. Assessment of the expression of amino acid transporters CD98, LAT1 and EZH2 in B cells in RA and SLE patients showed overexpression of CD98 and EZH2, but not LAT1, in SLE, compared with RA and control.

In SLE patients, EZH2 expression level correlated with that of CD98 in B cells. EZH2 expression also correlated with ESR and disease activity scores, such as of SLEDAI and BILAG, in SLE patients.

Conclusion: The results indicate that essential amino acid methionine plays an important role in PB differentiation through the CD98-EZH2-axis. The pathological process of SLE seems to involve essential amino acids and their metabolic/activation pathways throughout the process of PB differentiation.


SLE, Sjögren’s and APS – clinical aspects (other than treatment)

THU0244 PULMONARY MANIFESTATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by inflammation and tissue damage mediated by the immune system. Respiratory manifestations are common in SLE, appearing in up to 50% of patients throughout their lives. Furthermore, it is associated with higher mortality.

Objectives: To describe the prevalence and characteristics of pulmonary involvement in patients with SLE

Methods: Observational, descriptive, cross-sectional, retrospective study performed in patients with SLE in follow-up by the Rheumatology Department of Valme Hospital. The following information is collected from medical records: age, sex, mean age at diagnosis, characteristics of pleuropulmonary involvement and ANA and antiDNA positivity.

Results: We studied 165 patients with SLE, with mean age of 37.01 +/- 14.65 years, predominance of the female patients 153 (92.72%). Thirty eight of them had pulmonary involvement (23.03%), with a total of 47 episodes related to lung manifestations. Mean age at diagnosis was 39.70 +/- 15.50 years. Below is shown information about lung involvement:

<table>
<thead>
<tr>
<th>Variable</th>
<th>Prevalence</th>
<th>ANA</th>
<th>antiDNA</th>
<th>Hospitalization required</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatis</td>
<td>19</td>
<td>16</td>
<td>16</td>
<td>18</td>
</tr>
<tr>
<td>Lupus pneumonitis</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>ILD</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>1</td>
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</table>

Eleven patients (28.94%) presented pulmonary involvement at the time of diagnosis; pleuritis (10.63%) and only one case of interstitial lung disease, varicella pneumonia, shrinking lung syndrome, pulmonary embolism (PE) and bronchiolitis obliterans with organizing pneumonia. Two patients (4.24%) died due to severe respiratory failure secondary to bilateral pneumonia. Three of the 5 patients with PE were diagnosed with antiphospholipid syndrome secondary to SLE. Regarding treatment, most of patients who required hospitalization were in basic treatment with synthetic DMARDs (78.57% in monotherapy and 21.43% with double therapy) and only 2 patients with biologic DMARDs (Rituximab and etanercept).

Six patients had no treatment because the pulmonary event was at time of diagnosis, 2 patients were with antiaggregating therapy and there was no information registered in two patients (episode before 1997). 91.10% of the patients presented positive for ANA, of which 37.14% (13 patients) also presented positive antiDNA. No information was collected about autoimmunity in one patient (2.12%).

Conclusion: Pulmonary involvement in SLE is prevalent, although a significant proportion may remain asymptomatic. The little prevalence of pulmonary manifestations in our series might be due to low mean age, according to the result of a recent systematic review where analysed more than 10000 patients and excluded pulmonary manifestations are more frequent in late-onset SLE. The differential diagnosis is broad and the infectious cause, the main cause of mortality in patients with SLE, must always be ruled out.

REFERENCES:
[1] 10.1016/j.semarthrit.2018.01.010

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Disclosure of Interests: NAHIA PLAZA: None declared, MARÍA JOSÉ PÉREZ: None declared, Sergio Rodriguez Montero: None declared, CAR- MEN TRAPERO: None declared, Jose Luis Marenco Speakers bureau: abbie, pfizer, novartis, janssen

THU0245 LOW SPECIFICITY OF THE PROPOSED 2017 ACR- EULAR CLASSIFICATION CRITERIA FOR SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) COMPARED TO PREVIOUS CRITERIA IN SLE PATIENTS WITH NEUROPSYCHIATRIC SYMPTOMS

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Background: New ACR-EULAR SLE criteria have been proposed in order to attempt to improve classification for clinical and translational research (1, 2).

Objectives: We evaluated the performance of the proposed 2017 ACR-EULAR classification criteria in a cohort of SLE patients with neuropsychiatric (NP) symptoms and compared to previous classification criteria.

Methods: Medical records of patients visiting the NP-SLE clinic of the Leiden University Medical Center (LUMC) between 2007-2017 were retrospectively evaluated. The performance of the proposed 2017 ACR-EULAR criteria, the 2012 SLICC criteria and the 1997 ACR criteria was evaluated using sensitivity and specificity.

Results: 360 patients were included, of which 294 were clinically diagnosed with SLE. The newly proposed 2017 ACR-EULAR showed a sensitivity of 87% (95% CI: 83-91%) and a specificity of 74% (95% CI: 62-84%) as shown in Table 1. The 2012 SLICC criteria had a sensitivity of 85% (95% CI: 80-89%) and a specificity of 76% (95% CI: 64-85%). The 1997 ACR criteria had a sensitivity of 89% (95% CI: 85-92%) and a specificity of 89% (95% CI: 80-96%). Sixty out of 294 patients fulfilled the proposed NP domain (delirium/psychosis/epilepsy). Using more specific criteria for NP symptoms related to SLE, as previously proposed by Bortoluzzi et al. (3), only 37 patients fulfilled this domain. However, this did not improve specificity, which remained 74% (95% CI: 62-84%).
In addition, the performance of the newly proposed criteria was evaluated including patients with more than 10 points, but negative ANA. This led to an increase of sensitivity to 90% (95% CI 86-94%), but also did not influence specificity.

**Proposed 2017 ACR-EULAR classification criteria in SLE patients with NP symptoms**

<table>
<thead>
<tr>
<th>With adjusted NP domain</th>
<th>Including ANA negative patients</th>
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<tbody>
<tr>
<td>Sensitivity (95% CI)</td>
<td>87% (83-91%)</td>
</tr>
<tr>
<td>Specificity (95% CI)</td>
<td>74% (62-84%)</td>
</tr>
</tbody>
</table>

**Table 1. Performance of the proposed 2017 ACR-EULAR classification criteria for SLE**

**Conclusion:** In a cohort of SLE patients with NP symptoms, the proposed 2017 ACR-EULAR classification criteria showed similar sensitivity as the 1997 ACR and the SLICC 2012 criteria, but lower specificity. Including ANA negative patients improved sensitivity.

**REFERENCES:**


**Disclosure of Interests:** Rory Monahan: None declared, H.J.L. Beart: None declared, M.A. Gegevona: None declared, E.G. Brilmam: None declared, L.J.J. Beart: van de Voorde: None declared, C. Mago Checa: None declared, Thomas Huizinga Consultant for: Merck, UCB, Bristol Myers Squibb, Biostat AG, Pfizer, GSK, Novartis, Roche, Sanofi-Aventis, Abbott, Crescendo Bioscience Inc., Nycomed, Boeringher, Takeda, Zyus, Eprus, Eli Lilly, G.M. Steup-Beekman: None declared


**THU0246 ASYMPTOMATIC MYOCARDIAL DYSFUNCTION DETECTED BY SPECKLED TRACKING ECHOCARDIOGRAPHY (STE) IN ACTIVE SLE PATIENTS**


**Background:** Clinical myocarditis is seen in 10% of SLE patients, but autopsy studies have shown myocardial involvement in up to 50% of patients. Lupus myocarditis may be silent and can be detected by newer echocardiographic technique like STE especially when SLE is active.1,11

**Objectives:** To study asymptomatic myocardial dysfunction by STE in active SLE patients.

**Methods:** All consecutive active SLE patients having a SLEDAI score ≥ 6 without any cardiac symptoms with disease duration ≤ 5 years aging between 18- 45 years, who attended the Rheumatology and Clinical Immunology department (Outpatient and Inpatient) of Medanta, The Medicity, Gurgaon, from May 2016 to March 2018, were enrolled. They were evaluated for myocardial dysfunction by using a novel ultrasound technique - STE, which was reviewed by one observer cardiologist. Global longitudinal systolic strain (GLSS) was calculated by STE in all patients. GLSS>19.7 was considered as an indicator of myocardial dysfunction.2,3 Age and sex matched controls in the form of thirty healthy volunteer subjects were enrolled and their echocardiography findings were compared with active lupus patients. Atherosclerotic risk factors like hypertension, Diabetes Mellitus and age >45 years were excluded to avoid confounding effects.

**Results:** Fifty eight active lupus patients were analysed. In the cohort female: male ratio was 8.6:1, median duration of disease was 22 months (0.5 - 10.1 years) and mean SLEDAI was 11.02 ± 2.30. GLSS was significantly lower in active lupus patients compared to healthy controls (p=0.0001) suggestive of myocardial dysfunction. In active lupus patients, abnormal echocardiographic findings (myocarditis, non-bacterial thromboembolic, pulmonary arterial hypertension and pericarditis) were seen in 62.1%. Myocardial dysfunction was found in 27 (46.6%), 20 (34.5%) patients had low GLSS with normal left ventricular ejection fraction (LVEF) and these were significantly associated with APLA and anti Sm/RNP antibodies. Multivariate Logistic Regression analysis of myocardial dysfunction with SLEDAI and other system parameters showed that musculoskeletal, CNS, haematological and nephritis were associated with increased risk for developing higher disease activity and myocardial dysfunction, although it was not statistically significant.

**Conclusion:** Almost half of active lupus patients have silent myocarditis. GLSS is more sensitive in detecting asymptomatic myocardial dysfunction than LVEF. Regular Echocardiography with Speckled tracking should be performed in Lupus patients especially when disease is active.

**REFERENCES:**


**Disclosure of Interests:** None declared


**THU0247 LRRN4: A NOVEL PROGNOSTIC BIOMARKER OF RENAL OUTCOME IN LUPUS NEPHRITIS PATIENTS**

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**Background:** Lupus nephritis (LN) is the most common organ-threatening manifestation of systemic lupus erythematosus (SLE) and can result in kidney deterioration and end-stage renal disease (ESRD). Newly discovered biomarkers exhibit qualities of disease activity and damage, predict long term preservation of renal function.

**Objectives:** Combine the transcriptomics profile of kidney with long-term renal outcome in LN patients, to explore the novel non-invasive predictive biomarker for renal outcome.

**Methods:** The transcriptomics profile of kidney in 24 LN patients was obtained by using Affymetrix human HTA 2.0 gene expression chip. Random Forest method was used to screen the candidate mRNA biomarkers by correlate the gene expression profile with eGFR slope during the follow-up (Mean time 5.2±1.2 years). In addition, in an independent LN cohort enrolled 45 patients, qRT-PCR and immunochemistry staining was performed to validate the correlation of mRNA level and protein level of candidate gene with renal outcome.

**Table 1. Comparison of GLSS and LVEF between active SLE patients and healthy control group patients**

**Table No1. Comparison of GLSS and LVEF between active SLE patients and healthy control group patients**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>No. of patients (n:58)</th>
<th>%</th>
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<tbody>
<tr>
<td>GLSS &lt;19.7</td>
<td>27</td>
<td>46.6</td>
</tr>
<tr>
<td>&lt; LVEF 50%</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>Both low</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>GLSS &lt; 19.7 with normal LVEF</td>
<td>20</td>
<td>34.5</td>
</tr>
</tbody>
</table>

**Table 2. Myocardial dysfunction in active SLE based GLSS <19.7 %**

**Conclusion:** In a cohort of SLE patients with NP symptoms, the proposed 2017 ACR-EULAR classification criteria showed similar sensitivity as the 1997 ACR and the SLICC 2012 criteria, but lower specificity. Including ANA negative patients improved sensitivity.
Results: (1) There were 3212 gene was regulated in LN kidney (Fold change>1.5, FDR<0.05, compared with healthy control. DCBLD2, NPNT, CPVL, RGS5, and LRRN4 were found to have the leading correlation with eGFR slope of LN patients by using random forest method. (2) In the independent cohort, we validate that the mRNA and protein level of DCBLD2, NPNT, CPVL, RGS5, LRRN4 was significantly evaluated in tubulointerstitial component in LN kidney, compared with healthy controls (p<0.05), and also significantly correlated with eGFR slope [LRRN4(r=−0.715), P<0.001, DCBLD2(r=0.6280, P=0.001, CPVL(r=−0.517, P=0.004, RGS5(r=−0.485, P=0.016), NPNT(r=−0.412, P=0.016). In addition, the mRNA level of LRRN4 and DCBLD2 in kidney was correlated with SLEDAI score(r=0.611and r=0.512, respectively, P<0.01 and serum C3 level (r=0.501, r=0.435, P<0.05). LRRN4 mRNA level also significantly associated with tubulointerstitial fibrosis scoring(r=0.432, P=0.05;3 he protein of LRRN4 was expressed both in glomeruli and tubulointerstitial tissue. And IHC level of LRRN4 protein was significantly associated with eGFR slope (r=0.534, P<0.05 in LN patients.

Conclusion: LRRN4 in kidney may be used as a novel predictive biomarker of renal outcome in LN patients.

REFERENCES:


Disclosure of Interests: None declared


THU0248

UTILITY OF A MOBILE PHONE BASED APPLICATION TO COLLECT PATIENT REPORTED OUTCOME INFORMATION FROM SUBJECTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Patient Reported Outcomes (PROs) can provide important data about the impact of a disease on an individual subject and/or the quality of the response to medication. However, in most circumstances, PRO information is collected only intermittently and usually at the point of care or treatment. The development of mobile technology to collect PRO data provided the opportunity to acquire this information more frequently, in real-time, and in the subject’s normal environment.

Objectives: To test the utility of a smart phone application (app) to collect PRO information in subjects with systemic lupus erythematosus (SLE).

Methods: A smart phone app was developed that collects data from a number of PRO instruments, including FACIT-Fatigue, SF-36 (health-related quality of life) and patient global assessment (PGA). Subjects with SLE were involved in the initial development and evaluation of the acceptability of the app. To test the utility of this app, a multi-center clinical study (VALUE, NCT03142711) was carried out in collaboration with subjects with SLE, in whom PRO information was collected with the app daily for 5 years (PGA) or weekly for 3 months (FACIT-F and SF-36) in the subject’s environment, and also with the app and a standard paper form monthly at each clinical site. Demographic information, compliance and intra-class correlation coefficients between information collected with the app and using a paper form at the clinical site were assessed.

Results: Of the 60 subjects enrolled in this study, 91.3% were women; 57.5%, 16.3% and 17.5% identified themselves as of European, African or Asian ancestry, respectively. The mean age of the subjects was 42.6 years and the mean duration of education was 15.6 years. Overall compliance with completing the PRO instruments with the app at the scheduled time was 88%. To determine the consistency of information collected with the app, PRO instruments were completed on three occasions: a) in standard fashion using a paper form and b) using the app, separated by an interruption at the clinical site. The mean (SD) PGA scores at baseline, month 1 and month 2 were 3.3(2.4), 3.5(2.4) and 3.5(2.5) using the app and 3.2(2.4), 3.5(2.3) and 3.3(2.4) using the paper form. The Intra-class Correlation Coefficient (ICC) and 90%CI were 0.97 (0.96-0.98), 0.96 (0.94-0.97) and 0.95 (0.93-0.97) at the three time points, respectively. For the FACIT-F instrument, the mean (SD) score with the app was 33.2 (11.7), 31.0(12.6) and 32.3(12.7) and with the paper form was 34.1(11.6), 32.0(12.2) and 32.0(12.5) at the 3 time points with ICCs of 0.94 (0.91-0.96), 0.96 (0.95-0.98) and 0.96 (0.94-0.97), respectively. For the SF-36 Physical Functioning score, the mean (SD) with the app was 66.3(26.1), 65.5(26.9) and 67.4(25.8) and with the paper form was 68.4(25.1), 66.1 (26.6) and 67.6(25.8) for the 3 time points, respectively. The ICCs were 0.96 (0.94-0.97), 0.94 (0.91-0.96) and 0.96 (0.94-0.97) for the 3 time points, respectively.

Conclusion: Compliance with completion of PRO instruments using a mobile app was excellent and the content collected with the app conformed with that collected using a standard paper form. Since patient compliance with the use of a mobile app to collect PRO information and the consistency of the information obtained compared to that obtained in standard fashion using a paper form were high, the app affords the potential opportunity to acquire frequent and highly reliable information about the impact of disease and response to medication in individual subjects with SLE.

Acknowledgement: The study was sponsored by the Lupus Research Alliance and funded by Pfizer. Development and support of the app was provided by TCS.

Disclosure of Interests: Brooke Williams: None declared, Bridget Muckian: None declared, Christine Peschken Consultant for: AstraZeneca, Richard Furie Grant/research support from: Biogen, UCB Pharma, but not in the last 12 months, Consultant for: Biogen, UCB Pharma, but not in the last 12 months, Elena Massarotti: None declared, Vanja sikirica: Employee of: Pfizer, Employee of: Pfizer, Steven Gilberg Consultant of: Pfizer, Employee of: Pfizer, Martin Hodge Consultant of: Pfizer, Employee of: Pfizer, Peter Lipsky Consultant for: Consulting fees from Horizon Pharma


THU0249

URINARY NEUTROPHIL GELATINASE ASSOCIATED LIPOCALIN AND PROSTAGLANDIN D-SYNTHETASE PREDICT DISEASE FLARES IN SYSTEMIC LUPUS ERYTHEMATOSUS

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1University of Campania Luigi Vanvitelli, Rheumatology, Naples, Italy

Background: Systemic Lupus Erythematosus (SLE) is a multisystem autoimmune disease commonly characterized by periods of flares and quiescence. Conventional markers of disease activity (serum complement and anti-dsDNA antibodies) have a limited predictive value of disease flares. Recent evidence suggests that urine biomarkers are able to discriminate between SLE patients with ongoing renal activity and those without nephritis (1). Objectives: To investigate if urinary Neutrophil Gelatinase Associated Lipocalin (NGAL) and Lipocalin-type Prostaglandin D-Synthetase (LP-GDS) are early biomarkers that could be used as flare predictors in SLE. Methods: Patients prospectively followed at our clinic from March 2017 to September 2018, who fulfilled classification criteria for SLE (3), were considered for the study. Flares were identified by SELENA-SLEDAI Flare Index (SFI) after 3 months of urine collection (4). NGAL and LP-GDS levels were measured in the second void urine sample by ELISA. Data were compared by the unpaired student’s t test or the Mann-Whitney U test as appropriate. Logistic regression analysis was used to assess the independent baseline predictors of flares. Receiver operating characteristic (ROC) analysis was used to calculate the area under the curve (AUC) with associated 95% confidence interval (CI) to find the best cut-off values. Results: Urine specimen was collected from 66 patients, including 64 females and 2 males with a median age at diagnosis of 27 years (IQR 21.5-38). During 3 months-follow-up, 18 (27%) out of the 66 patients experienced a single disease flare. Urinary levels of LP-GDS (Fig 1) and NGAL (Fig 2) significantly increased 12 weeks before a disease flare (p=0.0001 and p=0.002, respectively). Urinary NGAL levels correlated with anti-DNA antibody titre (r=0.254, p=0.042) and not with serum complement prior to the disease flare (p>0.05). Moreover, urinary LP-GDS slightly correlated with anti-DNA antibody titre (p=0.08), and was not associated with serum complement levels. Based on ROC analysis, urinary NGAL (AUC: 0.752) and LP-GDS (AUC: 0.811), outperformed conventional biomarkers (Table1). ROC analysis revealed that NGAL levels above 10.95ng/ml had a sensitivity of 84% and a specificity of 63% for flare prediction, while urine LP-GDS cut-off value in the ROC curve, 1500 ng/ml, predicted a flare with 78% sensitivity and 86% specificity. At multivariate analysis, NGAL and LP-GDS were independent predictors of flare with OR=10.34 (95% CI 1.46 – 73.03) and 24.85 (95% CI 4.32-
142.68), respectively. Increase in anti-dsDNA antibodies levels also predicted flares with an OR of 6.70 (p=0.040), while hypocomplementemia was not a significant risk factor.

Conclusion: Urine NGAL and L-PGDS perform better than conventional markers in predicting a lupus flare in its incipient phase, in particular preceding the corresponding change in serum complement. Urinary NGAL and L-PGDS levels seem to be potential tools for monitoring patients with SLE. Further studies are needed to determine their clinical utility in everyday practice.

REFERENCES:

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<th>Variables</th>
<th>AUC</th>
<th>95% CI</th>
<th>Cut off values</th>
<th>sensitivity</th>
<th>specificity</th>
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</thead>
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<tr>
<td>C3</td>
<td>0.683</td>
<td>0.555 - 0.703</td>
<td>107 mg/dl</td>
<td>94%</td>
<td>40%</td>
</tr>
<tr>
<td>Anti dsDNA antibodies</td>
<td>0.705</td>
<td>0.579 - 0.812</td>
<td>30 UI</td>
<td>55%</td>
<td>89%</td>
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<tr>
<td>PGDS</td>
<td>0.811</td>
<td>0.694 - 0.897</td>
<td>1500 ng/ml</td>
<td>78%</td>
<td>86%</td>
</tr>
<tr>
<td>NGAL</td>
<td>0.752</td>
<td>0.630 - 0.851</td>
<td>10.95 ng/ml</td>
<td>84%</td>
<td>63%</td>
</tr>
</tbody>
</table>

Table 1. Area under the curve (AUC), cut off values, sensitivity and specificity for L-PGDS, NGAL and standard biomarkers for disease flares.

Abstract THU0249 – Figure 1

Abstract THU0249 – Figure 2

Disclosure of Interests: Serena Fasano: None declared, Luciana Pierro: None declared, Alessia Borgia: None declared, Melania Alessia Coscia: None declared, Ranieri Formica: Grant/research support from: CELGENE, PFIZER, Consultant for: UCB, NOVARTIS, CELGENE, PFIZER, Lilly, Paid instructor for: UCB, NOVARTIS, CELGENE, PFIZER, Lilly, JANSSEN, MSD, ROCHE, AMGEN


THU0250

EARLY IMPROVEMENT IN SLEDAI-2K RESPONDER INDEX-50 PREDICTS SRI-4 RESPONSE IN A RANDOMIZED PLACEBO-CONTROLLED TRIAL OF USTEKINUMAB (UST) IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: While traditional Systemic Lupus Erythematosus (SLE) Disease Activity Index 2000 (SLEDAI-2K) scoring assesses complete SLE response for individual disease manifestations, the SLEDAI-2K Responder Index-50 (S2K RI-50) evaluates responses using partial improvement (≥50%) in each of the 9 organ systems of SLEDAI-2K. Usteekinumab (UST), a monoclonal antibody that targets the shared p40 subunit of the cytokines IL-12 & IL-23, is being investigated in patients with active SLE. We have previously shown in a Phase 2 placebo (PBO)-controlled trial of UST in SLE1 that not only SLEDAI-2K and the SLE Responder Index 4 (SRI-4), but also S2K RI-50 can discriminate a treatment effect of UST vs PBO at week 24.2

Objectives: Here, we aimed to ascertain whether a minimal threshold of partial improvement in S2K RI-50 could be used as an early predictor of SRI-4 response.

Methods: This phase 2, PBO-controlled study enrolled adults with seropositive, active disease (SLEDAI score ≥ 6 with ≥ 1 BILAG A &/or ≥ 2 BILAG B scores) despite standard therapy. Patients (n=102) were randomized (3:2) to receive UST IV 6 mg/kg or PBO at week 0, followed by SC injections of UST 90mg or PBO q8w beginning at week8, both added to standard of care. We calculated S2K RI-50 response through week 24 in all patients, including 60 patients receiving UST and 42 patients receiving PBO, using increasing cut-offs of S2K RI-50 reductions from baseline. To help determining a minimal cut-off that discriminated a treatment effect reflecting partial improvement, nominal p values are reported for this post hoc analysis. Logistic regression models were used to evaluate the relationship between reduction in S2K RI-50 at week 12 or week 16 and SRI-4 response at week 24, followed by correlation of binary response data between the two instruments.

Abstract THU0250 – Table 1

Table 1. Area under the curve (AUC), cut off values, sensitivity and specificity for L-PGDS, NGAL and standard biomarkers for disease flares.

<table>
<thead>
<tr>
<th>Variables</th>
<th>AUC</th>
<th>95% CI</th>
<th>Cut off values</th>
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<tr>
<td>Anti dsDNA antibodies</td>
<td>0.705</td>
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<td>55%</td>
<td>89%</td>
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<tr>
<td>PGDS</td>
<td>0.811</td>
<td>0.694 - 0.897</td>
<td>1500 ng/ml</td>
<td>78%</td>
<td>86%</td>
</tr>
<tr>
<td>NGAL</td>
<td>0.752</td>
<td>0.630 - 0.851</td>
<td>10.95 ng/ml</td>
<td>84%</td>
<td>63%</td>
</tr>
</tbody>
</table>

Results: A 2-point reduction from baseline (improvement) in S2K RI-50 appeared to be the lowest threshold of response to demonstrate a treatment difference in the proportion of responders at week 24 with UST (93.5%) vs PBO (79.3%) (Δ14.2%, p=0.03). The relationship between 2-point improvement in S2K RI-50 at week 12 or week 16 and SRI-4 response at week 24 is presented in the total study population and by treatment group (Table). In the total population, 78/102 (76.6%) patients at week 12 and 74/102 (72.5%) of patients at week 16 had at least a 2-point improvement in S2K RI-50. Of those, 47/78 (60.3%, r=0.62) at week 12 and 48/74 (64.9%, r=0.76) at week 16 achieved an SRI-4 response at week 24. Odds ratios for the association between SRI-4 response at week 24 and 2-point or greater improvement in S2K RI-50 were 7.6 (CI 2.4-24.3, p=0.0007) at week 12 and 15.4 (CI 4.2-55.8, p=0.0001) at week 16. Similar analyses performed by treatment group demonstrated that these relationships were consistent in the UST and PBO groups (Table).

Conclusion: 2K RI-50 captures partial improvement of ≥50% in SLE disease activity and could be a useful outcome in clinical trials to predict early clinical response. These findings will be confirmed in an ongoing Phase 3 study.
REFERENCE:


THU0251

ASSOCIATION OF SMOKING STATUS AND TOTAL AND INDIVIDUAL DAMAGE INDEX IN SYSTEMIC LUPUS ERYTHEMATOSUS

Romy Kallas, Li Jessica, Michelle A Petri. Johns Hopkins University, School of Medicine, Baltimore, United States of America

Background: Smoking is a risk factor for systemic lupus erythematosus (SLE). It has been associated with increased disease activity and decreased effectiveness of hydroxychloroquine in cutaneous lupus.

Objectives: The objective of the study was to determine the association between smoking status and total and individual damage items in SLE.

Methods: We analyzed data from the Hopkins Lupus Cohort. Damage was recorded using the Systemic Lupus Erythematosus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index. Fisher's exact test and Wilcoxon test were used in exploratory analysis. Logistic regression was used to estimate the association between damage and smoking status (ever/never). Odds ratios and 95% confidence intervals were reported. Stratification by ethnicity was done for individual damage items that were found to be significantly associated with smoking.

Results: The prevalence of ever smokers in our cohort was 36%. SLE patients who ever smoked had higher odds of total damage with higher mean total damage index scores (p <0.0001). Data for individual damage items significantly associated with smoking are presented in Table 1. The association between cataract and smoking was still present after adjusting for ethnicity, diabetes, and prednisone use in a multivariate analysis. Logistic regression was used to estimate the association between damage and smoking status (ever/never). Odds ratios and 95% confidence intervals were reported. Stratification by ethnicity was done for individual damage items that were found to be significantly associated with smoking.

Conclusion: Smoking is a modifiable factor for organ damage in SLE. It is already known that it interferes with the efficacy of hydroxychloroquine. Now we are able to prove that smokers have more cutaneous damage (scarring) even after stratification for ethnicity. As expected, smokers had more cardiovascular damage. New findings include associations with gastrointestinal damage, cataracts, pulmonary hypertension, pancreatitis and diabetes.

Disclosure of Interests: Romy Kallas: None declared, Jessica Li: None declared, Michelle A Petri: Shareholder of: Pfizer, Merck, Grant/research support from: AstraZeneca, Blackrock, Glenmark, UCB, and the Annenberg Center for Health Sciences

THU0251 - Table 1. Relationship between SLICC/ACR Damage Index Items and Smoking (ever/never)

<table>
<thead>
<tr>
<th>Damage Item</th>
<th>ALL (95% CI)</th>
<th>Caucasian</th>
<th>African American</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>p-value</td>
<td>OR (95% CI)</td>
<td>p-value</td>
</tr>
<tr>
<td>Total damage</td>
<td>1.73</td>
<td>1.55</td>
<td>0.0003</td>
</tr>
<tr>
<td>(1.44, 2.07)</td>
<td></td>
<td>(1.22, 1.97)</td>
<td></td>
</tr>
<tr>
<td>Cataract</td>
<td>1.50</td>
<td>0.96</td>
<td>0.8176</td>
</tr>
<tr>
<td>(1.17, 1.92)</td>
<td></td>
<td>(0.68, 1.36)</td>
<td></td>
</tr>
<tr>
<td>Scarring alopecia</td>
<td>2.08</td>
<td>1.63</td>
<td>0.3320</td>
</tr>
<tr>
<td>(1.42, 3.06)</td>
<td></td>
<td>(1.06, 1.45)</td>
<td></td>
</tr>
<tr>
<td>Extensive scarring or panniculitis</td>
<td>3.37</td>
<td>2.57</td>
<td>0.0522</td>
</tr>
<tr>
<td>other than scalp</td>
<td>(1.95, 5.85)</td>
<td>(1.01, 7.03)</td>
<td></td>
</tr>
</tbody>
</table>

N/C: data are not sufficient for calculating odds ratio


Thursday, 13 June 2019 403
HORMONE DEPENDENCE AND CANCER IN SYSTEMIC LUPUS ERYTHEMATOSUS

Tatiana Cobo-Ibáñez1, Ana Urruticoechea-Araná2, Ilfígo Rua-Figueroa2, María Auxiliadora Martín-Martínez3, Juan Ovallés2, María Galindo-Izquierdo3, Jaime Calvo-Alen4, Raquel Navarro-Cruces5, Rosa Menor-Almagro6, Eva Tomeno Munier7, Loretto Horcada8, Esther Uriarte Isacelaya9, Victor Martínez Taboada10, José Luis Andreu11, Alina Boteanu12, J. Narváez13, Cristina Bohorquez14, Carlos A. Montilla-Morales15, Gregorio Santos Soler16, Blanca Hernández-Cruz17, Paloma Vela-Casasempe18, Eva Salgado Perez19, Mercedes Freire González20, José A. Hernandez Betain21, Elvira Díez Alvarez22, Lorena Exposito23, Olalla Fernández Berbizetita24, José Luis Marenco25, José M Pego-Reigosa26, on behalf of RELESSER Study Group.

1Hospital Infanta Sofía, Madrid, Spain; 2Hospital Virgen Macarena, Sevilla, Spain; 3University of María Paredes, Jaén, Spain; 4Hospital de Jerez, Cádiz, Spain; 5Hospital La Princesa, Madrid, Spain; 6Complejo Hospitalario de Navarra, Navarra, Spain; 7Hospital Donostii, Guipuzcoa, Spain; 8Hospital Marqués de Valdecilla, Santander, Spain; 9Hospital Puerta de Hierro-Majadahonda, Madrid, Spain; 10Hospital Ramón y Cajal, Madrid, Spain; 11Hospital de Bellvitge, Barcelona, Spain; 12Hospital Príncipe de Asturias, Madrid, Spain; 13Hospital Clínico de Salamanca, Salamanca, Spain; 14Hospital Marina Baixa, Alicante, Spain; 15Hospital Virgen Macarena, Sevilla, Spain; 16Hospital General de Alicante, Alicante, Spain; 17Complejo Hospitalario de Ourense, Ourense, Spain; 18Hospital Juan Canalejo, A Coruña, Spain; 19Hospital de Canarias Gran Canaria, Spain; 20Hospital de León, León, Spain; 21Hospital Clínico de Tenerife, Tenerife, Spain; 22Hospital de Basurto, Basurto, Spain; 23Hospital Virgen de Valme, Sevilla, Spain; 24Complejo Hospitalario de Vigo, Instituto de Investigación Biomédica, Vigo, Spain

Objectives: To estimate the incidence of cancer in systemic lupus erythematosus (SLE) patients and to analyze factors associated with cancer differentiated between hormone-sensitive (HS) and non-HS cancers.

Methods: Multicenter retrospective study of a cohort of patients included in Spanish Society of Rheumatology Lupus Registry (RELESSER). The first cancer after the diagnosis of SLE, sociodemographic, clinical activity, cumulative damage, severity, comorbidity, treatments, and refractory disease data were collected. Cancers were classified into HS (prostate, breast, endometrial and ovarian) and non-HS (the rest). Standardized incidence ratio (SIR) was calculated and logistics regression models were built to identify factors associated with cancer.

Results: We included 3539 patients (90.4% women) with SLE (ACR-97 criteria), of whom 154 had cancer (91% women), and 44 were HS (100% women). The SIR for cancer was 1.37 (95% CI: 1.15-1.59), reaching higher values in women under 65 years [2.38 (95% CI: 1.84-2.91)]. The SIR in women with cancer vs. non-HS was 1.02 (95% CI: 0.91-1.91) and 1.93 (1.34-2.66) in HS. In HS vs. non-HS cancers, age at diagnosis of SLE [Odds ratio (OR) 1.04 (p = 0.002) vs. 1.04 (p = 0.019), respectively] and the evolution time [OR 1.01 (p < 0.001) vs. OR 1.00 (p = 0.029), respectively] were factors associated with cancer. SLE-ACR damage index [OR 1.27 (p = 0.022)] and Angiotensin-Converting Enzyme (ACE) inhibitors prescription [OR 2.87 (p = 0.048)] were associated with non-HS cancers.

Conclusion: The incidence of cancer in patients with SLE is increased compared to the Spanish population, specially in younger women. This increase might be due to non-HS cancers. SLE with more cumulative damage and more prescription of ACE inhibitors might associate with non-HS cancers.

Disclosure of Interests: Tatiana Cobo-Ibáñez: None declared. ANA URRUTICOECHEA-ARANA: None declared. Ilfígo Rua-Figueroa: None declared. María Auxiliadora Martín-Martínez: None declared, Juan Ovallés: None declared, María Galindo-Izquierdo: None declared, Jaime Calvo-Alen: None declared, Alejandro Oleive: None declared, Antonio Fernandez-Nebro: None declared, Raúl Menor-Almagro: None declared, Eva Tomero Munier: None declared, Alejandro Oleive: None declared, Esther Uriarte Isacelaya: None declared, Victor Martínez Taboada: None declared, José Luis Andreu: None declared, Alina Boteanu: None declared, J. Narváez: Consultant for: Bristol-Myers Squibb, Cristina Bohorquez: None declared, Carlos A. Montilla-Morales: None declared, Gregorio Santos Soler: None declared, Blanca Hernández-Cruz: None declared, Paloma Vela-Casasempe: None declared, Jordi A. Hernandez Betain: None declared, Elvira Díez Alvarez: None declared, Lorena Exposito: None declared, Olalla Fernández Berbizetita: None declared, José Luis Marenco Speakers bureau: abbie, pfizer, novartis, jammsen, Jose M Pego-Reigosa: None declared DOI: 10.1136/annrheumdis-2019-eular.6449

EFFECT OF GLUCOCORTICOIDS ON DAMAGE ACCRUAL IN SLE PATIENTS WITH NO CLINICAL OR SEROLOGICAL DISEASE ACTIVITY

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Background: Observational studies have previously found associations between glucocorticoid therapy and irreversible organ damage in SLE. As glucocorticoid use and lupus disease activity are highly concordant, disease activity potentially confounds analysis of the contribution of glucocorticoid use to organ damage. This could be obviated through the study of damage accrual in patients without detectable disease activity.

Objectives: We studied whether glucocorticoids contribute to damage accrual in SLE in the absence of disease activity, by analysing the effect of glucocorticoids on SLE damage accrual in patients with no clinical or serological lupus disease activity (SLEDAI-2K=0).

Methods: 1907 SLE patients were recruited from 13 centres in 8 countries and followed longitudinally between 2013-2016. As per a standardised protocol, disease activity (SLEDAI-2K) and treatment details were recorded at each visit, and organ damage measured annually (SDI). Co-proportional hazards analyses were used to examine time-dependent associations of glucocorticoid use with damage accrual.

Results: 196/1707 (11.4%) patients had no clinical or serological disease for the entire study period (time adjusted mean (TAM) SLEDAI2K=0). Of these, 95% were female; median (IQR) age at diagnosis 36.5yrs (26.0-46.5) years, median (IQR) baseline SDI 0 (0-1). 68% were exposed to prednisolone, with a median (IQR) TAM-prednisolone dose 2mg/day (0-5). Despite SLEDAI2K=0 throughout, irreversible damage accrual occurred in 13% of the cohort, with 26 damage events captured over median (range) 1.9 years (1.0-2.2) followup. Prednisolone exposure at doses in the upper two quartiles was associated with damage accrual (HR 1.11 (1.02, 1.22), p=0.02)

Conclusion: Irreversible damage accrual occurs in patients with no clinical or serological disease activity as captured by SLEDAI-2K, and glucocorticoid use contributes to the risk of organ damage in these patients.

THU0254  TRENDS OF SEVERITY, PROGRESSION AND BURDEN OF DISEASE IN THE ‘ATTIKON’ SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) COHORT: EVIDENCE FOR THE RULE OF ‘ONE THIRD’ IN DISEASE SEVERITY

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Background: SLE phenotype, severity and prognosis varies widely, while its course, progression and pattern of severity cannot be predicted with confidence.

Objectives: We analyzed the phenotype and severity patterns of a SLE cohort in the Attica area of Greece, based in “Attikon” University Hospital, and assessed whether these patterns change over the course of the disease.

Methods: Retrospective cohort study of 512 Caucasian SLE patients fulfilling the ACR 1997 and/or SLICC 2012 criteria. Data on clinical course, pattern of severity and SLICC damage index (SDI) were recorded for each patient at the time of diagnosis and at last evaluation. Severity of disease was stratified based on BILAG manifestations and patients were assessed for progression to a more severe phenotype over their disease course. Patients with disease duration < 12 months were excluded. Binary logistic regression was performed to identify independent predictors of such progression.

Results: More than half patients (53.7%, 275/512) presented with mild disease, while in approximately 20% (20.8%, n=106) lupus presented with severe manifestations at diagnosis. Median (IQR) follow-up was 96.5 (144) months. Of 246 patients with initially mild disease, 126 (56.4%) retained their mild phenotype, 73 (29.7%) progressed to a moderate phenotype, while the remaining 47 (19.1%) eventually developed severe lupus. Also, 30 patients (29.4%, 30/102) who initially manifested moderate severity patterns progressed to severe disease over time. At last evaluation, a nearly equal distribution in severity patterns was evident (mild 30%, moderate 34% and severe 36%). Independent factors for disease progression were older age at diagnosis (OR: 0.97 per 1-year, 95% CI 0.95-0.99), disease duration (OR: 1.10 per 1-year, 95% CI 1.06-1.13), positive anti-dsDNA (OR: 2.20, 95% CI 1.38-3.49) and presence of fever at diagnosis (OR: 1.67, 95% CI 1.00-2.77). By multivariate regression, only disease duration (OR: 1.09, 95% CI 1.05-1.12) and anti-dsDNA (OR: 1.73, 95% CI 1.05-2.85) were independently associated with disease progression.

Ninety-two subjects (18%) had organ damage at the time of diagnosis, mainly due to neuropsychiatric and thrombotic events. At last visit, mean (SE) SDI was 0.67 (0.57). Two-hundred eight patients (59.8%) had no damage (SDI=0), while high damage (SDI > 3) was measured in 25 subjects (7.2%).

Conclusion: In this SLE cohort of Caucasian patients, almost half of cases have mild disease at presentation; yet with significant damage accrual. Of patients with disease duration > 1 year, 43.1% progressed to more severe phenotypes, with patients distributed evenly in the mild, moderate and severe categories. These data reiterate the rule of one third for severity observed in other autoimmune diseases.


THU0255  IMPACT OF IL34, IFNA AND IFN-1 ON DISEASE ACTIVITY OF SLE PATIENTS IN EGYPT

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Background: SLE is a systemic inflammatory and autoimmune disease. IL-34 plays pivotal roles in the proliferation and differentiation of mononuclear phagocyte cells, osteoclastogenesis and inflammation [1]. IFN-α play an important role in SLE pathogenesis [2] and proportion of patients displays increased serum IFN-α and IFN-1 [3]. Interestingly, the gene signatures of IFN-1 and IFN-α overlap [4].

Objectives: Assessment of IL34, IFN-1 and IFN-α in SLE with relationship to clinical, laboratory parameters, treatment response and disease progression. We hypothesized a subgroup of patient with a concordance of high level of these cytokines that could have a different disease behavior.

Methods: 82 newly diagnosed SLE Egyptian patients. History, examination and laboratory investigation with assessment of disease activity. Pretreatment assessment of IL34, IFN-α and IFN-1 level by ILIZA. Patients started treatment (antiinflammation → steroid → immunosuppressive drugs) with response evaluation after six months.

Results: 14 male (17.1%) and 68 female (82.9%), age mean±SD (46 ±8.2). Mean±SD of IL34, INFα and INFβ were 175.9±125.9 pg/mL, 109.3±32.5 pg/mL and 227.9±144.8 pg/mL respectively. 21 patients (25.6%) had lupus nephritis, 32 patients (39%) with SLAM >6 and 22 patients (26.8%) with SLEDAI >6. IL34 was positively correlated with anti-dsDNA (P = 0.002) but inversely correlated with C3 level (P = 0.009). IL34 was highly presented with lupus nephritis (P = 0.005), SLAM >6 (P = 0.03), SLEDAI>6 (P = 0.007) and poor responder to treatment (P = 0.02). INFα was inversely correlated with C3 (P = 0.001). INFα was highly presented with lupus nephritis (P = 0.02) and poor responders (P = 0.01) however no relation with SLAM>6 nor SLEDAI>6. INFβ was positively correlated with anti-dsDNA (P = 0.02) but inversely correlated with C3 (P = 0.01). INFβ was highly presented with lupus nephritis (P = 0.001), high IL34 (P = 0.001) and high INF-1 (P = 0.001). We assigned high levels (i.e., > 75% or third quartile) of each cytokine. Triple high (IL34β>75%, INFα >75% and IFN-1 >75%) found in 17 patients (20.7%) and were positively correlated with anti-dsDNA (P = 0.001) but inversely correlated with C3 (P = 0.001). Triple cytokines level was highly presented with lupus nephritis (P = 0.001), SLAM >6 (P = 0.02), SLEDAI>6 (P = 0.03) and poor response to treatment (P = 0.01) indicating these patients have aggressive disease. 28 patients developed (3 – 8) accumulated clinical features during the disease course, out of them 15 patients (53.5%) have high level of the triple cytokines indicating a poor prognosis of these subgroup.

Conclusion: High pretreatment IL34 or IFN-1 has a prognostic significance in SLE. Patients with high IL34 or INFα or IFN-1 had more kidney affection and poor response to treatment. Triple cytokines elevation significantly associated with lupus activity, more kidney affection and poor response to treatment so, this aggressive phenotype may need combination of targets or multicytokines targeted therapy.

REFERENCES:

Disclosure of Interests: None declared

**THU0256**

**RISK OF LONG-TERM INCIDENT CARDIOVASCULAR EVENT AND MORTALITY IN PATIENTS WITH SLE AND POPULATION CONTROLS IS ASSOCIATED WITH A HIGHER CAROTID INTIMA-MEDIA THICKNESS**

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**Background:** Measurement of carotid intima-media thickness (cIMT) is promoted as one of the tools for cardiovascular (CV) risk assessment in primary prevention in general population. The diagnosis of systemic lupus erythematosus (SLE) is a strong risk factor for premature CV events and mortality. Whether assessment of cIMT has a value for prediction of CV morbidity and mortality in patients with SLE compared with population controls of similar age and sex is not established.

**Objectives:** To examine association of cIMT with risk of incident CV events and mortality in SLE and controls.

**Methods:** We used the cross-sectional SLEVIC (SLE vascular impact cohort study) cohort of consecutive patients with SLE aged <70 years who were regularly treated in a tertiary referral rheumatology center. Carotid ultrasound was performed at inclusion to the cohort (from September 2006 to January 2008) in 118 patients and in 122 population controls matched by age and sex. Incident CV events were defined as hospitalization for angina pectoris, myocardial infarction, bypass grafting, percutaneous coronary or peripheral artery intervention, ischemic stroke and TIA. Combined outcome of incident CV event and all-cause mortality was evaluated for a mean (SD) follow-up of 9.6 (1.5) years. Participants with prevalent CV before inclusion, n=18, and those who were lost to follow-up, n=14, were excluded from this analysis. Event-free survival rates in patients and controls were compared using Kaplan-Meier curves. Relative hazard ratios from Cox proportional-hazards regression models were used to estimate the effect of cIMT measurement on the outcome.

**Results:** At inclusion, mean age (SD) of the included 98 patients was 47 (13) years, 87% females, mean disease duration 12 (9) years, SLEDAI 4.0, and SLICC/ACR 1.0. Mean age of included 109 controls was 49 (12) years, 91% females. Baseline mean (SD) cIMT did not differ between the groups (p=0.345) and was 607 (127) µm in patients and 632 (118) µm in controls. During follow-up, 12 patients and 4 controls were defined with the outcome. The outcome was reached more often in patients than in controls, p=0.022. The mean time to outcome (SD) was 9.9 (0.2) years for patients and 10.3 (0.1) years for controls.

The hazard rate (HR) for the combined outcome of CV event and mortality was 3.7-fold (95% CI, 1.2-11.5) higher in patients than in controls, adjusted for age, sex and smoking history, p=0.025. A higher baseline mean cIMT was significantly associated with the outcome, HR 1.0 (95% CI, 1.0-1.01) per 1.0 µm increase in cIMT, p=0.040, irrespective of the group. Additional adjustment for traditional risk factors, disease duration, treatments, presence of anti-phospholipid antibodies and defining with carotid plaque yielded similar risk estimates.

**Conclusion:** In this analysis we confirm an elevated long-term risk of important adverse clinical events in patients with SLE compared with controls. A measure of cIMT is associated with incident CV event and mortality. This suggests that assessment with carotid ultrasound may have a value for CV risk stratification and would encourage validation in large-cohort prospective populations.

**Disclosure of Inter:** Sofia Ajeagova: None declared. Ingård Hafström: None declared, Johan Frostegård Shareholder of: Minor shareholder and inventor in startup-company Atera Biotechnologies, but they do not produce drugs yet and rheumatology is not in their focus. DOI: 10.1136/annrheumdis-2019-eular.5763

**THU0257**

**DIAGNOSTIC PERFORMANCE OF 2002 AECG, 2012 ACR AND 2016ACR/EULAR CLASSIFICATION CRITERIA FOR SJÖGREN’S SYNDROME IN A HISPANIC POPULATION**

Nicola Alfaro1, Janett Carmen Riegatorres1, Cesar Vidal Soils1, David Vega Morales1, Brenda Roxana Vázquez Fuentes1, Mario Alberto Garza Elizondo1, Cassandra Michele Skinner Taylor1, Dionicio Ángel Galarza-Delgado1, Jesús Mohamed Noriega2, Karim Mohamed Noriega3, Hospital Universitario Dr. José Eleuterio Gonzalez, Department of Rheumatology and Clinical Immunology, Monterrey, Nuevo León, Mexico; Hospital Universitario Dr. José Eleuterio Gonzalez, Department of Ophthalmology, Monterrey, Nuevo León, Mexico

**Background:** Primary Sjögren’s syndrome (pSS) has several classification criteria, whose diagnostic performances vary depending on the studied population1. Concordance and differences among these criteria should be evaluated for independent populations to determine the diagnostic performance.

**Objectives:** To compare the performance among 3 classification criteria for pSS and determine the level of concordance among them.

**Methods:** Descriptive, retrospective, and cross-sectional study including 172 patients from the Rheumatology Service of the Hospital Universitario “Dr. José Eleuterio González”, who were studied for dry syndrome. The clinical criterion of the attending physician was considered as the gold standard for diagnosis. Different parameters were collected: presence of xerostomia, xerophthalmia, Schirmer’s test, sialometry, ocular staining, ANA, anti-Ro/SSA and anti-La/SSB antibodies, RF isotypes (IgA, IgM, IgG), and focal lymphocytic infiltrate in minor salivary gland biopsy. The criteria proposed by the American European Consensus Group (AECG), ACR and, ACR/EULAR were used to evaluate the classification. Compliance was determined for each set of criteria.

**Results:** Sociodemographic characteristics and clinical manifestations are shown in Table 1. For the AECG, ACR, and ACR/EULAR criteria, the sensitivity was 89.1%, 98.9% and 88% and the specificity was 93.8%, 71.3%, and 96.3%, respectively (Table 2). The ACR/EULAR criteria have an adequate level of agreement (κ=0.663, P<0.001) with those of the AECG and with respect to the ACR criteria a moderate level of agreement (κ=0.561, P<0.001).

**Abstract THU0257 – Table 1. Clinical characteristics.**

<table>
<thead>
<tr>
<th><em>pSS</em></th>
<th>Dry Syndrome</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, Median (IQR)</td>
<td>59 (47-64)</td>
<td>51 (43-59)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>89 (97%)</td>
<td>74 (83%)</td>
</tr>
<tr>
<td>Xerostomia, n (%)</td>
<td>77/90</td>
<td>52/71 (73.2%)</td>
</tr>
<tr>
<td>Xerophthalmia, n (%)</td>
<td>79/89</td>
<td>58/69 (84%)</td>
</tr>
<tr>
<td>Schirmer test, n (%)</td>
<td>63 (68%)</td>
<td>36 (45%)</td>
</tr>
<tr>
<td>OSS ≥ 3, n (%)</td>
<td>60 (65%)</td>
<td>18 (22%)</td>
</tr>
<tr>
<td>OSS ≥ 5, n (%)</td>
<td>59/91</td>
<td>11/56 (19%)</td>
</tr>
<tr>
<td>USF &lt;1.5 ml/min, n (%)</td>
<td>74 (80%)</td>
<td>35 (43.8%)</td>
</tr>
<tr>
<td>USF ≥0.1 ml/min, n (%)</td>
<td>76 (83%)</td>
<td>35 (43.8%)</td>
</tr>
<tr>
<td>Minor Salivary Gland, n (%)</td>
<td>73/85</td>
<td>23/67 (34.5%)</td>
</tr>
<tr>
<td>Anti-Ro/SSA, n (%)</td>
<td>70/90 (78%)</td>
<td>5/69 (7%)</td>
</tr>
<tr>
<td>Anti-La/SSB, n (%)</td>
<td>27/86 (31%)</td>
<td>1/65 (2%)</td>
</tr>
<tr>
<td>ANA, n (%)</td>
<td>62/88</td>
<td>23/66 (35%)</td>
</tr>
<tr>
<td>Rheumatoid Factor, n (%)</td>
<td>51/88</td>
<td>24/66 (36%)</td>
</tr>
<tr>
<td>IgG, n (%)</td>
<td>17/86</td>
<td>7/67 (10%)</td>
</tr>
<tr>
<td>IgM, n (%)</td>
<td>50/85</td>
<td>23/63 (36%)</td>
</tr>
<tr>
<td>IgA, n (%)</td>
<td>34/83</td>
<td>8/63 (13%)</td>
</tr>
</tbody>
</table>

OSS: Ocular Staining Score; USF: unstimulated saliva flow.

* The diagnosis of primary Sjögren’s Syndrome was made based on clinical criteria P<0.001

**Abstract THU0257 – Table 2. Diagnostic criteria performance.**

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>2002 AECG</th>
<th>2012 ACR</th>
<th>2016ACR/EULAR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kappa Cohen</td>
<td>2012</td>
<td>2016</td>
<td></td>
</tr>
<tr>
<td>2002 AECG</td>
<td>89.10%</td>
<td>0.545</td>
<td>0.663</td>
</tr>
</tbody>
</table>
NERVOUS SYSTEM INVOLVEMENT IN PRIMARY SJÖGREN’S SYNDROME

Jose Luis Andreu1, Carlos Sánchez-Piedra2, Monica Fernandez Castro3, Victor Martínez Taboada4, Alejandro Olive5, Jose Rosas6, Raúl Menor-Almagro7, Beatriz Tofol5,3, Alejandro Olive4, Jose Rosas5, Raúl Menor-Almagro6, Beatriz Tofol5,3

Background: Primary Sjögren’s syndrome (pSS) is a systemic autoimmune disease characterized by the involvement of the exocrine glands, mainly salivary and lacrimal glands. Approximately half of patients will experience extraglandular complications throughout their evolution.

Objectives: To characterize the involvement of the nervous system (NS) in patients with pSS.

Methods: Multicenter cross-sectional study of a cohort of patients with pSS, constructed by random selection of pSS patients fulfilling the 2002 American-European Consensus Criteria for pSS. A total of 33 rheumatology units. Through review of clinical records and interview with patients, demographic, clinical, analytical, therapeutic data and disease activity indexes were collected. Univariate analysis was done by Chi square test, Mann-Whitney U test and Student’s t test. Multivariate analysis was done by linear logistic regression. A p <0.05 was considered significant. Patients signed an informed consent. The study was authorized by the ethics committees.

Results: 437 patients were included (95% women, median age of 58 years). 65 patients developed NS involvement: 26 patients central NS, 31 peripheral NS and 8 both. Multivariate analysis showed association between NS involvement and atherosclerotic stroke (OR 10.4, 95% CI 2.8-38.5), ear disease (OR 2.1, 95% CI 1.1-4.2) and myopathy (OR 6.5, 95% CI 1.3-31.6). Patients with NS involvement had higher probability of being treated with glucocorticoids (OR 3.3, 95% CI 1.5-7.2) and cyclophosphamide (OR 6.8, 95% CI 1.5-31).

Conclusion: 15% of patients with pSS develop NS involvement that is associated with atherosclerotic stroke, ear disease and myopathy.

REFERENCE:
p=0.01) when compared to patients with both abnormal SGUS findings and LGS local lymphocytic sialadenitis.

**Conclusion:** SGUS and LSG histopathology showed only a moderate correlation in patients with pSS. SGUS may be useful to identify pSS patients with a more severe inflammatory LSG infiltrates, ultimately contributing to prevent non-invasive phenotyping of multiple subsets in pSS.

**Disclosure of Interests:** Chiara Baldini: None declared, Francesco Ferro: None declared, Nicoletta Luciano: None declared, Giannarita Governato: None declared, Marta Mosca: Paid instructor for: GlaxoSmithKline, Lilly, UCB, Stefano Bombardieri: None declared, Valentina Donati: None declared


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**THU0260**

**SYSTEMIC LUPUS ERYTHEMATOSUS AND CYTOPENIAS: THE KEY FINDINGS IN BONE MARROW**

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**Background:** Cytopenias are common in systemic lupus erythematosus (SLE), and it is fundamental to determine their etiology in order to establish an adequate therapeutic strategy.

**Objectives:** To describe the findings in the bone marrow aspirations (BMA) and biopsies of patients with SLE and cytopenias, as well as clinical and laboratory features associated with the etiology of the hematological abnormalities.

**Methods:** We performed a retrospective study in a third-level hospital in Mexico City. We included patients who fulfilled ACR criteria for SLE, presented with cytopenias and had a BMA and biopsy performed before 2000 and 2016. We described the main aspirate and biopsy findings, and also analyzed the final diagnosis and its association with clinical, laboratory, and serological features.

**Results:** We included 101 patients; median age was 32 years and 81.2% were women. Leukopenia (<3000 cells/µL) was found in 47.5% of patients, with 29.7% having moderate or severe neutropenia (<1000 cells/µL). Lymphopenia (<1000 cells/µL) was a common finding (71.3% of patients). Moderate-to-severe thrombocytopenia (<50 K/µL) was present in 28.7% of patients. Finally, 25.8% of patients presented with pancytopenia. Regarding bone marrow findings, there was erythroid dysplasia in 50.5% of patients, granulocytic dysplasia in 28.7% and megakaryocytic dysplasia in 16%. Myelofibrosis was found in 2.6%. An increase in plasma cells (≥5%) was found in 21.8%. In 72.3% of patients, bone marrow interpretation was conclusive. The most common diagnoses were disease activity (24.8%) and drug-associated myelotoxicity (28.7%). When compared to other etiologies, in patients with cytopenias secondary to disease activity, it was more frequent for the bone marrow to be hypercellular (56 vs 23%, p=0.006) and to have increased megakaryocytes (40 vs 17.4%, p=0.048). Conversely, granulocytic dysplasia was less common in this group of patients (17.4% vs 54.3%, p=0.006).

We analyzed factors associated with both activity and toxicity as final diagnoses (Table 1). After multivariate analysis, a neutrophil count <1000 cells/µL was a protective factor for disease activity (OR 0.021; 95% CI 0.001-0.428, p=0.012). On the other hand, a history of renal activity (OR 0.012; 95% CI 1.3-14.2, p=0.024) and neutrophils less than 1000 cells/µL (OR 4.05; 95% CI 1.15-14.19, p=0.029) were found to be independent risk factors for myelotoxicity.

**Conclusion:** The main causes of cytopenias in our SLE patients were disease activity and bone marrow toxicity. Our findings suggest that when patients present with less than 1000 neutrophils/µL, it is unlikely for the cytopenias to be secondary to disease activity. Our study reinforces the diagnostic utility of BMA and biopsy, and the associations we described may assist clinicians to determine the etiology of cytopenias in SLE patients, in order to make appropriate therapeutic decisions.

**Disclosure of Interests:** Ana Barrera-Vargas: None declared, Jonathan Campos-Guzmán: None declared, Samuel Goeva-Peláez: None declared, Aldo García-Ramos: None declared, Roberta Demichelis-Gómez: None declared, Christianne Bourlon: None declared, Javier Merayo-Chalico: Speakers bureau: Pfizer, Jorge Alocer-Varela: None declared


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**THU0261**

**THE URINARY CELLULAR PROFILE AS A BIOMARKER FOR LUPUS NEPHRITIS**

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**Background:** Proliferative lupus nephritis is one of the most common and serious manifestation of SLE and is a major cause of morbidity. A search for the ideal biomarker for LN is still underway, one that can be used for early detection, and correlate with the class & activity of LN. Urine is normally devoid of leucocytes, however it has been observed that macrophages and T-lymphocytes are routinely present in the urine of LN patients and those with other proliferative renal diseases. This provided the idea for their potential use as biomarkers for proliferative LN.

**Objectives:** To study the urinary CD4+, CD8+ T Lymphocytes, and CD14 Monocytes in patients with proliferative lupus nephritis, and explore their use as a biomarker for LN.

**Methods:** Our subjects included 30 patients with biopsy proven proliferative LN and 30 SLE patients without clinical or lab evidence of LN as controls. Lab investigations included serum creatinine, urine analysis, protein, creatinine ratio, anti-ds DNA Ab, C3 and C4. For the flowcytometric analysis 100 ml of freshly voided urine in a sterile container were obtained from patients and controls. All samples were processed within 2-4 hours of collection to ensure viability of the cells. Urine mononuclear cell count was done using a hemocytometer. The urine samples were centrifuged then washed twice by phosphate-buffered saline/bovine serum albumin (PBS/BSA) and resuspended in about 300 µl PBS. The cells were stained with anti-CD8- FITC, anti-CD4- PE, anti CD14-PE/PerCP and anti-CD3-APC monoclonal antibodies. The flow cytometric analysis was done using Becton Dickinson, FACS Calibur multi-parameter flow cytometer equipped with BD CellQuest Pro software for data analysis.

**Table 1**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Disease activity</th>
<th>Drug-associated toxicity</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(N=25)</td>
<td>(N=28)</td>
<td></td>
</tr>
<tr>
<td>History of disease activity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Mucocutaneous</td>
<td>80%</td>
<td>86%</td>
<td>0.719</td>
</tr>
<tr>
<td>- Renal</td>
<td>50%</td>
<td>96.4%</td>
<td>0.012</td>
</tr>
<tr>
<td>Neutrophils (cells/µL)</td>
<td>16%</td>
<td>17.9%</td>
<td>0.004</td>
</tr>
<tr>
<td>- Mild neutropenia (1000-1499)</td>
<td>4%</td>
<td>7.1%</td>
<td></td>
</tr>
<tr>
<td>- Moderate neutropenia (500-999)</td>
<td>4%</td>
<td>39.3%</td>
<td></td>
</tr>
<tr>
<td>- Severe neutropenia (&lt;500)</td>
<td>68%</td>
<td>70%</td>
<td></td>
</tr>
</tbody>
</table>

**Abstract THU0261 – Figure 1**

**Scientific Abstracts**
Results: CD14+ cells were the most abundant cells in the urine of LN patients. The mean numbers of urinary CD6+, CD4+ and CD14+ cells/ml were significantly higher in patients with LN (405.6 ± 200.0, 281.1 ± 195.3, and 1554.7 ± 606.8 respectively) than in those without (39.30 ± 17.56, 34.33 ± 16.41, and 161.17 ± 90.91 respectively). AUC for ROC = 1.0 for all 3 markers with CD8+ >85 cells/ml, CD4+ >80 cells/ml, and CD14+ >400 cells/ml being observed exclusively in LN. The cell counts correlated significantly with the protein:creatinine ratio, but not with other markers of disease activity. The CD4:CD8 ratio was significantly lower in LN patients (0.65 ± 0.21) than in those without (0.91 ± 0.31). Urinary CD14+ cells seem to occur in much higher counts in Class IV (1736.7 ± 522.0) than Class III LN (898.5 ± 17.68). p=0.084. Figure 1 shows a dot plot of flow cytometric analysis of urinary T cells and monocytes (dim CD4 expression and CD14 positive/not shown)

Conclusion: Urinary CD6+, CD4+, and CD14+ cells are highly sensitive and specific markers for detecting proliferative LN. A low CD4:CD8 ratio provides a further clue. The cell counts correlate with proteinuria. CD14 cell counts may be a potential biomarker to differentiate between the different classes of proliferative LN.

REFERENCES:

Disclosure of Interests: None declared

THU0262

FATIGUE IN PRIMARY SJÖGREN’S SYNDROME AS A DISEASE MANIFESTATION REFLECTING THE DEGREE OF MUCOSA-ASSOCIATED LYMPHOID TISSUE (MALT) INVOLVEMENT

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Background: fatigue in primary Sjögren’s syndrome (pSS) is a very common and complex symptom, heavily impairing a wide range of patient functions, quality of life and health policies. To date, measures of fatigue and other patient-reported symptoms/outcomes (PROs) poorly correlate with pSS disease activity assessed by ESSDAI. On the other hand, therapeutic interventions reducing pSS disease activity proved useful to improve fatigue burden in pSS.

Objectives: to evaluate if fatigue correlates to other pSS disease manifestations which may also reflect disease activity, by investigating if: a) higher levels of fatigue shows a higher frequency of a heavier involvement of mucosa-associated lymphoid tissue (MALT) documented by histopathology, persistent glandular swelling, or cryoglobulinemia (1); and b) if fatigue correlates to other pSS-related somatic symptoms, such as dryness and arthralgias.

Methods: among pSS patients undergoing clinical evaluation in our Sjögren’s Clinic in a six-months period, 86 consecutive unselected patients, fulfilling the latest ACR/EULAR pSS classification criteria, accepted to report their degree of fatigue, general dryness, ocular dryness, oral dryness and pain on 10-cm VAS (range 0-100), and to complete the ESSPRI (range 0-10), the PROFAD (range 0-28) and the EQ-5D scale (0-100) questionnaires. Four subgroups of fatigue severity were preliminarily defined representing, as previously described (3): no fatigue (VAS=0); 12.8% (n=11); low fatigue (VAS=1-24): 25.3% (n=19); moderate fatigue (VAS=25-74): 58.7% (n=44); high fatigue (VAS=75-100): 16% (n=12). As previously reported (3) no significant age or sex difference was present between subgroups, and potential contributors to fatigue, such as autoimmune thyroiditis, anemia and fibromyalgia did not play a role.

The frequencies of peculiar manifestations related to an increased activity in MALT involvement in pSS, such as persistent salivary gland swelling, cryoglobulinemia and biopsy-proven diagnosis of myoepithelial saliadenitis (MESA) or of pSS-related MALT lymphoma, at any time in the clinical history of patients, were evaluated for each subgroup.

Secondly, the correlations between fatigue VAS and PROs reflecting somatic symptoms were performed.

Results: pSS patients reporting moderate or high fatigue VAS showed significantly higher frequencies of salivary gland swelling (p=0.0274), of MESA or lymphoma proven by histological diagnosis (p=0.0397), if compared to pSS patients with no or low levels of fatigue. Cryoglobulinemia was not significantly increased, although more frequent, in patients with moderate or high fatigue (10.7%) compared to patients with no or low fatigue (6.6%).

Fatigue VAS score did not correlate with ESSPRI. Patients with higher levels of fatigue showed significant (p<0.0001) higher scores in total ESSPRI, dryness-ESSPRI, pain-ESSPRI, ocular dryness VAS, oral dryness VAS, pain VAS, somatic fatigue domain of PROFAD, arthralgia domain of PROFAD, total SSI and PROFAD-SSI-SF.

Finally, patients with higher levels of fatigue reported worst scores in quality of life EQ-5D-scale.

Conclusion: The severity of fatigue appears to mirror the degree of MALT involvement, and this involvement is the biological substrate of pSS itself. This represents a demonstration that fatigue is biologically related to pSS, and supports the notion that fatigue should be treated by disease-modifying drugs rather than only with symptomatic therapies in pSS. In addition, dedicated scores of pSS activity can be developed for pSS patients where fatigue is one of the dominant symptoms. Since fatigue may also correlate with pSS somatic symptoms, such as dryness and arthralgia, they could also be included.

REFERENCES:

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THU0263

NOVEL SUBSETS OF SLE PATIENTS ENRICHED FOR RENAL MANIFESTATIONS IDENTIFIED BY CLUSTERING WITH EXPANDED AUTOANTIBODY PROFILES OF NATIVE AMERICAN (NA), AFRICAN AMERICAN (AA), AND EUROPEAN AMERICAN (EA) SLE PATIENTS

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Background: Autoantibodies (AAbs) are a hallmark of systemic lupus erythematosus (SLE). Common SLE AAbs show differences in specificity, levels and associations with clinical characteristics of disease which may be influenced by ethnicity.(1-2) NA SLE patients do not always exhibit classical AAb profiles.(2) Understanding how AAb profiles associate with clinical disease, including in NA patients, is important to better inform disease management.

Objectives: To identify patient subsets enriched for renal disease by clustering with expanded autoantibody profiles of Native American (NA), African American (AA), and European American (EA) SLE patients

Methods: Serum samples from 49 NA, 49 AA, and 49 EA age, sex and ANA tier-matched SLE patients who met ACR classification and 10 sex and age matched controls from each ethnicity were tested for AAb reactivity by autoantigen microarray. Normalized fluorescence intensity (NF) for AAB binding was determined for each individual for all autoantigens. Ratios of NFIs to total Igs were calculated and converted to Z-scores. Kruskal-Wallis analysis of Z-score transformed AAB ratios were used to identify AAbs that differed significantly between patients and controls for each ethnicity; these AAbs were used for hierarchical clustering of SLE subjects within each ethnicity. The enrichment of SLE clinical criteria within each cluster was determined by Fisher’s exact test.

Results: AAbs to nucleic acids and Ro52 were present in SLE patients of all three ethnicities. On average, NA SLE patients, but not EA or AA SLE patients, had lower levels of AAbs against extracellular matrix (ECM) antigens compared to controls. AA and EA, but not NA, SLE patients had significantly higher levels of AAbs to Sm, RNP and histones compared to matched controls. In each ethnicity four clusters of SLE subjects were identified by ethnicity-specific AAbs. All three groups had a cluster of subjects enriched in nucleic acid-specific AAbs and a cluster of subjects enriched in Ro52 AAbs. The NA group also had two clusters enriched in ECM AAbs. The AA group had an Sm/RNP AAb enriched cluster and a nucleolin/histone AAb enriched cluster. Two additional EA
SLE clusters had similar levels of nucleic acid-specific AAbs and Ro52 AAbs, but were distinguished by significant differences in histone 2A (H2A) AAb levels. Renal manifestations were significantly enriched in the NA Ro52 cluster and the AA nucleolin/histone cluster compared to other SLE patient clusters of the same ethnicity.

Conclusion: Expanded AAb profiles can be used to identify SLE subsets that are more likely to have renal manifestations of disease.

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Disclosure of Interests: None declared


THU0265

IDENTIFYING COMORBID FIBROMYALGIA IN SYSTEMIC LUPUS ERYTHEMATOSUS USING PATIENT-REPORTED OUTCOMES

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Background: Fibromyalgia (FM) is disproportionately common in patients with systemic lupus erythematosus (SLE) and difficult to diagnose on a background of classical SLE symptoms [1]. The Multi-Dimensional Health Assessment Questionnaire (MDHQ) has been shown to be useful to recognise improvement over 2 months in a variety of rheumatic conditions including SLE [2] but has not previously been shown to be useful to alert the clinician to comorbid FM in the latter condition. Conversely, the 2011 FM self-report questionnaire is disease-specific and available for use in clinical and epidemiological studies. Administration of multiple forms may be difficult in a busy clinical setting.

Objectives: To identify comorbid FM in patients with SLE using patient-reported outcomes (PROs) from the routinely distributed MDHQ, in comparison to the 2016 revision of the 2010/2011 FM criteria.

Methods: Patients with SLE completed an MDHQ and the 2011 FM Criteria questionnaire. FM status was assigned using the 2016 revision of the 2010/2011 FM criteria as the gold standard. The MDHQ features 13 items with an 11-point numeric rating scale (NRS) designed to alert the clinician to comorbid FM in the latter condition. Conversely, the 2011 FM self-report questionnaire is disease-specific and available for use in clinical and epidemiological studies. Administration of multiple forms may be difficult in a busy clinical setting.

Objectives: To identify comorbid FM in patients with SLE using patient-reported outcomes (PROs) from the routinely distributed MDHQ, in comparison to the 2016 revision of the 2010/2011 FM criteria.

Methods: Patients with SLE completed an MDHQ and the 2011 FM Criteria questionnaire. FM status was assigned using the 2016 revision of the 2010/2011 FM criteria as the gold standard. The MDHQ features 13 items with an 11-point numeric rating scale (NRS) designed to alert the clinician to comorbid FM in the latter condition. Conversely, the 2011 FM self-report questionnaire is disease-specific and available for use in clinical and epidemiological studies. Administration of multiple forms may be difficult in a busy clinical setting.

Conclusion: SLE-PAH had 3.8-fold increase in mortality despite treatment with PAH specific therapy and immunosuppressants. Hyponatremia and renal disease were associated with poor survival outcome in SLE-PAH patients.

REFERENCE:

Disclosure of Interests: None declared

six main PROs: body pain, patient global and fatigue score on a 0-10 visual analogue scale, as well as a functional impact score, self-report joint count and symptom checklist while having a range of 0-10, 0-48 and 0-60 respectively. Composite indices consisting of either two or three of patient pain score 6, self-report joint count 16 and symptom checklist 16 or three of four of the same measures plus a fatigue score 6 have been described previously to provide clues to comorbid FM in other rheumatic diseases [4,9]. Individual PROs and these composite indices were compared between patients with and without FM by student’s unpaired t test and Area Under the Curve (AUC) analysis. The physician’s diagnosis of FM was analysed against the FM criteria using Cohen’s kappa. Physicians were blinded to the results of the 2016 FM criteria.

Results: 88 patients with SLE were studied, of whom 23 (26%) satisfied FM criteria. Those with FM reported higher scores in all PROs. A patient global of 6 could correctly classify 90% of patients and provided the highest AUC of 0.95, followed by the symptom checklist and body pain. An index of three measures (pain score, self-report joint count and symptom checklist) gave an AUC of 0.90. An index of four measures (additional fatigue criterion) gave an AUC of 0.93. Both indices correctly classified 89% of patients with a cut-off of 2 and 3 respectively. The physician’s diagnoses had moderate agreement with the FM criteria (kappa = 0.43).

Table 1

<table>
<thead>
<tr>
<th>3 PROs (≥2)</th>
<th>4 PROs (≥3)</th>
<th>Patient global</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>0.90</td>
<td>0.93</td>
</tr>
<tr>
<td>Specificity</td>
<td>78%</td>
<td>74%</td>
</tr>
<tr>
<td>Correctly classified</td>
<td>92%</td>
<td>94%</td>
</tr>
</tbody>
</table>

Conclusion: Comorbid FM is prevalent in SLE yet often missed by physicians. In busy clinical settings, composite indices provide useful clues to coexisting FM in SLE, although a simple MDHAQ patient global is quick and potentially just as valuable in this patient group. These findings require further validation in a larger cohort.

REFERENCES:

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THU0267

THE SLE DISEASE ACTIVITY SCORE (SLE-DAS) ENABLES ACCURATE DEFINITIONS OF SLE REMISSION AND LDA AS ACHIEVABLE TARGETS IN DISEASE MANAGEMENT

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Background: The treat-to-target strategy in Systemic Lupus Erythematosus (SLE) aims to achieve remission. However, to define a target based on the SLE Disease Activity Index (SLEDAI) is questionable, due to its limitations (especially its dichotomous nature). The SLE Disease Activity Score (SLE-DAS) is a recently validated continuous disease activity score which has a higher accuracy in measuring SLE activity and a higher sensitivity-to-change compared to SLEDAI.

Objectives: To assess the ability of SLE-DAS to define SLE remission and other disease activity states.

Methods: Cross-sectional study of SLE patients fulfilling the ACR/1972 and/or SLEDAI12 classification criteria and followed at the Padua Lupus Clinic from March to June 2018. Each outpatient visit, the attending clinician scored SLE disease activity (in the last 30 days) using Physician Global
Assessment (PGA) (0-3 points, 10 cm scale), SLEDAI-2K and SLE-DAS. A senior rheumatologist expert in SLE, blinded to the disease activity scores, classified each patient in 1 of 4 categories: (i) remission, (ii) low disease activity (LDA), (iii) mild disease activity and (iv) moderate/severe disease activity. The best cut-off values of SLE-DAS to define these categories were estimated using Receiver Operating Characteristic (ROC) curve analysis. Accuracy, precision, sensitivity and specificity values for these cut-off values were then calculated. The agreement between the SLE-DAS and physician’s classification was measured using Kappa coefficient. Statistical significance was set at 0.05.

**Results:** We included 221 patients (84.2% female, mean age of 45.4 ±13.5 years, mean disease duration of 15.4±9.5 years). In this preliminary study, the proposed cut-off values of SLE-DAS to define each disease activity category were: remission SLE-DAS≤2.08, LDA 2.08<SLE-DAS<3.77, mild disease activity 3.77<SLE-DAS<7.64, and moderate/severe disease activity SLE-DAS>7.64 for (Table 1). The overall accuracy of these SLE-DAS cut-off values to identify each disease activity state was 96.4%. The agreement between SLE-DAS and physician’s classification was very high (k=0.925, p<0.001). Distribution of SLE-DAS and SLEDAI-2K scores in each disease activity state is presented in Figure 1. According to the SLE-DAS cut-offs, 68.8% of the patients were in remission, 2.3% in LDA, 10.9% in mild disease activity and 18.1% in moderate/severe disease activity.

**Conclusion:** The SLE-DAS has a high precision in identifying remission, LDA, and other disease activity states in SLE. These results suggest that the SLE-DAS is an accurate tool in defining achievable targets in SLE management.

**Abstract THU0267 – Table 1. Performance of SLE-DAS to assess each disease activity state.**

<table>
<thead>
<tr>
<th>Disease activity state</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Precision (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remission</td>
<td>99.3</td>
<td>97.1</td>
<td>98.7</td>
</tr>
<tr>
<td>(SLE-DAS≤2.08)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low Disease Activity</td>
<td>66.7</td>
<td>99.5</td>
<td>80</td>
</tr>
<tr>
<td>(2.08&lt;SLE-DAS&lt;3.77)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild Disease Activity</td>
<td>88.0</td>
<td>99.0</td>
<td>91.7</td>
</tr>
<tr>
<td>(3.77&lt;SLE-DAS&lt;7.64)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate/Severe Disease Activity</td>
<td>94.9</td>
<td>98.4</td>
<td>92.5</td>
</tr>
<tr>
<td>(SLE-DAS&gt;7.64)</td>
<td></td>
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</tbody>
</table>

**References:**


**Disclosure of Interests:** None declared

**THU0269**

**CLINICAL AND LABORATORY FEATURES OF PRIMARY SJÖGREN’S SYNDROME ASSOCIATED WITH ANTICENTROMEREB ANTIBODIES**

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**Background:** The prevalence of ACA among patients with pSS ranges from 2% to 27%. Among experts, there is a lot of controversy about whether primary Sjogren’s syndrome with ACA is a separate disease subtype or overlap-syndrome with systemic sclerosis.

**Objectives:** To evaluate clinical and laboratory features of anticientromere antibody-positive (ACA) primary Sjögren’s syndrome (pSS); to evaluate the spectrum of autoantibodies in patients of this group; to evaluate conformity of the patients to the pSS and systemic sclerosis (SSc) classification criteria; to evaluate prevalence of salivary MALT-lymphoma in this group of patients; to evaluate prevalence of primary biliary cirrhosis (PBC)/biliary lesions in this group of patients.

**Methods:** From 2012 to 2018, we examined 83 patients with pSS and ACA. Inclusion criteria were conformity to the 2001 Russian Sjögren’s syndrome criteria and high ACA titer. We used ACR 2012 and ACR/EULAR 2016 criteria to evaluate conformity to the pSS, and ACR 2013 criteria to evaluate conformity to the SSc. Diagnosis of salivary MALT lymphoma was established on the basis of histological, immunohistochemical and PCR studies of biopsy specimens of parotid salivary glands.

**Results:** We found a low detection rate of anti-Ro antibodies (32.5%), anti-La antibodies (7.2%), RF (21.7%), increased ESR (14%), leukenopia (7%), hypergammaglobulinemia (17.6%), increased IgG (9.5%), increased IgA (18.7%) hypocomplementemia (16.1%) in the group of patients with pSS and ACA. Despite the low frequency of detection of the RF, some patients of this group had MALT-lymphoma: 14 patients had salivary MALT-lymphoma (16.8%), one patient had tonsil MALT-lymphoma with nodal involvement (1.2%). In addition, patients of this group are characterized by a high frequency of detection of AMA antibodies 17/52(32.7%), increased IgM (29.7%) and increased risk of biliary lesions (14.4%). According to our data increased risk of developing biliary lesions (28.5%), primary biliary cirrhosis (28.5%), autoimmune hepatitis (AIH) (28.5%), overlap-syndrome between PBC and AIH (14.5%) was observed in patients with functional signs of liver damage (ALT/AST, GGT, ALP >2N), AMA-positivity, high levels of IgM. Only two patients, who were diagnosed with liver disease according to studies of biopsy specimens, lacked AMA-antibodies. Damage to the nervous system, kidneys, antiphospholipid syndrome, rheumatoid arthritis, hypergammaglobulinemia, purpura and cryoglobulinemic vasculitis were much less common and were single. Also patients with pSS and ACA often have Raynaud’s phenomenon (54.9%) with capillaroscopic changes of the scleroderma type (68%) and an increased risk of developing limited form of systemic scleroderma (24%).

Conclusion: pSS associated with ACA is a subtype of the disease, significantly different from the “classic” in a number of clinical and laboratory signs and characterized by an increased risk of SSc and PBC/biliary lesions which in some cases leads to the underdiagnosis of pSS. ACA should be considered as pathogenetically related to pSS antibodies and all ACA-positive patients should be examined for pSS and PBC/biliary lesions regardless of whether they have SSc or not. Patients with a significant enlargement of salivary glands should be biopsied to confirm the presence of MALT-lymphoma before initiating hormonal, antilymphoproliferative and anti-B-cell therapy.

**Disclosure of Interests:** None declared


**THU0269**

**SERUM IL-6 AND CIRCULATING IMMUNE COMPLEXES AS BIOMARKERS OF DISEASE ACTIVITY IN MULTI-ETHNIC ASIAN SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Background:** IL-6 plays an important role in B cell hyperactivity and immunopathology of systemic lupus erythematosus (SLE), and may have a direct role in mediating tissue damage [1]. Elevated levels of serum
circulating immune complexes (CICs) have been described in SLE but the relationship with disease activity in our multi-ethnic Asian patients remains unclear.

Objectives: To determine the correlation between disease activity and the levels of CICs, serum and urine IL-6 in a Singapore cohort of multi-ethnic Asian SLE patients.

Methods: Serum levels of CICs, IL-6 and urine IL-6 were measured in 88 SLE patients using CIC-C1q and high sensitivity IL-6 ELISAs. All patients fulfilled the 1997 revised American College of Rheumatology (ACR) classification criteria. Clinical and laboratory manifestations, therapy, disease activity and damage at the time of sample collection was collated. Disease activity was scored with the SLE Activity Measure-revised (SLAM-R) and damage with the ACR/Systemic Lupus International Collaborating Clinic SLE damage index (SDI). The correlation between disease activity score and CICs, serum and urine IL-6 were assessed using Spearman’s correlation. Receiver operator characteristic (ROC) curve analysis was performed to assess the performance of the individual biomarkers in discriminating SLE disease activity.

Results: The cohort of 88 patients were predominantly female (n = 78, 89.6%), with a mean age of 40 years±13.1. The majority were of Chinese ethnicity (n = 73, 83%), 13% were Malay (n = 11) and 4 individuals were of other races. The mean disease duration was 98.4 months ± 86.4. The mean scores of SLAM-R and SDI were 2.9 ± 2.2 and 0.9 ± 0.9 respectively. SLE disease manifestations at the time of sample collection included mucocutaneous involvement (5.7%) and active urine sediment (28.7%). 77% had hypocomplementemia and 70.1% had elevated titres of anti-dsDNA antibody. The majority were on corticosteroids (75.9%) and hydroxychloroquine (65.5%). Immunosuppressive drugs included azathioprine in 37.9%, mycophenolate in 69.4%, intravenous pulse cyclophosphamide in 6.9% and cyclosporin in 1 patient. There was significant positive correlation between SLAM-R and serum CICs (R = 0.4121, p < 0.01), serum IL-6 (R = 0.4227, p < 0.01) and urine IL-6 (R = 0.3142, p = 0.01). Based on the area under the curve(AUC), CICs and urine IL-6 were better in discriminating active SLE (AUC 0.8002, p < 0.01 and AUC 0.7397, p < 0.01 respectively) compared to serum IL-6 (AUC 0.5554, p = 0.1718).

Conclusion: Our study observed significant correlation between levels of serum circulating immune complexes, serum and urine IL-6 with SLE disease activity in our multi-ethnic Asian SLE patient cohort. ROC curve analysis suggests that serum CICs and urine IL-6 may serve as sensitive biomarkers to identify SLE patients at risk of flares.


be the strongest inhibitor of TNF-α among cytokines involved in pSS pathogenesis, iii) results may explain the ineffectiveness of anti-TNF drugs in the treatment of pSS

REFERENCES:


Disclosure of Interests: None declared

THU0272

FUNCTIONAL GASTROINTESTINAL DISORDERS IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with multisystemic involvement. Gastrointestinal (GI) manifestations are frequent in patients with SLE, but functional gastrointestinal disorders (FGIDs), a heterogeneous group of GI diseases have hardly been evaluated in SLE patients.

Objectives: We evaluated the prevalence of FGIDs in SLE patients compared with age-matched controls and the role of potential risk factors for FGIDs.

Methods: SLE patients who met the ACR classification criteria for SLE and age-matched controls completed the Rome III questionnaire to assess the prevalence of FGIDs. Exclusion criteria were organic gastrointestinal disorders. Patients completed a structured interview to assess sociodemographic, clinical and treatment variables. Logistic multivariate analysis was performed to determine potential clinical factors (alcohol ingestion and medications) for FGIDs.

Results: The study responders included 116 SLE patients and 122 controls. The prevalence of FGIDs was higher in SLE patients than in controls (74.1% vs. 54.1%; p = 0.01). The most frequent FGIDs were nausea and vomiting disorders, belching disorders and globus pharyngeus. Anorectal disorders, mainly anorectal pain, were more frequent in SLE patients than controls (14.7% vs. 5.7%). After adjusting for confounding variables, SLE was associated with globus pharyngeus (OR: 3.5, 95% CI: 1.3-9.3), functional heartburn (OR: 2.5, 95% CI: 1.5-4.4), nausea and vomiting disorders (OR: 7.1, 95% CI: 2.7-19.1) and anorectal disorders (OR: 3.4, 95% CI: 1.4-8.4). Overlap symptoms were present in 69.8% of patients vs. 31.6% of controls. When only SLE patients were evaluated, glucocorticoid therapy and non-steroidal anti-inflammatory drugs (NSAIDs) were associated with any FGID and functional bowel disorders, while alcohol ingestion was associated with gallbladder and sphincter of Oddi disorders.

Conclusion: There is a higher prevalence of FGIDs in patients with SLE and a wider distribution of various GI tract symptoms compared with controls. Medication that may alter gastrointestinal homeostasis, such as NSAIDs and protein pump inhibitors, were associated with FGIDs in SLE patients.

Disclosure of Interests: None declared

THU0273

EVALUATION OF RELAPSE RATE AND LIFE PROGNOSIS AFTER INDUCTION THERAPY IN PROLIFERATIVE AND MEMBRANOUS LUPUS NEPHRITIS

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Background: The most common cause of morbidity and mortality in systemic lupus erythematosus (SLE) is lupus nephritis (LN). Renal flares are disadvantageous to the renal function of patients with severe LN, and the flares contribute to morbidity in patients with SLE. The reported incidence of renal flares has varied with the populations studied, the distributions of histological classes of LN, the treatment administered and the definitions of renal flare.

Objectives: Here we evaluated the relapse rate and life prognosis after induction therapy in proliferative and membranous LN.

Methods: We retrospectively analyzed the cases of 151 patients who underwent renal biopsy at our hospital and community hospitals from 1993 to 2016. We determined the complete response (CR) rate at 6 and 12 months after induction therapy and evaluated the predictive factors for CR, relapse rate, and life prognosis in proliferative and membranous LN.

Results: We were able to evaluate the therapeutic response, relapse rate and life prognosis at 6 and 12 months after therapy was introduced in 140 cases. Most of the patients were female (84.3%). The median age at LN onset was 34.0 years (interquartile range [IQR] 25.3–45.0 years), and the disease duration of SLE was 42 months (IQR: 2.0–121.0 months). The median follow-up duration after renal biopsy was 96 months (IQR: 44.0–168.0 months). The renal pathology of 99 (70.7%) patients was classified as ISN/RPS Class III or IV, and 41 (29.3%) patients were ISN/RPS Class V. Thirty-five patients (35.4%) were Class III or IV, and 17 patients (41.5%) in Class V achieved a CR at 6 months. Fifty patients (50.5%) in Class III/IV and 22 patients (53.7%) in Class V achieved a CR at 12 months. A multivariate analysis showed that the relapse rate and life prognosis were not different between proliferative and membranous LN.

Conclusion: Our results suggest that the predictive factors for a CR at 12 months after induction therapy are a lower index of chronicity in class III/IV, and neutrophil infiltration and CH50 in Class V were predictive factors for achieving a CR at 12 months. A Kaplan-Meier analysis showed that the relapse rate and life prognosis were not different between proliferative and membranous LN.

REFERENCES:


Disclosure of Interests: Momoko Okamoto: None declared, Kunihiro Ichinose: None declared, Mineaki Kitamura: None declared, Shuntaro Sato: None declared, Keita Fujikawa: None declared, Yoshiro Horai: None declared, Naoki Matsuoka: None declared, Masahiko Tsubo: None declared, Fumiaki Nonaka: None declared, Yukitaka Ueki: None declared, Toshimasa Shimizu: None declared, Tomohiro Koga: None declared, Shin-ya Kawashiri: None declared, Naoki Iwamoto: None declared, Mami Tamai: None declared, Hideki Nakamura: None declared, Tomoki Oriuchi: None declared.
None declared, Tomoya Nishino: None declared, Atsushi Kawakami Grant/research support from: Astellas Pharma, Consultant for: Astellas Pharma, Speakers bureau: Astellas Pharma.


THU0274 QUALITATIVE AND QUANTITATIVE ANALYSIS OF THE IMMUNOLOGIC CHARACTERISTICS OF THE MINOR SALIVARY GLAND BIOPSY IN SJÖGRÖN'S SYNDROME

Luisa Llorca1, Laura Martínez-Martínez1, Mª Berta Magallares1,2, Ivan Castellvi1, Cesar Díaz-Tormé1, Ana Laiz1, Patricia Moya2,3, Ana Milena Millán Acínegas1, Andrea García-Guillén1,1, Sylvie Jeria1, David Lobo1, Susana P. Fernandez-Sánchez1, Conceita Pitarlech1, Manel Riera1, María Carmen Hernández Lafuente1,2, Conchita Pitarch1,2, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain; Hospital Dos de Maig, Barcelona, Spain

Background: Minor salivary gland biopsy (MSGB) is the most important diagnostic test of Sjögren’s Syndrome (SS). It demonstrates the presence of the inflammatory infiltration in the most affected site. It’s possible role as a biomarker in the disease is still unknown. The Immunology Department of our center conducts a detailed analysis of the MSGB about the leukocyte infiltration and quantities number of each cell.

Objectives: To describe the immunologic features of the MSGB and carry out an association analysis with clinical variables.

Methods: Clinical variables, ESSDAI index at the moment of diagnosis and laboratory parameters were recorded. As from the MSGB, number of infiltration focus (1, 2 or several), big infiltrations (>100 cells), number of B and T cells, CD4/CD8 ratio and presence of isolated lymphocyte were collected. Categorical variables were described as frequencies and analyzed using Fisher exact test. T patient and Wilcoxon Rank Sum Test were used for comparison of means (μ).

Results: In total, a mean of 104 MSGB were carried out in our center. Among them 58 were diagnosed as SS by medical and ACR/EULAR 2016 criteria. Finally 41 patients with SS and abnormal MSGB result were included for this study.

<table>
<thead>
<tr>
<th>Basal characteristics of patients</th>
<th>Frequency (number/percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>8/19.5%</td>
</tr>
<tr>
<td>Extraglandular disease</td>
<td>18/43.9%</td>
</tr>
<tr>
<td>ESSDAI≥2</td>
<td>17/41.46%</td>
</tr>
<tr>
<td>Other autoimmune diseases</td>
<td>2/4.87%</td>
</tr>
<tr>
<td>Ac, Ro,La</td>
<td>0/0</td>
</tr>
<tr>
<td>CRP</td>
<td>13/31.71%</td>
</tr>
<tr>
<td>ANA pattern</td>
<td>(μ 9.79mg/dl)</td>
</tr>
<tr>
<td>Negative</td>
<td>8/19.51%</td>
</tr>
<tr>
<td>Homogenous</td>
<td>5/12.44%</td>
</tr>
<tr>
<td>Speckled</td>
<td>16/39.02%</td>
</tr>
<tr>
<td>Speckled and Homogeneous</td>
<td>10/24.39%</td>
</tr>
<tr>
<td>Other</td>
<td>6/14.64%</td>
</tr>
</tbody>
</table>

Biopsy: Patients with active disease (ESSDAI≥2) had greater amount of cells (μ 159 cells vs 509 cells; p=0.055) as well as those with extraglandular disease (μ 160 vs 488; p=0.08). Patients with active disease also had larger number of infiltration focus (p= 0.062). The presence of isolated CD8+ T cells was observed in 13 patients and they had lesser (μ 136 vs 381; p=0.35). In those with predominance of T cells over B cells had larger number of infiltrate focus (7/20; 35% vs 12/21; 57.14%; p<0.155). No association with disease activity or extraglandular manifestation was found.

Extraglandular manifestation and disease activity: 18 patients had extraglandular disease. Moderate or severe ESSDAI activity was found in 14 of these patients (34.2%, p=0.00). The biopsy of patients with extraglandular disease had larger amount of cells (μ 200 vs 145; p=0.01). Patients with active disease had more infiltrate focus (6/22 vs 11/19; p=0.047).

Disease evolution time was similar with a mean duration of 8-9 years in both groups.

Corticosteroids: There were 3 patients with active steroid treatment (>prednisone 10mg/d) at the moment of the biopsy. All 3 of them had >1 focus in the sample and 2 of them had large infiltrate with >150 cells. Eight of them had received steroids in the last 5 years, 6 of them had large infiltrate with >150 cells and 4 had >1 infiltrate focus in the biopsy. A study with more sample should be carried out to study the influence of steroids in the biopsy results.

Conclusion: Patients with extraglandular disease have larger amount of cells in the composition of infiltration. Those with more disease activity had more number of infiltration focus.

In 14 patients specific antibodies and antinuclear antibodies were negative. In these patients the biopsy is the most useful diagnostic test.

Possible association of those variables that were statistically not significant should not be ruled out due to the small sample size of the study.

Disclosure of Interests: HYE SANG PARK: None declared, LAURA MARTINEZ MARTINEZ: None declared, Berta Magallares: None declared, Ivan Castellvi Consultant for: I received fees less than 500USD as a consultant for Kern and Actelion, Paid instructor for: I received fees less than 2000USD as a instructor for Boehringer -Ingehelm, Novartis and Gebro, Speakers bureau: ND, Cesar Diaz-Tormé: None declared, Ana Laiz Consultant for: Lilly, Novartis, AbbVie, MSD, UCB and Janssen, Speakers bureau: Lilly, Novartis, Abvieve, MSD, UCB and Janssen, Patricia Moya: None declared, Ana Milena Millán Acínegas: None declared, Andrea García-Guillén: None declared, Sylvie Jeria: None declared, David Lobo: None declared, Susana P. Fernandez-Sanchez: None declared, Conchita Pitarch: None declared, Manel Riera: None declared, María Carmen Hernández Lafuente: None declared, Conchito Juarez: None declared, Hector Corominas: None declared.


THU0275 NEW PROSPECTIVE OF COGNITIVE IMPAIRMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: A PRAGMATIC LANGUAGE EVALUATION

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Background: Cognitive impairment (CI) in Systemic Lupus Erythematosus (SLE) is a frequent neuropsychiatric manifestation affecting several domains, even in apparently asymptomatic patients. Current research revealed that the typical CI pattern affects frontal-subcortical circuit and thus executive functions. The impairment of non-literal language or Pragmatic Language (PL), including metaphors, idioms, inferences or irony has been well described in several conditions such as autism disorders, Parkinson’s disease, brain injury and even in earlier phases of neurodegenerative processes. Even if PL neuro-anatomy remains controversial, correlation between executive dysfunctions and non-literal language involvement has been reported both in traumatic injury and mild cognitive impairment patients. Nonetheless, no specific study has been performed to evaluate PL impairment in SLE patients so far.

Objectives: We aimed at assessing the PL domain in a monocentric SLE cohort in comparison to healthy controls, matched to age and education, through a specific battery, BLED [1]. Secondly, we focused attention on possible correlations between CI and clinical and laboratory SLE-related features.

Methods: Forty adult patients affected by SLE, according to the ACR criteria, and thirty healthy subjects were enrolled consecutively in this cross-sectional study. The protocol included complete physical examination, extensive clinical and laboratory data collection (comprehensive of demographics, past medical history, co-morbidities, disease activity, chronic damage evaluation, previous and concomitant treatments) and cognitive assessment for five different domains: memory, attention, pragmatic language, executive and visuospatial functions. Self-reported scale for anxiety and depression were performed to exclude the influence of mood disorders on cognitive dysfunction.

Results: We enrolled forty Caucasian SLE patients (M/F 3/37; mean±SD age 45.9±10.1 years, mean±SD disease duration 120.8±81.2 months) and thirty healthy subjects (M/F 9/21; mean±SD age 41.3±13 years). According to the low level of disease activity and damage (mean±SD SLEDAI-2K of 1.3±2.3, mean±SD SDI of 0.2±0.5), only 30% of patients was on glucocorticoid treatment at the study entry. PL was the most compromised domain in terms of Mean Domain Z scores (Fig. 1). As regards the Domain Cognitive Dysfunction score, a deficit of PL was observed in 45% of participants and significantly prevalent than memory, executive and visuospatial functions impairment (P=0.0002, P=0.0002 and P<0.000001, respectively). According to Global Cognitive Dysfunction score 25% of patients experienced a mild impairment and 7.5% a moderate one. Anti-phospholipid antibodies positivity was significantly associated with memory impairment (P<0.0005), whereas the presence of other neuropsychiatric events was associated with executive dysfunctions (P<0.05); neither further significant association nor correlation were identified.
CHARACTERISTICS OF NEUROLOGIC INVOLVEMENT AND ITS RELATED FACTORS IN PRIMARY SJÖGREN SYNDROME

mindi qiu, Yutong Jiang, Wen Yang, Jieruo Gu. The third affiliated Hospital of Sun Yat-sen University, rheumatology, guangzhou, China

Background: Neurological manifestations seem common in primary Sjögren’s syndrome (pSS), but their reported prevalences vary in Chinese. And few studies reveal if the disease activity is associated with neurological involvement.

Objectives: To analyze the clinical neurological manifestations of primary Sjögren syndrome (pSS), and to evaluate the relationship with disease activity.

Methods: 112 patients (79 male, 33 female) who fulfilled the 2002 American-European Consensus Group criteria for pSS were enrolled in the study. For each patient, the clinical features were evaluated by medical data including clinical, laboratory and immunologic data, and neurological examinations including electromyography, magnetic resonance imaging, cerebrospinal fluid, and electroencephalogram. Statistical methods used were t-test, chi-square test and Logistic regression.

Results: Data were available for 112 patients, whose mean age was 55±10 years. Neurological involvement was noted in 19.6(22/112) patients, including 17(15.2%) with peripheral nervous system (PNS) manifestations and 2(1.8%) with central nervous system (CNS) manifestations and 2(1.8%) with both PNS and CNS involvements. Optic neuritis and trigeminal neuralgia were revealed frequently in cranial neuropathy. Anti-aquaporin 4 antibody was detected in two patients with optic neuritis. The clinical spectrum of peripheral neuropathies encountered in Sjögren’s syndrome patients was wide with sensory neuropathies being the most common. Tibal neuralgia, peroneal nerve and sural nerve were the most likely involved and lower limb involvement accounted for 68.4%(13/19). The frequency of Raynaud’s phenomenon was significantly higher(31.8%(7/22) vs 4.4%(4/90), P=0.01) as well as acroanesthesia(72.7% vs 8.9%, P=0.01) in pSS with neurological involvement than in pSS without neuropathy. The median values of EULAR Sjögren’s syndrome disease activity index (ESSDAI) were 5.6(range 2.6-7.6) and 3.2(range 1.4-5.2) in the NS and non-NS groups respectively(P<0.01). We found a significant rise of neuropathy risk associated with Raynaud’s phenomenon(relative risk 9.365, 95%CI 3.191 to 24.039, P<0.001) as well as acroanesthesia(relative risk 1.628, 95%CI 1.169 to 2.231, P=0.001). Elevated levels of rheumatoid factor(P<0.05) and ANA(P<0.01) were common in patients with neuropathy.

Conclusion: Neuropathy is not a rare manifestation of pSS. Prevalence of neurological involvement in pSS is 19.6%. Raynaud’s phenomenon and high disease activity may be the risk factors for neuropathy. Autoantibodies might contribute to the injury of the nervous system.

REFERENCES:

THU0277

HOW THE AGE AT DIAGNOSIS MODIFIES THE PHENOTYPE OF PRIMARY SJÖGREN SYNDROME: ANALYSIS IN 11,420 PATIENTS (BIG DATA SJÖGREN PROJECT)

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Objectives: To analyse how the age at diagnosis modifies the phenotype of primary Sjögren syndrome (SS). Methods: The Big Data Sjögren Project was formed in 2014 to take a high-definition picture of the main features of primary SS at diagnosis by merging international SS databases. By January 2019, the database included 11,420 patients from 24 countries of the 5 continents.

Results: Women (52.7 vs 54.6 yrs in men, p<0.001) and non-White patients (49.6 vs 53.5 yrs in Whites, p<0.001) were diagnosed at a younger age. Patients without sicca symptoms, with normal oral/ocular diagnostic tests and with positive biopsy were also diagnosed at younger ages (p<0.001 all comparisons).

REFERENCES:
Patients with positive immunological markers had a younger diagnostic age, except for cryoglobulins (p<0.001 all comparisons).

Patients without systemic activity (ESSDAI score = 0) were diagnosed at an older age (55.5 vs 52.1 yrs in those with systemic activity, p<0.001). There was a wide variation in the age at diagnosis of patients presenting with systemic activity according to the organ involved.

**Conclusion:** Age at diagnosis plays a key role in the glandular and systemic phenotype expressed by primary SjS patients at the time of diagnosis.

**Disclosure of Interests:** Soledad Retamozo: None declared, Nihan Acar-Denizli: None declared, Wan Fai Ng: None declared, Idledi Fanny Horváth: None declared, Astrid Rasmussen: None declared, Raphaèle Seror-Grat/research support from: Pfizer, Consultant for: Bristol-Myers Squibb, Pfizer, Amgen, Eli Lilly, Roche, Celgene, GlaxoSmithKline, MedImmune, Xiaomei Li: None declared, Chiara Baldini: None declared, Jacques-Eric Gottenberg Grant/research support from: Bristol-Myers Squibb, Grant/research support from: Bristol-Myers Squibb, Consultant for: Bristol-Myers Squibb, Lilly, Pfizer, Sanofi-Genzyme, UCB Pharma, Consultant for: Bristol-Myers Squibb, Eli Lilly, UCB, Sanofi-Genzyme, Pfizer, Pulukool Sandhya: None declared, Luca Quartuccio: None declared, Roberta Priör: None declared, Gabriela Hernandez-Molina: None declared, Berkan Arman: None declared, Aike A. Kruize: None declared, Seung-Ki Kwok: None declared, Gabriela Hernandez-Molina: None declared, Berkan Arman: None declared, Aike A. Kruize: None declared, Seung-Ki Kwok: None declared, Gabriela Hernandez-Molina: None declared, Berkan Arman: None declared, Aike A. Kruize: None declared, Seung-Ki Kwok: None declared, Gabriela Hernandez-Molina: None declared, Berkan Arman: None declared, Aike A. Kruize: None declared, Seung-Ki Kwok: None declared.
supplementation with omega-3 PUFAs might be beneficial. Omega-3 PUFAs can be metabolized to specialized pro-resolving mediators (SPMs) in inflamed tissues. PUFAs, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), give rise to protectins and E-series and D-series resolvins, respectively. These SPMs help promote tissue repair and healing in addition to reducing neutrophil infiltration.

**Objectives:** To investigate (1) if SPMs can be measured in lupus patient serum and plasma. Both EPA and DHA were significantly decreased in SLE patients compared to controls. (2) To evaluate if history of nephritis and disease activity were correlated with lower levels of PUFAs and some SPMs are associated with history of nephritis.

**Methods:** Blood samples were collected from 12 patients enrolled in the Autoimmune Disease Registry and Repository, a single center registry (1996-present) of patients meeting ACR SLE classification criteria. Samples were collected from 12 non-SLE-controls who were age (± 5 years) and race/ethnicity matched. Metabolomic profiling via tandem mass spectrometry (LC-MS-MS) was performed on serum and plasma to assess the PUFAs and SPM levels. Results: Levels of EPA and DHA were highly correlated in serum and plasma. Both EPA and DHA were significantly decreased in SLE patients compared to controls (Table 1). Neither plasma nor serum DHA or EPA levels was correlated with disease activity assessed by SLEDAI score. SPMs including D1 and RvE1 as well as their precursors, 17-HDHA and 18-HEPE, were identified in plasma and serum samples from SLE patients. Plasma levels of 17-HDHA, as well as serum levels of PD1, 17-HDHA, and 18-HEPE tended to be reduced in SLE (Table 1). The SLE patients with a history of nephritis had significantly lower levels of DHA (p<0.03), EPA (p<0.05), 18-HEPE (p<0.03), and 17-HDHA (p<0.04) than SLE patients without nephritis. Conclusion: SLE patients have lower levels of circulating EPA and DHA, the substrates for SPMs, relative to individuals without SLE. Lower levels of these PUFAs and some SPMs are associated with history of nephritis. Additionally, the levels of PD1, 17-HDHA, and 18-HEPE were measurable in SLE serum and plasma and tended to be reduced, especially in subjects with lupus nephritis. SPMs suppress the production of inflammatory mediators and promote resolution of inflammation. The lower levels of PUFAs and SPMs could contribute to the likelihood of developing lupus nephritis. Further evaluation of this relationship is warranted.

Abstract THU0279 – Table 1. Metabolomics of SLE and Control Serum

<table>
<thead>
<tr>
<th>Metabolite (in serum) mean (SD)</th>
<th>Control (n=12)</th>
<th>SLE (n=12)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>EPA (3.802.9)</td>
<td>0.013</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DHA (561.3)</td>
<td>0.003</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PD1 (57.1)</td>
<td>0.498</td>
<td></td>
<td></td>
</tr>
<tr>
<td>17-HDHA (14.9)</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18-HEPE (1.3)</td>
<td>0.195</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Disclosure of Interests:** Julia Davis-Porada: None declared, Charles Serhan: None declared, Peter Lipsky Consultant for: Consulting fees from Horizon Pharma, Jane E. Salmon Shareholder of: Biogen-Idec, BMS, Johnson & Johnson, Regeneron, Merck, Grant/ research support from: UCB, Consultant for: BMS, Ionis


THU0280 SEXUAL FUNCTION IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A CASE-CONTROL STUDY

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**Background:** Normal sexual function consists in the transition, during sexual activity, through the phases of excitement to relaxation without problems, and with a feeling of pleasure, satisfaction and fulfillment (1). The effect of systemic lupus erythematosus (SLE) in sexual function has been one of the least studied areas, but it is thought that some disease-related characteristics could have a negative effect. There are few previous studies that investigate sexual function in SLE, general results indicate a negative impact (2).

**Objectives:** The main aim of this study is to determine if there is an altered sexual function in Mexican women with SLE and compare it if it occurs in a greater proportion than in healthy women.

**Methods:** A case-control study with 102 Mexican women between 18 and 60 years, with SLE diagnosis (according to SLICC 2012 criteria) and a control group of healthy women (n=156) matched by age. Patients were excluded if they couldn’t answer the questionnaires reliably and pregnant women. They were asked about the presence of active sexual life in the last month and the Female Sexual Function Index (FSFI) self-questionnaire was applied. Variables between groups were compared with Chi-square and Mann U Whitney test.

**Results:** Baseline demographic characteristics between groups are shown in table 1. Women with SLE had less sexual activity, during the last month, than controls (63.7% vs 77.5%, p = 0.01). Out of the total women included, the FSFI was applied only to those that had an active sexual life, 65 with SLE and 121 healthy women. Sexual dysfunction (>26.5 points) was found in 28% women with SLE and in 22% of controls, with no significant differences (p=0.4). In the SLE group, a worse total score was found, as well as alteration in the desire and excitation domains when compared to healthy women (Table 2). In the multivariate linear regression analysis (using FSFI as the variable), no relationship was found with any demographic or disease-related variables.

Abstract THU0280 – Table 1. Comparison of demographic variables between the SLE and control group.

<table>
<thead>
<tr>
<th>Age, years (±SD)</th>
<th>Control group (n=156)</th>
<th>SLE group (n=102)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Civil Status</td>
<td></td>
<td></td>
<td>0.977</td>
</tr>
<tr>
<td>Single, n (%)</td>
<td>56 (35.9)</td>
<td>38 (37.3)</td>
<td></td>
</tr>
<tr>
<td>Married, n (%)</td>
<td>76 (48.7)</td>
<td>47 (46.1)</td>
<td></td>
</tr>
<tr>
<td>Divorced, n (%)</td>
<td>8 (5.1)</td>
<td>6 (5.9)</td>
<td></td>
</tr>
<tr>
<td>Domestic partnership, n (%)</td>
<td>16 (10.3)</td>
<td>11 (10.8)</td>
<td></td>
</tr>
<tr>
<td>Widowed, n (%)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Education &lt; 10 Years, n (%)</td>
<td>91 (58.3)</td>
<td>58 (56.9)</td>
<td>0.815</td>
</tr>
<tr>
<td>Menopause, n (%)</td>
<td>21 (13.5)</td>
<td>23 (22.5)</td>
<td>0.058</td>
</tr>
<tr>
<td>Has children, n (%)</td>
<td>82 (52.6)</td>
<td>69 (67.6)</td>
<td>0.016</td>
</tr>
</tbody>
</table>

Abstract THU0280 – Table 2. Female Sexual Function Index according to group.

<table>
<thead>
<tr>
<th>Female Sexual Function Index</th>
<th>Control group (n=121)</th>
<th>SLE group (n=65)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total, 2–36 points</td>
<td>30.5 (34.8)</td>
<td>29.3 (25.7)</td>
<td>0.017</td>
</tr>
<tr>
<td>Desire (1-6)</td>
<td>5.1 (6)</td>
<td>4.5 (4.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Excitement (0-6)</td>
<td>5.2 (6)</td>
<td>4.8 (4.8)</td>
<td>0.046</td>
</tr>
<tr>
<td>Lubrication (0-6)</td>
<td>5.6 (6)</td>
<td>5.2 (4.8)</td>
<td>0.181</td>
</tr>
<tr>
<td>Orgasm (0-6)</td>
<td>4.2 (4.8)</td>
<td>4.2 (4.2)</td>
<td>0.254</td>
</tr>
<tr>
<td>Satisfaction (0-6)</td>
<td>5.4 (6)</td>
<td>5.4 (4.8)</td>
<td>0.409</td>
</tr>
<tr>
<td>Pain (0-6)</td>
<td>5.6 (6)</td>
<td>5.2 (4.8)</td>
<td>0.590</td>
</tr>
</tbody>
</table>

**-Mann U Whitney or Chi-Square test according to type of variable. SD – Standard Deviation.**

References:


SALIVARY GLAND ULTRASOUND FINDINGS ARE ASSOCIATED WITH CLINICAL AND SEROLOGIC FEATURES IN PRIMARY SJÖGREN’S SYNDROME PATIENTS

Joana Silva1, Daniela Faria1, Joana Neves2, Marcos Cerqueira1, Joana Rodrigues1, Soraia Azevedo1, Sérgio Alcino1, José Tavares-Costa1, Carmo Afonso1, Daniela Peixoto1, Filipa Teixeira1.

Background: Primary Sjögren’s syndrome (pSS) is a multisystem immune-mediated disease characterized by hypofunction of salivary and lacrimal glands and possible multi-organ systemic manifestations. Over the past years, three sets of diagnostic criteria have been proposed, but none included salivary gland ultrasound (SGUS). However, SGUS has been recently applied for diagnosis and there are some reports regarding the correlation of SGUS findings with immunological and serological features in pSS patients (1, 2).

Objectives: To investigate the association of SGUS findings with clinical and analytical features of pSS patients.

Methods: A total of 54 patients diagnosed with pSS, fulfilling both the 2016 ACR/EULAR and 2002 AECG criteria for the disease, followed-up at our Rheumatology department, underwent SGUS evaluation. The par enchymal homogeneity of bilateral parotid and submandibular glands was graded using a score of 0 (normal) to 4 (gross inhomogeneity). Patients were classified into two groups according to the highest US score obtained. The grades 1 and 2 were considered to be normal and grades 3 and 4 to represent pathological SGUS findings. Demographics (age, sex and disease duration), European League Against Rheumatism Sjögren’s Syndrome Disease Activity Index (ESSDAI) and laboratory data (erythrocyte sedimentation rate, autoantibodies, rheumatoid factor, hypergammaglobulinemia, β2-microglobulin and complement levels) were collected and compared between the two SGUS groups.

Results: Differences between the group with pathological SGUS versus the group with normal SGUS are depicted in table 1. Multivariate logistic regression revealed that anti-SSB (OR = 6.6, 95% CI 1.7 to 25.8, p = 0.006) was independently associated with the presence of pathological features in SGUS.

Table 1. Comparison of demographics, clinical and serologic features of pSS according to SGUS.

<table>
<thead>
<tr>
<th></th>
<th>Pathological SGUS (n=19)</th>
<th>Normal SGUS (n=35)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years</td>
<td>54.3±12.6</td>
<td>59.2±13.5</td>
<td>0.497</td>
</tr>
<tr>
<td>Mean disease duration, years</td>
<td>6.6±6.1</td>
<td>7.7±5.2</td>
<td>0.976</td>
</tr>
<tr>
<td>ESSDAI (IQI)</td>
<td>2.2 (0-5)</td>
<td>0.9 (0-1)</td>
<td>0.044</td>
</tr>
<tr>
<td>Mean Sedimentation rate, mm</td>
<td>36.3±22.1</td>
<td>22.7±15.8</td>
<td>0.160</td>
</tr>
<tr>
<td>Antinuclear antibody, n (%)</td>
<td>19 (100)</td>
<td>32 (91.4)</td>
<td>0.544</td>
</tr>
<tr>
<td>Anti-SSA, n (%)</td>
<td>18 (94.7)</td>
<td>27 (77.1)</td>
<td>0.137</td>
</tr>
<tr>
<td>Anti-SSB, n (%)</td>
<td>14 (73.7)</td>
<td>9 (25.7)</td>
<td>0.001</td>
</tr>
<tr>
<td>Rheumatoid factor, n (%)</td>
<td>14 (73.7)</td>
<td>14 (40.0)</td>
<td>0.018</td>
</tr>
<tr>
<td>Hypergammaglobulinemia, n (%)</td>
<td>12 (63.2)</td>
<td>14 (40.0)</td>
<td>0.104</td>
</tr>
<tr>
<td>Mean β2-microglobulin, mg/L</td>
<td>2.9±0.9</td>
<td>2.2±0.7</td>
<td>0.378</td>
</tr>
<tr>
<td>Mean Complement 3, mg/dL</td>
<td>115.1±28.9</td>
<td>120.7±24.5</td>
<td>0.938</td>
</tr>
<tr>
<td>Mean Complement 4, mg/dL</td>
<td>21.6±6.0</td>
<td>21.8±8.1</td>
<td>0.165</td>
</tr>
<tr>
<td>Hydroxychloroquine treatment, n (%)</td>
<td>15 (78.9)</td>
<td>21 (60.0)</td>
<td>0.229</td>
</tr>
</tbody>
</table>

Conclusion: In our study, pathological US findings were associated with higher disease activity and positivity for rheumatoid factor and anti-SSB. Additionally, anti-SSB antibody was strongly and independently associated with pathological US findings in the salivary gland of pSS patients. Further and larger studies are necessary to support these findings and include SGUS as part of the diagnostic criteria for Sjögren’s syndrome.

REFERENCES:

Disclosure of Interests: None declared

THU0282
ULTRASOUND FINDINGS IN THE SALIVARY GLANDS IN A COHORT OF PATIENTS WITH SUSPECTED SJÖGREN’S SYNDROME

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Background: Ultrasound has been shown to be a promising tool in the evaluation of salivary glands for parenchyma changes with the potential to improve diagnosis. The changes range from mild inhomogeneity of the glandular tissue to large vesicular changes almost eliminating all normal glandular tissue. American-European Consensus Group (AECG) classification criteria for SS are often used diagnostically (1).

Objectives: To describe ultrasound findings in salivary glands (SGUS) in a cohort of patients with suspected Sjögren’s syndrome (SS) and assess their positive and negative predictive value for the diagnosis.

Methods: 191 consecutive patients with suspected SS (ocular and/or oral dryness) referred to the department of Rheumatology between March 2017 and March 2018 were evaluated by SGUS as part of the initial evaluation. All had unstimulated sialometry, Schirmer’s test and laboratory test done (including autoantibodies (ANA screening, Rheumatoid factor and anti-cyclic citrullinated peptide, anti-Ro/SSA and anti-La/SSB), and screenings test for hepatitis B+C). In doubtful cases, a minor salivary gland (MSG) biopsy was performed. SGUS was performed with a GE Logiq E9 equipped with a linear ML6-15 probe and included grey-scale evaluation of the submandibular and parotid gland bilaterally. SGUS was considered abnormal when moderate to severe inhomogeneity with anechoic or hypoechoic areas was present in at least one gland.

Results: 63 patients were diagnosed with SS according to the AECG classification criteria - 57 patients with primary SS, 6 with secondary SS. 128 patients with sicca symptoms did not fulfill AECG criteria for SS and none were diagnosed with SS based on other parameters. Demographic data for the cohort is shown in table 1. 55 patients had MSG biopsy performed. The SGUS examination and evaluation was performed in less than 15 min per patient. The sensitivity of SS is 0.51 and the specificity 0.88; the PPV of SGUS for the SS diagnosis was 0.68 and the NPV was 0.78.

The sensitivity of SGUS for positive MSG biopsy was 0.29 and the specificity 0.82 – the PPV was 0.50 and the NPV was 0.65; for abnormal sialometry the sensitivity of SGUS was 0.32 and the specificity 0.82 – the PPV for SGUS was 0.64 and NPV was 0.55.

Table 2 shows the association between SGUS and final diagnosis, MSG biopsy and sialometry, respectively.

Abstract THU0282 – Table 1.

<table>
<thead>
<tr>
<th></th>
<th>Primary SS</th>
<th>Secondary SS</th>
<th>Not fulfilling SS classification criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESSDAI, n (%)</td>
<td>65 (82%)</td>
<td>62 (55%)</td>
<td>105 (27)</td>
</tr>
<tr>
<td>Mean age, years</td>
<td>56 (2-86)</td>
<td>54 (12-80)</td>
<td>56 (12-80)</td>
</tr>
<tr>
<td>Positive pyoderma, n (%)</td>
<td>24 (6%)</td>
<td>22 (38%)</td>
<td>6 (6%)</td>
</tr>
<tr>
<td>Positive Sjögren’s syndrome, n (%)</td>
<td>44 (7%)</td>
<td>45 (7%)</td>
<td>45 (7%)</td>
</tr>
<tr>
<td>Anti-Ro/SSA, n (%)</td>
<td>48 (83%)</td>
<td>48 (83%)</td>
<td>48 (83%)</td>
</tr>
<tr>
<td>Anti-La/SSB, n (%)</td>
<td>31 (57%)</td>
<td>31 (57%)</td>
<td>31 (57%)</td>
</tr>
<tr>
<td>n number, 55 SS &amp; 58 Sjögren’s Syndrome</td>
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</tbody>
</table>

Abstract THU0282 – Table 2.

<table>
<thead>
<tr>
<th></th>
<th>Fulfilled SS classification criteria</th>
<th>Not fulfilling SS classification criteria</th>
<th>Positive MSG biopsy</th>
<th>Negative MSG biopsy</th>
<th>Positive sialometry for SS</th>
<th>Negative sialometry for SS</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESSDAI, n (%)</td>
<td>32 (53%)</td>
<td>45 (78%)</td>
<td>6 (29%)</td>
<td>6 (29%)</td>
<td>30 (52%)</td>
<td>10 (18%)</td>
</tr>
<tr>
<td>Mean age, years</td>
<td>56 (2-86)</td>
<td>54 (12-80)</td>
<td>6 (29%)</td>
<td>6 (29%)</td>
<td>30 (52%)</td>
<td>10 (18%)</td>
</tr>
</tbody>
</table>

n number, 55 SS & 58 Sjögren’s Syndrome, 55/80 mm sialometry salivary gland

Conclusion: SGUS has a high specificity but poor sensitivity for the SS diagnosis with a good NPV and a high specificity for positive MSG.
biopsy and positive sialometry, SGUS is a feasible method for the evaluation of structural changes in the salivary gland and may aid in the diagnosis and classification of SS.

REFERENCE:

Disclosure of Interests: Viktoria Fana: None declared, Uffe Møller Dahn Speakers bureau: Speakers fee from Eli Lilly, Novartis and Roche, Lene Terslev Speakers bureau: Speakers fee from : Roche, Novartis, Pfizer, MSD, BMS, Celgene


THU0283 PATIENT ACCEPTABLE SYMPTOMS STATE (PASS) QUESTIONNAIRE APPLICATION IN THE COHORT OF SLE PATIENTS FROM THE SPANISH SOCIETY OF RHEUMATOLOGY (RELESSER): ASSOCIATION WITH ACTIVITY INDEX


HOSPITAL LUCUS AUGUSTI, LUIGI, Spain; HOSPITAL GRAN CANARIA DR NEGRIN, Gran Canaria, Spain; COMPLEJO HOSPITALARIO UNIVERSITARIO DE VIGO, Vigo, Spain; HOSPITAL DE BELLVITGE, Barcelona, Spain; HOSPITAL GENERAL UNIVERSITARIO GREGORIO MARAÑON, MADRID, Spain; HOSPITAL UNIVERSITARIO 12 DE OCTUBRE, Madrid, Spain; HOSPITAL UNIVERSITARIO ARABA, Añana, Spain; HOSPITAL REGIONAL UNIVERSITARIO DE MALAGA, Malaga, Spain; HOSPITAL GENERAL UNIVERSITARIO GREGORIO MARAÑON, Madrid, Spain; HOSPITAL GERMANS TRIAS I PUJOL, Badalona, Spain; HOSPITAL DE LA PRINCESA, Madrid, Spain; HOSPITAL DE DONOSTIA, Donostia, Spain; HOSPITAL MIGUEL SERVET, Zaragoza, Spain; HOSPITAL JUAN CANALEJO A CORUNA, A Coruña, Spain; HOSPITAL MARQUES DE VALDECILLA, Santander, Spain; HOSPITAL UNIVERSITARIO DE CANARIAS, Las Palmas de Gran Canaria, Spain; HOSPITAL SON LÄTZER, Mallorca, Spain; HOSPITAL CLINICO UNIVERSITARIO SALAMANCA, Salamanca, Spain

Background: Little is known about the patient related outcomes and disease activity in systemic lupus erythematosus. Damage and impact are issues that have not been associated with activity in lupus previously.

Objectives: In a large cohort of systemic lupus erythematosus (SLE) patients, to evaluate the association between a Patient Acceptable Symptoms State (PASS) and three different domains of the disease: activity, patients, PASS was associated with other domains of the disease: activity, impact and effect on patients life. PASS is a simple and reliable patient-reported outcome that can be a useful tool to evaluate patients well-being.

Conclusion: In the largest observational European Registry of SLE patients, PASS was associated with other domains of the disease: activity, impact and impact on patients life. PASS is a simple and reliable patient-reported outcome that can be a useful tool to evaluate patients well-being.

Disclosure of Interests: Tomas Vazquez Rodriguez: None declared, Ilonio Rua Figueiroa: None declared, Victor del Campo Perez: None declared, J. Navarrete Consultant for: Bristol-Myers Squibb, Francisco J Lopez-Longo: None declared, Maria Galindo-Izquierdo: None declared, Eva Tomero Muriel: None declared, Coral Moroñito Rodriguez: None declared, Esther Uriarte Ibañecia: None declared, Antonio Fernandez-Nebro: None declared, Juan Ovallés: None declared, Pilar Rubio Munoz: None declared, Eva Tomero Muriel: None declared, Coral Moroñito Rodriguez: None declared, Esther Uriarte Ibañecia: None declared, Angela Pecondon-Espanol: None declared, Mercedes Freire Gonzalez: None declared, Ricardo Blanco: None declared, Marian Gantes Mora: None declared, Mónica Ibañez Barceló: None declared, Carlos A. Montilla-Morales: None declared, Jose M Pego-Reigosa: None declared


THU0284 WHAT DO HEMATOLOGICAL ABNORMALITIES TELL US IN SLE? RESULTS FROM TWO INDEPENDENT MULTICENTER EUROPEAN SLE COHORTS

Sule Yavuz1, Dondu Canısu2, Dionisios Nikolopoulos2, Francesca Crisafulli3, Ana M Arantunes4, Cristina Adamichou5, Sara Reid6, Chiara Saltanaro7, Laura Andreoli8, Angela Tincani9, Maria Moraes-Fonse2, George Bertisias10, Marta Mosca12, Dan Leonard11, Antonis Fanouriakis13, Lars Ronnlund14, Swedish SLE Network15, The Authors would like to thank Dr. Koray Taslilar for his technical assistance. Uppsala University, Uppsala, Sweden; Eskisehir Jaime Calvo-Alen16, Osmangazi University Hospital, Eskisehir, Turkey; 3.Attikon University Hospital, Athens, Greece; 4.Rheumatology and Clinical Immunology Unit, Spedalì Civilì and University of Brescia, Brescia, Italy; 5.Centro Hospitalar de Lisboa Centro, Lisboa, Portugal; 6.University of Crete, Crete, Greece; 7.University of Pisa, Pisa, Italy; 8.Spedalì Civilì and University of Brescia, Brescia, Italy; 9.Rheumatology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy; 10.SWEedishSLENetwork, Stockholm, Sweden

Background: Detailed analysis of hematological manifestations are limited and their clinical impact on disease remain obscure.

Objectives: To scrutinize factors associated with different hematological abnormalities (HA) in SLE patients and their impact on infections, bleeding and damage accrual.

Methods: A dataset (GIPTSLE) originated from SLE patients in Europe was studied. The dataset consisted of six monthly visits of each patients for at least 2 years. Results were compared with another well-established SLE cohort from Sweden (Swedish SLE network). Patients in both cohorts fulfilled the ACR1997 SLE criteria. Variables collected at each visit included CBC, presence or absence of haemolytic anemia, all domains of SLEDAI\-2K, medications, infection or bleeding episodes, Systemic Lupus International Collaborating Clinics/ACR damage index (SDI), HA occurring at the beginning or during follow-up were defined according to the ACR criteria. HA was only considered in patients with no previous use of immunosuppressives or biologic agents at least 3 months before the first HA events. The Swedish confirmation cohort included all the variables of interest. We excluded all haematological domains from SLEDAI\-2K (SLEDAI) for the analysis. Based on six monthly change in SDI, each visit was labelled either “damage transition/or “non-damage transition”. Generalized estimating equations (GEE), multiple logistic regression, Chi-square test and independent samples t test were used where it was appropriate.

Results: Of the 1430 visits of 286 patients analysed from the first cohort (89.5% female, 95.8% Caucasian, 64.7% dsDNA positive) 60% had at least one HA. At the enrolment, the median (range) disease duration was 8 years (0-38), asSLEDAI\-2K was 6 (0-25) and SDI was 0 (0-6). Upon GEE analysis, lymphopenia was significant for SDI (OR=2.5, 1.0-5.9) Upon GEE analysis after further adjusting prednisolone exposure, HA found be significant for SDI was thrombocytopenia (OR=3.6, 1.04-12.1) but no significant evidence for the dependence of this relationship on time. The effect of lymphopenia was attenuated. HR for bleeding was significant when platelets were below 50K (HR=2.6, 1.15-6.1) Of the 1395 patients when platelets were below 50K (HR=2.6, 1.15-6.1) Of the 1395 patients analysed from the second set (86.8%female, 93.0% Caucasian, 61.6 dsDNA positive), 63.4% had HA. At the last visit, the median (range) disease duration was 14 years (1-65) and SDI was 0 (1-14). Upon multiple regression analysis after adjusting age, sex and prednisolone exposure both thrombocytopenia (OR=2.2, 1.3-3.6) and lymphopenia (OR=1.8, 1.2-
UMBILICAL ARTERIAL DOPPLER ULTRASONOGRAPHY PREDICTS LATE PREGNANCY OUTCOMES IN PATIENTS WITH LUPUS NEPHRITIS: A Multicenter Study From Southern China

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Background: Compared with the general population, patients with lupus nephritis (LN) are still at high risk of adverse pregnancy outcomes (APOs). Umbilical artery is the last vessel upstream of the placenta and is particularly important for placental perfusion and foetal development. Increased umbilical artery resistance could be traced by Doppler velocimetry, which is frequently related to pre-eclampsia, intrauterine growth restriction (IUGR), and foetal distress. Umbilical artery Doppler is used as a screening tool for placenta-related diseases in the general population. However, the predictive value in complications of LN pregnancies has not been widely assessed.

Objectives: To investigate the fetal adverse pregnancy outcomes (APOs) and the predictive value of umbilical arterial Doppler ultrasonography in the third trimester in pregnant women with LN.

Methods: A retrospective cohort study enrolling 203 LN patients with pregnancies from 2007 to 2017 from three centers was performed. These patients received umbilical arterial Doppler ultrasound examination during 28-34 gestational weeks. Doppler velocity waveforms of the umbilical arteries were assessed with resistance index (RI), systolic-diastolic ratio (S/D) and pulsatility index (PI).

Results: Fetal APOs occurred in over half of the patients (103/203, 50.7%). Sixty-six pregnancies (66/203, 32.5%) ended with preterm births. The incidence rate of IUGR was 18.2% (37/203). Fetal distress was noted in 23 pregnancies (23/203, 11.3%). All the Doppler parameters were higher in patients with IUGR, fetal distress and composite APOs than in patients without any APOs. Patients with IUGR and fetal distress had significantly higher values of PI, RI and S/D. It was noted that PI, RI and S/D was higher in patients with premature delivery than those with full-term delivery. However, only the difference of RI and S/D reached statistical significance. RI indicated the highest risk of IUGR and composite APOs. The cut-off values were 0.66 and 0.67, respectively. Sensitivities were 51.4% and 33.7%, and specificities were 87.4% and 92.1%. S/D was also a best predictor for IUGR, with the optimal cut-off value of 2.88. Sensitivity and specificity were comparable with RI. PI over 0.84 was an ideal indicator for fetal distress with an optimal combination of sensitivity (89.5%) and specificity (51.6%).

Conclusion: Fetal complications were frequent in patients with LN. Umbilical arterial Doppler ultrasonography was a useful measure to predict late IUGR, fetal distress and the composite APOs.

Acknowledgement: No

Disclosure of Interests: None declared

ANEURYSM IN BEHÇET’S DISEASE: MANAGEMENT, PROGNOSIS AND MORTALITY

Berkan Armagan,1 Ertuşğan Çağrı Bölek2, Alper Sarı1, Gözde Kübfa Yardımcı1, Bayram Farsızoğlan1, Emre Bilgin1, Fatma Gonca Eldem2, Levent Kılıç3, Omer Karadayı4, Bora Peynircioğlu1, Barbaros Erhan Çil2, Metin Demircin3, Ali Akdoğan1, Sule Araş Bilgen1, Ali İhsan Ertenli1, Sedat Kiraz1, Umut Kalyoncu1, Bayram Farisoğlan1, Carmen Carrasco-Cubero1, Julio Sánchez, Santos Castañeda, Lara Sánchez-Bilbao1, Iñigo González-Mazón1, Monica Calderón-Gorbeck, D. Prieto-Peña1, Miguel Á. González-Gay, Ricardo Blanco2.

Abstract THU0287

Background: Arterial aneurysms are one of the unique features of Behçet’s disease (BD). Although arterial aneurysms are relatively rare, they carry risk of rupture and have poor prognosis.

Objectives: To evaluate the medical and interventional therapies and long-term outcomes of BD patients with extracranial arterial aneurysms.

Methods: We retrospectively reviewed the medical records of 441 BD patients according to ISG criteria between 2013 and 2018 at the Hacettepe University Vaşcitsus University (HUVAC). We determined 45 BD patients with an arterial aneurysm. Six patients with isolated carotid and/or cranial arterial aneurysms who were followed by other clinics excluded from the analysis. Overall, 39 BD patients with an extracranial and extra cranial arterial aneurysm included in the study. Data regarding demographic characteristics, clinical, laboratory and vascular imaging findings, history of medical treatments and outcomes were collected. Vascular intervention of patients were grouped as surgery or endovascular intervention. Radiological response after vascular intervention divided into 3 groups as regression, stable and progression according to radiological evaluation. Regression was defined as a decrease or disappearance of the aneurysm. Stable was defined as no change in the aneurysm diameter. Progression was defined as an increase in diameter of a previous aneurysm or occurrence of a new vascular event. We colligated the stable and regression groups and compared with the progression group. Relapse was defined the progression of the aneurysm which underwent an intervention.

Results: A total of 39 BD patients (Male, 80%) with an arterial aneurysm were analyzed in this study. Mean age and mean age of diagnosis patients were 40.8±11.0 and 29.7±7.7 years, respectively. The clinical features of BD was as follows; oral ulcer 100%, genital ulcer 80.6%, acneiform lesion 47.2%, erythema nodosum 33.3%, pathergy positivity 34.5%, arthritis 27.8%, fever 24.3%, uveitis 34.5%, neurological involvement 30.6% and gastrointestinal involvement 7.7%. Distribution of arterial aneurysms was 51% subclavian, 51% coronary artery & cardiac, 38.8% pulmonary, 10.3% thoracic aorta, 33.3% abdominal aorta, 5.1% renal, 25.6% iliac and 12.8% femoral. Induction and maintenance treatments are characterised in Table 1. Distribution of arterial involvement was as follows; carotid 34.5%, arthritis 27.8%, fever 24.3%, uveitis 34.5%, neurological involvement 30.6% and, gastrointestinal involvement 7.7%. Distribution of arterial involvement was as follows; carotid 34.5%, arthritis 27.8%, fever 24.3%, uveitis 34.5%, neurological involvement 30.6% and, gastrointestinal involvement 7.7%.

Conclusion: Arterial aneurysms in BD have poor prognosis and high mortality. Glucocorticoids, cyclophosphamide and interferon-α are the most preferred treatments for induction and maintenance therapy for aneurysm of the BD. Approximately 2/3 of the patients required a vascular intervention. Clinical and radiological progression was more prominent in the aorta and its branches. As expected, there is more progression in interventional procedures without medical treatment.

Disclosure of Interests: Berkan Armagan: None declared, Ertüşğan Çağrı Bölek: None declared, Alper Sarı: None declared, Gözde Kübfa Yardımcı: None declared, Bayram Farsızoğlan: None declared, Emre Bilgin: None declared, Fatma Gonca Eldem: None declared, Levent Kılıç: None declared, Omer Karadayı: None declared, Bora Peynircioğlu: None declared, Barbaros Erhan Çil: None declared, Metin Demircin: None declared, Ali Akdoğan: None declared, Sule Araş Bilgen: None declared, Ali İhsan Ertenli: None declared, Sedat Kiraz: None declared, Umut Kalyoncu Grant/research support from: MSD, Roche, UCB, Novartis and Pfizer, Consultant for: MSD, Abbvie, Roche, UCB, Novartis, Pfizer and Abdı Ibrahim, Speakers bureau: MSD, Abbvie, Roche, UCB, Novartis, Pfizer and Abdı Ibrahim.


LONG-TERM FOLLOW-UP OF ANTI-IL-6-RECEPTOR TOCILIZUMAB IN REFRACTORY UVEITIS IN PATIENTS WITH BEHÇET’S DISEASE. MULTICENTER STUDY OF 14 PATIENTS IN CLINICAL PRACTICE


Background: Ocular involvement in Behçet’s disease (BD) is a potential severe and disabling complication. Anti-TNF-α agents have shown an improvement of visual outcome in BD-related uveitis refractory to conventional immunosuppressive (IS) drugs. However, these drugs do not achieve control of intraocular inflammation in all patients or are not well tolerated. Tocilizumab (TCZ) has shown efficacy in different refractory ocular inflammatory diseases.

Objectives: To assess the efficacy of long-term therapy with TCZ in refractory uveitis associated to extraocular manifestations (EOM) due to BD.

Methods: Multicenter study of patients with BD refractory to standard systemic therapies.

Results: We followed up 14 patients (9 men/5 women) (26 affected eyes); mean age 40.8±19.5 years. Pattern of ocular involvement: panuveitis (10); 4 with retinal vasculitis), anterior (3) and posterior (1) uveitis; 8 recurrent and 6 chronic; 9 with cystoid macular edema. At TCZ onset, the following EOM were present: oral and/or genital ulcers (10), arthritis (10), folliculitis/pseudofolliculitis (6), erythema nodosum (5), intestinal affection (1) and neurological involvement (3). Before TCZ, they had received corticosteroids (13 intraocular, 12 oral and 1 iv), conventional IS drugs and biologic agents: methotrexate (11), cyclosporine (8), azathioprine (10), colchicine (1), cyclophosphamide (2), mycophenolate mofetil (1), adalimumab (10), infliximab (6), golimumab (3), canakinumab (1), or etanercept (1). TCZ was used in monotherapy (7) or

Abstract THU0288 – Table 2.

Table 2. Figure 2. Evaluation of response according to vascular intervention and induction treatments.

** TCZ was used in monotherapy due to previous intolerance.
combined with conventional IS drugs (7) at 8 mg/kg/iv/4 w (11) or 162 mg/sc/w (3). 

Objectives: The aim of this study was to assess the persistency rate of MCS-related clinical and laboratory indexes after successful treatment with DAA.

Methods: CRESO (Cryoglobulinemia Eradication Study Observational) is a multicentre observational study promoted by the Italian Society of Infectious and Tropical Diseases (SIMIT) and the Italian Group for the Study of Cryoglobulinemias (GISC), aimed to assess the impact of DAA therapy on MCS symptoms and cryoglobulin production. Patients could be enrolled if they presented, during the 12 months before the enrolment, a cryocrit >0.5% and, at least, one episode of palpable purpura or, alternatively, arthralgia and fatigue with at least one symptom among peripheral neuropathy, Raynaud’s phenomenon, lower limb ulcers or nephropathy, and a C4 level <8 mg/dL.

Results: The present analysis was based on clinical and laboratory data of 94 patients (75.5% female with a median age of 67.5 years) that have been followed up for a median time of 24 weeks (IQR 12-24) after SVR12 achievement. At baseline the cryocrit was frankly positive in 85 (90.4%), detectable (>0.5%) in 4 and negative in 4 cases; patients with type II cryoglobulins and C4 levels <8 mg/dL were prevalent, respectively, with 81.5% and 75.9%. Low eGFR values (<45 mL/min/1.73m²) were present in 12 cases (12.8%), 10 patients (10.6%) had a history of B-cell non-Hodgkin’s lymphoma (NHL), and 1 of hepatocellular carcinoma, while liver cirrhosis was diagnosed in 22 cases (23.4%) and glomerulonephritis in 17 cases (18.1%). Patients were treated for 12 (72 cases) or 24 (21 cases) weeks with a total of ten different IFN-free DAA regimens. SVR12 was achieved in all 94 cases. Both prevalence and median cryocrit values decreased significantly after DAA treatment (p<0.0001), however, at the time of the last observation 56.4% of patients were still positive for MCS. The prevalence of purpura and fatigue significantly decreased (p<0.0001) as well sicca syndrome prevalence (p<0.015), while arthralgia and lower limb ulcers decrease did not reach statistical significance. In multivariate analysis, eGFR<45 mL/min/1.73m² was an independent predictor of persistence of cryoglobulin production (AOR 7.7, CI 95% 1.6-37.2; p=0.011). 

Conclusion: CRESO study data confirm the persistence of cryoglobulin production and MCS symptoms in some patients, despite the eradication of HCV. This finding rises questions about the possible further evolution of the disease over time regardless the persistency of its original trigger.

Disclosure of Interests: None declared


THU0290

DISEASE AND TREATMENT-RELATED MORBIDITY IN YOUNG AND ELDERLY PATIENTS WITH ANCA-ASSOCIATED VASCULITIS

Alvise Bert1, Mara Felicetti2, Sara Monti3, Augusta Orlotan3, Roberto Padovan3, Giuliano Brunoni4, Roberto Bortoloti4, Roberto Caporalì5, Carlomaurizio Montecucco6, Franco Schiavon7, Giuseppe Paolozzi7, Santa Chiara Hospital, Rheumatology, Trento, Italy; 6University of Padua, Rheumatology, Padua, Italy; 7University of Padua, Rheumatology, Padua, Italy

Background: Advancing age may be a risk factor for morbidity in antimalarials (ANCA)-associated vasculitides.

Objectives: We aimed to compare the rates and better characterize the type of disease- and treatment-related complications affecting young and elderly patients with AAV.

Methods: All new cases of granulomatosis with polyangiitis or microscopic polyangiitis diagnosed between 2000 and 2016 in referral centers in Northern Italy were included. Patients were stratified by age into young or elderly (<65 years old). Data were collected from time of diagnosis until end of follow-up, with scheduled annual visits or additional visits in case of relapse or complication requiring hospitalization.

Results: Of 141 patients included, 99 were young and 42 elderly at the time of AAV diagnosis. Median follow-up was 58.0 months (25-75% IQR, 31.0-60.0) in young and 48.0 months (25-75% IQR, 23.25-60.0) in elderly patients (p=0.05).

Overall, total chronic damage assessed by Vasculitis Damage Index (VDI) significantly increased in elderly patients compared to young ones during follow-up (+0.28, p<0.05). Although rates of the most common complications scored in the VDI (i.e. arterial hypertension, heart failure, ischemic cardiac vascular complications, diabetes, and malignancy) accumulated over time when analyzed singularly, no difference between the two age groups was observed (p>0.05). Sixty-three (44.7%) patients had acute kidney injury due to AAV-glomerulonephritis at diagnosis, 37 were young and 26 were elderly. In these patients, renal function recovery in the first 6 months was significantly lower for elderly (median 2eGFR (25-75% IQR), 5.3 (0.4-14) mL/min/1.73m² compared to young patients (22.8 (5.9-52.1) mL/min/1.73m², p=0.008) while on induction treatment. Stratification for
ANCA status (MPO-ANCA+ versus PR3-ANCA+), did not change these results. Despite similar immunosuppressive therapy approaches and relapse rates, elderly patients had a higher rate of severe infections compared to younger patients (OR 2.1, 95% CI: 1.1-4.4, p=0.043; Figure below).

Conclusion: Our findings indicate that elderly patients had higher susceptibility to morbidity related to vasculitis or its treatment than younger patients, particularly to worst renal function recovery and higher infection rate.

REFERENCES:

Disclosure of Interests: Alivise Berti: None declared, Mara Felicetti: None declared, Sara Monti: None declared, Augusto Ortolan: None declared, Roberto Padoan: None declared, Giuliano Brunori: None declared, Roberto Bilginer: None declared, Seza Özen Consultant for: Seza Ozen is receiving consultancy fees from Novartis, Speakers bureau: Roche.

THU291

THE CHARACTERISTICS OF PEDIATRIC BEHÇET’S DISEASE IN TURKEY VERSUS ISRAEL

Yonatan Butbul1, Ezgi Deniz Batu2, Hatife Emine Sonmez2, Betül Sözeri3, Nuray Alçak4, Bilginer: None declared, Seza Özen Consultant for: Seza Ozen is receiving consultancy fees from Novartis, Speakers bureau: Roche.


Table 1

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All patients (n=205)</th>
<th>Patients from Turkey (n=165)</th>
<th>Patients from Israel (n=40)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>98 (47.8)</td>
<td>86 (52.1)</td>
<td>12 (30)</td>
<td>0.012</td>
</tr>
<tr>
<td>Age at symptom onset, months, median (min-max)</td>
<td>133 (12)</td>
<td>132 (12-191)</td>
<td>134 (12-190)</td>
<td>1</td>
</tr>
<tr>
<td>Age at diagnosis, months, median (min-max)</td>
<td>156 (49)</td>
<td>156 (48-191)</td>
<td>153 (55-191)</td>
<td>0.96</td>
</tr>
<tr>
<td>Oral aphthosis</td>
<td>204 (99.5)</td>
<td>165 (100)</td>
<td>39 (97.5)</td>
<td>0.195</td>
</tr>
<tr>
<td>Genital aphthosis</td>
<td>134 (65.4)</td>
<td>107 (64.8)</td>
<td>27 (67.5)</td>
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</tr>
<tr>
<td>Skin involvement</td>
<td>100 (48.8)</td>
<td>91 (55.2)</td>
<td>9 (22.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Eye involvement</td>
<td>29 (14.1)</td>
<td>22 (13.3)</td>
<td>7 (17.5)</td>
<td>0.49</td>
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<tr>
<td>Neurologic involvement</td>
<td>30 (14.6)</td>
<td>25 (15.8)</td>
<td>4 (10)</td>
<td>0.35</td>
</tr>
<tr>
<td>Vascular involvement</td>
<td>22 (10.7)</td>
<td>19 (11.5)</td>
<td>3 (7.5)</td>
<td>0.77</td>
</tr>
<tr>
<td>Pathergy positivity</td>
<td>45 (22.3)</td>
<td>42 (25.6)</td>
<td>3 (13)</td>
<td>1.00</td>
</tr>
<tr>
<td>BDCAF at first visit</td>
<td>3 (0-15)</td>
<td>4 (1-15)</td>
<td>2 (0-5)</td>
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<td>BDCAF at last visit</td>
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Conclusion: This is the largest cohort of pediatric BD reported to date. The disease manifestations and disease activity significantly differ among pediatric BD patients from Turkey and Israel which emphasizes the effect of the ethnicity on disease phenotype.

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THU292

EXTRACRANIAL VESSEL INVOLVEMENT IN PATIENTS WITH GIANT CELL ARTERITIS

Monica Calderón-Gómeze1, J. Loricerac, D. Prieto-Peñaa, J. Narváezb, Santos Castañead1, Elena Arrecochea1, Ignacio Villa-Blanco1, Catalina Gomez-Aragoe2, Eva Perez-Pampín2, Vicente Aldasono3, Noelia Alvarez-Rivas4, Nagore Fernandez-Lianto5, María Alvarez del Bueno6, Luisa Marena Rojo7, Francisco Sivera1, Eva Galindez1, Roser Solans-Laqué2, Natalia Palfona8, Jose Ignacio Barno9, Isabel Martinez-Rodrigueze10, Carmen Gonzalez-Vela11, Raquel Dos-Santos12, J. Luis Hernandez1, Miguel A Gonzalez-Gaye1, Ricardo Blanco1,13, Santander, Santander, Spain; Barcelona, Barcelona, Spain; Madrid, Madrid, Spain; Torrelavega, Torrelavega, Spain; Mondragon, Mondragon, Mondragon, Spain; Santiago, Santiago de Compostela, Spain; Lugo, Lugo, Spain; Leiria, Leiria, Spain; Palencia, Palencia, Spain; Alcalaz San Juan, Alcalaz de San Juan, Spain; Alcalaz de San Juan, Spain; Villoria, Villoria, Spain; Pontevedra, Pontevedra, Spain; Granada, Granada, Spain; Vigo, Vigo, Spain; Ourense, Ourense, Spain; Avilés, Avilés, Spain.

Background: Giant cell arteritis (GCA) is a large vessel vasculitis with a predisposition for the cranial branches of the external carotid artery. However, aorta and/or its main branches may also be involved.

THE CHARACTERISTICS OF PEDIATRIC BEHÇET’S DISEASE IN TURKEY VERSUS ISRAEL

Yonatan Butbul1, Ezgi Deniz Batu2, Hatife Emine Sonmez2, Betül Sözeri3, Nuray Alçak4, Bilginer: None declared, Seza Özen Consultant for: Seza Ozen is receiving consultancy fees from Novartis, Speakers bureau: Roche.


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**Objectives:** In a series of patients with GCA who presented extracranial vessel involvement, our aim was to assess a) the vascular territories most frequently affected and b) correlation of a major extension of extracranial vascular involvement with a more severe clinical and analytical features.

**Methods:** Multicenter study of 68 patients with GCA who presented a compromise of extracranial vessels confirmed by PET/CT. Visual analysis of vascular uptake was performed on supra-aortic trunks (SAT), aortic arch (AA), thoracic aorta (TA), abdominal aorta (AbA), iliac arteries (IA), lower limb arteries (LLA), and upper limb arteries (ULA).

**Results:** We evaluated 68 patients with GCA (51±17m) with a mean age of 68±8.3 years. The vascular territories affected were: TA (n=58, 85.29%), SAT (n=38, 55.88%), AbA (n=28, 41.18%), AA (n=18, 26.47%), LLA (n=17, 25%), IA (n=13, 19.12%) and ULA (n=6, 8.82%). We considered 3 groups according to the number of vascular territories affected: a) 1 or 2 territories, b) 3 or 4 territories and c) 5 or more territories and made a comparative study between this groups. In patients with ≥5 vascular territories affected, we observed a higher baseline ESR, and the most frequent systemic manifestations were polymyalgia rheumatica and constitutional symptoms with statistical significance (TABLE). Distribution of categorical variables was compared by the Pearson Chi-squared test. Quantitative variables were analyzed using the ANOVA test.

**Conclusion:** In patients with GCA the involvement of TA is very frequent, followed by the SAT and the AbA. Regarding the laboratory findings, patients with higher levels of ESR presented a major extension of extracranial vascular involvement, as well as presenting PMR and/or constitutional symptoms was also related to more affection of extracranial territories.

**Abstract THU0292 – Table 2.**

<table>
<thead>
<tr>
<th>bDMARDs</th>
<th>N° of previous bDMARDs associated</th>
<th>24-month DRR</th>
<th>Reasons for bDMARDs discontinuation</th>
<th>24-month DRR</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Inefficacy</td>
<td>Toxicity</td>
</tr>
<tr>
<td><strong>BF</strong></td>
<td>0 (0-2)</td>
<td>38 (90%)</td>
<td>69%</td>
<td>5 (12%)</td>
</tr>
<tr>
<td>ADA (12)</td>
<td>0 (0-5)</td>
<td>11 (92%)</td>
<td>56%</td>
<td>4 (33%)</td>
</tr>
<tr>
<td>GOL (7)</td>
<td>2 (0-6)</td>
<td>5 (71%)</td>
<td>71.4%</td>
<td>1 (14%)</td>
</tr>
<tr>
<td>TCZ (17)</td>
<td>1 (0-4)</td>
<td>15 (88%)</td>
<td>41%</td>
<td>7 (41%)</td>
</tr>
<tr>
<td>ANK (4)</td>
<td>2.5 (1-3)</td>
<td>2 (50%)</td>
<td>0%</td>
<td>2 (50%)</td>
</tr>
<tr>
<td>ABT (2)</td>
<td>4.5 (4-5)</td>
<td>1 (50%)</td>
<td>50%</td>
<td>1 (50%)</td>
</tr>
<tr>
<td>RTX (2)</td>
<td>2.5 (2-3)</td>
<td>1 (50%)</td>
<td>0%</td>
<td>2 (100%)</td>
</tr>
<tr>
<td><strong>Overall</strong></td>
<td>0.5 (0-6)</td>
<td>75 (86%)</td>
<td>60%</td>
<td>22 (26%)</td>
</tr>
</tbody>
</table>

**REFERENCES:**


**Disclosure of Interests:** Monica Calderón-Goecke: None declared, J. Loricer: None declared, D. Prieto-Peña: None declared, J. Narváez Consultant for: Bristol-Myers Squibb, Santos Castañeda Consultant for: Amgen, BMS, Pfizer, Lilly, MSD, Roche, Sanofi, UCB, Elena Aurrecoechea: None declared, Ignacio Villa-Blanco: None declared, Catalina Gomez-Arango: None declared, Eva Perez-Pampin: None declared, Vicente Aldasoro: None declared, Noelia Alvarez-Rivas: None declared, Nagore Fernandez-Llano: None declared, Maria Alvarez del Buergo: None declared, Luisa Marena Rojas: None declared, Francisca Sivera: None declared, Elena Galindez: None declared, Roser Solans-Laqué: None declared, Susana Romero-Yuste: None declared, Norberto Ortego: None declared, Marcelino Revenga: None declared, Rafael Milero: None declared, Eva Salgado-Pérez: None declared, Sabela Fernández: None declared, Vanesa Calvo-Rio: None declared, Natalia Palomu-Fontana: None declared, Jose Ignacio Banzo: None declared, Isabel Martinez-Rodriguez: None declared, Carmen González-Vela: None declared, Raquel Dos-Santos: None declared, J. Luis Hernández: None declared, Miguel A González-Gay Grant/research support from: Prof. MA Gonzales-Gay received grants/research supports from Abbvie, MSD, Jansen and Roche., Speakers bureau: Consultation fees/participation in company sponsored speaker’s bureau from Pfizer, Lilly, Sobi, Celgene, Novartis, Roche and Sanofi., Ricardo Blanco Grant/research support from: Abbvie, MSD, and Roche, Consultant for: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen, Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen.

**DOi:** 10.1136/annrheumdis-2019-eular.2184
TREATMENT PATTERNS, DISEASE BURDEN AND OUTCOMES IN PATIENTS WITH GIANT CELL ARTERITIS AND POLYMYALGIA RHEUMATICA

Gary Craig1,2, Keith Knapp2, Bob Salim3, Shalini Mohan4, Margaret Michalska2,4
1Arthritis Northwest, Spokane, United States of America; 2Discus Analytics, Spokane, United States of America; 3Axio Research, Seattle, United States of America; 4Genentech, Inc., South San Francisco, United States of America; 5Genentech, Inc, South San Francisco, United States of America

Abstract THU294

Background: For patients with giant cell arteritis (GCA) and/or polymyalgia rheumatica (PMR), glucocorticoids are the mainstay of treatment. However, due to the chronic nature of these diseases, patients may require continued glucocorticoid treatment to achieve treatment targets or prevent disease relapse, over time resulting in high cumulative doses and associated adverse events.

Objectives: To assess patterns of glucocorticoid use and outcomes in patients with GCA, PMR or both.

Methods: This retrospective cohort study used electronic medical records from a single US community-based rheumatology clinic utilizing the Joint-Map rheumatology software application. Patients age ≥ 50 years with a diagnosis of either GCA or PMR and ≥ 1 entry for glucocorticoid following the diagnosis were included and followed until lost to follow-up or the end of the study period (30 Nov 2017). The index date was defined as the date of first glucocorticoid prescription received at or after the earliest GCA or PMR diagnosis date. Outcomes at 2 years included the proportion of patients achieving remission (defined as not receiving steroids for ≥ 6 months), time to remission, persistence of remission (defined as not receiving steroids for ≥ 6 months and still not receiving steroids at 2 years) and prednisone dose at follow-up, and were compared between patients with GCA only, PMR only or both GCA and PMR. P values are reported using F-test (ANOVA) for continuous variables and Chi-squared test for categorical variables.

Results: We identified 81 patients with GCA only, 779 with PMR only and 97 with GCA and PMR. Mean (SD) age was 70.0 (9.1) years; 64.2% were women. Mean (SD) daily prednisone dose at the index date was 46.7 (30.9) mg for patients with GCA only, 20.1 (14.2) for PMR only and 29.0 (23.4) for patients with both GCA and PMR. Two years after the index date, 32% of patients with GCA only, 32% with PMR only and 27% with GCA and PMR had achieved remission; 17%, 23% and 18% were in persistent remission, respectively (Table 1), with no significant differences between groups. Among patients who achieved remission, overall median time to first remission was 202.5 (0-635) days and was shorter for patients with both GCA and PMR (157 [0-619] days) vs GCA (213 [0-577] days) or PMR (203.5 [0-635] days) only. Kaplan-Meier estimates of time to remission for each group are shown (Figure 1). Most patients required a daily prednisone dose at 2 years, with similar doses observed between groups (Table 2).

Conclusion: Patients with either GCA and/or PMR are exposed to significant doses of prednisone. In this study, fewer than one-third of patients with GCA and/or PMR achieved remission; the majority of patients continued to require prednisone therapy for at least 2 years after its initiation. These data highlight the need for the use of more efficacious and steroid-sparing therapies in patients with GCA and/or PMR.

Abstract THU294 – Table 1. Outcomes at 2 Years Post-Index Date

<table>
<thead>
<tr>
<th>Total patients</th>
<th>GCA Only (N = 81)</th>
<th>PMR Only (N = 779)</th>
<th>GCA and PMR (N = 97)</th>
<th>Total (N = 957)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Achieved remission, n (%)</td>
<td>26 (32.1)</td>
<td>248 (31.8)</td>
<td>26 (26.8)</td>
<td>300 (31.3)</td>
<td>0.7921</td>
</tr>
<tr>
<td>Persistent remission, n (%)</td>
<td>14 (17.3)</td>
<td>176 (22.6)</td>
<td>17 (17.5)</td>
<td>207 (21.6)</td>
<td>0.5139</td>
</tr>
<tr>
<td>Time to remission, days*</td>
<td>224.3 (171.7)</td>
<td>226.5 (198.6)</td>
<td>208.4 (186.6)</td>
<td>224.7 (194.9)</td>
<td>0.0361</td>
</tr>
<tr>
<td>Median (range)</td>
<td>213 (0-577)</td>
<td>203.5 (0-635)</td>
<td>157 (0-619)</td>
<td>202.5 (0-635)</td>
<td>0.0361</td>
</tr>
</tbody>
</table>

* Among patients who achieved remission.

Abstract THU294 – Table 2. Prednisone Dose at 2 Years Post-Index Date

<table>
<thead>
<tr>
<th>Total patients</th>
<th>GCA Only (N = 26)</th>
<th>PMR Only (N = 341)</th>
<th>GCA and PMR (N = 60)</th>
<th>Total (N = 427)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prednisone dose, mg/day*</td>
<td>9.5 (10.6)</td>
<td>8.8 (9.2)</td>
<td>12.6 (15.9)</td>
<td>9.4 (10.5)</td>
<td>0.0819</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>5.0 (4.0)</td>
<td>5.0 (6.6)</td>
<td>7.5 (8.0)</td>
<td>5.0 (6.0)</td>
<td>0.0819</td>
</tr>
</tbody>
</table>

* Among patients who had prednisone dose information available at 2 years.


POLYMYALGIA RHEUMATICA ASSOCIATED WITH GIANT CELL ARTERITIS CONFIGURES A SUBTYPE WITH LOWER MORTALITY WITHIN GIANT CELL ARTERITIS

Carmen de Frutos Fernández1, Maria Angeles Martinez Huedo2, Irene Monjo3, Ezequiel de Miguel4, Carmen de Frutos Fernández5, 1Medicine Student Universidad Autónoma de Madrid. Rheumatology service, Hospital Universitario la Paz-IDiPaz., Madrid, Spain; 2U. Docencia e Investigación. Hospital Universitario La Paz. Madrid, Madrid, Spain; 3Rheumatology service, Hospital Universitario la Paz-IDiPaz., Madrid, Spain

Background: Giant cell arteritis (GCA) is the most frequent systemic vasculitis in older than 50 years old, with marked general state involvement or ischemic phenomena that can cause blindness to the patient’s death. Its form of presentation is heterogeneous however the therapeutic approach tends to be homogeneous. In recent years, the possible existence of subtypes of the disease has been pointed out and this can have important repercussions in the prognosis and approach of the disease. Two studies have suggested that the coexistence of GCA and Polymyalgia rheumatica (PMR) identifies a subgroup of patients at low risk for developing cranial ischemic symptoms. However, this was refuted by three other studies that did not find that effect.

Objectives: To study if, excluding the articular manifestations, the GCA against the association of PMR with ACG presents a phenotype with clinical differences relevant in clinical practice.

Methods: Retrospective observational study based on data from the Data-base of Hospital from the Spanish National Health Service with primary or secondary diagnostic of GCA between January 1st, 2005 and December 31st, 2015. In this substudy the data demographics and comorbidities and mortality, presenting patients with GCA were collected and compared with patients with GCA and PMR.

Results: The study cohort included 29.576 patients with GCA, of whom 4.189 had PMR as an associated diagnosis. The comorbidities associated with ACG and ACG/PMR and the statistical significance of the differences can be seen in the table. As a relevant fact, a lower risk of mortality was observed in patients presenting GCA along with PMR (OR 0.682 [95% CI 0.581-0.801]) and a lower frequency of cerebrovascular events and ischemic optic neuropathy.

Table 1. Differences between GCA associated with PMR vs ACG without PMR

<table>
<thead>
<tr>
<th></th>
<th>WITHOUT PMR</th>
<th>WITH PMR</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex*</td>
<td>Men 9533</td>
<td>37.6%</td>
<td>1474</td>
</tr>
<tr>
<td></td>
<td>Woman 15853</td>
<td>62.4%</td>
<td>2715</td>
</tr>
<tr>
<td>Age ≤ 74</td>
<td>5646</td>
<td>22.2%</td>
<td>997</td>
</tr>
<tr>
<td>group*</td>
<td>75-79 5779</td>
<td>22.8%</td>
<td>954</td>
</tr>
<tr>
<td></td>
<td>80-84 6789</td>
<td>26.7%</td>
<td>1210</td>
</tr>
<tr>
<td>≥ 85</td>
<td>7177</td>
<td>28.3%</td>
<td>1528</td>
</tr>
<tr>
<td>DM2*</td>
<td>6486</td>
<td>25.5%</td>
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</tr>
</tbody>
</table>
Correlations Among Vascular Ultrasound Abnormalities of the Temporal and Large Arteries in Giant Cell Arteritis

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Background: Vascular ultrasound (VUS) is a sensitive and specific method for evaluating giant cell arteritis (GCA). Understanding patterns of temporal artery (TA) and large artery involvement may be important for aiding in diagnosis.

Objectives: To determine correlations among VUS abnormalities in patients with GCA.

Methods: We performed a retrospective study among 503 patients that underwent VUS to evaluate suspected or known GCA at an academic medical center, 2013-2017. Demographics, clinical features, VUS reports, and pathology data were extracted through electronic medical record review. Trained cardiovascular sonologists imaged the right and left temporal, common carotid (CCA), subclavian (SCA), and axillary (AXA) arteries. The superficial temporal arteries (STA) and their frontal (TA-F) and parietal (TA-P) branches were abnormal if halo sign or hyperechoic wall thickening was present; the CCA, SCA, and AXA were abnormal if those findings and/or stenosis or occlusion were present. Cardiovascular medicine physicians trained in VUS interpreted studies as acute arteritis, no arteritis, or hyperechoic wall thickening without acute arteritis. Among patients diagnosed with GCA by the treating physician (n=139), we determined correlations between abnormal vessels using phi coefficients (φ).

Results: Among 139 patients, 50% were diagnosed before VUS (median disease duration 17 months). Median age at VUS was 73 years; 75% were female and 93% White. Forty patients (29%) had TA biopsy-proven GCA; an additional 14 (10%) had biopsy-proven giant cell arteritis. Prevalence of abnormalities of TAs and large arteries were similar (20% of right and 27% of left TAs; 20% of right and 24% of left large arteries). VUS was consistent with acute arteritis in 32%, no arteritis in 53%, and hyperechoic without acute arteritis in 15%. Abnormalities in the STA, TA-F, and TA-P were moderately correlated ipsilaterally (φ = 0.46-0.62, p<0.0001) and contralaterally (φ = 0.51-0.58, p<0.0001) (Table). Abnormalities in the AXA and SCA were strongly correlated with the ipsilateral and contralateral AXA and SCA (φ = 0.64-0.82, p<0.0001). Correlation between right and left TAs was moderate (φ = 0.59, p<0.0001), while a stronger relationship was found between right and left large arteries (φ = 0.77, p<0.0001). Abnormalities in TAs were not correlated with large arteries (φ = 0 for all comparisons; not significant).

Conclusions: We observed moderate correlations of TA branches and strong correlations of large artery branches on VUS among GCA patients. Abnormalities in the TAs and large arteries were not correlated, under-scoring the importance of scanning both groups of vessels with VUS.

Table. Notable correlations between abnormal arteries on VUS among 139 GCA patients

<table>
<thead>
<tr>
<th>Artery</th>
<th>Correlated Artery</th>
<th>φ</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>L STA</td>
<td>R STA</td>
<td>0.60</td>
<td>†</td>
</tr>
<tr>
<td>L TA-F</td>
<td>R TA-F</td>
<td>0.62</td>
<td>†</td>
</tr>
<tr>
<td>L STA</td>
<td>R STA</td>
<td>0.58</td>
<td>≈</td>
</tr>
<tr>
<td>L TA-F</td>
<td>R TA-F</td>
<td>0.51</td>
<td>≈</td>
</tr>
<tr>
<td>L STA</td>
<td>R STA</td>
<td>0.58</td>
<td>≈</td>
</tr>
<tr>
<td>L TA-F</td>
<td>R TA-F</td>
<td>0.46</td>
<td>NS</td>
</tr>
<tr>
<td>R CCA</td>
<td>L CCA</td>
<td>0.66</td>
<td>≈</td>
</tr>
<tr>
<td>R AXA</td>
<td>L AXA</td>
<td>0.81</td>
<td>≈</td>
</tr>
<tr>
<td>L AXA</td>
<td>R AXA</td>
<td>0.62</td>
<td>≈</td>
</tr>
<tr>
<td>L SCA</td>
<td>R SCA</td>
<td>0.81</td>
<td>≈</td>
</tr>
<tr>
<td>L AXA</td>
<td>R AXA</td>
<td>0.69</td>
<td></td>
</tr>
<tr>
<td>L SCA</td>
<td>R SCA</td>
<td>0.64</td>
<td></td>
</tr>
<tr>
<td>L temporal composite</td>
<td>R temporal composite</td>
<td>-0.07</td>
<td>NS</td>
</tr>
<tr>
<td>L large composite</td>
<td>R large composite</td>
<td>-0.07</td>
<td>NS</td>
</tr>
<tr>
<td>L temporal composite</td>
<td>R large composite</td>
<td>0.06</td>
<td>NS</td>
</tr>
<tr>
<td>L large composite</td>
<td>R large composite</td>
<td>0.05</td>
<td>NS</td>
</tr>
</tbody>
</table>

Temporal composite: abnormal superficial TA, TA-frontal branch, and/or TA-parietal branch. Large composite: abnormal common carotid, subclavian, and/or axillary artery, NS: not significant for p<0.0001

Disclosure of Interests: None declared

Steroid Treatment May Improve Arterial Stiffness in Patients With Polymyalgia Rheumatica and Giant Cell Arteritis: A Prospective Cohort Study

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Background: Polymyalgia rheumatica (PMR)/Giant cell arteritis (GCA), common inflammatory diseases, are associated with increased risk of aortic stiffness, possibly due to an inflammatory process.1,2

Objectives: To evaluate the effect of steroid treatment on aortic stiffness in patients with PMR/GCA.

Methods: This is an ongoing 1-year prospective cohort study. 37 consecutive patients with newly diagnosed PMR/GCA were included. Aortic pulse wave velocity (PWV) and aortic augmentation index normalized to heart rate of 75 beats per minute (Aix@75) were measured at baseline and subsequently at 1st and 4th months of treatment initiation with oral prednisolone.

Results: Of 37 patients, 3 pts. were excluded from the study because of lack of interest or a change in the initial diagnosis. Of all included pts. 61.8% were female and mean age was 71 (69-74) years. At diagnosis, 24 pts. presented with pure PMR symptoms, 2 pts. with pure cranial GCA, 8 pts. with concurrent PMR and GCA. The mean of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) at baseline were 62.3±22.9 and 46.4±43.7, respectively. Aix@75 was significantly decreased after 4 months of treatment initiation (from 62.1±11.6 to 19.5±11.5, p=0.016). Though aortic PWV was decreased after 4 months of treatment initiation (from 12.3±2.4 to 11.6±2.4), the results was not statistically significant (p=0.070). We did not find any significant changes at 1st month, nor in aortic PWV neither in Aix@75.

Conclusion: Steroid treatment may improve arterial stiffness in PMR/GCA patients due to suppression of the inflammatory process. However this is a time consuming effect and may not be seen as early as the first month.

References:
Objectives: The aim of this study is to highlight the magnitude of this existing manifestations. Several patients initially have few of these manifestations, but were followed and treated for manifestations strongly suggesting Behçet's syndrome by surveying the frequency, presentation patterns and outcome of patients who did not fulfill ISG criteria when they presented to our clinic, but were followed and treated for manifestations strongly suggesting BS.

Methods: We conducted a retrospective chart review of all BS patients who were registered between 2003 and 2008. Among these 2385 patients, 199 (8%) BS patients who did not fulfill ISG criteria at their initial visit were included in this study. Patients were called and a standard form was used for collecting demographic characteristics, BS manifestations at initial visit and during follow-up and treatment.

Results: Among the 199 patients (M/W: 90/109, mean age: 34 ± 11 years) who did not fulfill ISG criteria when they presented to our clinic, 70 (35%) had major organ involvement. The types of major organ involvement that led to a diagnosis of BS at initial visit despite not fulfilling ISG criteria were eye involvement in 37, vascular involvement in 29 (venous thrombosis in 22, arterial aneurysms in 7), nervous system involvement in 3 and gastrointestinal (GI) involvement in 1 patient. Thirty-five patients (18%) had a family history of BS. Of 199 patients, 167 had at least one more visit with a median follow-up of 11 years (IQR: 7-12). We were able to contact 116 of these patients and saw that 73 had fulfilled ISG criteria in the meantime. Among the 51 patients that we were not able to contact, 17 had fulfilled criteria while they were being followed in our clinic. Thus, a total of 70 (42%) patients fulfilled ISG criteria after a median follow-up of 1.5 years (IQR: 1-4.25). All but 2 patients who developed eye involvement during the follow-up had fulfilled ISG criteria with a new mucocutaneous manifestation. After a median follow-up of 4 years (IQR: 1-7), 23 (14%) patients had developed at least one non-criteria BS manifestation, including vascular involvement in 10, arthritis in 13, neurologic involvement in 2 patients and GI involvement in 1 patient. Among the 81 patients who developed at least one new manifestation, 16 (20%) were under immunosuppressive or interferon-alpha treatment at the time they developed their new manifestation. The remaining 65 patients had only received colchicine. Among the 29 patients who had vascular involvement at initial visit, 7 (24%) had a vascular relapse at different vascular site. Three patients had another rheumatologic diagnosis (ankylosing spondylitis, seropositive rheumatoid arthritis and sarcoidosis) at the end of the follow-up.

Conclusion: In our 10-year follow-up cohort study, 42% of the 167 incomplete BS patients had fulfilled ISG criteria within a median duration of 1.5 years. Sixty-two (37%) of these had major organ involvement that could have caused severe morbidity and mortality if the diagnosis of BS was missed and patients were untreated.

Disclosure of Interests: Sinem Nihal Esatoglu: None declared, Seyda Bilgin: None declared, Cem Sulu: None declared, Vedat Hamuryudan Consultant for: Abbvie, Amgen, BMS, Jansen, MSD, Pfizer, UCB, Speakers bureau: Abbvie, Amgen, BMS, Jansen, MSD, Pfizer, UCB, Zekayi Kutluýan: None declared, Serdal Uğurlu: None declared, Emire Seyah: None declared, Melike Melikoglu: None declared, Izzet Fresko: None declared, Sebahattin Yurdakul: None declared, Hasan Yazici: None declared, Gulen Hatemi Consultant for: Abbvie, Amgen, BMS, Jansen, MSD, Pfizer, UCB, Speakers bureau: Abbvie, Amgen, BMS, Jansen, MSD, Pfizer, UCB, DOI: 10.1136/annrheumdis-2019-eular.4287
IMPACT OF VASCULAR ULTRASOUND ON EVALUATION OF GIANT CELL ARTERITIS AMONG 503 PATIENTS IN AN ACADEMIC MEDICAL CENTER

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2Brigham and Women’s Hospital, Department of Medicine, Division of Cardiovascular Medicine, Boston, United States of America

Background: As vascular ultrasound (VUS) is increasingly used in evaluation of giant cell arteritis (GCA), its impact on clinical care is of great interest.

Objectives: To describe utilization of VUS in GCA evaluation at a large academic medical center and investigate impact of VUS on clinical impression.

Methods: We performed a retrospective cohort study of patients who underwent VUS at a single center in Boston, 2013-2017, to evaluate suspected or known GCA. Trained cardiovascular ultrasound technicians used a standardized protocol to image the temporal, carotid, subclavian, and axillary arteries for presence of hypoechoic circumferential wall thickening (halo sign), hypeechoic wall thickening, stenosis, and occlusion. VUS images were interpreted by trained cardiovascular medicine physicians as consistent with acute arteritis ("acute"), no evidence of arteritis ("none"), or hypeechoic wall thickening without halo sign ("hypeechoic"). Demographic, laboratory, medication, pathology and clinical data including the treating physician’s clinical suspicion for GCA pre- and post-VUS were obtained by electronic medical record review. Fisher’s exact test and Wilcoxon rank-sum tests compared baseline characteristics among patients with VUS positive for acute arteritis ("acute") vs. negative for acute arteritis ("none" or "hypeechoic"). We compared the treating physician’s pre- and post-VUS clinical suspicion for GCA among patients with no history of GCA or aneurysms.

Results: We identified 503 patients with median age 70.4 years; 69.0% were female and 87.5% White. VUS interpretation was acute in 48 patients (9.5%), none in 427 (84.9%), and hypeechoic in 28 (5.6%). Baseline characteristics are presented in Table 1. Weight loss, cranial symptoms, higher ESR, and steroid use were more common in patients with VUS positive for acute arteritis. Change in the treating physician’s clinical suspicion for GCA in 73/95 (77%) cases, and VUS negative for acute arteritis lowered suspicion for GCA in 303/396 (77%). Of 110 patients with a temporal artery biopsy after VUS, 16 (14.6%) biopsies showed active arteritis; 11 of these were in patients with VUS negative for acute arteritis.

Conclusions: VUS result changed the clinical suspicion for GCA in approximately 75% of patients in this large cohort.

Table 1. Characteristics at the time of VUS

- **Objective**: To describe utilization of VUS in GCA evaluation at a large academic medical center and investigate impact of VUS on clinical impression.
- **Methods**: We performed a retrospective cohort study of patients who underwent VUS at a single center in Boston, 2013-2017, to evaluate suspected or known GCA. Trained cardiovascular ultrasound technicians used a standardized protocol to image the temporal, carotid, subclavian, and axillary arteries for presence of hypoechoic circumferential wall thickening (halo sign), hypeechoic wall thickening, stenosis, and occlusion. VUS images were interpreted by trained cardiovascular medicine physicians as consistent with acute arteritis ("acute"), no evidence of arteritis ("none"), or hypeechoic wall thickening without halo sign ("hypeechoic"). Demographic, laboratory, medication, pathology and clinical data including the treating physician’s clinical suspicion for GCA pre- and post-VUS were obtained by electronic medical record review. Fisher’s exact test and Wilcoxon rank-sum tests compared baseline characteristics among patients with VUS positive for acute arteritis ("acute") vs. negative for acute arteritis ("none" or "hypeechoic"). We compared the treating physician’s pre- and post-VUS clinical suspicion for GCA among patients with no history of GCA or aneurysms.
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- **Conclusions**: VUS result changed the clinical suspicion for GCA in approximately 75% of patients in this large cohort.

**Abstract THU300** – **Table 1.** Characteristics at the time of VUS

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Age, years</th>
<th>History of GCA or aneurysm</th>
<th>History of PMR</th>
<th>Weight loss</th>
<th>Fatigue</th>
<th>Jaw claudication</th>
<th>Scalp tenderness</th>
<th>TA tenderness/decreased TA pulse</th>
<th>Transient vision loss</th>
<th>Permanent vision loss</th>
<th>CRP*, mg/L</th>
<th>ESR*, mm/h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range</td>
<td>70.4 (62.7, 77.5)</td>
<td>14.3 (21.1)</td>
<td>31.2 (22.9)</td>
<td>51.3 (60.9)</td>
<td>13.3 (22.9)</td>
<td>36.2 (45.8)</td>
<td>10.9 (33.3)</td>
<td>17.1 (37.5)</td>
<td>14.5 (29.2)</td>
<td>7.8 (10.4)</td>
<td>3.0 (6.3)</td>
<td>15.7 (3.1, 76.0)</td>
</tr>
<tr>
<td>Median</td>
<td>73.2 (65.8, 79.7)</td>
<td>32.1 (NS)</td>
<td>67.0 (50.3)</td>
<td>12.3 (0.05**)</td>
<td>35.2 (NS)</td>
<td>8.6 (&lt;0.01)</td>
<td>15.0 (&lt;0.01)</td>
<td>3.0 (NS)</td>
<td>13.0 (NS)</td>
<td>7.5 (NS)</td>
<td>2.6 (NS)</td>
<td>36.3 (8.1, 81.9)</td>
</tr>
<tr>
<td>IQR</td>
<td>69.9 (77.3)</td>
<td>0.02</td>
<td>32.1 (NS)</td>
<td>0.05**</td>
<td>35.2 (NS)</td>
<td>8.6 (&lt;0.01)</td>
<td>15.0 (&lt;0.01)</td>
<td>2.6 (NS)</td>
<td>13.0 (NS)</td>
<td>7.5 (NS)</td>
<td>2.6 (NS)</td>
<td>13.7 (7.9, 13.7)</td>
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<tr>
<td>Statistics</td>
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<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
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<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

Presented as% or median (interquartile range).

**CRP**: C-reactive protein; **ESR**: erythrocyte sedimentation rate; **GCA**: giant cell arteritis; **PMR**: polymyalgia rheumatica; **TA**: temporal artery; **VUS**: vascular ultrasound. NS: not significant.

*Among 418 patients with CRP and 370 with ESR checked within 3 weeks before VUS.
**p<0.046
Figure 1. Treating physician’s clinical suspicion for GCA before and after VUS among 431 patients without a history of GCA/sortitis

<table>
<thead>
<tr>
<th>VUS positive for acute arteritis (n=335)</th>
<th>Post-test impression</th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Definite GCA</td>
<td>Very Likely GCA</td>
</tr>
<tr>
<td>Definite GCA</td>
<td>3</td>
<td>-</td>
</tr>
<tr>
<td>Very likely GCA</td>
<td>13</td>
<td>9</td>
</tr>
<tr>
<td>Possible GCA</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Unlikely GCA</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Not GCA</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>VUS negative for acute arteritis (n=396)</th>
<th>Post-test impression</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Definite GCA</td>
<td>Very Likely GCA</td>
</tr>
<tr>
<td>Definite GCA</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Very likely GCA</td>
<td>4</td>
<td>9</td>
</tr>
<tr>
<td>Possible GCA</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Unlikely GCA</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Not GCA</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Increased suspicion | No change | Decreased suspicion

Abstract THU0300 – Figure 1

Disclosure of Interests: None declared

THU0301

SPLENIC INVOLVEMENT IS NOT RARE IN ANCA-ASSOCIATED VASCULITIS HOWEVER SPLENIC INFARCT MIGHT ONLY BE ASSOCIATED WITH GRANULOMATOSIS WITH POLYANGIITIS

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Background: Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a systemic necrotizing vasculitis of small and medium-sized arteries. Although, upper and lower respiratory tracts and kidneys are predominantly affected; other organs/systems can also be involved in the course of the disease and in some cases, it might be difficult to differentiate subgroups based on the clinical presentation. Splenic involvement has been rarely reported, mainly in patients with granulomatosis with polyangiitis (GPA), in fact, it was thought to be underestimated, as it is often asymptomatic.

Objectives: In this study, we aimed to investigate systematically the frequency of splenic infarct and related factors in our AAV patients. We also evaluated the role of splenic involvement in the differentiation of AAV subgroups.

Methods: Patients with a diagnosis of AAV in whom abdomen/thorax computed tomography (CT) was performed were included in the study. An experienced radiologist examined CT images for the presence of splenic involvement. The clinical and demographic data were retrospectively collected.

Results: In total 70 (30 [43%] female and mean age 56.1 ± 15.7 years) AAV patients (38 [54%] had granulomatosis with polyangiitis (GPA); 20 [29%] microscopic polyangiitis; 11 [16%] renal-limited disease and 1 [1%] eosinophilic granulomatosis with polyangiitis) were included in the analysis. Splenic pathologies including splenomegaly, hypodense lesion/s, lobulation, and infarction were seen in 21 (30%) patients with AAV. Splenic infarct was observed in seven (10%) patients and all had GPA with renal involvement and PR3ANCA positive. Three of them had total splenic infarct or auto-splenectomy. None of these patients had a history of endocarditis, shock or malignancy before CT. Splenic infarction was found to be negatively correlated with age at diagnosis (p=0.017; rho=–0.285), and positively associated with ENT (ear-nose-throat) (p= 0.002; rho=0.370) and eye involvements (p=0.013; rho=0.324).

Conclusion: Our results show that splenic pathologies might not be rare in AAV however, infarction can help to separate GPA from other AAVs. In young GPA patients, in particular, those with ENT and eye involvement, physicians should remember splenic infarction. Since almost half of our cases had severe infarction or auto-splenectomy, clinicians might consider immunization in GPA patients for vaccine-preventable infections.

REFERENCES:

THU0302

OUTCOMES OF PREGNANCY IN BEHCET’S DISEASE

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Background: Behcet’s disease (BD) is multisystemic disease of unknown cause. The relationship between BD and pregnancy is reported in limited number of studies.

Objectives: To evaluate outcomes of pregnancies in BD patients (pts).

Methods: We retrospectively collected data of 22 women with BD diagnosis (according to ISGBD 1990 and ICBD 2014) and their 68 pregnancies. Pts’ mean age was 30 [26;35] yrs, disease duration 7 [2;10] yrs. Ten (45,5%) pts had severe BD according to Ch.Zouboulis classification (due to generalized uveitis, retinal vasculitis and parenchymatous CNS lesions), while other 10 (45,5%) pts had mild disease with mainly dermal-mucous manifestations, and remaining two (9%) pts had moderate disease. These patients did not receive cytotoxic therapy.

Results: Sixty-eight pregnancies in 22 pts resulted in 45 live birth (4 cesarean section in 2 pts). Four patients had 11 medical abortions on request before 12 weeks of gestation, one patient - due to medical reasons. Unfavorable outcomes of pregnancy were documented in pts with splenic infarction; transverse (a) and coronal images (b) show an irregular contoured shrunken spleen (arrows).

Disclosure of Interests: Önay Gerçik: None declared, Şebnem Karasu: None declared, Dilek Solmaz: None declared, Zeki Soyapaçak: None declared, Fulya Çakalağaoğlu: None declared, Servet Akar Grant/research support from: MSD, Abbvie, Roche, UCB, Novartis, Pfizer, Amgen, Consultant for: MSD, Abbvie, Roche, UCB, Novartis, Pfizer, Amgen, Speakers bureau: Pfizer

REFERENCE:

Disclosure of Interests: None declared

THU0303
THE OMERACT CORE DOMAIN SET FOR CLINICAL TRIALS IN BEHÇET’S SYNDROME
Gulen Hatemi1, Alexa Meara2, Yesim Ozguler3, Haner Direskeneli4, Alfred Mahf4, Beverley Shea5, Esen Cam6, Ahmet Gül7, Yusuf Yazici8, Peter Tugwell5, Hasan Yazici9, Peter Merkel10.

Objectives: The Outcome Measures in Rheumatology Clinical Trials (OMERACT) Behçet’s Syndrome Working Group has worked to advance the creation of a data-driven Core Domain Set for use in all clinical trials.

Methods: The Core Domain Set was developed through a comprehensive, iterative, multi-stage, multi-year project that followed the methodologically rigorous processes and standards set forth by OMERACT; i) a systematic review; ii) a survey among experts in BS; iii) an outcomes interest group meeting during the International Conference on Behçet’s Disease; iv) qualitative patient interviews; v) a three-round modified Delphi exercise involving both patients with BS and a multidisciplinary set of physicians expert in BS, focused on obtaining consensus on the domains of illness necessary in the study of BS; and vi) utilization of the data, insight, and feedback generated by the outlined processes to develop a final Core Domain Set. The final Core Set was presented and put up for a vote of endorsement at the 2018 OMERACT meeting.

Results: All steps in the processes outlined were completed. The systematic review clearly demonstrated the substantial variability in the domains studied in clinical trials of BS and a lack availability of validated outcome measures in BS. The survey of physicians, the in-person meeting of experts, and the qualitative research with patients all helped generate an extensive list of candidate domains and sub-domains to consider for use in clinical trials. It also become clear that there was a need and strong interest in delineating domains across the several major organ systems involved in this disease and in recognizing that clinical trials in BS often focus on specific manifestations and not the disease in its entirety. The Delphi involved 74 physicians expert in BS from 21 countries and from a wide range of specialties, and 64 patients from 10 countries. The Delphi utilized both ratings and rankings to prioritize the 56 domains and sub-domains originally under consideration.

The final proposed Core Set included 5 sub-domains mandatory for study in all trials in BS, with additional sub-domains mandatory for study of specific organ systems when that system is the focus of a trial: mucocutaneous (2 additional sub-domains), ocular (4), central nervous system (3), musculoskeletal (2), vascular (4), and gastrointestinal (2). The final Core Set was strongly endorsed at the 2018 OMERACT meeting.

Disclosure of Interests: Gulen Hatemi Consultant for: Abbvie, Amgen, BMS, Janssen, MSD, Pfizer, UCB, Speakers bureau: Abbvie, Amgen, BMS, Janssen, MSD, Pfizer, UCB, Alexa Meara: None declared, Yesim Ozguler: None declared, Haner Direskeneli: None declared, Alfred Mahf: None declared, Beverley Shea: None declared, Esen Cam: None declared, Ahmet Gül: None declared, Yusuf Yazici: Shareholder of: Samumed, LLC, Consultant for: Celgene Corporation, BMS, Genentech, Sanofi, Employee of: Samumed, LLC, Peter Tugwell: None declared, Hasan Yazici: None declared, Peter Merkel: None declared

THU0304
PREVALENCE AND MANAGEMENT OF CARDIOVASCULAR RISK FACTORS IN ANCA-ASSOCIATED VASCULITIS: A CROSS-SECTIONAL STUDY IN THE NETHERLANDS AND CANADA
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Background: Patients with ANCA-associated vasculitis (AAV) are at increased risk of cardiovascular (CV) disease.

Objectives: The aim of the present study was to determine the prevalence of CV risk factors in patients with AAV and to evaluate the management of CV risk factors according to current guidelines.

Methods: A cross-sectional study was performed in patients with AAV in the Netherlands and Canada. Information on traditional CV risk factors, as well as markers of inflammation and kidney function, were collected. Their prevalence and treatment were studied and compared with recommendations in current guidelines.

Results: A total of 144 consecutive patients with AAV were included (71 from the Netherlands; 73 from Canada). Mean age was 62 ± 15 years, and 56% were male. The disease duration was 7.0 ± 6.6 years; 69% had granulomatosis with polyangiitis, 17% microscopic polyangiitis, and 14% eosinophilic granulomatosis with polyangiitis. Mean body mass index was 28 ± 6 kg/m² and 65 patients (45%) had an estimated glomerular filtration rate <60 ml/min. The mean C-reactive protein was 6.5 ± 12.3 mg/l. Dyslipidemia was present in 69% and hypertension in 72%. In 36% and 25% of the included patients, blood pressure and dyslipidemia, respectively, were not managed in accordance with national guidelines.

Conclusion: Patients with AAV have a high prevalence of traditional CV risk factors. Whether past or persistent inflammation and chronic kidney disease further increases the CV risk remains to be studied. Strict adherence to CV risk management guidelines should be encouraged.

REFERENCE:

Disclosure of Interests: None declared

THU0305
ABSTRACT WITHDRAWN

THU0306
NEUTROPHIL ADHESION MOLECULES AND INFLAMMATORY CYTOKINES AS BIOMARKERS FOR MONITORING DISEASE PROGRESSION IN GIANT CELL ARTERITIS
Tadeja Kurz1,2, Katja Lakota1,3, Gerhard Thallinger4,5, Polona Zigon1, Sasa Cučić1,2, Matija Tomsić1,6, Snežna Sodin-Senn7,8, Alojzija Hocevar1.

1University Medical Centre Ljubljana, Department of Rheumatology, Ljubljana, Slovenia, 2University of Ljubljana, Faculty of Pharmacy, Ljubljana, Slovenia, 3University of Primorska, FAMNIT, Koper, Slovenia, 4Graz University of Technology, Institute of Computational Biotechnology, Graz, Austria, 5OMICS Center Graz, Graz, Austria, 6University of Ljubljana, Faculty of Medicine, Ljubljana, Slovenia

Background: Monitoring giant cell arteritis (GCA) activity with appropriate biomarkers is important, as current evaluation, based mainly on clinical symptoms/signs and traditional markers of inflammation, is not always sufficient and reliable.

Objectives: Our goal was to identify cellular and molecular biomarkers that could help clinicians to closely monitor GCA progression and/or treatment response.

Methods: Peripheral blood was obtained from 27 GCA patients at time of diagnosis (before glucocorticoid (GC) treatment), and subsequently at...
weeks 1, 4, 12, 24 and 48 of follow-up (FU). At diagnosis, all patients received GC in line with EULAR recommendations with a slow GC tapering starting after week 4. At week 12, some of the patients (16/27) received additionally leflunomide (10 mg). Whole blood samples were stained, lysed, fixed and analyzed by flow cytometry. The expression of adhesion molecules (CD62L, CD11b) was determined on neutrophils. Serum levels of serum amyloid A (SAA) and IL-6 were measured by nephelometry and ELISA, respectively. Levels of IL-6, IL-18, IL-23, L-selectin and CHI3L1 were determined by MagPix using human pre-mixed multi-analyte kits.

Results: At weeks 1 and 4 of FU we detected a decrease in neutrophil expression of CD62L and CD11b, as well as in sera levels of SAA, IL-6, IL-8, IL-18, L-selectin and CHI3L1 in all GCA patients. At week 12 (8 weeks after GC tapering) an elevation of CD11b, SAA, IL-6 and IL-23 as compared to week 4 was observed (Figures 1 and 2). At weeks 24 and 48 of FU we identified four different groups of biomarkers. The first group consisted of neutrophil CD62L (p<0.05) and serum IL-6, that showed a marked increase in patients receiving GC therapy only, while decreasing in patients receiving GC in combination with leflunomide. The second group is represented by neutrophil CD11b and serum IL-8 that were higher at week 24 in the GC-treated group (the first FU after receiving leflunomide), however their levels were equal at week 48 in both groups of GCA patients (Figures 1 and 2). In the third group, the serum levels of SAA, IL-18 and L-selectin decreased at week 24 and remained stable through week 48, regardless of therapy used. The fourth group of biomarkers included serum IL-23 and CHI3L1, levels of which declined at weeks 24 and 48 in patients receiving GC only and substantially increased in patients receiving leflunomide and GC (Figure 2).

Conclusion: Neutrophil surface markers CD62L and CD11b together with inflammatory parameters (SAA, IL-6, IL-8 and IL-23) could represent informative biomarkers for monitoring disease progression in GCA patients. Important biomarker differences were observed between GC-treated GCA patients, in the presence and absence of leflunomide, serving as a good basis for predicting relapses.
Methods: The patients, fulfilling the International Criteria for Behçet’s disease (ICBD), and healthy controls, of a comparable age, were evaluated in the Rheumatology and Urology Clinics. The demographic and clinical data was collected. Disease activity of the patients was assessed using Behçet’s Syndrome Activity Score (BSAS). For both groups, the sexual function and the psychological status were evaluated using the Internationa l Index of Erectile Functions (IIIF-5) and the Beck Depression Inventory (BDI), respectively. Spearman’s ρ, Chi-Square and Mann-Whitney U tests were used as appropriated.

Results: The number of BD patients was 26 and that of the controls was 27. The mean age of the patients was 36±7.4 and that of controls was 40.9±5.2. Though BD patients were younger in age they exhibited significantly lower scores in sexual function, and scored higher in depression as illustrated in Table 1.

Abstract THU0308 – Table 1. Demographic and clinical data of the participants

<table>
<thead>
<tr>
<th>Patients (n=26)</th>
<th>Controls (n=27)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking, n (%)</td>
<td>8 (30.8%)</td>
<td>4 (14.8%)</td>
</tr>
<tr>
<td>Disease duration (years), mean ± SD</td>
<td>4.2±1.9</td>
<td>NA</td>
</tr>
<tr>
<td>Erectile dysfunction (IIIF-5 score), median (interquartile range)</td>
<td>15 (9-20)</td>
<td>20 (20-25)</td>
</tr>
<tr>
<td>Depression score (Beck questionnaire), median (IQR)</td>
<td>13 (9-18)</td>
<td>9 (7-14)</td>
</tr>
</tbody>
</table>

There were no associations between the disease duration, smoking status or different clinical phenotypes and the sexual or psychological functions. However, there was an inverse relationship between BSAS and the sexual function (rho = -0.45, p = 0.024). The duration of corticosteroids intake was negatively correlating with the sexual function (rho= -0.604, p= 0.001) as well. The depression scores correlated significantly with the presence of inflammatory back pain (rho= -0.413, p=0.036). There was no association between the severity of sexual dysfunction and that of depression. The patients showed different degrees of depression, and there was a tendency towards increased rates of erectile dysfunction in all groups as shown in Table 2.

Abstract THU0308 – Table 2. Correlation of IIIF-5 and BDI

<table>
<thead>
<tr>
<th>Sexual function</th>
<th>Beck Depression Inventory (BDI)</th>
<th>Total P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(IIIF-5 score)</td>
<td>(BDI)</td>
<td>Minimal (n=14)</td>
</tr>
<tr>
<td>No ED or Mild ED ≥ 17, n (%)</td>
<td></td>
<td>4 (28.6%)</td>
</tr>
<tr>
<td>ED ≤ 16, n (%)</td>
<td></td>
<td>10 (71.4%)</td>
</tr>
</tbody>
</table>

ED; erectile dysfunction.

Conclusion: BD has a negative impact on men’s psychological state and sexual function. Severe disease states, evident in the long duration of corticosteroids use and the high activity scores, are linked to sexual dysfunction.


Methods: Rituximab pharmacokinetics was described in 92 AA patients from the RAVE trial (rituximab for ANCA- associated vasculitis) using a population modeling approach. A semi-mechanistic model including a latent target antigen turnover allowed the estimation of specific target-mediated elimination of rituximab in addition to its non-specific elimination. Sex, body surface area (BSA), BVAS/WG score, and status newly diagnosed on pharmacokinetic parameters were investigated as covariates.

Results: A two compartments model including target mediated elimination best described rituximab pharmacokinetics. The mean (individual standard deviation) estimated central volume of distribution was 3.06 L (2.61%), systemic clearance was 0.135 L days⁻¹ (6.43%), and target-mediated elimination rate constant was 19.13 x 10⁻⁶ nmol⁻¹ days⁻¹ (fixed to 0). The initial activity of the disease was higher in male than in female (p=4.09 x 10⁻¹⁰). Moreover, systemic clearance was slightly lower in granulomatosis with polyangiitis group than in other AAV groups (p=3.6 x 10⁻³). Neither BVAS/WG score nor BSA were significant covariates in a multivariate analysis.

Conclusion: We report a nonlinear target-mediated elimination of rituximab in AAV patients. Granulomatosis with polyangiitis patients have a lower global clearance of rituximab than other AAV groups. Our study not support the utility of BSA based individualized dosing protocols, as previously reported (1).

REFERENCE:

Disclosure of Interests: Denis Mulleran Speakers bureau: Pfizer, Novartis, Grifols, Amina Bensalem: None declared, David Ternant Speakers bureau: Sanofi, Amin, Gilles Paoutand Grant/research support from: Novartis, Roche Pharma, Sanofi-Genzyme, Chuagi, Pfizer and Shire, Divi Comec: None declared, Ulrich Specks: None declared DOI: 10.1136/annrheumdis-2019-eular.4897

THU0310

OPTIMAL INITIAL DOSE OF GLUCOCORTICOID FOR ELDERLY-ONSET ANCA ASSOCIATED VASCULITIS: SAFETY OUTCOME ANALYSIS OF TWO NATIONWIDE, PROSPECTIVE, INCEPTION COHORT STUDIES

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Background: Glucocorticoid (GC) is still the mainstay of treatment for antineutrophil cytoplasmic antibody (ANCA) -associated vasculitis (AAV) while GC use, disease severity, and older age are risk factors for accrual of damage and infection in AAV(1,2). Objectives: To explore optimal initial dose of GC for patients with elderly-onset AAV based on safety outcome analysis using data from two nationwide prospective inception cohort studies (RemIT-JAV and RemIT-JAV-RPGN).

Methods: RemIT-JAV and RemIT-JAV-RPGN enrolled consecutive patients with newly diagnosed AAV fulfilling the criteria for primary systemic vasculitis as proposed by the European Medicines Agency algorithm and requiring immunosuppressive treatment. From the cohort studies, elderly-onset (<65 years) patients with microscopic polyangiitis and granulomatosis with polyangiitis, classified as generalized or severe disease type according to the European Vasculitis Study Group-defined disease severity, were enrolled in this analysis. The primary outcome measures were Vasculitis Damage Index (VDI) at 24th month and serious infections during 2 years after starting treatment for AAV. The patients were divided into three groups based on initial dose of GC: high-dose (HD) group, prednisolone (PSL) >0.8 mg/kg/day; medium-dose group (MD), 0.6: PSL <0.8 mg/kg/day; low-dose (LD) group, PSL <0.6 mg/kg/day. The VDI were classified into treatment-related VDI(3) and disease-related VDI.

Nonlinear Pharmacokinetics of Rituximab in Anti-Neutrophil Cytoplasmic Antibody Associated Vasculitis

Denis Mulleran1,2, Amina Bensalem1, David Ternant3,1, Gilles Paintaud1,3, Divi Comec1,2, Ulrich Specks1.

Rituximab (RTX) was approved in patients with anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis (AAV), to describe the pharmacokinetics of rituximab in AAV patients and to explore its sources of variability.
PERSISTENT LOW-GRADE VASCULAR INFLAMMATION IN LARGE VESSEL VASCULITIS: A LONGITUDINAL STUDY USING FULLY INTEGRATED 18F-FDG PET/MR

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1Operative Unit of Rheumatology, Department of Medicine DIMED, University of Padova, Italy, 2Operative Unit of Radiology, Department of Medicine DIMED, University of Padova, Italy, 3Operative Unit of Nuclear Medicine, Department of Medicine DIMED, University of Padova, Italy, Padova, Italy

Background: Persistent low-grade vascular inflammation in large vessel vasculitides (LVV) treated patients could represent the expression of persistent subclinical disease activity or post-inflammatory vascular remodelling. Whether these findings have any impact on future vascular outcomes is still an unmet need.

Objectives: To evaluate the frequency and evolution of the low-grade vascular inflammation using a fully integrated 18F-FDG PET/MR in a longitudinally followed cohort of LVV patients.

Methods: All consecutive patients with LVV who underwent at least 2 PET/MR scans (median time 9[6] months) between January 2015 and February 2019 were included. For each scan vessel’s metabolic activity was assessed using the Meller’s grading and the standard uptake value. Low-grade inflammation was defined as Meller 1 and 2 (inferior or equal to liver), as previously reported. Demographic and clinical data, as well as disease remission or flares, were recorded and compared to vascular metabolic activity.

Results: In total, 107 PET scans were performed (from min. 2 scans to max. 5 scans per patient), mainly during follow-up (78.6%) in 33 LVV patients (72.7% GCA, 27.3% TAK), predominantly female (84.8%), with a regular BMI (24[5.5]) and with a long-standing disease (30[29] months). At PET examination, low-grade metabolic activity was reported in 60% of the cases (86.4% GCA and 13.6% TAK), while complete remission in 15% and highly pathological in 25%. Comparing patients with low-grade vascular inflammation to those with complete remission (Meller 0), they resulted significantly older (64[12] vs 57[33] years, p<0.005), with a lower disease duration (26.5[21.4] vs 52.5[34.8] months, p<0.001) and with higher daily prednisone dosage, but without significance (5[7.5] vs 2.5 [8.75], p=0.096). No significant differences were noted in acute phase reactants and type of treatment. Moreover, when compared to those with high metabolic activity (Meller 3), patients with low-grade inflammation resulted significantly older (64[12] vs 62[25] years, p<0.025), with a lower disease duration (26.5[21.4] vs 33[46] months, p=0.041), lower CRP level, but without significance (3.03[5.92] vs 10.35[13.75], p=0.069). Clinical remission, before PET examination, was registered in 55.6% of patients with Meller lower activity, significantly lower compared to those with Meller 1+2 (87.5%, p=0.002). Steroids and immunosuppressants tapering rate did not differ between patients with low-grade metabolic activity and those without activity.

Among all patients with low-grade vascular inflammation, 60% underwent to steroids or immunosuppressants tapering. At the subsequent PET examination, a persistence/worsening of metabolic activity was found in 88.5% of them. Change or increase of the treatment regimen led to an improvement (complete remission) in 58.9% of the cases. Low-grade metabolic activity was associated with a significant increased risk of worsening/flare at the subsequent PET examination (RR 5.29[1.87-16.11], p=0.002).

Conclusion: Low-grade vascular inflammation at PET examination is a common feature in LVV treated patients, especially GCA. It is significantly associated with an older age, lower disease duration and clinical remission. However, steroids or immunosuppressants tapering is these patients is associated with an increased risk of worsening/flare. Further research is urgently needed to address this issue.

REFERENCES:

ADVENTITIAL FIBROBLAST, AN IMPORTANT PLAYER IN GIANT CELL ARTERITIS

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Background: Giant cell arteritis (GCA) is a systemic vasculitis affecting large vessels. The diagnosis is based on the temporal artery biopsy (TAB) which shows a segmental and focal arterial infiltration composed of CD4 T cells and macrophages. It is accompanied by a destruction of the internal elastic layer of the media and a hyperplasia of the intima by proliferation of myofibroblasts (Weyand). The origin of these myofibroblasts is controversial (Ly). Evidences suggest the activation of adventitial fibroblasts into myofibroblasts and their migration into the intima (Stenmark).

Objectives: The objective of this study was to determine whether adventitial fibroblasts migrate to the intima and thereby contribute to intimal hyperplasia during GCA.

Methods: Arterial sections from TAB of patients with GCA (n=24) and control subjects (n=24) were analyzed. Immunohistochemical analysis was
performed using antibodies directed against fibroblasts (CD90, vimentin), myofibroblasts (alpha smooth muscle actin (ASMA)) and vascular smooth muscle cells (desmin). Staining of prolly-4-hydroxylase (P4H) and myosin were also performed. Stainings were quantified using the ODPviewer® software (Kamax Innovative System, France) by two double-blind observers. Moreover, co-expression of CD90 with different stainings (ASMA, myosin and P4H) was also performed. Cells in culture were identified by immunocytochemistry using anti-CD90 and markers of activity such as myosin and P4H. Functional assays were performed using culture cells obtained from GCA patients’ BATs (n=4) and controls (n=4). The BATs were dissected to separate the adventitia from the other two layers. Each dissected fragment was seeded separately. The proliferation was studied using a bromodeoxyuridine incorporation test under different conditions: DMEM, fetal calf serum (FCS), PDGF and supernatants of cells in culture. The study of migration was performed using a scratch test under the same conditions.

Results: CD90 was significantly higher in GCA than controls in adventitia and intima. Vimentin and ASMA were significantly higher in the 3 tunics of patients with GCA. Expression of desmin was only present in the media for both groups with no significant difference. P4H was present in adventitia with significant differences between both groups. The adventitial and intimal CD90+ cells co-expressed P4H, ASMA and myosin more importantly during GCA. Cultured cells from BATs’ adventices expressed CD90 and did not express desmin. These cells had a greater myosin staining during GCA and had an increased proliferation ability during GCA in the presence of FCS, PDGF and fibroblast supernatants of control or GCA patients. The migration rates of these cells were also significantly increased during GCA in the presence of FCS or PDGF.

Conclusion: Vascular remodeling during GCA would start in the adventitial layer with a key role of fibroblasts. Advenitial fibroblasts could be activated into myofibroblasts and acquire proliferative and migratory abilities. They would participate in the intimal hyperplasia, responsible for ischemic complications. Their inhibition could be a therapeutic way to limit these complications. The activating signal of adventitial fibroblasts into myofibroblasts is not yet known during GCA and requires further studies.

REFERENCES:

Disclosure of Interests: None declared

THU0313 COMPARATIVE STUDY OF CLINICAL, ANALYTICAL AND VASCULAR 18F-FDG UPTAKE EVOLUTION IN PATIENTS WITH GIANT CELL ARTERITIS TREATED WITH METHOTREXATE VS TOCILIZUMAB


Background: Glucocorticoids remain to be the cornerstone therapy in giant cell arteritis (GCA). However, relapses are common when the prednisone dose is tapered. Thus, additional therapies are required in relapsing GCA. The most widely used conventional immunosuppressive drug is methotrexate (MTX) which efficacy is modest. Consequently, in some cases biological therapy in needed. Among them, the most frequently used is the recombinant humanized anti-IL6 receptor antibody tocilizumab (TCZ).1

Objectives: To compare clinical evolution, normalization of acute phase reactants and normalization of vascular 18F-FDG uptake assessed by PET/CT in patients with GCA treated with MTX vs TCZ.

Methods: Comparative multicentric study of 23 patients with GCA treated with MTX vs 36 patients with GCA treated with TCZ who had a baseline and follow-up PET/CT scan. We assessed clinical improvement (no improvement/partial/complete), normalization of acute phase reactants (CRP ≤ 0.5mg/dl, and/or ESR ≤ 20 mm/1st hour) and reduction of 18F-FDG uptake in PET/CT (no reduction/partial/complete normalization). Images were evaluated qualitatively by experienced nuclear medicine physicians. Prednisone tapering was also assessed. Statistical analysis was performed with SPSS. Student’s t test or Mann-Whitney U test was used to compare continuous variables, and Chi-squared test or Fisher’s exact test for categorical variables as appropriate.

Results: We included 23 patients with GCA treated with MTX (20 women/3 men); mean age 65.6 ± 7.9 years; and 36 patients treated with TCZ (27 women/9 men); mean age 67.5 ± 8.3 years. Clinical, analytical and vascular 18F-FDG uptake evolution is shown in the TABLE. After one year of treatment, the percentage of patients who experienced complete clinical improvement was higher in those who received TCZ (88.9% vs 44.4%; p=0.003). Normalization of acute phase reactants was also more frequent in patients who received TCZ (92.6% vs 47.6%; p=0.001). In regard with reduction of vascular 18F-FDG uptake, complete normalization was only achieved in 25% of patients who received TCZ and 14.3% of those who received MTX.

Conclusion: Patients with GCA who received TCZ experienced a more rapid and effective clinical and analytical improvement than patients who received MTX. Besides, prednisone tapering was quicker in patients with TCZ. However, no significant differences were found in complete normalization of 18F-FDG vascular uptake between both treatments.

Abstract THU0313 –Table 1.

<table>
<thead>
<tr>
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<th>MTX (n=23)</th>
<th>TCZ (n=36)</th>
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</tr>
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<tbody>
<tr>
<td>Age, mean ± SD</td>
<td>65.6 ± 7.9</td>
<td>67.5 ± 8.3</td>
<td>0.39</td>
</tr>
<tr>
<td>Complete clinical improvement, n/ (%)</td>
<td>20 (87.0)</td>
<td>27 (77.0)</td>
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</tr>
<tr>
<td>6 months</td>
<td>7/13 (53.8)</td>
<td>9/23 (39.1)</td>
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</tr>
<tr>
<td>12 months</td>
<td>8/13 (61.5)</td>
<td>23/27 (85.2)</td>
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</tr>
<tr>
<td>18 months</td>
<td>7/11 (63.6)</td>
<td>21/32 (65.6)</td>
<td>0.03</td>
</tr>
<tr>
<td>24 months</td>
<td>7/9 (77.8)</td>
<td>17/28 (60.7)</td>
<td>0.25</td>
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**Normalization of ESR and/or CRP, n/ (%)**

<table>
<thead>
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<th>TCZ (n=36)</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td>6 months</td>
<td>7/13 (53.8)</td>
<td>10/23 (43.5)</td>
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</tr>
<tr>
<td>12 months</td>
<td>10/12 (83.3)</td>
<td>25/27 (92.6)</td>
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<tr>
<td>18 months</td>
<td>10/11 (90.9)</td>
<td>21/23 (91.3)</td>
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<tr>
<td>24 months</td>
<td>9/10 (90.0)</td>
<td>15/19 (78.9)</td>
<td>0.99</td>
</tr>
</tbody>
</table>

**Normalization of 18F-FDG PET/CT, n/ (%)**

<table>
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<td>6 months</td>
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<td>10/16 (62.5)</td>
<td>0.21</td>
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<tr>
<td>12 months</td>
<td>7/13 (53.8)</td>
<td>23/24 (95.8)</td>
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</tr>
<tr>
<td>18 months</td>
<td>7/14 (50.0)</td>
<td>7/14 (50.0)</td>
<td>0.51</td>
</tr>
<tr>
<td>24 months</td>
<td>7/17 (41.2)</td>
<td>17/24 (70.8)</td>
<td>0.99</td>
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</tbody>
</table>

**Dose of Prednisone (mg/day), mean (SD)**

<table>
<thead>
<tr>
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<th>MTX (n=23)</th>
<th>TCZ (n=36)</th>
<th>P</th>
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<td>6 months</td>
<td>7.5 ± 3.0</td>
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<td>0.05</td>
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<td>12 months</td>
<td>5.0 ± 3.0</td>
<td>6.0 ± 3.0</td>
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<tr>
<td>18 months</td>
<td>5.0 ± 3.0</td>
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<td>0.03</td>
</tr>
<tr>
<td>24 months</td>
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</table>

**REFERENCE:**

Disclosure of Interests: D. Prieto-Peña: None declared, Monica Calderón-Goercke: None declared, Javier Lorícora: None declared, J. Narváez Consultant for: Bristol-Myers Squibb, Elena Aurrecoechea: None declared, Ignacio Villa-Blanco: None declared, Santos Castañeda Consultant for: Amgen, BMS, Pfizer, Lilly, MSD, Roche, Sanofi, UCB, Catalina Gonzalez-Arango: None declared, ANTONIO MERA VARELA: None declared, Eva Perez-Pampín: None declared, Vicente Aldasoro: None declared, Noelia Alvarez-Rivas: None declared, Nagore Fernández-Llano: None declared, Maria Álvarez del Buergo: None declared, Luisa Marena Rojas: None declared, Francesca Sivera: None declared, Eva Galindez: None declared, Roser Solans-Laqué: None declared, Susana Romero-Yuste: None declared, Isabel Martinez-Rodriguez: None declared, Jose Ignacio Landa: None declared, Miguel A Gonzalez-Gay Grant/research support from: Prof. MA Gonzalez-Gay received grants/research support from: Abbvie, MSD,
Outcomes of patients treated with tocilizumab or abatacept as steroid-sparing agents with giant cell arteritis

Daniela Rossi, Irene Cecchi, Elena Rubini, Massimo Radin, Savino Sciascia, Dario Roccatello, University of Turin, Turin, Italy

Background: Giant cell arteritis (GCA) is a common form of systemic vasculitis. The current mainstay of GCA management is glucocorticoid (GC) therapy. Recently, at least 2 biological therapies (tocilizumab (TCZ) and abatacept (ABA)) have been proven to be effective in the management of GCA in randomized controlled trials. Nevertheless, their use as steroid sparing agents might need further investigation.

Objectives: We aimed to investigate the steroid-sparing effect of biological therapies, namely TCZ and ABA, in a cohort of GCA patients when compared to standard GC treatment.

Methods: We retrospectively collected data from GCA patients who attended the S.G. Bosco Hospital, Turin, Italy, who were treated with TCZ, both intravenous (IV) and subcutaneous (SC), and/or ABA SC (8 mg/kg/month, 162 mg/week, and 125 mg/week respectively). These therapies were prescribed as first line agents or as second line when patients refractory/intolerant/contraindicated to standard immunosuppressive therapies. Complete response to the treatment was defined as a clinical and serological remission after 12 months of therapy; partial response was defined as clinical or serological remission after 12 months of therapy.

Results: This retrospective study included 33 GCA patients (mean age 74 (range 85-57), females 63%, mean follow-up from GCA diagnosis 44.4-33.5 months). Table 1 resumes the characteristics of the GCA patients included in the study. Twenty-eight patients out of 33 (85%) received one biologic agent. Five patients (15%) needed a therapeutic switch (one patient from TCZ to ABA, and 4 patients from ABA to TCZ). Patients were treated as follow: 9 with TCZ IV, 11 with TCZ SC, and 18 with ABA. Among the TCZ IV group, all patients experienced a response (57% complete response, and 43% partial response). Among the TCZ SC group, 83% experienced a response (67% complete response, and 16% partial response). Among the ABA group, 86% experienced a response (36% complete response, and 50% partial response). After 12 months of therapy, 100% of patients in TCZ groups, both IV and SC, and 64.2% of ABA group were treated with low doses of oral prednisone (≤ 7.5 mg/day) as maintenance. We noticed a significant reduction of inflammatory parameters [C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR)] after 12 months of therapy with TCZ (TCZ IV group: mean baseline CRP (mg/dl) 1.9±2.3, mean CRP after 12 months of therapy 0.3±0.2; mean baseline ESR (mm/h) 58.1±25.6, mean ESR after 12 months 9.5±4.2; TCZ SC group: mean baseline CRP 4.5±3.8, mean CRP after 12 months 0.2±0.2; mean baseline ESR 51.9±27, mean ESR after 12 months 6.5±6]. When compared to standard GC regimen [1], in patients treated with TCZ, both IV and SC, we estimated a median steroid-sparing effect quantifiable in 30 mg/daily in the first month and an overall steroid-sparing effect of 15 mg/daily when assessed in 12 months.

Conclusion: This retrospective study confirms the efficacy of biological therapies in the management of GCA. Besides, in our experience TCZ allowed a significant reduction of GCs use, especially in the first month of therapy, when compared to standard GCs based regimens.

REFERENCE:


Disclosure of Interests: None declared

induction therapy was more common in severe patients (71.8% of patients having at least one comorbidity) compared to mild patients (55.1%). Since BVAS was not measured routinely, clinical response was categorized as full (no vasculitis activity and GC taper on track), partial (reduction in vasculitis activity and major organ damage arrested) and no response (no improvement in vasculitis). Clinical response is presented below (% patients) for combination of incident and relapsing patients demonstrating that response varied with many patients having slow and/or incomplete response. Response varied by severity of the disease when induction therapy commenced.

**Conclusion:** Incident and relapsing AAV patients have variable disease severity at the time of induction therapy. Response to induction therapy is with few exceptions better in patients with milder AAV but overall many patients are slow to respond or have only a partial response to current induction therapy.

**Acknowledgement:** This work was supported by Vifor Pharma

**Disclosure of Interests:** Peter Rutherford Employee of: Vifor Pharma, Dieter Götte Employee of: Vifor Pharma


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**THU0316 PROTEINASE-3 REGULATING MICRO-RNA IN GRANULOMATOSIS WITH POLYANGIITIS**

Susanne Schinke1, Nick Reichard2, Barbara Russo2, Antje Müller3, Martin Lauden4, Robert Häsl4, Gabriela Riemekasten1, Peter Lamprecht1.

1University Lübeck, UKSH Campus Lübeck; 2Rheumatology and Clinical Immunology, Lübeck, Germany; 3University Lübeck, Lübeck, Germany; 4University Hospital and School of Medicine, Immunology and Allergy, Geneva, Switzerland; 5Christian-Albrechts-University Kiel, Kiel, Germany

**Background:** Dysregulated miRNA expression profiles have been described in diverse chronic inflammatory diseases. We previously did a microarray screening of 847 miRNAs in nasal tissue from GPA patients and we found a disease associated alteration of miRNA expression compared to healthy controls (HC) and chronic rhinosinusitis (CRS).

**Objectives:** In order to identify new miRNA targets of potential pathophysiological relevance in GPA, we validated dysregulated miRNAs by qPCR in GPA nasal tissue biopsies and sera. Moreover, we screened GPA associated miRNAs for their potential to regulate proteinase-3 (PTRN3).

**Methods:** In an independent validation cohort (tissue and sera from 14 GPA-patients, 10 disease controls: CRS and Crohn’s/CD) 12 miRNAs were examined by qPCR. Validated and computational miRNA targets were identified by miDIP algorithms. The inhibitory capacity of miRNAs on Proteinase-3 (PTRN3) was estimated by a dual-luciferase reporter system (Promega®). The 3’UTR-PTRN3 sequence was cloned and inserted into the pmirGlo vector and co-transfected with the hsa-mirna mimics (Dharmacon®) into HeLa cells. As a second method, the effect of miR-184 transfection on the endogenous PRTN3 expression in the human myeloid leukemia cell line HL-60 was estimated by western blot.

**Results:** Microarray screening revealed alteration of 24 miRNAs in GPA nasal tissue compared to HC and CRS. qPCR confirmed dysregulation of 6 tissue related miRNAs also in GPA sera. Compared to CD 4 miRNAs (miR-10b, -99a/100, -125b, -532-3p) were down regulated in GPA tissue. The miRNA with the highest expression level in nasal tissue from GPA was miR-184. miR-184 along with miR-708 and miR-214-5p were also predicted to target PRTN3 by the miDIP algorithm. The dual-luciferase reporter assay revealed a significant reduction of PRTN3 expression by miR-184, while these effects could not be observed for miR-708 or miR-214-5p. The transfection of miR-184 into HL-60 cells resulted in a dose-dependent knockdown of PRTN3 expression as detected by Western blot.

**Conclusion:** Characteristic miRNA signatures in GPA, CRS and CD suggest distinct pathophysiological mechanisms. It indicates at a local miRNA dysregulation in inflamed GPA tissue with a corresponding serum signature that might serve as novel biomarkers. To our knowledge this is the first analysis that attempts to correlate GPA-associated miRNA expression patterns in tissue with serum. Moreover, this is the first description of a miRNA (miR-184) that potentially regulates the expression of the GPA autoantigen PRTN3.

**REFERENCES:**


**Disclosure of Interests:** Susanne Schinke Grant/research support from: travel and congress expenses from different companies pfizer, ucb, chemocentryx; Janissen-Clag, msi; Nick Reichard: None declared, Barbara Russo: None declared, Antje Müller: None declared, Martin Lauden: paid instructor for: Olympus, Speakers bureau: Novartis, Robert Häsl: None declared, Gabriela Riemekasten Consultant for: Chugai, F. Hoffmann-La Roche, Speakers bureau: Chugai, F. Hoffmann-La Roche, Peter Lamprecht: None declared

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**THU0317 IDENTIFICATION OF ENDOTHelial PROTEIN C RECEPTOR AND SCAVENGER RECEPTOR CLASS B TYPE 1 AS MAJOR AUTOANTIGENS IN TAKAYASU ARTERITIS**

Tsuyoshi Shiri, Tomoyuki Mutoh, Tomonori Ishii, Hiroshi Fujii, Hideo Harigae.

**Background:** Takayasu arteritis (TAK) affects the aorta and its major branches. It has been recognized that high numbers of patients with TAK possessed endothelial cell antibodies (AECA), which have potential to induce vascular lesion. However, their major target antigens remain unclear. The target antigens of AECA are plasma membrane proteins, and traditional methods to identify autoantigens do not differentiate between cell-surface molecules and intracellular molecules. To overcome this problem, we have developed an expression cloning system to identify cell-surface antigens: serological identification system for autoantigens using a retroviral vector and flow cytometry (SARP)-3,5. Because there...
exists no disease-specific testing for TAK, identification of autoantigens would be extremely important.

Objective: To identify major autoantigens in TAK using SARF and analyze clinical significance of autoantibodies

Methods: Two hundred and seventy-eight patients with collagen diseases were enrolled: 20, TAK; 10, giant cell arteritis (GCA); and 188, other collagen diseases. A cDNA library of human umbilical vein endothelial cells (HUVECs) was retrovirally transfected into a rat myeloma cell line. Cells expressing the cDNA library were stained with prototype AECA and fluorescence-conjugated secondary anti-human IgG, and cells with fluorescence were sorted with flow cytometry. Autoantigen identification was performed by analyzing the cDNA inserted into the sorted cells. Cells expressing the identified autoantigens were generated, and the presence of autoantibodies was confirmed. The autoantibodies against identified autoantigens were measured in TAK and other collagen diseases, and the prevalence and clinical characteristics of each autoantibody were evaluated.

Results: AECA activity against HUVECs were measured in patients with TAK and nine AECA serum samples were selected for subsequent SARF. Four distinct AECA-positive clones were successfully isolated using serum IgG from TAK patients. Two clones were identical to the cDNA of PROCR encoding protein C receptor (EPCR), and others, to SCARB1 encoding scavenger receptor class B type 1 (SR-BI). A validation experiment involving 52 patients with TAK confirmed disease specificity in TAK; autoantibodies against EPCR or SR-BI accounted for 34.6% or 36.5% cases, respectively, with minimal overlap (3.8%). Measurement of these autoantibodies in other collagen diseases was performed, and the sensitivity and specificity of these two autoantibodies were 67.3% and 96.5%, respectively. Importantly, these autoantibodies were not detected in patients with GCA who were positive for temporal artery biopsy. TAK was classified into three subtypes based on the profile of these autoantibodies. Anti-EPCR positive group showed high prevalence of stroke, ulcerative colitis, and type II artery lesion. Anti-SR-BI positive group presented higher levels of inflammatory markers, type V artery lesion, and older age at onset. Aortic regurgitation was rare in anti-SR-BI positive group. Double-negative group presented higher rates of vascular surgery.

Conclusion: We identified EPCR and SR-BI as novel autoantigens in TAK. Autoantibodies against EPCR or SR-BI were observed in 66.7% of patients, and different types of autoantibodies showed distinct clinical characteristics. These autoantibodies would aid in clinical application and elucidating pathomechanisms.

REFERENCES:

Disclosure of Interests: Tsuyoshi Shirai: None declared, Tomoyuki Mutoh: None declared, Tomonori Ishii Grant/research support from: GSK, Janssen, Consultant for: GSK, Janssen, Speakers bureau: Mitsubishi-Tanabe, Janssen, Chugai, Ono, Sanofi, Abbvie, Eisai, Astellas, UCB, Teijin, Daiichi-Sankyo, Pfizer, Takeda, Asahi, and Kasei Pharma, Hiroshi Fuji: None declared, Hideo Hanag: None declared


THU0318 ANCA-ASSOCIATED GLOMERULONEPHRITIS WITHOUT CRESCENT FORMATION HAS ATYPICAL CLINICOPATHOLOGICAL FEATURES: A MULTICENTER RETROSPECTIVE STUDY

Kazuyuki Suzuki, Takeshi Zoshima, Hajime Sanada, Fae Suzuki, Satoshi Hara, Mitsuhiro Kawano, Kanazawa University Hospital, Kanazawa, Japan

Background: The most typical histopathological feature of ANCA-associated glomerulonephritis (ANCA-GN) is crescentic GN. However, ANCA-GN is also complicated by other renal lesions, including vascular ones (arteritis and arteriolitis) and tubulointerstitial ones (tubulitis and peritubular capillaritis) [Reference 1], and tubulointerstitial or vascular dominant inflammation without glomerulopathy sometimes exists. Few reports have focused on ANCA-GN without crescent formation in a large multicenter study.

Objectives: To identify the clinicopathological features of ANCA-GN without crescent formation.

Methods: We enrolled 122 Japanese ANCA-GN patients who were subjected to renal biopsy in 16 hospitals from 2001 to 2018. We measured various clinical parameters at the time of renal biopsy, including creatinine (Cr), estimated glomerular filtration rate (eGFR), C-reactive protein (CRP), MPO-ANCA, PR3-ANCA in the sera, urinalysis findings, and presence of comorbidities (hypertension, hyperlipidemia, diabetes mellitus, and hyperuricemia). Renal biopsy findings were evaluated by light microscopy. We also measured serum Cr and eGFR at the last patient visit, and recorded medications prescribed for ANCA-GN. We retrospectively compared these clinical and histological findings between those with crescent (C+ group) and without crescent (C- group). The primary endpoint was the cumulative percentage of patients who died from any cause.

Results: Of 122 patients (63 females; mean age 69.5 years; observation period 37.1±14.8 years), C- group included 20 (16.4%). Although C+ group had higher CRP levels (11.2±8.5 vs 6.6±5.2 mg/dl, p=0.01), they had less proteinuria (0.8±0.9 vs 1.6±1.7 mgCr, p=0.04) and better renal function (eGFR; 52.1±29.5 vs 30.2±25.4 ml/min/1.73m2, p<0.01) than C+ group. There were no significant differences in any other clinical findings including ANCA serology. In histological findings, C- group had a higher frequency of arteritis (40.0% vs 16.8%, p=0.03), while other histological findings such as arteriolitis, tubulitis and peritubular capillaritis did not differ. There were no significant differences in medications or observational period. C+ group had better latest renal function (eGFR; 57.3±27.8 vs 39.0±23.6 ml/min/1.73m2, p=0.02) than C+ group. However, overall survival rate did not differ (68.4% vs 78.7%, p=0.37).

Conclusion: ANCA-GN without crescent formation had specific clinicopathological features including higher systemic inflammation and frequency of renal arteritis than ANCA-GN with crescent formation. Though renal function throughout the clinical course was better in ANCA-GN without crescent formation, overall survival rate was similar with ANCA-GN with crescent formation.

REFERENCE:

Disclosure of Interests: None declared


THU0319 TAKAYASU’S ARTERITIS: BEYOND THE VESSELS

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Background: Takayasu arteritis (TAK) is an inflammatory disease which primarily affects large vessels1. However, as a systemic disease, the spectrum of its manifestations is not limited to the arterial wall2.3.

Objectives: To describe characteristics of extravascular manifestations of TAK patients from a single Italian Centre.

Methods: Data records of TAK patients diagnosed according to the 1990 ACR criteria and followed-up at our Large Vessel Vasculitis Clinic were reviewed. Any significant inflammatory/autoimmune comorbidity and family history for inflammatory/autoimmune diseases were considered. For each comorbidity, temporal correlation with TAK diagnosis was assessed. Need for biological therapy for TAK control, as an indirect measure of TAK aggressiveness, was evaluated. Non-parametric statistic tests were used.

Results: In our cohort of 129 TAK patients, 46 patients (37.5%) were identified as having an inflammatory/autoimmune comorbidity, for a total of 64 comorbidities (14 patients experienced >1 comorbidity). Comorbidities were classified into 6 categories: systemic inflammatory diseases (17.2%); gastrointestinal (9.4%), articular (10.9%), ocular (20.3%) and mucocutaneous (39.1%) involvement; miscellaneous (autoimmune hepatitis (1.6%), retroperitoneal fibrosis (1.6%). In 33 cases (51.6%) the comorbidity onset preceded, in 25 (39%) followed and in 6 (9.4%) was synchronous with TAK diagnosis (Table 1). In 25 patients (54.3%) use of a biological therapy to control TAK activity was needed (versus 35.4% in patients without comorbidities, p=0.042). Having a comorbidity increased the risk for the introduction of a biologic therapy, odds ratio=2.176 (1.6%-4.541). Of the 129 TAK patients, 17 (13.2%) had a positive family
Abstract THU0319 – Table 1. Prevalence and characteristics of inflammatory/autoimmune extravascular comorbidities in a cohort of 129 TAK patients, temporal correlation with TAK diagnosis, and need for biological therapy.

<table>
<thead>
<tr>
<th>DISEASE</th>
<th>N° OF CASES</th>
<th>ANTECEDENT TO TAK DIAGNOSIS</th>
<th>SUBSEQUENT TO TAK DIAGNOSIS</th>
<th>SYNONCHRONOUS WITH TAK DIAGNOSIS</th>
<th>NEED FOR BIOLOGICAL THERAPY</th>
</tr>
</thead>
<tbody>
<tr>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
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<td>0</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
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<td>4</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
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<td>1</td>
<td>2</td>
<td>2</td>
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<tr>
<td>GUT</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<td>2</td>
<td>1</td>
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<td>0</td>
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<td>0</td>
<td>0</td>
<td>1</td>
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<td>Undifferentiated Colitis</td>
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<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
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<tr>
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<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
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<tr>
<td>TOT.</td>
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<td>4</td>
<td>2</td>
<td>0</td>
<td>4 (66.7%)</td>
</tr>
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<td>0</td>
<td>4</td>
<td>0</td>
<td>3</td>
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<td>2</td>
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<td>2</td>
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<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>TOT.</td>
<td>7</td>
<td>1</td>
<td>6</td>
<td>0</td>
<td>6 (85.7%)</td>
</tr>
<tr>
<td>EYE</td>
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<td></td>
</tr>
<tr>
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<td>3</td>
<td>3</td>
<td>0</td>
<td>4</td>
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<tr>
<td>Serpiginous Choroiditis</td>
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<tr>
<td>TOT.</td>
<td>13</td>
<td>8</td>
<td>5</td>
<td>0</td>
<td>6 (46.2%)</td>
</tr>
<tr>
<td>SKIN/MUCOSA</td>
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<tr>
<td>Erythema Nodosum</td>
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<td>8</td>
<td>8</td>
<td>2</td>
<td>10</td>
</tr>
<tr>
<td>Chronic Urticaria</td>
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<td>3</td>
<td>4</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Chronic Recurrent Oral</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>0</td>
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<tr>
<td>Aphthous Ulcers</td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Skin Psoriasis</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>TOT.</td>
<td>25</td>
<td>13</td>
<td>10</td>
<td>2</td>
<td>15 (60%)</td>
</tr>
<tr>
<td>MISCELLANEOUS</td>
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<td>0</td>
<td>0</td>
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<td>0</td>
</tr>
<tr>
<td>Autoimmune Hepatitis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>TOT.</td>
<td>64</td>
<td>33</td>
<td>25</td>
<td>6 (9.4%)</td>
<td>38</td>
</tr>
</tbody>
</table>

|ieron | 25 (patients) |

THU0320 RISK FACTORS OF INTRAVENOUS IMMUNOGLOBULIN RESISTANCE AND CORONARY ARTERIAL LESIONS IN TURKISH CHILDREN WITH KAWASAKI DISEASE

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Background: Kawasaki Disease (KD) is an acute, systemic, febrile vasculitis that occurs during infancy and is the most common cause of childhood coronary artery disease. The incidence of coronary artery lesions (CALs) has declined with the routine use of intravenous immunoglobulin (IVIG) treatment, but there is still considerable risk for resistance to IVIG treatment and development of CALs (1). Objectives: Previously defined risk scoring systems have limited predictive capacity for IVIG resistance of KD in Turkish children. The present study was aimed to determine the risk factors in Turkish children with IVIG resistant KD and coronary artery involvement. Methods: Clinical, laboratory and echocardiographic data were retrospectively analyzed in 94 Kawasaki patients. IVIG resistant and responsive groups were compared. Results: Of the 94 patients included in the study, 55 (58.5%) were male and 39 (41.5%) were female and the ratio was 1.41. The median (25–75 percentage) age at the time of diagnosis was 35 (19-52) months. CALs were observed at echocardiographic evaluation in 31 patients (33%) and 17 patients (18.1%) were IVIG resistant. IVIG resistant group had a higher rate of CALs compared to the IVIG responsive group (p<0.05). When two groups were compared prior to IVIG, neutrophil/lymphocyte ratio (NLR) and C-reactive protein (CRP) parameters were statistically higher in IVIG resistant group. NLR values still remained as statistically higher in the IVIG-resistant group after initial IVIG. Regarding IVIG resistance, duration of fever ≥ 9.5 days, CRP ≥ 88 mg/L and NLR > 1.69 were the best cutoff values. The criteria for at least two of these three predictors were considered to be statistically significant risk factors for detecting IVIG resistance in KD before treatment (76.47% sensitivity, 71.05% specificity and 95% confidence intervals were 50.1-93.19% and 59.51-80.89%, respectively). Regarding risk for CALs, duration of fever ≥ 9.5 days before IVIG, (OR: 3.4) and Pit count after IVIG ≥ 670x10⁴/mL, (OR: 5.5), were the best cutoff values.

Abstract THU0320 – Table 1. ROC analyses and Odds ratios for best cut-off values of variables for predicting IVIG resistance before IVIG treatment.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Duration of fever before IVIG (days)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Discriminative ability</th>
<th>Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>9.5</td>
<td>85.8%</td>
<td>72.7%</td>
<td>0.667±0.080</td>
<td>3.809</td>
</tr>
<tr>
<td></td>
<td>9.5</td>
<td>95% (CI: 510-128)</td>
<td>95% (CI: 1.1-2.8)</td>
<td>0.824, p=0.032</td>
<td>11.31 (p=0.016)</td>
</tr>
<tr>
<td>CRP before IVIG mg/L</td>
<td>88.0</td>
<td>70.0%</td>
<td>64.7%</td>
<td>0.696±0.076</td>
<td>4.40</td>
</tr>
<tr>
<td></td>
<td>95% (CI: 0.520-1.38)</td>
<td>95% (CI: 1.38)</td>
<td>0.817, p=0.032</td>
<td>13.97 (p=0.012)</td>
<td></td>
</tr>
<tr>
<td>NLR before IVIG</td>
<td>1.69</td>
<td>93.3%</td>
<td>43.4%</td>
<td>0.678±0.070</td>
<td>4.40</td>
</tr>
<tr>
<td></td>
<td>95% (CI: 0.541-13.97)</td>
<td>95% (CI: 1.38)</td>
<td>0.817, p=0.031</td>
<td>13.97 (p=0.012)</td>
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</tr>
</tbody>
</table>

p<0.05
Conclusion: This study defined three criteria for IVIG resistance in KD prior to treatment: Duration of fever before IVIG > 9.5 days, CRP > 88 mg/L and NLR value > 1.69. Presence of two of these three criteria were found as a significant risk factor for IVIG resistance. Following initial therapy with IVIG, if NLR value is > 1.25, it also predicted ongoing inflammation and IVIG resistance, possibly a need for steroid therapy instead of second IVIG.

Based on the clinical and laboratory features, we established a new risk-scoring system for predicting IVIG resistance in Turkish children with KD. This may be useful for choosing optimal treatment for KD before corona artery involvement.

REFERENCE:

Disclosure of Interests: Serkan Turkuca; None declared, Kaan Yildiz; None declared, Ceyhun Acari; None declared, Hatice Adiguzel Dundar; None declared, Serkan Turkucar; None declared, Kaan Yildiz; None declared.


Background: Approximately 50% of patients with giant cell arteritis (GCA) also have polymyalgia rheumatica (PMR) symptoms. 1

Approximately 50% of patients with giant cell arteritis (GCA) have polymyalgia rheumatica (PMR) symptoms. 1

Clinical manifestations of disease onset, n (%)

Table 1

<table>
<thead>
<tr>
<th>Symptom</th>
<th>With PMR (n = 32)</th>
<th>Without PMR (n = 29)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Localized headache</td>
<td>28 (87.5)</td>
<td>19 (68.9)</td>
</tr>
<tr>
<td>Scalp tenderness</td>
<td>15 (46.9)</td>
<td>11 (39.3)</td>
</tr>
<tr>
<td>Jaw clausitication</td>
<td>16 (50.0)</td>
<td>15 (51.7)</td>
</tr>
<tr>
<td>Amaurosis fugax</td>
<td>5 (15.6)</td>
<td>6 (21.4)</td>
</tr>
<tr>
<td>Blurry vision</td>
<td>9 (28.1)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Permanent vision loss</td>
<td>2 (6.3)</td>
<td>6 (21.4)</td>
</tr>
<tr>
<td>Diplopia</td>
<td>1 (3.1)</td>
<td>1 (3.6)</td>
</tr>
<tr>
<td>Weight loss</td>
<td>9 (28.1)</td>
<td>14 (48.3)</td>
</tr>
<tr>
<td>PMR symptoms (s) only, n (%)</td>
<td>2 (6.3)</td>
<td>0</td>
</tr>
<tr>
<td>ESR (mm/hr), mean (SD)</td>
<td>67.9 (36.52)</td>
<td>78.3 (20.41)</td>
</tr>
<tr>
<td>CRP (mg/L), mean (SD)</td>
<td>63.1 (56.69)</td>
<td>92.4 (84.65)</td>
</tr>
<tr>
<td>Positive TA test, n (%)</td>
<td>14/27 (48.3)</td>
<td>11/24 (45.8)</td>
</tr>
</tbody>
</table>

Abstract THU0321 – Table 1

Table 1. Patient characteristics at GCA diagnosis and treatment received

<table>
<thead>
<tr>
<th>Age, mean (SD)</th>
<th>67.6 (8.27)</th>
<th>71.0 (9.09)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, n (%)</td>
<td>23 (71.9)</td>
<td>20 (71.4)</td>
</tr>
<tr>
<td>White, n (%)</td>
<td>27 (84.4)</td>
<td>20 (69.2)</td>
</tr>
<tr>
<td>Clinical manifestations at disease onset, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Localized headache</td>
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<td>Weight loss</td>
<td>9 (28.1)</td>
<td>14 (48.3)</td>
</tr>
</tbody>
</table>

PMR symptoms (s) only, n (%)

| With PMR symptom(s) | 2 (6.3) | 0 |
| Without PMR symptom(s) | 3 (9.4) | 3 (9.4) |
| PMR symptom(s) (s), n (%) | 5 (15.6) | 6 (21.4) |
| No. of flares | 60 | 23 |
| With PMR symptom(s), n (%) | 50 (83.3) | 18 (78.3) |
| Without PMR symptom(s) | 10 (16.7) | 5 (21.7) |
| Annual flare rate (95%) | 1.34 | 0.54 |
| Time to flare (years), median (IQR) | 0.3 (0.2-0.7) | 2.1 (0.6-2.6) |

Abstract THU0321 – Table 2

Table 2. Clinical outcomes before and after TCZ initiation

<table>
<thead>
<tr>
<th>Before TCZ Initiation</th>
<th>After TCZ Initiation</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with ≥ 1 flare, n (%)</td>
<td>24 (75.0)</td>
<td>11 (33.4)</td>
</tr>
<tr>
<td>With PMR symptom(s)</td>
<td>21 (65.6)</td>
<td>8 (25.0)</td>
</tr>
<tr>
<td>Without PMR symptom(s)</td>
<td>3 (9.4)</td>
<td>3 (9.4)</td>
</tr>
<tr>
<td>No. of flares</td>
<td>60</td>
<td>23</td>
</tr>
<tr>
<td>With PMR symptom(s), n (%)</td>
<td>50 (83.3)</td>
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<td>1.34</td>
<td>0.54</td>
</tr>
<tr>
<td>Time to flare (years), median (IQR)</td>
<td>0.3 (0.2-0.7)</td>
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</tr>
</tbody>
</table>

Abstract THU0322 – Table 2

Table 2. Clinical outcomes before and after TCZ initiation

<table>
<thead>
<tr>
<th>Before TCZ Initiation</th>
<th>After TCZ Initiation</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with ≥ 1 flare, n (%)</td>
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<tr>
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</tr>
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<td>0.3 (0.2-0.7)</td>
<td>2.1 (0.6-2.6)</td>
</tr>
</tbody>
</table>

GC, glucocorticoids; GCA, giant cell arteritis; IQR, interquartile range; PMR, polymyalgia rheumatica; TCZ, tocilizumab.
* Symptoms are after GCA diagnosis.
† Rates are estimated from a Poisson regression model with treatment, age, smoking history and new and relapsing GCA as covariates and random patient effect.

Disclosure of Interests: Sebastian Unizony Grant/research support from: F. Hoffmann-La Roche, Genentech, Consultant for: Kiniksia, Sanofi, GSK, Robert Spiera Grant/research support from: Roche-Genentech, Xencor, GlaxoSmithKline, Bristol-Myers Squibb, Boehringer Ingelheim, Cytori, Chemocentryx, Corbux, Consultant for: Roche-Genentech, GlaxoSmithKline, CSL Behring, Sanofi Aventis, Jinglan Pei Employee of: Genentech, Paris Sidiropoulos Employee of: Genentech, Jennie H. Best Shareholder of: Genentech, Employee of: Genentech, John H. Stone Grant/research support from: F. Hoffmann-La Roche, Genentech, Xencor, Consultant for: Chugain, F. Hoffmann-La Roche, Genentech, Xencor


THU0322

Clinical characteristics of biopsy-proven IGA vasculitis in children and adults: A retrospective cohort study

Michel Villatoro Villar1, Cynthia S. Crowson1,2, Ashima Makol1, Kenneth J Warrington1, Steven R. Ytterberg1, Matthew Koster1

Rheumatology, Rochester MN, United States of America; Mayo Clinic, Rochester MN, United States of America; Mayo Clinic, Health Sciences Research, Rochester MN, United States of America

Background: Differences in both presentation and outcome based on age of diagnosis have been described in patients with IGA vasculitis (lGAV) but data are limited due to cohort size and follow-up duration.

Objectives: To describe the differences in clinical characteristics and outcome between adult- and child-onset biopsy-proven IGA vasculitis (lGAV) in North America.

REFERENCE:
Methods: Patients with IgAV from January 1, 1997, through December 31, 2016 were retrospectively identified. Clinical characteristics, laboratory parameters and outcomes were abstracted from direct medical chart review. Proteinuria was classified as non-nephrotic (>0.2 g/dl, >3.5 g/dl) or nephrotic (>3.5 g/dl). Microscopic hematuria was defined as ≥5 RBCs/hpf or ≥2+ on dipstick. Disease activity at each follow-up visit was categorized as complete response (normalization of all baseline abnormalities due to IgAV), partial response, non-response (lack of improvement of any abnormalities) or relapse (development of clinical signs of IgAV after a symptom-free period of at least one month). Prevalence of disease activity and competing risks were estimated using multi-state models.

Results: A total of 243 IgAV patients were identified (97% Caucasian, 58% male). 174 patients were adults (>21 years) and 69 were <21 years. Compared to patients <21 years, adults at baseline had more frequent ulcerative skin lesions (11% vs. 9%; p=0.02) and nephrotic-range proteinuria (22% vs. 3%; p=0.007) but less commonly had abdominal pain (34% vs. 61%; p=0.01), ischemic gastrointestinal involvement (10% vs. 20%; p=0.04) and arthralgias (38% vs. 61%; p=0.001). Frequency of microscopic hematuria was similar between groups (47%). Oral corticosteroids were the most common initial treatment used (80%). Dialysis was required in 13 patients (8 adults) and renal transplant was performed in 4 cases (1 adult). Of 137 patients with hematuria during the study, 72% had complete resolution by 1 year after onset, compared to 50% of 179 patients with proteinuria. The prevalence of disease activity state at each follow-up time point is shown in figure 1. During 389 person-years of follow-up, 29 deaths were observed. The main causes of death were cancer, cardiovascular disease, infection and vasculitis. Five person-years of follow-up, 29 deaths were observed. The main causes of death were cancer, cardiovascular disease, infection and vasculitis. Five year survival rates (95% CI) for patients aged <21, 21-50, and 51+ years were 100%, 94% (87, 100) and 40% (26, 63), respectively (p<0.001). Standardized mortality ratio for patients aged 21-50 years at diagnosis was 5.62 (0.68, 20.3) and 7.60 (5.0, 11.1) for those 51 or older.

Conclusion: IgAV in adults is associated with more severe skin/kidney involvement and poorer renal outcome. Among adults with IgAV, patients aged 51 years or older at diagnosis have significantly higher mortality.

Abstract THU0322 - Figure 1

REFERENCES:

Disclosure of Interests: None declared
AXONAL DYSFUNCTION IN CEREBRAL WHITE MATTER IN SYSTEMIC SCLEROSIS: A PROTON MAGNETIC RESONANCE SPECTROSCOPIC IMAGING (1H-MRSI) STUDY

Danilo Pereira, Mariana Freschi, Renan Frittoli, Tiago Amaral, Sergio Dertkigil, Ana Paula del Rio, Gabriela Castellano, Fernando Cendes, Leticia Rittner, Simone Appenzeller. University of Campinas, Campinas, Brazil

Background: Systemic sclerosis (SSc) is a diffuse connective tissue disease characterized by varying degrees of cutaneous and visceral fibrosis, presence of autointerandies and vasculopathy. In addition, central nervous system (CNS) involvements are often observed [1].

Objectives: The aim of the present study was to investigate the presence of axonal dysfunction in systemic sclerosis (SSc) and to determine if clinical, laboratory and treatment features are associated with its occurrence.

Methods: In this longitudinal study we included 38 SSc patients (32 woman, mean age of 50.86, SD=11.66 years; range 31-74) and 38 healthy volunteers (32 woman, mean age of 49.23, SD=12.03 years; range 26-77). All individuals were evaluated (neuropsychiatric evaluation and MRI) at study entry and after 12 months. Cognitive evaluation was performed using the Montreal Cognitive Assessment (MoCA), mood disorders were determined through Beck’s Depression (BDI) and Beck’s Anxiety Inventories (BAI). Individual with scores: MoCA ≥26, BDI ≥11 and BAI ≥7 were considered impaired. SSc patients were further assessed for clinical and laboratory SSc manifestations, disease activity (Medsger Activity Index), severity activity (Medsgier Severity Index). We performed multi-voxel 1H-MRSI over the superior-posterior region of the corpus callosum. Our MR/MRSI protocol consisted of: T1-weighted images; 2D pulse sequence (PRESS); excitation angle of 90˚. Our MRI/MRSI protocol consisted of: T1-weighted images; 2D pulse sequence (PRESS); excitation angle of 90˚.

Results: We observed a significant reduction in NAA/Cr (mean value=1.72; SD=2.4) and Cho/Cr(mean value=2.4; SD=2.04) ratio in SSc when compared to controls (NSC/Cr mean value=1.85; SD=2.7; p = 0.36; Cho/Cr mean value=0.377; SD=0.169; p<0.001). Reduction in NAA/Cr ratio was associated with cognitive impairment (p = 0.017), presence of migraine (p = 0.001), current use of prednisone (p=0.010) and current use of methotrexate (p < 0.001). NAA/Cr ratio correlated with MoCA scores (r=0.4; p=0.015).

Follow up study showed a reduction in NAA/Cr values when compared to patients’ baseline values (p = 0.0341).

Conclusion: Our results showed a significant reduction in NAA/Cr ratio in SSc patients associated with cognitive impairment and the use of some drugs (MTX and prednisone) during the treatment. Therefore, NAA/Cr ratios may be a useful biomarker in follow-up studies of SSc.

REFERENCES:

Disclosure of Interests: None declared


9. Systemic sclerosis, myositis and related syndromes – etiology, pathogenesis and animal models

THU0325 THE HMGB1/AGE-RAGE AXIS IN SYSTEMIC SCLEROSIS PATIENTS: A POTENTIAL ROLE IN ITS VASCULOPATHY?

Isabella Atzeni1, Amaan Emam Abdullah1, Anniek van Roon1, Gilles Diercks2, Harry van Goor3, Andreas Smil1, Johanna Westra4, Douwe J Mulder4. 1University of Groningen, University Medical Center Groningen, Internal Medicine, Division of Vascular Medicine, Groningen, Netherlands; 2University of Groningen, University Medical Center Groningen, Pathology and Medical Biology, Groningen, Netherlands; 3University of Groningen, University Medical Center Groningen, Rheumatology and Clinical Immunology, Groningen, Netherlands

Background: Systemic sclerosis (SSc) is a progressive fibro-inflammatory autoimmune disease of which the pathogenetic pathways are incompletely understood. Advanced glycation endproducts (AGEs) are oxidative stress derived compounds with potential proinflammatory effects. Their exact role in fibrosis remains unknown. The receptor for AGEs is RAGE, which is also the receptor for high mobility group box 1 (HMGB1), a nuclear protein, which is proinflammatory when released from activated or apoptotic cells. We hypothesize that AGEs and HMGB1 may promote inflammation and profibrotic processes, presumably mediated by RAGE.

Objectives: To study the role of the HMGB1/AGE-RAGE axis in the pathogenesis of SSc.

Methods: Distribution of N-(carboxymethyl)lysine (CML) and N^ε-(5-hydroxymethyl-4-imidazol-2-yl)-ornithine (MG-H1) was assessed by immunohistochemistry in skin biopsies of 12 SSc patients [median age 56 years (IQR 52-61); 6 of affected, 6 of unaffected skin]. The intensity was assessed semi-quantitatively on endothelium and fibroblasts. In vitro experiments were performed on healthy human dermal fibroblasts, which were stimulated with 0 μg/ml HMGB1. All cells were treated for 24 hours. Detection was performed using the 1H-MRSI protocol consisting of: T1-weighted images; 2D pulse sequence (PRESS); excitation angle of 90°; Long TE: 144ms and TR: 2000ms; VOI (MRSI) size (mm³) = (116 x 79 x 16) grid with 208 voxels. Scans were performed with a Philips 3.0T MRI scanner. We measured signals from N-acetyl-compounds (NAA), creatine (Cr), choline (Cho), glutamate (Glu), glutamine (Gln) and Glx (the sum of Glu and Gln) using TROQUIN software.

Statistics was performed according nature of the variable.

Results: We observed a significant reduction in NAA/Cr (mean value=1.72; SD=2.4) and Cho/Cr (mean value=2.4; SD=2.04) ratio in SSc when compared to controls (NSC/Cr mean value=1.85; SD=2.7; p = 0.36; Cho/Cr mean value=0.377; SD=0.169; p<0.001). Reduction in NAA/Cr ratio was associated with cognitive impairment (p = 0.017), presence of migraine (p = 0.001), current use of prednisone (p=0.010) and current use of methotrexate (p < 0.001). NAA/Cr ratio correlated with MoCA scores (r=0.4; p=0.015).

Follow up study showed a reduction in NAA/Cr values when compared to patients’ baseline values (p = 0.0341).

Conclusion: Our results showed a significant reduction in NAA/Cr ratio in SSc patients associated with cognitive impairment and the use of some drugs (MTX and prednisone) during the treatment. Therefore, NAA/Cr ratios may be a useful biomarker in follow-up studies of SSc.

REFERENCES:

Disclosure of Interests: None declared


THU0325 – Figure 1. Smooth muscle actin (α-SMA) expression by immunohistochemistry in stimulated and unstimulated human skin fibroblasts. Fibroblasts were treated with 0 (A), 1 (B), 10 (C) or 50 (D) ng/ml TGF-β1, 10 (E) or 100 (F) μg/ml AGE-BSA or 1 (G) or 10 (H) μg/ml HMGB1. All cells were treated for 24 hours. Detection was performed with 2 μg/ml anti-α-SMA. Bar 100 μm.

Scientific Abstracts

442 Thursday, 13 June 2019
**THU0325**  
**ANALYSIS OF PHOSPHATIDYLINOSITOL 3-KINASE PATHWAY IN B CELL ACTIVATION OF SYSTEMIC SCLEROSIS PATIENTS**

Judith Rapp, Vivien Telek, Tunde Minier, László Czirják, Times Berki; Diana Simon.  
University of Pécs Medical School, Pécs, Hungary

**Background:** B cell activation is an early event in the development of systemic sclerosis (SSc) as transcriptome profiling identified local B-cell activation in early diffuse cutaneous (dc) SSc skin biopsies. Autoantibody production is a widely investigated function of B cells in SSc but less attention has been devoted to the role of innate immune molecules and their receptors, like Toll-like receptors (TLRs). The classical B cell activation downstream of BcR and CD19 co-receptor engagement involves phosphatidylinositol-3 kinases (PI3K) signaling pathway that integrates the effects of multiple co-stimulatory receptors.

**Objectives:** Our goal was to examine PI3K signaling by investigating the mRNA expression of 92 pathway related genes in B cells from early dcSSc patients. Akt is a central element of PI3K pathway, but it can also converge into innate receptor mediated pathways such as mTOR and MAPK. Thus for functional relevance we also analyzed the phosphorylation of Akt, S6 and NF-κB in B cells from early dcSSc patients.

**Methods:** Twenty-one patients with early dcSSc were enrolled with disease duration of 2.0 (±1.2) years based on the date of the first non-Raynaud’s symptom. 30% of patients received immunosuppressive therapy. Peripheral blood CD19+ B cells were purified from dcSSc patients and age- and sex-matched healthy controls (HC, n=15). mRNA expression of 92 B cell specific PI3K pathway related genes was measured using a Taqman qPCR array and was validated by individual qPCR. Isolated B cells were activated through BcR using anti-IgG/M antibody or anti-CD180 antibody, and their combination followed by flow cytometric analysis of phospho-Akt (S473), phospho-S6 (S235/S236) and phospho-NF-κB p65 (S529) positive cells.

**Results:** Analyzing the expression of 92 PI3K pathway associated genes we found altered expression of molecules playing a role in alternate B cell activation and innate signaling. The expression of both IL-4 receptor and osteopontin (SPP1) was upregulated in B cells of untreated dcSSc patients, but became downregulated upon immunosuppressive therapy. Innate molecules like TLR4 and complement component 3 remained highly upregulated and the downregulation of CD180 was not inhibited by immunosuppressive treatment, thus may preserve the activated state of B cells in dcSSc. We aimed to model B cell activation via TLR4 and CD180 and pus and endogenous ligands of TLR4 failed to activate isolated B cells. Since there are not known ligands of CD180, we investigated the effects of anti-CD180 itself and also its combination with BcR mediated stimulation of B cells. Analyzing the phosphorylation of the PI3K pathway-associated molecules revealed an impaired responsiveness of dcSSc B cells to anti-CD180 alone, and the combination of anti-CD180 and anti-Ig induced different phosphorylation patterns of Akt, S6 and NF-κB molecules in dcSSc and healthy controls (HC).

**Conclusion:** Analysis of B cells from early dcSSc patients revealed that B cells possess molecular changes in PI3K pathway that involves innate immune components. Gaining new insight into innate B-cell activation in SSc could be helpful for finding new therapeutic targets.

**REFERENCES:**  

**Acknowledgement:** This work was supported by GINOP-232-15-2016-00050 and EFOP 361-16-2016-0004 grants.

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.3313

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**THU0326**  
**ANALYSIS OF PHOSPHATIDYLINOSITOL 3-KINASE PATHWAY IN B CELL ACTIVATION OF SYSTEMIC SCLEROSIS PATIENTS**

Diercks: None declared, Harry van Goor: None declared, Andries Smit Abdulle : None declared, Anniek van Roon: None declared, Gilles Diercks: None declared, Harald van Goor: None declared, Andries Smit

**Background:** AUTOANTIBODIES PRODUCED BY PATIENTS WITH SYSTEMIC SCLEROSIS (SSC) contribute to the pathogenesis of the disease. Autoantibodies targeting Topo-I and Cenp B to directly induce pro-fibrotic activation of fibroblasts.

**Methods:** Dermal fibroblasts were isolated from unaffected and affected skin samples of (n=10) limited cutaneous SSc (LCSSc) patients, from affected skin samples of (n=10) diffuse cutaneous (DcSSc) patients and from (n=20) healthy subjects. Fibroblasts were stimulated with serum-isolated fractions of Topo-I, Cenp B and control IgGs in ratios 1:100 and with Cenp B and Topo-I IgGs and with Cenp B+ and Topo-I+ sera statistically increased all the profibrotic markers compared to control ones. Stimulation with Cenp B and Topo-I (p<0.01) IgGs reduced unaffected LCSSc and control fibroblast viability in a time- and dilution-dependent manner compared to control IgGs. Similar results were obtained with Cenp B+ (p<0.05) and Topo-I+ (p<0.05) sera compared to control sera. Flow cytometry analysis revealed that both Cenp B/Topo-I IgGs and Cenp B+/Topo-I+ sera induce apoptosis in unaffected LCSSc and control fibroblasts only, while affected LCSSc/DcSSc fibroblasts showed apoptosis resistance. qPCR showed that basal levels of pro-fibrotic markers ACTA2, COL1A1 and TGFBI were upregulated in affected LCSSc/DcSSc fibroblasts correlated with LCSSc unaffected and to control ones. Stimulation with Cenp B and Topo-I IgGs and with Cenp B+ and Topo-I+ sera statistically increased all the profibrotic markers compared to control IgGs (p<0.05) and to control sera (p<0.05). ICC proved that α-SMA, Coll-I and SM22 levels were upregulated in a time- and dilution-dependent manner in unaffected LCSSc and control fibroblasts upon stimulation with Cenp B and Topo-I IgGs and with Cenp B+ and Topo-I+ sera, while they remained stably high in affected LCSSc/DcSSc fibroblasts.

**Conclusion:** This study demonstrates the pathogenetic role of antibodies targeting Topo-I and Cenp B to directly induce pro-fibrotic activation of fibroblasts. Therefore, besides the diagnostic and prognostic use of those autoantibodies in SSC, these data justify the importance of therapeutic use of immunosuppressive drugs in the early stages of the disease.
REFERENCES:

Disclosure of Interests: None declared

THU0328

DO PATIENTS WITH SYSTEMIC SCLEROSIS HAVE ULTRASONOGRAPHIC MODIFICATIONS OF SALIVARY GLANDS SUGGESTIVE OF SJOGREN SYNDROM?

Marion Couderc, Anne Toumadre, Sylvain Mathieu, Martin Soubrier, Jean-Jacques Dubost, CHU Clermont-Ferrand, Rheumatology, Clermont-Ferrand, France

Background: Modificiations in ultrasonographic aspect of major salivary glands have been reported in patients with primary Sjogren Syndrome (pSS) with good diagnostic accuracy. Sicca symptoms are frequently observed in Systemic sclerotic (SSc).

Objectives: To assess the ultrasonographic echostructure of major salivary glands in patients with SSC and compare the modifications with those of patients with pSS or controls with sicca symptoms.

Methods: We performed a mononcentre case-control study between 2014 and 2017 in the university hospital of Clermont-Ferrand (France). Patients with SSc and pSS were fulfilling the American College of Rheumatology/European League against Rheumatism (ACR/EULAR) 2013 and the ACR 2012 classification criteria respectively. Controls patients were complaining of sicca symptoms but did not meet the ACR 2012 criteria. Bilateral parotid and submandibular glands ultrasound (US) were performed in all patients by the same operator blinded to the diagnosis. Inhomogeneity of each of the 4 major salivary glands in B-Mode was graded using the Jousse-Joulin scoring system (scale of 0 to 4) as previously described.[1] The highest grade among the 4 glands was retained as suggestive of Sjogren Syndrome if ≥ 2.

Results: A total of 108 patients were included: SSc (n=25), pSS (n=48) and controls (n=35). Among the 48 patients with pSS, 12 were receiving hydroxychloroquine, 4 an immunosuppressor, 77% had antinuclear antibodies at a significant level (≥1:640), 26 (54%) anti-SSA antibodies, 40/45 (89%) had a labial salivary biopsy suggestive of pSS (Chisholm and Mason score ≥3). Comparing the pSS and the control groups, performance of a US echostructure grade ≥ 2 for the diagnosis of pSS was good: Se=75%, Sp=91.4%, positive predictive value= 92.3%, negative predictive value= 72.7%.

Among the 25 SSc patients, 7 had immunosuppressor therapy, 8 had a localized SSc. Shimier’s test ≤ 5 mm in 5 minutes was present in 9/18 (53%), unstimulated salivary flow ≤ 0.1 mL/minute in 8/14 (57.1%). In the SSc group, 12 patients had an US echostructure grade 0, 6 grade 1, and 7 patients (28%) had an US echostructure grade of ≥ 2: US score=3 (n=5), US score=4 (n=2). Anti-SSA antibodies were found in 1/7 patients with an US echostructure grade ≥ 2 and 2/18 patients with US echostructure grade 0 or 1.

Conclusion: Nearly one third of patients with SSc have US echostructure changes suggestive of Sjogren Syndrome regardless of the presence of anti-SSA antibodies.

REFERENCES:

Disclosure of Interests: None declared

THU0329

RED FLAG SIGNS OF SYSTEMIC SCLEROSIS ARE PREVALENT IN SUBJECTS WITH RAYNAUD’S PHENOMENON: THE GENERAL POPULATION AND MAY BE A PROXY FOR LUNG INVOLVEMENT

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Background: Pulmonary involvement in systemic sclerosis (SSc) is very difficult to treat when diagnosed too late. Therefore, in order to optimally use the “window of opportunity” more attention should be given to the early identification of SSc. To the best of our knowledge, no studies exist that have structurally assessed the epidemiology of red flag signs and potential signs of pulmonary involvement in patients with Raynaud’s phenomenon (RP).

Objectives: To assess the prevalence of red flag signs in patients with RP. Moreover, we aim to investigate the occurrence of pulmonary signs and symptoms in participants with red flag signs.

Methods: We retrospectively analyzed data from the LifeLines Cohort Study, which is a large population-based cohort study in the Northern parts of the Netherlands. A total of 74011 participants completed the connective tissue disease questionnaire. The presence of RP and red flag signs for SSC (i.e., puffy fingers, skin thickening distal, skin thickening proximal, and pitting scars) were obtained. Participants were classified as having red flag signs by the presence of at least one red flag sign in addition to RP. In addition, patient characteristics, self-reported pulmonary complaints, spirometry (screening for interstitial lung disease (ILD)), and uric acid (global screening for pulmonary arterial hypertension (PAH)) were also obtained. Three groups of participants were formed, namely: participants with RP and red flag signs (n=981), participants with RP without red flag signs (n=2946), and participants without RP and without red flag signs (n=70037).

Results: The prevalence of red flag signs was 5 fold higher in participants with RP, as compared to the non-RP group: RP 25% [23.7-26.4], non-RP 5% [4.9-5.2], p<0.001. A total of 413(42.1%) of the participants with RP and red flag signs reported dyspnea, which was 1.5 fold higher than in those with RP but without red flag signs, and two-fold higher compared to participants without RP and without red flag signs (p<0.001). Moreover, dyspnea in rest and after exertion was more prevalent in participants with RP and red flag signs (p<0.001). In addition, participants with RP and red flag signs more frequently reported to suffer from pulmonary fibrosis (p<0.001, table 1), and had the lowest forced vital capacity, as compared to the other groups (p<0.001). Conversely, uric acid was not found to be elevated in participants with RP and red flag signs.

Conclusion: This unselected cohort study from the general population demonstrates that the prevalence of red flag signs in subjects with RP may be as high as 25%. Potential signs and symptoms of pulmonary complaints are more prevalent in participants with RP who also reported red flag signs. This could indicate an increased risk of pulmonary involvement (i.e., ILD and PAH) in RP patients with red flag signs, although additional specific tests are mandatory to substantiate definite disease.

Disclosure of Interests: Amaal Eman Abdulle : None declared, Elisabeth Brouwer Speakers bureau: Dr. Brouwer as an employee of the UMCG, Harry van Goor: None declared, Johanna Westra: None declared, Karina de Leeuw: None declared, Douwe J Mulder Grant/Research support from: My University has received research grants for my research from: Boehringer Ingelheim and Actelion, Speakers bureau: My University has received speakers fee from: Sanofi

Abstract THU0329 – Figure 1. Prevalence of red flag signs in participants with and without Raynaud’s phenomenon.

Disclosure of Interests: Amaal Eman Abdulle : None declared, Elisabeth Brouwer Speakers bureau: Dr. Brouwer as an employee of the UMCG received speaker fees and consulting fees from Roche which were paid to the UMCG, Harry van Goor: None declared, Johanna Westra: None declared, Karina de Leeuw: None declared, Douwe J Mulder Grant/ Research support from: My University has received research grants for my research from: Boehringer Ingelheim and Actelion, Speakers bureau: My University has received speakers fee from: Sanofi
Background: Although several previously conducted studies reported on the prevalence of Raynaud’s phenomenon (RP) in different regions of the world, these studies often included a limited number of selected individuals. Moreover, no studies exist that have systematically assessed the relative contribution of known etiological factors of RP in the general population of the Netherlands.

Objectives: To assess the prevalence of RP, and gender-specific etiological factors associated with RP in the Northern parts of the Netherlands.

Methods: Data from the Lifelines cohort were analyzed, in which all participants completed the self-administered validated connective tissue disease questionnaire. Subjects who reported cold-sensitive fingers and biorhythmic colour changes in response to cold were considered to suffer from RP. Known etiological factors such as hormonal status, body mass index (BMI), smoking behaviour, and comorbidities were all assessed in a standardised way.

Results: In total 93,935 participants completed the questionnaire (mean age 45.6 ±12.9). The prevalence of RP was 4.2% [95% CI 4.1-4.4] which was approximately three-fold higher in females (5.7%, 95% CI [5.5-5.9]), as compared to males (2.1%, 95% CI [1.9-2.2] p-value <0.001, figure 1). Regarding gender-specific risk factors associated with RP, we observed that BMI <18.5 (OR 4.6 [2.4-8.7], p<0.001), cardiovascular disease (OR 1.93 [95% CI 1.31-1.78], p<0.001), history of cancer (OR 1.40 [1.00-1.95], p=0.049), use of beta-blockers (OR 1.39 [1.06-1.83], p=0.01), and smoking (OR 1.28 [1.09-1.51], p=0.003) were associated with an increased odds of RP in men. Conversely, alcohol consumption, diabetes and age were not associated with RP in men. In females, BMI<18.5 (OR 2.8 [2.2-3.64], p<0.001), cardiovascular disease (OR 1.42 [1.32-1.54], p<0.001), receiving hormonal contraception (OR 1.17 [1.08-1.26], p<0.001), and hormonal replacement therapy (OR 1.14 [1.04-1.25], p=0.007) were associated with increased odds of RP. Moreover, smoking behavior, use of beta-blockers, alcohol consumption, and diabetes were not associated with RP in women. A BMI<30 was associated with a strongly decreased odds of RP in both men (OR 0.22 [0.11-0.42], p<0.001) and women (OR 0.35 [0.28-0.44], p<0.001).

Conclusion: This large cohort study found a prevalence of 4.2% of RP in the Northern part of the Netherlands, with an expected predominance in young female subjects. Moreover, the etiologic risk factors of RP are multifactorial and clearly gender-specific (e.g., hormonal status in women, smoking behavior and use of beta-blockers in men), with underweight strongly increasing and obesity strongly decreasing the likelihood of RP in both sexes. This might suggest that different mechanisms influence the expression of RP in men and women.

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Abstract THU0330 - Figure 1. Prevalence of RP depicted for men and women.

REFERENCE:

Disclosure of Interests: Katrina Bamberg: None declared, Laura Mehtälä: None declared, Olli Arola: None declared, Seppo Laitinen: None declared, Paulina Nordling: None declared, Marjatta Strandberg: None declared, Niko Strandberg: None declared, Johanna Paltta: None declared, Mariku Mali: None declared, Fabricio Espinosa-Ortega: None declared, Laura Pirilä: None declared, Ingrid E. Lundberg Grant/research support from: Dr. Lundberg has received honoraria from Bristol Myers Squibb and Medimmune and is currently receiving a research grant from Bristol Myers Squibb and from Astra Zeneca., Consultant for: She is a scientific advisor for Bristol Myers Squibb, and aTyr, Tanja Savukoski: None declared, Kim Pettersson: None declared


THU0331 SKELETAL TROPOIN I A POSSIBLE NOVEL BIOMARKER FOR MANAGEMENT OF PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

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Background: The current biomarkers for the diagnosis and monitoring of diseased and injured skeletal muscles, such as creatine kinase (CK), have limited tissue specificity and incapability to differentiate between pathological and physiological changes. Thus, new biomarkers with improved diagnostic certainty are needed. Skeletal troponin I (skTnI) is a promising new biomarker for injured and diseased skeletal muscle tissue. Although studies have reported that circulating skTnI levels are elevated in response to trauma, exercise and various muscular diseases (1), its clinical utility to serve as a diagnostic indicator has largely been unexplored.

Objectives: Our aim was to develop and validate a novel assay for skTnI and to assess its clinical performance with idiopathic inflammatory myopathy (IIM) patients.

Methods: A two-step fluorimunoassay was used to analyze the levels of skTnI in samples from healthy reference individuals (n=125), trauma patients (n=151), and patients with IIM (n=94). Later, skTnI and CK levels in patients with IIM were compared according to their disease activity status (active, pre-active or stable).

Results: The limit of detection was 1.2 ng/ml, and the upper reference limit (90th percentile) was 5.4 ng/ml. The median skTnI concentrations were <LoD, 2.7 ng/ml, and 9.8 ng/ml in reference, trauma, and IIM cohorts, respectively. Differences in measured skTnI levels were statistically significant between all three study cohorts (Mann-Whitney p<0.001 for all). skTnI and CK had a strong positive correlation (Spearmans’s r=0.848, p<0.001). With skTnI, patients in both pre-active and active IIM were differentiated from stable phase patients (33.9 and 34.5 ng/ml vs 5.1 ng/ml, p<0.001 for both). This was not possible with CK as significantly elevated CK levels were mainly present in active IIM (median 16.5 ikat/L) and the medians of pre-active and stable phase skeletal muscle tissue (i.e., skat/L vs 1.7 ikat/L, p=0.060) remained close to normal reference ranges. The area under the receiver operator characteristic curve was 0.87, 0.84, and 0.87 for skTnI and CK individually and combined, respectively.

Conclusion: With the developed skTnI assay, IIM patients were identified from healthy individuals and from patients with traumatic muscular injuries. Also, skTnI was shown to outperform CK in detecting IIM patients in different disease activity statuses.

Disclosure of Interests: Katrina Bamberg: None declared, Laura Mehtälä: None declared, Olli Arola: None declared, Seppo Laitinen: None declared, Paulina Nordling: None declared, Marjatta Strandberg: None declared, Niko Strandberg: None declared, Johanna Paltta: None declared, Markku Mali: None declared, Fabricio Espinosa-Ortega: None declared, Laura Pirilä: None declared, Ingrid E. Lundberg Grant/research support from: Dr. Lundberg has received honoraria from Bristol Myers Squibb and Medimmune and is currently receiving a research grant from Bristol Myers Squibb and from Astra Zeneca., Consultant for: She is a scientific advisor for Bristol Myers Squibb, and aTyr, Tanja Savukoski: None declared, Kim Pettersson: None declared

ABSOLUTE REDUCTION OF REGULATORY T CELLS AND EFFICACY OF SHORT-TERM AND LOW-DOSE IL-2 IN PATIENTS WITH DERMATOMYOSITIS OR POLYMYOSITIS

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Background: Dermatomyositis (DM) and polymyositis (PM) are heterogeneous, chronic and progressive autoimmune disorders characterized by symmetrical, proximal muscle weakness[1,2]. Although the pathogenesis of PM/DM remains unclear, immune intolerance caused by the deficiency of regulatory T (Treg) cells may be an important cause of PM/DM, and quantitative status of peripheral Treg cells is unclear in this disease. Low-dose interleukin-2 (ld-IL2) has been found to enhance proliferation, function and survival of Treg cells to regulate immune tolerance[3]. However, the therapeutic effect of ld-IL2 on PM/DM has not been reported.

Objectives: To investigate whether peripheral Treg cells are reduced and whether ld-IL2 has therapeutic efficacy in PM/DM.

Methods: Total 71 PM/DM inpatients (10 PM and 61 DM) were retrospectively studied. Five PM and 35 DM patients were treated with ld-IL2 (5.0*10^5 international units (IU) per day for 5 days) accompanied by conventional therapy, while the rest PM/DM patients only with conventional therapy. Thirty of age- and gender-matched healthy adults were regarded as healthy controls (HCs). CD3+T, CD4+T, CD8+T, B, NK, Th1, Th2, Th17 and Treg cells, as well as cytokines [interleukin-2 (IL-2), interleukin-4 (IL-4), interleukin-6 (IL-6), interleukin-10 (IL-10), tumor necrosis factor-α (TNF-α), interferon-γ (IFN-γ) and interleukin-17 (IL-17)] were measured by flow cytometry. The correlation coefficients between various indicators and Myositis Disease Activity Assessment Visual Analogue Scale (MYOACT) were calculated by Spearman correlation test.

Results: Both PM and DM patients had significantly lower number of CD3+T (P=0.018, P=0.003) and CD4+T cells (P=0.035, P=0.016) than HCs, as well as the number and percentage of Treg cells (P<0.001) in PM/DM and these of NK, Th1 cells in DM, while Th2 and Th17 cells didn’t exhibit any significant difference. In addition, the ratio of Th1/Th2 in DM (P<0.015, P=0.001). Meanwhile, the production of serum IL-2 was reduced in PM/DM (P=0.001), while, in contrast, IL-4, IL-6, IL-10, TNF-α, IFN-γ and IL-17 increased. ld-IL2 could significantly increase the number of Treg cells but have little effect on Th17 cells in DM. In addition, MYOACT was correlated with the number of CD3+T, CD4+T, CD8+T, Th1, Th2, Treg cells, PLT and lymphocyte (r=-0.388, P=0.002; r=-0.360, P=0.004; r=-0.364, P=0.004; r=-0.386, P=0.002; r=-0.282, P=0.028; r=-0.262, P=0.041; r=-0.311, P=0.015; r=-0.388, P=0.002; respectively) negatively, as well as the percentage of CD3+T and CD8+T cells (r=0.277, P=0.030; r=-0.291, P=0.023), opposite to aspartate transaminase (AST) (r=0.289, P=0.025) in DM.
2-CARBA CYCLIC PHOSPHATIDIC ACID (2CCPA) SUPPRESSES PROFIBROTIC ACTIVITY IN SYSTEMIC SCLEROSIS SKIN FIBROBLASTS AND BLEOMYCIN-INDUCED SKIN FIBROSIS IN MICE

Tomoaki Higuchi1, 2, Kae Takagi3, Akiko Tochimoto1, Yuki Ichimura1, Takanari Norose1, Yasuhiro Katsumata1, Ikuko Masuda4, Hisashi Yamakawa5, Toshihiro Moroboshi6, Yasushi Kawaguchi7, Tokyo Women’s Medical University, Department of Rheumatology, Tokyo, Japan; 8SANSHO, Co., Ltd, Tokyo, Japan

Background: Systemic sclerosis (SSc) is a connective tissue disorder with progressive fibrosis in multiple organs including skin, lung and the gastrointestinal tract. Fibrosis is thought to be driven by activated fibroblasts. Therefore, inhibition of the profibrotic activity of activated fibroblasts may be a promising therapeutic approach in skin fibrosis in SSc. The autotaxin (ATX)/lysophosphatic acid (LPA) axis is reportedly involved in fibrotic pathogenesis in SSc1, 2-carba cyclic phosphatic acid (2ccPA) is a naturally occurring lipid mediator and one of its pleiotropic properties is to inhibit the ATX/LPA axis. Therefore, we investigated the anti-fibrotic effect of 2ccPA on human SSc skin fibroblasts and bleomycin-induced skin fibrosis in mice.

Methods: This study was approved by the ethics committee and the ethical review committee of animal experiments of Tokyo Women’s Medical University. We informed all participants of the content of this study, and written consent was obtained. Skin fibroblasts were obtained from SSc patients and adult healthy individuals were purchased. The cells were incubated with 1-10 μM 2ccPA in the presence or absence of 10 ng/ml transforming growth factor-β1 (TGF-β1). Messenger RNA (mRNA) and protein expression for type I collagen, connective tissue growth factor (CTGF), α smooth muscle actin (αSMA), fibronectin (FN) and TGF-β1 were assessed by qRT-PCR or Western blotting. Procollagen type I (CPII), procollagen E3 (PGE3) and hepatocyte growth factor (HGF) levels in the supernatant were assessed by ELISA. Intracellular cyclic adenosine monophosphate (cAMP) levels were calculated using a commercially available EIA kit. Forskolin was used to increase intracellular cAMP levels in cultured SSc skin fibroblasts. An inhibitor of denylate cyclase (AC), 2′-deoxyadenosine, was used to investigate whether the anti-fibrotic effect of 2ccPA was mediated via the AC/cAMP pathway. Furthermore, we used a mouse model of bleomycin-induced skin fibrosis to investigate the safety and anti-fibrotic effects of 2ccPA.

Results: Ten μM 2ccPA significantly reduced mRNA and protein expression for type I collagen, CTGF, αSMA in SSc skin fibroblasts and adult healthy skin fibroblasts treated with TGF-β1. PGE2 and HGF levels in the supernatant of SSc skin fibroblasts were also reduced by 2ccPA treatment. 2ccPA increased intracellular cAMP levels as well as the AC stimulator, forskolin. In addition, forskolin decreased the mRNA expression of profibrotic markers. Reduction of COL1A1 mRNA expression by 2ccPA was blocked by treatment with 2′-deoxyadenosine in cultured SSc skin fibroblasts, suggesting that the anti-fibrotic activity of 2ccPA was partially mediated via AC stimulation. In mouse experiments, intraperitoneal injection of 10 mg/kg 2ccPA significantly reduced the development of skin thickness, collagen content and αSMA-positive cell counts.

Conclusion: 2ccPA suppressed the profibrotic activity of SSc skin fibroblasts and the development of bleomycin-induced skin fibrosis. Our experiments suggested that the anti-fibrotic property of 2ccPA was at least in part due to increased intracellular cAMP levels in skin fibroblasts. 2ccPA has been reported to be well tolerated in clinical trials of other diseases and may be expected for the treatment of fibrotic lesions in SSc.

REFERENCE:

Disclosure of Interests: None declared.

Background: In inflammatory diseases, such as rheumatoid arthritis, early treatment has demonstrated to improve disease control and decrease mortality. It is not known if an early treatment could have similar effects on inflammatory myositis (IM) patients.

Methods: All patients from REMICAM were included (1). The influence of time elapsed between initial symptoms and diagnosis or start of therapy, and the year of diagnosis (before or after 2000), on mortality and disease control (defined as the possibility of glucocorticoid (GC) withdrawal due to IM improvement), was studied by means of survival analysis and regression proportional hazard bi and multivariate Cox models. All factors with p<0.2 in bivariate analysis were included in multivariate models. The mortality analysis was controlled for age, sex, and other known mortality factors: cardiovascular risk factors, interstitial lung diseases (ILD), cardiac involvement and cancer. The disease control analysis was controlled for age, sex, and other known severity factors such as ILD, cardiac involvement and IM subtypes.

Results: From 479 patients (74% females, 52% polymiositis, 44±22 years at diagnosis, 10±8 years follow up), 208 (43%) were diagnosed before year 2000, and 271 (57%) after year 2000. Mortality was independently associated with less ILD presence, lower n° of therapies and a shorter time between the initial symptoms and the start of IS therapy (Table 1). Risk factors for mortality were age, male sex and cancer, but not the delay in diagnosis or in the start of therapy (Table 2).

Abstract THU0334 – Table 1.

<table>
<thead>
<tr>
<th>Bivariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (IC95%)</td>
<td>p</td>
</tr>
<tr>
<td>Age at diagnosis</td>
<td>0.97 (0.96-0.98)</td>
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<tr>
<td>ILD</td>
<td>0.3 (0.2-0.5)</td>
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<tr>
<td>Diagnosis &lt; 2000</td>
<td>0.1</td>
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<tr>
<td>N therapies</td>
<td>0.8 (0.7-0.9)</td>
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<tr>
<td>Any IS</td>
<td>0.6 (0.4-0.8)</td>
</tr>
<tr>
<td>Initial symptoms to diagnosis</td>
<td>0.987 (0.981-0.990)</td>
</tr>
<tr>
<td>IS</td>
<td>0.993</td>
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</table>

Abstract THU0334 – Table 2.

<table>
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<th>Bivariate</th>
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<tbody>
<tr>
<td>HR (IC95%)</td>
<td>p</td>
</tr>
<tr>
<td>Sex</td>
<td>0.5 (0.3-0.8)</td>
</tr>
<tr>
<td>Age at diagnosis</td>
<td>1.05 (1.04-1.06)</td>
</tr>
<tr>
<td>Cancer</td>
<td>3.4 (2.2-5.2)</td>
</tr>
</tbody>
</table>

Conclusion: In the REMICAM cohort, disease control is more frequent in younger patients, diagnosed after 2000, with early initiation of IS therapy. Mortality was not associated with the delay in diagnosis or therapy in our study. Our data support the hypothesis that, in IM, as in other inflammatory diseases, an early treatment is essential to decrease inflammation and achieve disease control.
Objectives: This pilot study aims to establish a novel ex vivo experimental model that can demonstrate fibrotic change in mouse skin and represent ADSC loss within days rather than within weeks needed for current models.

Methods: Six B6 mice were sacrificed at between 12-16 weeks of age and skin tissues were obtained from the back by 8mm punch biopsies. Skin samples were immersed in Dulbecco’s Modified Eagle’s Medium containing either bleomycin (5 or 10mU/ml) or PBS as control for one or three days. After harvesting, H&E staining was performed on skin samples to assess phenotypic fibrotic changes. Flow cytometry (FACS Canto) was used to measure the viability, total cell number and ADSC change. A total collagen assay quantified collagen production in samples.

Results: On H&E staining, compared to controls, samples cultured with 5mU/ml bleomycin for a day showed increased density of dermis and deposition of amorphous pink material, likely representing increased collagen. With 10mU/ml bleomycin, these changes were greater and especially affected the upper dermis. On day 3, samples in 5mU/ml and 10mU/ml bleomycin appeared to have denser fibrosis, broader dermis band, and narrower DWAT layer. The histopathological change was most prominent on day 3 sample in 10mU/ml bleomycin, with the dermis layer 40% thicker and the DWAT layer 37% narrower than the control. However, all the samples on day 3 showed stress, such as epidermis detachment and apoptosis in the epidermis. On the Total Collagen Assay, collagen deposition on day 1 in control sample was 7.7ug/mm, compared to 33ug/mm from sample in 10mU/ml bleomycin. On day 3, collagen deposition in 10mU/ml bleomycin was 37ug/mm which was 2.5 to 5 times higher than control. On FACS, the decrease in ADSC level correlated to the increase in concentration of bleomycin and the number of days treated, with the greatest drop in samples in 10mU/ml bleomycin on day 3.

Conclusion: Our results thus far suggest that we are creating a novel ex vivo model of skin fibrosis that can help better understand how ADSCs can be of therapeutic benefit in SSc. This rapid ex vivo model will complement the existing in vivo model. Our next step will be to investigate the changes of profibrotic cytokines before and after applying ADSCs purified from healthy mice to understand how skin fibrosis can be reversed.

REFERENCES:

Abstract THU0356 – Figure 1. H&E. Blue arrows showed the areas where there are increased collagen deposition and density.


**Abstract THU0356 – Figure 2. Total collagen content**

**Disclosure of Interests:** None declared

**Abstract THU0356 – Figure 3. ADSC cell count measured by flow cytometry**

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.1881

**THU0337**

**COMPARISON OF THE EFFICACY OF TWO RITUXIMAB SIMVASTATIN-CONJUGATED NANO PARTICLE REGIMENS IN THE PATIENTS WITH SYSTEMIC SCLEROSIS ASSOCIATED WITH INTERSTITIAL LUNG DISEASE**

Olga Ovsyannikova, Mayya Starovoytova. Disclosure of Interests: None declared

**Background:** Rituximab (RTM) is considered as a promising therapeutic agent for treatment of interstitial lung disease (ILD) in the patients with systemic sclerosis (SSc). However, the limited number of RTM-treated patients, heterogeneity of the studies in relation to main parameters, considerably different dose regimens, cumulative doses, and observation periods does not allow univocal conclusions on RTM efficacy or definitive recommendations on RTM use in the patients with SSc. The question whether to combine RTM with immunosuppressants (IS) or it is possible to use it as a single-agent therapy in the patients with SSc associated with ILD is still relevant.

**Objectives:** To compare the time courses of pulmonary function parameters and dermal fibrosis parameters during the use of RTM in combination with IS and as a single-agent therapy in the patients with SSc associated with ILD in the open-label prospective non-randomized study. **Methods:** 90 patients with the confirmed SSc diagnosis and ILD evidence associated with ILD in the open-label prospective non-randomized study. **Results:** In Groups A and B during the therapy significant decrease in mRss was observed. The treatment groups did not differ significantly in the median FVC increments, clinically meaningful FVC and DLCO increments of decrements, and EScSG and mRss time courses.

**Conclusion:** RTM administration both in combination with IS and as a single-agent therapy in the patients with SSc associated with ILD effectively alleviated skin induration and EScSG, improved or stabilized the pulmonary function parameters. The absence of statistically significant difference in the time course of evaluated parameters between the groups substantiate potential RTM use as a single-agent therapy that, this is most important for the patients with poor tolerability or contraindications to IS administration.

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.6870

**THU0338**

**SIMVASTATIN-CONJUGATED NANO PARTICLE ENHANCES THE THERAPEUTIC EFFECT OF ADIPOSE-DERIVED STEM CELLS ON INTERSTITIAL LUNG DISEASE**

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**Background:** Interstitial lung disease (ILD) associated with connective tissue disease is a life-threatening pathological condition that causes respiratory failure when it progresses. Lung inflammation is treated with corticosteroids and immunosuppressants, and pulmonary fibrosis is treated with anti-fibrosis agents such as pirfenidone and nintedanib. However, many cases are treatment-resistant and the outcome is poor. Moreover, adverse effects such as infections resulting from immunosuppressive therapy are problematic. The development of new treatments is thus required for ILD from the viewpoint of the poor effect and adverse effects of the currently available treatments. Research and development with adipose-derived stem cells (AdSCs) in immunosuppressive therapy have progressed for autoimmune diseases, and favorable outcomes have been reported. In recent years, the effectiveness of AdSCs in ILD model mice has been demonstrated (ref). The statin preparation has not only an anti-fibrotic action but also an action of promoting a cellular function including angiogenesis promoting action, an immunosuppressive action, an anti-fibrotic action, an action of promoting a cellular function including angiogenesis promoting action, an immunosuppressive action, and favorable outcomes have been reported. In recent years, the effectiveness of AdSCs in ILD model mice has been demonstrated (ref).

**Methods:** To compare the time courses of pulmonary function parameters and dermal fibrosis parameters during the use of RTM in combination with IS and as a single-agent therapy in the patients with SSc associated with ILD in the open-label prospective non-randomized study. **Results:** In Groups A and B during the therapy significant decrease in mRss was observed. The treatment groups did not differ significantly in the median FVC increments, clinically meaningful FVC and DLCO increments of decrements, and EScSG and mRss time courses.

**Conclusion:** RTM administration both in combination with IS and as a single-agent therapy in the patients with SSc associated with ILD effectively alleviated skin induration and EScSG, improved or stabilized the pulmonary function parameters. The absence of statistically significant difference in the time course of evaluated parameters between the groups substantiate potential RTM use as a single-agent therapy that, this is most important for the patients with poor tolerability or contraindications to IS administration.

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.6870

**Notes:** in Parameters column 1 = before treatment, 2 = after treatment; M ± SD = mean value and standard deviation; * = significant difference between the values measured before and after the treatment

**Conclusion:** RTM administration both in combination with IS and as a single-agent therapy in the patients with SSc associated with ILD effectively alleviated skin induration and EScSG, improved or stabilized the pulmonary function parameters. The absence of statistically significant difference in the time course of evaluated parameters between the groups substantiate potential RTM use as a single-agent therapy that, this is most important for the patients with poor tolerability or contraindications to IS administration.

**Disclosure of Interests:** None declared

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OBJECTIVES: We have investigated the hypothesis that statin, an agent with pleiotropic effects, could augment the therapeutic potential of AdSCs. Methods: ILD was induced by bleomycin (BLM) in C57BL/6 mouse, and the mice were assigned in the following groups: 1) Control, 2) NP-AdSCs (2.5×10⁶ cells), and 3) STNP-AdSCs (2.5×10⁶ cells). Results: Simvastatin-conjugated nanoparticles (STNP) significantly promoted the migration activity and cell survival without changing the proliferation activity, and up-regulated transforming growth factor (TGF)-β1 in vitro assays. Lung inflammation and fibrosis assessed were significantly suppressed at 4 weeks after starting BLM administration in STNP-AdSCs group (Figure). The levels of IL-4, IFN-gamma, TNF-alpha, CCL1A1, and TIMP1 mRNA expression at 28 days after BLM administration were significantly lower in STNP-AdSCs group compared with that in other groups. Conclusion: Simvastatin-conjugated nanoparticles enhanced the therapeutic effect of a small number of AdSCs transplantation.

Abstract THU0338 – Figure 1

REFERENCE:

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THU0339
PULMONARY INVOLVEMENT AND OUTCOME IN SYSTEMIC SCLEROSIS (SSC) – ILD-PH AS AN IMPORTANT SUBSET

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Background: Pulmonary involvement is the leading cause of death in SSc and can manifest as interstitial lung disease (ILD), pulmonary hypertension (PAH) or a combination (ILD-PH). Aim of this analysis was to determine prevalence, clinical characteristics and outcomes of different forms within the German SSC network.

Objectives:
Methods: SSC patients were analyzed for pulmonary involvement, clinical characteristics and outcome.

Results: There were 3699 pts in 42 centers with a mean follow-up time of 34.4±12.6 months. At baseline, ILD was frequent (29.5%), while ILD-PH and PAH had lower prevalences (7.5%, 6.1%). At the end of follow-up, 32% of SSC pts had ILD, 13% ILD-PH and 7% PAH. ILD and ILD-PH were more frequent in the diffuse form (47%, 12%), while PAH did not differ between subforms. Significant differences in baseline characteristics between PAH vs. ILD-PH vs. ILD were found for age (62, 59, 54 years), sex (males: 15%, 22%, 24%) and smoking prevalence (non-smokers 49%, 63%, 57%). Mean DLCO and FVC were 56%/93% for PAH, 49%/78% for ILD-PH and 56%/81% for ILD. Significant decreases for DLCO (≥15%) and FVC (≥10%) were found in 45%/26% in PAH, 45%/26% for ILD-PH and 36%/16% in ILD. All-cause mortality was 8.1% for the total cohort and differed significantly between patients without pulmonary involvement (4%), ILD (7.8%), PAH (14.2%), and ILD-PH (21%, p<0.001).

Conclusion: ILD is the most prevalent pulmonary involvement in SSC, while PH-ILD is associated with the most detrimental survival. Significant differences in baseline characteristics of types of pulmonary SSC involvement may help to identify patients at risk in the future.

Disclosure of Interests:

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IMPACT OF LANIFIBRANOR, A PAN-PPAR AGONIST, ON THE PULMONARY VASCULAR TONE

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Background: Pulmonary hypertension (PH) is common in patients with fibrosing interstitial lung diseases (ILDs) such as systemic sclerosis (scleroderma) and has a significant impact on survival. The pan-peroxisome proliferator-activated receptor (PPAR) agonist lanifibranor is currently being tested in a phase II clinical trial in scleroderma patients. Although, the antifibrotic effects of lanifibranor have been previously shown in preclinical mouse models of scleroderma and related PH (1), its effects in modulating the pulmonary vascular tone are largely unknown.

Objectives: To evaluate the acute effect of lanifibranor (pan-PPAR agonist) and selective PPAR agonists on the pulmonary vascular tone.

Methods: Freshly isolated intra-pulmonary arteries from explanted human and rat lungs were used in wire myography experiments to assess the acute effect on pulmonary vascular tone of pan-PPAR agonist -lanifibranor and the selective PPAR agonists PPARγ -GW50156 and PPARγ -GW50156 and PPARγ -trogoltiazine (0.01M-30μM) versus vehicle (DMSO). The intra-pulmonary arteries were pre-constricted with 300M of the thromboxane A2 receptor agonist U46619. The contribution of endothelium and nitric oxide was investigated using both native and endothelium-denuded vessels, with and without the nitric oxide synthase inhibitor L-NAME.

Results: Isometric tension measurements in rat pulmonary arteries showed that lanifibranor and the selective PPAR agonists PPARγ -GW50156 and PPARγ -trogoltiazine, induced a significant relaxation compared to their vehicle controls, whereas the PPARα agonist fenofibrate did not show any vasoactive effect on the pre-constricted arteries. Lanifibranor showed a significant vasodilatory effect already at 1μM whereas GW50156 and troglitiazine showed significant vasodilator effects starting from 10μM as compared to their vehicle controls. At the maximum concentration used (30μM), lanifibranor caused a relaxation response of ~85% whereas GW50156 and troglitiazine caused just ~45% and ~50% vasorelaxation (n=6), respectively. The vasodilation induced by pan-PPAR and selective PPAR agonists remained unaffected by pre-treatment of L-NAME or denuded endothelium. Lanifibranor had vasodilatory effects that were strongly superior to any of the selective PPAR agonists in the isolated pulmonary artery from the explanted human lungs (n=3).

Conclusion: The current study revealed that the pan-PPAR agonist lanifibranor caused a rapid dose-dependent relaxation in both rat and human intra pulmonary arteries which were superior to any other PPAR agonists suggesting additive effects of the pan-PPAR agonism. The observed vasoactive effects of pan-PPAR are independent of nitric oxide and endothelium, delineating the specific effect of PPAR agonism on the pulmonary artery smooth muscle cells. These results suggest that lanifibranor could be a promising therapy for vasculopathies such as PH observed in scleroderma patients.

REFERENCE:


MICRONR27A3P REGULATES WNT SIGNALLING BY TARGETING SFRP-1 IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is an autoimmune idiopathic connective tissue disease that results in fibrosis of the skin and lungs. Wnt signalling is a highly conserved signalling pathways that is involved in organogenesis and tissue homeostasis. In recent years it has emerged that aberrant Wnt signalling is key in SSc and animal models of the disease. The Wnt pathway comprises of secreted glycoproteins that bind to specific receptors that initiate the pathway and result in beta catenin stabilization. However, secreted antagonists are secreted to block and negatively regulate Wnt signalling. We and others have found reduced sSFRP-1 in SSc, a key Wnt antagonist. Although lower in SSc skin and isolated fibroblast from patients the mechanism governing this is unknown. This work seeks to identify epigenetic mechanisms.

Objectives: Determine the epigenetic regulation of sSFRP-1 in SSc.

Methods: Serum sSFRP-1 was measured in healthy and diffus SSc patients to ascertain the levels of sSFRP-1. Mir27a was identified as a possible microRNA that targets sSFRP1 using siRNA and miRNA. mir27a was transfected into healthy dermal fibroblasts using transfection methods and sSFRP-1 was measured. Collagen was also measured by western blotting after transfection. Mir27a was also measured in SSc dermal fibroblasts using specific Taqman probes and normalized to RNU4 miR. Cloning of the 3’UTR of sSFRP1 into a luciferase reporter vector was performed and then transfected into HEK293 cells with mir27a mimics or with concentration matched scramble and after 24 hours luciferase was monitored.

Results: Significantly reduced expression of sSFRP-1 was found in SSc serum compared to controls (n=10). SSc dermal fibroblasts had 3 fold higher levels of mir27a compared to healthy fibroblasts. Increased mir27a in healthy dermal fibroblasts resulted in significantly less sSFRP-1 secreted into conditioned media and this was co-incident with an increase of collagen1 levels. Finally cloning of the 3’UTR binding site in a luciferase plasmid and overexpression of mir27a led to reduced levels of luciferase in HEK293 cells in vitro.

Conclusion: Reduced sSFRP-1 in systemic sclerosis is mediated by mir27a and this leads to fibrosis via enhanced Wnt signaling. Targeting the epigenetic changes that mediate this may be a therapy in SSc.


SYSTEMIC SCLEROSIS IS A DISEASE OF A PREMATURELY SENESESCENT, INFLAMMATORY AND ACTIVATED IMMUNOME

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Background: Systemic sclerosis (SSc) is an autoimmune disease characterised by excessive fibrosis of skin and internal organs, and vascular dysfunction (1). Association of T and B cell subsets have been reported in SSc, however there is lack of systematic studies of functional relations between immune cell subsets in this disease (2,3,4). This lack of mechanistic knowledge hampers targeted intervention.

Objectives: In the current study we sought to determine differential immune cell composition and their interactions in peripheral blood of SSc patients and its impact on disease severity and progression.

Methods: Mononuclear cells from blood of SSc patients (n=20) and healthy controls (n=10) were analysed by mass cytometry using a 36 marker (cell-surface and intracellular) panel to aid in identification of major PBMC lineages including T cells, B cells, monocytes and NK cells and their subsets. Transcriptome analysis (m-RNA sequencing) was performed on sorted T and B cell subsets. Unsupervised clustering of mass cytometry data was performed using in-house developed analysis software MARVIS. This software combines dimension reduction and clustering steps to identify all possible cellular subsets. Further, custom R scripts helped in identifying nodes that were differentially expressed between the study groups and also phenotype of these nodes.

Results: Unsupervised clustering analysis revealed significant differences in the frequencies of T and B cell subsets in patients. Correlation network analysis highlighted an overall dysregulated immune architecture coupled with domination of inflammatory senescent T cell modules in SSc patients. Transcriptome analysis of sorted immune cells revealed an activated phenotype of CD4 and MAIT cells in patients, accompanied with increased expression of inhibitory molecules, reminiscent of
PU.1 INHIBITOR DB1976 CONTROLS FIBROBLAST POLARIZATION IN SYSTEMIC SCLEROSIS AND LEADS TO REPRESSION OF FIBROSIS IN DIFFERENT MODELS OF ORGAN FIBROSIS

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Background: Persistent activation of fibroblast with excessive release of extracellular matrix is a hallmark of systemic sclerosis (SSc). Fibroblasts can either acquire a “pro-fibrotic” phenotype with excessive matrix production or a “pro-inflammatory” phenotype with releasing of matrix-degrading enzymes and subsequent tissue destruction. Despite these well-characterized phenotypic differences, the molecular mechanisms that drive polarization of fibroblasts into these two functionally opposing phenotypes remain enigmatic.

Objectives: We aimed to evaluate the transcriptional network that promotes the extracellular matrix-producing fibroblast fibrotic fate.

Methods: We established the transcriptional network that induces the pro-fibrotic phenotype of fibroblasts by in silico and immunofluorescence analyses of human fibrotic skin, lung, liver and kidney, and performed functional assays to address the fibrogenic potential of fibroblasts in vitro and in several mouse models of systemic sclerosis. The heterocyclic diazidine DB1976 was used as new therapeutic compound to induce regression of fibrosis.

Results: We identified the ETS transcription factor PU.1 as molecular checkpoint for acquisition of a “pro-fibrotic” phenotype of fibroblasts. Our data demonstrate that expression of PU.1 is effectively silenced in fibroblasts during tissue homeostasis. When the epigenetic control of PU.1 is lost and PU.1 expression is induced, fibroblasts differentiate into a fibrotic phenotype that includes the transcription of numerous pro-fibrotic mediators. PU.1 polarized resting fibroblasts and even repolarized extracellular matrix-degrading inflammatory fibroblasts to an extracellular matrix-producing fibroblastic phenotype. PU.1 is associated with a network of pro-fibrotic factors including members of the TEAD-HIPPO, canonical TGF-β–SMAD and AP1 signaling pathways. Other transcription factors with fibrotic abilities, such as SNAI2 and myocyte enhancer factor (MEF) 2, bind in close vicinity to PU.1-binding sites within the genome and contribute to the recruitment of the transcription machinery that drives the switch towards the fibrotic phenotype. PU.1 has a major coordinating role within this complex network of transcription factors in fibroblasts, as the inactivation of PU.1 alone is sufficient to prevent fibrotic polarization in vitro and in vivo. Finally, we investigated pharmacological targeting of PU.1 as a potential strategy to prevent uncontrolled fibrotic tissue remodeling. DB1976 showed anti-fibrotic effects in vivo in various fibrosis models and across several organs. Treatment with DB1976 not only prevented bleomycin-mediated skin fibrosis, but also induced regression of pre-established fibrosis, and was well tolerated.

Conclusion: These findings suggest that PU.1 inhibition may represent a novel and effective therapeutic approach to treat a wide range of fibrotic diseases. Inactivation of PU.1 effectively reverted the fibrotic phenotype of fibroblasts to a resting state and induced the regression of tissue fibrosis.

Disclosure of Interests: None declared


THU0344 A PILOT STUDY ASSESSING THE EFFECT OF AIR POLLUTION ON EXTRACELLULAR VESICLES IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a severe autoimmune disease characterized by a progressive multi-organ fibrosis. The identification of specific diagnostic and prognostic biomarkers remains an unmet need. Over the past few years, it has been suggested that extracellular vesicles (EVs) and environmental toxicants, such as particulate matter (PM), may have an important role in the pathogenesis of autoimmune diseases. At present, no data are available on the impact of PM exposure on EVs from patients with SSc.

Objectives: Our aim was to evaluate the effects of PM with aerodynamic diameter ≤ 10 μm (PM10) and ≤ 2.5 μm (PM2.5) on EVs in SSc and osteoarthritis (OA) as control.

Methods: Plasma EVs were analyzed by Nanosight and flow cytometry after labeling with the following markers: CD14 (monocyte), CD61 (platelet), CD25 (T-reg), human endogenous retrovirus w (HERV-w), human leukocyte antigen G (HLA-G). Demographic and clinical data were collected for each patient. Plasma EV concentrations were measured in SSc and OA patients and were analyzed by generalized linear regression models. Daily PM concentrations, estimated by Regional Environmental Protection Agency at municipality resolution, were used to assign short-term exposure (mean of the 7 days preceding the evaluation) to each study subject.

Results: 12 consecutive patients with limited cutaneous SSc (11 female, median age 66.8, median disease duration 12.3, 7 anti-centromere positive, median mRSS 3.5) and 12 patients with OA (median age 67.1, median disease duration 9.3, 8 female) were enrolled. The increase of PM2.5 led to a decrease of HERV-w+ microvesicles (MV) in both SSc (β=-0.10; p<0.01) and OA (β=-0.09; p=0.01) and of HLA-G+ (β=-0.11; p<0.01) only in SSc. Similar results were observed analyzing PM10 exposure. Analysis of EVs concentration according to their dimension showed a negative association in the size range of exosomes (83-
TEXTURE-BASED RADIOMICS FEATURES DISCRIMINATE DIFFERENT STAGES OF EXPERIMENTAL INTERSTITIAL LUNG DISEASE

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Background: Interstitial lung disease (ILD) is a life-threatening complication of systemic sclerosis (SSc). There is an unmet need for validated, routinely available biomarkers for disease staging and individualized patient stratification. In that respect, high-resolution computed tomography (HRCT), routinely performed in the work-up of SSc-ILD patients, has great potential as a source for non-invasive imaging biomarkers. Recently, radiomics, the quantitative extraction of hundreds of radiologic image features has great potential to provide biological and stage-specific quantitative information on lung (micro-)architecture and thus could serve as quantitative imaging biomarkers for guided decision making in SSC-ILD.

Objectives: To evaluate the performance of CT-based radiomics for differentiation of IIM subtypes.

Methods: The study included 464 patient samples collected at Hospital Vall d’Hebron, Autonomous University of Barcelona, most of whom had a diagnosis of IIM (n=264). As controls, samples from patients with myositis like conditions (ML, n=20), rheumatoid arthritis (RA, n=33), systemic lupus erythematosus (SLE, n=40), Sjogren’s syndrome (SS, n=25), infectious diseases (ID, n=40) and healthy individuals (HI, n=42) were included. All samples were tested using a novel fully automated particle-based multi-analyte technology (PMAT, Inova Diagnostics, research use only; Jo-1, PL-7, PL-12, EJ, Mi-2b, NXP2, SAE, TIF1y, MDA5, HMGCR, SRP) which utilizes paramagnetic particles with unique signatures and a digital interpretation system.

Results: CT imaging visualized morphological changes of the lung architecture in BLM-treated mice, as evidenced by a time-dependent increase of grey areas on chest CT images and a gradual increase in tissue density on density-masked lungs. Accordingly, 6 out of 17 classical histogram features (e.g. mean CT density, skewness and kurtosis) distinctly distinguished diseased from healthy mice with area under the curve values (AUCs) >0.87 (p<0.05) and thus detected lung remodelling. However, histogram-based features failed to differentiate between the different time points and thus stages of experimental lung fibrosis as investigated by receiver operating characteristic curve analysis and by hierarchical clustering. In contrast, 59 out of 137 texture-based radiomics features, including features describing image homogeneity or contrast detected ILD and distinguished the different stages with excellent accuracy (AUCs>0.84; p<0.05) thus outperforming the classical histogram features.

Conclusion: We confirmed the potential of CT-based texture features for diagnosis and also help to stratify idiopathic inflammatory myositis (IIM) patients with particular clinical features, treatment responses, and disease outcome. Standardization of MSA detection is of high importance because these antibodies also have the potential to be used in classification criteria.

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Results: The sensitivity/specificity of the individual MSA were: 19.7%/100% (Jo-1), 7.2%/100.0% (M2), 3.0%/99.0% (NXP2), 3.8%/100.0% (SAE), 2.7%/100.0% (PL-7), 1.9%/99.5% (PL-12), 1.1%/100.0% (EJ), 15.5%/99.5% (TIF1Y), 8.3%/98.5% (MDAS), 6.1%/99.0% (HMGCR) and 1.9%/98.5% (SRP). The overall clinical performance was: sensitivity 68.2% (95% confidence interval 62.3-73.5%), specificity 94.0% (95% CI 89.8-96.5%) and odds ratio 33.8. In the table below, the sensitivity and specificity of each analyte for IIM subtypes was calculated along with odds ratio.

Conclusion: The novel PMAT used to detect a spectrum of MSA in IIM on a fully automated system showed good sensitivity and specificity in line with the known associations of MSA. Sensitivities and specificities of the individual MSA are within expected ranges. Lastly, the individual markers help to stratify patients into IIM subtype which is important for management of the patients.


REFERENCES:

Disclosure of Interests: None declared.


THU0348 TESTING THE IN VITRO EFFECTS OF NINTEDANIB ON CIRCULATING FIBROCYTES AND RESIDENT SKIN FIBROBLASTS FROM THE SAME SYSTEMIC SCLEROSIS PATIENTS: PRELIMINARY RESULTS

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Background: The fibrosis in systemic sclerosis (SSc) progresses from microvascular alterations, immune system activation, and increased extracellular matrix protein synthesis into the skin and internal organs, primarily mediated by myofibroblasts.1 Myofibroblasts are characterized by a high expression of α-smooth muscle actin (αSMA) and by the overproduction of type I collagen (COL1) and fibronectin (FN).2 Although myofibroblasts primarily derive from fibroblasts Varela-Smires et al.1 Varela-Smires et al.1, Stefano Soldano1

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Background: Systemic sclerosis (SSc) is characterized by immune system alterations, vascular damage and fibrosis (1). Macrophages seem to play an emerging role in SSc, and the characterization of their polarized phenotype, starting from the dichotomous definition of classically activated (M1) or alternatively activated (M2) macrophages, is a recent research topic of interest (2).

Objectives: The study investigated a possible imbalance in the distribution of circulating cells expressing M1 and M2 markers in SSc patients (pts) compared to healthy subjects (HSs), and the presence of circulating cell co-expressing M1 and M2 surface markers. Possible correlations between their percentage and selected SSc clinical aspects were investigated.

Methods: In the study 55 SSc pts (50 females/5 males, mean age 64 ± 13 yrs), fulfilling the new EULAR/ACR criteria for SSc diagnosis, and 27 age-matched HSs (25 females/2 males, mean age 57±7 yrs) were enrolled. Blood and skin biopsies were performed. In particular, circulating cells belonging to the leukocyte and monocyte populations (CD45+ and CD14+ cells) were investigated by flow cytometry (FC) using the surface markers characterizing M1 (CD80, CD86, TLR2, TLR4) and M2 phenotypes (CD204, CD206, CD163). Statistic analysis was performed using Mann-Whitney and Kruskal-Wallis tests, and correlations were explored by bivariate Pearson’s analysis.

Results: Increased circulating cells showing an M2 phenotype and characterized as CD204+CD206+CD163+cells was observed in SSc pts compared to HSs (p<0.0001), whereas no difference in CD80+CD86+TLR2+TLR4+ (M1) cell percentage was observed. A significant higher percentage of circulating cells showing a hybrid M1/M2 phenotype (CD204+CD206+CD163+TLR4+CD80−CD86− cells) was observed in SSc pts compared to HSs. These hybrid M1/M2 cells were significantly increased in SSc pts either treated with steroids or under no immunosuppressive treatment (p<0.01; p<0.05, as well as in ScI70+ pts (p<0.05 vs. ScI70- pts)
and SSc pts with interstitial lung disease (ILD) and high systolic pulmonary artery pressure (PAP). A linear negative correlation between the high hybrid M1/M2 cell percentage and diffusing capacity of the lungs for carbon monoxide (DLCO)%, and the forced vital capacity (FVC)/DLCO ratio higher than 1.5 was observed. No significant correlations were reported with SSc duration, other treatments, NVC patterns, renal artery resistive index, heart and kidney involvements, digital ulcers, telangiectasias, calcinosis.

Conclusion: The study identified a circulating cell population expressing both M1 and M2 surface markers, which is increased together with circulating M2 cells in SSc pts, in particular affected by ILD and high PAP, suggesting their possible involvement in the pathogenesis of those disease complications. Further evaluations are in progress.

REFERENCES:

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THU0349

AUTOLOGOUS FAT GRAFTING IN THE TREATMENT OF PATIENTS WITH SYSTEMIC SCLEROSIS: CURRENT EXPERIENCE AND FUTURE PROSPECTS

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Background: Systemic Sclerosis (SSc) is a connective tissue disease, characterized by endothelial dysfunction and fibrosis, potentially affecting internal organs and reducing life expectancy. Digital ulcers (DUs), as well as hand and face skin thickening, are the hallmarks of the disease. These alterations lead to pain, functional impairment, aesthetic damages, and psychological distress. Autologous fat grafting (AFG) is a surgical technique used also to promote tissue regeneration. In the last decade, AFG has been successfully developed to treat clinical conditions characterized by skin atrophy or fibrosis. AFG composition of multipotent cells, carrying angiogenic, and immunogenic properties, may be able to restore the damaged tissues.

Objectives: Evaluate our experience with AFG to treat and prevent damage and disability due to DUs and SSc skin complications.

Methods: We analyzed 25 SSc patients, extrapolated from a larger series of 45 subjects, complaining about mouth and/or hand impairment, due to skin involvement, and, in some cases, long-lasting DUs (M/F 6/19, mean age 55.69±9.25 SD-years, mean disease duration 184.68±121.09 SD-months, L/D cutaneous subsets 21/4). Surgical procedures consisted in the injection of centrifuged and purified autologous fat, harvested from hips or abdomen. 2ml of fat were grafted in each of the 8 sites around the mouth, while 0.5 or 1 ml around the neurovascular bundle at the base of each finger. The study included: preoperative data collection; 2 or 3 surgical sessions at a distance of 6 months one from the other; data collection at 3 months after each surgical session; data collection at 3 and 6 months of follow up-FU after the last surgical procedure. Data collection consisted of clinic-serological SSc features and clinimetric measures of MODA and the following: 1. Control (BLM-SSc), 2. mAdSCs (1.0×10⁴ cells), 3. mAdSCs (1.0×10⁵ cells). After the administration of BLM, mAdSCs were injected via a tail vein on day 7. The mice were sacrificed at 14 days after mAdSCs injection, and the skins were harvested for histological analysis.

Results: In mAdSCs (1.0×10⁵ cells) group, thickening of skin, hydroxyproline content, infiltration of inflammatory cells, gene expression of inflammatory cytokines, and fibrotic factors were significantly reduced compared with control group (Figure). In mAdSCs (1.0×10⁴ cells) group, there were no reduction of them. mAdSCs did not accumulate in skin. The levels of MMP-2, MMP-9, and COL1A1 mRNA expression at 21 days after BLM administration were significantly lower in mAdSCs (1.0×10⁵ cells) group compared with those in control group.

Conclusion: Intravenous mAdSCs inhibited both skin inflammation and fibrosis of BLM-SSc mice in a dose-dependent manner.

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THU0350

ANTI-INFLAMMATORY AND ANTI-FIBROTIC EFFECTS OF INTRAVENOUS ADIPOSE-DERIVED STEM CELL TRANSPLANTATION IN A MOUSE MODEL OF BLEOMYCIN-INDUCED SCLERODERMA

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Background: Systemic sclerosis (SSc) is a systemic autoimmune disease characterized by microvascular damages and fibrosis. The main lesions of SSc are peripheral circulation insufficiency, scleroderma, and interstitial pneumonia. Skin lesions are related to patient’s ADL and QOL, however there is no effective treatment for normalizing the disease state. Adipose-derived stem cells (AdSCs) have recently been considered a useful treatment tool for autoimmune disease because of their anti-inflammatory and immunosuppressive effects (ref).

Objectives: We investigated the therapeutic effect of intravenous mouse AdSCs (mAdSCs) transplantation in a SSc mouse model.

Methods: SSc was induced by bleomycin (BLM) in Balb/c mice, and the mice were assigned in the following groups: 1. Control (BLM-SSc), 2. mAdSCs (1.0×10⁴ cells), 3. mAdSCs (1.0×10⁵ cells). After the administration of BLM, mAdSCs were injected via a tail vein on day 7. The mice were sacrificed at 14 days after mAdSCs injection, and the skins were harvested for histological analysis.

Results: In mAdSCs (1.0×10⁵ cells) group, thickening of skin, hydroxyproline content, infiltration of inflammatory cells, gene expression of inflammatory cytokines, and fibrotic factors were significantly reduced compared with control group (Figure). In mAdSCs (1.0×10⁴ cells) group, there were no reduction of them. mAdSCs did not accumulate in skin. The levels of MMP-2, MMP-9, and COL1A1 mRNA expression at 21 days after BLM administration were significantly lower in mAdSCs (1.0×10⁵ cells) group compared with those in control group.

Conclusion: Intravenous mAdSCs inhibited both skin inflammation and fibrosis of BLM-SSc mice in a dose-dependent manner.

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THE ROLE OF PRURITOGENIC MEDIATORS IN DERMATOMYOSIS RELATED ITCH

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Background: Pruritus is a common symptom in systemic autoimmune diseases like dermatomyositis (DM). Recent researches have indicated that interleukin-31 (IL-31), IL-33, IL-6, or inflammatory cytokines, such as tumor necrosis factor (TNFα), peroxisome proliferator-activated receptor γ (PPARγ) and ion channels belonging to the transient receptor potential (TRP) family are involved in pruritogen mediated itch. The objective of the present study was to evaluate a novel highly selective orally available 5-HT2B receptor antagonist, AM1476, for its ability to reduce pulmonary and dermal fibrosis in the sclerodematous animal model of dermatomyositis related itch.

Methods: Gene expression of TNFα, PPARγ, IL-33, IL-6 and TRPV channels in lesional DM skin was evaluated by RT-qPCR and was compared with non-lesional DM skin samples. Pruritus and disease activity of DM was evaluated by the 5-d itch scale and Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI), respectively. Statistical analysis was performed with IBM SPSS 20.0 software.

Results: Skin samples of 17 active DM patients were analyzed. We could show, that itching index in DM was positively correlated with CDASI score with a correlation coefficient of 0.82 (p=0.001). TNFα gene expression was significantly higher (34.87%) in lesional DM skin than non-lesional DM skin (p=0.03). The normalized TNFα mRNA expression was positively correlated with itch scale (R= 0.605, p=0.022) and its level was significantly higher in skin samples of patients with severe itch (itch score: 15-20) versus mild itch (itch score: 5-10) (2.02±0.38 vs. 1.12±0.20; p<0.01). The level of PPARγ was decreased in lesional DM skin, but this was statistically not significant. The mRNA expression of normalized PPARγ was negatively correlated with itch scale (R= -0.518, p=0.019), and its level was significantly lower in skin samples of patients with severe itch versus mild itch (0.28±0.36 vs. 1.53±0.98; p=0.038). Lesional IL-6 mRNA levels were associated with CDASI activity score (R=0.619, p=0.018). The mRNA levels of TRPV1-4 channels were not associated with 5-D itch score, but normalized TRPV1 and TRPV4 mRNA expressions were positively correlated with CDASI damage score (R=0.699, p=0.008; R=0.789, p=0.001). Interestingly, itching sensation of DM patients was not correlated with IL-33 mRNA levels measured in skin samples.

Conclusion: Our results argue for that higher cutaneous disease activity generate pruritus. TNFα and PPARγ might play a determining, but opposite role in DM-associated itch. Furthermore IL-6, TRPV1 and TRPV4 channels might participate in pathomechanism of cutaneous manifestation of the disease.

DISCLOSURE OF INTERESTS: : None declared

chronic graft-versus-host disease model and dermal fibrosis in the tight-skint-1 model of systemic sclerosis. Effects on the TGF-β-Smad signaling pathway were investigated in vivo. Exposure of AM1476 was measured to ensure proper target engagement.

Methods: The murine sclerodermatous chronic graft-versus-host disease (cGvHD) model was used to evaluate anti-fibrotic effects after therapeutic dosing of the 5-HT2B receptor antagonist, AM1476. The compound was orally administered at 1, 10 and 30 mg/kg b.i.d. from day 21, several days after the first skin biopsies were collected. In cGvHD model, myofibroblast counts and collagen production were used to evaluate dermal fibrosis. Effects on pulmonary fibrosis were measured using hydroxyproline content, Sirius Red staining and Ashcroft score. Plasma was collected for PK analysis at different timepoints in each treatment group using sparse sampling, on the last day of the experiment. The tight-skint-1 model was used to evaluate anti-fibrotic effects after therapeutic treatment. AM1476 was orally administered at 10 mg/kg, b.i.d. from week 5 to week 10. Hypodermal thickening, myofibroblast counts and hydroxyproline content in skin biopsies were evaluated at the end of the treatment period. The number of phosphorylated Smad3 (pSmad3) positive cells was used to evaluate inhibition of TGF-β signaling.

Results: The 5-HT2B receptor antagonist AM1476, significantly reduced all measured dermal and pulmonary fibrosis readouts in the cGvHD model using an oral therapeutic treatment approach. Pharmacokinetic analysis of plasma samples supported 5-HT2B receptor engagement. Therapeutic treatment of dermal fibrosis in the tight-skint model effectively and significantly reduced hypodermal thickening, number of myofibroblast and hydroxyproline content. The number of pSmad3 positive cells was significantly reduced in skin samples isolated from treated animals.

Conclusion: Inhibition of 5-HT2B receptor activity resulted in pronounced anti-fibrotic effects in pulmonary and dermal fibrotic tissues. AM1476 was well tolerated without obvious signs of toxicity. Effects on pSmad3, reflecting TGF-β-inhibition, will be evaluated as a potential biomarker in upcoming clinical trials. The highly selective 5-HT2B receptor antagonist AM1476 represents a promising drug candidate for treatment of fibrotic conditions and is currently in development for systemic sclerosis.


THU0354 MACHINE LEARNING CLASSIFICATION OF SKIN GENE EXPRESSION IDENTIFIES A SUBSET OF SYSTEMIC SCLEROSIS PATIENTS MOST LIKELY TO SHOW CLINICAL IMPROVEMENT IN RESPONSE TO ABATACEPT

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Background: A prior pilot study of abatacept in SSc with molecular gene expression data in skin (1) found that four of five patients who improved on abatacept, as determined by change in mRSS, were in the inflammatory intrinsic gene expression subset. Improvement was accompanied by a decrease in gene expression for immune pathways, including the CD28 and CTLA4 receptors—the target of abatacept. Here we tested our a priori hypothesis that the inflammatory subset shows a significant decline in mRSS during abatacept therapy.

Objectives: ASSET (Abatacept Systemic Sclerosis Trial) is a Phase 2 study designed to assess the efficacy of subcutaneous abatacept to treat diffuse cutaneous systemic sclerosis. We performed RNA-sequencing (RNA-seq) analysis of skin biopsies and analyzed associations between intrinsic molecular subsets and clinical outcomes in the ASSET trial.

Methods: RNA-seq was performed on skin biopsies from 84 participants in the ASSET trial. A machine learning classifier was trained on independent cohorts and used to objectively classify patients into intrinsic gene expression subsets prior to study unblinding (2). Treatment differences in longitudinal outcomes were assessed using linear mixed effect models.

Results: 84 participants were assigned to intrinsic subset at baseline resulting in 33 inflammatory, 18 fibroproliferative, and 33 normal-like samples. Change in mRSS over 12 months was significantly different between the abatacept and placebo treatment arms for the inflammatory (p<0.001) and normal-like (p=0.03) subsets, but there was no difference in the fibroproliferative subset of patients (p=0.47) (Figure 1). For FVC% predicted, the fibroproliferative subset showed a numerical increase in FVC% in the abatacept arm (p=0.19) while all other groups showed decreases in FVC%. All gene expression subsets showed decreases in HAQ-DI in the abatacept arm not observed in the placebo arm, with the most robust changes occurring in the inflammatory (p=0.09) and normal-like (p=0.06) subsets.

Conclusion: There was a marked divergence of the trajectory for mRSS change for the inflammatory subset and no apparent impact for the fibroproliferative subset (1). In contrast, only the fibroproliferative subset showed a clinically meaningful FVC change for abatacept. For the broader functional measure of HAQ-DI, there were similar impacts of abatacept on all three intrinsic skin gene expression subsets but is numerically greatest for the normal-like and fibroproliferative subsets. Together these data show for the first time in a placebo-controlled trial that intrinsic skin gene expression subsets may predict differential response to a targeted biological therapy, and also that this may reflect impact on different facets of SSc pathogenesis in skin or lung. This suggests that stratification of cases according to intrinsic gene expression subsets may maximize the number of informative SSc cases in clinical trials, and potentially improve future clinical practice.

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THU0355  IGURATIMOD MIGHT TREAT SCLERODERMA WITH INTERRUPTED EGR1-TGF-β LOOP

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Background: Systemic sclerosis (SSc) is an autoimmune disease characterized with multiple organ fibrosis. Previous studies showed transcription factor early growth response 1 (Egr1) overexpressed in the lesional skin of SSc patients, as well as Egr1 inducible genes. Egr1 forms a positive feedback loop with master pro-fibrolic cytokine TGFβ and thus promotes fibrosis.

Objectives: To investigate the anti-fibrotic effect of a novel DMARD iguratimod in scleroderma models and patient skin grafts.

Methods: We used iguratimod to treat TGFβ-stimulated human skin fibroblast, bleomycin induced mice, tight skin 1 (Tsk-1) mice and SSc skin grafts. The bleomycin model contained pre-establish fibrosis and late onset treatment. The skin grafts came from three SSc patients and was planted into irradiated nude mice.

Results: Igarutimod down-regulated egr1 expression in human skin fibroblast with decreased collagen production and α-SMA expression. Knocking down Egr1 in fibroblast could mimic these effects. Both oral and topical iguratimod could reduce dermal thickening and collagen deposition in bleomycin induced skin fibrosis. α-SMA (+) myofibroblast counts, as well as Egr1 (+) and/or TGFβ (+) fibroblast counts in iguratimod treated groups were significantly less than the controls. Similarly, topical iguratimod ameliorated fibrosis with deduced dermal thickening in bleomycin induced skin fibroblast, α-SMA (+) myofibroblast counts, as well as Egr1 (+) and/or TGFβ (+) fibroblast counts in iguratimod treated groups were significantly less than the controls. Furthermore, inhibition of endocytosis by pigmmalinolide B12, an inhibitor of α-SMA, reduced the induction of Egr1 and TGFβ in skin tissue were inhibited after iguratimod treatment simultaneously.

Conclusion: We found the potential of iguratimod to treat SSc, which was characterized as an Egr1 inhibitor. Further clinical investigation is needed to establish its safety and efficacy.

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Disclosure of Interests: None declared


THU0356  STAPHYLOCOCCUS AUREUS REGULATES FIBROBLAST FUNCTIONS – IMPLICATIONS FOR TISSUE REPAIR IN CHRONIC DIGITAL ULCERS IN SYSTEMIC SCLEROSIS

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Background: Chronic digital ulcers (DU) are a major complication in systemic sclerosis (SSc). Non-healing wounds are characterized by persistent inflammation, defective re-epithelialization and impaired matrix remodeling, and are often accompanied by bacterial colonization. In DU, the breach of the basement membrane exposes tissue and cell layers to commensal and pathogenic bacteria.

Objectives: To investigate whether interactions between commensal skin bacteria and dermal fibroblasts affect tissue repair mechanisms.

Methods: Dermal fibroblasts isolated from healthy controls (HC) and patients with diffuse cutaneous SSc (dcSSc) (n=3, each) were co-cultured with Staphylococcus aureus (SA) for 3 h at using a lower inoculum rather representing colonization (1 x 10⁶ CFU/ml) and a higher inoculum reflecting infection (1 x 10⁷ CFU/ml). Thereafter, fibroblasts were cultured with flucloxacillin-containing medium to kill extracellular and adherent bacteria. For mechanistic studies, a fibroblast cell line (Bi-5ta) was used. IL-6, IL-8, pro-collagen Iα1, and interferon (IFN)-β proteins in culture supernatants were measured by ELISA.

Results: SA increased pro-collagen Iα1 secretion by 5.2/2.5-fold (HC/dcSSc; p=0.08/<0.05). Staining of Egr1 and TGFβ in SA treated fibroblasts were 8.4/31.7-fold (HC/dcSSc; p<0.05 each). SA induced apoptosis and necrosis. SA invaded fibroblasts via endocytosis (25-50% of inoculated SA). TNFα secretion was induced 8.4/31.7-fold (HC/dcSSc; p<0.05 each). The genes of cytosolic dsDNA sensor molecules such as cyclic GMP-AMP synthase (cGAS) were upregulated 11.9/8.6-fold (HC/dcSSc; p<0.05 each). TLR9, an endosomal DNA sensor, was constitutively expressed. Knockdown of STING or MYD88, downstream mediators of cGAS and TLR9 respectively, reduced the induction of IFN-β (down to 24.6%; p<0.05), IL-6 (down to 34.9%; p<0.05), and IL-8 (down to 27.6%; p<0.05). In contrast, inhibition of endocytosis did not affect induction of apoptosis. This suggests that the invasion of fibroblasts by SA and the subsequent intracellular DNA sensing are crucial for the induction of these genes independently of apoptosis.

Conclusion: Invasion of dermal fibroblasts by SA with activation of the cGAS/STING and TLR9-MYD88 pathways is a key element in the impairment of tissue repair responses.

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Disclosure of Interests: None declared


THU0357  VENTRICULAR-ARTERIAL COUPLING AS A PREDICTOR OF CARDIOVASCULAR EVENTS IN SYSTEMIC SCLEROSIS

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Background: Standard Transthoracic Echocardiography (TTE) parameters have shown a low sensitivity in the detection of primary myocardial involvement (PMI) in systemic sclerosis (SSc). Arterial-ventricular coupling (VAC) is calculated by TTE as the ratio between arterial elastance (Ea) and ventricular end-systolic elastance (Ees), which reflects left ventricle stiffness. VAC is a central determinant of cardiovascular performance.

Objectives: We aimed to assess TTE-derived measures of cardiac mechanics and the prognostic role of VAC in SSc.

Methods: 75 patients affected by SSc without symptoms of cardiac involvement and 10 controls matched for sex and age were retrospectively evaluated. We collected data at the first TTE examination. Arterial-ventricular coupling (VAC=Ees/Ea), arterial elastance (Ea), ventricular arterial coupling (VAC=Ees/Ea), and diastolic elastance (Eed) were considered. A value of VAC > 0.62 was considered indicative of altered VAC (i.e. uncoupling), whereas a lower value as normal (i.e. coupling). Finally, we considered the hospitalization for cardiovascular event during a mean follow-up of 10.6±1.8 years.
Results: Among the 75 patients 42 (59.2%) had a diffuse cutaneous form of SSC (dSSc) and 64 (85.3%) were female; in SSC patients the median age was 53 (12.1) yrs and the mean disease duration 10.1±2.3 yrs. 36 (52.2%) patients had positive SCl70, 31 (44.9%) ACA, and 2 (2.9%) anti-RNA pol III. Compared to controls, SSC patients had higher Ea (2.28 vs 0.95 mmHg/ml, p=0.003) and Ees (3.95 vs 2.98 mmHg/ml, p=0.05), and increased diastolic stiffness (Eed) (0.210 vs 0.146 mmHg/ml, p=0.01). VAC was consequently comparable to controls. SSC patients affected by dcSSc had a lower Ees (2.90 vs 4.367, p<0.001) and Eed (0.34 vs 0.17; p=0.032) and a higher VAC (0.52 vs 0.70; p=0.01) compared to lSSc. No differences were found between patients with anti-Scl70 and ACA. At 10 years, 23% of patients was hospitalized for at least one cardiovascular event. The analysis of survival free hospitalization or death in all SSC patients demonstrated a worse outcome and poor prognosis in patients with an altered VAC (31, 47.7%) compared to those with a normal VAC (34, 52.3%) (Figure 1).

Conclusion: Our study suggests that both ventricular and arterial stiffness may be increased in SSC patients without signs and symptoms of heart disease. Since VAC seems to have a prognostic role in the prediction of cardiovascular events in SSC, it could be helpful to define an early therapeutic strategy to prevent or delay cardiac manifestations in these patients.

REFERENCE:

Disclosure of Interests: None declared

20. Spondyloarthritis – clinical aspects (other than treatment)

THU0358 DEVELOPMENT OF A SET OF ASAS QUALITY STANDARDS FOR ADULTS WITH AXIAL SPONDYLOARTHRITIS

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The ASAS QS group, established in 2015, developed a stepwise approach starting with (I) an overview and open discussions resulting in a proposal for possible key areas for quality improvement. Thereafter, (II) ASAS members and invited patients discussed and commented on a provisional list via a web-based survey with the possibility to propose additional key areas for quality improvement. (III) The complete list was then evaluated by ASAS members and invited patients. (IV) Then, the ASAS QS group prioritized key areas for which quality statements and measures are to be developed, and (V) phrased QS for the most important key areas. Finally (VI), a draft version was commented on, discussed and finally agreed by the ASAS members at the Annual ASAS Meeting 2019. Results: The ASAS QS group, consisting of 20 rheumatologists, 2 physiotherapists and 2 patients, provided 34 potentially key areas for quality improvement which were commented by 140 participants (86 physicians, 42 patients). Within that process 3 new key areas were proposed and all 37 key areas for improvement were again evaluated by 120 participants (86 physicians, 29 patients). Five key areas were identified to be most important to phrase QS: referral, rheumatologic assessment, treatment, education/self-management and comorbidities. Altogether, 9 QS, each accompanied by a rationale and a measure (figure), were endorsed by ASAS.

Conclusion: ASAS successfully developed the first QS set for improvement of health care provided for adults with axSpA. All QS are achievable in daily care in an optimized situation and intended to minimize variation in quality of care. It is emphasized that ASAS is well aware that all QS are ideal visions of an optimal care which may currently not be realistic in many countries.

THU0358 – Figure 1. ASAS quality standards for patients with axial spondyloarthritis

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WHAT IS THE LEVEL OF AGREEMENT BETWEEN LOCAL AND CENTRAL READERS IN THE DETECTION OF ACTIVE AND STRUCTURAL LESIONS ON MRI OF AXIAL Spondyloarthritis? DATA FROM THE ASAS CLASSIFICATION COHORT STUDY

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Background: There has been no central reader evaluation of MRI scans from the ASAS Classification Cohort (ASAS-CC) to compare detection of lesions in the sacroiliac joints (SIJ) between central and ASAS-CC local site readers. Active MRI lesions typical of axSpA were reported in 61.6% and 2.2% of patients from this cohort diagnosed with axSpA and non-axSpA back pain, respectively1. Structural lesions were recorded but not reported in the literature.

Objectives: We aimed to compare detection of active and structural lesions on MRI images of the SIJ from the ASAS-CC between ASAS-CC local site readers and central readers from the ASAS-MRI group.

Methods: MRI images were available from 258 of the 495 cases who had MRI performed in the ASAS-CC and also had a local rheumatologist diagnosis. Seven central readers recorded MRI lesions in an eCRF that included wording of lesions defining active and structural lesions typical of axSpA that was exactly the same as in the original ASAS-CC eCRF permitting comparisons between central and local readers. In addition, lesions that met the criteria for an ASAS positive MRI were recorded by central readers. Active and structural lesion frequencies were assessed descriptively according to majority agreement (r4/7) of central reader data and also any 2 central readers. Reliability of detection of MRI lesions was compared between central and local readers using the kappa coefficient.

Results: Significant differences in lesion frequencies were observed according to diagnostic category (Table 1). The frequency of active lesions reported by local readers (61%) was greater than for central readers that agreed on the presence of an active lesion (49.7%). Structural lesions were reported less frequently by local readers (44.0%) compared to central readers that agreed on the presence of a structural lesion (54.9%). Reliability of local readers for detection of active lesions was good but only fair for structural lesions (Table 2).

Conclusion: Local readers may have overestimated the presence of active lesions and underestimated the presence of structural lesions in the ASAS-CC. Their reliability for detection of structural lesions was limited which could reflect lack of awareness of structural lesions related to axSpA.

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Disclosure of Interests: Walter P Maksymowych Grant/research support from: AbbVie, Pfizer, Janssen, Novartis, Consultant for: AbbVie, Eli Lilly, Boehringer, Galapagos, Janssen, Novartis, Pfizer and UCB Pharma; Chief Medical Officer for Canadian Research and Education Arthritis, Xenofon Baraliakos Grant/research support from: AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Centocor, Chugai, Janssen, MSD, Novartis, Pfizer Inc, Roche and UCB, Grant/research support from: AbbVie, Pfizer, Merck Sharp & Dohme, UCB Pharma, Novartis, Consultant for: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Chugai, Janssen, Janssen Biologies, Novartis, Pfizer, UCB Pharma, Galapagos, Speakers bureau: AbbVie, Chugai, Janssen, Novartis, Pfizer, UCB Pharma, Robert G Lambert Consultant for: Bioclinica, Parexel, AbbVie, Ulrich Weber Consultant for: AbbVie, Joachim Sieper Consultant for: AbbVie, Böhringer Ingelheim, Janssen, Lilly, Merck, Novartis, Pfizer, UCB, Speakers bureau: Abbvie, Böhringer Ingelheim, Janssen, Lilly, Merck, Mylan, Novartis, Pfizer, UCB, Stephanie Wichuk: None declared, Denis Poddubnyy Grant/research support from: AbbVie, Merck Sharp & Dohme, Novartis, Consultant for: AbbVie, Bristol-Myers Squibb, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, UCB Pharma, Speakers bureau: AbbVie, Bristol-Myers Squibb, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, UCB Pharma, Mikkel Østergaard Grant/research support from: AbbVie, Chugai, Centocor, Merck, Novartis, Consultant for: AbbVie, BMS, Boehringer-Ingelheim, Chugai, Eli Lilly, Hospira, Janssen, Merck, Novartis, UCB, Regeneron, Roche, and UCB, Speakers bureau: Abbvie, BMS, Boehringer-Ingelheim, Chugai, Eli Lilly, Hospira, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, and UCB, Speakers bureau: AbbVie, BMS, Chugai, Janssen, MSD, Novartis, Pfizer, Roche and UCB, Speakers bureau: AbbVie, BMS, Chugai, Janssen, MSD, Novartis, Pfizer, Roche and UCB, Speakers bureau: AbbVie, BMS, Chugai, Janssen, MSD, Novartis, Pfizer, Roche and UCB.

THU0360

INCREASING IMPACT ON STRUCTURAL DAMAGE WITH INCREASING CUMULATIVE INFLAMMATION AT THE SI-JOINT QUADRANT LEVEL IN AXIAL SPONDYLOARTHRITIS – 5-YEAR DATA FROM THE DESIR COHORT

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Background: Axial inflammation is a key feature in axial SpA (axSpA). There is lack of data relative to the persistence of BME in the same anatomical quadrant (Q, 8 in total for both SIJ together), regardless of the overall presence of BME.

Objectives: This study aims to investigate particular patterns of distribution of SIJ-BME across quadrants over time, their persistence over time, and their impact on clinical and structural outcomes.

Methods: Patients from the DESIR cohort (early axSpA according to the rheumatologist) with MRI-SIJ available at baseline, 2 and 5 years were included. Each image was scored by 3 trained central readers blinded to chronological order. BME was considered positive if detected in ≥1/6 slices in each of the 8 quadrants, according to each individual reader. Four different patterns of BME over time were defined (no BME, sporadic pattern, fluctuating BME and persistent BME) considering all 8 quadrants (Figure). The effect of BME patterns on 5-year structural (mNY, mSASSS, ≥5 erosions and/or fatty lesions in MRI-SIJ) and clinical outcomes (BASI, BASMI and ASQoL) was evaluated using multilevel generalised estimating equations (GEE) models (taking the individual reader data into account) and linear regression (using the agreement of ≥2 out of 3), as appropriate. All models were adjusted for relevant confounders including treatment (Table).

Results: In total, 136 patients were included (age 34 (SD 9) years, 50% male, and 63% HLA-B27 positive). No BME was seen in 63 patients (46%), the ‘sporadic pattern’ in 34 patients (25%), the ‘fluctuating pattern’ was seen in 21 patients (15%) and the ‘persistent BME pattern’ was seen in 18 patients (13%). Compared to the ‘no BME’ pattern (reference), the ‘sporadic’ [OR (95% CI): 2.1 (1.0;4.5)], ‘fluctuating’ [OR: 5.6 (2.2;14.4)] and ‘persistent’ [OR: 7.5 (2.8;19.6)] patterns were associated with higher likelihood to be mNY positive at 5-years, suggesting a gradient between cumulative inflammation and damage. Similar findings were observed for mSASSS as a continuous outcome variable and for ≥5 erosions and/or fatty lesions in MRI-SIJ (Figure). The effect of BME patterns on 5-year structural (mNY, mSASSS, ≥5 erosions and/or fatty lesions in MRI-SIJ) and clinical outcomes (BASI, BASMI and ASQoL) was evaluated using multilevel generalised estimating equations (GEE) models (taking the individual reader data into account) and linear regression (using the agreement of ≥2 out of 3), as appropriate. All models were adjusted for relevant confounders including treatment (Table).

Conclusion: Only 13% of the patients showed persistent inflammation in the same Q over a 5-year period and in 15% inflammation was fluctuating across different Qs. More structural damage was found in patients with increasing cumulative level of local inflammation in the quadrant. Even when BME (temporarily) disappears there is an important effect on structural outcomes, and that effect t is independent of treatment.

Disclosure of Interests: Santiago Rodríguez-Manicà Grant/research support from: Novartis, MSD, Speakers bureau: Novartis, Alexandre Sepriano: None declared, Sofia Ramiro Grant/research support from: MSD, Consultant for: AbbVie, Lilly, MSD, Novartis, Pfizer, Sanofi, Speakers bureau: AbbVie, Lilly, MSD, Novartis, Pfizer, Sanofi, Robert B.M. Landewé: None declared, Pascal Claudépière Consultant for: Honoraria from Novartis as steering committee of this study, Anna Molto: None declared, maxime dougdas Grant/research support from: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma, Consultant for: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma, Miranda van Lunteren: None declared, Désirée van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Daichi, Eli Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, Union Chimique Belge

THU0361

DIAGNOSTIC PERFORMANCE OF MRI LESIONS IN THE SACROILIAC JOINTS ACCORDING TO UPDATED ASAS LESION DEFINITIONS: A CENTRAL READER ASSESSMENT OF MRI SCANS FROM THE ASSESSMENTS IN SPONDYLOARTHRITIS CLASSIFICATION COHORT

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Background: The ASAS MRI group has generated updated lesion definitions for MRI lesions in the SI. While the ASAS definition of a positive MRI for classification purposes remains unchanged, these additional ASAS definitions for active and structural lesions may also be of diagnostic value. It is important to understand their relative contribution and complementarily as diagnostic indicators.

Objectives: To determine optimal cut-offs for the number of SIJ quadrants with MRI lesions reflecting diagnosis of axSpA in patients with undiagnosed back pain.

Methods: MRI lesions on baseline scans from the ASAS Classification Cohort were recorded by 7 experienced readers from the ASAS-ASAS MRI group. Detailed scoring of lesions per SIJ quadrant (SPARCC SIJ quadrant method) was available for assessment of bone marrow edema (BME) and structural lesions in 158 and 146 cases, respectively, who were diagnosed by the local rheumatologist at baseline. Of these, 86 and 79 cases with BME and structural lesion data, respectively, were also diagnosed by the local rheumatologist at follow up (mean 4.4 years). We calculated sensitivity and specificity for varying numbers of SIJ quadrants with MRI lesions with rheumatologist diagnosis of axSpA at baseline and follow up as gold standard.

Results: Rating cut-offs based on BME were most sensitive for diagnosis at baseline and follow up but erosion- and fatty-lesion cut-offs were more specific (Table). At least 2 SIJ quadrants with erosion or fat metaplasia were associated with >90% specificity for the diagnosis of axSpA. There was also a consistent improvement in the sensitivity and specificity performance of cut-offs based on erosions and fatty lesions according to diagnosis at baseline and at follow up after 4.4 years but not for cut-offs based on BME. Lesion cut-offs that combined BME and/or erosion enhanced sensitivity without compromising specificity.
Conclusions: The updated ASAS definitions based on the presence of MRI lesions in 2-3 SIJ quadrants have comparable diagnostic performance. This performance improves for erosion and fatty lesion cut-offs after follow-up.

Disclosure of Interests: Walter P Maksymowych Grant/research support from: AbbVie, Pfizer, Janssen, Novartis, Consultant for: AbbVie, Eli Lilly, Boehringer, Galapagos, Janssen, Novartis, Pfizer and UCB Pharma; Chief Medical Officer for Canadian Research and Education Arthritis, Robert G Lambert Consultant for: Bioclinica, Parexel, Abbvie, Xenofon Baraliakos Grant/research support from: AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Centocor, Chugai, Janssen, MSD, Novartis, Pfizer Inc, Roche and UCB, Grant/research support from: AbbVie, Pfizer, Merck Sharp & Dohme, UCB Pharma, Novartis, Consultant for: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Chugai, Janssen Biologics, Novartis, Pfizer, UCB Pharma, Galapagos, Speakers bureau: AbbVie, Chugai, Janssen, Novartis, Pfizer, UCB Pharma, Susanne Juhi Pedersen: None declared, Pedro Machado Consultant for: Abbvie, BMS, Celgene, Janssen, MSD, Novartis, Pfizer, Roche and UCB, Speakers bureau: Abbvie, BMS, Celgene, Janssen, MSD, Novartis, Pfizer, Roche and UCB, Joachim Sieper Consultant for: Abbvie, Böhringer Ingelheim, Janssen, Lilly, Merck, Mylan, Novartis, Pfizer, UCB, Speakers bureau: Abbvie, Böhringer Ingelheim, Janssen, Lilly, Merck, Mylan, Novartis, Pfizer, UCB, Joachim Sieper Consultant for: Abbvie, Böhringer Ingelheim, Janssen, Lilly, Merck, Mylan, Novartis, Pfizer, UCB, Speakers bureau: Abbvie, BMS, Celgene, Janssen, MSD, Novartis, Pfizer, Roche and UCB, Joachim Sieper Consultant for: Abbvie, Böhringer Ingelheim, Janssen, Lilly, Merck, Mylan, Novartis, Pfizer, UCB, Speakers bureau: Abbvie, BMS, Celgene, Janssen, Lilly, Merck, Mylan, Novartis, Pfizer, UCB, Speakers bureau: Abbvie, BMS, Celgene, Janssen, Lilly, Merck, Mylan, Novartis, Pfizer, UCB, Ulrich Weber Consultant for: Abbvie DOI: 10.1136/annrheumdis-2019-eular.6455

References:


Abstract THU0361 – Table 1.

<table>
<thead>
<tr>
<th>MRI lesion SIJ quadrant cut-offs, Agreement by central reader data</th>
<th>axSpA Diagnosed at Baseline</th>
<th>axSpA Diagnosed at Follow up</th>
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</thead>
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<tr>
<td></td>
<td>Sensitivity (95% CI)</td>
<td>Specificity (95% CI)</td>
</tr>
<tr>
<td>BME Score ≥2</td>
<td>50.0 (46.0-54.0)</td>
<td>82.5 (70.1-91.4)</td>
</tr>
<tr>
<td>BME Score ≥3</td>
<td>40.5 (31.5-50.0)</td>
<td>94.7 (85.4-97.1)</td>
</tr>
<tr>
<td>Erosion Score ≥2</td>
<td>35.3 (26.7-44.8)</td>
<td>93.0 (83.0-95.7)</td>
</tr>
<tr>
<td>Erosion Score ≥3</td>
<td>31.0 (22.8-40.3)</td>
<td>93.0 (83.0-95.7)</td>
</tr>
<tr>
<td>Fatty lesion ≥2</td>
<td>34.5 (25.9-43.9)</td>
<td>90.0 (83.0-95.5)</td>
</tr>
<tr>
<td>Fatty lesion ≥3</td>
<td>31.9 (23.6-41.2)</td>
<td>94.7 (85.4-97.1)</td>
</tr>
<tr>
<td>Erosion Score ≥2</td>
<td>32.8 (24.3-42.1)</td>
<td>82.5 (70.1-91.4)</td>
</tr>
<tr>
<td>Erosion Score ≥2</td>
<td>37.6 (28.5-49.2)</td>
<td>93.0 (83.0-95.5)</td>
</tr>
<tr>
<td>Erosion score ≥1 and</td>
<td>36.1 (28.6-41.3)</td>
<td>92.1 (78.6-95.7)</td>
</tr>
<tr>
<td>Erosion score ≥2</td>
<td>46.5 (38.0-54.0)</td>
<td>93.0 (83.0-95.5)</td>
</tr>
<tr>
<td>Erosion score ≥2 and/or</td>
<td>58.8 (48.3-69.3)</td>
<td>81.6 (65.7-87.2)</td>
</tr>
<tr>
<td>Erosion score ≥2</td>
<td>68.7 (54.8-83.8)</td>
<td>92.3 (79.5-95.0)</td>
</tr>
<tr>
<td>Erosion score ≥2 and/or</td>
<td>51.6 (41.2-61.8)</td>
<td>86.8 (69.9-93.1)</td>
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<tr>
<td>Erosion score ≥2</td>
<td>61.8 (49.3-74.8)</td>
<td>93.0 (83.0-95.5)</td>
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</table>

Abstract THU0362 – Figure 1. Estimated mean RMDQ scores over time for the overall intervention and usual care group.

Bars indicate 95% confidence intervals for the mean estimates.
DO ILLNESS PERCEPTIONS AND COPING CHANGE OVER TIME IN PATIENTS RECENTLY DIAGNOSED WITH AXIAL SPONDYLOARTHRITIS? A 2-YEAR FOLLOW-UP STUDY IN THE SPACE COHORT

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Background: In recently diagnosed axial spondyloarthritis (axSpA), illness perceptions are important in the relationship between back pain and Health-Related Quality of Life (HRQoL). Illness perceptions and coping remain stable over time. However, hardly any information is available, especially for early axSpA, as the few studies that have been conducted mostly had a cross-sectional design and investigated patients with long-standing radiographic axSpA.

Objectives: To investigate if illness perceptions and coping strategies change in the first 2 years after diagnosis of axSpA.

Methods: Patients diagnosed with axSpA and ≥1 follow-up visit (1 year and/or 2 years) in the SPACE cohort were included in the analysis. Mixed linear models were used to test if illness perceptions (measured by the Revised Illness Perception Questionnaire (IPQ-R, scale 1-5)), coping did not have an additional impact on this relationship, but was associated with HRQoL. Therefore, health outcomes might be improved by influencing illness perceptions and possibly coping. With respect to disease management, it is important to know if illness perceptions and coping remain stable over time. However, hardly any information is available, especially for early axSpA, as the few studies that have been conducted mostly had a cross-sectional design and investigated patients with long-standing radiographic axSpA.

Results: In total, 150 axSpA patients (mean age 30.4 years, 51% female, 65% HLA-B27+) were analysed. Baseline mean back pain (SD) was 4.0 (2.5), PCS was 28.8 (14.0), MCS was 47.8 (12.4), WPL was 34.1% (29.8) and activity impairment was 38.7% (27.9). Illness perceptions and coping strategies showed minimal changes over time (Table 1, 2). Over two years patients remained having negative illness perceptions (which were important in the association between back pain and health outcomes in the previous study). For example, over 2 years patients had strong beliefs in severe consequences (‘consequences’), had still negative emotions towards their disease (‘emotional representation’) and had strong beliefs in chance (‘chance’) as a cause for axSpA.

Conclusion: Despite clear improvements in back pain and health outcomes over 2 years, illness perceptions experienced and coping strategies applied by the patients showed little change in recently diagnosed axSpA patients. Further research is recommended why despite improved outcomes illness perceptions do not change, to investigate the impact of these unchanged illness perceptions and coping strategies on health outcomes and how these negative perceptions can be improved.

REFERENCES:

THE DIAGNOSTIC UTILITY OF THE RELATION BETWEEN MRI BONE MARROW EDEMA AND OTHER TYPES OF MRI LESIONS IN THE SACROILIAC JOINTS IN AXIAL SPONDYLOARTHRITIS

Serejil Seven1, Pernelle Hededå2, Mikkel Østergaard3, Lone Morselt-Cartensen4, Inge Juul Sørensen5, Birthe Bonde5, Gorm Thamsborg5, Jens Jørgen Lykkegaard5, Oliver Hendricks4, Niklas Rye Jørgensen5, Susanne Juul Pedersen4, Roberta Ramonda5, Désirée van der Heijde1, Floris A. van Gaalen1,1, LUMC, Leiden, Netherlands; 2Aalborg Rheumatism Hospital, Gråsten, Denmark; 3Aalborg Rheumatology and Spine Diseases, Glostrup, Denmark; 4Rigshospitalet – Glostrup, Copenhagen Center for Arthritis Research Center for Rheumatology and Spine Diseases, Glostrup, Denmark; 5Rigshospitalet – Glostrup, Department of Radiology, Glostrup, Denmark; 6Bidragende klinikker, Köbenhavn, Denmark; 7King Christian X’s Rheumatism Hospital, Gråsten, Denmark; 8Rigshospitalet – Glostrup, Department of Clinical Biochemistry, Glostrup, Denmark

Background: MRI detected bone marrow edema (BME) plays a central role in the ASAS (Assessment of Spondyloarthritis International Society) classification criteria for axial spondyloarthritis (axSpA)[1, 2]. However, BME in the sacroiliac joints (SIJs) is also present in other conditions[3-7].

Objectives: The aim was to investigate the diagnostic utility of MRI BME and its relation to different types of MRI SIJ lesions to separate patients with axSpA from persons with other conditions.

Methods: The MASH study is a prospective cross-sectional study of 204 participants, aged ≤45 years. The study included patients with axSpA (n=41), women with (n=46) and without (n=14) postpartum pain, patients with lumbar disc herniation (n=25), persons with hard physical labor (cleaning assistants) (n=25), long-distance runners (<30 km/week) (n=23) and healthy men (n=29). Participants with pain should all have VAS pain >2 (on a scale 0-10) for ≥2 months. Participants in the non-axSpA groups were not allowed to have any clinical SIJ features or rheumatological conditions.

Participants underwent clinical, laboratory and MRI examination (semi-structural STIR and T1W sequences) of the SIJs. MRIs were evaluated for BME, erosion, fat, ankylosis, and sclerosis according to the SPARCC MRI definitions of lesions[8, 9] by two independent readers. In nine slices of the cartilaginous compartment each SIJ was separately assessed for the presence of BME in relation to joint space and each of the above-mentioned structural lesions (range of total score per patient: 0-18).

Results: The table shows the clinical characteristics of each group, the mean MRI scores and MRI cut-off levels for the concordant reads. BME were more frequent in patients with axSpA, but these lesions were also seen in the other study groups, mainly women with postpartum pain. When increasing amounts of lesions were required (higher cut-offs),...
almost only AxSpA patients fulfilled the requirements. BME adjacent to sclerosis was most frequent in women with postpartum pain, whereas BME adjacent to fat was most frequently, but not exclusively, occurring in patients with axSpA, whilst BME adjacent to sclerosis was most frequent in women with postpartum pain. Detailed analysis of lesions and their anatomical location may help differentiate axSpA from other conditions.

Disclosure of Interests: Sengül Seven: None declared, Pernille Hededal: Disclosure of Interests:

REFERENCES:

Abstract THU0364 – Table 1.

Clinical characteristics and relations between MRI and other ML measures

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>AxSpA</th>
<th>No AxSpA</th>
<th>Relative risk (RR)</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Axial enthesitis</td>
<td>0.33*</td>
<td>0.26*</td>
<td>1.25 (1.03, 1.51)</td>
<td>0.02</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Peripheral enthesitis</td>
<td>0.33*</td>
<td>0.26*</td>
<td>1.25 (1.03, 1.51)</td>
<td>0.02</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Axial enthesitis</td>
<td>0.33*</td>
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<td>1.25 (1.03, 1.51)</td>
<td>0.02</td>
<td>&lt;0.0001</td>
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<tr>
<td>Peripheral enthesitis</td>
<td>0.33*</td>
<td>0.26*</td>
<td>1.25 (1.03, 1.51)</td>
<td>0.02</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Results: A total of 1,729 patients with axSpA were included in the analyses; mean age was 55.9 years and 46.1% were female. The prevalence was 9% (27%) for recent (ever) uveitis, 10% (15%) for recent (ever) psoriasis, and 6% (9%) for recent (ever) IBD. In 0.5% of the patients, all three conditions were recently (ever) present.

Abstract THU0365 – Table 1.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Prevalence</th>
<th>Reference</th>
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</thead>
<tbody>
<tr>
<td>Uveitis</td>
<td>9%</td>
<td>0.09 (0.05, 0.13)</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>10%</td>
<td>0.10 (0.06, 0.15)</td>
</tr>
<tr>
<td>IBD</td>
<td>6%</td>
<td>0.09 (0.05, 0.13)</td>
</tr>
</tbody>
</table>

Background: Uveitis, psoriasis and inflammatory bowel disease (IBD) are common in axial spondyloarthritis (axSpA) and data on their impact on activity of musculoskeletal manifestations and functional status in general are contradictory.

Objectives: The aim of this study was to assess the impact of uveitis, psoriasis and IBD on disease activity and functional status in a population-based cohort of patients with axSpA.

Methods: A stratified random sample of subjects with a diagnosis of axSpA (ICD-10 M45) was drawn from health insurance data in Germany. These patients received a questionnaire on disease-related, demographic and socioeconomic parameters. Age, sex, drug prescriptions and non-pharmacological treatment were retrieved from claims data and linked to the questionnaire data. Information on recent occurrence of uveitis, psoriasis and IBD (within one year) was obtained from claims data; in addition, information on history of uveitis, psoriasis and IBD was obtained from survey data. Patients with uveitis, psoriasis or IBD were compared to those without uveitis, psoriasis or IBD. Separate multivariable linear regression models were calculated to determine the effect of uveitis, psoriasis and IBD on disease activity and functional status, and further adjustment was performed for other relevant parameters including treatment.

Conclusion: Disease activity and functional impairment are higher in axSpA patients with a history of psoriasis or IBD, whereas history of uveitis was associated with lower disease activity according to the BASDAI even after adjustment for treatment.
MAGNETIC RESONANCE IMAGING IN COMPARISON WITH CONVENTIONAL RADIOGRAPHY FOR DETECTION OF STRUCTURAL CHANGES TYPICAL FOR SPA – DATA FROM THE ASSESSMENT OF Spondyloarthritis International Society (ASAS) COHORT

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Background: In axial spondyloarthritis, magnetic resonance imaging (MRI) is useful for depicting active inflammatory lesions. The utility of MRI to display structural changes is not that well established.

Objectives: Comparison of MRI and conventional radiography of the sacroiliac joints (SIJs) for detection of structural lesions typical for axial spondyloarthritides (axSpA) in an international multireader exercise.

Methods: Patients from the ASAS Cohort with symptoms suggestive of axSpA and both radiographs and T1-weighted MRIs of SIJs available for central reading were included. SIJs radiographs were scored by 3 central readers according to the modified New York (mNY) criteria grading system. Structural damage on radiographs was defined as fulfillment of the mNY criterion (patient level) or presence of grade 2 sacroiliitis (single joint level) (majority decision). MRI scans were assessed for structural changes compatible with axSpA (global statement) and separate changes (erosion, sclerosis, periarticular fat metaplasia and ankylosis) by 7 central readers (majority decision). Absolute agreement between MRI and radiography (Table 1).

Results: Overall, 199 patients (398 joints) were included, 149 (74.9%) had a diagnosis of axSpA. 102 (51.3%) had definite radiographic sacroilitis, 65 (32.7%) had structural changes suggestive of SpA on MRI (global assessment). The absolute agreement between MRI and radiography was 69.3%, kappa - 0.39 (Table 1). Structural damage on radiographs often (48.1% of cases) could not be confirmed by MRI. Among structural lesions, erosions on MRI showed the best discriminative capacity regarding the structural damage on radiographs (Table 1).

Conclusion: Only modest agreement between MRI and conventional radiography in detection of structural changes typical for SpA in the SIJs was revealed; erosions on MRI showed the best agreement with the presence of definite structural damage on radiographs.

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ANALYSING IMPAIRMENTS IN PHYSICAL PERFORMANCE (AS ASSESSED BY THE AS PERFORMANCE INDEX (ASPI)) IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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BACKGROUND: In patients with axial spondyloarthritis (axSpA) physical functioning is often impaired. The current gold standard to assess physical functioning is self-reported questionnaires (i.e. BASFI), which can be influenced by patients' subjective feelings. Therefore, a performance-based test-battery was designed to measure physical functioning more objectively: the ankylosing spondylitis (AS) Performance Index (ASPI) [1]. Based on domains taken from BASFI tasks were designed to imitate activities of daily living (ADL). Although the ASPI has been evaluated for a thorough analysis of the deficits of physical functioning and factors which influence the performance of patients with axSpA has not been performed to date.

OBJECTIVES: The aim of the present study assesses the relation between self-reported assessments of physical functioning and actual performance of patients, and to detect influencing factors.

METHODS: Consecutive axSpA patients underwent standardized assessments concentrating on the following variables: patient and disease characteristics, patient-reported outcomes (ASDAS, BASFI, BASMI, ASAS Health Index (ASAS HI), PHQ-9, IPAQ), mSASSS and ASPI (ASPI 1: Bending, 2. Putting on socks, 3. Getting up from the floor) [1]. The performance was measured in seconds as time to complete a task based on published instructions. Impairment in physical performance was defined as inability of patients to perform > 1 ASPI test. Spearman Rho correlation was used to compare self-reported functioning and performed physical functioning. Logistic regression analysis was used to identify factors associated with impaired physical performance.

RESULTS: A total of 200 patients (AS 66%, nr-axSpA 34%) was included: 69% males, 44.3±12.5 years old, mean symptom duration 17.9±12.6 years, BMI 27.2±5.5, mean ASDAS 2.5±1.1, BASFI 4.0±2.7, BASMI 3.5±1.8, ASAS HI 7.0±4.1, PHQ-9 8.8±6.2, and mSASSS (n=157) 10.2±18.8. 133 patients were treated with bDMARDs (66.5%). In total 44 patients (22%) were not able to perform one or more ASPI tests. The mean time for bending was 18.5±5.5 sec (n=179/90%), for putting on socks 12.8±6.4 sec (n=156/78%), and for getting up from floor 6.5±5.0 sec (n=187/94%). A significant correlation was found for all three ASPI tests with BASFI (0.5-0.7), ASAS HI (0.4-0.6) and spinal mobility as assessed by BASMI (0.4-0.7). Self-reported physical activity (IPAQ) correlated weakly with ASPI (all 0.2) and structural damage correlated only with the test putting on socks (r=0.3), whereas the other tests did not correlate. Logistic regression showed influence of obesity, spinal mobility and global functioning on actual performance but not of disease activity and self-reported physical function, (Figure 1).

CONCLUSION: This study confirms a good correlation of the ASPI with standard questionnaires but it showed a substantial floor effect strongly suggesting that additional information on actual performance is needed. Thus, to obtain a complete picture of function and impairments of patients with axSpA the actual performance needs also to be assessed. Moreover, obesity should be addressed as a potential modifying factor contributing to limitation in actual performance.

THU0367 – Figure 1. Association between clinical characteristics of patients with SpA and physical performance

REFERENCE:

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THU0368 
THE IMPACT OF PROFESSIONAL ACTIVITY IN ANKYLOSING SPONDYLITIS

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Background: The mechanical stress due to strenuous professional activity cannot be easily quantified, yet it may lead to a wide range of musculoskeletal complaints. In ankylosing spondylitis (AS) patients, mechanical stress may lead to the occurrence and the aggravation of enthesitis (1) and a profession involving an intense physical strain is correlated with the radiologic progression (2). While studies regarding the professional activities in ankylosing spondylitis patients are focused on the disease's impact on the work capacity, the type of labor may also influence the disease progression (3).

Objectives: To assess the relationship between the professional activity in AS patients, disease activity and radiological changes.

Methods: We enrolled 193 patients with AS admitted in the Rheumatology Department of the “St. Apostol Andrei” Emergency Clinical County Hospital. Patient evaluation was performed by a rheumatologist. All the data obtained from the medical history, clinical examination, laboratory tests and imaging studies was recorded at the same date. Data regarding the professional history, type of labor involved was also recorded. The physical strain due to professional activity was done using the methodology established by the National Institute for Medical Expertise and Recovery of Work, which takes into account the amount of energy used in order to perform certain tasks.

Results: We included 193 patients, mostly men, 171 men (81.9%), with a mean age of 47.9±12.04 years and a mean disease duration of 20.07±11.18 years. At the moment of the evaluation, 49.7% were still employed and 50.3% were retired due to work disability. Most patients had a professional qualification (89.2%), and manual labor was identified in 132 (6.4%) of the patients. In the study cohort the professional physical strain was mostly low (39.4%) and medium (50.8%). Manual laborers (77.3%) had an active disease, with a mean BASDAI of 5.6±1.0, and a mean ASDAS-PCR of 3.2±1.23, the high and very high disease activity (ASDAS-PCR >2.1) being registered in 86.1% of them (p=0.001). Manual workers had an important functional deficit (BASFI=6.3±2.41) (p=0.001). Regarding radiological features, manual laborers had stage IV sacroiliitis in 68.9% of the cases, 82.6% had syndesmophytes, which were generalised in 59.8% of the cases (p=0.005).

A high professional physical strain correlates with active disease (BASDAI=4.1), with the presence of bridging syndesmophytes (81.8%, p=0.009), and generalized syndesmophytes (68.8%, p=0.007).

Conclusion: Manual labor, with strenuous physical activities correlates with high disease activity, severe functional impairment and radiological changes in AS patients.

REFERENCES:

Disclosure of Interests: None declared

THU0369 
INCREASED PREVALENCE OF CARDIAC DISORDERS IN DUTCH ANKYLOSING SPONDYLITIS PATIENTS: THE CARDAS STUDY

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Background: The overall mortality rate in ankylosing spondylitis (AS) patients is increased by 60–90% compared with the general population. This higher mortality rate is predominately caused by cardiovascular disease (CVD) comprising both by increased prevalence of cardiac diseases such as valvular heart disease, conduction disturbances and cardiomyopathies as well as atherosclerotic diseases such as myocardial infarctions. However, there is some diversity in the literature and there is a lack of contemporary studies. Therefore, we investigated current prevalences of cardiac disorders in a well characterized cohorts of Dutch patients with AS.

Objectives: The CARDAS study aims to describe the prevalence of CVD in AS patients in a Dutch cohort.

Methods: We performed a cross-sectional study in consecutive AS patients between 50-75 years. Subjects were recruited from a large rheumatology outpatient clinic (Reade) in Amsterdam, the Netherlands. Patients underwent echocardiography with 2D, spectral and Color Doppler imaging. Diastolic dysfunction was evaluated by an experienced cardiologist based on the 2008 ASE guideline. Furthermore, an ECG, blood sample, surveys and physical examination were performed. Disease activity and function were measured with the BASFI, BASDAI and the ASDAS-PCR.

Results: 191 Consecutive AS patients were included with a median age of 58 years (54-65) of which mostly men (136/191, 71%) (Table 1). The mean disease duration was 34.9 years (+11.9) The disease activity measures, BASDAI, ASDAS-PCR and BASFI, indicated moderate disease activity and were, respectively 3.1 (+2.3), 2.1 (+1.0) and 3.5 (1.6-5.7). The percentage of AS patients was present in 42% of the AS patients. As cardiac manifestations are age related, AS patients were divided in 3 age categories, respectively 50-59 years, 60-69 years and 70-75 years. Hypertension was diagnosed in respectively 45.3%, 64.1% and 85.7%. History of CVD described as angina pectoris, myocardial infarction, stroke and/or peripheral ischemia were present in respectively 7.5%, 9.4% and 19%. Diastolic dysfunction was present in respectively 40.4%, 61.9% and 89.5% of the AS patients. The diastolic dysfunction present in this population was mainly mild with 60.2% of patients presenting with grade 1 and 39.8% with grade 2 diastolic dysfunction. Moderate to severe aortic regurgitation was present in respectively 10.4%, 12.5% and 42.9% of the AS patients. These prevalences are substantially increased in comparison to the general Dutch population.

Conclusion: We demonstrated increased prevalences of diastolic dysfunction, aortic valve regurgitation, mitral valve regurgitation and hypertension in Dutch AS patients compared to age matched general population. Although our results suggest mandatory echocardiography screening, this first needs to be established in prospective follow-up studies.

Abstract THU0369 – Table 1. Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>50-59 years</th>
<th>60-69 years</th>
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<tr>
<td>N</td>
<td>191</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
<td>131 (71%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>58 (54-65)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease activity</td>
<td>BASDAI=3.1 (±2.3)</td>
<td>ASDAS-PCR=2.1 (±1.0)</td>
<td>BASFI=3.5 (1.6-5.7)</td>
<td></td>
</tr>
<tr>
<td>CVD</td>
<td>History of CVD**</td>
<td>Hypertension</td>
<td>Aortic valve regurgitation**</td>
<td>Mitral valve regurgitation**</td>
</tr>
<tr>
<td></td>
<td>7.5%</td>
<td>45.3%</td>
<td>10.4%</td>
<td>33%</td>
</tr>
<tr>
<td></td>
<td>9.4%</td>
<td>64.1%</td>
<td>12.5%</td>
<td>31.1%</td>
</tr>
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<td></td>
<td>19%</td>
<td>85.7%</td>
<td>33.4%</td>
<td>42.9%</td>
</tr>
</tbody>
</table>

* Described as angina pectoris, myocardial infarction, stroke and/or peripheral ischemia
** moderate – severe regurgitation.

Disclosure of Interests: Milad Baniaamam: None declared, Sjoerd C. Heslinga: None declared, Thelma Konings: None declared, Otto Kamp: None declared, Vokko P. van Halm: None declared, Irene van der Horst-Bruinsma Grant/research support from: MSD, Pfizer, AbbVie, Consultant

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Conclusion: The ASDAS demonstrated similar construct validity in all patients with pSpA and axSpA in clinical practice. Therefore, the ASDAS can also be used to measure disease activity in pSpA in daily practice.

REFERENCE:

Disclosure of Interests: None declared

predictors of improvement in work productivity at 6 months, while increased baseline work productivity was a positive predictor of improvement. In the PsA group, other than higher baseline work productivity (positive predictor of improvement), no significant predictors were identified at 6 months. However, a negative trend was observed for the presence of depression (LSM: -0.4% vs. -2.5%; p=0.068).

Conclusion: We observed a significant proportion of AS and PsA patients unemployed in this real-world Canadian cohort. Treatment with adalimumab or non-biologic DMARDs was associated with significant improvement in work productivity irrespective of potential risk factors. Presence of depression was identified as an independent negative predictor of improvement in work performance/productivity.

REFERENCES:
N/A.

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THU0372 NEUROPATHIC PAIN IN THE PATIENTS WITH SPONDYLOARTHRITIS: RELATIONSHIP WITH FATIGUE, SLEEP QUALITY AND QUALITY OF LIFE

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Background: Neuropathic pain is defined as the pain that arises as a direct consequence of a lesion or diseases affecting the somatosensory system. Low back pain has nociceptive, neuropathic or mixed components. Inflammatory back pain is one of the key clinical criteria for the classification of spondyloarthritis (SpA). There are no accurate data for the overall prevalence of neuropathic pain in the inflammatory disorders.

Objectives: In the present study we aimed to determine whether there is a neuropathic component in SpA and also to determine the relationship with disease activity, clinical findings, fatigue, sleep quality and quality of life.

Methods: Eighty SpA patients fulfilling the Assessment of SpondyloArthritis International Society (ASAS) classification criteria for SpA (MF=42/38) (37.±11.7 years), 53 patients with chronic low back pain (CLBP) (MF=22/31) (45.5±13.6 years) and 50 healthy controls (MF=28/22) (38.1±12.7 years) were enrolled in the study. Pain was assessed with visual analogue scale (VAS rest and activity), disease activity with Ankylosing Spondylitis Disease Activity Index (BASDAI), functional capacity with Bath Ankylosing Spondylitis Functional Index (BASFI), fatigue with multidimensional assessment of fatigue (MAF), sleep quality with Pittsburgh Sleep Quality Index (PSQI) and quality of life was assessed with Short Form 36 (SF-36). Neuropathic pain was determined by using pain-Detect questionnaire, a simple and reliable screening questionnaire. Scores ≤12 indicate that a neuropathic pain component is unlikely, and scores ≥19 indicate that neuropathic component is very likely to be present. Scores between 12 and 19 suggest that the result is unclear.

Results: The PainDetect score of the SpA patients, CLBP patients and healthy controls were 12.06±5.9, 13.8±7.5, 2.6±4.2, respectively. While there was no significant difference between the patients with SpA and CLBP (p=0.05), the SpA patients had significantly higher scores than the healthy controls (p<0.0001). 14 (17.5%) of the SpA patients, 14 (26.4%) of the CLBP patients and none of the healthy controls had PainDetect score ≥19 (p=0.05). The MAF score and all subscales of SF 36 all components were significantly different in the three groups (p<0.05).

There were also statistically significant differences between three groups for all subscales of PSQI except duration of sleep and need medications to sleep (p<0.05). PainDetect score was positively correlated with VAS rest, BASDAI, and BASFI in the patients with SpA. While PainDetect score was positively correlated with VAS rest (p<0.05). PainDetect score was positively correlated with VAS rest and activity, depression was identified as an independent negative predictor of improvement in work performance/productivity.

REFERENCES:

Disclosure of Interests: None declared

THU0373 ACTIVE SACROLILITIS ON MAGNETIC RESONANCE IMAGING IN PATIENTS WITH ANTERIOR UVEITIS

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Background: Anterior uveitis (AU) is a common extraarticular manifestation in spondyloarthritis (SpA). The disease can precede the typical axial and peripheral features. Additionally, some studies had described positive bone marrow edema (BME) in patients with AU lacking chronic back pain.

Objectives: The aim of this study was to examine patients with AU, to determine whether the patients already fulfill criteria for axial and/or peripheral SpA and compare the findings to healthy controls (HC).

Methods: We recruited 65 patients without prior rheumatologic diagnosis who developed at least one episode of AU and 33 age and sex matched HC. The clinical data were collected and rheumatology examinations were performed by trained rheumatologists. Magnetic resonance imaging (MRI) of sacroiliac joints (SIJ) was read by trained rheumatologist who was blinded to the patient’s data. Patients were divided into SpA subsets (axial: imaging and clinical arm and peripheral SpA) fulfilling The Assessment of SpondyloArthritis international Society (ASAS) classification criteria and non-SpA subset. The ASAS modified Berlin algorithm for diagnosis of axial SpA (axSpA) was also applied.

Results: Altogether, 72% (n=47) patients referred back pain including 22.0% (n=14) patients referring inflammatory back pain. 28% (n=18) did not refer back pain. Similar results were found in HC subset. Bone marrow edema (BME) was found in 51% (n=33) of all patients with AU, however 35% (n=23) had highly suggestive BME (hsBME) corresponding to typical findings in sacrolilitsis compared to HC where 30% (n=10) had BME, however none had hsBME (p=0.08, p< 0.0001, respectively). Furthermore, patients with AU had higher serum CRP levels compared to HC (p<0.001); no other significant differences were observed. The diagnosis of SpA was confirmed in 46% (n=29) of all patients with AU, 34% (n=22) patients fulfilled the imaging arm and 12% (n=7) fulfilled the clinical arm of ASAS classification criteria for axSpA. 3% (n=2) patients fulfilled ASAS classification criteria for peripheral SpA. Two patients lacking back pain developed hsBME on SIJ. The diagnosis of axSpA according to the ASAS modified Berlin algorithm was confirmed in 42% (n=27) patients. Analysis of clinical characteristics showed significant difference between baseline BASDAI in SpA vs. non-SpA (1.6±1.5 vs. 0.8±1.0, p=0.007 respectively), and remained significant in those fulfilling imaging arm of axial SpA (p=0.04). The levels of CRP were significantly higher in SpA compared to non-SpA subsets (8.6±9.7 vs 2.6±2.7 mg/L, p=0.003). Presence of back pain and inflammatory back pain were more often in SpA compared to non-SpA subsets (79% and 43% vs. 51% and 3%, p=0.001 and p<0.001 respectively). Patients with hsBME had significantly higher serum CRP levels compared to patients lacking hsBME (9.0±10.4 vs 3.3±4.2 mg/L, p=0.005) no other significant differences were observed.

REFERENCES:

Disclosure of Interests: None declared
Conclusion: More than one third of patients with AU fulfilled the criteria for axial or peripheral SpA. Furthermore, the prevalence of back pain, increased BASDAI and serum CRP levels was significantly higher in AU patients with SpA compared to non-SpA subjects and HC. Inflammatory back pain was significantly more often in patients with AU classified as axSpA. Patients with hsBMI had significantly higher serum CRP levels compared to the rest of the patients.

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Disclosure of Interests: Kristýna Bubová: None declared, Monika Gregorvá: None declared, Katerina Zegzulková: None declared, Karel Pavelka: None declared, Jarmila Heissigerová: None declared, Ladislav Šenolt Grant/ research support from: Abbvie, Consultant for: Abbvie, Bristol-Myers Squibb, Celgene Corporation, Merck Sharp and Dohme, Novartis, Pfizer, Roche, UCB, Agen, Takeda, Speakers bureau: Abbvie, Amgen, Bristol-Myers Squibb, Celgene Corporation, Eli Lilly, Merck Sharp and Dohme, Novartis, Pfizer, Roche, UCB


GENDER DIFFERENCE IN ASAS HEALTH INDEX IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: The Assessment of Spondyloarthriss international Society Health Index (ASAS HI) has been developed and validated to assess health and function in patients with spondyloarthritis. However, whether ASAS HI differs between men and women is unknown. The aim of this study was to compare ASAS HI between men ans women in patients with ankylosing spondylitis (AS).

Objectives: The aim of this study was to compare ASAS HI between men ans women in patients with ankylosing spondylitis (AS).

Methods: Since November 2016, we measured and recorded data of demography, comorbidity, family history, medication use, the Ankylosing Spondylitis Disease Activity Score (ASDAS), the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), the Bath Ankylosing Spondylitis Functional Index (BASFI), the modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) and the ASAS HI for AS patients in clinical prac-
tice using an electronic patient reported data system linked to an electronic medical record system in Taichung Veterans General hospital (TVCGH). We retrieved the last recorded data of AS patients in TVCGH during 2017/11–2018/10. We assessed the association between gender and the ASAS HI using a multivariable linear regression model. Variables from the univariable linear regression analysis with p < 0.2 were included in then multivariable analysis. We used a forward selection method to build the models.

Results: A total of 307 AS patients [62 (20.2%) females, mean age 46.4 years (S.D. 13.3), mean symptom duration 20.6 years (S.D. 12.1)] were included. Female patients had an older age at onset (29.2 ± 12.6 vs 24.9 ± 9.6 years, p = 0.015), a shorter symptom duration (15.7 ± 11.6 vs 21.8 ± 12.0 years, p < 0.001), a lower proportion of smoking (65.8% vs 48.2%, p < 0.001), higher ASAS HI (5.9 ± 3.8 vs 4.3 ± 3.4, p = 0.001), higher ASDAS-ESR (1.9 ± 0.8 vs 1.5 ± 0.8, p < 0.001) and lower mSASSS (6.0 ± 11.4 vs 21.8 ± 23.1, p < 0.001) than male patients. There were no significant differences in BASFI (1.1 ± 1.5 vs 1.6 ± 1.7, p = 0.26), ASDAS-CRP (1.5 ± 0.8 vs 1.5 ± 0.9, p = 0.972) and BASDAI (2.4 ± 1.8 vs 2.0 ± 1.4, p = 0.115) between females and males. In multivariable analysis, male gender was significantly associated with a better ASAS HI (β = -1.73, 95% CI: -2.55, -0.91, p < 0.001). Other significant predictors of ASAS HI included BASDAI (β = 1.29, 95% CI: 1.07, 1.50, p < 0.001), disease duration (β = 0.04, 95% CI: 0.01, 0.06, p = 0.015), mSASSS (β = 0.01, 95% CI: 0.00, 0.02, p = 0.003) and hepatitis B (β = 0.99, 95% CI: 0.03, 1.96, p = 0.044).

Conclusion: This single center, cross-sectional study revealed that male gender was significantly associated with lower ASAS HI in AS patients.

REFERENCE:

CLINICAL FEATURES OF AXIAL SpondyloarthritIS PATIENTS DiAGNOSED IN PERIPHERAL VERSUS AN ACADEMIC HOSPITAL

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Background: Diagnosis of axial spondyloarthritis (axSpA) often relies on a positive magnetic resonance image of the sacroiliac joints (MRI-SIJ). However, pitfalls in interpretation of MRI-SIJ were recently acknowledged (1). Thus reader’s expertise might be a source of heterogeneity in patient populations diagnosed with non-radiographic axSpA.

Objectives: We compared clinical characteristics of axSpA patients diagnosed in peripheral hospitals (MRI evaluation by local experts) versus an academic hospital (MRI central reading by trained radiologists and rheumatologists).

Methods: Patients originate from the Be-Giant cohort, a Belgian nation-
wide observational registry of axSpA patients diagnosed by expert opin-
ion. Included patients fulfilled the Assessment of SpondyloArthritis international Society (ASAS) classification criteria for axSpA and are anti-
tNF-κBp province to inclusion. Patient enrollment started in 2010 and 2012 at the outpatient clinic of 1 academic and 7 peripheral hospitals respectively. Patients were free to visit a rheumatologist of their choice without necessity for referral by a general practitioner.

Results: By January 2019, 291 axSpA patients were included. Table 1 presents demographic and clinical characteristics according to the diag-
nostic echelon. The patient fraction fulfilling the imaging arm of the ASAS classification criteria was similar in both settings (75.4% vs. 88.7%, p = 0.21). However, because of a higher HLA B27 positivity rate in patients diagnosed in an academic versus peripheral hospitals (73.5% vs. 57.4%, p = 0.01), a significantly higher fraction of patients fulfilled both the clinical and imaging arm in the former diagnostic setting (63.0% vs. 37.7%, p = 0.01).

Conclusion: Patients diagnosed with axSpA in peripheral versus an aca-
demic hospital generally show similar demographic and clinical charac-
teristics. In an academic center, patients diagnosed with axSpA are more likely to be HLA B27 positive and to fulfill both ASAS classification arms, suggesting that rheumatologists in peripheral hospitals seem to assign more value to MRI findings compared to HLA B27 status in the diagnost-
ic process.

REFERENCES:
Abstract THU0375 – Table 1

<table>
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<tr>
<th>Age at diagnosis (years)</th>
<th>Peripher al center (n = 61)</th>
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<td>Male gender</td>
<td>20 (32.8)</td>
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<td>HLA B27 positivity</td>
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<td>145 (60.0)</td>
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<td>Arthritis</td>
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<td>Psoriasis</td>
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<td>Inflammatory bowel disease</td>
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<td>Acute anterior uveitis</td>
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<td>BMI (kg/m²)</td>
<td>23.8 (3.86)</td>
<td>24.4 (4.02)</td>
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<td>BASMI</td>
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<td>BASDAI (/100)</td>
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<td>30 (22.5)</td>
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<tr>
<td>ASDAS – CRP</td>
<td>2.43 (0.85)</td>
<td>2.47 (0.93)</td>
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Continuous variables: mean (SD); other: counts(%) .

Disclosure of Interests: Ann-Sophie De Craemer: None declared, Thomas Renson: None declared, Philippe Carron: None declared, Peggy Jacques: None declared, Jan Lenaerts: None declared, Lieve Gyselbrecht: None declared, Rik Joos: None declared, Filip van den Bosch Consultant for: AbbVie, BMS, Galapagos, Janssen, Lilly, Merck, Novartis, Pfizer and UCB, Speakers bureau: AbbVie, BMS, Janssen, Lilly, Merck, Novartis, Pfizer and UCB, Dirk Eewout: None declared

THU0376

THE VALUE OF SACRILIC JOURNAL RADIOGRAPHS IN THE EARLY SPONDYLOARTHROPATHIES: RESULTS FROM THE ASAS-COMOSPA STUDY

Eugenio de Miguel1, Beatriz Joven-Ibáñez2, Eva Galindez3, Claudia Urrego-Laurín4, Maria Luz García-Vivar5, Cristina Fernández-Carballedo6, Jose Francisco Garcia Llorente7, Maria del Carmen Castro Villegas8, Carolina Torner9, Xavier Juanola-Roura10, Esperanza Working Group, La Paz University Hospital, Rheumatology, Madrid, Spain; 12 de Octubre University Hospital, Madrid, Spain; 2Basurto University Hospital, Rheumatology, Bilbao, Spain; 3Moncloa University Hospital, Madrid, Spain; 4San Juan University Hospital, Rheumatology, Alicante, Spain; 5Galdakao University Hospital, Rheumatology, Bilbao, Spain; 6Reina Sofia University Hospital, Rheumatology, Córdoba, Spain; 7Bellvitge University Hospital, Rheumatology, Barcelona, Spain

Background: X-Ray sacroiliitis is the cornerstone in the diagnosis of the ankylosing spondylitis (AS). It is clear that the presence of sacroiliitis is a specific lesion in long standing AS, but little evidence exists on the reliability of this image technique in early axial spondyloarthritides (axSpA), which associates with reduced structural damage. It is relevant because some rheumatologists and pharmaceutical authorities feel more confident with the diagnosis of AS rather than with non radiographic axial spondyloarthritides (nr-axSpA) forms. On the other hand, according to various research studies, clinicians are subject to potential bias when interpreting radiographs, influenced by their pretest clinical judgment.

Objectives: The aim of this study is to determine the value of X-Ray sacroilitis in the early diagnosis of axSpA.

Methods: This study included 290 radiographs of the SI joints from patients in the ASAS-COMOSPA cohort. Nine readers, blinded for the diagnosis, participated in the reliability exercise, all of them experienced rheumatologists and members of the Spanish spondyloarthritides working group (GRESSER). Patients with axSpA were classified as having AS if the radiographic criteria of the modified NY criteria (presence of radiographic changes in the SIJ of at least grade II bilaterally or at least grade III unilaterally) were fulfilled. The gold standard was the categorical opinion of at least five of the expert readers. For the statistical analysis, the Chi-square and Kappa tests were performed.

Results: The radiographic diagnosis, sensitivity, specificity, likelihood ratio, grade of agreement and mean K values compared to gold standard are shown in table 1. The concordance Kappa test was highly variable among the readers, ranging from fair to excellent. The agreement with the gold standard varied from 68 to 94% and the sensitivity and specificity, from 50-100% and 64-96%, respectively. Additionally, the number of AS was 61, with an inter-reader variability rate of 31 to 138. Larger discrepancies were observed when assessing sacroilitis grade 2.

Conclusion: The diagnosis of AS in early axSpA is characterized by a marked variability. At least in doubtful cases, a second central evaluation performed by highly qualified experts should be advisable.

Disclosure of Interests: Eugenio de Miguel: None declared, Beatriz Joven-Ibáñez: Speakers bureau: Celgene, Novartis, MSD, Pfizer, AbbVie, and Janssen, Eva Galindez: None declared, Claudia Urrego-Laurín: None declared, Maria Luz García-Vivar: None declared, Cristina Fernández-Carballedo: None declared, Jose Francisco Garcia Llorente: None declared, Maria del Carmen Castro Villegas Paid instructor for: MSD, Abbvie, Pfizer, Janssen, Lilly, Roche, Carolina Torner: None declared, Xavier Juanola-Roura: None declared

THU0377

THE CARDIOVASCULAR ASSOCIATIONS WITH ENTHESITIS AND DACTYLITIS IN PATIENTS WITH SPONDYLOARTHROPATHIES: RESULTS FROM THE ASAS-COMOSPA STUDY

Mohammad H. Derakhshan1, Nicola Goodson2, Jonathan Packham2, Raj Sengupta3, Anna Mollo4, Helena Marzo-Ortega5, Stefan Siebert6, On behalf of BRITSpA and the ASAS-COMOSPA investigators. 1University of Glasgow, Institute of Infection, Immunity and Inflammation, Glasgow, United Kingdom; 2University of Liverpool, Department of Rheumatology, Liverpool, United Kingdom; 3Keele University, Haywood Rheumatology Centre, Stoke on Trent, United Kingdom; 4Royal National Hospital for Rheumatic Diseases, Bath, United Kingdom; 5Hopital Cochin, Paris, France; 6University of Leeds, NIHR LBRC, Leeds, United Kingdom

Background: Enthesitis and dactylitis are considered characteristic inflammatory musculoskeletal manifestations of spondyloarthritides (SpA). These manifestations are usually assessed in the context of their assumed underlying specific condition rather than as distinct entities. Data from the ASAS-COMOSPA cohort have recently been shown that duration of SpA disease is associated with higher odds of hypertension particularly in axial SpA (1).

Objectives: To evaluate the possible associations of dactylitis and enthesitis phenotypes with cardiovascular comorbidities in a heterogeneous cohort of patients with SpA.

Methods: ASAS-COMOSPA is a global cross-sectional study assessing comorbidities in 3984 patients with SpA. History of enthesitis or dactylitis was based on self-report with confirmation using the medical records. Associations between dactylitis or enthesitis with hypertension, dyslipidemia, diabetes, ischemic heart diseases (IHD) and stroke were analysed by separate logistic regression models unadjusted, adjusted for age and sex (models 1), and adjusted for age, sex and BMI (model 2).

Results: The data of 3905 participants were available for analysis. There were 1480 (37.9%) with history of enthesitis and 611 (15.6%) with dactylitis, while 1814 (46.5%) had neither. Presence of dactylitis was associated with hypertension in the univariable analysis [OR=1.68; 95%CI: 1.39–2.03]. The association remained significant when adjusted for age and sex, but not following further adjustment for BMI (Table). Similarly, enthesitis was associated with hypertension in the univariable analysis [OR=1.36; 95%CI: 1.17-1.59], which remained after adjusted for age and sex, as well as after further adjustment for BMI (Table). Similar associations were seen for dyslipidemia and dactylitis [OR=1.60; 95%CI: 1.29–1.98] or enthesitis [OR=1.50; 95%CI: 1.26–1.77], with the association with dactylitis lost after further adjustment for BMI while the association with enthesitis remained significant (Table). While there were significant associations between dactylitis and diabetes [OR: 1.50 (95% CI: 1.07–2.11)], and between enthesitis and diabetes [OR=1.35; 95%CI: 1.02-1.78] in unadjusted models, no associations were
COEXISTENCE OF ANKYLOSING SPONDYLITIS AND DACTYLITIS

Both ankylosing spondylitis and rheumatoid arthritis are common entities. The coexistence of both diseases in the same person is not known exactly, however, with the data obtained, there seems to be a greater aggressiveness in the evolution, since most of them present an erosive radiological pattern, positivity for RF, involvement of the axial skeleton and presence of rheumatoid nodules in a frequency higher than that which occurs in patients with diagnosis isolated from either of the two entities.

REFERENCE:

Disclosure of Interests: Mohammad H. Derakhshan: None declared, Nicola Goodson Grant/research support from: Research support grant from Novartis, Speakers bureau: Paid speaker UCB, Jonathan Packham Consultant for: Educational speaker grant from Abbvie, Raj Sengupta Grant/research support from: Celgene, Novartis, Consultant for: Abbvie, Biogen, Celgene, Novartis, UCB, Speakers bureau: Abbvie, Biogen, Celgene, Novartis, UCB, Anna Moltõ: None declared, Helena Marzo-Ortega Grant/ research support from: Janssen, Novartis and Pfizer, Consultant for: Abbvie, Celgene, Janssen, Eli-Lilly, Novartis and UCB, Speakers bureau: Abbvie, Biogen, Celgene, Novartis, UCB, Anna Moltõ: None declared, Helena Marzo-Ortega Grant/ research support from: Janssen, Novartis and Pfizer, Consultant for: Abbvie, Biogen, Celgene, Janssen, Eli-Lilly, Novartis and UCB, Stefán Siebert Grant/research support from: AbbVie, Novartis, Pfizer, Janssen, BMS, Celgene, UCB, and Boehringer Ingelheim, Consultant for: Abbvie, UCB, Pfizer, Janssen, Boehringer Ingelheim, Celgene, and Novartis, Speakers bureau: Abbvie, UCB, Pfizer, Janssen, Boehringer Ingelheim, Celgene, and Novartis

Conclusion: In patients with SpA, both dactylitis and enthesitis are associated with higher risk of hypertension and dyslipidaemia. The loss of associations with dactylitis with adjustment for BMI could suggest a potential shared underlying metabolic mechanism.

REFERENCE:

Disclosures of Interests: Bryan-Josué Flores Robles, Valvanera Pinillos, Angel Elena-Ibáñez, Ezditen Labrador-Sánchez, Leticia Merino-Meléndez, Juan Antonio López-Martin, Enrique Ramalle-Gomara: None declared, Medrano San Pedro, Logroño, La Rioja, Spain

Disclosure of Interests: AbbVie, Celgene, Janssen, Eli-Lilly, Novartis and UCB, Pfizer, Consultant for: Abbvie, UCB, Pfizer, Janssen, Boehringer Ingelheim, Celgene, and Novartis, Branch: None declared, Angel Elena-Ibáñez: None declared, Ezditen Labrador-Sánchez: None declared, Leticia Merino-Meléndez: None declared, Juan Antonio López-Martin: None declared, Enrique Ramalle-Gomara: None declared


THU0378

COEXISTENCE OF ANKYLOSING SPONDYLITIS AND RHEUMATOID ARTHRITIS (ANALYSIS OF 73 CASES)

Bryan-Josué Flores Robles, Valvanera Pinillos, Angel Elena-Ibáñez, Ezditen Labrador-Sánchez, Leticia Merino-Meléndez, Juan Antonio López-Martín, Enrique Ramalle-Gomara

Hospital San Pedro, Logroño, La Rioja, Spain

Background: The coexistence of rheumatoid arthritis (RA) and ankylosing spondylitis (AS) in the same person is a rarely described phenomenon. Both ankylosing spondylitis and rheumatoid arthritis are common entities in the field of rheumatic diseases with a high impact on the patient’s quality of life and morbidity and mortality. The possibility of the coexistence of both diseases in the same person is not known exactly, however, with the data published to date, it is estimated that it ranges from 1 in 500,000 to 1 in 2,000,000.

Objectives: The epidemiological, clinical and study characteristics (radio-graphic/laboratory) of 73 patients with coexistent diagnosis of RA and AS are described. It includes 71 patients detected in the literature (32 articles) and 2 own cases

Methods: The platforms used for the search using the terms AR and AS (coexistence/concomitance/concurrency) were PubMed, Medline, Embase, Scopus, hospital virtual libraries, non-indexed journals and a secondary manual search. All the articles were taken into account, regardless of the language in which they were written, making the relevant translations (1 article in French, 1 article in Portuguese, 1 article in Spanish and the rest in English), and only those well documented cases were included.

Results: Of the total of registered cases, 55 patients were men (75.3%), with a mean age of 54 years, and a mean age of onset of the disease at 35.7 years (SD 14.0). Ankylosing spondylitis was the first of the two diseases diagnosed in 52.2% of cases (35/67). The mean duration of the disease (RA or AS) up to the time of diagnosis of both was 19 years. The first symptom of onset was low back pain in 50% of cases (34/68), followed by arthritis in 46% of cases (32/68), 56% of patients (36/64) had nodules rheumatoid and 85% of patients had presented low back pain at some point of their assessment. In 15% of the patients (11/73) the presence of uveitis was documented (in some old articles the term of iritis was limited), in 22% of cases there was extra-articular involve-ment (16/73), being the most frequent was the presence of Felty syndrome with 4 cases. (table 1)

Regarding the findings in the imaging studies, up to 78% of the patients had syndesmophytes in the spine (either in plain radiography). 88% (62/70) presented erosions in the X-rays of the hands and/or feet. The Radiological sacroiliitis was present in almost all patients 72/73, RA was positive in 90%, in 9 of the 11 patients in whom anti-CCP was performed were positive, and, in addition, almost 90% of the cases were HLA B-27 positive

Conclusion: The coexistence of AR and SpA is highly uncommon. With the data obtained, there seems to be a greater aggressiveness in the evolution, since most of them present an erosive radiological pattern, positivity for RF, involvement of the axial skeleton and presence of rheumatoid nodules in a frequency higher than that which occurs in patients with diagnosis isolated from either of the two entities.

REFERENCE:

Disclosure of Interests: Bryan-Josué Flores Robles Grant/research support from: Transport and hotel, Valvanera Pinillos: None declared, Angel Elena-Ibáñez: None declared, Ezditen Labrador-Sánchez: None declared, Leticia Merino-Meléndez: None declared, Juan Antonio López-Martin: None declared, Enrique Ramalle-Gomara: None declared


THU0379

DEPRESSIVE SYMPTOMS AND FUNCTIONAL IMPAIRMENT ARE FREQUENT AND AFFECT QUALITY OF LIFE IN ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS: A QUESTIONNAIRE-BASED ASSESSMENT OF 300 PATIENTS COMPARED WITH 150 PATIENTS WITH PSORIASIS AND 150 PATIENTS WITH MECHANICAL BACK PAIN

Natalie Friede1, Sonja Hiestand1, Franziska Schauer2, Christoph Schempf2, Georg Herget2, Dominique Endres3, Ludger Tebartz van Elst4, Reinhard Völ3, Jens Thiel1, Nils Venhoff1, 1Medical Center – University of Freiburg, Faculty of Medicine, University of Freiburg, Department of Rheumatology and Clinical Immunology, Freiburg im Breisgau, Germany; 2Medical Center – University of Freiburg, Faculty of Medicine, University of Freiburg, Department of Dermatology, Freiburg im Breisgau, Germany; 3Medical Center – University of Freiburg, Faculty of Medicine, University of Freiburg, Faculty of Medicine, University of Freiburg, Department of Orthopedic and Trauma Surgery, Freiburg im Breisgau, Germany; 4Medical Center – University of Freiburg, Faculty of Medicine, University of Freiburg, Section for Experimental Neuropsychiatry, Department of Psychiatry and Psychotherapy, Freiburg im Breisgau, Germany

Background: Axial ankylosing spondylitis (axSpA) and psoriatic arthritis (PsA) constitute chronic inflammatory conditions affecting the axial skeleton as well as peripheral joints. Insufficient treatment may lead to joint destruction associated with a high rate of disability. Extra-articular manifestations contribute to morbidity and a reduced quality of life.

Abbreviations: DT= Typical deviation
Furthermore, both, axSpA and PsA have been associated with an increased risk of depression.

Objectives: The aim of this project was to assess quality of life, functional impairment in everyday life as well as the prevalence of depression in axSpA and PsA and determine associated factors.

Methods: A questionnaire-based screening tool (FBBH, WHOQOL-BREF, Phq9, GHQ-12) was used to assess 150 patients with PsA and 150 patients with axSpA as well as 300 controls (150 with skin psoriasis only and 150 mechanical back pain patients) for quality of life, functional impairment as well as signs of depression.

Results: Both, SpA and PsA patients had a significantly reduced health-related quality of life compared to published normal values as well as psoriasis only patients (p<0.0003). Pain and functional impairment in everyday life correlated highly with perceived overall quality of life (r=0.8). Both, physical health as well as psychological health in turn highly correlated with the presence of depressive symptoms. In total, 35.4% of SpA and 41.2% of PsA patients had mild signs of depression, whereas 25% respectively 28.4% of SpA and PsA had patients moderate to severe signs of depression. Patients with active disease (BASDAS4) at the time of evaluation showed significantly more frequent depressive symptoms compared to patients with no or low disease activity (p<0.0001). Female patients had a significantly reduced physical and psychological health-related quality of life compared to male patients (p=0.0190). In our cohort, also age correlated with perceived quality of life. SpA and PsA patients <45 years of age reported a significantly higher perceived overall quality of life compared to patients >45 years (p=0.0001). Quality of life regarding physical health, mental health as well as social relationships was significantly better in younger patients (p=0.0014, p=0.0109, p=0.0196 respectively). However, this did not translate into a reduced rate of depressive symptoms in young patients. Body mass index (BMI) was associated with reduced health-related quality of life and psychological wellbeing, but did not correlate with depression. Smoking was neither associated with quality of life nor depression.

Conclusion: Despite treatment many SpA and PsA patients suffer from a reduced quality of life. Depression constitutes an important comorbidity, which needs to be addressed. Adequate therapy is not only important to reduce irreversible joint damage and disability but may also have a role in avoiding comorbidities such as depression.

Disclosure of Interests: None declared


THU0380 LUMBOPELVIC RHYTHM IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS COMPARED WITH LOW BACK PAIN AND HEALTHY SUBJECTS

Juan L. Garrido-Castro1, Inmaculada Concepcion Aranda-Valera1, Sandra Alcaraz-Ciurana1, Luzdary Garcia-Luque2, Diana Rodriguez-de-Souza2, Cristina Gonzalez-Nava3, Francisco Alburquerque-Sendin3, Philip Gardiner3, Eduardo Collantes Estevez1, 1IMIBIC, Cordoba, Spain; 2University of Cordoba, Cordoba, Spain; 3WHSCF, Londonerney, United Kingdom

Background: Lumbar back pain reduces spinal mobility in patients. Although there are some symptoms that characterise ‘back pain’, these are non-specific and the diagnosis is often delayed. It is not clear if there are kinematic differences between axial Spondyloarthritis (axSpA) and other types of back pain. Inertial motion sensors are now available that can accurately and reliably measure spinal mobility. The ViMove system uses two inertial sensors located at L1 and S1 allowing spinal flexion to be separated into its lumbar and pelvic components. The relation between different parts of the spine during a full flexion movement is known as lumbopevic rhythm. The trunk sensor measures the total flexion, whilst the contribution of hip is measured by the pelvic sensor leaving lumbar flexion as the difference between the two angles.

Objectives: To analyse relation of lumbopevic angles in axSpA patients, LBP patients and healthy controls.

Methods: 92 subjects were included in our study: 56 axSpA (from the COSPAR cohort of the Reina Sofia University Hospital), 14 LBP and 22 healthy controls. Inertial based system, the ViMove, was used to measure mobility. axSpA patients were stratified in three groups according their overall mobility using the BASMI: axSpA Low (< 2), Med (2-4) and High (>4).

Results: Table shows the results of spinal mobility tests in each group. The trunk, pelvis and lumbar angles are expressed in degrees (Mean and SD). cPelvis is the contribution of pelvis to the overall movement as percentage. Three of the five measurements in BASMI are outside the lower back so unlikely to be affected in LBP patients.

<table>
<thead>
<tr>
<th>n</th>
<th>Trunk</th>
<th>Pelvis</th>
<th>Lumbar</th>
<th>cPelvis</th>
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<tr>
<td>Control</td>
<td>22</td>
<td>114.8</td>
<td>56.7</td>
<td>58.0 (9.6)</td>
<td>48.7% (9.5%)</td>
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<tr>
<td>axSpA</td>
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<td>103.7</td>
<td>56.0</td>
<td>47.7</td>
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<td>LBP</td>
<td>14</td>
<td>101.3</td>
<td>52.8</td>
<td>48.5</td>
<td>52.0%</td>
</tr>
<tr>
<td>axSpA Low</td>
<td>21</td>
<td>111.3</td>
<td>54.2</td>
<td>57.0 (9.2)</td>
<td>48.5% (6.6%)</td>
</tr>
<tr>
<td>axSpA Med</td>
<td>22</td>
<td>105.9</td>
<td>56.2</td>
<td>49.6</td>
<td>52.0%</td>
</tr>
<tr>
<td>axSpA High</td>
<td>13</td>
<td>87.8 (19.4)</td>
<td>58.3</td>
<td>29.4</td>
<td>68.5%</td>
</tr>
<tr>
<td>LBP</td>
<td>14</td>
<td>101.3</td>
<td>52.8</td>
<td>48.5</td>
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<td>58.3</td>
<td>29.4</td>
<td>68.5%</td>
</tr>
</tbody>
</table>

There were significantly differences in the trunk, lumbar and pelvis angles between control and axSpA patients (p<0.01). The only significant difference between LBP and axSpA was in the lumbar angles (p<0.05).

Conclusion: A reduction in spinal flexion was found in all patient groups, but there are interesting differences in the pattern of movement. LBP patients were characterised by a greater reduction in pelvic movement compared to the axSpA patients, although the final trunk flexion angle is actually lower in axSpA. When we compared more and less affected axSpA patients (according to BASMI), the most severely affected had severe restriction in lumbar movement whilst pelvic movement was increased. Lumbo-pelvic rhythm can also be analysed throughout early, middle and the end of the movement. Investigating spinal kinematics could help us to understand better axSpA and how it affects spinal mobility.

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Disclosure of Interests: None declared

THU0381  PATIENT-REPORTED IMPACT OF AXIAL SPONDYLOARTHRITIS ON WORKING LIFE: RESULTS FROM THE EMAS SURVEY

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Background: Axial spondyloarthritis (axSpA) impacts multiple dimensions of patients’ lives, including working life.

Objectives: To evaluate work-related issues, their associations and determinants among European axSpA patients.

Methods: The European Map of Axial Spondyloarthritis (EMAS), conducted from July 2017 to February 2018, was a cross-sectional on-line survey of unscreened patients with self-reported axSpA from Austria, Belgium, France, Germany, Italy, Netherlands, Norway, Russia, Slovenia, Spain, Sweden, Switzerland, and the UK. Participants were recruited through an on-line panel and patient organizations. Participants were classified as active (employed, unemployed between 15-64 years) or inactive (retirees, on sick leave, students and homemakers). Those employed were asked to report work-related issues (sick-leave, difficulty fulfilling work hours, missing work for doctors’ appointments, reducing working hours or taking days off) in the past 12 months. Disease activity (BASDAI), self-reported spinal stiffness, diagnostic delay and psychological distress (General Health Questionnaire, GHQ-12) were compared between employed patients with or without work-related issues using a Mann-Whitney and Kruskal-Wallis test. Two-stage regression analysis was conducted to determine explicative sociodemographic (using stepwise method for income, age, gender, education) and disease-related factors (enter method for BASDAI, self-reported spinal stiffness, functional limitation) over work-related issues.

Results: 2846 axSpA patients participated in EMAS: mean age was 44 ±12 years. 61.3% were female and 48.1% were university educated. Mean disease duration and diagnostic delay were 17.2±12.4 and 7.4±8.4 years, respectively, and mean BASDAI was 5.5±2.0. 61.3% (n=1653) were considered active, of which 87.7% (n=1450) were employed. Of those employed, 67.7% reported a work-related issue, specifically 56.3% took sick leave, 44.6% had difficulties in fulfilling the working hours, 34.6% missed work due to doctor’s appointments, 31.6% requested days off, and 25.7% reduced their number of working hours (Table 1). Among all patients, 74.1% faced or believed they would face difficulties finding a job due to axSpA. Experiencing work-related issues due to axSpA was significantly associated with higher disease activity, self-reported spinal stiffness, longer diagnostic delay, and higher level of psychological distress (p<0.001). First regression step showed gender and educational level as explanatory sociodemographic control factors, while educational level and BASDAI were the only statistically significant explanatory factors in the second step (p<0.001) (Table 2).

Abstract THU0381 – Table 1.

<table>
<thead>
<tr>
<th>Work-related issues (mean ± SD)</th>
<th>No work-related issues (mean ± SD)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>41.8 ± 9.7</td>
<td>42.3 ± 10.4</td>
</tr>
<tr>
<td>Gender (Male)</td>
<td>37.3%</td>
<td>47.9%</td>
</tr>
<tr>
<td>Education level (University)</td>
<td>62.7%</td>
<td>56.0%</td>
</tr>
<tr>
<td>Marital status (Married)</td>
<td>67.3%</td>
<td>69.3%</td>
</tr>
<tr>
<td>BASDAI (0-10)</td>
<td>5.4 ± 1.8</td>
<td>4.0 ± 2.0</td>
</tr>
<tr>
<td>BASDAI (≥11)</td>
<td>79.0%</td>
<td>50.2%</td>
</tr>
<tr>
<td>Stiffness index (0-12)</td>
<td>7.5 ± 2.4</td>
<td>6.3 ± 2.5</td>
</tr>
<tr>
<td>GHQ-12 (0-12)</td>
<td>5.1 ± 4.0</td>
<td>2.0 ± 3.2</td>
</tr>
<tr>
<td>GHQ-12 (≥13)</td>
<td>68.8%</td>
<td>34.1%</td>
</tr>
<tr>
<td>Depression, 1-36</td>
<td>26.1%</td>
<td>31.1%</td>
</tr>
<tr>
<td>Anxiety, 1-36</td>
<td>32.2%</td>
<td>16.1%</td>
</tr>
</tbody>
</table>

Abstract THU0381 – Table 2.

<table>
<thead>
<tr>
<th>Sip of change in first step</th>
<th>Second stage Coefficients</th>
<th>Sip of coefficients</th>
<th>Goodness of fit statistics</th>
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</thead>
<tbody>
<tr>
<td>Income</td>
<td></td>
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</tr>
<tr>
<td>Gender</td>
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<tr>
<td>Education level</td>
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<tr>
<td>Stiffness index</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BASDAI</td>
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</tbody>
</table>

Conclusion: Nearly two-thirds of employed patients experienced work-related issues due to axSpA. The strongest factor associated with work-related issues was high disease activity. Understanding the determinants of work-related issues is needed to ensure that patients have adequate workplace and holistic medical support to lead productive work-lives.

Acknowledgement: EMAS was funded by Novartis Pharma AG

Disclosure of Interests: Marco Garrido-Cumbra Consultant for: Honoraria from Novartis as steering committee of this survey, Laure Gossec Grant/research support from: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis-Sandoz, Pfizer, Sanofi, and UCB, Consultant for: AbbVie, Biogen, BMS, Celgene, Janssen, Lilly, MSD, Nordic Pharma, Novartis-Sandoz, Pfizer, Roche, Sanofi, and UCB, Consultant for: L Gossec has received honoraria from Celgene as investigator for this study, Victoria Navarro-Compán: None declared, David Gálvez-Ruiz Consultant for: Honoraria from Novartis as steering committee of this survey, Christine Bundy Consultant for: Honoraria from Novartis as steering committee of this survey, Raj Mahapatra Consultant for: Honoraria from Novartis as steering committee of this survey, Souzi Makri: None declared, Sergio Sanz-Gómez: None declared, Carlos Delgado Domínguez Consultant for: Honoraria from Novartis as steering committee of this survey, Denis Poddubny Grant/research support from: AbbVie, Merck Sharp & Dohme, Novartis, Consultant for: AbbVie, Bristol-Myers Squibb, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, UCB Pharma, Speakers bureau: AbbVie, Bristol-Myers Squibb, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, Roche, UCB Pharma.


THU0382  FACTORS ASSOCIATED WITH POOR WORK OUTCOMES IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS IN SINGAPORE

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Background: Axial spondyloarthritis (axSpA) can lead to significant limitation of mobility and function, resulting in poor work outcomes.1 Factors associated with poor work outcomes have not been identified in an Asian population. Singapore is an urban Asian city with a low unemployment rate and a healthcare model with heavy emphasis on self-reliance.2 This socio-cultural context may influence risk factors for poor work outcomes.

Objectives: To identify factors associated with poor work outcomes in patients with axSpA in Singapore.

Methods: A cross-sectional study was performed in two tertiary centres in Singapore. Patients ≥21 years fulfilling Assessment in Spondyloarthritis International Society (ASAS) 2009 criteria for axSpA were included. We collected sociodemographic, clinical data, treatment modalities and patient reported outcomes, including the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), EQ-5D index, and Work Productivity and Activity Impairment scale (WPAI:SpA). WPAI:SpA was used to derive scores for presenteeism (reduced productivity while at work), absenteeism (time absent from work), work impairment (combining presenteeism and absenteeism scores) and activity impairment (impairment in activities performed outside of work). Univariable and multivariable linear regressions were used to

*Fig 2a* and Mann-Whitney to indicate if there is an association between the variables.
examine factors associated with presenteeism, absenteeism, work impairment and activity impairment.

Results: A total of 156 patients with axSpA were included: 72.4% employed, 80.1% male, 86.5% Chinese, mean age 39.2 (13.0) years, mean disease duration 8.5 (8.9) years. The mean BASDAI was 3.2 (2.0), mean BASFI was 2.1 (2.1), mean EQ-SQD was 0.8 (0.1) and mean activity impairment was 28.2%. Among employed patients, mean absenteeism was 4.5%, mean presenteeism was 24.9% and mean work impairment was 27.6%. In multivariable analysis, absenteeism was associated with disease duration (ß: -0.44; 95% CI: -0.80, -0.07;p=0.02) and EQ-SQD (ß: -46.28; 95% CI: -89.63, -2.92; p=0.04). Presenteeism was associated with BASDAI:4 (ß: 8.23; 95% CI: 0.24, 16.22; p=0.04), BASFI (ß: 3.59; 95% CI: 1.25, 5.92; p<0.01) and EQ-SQD (ß: -64.40; 95% CI: -115.79, -13.02; p=0.02). Work impairment was associated with BASFI (ß: 3.57; 95% CI: 0.04; 6.84; p=0.04), EQ-5D (ß: -88.00; 95% CI: -150.87, -25.13; p<0.01). Activity impairment was associated with age (ß: -0.21; 95% CI: -0.41, -0.01; p=0.04), BASDAI:4 (ß: 19.94; 95% CI: 13.79, 26.09; p<0.01), BASFI (ß: 3.29; 95% CI: 1.63, 4.95; p<0.01), EQ-SQD (ß: -82.28; 95% CI: -125.15, -39.41; p<0.01).

Conclusion: Factors such as active disease, reduced physical function and poorer quality of life are associated with reduced work outcomes in patients with axSpA in Singapore. These factors need to be addressed to improve work outcomes.

REFERENCES:


THU0383 PREVALENCE OF SPONDYLOARTHRITIS IN FIRST DEGREE RELATIVES OF PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Ankylosing spondylitis (AS) is a common rheumatic disease with higher prevalence in relatives of patients already diagnosed with the disease. HLA-B27 positivity in twins is estimated to 90%.

Objectives: The aim of this study was to examine first degree relatives (FDR) of AS patients, to determine whether the patients already fulfill criteria for axial and/or peripheral spondyloarthritis (SpA) and compare the findings to healthy controls (HC).

Methods: We recruited 32 patients without prior rheumatologic diagnosis with first degree relative treated for AS and 20 age and sex matched HC. The clinical data were collected and rheumatology examinations were performed by trained rheumatologists. Magnetic resonance imaging (MRI) of sacroiliac joints (SIJ) was read by trained rheumatologist who was blinded to the patient’s data. Patients were further divided into the subsets of axial SpA (imaging and clinical arm) and peripheral SpA fulfilling the Assessment of SpondyloArthritis international Society (ASAS) classification criteria for axial and/or peripheral SpA.

Results: Altogether, 78% (n=25) FDR referred back pain, 34% (n=11) referred inflammatory back pain (IBP), and 22% (n=7) did not refer back pain, which was significantly different from that in HC (65% referred back pain, 0% referred IBP, 35% referred no back pain, p=0.0038 and p=0.03, respectively). Bone marrow edema (BME) was found in 50% (n=16) of FDR, and 22% (n=7) had highly suggestive BME (hsBME) corresponding to typical findings of active sacroiliitis compared to HC where 10% (n=2) had BME, and none had hsBME (p=0.063, p=0.035, respectively). Furthermore, FDR had higher BASDAI and higher prevalence of HLA-B27 positivity compared to HC (2.0 (±1.5) and 75% vs. 0.4 (±0.6) and 5%, p= 0.001 and p= 0.001, respectively). No other significant differences were observed. The diagnosis of SpA was confirmed in 37% (n=12) of all FDR, 25% (n=8) patients fulfilled the imaging arm and 6% (n=2) fulfilled the clinical arm of ASAS classification criteria for axSpA, 6% (n=2) patients fulfilled ASAS classification criteria for peripheral SpA. The diagnosis of axSpA according to the ASAS modified Berlin algorithm was confirmed in 41% (n=13) patients. Analysis of clinical characteristics showed significant difference between serum CRP levels in SpA vs. non-SpA (8.2 (±12.5) vs. 2.3 (±4.4), p=0.02, respectively) and HLA-B27 positivity (100% vs. 60%, p=0.01, respectively). Presence of back pain and inflammatory back pain were more often in SpA compared to non-SpA subsets (100% and 67% vs. 65% and 15%, p=0.03 and p=0.06, respectively).

Conclusion: More than one third of first degree relatives of patients with AS fulfilled the criteria for axial or peripheral SpA, and had significantly higher prevalence of inflammatory back pain and increased BASDAI compared to HC. Based on these data, screening of family members of patients with AS should be recommended.

REFERENCES:

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THU0384 IMAGING OF SACRIOILIAC JOINTS IN EARLY SPONDYLOARTHRITIS: SHOULD WE CHOOSE COMPUTED TOMOGRAPHY OR MAGNETIC RESONANCE IMAGING?

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Background: In view of the limited utility of pelvic radiography to recognize sacroiliitis in its earliest stages, magnetic resonance imaging (MRI) has been considered as a reliable imaging modality to detect acute subchondral inflammation at disease onset. However, several recent studies reported a high proportion of false-positive of sacroiliac joints (SIJ) MRI. Other studies demonstrated that computed tomography (CT), by its ability to detect early structural damage, may be helpful. Consequently, strengths and limitations of each imaging technique need to be considered when choosing the most appropriate first-line modality in clinical practice.

Objectives: We aimed to assess the performance of CT scanning and MRI for detecting sacroiliitis in early SpA by estimating the sensitivity and specificity of each imaging technique.

Methods: Consecutive patients, aged 16 years and over, referred for symptoms suggestive of SpA from February 2014 to February 2017 were enrolled in this cohort. After excluding patients whose conventional radiography showed a confirmed sacroiliitis, eligible patients underwent SI CT and/or MRI. The CT and MR images were reviewed by 2 musculoskeletal radiologists blinded to clinical findings. Then, 2 rheumatologists recorded from the clinical files if patients fulfilled the ASAS (Assessment of SpondyloArthritis international Society) classification criteria for SpA. This classification was considered as the gold standard of this study.

Results: Fifty-three patients were included: 14 men and 39 women. The mean age was 36 years. The prevalences of HLA-B27 and elevated C-reactive protein (CRP) levels were 37.4% and 16.3%, respectively. Fifty-eight percent of the patients (n=31) fulfilled the ASAS criteria for axial SpA. Among these patients, 30 patients underwent SI CT and 27 underwent SI MRI. Sacroiliitis was visualized by CT in 28 out of 30 patients (93.3%) and by MRI in 17 out of 27 patients (63%). Among the 22 patients who did not
fulfill the ASAS criteria for SpA, 21 patients underwent SU CT and 20 underwent SU MRI. Sacroiliitis was not visualized by CT in any patients and was visualized by MRI in 2 out of 20 patients (10%). Sensitivity, specificity, positive and negative likelihood ratio of CT calculated with ASAS classification as golden standard were respectively estimated at 93.3%, 100%, 90% and 91.3%. Youden index was estimated at 0.93 and Q Yule coefficient at 1. Sensitivity, specificity, positive and negative likelihood ratio of MRI calculated with ASAS classification as golden standard were respectively estimated at 62.9%, 90%, 89.5% and 64.3%. Youden index was estimated at 0.53 and Q Yule coefficient at 0.88.

Conclusion: In our study, the evaluation of sacroiliitis by CT, in comparison with MRI, has shown to be more sensitive and more specific. However, other factors should also be taken into account while comparing CT and MRI such as the high radiation exposure of CT scanning in the one hand and the cost and the restricted accessibility of MRI in the other hand.

Disclosure of Interests: None declared


**COMPARISON OF CLINICAL AND DEMOGRAPHIC FEATURES OF JUVENILE SPONDYLOARTHRITIS BETWEEN ISRAELI AND US CHILDREN**

Merav Heshin-Bekenstein1, Naseem Ghantous2, Irir Tiross3, Yonatan Butbul2, Liora Harel2, Yaniv Lakovsky2, Pamela Weiss4, Nadav Rappoport3, Kimberly Dequatro2, Emily von Scheven1, Lianne S. Gensler1, Amir Hendel2, John MacKenzie1, Gil Amaramy2, 1University of California San Francisco, San Francisco, United States of America; 2Tel Aviv University, Tel Aviv, Israel, 3Rambam Medical Center, Haifa, Israel, 4Children’s Hospital of Philadelphia, Pennsylvania, United States of America

**Background:** Clinical observations among Israeli pediatric rheumatologists reveal that some of the clinical and demographic features of Israeli children diagnosed with Juvenile Spondyloarthritis (JSpA) are different as compared to the typical characteristics described in US studies.

**Objectives:** In this study, we compared clinical, laboratory and radiographic features to determine whether differences occur between the two populations of JSpA.

**Methods:** We performed a retrospective, cross-sectional, multicenter comparison of JSpA patients from 3 large Israeli pediatric rheumatology centers and a large US pediatric rheumatology center. Patients with a diagnosis of Juvenile Ankylosing Spondylitis (JAS) and/or Enthesitis-related Arthritis (ERA) were included. The demographic, clinical and imaging features of the subjects upon presentation were compared, including MRI of the sacroiliac joints. Inter Center Comparison (ICC) between the Israeli and US musculoskeletal radiologists was conducted.

**Results:** Overall 87 patients met the inclusion criteria (39 Israeli, 48 US). As compared to the US population, the Israeli population was less likely to be male (56% vs. 75%, p<0.11), and more likely to be older at time of diagnosis (14.3 vs. 11.9 years, p<0.001). Upon presentation, axial symptoms (inflammatory back pain) and physical examination findings consistent with sacroiliitis (SU tenderness, modified Schober test), were significantly more prevalent among Israeli patients (59% vs. 35.4%, 48.7% vs. 16.7%, and 41.2% vs. 21.5%, respectively, all p<0.05), whereas peripheral arthritis and enthesitis were significantly more prevalent among the US patients (43.6% vs. 91.7% and 7.7% vs. 39.6% in Israeli patients vs. US patients, p<0.05). For HLA-B27, 32% of the Israeli patients vs. 66.7% of the US patients were positive (p<0.007). In addition, of those who had imaging (N=30 and N=37 for Israeli and US cohorts) 96.7% of the Israeli patients versus 29.7% of the US patients demonstrated positive MRI findings that were consistent with sacroiliitis (p=0.005, overall N=67). An excellent level of agreement was observed between the Israeli and US musculoskeletal radiologists (kappa=0.9).

**Conclusion:** We found important distinctions between two populations with JSpA. Israeli children were more likely to present with axial disease, less likely to demonstrate HLA B27 carrier positivity, and more likely to demonstrate sacroiliitis on MRI than US children, who more commonly presented with peripheral arthritis and enthesitis, HLA-B27 positivity and negative MRI findings. These unique findings of the Israeli JSpA population, also as compared to descriptions of JSpA patients in the medical literature, point to environmental and/or cultural factors that merit additional studies in order to unravel the differences in disease presentation between the two countries.

**COMPARISON OF CLINICAL AND DEMOGRAPHIC FEATURES OF JUVENILE SPONDYLOARTHRITIS BETWEEN ISRAELI AND US CHILDREN**

Merav Heshin-Bekenstein1, Naseem Ghantous2, Irir Tiross3, Yonatan Butbul2, Liora Harel2, Yaniv Lakovsky2, Pamela Weiss4, Nadav Rappoport3, Kimberly Dequatro2, Emily von Scheven1, Lianne S. Gensler1, Amir Hendel2, John MacKenzie1, Gil Amaramy2, 1University of California San Francisco, San Francisco, United States of America; 2Tel Aviv University, Tel Aviv, Israel, 3Rambam Medical Center, Haifa, Israel, 4Children’s Hospital of Philadelphia, Pennsylvania, United States of America

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**CHILEAN AXIAL SPONDYLOARTHRITIS PATIENTSREPORT HIGH DISEASE BURDEN AND IMPAIRED WORK ACTIVITY – AN INTERNET SURVEY IN 472 PATIENTS**

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**Background:** Axial spondyloarthritis (axSpA) can be associated with significant burden and impaired work activity. In Chile, several barriers impede adequate treatment, such as insufficient access to specialists and biological treatment. Furthermore, there is an important lack of insight into the local situation. This hampers the development of adequate national treatment standards and financial support.

**Objectives:** 1. To evaluate the disease burden, quality of life and work participation in Chilean axSpA patients. 2. To assess gender differences in disease burden and 3) compare patients with and without biologics.

**Methods:** A cross sectional online survey among Chilean SpA patients, recruiting via the internet website and associated social media of the Chilean SpA Patient Foundation (“Espondilitis Chile”). The survey was written in Spanish and requested information, mostly via multiple choice options, on gender, age, disease characteristics (diagnosis, disease duration, treatment), disease burden (BASDAI and BASFI), quality of life (ASAS Health Index) and work participation (WPAI). Only axSpA patients were included for further analyses. The association between BASDAI, quality of life or work participation (presenteeism, absenteeism) and subgroups (gender, biologics) was assessed through univariable regression and subsequently multivariable regression analyses, correcting for age, disease duration and concomitant treatment (NSAIDs, DMARDs, opiates).

**Results:** Between July and October 2018, 625 patients completed the website survey, of whom 472 reported a diagnosis with axSpA (91% radiographic axSpA, 37% male, mean age 42 years, 83% BASDAI>4, table 1). Twenty percent used a biological and patients with biologics were more likely to have a paid job (p<0.01) and had significantly lower BASDAI, BASFI, ASAS HI and risk of absenteeism. In multivariable analyses, biologics remained significantly associated with a lower BASDAI.

**Conclusion:** The results of the web survey demonstrate a high level of disease burden and work impairment in Chilean axSpA patients. The use of biologics is low, although its use is independently associated with having a lower disease activity. Women used significantly less biologics despite reporting a worse disease state (BASDAI, ASAS HI) and greater work disability, suggesting inequality in access to treatment.
Enteropathic arthritis patients under biMDrm treatments had frequently radiographic sacroilitis: Hur-Bio real-life results

Gözde Kübra Yardımcı, Bayram Farişoğlu, Alper San, Levent Kılıç, Berkan Amagan, Emre Bilgin, Ertuğrul Çağrı Bölek, Ömer Karadag, Ali Akdoğan, Süleyman Bilgen, Sedat Kiraz, Ali İhsan Erenteli, Umut Kalyoncu, Hacettepe University Medical School Internal Medicine, Rheumatology, Ankara, Turkey

Background: Enteropathic spondylarthritis (eSpA) is one of the diseases in the Spondyloarthritis (SpA) spectrum and occurs in patients with inflammatory bowel disease (IBD). Sacroilitis is frequently found in patients with IBD and can be over-looked because of focusing on IBD.

Objectives: Aim of this study is to evaluate the general features of eSpA and compare with psoriatic spondylitis (PsA), and ankylosing spondylitis (AS).

Methods: Hur-Bio (Hacettepe University Rheumatology Biologic Registry) is a prospective, single-center database of biological treatments since 2005. eSpA patients were enrolled from Hur-Bio registry. Sacroilitis was defined as modified New York criteria or based on ASAS magnetic resonance imaging criteria. Age and disease duration matched 128 ankylosing spondylitis and 96 psoriatic spondylitis patients were selected as a control group from Hur-Bio database. Demographic, clinical, laboratory, therapeuetic data and imaging features were collected from this database: age, gender, age at disease onset, disease duration, type of IBD, Baseline disease activity before the first biologic therapy use was assessed with BASDAI, BASFI, VAS-patient global assessment, ESR and CRP.

Results: Hur-Bio Bio registry included 2576 SpA patients, and 90 (3.5%) patients had enteropathic arthritis (EA). Sixty four of 90 (71.1%) patients had sacroilitis according to modified NY criteria, and these patients were included in the study. Of the 64 patients with eSpA, IBD type was ulcerative colitis (UC) in 34 (53%) patients, Crohn’s disease (CD) in 30 (47%) patients. For eSpA patients, initial biological DMARDs were infliximab in 26 (40.6%), adalimumab in 23 (35.9%), etanercept in 10 (15.6%), golimumab in 4 (6.3%), and certolizumab in 1 patient (1.6%). The proportion of bDMARDs were similar with control group. Baseline disease activity were similar between eSpA and control group. However, baseline ESR levels were higher in eSpA than AS (p=0.037) and psoriatic spondylitis (p=0.001), as well. Baseline demographic and clinical features were summarized in Table 1.

Conclusion: Enteropathic spondylarthritis was present only a small part of all SpA patients. Sex, SpA family history, and uveitis were different from other SpA subgroups. Disease activities were similar with other spondylarthritis, but particularly ESR level was higher in eSpA probably due to bowel disease activity. Sacroilic and spine involvement seems to be the main reason for starting biDMARD in IBD patients, rather than peripheral arthritis.

Data were given as mean (standard deviation) or median (min-max)

HLA-B27 were assessed in 27 eSpA, 52 AS and 33 PSA patients.

Disclosure of Interests: Gözde Kübra Yardımcı: None declared, Bayram Farişoğlu: None declared, Alper San: None declared, Levent Kılıç: None declared, Berkan Amagan: None declared, Emre Bilgin: None declared, Ertuğrul Çağrı Bölek: None declared, Ömer Karadag: None declared, Ali Akdoğan: None declared, Süleyman Bilgen: None declared, Sedat Kiraz: None declared, Ali İhsan Erenteli: None declared, Umut Kalyoncu: Grant/research support from: MSD, Roche, UCB, Novartis and Pfizer, Consultant for: MSD, Abbvie, Roche, UCB, Novartis, Pfizer and Abdi Ibrahim, Speakers bureau: MSD, Abbvie, Pfizer, UCB, Roche, Novartis, Pfizer and Abdi Ibrahim.


THU0388

Clinically relevant deficits in performance tests in patients with axial spondyloarthritis (axSpA): More than collecting questionnaires needs to be done

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Background: Physical function in axial spondyloarthritis (axSpA) usually assessed by the BASFI questionnaire is an established core domain of that disease. There is evidence that self-reported physical function is not equivalent with the actual performance of patients. Physical performance can be assessed as a single task such as grip strength or single stance, or as a generic compound measure such as the short physical performance battery test (SPPB). SPPB comprises a chair rising test, a balance test and gait speed.

Objectives: To investigate which performance tests are most frequently impaired in patients with axSpA.

Methods: Consecutive axSpA patients presenting to our tertiary hospital underwent a standardized assessment including patient and disease characteristics, patient-reported outcomes (ASDAS, BASFI, BASMI, ASAS Health Index (ASAS HI), PHQ-9) and performance tests (SPPB, grip strength and single stance). Structural damage was assessed by mSASSS. Validated cut-offs were used for SPPB, chair rise test, grip strength and gait speed. Impairment of performance tests as well as discrimination between subgroups was analysed.

Results: A total of 200 patients (n=axSpA 65.5%, nr=axSpA 34.5%) were included: 69% males, 44.3±12.5 years of age, mean symptom duration

Abstract THU0386 – Table 1. Patient characteristics of Chilean axSpA patients (n=472).

<table>
<thead>
<tr>
<th>Overall (n=472)</th>
<th>Men (n=299)</th>
<th>Women (n=173)</th>
<th>p=</th>
<th>Biologics (n=92)</th>
<th>No Biologics (n=372)</th>
<th>p=</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, men</td>
<td>173 (37)</td>
<td>45 (49)</td>
<td>124 (33)</td>
<td>0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age, yrs</td>
<td>42 ±10</td>
<td>43 ±11</td>
<td>41 ±9</td>
<td>&lt;0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disease duration, yrs</td>
<td>13 ±10</td>
<td>13 ±15</td>
<td>15 ±12</td>
<td>&lt;0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BasDAI</td>
<td>6.1 ±2.1</td>
<td>5.8 ±2.3</td>
<td>6.3 ±2.1</td>
<td>0.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BASFI</td>
<td>5 ±3</td>
<td>5.1 ±2.8</td>
<td>5.4 ±2.4</td>
<td>&lt;0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ASAS Health Index</td>
<td>10 ±4</td>
<td>9 ±4</td>
<td>10 ±3</td>
<td>&lt;0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presenteism, patients</td>
<td>202 (81)</td>
<td>46 (79)</td>
<td>151 (83)</td>
<td>0.04</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Acknowledgement: This study was conducted with help of the Chilean spondyloarthritis patient foundation “Espondilitis Chile”.

Disclosure of Interests: Sebastian Ibáñez Consultant for: Novartis, Paid instructor for: Bristol Myers Squibb, Speakers bureau: Abbvie; Alire, Rianne dis Bentum: None declared, Omar Valenzuela Consultant for: Novartis, Paid instructor for: Bristol Myers Squibb, Speakers bureau: Abbvie, Irene van der Horst-Bruinser Grant/research support from: MSD, Pfizer, AbbVie, Consult: for: Abbvie, UCB, MSD, Novartis, Speakers bureau: BMS, AbbVie, Pfizer, MSD.

A SYSTEMATIC REVIEW OF PREGNANCY OUTCOME IN ANKYLOSING SPONDYLITIS

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Background: Ankylosing spondylitis (AS) is a chronic, systemic inflammatory arthritis predominantly affecting spine and sacroiliac joints. AS affects young individuals in their third and fourth decades of life. Pregnancy poses challenges in AS patients. Unlike other chronic autoimmune diseases, not much is known regarding pregnancy outcome in AS and a systematic review would help treating clinicians and health professionals.

Objectives: Our main objective was to evaluate the pregnancy outcomes in ankylosing spondylitis. We reviewed the management and care related to preconception counselling, antenatal, intrapartum and postpartum period, particularly disease activity, medications and birth outcomes.

Methods: A systematic search of PUBMED and EMBASE was performed. Relevant peer-reviewed papers were identified using inclusion criteria which included articles on pregnancy outcomes in AS patients above 16 years. We included only English articles covering systematic reviews, randomized control trials, case reports, observational studies published in medical literature between 1970 and March 2017. We excluded papers discussing general management of AS and articles on other autoimmune diseases and pregnancy. Each author screened the titles and abstracts individually based on our criteria. A standardized data collection form was used for assessment of study quality and evidence synthesis. Systematic review was registered in PROSPERO and we followed the PRISMA flow chart.

Results: Our search yielded 544 papers. After initial screening of the titles and abstracts 443 papers were identified of which 42 potentially relevant papers were selected for full text review. 18 papers were finally included. Our initial results are based on individual papers. Zhou et al. studied 12 AS patients retrospectively with no adverse outcomes, all had term pregnancies with 5 normal vaginal delivery, 7 caesarean delivery was based on obstetric reasons. Nai Lee Lui et al. observed a reduction in pain in the first trimester, first month postpartum, in the second and third trimester and in up to 6 months postpartum. Monika Ostensen et al. observed unaltered or aggravated disease symptoms during pregnancy in 80%. Delivery was mainly uncomplicated and was normal in most cases. A postpartum flare during the first 3 months occurred in 90% of AS pregnancies. Hakan Timur et al. did not notice any adverse pregnancy outcomes. Worsening of symptoms was seen in 60-90% of patients up to 6 months after delivery. Jakobsson et al. noticed women with AS had a higher prevalence for several adverse birth outcomes with an influence by both disease severity and comorbidities. Case reports highlighted anaesthetic difficulties during delivery. There was paucity of articles studying the treatment aspects and complications only in AS patients.

Conclusion: To the best of our knowledge, this systematic review is the first one reviewing the outcome of pregnancy in ankylosing spondylitis. As the studies were heterogeneous, the pregnancy outcome was not consistent. There is paucity of data about pregnancy management for women with AS and further research is needed in this area to guide evidence based management of these pregnancies.

REFERENCE:
THU0390  GENETIC STUDY OF MEDICAL IMAGE PROGRESSION IN A CHINESE AS POPULATION FOR SIX MONTHS’ FOLLOW-UP

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Background: Genetic factors accounts for about 90% pathogenesis of ankylosing spondylitis (AS), and may predict the disease progression. MRI is an important tool for evaluating disease progression and assessing treatment response in patients with AS.

Objectives: This study aims to define correlation between AS-associated genetic variations and MRI scores of AS patients in Chinese population.

Methods: A total of 62 AS patients treated with TNF blockers from Guanghua medical center (Shanghai, China) were recruited in this study. All of AS patients were evaluated for disease progression with MRI (SPARCC) [1-3]. Measures of inflammation (bone marrow edema (BME) of sacroiliac joints (SIJ) and spine) and structural damage (fat metaplasia, erosion, backfill and ankylosis of SIJ) were recorded at baseline and six months’ follow-up. The changes of MRI scores were defined as the score of six months’ follow-up minus that of baseline. All of patients were examined with whole exon sequencing for genetic polymorphisms. Logistic regression analysis was performed and genetic variants with p < 1E-4 were considered as significant.

Results: The results showed that seven genetic variants significantly enriched in extracellular matrix pathways were associated with the changes of BME score of SIJ and spine. Four genetic variants regulating bone homeostasis, such as ABCA4, were significantly associated with the changes of fat metaplasia. Twelve variants were associated with the changes of erosion, one of which regulated expression of FBFI according to GTex database (p-value = -5.0/1.1E-5). Mouse with Fat4 knockout showed abnormality in insulin metabolism and skeleton (MGI database). Genetic variants of the adipose related gene (CTBP2) and bone related genes (RGMA, BMP8A) were associated with the changes of backfill. In addition, genetic variants of FAT4 was associated with the changes of ankylosis (p-value = 6.8/1.4E-8). Mutation of FAT4 caused two bone related diseases and mouse with Fat4 knockout showed severe abnormality of skeleton (MGI database).

Conclusion: Overall, the results suggested that the polymorphisms of genes involved in extracellular matrix were associated with BME, and genetic variants involved in adipose and bone metabolism were associated with structural damage in AS patients.

REFERENCES:

Disclosure of Interests: JING LIU: None declared, Qi Zhu: None declared, Weilin Pu: None declared, Dongyi He: None declared, Heijan Zou: None declared, Xiaodong Zhou: None declared, John D Reveille Grant/research support from: Janssen Research & Development, LLC, Jiucun Wang: None declared.


THU0391  COMPARISON OF CHARACTERISTICS AND BURDEN OF DISEASE IN PATIENTS WITH RADIOGRAPHIC AND NON-RADIOGRAPHIC AXIAL SPONDYLOARTHRITIS: A SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS

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Background: In 2009, the ASAS criteria allowed to classify patients with radiographic (r-axSpA) and non-radiographic (nr-axSpA) axial Spondyloarthritis (axSpA), and enhanced the concept of axSpA as a whole disease with different phenotypic presentations. However, some have claimed that the burden of r-axSpA and nr-axSpA is so different that they should be considered as different forms of the same disease.

Objectives: To compare the characteristics, burden of disease and treatment effect in patients with r-axSpA and nr-axSpA.

Methods: A systematic literature review until October 2018 was performed using PubMed, EMBASE and Cochrane databases. The PICO approach was used to formulate the research questions: P (r-axSpA patients), I (no intervention/drugs (only for the treatment effect evaluation), C (nr-axSpA patients), O (clinical presentation, disease activity, structural damage, function, quality of life, mobility, treatment modalities and treatment effect). Only observational studies and Randomized Controlled Trials (RCT) published after 2009 (year of publication of the ASAS criteria) were included. For the evaluation of the treatment effect, only RCT were considered. Risk of bias was evaluated on each manuscript with the Cochrane Risk of Bias tool for RCT and Hayden tool for observational studies. Pooled analysis was performed (Standardized Means Differences (SMD) and Relative Risk (RR) for continuous and binary variables, respectively) with a random effects model after evaluation of the heterogeneity of the studies.

Results: A total of 60 studies out of 787 references were included. Clinical presentation, disease activity, burden of disease (function, quality of life and mobility), treatment and treatment effect were evaluated in 54 (90.0%), 40 (67.7%), 37 (61.7%), 18 (30.0%) and in 9 (15.0%) manuscripts, respectively. Only 3 cross-sectional studies were classified as high risk of bias. Pooled analysis comparing continuous and binary variables are represented in tables 1 and 2. Only two RCTs (Etanercept vs. Sulfasalazine and Cetolizumab vs. Placebo) directly compared the treatment effect between both groups, and none of them showed differences regarding ASAS partial remission, ASDAS major improvement and ASAS 40.

Conclusion: Published data suggest that r-axSpA and nr-axSpA patients share a similar clinical presentation except for peripheral manifestations (which are more prevalent among nr-axSpA), males and smokers (which are more frequent among r-axSpA). Disease activity and burden of disease are identical in both groups, except mobility, which is poorer among r-axSpA. The treatment effect was similar in both groups.

Abstract THU0391 – Table 1.

Table 1. Pooled results for clinical presentation, disease activity, burden of disease and treatment for continuous variables in r-axSpA vs. nr-axSpA patients.

<table>
<thead>
<tr>
<th>Variable</th>
<th>r-axSpA</th>
<th>nr-axSpA</th>
<th>SMD (95%CI)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical presentation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at symptom onset</td>
<td>26.3(24.8 to 27.9)</td>
<td>27.8(26.2 to 25.4)</td>
<td>-0.61(-0.92 to 0.01)</td>
</tr>
<tr>
<td>Time to diagnosis</td>
<td>6.6(0.5 to 6.6)</td>
<td>4.2(3.2 to 6.2)</td>
<td>0.41(0.11 to 0.71)</td>
</tr>
<tr>
<td>MRI Inflammation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPARCC total SI</td>
<td>7.7(5.4 to 10.1)</td>
<td>7.2(5.9 to 8.6)</td>
<td>0.01(-0.37 to 0.38)</td>
</tr>
<tr>
<td>Berlin activity score: spine</td>
<td>3.8(2.8 to 4.9)</td>
<td>3.2(2.0 to 5.9)</td>
<td>0.07(0.55 to 0.6)</td>
</tr>
<tr>
<td>Structural damage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>mSASSS</td>
<td>6.9(5.3 to 8.0)</td>
<td>7.3(6.7 to 8.3)</td>
<td>0.34 (0.4 to 0.6)</td>
</tr>
<tr>
<td>Disease activity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BASDAI</td>
<td>4.6(3.3 to 5.9)</td>
<td>4.8(3.0 to 5.3)</td>
<td>-0.09 (0.11 to 0.0)</td>
</tr>
<tr>
<td>CDAI</td>
<td>3.0(1.7 to 4.3)</td>
<td>2.5(1.5 to 3.5)</td>
<td>0.29 (0.29 to 0.3)</td>
</tr>
<tr>
<td>ASDAS-CRP</td>
<td>2.6(1.2 to 3.7)</td>
<td>2.3(1.2 to 3.6)</td>
<td>0.30 (0.15 to 0.5)</td>
</tr>
<tr>
<td>Function</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BSAI</td>
<td>3.4(2.3 to 4.7)</td>
<td>3.0(2.7 to 3.5)</td>
<td>0.19 (0.15 to 0.3)</td>
</tr>
<tr>
<td>MHAQ</td>
<td>0.6(0.5 to 0.8)</td>
<td>0.6(0.5 to 0.9)</td>
<td>0.06 (-0.01 to 0.2)</td>
</tr>
<tr>
<td>Quality of life</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SF36-ROC</td>
<td>48.5(46.5 to 50.6)</td>
<td>48.2(44.1 to 52.3)</td>
<td>0.02 (-0.01 to 0.0)</td>
</tr>
<tr>
<td>SF36-PFS</td>
<td>46.3(27.0 to 47.7)</td>
<td>41.5(27.0 to 46.7)</td>
<td>-0.04 (-0.02 to 0.0)</td>
</tr>
<tr>
<td>Mobility</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BASMI</td>
<td>2.8(2.3 to 3.3)</td>
<td>2.8(2.3 to 3.3)</td>
<td>0.08 (0.05 to 0.3)</td>
</tr>
</tbody>
</table>

*SMOD < 0.2 = irrelevant difference / 0.2 ≤ SMD < 0.5 = small difference / SMD ≥ 0.5 = meaningful difference
Results: A total of 246 patients were recruited, 47.6% were diagnosed with axSpA, and these included 85.8% of B27 positive patients (Table 1). Diagnosis of axSpA was established in 45.7%, 61.6%, and 40.2% of patients, while ASAS classification criteria were met by 26.1%, 71.2%, and 27.6% of patients with psoriasis, AAU, and IBD, respectively. Features of inflammatory back pain, male gender, and B27 positivity, but not physical measures discriminated axSpA from other causes of back pain (Table 2).

Abstract THU0392 – Table 1.

Table 2. Pooled results for clinical presentation and treatment for binary variables in r-axSpA vs. non-axSpA patients.

<table>
<thead>
<tr>
<th>r-axSpA</th>
<th>non-axSpA</th>
<th>RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male)</td>
<td>55.2%</td>
<td>37.6%</td>
</tr>
<tr>
<td>Smoker</td>
<td>34.5%</td>
<td>25.6%</td>
</tr>
<tr>
<td>HLA-B27 positive</td>
<td>20.2%</td>
<td>6.9%</td>
</tr>
<tr>
<td>Good NSAID response</td>
<td>68.5%</td>
<td>50.0%</td>
</tr>
<tr>
<td>Peripheral arthritis</td>
<td>138.5%</td>
<td>56.5%</td>
</tr>
<tr>
<td>Dactylitis</td>
<td>4.5%</td>
<td>2.1%</td>
</tr>
<tr>
<td>Any enthesitis</td>
<td>3.5%</td>
<td>0.9%</td>
</tr>
<tr>
<td>Uveitis</td>
<td>0.5%</td>
<td>0.1%</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>6.5%</td>
<td>12.6%</td>
</tr>
<tr>
<td>IBD</td>
<td>6.5%</td>
<td>5.2%</td>
</tr>
</tbody>
</table>

Table 3.

Disclosure of Interests: Clementina López-Medina: None declared, Sofia Ramiro Grant/research support from: MSD, Consultant for: AbbVie, Lilly, MSD, Novartis, Pfizer, Sanofi, Speakers bureau: AbbVie, Lilly, MSD, Novartis, Pfizer, Sanofi, Désirée van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Daichii, Eli-Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, Union Chimique Belge, maxime dougados Grant/research support from: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma, Consultant for: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma, Anna Molto: None declared


Abstract THU0392 – Table 2.

Table 1.

Demographics

<table>
<thead>
<tr>
<th>axSpA YES</th>
<th>axSpA NO</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, N (%)</td>
<td>72 (61.5%)</td>
<td>57 (44.2%)</td>
</tr>
<tr>
<td>Mean (SD) age, years</td>
<td>33.7 (6.7)</td>
<td>35.2 (6.7)</td>
</tr>
<tr>
<td>Inflammatory Back Pain Yes, N (%)</td>
<td>102 (87.2%)</td>
<td>72 (55.8%)</td>
</tr>
<tr>
<td>Duration stiffness &gt; 60 mins, N (%)</td>
<td>57 (48.7%)</td>
<td>30 (23.3%)</td>
</tr>
<tr>
<td>Nocturnal awakening 2nd half of night, N (%)</td>
<td>72 (61.5%)</td>
<td>51 (39.5%)</td>
</tr>
<tr>
<td>Alternating buttock pain, N (%)</td>
<td>53 (45.3%)</td>
<td>21 (16.3%)</td>
</tr>
<tr>
<td>Improvement with exercise but not rest, N (%)</td>
<td>77 (65.8%)</td>
<td>48 (37.2%)</td>
</tr>
<tr>
<td>Respond to NSAID within 48 hrs, N (%)</td>
<td>58 (49.6%)</td>
<td>59 (45.7%)</td>
</tr>
<tr>
<td>Family history of SpA, N (%)</td>
<td>22 (18.8%)</td>
<td>28 (21.7%)</td>
</tr>
<tr>
<td>B27+ positive</td>
<td>61 (52.1%)</td>
<td>28 (21.7%)</td>
</tr>
<tr>
<td>Elevated CRP (&gt; 6.0mg/L)</td>
<td>43 (36.8%)</td>
<td>32 (24.8%)</td>
</tr>
<tr>
<td>Radiographic sacroiliitis, N (%)</td>
<td>54 (46.2%)</td>
<td>7 (5.4%)</td>
</tr>
</tbody>
</table>

Conclusion: Patients with extra-articular manifestations and undiagnosed back pain have a high prevalence of axSpA and refer to a rheumatologist should constitute standard of care, especially if B27 positive.

Disclosure of Interests: Walter P Maksymowycz Grant/research support from: AbbVie, Pfizer, Janssen, Novartis, Consultant for: AbbVie, Eli Lilly, Boehringer, Galapagos, Janssen, Novartis, Pfizer and UCB Pharma; Chief Medical Officer for Canadian Research and Education Arthritis, Raj Carmona Grant/research support from: Amgen, Abbvie, BMS, Eli Lilly, Merck, Novartis, Janssen, Takeda, UCB, James Yeung: None declared, Jon Chan Grant/research support from: Janssen, UCB, Novartis, Pfizer, Celgene, Consultant for: Amgen, Celgene, UCB, Novartis, Janssen, Sanofi, Diagne Mosher: None declared, Ariel Masetto Consultant for: Abbvie, Celgene, UCB, Novartis, Janssen, Sanofi, Dianne Mosher: None declared, Ariel Masetto Consultant for: Abbvie, Celgene, UCB, Novartis, Janssen, IBD, Psoriasis, Acute Anterior Uveitis, and Inflammatory Bowel Disease Presenting with Undiagnosed Back Pain

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Background: There are limited prospective data as to the frequency of axial spondyloarthritis (axSpA) in unselected patients referred to rheumatologists with undiagnosed back pain. It is also unclear which clinical features discriminate between axSpA and non-specific causes of back pain that might inform the development of a screening strategy.

Objectives: To determine the prevalence of axSpA in unselected patients referred with undiagnosed back pain presenting with AAU, psoriasis, or colitis and determine which clinical characteristics define patients with axSpA.

Methods: The multicenter Screening for Axial Spondyloarthritis in Psoriasis, Iritis, and Colitis (SASPIC) Study is aimed at facilitating early detection of axial SpA. First and last patients were recruited on February 2013 and March 2018, respectively. Consecutive patients ≤45 years of age with ≥3 months undiagnosed back pain with any one of psoriasis, AAU, or colitis had routine clinical evaluation by a rheumatologist for axial SpA and MRI evaluation ordered per rheumatologist decision. Differences in clinical characteristics between those who were diagnosed as axSpA or non-specific back pain were analyzed using chi-squared and t-tests.

Conclusion: Patients with extra-articular manifestations and undiagnosed back pain have a high prevalence of axSpA and refer to a rheumatologist should constitute standard of care, especially if B27 positive.

Disclosure of Interests: Walter P Maksymowycz Grant/research support from: AbbVie, Pfizer, Janssen, Novartis, Consultant for: AbbVie, Eli Lilly, Boehringer, Galapagos, Janssen, Novartis, Pfizer and UCB Pharma; Chief Medical Officer for Canadian Research and Education Arthritis, Raj Carmona Grant/research support from: Amgen, Abbvie, BMS, Eli Lilly, Merck, Novartis, Janssen, Takeda, UCB, James Yeung: None declared, Jon Chan Grant/research support from: Janssen, UCB, Novartis, Pfizer, Celgene, Consultant for: Amgen, Celgene, UCB, Novartis, Janssen, Sanofi, Dianne Mosher: None declared, Ariel Masetto Consultant for: Amgen, Sanofi, Consultant for: Sanofi, Pfizer, Bristol-Myers Squibb, Novartis, Boehringer Ingelheim, Speakers bureau: Novartis, Stephanie Keeling Consultant for: AbbVie, Pfizer, Eli Lilly, Janssen, Amgen, Astrezeneca, UCB., Olga Ziouzina: None declared, Sherry Rohekar Consultant for: Abbvie, Amgen, BMS, Celgene, Eli Lilly, Janssen, Merck, Novartis, Pfizer, Roche, Sanofi, UCB, Joel Paschke: None declared, Amanda Carapellucci: None declared, Robert G Lambert Consultant for: Bicodina, Paralex, Abbvie

PERFORMANCE OF THE ASAS CLASSIFICATION CRITERIA PRESENTING WITH UNDIAGNOSED BACK PAIN: DATA FROM THE SCREENING IN AXIAL SPONDYLOARTHRITIS IN PSORIASIS, IRITIS, AND COLITIS (SASPIC) COHORT

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Background: Classification criteria for axial spondyloarthritis (axSpA) that capture the spectrum of disease present challenges due to the frequency of back pain, the relative infrequency of axSpA, and limited physical and laboratory findings in early disease. Several cohorts have reported the performance of the ASAS classification criteria in settings where patients have been selected for certain features such as the presence of inflammatory back pain and/or short symptom duration.

Objectives: We aimed to test the performance of the ASAS classification criteria in unselected patients referred with undiagnosed back pain who have presented with acute anterior uveitis (AAU), psoriasis, or colitis to their respective specialists and whether performance varied according to demographic factors and symptom severity.

Methods: We multicenter Screening for Axial Spondyloarthritis in Psoriasis, Iritis, and Colitis (SASPIC) Study is aimed at early detection of axial SpA. Consecutive patients ≤45 years of age with ≥3 months undiagnosed back pain with any one of psoriasis, acute anterior uveitis (AAU), or colitis undergo routine clinical evaluation by a rheumatologist for axial SpA and MRI evaluation is ordered per rheumatologist decision. The rheumatologist determines the presence or absence of axial SpA and the degree of confidence in the diagnosis (-10 (definitely not SpA) to +10 (definite SpA)) at 3 consecutive stages: 1. After the clinical evaluation; 2. After the results of labs (B27, CRP) and radiography; 3. After the results of MRI evaluation. Assessment of imaging was conducted by local and central readers. We calculated the sensitivity and specificity of the ASAS criteria and the component imaging and clinical arms using the stage 3 diagnostic assessment by the local rheumatologist as gold standard.

Results: A total of 246 patients were recruited, 47.6% being diagnosed with axSpA (61.5% male, age 33.7 years, symptom duration 7.6 years, B27 positive 52.1%), after stage 3 evaluation. Sensitivity/specificity of the ASAS criteria, imaging arm, clinical arm were 74.4/79.8%, 55.6/93.8%, 50.4/82.2%, respectively (Table). For patients diagnosed with a high degree of confidence sensitivity/specificity was 87.5/82.7%, 68.8/94.5%, 56.3/84.5%, respectively. Specificity, especially for the clinical arm, was notably higher in patients with a higher degree of back pain (≥5/10), and in those with longer symptom duration (>5 years).

Conclusion: The performance of the ASAS criteria in the SASPIC cohort is comparable to the findings in the original ASAS classification study. Performance may vary according to symptom duration and severity of symptoms which likely impacts diagnostic ascertainment.

Disclosure of Interests: Walter P. Maksymowych Grant/research support from: AbbVie, Pfizer, Janssen, Novartis, Consultant for: AbbVie, Eli Lilly, Boehringer, Galapagos, Janssen, Novartis, Pfizer and UCB Pharma; Chief Medical Officer for Canadian Research and Education Arthritis, Raj Carmona Grant/research support from: Amgen, Abbvie, BMS, Eli Lilly, Merck, Novartis, Janssen, Takeda, UCB, James Yeung; None declared, Jon Chan Grant/research support from: Janssen, UCB, Novartis, Pfizer, Celgene, Consultant for: Amgen, Celgene, Eli Lilly, Janssen, Amgen, Abbvie, Novartis, Pfizer, UCB, San doz, Merck, Liam Martin; None declared, Sibel Aydin Consultant for: Abbvie, Celgene, UCB, Novartis, Janssen, Sanofi, Dianne Moshe; None declared, Ariel Masotto Consultant for research support from: Amgen, Sanofi, Consultant for: Sanofi, Pfizer, Bristol-Myers Squibb, Novartis, Boehringer Ingelheim, Speakers bureau: Novartis, Stephanie Keeling Consultant for: AbbVie, Pfizer, Eli LILy, Janssen, Amgen, AstraZeneca, UCB, Olga Ziouzina; None declared, Sherry Rohekard Consultant for: Abbvie, Amgen, BMS, Celgene, Eli-Lilly, Janssen, Merck, Novartis, Pfizer, Roche, Sanofi, UCB, Joel Paschke; None declared, Amanda Carapellucci; None declared, Robert G Lambert Consultant for: Bioclinica, Parexel, Abbvie DOI: 10.1136/annrheumdis-2019-eular.6354

THE PREVALENCE OF EXTRA-ARTICULAR MANIFESTATIONS IN AXIAL SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS IS ASSOCIATED TO DISEASE DURATION: RESULTS FROM THE LEEDS SPECIALIST SPONDYLOARTHRITIS SERVICE

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Background: Psoriasis, uveitis and inflammatory bowel disease (IBD) are extra-articular manifestations (EAMs) that can occur in both axial Spondyloarthritis (axSpA) and psoriatic arthritis (PsA). Their prevalence has been outlined independently in a recent meta-analysis1 for axSpA and in several series in PsA with variable results. Although the diagnostic delay of inflammatory arthritis has been reduced in the last years, it remains a significant unmet need, particularly in axSpA. There are limited data on the relationship between diagnostic delay and the appearance of EAMs.

Objectives: To explore the prevalence of EAMs in a cohort of axSpA and PsA patients, and its relationship to disease duration and possible diagnostic delay in both groups.

Methods: Cross-sectional, single centre, observational cohort study of consecutive patients attending a large tertiary specialist clinic. All subjects provided written consent (2005-2018). Only patients fulfilling the modified New York (mNY) criteria for ankylosing spondylitis and CASPAR criteria for PsA were considered for this analysis. Demographic and clinical data were retrieved during enrolment and cross-referenced with the clinical notes to explore the relationship between presence of EAMs and diagnostic delay in both groups.

Results: Data from 988 patients were available for analysis (n= 418 axSpA, n=570 PsA). Demographic and clinical characteristics are summarised in Table 1.

In the axSpA group, 187 cases (44.7%) presented with EAMs (including psoriasis) and 67 (16.02%) of these had more than 1 EAM. In the PsA group, 32 cases (5.6%) presented with EAM (excluding psoriasis) and only 3 cases (0.5%) had more than one EAM. In the PsA group, a median delay of 4 years (IQR 2-9) was observed between psoriasis onset and PsA. In 42 cases the psoriasis appeared after the PsA onset. The predominant PsA phenotype was polyarticular (n=298; 52.3%) of which n=118, 20.7% had erosive disease. 101 (17.7%) had a predominantly axial phenotype.

Conclusion: Disease duration and delay to diagnosis were longer in the axSpA group (p<0.0001). Further univariate analysis showed an association between disease duration and the presence of EAMs when analysing the whole cohort (p<0.001) and the axSpA group (p<0.001), but not in the PsA group (p=0.832). The diagnostic delay was associated to the presence of EAMs in the whole cohort (p<0.001), but not in the individual disease groups. In the multivariate analysis only disease duration was related to presence of EAMs in the whole cohort (OR 1.064 95%IC 1.044-1.086) and axSpA group (OR 1.043 95%IC 1.016-1.070).

Abstract THU0393 – Table 1.

<table>
<thead>
<tr>
<th>Patient Category</th>
<th>Number</th>
<th>ASAS criteria</th>
<th>Imaging arm</th>
<th>Clinical arm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Sens</td>
<td>Spec</td>
<td>Sens</td>
</tr>
<tr>
<td>All patients</td>
<td>246</td>
<td>74.4</td>
<td>79.8</td>
<td>55.6</td>
</tr>
<tr>
<td>Patients diagnosed with confidence &gt;7 for axSpA yes and ≤4 for not axSpA ≤10 to ≤10 scale</td>
<td>190</td>
<td>87.5</td>
<td>82.7</td>
<td>68.8</td>
</tr>
<tr>
<td>Patients with back pain ≤5 (0-10 scale)</td>
<td>165</td>
<td>74.7</td>
<td>83.7</td>
<td>54.4</td>
</tr>
<tr>
<td>Patients with back pain ≤5 (0-10 scale)</td>
<td>81</td>
<td>73.7</td>
<td>72.1</td>
<td>57.9</td>
</tr>
<tr>
<td>Patients with symptom duration ≤5 years</td>
<td>143</td>
<td>78.1</td>
<td>85.7</td>
<td>53.4</td>
</tr>
<tr>
<td>Patients with symptom duration ≤5 years</td>
<td>103</td>
<td>68.2</td>
<td>72.9</td>
<td>59.1</td>
</tr>
<tr>
<td>Males</td>
<td>129</td>
<td>73.6</td>
<td>78.9</td>
<td>61.1</td>
</tr>
<tr>
<td>Females</td>
<td>117</td>
<td>75.6</td>
<td>80.6</td>
<td>46.7</td>
</tr>
</tbody>
</table>
Conclusion: The prevalence of EAMs (uveitis and IBD) in this cohort appears higher in axSpA than PsA and is related to disease duration. Diagnostic delay occurs in both groups being more significant in axSpA, and should be highlighted as a priority research area in order to improve the outcome of people affected by SpA.

REFERENCES:


and little has been explored in the alterations at the level of the jejunum. The tests for its detection are expensive, unavailable and invasive. The breath test is used to detect small intestine bacterial overgrowth (SIBO), being a non-invasive, simple and inexpensive test.

Objectives: To determine the frequency of SIBO and the relation to the clinical activity of SpA.

Methods: An analytical cross-sectional study was conducted in the period March 2018–October 2018. Patients older than 18 years, who signed informed consent, who met modified New York criteria and Caspar criteria were included. Patients were excluded who were diagnosed with active lung infection, active oral infections, interstitial lung disease, chronic obstructive pulmonary disease, acute diarrheal disease, short bowel syndrome, abdominal surgery in less than 6 months, and oral or IV antibiotics used one month before the test.

Patients who fulfilled the inclusion criteria were collected demographic and clinical data, gastrointestinal manifestations were interrogated and ASDAS pcr, BASMI, BASDAI, BASFI activity scales were measured. The breath test was performed by a gastroenterologist. The concentrations of hydrogen produced by bacteria were measured by GASTROLYZER® according to the recommendations of the consensus of the American Gastroenterology Association. It was considered a positive test to change the concentrations of more than 20 ppm with respect to the basal test. To compare the frequency of SIBO, a historical cohort of patients without rheumatic diseases matched by age was taken. The data were presented in means and percentages. Student’s T and Mann-Whitney U were performed for numerical variables. Groups with chi square were compared.

Results: We studied 20 patients with ankylosing spondylitis (M/F 9/11) and 11 psoriatic arthritis (M/F 1/12), mean age 54.45 ±13.52. 33 healthy controls matched by age. Positive test was found in 11 (33%) patients (8/3 EA/APS) vs 1 (3%) in controls. When comparing groups with positive test versus negative test groups, patients with SIBO consumed less SSZ (72.7 vs 90.9, p 0.008), had higher frequency of irritable bowel (54 vs 9, p 0.004), antecedent of cholecystectomy (27.3 vs 9.1 p 0.01), steatorrhea (18.2 vs 0, p 0.001), and higher activity: ASDAS> 2.1 (100% vs 86.4%, p 0.199), BASMI> 4 (36.4% vs 31.8% p 0.79), BASFI> 4 (72.7% vs 50%, p 0.21), enthesitis> 1 (45.5% vs 13.6%, p 0.61).

Conclusion: We found a higher frequency of SIBO in patients with SpA compared to healthy controls, but not related to disease activity. This is the first study to investigate SIBO by breath test in patients with SpA.

REFERENCES:

Disclosure of Interests: None declared
Abstract THU0398

Table 1. Demographic and Clinical Characteristics and Treatment Profiles Among Patients with AS Who Initiated Secukinumab or Other Biologic*.  

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Secukinumab Initiators (n = 26)</th>
<th>Other Biologic Initiators (n = 26)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD) years</td>
<td>47.1 (12.0)</td>
<td>48.2 (12.0)</td>
<td>0.88</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>14 (53.8)</td>
<td>11 (42.3)</td>
<td>0.75</td>
</tr>
<tr>
<td>BMI, centrally measured, mean (SD) kg/m²</td>
<td>28.5 (6.6)</td>
<td>29.3 (6.1)</td>
<td>0.47</td>
</tr>
<tr>
<td>Work status, n (%)</td>
<td>19 (73.1)</td>
<td>19 (73.1)</td>
<td>0.87</td>
</tr>
<tr>
<td>Fibromyalgia</td>
<td>3 (11.5)</td>
<td>4 (15.4)</td>
<td>0.83</td>
</tr>
<tr>
<td>Depression</td>
<td>7 (26.9)</td>
<td>8 (30.8)</td>
<td>0.74</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>2 (7.7)</td>
<td>6 (23.1)</td>
<td>0.14</td>
</tr>
<tr>
<td>NSAID use, mean (SD) mg/day</td>
<td>6.5 (4.6)</td>
<td>6.8 (4.9)</td>
<td>0.75</td>
</tr>
<tr>
<td>Dual (COX-2, COX-1) inhibitors, n (%)</td>
<td>10 (38.5)</td>
<td>10 (38.5)</td>
<td>1.00</td>
</tr>
<tr>
<td>Current smoking, n (%)</td>
<td>11 (42.3)</td>
<td>18 (69.2)</td>
<td>0.16</td>
</tr>
<tr>
<td>Age ≥50, n (%)</td>
<td>21 (80.8)</td>
<td>22 (84.6)</td>
<td>0.74</td>
</tr>
<tr>
<td>Inflammatory IBD</td>
<td>1 (3.8)</td>
<td>6 (23.1)</td>
<td>0.10</td>
</tr>
</tbody>
</table>

Conclusion: In this real-world study of US patients with AS, secukinumab initiators had similar demographics, clinical outcomes, disease burden and patient reported outcomes compared with other biologic initiators, with the exception of higher prior biologic use.

Acknowledgement: This study was sponsored by Corrona, LLC. Corrona is supported through contracted subscriptions with multiple pharmaceutical companies. The abstract was a collaborative effort between Corrona and Novartis, with financial support provided by Novartis. The abstract was a collaborative effort between Corrona and Novartis.

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Gait 3D Kinematics Unveils a Specific Pattern in Patients in Early Years of Axial Spinal Arthritis: Evidence of Their Body Composition and Muscle Performance Variables

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Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory rheumatic disease characterized by a progressive mobility reduction of the rachis. The posture changes may cause balance problems with gait repercussions. However, we lack information during the early years of the disease regarding gait pattern and the possible variables that may influence gait parameters.

Objectives: In order to gain insight into the gait patterns in patients at early stages of axSpA and the potential influence of some patient-specific features, the aim of this study was therefore to evaluate: (i) the 3D gait signature in patients at early years of axSpA; and (ii) the relation between gait parameters, and body composition and muscle performance variables.

Methods: A cross-sectional study was conducted on 46 participants (18-50 years old), 23 patients with axSpA (according to ASAS criteria, with less than 10 years since symptoms onset) and 23 healthy controls, matched by gender and age, with a mean age of 37±7.5 years, predominantly males (60%). The patients with axSpA had 5±3.2 years of disease duration, with BASDAI and BASFI of 3±2.2 and 2±2.9, respectively. Subjects’ movement was reconstructed using a 3D full-body kinematic model (Kinetikos, Coimbra, Portugal) fed by 15 inertial sensors placed in the head, arms, trunk, pelvis, thighs, shanks and feet. The primary outcomes comprised the general gait parameters such as gait pattern (step length, cadence, stance duration, body vertical regularity (sample entropy), step length, range of movement and peak velocity of the different joints. Body composition was assessed by performing octopolar multifrequency bioelectrical impedance analysis (BIA; InBody 770). Muscle performance was assessed with a 60 second sit-to-stand test (STS60), while physical activity was controlled by the international physical activity questionnaire (IPAQ). Variables (except age, disease duration, BASDAI, BASFI) are presented as median. Non-parametric tests were used to compare groups. Correlations between gait, body composition and skeletal muscle function parameters, were performed.

Results: Gait analysis showed statistically significant differences between axSpA and healthy control groups on gait deviation index (median 83 vs 87%, p=0.022, with higher score values representing similar performance to normal movement), speed (median 0.79 vs 0.85m/s, p=0.015), stance duration at the left side (median 68 vs 67s, p=0.027), left step length (median 0.47 vs 0.49m, p=0.008), and vertical regularity (median 0.39 vs 0.33, p=0.029 with higher values representing a less regular and predictable movement pattern). At the sagittal plane, patients showed higher values of left arm maximum flexion (median 14° vs 10°, p=0.011), lower lumbar extension peak velocity (median 45° vs 60°s, p=0.016) and higher ankle angular peak velocity on right side (median 530° vs 299°s, p=0.020). However, no statistically significant differences between groups were found for physical activity parameters. Reduction in statistically significant correlation was found between the gait parameters and weight, body fat, torso fat, visceral fat, body mass index, total body water, extracellular water, fat free mass, lean mass, bone mineral content and STS60.

Conclusion: These results provide evidence that although young axSpA patients at early years of the disease display a particular gait pattern...
and this behavior does not seem to be influenced by the body composition and muscle performance. The main determinant for this gait pattern remains an open question.

Disclosure of Interests: Fernando Pimentel dos Santos Grant/research support from: From Abbvie and Novartis, Speakers bureau: Abbvie, Novartis, Pfizer, Biogen, Lucia Domingues: None declared, César Mendes: None declared, Ricardo Matias: None declared, Santiago Rodrigues-Manica: None declared, Carolina Crespo: None declared, Jaime Branco: None declared.


THU0399 DEVELOPMENT OF AN OPTIMIZED ONLINE SELF-REFERRAL TOOL FOR EARLY RECOGNITION OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS (AXSPA) – DATA FROM THE ‘OPTIREF’-STUDY

Fabian Proft1, Laura Spiller1, Mikhail Protopenov1, Valeria Rios Rodriguez1, Burkhard Muche1, Judith Rademacher1, Susanne Lüders1, Anne Katrin Weber1, Imke Redeker1,2, Denis Poddubnyy1,2.

Background: One of the major reasons for a long diagnostic delay in axial spondyloarthritis (axSpA) is the late referral of patients by primary care physicians dealing with patients with chronic back pain. We developed and implemented an online self-referral tool (www.bechterew-check.de), which gave access to a rheumatological consultation if patients declared suffering from chronic back pain (≥ 3 months) with a symptom onset ≤ 45 years of age, and at least one feature indicative of SpA. In the prospective “Identification of the Optimal Referral Strategy for Early Diagnosis of Axial Spondyloarthritis (OptiRef) Study” we could diagnose axSpA in 19% of the self-referred patients [1].

Objectives: To optimize the online-self-referral tool for recognition of patients with high suspicion of axSpA in order to increase the specificity by keeping the high level of sensitivity.

Methods: 181 patients who had fulfilled the online self-referral strategy were included and underwent a standardized rheumatological examination. The final diagnosis of axial SpA/no axial SpA by the rheumatologist served as the gold standard. The performance of all possible combinations of the referral parameters (13 parameters in total including 5 features of inflammatory back pain (IBP) and 8 other SpA features) added to both stem parameters (chronic back pain, starting at age of ≤ 45 years) was tested. In addition, the following pre-specified combinations were evaluated: 1) ≥ 1 IBP parameter AND ≥ 1 other SpA parameter, 2) ≥ 1 IBP parameter OR ≥ 1 other SpA parameter. For all combinations, a sensitivity, a specificity, positive and negative predictive values (PPV and NPV), as well as a positive and negative likelihood ratio (LR+ and LR-) were calculated. We targeted the maximal specificity by acceptable sensitivity (defined as ≥ 90% of the original strategy).

Results: For 163 of the included patients, full data of the online questionnaire as well as of rheumatology examination including the final diagnosis of Axial Spondyloarthritis were available. 31 (19%) of them were diagnosed with axial SpA.

For 163 of the included patients, full data of the online questionnaire as well as of rheumatology examination including the final diagnosis of Axial Spondyloarthritis were available. 31 (19%) of them were diagnosed with axial SpA.

Conclusion: The data-driven optimized online self-referral tool (figure 1) requires the following parameters to be positive: chronic back pain (≥ 3 months) plus back pain onset before 45 years of age plus ≥ 2 IBP parameters plus ≥ 1 other SpA feature. The performance of this tool should be confirmed in a prospective study.

Disclosure of Interests: Fabian Proft Grant/research support from: Novartis, Consultant for: yes but less than 10.000, Paid instructor for: yes but less than 10.000, Speakers bureau: yes but less than 10.000, Laura Spiller: None declared, Mikhail Protopenov: None declared, Valeria Rios Rodriguez: None declared, Burkhard Muche Speakers bureau: Yes less than 10.000, Judith Rademacher: None declared, Susanne Lüders: None declared, Anne Katrin Weber: None declared, Denis Poddubnyy Grant/research support from: Novartis, Pfizer, Biogen, Lucia Domingues: None declared, César Mendes: None declared, Ricardo Matias: None declared, Santiago Rodrigues-Manica: None declared, Carolina Crespo: None declared, Jaime Branco: None declared.


THU0400 COMPLICATIONS OF ANTERIOR UVEITIS ASSOCIATED WITH HLA-B27 ANTIGEN IN PATIENTS WITH AND WITHOUT SPONDYLOARTHRITIS

Irina Razumova1, Alla Godzenko2, Irina Guseva2, Research Institute of Eye Disease, Moscow, Russian Federation; 2Nasonova Research Institute of Rheumatology, Moscow, Russian Federation

Background: HLA-B27-associated anterior uveitis (AU) can be an isolated disease or part of a systemic inflammatory process, such as spondyloarthritis. Differences in the outcome of uveitis with and without spondyloarthritis still under research.

Disclosure of Interests: Fabian Proft Grant/research support from: Novartis, Consultant for: yes but less than 10.000, Paid instructor for: yes but less than 10.000, Speakers bureau: yes but less than 10.000, Laura Spiller: None declared, Mikhail Protopenov: None declared, Valeria Rios Rodriguez: None declared, Burkhard Muche Speakers bureau: Yes less than 10.000, Judith Rademacher: None declared, Susanne Lüders: None declared, Anne Katrin Weber: None declared, Denis Poddubnyy Grant/research support from: AbbVie, Merck Sharp & Dohme, Novartis, Consultant for: AbbVie, Bristol-Myers Squibb, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, UCB Pharma, Speakers bureau: AbbVie, Bristol-Myers Squibb, Janssen, Merck Sharp & Dohme, Novartis, Pfizer, Roche, UCB Pharma.

This abstract is a summary of a recent publication in which the following results were found:

- **EULAR 2018 abstract abstract THU0230**
  - **Objective:** To optimize the online-self-referral tool for recognition of patients with high suspicion of axSpA in order to increase the specificity by keeping the high level of sensitivity.
  - **Methods:** 181 patients who had fulfilled the online self-referral strategy were included and underwent a standardized rheumatological examination. The final diagnosis of axial SpA/no axial SpA by the rheumatologist served as the gold standard. The performance of all possible combinations of the referral parameters (13 parameters in total including 5 features of inflammatory back pain (IBP) and 8 other SpA features) added to both stem parameters (chronic back pain, starting at age of ≤ 45 years) was tested. In addition, the following pre-specified combinations were evaluated: 1) ≥ 1 IBP parameter AND ≥ 1 other SpA parameter, 2) ≥ 1 IBP parameter OR ≥ 1 other SpA parameter. For all combinations, a sensitivity, a specificity, positive and negative predictive values (PPV and NPV), as well as a positive and negative likelihood ratio (LR+ and LR-) were calculated. We targeted the maximal specificity by acceptable sensitivity (defined as ≥ 90% of the original strategy).
  - **Results:** For 163 of the included patients, full data of the online questionnaire as well as of rheumatology examination including the final diagnosis was available. 31 (19%) of them were diagnosed with axial SpA.
  - **Conclusion:** The data-driven optimized online self-referral tool (figure 1) requires the following parameters to be positive: chronic back pain (≥ 3 months) plus back pain onset before 45 years of age plus ≥ 2 IBP parameters plus ≥ 1 other SpA feature. The performance of this tool should be confirmed in a prospective study.

**Table 1: Performance of self-referral strategies based on combinations of SpA parameters in addition to the stem parameters (chronic back pain starting at age of 45 years).**

<table>
<thead>
<tr>
<th>Number of parameters</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>LR+</th>
<th>LR-</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 2</td>
<td>0.70 (0.59–0.79)</td>
<td>0.89 (0.80–0.92)</td>
<td>0.49 (0.38–0.60)</td>
<td>2.41</td>
<td>0.08</td>
</tr>
<tr>
<td>≥ 1</td>
<td>0.68 (0.58–0.77)</td>
<td>0.91 (0.83–0.95)</td>
<td>0.47 (0.36–0.60)</td>
<td>2.40</td>
<td>0.08</td>
</tr>
<tr>
<td>≥ 1 other SpA feature</td>
<td>0.67 (0.56–0.76)</td>
<td>0.90 (0.82–0.94)</td>
<td>0.47 (0.36–0.60)</td>
<td>2.42</td>
<td>0.05</td>
</tr>
<tr>
<td>≥ 1 IBP parameter</td>
<td>0.70 (0.59–0.79)</td>
<td>0.89 (0.80–0.92)</td>
<td>0.47 (0.36–0.60)</td>
<td>2.40</td>
<td>0.08</td>
</tr>
<tr>
<td>≥ 1 other SpA parameter</td>
<td>0.68 (0.58–0.77)</td>
<td>0.91 (0.83–0.95)</td>
<td>0.47 (0.36–0.60)</td>
<td>2.42</td>
<td>0.05</td>
</tr>
</tbody>
</table>

**The influence of stem features on the assessment of the self-referral tool is not shown.**

**References:**


**Disclosure of Interests:** None declared, Carolina Crespo: None declared, Jaime Branco: None declared.
OBJECTIVES: To compare the incidence of complications in HLA-B27- associated anterior uveitis patients with and without spondyloarthritides (SpA).

METHODS: 189 patients with HLA-B27- associated anterior uveitis were observed in Research Institute of Eye Disease for 10 years. The pts were underwent standard ophthalmological examination, and, if necessary, computer perimeter, ultrasound examination (B-scan), optical coherence tomography of the retina and optic nerve (OCT), fluorescence fundus angiography (FAGD) and electrophysiological studies (EFEI). All pts were examined for clinical and imaging signs of SpA: inflammatory back pain, arthritis, enthesitis, sacroiliitis.

Different variants of SpA were diagnosed in 108 pts: ankylosing spondylitis – in 48 (44,4%), reactive arthritis – in 9 (8,3%), psoriatic arthritis - in 9 (8,3%), inflammatory bowel disease – in 2(1,9%), juvenile SpA – in 4 (3,7%), undifferentiated SpA - in 36 (33,3%). In 81 pts SpA was not confirmed: 11 had a viral infection (13,5%), 7- bacterial infection (8,6%), 1 (1,2%)-multiple sclerosis, 3 (3,7%) -psoriasis, 59 (72.8%) -idiopathic AU.

RESULTS: Complications were identified in 74 of 110 (67.3%) eyes in SpA-group and in 39 of 81(48,1%) – 110 eyes in group without SpA. Cataract was identified in 89 (60,5%) of 147 eyes in SpA-group and in 35(1,8%) of 110 eyes in group without SpA, p=0,0001;glaucoma – in 24(16,3%) and in 8 (7,3%) of 110 eyes in group with SpA respectively, p=0,021;vitreous detachment - in 59(40,1%) and in 26 (23,6%), p=0,005. Maculopathy, optic atrophy, corneal degeneration, panuveitis were observed more often in SpA-group, but the differences were not significant. Combinations of several complications were detected in 59 (40,1%) in SpA-group and in 31 (28,2%) in group without SpA, p=0,03.

Conclusion: Women with SpA have higher RAPID3 scores than men, in contrast to a modified ASDAS-CRP based on scores from the MDHAQ which did not show gender differences. These data suggest that RAPID3 scores in women may be attributable in part to a gender bias rather than clinical severity and a careful interpretation in the context of gender is necessary.

REFERENCES:
AXIAL SPONDYLOARTHRITIS INDUCES MUSCLE DISFUNCTION, THE ROLE OF BODY COMPOSITION PARAMETERS: MYOSPA STUDY

Maria Luisa Sequeira1, Inês Da Costa Santos2, Rita Amador1, Lucia Domingues1, Carolina Crespo1, Santiago Rodrigues-Manica1, José Ribeiro1, Andreia Sepeirano1, Diana Teixeira1, Agena Neto1, Rita Pinheiro Torres1, Conceição Calhau1, Jaime Branco1, Fernando Pimentel Dos Santos1, NOVA University of Lisbon, CEDOC NOVA Medical School | FCM, Lisboa, Portugal. 1Leiden University Medical Center, Rheumatology, Leiden, Netherlands. 2CHLO, Hospital de Egas Moniz, Rheumatology Department, Lisboa, Portugal

Background: Sarcopenia as well as abnormalities in body composition are common features in several chronic diseases and have been shown to lead to increased morbidity and mortality. However, their assessment in young patients with axial spondyloarthritis (axSpA) has not been performed thus far.

Objectives: To assess the skeletal muscle mass, strength and performance as well as body composition in patients with axSpA compared to healthy controls.

Methods: Patients between 18 and 50 years of age with the diagnosis of axSpA and short disease duration (under 10 years) and classified as male (34%) and type 1 back (2%). Spinal deformities were more frequent in women (p=0.004) and associated with a longer duration of the disease (p<0.0001) and a longer duration before initiation of treatment (p<0.0001) (Table 1).

Conclusion: Our study showed that the EOS system was a useful technique in assessing pelvic and spinal stature in patients with SA.

Table 1. Association of the spinal deformities with clinical parameters.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Spinal deformities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex</td>
<td>p=0.004</td>
</tr>
<tr>
<td>Age</td>
<td>p=0.126</td>
</tr>
<tr>
<td>Duration of the disease</td>
<td>p&gt;0.0001</td>
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<tr>
<td>Active disease</td>
<td>p=0.233</td>
</tr>
<tr>
<td>Axial spondyloarthritis</td>
<td>p=0.146</td>
</tr>
<tr>
<td>Duration before treatment</td>
<td>p=0.0001</td>
</tr>
</tbody>
</table>

Disclosure of Interests: None declared


THU0403

AXIAL SPONDYLOARTHRITIS INDUCES MUSCLE DISFUNCTION, THE ROLE OF BODY COMPOSITION PARAMETERS: MYOSPA STUDY

THU0404

DICKKOPF-1 SERUM LEVELS AND THEIR CORRELATION WITH ACTIVE AND CHRONIC MRI-CHANGES OF SACROILIAC JOINTS AND CLINICAL INDICES IN PATIENTS WITH SPONDYLOARTHRITIS

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Background: The lack of valid biochemical markers for spondyloarthritis (SpA) patients requires searching the additional options to increase sensitivity of clinical and radiological methods in validation of changes in sacroiliac joints (SI). The molecular basis for the link between inflammation and new bone formation in SpA is still not clear. It has recently been shown that low serum levels of the Dickkopf-1 (Dkk-1), the natural inhibitor of Wnt protein, is associated with the formation of new syndesmophytes in patients with SpA [1]. Dkk-1 may be a main factor in blocking new bone formation [2], and might play a role of potential biomarker in SpA patients.
**THU0404**

**PREVALENCE OF FIBROMyalGIA IN INFLAMMATory BOWEL DISEASE (IBD) PATIENTS: A SINGLE CENTRE OBSERVATIONAL PROspective STUDY**

Ilaria Tinazzi¹, Angela Variol², Andrea Ceccherle³, Antonio Marchetta³

Dennis McGonagle³.

1Sacro Cuore Hospital, Unit of Rheumatology, Negrar Verona, Italy; 2Sacro Cuore Hospital, IBD Unit, Negrar Verona, Italy; 3NIHR Leeds Musculoskeletal Biomedical Research Unit, Leeds Teaching Hospitals Trust and The University of Leeds, Leeds, United Kingdom

**Background:** Joint pain is frequently reported by IBD patients and can be associated to extra-intestinal manifestations of diseases or adverse events associated to anti-TNF or vedolizumab therapy and also associated with other non-SpA-disease related factors including mechanical/degenerative problems. The appropriate rheumatological referral pathway is crucial to drive therapeutic strategy in case of concomitant spondyloarthritis (SpA). Fibromyalgia is a frequent cause of chronic pain that needs to be identified in order to not overestimate the prevalence of SpA in IBD patients.

**Objectives:** The aim of the study was to assess the prevalence of FM in a cohort of IBD outpatients.

**Methods:** Consecutive patients of the IBD Unit coming for a routine visit were screened by a rheumatologist in order to identify cases presenting the 2010 ACR criteria for FM or ASAS criteria for SpA. Patients affected by other rheumatic conditions such as rheumatoid arthritis and crystal arthropathies were excluded from the study. The rheumatological assessment included a 26 swollen joint count (SJC) and 6 TJC, MASEI, LEI and the fibromyalgia tender points examination. The patient completed BASDAI and BASFI on the day of clinical evaluation. Imaging exams (MSK ultrasound, MRI) and HLA-B27 determination were requested if needed for diagnostic confirmation.

**Results:** Between January to May 2018, 210 patients were enrolled in the study and 181 completed the clinical and imaging/laboratory assessment. A total of 44 patients (24.3%) in the IBD cohort met the ACR 2010 criteria for FM, 34 patients (18.8%) met the criteria for primary FM, and 10 patients (5.5%) presented FM and SpA. Of note, FM patients presented LEI; BASDAI and BASFI scores higher than SpA patients.

**Conclusion:** FM is a common comorbidity in IBD patients and can be associated to SpA. An appropriate rheumatological referral is crucial to exclude a concomitant SpA and to manage FM.

**REFERENCES:**


**Disclosure of Interests:** Ilaria Tinazzi: None declared, Angela Variola: None declared, Andrea Ceccherle: None declared, Antonio Marchetta: None declared, Dennis McGonagle Consultant for: Lilly, Novartis UCB, Speakers bureau; Lilly, Novartis UCB.

**DOI:** 10.1136/annrheumdis-2019-eular.5847

**THU0406**

**ULTRASONOGRAPHIC INVOLVEMENT OF THE ANTERIOR CHEST WALL IN SPONDYLOARTHITIS, A FIVE YEARS FOLLOW UP STUDY**

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**Background:** Spondyloarthritis is characterized by inflammatory back pain. Anterior chest wall pain is common and a previous study reports a prevalence à 37% of ultrasonographic lesions of this anatomical region [1].

**Objectives:** The objective of this study is to evaluate, in patient with Spondyloarthritis, the prevalence of ACW ultrasonographic lesions after a follow up of 5 years and to identify factors associated with the development of new lesions.

**Methods:** This is a monocentric and prospective study including patients with Spondyloarthritis meeting the ASAS 2009 criteria. Patients were followed during five years. ultrasound B mode and power Doppler examination of the two sternoclavicular joint and the manubrio-sternal joint were performed by the same two examiners at baseline and five years later. The presence of erosion, synovitis, ankylosis, power Doppler signal, joint effusion and bone margin narrowing were assessed. Clinical characteristics and disease activity were evaluated at 5 years.

**Results:** In the 136 patients at baseline, 58 patients were evaluated 5 years later. The mean age was 48.2 +/- 11.9 years old, with 86% male and 89% HLA B27. 60.3% of these patients had a history of pain of the ACW. The prevalence of ultrasonographic involvement of the ACW was 34% at baseline and 67.2% five years later. The most frequent lesions were ankylosis of the manubriotelial joint (38%) and erosions of the sternoclavicular joint (29%). At 5 years, patients with lesions of the ACW are significantly older (51.4 +/- 11.5 VS 41.5 +/- 9.98, p<0.01). There were no differences concerning the presence of HLA B27 and the presence of a radiographic sacroiliitis or syndesmophytes. Among these 58 patients, 31 (53%) developed a new lesion of the ACW. There is a statistically significant association between a higher ASAS CRP and new lesions of the ACW (1.56 +/- 1.07 VS 3.0 +/- 2.17 p < 0.001) and with the level of CRP (5.34 +/- 7.85 VS 16.2 +/- 35, p = 0.035). Baseline ASAS CRP is not a predictor of new chest wall lesions prior to 5 years of age. Nevertheless, poor control of disease activity is associated with the development of new lesions. Patients with new lesions have an ASAS CRP score that increase (0.882 +/- 2.48) between 2013 and 2018, while patients with no new lesions have an ASAS CRP score that decrease (-0.641 +/- 1.50) between 2013 and 2018.

**Conclusion:** The prevalence of ultrasonographic lesions of the ACW increased after 5 years of follow up. The development of new lesions is associated with a higher disease activity, a higher CRP and an increased disease activity over 5 years.

**REFERENCES:**

THU0408

ACHIEVING DISEASE REMISSION IN AXIAL SPONDYLARTHROPATHY: A TWO-CENTRE RETROSPECTIVE ANALYSIS OF RELEVANT BASELINE PATIENT CHARACTERISTICS

Thomas Williams 1, Karl Gaffney 2, Alison Waleyde 2, Charlotte Cavill 1, Mandy Freeth 1, Alan Brooksby 3, Raj Sengupta 1. 1 Royal National Hospital for Rheumatic Diseases, Bath, United Kingdom; 2 Norfolk and Norwich University Hospital, Norwich, United Kingdom; 3 Bath Spa University, College of Liberal Arts, Bath, United Kingdom

Background: ASAS-EULAR Axial Spondyloarthritis (AxSpA) guidelines recommend that AxSpA treatment should be guided according to a predefined target 1, following increasing evidence that persistent, uncontrolled inflammatory disease activity results in long-term damage and poor outcomes 2-3. Despite this, there remains no single definition for ‘remission’ in AxSpA.

Objectives: To identify baseline characteristics of individuals achieving AxSpA disease ‘remission’ 6 months after initiation of biologic disease-modifying therapy (bDMARD).

Methods: A two-centre retrospective cross-sectional analysis was performed, of AxSpA patients receiving their first bDMARD at the Royal National Hospital for Rheumatic Diseases, Bath, and Norfolk and Norwich University Hospital, Norwich. AxSpA ‘remission’ was defined as Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) <1; Bath Ankylosing Spondylitis Functional Index (BASFI) <3.8 or serum C-reactive protein (CRP) <5. A non-parametric (2-tailed Chi-Square) test was applied to identify differences in baseline characteristics which distinguished those patients achieving ‘remission’ after 6 months bDMARD treatment from others.

Results: 538 patients were included. Sufficient BASDAI data was available for 440, CRP data for 448 and BASFI data for 354. Overall, 42 (9.5%) patients achieved BASDAI <1; 275 (61.4%) achieved CRP <5 and 206 (58.2%) achieved BASFI <3.8. The differences in baseline characteristics of individuals achieving these AxSpA ‘remission’ outcomes compared with others are summarised in Table 1, with statistically significant results at the 95% level highlighted.

Abstract THU0408 – Table 1. p-values of 2-tailed non-parametric test comparing baseline characteristics of individuals achieving AxSpA ‘remission’ outcomes after 6 months versus others.

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>p-values</th>
</tr>
</thead>
<tbody>
<tr>
<td>BASDAI &lt;1</td>
<td>N=275/448</td>
</tr>
<tr>
<td>Lower mean age at AxSpA diagnosis</td>
<td>0.04</td>
</tr>
<tr>
<td>Less mean time from diagnosis to bDMARD</td>
<td>0.56</td>
</tr>
<tr>
<td>Lower mean baseline BASDAI</td>
<td>0.35</td>
</tr>
<tr>
<td>Lower median baseline CRP</td>
<td>0.01</td>
</tr>
<tr>
<td>Lower median baseline BASFI</td>
<td>0.08</td>
</tr>
<tr>
<td>Lower median baseline BASMI</td>
<td>0.73</td>
</tr>
<tr>
<td>HLA B27+</td>
<td>0.21</td>
</tr>
<tr>
<td>Male sex</td>
<td>0.87</td>
</tr>
</tbody>
</table>

Conclusion: Our self-defined measures of BASDAI and CRP remission were most achievable in our cohort for patients with lower CRP and less functional limitation before bDMARD initiation. This may reflect remission being more achievable when treating milder disease. Functional ‘remission’ was influenced by baseline BASMI and BASDAI in our cohort, highlighting the importance of both disease activity and pre-existing structural damage on functional outcomes. Further work could include longitudinal follow-up of outcomes in these patients to establish the relevance of target achievement. ‘BASDAI remission’ was very narrowly defined in this study, and this analysis could be repeated with a more achievable target eg BASDAI <3.

REFERENCES:


THU0409

PATTERN AND INFLUENTIAL FACTORS IN PROMOTING TREAT-TO-TARGET (T2T) FOR FOLLOW-UP ANKYLOSING SPONDYLITIS (AS) PATIENTS WITHIN A RHEUMATIC DISEASE-PATIENT INTERACTIVE SMART SYSTEM OF DISEASE MANAGEMENT (SSDM): A COHORT STUDY FROM CHINA

Jing Yue 1, Hui Song 1, Jing Yang 1, Zhenchun Zhang 1, Li Hongbin 2, Junli Zhang 2, Zongzhou Huang 4, Wei Wang 5, Hua Wu 6, Li Yang 6, Li Zhijun 6, Lijun Liu 6, Yuhua Jia 6, Fei Xiao 6, Huaxiang Wu 6. SSDM Collaboration Group, China; 1 The Second Affiliated Hospital of Zhejiang University School of Medicine, Hangzhou, China; 2 Beijing Jishuitan Hospital, Beijing, China; 3 Central Hospital of MianYan, MianYang, China; 4 Linyi people’s Hospital, Linyi, China; 5 The Affiliated Hospital of Inner Mongolia Medical University, Huhehaote, China; 6 The First Affiliated Hospital of Anhui Medical University, Hefei, China; 7 The First Affiliated Hospital of The Fourth Military Medical University, Xi An, China; 8 Dongguang Donghua Hospital, Dongguan, China; 9 Beijing Hospital of Traditional Chinese Medicine (TCM), Beijing, China; 10 Jilin Jiangsu People’s Hospital, Yanzhou, China; 11 Zhejiang Provincial People’s Hospital, Hangzhou, China; 12 The First Affiliated Hospital of Bengbu Medical College, Bengbu, China; 13 Yong Liao City Hospital, Tongliao, China; 14 Shanghai Gothic Internet Technology Co., Ltd., Shanghai, China

Background: Ankylosing Spondylitis Disease Activity Score (ASDAS) is adopted to evaluate the degree of disease activity and the inflammatory response in AS patients. ASDAS score ≤ 1.3 represents inactive disease status and achievement of T2T.

Objectives: To evaluate the patterns of T2T and related influential factors among AS patients after applying SSDM in the real world.

Methods: SSDM is a mobile application for disease management. Patients were trained to master SSDM by healthcare professionals and to conduct ASDAS self-assessments. Patients were also required for repeating self-evaluation after leaving the hospital. After entry by patients, data can be synchronized to the SSDM terminal of authorized rheumatologists.

Results: From Jan 2015 to Jan 2019, 667 AS patients across China were followed up for more than 6 months through SSDM. The results at baseline and in final follow up were summarized in Table 1. The rate of T2T achievers were 28.49% (190/667) at baseline, and improved significantly to 41.38% (276/667) after 6 months follow up, p<0.01. Among T2T achievers at baseline, 64.21% (122/190) maintained T2T, 35.79% (68/190) relapsed. Of patients who didn’t achieve T2T at baseline, only 32.29% (154/477) of the other AS patients achieved T2T after 6 months follow up. We further analyzed the impact of the times of self-assessment for ASDAS on T2T. The patients were stratified according to their frequency of self-assessment: more than 3 times, less than or equal to 3 times. After adjusting for 6 months follow-up. Results show that the more frequent of the self-assessment, the higher improvement of T2T rate than others. Significance analysis of variables in three times of self-assessment and parameter estimation was conducted by least square method. The improvement of T2T rate(y) was positively correlated with times of self-assessment for ASDAS(x) independently (Figure 1).

Conclusion: Significant improvement was observed under applying SSDM through empowering AS patients. After proactive disease management via SSDM for more than 6 months, Patients with ASDAS≥1.3 score at baseline had a significantly higher retention rate of disease activity. The patients who performed more self-assessments through SSDM had lower probability of relapse and higher rate of T2T. SSDM is a valuable tool for long term follow-up through empowering patients.
UVEITIS RELATED FACTORS IN PATIENTS WITH SPONDYLOARTHRITIS

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Background: Uveitis is the most common extra-articular feature of spondyloarthritis (SpA). Sometimes uveitis may be the only clinical finding of SpA leading to diagnosis. In the current literature, there is information about frequency and characteristics of uveitis in SpA patients; however, factors associated with uveitis are not clear.

Objectives: Our aim in this study was to analyze uveitis-related factors in a large cohort of SpA patients.

Methods: This multicenter, prospective observational cohort study used the TReasure database in which web-based registration of rheumatoid arthritis and SpA patients are being performed in 15 centers across different regions of Turkey. Age, gender, duration of illness, delayed onset, SpA clinical findings, HLA B27 and acute phase responses (erythrocyte sedimentation rate and C-reactive protein, BASDAI and BASFI values, clinical findings and direct X-ray findings of SpA patients with and without uveitis were retrospectively evaluated.

Results: As of January 2019, there were 4557 registered SpA patients. Overall, 491 (10.8%) patients had experienced one or more episodes of uveitis. The median (Q1-Q3) uveitis onset age was 46 years (38-53 years) and the median (Q1-Q3) uveitis attack number was 2 (1-4). Uveitis was usually unilateral (74.2%). Records of eye damage was available in 373 patients, of whom 45 (12.1%) had permanent damage in the eye. Patients with permanent eye damage had more frequent uveitis attack (3 (2-6)) vs. 2 (1-3), p=0.003) and had tendency of bilateral uveitis attack (41.5% vs 24%, p=0.017).

Duration between the first uveitis attack and onset of SpA symptoms was 68 months (7-141). On the other hand, the mean duration between the first uveitis attack and SpA diagnosis is 7 months (17-68 months). In 320 (70%) patients, uveitis was diagnosed before the onset of SpA symptoms and 52% (n=240) of the patients had uveitis before SpA diagnosis.

Demographic and clinical features of the patients are given in Table 1.

Conclusion: In our cohort, genetic background, radiographic severity, and disease duration may be related with uveitis. HLA B27 positivity and family history may be risk factors for development of uveitis. First attack of uveitis is nearly always before the onset of symptoms and diagnosis of SpA. Although uveitis is usually self-limited; however, almost 10% of SpA patients may have permanent eye damage. Thus, patients with uveitis should be carefully investigated because it may be the diagnostic feature of SpA.

Disclosure of Interests: None declared

Background: Delayed diagnosis in patients with axial spondyloarthritis (AxSpA) has been shown to negatively impact disease prognosis and contribute to worse economic and quality of life outcomes; however, there is limited evidence available regarding the association of delayed diagnosis of AxSpA with the comprehensive burden of disease.

Objectives: To identify and summarize current published literature evaluating the clinical, economic, and humanistic burden associated with delayed diagnosis in patients with AxSpA.

Methods: This systematic literature review was conducted and reported according to the PRISMA guidelines (Figure 1).1 Publications were retrieved from the MEDLINE®, Embase® and Embase databases. English-language publications of original research articles (up to July 12, 2018) and conference abstracts (2014 to 2018) reporting studies of delayed diagnosis of adult patients with AxSpA associated with clinical, economic, or humanistic burden were eligible for inclusion. Abstracts from all records retrieved from the literature search were screened by two independent reviewers (first-level screening) (Table 1). Patents with delayed diagnosis of AxSpA generally had worse clinical outcomes, including higher disease activity (Bath Ankylosing Spondylitis Disease Activity Index), poorer mobility and physical function (Bath Ankylosing Spondylitis Functional Index), and more structural damage, compared with patients who had an earlier diagnosis (Table 1). Patients with delayed diagnosis also had higher healthcare costs, including costs of unnecessary treatments, and greater likelihood of work disability compared with those who had an earlier diagnosis (Table 1). Delayed diagnosis was associated with worse quality of life, including greater likelihood for depression and negative psychological impact (Table 1).

Conclusion: Delayed diagnosis in patients with AxSpA demonstrated a decrease in physical function, higher direct and indirect costs, and poorer quality of life. This study highlights the importance of early recognition and diagnosis of AxSpA in order to improve outcomes and mitigate extensive burden on patients and society. Therefore, further efforts by the healthcare community are warranted to increase awareness of early signs of disease and reduce the delay in diagnosis of AxSpA.

Table 1

<table>
<thead>
<tr>
<th>Study</th>
<th>Delayed Diagnosis</th>
<th>Clinical Burden</th>
<th>Economic Burden</th>
<th>Humanistic Burden</th>
</tr>
</thead>
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<td>High</td>
<td>High</td>
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<tr>
<td>Study 2</td>
<td>No</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>Study 3</td>
<td>Yes</td>
<td>High</td>
<td>High</td>
<td>Low</td>
</tr>
</tbody>
</table>

Abstract THU0411 - Figure 1

REFERENCE:

Acknowledgement: This study was sponsored by Novartis Pharmaceuticals Corporation, East Hanover, NJ.
1 and STT joints were assessed for synovitis (0-3) and bone marrow lesions (BMLs; 0-6 and 0-9, respectively). Radiographs were assessed for the presence of osteophytes in CMC-1 and STT joints following the OARSI atlas by two readers. Since pain was assessed for the TB as a whole, imaging scores of CMC-1 and STT joints were combined, comparing no change in both joints (i.e. ‘stable’) versus change in at least one joint. In TBs without maximum baseline pain, associations between increase in MRI features and increase in TB pain were investigated using logistic regression, presented as odds ratios (ORs) with 95% confidence intervals (CIs). Similarly, in TBs with pain and MRI features present at baseline, associations between decrease in imaging features and decrease in TB pain were investigated.

Results: Out of 161 patients (82.6% women, mean age 60.8 years, 91.3% fulfilling ACR hand OA criteria) 64 had TB pain at baseline (of whom 11 with maximal score). At the two-year follow-up visit, pain had decreased in 31 patients and increased in 33 patients. The majority had stable synovitis (n=106) and BML (n=96) scores over two years, although decreased (n=22, n=26, resp.) and increased (n=29, n=36, resp.) scores were common. Increase in radiographic osteophytes was rarely (n=10) observed. Increase in synovitis or BML was associated with increased pain, also after adjusting for baseline osteophyte status (Table). A decrease in BML was associated with a decrease in pain, although it did not reach statistical significance. Presence of osteophytes on baseline radiographs was weakly associated with change in pain in univariate analyses and attenuated when adjusting for the change in MRI features. Decrease of synovitis in patients with baseline pain was scarce (n=7), therefore ORs were not computed.

Conclusion: In this cohort of hand OA patients, thumb base pain levels varied over the course of two years in approximately forty percent of patients. Changes in MRI-defined synovitis and BMLs of the TB joints were positively associated with change in pain on palpation. Baseline osteophytes were not significantly associated with change in pain. While cross-sectionally MRI-defined inflammation may be a less important determinant of pain than radiographic damage, this study shows that a change in inflammatory features may indeed be relevant.

Disclosure of Interests: Sjoerd van Beest: None declared, H.M. Kroon: None declared, Monique Reijnierse Grant/research support from: Funding from the Dutch Arthritis Foundation. The funding source had no role in the design and conduct of the study., Frits Rosendaal: None declared, Margreet Klöppenburg Grant/research support from: Pfizer, IMI-APPROACH (Grant Agreement n° 115770), Consultant for: GlaxoSmithKline, Merck-Serono, Abbvie, Levicetix, Pfizer, Félize P.B. Kroon: None declared DOI: 10.1136/annrheumdis-2019-eular.1593

REFERENCES:

THU0414  COMPARISON OF INTRA-ARTICULAR SHAM AND VEHICLE INJECTIONS FROM A PHASE 2B TRIAL OF SM04690, A SMALL-MOLECULE WNT PATHWAY INHIBITOR FOR KNEE OSTEOARTHRITIS

Yusuf Yazici1, Jeyanesh Tambiah1, Christopher Swearengen1, Sarah Kennedy1, Vibeke Strand2, Brian Cole3, Marc Hochberg4, Raveendhara Bannuru2, Timothy McAlindon5, 1Samumed, LLC, San Diego, United States of America; 2Stanford University School of Medicine, Stanford, United States of America; 3Rush University, Chicago, United States of America; 4University of Maryland, Baltimore, United States of America; 5Tufts Medical Center, Boston, United States of America

Background: Intra-articular (IA) saline, commonly used as a placebo (PBO) comparator in knee osteoarthritis (OA) trials, has consistently shown improvements from baseline in patient-reported outcomes (PROs). These effects have been attributed to contextual and/or physiological benefits of saline, thus causing interpretation of potential IA therapeutics trial results to be questioned.1,2

Objectives: A prospective, randomized, controlled, 24-week phase 2b study compared effects of vehicle PBO to sham and SM04690 (an IA Wnt pathway inhibitor in development as a potential disease-modifying knee OA drug (DMOAD)) injections. Potential unblinding impact of PBO or sham was also tested. Primary study results are presented separately.

Methods: Knee OA subjects with Kellgren-Lawrence (KL) grades 2-3 and Pain Numeric Rating Scale (NRS) ≥4 and ≥8 in the target knee and <4 in the contralateral knee were randomized to receive a single blinded IA injection of 2 mL vehicle (PBO, 0.5% carboxymethylcellulose sodium, 0.05% polysorbate 80 in pH 7.4 saline), sham (dry needle), or SM04690 in the target knee on Day 0. PROs included change from baseline in weekly average of daily pain in the target knee by NRS, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain, WOMAC Physical Function, and Patient Global Assessment (PGA). Subjects were asked which treatment assignment they thought they received; their accuracy was compared using Bang’s Blinding Index (BBI), a method used to evaluate blinding across clinical trial treatment arms. The index scale is -1 < 0 < +1, with values toward -1 indicating more subjects incorrectly guessing treatment allocations, toward 0 indicating perfect blinding, and toward +1 indicating more subjects correctly identifying treatment allocations.

Results: In the full analysis set of PBO and sham subjects (N=233; 207 [89%] completed), both groups showed clinically relevant improvements in the full analysis set of PBO and sham subjects (N=233; 207 [89%] completed), both groups showed clinically relevant improvements from baseline at first measurement that persisted [89%] completed), both groups showed clinically relevant improvements from baseline at first measurement that persisted.

Conclusions: Subjects with knee OA receiving a single IA injection of PBO reported no differences in changes from baseline in knee OA PROs compared to subjects who received sham injections. These data suggested the effects were “contextual,” meaning they resulted from the injection procedure, rather than from direct therapeutic effects of PBO or saline in the joint.

REFERENCES:

THU0415  EXPLORATORY PROTEIN PROFILING OF HUMAN SYNOVIAL FLUID FROM KNEE OSTEOARTHRITIS

Neserin Ali1, Jon Tjörnstrand2, Paul Neuman2, Elin Folkeson1, Velocity Hughes1, Patrik Onnerfjord1, Martin Englund1, 1Lund University, Lund, Sweden; 2Skåne University Hospital, Lund, Sweden

Background: There is a lack of valid and robust biomarkers in the field of OA diagnosis, prognosis, and treatment evaluation [1]. Synovial fluid is in direct contact with articular cartilage, ligament, meniscus and joint capsule it is therefore an excellent sample to explore the protein profile in which could provide pathogenesis information from several surrounding parts.

Objectives: The aim with this project was to perform mass spectrometry (MS) of human synovial fluid using a global discovery approach, to identify biomarker candidates associated with meniscus degradation and/or knee OA.

Methods: Synovial fluid was sampled from 3 different subject groups: i) end-stage medial compartment knee OA patients undergoing arthroplasty (n=11, age range 55-80 years), ii) knee arthroscopy patients who typically had a degenerative meniscal tear (n=7, age range 50-64 years), and iii) deceased human donors without known chronic knee disease (n=13, age range 19-79 years). All synovial fluids were centrifuged and freshly frozen and stored at -80°C. For the analysis, 50 μL of synovial fluid was mixed with MS-safe protease inhibitor cocktail, hyaluronidase, depleted, reduced, alkylated, precipitated, digested with sequencing grade trypsin (Promega), filtered and desalted. The samples were further analyzed with an EASY-nLC 1000 coupled to an Orbitrap Fusion mass spectrometer.

Figure: Observations over time depicting mean improvements (± 95% CI) of PBO compared to sham injection adjusted for baseline. A. Pain NRS, B. WOMAC Pain, C. WOMAC Function, and D. Patient Global; in all subjects.


using data-independent acquisition. The raw MS data were further analysed with Spectronaut™ for protein identification and quant data extraction. Differences in protein levels were analyzed in two steps: 1) Donors vs arthroplasty 2) Between all 3 different groups. Analyses were adjusted for age, gender and weight. Differentially expressed proteins between the groups were clustered using Pearson correlation coefficient as the distance metric.

Results: In total, 529 proteins were identified in the 31 different synovial fluid samples analyzed. Principal component analysis suggested a profound difference between the protein profiles of synovial fluid from donors vs arthroplasty patients, while the arthroscopy group had a protein profile that was in-between donors and the arthroplasty group (Figure 1A). Statistical differential analysis yielded significant differences in the levels of 43 proteins comparing donors vs arthroplasty patients. 36 proteins differed between the 3 groups when comparing all groups in the same statistical model. Extracellular matrix proteins like collagens and aggrecan showed higher expression in donors than in arthroplasty patients. Collagen on the other hand was higher in arthroscopy patients compared to donors. Decorin was significantly higher in donors compared to both arthroscopy and arthroplasty patients. The differentially expressed proteins associated with the inflammatory response were higher in the arthroscopy group compared to both donors and arthroplasty patients. Generally, extracellular matrix proteins like collagens and aggrecan showed higher expression in donors than in arthroplasty patients. Collagen on the other hand was higher in arthroscopy patients compared to donors. Decorin was significantly higher in donors compared to both arthroscopy and arthroplasty patients. The differentially expressed proteins associated with the inflammatory response were higher in the arthroscopy group compared to both donors and arthroplasty patients. Generally, extracellular matrix proteins like collagens and aggrecan showed higher expression in donors than in arthroplasty patients. Collagen on the other hand was higher in arthroscopy patients compared to donors. Decorin was significantly higher in donors compared to both arthroscopy and arthroplasty patients. The differentially expressed proteins associated with the inflammatory response were higher in the arthroscopy group compared to both donors and arthroplasty patients. Generally, extracellular matrix proteins like collagens and aggrecan showed higher expression in donors than in arthroplasty patients. Collagen on the other hand was higher in arthroscopy patients compared to donors. Decorin was significantly higher in donors compared to both arthroscopy and arthroplasty patients. The differentially expressed proteins associated with the inflammatory response were higher in the arthroscopy group compared to both donors and arthroplasty patients. Generally, extracellular matrix proteins like collagens and aggrecan showed higher expression in donors than in arthroplasty patients. Collagen on the other hand was higher in arthroscopy patients compared to donors. Decorin was significantly higher in donors compared to both arthroscopy and arthroplasty patients.

Conclusion: There is a profound difference in the protein profile of synovial fluid in donors vs knee OA patients (Figure 1). The inflammatory response seems to be higher in the early stages of OA than in later stage. Our findings emphasize the importance of OA staging in the development and use of biomarkers.

REFERENCE:
HOA cohort showed a positive association between soft tissue swelling, tenderness upon pressure with pain and radiographic progression.6

Objectives: To identify new prognostic factors and to confirm existing evidence on already identified prognostic factors for radiographic progression in HOA.

Methods: All 270 patients from this cohort were contacted to participate in a second follow-up visit after ten years at the Ghent University Hospital. A total of 106 patients consented to this follow-up visit. Presence of tender and swollen joints was assessed. Grip strength was measured. Functional Index for HOA (FIHOA) and Australian/Canadian OA Index questionnaires (AUSCAN) were completed by the patients. Pain was scored on a visual analogue scale from 0-100mm (VAS pain). Radiographs of hands were taken and scored using the anatomical phase scoring system for HOA by Verbruggen and Veys5. Patients were defined as radiographic progressor when two or more joints progressed to another phase within the scoring system, except for N-phase to S-phase. Logistic regression was performed on the clinical data and outcomes such as presence of tenderness (yes or no), soft tissue swelling (yes or no), VAS pain, disease duration, FIHOA and AUSCAN. VAS pain was dichotomized into two groups: VAS ≤33mm and VAS >33mm. Disease duration was dichotomized in ≤5 years and >5 years; p-values and odds ratios (OR) with 95% confidence intervals (95% CI) were calculated.

Results: After a mean follow-up of 9.7 years, 73.3% of the patients showed radiographic progression. The following clinical factors were associated with radiographic progression on patient level (OR [95%CI]): presence of tenderness (4.19 [1.52-11.61]), presence of soft tissue swelling (2.73 [1.08-6.92]) and disease duration > five years (4.00 [1.50-10.66]). Other outcomes were retained as prognostic factors for radiographic progression (OR [95%CI]): VAS pain (1.02 [1.00-1.04], total FIHOA (1.12 [1.03-1.23]), total AUSCAN (1.02 [1.01-1.04] and AUSCAN pain (1.07 [1.02-1.12], AUSCAN function (1.03 [1.01-1.06]) and VAS pain > 33mm (2.87 [1.14-7.24]). The mean number of E and R joints was 1.2 and 1.4 at baseline, and 0.2 and 0.5 after 10 years (p<0.001). The total number of joints that progressed to the E-phase and R-phase over a period of ten years was respectively 20 (1.05%) and 399 (21%).

Conclusion: Clinical presence of pain and soft tissue swelling at baseline remain strong predictors of radiographic progression in HOA after ten years. Tenderness upon pressure, moderate VAS pain and moderate impaired function at baseline are identified as new predictors. After ten years, more remodelling and less erosive joints are seen.

REFERENCES:

Disclose of Interests: None declared

THU0417 – THE SEVERITY OF STRUCTURAL AND INFLAMMATORY FEATURES OF HAND OSTEOARTHRITIS ASSOCIATE WITH PERIPHERAL PAIN SENSITIZATION

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Background: Increased sensitivity to pain in the area around joints with osteoarthritis (OA), i.e., peripheral sensitization, is associated with higher pain severity. The mechanisms underlying peripheral sensitization in hand OA have not been substantially explored in previous studies.

Objectives: We aimed to explore whether the severity of structural or inflammatory OA features in the distal and proximal interphalangeal (DIP/PIP) joints were associated with lower pressure pain thresholds (PPT) at the same joint in a large study sample of persons with hand OA.

Methods: In these cross-sectional analyses we included 277 persons with hand OA from the Nor-Hand cohort. All participants underwent radiographic and ultrasound examination (GE S8, ML 6-15MHz probe) of both hands. Pressure pain threshold (PPT) was tested with a hand-held algometer (FPX025, 1cm² flat rubber probe) in perpendicular position at the dorsal side of the DIP/PIP joint reported to be the most painful. Information about demographics and psychosocial factors was collected with questionnaires. We examined whether increasing radiographic severity (Kellgren-Lawrence 0-4 score) and ultrasound-detected inflammation (grey-scale synovitis 0-3 score and presence of power-Doppler activity) were associated with PPT at the same joint. We conducted separate analyses of linear regression with adjustments for age, sex, BMI, education level, use of analgesics, sleep disturbance, the Pain Catastrophizing Scale and the Hospital Anxiety and Depression Scale.

Results: The majority of the study population were women (89%), median age was 61 (IQR 57-66) years, mean BMI was 26.3 (SD 4.6) kg/m² and mean duration of hand OA symptoms was 6 (IQR 3-13) years. The DIP/PIP joints demonstrated a wide range of PPT (mean [SD] 3.9 [1.9], range 0.6-11.4 kg/cm²) and OA severity (Table). We found that both increasing radiographic severity and inflammation were associated with lower PPTs (Table). When including grey-scale synovitis and power Doppler as confounders in analysis of radiographic severity, the results became weaker but remained significant (Table).

Abstract THU0417 – Table 1. Associations of structural and inflammatory OA features of DIP/PIP joints to pressure pain thresholds at the same joint, n=277.

<table>
<thead>
<tr>
<th>Radiographic severity (Kellgren-Lawrence)</th>
<th>PPT (SD), kg/cm²</th>
<th>Adjusted beta (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 0 (n=63)</td>
<td>4.5 (1.9)</td>
<td>0.0 (ref.)</td>
</tr>
<tr>
<td>Grade 1 (n=39)</td>
<td>4.3 (1.8)</td>
<td>-0.4 (-1.1, -0.03)</td>
</tr>
<tr>
<td>Grade 2 (n=61)</td>
<td>4.6 (2.2)</td>
<td>-0.1 (0.7, 0.6)</td>
</tr>
<tr>
<td>Grade 3 (n=54)</td>
<td>3.2 (1.6)</td>
<td>-1.5 (-2.2, -0.8)</td>
</tr>
<tr>
<td>Grade 4 (n=60)</td>
<td>2.9 (1.2)</td>
<td>-2.0 (-2.6, -1.3)</td>
</tr>
</tbody>
</table>

p for trend <0.001 *<0.001

Grey-scale synovitis
Grade 0 (n=155) | 4.3 (2.0) | 0.0 (ref.) |
Grade 1 (n=56)  | 3.8 (2.0) | -0.6 (-1.2, -0.1) |
Grade 2 (n=42)  | 3.3 (1.2) | -1.1 (-1.8, -0.4) |
Grade 3 (n=24)  | 2.6 (1.5) | -1.7 (2.5, -0.9) |

p for trend <0.001

Power Doppler
Grade 0 (n=266) | 4.3 (2.1) | 0.0 (ref.) |
Grade 1.3 (n=14) | 3.0 (1.3) | -1.3 (-1.8, -0.9) |

Adjusted for age, sex, BMI, analgesics, education, sleep disturbance, the Pain Catastrophizing Scale and the Hospital Anxiety and Depression Scale. *Additional adjustments for grey-scale synovitis and power Doppler.

Conclusion: Both structural and inflammatory hand OA features in DIP/PIP joints were associated with lower pressure pain thresholds, i.e. pain sensitization, at the same joint. Our results suggest that peripheral sensitization might be driven by structural and inflammatory features, and that targeting the disease early might prevent peripheral sensitization and reduce pain.

Disclosure of Interests: None declared
THU0418 NEUROPATHIC-LIKE PAIN IN PERSONS WITH HAND OSTEOARTHRITIS AND ASSOCIATIONS WITH PERIPHERAL AND CENTRAL SENSITIZATION

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Background: Despite no current knowledge of lesions or disease of the sensory nervous system in osteoarthritis (OA), subgroups of knee OA patients report neuropathic-like pain. The neuropathic-like pain component has been suggested to reflect central sensitization.

Objectives: To describe the prevalence of neuropathic-like pain in persons with hand OA and explore whether neuropathic-like pain associate with peripheral and/or central sensitization.

Methods: These cross-sectional analyses included 280 participants with hand OA from the Nor-Hand study. A modified PainDETECT questionnaire was used to characterize neuropathic-like hand pain (mPD-hand, 0-36 scale). We conducted quantitative sensory testing (QST) of pressure pain thresholds (PPT) and temporal summation (TS). Low PPTs at local sites (painful finger joint and non-painful finger joint) indicate peripheral and/or central sensitization, while low PPTs at extra-segmental sites (radionuclar joint, musculus trapezius and tibialis anterior) indicate central sensitization. TS, defined as an increase in pain ≥2 on a numeric rating scale (NRS) at 0-10 during a repetition of ten punctuate stimuli at the wrist, indicates central sensitization. Participants with painful hand OA (NRS of hand pain above the patient acceptable symptom score of >4), were categorized as having either nociceptive pain (mPD-hand ≤12) or neuropathic-like pain (mPD-hand score >12). We examined whether reporting nociceptive or neuropathic-like pain, as compared to no/mild pain (NRS hand pain below 4) was associated with QST results using regression analyses.

Results: In this study sample, 88% were female, median age was 61 (IQR 57-66) years and 94% fulfilled the ACR criteria for hand OA. Median mPD-hand score was 8 (IQR 3, 13). Half of the participants (n=144, 51%) reported NRS pain ≥4, of whom 58% (40%) had neuropathic-like pain. Those with neuropathic-like pain reported higher mean (SD) NRS pain severity than persons with nociceptive pain (5.9 (1.6) vs 5.3 (1.5), p=0.01). We found that neuropathic-like pain was associated to higher pain sensitization reflected by lower PPT at the painful finger joint (Table), non-painful finger joint (β -1.1, 95% CI -2.3, -0.9), radionuclar joint (β -1.1, 95% CI -1.8, -0.4), trapezius (Table) and tibialis anterior (β -1.0, 95% CI -1.8, -0.2) and presence of TS (Table). The associations between neuropathic-like pain and QST were weaker than the association between nociceptive pain and sensitization were weaker than the association between nociceptive pain and sensitization.

Conclusions: In this study, the prevalence of neuropathic-like pain was 51% in hand OA. The presence of neuropathic-like pain was associated with decreased pain thresholds and increased pain sensitization.

THU0419 BIOMARKERS OF BONE AND CARTILAGE TURNOVER CTX-I AND CTX-II PREDICT TOTAL JOINT REPLACEMENTS IN OA

Jonathan Bierne-Bastos1, Anne-Christine Bay-Jensen2, Morte Mandel1, Inger Bjyrjallsen2, Jeppe Ragnar Andersen3, Bente Juel Riis2, Claus Christiansen1, Asger Reinsup Bihlet1. 1Nordic Bioscience, Clinical Development, Herlev, Denmark; 2Nordic Bioscience, Biomarkers and Research, Herlev, Denmark; 3Nordic Bioscience, Herlev, Denmark.

Background: Osteoarthritis (OA) can lead to joint failure and ultimately total joint replacement (TJR). Identifying risk-factors of developing joint failure is of interest for clinicians and researchers. Currently late-stage clinical trial design for new treatments in OA is evolving with the possible utilization of accelerated approval pathways. This may require outcome studies with longer duration, in which joint failures may qualify as an endpoint. However, TJRs are relatively rare events and are known to be biased by doctor/patient interactions as well as local practice guidelines, and consequently, there is a need for objective non-invasive measures, such as soluble biomarkers (BM), to enrich the population for this outcome. BM may act as important tools in investigating the association between biochemical/pathological processes and risk of joint failure. Destruction of collagen types I and II are known to be involved in OA disease progression, and the biomarkers CTX-I (C-telopeptide of crosslinked collagen type I), a marker of bone degradation, and CTX-II (C-telopeptide of crosslinked collagen type II), a marker of cartilage degradation, may reflect disease progression with clinical relevance for the risk of joint failure.

Objectives: To evaluate baseline (BL) BM sCTX-I and uCTX-II as predictors of TJR.

Methods: Data from two clinical trials investigating on salmon calcitonin (SNC) in OA, NCT00486434 and NCT00704847, was analyzed post-hoc. Data was dichotomized by the bottom and top quartile of the respective BM concentration at BL to compare the number TJRs of the knee or hip in groups with high vs. low sCTX-I or uCTX-II, respectively. For means of visualization, plotted in Kaplan-Meier curves. Cox Proportional Hazard Regression was performed to determine the association of BL sCTX-I and uCTX-II to the incidence of TJR while adjusting for co-variates; age, BMI, and gender. Data from both treatment groups were analyzed. Only the first reported incident was included in the analysis for each subject.

Results: A total of 68 TJRs of knee or hip were reported, of which 49 were knees and 18 were hips. One patient underwent two TJRs, resulting in 67 subjects with events.

Results from the Cox Proportional Hazard Regression adjusted for covariates of age, BMI, and sex (table 1), indicate that high BL sCTX-I compared to low was associated with a 3.4 times higher risk of undergoing an arthroplasty of the knee or hip within a two-year period (p=0.04). High BL uCTX-I compared to low was associated with a 3.1 times higher risk of undergoing a TJR of the knee or hip during the study period (p=0.04), and an 8.9-fold increased risk of undergoing a knee replacement during the study period (p=0.02). TJR events over time in groups of high or low uCTX-II through the study are illustrated in figure 1.

Abstract THU0418 –Table 1. Associations between neuropathic-like pain and quantitative sensory testing

<table>
<thead>
<tr>
<th></th>
<th>PPT painful finger joint1</th>
<th>PPT trapezius muscle2</th>
<th>Temporal summation3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (β/95% CI)</td>
<td>Mean (β/95% CI)</td>
<td>N(%) OR(95% CI)</td>
</tr>
<tr>
<td>No/Mild pain</td>
<td>4.3 (0.0) (ref.)</td>
<td>4.9 (0.0) (ref.)</td>
<td>43 (0.0) (ref.)</td>
</tr>
<tr>
<td>(n=136)</td>
<td>(2.1)</td>
<td>(2.1)</td>
<td>(32%)</td>
</tr>
<tr>
<td>Nociceptive pain</td>
<td>3.9 (-0.5, -1.0)</td>
<td>-0.6 (-1.1, 0.1)</td>
<td>35 (1.3, 0.7)</td>
</tr>
<tr>
<td>(n=146)</td>
<td>(1.7)</td>
<td>(1.0)</td>
<td>(41%, 2.4)</td>
</tr>
<tr>
<td>Neuropathic-like</td>
<td>2.9 (-1.2, -0.2)</td>
<td>-0.9 (-1.5, -0.2)</td>
<td>39 (1.8, 1.8)</td>
</tr>
<tr>
<td>pain</td>
<td>(n=58)</td>
<td>(1.4)</td>
<td>(67%, 8.2)</td>
</tr>
</tbody>
</table>

1Linear regression, 2logistic regression. Adjusted for age, sex, BMI, use of analgesics, level of education, sleep disturbance, Pain Catastrophizing Scale, the Hospital Anxiety and Depression Scale and radiographic hand OA severity (Kelgren-Lawrence score sum score).

Conclusion: Of persons with painful hand OA, 40% have a neuropathic-like pain component. Reporting neuropathic-like pain is associated with peripheral and central sensitization, indicated by low PPTs and presence of TS. Our results suggest that patients who report neuropathic-like symptoms are more likely to have sensitization and increased pain.

Disclosure of Interests: Pernille Steen Petersen: None declared, Tuhina Neogi: None declared, Marthe Glearsen: None declared, Karin Magnusson: None declared, Hilde Bernt Hammer Grant/research support from: AbbVie, Pfizer and Roche, Paid advisor for: AbbVie, Pfizer, UCB, Novartis, Roche, Speakers bureau: AbbVie, Pfizer, UCB, Novartis, Roche, Tore K. Kviën Grant/research support from: AbbVie, BMS, MSD, Pfizer, Roche and UCB, Consultant for: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celgene, Celntron, Eli Lilly, Hospira, Merck-Serono, MSD, Novartis, Oktal, Oniron Pharma, Pfizer, Roche, Sandoz, Sanofi, Mylan and UCBS, Speakers bureau: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celgene, Celntron, Eli Lilly, Hospira, Merck-Serono, MSD, Novartis, Oktal, Oniron Pharma, Pfizer, Roche, Sandoz, Sanofi and UCB, Till Uhlig Consultant for: Grünenthal, Novartis, Speakers bureau: Grüenthal, Novartis, Ida Kristin Haugen Grant/research support from: ADVANCE research grant from Pfizer, Consultant for: Advisory board Abbvie DOI: 10.1136/annrheumdis-2019-eular.4060
Conclusion: High levels of sCTX-I and uCTX-II at BL were associated with increased risk of undergoing TJR of the knee or hip during the two-year study. Our findings support the role of sCTX-I and uCTX-II as important biomarkers in clinical OA trials evaluating incidence of TJR.

Disclosure of Interests: None declared


THU0421

EFFECT OF GAME BASED EXERCISE PROGRAMS ON PAIN, FUNCTIONAL MOBILITY AND BALANCE IN PATIENTS WITH KNEE OSTEOARTHRITIS: RANDOMIZED CONTROLLED STUDY

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2Zonguldak Bulent Ecevit University Faculty of Medicine, Physical Medicine and Rehabilitation, Zonguldak, Turkey

Background: Osteoarthritis is a chronic joint disease affecting the knee, hip and hand joints. Exercise is an integral component of conservative treatment for osteoarthritis. However, virtual reality applications using interactive games for rehabilitation have become a focus of interest in recent years.

Objectives: The aim of this study was to evaluate the effects of virtual reality games on knee pain, functional mobility and balance in patients with knee osteoarthritis.

Methods: Fifty patients who were complaining of knee pain, aged 40-70 years, and were diagnosed with Kellgren-Lawrence stage 2, 3, 4 idiopathic knee osteoarthritis was included. Patients were randomly assigned to two equal groups (n = 25) as the control and the study group. Age, sex, weight, height, duration of illness was recorded for all patients. In to two equal groups (n = 25) as the control and the study group. Age, sex, weight, height, duration of illness was recorded for all patients. In the study group, all patients received virtual reality games on knee pain, functional mobility and balance in patients with knee osteoarthritis.

Results: In both groups, significant change in VAS, WOMAC knee osteoarthritis index, and CB&M score was observed (p<0.05). In the study group, VAS, WOMAC osteoarthritis index, and CB&M scores were significantly different than control group (p<0.05). The differences between baseline scores were significant in the study group.

Conclusion: MetS is predominantly associated with trajectories of localised and generalised pain through central obesity, suggesting that weight management is important in the prevention and therapy of pain over time.

Disclosure of Interests: None declared


THU0420

METABOLIC SYNDROME AND TRAJECTORIES OF LOCALISED PAIN AND GENERALISED PAIN

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Background: Metabolic syndrome (MetS) has been suggested as having a link to the pathophysiology of pain; however, no study has assessed whether MetS and its components are associated with localised pain and generalised pain and their courses over time.

Objectives: To describe the associations of MetS and its components with trajectories of localised knee pain (pain severity) and generalised pain (number of painful sites (NPS)) in a general older population.

Methods: 1,099 participants from a population-based older adult cohort study were recruited at baseline. 875, 768 and 563 participants attended years 2.6, 5.1 and 10.7 follow-up, respectively. Data were collected on demographic, psychological, lifestyle and comorbidities, blood pressure, glucose, triglycerides, and high-density lipoprotein (HDL) cholesterol. MetS was defined based on the National Cholesterol Education Program-Adult Treatment Panel III criteria. Radiographic knee osteoarthritis (ROA) was assessed by X-ray. Knee pain was measured by Western Ontario and McMaster Universities Osteoarthritis Index pain questionnaire at each time-point. Presence/absence of pain at the neck, back, hands, shoulders, hips, knees and feet was collected by questionnaire at each time-point.

Group-based trajectory modelling was applied to identify pain trajectories. Multi-nominal logistic regression was used for the analyses.

Results: Of 895 participants included in this study, 32% of participants had MetS and 60% had ROA at baseline. Three localised knee pain severity trajectories were identified: ‘Minimal pain’ (52%), ‘Mild pain’ (33%) and ‘Moderate pain’ (15%). Three NPS trajectories were identified: ‘Low NPS’ (12%), ‘Medium NPS’ (38%), and ‘High NPS’ (49%). In multivariable analysis without adjusting for central obesity, central obesity increased risk of belonging to both mild pain and moderate pain trajectories as compared to the ‘Minimal pain’ trajectory group, but MetS, hypertglycemia and low HDL were only associated with ‘Moderate pain’ trajectory [relative risk (RR): 1.67-2.26, all P<0.05]. Similarly, central obesity was also associated with both ‘Medium NPS’ (RR 2.35, 95%CI 1.40–3.92) and ‘High NPS’ trajectories (RR 3.07, 95%CI 1.85–5.08) compared to ‘Low NPS’ trajectory group, whereas MetS was only associated with ‘High NPS’ trajectory (RR 2.60, 95%CI 1.54–4.41). These associations became weak and non-significant after further adjustment for central obesity.

Conclusion: MetS is predominantly associated with trajectories of localised and generalised pain through central obesity, suggesting that weight management is important in the prevention and therapy of pain over time.

Disclosure of Interests: None declared

and final scores of VAS and WOMAC were significantly higher (p<0.05) in study group.

Conclusion: The results of the present study showed that virtual reality game-based exercise programs performed better results than conventional treatment program in patients with knee osteoarthritis.

REFERENCES:


Disclosure of Interests: None declared

THU0422
COMPARISON OF PRP DERIVED GROWTH FACTOR
(PRGF) VERSUS HYALURONIC ACID (HA)
IN MODERATE TO MODERATE KNEE OSTEOARTHRITIS; A SINGLE BLIND
ONE YEAR RANDOMIZED CLINICAL TRIAL STUDY

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Background: Osteoarthritis (OA) is the most common joint disease with characteristics of progressive loss of joint cartilage.

Objectives: Aim of this study was to evaluate clinical outcomes of intra-articular injection of PRP derived growth factor (PRGF) versus hyaluronic acid (HA) in patients with knee osteoarthritis.

Methods: 102 patients with grade II or grade III knee OA were randomly assigned to 2 intra-articular injections of PRGF 3 weeks apart or 3 weekly injections of HA. Primary outcome was the mean change from baseline until 2, 6 and 12 months post intervention in scores of visual analog scale (VAS), WOMAC and Lequesne index.

Results: The mean age of patients was 57.08±7.3 in PRGF compared to 58.65±7.09 in HA group. In PRGF group, VAS decreased from 7.8±1.5 to 5.4±1.7, and from 7.8±1.1 to 6.1±1.8 in the HA group after 12 months (P<0.0001). Total WOMAC score decreased from 41.96±11.71 to 27.10±12.3 (P<0.001), and from 39.71±10.4 to 32.41±11.8 after 12 months, respectively (P<0.05). In Lequesne index, all scores were significantly decreased after 12 months in PRGF group in comparison to HA group (P<0.001).

Conclusion: Although PRGF and HA were both effective, but PRGF injection resulted in significantly higher satisfaction, lower VAS and WOMAC and Lequesne total at baseline, 2, 6 and 12 months after injection. PRGF indicates plasma rich in growth factor.

Disclosure of Interests: None declared

THU0423
ANTEROIOR TIBIALATAR FAT PAD MORPHOLOGY AND
IGNAL INTENSITY ON MAGNETIC RESONANCE
AGING ARE CORRELATED WITH PATIENT
CHARACTERISTICS AND JOINT PATHOLOGY

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Background: Ankle sprains are the most frequent form of trauma in the ankle and up to 33% of patients experience ongoing pain 1 year after the initial trauma.1 In the ankle, trauma is the primary etiology of osteoarthritis with an overwhelming proportion of 70-78%.2 Recently, our group completed a small pilot study that suggested that the anterior tibial fat pad (ATFP) should be investigated as a source of inflammation and pain.3

Objectives: In this study, we tried to investigate the innovative concept of the ATFP as missing link in the pathogenesis of persistent complaints and potential source driving inflammation in the development of osteoarthritis.

Methods: The present study is a secondary analysis of an observational case control study by Van Ochten et al.4 We included 106 patients with a Kellgren & Lawrence score of 0 in the tibial joint on x-ray. T1 MRI scans were assessed for the signal intensity and area of the ATFP. T1 MRI scans in the program 'MATHLAB', quantitative values of intensity and area were generated. Those values were statistically tested for correlations with patient characteristics and structural abnormalities by univariate and multivariate linear regression.

Results: MRI signal intensity of the ATFP is associated with BMI (p=0.03), sex (p<0.01) and age (p<0.01). ATFP area is correlated with sex (p<0.01) and presence of pre-OA signs in the subtalar joint (p=0.01). After multivariate analysis, correcting for sex, subtalar pre-OA signs and BMI, persistent complaints were associated with ATFP area (p=0.04).

Conclusion: This study demonstrates the involvement of the ATFP in hindfoot joint pathology. ATFP MRI characteristics were also influenced by patient characteristics. Further research should confirm these findings in a more elaborate population including OA patients, focus on histological validation and determine underlying pathogenic processes that may explain the observed correlations.

REFERENCES:
THE NEW TREATMENT APPROACH IN KNEE OSTEOARTHRITIS: EFFICACY OF CELLULAR MATRIX COMBINATION OF PLATELET RICH PLASMA WITH HYALURONIC ACID VERSUS TWO DIFFERENT TYPES OF HYALURONIC ACID (HA) (PROSPECTIVE, RANDOMIZED, DOUBLE BLIND CONTROL STUDY)

Blanko Barac, Nemanja Damjanov, Ana Zekovic. Institute of rheumatology, Belgrade, Serbia

Background: Osteoarthritis pathogenesis is a complex process associated with decreased ability to regenerate cartilage mainly due to lack of physiologic vascularization. One of the most commonly affected joints is the knee.

Objectives: The aim of this study was to compare the efficacy of intra-articular (IA) injections of platelet rich plasma (PRP) combined with hyaluronic acid (HA) prepared with the Cellular Matrix device versus IA injections with two different types of hyaluronic acid for treatment of knee osteoarthritis.

Methods: This is a prospective, randomized, double-blind, controlled study on 53 patients (90 knees) suffering from knee osteoarthritis, divided in 3 groups. The first group comprised 19 patients (30 knees) treated with 3 IA injections, one every second week, of Cellular Matrix (CM) PRP-HA combination. The second group of 19 patients (30 knees) was treated with 3 weekly IA injections of 2% non-cross-linked sodium hyaluronate and the third group of 15 patients (30 knees) treated with 3 weekly IA injections of 2% non-cross-linked sodium hyaluronate with mannitol. All groups were homogeneous concerning gender, age and Kellgren Lawrence scale (I to III). For all patients visual analog pain scale (VAS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Knee Injury and Osteoarthritis Outcome Score (KOOS), The International Knee Documentation Committee (IKDC) score (‘well-being’ scale for all 4 regions) were used as outcome measures. Responsiveness was assessed using standardised response means (SRM) (CIs were assessed using the bootstrap method of EFron) and derived the number of patients per arm in a putative trial to demonstrate 50% change, at 80% probability, α=0.05.

Results: 6,945 knees (3,667 subjects, 2,085 female) were included (KL 0: 2,796; KL1: 1,338 knees; KL2: 1,879 knees; KL3: 924 knees). Table 1 provides summary results and Figure 1 shows SRM and putative trial cohort numbers by KL grade for bone shape and cartilage thickness.

Conclusion: The Cellular Matrix PRP-HA combination might be one of the most potent, safe, fast and novel therapeutic option for osteoarthritis of the knee, as well as a useful tool for postponing arthroplasty surgery when it is necessary.

REFERENCES:

COST-EFFECTIVE OA TRIALS REQUIRE ENROLMENT OF KNEES WITH DEFINITE JOINT SPACE NARROWING (KELLGREN LAWRENCE 3); DATA FROM 6,939 KNEES FROM THE OSTEOARTHRITIS INITIATIVE

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Background: The design of clinical trials for osteoarthritis is challenging; structural changes in tissues are quantitatively small and proceed very slowly. No clear guidance exists on how to optimise recruitment. We have previously shown that the use of radiographic joint space width of 2 to 4.5 mm is of major importance for improving responsiveness in clinical trials using MRI bone and cartilage outcomes. However, it can be technically challenging to screen for joint space width this carefully, so we considered whether Kellgren-Lawrence (KL) grade could be used as an enrichment strategy. As no other commonly used covariates have been shown to reliably increase responsiveness, it would be useful to know the numbers needed using ONLY an expert-read KL grade structural inclusion criterion.

Objectives: To determine responsiveness of change in femur bone shape and cartilage thickness using a large observational dataset and calculate likely trial cohort sizes per arm for each KL grade.

Methods: We used all knees from the Osteoarthritis Initiative which had MR images at baseline, 1 and 2 years, and a baseline KL grade (centrally read and adjudicated by 2 experienced radiologists). Quantitative 3D femur bone shape, and cartilage thickness in the central medial femoral region were used as outcome measures. Responsiveness was assessed using standardised response means “SRM” (CIs were assessed using the bootstrap method of Efron) and derived the number of patients per arm in a putative trial to demonstrate 50% change, at 80% probability, α=0.05.

Results: 6,939 knees (3,667 subjects, 2,085 female) were included (KL 0: 2,796; KL1: 1,338 knees; KL2: 1,879 knees; KL3: 924 knees). Table 1 provides summary results and Figure 1 shows SRM and putative trial cohort numbers by KL grade for bone shape and cartilage thickness.

Conclusion: Expert-read KL3 inclusion, using 2 independent radiologists, with strict attention to standards provides increased responsiveness for common MRI OA outcomes. It is worth noting that 80% of KL3 knees have OARSI JSN grade 3, and 78% of KL3 knees have radiographic JSN of 2 to 4.5 mm, and similar enrichment can be expected using these alternatives. Few clinical studies can afford cohort sizes of greater than 200 knees, and for these studies, using a large proportion of KL3 knees is critical, especially if cartilage thickness is to be used as the outcome.
Abstract THU0425 – Figure 1. SRM and cohort numbers by KL grade for bone shape and cartilage thickness in 6,939 knees. Top row shows SRM values at 1 year (left) and 2 years for femur bone shape and central medial femur cartilage thickness, with 95% confidence limits calculated using a bootstrap method. Bottom row shows numbers needed per cohort arm, assuming 50% change, 80% probability, alpha 0.05. Units are in vector units for bone shape, and mm for cartilage thickness.

Abstract THU0426 – Table 1. Responsiveness of bone shape and cartilage thickness by KL Grade

Detailed breakdown of SRM values, cohort size, mean change, and SD of that change for Figure 1. Units are in vector units for bone shape, and mm for cartilage thickness.

Disclosure of Interests: Michael Bowes Shareholder of: Stryker Corporation, Employee of: Stryker Corporation, Philip G Conaghan Consultant for: Flexion Therapeutics, AbboVie, Medivir, Merck Serono, Novartis, GlaxoSmithKline


THU0426 EFFECTS OF SODIUM SUCCINATE AND HYALURONIC ACID IN KNEE OSTEOARTHRITIS TREATMENT

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Background: At present hyaluronic acid (HA) is rather widely used in treatment of patients with osteoarthritis (OA). HA normalizes the properties of the synovial fluid; has a protective effects; promotes the cartilage nutrition and so improves the signs of OA and function of the joints. Sodium succinate (the salt of the succinic acid) helps to normalize intracellular metabolism and tissue respiration in hypoxic conditions via mitochondrial mechanism of action; normalizes acid – alkaline balance; takes part in K+ and Ca2+ transportation and provides antioxidant defense, - so is a promising compound for cartilage treatment

Objectives: To investigate the clinical efficacy of combination of hyaluronic and sodium succinate in treatment of early OA stages

Methods: The study included 126 patients with knee OA (stages I-II), Kelgren and Lawrence, mean age (54.3 ± 2.7) years, among them - 75 women (60%) and 51 men - (40%). All enrolled patients had OA exacerbation (without clinically evident synovitis) and received standard OA treatment (NSAIDs, exercises, orthopedic devices) for 15 days; Gr.1 patients (58) also got 5 intra-articular injections of 1.1% hyaluronic acid, stabilized with sodium succinate (2 ml, once a week); patients of Gr.2 (68) in addition to standard treatment received 5 intra-articular injections of 1.1% solution of non-stabilized HA (2 ml, once a week). Clinical observation and evaluation of the results were performed at the beginning of the treatment, at 6th, 12th and 24th week after the study beginning

Results: During the treatment period, patients in both groups showed the positive changes in clinical signs and symptoms of OA which led to the lowering of the WOMAC index (from (78.3 ± 4) to (75.4 ± 3.8) in Gr. 2 at the beginning of the study to (27.9 ± 2.6) and (29.8 ± 1.9) accordingly at week 12 (p<0.05 for both groups). The VAS score in both groups indicated a significant pain reduction, but the stability and duration of the clinical effect in the groups was different. In patients of Gr.1, the pain syndrome continued to decrease after 12 weeks till 24th week, whereas in Gr.2 after the treatment course there was no significant changes in further pain regression after 6th week point. The changes in Lisholm score were also significantly better in Gr.1 than in Gr. 2 (before treatment (21.7 ± 4.6) and (22.6 ± 5.3), at week 6 - (86.4 ± 5.7) and (71.3 ± 4.8), at week 12 – (87.6 ± 5.2) and (83.7 ± 5.3), respectively. p<0.05 between groups at week 12th

Conclusion: Combination of the hyaluronic acid and sodium succinate biochemical and physiologic properties in early stages of knee OA (as intra-articular injections) allows to increase the treatment efficacy, achieve better pain control, and more stable remission comparing to use of the hyaluronic acid alone

Disclosure of Interests: None declared


THU0427 THE LIFETIME RISK OF KNEE AND HIP REPLACEMENT FOLLOWING A GP DIAGNOSIS OF OSTEOARTHRITIS: REAL WORLD COHORT DATA FROM CATALONIA INCLUDING 48,311 PARTICIPANTS WITH UP TO 9 YEARS OF FOLLOW-UP

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Background: The lifetime risk of knee and hip replacement following a primary care diagnosis of knee or hip osteoarthritis is unknown and overly negative beliefs about prognosis act as a barrier to implementing recommended management strategies.

Objectives: To estimate lifetime risk of knee and hip replacement following a GP diagnosis of osteoarthritis and assess how this risk varies with patient characteristics.

Methods: Primary care and linked hospital data from Catalonia, covering 2006 to 2015, were used. Study participants had a newly recorded GP diagnosis of knee or hip osteoarthritis. Parametric survival models were specified for risk of knee/hip replacement and death following diagnosis. Survival models were combined and extrapolated using a Markov model and lifetime risk estimated for the average patient profile. The effects of age at diagnosis, sex, comorbidities, socioeconomic status, body mass index (BMI), and smoking on risk were assessed.

Results: 48,311 individuals diagnosed with knee osteoarthritis were included with a median follow-up of 4.3 years (IQR: 2.1 to 6.5) and of whom 2,561 underwent knee replacement. Reference figures for hip osteoarthritis were 15,105 individuals diagnosed with a median follow-up of 3.8 years (IQR: 1.8 to 6.1) and 1,247 hip replacements. The average participants’ lifetime risk for knee replacement was 30% (95% CI: 25% to 36%) and for hip replacement was 14% (10% to 19%). Notable patient characteristics influencing lifetime risk were age at diagnosis for knee and hip replacement, sex for hip replacement, and BMI for knee replacement. BMI increasing from 25 to 35 was associated with lifetime risk of knee replacement increasing from 24% (20% to 28%) to 32% (26% to 37%) for otherwise average patients.

Conclusion: Knee and hip replacement are not bound to happen for most after a GP diagnosis of osteoarthritis, with average lifetime risks of less than a third and a sixth, respectively. Patient characteristics influence lifetime risks with, most notably higher BMI associated with a meaningfully increased risk of knee replacement.

Disclosure of Interests: Edward Burn: None declared, David W Murray: Research support from: Grants from Zimmer Biomet, Consultant for: Personal fees from Zimmer Biomet, Gillian A Hawker: None declared, Rafael Pinedo-Villanueva: None declared, Daniel Prieto-Alhambra Grant/ research support from: Grants from Amgen, UCB Biopharma and Servier outside the submitted work, Consultant for: UCB Biopharma, Speakers bureau: Amgen

Background: Even though Neuromuscular electrical stimulation (NMES) has been widely used as a non-pharmacological intervention in patients with knee osteoarthritis (OA) to improve muscle strength and function, prior research has shown conflicting results regarding NMES effectiveness in knee OA treatment.

Objectives: The aim of this systematic review and meta-analysis was to investigate the effectiveness of NMES in muscle strengthen, pain, and function in individuals with knee OA.

Methods: Only randomized controlled trials (RCTs) were included in this study. Two authors independently performed the study selection. We used Pubmed, Embase, LILACS, PEDro and Cochrane Central Register of Controlled Trials as data sources. The main outcome evaluated was muscle strength. Function and pain were assessed as secondary outcomes using the Western Ontario Macmaster (WOMAC) questionnaire and Timed up and go (TUG) test. The methodological quality was assessed using PEDro scale.

Results: A total of 23,215 were initially identified. After selection of titles and abstracts, studies were selected for the full-text analysis, ten studies were included with a total sample size of 622 patients. The methodological quality of the selected studies was moderate, with a mean score of 5.5 on a 0-10 scale (PEDro). The following analysis were performed:

Legend: Data homogeneity (Chi² = 5.03; I² = 21%) was identified, with no significant difference in favor of NMES (Z = 0.07, p = 0.95). NMES - Neuromuscular electro stimulation.

Conclusion: NMES increased muscle strength in patients with OA compared to the active control group. However, the evidence to date did not demonstrate effects for pain control nor improvement in physical function.

REFERENCES:

Acknowledgement: This research was supported by University of Brasilia.

Disclosure of Interests: None declared

frequent impairment on work (66%) and personal life (87%) and the highest use of analgesics (60% NSAIDs, 25% opioids and 40% others). In the regression analyses, BMI per 5 units and WHO-S 10% worsening were associated with an increase in WOMAC values of 3-4 points, irrespective of the joint manifestations.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Reference</th>
<th>Polyarthropathy</th>
<th>Hip OA</th>
<th>Knee and Hip OA</th>
<th>Knee OA</th>
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<tr>
<td>Age</td>
<td>per 10 years</td>
<td>0.7 (0.6-2.0)</td>
<td>0.7 (1.2-4.2)</td>
<td>2.0 (0.5-8.5)</td>
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<tr>
<td>Gender: Male</td>
<td>Female</td>
<td>3.4 (1.7-6.4)</td>
<td>0.0 (3.5-15.0)</td>
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<tr>
<td>BMI, kg/m²</td>
<td>per 5 units</td>
<td>0.1 (0.3-3.2)</td>
<td>1.3 (1.0-5.2)</td>
<td>3.1 (1.8-6.6)</td>
<td>6.1 (0.6-76.7)</td>
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<td>Symptom duration per year</td>
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<td>0.9 (0.2-1.0)</td>
<td>0.2 (0.9-2.4)</td>
<td>0.4 (0.08-0.8)</td>
<td></td>
</tr>
<tr>
<td>MSACRAH</td>
<td>with 5% worsening</td>
<td>4.1 (1.0-15.0)</td>
<td>1.3 (1.0-4.1)</td>
<td>3.5 (1.5-9.1)</td>
<td>5.9 (0.7-51.5)</td>
</tr>
</tbody>
</table>

Table: Results of four separate multiple linear regression models with the WOMAC as the dependent variable. Regression coefficients with 95% confidence intervals are shown.

Discussion: The outcome of the consultation.

Results: No differences between groups were observed on the 3 subscales of the COQ (group difference (95% CI): communication 0.009 (-0.10, 0.12), conduct -0.02 (-0.12, 0.07) and information provision 0.02 (-0.18, 0.21)). Between group differences (95% CI) were in favour of the intervention group for knowledge (1.4 (0.6, 2.2)), negative beliefs regarding physical activity (-0.12 (-0.23, -0.02)) and pain medication (-0.30 (-0.49, -0.01)). We found no differences on other secondary outcomes.

Conclusion: An educational eHealth tool to prepare a first orthopaedic consultation for hip or knee OA does not result in higher patient satisfaction with the consultation, but it does influence cognitions about osteoarthritis.

References:

Disclosure of Interests: None declared


Preparing an Orthopaedic Consultation Using an EHealth Tool: A Randomized Controlled Trial in Patients with Hip and Knee Osteoarthritis

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Background: Hip and knee OA patients who are referred to an orthopaedic surgeon often expect action to be taken.1 However, the majority of those patients is not (yet) eligible for a joint replacement.2,3 We hypothesized that a solid preparation using the eHealth tool is likely to streamline patients’ expectations and increase satisfaction, irrespective of the outcome of the consultation.

Objectives: To evaluate the effect of a stand-alone mobile and web-based educational intervention (eHealth tool) compared to usual preparation of a first orthopaedic consultation of patients with hip or knee osteoarthritis (OA) on patients’ satisfaction.

Methods: A two-armed unblinded randomized controlled trial involving 286 patients with (suspicion of) hip or knee OA, randomly allocated to either receiving an educational eHealth tool to prepare their upcoming consultation (n=144) or usual care (n=142). Satisfaction with the consultation on three subscales (range 1-4) of the Consumer Quality Index (CQI - primary outcome) and knowledge (assessed using 22 statements on OA, range 0-22), treatment beliefs (assessed by the Treatment beliefs in OsteoArthritis questionnaire, range 1-5), pain medication use (yes/no), assessment of patient’s involvement in consultation by the surgeon (assessed on a 5-point Likert scale) and patient satisfaction with the outcome of the consultation (numeric rating scale), were assessed.

Results: No differences between groups were observed on the 3 subscales of the COQ (group difference (95% CI): communication 0.009 (-0.10, 0.12), conduct -0.02 (-0.12, 0.07) and information provision 0.02 (-0.18, 0.21)). Between group differences (95% CI) were in favour of the intervention group for knowledge (1.4 (0.6, 2.2)), negative beliefs regarding physical activity (-0.12 (-0.23, -0.02)) and pain medication (-0.30 (-0.49, -0.01)). We found no differences on other secondary outcomes.

Conclusion: An educational eHealth tool to prepare a first orthopaedic consultation for hip or knee OA does not result in higher patient satisfaction with the consultation, but it does influence cognitions about osteoarthritis.

References:

Disclosure of Interests: None declared


Frequency of Tendon Involvement and Its Effect on Hand Function in Hand Osteoarthritis

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Background: Tenosynovitis and consequent tendon damage are common findings in inflammatory arthritides. In contrast to rheumatoid arthritis (RA) and psoriatic arthritis, little is known about the frequency of tendon involvement in hand osteoarthritis (HOA) and the influence thereof on hand function. Ultrasound has been reported to have a high specificity in diagnosing tenosynovitis and tendon damage.

Objectives: We aimed to appraise the frequency of tendon involvement in HOA and to assess the agreement between ultrasound (US) and clinical diagnosis of tenosynovitis and tendon damage in HOA. In addition, we wanted to assess the influence of tendon involvement on hand function.

Methods: We included 73 patients with HOA in the study. Each patient underwent a clinical as well as a US examination of the 6 extensor tendon compartments and 6 flexor tendons of the hand (fig. 1). They were assessed for US signs of tenosynovitis and tendon damage as well as osteophytes (presence/absence) by a sonographer blinded to clinical information, as well as for clinical tendon involvement (presence/absence) by a biometrician blinded to the US results. Difference in frequency of sonographically detected tendon involvement between flexor and extensor tendons and between right and left hand were calculated by Chi-Square test. Osteophytes were also evaluated on standard radiographs. Agreement between US and clinical examination was calculated by Cohen’s kappa. Hand function was quantified using the Score for the Assessment and Quantification of Chronic Rheumatoid Affections of the Hands (SACRAH) questionnaire as well as the Mobberg pick-up test (MPUT). Correlation between MSACRAH and tendon involvement was calculated by Spearman’s correlation.

Results: In 41 patients (56.2%), at least one tenosynovitis was observed and in 8 (11%) patients, at least one tendon damage was detected by US. Tendon damage was found more often in flexor tendons (0.2% vs. 2.2%, p<0.001), while tenosynovitis was found more often in extensor
Abstract THU0431 – Figure 1.

Conclusion: This study revealed a high frequency of tendon involvement in HOA. The prevalence of tenosynovitis was similar as reported for RA and other inflammatory arthritides. The fact that we could demonstrate marked differences in the distribution of tenosynovitis and tendon damage between and among flexor and extensor tendons as assessed on US, coupled with the overall homogenous clinical involvement, suggests that clinical examination may be less specific for tendon involvement as compared to US. Tendon involvement on US does not seem to have an impact on hand function in HOA.

Disclosure of Interests: Irina Gessl Grant/research support from: Travel Grant, Anna Vinatzer: None declared, Gabriela Supp: None declared, Michael Zauner: None declared, MichaelaLosikandl: None declared, Martina Dunelova: None declared, ValentinRitschl: None declared, Josef S. Smolen Grant/research support from: AbbVie, Eli Lilly, Janssen, MSD, Pfizer, Roche, Consultant for: AbbVie, Amgen, Astra-Zeneca, Astro, Celgene Corporation, Celtrion, Eli Lilly, Glaxo, ILTOO, Janssen, MedImmune, MSD, Novartis, Pfizer, Roche, Samsun, Sanofi, UDB, Speakers bureau: AbbVie, Amgen, Astra-Zeneca, Astro, Celgene Corporation, Celtrion, Eli Lilly, Glaxo, ILTOO, Janssen, MedImmune, MSD, Novartis, Pfizer, Roche, Samsun, Sanofi, UDB, Daniel Aletaha Grant/research support from: AbbVie, Bristol-Myers Squibb, and MSD, Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medac, Merck, MSD, Pfizer Inc, Roche, and UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medac, Merck, MSD, Pfizer Inc, Roche, and UCB, Peter Mandl: None declared.


THU0433

THE BURDEN OF OSTEOARTHRITIS PAIN FROM THE PATIENT’S PERSPECTIVE IN EUROPE

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Background: Pain, the primary symptom of osteoarthritis (OA), affects multiple aspects of a patient’s life.

Objectives: To evaluate the burden of OA pain from the patient’s perspective in 5 European countries (France, Germany, Italy, Spain, the United Kingdom; EUS).

THU0432

LUMBAR FACET JOINT OSTEOARTHRITIS IS A RISK FACTOR OF SACROILIAC JOINTS DEGENERATION

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Background: Degeneration of sacroiliac joints (SLJ) is common in the general population, which associates with age, gender and body mass index (BMI). This degenerative disease relates to various lumbar disorders. Lumbar facet joint osteoarthritis (LFJOA) is highly prevalent, but relationship between this disease and SLJ degeneration remains poorly evaluated.

Objectives: This study aimed to investigate the relation between LFJOA and SLJ degeneration. We hypothesized that LFJOA patients might suffer more serious SLJ degeneration, thus multiple linear regression was employed to compare the effect of LFJOA and demographic characteristics on degeneration of SLJ.

Methods: We reviewed pelvic and lumbar computed tomography (CT) examinations of LFJOA patient with low back pain (LBP) through a picture archiving and communication system. The controls were age, gender and BMI-matched individuals who were free of LFJOA and LBP, and underwent pelvic and whole abdomen CT scans due to the non-musculoskeletal symptoms. Severity of SLJ degeneration was scored using a quantitative method which has been described by Bäcklund et al [1]. LFJOA was graded using a method which has been mentioned by Weishaupt et al [2]. Briefly, this method concerns facet joint space, osteophytes, hypertrophy of the articular processes, and subarticular bone erosions, which ranges from 0 to 3 for a joint. If there is a discrepancy between 2 joints in the same level, the greater one was used. LFJOA was defined as at least one level ≥2 from L1-2 to L5-S1. Scores of SJU degeneration were compared between LFJOA patients and the controls. Correlation analysis between SJU degeneration score and number of LFJOA levels, number of LFJOA joints, sum of LFJOA grades were performed. Stepwise multiple linear regression model was used to find the most important contributor of SJU degeneration among LFJOA, gender, age and BMI.

Results: (1) CT examinations of 992 LFJOA patients and 399 controls were reviewed. (2) Score of SJU degeneration in LFJOA patients were higher than that of the controls (8.85±2.94 vs. 4.31±2.52, P<0.05). (3) SJU degeneration score positively correlated with number of LFJOA levels (r=0.11, P<0.05), number of LFJOA joints (r=0.09, P<0.05) and sum of grades (r=0.10, P<0.05). (4) Results of multiple linear regression were shown in Table 1. LFJOA had the greatest standardized coefficient in the regression model.

Conclusion: LFJOA patients suffers more significant SJU degeneration, and more severe LFJOA leads to more serious SJU degeneration. Influence of LFJOA on SJU degeneration is stronger than demographic characteristics.

References:

Abstract THU0432 – Table 1. Stepwise multiple linear regression model for sacroiliac joints degeneration score

<table>
<thead>
<tr>
<th>Independent variables</th>
<th>Unstandardized coefficient</th>
<th>Standardized coefficient</th>
<th>P value</th>
<th>95% confidence interval for B</th>
<th>Variance inflation factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>LFJOA</td>
<td>4.49</td>
<td>0.12</td>
<td>0.58</td>
<td>&lt;0.001</td>
<td>4.73</td>
</tr>
<tr>
<td>BMI</td>
<td>0.12</td>
<td>0.05</td>
<td>0.55</td>
<td>&lt;0.001</td>
<td>0.12</td>
</tr>
<tr>
<td>Age</td>
<td>0.05</td>
<td>0.01</td>
<td>0.06</td>
<td>&lt;0.001</td>
<td>0.02</td>
</tr>
<tr>
<td>Gender</td>
<td>0.30</td>
<td>0.11</td>
<td>0.04</td>
<td>0.009</td>
<td>0.08</td>
</tr>
</tbody>
</table>

SE standard error, LFJOA lumbar facet joint osteoarthritis, BMI/body mass index P²=0.65, adjusted R²=0.65

Acknowledgement: None.

Disclosure of Interests: None declared

KNEE JOINT DISTRACTION AS STANDARD OF CARE
TREATMENT FOR KNEE OSTEOARTHRITIS: A COMPARISON WITH CLINICAL TRIAL PATIENTS

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Background: Knee joint distraction (KJD) has been evaluated as joint-preserving treatment for patients with knee osteoarthritis (OA) in 3 clinical trials since 2004. KJD aims to delay a total knee arthroplasty (TKA) in serving treatment for patients with knee osteoarthritis (OA) in 3 clinical trials since 2004. KJD showed cartilage regeneration and clinical improvement. Since 2014, KJD is a standard of care treatment option in several Dutch hospitals for younger (<65 yrs) knee OA patients.

Objectives: Compare baseline characteristics and clinical outcome at 1 year post-treatment between KJD patients treated in regular care vs study conditions.

Methods: In the OPS, patients (n=20; age <60 years) with end-stage OA indicated for TKA were treated with KJD for 8 weeks between 2004 and 2006. In an RCT comparing KJD with TKA, end-stage knee OA patients considered for TKA were treated with KJD (n=19; age <65 years) and completed 1-year follow-up. In an RCT comparing KJD with HTO, medial knee OA patients considered for HTO were treated with KJD (n=22; age <65 years). In both RCTs, patients were treated with KJD for 6 weeks between 2011 and 2014. From 2014-2017, 84 patients were treated with 6-week KJD in regular care and available for 1-year follow-up.

All distraction surgery was performed using two external fixators with built-in springs. The knee was distracted 5 mm and weight-bearing was supported. WOMAC questionnaires were assessed at baseline (0) and 12 months. Only regular care patients completed both questionnaires were included in analyses.

Abstract THU0434 –Table 1.

Table 1: Baseline characteristics of patients treated with knee joint distraction.

<table>
<thead>
<tr>
<th>Study patients (n=21)</th>
<th>Regular care patients (n=21)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (mean±SD)</td>
<td>51.7±10.6</td>
<td>54.0±8.5</td>
</tr>
<tr>
<td>Male gender; n (%)</td>
<td>35 (57)</td>
<td>25 (50)</td>
</tr>
<tr>
<td>BMI, kg/m² (mean±SD)</td>
<td>28.1±3.7</td>
<td>27.4±3.4</td>
</tr>
<tr>
<td>Left knee index, n (%)</td>
<td>24 (43)</td>
<td>10 (18)</td>
</tr>
<tr>
<td>Range of motion, degrees (mean±SD)</td>
<td>127±14 (49)</td>
<td>137±14 (41)</td>
</tr>
<tr>
<td>Leg pain, degree (mean±SD)</td>
<td>4.6±1.0</td>
<td>4.6±1.7</td>
</tr>
<tr>
<td>KLF pain–disability grade, n (%)</td>
<td>4.0±0.6</td>
<td>3.5±0.9</td>
</tr>
<tr>
<td>Grade 0</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Grade 1</td>
<td>1 (5.0%)</td>
<td>1 (5.0%)</td>
</tr>
<tr>
<td>Grade 2</td>
<td>1 (5.0%)</td>
<td>1 (5.0%)</td>
</tr>
<tr>
<td>Grade 3</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Grade 4</td>
<td>1 (4.8%)</td>
<td>1 (4.8%)</td>
</tr>
<tr>
<td>Distraction duration, days (mean±SD)</td>
<td>48.3±1.2</td>
<td>45.5±2.2</td>
</tr>
<tr>
<td>- without OPS</td>
<td>48.3±1.3</td>
<td>45.5±2.3</td>
</tr>
<tr>
<td>WOMAC Baseline, points (mean±SD)</td>
<td>49.9±13.9</td>
<td>49.8±13.7</td>
</tr>
<tr>
<td>- Pain</td>
<td>49.8±13.9</td>
<td>49.8±13.7</td>
</tr>
<tr>
<td>- Stiffness</td>
<td>44.5±13.8</td>
<td>45.0±13.8</td>
</tr>
<tr>
<td>- Function</td>
<td>51.0±13.2</td>
<td>51.0±13.2</td>
</tr>
</tbody>
</table>

Baseline patient characteristics were compared between ‘study’ (OPS/ RCT) and ‘regular care’ patients. For each group, the total WOMAC scores and subscales at follow-up were compared to baseline. The influence of different characteristics on the 1-year change in WOMAC scores was analyzed. Characteristics predicting being a responder to KJD treatment were analyzed according to the OMERACT-OARSI responder criteria, defined as an increase of ≥50% and ≥20 points in WOMAC pain or function scales, or a ≥20% and ≥10-point improvement in both scales.

Results: In regular care, 41 patients completed both questionnaires. Base-line characteristics for both groups are shown in table 1, showing a significant, but small difference in distraction duration, which was longer for study patients, but shorter when excluding the OPS patients who received distraction 2 weeks longer. The total WOMAC score and subscales for both groups increased significantly at 1 year compared to baseline (figure 1). The increase in total WOMAC and all subscales was over 15 points and thus clinically significant for both groups. The increase in the WOMAC function subscale was statistically, but not clinically, significantly higher for study patients (6.7 points) than regular care patients, while the total WOMAC, pain and stiffness were not different between groups (figure 1). After 1 year, 69% of patients were responders (60% regular care, 75% study patients, p=0.120). None of the baseline characteristics could significantly predict being a responder or had a significant influence on the increase in total WOMAC.

**Abstract THU0434 – Figure 1**

Conclusion: KJD results in a statistically and clinically significant 1-year improvement in total WOMAC and subscales for most patients. There were no clinically relevant differences between study and regular care patients. Longer follow-up will show whether this is maintained. As such, KJD not only shows good efficacy in study conditions, but also in regular care and can be a joint-preserving treatment of choice for young knee OA patients.

**REFERENCES:**

**Disclosure of Interests:** Mylène Jansen: None declared, Simon Mastberger Grant/research support from: FOREUM; Dutch Arthritis Society, Michelle Van Empelen: None declared, Esmee Kester: None declared, Floris Lafeber Shareholder of: ArthroSave, Grant/research support from: FOREUM; Dutch Arthritis Society, Roel Custers: None declared

**DOI:** 10.1136/annrheumdis-2019-eular.2786

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**THU0435 ASSESSING THE EFFECTS OF PULSED ULTRASOUND TREATMENT ON PAIN, FUNCTIONALITY, SYNOVIAL FLUID AND CARTILAGE THICKNESS, IN KNEE OSTEOARTHRITIS**

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**Background:** Osteoarthritis (OA) is a progressive rheumatic disease which is the most common cause of musculoskeletal pain and functional impairment, particularly in the elderly group. Ultrasound therapy is one of the most commonly used physical modalities in the OA treatment. It has deep heating effect and increases tissue regeneration, blood flow and metabolic effects while reducing the inflammation. In addition, it increases the cartilage regeneration according to certain in vivo and in vitro studies (1).

**Objectives:** To research the effect of pulsed ultrasound treatment on pain, functionality, synovial fluid and cartilage thickness in knee osteoarthritis.

**Methods:** This study was a randomised-controlled and parallel group study. 96 patients (79 females and 17 males) were included to study who had knee pain, aged between 45-75 years. They also have diagnosed as knee osteoarthritis according to ACR diagnostic criteria and their Kellgren-Lawrence grades were <3. These patients were divided in two groups randomly: Treatment group (exercise + US), (9 male, 39 female), control group (exercise + Sham US), (8 male, 40 female). The patients in the treatment group were treated with a 1 MHz probe and a density of 1w/cm², 1: 4 for 10 minutes, and 3 sessions a week for 8 weeks. Sham US treatment was applied to each group at the same time. Both groups received a home exercise program including knee range of motion and isometric strengthening exercises. All patients were evaluated by ultrasonographic measurements and quality of life tests; VAS (Visual Analog Scale) rest, VAS walking, Timed Up and Go Test, WOMAC Questionnaire scores (before treatment, after treatment, 3 months after treatment).

**Results:** 9 out of 48 patients in the treatment group and 12 out of 48 patients in the control group were excluded from the study because they did not continue treatment or come to the control. The distribution of groups was similar (Table-1). VAS rest, VAS walking, Timed up and go test, WOMAC questionnaire scores, were improved statistically significant in both groups (P<0.05), but group effect could not be demonstrated (P>0.05) There were no statistically significant results in terms of both synovial fluid and femoral cartilage thickness measurements (P>0.05) (Table 2).

**Conclusion:** Therapeutic ultrasound treatment in addition to home exercise program has not been shown to be effective rest and walking pain, functionality, synovial fluid and femoral cartilage thickness in the treatment of knee osteoarthritis. This is the first study to evaluate the effect of therapeutic intermittent ultrasound on synovial fluid and cartilage thickness by
ultrasound, international collaborative studies and randomized clinical trials will help in clarifying these areas of uncertainty.

REFERENCES:

Disclosure of Interests: None declared

THU0436
THE RELATIONSHIP OF BONE MINERAL DENSITY OF THE AXIAL SKELETON ON THE RISK OF PROGRESSION OF OSTEARTHRITIS OF THE KNEE

Natalia Kashevarova, Elena Taskina, Ludmila Alekseeva, Nikolay Demin, Aleksandr Lila. VA Nasonova Research Institute of Rheumatology, Moscow, Russian Federation

Objectives: To find the relationship between bone mineral density (BMD) and risk of knee OA progression in a 5-year prospective study.

Methods: 110 females with knee OA were examined twice with 5-year interval. Examination included filling questionnaires, VAS pain assessment, plain knee radiography and axial skeleton densitometry. I stage knee OA was established in 33 (30%) patients, II stage - in 46 (41.8%), III stage - in 26 (23.6%), and IV - in 5 (4.5%). Normal lumbar vertebral densitometry BMD values were found in 45 patients (40.9%), osteopenia-corresponding BMD values - in 33 (30.0%), and osteoporosis - in 32 (29.1%). Normal femoral neck BMD values were identified in 60 (54.5%) patients, osteopenia-level BMD - in 48 (43.7%), osteoporosis - in 2 (1.8%). In all premenopausal patients (n = 15) axial skeleton BMD values were normal.

Results: In 5-year interval radiographic progression was established in 40 patients (Group 2), while in 70 (Group 1) patients no progression occurred. Both groups were comparable in terms of age and disease duration, although, more patients from Group 2 tended to have normal baseline densitometry BMD values - both in lumbar vertebral and femoral neck: 47.5% vs 37.1%, and 62.5% vs 44.3% as compared to Group 1 patients. Patients from Group 1 more often had BMD values corresponding to osteoporosis and osteopenia: 32.9% vs 22.5%, and 55.7% vs 37.5%, respectively, as compared to Group 2 patients, although not achieving statistical significance. These differences were still identifiable after 5-year interval. Absolute BMD values at the second examination in 5 years were indicative of statistically significant increase in femoral neck and total hip BMD in Group 2 patients with knee OA progression: 0.79 ± 0.11 vs 0.73 ± 0.16, p<0.01, and 0.93 ± 0.14 vs 0.84 ± 0.25, p<0.05, respectively.

Abstract THU0436 - Table 1

<table>
<thead>
<tr>
<th>Baseline BMD Difference between OA stage</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>I stage</td>
<td>0.64±0.15</td>
</tr>
<tr>
<td>II stage</td>
<td>0.76±0.16</td>
</tr>
<tr>
<td>III stage</td>
<td>0.75±0.15</td>
</tr>
<tr>
<td>IV stage</td>
<td>0.73±0.17</td>
</tr>
</tbody>
</table>

Abstract THU0436 - Table 2

<table>
<thead>
<tr>
<th>Femoral neck BMD Difference between OA stage</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>I stage</td>
<td>0.07±0.07</td>
</tr>
<tr>
<td>II stage</td>
<td>0.17±0.20</td>
</tr>
<tr>
<td>III stage</td>
<td>0.16±0.13</td>
</tr>
<tr>
<td>IV stage</td>
<td>0.15±0.14</td>
</tr>
</tbody>
</table>

Thorough analysis of lumbar vertebrae BMD (g/cm²) relationship with OA stages revealed that in patients with stage IV OA lumbar BMD values were significantly higher than in patients with stages I-II OA (stage I OA - BMD 0.87±0.12 g/cm²; stage II OA - 0.92±0.21 g/cm²; stage III OA - 0.88±0.13 g/cm², stage IV OA - BMD 1.07±0.17 g/cm²) (Table1). Femoral BMD values didn’t show evident correlation with knee OA stage, although there was a trend towards higher BMD values in patients with stage IV OA compared to stage III OA (p = 0.06). Total hip BMD values were quite similar to lumbar BMD values (p = 0.01) (Table 2). BMD values were statistically significantly higher in patients with stage IV OA, than in patients with stages I and III (respectively, IV - 0.98 ± 0.13 g/cm², I - 0.85 ± 0.10 g/cm² and III - 0.86 ± 0.16 g/cm²). Correlation analysis also confirmed direct correlation between knee OA stage and BMD values in all evaluated compartments (p<0.05).

Conclusion: Increasing during the 5-year follow up period femoral neck and total hip BMD values can be interpreted as the predictor of knee PA progression. More advanced OA stages are associated with higher BMD values. Future multicenter prospective studies are deemed to better establish the correlation between BMD and knee OA progression.

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THU0437
INCIDENCE OF OSTEOARTROPOIC FRACTURE IN PATIENTS WITH KNEE OSTEOARTHRITIS: CLINICAL IMPACT OF FRAX-BASED OSTEOPOROSIS TREATMENT

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Background: The relationship between osteoporosis and osteoarthritis is complex and controversial. Several previous studies have indicated inverse relationship between osteoporosis and osteoarthritis [1-2]. However, the increased bone mineral density in osteoarthritis does not confer a reduce risk for fractures in other studies [3-4]. From the Rotterdam study, although patients with knee osteoarthritis had a higher bone mineral density, their incident fracture risk was increased as compared with those without knee osteoarthritis [5]. Therefore, fracture risk assessment in patients with knee osteoarthritis should not be overlooked.

Objectives: We aimed to evaluate the incidence of high risk group of osteoporotic fracture in patients with knee osteoarthritis comparing the FRAX and WHO criteria. We also examined whether patients with knee OA differ from age, sex, and BMI matched community-based control group without knee OA in terms of the incidence of high risk group of osteoporotic fracture.

Methods: We retrospectively assessed 282 Korean patients with knee OA who visited 5 medical centers between November 2012 and November 2015. For control group, 991 subjects aged of > 50 years-old were enrolled in database of health checkup centers. After matching for age, sex and body mass index, 552 subjects (276 subjects in knee OA group and 276 subjects in control group) included for this study.

Results: Osteoporosis according to WHO criteria was detected 110 (39.86%) subjects in OA group, and 101 (36.59%) subjects in control group; these difference were not significant. However, mean FRAX major osteoporotic fracture probabilities calculated with femur neck T-score were significant different between OA group and control group (7.72% vs 6.10%, p<0.001). Mean FRAX major osteoporotic fracture probabilities calculated without femur neck T-score were also significant different between OA group and control group (8.85% vs 6.86%, p<0.001). Mean FRAX hip fracture probabilities calculated with femur neck T-score were significant different between OA group and control group (2.48% vs 1.73%, p<0.001). Mean FRAX hip fracture probabilities calculated without femur neck T-score were also significant different between OA group and control group (3.50% vs 2.37%, p<0.001). When FRAX calculations without the use of femur neck BMD was adjusted for knee OA group rather than control group, 5.9% more patients would be recommend for osteoporosis treatment. Among the clinical risk factors of FRAX, previous fracture was significant different between knee OA group and control group (15.9% vs 0%, p<0.001).
Conclusion: We demonstrated that knee OA patients have an increased risk of osteoporotic fracture according to FRAX criteria, but not WHO criteria. Our study suggests that FRAX supports clinical decision to reduce the risk of osteoporotic fracture in patients with knee OA.

Disclosure: All authors agree that there are no conflicts of interest (both personal and institutional) regarding scientific financial interests that are relevant to the work conducted or reported in this manuscript.

REFERENCES:

Disclosure of Interests: None declared


THU0438

DO CORTICOSTEROIDS OR HYALURONIC ACID INTRA-ARTICULAR INJECTIONS IMPACT THE RISK OF TOTAL KNEE REPLACEMENT? REAL-LIFE DATA FROM THE KHOALA COHORT

Augustin Latourte1,2, Anne-Christine Rat3,4, Willy Nguyen Sime5, Abdou Omorou6,7, Florent Eymard8,9, Jeremie Sellam10, Christian Roux6,7, Francis Guillemin4,5, Pascal Richette2,9.

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Background: Long-term structural outcomes of corticosteroids (CS) or hyaluronic acid (HA) intra-articular injections in knee osteoarthritis (KOA) are unclear. Whether HA injections delay the need for total knee replacement (TKR) remains controversial, and an increased risk of cartilage damage has been reported with repeated CS injections.

Objectives: We conducted this study to compare, in real-life setting, the risk of TKR in patients receiving CS or HA vs. in those who did not receive intra-articular injections.

Methods: Khoala cohort is a French nationwide population-based cohort of 878 patients with symptomatic hip or knee OA (ACR criteria), aged 40-75 years. This study included patients with baseline KOA only. Patients were followed annually by self-reported questionnaires and by clinical examination and radiography at baseline (year 0), years 3 and 5.

The risk of incident TKR was compared between patients who had never received intra-articular injections vs. patients who received at least 1 CS or HA injection during follow-up.

The model allows for adjustment for time-varying confounding factors (i.e. pain, function and mental health scores) in addition to constant confounders (i.e. baseline age, sex, BMI, Kellgren-Lawrence grade).

Results: This study involved 656 patients (mean age 62.2 ± 8.5 years; 70.3% females) of which 91 (13.9%) underwent TKR during follow-up. CS or HA injections were performed in 143 (21.8%) and 191 (29.1%) patients, respectively, and 92 (14.0%) received both treatments. The 5-year relative risk of incident TKR in treated vs. untreated knee was 0.98 (95% CI 0.35 to 2.66; p=0.94) CS-treated knees and 0.38 (95% CI 0.15 to 1.03; p=0.06) in HA-treated knees.

Conclusion: In this study, CS injections for symptomatic KOA did not increase the 5-year risk of incident TKR. There was a non-significant trend for a reduced risk of TKR in HA-treated knees.

Acknowledgement: This work was supported by the French Society of Rheumatology and ART-Viggo Association.

Disclosure of Interests: Augustin Latourte: None declared, Anne-Christine Rat: None declared, Willy Nguyen Sime: None declared, Abdou Omorou: None declared, Florent Eymard: None declared, Jeremie Sellam: None declared, Christian Roux: None declared, Francis Guillemin Grant/research support from: Expanscience, Pascal Richette Consultant for: Grunenthal, Horizon, Speakers bureau: AstraZeneca, Grunenthal

Disclosure of Interests: None declared


THU0439

MEASUREMENT PROPERTIES OF PAIN CATASTROPHIZING SCALE IN PATIENTS WITH KNEE OSTEOARTHRITIS

Weij Ong1, Yu Heng Kwan1,2, Julian Thumboo1,2, Seng Jin Yeo3, William Yeo3, Ying Ying Leung1,2, William Yeo3, Ying Ying Leung1,2.


1.03; p=0.06). There was a non-significant trend for a reduced risk of TKR in HA-treated knees.

Conclusion: In this study, CS injections for symptomatic KOA did not increase the 5-year risk of incident TKR. There was a non-significant trend for a reduced risk of TKR in HA-treated knees.

Acknowledgement: This work was supported by the French Society of Rheumatology and ART-Viggo Association.

Disclosure of Interests: Augustin Latourte: None declared, Anne-Christine Rat: None declared, Willy Nguyen Sime: None declared, Abdou Omorou: None declared, Florent Eymard: None declared, Jeremie Sellam: None declared, Christian Roux: None declared, Francis Guillemin Grant/research support from: Expanscience, Pascal Richette Consultant for: Grunenthal, Horizon, Speakers bureau: AstraZeneca, Grunenthal
Abstract THU0439 – Table 1. Hypothesized and actual correlations for hypothesis testing

<table>
<thead>
<tr>
<th>PCS total score</th>
<th>Hypothesized Correlations</th>
<th>Actual Correlation</th>
<th>Hypothesis met</th>
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<tbody>
<tr>
<td>Internal resource</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain self-efficacy questionnaire</td>
<td>Moderate + -0.4186 ** Yes</td>
<td></td>
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<tr>
<td>Mental well-being</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>HADS</td>
<td>Strong + 0.5823 ** Yes</td>
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<td></td>
</tr>
<tr>
<td>SF-36 mental health</td>
<td>Moderate - 0.3323 ** Yes</td>
<td></td>
<td></td>
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<tr>
<td>Physical well-being</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WOMAC physical function</td>
<td>Moderate + 0.4767 ** Yes</td>
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<td></td>
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<tr>
<td>WOMAC pain</td>
<td>Moderate + 0.4671 ** Yes</td>
<td></td>
<td></td>
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<tr>
<td>SF-36 physical functioning</td>
<td>Moderate - 0.2632 ** No</td>
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<tr>
<td>Social well-being</td>
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<td></td>
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<tr>
<td>Lubben’s social network score</td>
<td>Weak +/- -0.0486 Yes</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

** p < 0.001: HADS: Hospital Anxiety and Depression Scale

Disclosure of Interests: Wei Jie Ong: None declared, Yu Heng Kwan: None declared, Julian Thumboo: None declared, Seng Jin Yeo: None declared, William Yeo: None declared, Ying Ying Leung: Grant/research support from: Abbvie, Novartis, Speakers bureau: Abbvie and Novartis, Speakers bureau: Novartis


THU0440 – THE ASSOCIATION OF PLASMA FATTY ACIDS LEVELS WITH HAND AND KNEE OSTEOARTHRITIS

Mareike Loef1, Andrea Ioan-Facsinay1, Dennis Moock2, Ko Willems van Dijk3, Renée de Mutsert3, Margreet Rospenkrog2,3, Frits Rosendaal3,1, LUMC, Rheumatology, Leiden, Netherlands; 2LUMC, Epidemiology, Leiden, Netherlands; 3LUMC, Human Genetics, Leiden, Netherlands

Background: Obesity is one of the most important risk factors for osteoarthritis (OA). For long the association between obesity and OA was thought to be explained by increased mechanical loading. However, the role of systemic factors is increasingly recognized, especially in non-weightbearing joints. Obesity is strongly associated with increased levels of circulating fatty acids, which may result in lipotoxicity. However, our knowledge about the effect of different fatty acids on OA is sparse.

Objectives: To investigate the association of plasma saturated fatty acids (SFAs), monounsaturated fatty acid (MUFAs), polyunsaturated fatty acids (PUFAs), omega (n-3) and n-6 PUFAs with clinically defined hand and knee OA.

Methods: In the population-based Netherlands Epidemiology of Obesity (NEO) study, a total of 6,671 middle-aged participants were recruited from the greater area of Leiden. Clinical hand and knee OA were defined by the ACR clinical classification criteria. Blood samples were obtained after an overnight fast and 150 minutes after consumption of a standardized liquid mixed meal containing 600kCal, with 16% of energy (En%) derived from protein, 40 En% from carbohydrates and 34 En% from fat. EDTA-plasma samples were used for a high-throughput proton nuclear magnetic resonance (NMR) metabolomics platform (Nightingale Health Ltd., Helsinki, Finland) to quantify 159 lipid and metabolite measures. For the present analyses the concentrations of fasting and postprandial total fatty acids, SFAs, MUFAs, PUFAs, n-6 PUFAs and n-3 PUFAs in mmol/l were used. Since we are in a postprandial state most of the day, these samples were used for the primary analyses. All fatty acid concentrations were standardized (mean 0, SD 1), to ensure a similar interpretation of the estimated effect. We excluded participants who reported to have inflammatory rheumatic disease or fibromyalgia, with missing physical examination, who were non-fasting at baseline, or reported using lipid-lowering medication. Logistic regression analyses were used to investigate the association between fatty acids and clinical OA phenotypes. All analyses were stratified by sex and corrected for age, education, ethnicity and total body fat percentage. Data are presented as odds ratios (OR) with 95% confidence intervals (CI).

Results: In the current analysis 5,328 NEO participants were included, with a mean age of 56 years and 56% were women. Hand OA, knee OA and concurrent hand and knee OA were defined in 8%, 10% and 4% of participants, respectively. After correction for possible confounders, total fatty acids, SFA, total PUFA and omega-3 PUFA levels were positively associated with clinical hand OA in men, with OR (95% CI) of 1.24 (1.01 – 1.50), 1.23 (1.00 – 1.50), 1.26 (1.00 – 1.58) and 1.24 (1.01 – 1.52), respectively. Although not significant, similar effect estimates were observed for men with concurrent hand and knee OA, but not for clinical knee OA alone. In women no associations were seen of any of the fatty acids with clinical hand or knee OA. Analyses of the association between fasting fatty acid levels and clinical hand and knee OA showed rather similar results, with slightly lowered ORs and wider confidence intervals.

Conclusion: Quantitatively measured plasma postprandial SFA and PUFA levels were significantly associated with hand OA in men. In women no associations were found. Intriguingly, although SFA and omega-3 PUFAs are deemed to have opposing effects on inflammation, both were positively associated with hand OA. Future research is warranted to replicate the association and determine whether there is a causal role for plasma fatty acid levels in hand OA.

Disclosure of Interests: Mareike Loef Grant/research support from: Innovative Medicines Initiative Joint Undertaking under Grant Agreement n° 115770, Andrea Ioan-Facsinay Shareholder of: Johnson & Johnson, Dennis Moock Consultant for: Part-time clinical research consultant for Metabolon, Inc., Ko Willems van Dijk: None declared, Renée de Mutsert: None declared, Margreet Rospenkrog Consultant for: Frits Rosendaal: None declared

**THU0441**

**IMPROVED KNEE PHYSICAL FUNCTION CORRELATES SIGNIFICANTLY WITH TIBIOFEMORAL CARTILAGE THICKNESS INCREASE AFTER IA TPX-100: RESULTS OF A POST HOC ANALYSIS**

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**Background:** In new draft guidance for OA drugs, the U.S. FDA notes the “well-recognized discordance” in clinical trials between structural imaging and patient benefit. In a randomized doubleblind, placebo-controlled trial, IA TPX-100 was associated with statistically significant and clinically meaningful improvement in knee functions among subjects (n=93) recruited for mild-moderate (ICRS grades 2-3) bilateral patellofemoral OA. No treatment differences in PF cartilage were detected, consistent with FDA concerns. However, only 14% of knees had measurable PF cartilage change on follow-up MRIs, limiting power for analysis of treatment differences in PF cartilage (ACR/ACHP 2017).

**Objectives:** To conduct a subset analysis of knee function and cartilage thickness correlations among the 73% of subjects (n=68) who had, in addition to PFOA, bilateral tibiofemoral OA (TFOA).

**Methods:** Subjects received 4 weekly injections of IA TPX-100 in one knee and identical saline placebo in the contralateral knee, as randomly assigned. MRIs were obtained at baseline, 6 and 12 months; and patient-reported outcomes (KOOS/WOMAC) were obtained at baseline, 3, 6 and 12 months. Subjects, sites, sponsor and central readers were blind to treatment assignment. All subjects receiving 4 weekly injections of 200 mg TPX-100 with at least one follow-up MRI were included for efficacy. The database was locked prior to all analyses, and clinically meaningful differences in outcome measures were selected a priori, based on the literature (Roos 2003).

**Results:** Of 68 subjects with bilateral TFOA, 47% had ICRS grade 4 (severe) TFOA at baseline, and 43% had ICRS grade 3 (moderate) disease. Demographic data for the cohort were consistent with the U.S. OA population in mean age (60.8 years), BMI (30.6), and gender distribution (60% females). IA TPX-100 was safe and well tolerated, with no drug-related serious adverse events or safety concerns. The mean functional improvement of TPX-100-treated knees was significantly higher than that of placebo-exposed knees at 6 and 12 months (p<0.004 and p<0.02, respectively). Responder knees, defined a priori with ≥8 points increase in KOOS physical function, had mean improvements in function of 20.5 and 22.4 at 6 and 12 months, respectively. Pearson analysis revealed a significant positive 12-month correlation (p=0.05) between degree of functional improvement and cartilage thickness increase/stabilization in TF cartilage in TPX-100-treated knees (Table 1).

**Table 1.**

<table>
<thead>
<tr>
<th>Cartilage Thickness vs. Knee Function (KOOS ADL)</th>
<th>Month</th>
<th>Cartilage Thickness</th>
<th>Pearson Correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>12</td>
<td>Correlation</td>
<td>p-value</td>
</tr>
<tr>
<td>Lateral TF</td>
<td>0.359</td>
<td>0.003</td>
<td></td>
</tr>
<tr>
<td>Medial TF</td>
<td>0.242</td>
<td>0.048</td>
<td></td>
</tr>
<tr>
<td>Entire TF</td>
<td>0.332</td>
<td>0.007</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** In subjects with bilateral TFOA, statistically significant and clinically meaningful robust functional improvements in TPX-100-treated knees were seen at 6 and 12 months compared with placebo-exposed knees. Formal analysis revealed statistically significant correlations between functional improvement and increase or stabilization of lateral, medial and total TF cartilage thickness. To our knowledge, TPX-100 is the first candidate DMOAD to show improvement in critical knee function concordant with increase/stabilization of cartilage structure compared with placebo-exposed knees.

**REFERENCE:**


**Acknowledgement:** We thanks Drs. Felix Eckstein and Ali Guermazi for central readings of MRIs.


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**THU0442**

**SOCIAL VULNERABILITY AND DISCHARGE DISPOSITION AFTER ELECTIVE TOTAL HIP REPLACEMENT? RISK-ADJUSTED ANALYSIS OF LARGE REGIONAL DATASET**

Bella Mehta1, Susan Goodman1, Kaylee Ho2, Debra D’angelo2, Michael Parks3, Said Ibrahim2, 1Hospital for Special Surgery, Main Campus, New York, United States of America; 2Weill Cornell Medical College, New York, United States of America

**Background:** With the aging of the world population and the rising prevalence of Osteoarthritis (OA), elective joint replacement (JR) has become one of the fastest growing procedures in the management of end-stage OA. There is also increasing evidence that social determinants of health such as where one lives impact healthcare utilization and decision-making. Furthermore, elective JR of the hip and knee is one of the most important cost-centers for Medicare, the largest payer in the US, and has therefore been the subject of ongoing payment reform models that shape discharge destination and risk of readmission.

**Objectives:** In a large regional dataset, we sought to examine how social vulnerability impacts discharge destination after elective THR, and what is the role in this relationship of patient race, another key social determinant of health which has been previously associated with disposition after surgery.

**Methods:** We used the Pennsylvania Health Care Cost Containment Council (PHC4) database to identify all patients who underwent elective THR between 2012 and 2016. Community level Social Vulnerability Index (SVI) was derived from the American Census Survey, which draws 15 different measures of vulnerability including socioeconomic, housing, and disability among others. SVI ranges from 0 (least vulnerable) to 1 (most vulnerable). SVI was dichotomized into low versus high (median) and high (above median). We used binary logistic regression to test the association between community SVI and discharge disposition: Institution (Nursing home or inpatient rehabilitation vs Home). We adjusted for important clinical, demographic, and facility level covariates.

To examine the role race (African American (AA) vs White) in this relationship, we included in the model an interaction term for SVI and race.

**Results:** There were a total 86,215 THR done between Jan 2012 and Dec 2016 that met our inclusion criteria. About 40,881 were ≥65 years of age, and 45,334 were ≥65 years of age. Patients from low SVI community went to high volume hospitals as compared to high SVI in all age groups. Figure 1 shows the geospatial localization and relationship of THR patients in the State of Pennsylvania by community SVI level. Compared to white patients, AA patients were more likely to live in higher SVI communities (median SVI AA 0.66; IQR 0.48-0.83 vs median SVI W 0.42; IQR 0.28-0.55, respectively). Compared to low SVI communities, patients from high SVI communities were more likely to be discharged to an institution (vs home) for age <65, aOR= 1.11, 95% CI: 1.07-1.16, p<0.001). The odds of discharge to an institution (vs Home) for patients living in high SVI communities (vs low SVI) was higher in AA compared to whites in all age groups. [Figure 2].

**Conclusion:** In this large regional dataset of patients who underwent THR, social vulnerability index of the community is associated with discharge disposition after surgery. Moreover, this association was stronger in African-Americans compared to Whites. This association when coupled with ongoing payment reform models may have implications for access to care for socially vulnerable populations.
ASSESSING PAIN CHARACTERISTICS IN PERSONS WITH HAND OSTEOARTHRITIS USING THE MCGILL PAIN QUESTIONNAIRE

Elisabeth Mulrooney,1, Karin Magnusson,2, Hilde Bemer Hammer,2, Hanne Solveig Dagfinруд,2, Tore K. Kvien,1,2, Ida Kristin Haugen1,1. Oslo University Hospital, Department of Rheumatology, Oslo, Norway,2Diakonhjemmet Hospital, National Advisory Unit on Rehabilitation in Rheumatology, Oslo, Norway,2Lund University, Department of Orthopedics, Lund, Sweden,1University of Oslo, Department of Interdisciplinary Health Sciences, Oslo, Norway,1University of Oslo, Department of Orthopaedics, Oslo, Norway

Background: Pain in osteoarthritis (OA) causes significant physical, psychological and social limitations. Increased understanding of the pain experience is important for improved patient care.

Objectives: We aimed to assess the pain characteristics of hand OA using the McGill Pain Questionnaire, a multidimensional self-reporting questionnaire that assesses the quality and intensity of the pain. Secondly, the external validity was examined.

Methods: Three-hundred persons with hand OA from the Nor-Hand study completed questionnaires, including a modified McGill questionnaire. The participants are presented with a list of 106 pain descriptors in 18 sections. The questionnaire consists of three subscales: sensory (12 sections, 0-71.3 scale), affective (5 sections, 0-32.9 scale) and evaluative (one section, 0-8.6 scale), and an intensity score (no pain – severe pain). The total scale is rated from 0-112.8. The subscales and total scale were normalized to 0-100 scales. The participants also completed the Numeric Rating Scale (NRS, 0-10 scale) about hand pain, the Australian/Canadian (AUSCAN) hand pain subscale (0-20 scale) and questionnaires about psychological factors; Hospital Depression and Anxiety Scale (HADS, 0-42 scale), Pain Catastrophizing Scale (PCS, 0-52 scale) and the pain subscale of the Arthritis Self Efficacy Scale (ASES, 10-100 scale). For all scales except ASES, high scores indicate poor health. We identified the adjectives in the McGill questionnaire with most frequent responses. To determine the external validity, the McGill questionnaire was correlated to other questionnaires (AUSCAN, NRS, HADS, PCS and ASES) using Spearman correlation coefficients.

Results: The participants (89% women) with median (IQR) age of 61 (57-66) years demonstrated a wide range in pain characteristics and intensity, with a median (IQR) of 34.5 (0-62.3), 14.9 (0-39.2) and 44.2 (34.9-48.8) for the sensory, affective and evaluate subscales, respectively. The median for the total pain sum score was 29.7 (7.0-53.2). A floor effect was detected for the sensory (23.7% with score 0) and affective (40.3% with score 0) subscales. The reported adjectives with highest frequency were “sore” (n=208, 69.3%), “inhibiting” (n=124, 41.3%) and “annoying” (n=97, 32.3%). The participants frequently reported neuropathic-like characteristics such as sticking/stabbing/pricking (n=137, 45.7%), smarting/burning (n=95, 36.6%), smarting/burning (n=137, 45.7%), smarting/burning (n=95, 36.6%), smarting/burning (n=95, 36.6%) and smarting/burning (n=95, 36.6%).

The McGill total scale showed moderate correlations with AUSCAN and NRS pain (Table). Similar strength of correlations was found for all the subscales, and stronger for the intensity score (0.63-0.64). The correlation with HADS was similar for the McGill questionnaire, AUSCAN and NRS pain. The correlations with PCS and ASES were weaker for McGill than for the other pain questionnaires.

Abstract THU0443—Table 1. Correlations between the McGill questionnaire and questionnaires assessing pain and psychological health.

<table>
<thead>
<tr>
<th></th>
<th>McGill</th>
<th>AUSCAN</th>
<th>NRS</th>
<th>HADS</th>
<th>PCS</th>
<th>ASES</th>
</tr>
</thead>
<tbody>
<tr>
<td>McGill total</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>McGill total</td>
<td>1.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>AUSCAN</td>
<td>0.41</td>
<td>1.0</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>NRS pain</td>
<td>0.45</td>
<td>0.73</td>
<td>1.0</td>
<td></td>
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<td></td>
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<tr>
<td>HADS</td>
<td>0.31</td>
<td>0.24</td>
<td>0.29</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCS</td>
<td>0.26</td>
<td>0.48</td>
<td>0.41</td>
<td>0.47</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>ASES</td>
<td>-0.20</td>
<td>-0.35</td>
<td>0.40</td>
<td>-0.30</td>
<td>-0.42</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Conclusion: The McGill Pain questionnaire may be a useful tool in research settings for a broad evaluation of pain characteristics in hand OA. Moderate correlations with other pain questionnaires suggest that the McGill questionnaire measures other constructs. For the first time, we have shown that neuropathic-like pain characteristics are frequently reported by persons with hand OA.

Disclosure of Interests: Elisabeth Mulrooney: None declared, Karin Magnusson: None declared, Hilde Bemer Hammer Grant/research support from: AbbVie, Pfizer and Roche, Paid instructor for: AbbVie, Pfizer, UCB, Novartis, Roche, Speakers bureau: AbbVie, Pfizer, UCB, Novartis, Roche, Hanne Solveig Dagfinrud Consultant for: Honoraria from Novartis as a steering committee member on this survey, Tore K. Kvien Grant/research support from: AbbVie, BMS, MSD, Pfizer, Roche and UCB., Consultant for: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celgene, Celtriton, Eli Lilly, Hospira, Merck-Serono, MSD, Novartis, Oktal, Orion Pharma, Pfizer, Roche, Sandod, Sanofi, Mylan and UCB, Speakers bureau: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celgene, Celtriton, Eli Lilly, Hospira, Merck-Serono, MSD, Novartis, Oktal, Orion Pharma, Pfizer, Roche, Sandod, Sanofi and UCB, Ida Kristin Haugen Grant/research support from: ADVANCE research grant from Pfizer, Consultant for: Advisory board Abbvie, Ida Kristin Haugen Grant/research support from: AbbVie, Pfizer, UCB, Roche, Sandod, Sanofi, Mylan and UCB, Speakers bureau: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celgene, Celtriton, Eli Lilly, Hospira, Merck-Serono, MSD, Novartis, Oktal, Orion Pharma, Pfizer, Roche, Sandod, Sanofi and UCB, Ida Kristin Haugen Grant/research support from: ADVANCE research grant from Pfizer, Consultant for: Advisory board Abbvie.


THU0444

CROSS-CULTURAL TRANSLATION, ADAPTATION AND VALIDATION OF A JAPANESE VERSION OF THE FUNCTIONAL INDEX FOR HAND OSTEOARTHRITIS (J-FIHOA)

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Background: Hand osteoarthritis (HOA) is a highly prevalent and heterogeneous musculoskeletal disorder. Although well-designed clinical trials and guidelines have been published, there are comparatively few HOA

Abstract THU0442—Figure 2. Adjusted odds of discharge to an institution (vs Home) for patients living in High SVI compared to Low SVI stratified by race

*Adjusted covariates for all models include patient sex, age, insurance, facility metro status, number of cases, surgical complications, and Elixhauser Index.

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THU0443

ASSESSING PAIN CHARACTERISTICS IN PERSONS WITH HAND OSTEOARTHRITIS USING THE MCGILL PAIN QUESTIONNAIRE

THU0444

CROSS-CULTURAL TRANSLATION, ADAPTATION AND VALIDATION OF A JAPANESE VERSION OF THE FUNCTIONAL INDEX FOR HAND OSTEOARTHRITIS (J-FIHOA)
studies concerning Asian countries. To both pursue appropriate clinical courses for patients and to engage in future research, physicians need to discriminate symptomatic HOA. The Functional Index for Hand Osteoarthritis (FIHOA) assesses hand OA-related functional impairment and is accepted as a gold standard with excellent reliability and responsiveness [1,2].

**Objectives:** Our objective was to make a Japanese version of the FIHOA (J-FIHOA) and to validate it among Japanese HOA patients.

**Methods:** J-FIHOA was created following forward/backward translation processes distilled from the established guidelines. A prospective, multi-center study was undertaken for its validation. Seventeen collaborating hospitals recruited hand OA patients from September 2017 to September 2018. Patients who met the ACR classification criteria were included. A medical record review and the following patient-rated questionnaires were collected: J-FIHOA, Japanese Health Assessment Questionnaire (J-HAQ), and the Short Form 36 Health Survey (J-SF-36). As item 7 is a gender-role question, an item total correlation needed to be calculated independently for women and men. The J-FIHOA scores at enrollment were used to assess Cronbach’s alpha coefficient/item-total correlation and compared with the J-HAQ, NRS pain and J-SF-36 yielding respective Spearman’s rank correlation coefficients.

To assess reliability, we used test-retest methods for patients with unchanged symptoms/treatments. The interval was 1-2 weeks and data sets were assessed with the intraclass correlation coefficient (ICC). To evaluate responsiveness, those who started new pharmacological treatments were required to answer the questionnaires and to have a 1-month follow-up visit. Differences between pre- and post-pharmacological treatments were used to calculate the effect size (ES).

**Results:** Twenty-nine male and 145 female HOA patients participated (mean age 65 years). Cronbach’s alpha was 0.91, showing high internal consistency. Each item was well correlated with the total score (all values >0.30; range 0.46 to 0.89). Construct validity between J-FIHOA and other scales was: 0.73 (J-HAQ), 0.56 (NRS pain), -0.31 (J-SF-36 physical component) and -0.21 (J-SF-36 mental component). Although the FIHOA has no pain-related question, previous reports showed moderate correlations between the FIHOA and pain. Our results were concordant with these reports. It was expected that J-SF-36 mental component had the weakest correlation. One hundred fifty-seven longitudinal data sets were pooled and used to evaluate reliability (137 for test-retest) and responsiveness (20 for ES). ICC for test-retest was 0.83 (95% CI, 0.77 to 0.88). The ES were 0.56 for J-FIHOA and 0.44 for J-HAQ. We assumed that this higher ES related on the HOA specificity of J-FIHOA.

**Conclusion:** We created a cross-culturally adapted J-FIHOA. Our results showed its good metric qualities to assess dysfunction in HOA and equivalence with the original FIHOA.

**REFERENCES:**

**Disclosure of Interests:** None declared


**THU0445**

**ASSOCIATION BETWEEN PATIENT’S EXPECTATION AND SATISFACTION FOLLOWING TOTAL KNEE REPLACEMENT FOR OSTEOARTHRITIS**

María Noviani1, Julian Thumboo1,2, Seng Jin Yeo3, Steven Bak-Siew Wong4, Vikki Wyld4, Bibhas Chakraborty5, Ngai Nung Lo6, William Yeo7, Hwei Chi Chong8, Mann Hong Tan9, Darren Tay2, Ying Ying Leung1,2

1Singapore General Hospital, Department of Rheumatology and Immunology, Singapore, Singapore; 2Duke-NUS Medical School, Singapore, Singapore; 3Singapore General Hospital, Department of Orthopaedic Surgery, Singapore, Singapore; 4Singapore General Hospital, Department of Radiology, Singapore, Singapore; 5University of Bristol, Musculoskeletal Research Unit, Translational Health Sciences, Bristol, United Kingdom

**Background:** Up to 20% of patients are dissatisfied with the outcome of total knee replacement (TKR). Pre-operative expectations may affect patient’s outcomes, including satisfaction after surgery. Better understanding of patient’s expectation could aid the development and improvements of pre-operative education. Pre-operative expectations and post-operative satisfaction may vary across cultures and have not been described in an Asian context.

**Objectives:** We aimed to evaluate the association between patient’s pre-operative expectation and post-operative satisfaction following TKR for osteoarthritis.

**Methods:** Patients listed for TKR because of OA in a tertiary referral centre were recruited. Pre-operatively, participants completed sociodemographic questions, Western Ontario and McMaster Universities Index (WOMAC) pain and function, and the Hospital for Special Surgery (HSS) KR expectation survey. At 6 months after TKR, patients rated their satisfaction with each expectation on the HSS as completely satisfied, partially satisfied or dissatisfied. Overall satisfaction with TKR was assessed with a 4-point Likert scale and dichotomized to satisfied or dissatisfied. Association between overall satisfaction at 6 months and pre-operative expectation was analysed using logistic regression after adjustment for demographic data.

**Results:** Between June 2017 and December 2017, 215 patients were recruited and completed follow up at 6 months after TKR (71% female, 82% Chinese, mean age 65±7 years). The overall satisfaction rate was 92%. The most prevalent pre-operative expectations were improved ability to perform daily activities (85%), participation in recreation (83%), pain relief (81%) and ability to change position (81%) (Figure 1). At 6 months after TKR, the top five fulfilled expectations (defined as ‘completely satisfied’) were improvement in the ability to perform daily activities (82%), walking short distance (66%), improvement in psychological well-being (64%), pain relief (64%) and position change (56%) (Figure 1). For most items on the questionnaire, expectations were high and not fully met; however most patient’s expectations were at least partially met. In the logistic regression model, post-operative HSS total score, but not pre-operative HSS score, was associated with overall satisfaction (P<0.01) after adjusting for demographic data (Table 1).

**Abstract THU0445 – Table 1. Variables Associated with Overall Satisfaction at 6 Months after TKR by Logistic Regression Analysis**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Exp(B), (95% Confidence Interval) P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>0.985 (0.869, 1.115) 0.809</td>
</tr>
<tr>
<td>Gender</td>
<td>0.589 (0.128, 2.700) 0.496</td>
</tr>
<tr>
<td>Ethnic group</td>
<td>0.729 (0.093, 5.741) 0.764</td>
</tr>
<tr>
<td>Education level</td>
<td>0.142 (0.010, 2.065) 0.153</td>
</tr>
<tr>
<td>BMI</td>
<td>0.992 (0.872, 1.128) 0.901</td>
</tr>
<tr>
<td>Radiographic index of knee</td>
<td>0.917 (0.228, 3.689) 0.902</td>
</tr>
<tr>
<td>WOMAC pain, baseline</td>
<td>0.988 (0.926, 1.053) 0.710</td>
</tr>
<tr>
<td>WOMAC function, baseline</td>
<td>0.978 (0.903, 1.060) 0.589</td>
</tr>
<tr>
<td>HSS total score at baseline</td>
<td>1.024 (0.967, 1.084) 0.421</td>
</tr>
<tr>
<td>HSS total score at 6 months</td>
<td>1.172 (1.092, 1.259) &lt;0.001</td>
</tr>
</tbody>
</table>

**Conclusion:** Although most patient’s expectations were at least partially met, they were not fully met. This suggests that many patients have unrealistic expectations of TKR outcome. Fulfillment of expectations, rather than expectation per se, was the most important variable associated with patient’s overall satisfaction.

**Disclosure of Interests:** Maria Noviani: None declared, Julian Thumboo: None declared, Seng Jin Yeo: None declared, Steven Bak-Siew Wong: None declared, Ngai Nung Lo: None declared, William Yeo: None declared, Hwei Chi Chong: None declared, Mann Hong Tan: None declared, Hwei Chi Chong: None declared, Mann Hong Tan: None declared, Hwei Chi Chong: None declared, Mann Hong Tan: None declared, Hwei Chi Chong: None declared, Mann Hong Tan: None declared.
DIACEREIN PROVEN AS EFFECTIVE AS CELECOXIB IN REDUCING PAIN AND SYMPTOMS IN KNEE OSTEOARTHRITIS PATIENTS IN A MULTICENTRE DOUBLE-BLIND RANDOMISED STUDY (DISSCO)

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Background: There was a need to ascertain in a clinical trial the comparative efficacy of diacerein, an IL-1 inhibitor, vis-à-vis celecoxib, a COX-2 inhibitor, in relieving knee osteoarthritis (OA) symptoms.

Objectives: The primary outcome of this study was to show that diacerein is non-inferior to celecoxib in terms of pain reduction (WOMAC A pain subscale) after 6 months of treatment in moderate-to-severe symptomatic knee OA patients.

Methods: A randomised double-blind multicentre trial was conducted in four European countries (Spain, Belgium, Austria, Czech Republic) and in Canada evaluating treatment with diacerein versus celecoxib in patients with OA diagnosed according to ACR criteria, with KL grade 2-3 knee OA and moderate-to-severe pain (VAS pain score [0-100] while walking on a flat surface > 40 mm). Eligible patients were randomised to treatment for 6 months with either diacerein 50 mg once daily for the first month and twice daily thereafter, or celecoxib 200 mg once daily. The primary outcome was the change from baseline in WOMAC pain subscale (0-50 scale) after 6 months of treatment. Secondary outcomes included WOMAC function and stiffness, VAS pain, presence of joint swelling/effusion, rescue medication consumption, percentage of OMERACT-OARSI responders, and SF-36. A total of 380 patients were randomised in the study. The primary outcome assessment on the per protocol set (PPS) (n=288) was followed by sensitivity analysis on the ITT population (n=370).

Conclusion: This clinical trial showed that in patients with moderate-to-severe knee OA pain, diacerein has comparable efficacy to celecoxib with respect to reducing pain and stiffness and improving function after 6 months in a clinically relevant manner. The drug also demonstrated a good safety profile with positive benefit to risk ratio.


THE RELATIVE EFFICACY OF TOPICAL NON-STEROIDAL ANTI-INFLAMMATORY DRUGS AND CAPSAICIN IN OSTEOARTHRITIS: MOVING FROM AVERAGE TREATMENT EFFECTS TO INDIVIDUAL TREATMENT PREFERENCES

Monica Persson1, Joanne Stocks1, Aliya Sarmanova2, Gwen Fernandes2, Gyula Varadi2, Mohammad Hashem Hashempur2, Robbert van Haselen3, David Walsh4, Michael Doherty4, Weiya Zhang4, University of Nottingham, Nottingham, United Kingdom; University of Bristol, Bristol, United Kingdom; 2Biophysics Pharma, Inc., Beverly, United States of America; 3Fasa University of Medical Sciences, Fasa, Iran (Islamic Republic of); 4International Institute for Integrated Medicine, London, United Kingdom

Background: Pain is an important issue for people with osteoarthritis (OA). Topical non-steroidal anti-inflammatory drugs (tNSAIDs) and capsaicin are recommended treatments, but reduce OA pain by different mechanisms.

Objectives: To [1] determine the relative efficacy of tNSAIDs and capsaicin in OA and [2] identify predictors of response that may allow tailoring of topical therapy to the individual.

Methods: Systematic literature searches were conducted up to 16/11/2015 for randomised controlled trials (RCTs) of tNSAIDs or capsaicin in OA. Placebo-controlled RCTs were pooled in conventional meta-analyses (CMA) for specific (difference between treatment and placebo) and overall (pain reduction in treatment arm) treatment effects. Bayesian network meta-analysis (NMA) compared treatment effects via placebo. RCT discrepancy analyses were conducted and an individual patient data meta-analysis (IPDMA) examined for predictors of response.

A pilot n-of-1 trial series (PNTS) examined treatment effects, patient preferences, and predictors of response. Participants with painful radiographic knee OA were allocated to three treatment cycles, each comprising four weeks treatment with 5% ibuprofen gel and 0.025% capsaicin cream in a random order.

Effect sizes (ES) are Hedges’ g and 95% confidence interval (CI) or credible interval (Crl). Predictors of response were identified in regression modelling for treatment-by-covariate interactions (specific effect) or covariate associations (overall effect). 9 and 25 predictors were examined in IPDMA and PNTS, respectively.

Results: CI 63 tNSAID and 10 capsaicin RCTs identified, CMA and NMA analysed 21 tNSAID (n=6191) and five capsaicin (n=415) RCTs. The quality of evidence was moderate for tNSAIDs and very low for capsaicin. Overall treatment effects were large and likely clinically significant (tNSAIDs ES 1.23, 95%CI 1.06-1.41; capsaicin ES 1.05, 95%CI 0.52-1.57). tNSAIDs (all drugs/doses grouped) were superior to placebo (ES 0.31, 95%CI 0.20-0.41), but capsaicin was only effective at 0.025% concentration (ES 0.41, 95%CI 0.17-0.64; ES of all capsaicin RCTs 0.28, 95%CI -0.04-0.60). On average, tNSAIDs and capsaicin were equally effective (ES 0.04, 95%CI -0.29-0.37).

IPD were provided for 15 (n=3889) tNSAID RCTs, including 11 (n=3140) placebo-controlled RCTs. No IPD were obtained for capsaicin. A significant but small interaction was observed between sex and tNSAID use for pain relief, with women reporting greater effect (11 RCTs, n=2939, p=0.023).

22 participants enrolled in the PNTS and completed 104 treatment periods. Clinically important pain relief (≥1 on 0-10 numeric rating scale) was achieved in 64% of periods, with no difference in efficacy between treatments overall (p=0.271). Individual responses to treatment varied, with 60% of people preferring one treatment over the other, but without clear predictors for the preference.

Conclusion: tNSAIDs and capsaicin may relieve OA pain, but treatment effects from group comparisons do not directly translate to treatment outcomes at an individual level. No baseline characteristics robustly determine which treatment is more likely to benefit an individual. Patients may benefit from trying both treatments to determine which is better for them.

Acknowledgement: M Underwood (Warwick University), A Suter (Bioforce AG/A.Vogel Produkte), GR Matoune (IBSA Institut Biochimique SA), and GSK for sharing IPD; D Burke for statistical advice; and D McWilliams for trial randomisation.

Disclosure of Interests: Monica Persson: None declared, Joanne Stocks Grant/research support from: Co-I on research grant from Pfizer/Eli Lilly, Aliya Sarmanova: None declared, Gwen Fernandes: None declared, Gyula Varadi Employee of: Inpellis, Inc. (previous); Biophysics Pharma, Inc (current), Mohammad Hashem Hashempur: None declared, Robbert van Haselen Consultant for: Consultancy services for homeopathic pharmaceutical companies, David Walsh Consultant for: Pfizer, GlaxoSmithKline, Consultancies on arthritis pain, Speakers bureau: Pfizer Ltd for a talk at OARSI 2018, Michael Doherty Grant/research support from: AstraZeneca funded the Nottingham Sons of Gout study, Consultant for: Advisory Boards on Grunenthal and Mallinckrodt, Weiya Zhang Consultant for:
DISEASE BURDEN IN OSTEOARTHRITIS (OA) IS SIMILAR TO RHEUMATOID ARTHRITIS (RA) FROM THE PATIENT’S PERSPECTIVE, SLIGHTLY HIGHER IN RA AT PRESENTATION, SIMILAR ONE YEAR LATER, AND SLIGHTLY HIGHER IN OA TWO YEARS LATER AT ONE PRIVATE PRACTICE SETTING

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Background: Disease burden traditionally has been regarded as considerably greater in rheumatoid arthritis (RA) versus osteoarthritis (OA). However, recent reports of cross-sectional data indicate similar disease burden in OA vs RA according to MDHAQ/RAPID3 (multidimensional health assessment questionnaire/routine assessment of patient index data). One concern is that these findings may reflect only better treatment for RA, and initial disease burden may be considerably higher in RA vs OA.

Objectives: To analyze disease burden in patients with OA vs RA at baseline and 1- and 2-year follow-up according to MDHAQ/RAPID3 scores in routine care at a single rheumatologist private practice site.

Methods: All patients seen in routine care at this site complete an MDHAQ at each visit in the waiting area prior to seeing the rheumatologist. The MDHAQ includes three 0-10 scores for physical function, pain visual analogue scale (VAS), and patient global VAS, compiled into a 0-30 RAPID3, as well as 0-10 fatigue VAS, and 0-48 self-report painful joint count scores. Mean MDHAQ scores were compared in OA versus RA patients at 1st visit and visits 1 and 2 years later, using t tests, adjusted for age and body mass index (BMI) using analysis of variance (ANOVA).

Results: Among 101 OA and 175 patients with RA, at first visit, all MDHAQ scores except pain VAS were statistically significantly higher in RA vs OA, e.g., mean 0-30 RAPID3 was 11.9 in OA and 13.7 in RA. However, none of these differences appear clinically significant (Table). After 1-year, all scores improved, but more in RA vs OA patients (Table), e.g., mean RAPID3 of 11.5 in OA and 10.9 in RA; no differences between OA and RA were statistically or clinically significant. After 2-years, mean RAPID3 was 11.9 in OA vs 9.0 in RA, indicating continued improvement in RA but little change in OA. All scores other than fatigue VAS were higher in OA, including the self-report painful joint count. Differences between OA and RA were explained only minimally by age and BMI.

Conclusion: Most MDHAQ/RAPID3 scores were higher in RA than in OA at the first visit, indicating greater severity of RA, although OA was almost as severe. One year later, scores were similar with no statistically significant differences. Two years later, most scores were higher in OA. These findings are largely independent from better treatment for RA vs OA. At an individual level, patients with primary OA may be better or poorer than other patients with primary RA. Nonetheless, at a group level, the severity of disease burden in OA appears almost as great as in RA, and becomes greater over the next 2 years, likely as a result of better treatment. The severity of OA is understated, suggesting a need for increasing resources for research toward better treatment for OA.

Abstract THU0449 – Figure 1

EFFECT MODERATION OF ANALGESIC TREATMENT OUTCOMES BY DEPRESSION IN PERSONS WITH OR AT-RISK FOR SYMPTOMATIC KNEE OSTEOARTHRITIS

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Background: Depression often accompanies knee osteoarthritis (OA), exacerbates pain severity, and may negatively affect analgesic treatment outcomes.

Objectives: To determine whether depression moderates the effect of analgesics on pain severity in persons with or at-risk for symptomatic knee OA.

Methods: Participants (n=2059) were from the Osteoarthritis Initiative, with or at-risk for symptomatic knee OA, and had complete data on selected measures at baseline and four annual follow-up visits. Analgesic initiation (acetaminophen, non-steroidal anti-inflammatory drugs, opioids) was assessed at three annual follow-up visits in those who were not analgesic users at baseline. Depression was evaluated concurrent to assessment of analgesic use with the Center for Epidemiological Studies Depression (CES-D) scale using the corresponding CES-D screening threshold (CES-D score ≥ 16). Pain severity at the fourth annual follow-up visit was the outcome and measured with the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain scale (rescaled range = 0-100).

Conclusion: The persistent use of analgesics at years one and two (β = -2.17; 95% CI: -4.62, 0.27) or years one, two, and three (β = -1.36; 95% CI: -4.22, 1.50) did not increase the magnitude of the treatment effect in non-depressed participants. In contrast, time-specific associations in depressed participants increased during follow-up from 0.61 (95% CI: -9.17, 10.38) to -9.64 (95% CI: -17.96, -1.33), and the treatment effect of year three analgesic use on year four pain severity was statistically significant. The magnitude of the treatment effect increased from year one with persistent analgesic use at years one and two (β = -5.76; 95% CI: -20.65, 9.15) and years one, two, and three (β = -15.39; 95% CI: -33.99, 3.21). However, effect moderation was only significantly concerning year three analgesic use, where the subsequent difference in treatment effect between depressed and non-depressed participants was -10.46 (95% CI: -18.97, -1.94). Time-varying confounders measured at three annual follow-up visits were: WOMAC pain score, Kellgren-Lawrence grade, body mass index, physical performance, knee injuries, and knee injections. Structural nested mean models appropriate for evaluating time-varying effect moderation of dynamic treatments by evolving effect modifiers were implemented using an inverse-probability-of-treatment-weighting regression with-residuals approach.

Results: In non-depressed participants, analgesic treatment effect at years one, two, and three on pain severity at year four was minimal (Figure 1).
QUALITY OF LIFE OF PATIENTS WITH A COMBINATION OF SARCOPENIA AND OSTEOARTHRITIS OF LOWER EXTREMITY

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Background: In accordance with the updated recommendations of the EWGSOP (2018), sarcopenia is a muscle disease (muscle failure) rooted in adverse muscle changes that accrue across a lifetime [1]. Sarcopenia and osteoarthritis significantly affect the self-esteem quality of life which is associated with a decrease in muscle strength and muscle performance, falls, joint pain [2]. In 2015, the SarQoL® questionnaire (Sarcopenia and Quality of Life, www.sarqol.org) was developed, specific to patients with sarcopenia. Improvement of quality of life should be the priority of any interventions to prevent and treat osteoarthritis and sarcopenia in the ageing population [3].

Methods: Prospective study of 159 women, mean age 74 ± 13.3. Sarcopenia was diagnosed according to the algorithm proposed by the European Working Group on Sarcopenia in Older People (EWGSOP, 2010). Life quality assessment was performed using EQ-5D questionnaires and a specific questionnaire in patients with sarcopenia SarQoL.

Results: 31.45% of people with OA older than 65 years had sarcopenia. The results of the study showed a statistically significant decrease in overall health on the questionnaire EQ-5D in patients with sarcopenia compared with patients without sarcopenia (0.48 ± 0.22 points and 0.74 ± 0.19 points, respectively, p <0.01) and no differences according to the EQ-VAS scale in the studied groups (p = 0.05). The decrease in the general health status of EQ-5D in patients with OA sarcopenic compared with non-sarcopenic is associated with a restriction of the usual daily activities: in 70% (95% CI: 55.4-82.1) and 52.3% (95% CI: 42.5-61.9) respectively, (p <0.01). In patients with OA, reduced global SarQoL in sarcopenic subjects compared to non-sarcopenic ones: 50.65±14.23 vs. 75.10±14.46, p<0.001. Significantly lower scores for all domains were found in patients with OA sarcopenic compared with non-sarcopenic patients (p<0.001).

Conclusion: In patients with OA sarcopenic, the quality of life is worse than that of non-sarcopenic due to a decrease in habitual daily activities, probably associated with low muscle strength.

REFERENCES:

Disclosure of Interests: None declared

in Spain, including peripheral (hip, knee and hand) and axial (cervical and lumbar spine) OA.

Objectives: To estimate in adult population the prevalence of symptomatic axial OA (cervical and lumbar spine) and associated factors.

Methods: EPISER 2016 study is a cross-sectional, population-based descriptive study. To estimate the OA prevalence, adult population aged 40 or older was selected. The initial recruitment was made through a call center. Participants who met the premises of an initial screening based on symptoms were also identified. In a second phase rheumatologists confirmed the diagnosis. The axial OA diagnostic criteria to confirm new diagnosis were both clinical and radiographic criteria. Clinical criteria: mechanical pain longer than 3 months of evolution and stiffness of less than 30 minutes or absence of it; and radiographic criteria: vertebral osteophytes or reduction of intervertebral space with sclerosis of vertebral plate and sclerosis of interarticular joints. To confirm the diagnosis, it was necessary that both clinical criteria and at least one radiographic criteria were met.

Results: The sample of the EPISER study was 3,336 subjects ≥ 40, of whom 978 had peripheral or axial OA. The mean age was 64.72 years, 730 were women, 62.6% had basic education, 64.8% were overweight or obese and 83.9% were ex-smokers or non-smokers (Figure 1). The prevalence of global OA (peripheral+axial) was 29.35%. Prevalence of peripher- al and axial OA was 19.62% and 19.17% respectively. The characteristics of patients with peripheral and axial OA follow similar patterns. Both types of OA are more frequent in women with basic education levels. Regarding age, there are more patients with axial osteoarthritis between 40-49 years than with peripheral OA. Obesity or overweight are more strongly associated with peripheral OA.

Prevalence of cervical OA was 10.10%. In the multivariate analysis, it was observed that cervical OA is more frequent in women and older subjects, with the prevalence peak between 60-69 years. It is also more frequent in subjects with obesity and in subjects with a basic education level (Figure 2). OA cervical prevalence is lower in subjects from northern Spain than in population from the Mediterranean area (including the Balearic islands) and central Spain. Smoking, living in a rural or urban environment or having been born abroad were not associated with cervical OA.

Prevalence of lumbar OA was 15.52%. Multivariate analysis also showed that lumbar OA is more frequent in women and it increases with age (prevalence peak in ≥ 80 years). Greater association was observed with obesity or overweight and with basic study levels. Lumbar OA prevalence was higher in population from centre of Spain compared with other areas. Tobacco consumption, living in a rural or urban environment or having been born abroad were not associated with lumbar OA.

Conclusion: EPISER2016 study shows similar prevalence of peripheral and axial OA. Lumbar OA is more prevalent than cervical OA. Axial OA in Spain is more frequent in women, increases in women with erosive disease at the third year between 60-69 years for cervical OA and ≥ 80 years for lumbar OA. Both cervical and lumbar OA are more frequent in patients with obesity or overweight and with basic studies.

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THU0453

PROGRESSION OF PAIN, NUMBER OF PAINFUL AND SWOLLEN JOINTS AND ULTRASOUND DETECTED CHANGES IN THE GROUP OF 133 PATIENTS WITH HAND OSTEOARTHRITIS OVER THREE YEARS

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Background: Hand osteoarthritis (HOA) is a common and frequent cause of pain, stiffness, physical impairment and ultrasound features in patients with erosive and non-erosive HOA in a three years longitudinal study.

Methods: Consecutive patients with symptomatic HOA fulfilling the American College of Rheumatology (ACR) criteria were included in this study. Joint pain and swelling were assessed. Patients reported joint pain on 100 mm visual analogue scale (VAS). Pain, joint stiffness and disability were assessed by the Australian/Canadian OA hand index (AUSCAN). Radiographs of both hands were examined, and erosive disease was defined by at least one erosive interphalangeal joint. Synovial hypertrophy and power Doppler signal (PDS) were scored with ultrasound. Synovitis was graded on a scale of 0–3 and osteophytes were defined as cortical protrusions seen in two planes. Patients were examined at baseline and at the first, second and third year of follow-up.

Results: Altogether, 133 patients (14 male) with symptomatic nodal HOA were included in this study and followed between April 2012 and January 2019. Out of these patients, 72 (6 male) had erosive disease. The disease duration (p<0.01) was significantly higher in patients with erosive compared with non-erosive disease. Pain reported on VAS was significantly higher (p<0.01) in patients with erosive compared with non-erosive disease, however the results are inconsistent.

Objectives: The aim of this study was to evaluate progression of pain, stiffness, physical impairment and ultrasound features in patients with erosive and non-erosive HOA in a three years longitudinal study.

Methods: Consecutive patients with symptomatic HOA fulfilling the American College of Rheumatology (ACR) criteria were included in this study. Joint pain and swelling were assessed. Patients reported joint pain on 100 mm visual analogue scale (VAS). Pain, joint stiffness and disability were assessed by the Australian/Canadian OA hand index (AUSCAN). Radiographs of both hands were examined, and erosive disease was defined by at least one erosive interphalangeal joint. Synovial hypertrophy and power Doppler signal (PDS) were scored with ultrasound. Synovitis was graded on a scale of 0–3 and osteophytes were defined as cortical protrusions seen in two planes. Patients were examined at baseline and at the first, second and third year of follow-up.

Results: Altogether, 133 patients (14 male) with symptomatic nodal HOA were included in this study and followed between April 2012 and January 2019. Out of these patients, 72 (6 male) had erosive disease. The disease duration (p<0.01) was significantly higher in patients with erosive compared with non-erosive disease. Pain reported on VAS was significantly higher (p<0.01) in patients with erosive compared with non-erosive disease at baseline. Progression of pain after the third year of follow up was significantly higher in patients with erosive disease (p<0.05). The number of painful and clinically swollen joints was significantly higher in patients with erosive compared with non-erosive disease at baseline. The number of painful and clinically swollen joints remained statistically higher (p<0.01) at the third year of follow up in patients with erosive disease. According to the AUSCAN, patients with erosive compared with non-erosive disease had more pain (p<0.05) and stiffness (p<0.01) at baseline. Pain (p<0.01) and function (p<0.01) but not stiffness, worsened in patients with erosive compared with non-erosive disease at the third year of follow up.

US-detected pathologies such as gray-scale synovitis (p<0.001), intensity of PDS (p<0.01) and number of osteophytes (p<0.01) were significantly higher in patients with erosive compared with non-erosive disease at

Abstract THU0452 – Figure 1

Abstract THU0452 – Figure 2
baseine. There were improvements in gray-scale synovitis total score and intensity of PDS in patients with non- erosive disease while patients with erosive disease worsened after the iso third year of follow up. On the other hand, the progression of US-determined osteophyte formation was observed in both groups but were significantly higher in patients with ero- sive compared with non- erosive disease after the third year of follow up.

Conclusion: The findings of this study show that pain and number of painful and clinically swollen joints associated with US-detected synovial changes and osteophyte formation is more severe in patients with erosive HOA than in patients with non- erosive disease. In addition, osteophyte formation is more likely to progress independent of synovial inflammation.


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THU0454

CONDITIONED PAIN MODULATION AND TEMPORAL SUMMATION IN PERSONS WITH HAND OSTEOARTHRITIS AND ASSOCIATIONS WITH PAIN SEVERITY

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Background: Conditioned pain modulation (CPM) assesses adequacy of descending modular pathways. Temporal summation (TS) reflects ascending facilitation of nociceptive signals in the central nervous system (central sensitization). Inadequate CPM and enhanced TS of pain are both known to contribute to pain in chronic pain conditions. Different pain phenotypes may respond to different treatments strategies and may therefore be important to assess in clinical practice. CPM has not previously been explored in persons with hand OA and its relation to pain severity in unknown.

Objectives: To examine the prevalence of CPM and central sensitization alone or in combination in persons with hand OA, and to explore their associations with pain severity.

Methods: These cross-sectional analyses included 248 participants with hand OA from the Nor-Hand study. Participants reported hand pain severity during the last 24 hours on a numeric rating scale (NRS, 0-10), CPM was tested with pressure pain threshold (PPT) at the left wrist before (PPT1) and during (PPT2) a painful ischemic cuff stimulating stimulus at the opposite upper arm. Adequacy of CPM was calculated as CPM-ratio (PPT1/PPT2). CPM-ratio < 1 (increased PPT) indicates adequate CPM, while CPM-ratio ≥ 1 (unchanged/decreased PPT) indicate inadequate CPM. Presence of TS was calculated as TS-index (PPT1/PDT2). The TS-index > 1.5 indicates presence of TS. TS and inadequate CPM were included as covariates in the analysis. Regression analyses adjusted for age, sex, BMI, use of analgesics, education level, sleep disturbance, the Pain Catastrophizing Scale, the Hospital Anxiety and Depression Scale and radiographic hand OA severity (Kellgren Lawrence sum score).

Results: Of the 248 participants included, 90% were women, median age was 61 (IQR 57, 66) years and mean BMI was 26.3 (SD 4.7) kg/m2. CPM-ratio ranged from 0.4 to 1.6 (mean 0.9, SD 0.2), and 32% showed inadequate CPM. Presence of TS was found in 46% of the study population. Overall, 38% had no TS and adequate CPM, 29% had inadequate CPM only, 16% TS only and 16% had both (Table). We found that persons with inadequate CPM only and TS only reported higher pain severity than persons with adequate CPM and no TS (Table). Those with both inadequate CPM and TS reported similar levels of pain as persons with inadequate CPM only and TS only.

Abstract THU0454 – Table 1. Associations of conditioned pain modulation (CPM) and temporal summation (TS) with pain severity in persons with hand OA. (n=248)

<table>
<thead>
<tr>
<th>TS-only</th>
<th>No TS and inadequate CPM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD)</td>
<td>NRS hand pain</td>
</tr>
<tr>
<td>No TS and adequate CPM (n=96)</td>
<td>3.2 (1.8)</td>
</tr>
<tr>
<td>Inadequate CPM-only (n=39)</td>
<td>3.9 (2.3)</td>
</tr>
<tr>
<td>TS-only (n=73)</td>
<td>4.2 (2.5)</td>
</tr>
<tr>
<td>TS and inadequate CPM (n=40)</td>
<td>4.6 (2.3)</td>
</tr>
</tbody>
</table>

Adjusted for age, sex, BMI, analgesics, education, sleep disturbance, Pain Catastrophizing Scale, the Hospital Anxiety and Depression Scale and Kellgren Lawrence sum score.

Conclusion: One third of persons with hand OA had inadequate CPM. Those with inadequate CPM, central sensitization or both reported higher pain severity than persons without any signs of altered central pain processing. Having both inadequate CPM and central sensitization was not associated with higher pain severity than having only one of the features. Our results are the first to demonstrate such a heterogenous variety of clinically relevant pain phenotypes in persons with hand OA.

Disclosure of Interests: Perrine Steen Peterssen: None declared, Tuhina Neogi: None declared, Karin Magnusson: None declared, Hilde Berner Hammer Grant/research support from: AbbVie, Pfizer and Roche, Paid for: AbbVie, Pfizer, UCB, Novartis, Roche, Speakers bureau: AbbVie, Pfizer, UCB, Novartis, Roche, Consultant for: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Hospira, Merck-Serono, MSD, Novartis, Oktal, Orion Pharma, Pfizer, Roche, Sandzo, Sanofi, Mylan and UCB, Speakers bureau: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Hospira, Merck-Serono, MSD, Novartis, Oktal, Orion Pharma, Pfizer, Roche, Sandzo, Sanofi and UCB, Till Uhlig Consultant for: Grü- nenthal, Novartis, Speakers bureau: Grüntenthal, Novartis, Ida Kristin Hau- gen Grant/research support from: ADVANCE research grant from Pfizer, Consultant for: Advisory board Abbvie


THU0455

PHARMACOKINETICS (PK) OF A SINGLE INTRA-ARTICULAR (IA) INJECTION OF CNTX-4975 (TRANS- CAPSAICIN) VS TOPICAL 8% CAPSAICIN PATCH

Randall Stevens1, Kimberly Guedes1, Eddie Armas2, Valerie Smith3, Andrew Volosov3, Centrexion Therapeutics Corp, Boston, United States of America, 2Well Pharma Medical Research Corp, Miami, United States of America, 3Premier Research, Durham, United States of America

Background: CNTX-4975 is in phase 3 trials for treatment of moderate to severe pain associated with knee osteoarthritis (OA). PK data from prior studies of CNTX-4975 in subjects with moderate to severe knee OA pain suggest low systemic and short-term exposure, similar to the FDA-approved topical capsaicin 8% patch.

Objectives: We compared single-dose systemic exposure to trans- and cis-capsaicin following IA injection of CNTX-4975 (>99.5% trans-capsaicin, <0.5% total impurities) with 8% capsaicin patch in subjects with moderate to severe knee OA pain.

Methods: This open-label, crossover study enrolled adults aged 50–75 y with moderate to severe knee OA pain in ≥1 knee (most painful knee index knee; nonindex knee, no to mild pain [0–1; NPRS 0–4 scale]). Subjects were randomized 1:1 to 2 sequences: A (CNTX-4975 1 mg IA, index knee) followed by B (topical capsaicin 8% patch, posterior rib cage for 60 min) or BA sequence, with ≥7-day washout between treatments. Plasma samples for trans- and cis-capsaicin concentration assays were taken before and at specified times after study treatment. PK parameters, including maximum observed plasma concentration (Cmax), area under the plasma concentration-time curve from time 0 to last quantifiable plasma concentration (AUCt), and to infinity (AUC∞), time to Cmax (Tmax), and half-life (t1/2), were determined. PK parameters were reported using descriptive statistics. Geometric means ratios of In-transformed AUCt0–∞, AUC∞0–∞, and Cmax, were evaluated using ANOVA.

Results: Sixteen subjects (median age, 62 y; female, 62.5%) were randomized to treatment (PK analysis population). Tmax showed more rapid absorption of trans-capsaicin from IA CNTX-4975 vs the topical patch (Table). AUCt0–∞ and Cmax indicated greater trans-capsaicin exposure

with CNTX-4975 vs the patch; however, exposure was short term, with mean t1/2 0.5 h. Cis-capsaicin concentrations were insufficient for calculating PK.

Conclusion: Trans-capsaicin from CNTX-4975 injection was rapidly absorbed and eliminated. The extent of systemic exposure to trans-capsaicin was significantly higher after CNTX-4975 vs the 8% capsaicin patch.

Abstract THU0455 – Table 1.

<table>
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<th>Parameter</th>
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<th>Topical 8% Capsaicin N=15</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC0-∞ (hpg/mL)</td>
<td>3477.72 (1935.05)</td>
<td>2077.57 (353.76)</td>
</tr>
<tr>
<td>GM (CV %)</td>
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<td>85.10 (137.3)</td>
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<td>Geometric LS mean</td>
<td>2000.10</td>
<td>81.72</td>
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<tr>
<td>GM ratio (90% CI)</td>
<td>35.85 (15.00-86.71)</td>
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</tr>
</tbody>
</table>

Disclosure of Interests: Randall Stevens Shareholder of: Centrexion Therapeutics Corp, Kimberly Guedes Employee of: Centrexion Therapeutics Corp, Eddie Armas: None declared, Valerie Smith Consultant for: Premier Research, Andrew Volosov Consultant for: Premier Research


THU0456 EVALUATION OF THE USE OF ORLISTAT IN THE COMPLEX TREATMENT OF OBESITY IN PATIENTS WITH KNEE OSTEOARTHRITIS

Ekaterina Strebkova, Ludmila Alekseeva. Nasonova research institute of rheumatology, Moscow, Russian Federation

Background: Currently in the world there is a pandemic of obesity, which leads to an increase in diseases associated with obesity. Obesity is an important factor in the development and progression of osteoarthritis (OA). The metabolic phenotype of OA, which is directly associated with obesity, is highlighted. Due to the growing number of patients with obesity and OA, a high level of comorbidity and the lack of effectiveness of non-drug therapy, the problem of the effectiveness and safety of the therapy of obesity is very relevant.

Objectives: To evaluate the efficacy and safety of drug therapy for obesity in patients with OA of the knee.

Methods: 50 female patients (45-65 y.o.) with Kellgren-Lawrence stage II-III KOA and obesity (BMI=30kg/m²). Patients in Group 1 (n = 25) took 120 mg of orlistat 3 times a day in combination with a low-calorie diet and exercise for 6 months. Patients in Group 2 (n = 25) were on a low-calorie diet combined with exercise for 6 months. All patients received a variety of non-steroidal anti-inflammatory drugs (NSAIDs) in tablet form. All patients were assessed for body mass, parameters of the WOMAC index, EQ-SD quality of life index, NSAID consumption, and orlistat therapy safety assessment.

Results: After 6 months of drug therapy for obesity, patients from Group 1 achieved a significant weight loss by 10.07% (p < 0.05). Patients from Group 2 showed the use of non-medical methods of treating obesity reduced body weight by 9.9% (p < 0.05). Patients from Group 1 improved the WOMAC index: pain decreased by 52.5% (p < 0.05), stiffness by 47.98% (p < 0.05), and functional insufficiency by 51.55% (p < 0.05). Patients from Group 2 also showed a decrease in the WOMAC index, but these changes were worse than in patients with greater weight loss. Patients from Group 1 showed a significant improvement in the quality of life for the EQ-SD index by 52.27% (p < 0.05). Patients from Group 2 against the background of insignificant changes in body weight, the quality of life index EQ-SD did not change. The need to take NSAIDs on the background of drug therapy for obesity and weight loss decreased by 4.6 times. On the contrary, in Group 2 of patients on the background of non-pharmacological treatment of obesity after 3 months of observation, the need for NSAIDs was maintained in 76%. The need for NSAIDs in patients of Group 2 decreased 1.3 times. In general, the tolerability of orlistat in patients of Group 1 was good. Adverse reactions were observed in two patients in the form of steatorrhea. The appearance of an undesirable reaction was associated with errors in nutrition (eating food saturated with animal fats), which did not require discontinuation of the drug. After correcting the diet, no adverse reactions were noted in patients.

Conclusion: The results of our study showed a significant decrease in body weight by more than 10% in the group of patients with OA while receiving orlistat. Significant weight loss helps reduce pain intensity, improve joint function, and improves the quality of life of patients with OA. Orlistat reduces the need for NSAIDs, which can help stabilize other comorbid diseases in patients with OA and obesity. The study noted good safety of therapy with orlistat; no serious adverse reactions were reported. Thus, drug therapy for obesity using orlistat can be included in the management of patients with OA and obesity, who cannot achieve weight loss using non-drug methods.

Disclosure of Interests: : Ekaterina Strebkova: None declared, Ludmila Alekseeva Speakers bureau: Bayer, Boeringer-Ingelheim, Gedeon-Richter, Servier


THU0457 EVALUATION OF THE EFFECTIVENESS OF COMPLEX TREATMENT OF OBESITY ON THE CLINICAL MANIFESTATIONS OF KNEE OSTEOARTHRITIS AND THE DYNAMICS OF CYTOKINES, DEPENDING ON THE DEGREE OF WEIGHT LOSS

Ekaterina Strebkova, Ludmila Alekseeva. Nasonova research institute of rheumatology, Moscow, Russian Federation

Background: Obesity is a risk factor and progression of the metabolic phenotype of osteoarthritis (OA). The decrease in body weight is important in the treatment of OA. Non-drug therapy aimed at altering the eating behavior, allows you to achieve a decrease in body weight of only 5%, which does not always contribute to the achievement of the clinical effect in patients with diseases of the joints.

Objectives: Assess the effectiveness of complex treatment of obesity with the use of orlistat (intestinal lipase inhibitor) on the clinical manifestations of the knee OA and the dynamics of cytokines (CRP, IL-6, TNF-α) depending on the degree of weight loss.

Methods: 50 female patients (45-65 y.o.) with Kellgren-Lawrence stage II-III KOA and obesity (BMI=30kg/m²). Patients in Group 1 (n = 25) took 120 mg of orlistat 3 times a day in combination with a low-calorie diet and exercise for 6 months. Patients in Group 2 (n = 25) were recommended non-drug therapy for obesity for 6 months. At baseline and after 6 months, the clinical parameters of the knee OA (WOMAC) were evaluated, the quality of life was assessed (EQ-SD). A laboratory study of peripheral blood was conducted at baseline and after 6 months: CRP, IL-6, TNF-α.

Results: After 6 months of complex treatment of obesity with the use of orlistat, patients in Group 1 achieved a significant weight loss of 10.07% (p = 0.03) and <5% (p = 0.02). Data for statistically significant changes
Efficacy and Safety From a Phase 2b Trial of SM04690, a Novel Intra-articular Wnt Pathway Inhibitor for the Treatment of Osteoarthritis of the Knee

Yusuf Yazici1, Timothy Micalidorn2, Allan Gibofsky3, Nancy Lane4, Christian Lattermann5, Nebojsa Skrepnik6, Christopher Sweerijgen1, Anita DiFrancesco1, Jeyashein Tambian7, Marc Hochberg7.

Background: A phase 2a study of SM04690, a small-molecule, intra-articular (IA) Wnt pathway inhibitor reduced knee pain and improved physical function and medial joint space width (mJSW) at 52 weeks in subgroups of subjects with unilateral symptomatic knee osteoarthritis (OA) compared to placebo (PBO).1

Objectives: A 24-week phase 2b study was conducted to refine patient-reported outcome (PRO) measures, target population, medication dose, and to evaluate safety. PRO results for Weeks 12 and 24 are presented here.

Methods: Study subject inclusion criteria required ACR-defined knee OA, Kellgren-Lawrence (KL) grades 2-3, and Pain Numeric Scale (NRS) ≥4 and ≤8 in the target knee and <4 in the contralateral knee. A single IA injection of 2 mL SM04690 (0.03, 0.07, 0.15, or 0.23 mg), vehicle PBO, or sham (dry needle only) was given in the target knee at baseline. PRO endpoints included change from baseline in weekly average of daily pain in the target knee by NRS diary (NRS) [0-10], Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain [0-100], WOMAC Physical Function, improvements were observed for 0.07 mg (Week 12 [P=0.031]) and 0.23 mg (Week 12 [P=0.010], Week 24 [P=0.033]) dose groups.

Conclusion: SM04690, in development as a potential disease-modifying OA drug, showed in this phase 2b study statistically significant improvements from baseline in both the 0.07 mg and 0.23 mg dose groups compared to vehicle PBO for Pain NRS, WOMAC Pain, WOMAC Physical Function, and PtGA. These data support the continued development of SM04690 as a treatment for knee OA. Phase 3 studies are being planned.


Abstract THU0458 – Figure 1. Dynamics of CRP depending on the degree of weight loss (p <0.05).

Figure. Actual observations over time and ladder plots depicting least squares mean (LSM) improvement of Pain NRS (± 95% CI) in SM04690 compared to vehicle PBO, adjusted for baseline.


Disclosure of Interests: Elena Taskina1, Ludmila Alekseeva1, Natalia Kashchevarova1, Sergey Anikin1, Evgenia Sharapova1, Ekaterina Strebkova1, Lena Zonova2, Tatiana Raskina3, Elvira Otteva4, Irina Vinogradova5, Aleksandr Lil4, Y. A. Nasonov Research Institute of Rheumatology, Moscow, Russian Federation; FSBIE HE Novosibirsk State Medical University, Novosibirsk, Russian Federation; SBIE HE KemSMU MOH, Kemerovo, Russian Federation, Regional SBH CDC MOH Khabarovsk kray, Khabarovsk, Russian Federation, SHI Ulyanovsk regional affiliated hospital, Ulyanovsk, Russian Federation.

Objectives: To identify knee OA rapid progression factors in a multicenter prospective study.

Methods: 185 female patients from 5 RF constituent territories aged 40-75 with confirmed Kellgren-Lawrence grade I-II knee OA were included into prospective study after signing the informed consent form. Mean age was 59.2±7.4 years (42-75), mean BMI=27.1±4.4 kg/m², mean disease duration–12±8.1 years. Individual patient’s medical record included relevant anthropometric data, records from case history and clinical examination, VAS articular pain assessment, WOMAC scores, comorbidities. Instrumental diagnostic methods included plain radiography of knee joints, DEXA of the lumbar spine and femoral neck, MRI examination of knee joints. Stage II knee OA was established in 135 (73%) out of 185 patients, stage III – in 50 (27%).


Abstract THU0459 – PREDICTORS ASSOCIATED WITH RAPID PROGRESSION OF KNEE OSTEOARTHRITIS

Elena Taskina1, Ludmila Alekseeva1, Natalia Kashchevarova1, Sergey Anikin1, Evgenia Sharapova1, Ekaterina Strebkova1, Lena Zonova2, Tatiana Raskina3, Elvira Otteva4, Irina Vinogradova5, Aleksandr Lil4, Y. A. Nasonov Research Institute of Rheumatology, Moscow, Russian Federation; FSBIE HE Novosibirsk State Medical University, Novosibirsk, Russian Federation; SBIE HE KemSMU MOH, Kemerovo, Russian Federation, Regional SBH CDC MOH Khabarovsk kray, Khabarovsk, Russian Federation, SHI Ulyanovsk regional affiliated hospital, Ulyanovsk, Russian Federation.

Objectives: To identify knee OA rapid progression factors in a multicenter prospective study.

Methods: 185 female patients from 5 RF constituent territories aged 40-75 with confirmed Kellgren-Lawrence grade I-II knee OA were included into prospective study after signing the informed consent form. Mean age was 59.2±7.4 years (42-75), mean BMI=27.1±4.4 kg/m², mean disease duration–12±8.1 years. Individual patient’s medical record included relevant anthropometric data, records from case history and clinical examination, VAS articular pain assessment, WOMAC scores, comorbidities. Instrumental diagnostic methods included plain radiography of knee joints, DEXA of the lumbar spine and femoral neck, MRI examination of knee joints. Stage II knee OA was established in 135 (73%) out of 185 patients, stage III – in 50 (27%).
**Results:** Knee OA progression (form radiographic stage II to stage III) within 1 year follow up was documented in 15 patients (Group 2 – with progressed OA), while 170 patients did not show any progression (Group 1 - no progression). Both groups were comparable in terms of age, age at RA onset, and duration of the disease. Although patients who progressed had higher body weight (97.1±14.0 vs 74.2±10.8 kg, p<0.001) and BMI (31.9±5.8 vs 27.3±4.1 kg/m², p<0.001). Patients from Group II had more intense knee pain during walking (VAS - 65.8±11.8 vs 47.5±16.7 mm (p<0.0003), and higher WOMAC pain: 330.5±56.6 vs 237.8±85.4 mm (p<0.0001). A function - 1044±190.4 vs 859.2±243.8 mm, p<0.007. Patients from Group II showed higher rates of varus knee alignment (66.7% vs 35.3%, RR=1.89, 95% CI 1.25-2.85, p=0.02) and H-VA1386 (86.7% vs 61.8%, RR=1.4, 95% CI 1.11-1.77, p=0.04), as well as higher rates of higher arteries hypertension (93.3% vs 71.8%, respectively, RR=1.3, 95% CI 1.1-1.53, p=0.05) and type 2 diabetes mellitus (DM) (33.3% vs 12.9%, RR=2.57, 95% CI 1.14-5.82, p=0.04). MRI showed higher percentage of medial and lateral tibia cartilage defects in Group 2 patients (57.2% vs 18.6%, respectively; RR=3.06, 95% CI 1.74-5.38, p<0.003; 57.2% vs 14%, RR=4.08, 95% CI 2.23-7.46 p=0.0006); bone marrow edema (BME) in medial (71.4% vs 12.2%, RR=5.3, 95% CI 3.38-10.1, p<0.000004) and lateral tibial compartments (21.4% vs 4.1%, RR=5.25, 95% CI 1.47-18.7, p=0.03); subchondral cysts, occupying more than 25% of the area in medial and lateral tibial compartments (respectively, 28.6% vs 7.4%, RR=3.84, 95% CI 1.4-10.5, p<0.03; and 35.7% vs 8.8%, RR=4.06, 95% CI 1.7-9.7, p<0.01). Synovitis (MRI findings) was documented in 100% patients from Group 2 and in 58.4% patients without OA progression (RR=1.71, 95% CI 1.5-2.0, p=0.002). A multivariate (discriminant) analysis showed that the most important risk factors for knee OA progression were: higher body weight, high WOMAC pain score, presence of type 2 DM, BME in medial tibial compartment, and cartilage damage in medial tibial compartment (MRI findings). A model capable of predicting rapid progression of knee OA in an individual patient with high accuracy (area under the ROC-curve 0.925 (95% CI 0.828–0.222)) has been developed based on identified RF and their coefficients.

**Conclusion:** In a prospective multicenter study, using comprehensive instrumental examination the following key predictors of rapid knee OA progression were identified: excessive body weight, high WOMAC pain score, presence of type 2 DM, BME in medial tibial compartment, and cartilage damage in medial tibial compartment (MRI findings).

**Disclosure of Interests:** Elena Taskina Speakers bureau: Bayer, Sandoz, Boeringer-ingelheim, Ludmila Alekseeva Speakers bureau: Bayer, Boer-inger-ingelheim, Gideon-Richter, Servier, Natalia Khashevarova: None declared, Sergey Anikin: None declared, Evgenia Sharapova: None declared, Ekaterina Strebkova: None declared, Lena Zonova Speakers bureau: Sandoz, Pfizer, Abbvie, Novartis, Bayer, Tatiana Raskina: None declared, Ekaterina Strebkova: None declared, Lena Zonova Speakers bureau: Sandoz, Pfizer, Abbvie, Novartis, Bayer

**DOI:** 10.1136/annrheumdis-2019-eular.4525

**THU0461**

**IDENTIFICATION OF DEFINITIONS OF POOR OUTCOME AFTER TREATMENT OF KNEE OSTEOARTHRITIS: A LITERATURE REVIEW**

Malou te Molder1, J.M.H. Smolders2, Petra Heesterbeek3, Cornelia van den Ende4, 1Sint Maartenskliniek, Research, Nijmegen, Netherlands; 2Sint Maartenskliniek, Orthopaedic Surgery, Nijmegen, Netherlands; 3Sint Maartenskliniek, Orthopaedic Research, Nijmegen, Netherlands; 4Sint Maartenskliniek, Rheumatology Research, Nijmegen, Netherlands

**Background:** Total knee replacement (TKR) is considered an effective intervention of the treatment of advanced knee osteoarthritis (OA) (Kelg-ren & Lawrence >2). However, a significant proportion of patients could be considered as a poor-responder to TKR (i.e. no or little improvement) in terms of chronic knee pain, functional disability, poor quality of life (QoL), and dissatisfaction after TKR. Both in research and in clinical practice it is challenging to identify those patients with an unfavourable course after TKR. It is difficult though to quantify the proportion of patients with poor response to TKR, as different definitions of, and perspectives (clinician’s and patient’s) on failure are being used.

**Objectives:** The aim of this study was to review the literature and summarize definitions of poor response to TKR.

**Methods:** A systematic search up to 2016 was performed to identify and review previously used definitions of poor response to primary TKR in the literature. Studies were included if dichotomous definitions of outcome after primary TKR were used, if a prospective design was used and in English full text available. The type, amount and combination of domains (i.e. pain and physical function), outcome measures, type of responses (absolute/relative, change/cut-off), values and moments of follow-up used in definitions were summarized.

**Results:** A total of 44 different dichotomous definitions of poor response to TKR, were extracted from 1849 initially identified studies. 34 definitions incorporated one domain, six definitions comprised two domains and four definitions comprised three domains. Eight different domains were used in identified definitions: pain, physical function (mobility), physical functioning
Disclosure of Interests: None declared


THU0463

OUTCOME PREDICTION FOR TREATMENT OF KNEE OSTEOARTHRITIS WITH A TOTAL KNEE ARTHROPLASTY. THE INFLUENCE OF DEMOGRAPHIC FACTORS, PAIN, PERSONALITY TRAITS, PHYSICAL AND PSYCHOLOGICAL STATUS

J.J. Toki1, R.P.A. Janssen1, T.M. Haanstra2, M. (Marike) C. van der Steen3, S.M. A. Bierma-Za\end{document}
Highest expectations were scored for pain relief and improvement of the ability to walk of short and medium distances. Patients had the lowest expectations for improvement of mobility, in knee and thigh, psychological well-being, sexual activity and the ability to have paid work.

Female sex, higher age, higher depression score and duration of complaints > 50 months showed to be significant predictors of lower expectations for the treatment outcome after TKA. Baseline pain and function scores were not related to the level of pre-operative expectations.

Conclusion: In conclusion, young, male patients with a short duration of complaints might be at risk of having too high expectations of the treatment result. On the contrary patients with depressive symptoms are more likely to have low expectations, with a potential negative influence on their treatment result. The present study aids in identifying patients at risk for having either too high or too low expectations. This knowledge can be utilized in individualized expectation management interventions.

Acknowledgement: We would like to thank C. van Doesburg and H. Kox for their support in data collection and study procedures.

Disclosure of Interests: None declared


THU0464 PHASE 2 CLINICAL TRIAL OF THE GI SAFETY OF A HYDROGEN SULFIDE-RELEASEING ANTI-INFLAMMATORY DRUG (ATB-346)

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1University of Calgary, Calgary, Canada; 2National Institute of Oncology, Budapest, Hungary; 3University of Sao Paulo, Sao Paulo, Brazil; 4University of Campinas, Campinas, Brazil

Background: Hydrogen sulfide (H2S) is a naturally occurring gaseous mediator produced by intestinal bacteria and various eukaryotic cells. H2S exerts anti-inflammatory, pro-resolution and cytoprotective effects in vivo. ATB-346 is an H2S-releasing derivative of naproxen, which in animals was shown to produce negligible gastrointestinal (GI) damage and bleeding. In human studies, ATB-346 was found to be much more potent and long-lasting than naproxen. A phase 2 open-label efficacy study demonstrated that ATB-346 (250 mg daily) significantly reduced pain in patients with osteoarthritis of the knee, and markedly suppressed cyclooxygenase (COX) activity. The aim of the present study was to determine if ATB-346 would induce less gastrointestinal ulceration than standard dose naproxen.

Objectives: To determine if healthy subjects taking ATB-346 for 14 days would develop significantly less gastrointestinal ulcers (<3 mm diameter with depth) than subjects taking an equi-effective dose of naproxen.

Methods: This was a double-blind, active control, endoscopic study. 244 healthy volunteers completed the study. Upper GI endoscopy was performed prior to and on day 14 after commencing treatment with naproxen (550 mg twice daily) or ATB-346 (250 mg) once daily in the morning and placebo once daily in the evening. Whole blood thrombocyte synthesis was measured on days 0, 7 and 14. Plasma H2S levels were also measured.

Results: 53 subjects taking naproxen (42.2%) developed at least one ulcer, while only 3 subjects (2.5%) treated with ATB-346 developed at least one ulcer (p = 0.0001). The two drugs suppressed COX activity to the same extent (>95%). Affected subjects in the naproxen group developed more ulcers (an average of 4 per subject) than in the ATB-346 group (an average of 1.3), and there was a much greater incidence of larger ulcers (>5 mm diameter) in the naproxen group than in the ATB-346 group (125 vs 0, respectively). The incidence of gastro-esophageal reflux was higher in patients and nausea was lower with ATB-346 than with naproxen. Plasma H2S levels were significantly elevated (by 50%; p=0.001) in the ATB-346 group.

Conclusion: Consistent with the pre-clinical studies, this phase 2 clinical trial demonstrated a dramatic reduction of upper GI ulcer formation in subjects treated with equi-effective doses of ATB-346 versus naproxen. The COX inhibition observed in this trial was consistent with a previous phase 2A trial that demonstrated significant pain relief with ATB-346 in patients with osteoarthritis of the knee. ATB-346 appears to be an effective and much safer alternative to existing NSAIDs.

Disclosure of Interests: John Wallace: None declared, André Buret Shareholder of: Antibe Therapeutics, Peter Nagy: None declared, Marcelo Muscara Grant/research support from: Antibe Therapeutics, Gilberto de Nucci Shareholder of: Antibe Therapeutics, Employee of: BioLab Brasil

THU0464B IS THERE AN ASSOCIATION BETWEEN METABOLIC SYNDROME AND SEVERITY OF HAND OSTEOARTHRITIS? RESULTS FROM A NATIONWIDE STUDY

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Background: Hand osteoarthritis (HOA) is a highly prevalent rheumatic disease that predominates in females and causes pain, joint deformities and loss of functional capacity. Overweight and metabolic syndrome have been previously suggested to associate with the severity of HOA, but clarity on these associations is yet to be achieved.

Objectives: To test the possible association between body mass index (BMI) and other individual components of metabolic syndrome with severity of HOA in females from a nationwide epidemiological study.

Methods: EpiReumaPt was a three-stage national health survey where, in the first phase, 10,661 adult participants were randomly selected and interviewed using a structured face-to-face questionnaire that included screening for rheumatic diseases, such as HOA. In the second phase, positive screeners for ≥1 rheumatic complaint plus 20% of the negative screeners were invited for an assessment by rheumatologists. Finally, 3 rheumatologists revised all the information and defined the final diagnosis by consensus. Female patients with a final clinical diagnosis of primary HOA were included in this analysis. Hand functional status as assed by the Cochin questionnaire was the outcome of interest. The explanatory variables of interest were: BMI evaluated as a categorical variable (Normal: 18-24.99; overweight: > 25-29.99; obesity: ≥ 30), diabetes mellitus, hypertension and hypercholesterolemia (all self-reported and as binary variables: yes/no). The possible associations between BMI and the individual components of the metabolic syndrome with the Cochin score were tested in a multivariable linear regression model. Only significant variables (p<0.05) were kept in the final model. Potential confounders of the associations of interest and the outcome were defined a priori on clinical grounds and included age and symptoms of depression (HADS score).

Results: Out of the 3,877 participants evaluated by Rheumatologists, 473 women had primary HOA (national prevalence: 6.6%). In this population, 40% were overweight and 29% were obese. Ninety-three (20%) participants had diabetes, 261 (56%) had hypertension and 261 (56%) had hypercholesterolemia. In the multiple regression model, BMI and diabetes were found to significantly associate with HOA severity, whereas hypertension and hypercholesterolemia did not, thus not being selected in the final model (table).

Abstract THU0464 – Table 1. Association between individual components of the metabolic syndrome and HOA severity (Cochin score). Multivariable linear regression model

<table>
<thead>
<tr>
<th>Variables</th>
<th>Coefficient (95% CI)</th>
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<tbody>
<tr>
<td>BMI (categorical)</td>
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<tr>
<td>Diabetes (yes vs no)</td>
<td>3.63 (0.13; 7.13)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>0.13 (0.01; 0.27)</td>
</tr>
<tr>
<td>HADS score (continuous)</td>
<td>0.90 (0.59; 1.22)</td>
</tr>
</tbody>
</table>

Conclusion: In this study, higher BMI and the presence of diabetes mellitus associated with a worse functional capacity on women with primary HOA. These data add to the body of evidence suggesting a possible role of metabolic factors in the severity of HOA.

REFERENCES:


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Disclosure of Interests: Margarida Cruz: None declared, Alexandre Sepriano: None declared, Sara Dias: None declared, Ana Maria Rodrigues: None declared, Helena Canháo: None declared, Nélia Gouveia: None declared, Mónica Eusebio: None declared, Sofia Ramiro: None declared, Jaime Branco: None declared.
The evaluation of the effectiveness of intra-articular steroid, tenoxicam and combined steroid-tenoxicam injections in the treatment of patients with knee osteoarthritis

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Background: Intra-articular corticosteroid injections are widely applied in the treatment of symptomatic knee osteoarthritis (OA). There is an evidence of short-term effects of intra-articular corticosteroid injection (up to 3-4 weeks), however there is no consensus for the long-term benefit of this treatment yet (1). Tenoxicam is an effective analgesic and anti-inflammatory drug for symptomatic treatment of OA. Additionally, apart from oral use, tenoxicam is also applied as an intra-articular treatment option to minimize gastrointestinal side effects of NSAIDs (2). Clinical evidence suggests that the combined use of NSAIDs and corticosteroids is synergistic (especially macular edema after cataract surgery in ophthalmology) (3).

Objectives: The aim of this study is to compare the effectiveness of intra-articular administration of these treatments and their combination and determine whether the combination of intra-articular steroid and tenoxicam was more effective for a long period rather than only tenoxicam and steroid injection alone in OA treatment.

Methods: In 90 patients (56 female, 34 male) with diagnosis of knee osteoarthritis, patients with knee osteoarthritis were randomly divided into three groups (30 patients per group): Group 1 were treated by intra-articular injection of triamcinolone hexacetonide. Group 2 were treated by intra-articular injection of triamcinolone hexacetonide combined with tenoxicam. The estimation of the severity of pain by the visual analog scale (VAS) were enrolled at baseline and 1, 3, 6 months post-injection. Additionally, the Western Ontario and McMaster Universities Index (WOMAC) was used to determine the outcome measures of pain, stiffness and physical functioning at baseline and 1, 3, 6 months post-injection.

Conclusion: The combination of triamcinolone hexacetonide and tenoxicam was more effective for a long period rather than only tenoxicam and steroid injection alone in OA treatment.

THU0465 PHARMACOKINETICS AND TOXICOKINETICS STUDIES OF A SUSTAINED RELEASE LIPOSOMAL FORMULATION OF DEXAMETHASONE SODIUM PHOSPHATE (TLC599) FOLLOWING INTRA-ARTICULAR INJECTION IN DOGS


Background: Osteoarthritis (OA) is a degenerative joint disorder with limited long-lasting treatment options. Various steroid formulations on the market are effective but required frequent intra-articular (IA) injections due to short-term symptomatic relief. IA steroids have been shown to increase cartilage loss in knee and the rapid absorption into systemic circulation could cause adverse side effects, limiting their effectiveness (1). To circumvent these issues, TLC599, a novel sustained-release liposome formulation of dexamethasone sodium phosphate (DSP) was developed to provide a sustained OA pain management over an extended period with reduced side effects and toxicity. TLC599 resulted in sustained presence in the synovial fluid without significant local and systemic side effects from OA treatments following IA injection.

Objectives: To evaluate pharmacokinetics (PK) and toxicokinetics (TK) of TLC599 following IA injection in dogs.

Methods: In two studies, the dexamethasone phosphate (DP) and dexamethasone (DEX) concentration was quantified and the PK/TK profile of TLC599 following IA injection in dogs.

Results: Study #8351851: Following a single-dose IA injection of TLC599, DP concentration declined after 15 days but remained at similar level from 30 days to 120 days post-dose. Overall, the prolonged 120-day residence time of TLC599 in synovial joint was observed (Figure 2).

Conclusion: TLC599, a novel extended-release liposome formulation of DSP, showed a long-lasting-profile up to 120 days in synovial joint after a single IA injection in a preclinical dog study. In addition, no significant systemic exposure and accumulation of DP and DEX in dog plasma was observed following multiple-dose administration of TLC599. Animal studies indicate that TLC599 may be an effective and superior chronic treatment for OA.

REFERENCE:

Acknowledgement: The authors thank Yingfang Li, Jiunmin Lai, Ruixue Chen, Ph.D. and Carl Brown Ph.D. for reviewing support.


Results: The mean age of patients was 65.97±9.29 years. In tenoxicam group, median pre- and post-treatment (at 1, 3 and 6 months) VAS/ WOMAC scores were 8.00/34.00, 0.00/8.00 and 8.00/34.00, respectively. In steroid group, median pre- and post-treatment (at 1, 3 and 6 months) VAS/WOMAC scores were 8.00/34.00, 1.00/8.00, 8.00/ 34.00 and 8.00/34.00, respectively. In steroid plus tenoxicam group, median pre- and post-treatment (at 1, 3 and 6 months) VAS/WOMAC scores were 7.00/34.00, 0.00/6.00, 1.00/8.00 and 2.00/10.00, respectively. VAS and WOMAC scores in 1 month after the injection significantly decreased in both groups compared to baseline (p<0.01). However, there was a pronounced improvement in only steroid plus tenoxicam group at 3 and 6 months post-injection (p<0.01). Steroid plus tenoxicam group showed significantly improved VAS and WOMAC scores when compared to only steroid and tenoxicam group at follow-up 3 and 6 months (p<0.01).

Conclusion: The combination of corticosteroids and tenoxicam seems to produce a more effective result than alone therapy in reducing pain and improving functional recovery.

REFERENCES:
OBJECTIVES: To examine the possible role of genetic susceptibility for fatigue in southern Spanish women with fibromyalgia, by looking at the possible associations of fatigue and single nucleotide polymorphisms in 34 fibromyalgia candidate-genes, at the interactions between genes, and at the associations between gene-physical activity.

METHODS: In this cross-sectional study participated 276 women with fibromyalgia. We extracted DNA from saliva in order to analyse gene-polymorphisms related to fibromyalgia susceptibility, symptoms, or potential neurological impacts. Accelerometers registered the participants' physical activity and sedentary time. Five dimensions of fatigue were assessed with the Multidimensional Fatigue Inventory. Age, body fat (%), and analgesics and antidepressants consumption were considered as confounders in all analyses. Based on the Bonferroni’s and False Discovery Rate (FDR) values, the statistical significance was interpreted.

RESULTS: AT carriers of the rs4435709 polymorphism (sodium channel protein type 9 subunit alpha, SCN9A, gene) showed the highest scores on fatigue. Carriers of the heterozygous genotype of the rs1801133 (methylene tetrahydrofolate reductase, MTHFR, gene) or rs4597545 (SCN9A gene) polymorphisms who were physically active reported lower fatigue compared to their inactive counterparts. Highly sedentary carriers of the homozygous genotype of the rs7607967 polymorphism (AA/AG genotype; SCN9A gene) presented higher fatigue than those with lower levels of sedentary time.

CONCLUSION: Physical (in)activity behaviours and the SCN9A and MTHFR genes were jointly related to fatigue. Thereby, the potential benefits of following an active lifestyle might be observed more clearly in women with fibromyalgia genetically predisposed to higher levels of fatigue.

REFERENCES:

Acknowledgement: This work was supported by the Spanish Ministry of Economy and Competitiveness [I+D+I-DEP2010-15639, I+D+I DEP2013-40908-R to M.D.-F.; BES-2014-06762 to F.E.-L.]; the Spanish Ministry of Education [FPU13/03410 to D.S.-T.; FPU 15/00002 to B.G.C.]; the Consejería de Turismo, Comercio y Deporte de Andalucía [CTCD-2010/00119242-TRA to MF-]; and the University of Granada, Plan Propio de Investigación 2016, Excellence actions: Units of Excellence; Unit of Excellence on Exercise and Health (UCEES).

Disclosure of Interests: None declared
Results: Replacing 30 minutes of ST with LPA was associated with better strength in upper limb (B=0.19), handgrip strength (B=0.02) and aerobic fitness (B=0.22); all p<0.02). Replacing 30 minutes of LPA with MPA was related to better strength and flexibility in lower and upper limb (B ranging from 0.43 to 1.97; all p<0.02). Finally, replacing 30 minutes of LPA with MPA was associated with better strength and flexibility in lower and upper limb, aerobic fitness and balance (B ranging from 0.15 to 8.54; all p<0.04).

Conclusion: Replacing short time periods (30 min) of ST by PA (especially of moderate intensity) was related to better physical fitness. Moreover, to replace 30 min of LPA by MPA was related to better physical fitness. Our findings support the implementation of experimental research to better understand the extent to which replacing sedentary time (by LPA or MPA) or replacing LPA (by MPA) might enhance difference components of physical fitness in fibromyalgia. Such findings would have direct clinical implications.

REFERENCES:

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THU0471
THE EFFECT OF VIRTUAL REALITY EXERCISES ON PAIN, FUNCTIONALITY, CARDIOPULMONARY CAPACITY AND QUALITY OF LIFE IN FIBROMYALGIA SYNDROME: A RANDOMIZED, SINGLE-BLIND, CONTROLLED STUDY

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Background: Fibromyalgia Syndrome (FMS) is a clinical condition with many symptoms such as chronic generalized pain, fatigue, sleep disorder, cognitive dysfunction and depressive mood. Management of FMS is difficult and the most important component is regular exercise. In this syndrome, patients generally have compliance and motivation problems in maintenance of exercises. In recent years, exercises, with fun and game components, have been prescribed to increase patient compliance.1 Motion-controlled video games targeting virtual reality are examples of these exercises.2

Objectives: To investigate the effect of motion controlled video games on pain, functionality, cardiopulmonary capacity and quality of life in fibromyalgia women.

Methods: Forty women (> 18 years) who have FMS were included in study. Patients were randomized into study and control groups. Control group performed aerobic exercise (cycling, 3 days/week, 20 minutes/day) for 4 weeks. Study group performed virtual reality exercise (Volleyball, Microsoft Xbox Kinect®, 3 days/week, 15 minutes/day) together with cycling exercise. After the four week supervised exercise program, both groups received the same home exercise program for four weeks. All patients were evaluated at baseline, 4th and 8th weeks. Primary outcome measure was Fibromyalgia Impact Questionnaire, Visual Analogue Scale (VAS), Hospital Anxiety and Depression Scale, Fatigue Severity Scale (FSS), Symptom Severity Scale, EuroQoL-Quality of Life/Visual Analogue Scale (EQ5D-QoL/VAS) and 6 Minute Walk Test (6MWT) were used as secondary outcome measures. Positive and Negative Affect Schedule (PANAS) was used for patient satisfaction. T-test was used to compare demographic data between two groups. Repeated measures ANOVA was used in evaluation of intra-group efficiency of treatment. Treatment group and time interaction was evaluated by two-way analysis of variance. We calculated 20 patients per group, in order to find 14% minimal clinical difference in Fibromyalgia Impact Questionnaire with 80% power and 0.05 error rate (Tip 1 error).3

Results: All patients completed supervised exercise program (4 weeks), 34 patients (17 study group, 17 control group) were evaluated at the 8th week. Age, body mass index, education status, comorbidities and drug use were similar in both groups (p > 0.05). After four weeks, all outcome measures improved significantly in both groups (p<0.05). However, there was no statistically significant difference in all outcome measures between 4th and 8th weeks. Group and time interactions for 6MWT (F (1,21, 46.33) = 4.04, p = 0.043), FSS (F (1,61, 61.24) = 4.21, p = 0.026), EQ5D-QoL Scale (F (2, 76) = 4.55, p = 0.014) and EQ5D-VAS Scale (F (1, 4, 53.55) = 3.59, p = 0.049) were significant only for the study group. In addition, PANAS score was significantly higher in study group (p <0.001).

Conclusion: Virtual reality exercises along with aerobic exercise increase cardiopulmonary capacity and quality of life in FMS. In addition, they increase patient satisfaction and may improve patient compliance to exercise.

REFERENCES:

Disclosure of Interests: None declared


THU0472
FIBROMYALGIA SYNDROME IN WEST AFRICA: ACR 1990 IS NOT SENSITIVE FOR THE UNDER-DIAGNOSED AND WIDELY MISUNDERSTOOD DISORDER

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Background: Like most poorly understood rheumatic conditions, Fibromyalgia is thought to be rare in West Africa. Many clinicians rely on the various ACR classification criteria to make a diagnosis of Fibromyalgia despite the unknown performance of these criteria among patients of sub-Saharan African origin.

Objectives: To describe the characteristics of fibromyalgia in Nigerian patients and determine the sensitivities of four ACR criteria sets.

Methods: Consecutive patients diagnosed with fibromyalgia for the first time by a rheumatologist were evaluated using ACR 1990, ACR 2010, 2011 modification of ACR 2010 (ACR 2011) and ACR 2016 classification criteria for fibromyalgia. Sleep quality was assessed with the Pittsburgh Sleep Quality Index (PSQI), fatigue with the Fatigue Severity Scale (FSS) and severity of fibromyalgia with the Revised Fibromyalgia Impact Questionnaire (FIQR). The overall characteristics and the beliefs of these patients regarding their disease were analysed.

Results: Of the one hundred and fourteen (114) patients, ninety six (96) were females; male-to-female ratio is 1:5.3. The median duration of symptoms before diagnosis is 54 months (3 to 273 months) and the mean age is 44.6±15.6 years. Mild, moderate, and severe fibromyalgia were found in 32(28.1%), 53(46.5%) and 29(25.4%) patients respectively. Sensitivities of ACR 1990, ACR 2010, ACR 2011, and ACR 2016 were 38.5%, 68.2%, 76.7% and 76.7%, respectively. Poor sleep was found in 83 (72.8%) patients. Patients in functional classes I, II, and III were 71 (62.3%), 19 (16.7%) and 24 (21.1%), respectively. There was none in class IV. There was positive history of widespread pain in at least one first degree relative of 56 (49.1%) patients. Twenty-one (18.4%) patients had changed or quit their job due to the disease and there was
significant association between job loss and number of tender points as well as disease severity. The Mean FFS score is 4.48±1.3 and 73 (64.0%) patients believed their problem is a spiritual attack while 43 (37.7%) had done one form of ritual or the other in search of cure.

**Conclusion:** Fibromyalgia syndrome exists in West Africa. It is poorly understood among the sufferers and ACR 1990 is not sensitive as a diagnostic tool for the condition.

**REFERENCES:**

**Disclosure of Interests:** None declared

**THU0473**  
**MINDFULNESS IN FIBROMYALGIA: MEAN LEVELS AND CORRELATION WITH DISEASE BURDEN**

**Marco Antivalle, Federica Rigamonti, Michele Agostì, Piercarlo Sarzi Puttini. L. Sacco University Hospital, Rheumatology, Milano, Italy**

**Background:** Limited evidence suggests that mindfulness-based interventions can have a role in the management of fibromyalgia (FMS) [1], with positive effects on quality of life, pain perception [2] and sleep problems [3]. However, there is little data on the levels of mindfulness in FMS and its relationship with the impact of disease.

**Objectives:** To evaluate the levels of mindfulness and its correlation with disease burden in FMS.

**Methods:** Mindfulness was assessed in 112 FMS patients (mean age 45.9±11.36 yrs, 86.5% females) and in 128 (43.60±14.35 yrs, 75% females) healthy control subjects by the Mindful Attention Awareness Scale (MAAS) questionnaire [4]. The MAAS, a 15-item scale developed to assess individual differences in the frequency of mindful states over time, is the most popular scale measuring mindfulness. Each item can be scored on a Likert scale from 1 to 6, lower scores indicating a greater tendency towards mindfulness. FMS patients were further evaluated by Widespread Pain Index (WPI) and Symptom Severity Scale Score as per 2016 criteria, by the revised FIQ score, and by the Facit-Fatigue scale. Data analysis, including ANOVA and Pearson correlations, was performed with the SPSS software.

**Results:** In the whole population, mean MAAS score was 4.17±0.72, a value comparable to literature data in different populations, and was correlated to age (r=-0.175, p= 0.008) but not significantly different in males vs females (4.28±0.67 vs 4.16± 0.72). FMS patients and control subjects showed similar values (4.12±0.80 and 4.22±0.63, p=0.291). In FMS patients, the MAAS score showed a significant direct correlation with FACIT-fatigue scores, and a significant inverse correlation with overall impact of disease, as assessed by the burden of somatic symptoms and FIQR score. MAAS score showed no significant correlations with variables directly related to pain domain (WPI, tender points), nor with disease duration (Table 1).

**Conclusion:** Mindfulness levels, as assessed by MAAS questionnaire, are not significantly different in FMS patients as compared to unselected healthy control subjects. However, levels of mindfulness are higher in patients reporting a higher disease burden, but lower in patients reporting lower levels of fatigue, and are not significantly correlated to pain. Mindfulness in FMS shows complex interactions with the different domains of the disease, and needs to be further investigated, in order to clarify its relationship with disease features, and eventually to establish guidelines for mindfulness-based interventions.

**REFERENCES:**

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.2191
PREVALENCE OF THYROIDIAN DISORDERS IN A POPULATION WITH FIBROMYALGIA

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Background: Fibromyalgia (FM) is a clinical syndrome characterized by diffuse pain associated with other symptoms such as fatigue, sleep disturbance and mood. It presents a series of differential diagnoses such as thyroid disorders, hypoparathyroidism, systemic inflammatory diseases and myopathies. Hypothyroidism is a disease with a prevalence of 4-6% of the population, having many symptoms in common with FM, such as fatigue, mood changes, constipation, and diffuse pain in some cases.

Objectives: The purpose is to evaluate the association between FM and thyroid disorders.

Methods: A retrospective monocentric case-control study in a tertiary hospital, with patients and controls having regular follow-up. The cases were composed of women over 40 years old, diagnosed with FM by the criteria ACR 1990 and ACR 2010, without autoimmune disease or other confounding diseases for pain. The control consisted of women over 40 years old, without autoimmune diseases. Laboratory tests included TSH and free T4 in all patients. Evaluation by ANA, anti-TPO and anti-thyroglobulin antibodies, only when appropriate. The sample was classified into euthyroid, clinical and subclinical hyperthyroid, clinical and subclinical hypothyroid. Statistical analysis included Fischer’s T-tests and others where appropriate. The p value was significant when ≤ 0.05.

Results: The sample consisted of 142 patients, (median age of 58 years) and controls with 136 patients (median age of 67 years). Patients with FM had a greater number of thyroid disorders (31.7%) than controls (14.7%) (p = 0.001). FM patients had a TSH higher than the controls (mean 9.06 vs 2.96; p = 0.0026), with a lower free T4 (mean 1.06 vs 1.31; p = 0.0001), ANA, anti-TPO and anti-thyroglobulin antibodies analysis showed no differences between both groups (p = 1; p = 0.08, p = 1; respectively), when performed. Because of the small difference in median age between the two groups, a sub analysis was performed separating patients between the ages of 40 to 60 years and over 60 years. The same results previously seen were found.

Conclusion: Patients with FM had a greater association with clinical hypothyroidism. However, we did not find any association with autoantibodies in our casistic.

REFERENCES:

Disclosure of Interests: Marco Antonio G Pontes Filho Speakers bureau: Novartis and Janssen, DIOGO SOUZA DOMICIANO: None declared, Rafael Pontes Andreussi: None declared, Leonardo Rodrigues da Silva: None declared


THU0475 THE EFFECT OF SUPERVISED DYNAMIC EXERCISE PROGRAM ON SOMATOSENSORY TEMPORAL DISCRIMINATION IN PATIENTS WITH FIBROMYALGIA SYNDROME

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Background: Somatosensory temporal discrimination (STD) is the detection of two separate stimuli applied to the body over a short period of time (1). It is thought that STD provides information about the central processing of sensory stimuli. It has recently been reported that STD is impaired in fibromyalgia syndrome (FMS), which is considered to be the prototype of central sensitization syndromes (2).

Objectives: To evaluate the effect of dynamic exercise program on STD in patients with FMS.

Methods: The study included 48 female FMS patients diagnosed according to the ACR 2010 classification criteria who applied to outpatient clinics of Physical Medicine and Rehabilitation Department. Patients with inflammatory rheumatic disease, peripheral and central neurological diseases, history of malignancy and cardiode problems, and those who started a new medical therapy or exercise program related to FMS in the last 3 months were excluded. Before the study, local ethics committee approval was obtained. The study was designed as a prospective, randomized, single blind and controlled study. The patients were divided into two groups. Those included in the supervised exercise group (SEG) were given an exercise program that consisted of submaximal aerobic exercise (treadmill) and low-medium resistant isometric exercises under the supervision of a physiotherapist, 1-hour per day, 3 days in a week for 4-weeks. Those included in the home exercise group (HEG) were given a home exercise program that consisted of low-to-medium resistance isometric exercises and aerobic exercises 1-hour per day, 3 days in a week for 4-weeks. All patients were evaluated at baseline and after 4 weeks of treatment. Visual analogue scale (VAS) for pain, hospital anxiety and depression scales (anxiety: HADA, depression: HADD), fibromyalgia effect questionnaire (FIO), symptom severity scale (SSS) were used for clinical assessment. Additionally somatosensory temporal discrimination threshold (STDT) was measured by a blinded investigator. In order to achieve a difference of 25ms in STDTs between two groups, we calculated 20 FMS patients per group (power: 80%, alpha: 0.05 two sided) (2). However, 24 patients were included in the study because of the 20% chance of discontinuation. For the demographic, basal clinical and neurophysiological comparisons between the two groups, the independent sample-T test was used for the normally distributed data, and the Mann Whitney U test was used for the non-normally distributed data. In order to assess the effect of treatment on outcome measures, 2-way repeated measures of variance analysis (Treatment group x time) was used. Intention to treat analysis was performed.

Results: There were statistically significant changes in the VAS, HADA, HADD, FIO and SSS scores and STDTs in both groups after treatment programs (p <0.001). In the 2-way repeated measures of variance analysis, the treatment group x time interactions for VAS, HADA, HADD, FIO and SSS scores were found to be significant in favor of the supervised exercise group (p <0.05). However, no statistically significant interaction (treatment group x time) was found for STDT (p: 0.18).

Conclusion: We demonstrated that STD improves with exercise in patients with fibromyalgia for 4 weeks. However, this change was similar in both groups. Additionally, we showed that dynamic exercise program ameliorates pain, psychological status, function and other symptoms related to fibromyalgia syndrome.

REFERENCES:

Disclosure of Interests: None declared


THU0476 NEW PARADIGMS IN FIBROMYALGIA RESEARCH: INFLAMMATORY CELLS-TO-LIPOPROTEINS RATIOS AS PREDICTIVE AND DISCRIMINATOR MARKERS

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Background: Fibromyalgia (FM) is a chronic idiopathic disease characterized by diffuse pain, fatigue, sleep disturbances, stiffness, anxiety and depression. Compared to healthy subjects. FM patients have significant high ratios of mean platelet volume, Neutrophil-to-lymphocyte, and platelet to lymphocyte. Fibromyalgia showed a significant abnormal lipid profile characterized by higher levels of fasting serum triglyceride and cholesterol.

Objectives: This study aimed to derive ratios from the circulating inflammatory cells and serum lipoprotein levels as markers of disease-severity in newly diagnosed fibromyalgia.

Methods: We carried out a cross-sectional study with 90 newly-diagnosed fibromyalgia patients and 25 aged-matched healthy subjects to determine the haematological indices and serum lipoprotein profile. Revised
fibromyalgia impact questionnaire (FIQR), Tender points (TPs), fatigue severity scale, insomnia severity index, and the Hamilton’s scale for depression were used to assess the disease severity.

Results: Monocyte-to-high density lipoprotein ratio (MHDR) correlated significantly and inversely with tender points and FIQR scores while lymphocyte-to-high density lipoprotein ratio (LNHDLR) and lymphocyte-to-apo lipoprotein-B100 (LAPOR) ratio correlated significantly and directly with FIQR. None of the circulating inflammatory cells-to-lipoprotein ratios correlated with fatigue, insomnia, and depression-related symptoms.

Multi-variable regression analysis revealed a significant mean score of FIQR-symptoms equal to 63.2 with prediction of 11.9% (R=0.346, F=5.903, p=0.004, β coefficients for MHLDR=−0.257, and for LNHDLR=−3.789). The area under the curve and 95% confidence intervals of LNHDL is 0.658 (0.545–0.771) at the cut-off score of the FIQR-related symptoms at 63.2.

Conclusion: Circulating inflammatory cell-to-lipoprotein ratios can serve as prognostic markers in the assessment of disease-severity in fibromyalgia patients.

REFERENCES:


Abstract THU0477 – Table 1. Correlations between disease-related symptoms with the ratios of circulating inflammatory cells-to-lipoproteins.

<table>
<thead>
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<th>Disease-related symptoms</th>
<th>MHLDR</th>
<th>LNHDLR</th>
<th>MAPOR</th>
<th>LAPOR</th>
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<tr>
<td>FIQR-Function</td>
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<td>Fatigue severity scale</td>
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<td>Insomnia severity index</td>
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Disclosure of Interests: None declared

THU0477
A FIBROMYALGIA ASSESSMENT SCREENING TOOL ON A MULTIDIMENSIONAL HEALTH ASSESSMENT QUESTIONNAIRE (MDHAQ) WHICH DOES NOT INCLUDE A SELF-REPORT PAINFUL JOINT COUNT (PAINFUL JC), FAST3nJC, RECOGNIZES FIBROMYALGIA SIMILARLY TO OTHER FAST3 INDICES WHICH INCLUDE A PAINFUL JC

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Background: Fibromyalgia (FM) generally is easily recognized, but a diagnosis may be difficult, particularly in patients with secondary FM who have other primary diagnoses. Criteria for FM initially were reported in 2000, and revised in 2011 and 2016, based entirely on a patient self-report questionnaire. However, FM criteria are not collected in most routine clinical care, as it is not feasible to use multiple patient questionnaires in busy clinical settings. MDHAQ/RAPID3 (multidimensional health assessment questionnaire/routine assessment of patient index data) has been found informative in all diseases in which it has been studied. Cumulative indices based on MDHAQ scales known as FAST3 (fibromyalgia assessment screening tool) recognize FM at levels of agreement with revised FM criteria of >80% and correlations of >0.80, p<0.001. Pragmatic recognition of FM in non-rheumatic diseases based on MDHAQ may be possible, as most components of the MDHAQ (as well as the HAQ) appear generic rather than disease-specific. One component of MDHAQ/FAST indices, a self-report painful joint count (painful JC), is rheumatology-specific. Therefore, a FAST3-nJC (no painful JC) index was analyzed vs revised FM criteria as gold standards for possible use in non-rheumatology patients to recognize FM.

Objectives: To analyze FAST3-nJC versus 2011 and 2016 FM criteria, and compared to other FAST3 indices which include a painful JC, to recognize FM.

Methods: All patients with all diagnoses complete an MDHAQ at all visits in routine care at one setting. The self-report questionnaire to recognize the 2011 and 2016 FM Criteria was added over a 6-month period to be completed by consecutive patients. The MDHAQ includes 0–10 scores for physical function, pain and patient global visual analog scales (VAS), compiled into 0–30 RAPID3, as well as a 0–10 fatigue VAS, 0–5 self-report painful joint count, and 0–60 symptom checklist. All MDHAQ scales were analyzed for agreement with FM Criteria according to receiver-operator-characteristic (ROC) curves for area under the curve (AUC). Optimal cut points for each measure were identified, based on specificity and sensitivity, to develop optimal cumulative indices for clues to FM versus the 2011 and 2016 Criteria as gold standards.

Results: Among 502 patients with complete data, primary ICD-10 diagnoses were FM in 49, OA in 74, RA in 78, SLE 88 and other rheumatic diseases in 213. Primary or secondary FM was identified in 131 (26%) who met 2011 FM criteria, and 112 (22%) who met 2016 FM criteria. The 4 MDHAQ scales with the highest AUC vs FM Criteria (0.829–0.889) were symptom checklist, painful JC, fatigue, and pain. Three cumulative FAST3 measures were: FAST3-P with symptom checklist, painful JC and pain VAS; FAST3-F with symptom checklist, painful JC and fatigue VAS; FAST3nJC with symptom checklist, pain and fatigue VAS, but no painful JC. All FAST3 indices agreed with FM Criteria >79% and kappas were >0.52, indicating good agreement (Table). As expected, lowest agreement was seen for FAST3nJC, since the FM criteria include a self-report painful joint count, but differences are quite small.

Abstract THU0477 – Table 1. Percent agreement and kappa of 3 FAST3 (fibromyalgia assessment screening tool) indices vs 2011 and 2016 FM Criteria

<table>
<thead>
<tr>
<th>FAST3 index</th>
<th>FAST3-P (pain)</th>
<th>FAST3-F (fatigue)</th>
<th>FAST3-nJC (no painful JC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>vs 2011 FM Criteria</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Agreement</td>
<td>84.3%</td>
<td>86.6%</td>
<td>81.5%</td>
</tr>
<tr>
<td>Kappa</td>
<td>0.63 (0.56–0.70)</td>
<td>0.68 (0.60–0.75)</td>
<td>0.58 (0.50–0.66)</td>
</tr>
<tr>
<td>vs 2016 FM Criteria</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>% Agreement</td>
<td>81.7%</td>
<td>83.8%</td>
<td>79.1%</td>
</tr>
<tr>
<td>Kappa</td>
<td>0.56 (0.48–0.53)</td>
<td>0.60 (0.51–0.68)</td>
<td>0.52 (0.44–0.60)</td>
</tr>
</tbody>
</table>

Conclusion: FAST3nJC had slightly lesser agreement with 2011 and 2016 FM criteria than FAST3-P and FAST3-F but would appear
satisfactorily as a candidate for clues to recognize FM in patients with non-rheumatic diseases, as a diagnosis of FM ultimately is made by a physician.

Disclosure of Interests: None declared


THU0478 IS FIBROMYALGIA ASSOCIATED WITH STRUCTURAL OR FUNCTIONAL ABNORMALITIES IN SKELETAL MUSCLE?

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Background: Fibromyalgia (FM) is a chronic nonarticular pain syndrome of unknown etiology characterized by diffuse muscular pain, fatigue and mood disturbances. Previous studies have shown absence of skeletal muscle degeneration, regeneration or inflammation. Altered muscle fiber size distribution and decreased capillary density were the only abnormalities reported. From the clinical point of view some FM symptoms (fatigue, pain, myalgias, trigger points, stiffness) suggest skeletal muscle involvement. Objectives: The objective of this study is to determine if there are structural and functional abnormalities in the skeletal muscle in patients with primary FM assessed by means of a non-invasive, low-cost multimodality approach.

Methods: Female patients > 18 years, with FM diagnosis (ACR 2010 criteria) and healthy controls matched by age. Skeletal muscle morpho-structure and function were assessed by: body mass index (BMI), total fat mass and total muscle mass calculated by direct segmental multi-frequency bioelectrical impedance analysis. Cross-sectional measurements of rectus femoris muscle area and tissue echogenicity were evaluated by ultrasound and pixel analysis. Maximum handgrip strength by digital dynamometry, gait speed (6-meter time walk test), and FM Health Assessment Questionnaire (FAHQ).

Results: A total of 94 FM patients and 140 healthy controls were included, mean age was 51.6 years +/- 10.8 vs 50.2 +/- 11.3, respectively (p = 0.27). FM patients compared with controls had similar BMI (27.9 kg/m2 +/- 4.9 vs 26.8 +/- 4.5, p = 0.14), higher total body fat mass (27.8 kg +/- 9.2 vs 25.1 +/- 7.6, p = 0.04), rectus femoris muscle area was also higher for FM patients (44.6 cm2 +/- 11.4 vs 41.7 +/- 13.9, p = 0.05); regarding ultrasound tissue echogenicity, FM patients demonstrated higher mean brightness in rectus femoris (157.2 pixels +/- 19.4 vs 149.8 +/- 22.4, p = 0.01); lesser handgrip strength (22.0 kg +/- 6.6 vs 26.2 +/- 5.4 p = 0.0001); slower gait speed (1.14 m/s +/- 0.2 vs 1.3 +/- 0.2 p = 0.0001); and major impairment in daily activities by FFAQ (47% vs 2.90% p = 0.0001).

Conclusion: This non-invasive multimodal evaluation of the skeletal muscle showed the presence of structural and functional abnormalities in women with FM. These changes can be attributed to sedentary and hyperactive lifestyle with consequent higher total body fat mass, skeletal muscle fat infiltration, and functional impairment of activities of daily living. Alternatively, these abnormalities may also be an expression of a small-fiber neuropathy (myoneuropastic deregulation). Further studies are required to elucidate its underlying pathological process.

REFERENCES:

Disclosure of Interests: None declared


THU0479 SAFETY AND Efficacy of MedicaL CANnaBiS in FIBROMYALGIA

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1Soroka Medical Center, Rheumatology, Beersheba, Israel; 2Soroka Medical Center, Beersheba, Israel

Background: Although chronic pain is a well established indication for medical cannabis therapy, there is scarce evidence to support the role of medical cannabis in the treatment of fibromyalgia.

Objectives: The aim of this study was to investigate the characteristics, safety and effectiveness of medical cannabis therapy for fibromyalgia.

Methods: A prospective study with 6 months follow-up period based on fibromyalgia patients who were willing to answer questionnaire in a specialized medical cannabis clinic between 2015 and 2017.

Results: Among the 367 fibromyalgia patients the mean age was 52.9 +/-15.1, of whom 301 (82.0%) were women, 28 patients (7.6%) stopped the treatment prior to the six months follow-up. The six months response rate was 70.8%. Pain intensity (scale 0-10) reduced from a median of 9.0 at baseline to 5.0 (p<0.001), and 194 patients (81.1%) achieved treatment response. In a multivariate analysis age above 60 years (Odds ratio [OR] 0.34, 95% C.I 0.16-0.72), concerns about cannabis treatment (OR 0.36, 95% C.I 0.16-0.80), spasticity (OR 2.26, 95% C.I 1.08-4.72) and previous use of cannabis (OR 2.46 95% C.I 1.06-5.74) were associated with treatment outcome. The most common adverse effects were mild and included dizziness (7.9%), dry mouth (6.7%) and gastrointestinal symptoms (5.4%).

Conclusion: Medical cannabis appears to be safe and effective alternative for the treatment of fibromyalgia symptoms. Standardization of treatment compounds and regimens are required.

Disclosure of Interests: Ittch Sagyi: None declared, Lihi Bar-Lev Schleider Employee of: employee of Tikun Olam Ltd. without shares or options, Mahmoud Abu-Shakra: None declared, Victor Novack Consultant for: paid member of the Tikun Olam Ltd. scientific advisory board


THU0480 IS PROLONGED SEDENTARY TIME ASSOCIATED WITH THE IMPACT OF THE DISEASE IN WOMEN WITH FIBROMYALGIA? THE AL-ANDALUS PROJECT

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Background: Spending time seated has previously shown to be associated with worse symptomatology in fibromyalgia. In addition, to accumulate sedentary time (ST) in prolonged, unbroken periods (bouts) has shown to be particularly harmful in the general population.

Objectives: To examine the association of prolonged ST with the impact of the disease in women with fibromyalgia.

Methods: Four-hundred-and-seven (51.4±7.6 years old) fibromyalgia women participated in this cross-sectional study. Sedentary time accumulated in bouts of ≥10, ≥20, ≥30 and ≥60 minutes, and moderate-to-vigorous physical activity (MVPA) were measured with triaxial accelerometer (GT3X+). To control for total ST, the percentage of ST spent in different bout categories were calculated (e.g., time spent in bouts ≥30 min/ total ST) ×100. We assessed different domains of fibromyalgia impact (function, overall, symptoms) and the global impact of fibromyalgia (total score) with the Revised Fibromyalgia Impact Questionnaire (FIQ). Separate linear regression models were built to assess the association of percentage of ST spent in different bout categories (independent variables) with the domains of fibromyalgia impact and the global impact of the disease (dependent variable) while controlling for age, fat percentage, medication for fibromyalgia and depression, and total accelerometer wear time.

Results: Greater percentage of ST spent in bouts ≥10 min (β=0.171, p<0.001), ≥20 min (β=0.163, p<0.001), ≥30 min (β=0.169, p<0.001), and ≥60 min (β=0.161, p<0.001) was associated with greater global impact of the disease. In model 2, greater percentage of ST spent in bouts ≥10 min (β=0.145, p<0.003), ≥20 min (β=0.138, p<0.004), ≥30 min (β=0.148, p<0.001) was associated with greater impact of the disease.

Disclosure of Interests: None declared

Sleep Disturbances in Fibromyalgia

Incidence of OSA in FM has been variably reported but estimated at 25-40% disorder, with an estimated incidence of 14% of males and 5% females.

References:

Acknowledgement: We thank all the study participants for their collaboration. Funding: This study was supported by the Spanish Ministry of Economy and Competitiveness (I+D+i DEP2010-15659; I+D+i DEP2013-40908-R; BES-2014-07612) and the Spanish Ministry of Education (FPU 15/0002).

Disclosure of Interests: None declared.


SLEEP DISTURBANCES IN FIBROMYALGIA – AN AUSTRALIAN TERTIARY HOSPITAL EXPERIENCE

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Background: Fibromyalgia (FM) is a central pain disorder with an estimated population prevalence of 2-7% and six times as common in women than men. Obstructive sleep apnoea (OSA) is a structural sleep disorder, with an estimated incidence of 14% of males and 5% females. Incidence of OSA in FM has been variably reported but estimated at 25-40% disorder, with an estimated incidence of 14% of males and 5% females.

REFERENCES:

Disclosure of Interests: None declared.


Abstract THU0481 – Table 2. Sleep Study Data

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<th>Female</th>
<th>T value</th>
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<tr>
<td>Awake Total Sleep Time (TST)</td>
<td>742.4 (98.7)</td>
<td>665.8 (93.1)</td>
<td>0.014</td>
</tr>
<tr>
<td>Sleep Efficiency (SE)</td>
<td>84.9 (7.2)</td>
<td>83.6 (7.0)</td>
<td>0.023</td>
</tr>
<tr>
<td>Number of Sleep Arousals</td>
<td>8.5 (4.2)</td>
<td>5.7 (2.0)</td>
<td>0.003</td>
</tr>
<tr>
<td>Number of Sleep Stages</td>
<td>20.4 (8.4)</td>
<td>24.2 (1.6)</td>
<td>0.003</td>
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</table>

<table>
<thead>
<tr>
<th>B. One to One Matched Group</th>
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<td>Awake Total Sleep Time (TST)</td>
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</tr>
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</table>

Conclusion: Female predominance and 3% population incidence of FM was congruent with literature. We note the mean age was nearing expected upper limits for FM. Increased age as a risk factor for OSA may have led this selection bias. Unexpectedly, overall severity of OSA as per AHI and number of desaturating events as per ODI3 was less in FM. We hypothesise that this is due to a higher proportion of females in the FM group compared to males, confirmation would require a larger study cohort, a limitation of this study. It was beyond the scope of this study to explore concomitant medication use and comorbidities and its effect on sleep. Another significant finding was in males, where sleep efficiency (SE) was lower in both matched and random groups. Furthermore, when matched for age, gender and BMI, males FM have reduced total sleep time. Suggesting that males with FM may have additional impediments to good sleep efficiency which may not be readily recognised during clinical evaluation. Similarly to Prados et al, we found females with FM (fig. 3) had a trend for better sleep quality and less sleep disturbance. However, no domain reached statistical significance, which again reflects low study power. This study emphasises the contribution of OSA as a comorbidity for patients with FM and its effect on sleep quality. Importantly, also the differences in gender.

REFERENCES:

Disclosure of Interests: None declared.


Abstract THU0481 – Table 3. Female Study Data

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REFERENCES:

Disclosure of Interests: None declared.

Back pain, mechanical musculoskeletal problems, local soft tissue disorders

**THU0482**

**HUMAN LUMBAR SPINE FACET JOINT OSTEOARTHRITIS DISPLAYS PREDOMINANT NGF EXPRESSION AND SIGNALING IN CAPSULAR SYNOVIOUM AND SUBCONDYRAL BONE MARROW TISSUES INDEPENDENT OF OSTEOARTHRITIS GRADE**

Matthias Seidel1, Nathalie Busso2, Veronique Chobaz2, Cordula Netzer3, Thomas Huegiele2, Jeroen Geurts3, Matthias Seidel1, Nathalie Busso2, Veronique Chobaz2, Cordula Netzer3, Thomas Huegiele2, Jeroen Geurts3.

**Background:** Increased nerve growth factor (NGF) levels are associated with chronic pain conditions, including low back pain and osteoarthritis (OA). NGF signalling through its receptor TrkA regulates pro-inflammatory neurotransmitters such as substance P (SP). Inhibition of NGF has shown therapeutic efficacy in knee OA [1] and chronic back pain [2], but trials have revealed rare cases of rapidly progressive OA of peripheral joints.

**Objectives:** To describe the tissue distribution of NGF, TrkA, SP and macrophages in facet joint osteoarthritis (FJOA) of the lumbar spine and their association with FJOA grade.

**Methods:** FJOA specimens were obtained by facetectomy from patients undergoing intervertebral fusion (n=10, average age 69 years, 5 males). FJOA severity and presence of synovial hypertrophy was graded using preoperative magnetic resonance imaging (MRI). Relative abundance of NGF, CD68 (macrophages), TrkA and SP in capsular synovium (SY), cartilage (CL), subchondral bone (SB) and subchondral bone marrow (BM) was evaluated semi-quantitatively on a scale ranging from 0-3 using immunohistochemistry. Association between imaging parameters and tissue expression was determined using Pearson correlation analysis.

**Results:** Synovial hypertrophy as determined by MRI was present in six cases (60%) and median Weishaupt grade of FJOA was 2 (1.5-3) corresponding with moderate to severe OA. NGF was abundantly expressed in SY (3 [0.5-3]) and to a lesser extent in BM tissues (2 [1-3], whereas TrkA expression was detected in BM exclusively. NGF abundance in SY and BM showed a strong correlation (r=0.94), but did not associate with synovial hypertrophy or FJOA severity. CD68+ macrophages were highly abundant in BM (3 [1.5-3]) and sparse in SY tissues (0.5 [0-1]). The relative abundance of macrophages and NGF was strongly correlated in SY tissue only (r = 0.78). SP as a downstream mediator of NGF signalling was also abundantly expressed in SY, CL and BM tissues. Tissue distributions of CD68, NGF and SP are summarized in the figure.

**Conclusion:** NGF expression and signalling is evident in lumbar spine FJOA specimens, but not strongly associated with synovial hypertrophy or disease severity. These results are in agreement with recent studies of human knee OA, which have shown osteochondral NGF expression as a hallmark of symptomatic OA independently of chondropathy or synovitis [3].

**REFERENCES:**


**Disclosure of Interests:** Matthias Seidel Grant/research support from: AbbVie, Lilly, Novartis and Pfizer, Speakers bureau: AbbVie, Lilly, Novartis and Pfizer, Jeroen Geurts: None declared

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**THU0483**

**DEMOGRAPHICS AND CLINICAL CHARACTERISTICS OF A NATIONAL COHORT OF 290 PATIENTS WITH JOINT HYPERMOBILITY SYNDROME, THEIR SOCIOECONOMIC BURDEN AND THE PERFORMANCE OF THE 2017 INTERNATIONAL CLASSIFICATION CRITERIA OF THE EHLERS DANLOS SYNDROMES**

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**Background:** Joint hypermobility syndromes (JHS) encompass a spectrum ranging from asymptomatic joint hypermobility through to Ehlers Danlos syndromes (EDS) including hypermobile EDS (equivalent to the former diagnosis of EDS type 3). Many EDS patients have significant musculoskeletal pain and other systemic comorbidities including autonomic, bowel and bladder dysfunction. We present data from a cohort of patients with JHS referred to our tertiary centre from December 2015 to May 2017.

**Objectives:** To increase the awareness of the hypermobility syndrome among general rheumatologists and other health professionals. To assess the impact of this condition on the patient general health and their work disability.

**Methods:** We undertook a retrospective analysis of medical records. Statistical analysis utilised non parametric Chi squared analysis for between group comparisons.

**Results:** There were 280 patients: 253 patients (90%) were female and 27 were male (10%) with a female to male ratio of 9:1. The age distribution was from 18 to 66 (mean age 42 years). The age at which they were first diagnosed ranged from 4 to 55 (mean age 29 years); 279 (96%) had Ehlers Danlos Syndrome type 3, one patient had Marfan’s, one Kyphoscoliotic EDS, and two patients had Tenascin X deficiency.

Family history of hypermobility was reported among 185 patients (86%). In relation to the autonomic dysfunction, 185 patients (86%) had orthostatic intolerance, 126 (45%) had gastrointestinal problems; 109 (39%) had bladder dysfunction with 2.5% of them requiring catheterisation. Chronic joint and muscle pain was reported in 91%; 49.6% of these used opioid analgesia long term. One hundred and twenty patients (43%) had work disability.

**Conclusion:** Treatment of JHS is likely to have work disability; 54% vs. 34% (p<0.001). Bladder problems were more common in the group taking opioids (46% vs 32%; p<0.02). A significant association between orthostatic intolerance and bowel problems was observed. Almost half (47%) of those with orthostatic hypotension had bowel problems, compared to only 19% without (p<0.001). Patients with bowel problems were more likely to have bladder problems compared to those without bowel problems (P <0.001).

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.8380

**REFERENCES:**


**Disclosure of Interests:** None declared

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**THU0484**

**ESTIMATION OF PATIENT ACCEPTABLE SYMPTOM STATE FOR PATIENT-REPORTED OUTCOMES BETWEEN 2 POPULATIONS OF PATIENTS WITH NON-SPECIFIC CHRONIC LOW BACK PAIN**

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**Background:** Clinical relevance of commonly used patient-reported outcomes (PROs) is unclear in people with non-specific chronic low back pain (cLBP). Our aim is to determine whether baseline variables contribute to an acceptable symptom state at 1 month.

**Objectives:** To estimate and compare patient acceptable symptom state (PASS) at 1 month post-intervention for 4 PROs between 2 populations of patients with non-specific cLBP and to determine which baseline variables contribute to having an acceptable symptom state at 1 month.

**Methods:** Overall, we included 256 patients: 135 patients with cLBP and active discopathy participated in a randomized controlled trial assessing the efficacy on pain at 1 month of a single glucocorticoid intradicinal injection compared to contrast alone (2), and 121 patients with cLBP and without active discopathy participated in a randomized controlled trial assessing the efficacy on pain at 4 months of 12 sessions of immersive virtual reality (VR) compared to usual care (3). Using an anchor-based method, PASS estimates for PROs were obtained using the 75th percentile method (4). Logistic regression was used to determine baseline variables contributing to achieving PASS at 1 month.

**Results:** At 1 month, 137/256 (53.52%) participants self-rated their health as acceptable. In the whole population, PASS (95% IC) was 47.50 (40.00 to 55.00) for the lumbar-pain VAS, 30.50 (30.00 to 40.00) for the radicular-pain VAS, 39.27 (33.60 to 45.26) for the QUEBEC score, 9.95 (9.16 to 10.00) for the HAD anxiety subscale and 6.70 (6.00 to 8.00) for the HAD depression subscale. The PASS estimates did not differ between the 2 populations of cLBP patients for any of the PRO. The only baseline variable contributing to having an acceptable symptom state at 1 month was symptom intensity.

**Conclusion:** PASS estimates at 1 month did not vary across 2 independent samples of people with cLBP and 2 distinct nociceptive sources of cLBP. The main contributor of the PASS was symptom intensity at baseline. Our findings can be useful in interpreting the clinical relevance of PROs values.

**References:**


**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.3604

**THU0485**

**EFFICACY OF EXTRACORPOREAL SHOCK-WAVE THERAPY IN THE TREATMENT OF SHOULDER CALCIFIC TENDINITIS IN INSUFFICIENT RESPONDERS TO LOCAL STEROID INJECTION THERAPY: A RETROSPECTIVE ANALYSIS**

Meryem Yılmaz Kayşin, Feyza Ünlü Ozkan, Aktas Ilknur, Pinar Akpinar. University of Health Sciences, Faith Sultan Mehmet Training and Research Hospital, Physical Medicine and Rehabilitation, Istanbul, Turkey

**Background:** Calcific tendinitis (CT) results from the deposit of calcium hydroxyapatite crystals in periacellar muscular attachments, and most commonly affects the tendons of the shoulder (1). Extracorporeal shock wave therapy (ESWT) is based on the use of shock waves, and used for pain reduction and tissue healing (2).

**Objectives:** The aim of this analysis is to demonstrate the effects of ESWT in patients with shoulder CT with inefficient response to local steroid injection.

**Methods:** Two-year data of shoulder outpatient clinic were scanned. 10 patients with shoulder calcific tendinitis without satisfying response to local steroid injection (less than 50% decrease in pain-visual analog scale (VAS) score) who were treated with ESWT were reviewed.

**Results:** 10 patients (9 women, 1 man) fulfilled the inclusion criteria. The mean patient age was 51.3 years (range, 32-70 years) and body mass index was 26.2 kg/m2. The affected shoulder was left in 6 (60%) patients and right in 4 (40%). The calcific tendinitis involved the dominant side in 5 (50%) patients and non-dominant side in other 5 (50%). All patients had one peritendinous local steroid injection-2 ml 2% prilocain and 1 ml steroid (5 mg of betamethasone dipropionate + 2 mg betamethasone sodium phosphate). Mean time from symptom onset to the ESWT treatment was 3.5 weeks (range, 2-6 weeks). Mean VAS score was 9 and Shoulder Disability Index (SDI) score was 84.4 before ESWT treatment. ESWT system Elmed-Vibrolith ver3.0 was used in the treatment, each treatment consisted 2000 shocks with a frequency of 150 shocks a minute with maximum tolerable energy density (range, 3.2-3.4 bar). Mean ESWT session was 3.3 (3 patients had 3, 1 patient had 4 and 1 patient had 5 sessions of treatment). Mean post-treatment VAS score was 4.2 (53.3% decrease) and SDI score was 43.8 (48.1% decrease) which were evaluated after the last ESWT session.

**Conclusion:** With its good tolerance and safety, ESWT might be an alternative treatment method for calcific tendinitis of the shoulder. Although limited number of patients, we hope that this study might give rise to future randomized-controlled studies about the efficacy of ESWT in acute-subacute shoulder calcific tendinitis.

**References:**


**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.4330

**THU0486**

**PREGBALFIN EFFICACY IN THE TREATMENT OF CHRONIC PAIN IN PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background:** Objectives: To study the efficacy of Pregabal in the treatment of chronic pain in patients with rheumatoid arthritis.

Methods: We enrolled 80 patients with rheumatoid arthritis. Screening with the DN4 neuropathic pain questionnaire showed that 31% of patients (n=25) had a neuropathic pain component (NCP+), DN4-4 points. Mean age was 57.0 ±7.49 years, disease duration - 9.87 ± 9.5 years, DAS28 disease activity - 5.5 ± 1.3, VAS pain intensity - 73.1 ± 17.4. All patients were randomized into two groups: group I received pregabalin in combination with DMARDs; group II received DMARDs only. All patients underwent a clinical and neurological examination, disease activity was assessed with the DAS28 index, the effect of treatment on neuropathic pain was assessed with the DN4 and Pain DETECT questionnaires, pain intensity at rest – with the VAS scale.

**Results:** There were no significant differences between groups before the start of the study (Table 1)

**Abstract THU0486 - Table 1**

<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>P&lt;0.05</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>58.2±9.15</td>
<td>56.2±6.9</td>
<td>0.6</td>
</tr>
<tr>
<td>Disease duration (years)</td>
<td>13.6±6.7</td>
<td>7.07±3.4</td>
<td>0.3</td>
</tr>
<tr>
<td>DAS28</td>
<td>5.3±3.6</td>
<td>4.8±1.6</td>
<td>0.4</td>
</tr>
<tr>
<td>DN4 (points)</td>
<td>5.2±1.1</td>
<td>5.0±0.6</td>
<td>0.7</td>
</tr>
<tr>
<td>Pain Detect (points)</td>
<td>17.0±3.2</td>
<td>18.2±2.9</td>
<td>0.4</td>
</tr>
<tr>
<td>HADS-Anxiety</td>
<td>6.8±3.2</td>
<td>12.0±4.8</td>
<td>0.7</td>
</tr>
<tr>
<td>HADS-Depression</td>
<td>8.4±2.2</td>
<td>8.0±2.6</td>
<td>0.7</td>
</tr>
<tr>
<td>VAS, mm</td>
<td>77.0±33.5</td>
<td>75.2±14.7</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Positive dynamics of VAS pain intensity was observed in both groups [Fig. 1] (77.0 ± 13.5 vs 75.2 ± 14.7, at week 2 48.8 ± 14.2 vs 72.9 ± 14.7).
PERINEURAL INJECTION THERAPY; A NEW MODALITY IN MANAGEMENT OF MECHANICAL LOW BACK PAIN; A COMPARATIVE STUDY

Mohammed Hassan Abu-Zaid, Samar Abd Alhamed Tabra. Faculty of Medicine Tanta University, Rheumatology and Rehabilitation, Tanta, Egypt

Background: Chronic mechanical low back pain represents the second leading cause of disability worldwide being a major welfare and economic problem².

Subcutaneous prolotherapy treats prolonged pathological peripheral neurogenic inflammation for several painful conditions. As it induces apoptosis of proliferating peptidergic nociceptors and neovessels by reducing vascular endothelial growth factor.²

Objectives: To assess the effectiveness of subcutaneous perineural injection therapy in management of pain, physical function, disability and psychological status in mechanical low back pain

Methods: Ninety patients with non-radiating non-specific chronic mechanical low back pain (LBP) that persisted for 12 weeks or more were selected in this study. (Patients with inflammatory LBP, radiating, or LBP due to specific cause, pregnant women or Patients with implanted pacemaker or spinal cord stimulator were excluded from this study). After giving written consent; the patients were randomly divided into 3 groups 30 patients in each. Group I received 8 weekly subcutaneous injections of 1 ml of buffered dextrose 5% in each chronic constriction injury points and tender points in back and buttock. Group II treated by using pulsed electromagnetic field stimulation (PEMFs) for 30 minutes over the lower lumbar region with frequency of 10 Hz and intensity of 2 millitesla every other day for 8 weeks. Group III received sham PEMFs. All patients will be instructed to follow an exercise program in the form of stretching for bar region with frequency of 10 Hz and intensity of 2 millitesla every day for 8 weeks.

Results: The mean age of patients in the 3 groups was 40.2±10.5, 38.3 ±9.9, and 43.1±10.8 respectively. The mean VAS was 7.9±1.4, 8.2±0.6, and 7.6±1.1 respectively. No baseline differences existed between all groups in all parameters. There was significant improvement in VAS, WOMAC and HDAS in group I & II (p<0.05) after treatment, and 4 months later (figure 1). While the improvement in group III was non-significant (p>0.05). The improvement in group I was better than in group II with significant difference between the two groups (p<0.05) after treatment and 4 months follow up.

Conclusion: This preliminary data shows greater effectiveness of Pregabalin in comparison with NSAID and DMARD treatment, both in terms of pain intensity and the neuropathic pain component, which is of practical importance.

Disclosure of Interests: Katerina Filatova: None declared, Shandor Erdes Consultant for: Development of studies concepts., Speakers bureau: Educational meetings organized or supported by companies.


ACHILLES TENDON RUPTURE ASSOCIATED WITH THE USE OF FLUOROQUINOLONES IN PATIENTS OLDER THAN 60 YEARS

Andrea Briones-Figueroa, Walter Alberto Silientes-Giraldo, Jose Luis Morell Hita, Mónica Vázquez Díaz. University Hospital Ramón y Cajal, Rheumatology, Madrid, Spain

Background: Fluoroquinolones (FQ) are a class of broad-spectrum antibiotics whose use has spread as they are considered safe and well tolerated drugs. Among its musculoskeletal side effects, Achilles tendon rupture (ATR) is a well-known complication that can be disabling, arising recent interest from the pharmacovigilance system after evaluating the reported side effects.

Objectives: To describe the epidemiological and clinical features of patients diagnosed with FQ-associated ATR in a Spanish tertiary hospital.

Methods: A retrospective observational study was performed, which included all patients older than 60 years who were diagnosed of ATR in our center during the period 2000-2017, identifying patients who had been previously treated with FQ. The demographic, clinical and outcome data were obtained from their medical records.

Results: During the study period, 44 patients with ATR were identified, 8 (14.6%) of them previously treated with FQ. In this group of patients, the mean age at diagnosis of ATR was 77.3±9.54 years, being male 6 (75%). Four of them (50%) received concomitant treatment with corticosteroids (CS) and one patient had undergone kidney transplantation due to nephroangiosclerosis. Seven patients (87.5%) were treated with Levofloxacin and one case received Ciprofloxacin, all of them orally. The indication for FQ treatment in half of the cases was acute bronchitis and in the other half exacerbations of underlying respiratory pathology (chronic obstructive pulmonary disease and diffuse interstitial lung disease). The mean duration of treatment with FQ was 6.16 ± 2.4 days, while the mean time from the start of treatment to the diagnosis of ATR was 19.25 ± 14.83 days. In seven patients (87.5%) the rupture was spontaneous, while one patient presented traumatic rupture (low impact traumatism). 87.5% of the ruptures were total ruptures and all cases required surgical treatment, without recurrence reported. The comparison of the characteristics of patients with ATR who had or not received treatment with FQ is shown in the table, identifying significant differences in favor of a higher percentage of patients who were smokers, received concomitant treatment with CS and had spontaneous rupture in the group of patients who had received FQ.

Disclosure of Interests: None declared


References:
Fluoroquinolones Non-Fluoroquinolones p-value

| Age (years) | 77.37 ± 9.54 | 70.13 ± 8.3 | 0.48 |
| Sex | Male 6 (75%) | 25 (69.4%) | 0.75 |
| | Female 2 (25%) | 11 (30.6%) |
| Smoking | 5 (62.5%) | 1 (2.8%) | 0.00 |
| Treatment with CS | 4 (50%) | 2 (5.6%) | 0.01 |
| Treatment with | 0 (0%) | 5 (13.9%) | 0.26 |

Type of rupture

Spontaneous 7 (87.5%) 8 (25.8%) 0.01

Traumatic 1 (12.5%) 23 (74.2%)

Conclusion: The Achilles tendon is the most frequent location of tendinopathy associated with FQ, being affected in 95% of cases. The risk factors associated to an increased risk to develop FQ-associated ATR includes age over 60 years, male gender, chronic treatment with CS and organ transplantation, all these being present in our cases. Despite being a relatively frequent adverse event, it is underdiagnosed and the risk of ATR is not usually assessed when indicating FQ treatment. It is important to perform a risk/benefit assessment, specially in patients with associated risk factors, because most ruptures are complete and require surgical treatment, and may be a potential cause of disability.

REFERENCES:

Disclosure of Interests: None declared

THU0489 REAL-WORLD EFFECTIVENESS OF FIXED-SITE HIGH-FREQUENCY TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION IN CHRONIC LOW BACK PAIN

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Background: Fixed-site high-frequency transcutaneous electrical nerve stimulation (FS-TENS) is a form of TENS in which the stimulator is designed for a predetermined location rather than for co-localization with the patient’s pain. A small wearable device for localized application while active and sleeping facilitates adequate dosing.

Objectives: To evaluate the effectiveness of regular FS-TENS use in a large, real-world chronic low back pain (CLBP) population.

Methods: This retrospective, observational study evaluated use of FS-TENS (worn on upper calf; providing semi-continuous stimulation of sensor nerves) to treat CLBP across a 10-week period using previously collected therapy utilization, demographic, and clinical (pain characteristics, ratings) data. Data collected by the device and companion smartphone app are stored in a cloud database. Device usage was significantly different between groups

Results: A total of 834 device users met the inclusion criteria and were assigned to the treatment (671, 80%) or reference (163, 20%) groups. With few exceptions, the two groups had similar demographic and pain characteristics at baseline: the treatment group was older (58±13 vs 56 ±14, P=0.035), had lower body mass index (30.5±8.8 vs 31.9±7.9 kg/m2, P=0.043), was more likely to have hip pain (P=0.037), and less likely to have diabetes (P=0.002) or prior neck injury (P=0.006). There was no difference in baseline composite pain (6.3±2.1, treatment; 6.5±1.9, reference; P=0.364). Device usage was significantly different between groups (86±15%, treatment; 31±13%, reference; P<0.001), as was duration of therapy per week (46±22 hrs/week, treatment; 11±7 hrs/week, reference; P<0.001), median stimulation intensity (ratio of stimulation to sensation level expressed in decibels) (5.3 dB, treatment; 6.0 dB, reference; P=0.045). Of the 163 participants in the original reference group, 143 (88%) served as matches for the treatment group. The baseline to 10-week follow-up change in composite pain was −0.89±2.30 for the treatment group and −0.01±2.3 for the matched reference group, with a standardized mean difference between the groups of 0.38 (95% confidence interval, 0.27–0.49; P<0.001).

Conclusion: This study demonstrated that 10 weeks of regular FS-TENS use improved pain outcomes in a real-world sample of CLBP patients compared with a reference group with low FS-TENS use. This study suggests that regular FS-TENS use may be effective in improving pain outcomes in CLBP patients.

Disclosure of Interests: Xuan Kong is an employee of NeuroMetrix, Inc., Dawn Chesser is an employee of Dawn Chesser is an employee of GlaxoSmithKline Consumer Healthcare.

THU0490 PREDICTORS OF CHRONIC PAIN RELIEF BY FIXED-SITE HIGH-FREQUENCY TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION

Xuan Kong, M, Dawn Chesser, M, NeuroMetrix, Inc., Waltham, United States of America; GlaxoSmithKline Consumer Healthcare, Weybridge, Surrey, United Kingdom

Background: Fixed-site high-frequency transcutaneous electrical nerve stimulation (FS-TENS) is a form of TENS in which the stimulator is designed for a predetermined location rather than for co-localization with the patient’s pain. Previous studies in individuals with chronic pain have demonstrated the efficacy and real-world effectiveness of a small wearable FS-TENS device designed for localized application to a single placement site to ensure comfort while both active and sleeping. Results demonstrated that 50–80% of FS-TENS users with chronic lower extremity or low back pain experience clinically meaningful pain relief, and daily use of the device was associated with greater pain relief relative to intermittent use.

Objectives: To determine predictors of a positive FS-TENS response.

Methods: This retrospective, observational study evaluated users of a FS-TENS device to treat chronic pain over a 10-week period. The device and companion smartphone app collected dosage data, demographics, pain characteristics, and pain ratings and all data were stored in a cloud database. The primary study outcome was the baseline to week 10 change in composite pain (average of pain intensity and pain interference with sleep, activity, and mood). Device users were included if they provided demographic data, pain characteristics indicative of chronic pain, and baseline and week 10 pain ratings. Participants were defined as a responder or comparator based on their change in composite pain (responder: ≥15% decrease; comparator: ≥15% increase). Stepwise forward probit regression was used to determine independent predictors.

Results: There were 451 responders and 263 comparators. Independent predictors (Table) that were associated with greater response to FS-TENS included age, baseline composite pain, adherence/utilization rate (defined as the percentage of days with at least 30 minutes of stimulation), and stimulation intensity (defined as the ratio of therapeutic stimulation to sensation threshold, expressed in decibels). Negative predictors (associated with lower response) included history of headache/migraine and diabetes.

REFERENCE:

Abstract THU0490 – Table 1. Independent predictors of responders from probit regression.

<table>
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<th>Variable</th>
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<tr>
<td>Age (years)</td>
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<tr>
<td>Baseline composite pain (0–10)</td>
<td>0.27</td>
</tr>
<tr>
<td>Headache or migraine</td>
<td>-0.37</td>
</tr>
</tbody>
</table>
null
A MULTICENTRE RANDOMISED CONTROLLED FOLLOW-UP STUDY OF EFFECTS OF THE UNDERRIGHTER TRACTION THERAPY IN CHRONIC LOW BACK PAIN

Tamas Gati1, Agota Kulisch2, Eva Czimer2, Györgyi Cserhát3, Judit Feher4, Mihály Oláh5, Zuzsanna Mándó2, Tamas Bender1.

1Polyclinic of The Hospitalier Brothers of St John of God, Budapest, Hungary; 2St. Andrew Hospital for Rheumatic Diseases, Hévíz, Hungary; 3Sóstógyógyfőkút, Nyíregyháza, Hungary; 4Kenézy Gyula Hospital and Clinic (Debrecent), Debrecen, Hungary; 5Hungarospor Hajdúszoboszló Private Limited Company, Hajdúszoboszló, Hungary

Background: Chronic low back pain established for more than 3 months is one of the most common problems in the world. The prevalence could reach the 33%.

Objectives: To investigate the effects of underwater traction therapy on chronic low back pain.

The primary objective was to prove the hypothesis that underwater traction therapy has favourable effect of LBP using the change in the clinical parameters. Our secondary objective was to evaluate whether it also leads to the improvement in the quality of life.

Methods: A prospective, multicenter, comparative (intervention arm vs. control arm), randomized follow-up study. Participants aged between 18 and 85 years with more than 3 months low back pain and selected from outpatient clinics.

The participants were randomized to three groups: underwater weight bath traction therapy, weight bath and non-steroidal anti-inflammatory drugs (NSAIDs) medication and only non-steroidal anti-inflammatory drugs (NSAIDs) medication.

During the traction therapy ankle weights were used. The following parameters were measured before, right after, and nine weeks after the three-week therapy: level of low back pain in rest, level during activity tested using the Visual Analog Scale (VAS); specific questionnaire on back pain (Oswestry); questionnaire on quality of life (EuroQ-ual-SD) and clinical parameters.

Results: 141 participants aged 57.67 (±13.04) years. All of the investigated parameters improved significantly (p<0.001) in the underwater weight bath traction therapy groups by the end of the treatment compared to the base period, and this improvement was persistent during the follow-up period. There were no significant changes in the measured parameters in the control group except for the Oswestry Disability Index, which may also be the result of that group receiving pain-relieving drug therapy.

Conclusion: Based on our results, underwater weight bath traction therapy, might have favourable impact on the clinical parameters and quality of life of patients suffering from chronic low back pain.

REFERENCES:

Disclosure of Interests: None declared


THU0495

ROLE OF PLATELET RICH PLASMA IN TREATMENT OF ROTATOR CUFF TENDINOPATHY AND PARTIAL THICKNESS TEAR: FOLLOW UP BY ULTRASOUND

Yasmin Khairy. Mona Nasr, Fatma Ali, Rashaa Ali, Mohammed Abdelhakem, Adham Khalil. Faculty of Medicine, Minia University, Egypt., Rheumatology and Rehabilitation Department, Minia, Egypt

Background: Shoulder pain is the third most common musculoskeletal reason for seeking medical care. The diagnosis of Rotator Cuff Tendinopathy (RCT), with supraspinatus partial thickness tendon tears and tendinosis, constitutes more than 50% of adult cases presenting with shoulder pains at any time. Platelet rich plasma (PRP) injections are nowadays being used as an alternative for treating the tendinopathies, who have failed to be managed by conservative management.

Objectives: This work aimed to asses the effect of PRP injection under musculoskeletal ultrasound (MSUS) guidance in patients with rotator cuff tendinopathy, and partial thickness tear in comparison with those who received a rehabilitation program only. Baseline assessment and after three months was done using clinical, functional and ultrasonographic evaluation.

Methods: Our study included 60 patients with RCT diagnosed both clinically and by MSUS. Patients were divided into two groups (gl, gii); group I included 30 patients who received a Supervised Rehabilitation Program and group II included 30 patients who received PRP injection. Patients in both groups were assessed clinically, functionally (VAS) and (SPADI) and sonographically at baseline and after 3 months. Rehabilitation Program included: hot packs, (TENS), and (therapeutic ultrasound). The Exercise Programs (supervised and home-based) were applied, including: (ROM, stretching and strengthening exercises of the rotator cuff and scapular muscles). PRP injection was prepared under complete sterile conditions by whole blood centrifugation with specific

THU0494

RELATIONSHIP BETWEEN THE AREA OF THE MEDIAN NERVE CROSS SECTION AND THE CIRCUMFERENCE OF THE CARPUS AS A DIAGNOSTIC TOOL FOR CARPAL TUNNEL SYNDROME

Carlos Guillen-Astete, Patricia García-Casado. Hospital Ramón Y Cajal, MADRID, Spain

Background: The diagnosis of carpal tunnel syndrome (CTS) is fundamentally electrophysiological, however, on diagnostic suspicion ultrasonography has been shown to correlate satisfactorily with the electromyogram. The limitations of the ultrasonography study of the median nerve in patients with STC are due to the fact that the intervals of normality of the area of the median nerve cross section (ACTNM) are variable according to the sources consulted, the sex and the anthropometry of the individual.

Objectives: The purpose of this study is to determine whether NMTA can be correlated with a simple measurement such as wrist circumference length (MCL) in patients with electrophysiological diagnosis of TCEs and healthy subjects and used to discriminate them better than with the simple measurement of NMTA.

Methods: We included 50 patients with electrophysiological diagnosis of CTS and 43 healthy subjects of white ethnicity, older and with different anthropometric characteristics. The patients came from the Rheumatology consultations of three different centres. Healthy volunteers were subjects without CTS clinic, thyroid alterations, diabetes or known autoimmune rheumatological diseases whose data were obtained from a previous study. Circumference was measured with a flexible tape measure around the carpus immediately distal to the interstyloid line. The ultrasound measurements were made at the height of the escoid and pisiform bones using three different ultrasound scanners according to the head-quarters: Toshiba Nemio XG, 13Mhz linear probe, Siemens HM70a 14 Mhz and Logiq e GE 12 MHz. All the measured images were captured for analysis and correction of circumference lengths by an observer not linked to the identity of the subjects nor to their character of patient or control. An association study between wrist circumference and ACTNM was performed for both groups and a correlation index was submitted to a validation test for the determination of sensitivity and specificity.

Results: ACTNM was 11.11 SD 1.18mm2 in the control group and 12.73 SD 1.50mm2 in the patient group (p<0.05). The LCM was 18.81 DE 1.50cm and 18.72 DE 1.85 (p=0.803). In healthy subjects, the correlation between ACTNM and carpal circumference showed a satisfactory correlation (Coef Pearson 0.809, p<0.01, bilateral) as well as in patients (Coef Pearson 0.876, p<0.01, bilateral). The ACTNM/LCM index in the control group was 0.590 and for the patient group 0.679 (p<0.01). The area under the ACTNM curve was 0.808 EE 0.049 while in the case of the ACTNM/LCM index was 0.954 EE 0.019. The area under the ACTNM curve was 0.808 EE 0.049 while in the case of the ACTNM/LCM index was 0.954 EE 0.019. With an index of 0.62 or a sensitivity of 93% and specificity of 78% are obtained for the diagnosis of CTS.

Conclusion: LCM correlates well with ACTNM in healthy patients. It could be considered as a good anthropometric marker for further studies of normal ultrasound ranges of the median nerve. The LCM/ACTNM index is a useful measure to discriminate controls of patients with electrophysiological diagnosis of JTS. In our series, this index exceeds the discriminatory capacity of the ACTNM as an individual measure.

Disclosure of Interests: None declared

protocol; blood was centrifuged firstly at 1000 rpm for 10 minutes. The plasma was then transferred to a new glass tube and centrifuged at 3000 rpm for 15 minutes. Platelets will form a pellet at the bottom of the tube. Finally, a pure platelet rich plasma was obtained with a concentration 4 times greater than baseline. Ca gluconate was mixed with PRP (in a ratio of 0.3 ml ca gluconate/ml PRP) immediately before the injection. Under ultrasound guidance, 3ml PRP was injected slowly into the bursa without usage of local anesthetics prior to injection. Post injection, patients were advised to rest, use cold packs and were allowed to do light range of motion exercises 2-5 days post injection. Acetaminophen was allowed for tolerable post injection pain.

Results: Statistical analysis was made to 60 patients. Intragroup analysis showed statistical significant difference in both groups at follow up compared to baseline regarding clinical, functional and radiological data. Inter-group analysis showed more significant results in PRP group regarding clinical improvement (p <0.001), functional assessment (SPADI, PS, DS and total) and WORC score (p <0.0001) and sonographic assessment in (subscapularis tendinopathy, supraspinatus tendinopathy, supraspinatus fibrillar tendon disruption and supraspinatus tendon thickness) (p <0.0001) and sonographic subacromial subdeltoid bursitis (p > 0.001).

Conclusion: Single PRP injection is an effective mean of treatment of RCT as it improves patients’ quality of life clinically, functionally and structurally, better than traditional physical therapy program.

REFERENCES:

Disclosure of Interests: None declared

THU0496 THE EFFECT OF ADDITION OF BUFFERED DEXTROSE SOLUTION ON PAIN OCCURRING DURING LOCAL STEROID INJECTION FOR PLANTAR FASCIITIS

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Background: 5% dextrose water (D5W) has been previously reported to decrease pain when co-administered with noxious agents as chemotherapeutics and micropherses1,2. It has also been reported to have an immediate analgesic effect on low back pain and radiculopathy when injected epidurally3.

Objectives: To evaluate the potential immediate analgesic effect of D5W when added to the injectate during local steroid injection for treatment of plantar fasciitis.

Methods: In this single blind study, a total of 122 patients with plantar fasciitis were randomly assigned to receive either 40 mg triamcinolone acetonide/1ml + 0.5ml lidocaine 2% (group A: 61 patients; 73 heels) or 40mg triamcinolone acetonide/1ml+0.5ml lidocaine2%+ 0.5ml buffered D5W (group B: 61 patients; 69 heels) as a local injection using the medial approach. Clinical assessment including disease duration, BMI, history of previous injection and post-injection complications and 2-week recurrence rate was performed. Plain X-ray lateral view on the painful heel was obtained for diagnosis of associated calcaneal spur. Visual analogue scale (VAS 0-10) was used to assess the degree of pain intensity during injection.

Results: There were no significant difference between both groups regarding age, sex or BMI where the mean for age was 42.56 years in group A and 43.39 years in group B (P = 0.86), the male to female ratio was 16:45 in both groups and the mean for BMI was 31.49 in group A and 30.86 in group B (P=0.51). The mean disease duration was 6.02 months in group A and 10.77 months in group B (P=0.005). Calcaneal spur was diagnosed in 60 patients (82%) in group A and in 47 patients (68%) in group B. A highly significant difference in VAS was observed as the mean was 8.26±2.00 in group A and 4.25±2.05 in group B (P <0.0001) with a confidence interval (95% CI) of 7.78 -8.74 for group A.

Conclusion: Early intervention by rheumatologists in patients with TD due to musculoskeletal disorders reduces the duration of the processes, saving costs to the health system.

Disclosure of Interests: None declared


Disclosure of Interests: None declared

THU0498 RISK FACTORS FOR SHOULDER PAIN PERSISTENCE IN ROTATOR CUFF DISORDERS

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Background: A large proportion of patients with atraumatic painful shoulder have an unfavorable outcome with long-term disability (1). Predictors of no recovery in patients with shoulder disorders were identified previously: repetitive overhead activity in sport and work (2) duration of complaints, somatization, low social support, older age, unemployment, musculoskeletal comorbidity, recurrent complaint (3,4).

Objectives: To identify the risk factors for over 6 month pain persistence in patients with rotator cuff disorders

Methods: Our prospective study included 51 hospitalized patients with atraumatic shoulder pain. The assessment was clinical and shoulder MRI for confirmation of rotator cuff disorders. We have studied the influence of the patient’s characteristics and the influence of the condition’s characteristics for pain persistence. Statistical analysis was performed in SPSS-18, p<0.05 was significant.

Results: No significant correlations were found between pain persistence and age, gender, smoking status, occupational overuse, physical demands before the onset of pain, marital status, continuous pain, lesions on shoulder MRI. The association with the following elements is statistically significant for pain persistence: opposite shoulder previously affected (p=0.01), diabetes mellitus (p=0.04), insidious onset (p=0.004), the high educational level (p=0.02), physical therapy (p=0.03), local injection (p=0.08).

Using multinominal regression we observed only acute onset of the pain shoulder (RR=7.1) and physiotherapy treatment (RR=0.1) with p=0.026.

Conclusion: The factors that determine the shoulder pain persistence are non-specific and can be sometimes psychosocial, local, physical or other comorbidities like diabetes.

REFERENCES:

Disclosure of Interests: None declared

THU0500 PELVIC CONGESTION SYNDROME, UNCOMMON CAUSE OF LOW BACK PAIN

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Background: The pelvic congestion syndrome (PCS) is an under and often misdiagnosed entity that appears more frequently in premenopausal age and multiparous women. The pathophysiology consists of a sum of phenomena including venous stasis and inversion of the pelvic venous flow that cause varicose veins and congestion. The left ovarian vein is usually the most affected. Typically it presents as a dull, chronic abdomi nal-pelvic (AP) pain, which worsens with menstruation and prolonged comparing a standard dose with a very low dose: Mature results after 12 months’ follow-up. Int J Radiat Oncol Biol Phys 2012;84:e455-462.

Disclosure of Interests: None declared
standing, and lasts longer than six months. Pain is associated with dyspareunia and varicosities in lower limbs (LL) and genitals. It is a challenging and important to consider typical clinical presentations that simulate osteoarthritic (OA) pathologies. It is usually diagnosed by Angio-CT, and a safe, definitive and successful treatment is the embolization of the affected vein.

Objectives: The objective of this study was to evaluate the characteristics of those patients diagnosed with PCS in our University hospital from January 2014 to May 2018, paying close attention to the atypical forms of presentation that simulate OA pathology.

Methods: We included all patients from our center who were operated by embolization due to a PCS from January 2014 to May 2018. Socio-demographic variables, forms of presentation, pain characteristics, associated symptoms, patient management and outcome data were collected.

Results: Sixty women were included with a mean age of 43 years at diagnosis, 87% (n=52) were multiparous, with a mean of 2 previous pregnancies. In 95% (57) of all cases the duration of symptoms until the diagnosis exceeded 6 months. Patients were classified according to presence and location of pain in 4 groups: 1. Women with AP pain, 23% (14); 2. Women with OA pain 5% (3); 3. Women with mixed AP and OA pain, 59% (35); and 4. Women with other symptoms 13% (8). Regarding patients from groups 2 and 3 (only OA pain or mixed pain) (38), 90% (34) of them presented low back pain, 53% (20) hip pain and 40% (15) sciatic pain. Only 5% (3) of all patients were evaluated by a rheumatologist.

As for the pain characteristics from groups 1, 2 and 3 (52), in 72% (37) of patients it was diurnal, in 48% (26) it worsened with menstruation, in 62% (32) it worsened with prolonged standing and in 35% (18) it worsened at rest. Among the associated manifestations, stand out the presence of LL varicose veins in 74% (38) of patients, genital varicosities in 58% (30), dyspareunia in 42% (22), dysmenorrhea in 40% (21), hemorroids in 37% (19) and dysuria in 18% (9). All patients underwent embolization of the affected vein, with an initial Visual Analogue Scale (VAS) mean of 7.38 over 10, and final VAS mean of 2.63. The mean recovery time was 36 days. The evolution was good or very good in 84% (32) of patients with mixed (AP and OA) pain and in 57% (8) of those who only had AP pain. Less than 2% (1) had a recurrence without the need for reoperation.

Conclusion: PCS is a rare entity, typically associated with long lasting AP pain, but, in more than half the cases, is accompanied with OA symptoms, mainly low back pain. It is important and challenging for the rheumatologist to identify these patients, since treatment is usually safe and effective, and diagnostic delay worsens their quality of life.

Disclosure of Interests: None declared


27. BACK PAIN, MECHANICAL MUSCULOSKELETAL PROBLEMS, LOCAL SOFT TISSUE DISORDERS

THU0501 MUSCULOSKELETAL DISORDERS IN TYPE 1 AND 2 DIABETIC PATIENTS: PREVALENCE AND ASSOCIATION WITH MICROVASCULAR COMPLICATIONS OF DIABETE

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Background: Diabetes mellitus (DM), a worldwide high prevalence disease, is associated with a large variety of musculoskeletal (MS) disorders. They are poorly treated, as compared to microvascular complications. However, they are a common source of disability.

Objectives: We designed this study to assess the prevalence of MS disorders among diabetic patients and their relation to microvascular complications of diabetes.

Methods: A cross-sectional study enrolled consecutive subjects with diabetes seen in the Endocrinology department. We recorded age of patients, sex, body mass index, type and duration of diabetes, Long-term glycemic control assessed by hemoglobin A1c levels, and lipid profile. Musculoskeletal and microvascular disorders assessment was done by detailed history with clinical examinations and investigations if needed.

Results: A total of 376 subjects were studied, (84.6% had type 2 diabetes). The mean age was 52.5±13.9 years, 41% had one or more microvascular complications, among which retinopathy was present in 28.2%, nephropathy in 16.1% and neuropathy in 12.8%. Moreover, 23.4% of the patients had one or more musculoskeletal disorders. Shoulder cap- sulitis was present in 12.5%; carpal tunnel syndrome in 8.8%; trigger finger in 5.9%; and 2.9% had diabetic cheiroarthropathy. Dupuytren’s contracture and Charcot foot, were found in 0.5% and 0.3% of the cases respectively. Symptomatic osteoarthritis was found in 19.4%. Musculoskeletal disorders prevalence increased with age, diabetes duration, presence of dyslipidemia and various microvascular complications.

Abstract THU0460 –Table 1. Distribution of cases according to MS disorders in relation to type of diabetes

<table>
<thead>
<tr>
<th>MS disorders</th>
<th>Type of diabetes</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Type 1 N = 58</td>
<td>Type 2 N = 318</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>3.4 ± 12.3</td>
<td>22.3 ± 0.001*</td>
</tr>
<tr>
<td>Shoulder capsulitis</td>
<td>3.4 ± 14.2</td>
<td>4.0 ± 0.023*</td>
</tr>
<tr>
<td>Carpel Tunnel Syndrome</td>
<td>8.6 ± 8.8</td>
<td>9.6 ± 3.3</td>
</tr>
<tr>
<td>Limited joint mobility</td>
<td>0.0 ± 11</td>
<td>3.5 ± 0.151</td>
</tr>
<tr>
<td>Trigger Finger</td>
<td>3.4 ± 6.3</td>
<td>3.9 ± 22</td>
</tr>
<tr>
<td>Dupuytren’s contracture</td>
<td>0.0 ± 2.0</td>
<td>0.6 ± 0.545</td>
</tr>
<tr>
<td>Charcot’s Foot</td>
<td>1.7 ± 0.154</td>
<td>1.0 ± 0.0</td>
</tr>
<tr>
<td>Total MS disorders</td>
<td>10.7 ± 7.8</td>
<td>24.5 ± 0.149</td>
</tr>
</tbody>
</table>

Conclusion: this study shows a high prevalence of musculoskeletal disorders in diabetic’s patients which were significantly associated with advanced age, longer duration of diabetes, presence of dyslipidemia and microvascular complications.

Disclosure of Interests: None declared


THU0502 DIFFERENTIAL DIAGNOSIS OF MONOARTHRITIS: THREE CASES WITH PIGMENTED VILLONODULAR SYNOVITIS

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Background: Pigmented Villonodular Synovitis (PVNS) is a proliferative disorder of synovium that affects synovial joints, tendon sheaths and bursas. The estimated incidence is around 1.8 cases per million people in a population. PVNS is usually found in adults aged 20-50 years, but it may occur also in children. As it is a rare pathology in children, diagnosis is often delayed, and it is difficult to distinguish from Juvenile Idiopathic Arthritis (JIA), hemophilic arthropathy, tuberculosis, and other neoplastic processes.

Objectives: The aim of this case series is to emphasize PVNS in the differential diagnosis of monoarthritis, and the importance of interpretation of imaging, i.e. MRI.

Methods: Three pediatric PVNS cases who were misdiagnosed as monoarticular JIA and familial Mediterranean fever (FMF) are presented as case series.

Results: Case-1: A 14-year-old male had swelling and pain on his left knee for one year. An MRI of knee was reported as joint effusion in suprapatellar bursa, and he was referred to our clinic as monoarticular JIA. He was on methotrexate (MTX) 15 mg/m²/wk. SC, and despite effective treatment there was no improvement. MRI was performed by a pediatric radiologist who was an expert on musculoskeletal diseases. Joint effusion and a lesion compatible with PVNS were observed in left suprapatellar recess (Figure-A). Arthroscopic synovectomy was performed and histopathological result was PVNS.

Case-2: A one year-old female had swelling on her right knee for three months after a minor trauma. On physical examination, she had effusion of the right knee which was confirmed on USG. She was diagnosed as monoarticular JIA and intraarticular triamcinolone injection was performed. She was unresponsive to adequate non-steroid drug therapy, and MTX was started. Despite intensive therapy, there was no change. MRI showed focal lesions with high signal in T2 weighted images in suprapatellar and intraarticular areas, and findings were evaluated as compatible with PVNS (Figure-B). Total synovectomy was performed and PVNS was confirmed in pathological evaluation (Figure-C). She is in complete remission without treatment.
The purpose of this study is to determine the ultrasound characteristics of the coxofemoral joint of patients who consult for acute inguinal pain, correlate it with its clinical presentation and propose a reasoned strategy for its management.

Methods: We reviewed the clinical records of patients under the age of 50 who consulted for direct non-traumatic hip joint pain. Only cases with less than one week of evolution were included. Patients who consulted on weekends or in the afternoon were not included in this register because of the lack of immediate ultrasound study during these periods of time. We excluded those patients who, during the consultation, acknowledged having used anti-inflammatory drugs in the last 24 hours and those whose records are incomplete. The ultrasounds were performed with a portable Logiq e ultrasound machine, equipped with a linear probe of up to 12MHz.

Results: Between 2014 and 2017, 211 patients under 50 years of age consulted for non-traumatic mechanical groin pain. Excluding patients who consulted outside of the immediate ultrasound study access hours, who had recently taken NSAIDs and whose clinical records were incomplete, we reviewed 116 clinical and image records. The mean age of the patients whose records were included was 37.8 SD 8.5. The mean time in days, between the consultation and the onset of symptoms according to history constancy was 4 SD 2. 59 subjects were male (50.9%). In the physical examinations described in the reports, 29 patients (25%) presented painful passive manoeuvres, 38 (32.8%) presented painful active manoeuvres, and 22 (19%) could not maintain standing due to the impossibility of loading due to coxofemoral pain. Regarding the ultrasound findings, 5 patients presented unequivocal capsular distension at the level of the upper anterior labrum (4.3%) and 32 (27.6%) presented distension of the anterior recess. One patient with capsular distension was finally diagnosed with ONA and another with APso.

Conclusion: Our results show that in the studied population (<50 years old, non-traumatic coxofemoral pain of sufficient intensity to be consulted in the emergency department in less than 7 days of evolution) synovitis is a finding present in a quarter of patients and that it is severe in approximately 4%. Its strong association with incapacity for load and passive joint dysfunction would condition the incorporation of these findings in therapeutic decision making, including -in these cases- rest in unload- ing. On the other hand, the absence of synovitis in ¾ parts of the patients strongly suggests a muscular etiology that with proper treatment will respond positively only to NSAIDs. The incorporation of ultrasound, in our opinion, plays a role of diagnostic clearance when the semiological exploration is doubtful.


THU0504 ROTATOR CUFF CALCIFICATION AND SHOULDER PAIN: A CLINICAL AND ECHOGRAPHIC STUDY OF 465 PATIENTS

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Background: Shoulder pain is a common cause for medical consultation and is commonly linked to lesions of the rotator cuff. Rotator cuff calcification (due to BCP crystal deposition) is also a common finding and can give rise to chronic pain as well as acute inflammatory episodes

Objectives: The goal of the study was to compare the clinical and the echographic characteristics of patients with BCP calcification in the rotator cuff and shoulder pain to those with no signs of calcification

Methods: A retrospective case-control study of 465 patients whose primary complaint was shoulder pain presenting between 1997 and 2011 and seen by one rheumatologist. 125 patients who had rotator cuff calcification (RCC) were identified and constituted the study group. We compared the patients with RCC with 125 patients without calcification who were randomly extracted from the same registry which constituted the control group. All had detailed demographic and clinical documentation as well as a precise description of the echographic findings. Subgroups
were defined according to the type and the duration of symptoms (Hyper-
acute painful shoulder, subacute inflammatory symptoms and chronic
mechanical pain). Short-term response (up to 6 weeks) to treatment was
also analyzed for the two first subgroups.

Results: 25% of the patients consulting for shoulder pain had evidence of
RCC as demonstrated by ultrasound. Hyperacute and subacute inflam-
matory symptoms were not linked to calcification (Hyperacute: 16 pts
with 13pts without (p value : ns), subacute: 32 pts in both groups). The
mean age (54 years) and female predominance (60%) were also similar
in patients with or without calcification. However, patients with hyperacute
painful shoulder with RCC were younger (mean years: 49 against 58
years; p: 0.007). None were <35 or > 60 years old and 75% of them
were females. In 60% of cases of hyperacute painful shoulder linked to
calcification, the acute flare was the first shoulder complaint compared to
<30% in the over 60 years group. More than a 1/3 of the patients with RCC
(35% in chronic and 43% in acute symptom groups) had no other echographic lesion compared to < 5% of patients without RCC. Calculifications were rarely associated with
partial or total rotator cuff rupture (<10% against 25%, p: 0.007).

Steroid infiltrations were mostly performed with rapid short-term response in
the acute and subacute groups linked to calcification: 15/16, 24/34
against 4/13 p=0.001, 10/34 p=0.001 without calcification. Surgery was
necessary in 7/101 pts with chronic symptoms without calcification against
only 1/95 when calcifications were present (p=0.03).

Conclusion: Clinical and demographic data cannot clearly predict the
presence of RCC in patients presenting with shoulder pain. However, acute
symptomatic (54 years) is found preferentially in middle aged women,
often with no degenerative or traumatic echographic lesions. Steroid infil-
tration appears to be the treatment of choice when acute inflammatory
symptoms linked to RCC are present.

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None declared, Pascal Zufferey: None declared


Basic science in paediatric rheumatology

THU0505

INTRINSIC AND EXTRINSIC B CELL DEFECT IN DADA2 PATIENTS

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Francesca Antonini5, Alice Grossi6, Gianluca Damonte6, Isabella Ceccherini6,
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Background: DADA2 Deficiency is an autoinflammatory disease character-
ized by systemic vasculopathy, strokes and mild immunodeficiency.
The defect is due to a mutation in ADA2 gene. It regulates the catabolism of
extracellular adenine, which is an important regulator of Class Switch
Recombination in B lymphocytes.

Objectives: We addressed if ADA2 mutation affects directly B-cell function
and the capacity of helper T cells to support B cells.

Methods: 14 patients carrying LOF mutations in ADA2 were examined. We analyzed immunophenotype by flow cytometry. B cells isolated from
DADA patients or HD have been cultured alone or in co-culture with
CD4+ T cells and in vitro B cell proliferation has been evaluated by
CFSE dilution, whereas B cell differentiation to Immunoglobulins secreting
cells in response to TLR9 agonist and T cell help has been evaluated by
ELISA assay.

Results: Flow-cytometric analysis showed a significant reduction of
switched memory B cells and of CD4+/CD8+ T cells. We identified an
significant expansion of circulating Tfh cells in DADA2. Then we investig-
gated a role of ADA2 in B cells: we found that it is expressed, secreted
but the activity is strongly impaired in DADA2. We also addressed the
interaction between B and T cells; we found that proliferation and differ-
entiation of patients' B cells were not sustained from patient's T cells.

Moreover DADA2 T cells showed an impairment in the IL21 production and
a downregulation of CD40L.

Conclusion: Our findings suggest that ADA2 mutation could affects
indirectly B cell function and T cell help functions.

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Deficiency of Adenosine Deaminase 2 sheds new lights on the disease in
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early onset polymyositis nodosa and stroke: a multicentre national study.

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Alberto Martiní Consultant for: I do not have any conflict of interests to declare since starting from 1 March 2016 I became the Scien-
tific Director of the G. Gaslini Hospital; therefore, my role does not allow
me to render private consultancies resulting in personal income.
I perform consultancy activities on behalf of the Gaslini Institute for the
companies listed below: AbbVie, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, EMD Serono, Janssen, Novartis, Pfizer, R-Pharm.
The money received for these activities are directly transferred to the
Gaslini Institute’s bank account. Before March 2016, I was the head of the
Pediatric Rheumatology Department at the G. Gaslini Hospital, where
the PRINTO Coordinating Centre is located. For the coordination activity
of the PRINTO network, the Gaslini Hospital received contributions from the
industries listed in this section. This money has been reinvested for
the research activities of the hospital in fully independent manners
besides any commitment with third parties. Elisabetta Traggia Employee of:
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THU0506

MAST CELL DEFICIENCY AMPLIFIES INFLAMMATORY RESPONSE IN A MOUSE MODEL OF KAWASAKI’S DISEASE

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Background: Kawasaki’s disease is a pediatric medium vessel vasculitis
causing coronary arteritis and potentially coronary artery aneurysms.
Higher systemic levels of Interleukin-6 (IL-6) in the first week of disease
has been shown to be associated with a higher risk of coronary artery
aneurysms (1, 2). Mice injected with Candida albicans water-soluble frac-
tion (CAWS) develop coronary and aortic arteritis like that seen in Kawa-
saki’s disease. Our prior work has demonstrated that mast cell
degranulation can inhibit lipopolysaccharide (LPS)-induced IL-6 gene
expression in the aorta and systemic IL-6 production (3).

Objectives: The objective of this study was to determine if mast cells
play a role in the IL-6 homeostasis in an established mouse model of
Kawasaki’s disease (CAWS) model.

Methods: 8-10-week-old male wild type controls (WT) and kitw-sh-w-sh-w mice (mast cell deficient, MCD) of C57Bl/6 background were randomly
distributed into four groups (WT-PBS, WT-CAWS, MCD-PBS, MCD-
CAWS). They were either injected intraperitoneally with PBS or CAWS (2
mg/mouse) daily for a period of 5 days. Eight animals from each group

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were sacrificed at either 7, 14 or 30 days after the last injection and blood, aorta and heart specimens were harvested. A pathologist (OT), blinded to treatment groups, examined aortic root and adjacent myocardium specimens and assigned a score for the degree of inflammation (0-6).

Results: Seven MCD-CAWS mice died unexpectedly within 24 hours of the first CAWS injection. Autopsies reviewed marked liver sinusoidal dilation in all and patchy necrosis of the liver in 4. Similar, liver findings were seen in 75% of MCD-CAWS after 7 days, but not in other groups. MCD-CAWS mice had higher systemic IL-6 compared to WT-CAWS at both 7 days (208 ± 21 vs 152 ± 12 pg/ml; p<0.001) and 14 days (226 ± 49 vs 169 ± 19 pg/ml; p<0.004), but not at 30 days. By 14 days mice in MCD-CAWS had significantly higher serum INFγ compared to WT-CAWS mice (97 ± 4 vs 87 ± 7 pg/ml; p=0.0086) which remained persistently elevated even at 30 days (103 ± 8 vs 91 ± 4 pg/ml; p=0.002). TNFα was higher in MCD-CAWS compared to WT-CAWS at 7 days (258 ± 8 vs 243 ± 6.5 pg/ml; p=0.0016), 14 days (266 ± 14 vs 239 ± 66 pg/ml; p<0.001) and 30 days (328 ± 52 vs 256 ± 8 pg/ml; p=0.002). The average aortic root inflammatory score was non-significantly higher in the MCD-CAWS group compared to WT-CAWS at both 7 days (1.5 ± 1.3) and 14 days (3.7 ± 2.4).

Conclusion: Mast cell deficiency resulted in higher systemic levels of IL-6, TNFα and INFγ in the CAWS mouse model of Kawasaki’s disease. Similarly, mast cell deficiency resulted in more intense inflammation at the root of the aorta in this model. These results support the novel concept that mast cells play a protective role in reducing the initial systemic inflammatory response in Kawasaki’s disease.

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Disclosure of Interests: None declared


THU0507

TYPE I INTERFERON SCORE AND INTERFERON INDUCED MEDIATORS CXL10 and NEOPTERIN ARE CORRELATED WITH DISEASE ACTIVITY IN JUVENILE DERMATOMYOSITIS

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Background: Interferons (IFNs) seem to play an important role in the pathogenesis of juvenile dermatomyositis (JDM). Our group previously reported that expression of both type I and type II IFN related genes is increased in muscle biopsies of JDM patients and correlates with histological and clinical features of the disease.

Objectives: The aim of this study was to investigate expression of interferon regulated genes (IRGs), as well as serum levels of type II and type I IFN induced chemokines (CXCL9, CXCL10) and neopterin in peripheral blood of JDM patients and to assess their correlations with clinical and laboratory findings.

Methods: We collected 189 blood samples from 39 JDM patients at different time points during follow-up. In 11 patients we obtained the first blood sample at time of muscle biopsy. We measured expression of type I IRGs (IFI27, IFI144L, IFI1, ISG15, RASD2, SIGLEC1), IFNγ and type II IRGs (CXCL9, CIITA, IDO1) by quantitative PCR (qPCR) and calculated a type I and type II IFN score for muscle and blood samples; serum levels of CXCL9, CXCL10 and neopterin were analyzed by ELISA. Ten healthy subjects were used as controls (HC). At each visit, the following clinical and laboratory data were recorded: physician’s global assessment (PGA) of disease activity VAS (Visual Analogue Scale), cutaneous VAS, Cutaneous Assessment Tool (CAT) activity score, Childhood Myositis Assessment Score (CMAS), serum levels of creatine phosphokinase (CK, IU/l), presence of myositis specific or myositis associated antibodies (MMAA), prednisone (or equivalent) dose (mg/kg/daily), ongoing immunosuppressive medications.

Results: Serum levels of CXCL9 where significantly correlated with muscle expression of IFNg and type II IFN score. The correlation of CXCL10 levels with muscle type I and type II IFN score was weaker. Muscle expression of CXCL9 and CXCL10 correlated with serum levels of these chemokines. Type I IFN score in blood of JDM patients was increased compared to HC and significantly correlated with PGA, cutaneous VAS, CAT activity score. Serum levels of CXCL9 and CXCL10 were significantly higher in JDM patients compared to HC. MSA positive JDM patients showed higher levels of CXCL9 and CXCL10 compared to MSA negative patients. CXCL10 levels correlated with PGA and CMAS, but not with cutaneous disease activity. CXCL9 showed no significant association with the evaluated clinical features. Neopterin levels significantly correlated with PGA, cutaneous VAS, CAT activity score and CMAS.

Conclusion: Our findings indicate that expression of IRGs, measured as type I IFN score, and serum levels of CXCL10 and neopterin reflect specific features of disease activity in JDM, supporting their role as valuable disease biomarkers.

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THU0508

CHANGES IN MIR-17–92 CLUSTER EXPRESSION LINK SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS, MONOCYTE-TO-MACROPHAGE DIFFERENTIATION, AND INTERFERON REGULATION

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Background: MicroRNAs (miRNAs) are small noncoding RNAs which post-transcriptionally regulate gene expression. The miR-17-92 cluster is well studied in cancer biology and cellular differentiation; its overexpression has been found to serve a major oncogenic role in the targeting and downregulation of tumor-suppressive pathways, such as PTEN or TGFB. Our previous work identified several members of the cluster – miR-18, miR-19a/b, miR-20a, and miR-92a – with significantly higher levels in monocytes from patients with active Systemic Juvenile Idiopathic Arthritis (SJIA). SJIA is a chronic inflammatory disease of childhood with features of autoinflammation, and innate immune cells including monocytes have important roles in disease pathogenesis. Children with SJIA are at risk for life-threatening complications including Macrophage Activation Syndrome (MAS), an episode of overwhelming inflammation characterized by macrophage proliferation and driven by IFN signaling.

Objectives: Characterize the regulation of the miR-17-92 cluster, define key targets, and determine the cluster’s role in inflammation and SJIA.
Methods: miRNA levels were examined in THP-1 cells, as well as primary human monocytes isolated from healthy donors over the course of the monocyte to monocyte-derived macrophage (M/M) transition. miR-17, miR-19a, and miR-20a were overexpressed via transfection in CD14+ monocytes for 2 days. Transcriptional profiles were performed using Ampliseq Transcriptome and the Ion Torrent S5 system and analyzed using AltaAnalyze. Potential targets of the miR-17-92 cluster determined from sequencing analysis were then validated via dual-lucerase reporter assay.

Results: Neither blood monocytes nor fully differentiated THP-1 cells showed significant changes in miR-17-92 levels under standard polarization conditions, including M1, M2a, and M2b conditions, or IL-6 and IL-10 stimulation. The most sizable changes in miR-17-92 levels were found during monocyte to macrophage transition. Interestingly, primary monocytes showed miR-17-92 clusters within the first 48 hours of differentiation towards MDM, variable by miRNA and experiment, similar to that seen in SJIA monocytes. In contrast, both PMA-differentiated THP1 cells and fully differentiated MDMs showed decreased miR-17-92 compared to undifferentiated monocyte cells. MiR-17-92 was overexpressed in vitro in primary monocytes to model these early transition changes. Genome-wide transcriptional profiling showed an upregulation of genes involved in Type I and II interferon pathways, including response to interferon-alpha (adjusted p=2.71x10^-10) and interferon-gamma (adjusted p=7.81x10^-5). Analysis of genes significantly downregulated by miR-17, miR-19a, or miR-20a identified several putative and previously validated miR-17-92 cluster targets, including ATG5, IFRD2, JAK1, PPARG, and PTEN2 which have interferon-regulatory functions. Dual-lucerase reporter assays experiments support that these genes are direct targets of miR-17, miR-19a, and/or miR-20a.

Conclusion: MiR-17-92 cluster members demonstrate initial increase followed by subsequent decrease in expression during 2-week human monocyte to macrophage differentiation. Overexpression of miR-17-92 miRNAs upregulates Type I and II interferon pathway genes, and these miRNAs target multiple genes involved in regulating interferon signaling and/or inflammatory response. Taken together, miR-17-92 cluster overexpression in SJIA monocytes may suggest a more differentiated phenotype, and contribute to IFN sensitivity and risk for MAS.

Disclosure of Interests: None declared


THU0509 MONOCYTES PROTEOMIC PROFILE OF PATIENTS WITH DIFFERENT AUTOINFLAMMATORY DISEASES: A NEW APPROACH TO CHARACTERIZE THESE DISEASES

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Background: Autoinflammatory diseases are a group of inherited diseases characterized by early onset and systemic inflammation. These pathologies are caused by mutations in genes involved in the regulation of innate immune response with a consequent inflammatory phenotype. The most common genetically defined periodic fever are Familial Mediterranean Fever (FMF), Cryopyrin-associated periodic syndromes (CAPS), TNF receptor-associated periodic syndrome (TRAPS) and mevalonate kinase deficiency (MKD/HIDS).

Some patients show clinical features similar to autoinflammatory diseases, but no genetic mutation has been found.

Objectives: Our aim is to evaluate the differences in the expression of proteins or pathway in monocytes, and plasma metabolites in patients with autoinflammatory diseases compared with healthy subjects to clusterize and better understand the mechanisms underlying different genetically defined disorders and try to characterize the genetically undefined pathologies.

Methods: Monocytes, purified from peripheral blood and incubated with or without LPS, were collected from patients and healthy donors; samples have been processed by IAT protocol. Each digested sample was analyzed by high-resolution liquid chromatography and tandem mass spectrometry (LC-MS/MS) based on Orbitrap technology. The quantification strategy is a label-free approach (LFQ) available in MaxQuant suite.

Results: Here we identified a median of about 5000 proteins from the monocyte samples of each 4000 are quantified by LFQ approach. PCA analysis and Person’s correlation show good reproducibility of data and a good separation between the different groups. The data were then submitted to an appropriate statistic. T-Tests highlighted differentially expressed proteins and through Cytoscape with the ClueGo app we obtained the differently regulated pathways in the different conditions. It has also been constructed, starting from significative proteins, a network, related to disease using the information of String Disease db. We observed that the expression of proteins is differently enriched according to the different conditions. For each autoinflammatory disease, a list of significantly modulated proteins was obtained: some of which are already known to be related to the disease, while others have not yet been described. In FMF, MEFV, RhoA and some related proteins were significantly up-regulated together with genes linked to the interferon pathway.

TRAPS relevant proteins turn up related to the maintenance of Golgi and cellular trafficking. The bioinformatics analysis allows us to better understand the functional interaction between these monocytes proteins and give a new explanation of the disease.

Conclusion: Here, we addressed how a high-resolution proteomics approach could be used to better understand the biology of autoinflammatory diseases. The characterization of a broad spectrum of proteins and their interaction network will allow us to identify new biomarkers for the different pathologies and better comprehend and recognize the genetically undefined disorders.

REFERENCES:

Disclosure of Interests: Federica Penco: None declared, Andrea Petetto: None declared, Chiara Lavarello: None declared, Ilaria Guelli: None declared, Anna Berton: None declared, Alessia Omenetti: None declared, Claudia Pastorino: None declared, Marco Gattorno Grant/research support from: MG has received unrestricted grants from Sobi and Novartis


THU0510 NEUTROPHIL FUNCTION IN PEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: While the role of adaptive immune system in pathogenesis of systemic lupus erythematosus (SLE) has been well characterized, there is paucity of literature on innate immunity in these patients. There are limited data on neutrophil function in pediatric lupus. In this study we analyzed neutrophil functions in a cohort of pediatric lupus from North India.

Objectives: To evaluate phagocytic and oxidative burst activity of neutrophils in patients with pediatric-onset SLE

Methods: This prospective study was carried out at a tertiary care center in North India in patients with SLE during the period July 2017 to December 2018. Diagnosis of lupus was based on SLICC 2012 criteria and patients who had disease onset below 18 years were included. Controls were age matched children attending the outpatient clinic of department. Disease activity was measured by SELENA-SLEDAI score. Phagocytic activity was estimating using the pH Rhodamine Escherichia coli BioParticles kit by flow cytometry. Phagocytic activity is normalized as% phagocytic activity of neutrophils, delta mean fluorescent intensity (%MFI), and stimulation index (SI). Oxidative burst activity was performed by Dihydroorhodamine (DHR) flow cytometry assay and% positivity of neutrophils, %MFI, and SI were calculated.

Results: Eighty-seven children with lupus (83 girls; 24 boys) comprised the study group. 44 healthy controls were also enrolled. Disease onset was 8.5±2.95 years whereas age at enrolment was 12.3±4.57 years. Phagocytic activity in neutrophils SLE and controls were 76.59±20.70% and 91.90±4.47% p<0.001 respectively. %MFI phagocytosis in patients with SLE and control were 0.09 (0.05-0.16), 0.18 (0.15, 0.22); (p.< 0.002) respectively. SI of phagocytosis in patients with SLE and controls were 2.79 (1.92, 3.79), 5.00 (4.50, 6.12); p<0.001. SLEDAI score was negatively correlated with phagocytic function in neutrophils in patients with SLE. Oxidative burst activity of neutrophils in patients with SLE and controls in form of positivity on neutrophils were 84.03±17.36%, 92.26±20.70% respectively.
5.49; p<0.001 respectively. ΔMFI and SI on DHR between patients and healthy controls were comparable. There was no difference in oxidative burst activity between active and inactive SLE patients. Two patients showed a double peak in DHR flow cytometry consistent with mosaic burst activity between active and inactive SLE patients. Two patients healthy controls were comparable. There was no difference in oxidative dysfunction and disease activity. The E.coli based phagocytic functions of neutrophils were significantly reduced in pediatric SLE patients compared to healthy controls. Phagocytic activity of neutrophil was significantly lower in patients with disease activity and coexistent infection in patients with pediatric SLE. Oxidative burst activity was reduced in patients with pediatric SLE compared to healthy controls. However, there was no significant correlation of oxidative burst activity to the age, disease activity and coexistent infections.

REFERENCES:

Acknowledgement:–

Abstract THU0510 – Figure 1. Phagocytic functions in patients with active SLE versus inactive disease

Abstract THU0510 – Figure 2. Correlation of SLEDAI and phagocytic activity

Disclosure of Interests: None declared

THU0511 COMPARISON OF PAXGENE AND TEMPUS WHOLE BLOOD RNA COLLECTION AND ISOLATION SYSTEMS FOR THE QUANTIFICATION OF TYPE I INTERFERON-STIMULATED GENE EXPRESSION

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Background: Type I interferons (IFN) have important roles in many pediatric and adult rheumatic diseases and are a new therapeutic target for which several “anti-interferon (anti-IFN)” treatments are currently in use or in development. Since the direct detection of these proteins in biological samples has proved challenging, indirect methods are often used to infer the presence of type I IFN. Most commonly this involves quantification of the relative expression of interferon-stimulated genes (ISGs) that are used to calculate an interferon score (IS) (1). This score has been used for example to assess type I IFN activity in pediatric patients with type I interferonopathies, systemic lupus erythematosus, dermatomyositis and systemic juvenile idiopathic arthritis (2). Both qPCR and Nanostring technology have similar sensitivity and reproducibility for IS determination (3). The use of different whole blood RNA collection systems on the IS have not been evaluated however despite evidence of method-dependent changes in gene expression (4).

Objectives: The aim of the study was to compare expression of six common ISGs (IFI27, IFI44L, IFIT1, ISG15, RSAD2, SIGLEC1) and the corresponding IS in RNA derived from two commonly used whole blood RNA collection systems (PAXgene and Tempus).

Methods: Whole blood was collected from ten healthy individuals (median age 25.5 years) in sodium heparin tubes and incubated without or with recombinant human interferon alpha 2b (rhIFNa, 2 IU/ml, 4 hrs, 37°C, 5% CO2). Next, samples were divided between PAXgene (PreAnalytiX, Becton Dickinson) and Tempus (Applied Biosystems) tubes and RNA was isolated according to the manufacturer’s protocols. cDNA was synthesized (500ng input RNA; qScript cDNA synthesis kit) and ISG expression measured on a QuantStudio 6 Real-Time PCR instrument using a TaqMan Fast Advanced Assay. For each ISG, expression was normalized against the geometric mean of two housekeeping genes (18s rRNA and HPRT1) and calculated using the formula 2-ΔΔCt. Relative gene expression is reported as the normalized expression of each ISG divided by the median of normalized expression of the same ISG in unstimulated samples. The median relative expression of all six ISGs was used to calculate the IFN score for each sample.

Results: There was no statistically significant difference in the normalized expression of any of the six ISGs in either the rhIFNa-stimulated or unstimulated samples derived from PAXgene or Tempus tubes. The greatest difference in mean normalized expression in both unstimulated and stimulated samples was observed for ISG15 (difference in mean normalized expression was 0.0034 and 0.11, respectively). Overall there was a strong correlation of the IFN score between PAXgene and Tempus tubes for both the unstimulated (R2 = 0.9117, p<0.0001) and rhIFNa-stimulated samples (R2 = 0.8529, p<0.0001).

Conclusion: Despite reported differences in gene expression patterns associated with samples collected in PAXgene versus Tempus tubes, our results demonstrate that 6-gene interferon scores do not differ significantly between RNA samples obtained with these two systems. These results suggest that health care and research centres can use either tubes for IFN score determination using these 6 ISGs and results can be directly compared irrelevant of the RNA collection system employed.

REFERENCES:

Disclosure of Interests: None declared
WHAT IS HIDDEN BEHIND SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS, ADULT ONSET STILL’S DISEASE, AND SECONDARY MACROPHAGIC ACTIVATION SYNDROME. THE UTILITY OF THE BIOMARKERS

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Background: Systemic Juvenile Idiopathic Arthritis (SJIA) and adult onset Still’s disease are rare diseases of unknown etiology that share several clinical and laboratory features. The pathogenesis of these two diseases is complex and multifactorial, with an important role of innate immunity: activation of neutrophils and macrophages and increased levels of cytokines dependent on the activation of the inflammasome. A proportion of these patients will develop a Macrophage activation syndrome (MAS), a serious and life-threatening complication.

Objectives: To identify immunological markers that allow a differential diagnosis between patients with inactive SJIA, active SJIA or MAS. To evaluate if there are differences between biomarkers in SJIA and adult onset Still’s disease.

Methods: Observational, prospective and multicenter study, inclusion criteria: patients with SJIA or adult onset Still’s disease, followed in Paediatric or Adult Rheumatology Department from 5 Madrid hospitals. Group 1: Patients with active SJIA or adult onset Still’s disease: diagnosis of secondary MAS at the first visit, have been followed-up performing a second clinical and analytical visit at 3 months. Group 2: Patients with reactive SJIA or adult onset Still’s. Clinical and analytical data were collected. PBMCs were obtained before and after treatment, and several leukocyte subtypes were evaluated by flow cytometry (FACS). The intracytoplasmic expression of TNF-α, IL-1b and IL-6 in monocytes was determined by flow cytometry before and after stimulation with lipopolysaccharides (LPS) in the presence of monensin ( Golgi inhibitor). In addition, IL-18 levels were determined by ELISA in all visits.

Results: A total of 25 patients were included (18 SJIA and 7 adult onset Still’s disease), 2 of them being excluded from the analysis because exclusions criteria. 30.4% patients presented MAS at the first visit (5 SJIA and 2 adult onset Still’s disease) and other 2 at some time during the disease. The median of IL-18 was 296.1 (CI 108.3-346.0) in patients who have never had MAS and 899.85 (CI: 397.32-1095.6) in the other group. Patients with active MAS had a CD4/CDC8 ratio close to the lower limit (1.1 +/- 0.1 SD) reflecting a decrease in the CD4 + population and an increase in CD8 +. On the other hand, the rest of the groups presented a CD4/CDC8 ratio of 2.6 +/- 0.5 SD in patients without disease activity and 2.0 +/- 0.7 SD in patients with active SJIA or adult onset Still’s disease but without MAS. No significant differences were found between patients with SJIA or adult onset Still’s disease.

Conclusion: The results of this study show that the analysis of three determinations: %CD4,%CD8 and the CD4/CD8 ratio can help in the early detection of patients with MAS secondary to SJIA or adult onset Still’s disease. The determination of IL-18 has been in our study a marker of MAS, similar to several published studies. No significant differences were found in the immunological tests between patients with SJIA and adult onset Still’s disease with active or inactive disease.

REFERENCE:

WHOLE BLOOD CELLS FROM PATIENTS WITH SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS (SJIA) IN CLINICAL INACTIVE DISEASE DISPLAY A DYSREGULATED RESPONSE TO TLR-4 STIMULATION

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Background: Systemic juvenile idiopathic arthritis (sJIA) is a polygenic autoimmune inflammatory disease. Innate immune mechanisms appear to play a central role in the pathogenesis of the disease. Nevertheless, a better understanding of the pathophysiology of sJIA is still needed to identify patients responsive to IL-1 or IL-6 targeted therapies.

Objectives: In this study, we evaluated the production of IL-1β, IL-6 and TNF-α by fresh whole blood cells isolated from sJIA patients in disease remission, after stimulation with the TLR-4 ligand lipopolysaccharide (LPS), and we investigated whether sJIA patients that respond or not respond to treatment with the IL-1 receptor antagonist anakinra show a different response.

Methods: We collected fresh whole blood samples from sJIA patients during clinical inactive disease (inactive sJIA, n=19) and sJIA patients during active disease (active sJIA n=4). Active and inactive disease was defined at time of sampling. As controls, fresh whole blood samples from healthy subjects (HS, n=10) were used. Whole blood cells were left unstimulated or stimulated with 10ug/mL of LPS for 24 hours. Cytokine levels (IL-1β, IL-6 and TNF-α) released in the supernatants were measured by ELISA. Response to anakinra was defined as achievement of clinical inactive disease off glucocorticoids at 6 months after initiation of anakinra treatment.

Results: We found that LPS-stimulated cells from inactive sJIA patients released significantly higher amounts of all the inflammatory cytokines tested, compared to HS (p<0.01). In addition, cells from inactive sJIA patients produced significantly higher levels of IL-1β also compared to active sJIA patients (p<0.05). When we divided inactive sJIA patients in two groups (responders and non-responders), depending on the clinical response to anakinra treatment, we observed that in both groups of patients IL-1β, IL-6 and TNF-α levels were significantly higher than those observed in HS. In addition, we found that LPS-stimulated whole blood cells from non-responder inactive sJIA patients released significantly higher levels of IL-1β and TNF-α compared to responder inactive sJIA patients. The CD4+ CD107a+ SJIA patients displayed significantly lower levels of IL-1β and TNF-α compared to the CD4+ CD107a+ SJIA patients.

Conclusion: Our preliminary results show a dysregulated production of inflammatory cytokines by whole blood cells from sJIA patients in remission disease, when stimulated with a TLR-4 agonist.

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ROLE OF THE ORAL MICROBIOME IN CHRONIC NON-BACTERIAL OSTEOMYELITIS IN CHILDREN

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Background: Chronic non-bacterial osteomyelitis (CNO) is a rare autoinflammatory disease of the bone and bone marrow. The presentation of the disease is broad, but pain and osteodema on MRI are the hallmark of CNO. While the activation of inflammasomes and the subsequent release of IL-18 seems to play a central role, the exact molecular pathophysiology of CNO is largely unexplained. In respect of the potential role of the microbiome to date only experimental data on mice are available, indicating that the manipulation of the microbiome through dietary modulation might alter the course of the disease and also plays a role in the release of IL-18 from innate immune cells.1


Disclosure of Interests: None declared

**Objectives:** To identify the impact of the oral microbiome on CNO in children and adolescents. Dysbiosis as a state of pathological alteration of the microbiome has been discussed as an environmental factor in rheumatic diseases in adults and in children. Human data in CNO are lacking.

**Methods:** 20 patients (12 male and 8 female, aged 3 to 13 years) with a median of 10.3 years were examined. Two different sites of the oral cavity (central and left part of the tongue) were swabbed. In total, 143 individual samples were retrieved and subjected to 16s r-RNA amplification sequencing; DNA was extracted using the QIAamp® DNA Microbiome Kit. The V4 region of the 16S ribosomal RNA gene was amplified by PCR with V4 specific primers. A limited cycle amplification step was performed. Libraries were normalized and pooled, and sequenced on a MiSeq system (Illumina). Raw sequence reads were demultiplexed and clustered into sub-OTUs (operational taxonomic units) via Deblur in QIIME. Qiime2 was used to calculate alpha- and beta- diversity for multiple alternative metrics. Statistical significance was calculated with non-parametric tests (Mann-Whitney and Permanova).

**Results:** The administration of medication in general (mostly NSAIDs) had a significant impact on the microbiome (p-value < 0.02). With limited statistical power of the small cohort, gender, age and disease activity do not significantly influence the microbiome. There is a significant difference between the variable swab sites at the 1% level (p<0.01). Whereas swabs from the center of the tongue exhibit more Streptococci salivarius, the left outer part of the tongue shows more Haemophilus parainfluenzae.

**Conclusion:** To the best of our knowledge, this is the first study of the oral microbiome in children and adolescents in CNO. Our data suggest that administration of medication to CNO patients alters the microbiome. It is also influenced by a change of the swab site. Limited patient numbers did not allow to show an effect on disease activity, but enrollment will continue.

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[2] Verwoerd A, Ter Haar NM, de Roock S, Vastert SH, Bogartt D. The V4 region of the 16S ribosomal RNA gene was amplified by PCR with V4 specific primers. A limited cycle amplification step was performed. Libraries were normalized and pooled, and sequenced on a MiSeq system (Illumina). Raw sequence reads were demultiplexed and clustered into sub-OTUs (operational taxonomic units) via Deblur in QIIME. Qiime2 was used to calculate alpha- and beta- diversity for multiple alternative metrics. Statistical significance was calculated with non-parametric tests (Mann-Whitney and Permanova).

**Disclosure of Interests:** None declared

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**Paediatric rheumatology**

**THU0515**

**PAIN IS THE MAIN DETERMINANT OF WELL-BEING IN OLIGO- AND POLYARTICULAR JIA: EVIDENCE FROM THE PHARMACHILD REGISTRY**

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**Background:** Juvenile idiopathic arthritis (JIA) affects patients’ well-being as the result of a complex interplay of multiple factors, including disease activity, symptoms, physical and emotional quality of life, and treatment burden. Little evidence exists about the relative contribution of these elements to disease impact.

**Objectives:** 1) To identify direct and indirect determinants of well-being, expressed by VAS-measured parent/patient global assessment of well-being (PGW), in children with oligo- and polyarthritis. 2) To assess whether the impact of the major determinants varies with level of disease activity.

**Methods:** We analyzed data of 1873 patients evaluated in 4464 prospective visits from the international JIA pharmacovigilance registry Pharmachild. Patient-reported outcomes were collected through the Juvenile Arthritis Multidimensional Assessment Report (JAMAR). Evaluated predictors of PGW included VAS-measured physician global assessment, inflammatory markers, active joint count, VAS-measured pain, morning stiffness duration, Juvenile Arthritis Functional Score (JAFS), Physical (PhHS) and Psychosocial (PsHS) subscales of the Pediatric Rheumatology Quality of Life (PRQL) scale, disease damage measured through the Juvenile Arthritis Damage Index (JADI) and adverse events (AE). We used path analysis to assess direct and indirect effects of variables on PGW. We repeated the analysis on subsets of visits stratified by disease activity, measured with JADAS10, to test differences across activity states.

**Results:** Pain severity proved the strongest direct determinant of PGW (b 0.521, p<0.001), followed by Psychosocial (b 0.191, p<0.001) and Physical Health (b 0.158, p<0.001). Stiffness (f2 0.041, p<0.001) and joint damage by the JADI (f2 0.032, p<0.001) were also indirectly associated with PGW, through their effects on function and PhHS. Patient-reported adverse events (AE) had a small effect on PGW (f2 0.025, p<0.001) through their impact on PsHS. Relations among variables and relative coefficients are depicted in the graph. Multi-group comparison between Remission, Low (LDA), Moderate (MDA) and High Disease Activity (HDA) groups revealed that for subjects in Remission, pain had a lower impact on function and physical health compared to those with LDA, while remaining the strongest predictor of PGW. Among the HDA group, the direct effect of pain on well-being and the impact of physical health on psychosocial health was greater than in other activity states (table). The effect of AE remained significant across all activity categories.

**REFERENCES:**


**Abstract THU0515 – Figure 1.**

**Table Coefficients (b) Comparison**

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<th>Pathway</th>
<th>REM</th>
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<th>MDA</th>
<th>HDA</th>
<th>REM</th>
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<td>Pain -&gt; JAFS</td>
<td>0.312</td>
<td>0.401</td>
<td>0.400</td>
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<td>Pain -&gt; PGW</td>
<td>0.367</td>
<td>0.420</td>
<td>0.467</td>
<td>0.614</td>
<td>0.524</td>
<td>0.502</td>
<td>0.496</td>
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<tr>
<td>Pain -&gt; PsHS</td>
<td>0.375</td>
<td>0.420</td>
<td>0.467</td>
<td>0.614</td>
<td>0.524</td>
<td>0.502</td>
<td>0.496</td>
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</tbody>
</table>

**Conclusion:** Pain was the main determinant of PGW in all disease activity states. The level of PGW also reflected other aspects of disease impact, particularly physical and psychosocial distress, and, to a lesser extent, treatment adverse events. The impact of pain and physical functioning on psychosocial health and well-being varies with disease activity, being greater in patients with higher disease activity.

**REFERENCE:**


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LONG-TERM SAFETY OF SUBCUTANEOUS TOCILIZUMAB ADMINISTRATION IN SYSTEMIC AND POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS

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Background: Tocilizumab (TCZ) administered intravenously (IV) was effective for the treatment of polyarticular (pJIA) and systemic (sJIA)1,2 Objectives: To evaluate the long-term safety and efficacy of subcutaneous (SC) TCZ in patients (pts) with pJIA or sJIA enrolled in a long-term extension (LTE) phase of two 52-week, open-label studies. Methods: Pts aged 1-17 years received body weight (BW)-based TCZ SC: pJIA pts who failed or could not tolerate MTX received TCZ 162 mg every 3 weeks for BW <30 kg or every 2 weeks (Q2W) for BW <30 kg; sJIA pts received a standard response to NSAIDs and glucocorticoids recibed TCZ 162 mg Q2W for BW <30 kg or every 2 weeks for BW ≥30 kg. All pts discontinued biologic DMARDs (approximately 50% switched from TCZ IV to TCZ SC). After 52 weeks, pts continued BW-based TCZ in a separate LTE study; safety data (adverse events [AEs], serious AEs [SAEs]) in the LTE study to clinical cutoffs December 1, 2017 (pJIA), and February 28, 2018 (sJIA), are reported for all pts who received ≥1 dose of TCZ SC and had >1 postdose safety assessment.

Results: Most pJIA (n=44) and sJIA (n=38) pts were female (72.7% and 55.3%) and white (88.6% and 84.2%); median (range) age was 9.0 (2-18) years. AE rates (Table) were similar regardless of BW. Most AEs were grade 1 or 2; grade ≥3 AEs were reported by 10.4% (20.8%) pJIA pts and 4/38 (10.5%) sJIA pts, most commonly nasopharyngitis (pJIA, 17/ 44 [38.6%]; sJIA, 11/38 [28.9%]). Other AEs reported in ≥15% of pts included arthralgia, gastroenteritis, cough, vomiting, diarrhea, pyrexia, headache, and oropharyngeal pain (pJIA) and upper respiratory tract infection, cough, pyrexia, arthralgia, and rash (sJIA). No opportunistic infections developed. Neutropenia AEs were reported by 6/44 (13.6%) pJIA pts and 7/38 (18.4%) sJIA pts. SAEs occurred in 5/44 (11.4%) pJIA pts (furuncle, appendicitis, pneumonia, eye pain/headache, infectious mononucleosis) and 2/38 (5.3%) sJIA pts (pneumonia, cranioencebral injury from a fall); only pneumonia (pJIA) was considered treatment related. Neutralizing anti-TCZ antibodies developed in 2 (4.7%) pJIA pts and no sJIA patients. No deaths were reported in the LTE study.

Conclusion: In this LTE study in children with pJIA or sJIA, SC TCZ continues to have an acceptable tolerability profile with no new safety concerns.

REFERENCES:

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Background: In 2008 the Paediatric Rheumatology European Society (PReS) promoted an International Project for the study of Autoinflammato-ry Diseases (AIDs) named Eurofever, whose main purpose is to create a web-based registry for the collection of information in AIDs patients.

Methods: The data were extracted from the Eurofever registry, which is hosted in the PRINTO website (http://www.printo.it). From February 2015 we started the longitudinal collection of follow-up data with particular focus on treatment, modification of the clinical picture, onset of complica-tion/adverse events. We have enrolled patients included in the registry up to 28 September 2018.

Results: Up to date 4175 patients have been enrolled (3843 of them with complete demographic information, 1903 M e 1940 F) from 62 coun-tries. For 3356 (87%) patients also clinical data from onset to diagnosis, with complete demographic information, were collected during the first visit performed at referred pediatric or adult cen-ter, are available. For each disease the number of enrolled patients is: FMF 1086 pts (951 with complete clinical data); TRAPS 273 pts (256 complete); CAPS 298 pts (279 complete); MKD 205 pts (190 complete); Blau’s disease 49 pts (26 complete); PAPA 42 pts (41 complete); NLRP12 mediated periodic fever 13 pts (11 complete); DADA2 14 pts (9 complete); DIFA 3 pts (all complete); SAVI 3 pts (all complete); CANDLE 1 pt (complete) and Majeed 4 pts (all complete). Among multifactorial autoinflammatory diseases: PFAPA 676 pts (551 complete); CNO 581 pts (540 complete); Behcet 214 pts (186 complete), undefined periodic fever 368 pts (292 complete) and Schnitzler 13 pts (all complete). The median onset age is 36 months (range 1 month – 75 years), the median diagnosis age is 8 years (range 1 month – 78 years). Most of patients (3509 /91%) presented disease onset during pediatric age (<16 years), 334% (9) during adult age (81 FMF, 31 CAPS, 53 TRAPS, 40 CRMO, 12 Schnitzler syndrome e 90 unknown fever), 405 of 3509 (12%) patients with pediatric onset received diagnosis during adult age. The median diagnos-tic delay is 5 years; diseases with longer diagnostic delay are: NLRP12 (24 years, range 4-76), CAPS (15 years, range 0-77), PAPA (14 years, range 2-57), TRAPS (12 years, range 0-77). 396 patients have been treated with at least one biologic drug, 1031 with DMARDs, 427 with systemic steroid and 686 with others drugs. The most frequent diseases treated with biologic drugs are: CAPS (38%), multifactorial diseases (28%), FMF (22%), MKD (11%), rare monogenic (8%: 1 CANDLE, 2 DIFA, 2 NLRP12, 3 Majeed, 8 DADA2 and 14 PAPA), and FMF (7%). Since February 2015, longitudinal visits have been inserted for 477 (12%) patients, with detailed data on treatment and safety.

Conclusion: The enrollment in Eurofever Registry is still ongoing. The analysis of data will improve our knowledge both on the natural history of the single disease and on the efficacy/safety of treatment commonly used in the clinical practice.

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I perform consultancy activities on behalf of the Gaslini Institute for the companies listed below:
Adverse events of special interest were uveitis (n=109), H. zoster (n=24), chronic inflammatory bowel disease (n=19), pregnancies (n=4), depression (n=11), malignancies (n=8), demyelination (n=2). Adverse Events of Special Interest (AESI) were in the MTX-cohort uveitis (n=52), H. zoster (n=4), chronic inflammatory bowel disease (n=1), depression (n=2), malignancies (n=4).

A total of 1606 patients (60.7%) discontinued treatment. Of these 638 (39.7%) discontinued due to remission, 565 (35.2%) due to lack of efficacy and 188 (11.7%) because of intolerance.

Conclusion: The current analysis adds to the established safety profile of cAcr and C21 because of intolerance.

A total of 1606 patients (60.7%) discontinued treatment. Of these 638 (39.7%) discontinued due to remission, 565 (35.2%) due to lack of efficacy and 188 (11.7%) because of intolerance.

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EARLY IDENTIFICATION OF VENTRICULAR DYSFUNCTION IN JUVENILE SYSTEMIC SCLEROSIS BY SPECKLE TRACKING ECHOCARDIOGRAPHY

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Background: Juvenile Systemic Sclerosis (JSSc) is a rare multisystemic connective tissue disease, with onset before the age of 16. Cardiac involvement, recognized in 8-24% of the patients [1], begins in early stages of JSSc and has a poor prognosis. The classical cardiac US imaging, including the left ventricular ejection fraction (EF), evaluates the global function of the heart, thus being inappropriate to assess the subclinical course of the disease. A new echocardiographic technique, the speckle tracking echocardiography (STE), has been shown to be able to identify regional ventricular dysfunctions also in early stages of adult-onset SSc[2,3].

Objectives: Aim of our study was to assess the longitudinal strain of right and left ventricle in JSSc patients, in order to identify ventricular dysfunctions earlier and more effectively than with traditional echocardiography. Furthermore, we investigated the evolution of cardiac involvement during follow-up, in order to establish a possible correlation between age and overall disease severity, measured by the Juvenile Systemic Sclerosis Severity Score (J4S)[4].

Methods: Consecutive patients with JSSc underwent clinical and cardiological evaluation. This included traditional echocardiography (such as M-Mode, EF, Pulsed- and Tissue-Doppler), 3D-Echocardiography and STE, measuring the global longitudinal strain of left ventricle (GLS) and the longitudinal strain of right ventricle free-wall (RVLS). Each patient was assessed several times by pediatric rheumatologists for J4S and by cardiologists with STE and standard echo.

Results: 18 JSSc patients (12 F, 6 M), mean age 12.3 years, disease duration 4.5 years, entered the study. At baseline evaluation, EF was abnormal in 1 patient, whereas GLS and RVLS were normal in 5. The diagnostic sensitivity of cardiac involvement of STE increased, with a prevalence rising from 22.2% to 38.8%. During the follow-up, last mean 30 months (range 17-43), the mean GLS values gradually worsened (-21.2; -20.1; -19.4%) while there was no significant variations of EF. The strong correlation between GLS and J4S, found at baseline, vanished during the follow-up. Speckle tracking echocardiography is a useful technique to evaluate the cardiac involvement in patients with JSSc. In comparison with traditional EKG or echocardiography, it allows to increase the diagnostic sensitivity of cardiac involvement. Over time, we observed a gradual worsening of GLS, sign of a progressive left ventricular dysfunction, that was not identified by EF. It is possible that the coronary microvascular damage compromises the subendocardial fibers function which are more sensitive to ischemia and whose contractility is well assessed by GLS [5]. Finally, the initial correlation between strain and J4S disappeared during the follow-up, maybe because of the pharmacological therapy, which was effective on several aspects of the disease but had low impact on the ventricular function.

REFERENCES:

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Clinical manifestations and comparison of subtypes of juvenile idiopathic inflammatory myopathies: data from the REMICAM registry

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Background: Juvenile idiopathic inflammatory myopathies (JIIM) are a heterogeneous group of autoimmune diseases affecting children, characterized by symmetric muscular weakness, cutaneous rash and systemic organ involvement. Given its low incidence, there are few studies describing the characteristics of this disease and its subtypes in Spanish patients.

Objectives: To describe the demographic, clinical and analytical characteristics of patients with JIIM from the registry of inflammatory myopathies in Madrid community (REMICAM), and to compare those measures with polyomysitis (PM) and juvenile dermatomyositis (JDM) subgroups.

Methods: A multicentre retrospective study from the REMICAM registry was performed. Patients were selected if they were 18 years or younger at onset of JIIM and met definite or probable criteria for JIIM by the modified Bohan and Peter criteria. We included patients with JDM or PM subgroups, overlap myositis patients were excluded.

Results: 86 patients were included, 12 classified as PM and 74 as JDM. 70% were women and 96% were Caucasian. Mean age at diagnosis was 11.8 years in PM group vs 7.2 years in JDM group. 44% presented arthritis and 93% presented muscular weakness. Gottron sign was present in 76% of the patients, and calcinosis was present in 31.4%. Cardiac and pulmonary manifestations were rare (<5%). There were no cases of neoplastic disease. Clinical features and complementary analysis are shown in table 1 and table 2.

<table>
<thead>
<tr>
<th>Phenomenon</th>
<th>PM (n=12)</th>
<th>JDM (n=74)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>23 (29.1%)</td>
<td>6 (50.0%)</td>
<td>17 (25.4%)</td>
</tr>
<tr>
<td>Weight loss</td>
<td>12 (15.2%)</td>
<td>2 (1.3%)</td>
<td>11 (16.4%)</td>
</tr>
<tr>
<td>Arthritis</td>
<td>39 (44.2%)</td>
<td>7 (53.3%)</td>
<td>31 (41.9%)</td>
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<tr>
<td>Gottron sign</td>
<td>24 (28.4%)</td>
<td>6 (50%)</td>
<td>18 (24.7%)</td>
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<tr>
<td>Heliotrope erythema</td>
<td>66 (76.7%)</td>
<td>65 (87.8%)</td>
<td>0 (0%)</td>
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<tr>
<td>Mechanic hands</td>
<td>10 (12.3%)</td>
<td>10 (14.5%)</td>
<td>0 (0%)</td>
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<tr>
<td>Skin ulcers</td>
<td>3 (3.7%)</td>
<td>3 (4.3%)</td>
<td>0 (0%)</td>
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<tr>
<td>Raynaud</td>
<td>12 (13.9%)</td>
<td>3 (25%)</td>
<td>9 (12.2%)</td>
</tr>
<tr>
<td>Calcinosis</td>
<td>27 (31.4%)</td>
<td>2 (16.7%)</td>
<td>25 (33.8%)</td>
</tr>
<tr>
<td>Muscular weakness</td>
<td>80 (93.0%)</td>
<td>11 (91.7%)</td>
<td>69 (93.2%)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>68 (83.9%)</td>
<td>8 (66.7%)</td>
<td>60 (82.5%)</td>
</tr>
<tr>
<td>Myocarditis</td>
<td>2 (2.3%)</td>
<td>0 (0%)</td>
<td>2 (2.7%)</td>
</tr>
<tr>
<td>Arhythmia</td>
<td>3 (3.5%)</td>
<td>1 (8.3%)</td>
<td>2 (2.7%)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>1 (1.2%)</td>
<td>1 (1.4%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Intestinal disease</td>
<td>1 (1.2%)</td>
<td>1 (1.4%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>19 (22.1%)</td>
<td>2 (16.7%)</td>
<td>17 (23.0%)</td>
</tr>
<tr>
<td>GI reflux</td>
<td>7 (8.1%)</td>
<td>1 (8.3%)</td>
<td>6 (8.1%)</td>
</tr>
<tr>
<td>GI hemorrhage</td>
<td>1 (1.2%)</td>
<td>1 (1.4%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

Conclusion: JDM was the most frequent form of MIU in our study (86%). The most frequent manifestations were the muscular and dermatological ones, but an important group also presented arthritis and fever. There was no statistical difference between both groups, regardless, myalgias and dysphagia were more common in JDM group, and they had higher CPK and aldolase values. PM patients were older, had more fever and arthritis, also, cytoptenia and ANA positivity were more common.

Reference:

Obesity is associated with severe renal involvement, persistent purpura and longer joint symptoms in children with Henoch Shölein purpura

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Background: Over the last 20 years, the prevalence of obesity is increased in the developed and developing countries. Adipose tissue has an effect on inflammatory processes and immune system besides metabolic and appetite regulating mechanisms. On this basis, it is now of major interest to clarify the relationship between obesity and autoimmune/inflammatory diseases (1,2).

Objectives: We aimed to evaluate the role of obesity on the clinical course and response to treatment in patients with Henoch Shölein Purpura (HSP).

Methods: Data charts of children with HSP followed in Dokuz Eylül University Children’s Hospital were reviewed retrospectively. Obesity was defined as BMI >95 percentile in conformity with Centers for Disease Control and Prevention (CDC) (3). Persistent purpura was defined as skin involvement persisting for >30 days. Mild nephropathy was defined by the presence of microscopic hematuria and/or nonnephrotic proteinuria, and severe nephropathy by nephrotic syndrome and/or acute nephritic syndrome and/or renal insufficiency (4). Patients were grouped as obese and non-obese depending on BMI. Two groups were compared for demographic, clinical and laboratory parameters.

Results: There were 199 patients [M:F=104:95; presenting age 7.1 years (range 5.0-9.2); follow-up period 17.5 months (range 3-50)]. Obesity was associated with severe renal involvement and persistent purpura.
ARE CHILDREN AND ADULTS HAVING DIFFERENT PHENOTYPE AND GENOTYPE OF FMF?

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Background: Familial Mediterranean fever (FMF) is an autosomal recessively inherited autoinflammatory disease and begins in childhood. In nearly 60% of patients, the first attack occurs before the age of 10, and in 94% of the before the age of 20 years. There is a prospective study designed for comparing childhood onset and adult onset FMF.

Objectives: To compare the demographic data, clinical features, genetic analysis, laboratory values and severity scores of both childhood and adult onset FMF. Compliance and resistance to colchicine, presence of accompanying diseases and complications due to FMF were also analyzed and reviewed.

Methods: The patients were divided into two groups; group I: children with FMF (symptoms begin before 18 years of age) and group II: adults with FMF (symptoms begin after 18 years of age). A questionnaire for collecting age at disease onset, sex, age at diagnosis, delay at diagnosis and duration of the disease, family history of FMF, consanguinity and accompanying diseases were filled. The questions were asked by an adult and pediatric rheumatologist to both groups by face to face interviews. Genetic analysis results and treatment protocols were taken from patient’s charts. Laboratory data concerning complete blood count, ratio of urine protein to creatinine, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), serum amyloid A (SAA) levels were obtained during their routine follow-up at attack-free period.

Results: There were 178 (60.3%) children with the diagnosis of FMF; 73 female and 104 male and 117 (39.7%) adults diagnosed as FMF after 18 years of age; 69 female and 48 male. The mean±SD age at symptom onset, at the diagnosis and current age was 12.9±3.03, 6.4±5.61, 11.9±4.38 for group I and was 18.35±10.34, 32.23±11.62, 38±11.64 for group II, respectively. Consanguinity was significantly more frequent among children with FMF (36.1%). A positive family history of FMF was similarly present in 102 (57.6%) of group I and 66 (56.4%) of group II. Twelve (10.2%) adult patient have FMF at their children. Family history of amyloidosis was equally distributed between groups; 6.2% in group I and 6.8% in group II. The median number of FMF attacks per year was 18 in children and 15 in adults. While children were having significantly more frequent attacks, the duration of attacks were longer in adults compared to children (p<0.001). The most frequent symptom was fever (91.5%) in children and abdominal pain (96.5%) in adults. Arthritis, chest pain and erysipelas like rash were seen similarly in both cohorts. Sacroiliitis (10.2%), amyloidosis (5.1%) and chronic renal insufficiency (5.1%) were significantly more common in patients with FMF diagnosed after 18 years of age. Colchicine resistance and compliance were evenly distributed among groups. In genotypic evaluation, groups were compared for homozygotes, compound heterozygotes and heterozygotes and had put forth similar results. Attack free acute phase reactants like CRP; median 2.8 mg/dl and SAA; median 3.86 mg/dl were significantly higher in group I.

Conclusion: Both clinical features and acute phase response in FMF were less pronounced in patients diagnosed at adulthood. Children were having more frequent attacks, but accompanying diseases were more common in adults. While following patients taking age of the patient in account will help to better understand the disease course.

REFERENCE:

Acknowledgement: None

Disclosure of Interests: None declared


THU0524B EXTRA-OCULAR MANIFESTATIONS OF CHILDREN WITH SACROID-LIKE UVEITIS

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Background: Paediatric sarcoidosis may represent a spectrum of disease. Early onset sarcoidosis & its genetically defined counterpart Blau syndrome associated with NOD2 mutations are characterized by fever, rash, arthiritis and organomegaly. Later onset sarcoidosis has wider organ involvement including lungs, kidneys, lachrymal and extra-ocular glands. Both presentations may lead to long term complications due to end-stage organ damage. Although similar disease manifestations can be seen in adults and children, some entities are essentially pediatric at onset, namely Blau syndrome and most forms of immunodeficiency associated granulomatous diseases. Ocular sarcoidosis has a well described uveitis phenotype (1). We created a retrospective cohort of patients currently followed at GOSH with likely ocular manifestation of sarcoidosis (1)

Objectives: To describe a retrospective cohort of children with sarcoid-like uveitis. To describe their extra-ocular manifestations at the time of the study. To describe their management.

Methods: Retrospective case review of children currently followed at GOSH with a phenotype of ocular sarcoidosis with uveitis (ophthalmologist define (5, 6)), or a diagnosis of idiopathic uveitis (anterior, posterior, intermediate or panuveitis) with raised ACE level at least once. We collected demographics and all extra-ocular involvement described in the study.

Results: 52 patients. 27/52 males. Median age onset of uveitis 4.20 yrs (1.41-15.16). 30/52 had onset <8 yrs. Median ACE 73 and mean ACE 77 at presentation (9-90UL normal). Median max ACE79% max mean ACE 88.2 (14.420).NOD2 done in 12 patients: 6+, 6-. Only 4/6 patients Blau phenotype.

Ethnicity: black 13, asian 10, caucasian 13, unknown 16.52. 49/52 had bilateral uveitis. Uveitis anterior 17/52, intermediate 5/52, posterior 2/52, panuveitis 25/52, unknown 1/52. ANA+15/47(32%). Extra-ocular (n=52): Lymphadenopathy: 15 (29%) clinically Liver: 16 (31%) - transaminitis 9, ultrasound(US)/USG abnormality (hepaticomegaly, calcification, increased echogenicity) 5 & both abnormal USS & blood 2 (glycogen 15%, 29%) large joints of lower limbs & joints hands. Tenosynovitis 4 (7.7%) Renal: 15 (29%) (USS or Blood/urine tests – raised serum creatinine,
raised urinary ca creat ratio, raised urinary NAG/RBP) — 4/15 on USS and 9/15 in blood/urine tests, 2/15 on both USS and blood/urine tests. Lungs: 7 (12.5%): 6 abnormal lung function test, 1 abnormal CXR, lung function & CT chest - severe interstitial lung disease & presented- progressive shortness of breath. Skin: 10 (19.2%), eczema-like/non-specific skin Pariod/plandulair: 1 (1.9%) on USS Spleonomegaly: 4 (7.7%) on USS Sensorineural hearing loss: 2 (3.8%).

Medications to treat uveitis and/or extra-ocular manifestations were: Methotrexate 13 (25%), Methotrexate + Adalimumab 11 (21.2%), MMF 6 (11.5%), topical steroids 6 (15.4%), systemic steroids 2 (3.8%). 10 patients no medication

Conclusion: Most of the sarcoid-like uveitis patients had at least one extra-ocular involvement. ACE does not appear to be a sensitive biomarker. Some patients (19.2%) have a mild phenotype and require no treatment. Our data demonstrate the importance of close monitoring for extra-ocular manifestations and highlight good clinical response to steroids, MTX, MMF and anti-TNF.

REFERENCE:

Disclosure of Interests: Abhay Shivpuri: None declared, Emily Kalms: None declared, Ameena Tola Solebo: None declared, Harry Petrushkin: None declared, Dhanes Thomas: None declared, Elizabeth Graham: None declared, Clive Edelson: None declared, Sandrine Compeyrot-Lacassagne Grant/research support from: Abbvie

THU0525 DEVELOPMENT OF A PREDICTIVE TOOL FOR RESPONSE TO ANTI-TNF-ALPHA THERAPY IN JIA USING GENE EXPRESSION PROFILES IN PERIPHERAL DERIVED MONONUCLEAR CELLS
Jedidja Baaji1, Rianne Scholman1, Rae Yeung2, Trang Duong3, Nico Wulfraat1, Joost F. Swart1, Sebastian Vaster1, Sytze De Roock1, 1UMC Utrecht, Department of Pediatric Rheumatology, Utrecht, Netherlands; 2Hospital for Sick Children, Department of Paediatrics, Toronto, Canada

Background: Heterogeneity in response to biological medication is a major challenge in the management of Juvenile Idiopathic Arthritis (JIA) (1). Biomarkers such as cytokines or whole blood RNA expression profiles that predict therapy efficacy prior to treatment pose a solution and could enable precision medicine. It was previously demonstrated that whole blood gene expression profiles can predict response to anti-TNF-α therapy in patients with JIA (2). These findings currently await validation in a multicenter prospective cohort study. Harmonization of data from different cohorts, however, is often hampered by site-dependent differences in biological sample collection and processing (3). For instance, the biological material that is retrospectively available from biobanks depends on what is stored exactly, e.g. whole blood versus peripheral blood mononuclear cells (PBMC). Furthermore, different blood collection tubes containing different additives can affect sample quality at an early stage and make interchangeability or comparability of data impossible.

Objectives: We evaluated the comparability of gene expression profiles when whole blood from patients with JIA is collected in different RNA collection tubes and processed accordingly. Next, we will investigate the predictive capacity for therapy response of RNA expression profiles from frozen PBMC of 63 JIA patients.

Methods: Peripheral blood from 11 children with non-systemic JIA with active disease was collected in PAXgene (PreAnalytX) and Tempus (Applied Biosystems) tubes. All tubes were subsequently stored in the freezer at ~80 °C. After thawing, RNA from the PAXgene tubes was extracted with use of the PAXgene Blood RNA Kit and RNA from the Tempus tubes was isolated by using the Tempus Preserved Blood RNA Purification Kit I; Gene expression of CSNK1D, C1D, ASAP2, SRRR, PPP1R3B, HLA-DOA1, PDZK1P1 and MZB1 was determined with qPCR. For our next experiment, frozen PBMC derived from patients with non-systemic JIA who are included in our longitudinal Pharmacology biobank will be used. Of the 63 patients, 28 (44.4%) children were diagnosed with oligo articular JIA, 19 (30.2%) with poly articular JIA, 9 (14.3%) with enthesis-related JIA, 4 (6.3%) with psoriatic JIA and 3 (4.8%) with undifferentiated JIA. The average age at sampling was 11.5 years ± 4.0 and 65% of the patients was female. These samples will be run on a 96-analyte NanoString panel and associated with clinical response at time points 3 and 6 months after start of TNF-α blockade.

Results: Both RNA blood collection systems yielded high-quality RNA, with overall higher RNA concentrations for blood collected in Tempus tubes in comparison to PAXgene tubes. qPCR data showed that gene expression of all measured genes is affected by the method of blood collection and processing. However, the inter-individual variation was similar between both collection tubes, indicating that similar RNA profiles were observed.

Conclusion: Gene expression profiles derived from whole blood collected in PAXgene or Tempus tubes are comparable, but are not interchangeable.

REFERENCES:

Disclosure of Interests: None declared

THU0526 LONG-TERM OUTCOME IN JUVENILE IDIOPATHIC ARTHRITIS – A POPULATION-BASED STUDY FROM SWEDEN
Elisabet Berthold1, Bengt Månsson1, Robin Kahn1, 2Clinical science Lund, Lund University, Department of Rheumatology, Lund, Sweden; 2Clinical science Lund, Lund University, Department of Pediatrics, Lund, Sweden

Background: Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in children. The incidence rate among Caucasians is reported to be 8-15/100 000/year (1, 2). The long-term prognosis is insufficiently studied in JIA, although it is known that the disease often proceeds into adulthood and may cause joint damage leading to significant morbidity and physical disability. There are many challenges in elucidating the long-term prognosis. Amongst others, frequent occurrence of disease misclassification in diagnostic registers and the heterogeneity of JIA have made it difficult to interpret results (3, 4).

Objectives: To study the epidemiology, incidence and long-term outcome of JIA in southern Sweden using a population-based cohort of children with a validated diagnosis of JIA collected over nine years.

Methods: Potential cases of JIA, diagnosed between 2002 and 2010 were collected from a local search at the Department of Rheumatology in Lund and at the National Board for Health and Welfare, using the ICD-codes M08-M09. The study area is Skåne, the southernmost county of Sweden (population 1.24 million; 19.1% aged < 16 years) and the median follow-up time was eight years. The JIA-diagnosis was validated and subcategorised through medical record review based on criteria defined by The International League of Associations for Rheumatism. Parameters on disease activity and pharmacologic treatment were recorded annually until the end of the study period.

Results: 251 cases of JIA were confirmed. The mean annual incidence rate for JIA was estimated to be 12.8/100 000/year. The highest age specific annual incidence is at the age of two years (36/100 000/year). This peak is consistent in the female group, but the incidence peak among males is at 12 years of age. Almost all patients are at some point during their disease course prescribed non-steroidal anti-inflammatory drugs (98%). Intra-articular steroid injections are also frequently used (78.9% in the total cohort). Methotrexate is the most common disease modifying anti-rheumatic drug prescribed (60.8%). Tumor necrosis factor alpha-inhibitors are used as treatment in 23.9% of the children.

Oligoarthritis was the largest subgroup (44.7%), followed by undifferentiated JIA (16.3%), polyarticular rheumatoid factor negative JIA (13.9%), enthesitis-related arthritis (8.8%), polyarticular rheumatoid factor positive JIA (6.8%), juvenile psoriatic arthritis (6.8%) and systemic JIA as the smallest subgroup (2.8%).
Uveitis, both acute and chronic, was seen in 10.8% of the children. Permanent joint affection was seen in 20.7% of the children and 8.8% have been treated with joint corrective orthopedic surgery. At five-year follow-up, 57% of the children had disease activity, defined as arthritis and/or uveitis (2.1% with uveitis as active disease).

**Conclusion:** This is a well-defined, population-based and validated cohort of children diagnosed with JIA investigating long-term outcome in the era of biologics. We found that a considerable part of the children still develop uveitis, permanent joint affection and need joint corrective surgery occasionally. More than 50% of the cohort has active disease five years after diagnosis. In conclusion, we still have long-term challenges in children with JIA, in spite of state-of-the-art treatment.

**REFERENCES:**


**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular1579

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**THU0527 RISK SCORE OF MACROPHAGE ACTIVATION SYNDROME IN PATIENTS WITH SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS**

Simone Carbogno1, Denise Pires Marafon2, Giulia Manucci3, Manuela Pardeo4, Antonella Insalaco5, Virginia Messi6, Emanuela Sacco7, Fehrat Derm8, Betul Sözen8, Alenka Gagro9, Nastasia Kifer10, Marija Jelusic11, Francesca Minoia12, Mikhail Kostik13, Olga Vougiouka14, Roberta Simoni15, Francesca Minoia16, Mikhail Kostik17, Olga Vougiouka18, Fabrizio De Benedetti19, Claudia Bracaglia20, 21

**Background:** Macrophage Activation Syndrome (MAS) is a severe, life-threatening, complication of rheumatic diseases in childhood, particularly of systemic Juvenile Idiopathic Arthritis (sJIA), occurring in approximately 25% of the patients with sJIA. A score that identifies sJIA patients who are at high risk to develop MAS would be useful in clinical practice.

**Objectives:** To evaluate whether routine laboratory parameters at disease onset may predict the development of MAS in patients with active sJIA. To define a risk score of MAS for sJIA patients using these parameters.

**Methods:** Laboratory parameters of disease activity and severity (WBC, N, PLT, Hb, ferritin, AST, ALT, gGT, LDH, TGL, fibrinogen, D-dimer and CRP), were retrospectively evaluated in 86 sJIA patients referred to our Division of Rheumatology from 1998 to 2017 with at least one year of follow-up. Laboratory parameters were evaluated during active sJIA, without MAS, at time of hospitalization (T1) and before treatment for sJIA was started (T2). Patients were divided in two groups: group 1 (patients without history of MAS), group 2 (patients with at least one MAS episode during disease course). To calculate a MAS risk score, laboratory parameters, collected at T2, with a statistical significant difference between the two groups of patients were selected.

**Results:** Thirty-three patients, who fulfilled the 2016 classification criteria for MAS [1] at time of sampling, were excluded from the analysis. Therefore, we analysed laboratory parameters of 53 patients with sJIA, 33 of whom without history of MAS (group 1) and 20 who developed at least one episode of MAS during disease course (group 2). Levels of ferritin, AST, ALT, gGT and TGL, collected at T2, were statistically significant higher in patients with a history of MAS compared to those without a history of MAS. For each of these parameters an arbitrary cut-off was defined. In order to define the final score an arbitrary rate was attributed to each parameter. Sensitivity (Se), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV) were calculated to define the most scoring system. The scoring system with the best sensitivity was chosen (Table 1). A MAS risk score >3 identified 19 out of 20 sJIA patients with a history of MAS and 4 out of 33 sJIA patients without history of MAS.

**Conclusion:** In conclusion we developed a MAS risk score based on routine laboratory parameters that are available worldwide, that can help clinicians to identify patients at higher risk to develop MAS. A validation on a larger population is necessary.

**REFERENCES:**


**Disclosure of Interests:** Simone Carbogno: None declared, Denise Pires Marafon: None declared, Giulia Manucci: None declared, Manuela Pardeo: None declared, Antonella Insalaco: None declared, Virginia Messi: None declared, Emanuela Sacco: None declared, Fehrat Derm: None declared, Betul Sözen: None declared, Alenka Gagro: None declared, Nastasia Kifer: None declared, Marija Jelusic: None declared, Francesca Minoia: None declared, Mikhail Kostik: None declared, Olga Vougiouka: None declared, Fabrizio De Benedetti: None declared, Claudia Bracaglia: None declared

**DOI:** 10.1136/annrheumdis-2019-eular5804

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**THU0528 DISCONTINUATION OF COLCHICINE THERAPY IN CHILDREN WITH FAMILIAL MEDITERRANEAN FEVER**

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**Background:** Clinical phenotype of FMF exists in some carriers of MEFV mutation. These patients tend to have a mild disease. Prolonged colchicine free remission was reported in a small group of FMF patients.

**Objectives:** To describe and characterize a group of children with FMF in whom colchicine was discontinued.

**Methods:** The study cohort consisted of all children with FMF followed at 2 referral centers in Israel. In conclusion, we still have long-term challenges in children with JIA investigating long-term outcome in the era of biologics.

**Results:** In order to validate the MAS risk score on a different population, we applied it on 53 patients from other paediatric Rheumatologic centres. Thirty-seven of these patients without history of MAS while 16 with at least one episode of MAS. Sensitivity and specificity were 0.750 and 0.784 respectively.

**Conclusion:** In conclusion we developed a MAS risk score based on routine laboratory parameters that are available worldwide, that can help clinicians to identify patients at higher risk to develop MAS. A validation on a larger population is necessary.

**REFERENCES:**


**Disclosure of Interests:** Yonatan Butbul: None declared, Rawan Sliman: None declared, Shade Fahoun: None declared, Yackov Berkun: None declared, Rappaport Children’s Hospital, Rambam Medical Center, Haifa, Israel, Pediatric Rheumatology Service, Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Department of Pediatrics B, Haifa, Israel; Rappaport Children’s Hospital, Rambam Medical Center, Haifa, Israel, Pediatric Rheumatology Service, Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel; Hadassah-Hebrew University Medical Center Mount Scopus, Jerusalem, Israel, Department of Pediatrics and FMF clinic, Haifa, Israel

**DOI:** 10.1136/annrheumdis-2019-eular5804

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**THU0527 – Table 1.**

<table>
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<tr>
<th>Laboratory parameters</th>
<th>Cut-off</th>
<th>Rate</th>
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<td>Ferritin (mg/ml)</td>
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<tr>
<td>AST (UI/L)</td>
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</tr>
<tr>
<td>LDH (UI/L)</td>
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<td>1</td>
</tr>
<tr>
<td>gammaLT (UI/L)</td>
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<td>1</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>&gt;250</td>
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</tbody>
</table>

**Sensitivity (Se) = 0.950**

**Specificity (Sp) = 0.982**

**Positive predictive value (PPV) = 0.826**

**Negative predictive value (NPV) = 0.967**

**THU0528**

**Table 1.**

**Laboratory parameters and cut-off used to create the MAS risk score in sJIA patients**

**Laboratory parameters:** Ferritin, AST, LDH, gammaLT, Triglycerides.

**Cut-off:**
- Ferritin: >900 mg/ml
- AST: >35 UI/L
- LDH: >50 UI/L
- gammaLT: >30 UI/L
- Triglycerides: >250 mg/dl

**Rate:**
- 1
- 1
- 1
- 1
- 2

**Sensitivity:** 0.950

**Specificity:** 0.982

**Positive predictive value:** 0.826

**Negative predictive value:** 0.967
Whole-body magnetic resonance imaging in juvenile dermatomyositis: a longitudinal study

**Objectives:** To compare whole-body MRI (WB-MRI) with clinical examination. Correlations between WB-MRI muscle score and disease activity is a challenge in clinical practice.

**Methods:** We included consecutive JDM patients followed in the rheumatology unit. All patients were submitted to clinical and laboratory evaluation. WB-MRI images were obtained using a 1.5 T MRI scanner and short T inversion recovery sequences (STIR). Muscle, peripheral inflammation and subcutaneous inflammations signal abnormalities were scored in 42 muscular groups. Muscle inflammation was classified as: 0 = absent; 1 = Mild to moderate/involvement less than 50% of muscle extension and 2 = Accentuated/greater than 50%. Peripheral and subcutaneous inflammations were classified as: 0 = absent; 1 = present; and on proximal and distal extremities. WB-MRI and clinical assessments were performed concurrently and results compared. Evaluation was repeated after 12 months. Statistics was performed according to the nature of the variable.

**Results:** WB-MRI revealed muscle inflammation in 6 (31.6%) at study entry. We observed grade 2 muscle inflammation of the right and left scapular girdle (1/19 patients), right and left pelvic girdle (2/19 patients) and right and left thigh (1/19 patients). Grade 1 inflammation was observed in peripheral right and left arm (2/19 patients), peripheral right and left thigh (1/19 patients). Grade 1 subcutaneous inflammation was observed in right and left thigh (1/19 patients) and left leg (1/19 patients). Additionally we observed sacroiliitis (1/19 patients), spinal cord infarction (21%), and osteonecrosis (5.2%). All patients were treated with standardized treatment. After 12 months 13/19 (68.4%) patients repeated the WB-MRI. Five (38.4%) patients had new/worsening of muscle and subcutaneous inflammation, one (7.7%) patient had tibial medullary infarction. Correlations between WB-MRI muscle score and disease activity measures were excellent (Manual Muscle Test: r = 0.88, Childhood Myositis Assessment Scale: r = 0.81). Patients with subcutaneous inflammation developed clinically evident subcutaneous calcifications during follow-up.

**Conclusion:** WB-MRI provides additional information to clinical evaluation and represents a promising tool to determine the grade of muscle inflammation to additional peripheral and subcutaneous tissue inflammation.

**References:**

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.2380
Background: Childhood uveitis is a group of heterogenous, potentially blinding inflammatory disorders. Management is complex. There is growing recognition of the importance of actively involving affected children and their families in their own care. Co-designed interventions, developed through active involvement of staff and patients, can provide effective solutions to problems identified by those affected.

Objectives: To use findings from a patient and family discussion group to inform the co-designed development of health care processes and interventions.

Participants: Five children/young people with uveitis (age ranges 8 to 17), seven parent/carers of children with uveitis and four health care professionals attended a 90 minute discussion group. Main discussion topic was the identification of areas in need of interventions or support structures. Sub-topics were determined a priori using previous PPI and existent research (REFS). They comprised: Direct health care; Impact on families; School, education and peers. Responses were collated. Consent was taken for use of direct quotes from participants.

Results: We outline the areas identified by children and families:

Direct health care: Four interconnected areas were identified: (1) Transitioning to adult services, (2) peer support (health care services being a valuable site for identifying peers), (3) communication between care structures to adult services, (2) peer support (health care services being a valuable site for identifying peers), (3) communication between care structures and (4) education for families. With regards to family education, there was identification of the need for specific services or interventions around the communication of (4a) diagnosis, (4b) treatment, (4c) likely long term outcomes/prognosis, (4d) and the child’s progress. There was also discussion on (4e) the formats used to communicate with families.

Impact on families: Participants discussed support around (1) family relationships, (2) the impact of systemic medication, They also discussed (3) a need for recognition of the changing nature of their lived experience as affected families over the disease course and the need for on-going psychologic support especially at presentation to help with acceptance.

School, education and peers: Participants discussed the need for support around: (1) the impact of treatment on school life, (2) communication with school professionals and peers, (3) impact of visual impairments, (4) education for families, With regards to family education, there was identification of the need for specific services or interventions around the communication of (4a) diagnosis, (4b) treatment, (4c) likely long term outcomes/prognosis, (4d) and the child’s progress. There was also discussion on (4e) the formats used to communicate with families.

Conclusion: Through the above approach, we have identified a range of issues affecting our patients and their families. Our findings are similar to those of other groups (1, 2) These lived experiences will be used to inform the co-design of supportive services (patient leaflets, videos, website, psychology intervention) and research on the effectiveness of these interventions in improving the management of affected children and their families.

REFERENCES:

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NEW CLASSIFICATION CRITERIA FOR RECURRENT AUTOINFLAMMATORY DISEASES APPLIED TO AN INDEPENDENT COHORT: EXPERIENCE FROM THE JIR COHORT DATABASE

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Background: New classification criteria for the inherited periodic fever syndromes (TRAPS, FMF, MKD and CAPS) have recently been developed during a Consensus Conference held in Genoa in March 2017.

Objectives: The aim of our study was to compare these new classification criteria for monogenic recurrent fever syndromes with the diagnoses of clinicians. For this purpose we used the JIR cohort database, an international platform gathering data of patients with pediatric inflammatory disease.

Methods: The Genoa classification criteria were applied to all the patients, then compared to the clinical diagnosis of the treating physician. As patient diagnosis could be confirmed or suspected, the patients could have up to two diagnoses. Classification criteria relied on genetical HRF pathogenicity classification. Finally, criteria performance were assessed by firstly determining sensitivity and specificity and secondly analyzing true positive, false positive and false negative patients.

Results: 455 patients included in the JIR cohort database with a recurrent fever syndrome were enrolled to the study.

CAPS: The analysis of the performance of the CAPS criteria showed sensitivity of 60% and specificity of 98%. 14 patients fulfilled Genoa CAPS classification criteria, with 6 true positive and 8 false positive patients. Patients with confirmatory genotype always fulfilled classification criteria. 4 patients, who carried heterozygous mutations, were false negative.

TRAPS: The analysis of the performance of the TRAPS criteria showed sensitivity of 100% and specificity of 98%. 22 patients fulfilled Genoa TRAPS classification criteria, all true positive patients with confirmatory and non-confirmatory genotype. 5 were false negative with 4 patients with contramatory genotype.

FMF: The analysis of the performance of the FMF criteria showed sensitivity of 96% and specificity of 89%. 118 patients were true positive while 35 were false positive patients. True positive patients were all patients with confirmatory genotype, patients with non-confirmatory genotype and no mutation. 37 were false positive patients. 5 patients were false negative with 3 patients with non-confirmatory genotype.

MKD: The analysis of the performance of the CAPS criteria showed sensitivity of 64% and specificity of 66%. 7 patients with confirmatory genotype were true positive patients. 148 were false positive patients with 44 patients diagnosed TRAPS, FMF, CAPS while the rest were SURF. 4 were false negative including 3 patients with non-confirmatory genotype.

Conclusion: This study confirms that classification was undertaken on a cohort of patients seen with recurrent fever. This descriptive study shows tremendous performance Genoa criteria for patients with confirmatory genotype and help classifying patients with non-confirmatory genotype. On the other hand, those classification criteria were less performant when patients did not display at least one gene mutation. Therefore, Genoa classification criteria for TRAPS outperformed the others, because mandatory genetic screening. This study also highlights permissive criteria for clinical CAPS, FMF and MKD. The implementation of biological criteria in MKD would improve MKD criteria.

Disclosure of Interests: None declared.


NATURE AND IMPACT OF THE FRENCH NETWORK RESRIP ON SCHOOLING, FOR CHILDREN WITH CHRONIC INFLAMMATORY RHEMATISM

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Background: Pediatric chronic inflammatory rheumatism (CIR) has a significant impact on daily life, especially on schooling, that can lead to child’s drop-out. In this context, a French paediatric health network, RESRIP (Réseau pour les Rhumatismes Inflammatoires Pédiatriques), has been created in 2014 for children with CIR and living in the Ile-de-France region. Patients are included in this network if they meet certain criteria such as the need to find trained health professionals close to their home or for support because of adverse social conditions or difficulties with their schooling. If the criteria are fulfilled, the patient and his family participate in an intake interview which allows RESRIP to understand the patient’s need and to set up targeted actions.

Objectives: In our study, we aim to describe and evaluate RESRIP’s role on improving school attendance and tackling absenteeism.

Methods: A descriptive retrospective study was performed regarding the support provided by RESRIP with respect to patients’ schooling and education professionals. Rates of non-attendance were collected at inclusion
and every 6 months from 2014 to 2017, through a standardized auto-questionnaire.

Results: 278 patients (M/F: 0.29) aged 12.7 years on average (± 4.9 range 2-21) were taken care of between 2014 and 2017 by RESRIP. Juvenile idiopathic arthritis (JIA) (n = 142), connective tissue disease (n = 49) and auto-inflammatory disease (AID) (n = 32) are the 3 main pathologies covered. Among the 278 patients, twenty-one percent of patients needed academic support when entering the network, including: 37% in the JIA group, 34% in the connective tissue group and 18% in the AID group. Educational assistance was set up for all patients with school difficulties at inclusion but also for all the patients during their follow-up. Patient Support: 178 Individual Action Plan (IAP) were implemented by RESRIP. Twelve patients benefited from additional time for their school exams and 10 were allowed to pass the baccalaureat (French final college exam) only two years instead of a year. In thirty patients, sports education has been adapted. Forty-one MDPH files (Departmental Houses for the Disabled) were produced to enable the establishment of a school life assistant (AVS), teaching materials and/or technical aids. Finally, 8 patients received home school assistance through Home Learning Assistance Services (SAPAD).

Education professional support: RESRIP established partnerships with the French National Education (FNE) and the SAPAD (home tuition service for ill children). For the FNE, RESRIP provided school doctors or nurses with: 8 continuing medical training and 25 personal interviews to explain the pathologies. In addition, 5 multidisciplinary meetings, within the institutions were organized, for 5 patients with social integration difficulties and school educational exemptions, has added a significant decrease in school absenteeism between 2014 and 2017: 3.2 days per year on average at age 1 to 0.5 days per year on average (p <0.05) at 42 months. Conclusion: Over time, a better understanding of the impact of chronic illness on school and education professionals, has allowed RESRIP to improve its support. The result is a notable decline in school absenteeism and in unjustified physical education exemptions. Several projects are underway: The development of a standard IAP available for doctors, the set-up of a partnership with school hospital, willing to help for the implementation of home school support courses in addition to SAPAD.

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THU0537 ANGIOMATOID FIBROUS HISTIOCYTOMA MIMICKING SYSTEMIC JIA VIA MUTATION-DRIVEN IL-6 PRODUCTION

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Background: Angiomatoid Fibrous Histiocytoma mimicking Systemic JIA via mutation-driven IL-6 production: Angiomatoid Fibrous Histiocytoma (AFH) is a rare tumour associated with mutation-driven production of Interleukin-6 (IL-6) which causes a systemic inflammatory picture similar to Systemic Juvenile Idiopathic Arthritis (sJIA). Objectives: A previously well 6-year old girl was referred with 6 weeks of abdominal pain, nausea, weight loss, night sweats, & lethargy. Examination was unremarkable apart from a 2cm lump in the right popliteal fossa. This had been reported on USS 2 months earlier, at an external hospital, to be a Sebaceous cyst. There was no rash, organomegaly, lymphadenopathy, or synovitis. She had persistent recurrent fevers of >39C, but not in the classical coutidial pattern of sJIA. Methods: Bloods showed persistent Hb <70, platelets >600, ESR >100 & CRP >200. Autoantibody & full infection screens were negative. Urine HMMA:creatinine ratio was minimally raised at 7.2 (normal 1.8 - 5). Faecal calprotectin, upper & lower GI endoscopy were normal. Bone-Marrow Aspiration was reported as being highly reactive but with no malignancy seen. Whole-body STIR MRI was reported as normal, but repeat localised USS of the knee showed a 27x18x21mm well circumscribed, mixed cystic/solid lesion with marked vascularity. The lesion was then biopsied, and subsequently excised Plasma IL-6 levels were significantly elevated at 46.7pg/ml (normal range: 0-2), but normalised after excision. TNF and IL1b levels were normal Results: Initial biopsy and FISH analysis confirmed the diagnosis of AFH via mutation-driven IL-6 production. Angiomatoid Fibrous Histiocytoma (AFH) is a rare tumour associated with mutation-driven production of Interleukin-6 (IL-6) which causes a systemic inflammatory picture similar to Systemic Juvenile Idiopathic Arthritis (sJIA).

Conclusion: No statistical differences were detected, although the scarce number of control subjects might have influenced this result. There is a trend towards a lower antibody persistence anti-Hb in patients compared to healthy children. The response to life virus vaccine and tetanus seem to be as good as in healthy children.

Disclosure of Interests: Laura Fernández Silveira: None declared, M.J Gimenez: None declared, E Andreu-Alapont: None declared, Patricia Falomir-Salcedo: None declared, E Serrano-Poveda: None declared, M.I. González-Fernández: None declared, B Lopez-Montesinos: None declared, Inmaculada Calvo Grant/research support from: received research grants from Pfizer, Roche, Novartis, Clementia, Sanofi, MSD, BMS and GSK, Consultant for: Advisory boards: Novartis, AbbVie, Speakers bureau: AbbVie, Roche, Novartis, SOBI DOI: 10.1136/annrheumdis-2019-eular.6378

THU0536 LONG TERM IMMUNITY IN A PAEDIATRIC COHORT OF PATIENTS WITH RHEUMATIC DISEASES FROM A TERTIARY HOSPITAL IN SPAIN

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Background: Pediatric patients with rheumatic diseases (RD) are at increased risk of infections. Vaccines have been proved to be very effective to prevent them. Nevertheless the long-term immunity after vaccination remains quite unknown in this group.

Objectives: To compare the long term seroprotection in pediatric patients with rheumatic diseases who received measles, rubella, mumps, tetanus, diphtheria, hepatitis B, Hib and meningococcus C vaccination according to the routine immunization schedule in Spain, and healthy children.

Methods: We designed a cross-sectional study including consecutive pediatric patients with RD who attended the rheumatology clinic and healthy children older than 10 y.o. The administered vaccines, treatment and pathology of each patient will be recorded. Their antibodies titers against each antigen were quantified and compared to healthy children.

Results: 60 patients (median age 13 y.o IQR 10.2-17) and 15 healthy children (mean age 11.3 y.o. IQR 11.3-12.7) were included. In the patients group 62% were female, and 35% in healthy. Diagnosis: 85% Idiopathic juvenile arthritis, 16% Lupus or juvenile dermatomyositis. 46% had received biologic treatment sometime. Seroprotection rate was (patient vs control): measles 89%/ vs 81%, rubella 78.8% vs 73.3%, parotiditis 84.7% vs 66.7%, VHB 27% vs 10.5%, diphtheria 89.5% vs 81%, tetanos 64.9% vs 61.1%. Hib 42% vs 53%, pneumococco 92.4% vs 100%, meningococcus C 12% vs 11%. p>0.05

Conclusion: No statistical differences were detected, although the scarce number of control subjects might have influenced this result. There is a trend towards a lower antibody persistence anti-Hb in patients compared to healthy children. The response to life virus vaccine and tetanus seem to be as good as in healthy children.

Disclosure of Interests: Laura Fernández Silveira: None declared, M.J Gimenez: None declared, E Andreu-Alapont: None declared, Patricia Falomir-Salcedo: None declared, E Serrano-Poveda: None declared, M.I. González-Fernández: None declared, B Lopez-Montesinos: None declared, Inmaculada Calvo Grant/research support from: received research grants from Pfizer, Roche, Novartis, Clementia, Sanofi, MSD, BMS and GSK, Consultant for: Advisory boards: Novartis, AbbVie, Speakers bureau: AbbVie, Roche, Novartis, SOBI DOI: 10.1136/annrheumdis-2019-eular.309
ABSTRACT WITHDRAWN

THU0539

SERUM SOLUBLE CD25: AN USEFUL BIOMARKER OF MACROPHAGE ACTIVATION SYNDROME IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

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Background: Systemic juvenile idiopathic arthritis (SJIA) is an auto-inflammatory disorder secondary to innate immune dysfunction with a propensity to develop macrophage activation syndrome (MAS), a life-threatening condition (1). sCD25 has been used as a sensitive biomarker for the diagnosis of Hemophagocytic lymphohistiocytosis which has similarities in clinical features and pathogenesis to MAS (2).

Objectives: To assay serum soluble CD25 in children with systemic juvenile idiopathic arthritis (SJIA) and to compare levels of sCD25 in children with inactive disease, active disease and those with macrophage activation syndrome (MAS).

Methods: This prospective study was conducted in a tertiary care referral centre in North India from January 2017 to June 2018. All patients fulfilling the International League of Associations for Rheumatology (ILAR) 2001 criteria for SJIA were eligible for enrolment. At enrolment, all patients were examined clinically for signs of disease activity. Appropriate investigations were carried out and sCD25 was analyzed by using commercially available sCD25/IL-2R ELISA kit.

Results: A total of 35 children (1-18 years) with 43 events were included in the study. Mean age at enrolment in the study was 7.3±3.59 years with male to female ratio of 2.5. Based on clinical features and investigations, events were categorized into 3 groups; SJIA with inactive disease (15; 34.9%), SJIA with active disease (15; 34.9%) and SJIA with MAS (13; 30.2%). Mean sCD25 levels in the study population were 10,966.02 ± 10,854.93 pg/ml. Children with inactive disease, active disease and disease with MAS had mean ± SD serum sCD25 levels of 4710.6 ± 1817.04 pg/ml, 7604 ± 2376.24 pg/ml, and 22062.9 ± 14335.97 pg/ml respectively. Although, Mean level of sCD25 in children with active disease was higher than those with inactive disease, but no significant difference could be found. sCD25 levels significantly (p value 0.0001) varied between MAS and other 2 groups. sCD25 cut off level of 10,385 pg/ml was found to have sensitivity of 100% and specificity of 96.7% in differentiating MAS in SJIA from disease flare and inactive disease. There was no significant correlation of sCD25 with demographic parameters. Total leucocyte count, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), platelet counts, urea, creatinine, prothrombin time, activated partial prothrombin time and fibrinogen levels. A correlation of sCD25 was found with levels of haemoglobin (p-value .01), ferritin (p-value .001), aspartate aminotransferase (AST) (p-value .00), alanine aminotransferase (ALT) (p-value .00), alkaline phosphatase (ALP) (p-value .005) and triglycerides (p-value .001). Higher sCD25 levels were found in patients who had low Hb, elevated ferritin, elevated AST, ALT, ALP and serum triglyceride levels.

Conclusion: sCD25 is a useful biomarker in differentiating MAS in SJIA from disease flare and inactive disease with sensitivity and specificity of 100% and 96.7% respectively at a cut off level of 10,385 pg/ml. Coupling sCD25 with other laboratory parameters may be useful for early diagnosis of MAS in SJIA.

REFERENCES:

Disclosure of Interests: None declared


THU0540

SYSTEMATIC REVIEW OF BIOLOGICAL TREATMENT OF DEFICIENCY OF INTERLEUKIN-36 RECEPTOR ANTAGONIST (DIRTA) IN CHILDREN AND ADOLESCENTS

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Background: Deficiency of interleukin-36 receptor antagonist (DIRTA) is a life threatening autoinflammatory disease caused by autosomal recessive mutations of the IL36RN gene leading to recurrent episodes of generalized purpuric psoriasis with systemic inflammation and fever. The disease is rare and no standardized treatment guidelines exist.

Objectives: To systematically review and analyze the literature on biologically treated pediatric DITRA patients.

Methods: A NCBI pubmed database research was performed to identify all relevant articles on pediatric DITRA patients treated with biologicals. According to defined response criteria therapeutic efficacy was analyzed.

Results: Our literature research revealed 13 pediatric patients with DITRA and biotreatment. Ten patients were homozygous including six with the p.Leu27Pro, three with the p.Arg10Argfs* and one with the p.Thr123Met mutation and three were compound heterozygous. We add an unreported DITRA patient with a compound heterozygous IL36RN p.Pro76Leu/pSer113Leu mutation. In total 29 flares in 14 patients were treated with biological agents-targeting IL-1/IL-17, IL-12/23 and TNF-α. Complete response was achieved in 15 (52%), partial in 4 (14%), and no response in 10 (34%) of the flares. Response rates were heterogeneous among the different agents. While complete/partial/no response with inhibition of TNF-alpha could be achieved in 6 (46%)/3 (23%)/4 (31%), the inhibition of IL-17 and of IL-12/23 led in each 4 flares to a 100% complete response. IL-1/3R inhibition led to complete/partial response in each 1 (13%) and was not effective in 6 (75%) flares. Of note, the unreported patient was successfully treated with weekly dosed adalimumab.

Conclusion: DITRA is a rare disease that has to be considered in patients with generalized purpuric psoriasis with systemic inflammation and fever. It can be effectively treated with specific biological inhibition of TNF-alpha, IL-12/23 and IL-17, while anti-IL-1/3R treatment seems less effective. Weekly dosed adalimumab appears to be a novel treatment option for pediatric patients. Further reports and studies of biological treated pediatric DITRA patients are warranted for evaluation of optimal treatment.

REFERENCE:

Disclosure of Interests: Toni Hospach Speakers bureau: Chugai, Roche, Novartis, Fabian Glowatzki: None declared, Friederike Blankenburg: None declared, Dennis Conzelmann: None declared, Christian Strinkorb: None declared, Chris Sandra Muellerschoen: None declared, Peter Driesch von den: None declared, Lisa Koehler: None declared, Meino Rohfils: None declared, Christoph Klein: None declared, Fabian Hauck: None declared


THU0541

ANTI-VACCINE ANTIBODY LEVELS IN JUVENILE IDIOPATHIC ARTHRITIS PATIENTS: PRELIMINARY DATA IN 90 PATIENTS

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Background: Patients with juvenile idiopathic arthritis (JIA) may have lower protective levels of anti-vaccine antibodies (AVA) due to high inflammatory activity, interrupted or incomplete vaccination schedule, using of immune-modulating drugs, e.g. systemic corticosteroids (CS), methotrexate (MTX) and biologics [1].

Objectives: The aim of our study was to evaluate levels of AVA in the patients with JIA.

Disclosure of Interests: None declared

Methods: We included data about 90 JIA (26 M and 64 F) aged from 2 to 17 years, who received scheduled vaccination before the age of 2 years and before JIA onset. In all patients the Ig G anti-measles (AM), anti-parotitis (AP), anti-hepatitis B (AHB), anti-diphtheria (AD) and anti-rubella (AR)AVA levels were detected with ELISA. In each patient we evaluate the type of the JIA (oligoarthritis – OA (n=38), polyarthritis – PA (n=36), systemic-SA (n=7) and enthesitis-related arthritis – ERA (n=10), routine disease activity and treatment. In healthy controls were measured anti-measles (n=40) and anti-parotitis (n=30) antibodies (AB) for comparison with JIA.

Results: The main demographic characteristics: age of inclusion in the study 11 (8-15) years, disease onset – 6 (4-8) years, JIA duration – 2 (7-2) years. The AM AB in JIA patients were 0.2 (0.0-0.5) IU/ml and in HC 0.3 (0.2-1.1) IU/ml (p=0.00002), despite the higher age of JIA patients than HC (p=0.0000001); AP AB were 2.6 (1.0-5.1) IU/ml vs 1.1 (0.0-4.9) IU/ml in JIA and HC, respectively (p=0.04). Protective levels of AM AB was detected in 50% of all JIA population, vs. HC – 87.5% (p=0.00005), AP – 67.7% vs. 60% in HC (p=0.076), AHB – 54.4%, AD – 50%, AR – 97.8%. The main data related to vaccination status in the table. We have found correlation between JIA duration and levels AM AB (r=-0.27, p=0.01). Differences in the study between studies can be explained by differences in the study populations (age, disease duration and disease state) and differences in the study methods (1-3). Depression and anxiety are the most common disorders, but most studies were based on questionnaires to investigate incidence of only these two diseases (1,3).

Objectives: To explore mental and behavioral disorders in JIA patients compared to the control population.

Methods: All incidents patients with JIA during 2000-2014 were collected from the nationwide register, maintained by the Social Insurance Institution of Finland (4). The National Population Registry identified three controls (similar regarding age, sex and residence) for each case. They were followed up together until 31Dec 2015. ICD-10 codes of psychiatric diagnosis (F10-F99) were picked up from the Care Register for Health Care of the National Institute for Health and Welfare.

Results: During 28,941 follow-up years, 974 (23%) JIA patients were diagnosed with mental or behavioral disorders, whereas the number in the control group was 1,807 (15%), (p<0.001). Neurotic, stress-related and somatoform disorders (F40-48) and mood (affective) disorders (F30-39) were the most common psychiatric diagnoses in the JIA (10.41% and 8.18%) and in the control group (5.44% and 5.13%). The odds ratio for neurotic disorders (F40-48) was 2.02 (95% CI 1.78-2.29) and for mood disorders (F30-39) 1.65 (95% CI 1.44-1.89). Additionally, JIA statistically significantly associated with behavioral and emotional disorders and disorders of psychological development (Table). Female patients with JIA had higher odds ratios than males for all mental and behavioral disorders except behavioral syndromes (F50-59), for which males with JIA had higher odds ratio.

Conclusion: The risk of psychiatric disorders in JIA patients is increased.

REFERENCES:

Disclosure of Interests: None declared


THU0542
THE PSYCHIATRIC DISORDERS IN CHILDHOOD, ADOLESCENCE AND YOUNG ADULTS WITH JUVENILE IDIOPATHIC ARTHRITIS PATIENTS IN FINLAND
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Background: Reported psychiatric morbidity among juvenile idiopathic arthritis (JIA) patients has varied between 9.3-51% (1-3). The variation between studies can be explained by differences in the study populations (age, disease duration and disease state) and differences in the study methods (1-3). Depression and anxiety are the most common disorders, but most studies were based on questionnaires to investigate incidence of only these two diseases (1,3). Depression and anxiety are the most common disorders, but most studies were based on questionnaires to investigate incidence of only these two diseases (1,3).

Objectives: To explore mental and behavioral disorders in JIA patients compared to the control population.

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Conclusion: The risk of psychiatric disorders in JIA patients is increased.

REFERENCES:

Disclosure of Interests: None declared


THU0543
LATENT TUBERCULOSIS INFECTION IN CHILDREN WITH PEDIATRIC RHEUMATOLOGIC DISEASES TREATED WITH CANAKINUMAB
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Background: Little is known about the long-term safety of canakinumab treatment (Table). In this study, we report the follow-up data of children with pediatric rheumatologic diseases treated with canakinumab (THU0543).

Disclosure of Interests: None declared

Objectives: To determine the incidence of latent tuberculosis infection and evaluate the follow-up protocol of the patients treated with canakinumab in a single pediatric rheumatology center from a TB-medium burden country.

Methods: The hospital charts of patients treated with canakinumab between 2012 and 2019 were retrospectively reviewed. The patients were screened for TB using tuberculin skin test (TST) and/or Quantiferon-TB Gold (QFT-G) test. They had no history of active TB prior to screening and no signs or symptoms of active TB. None of the patients had recent close contact with a person diagnosed as active TB. At initial evaluation, in patients who had never been given immunosuppressive therapy, TST ≥ 15 mm (if BCG vaccinated) and TST ≥ 10 mm (if BCG unvaccinated) were considered as positive. In the case of prior immunosuppressive drug use TST cut-off limit was accepted as 5 mm. Patients with either a positive TST or QFT-G result, in whom previous TB ruled out, were to receive appropriate treatment for latent TB one month prior to the first dose of canakinumab and continue throughout 9 months. Chest radiographs were performed prior to therapy and every 6 months. In case TST was anergic, both chest X-ray and TST were repeated after 3 months. Patients were evaluated for signs and symptoms of active TB by an infectious disease specialist every 3 months while on canakinumab therapy according to the guidelines of Ministry of Health for use of biologic agents\(^1\). The TST conversion was considered as a variation ≥ 5 mm between the two TSTs performed within an interval at least 3 months. If TB was suspected during the study, repeat TB testing (TST, QFT-G, and chest radiograph) was recommended.

Results: Twenty-six of 344 children had received a diagnosis of juvenile idiopathic arthritis, 1 TRAPS and 1 hyper Ig D syndrome patients were evaluated. The mean age at canakinumab onset was 12.4 ± 4.3 years (min: 2, max: 17 years). The average duration of canakinumab use was 2.3 ± 1.4 years (min: 1 max: 6.5 years). Among 37 patients, 5 patients had positive TST and one had positive QFT-G with normal chest X-ray prior to therapy. They were given isoniazid prophylaxis for latent TB. QFT-G was checked in 6 patients prior to canakinumab, 5 were negative. Seven patients had TST conversion during follow-up. Their chest X-rays were normal. None of them had active TB symptoms, such as; cough, fever, night sweats and weight loss. The mycobacterial cultures, mycobacterium tuberculosis PCR of induced sputum (via hypertonc saline nebulization) or morning gastric aspirates were negative in these patients. QFT-G was checked in 10 patients during follow-up and all were negative. None of the patients experienced active TB during follow-up.

Conclusion: To the best of our knowledge, this is the first study investigating the frequency of latent tuberculosis infection among patients treated with canakinumab. The results of this study suggest that although frequency of latent TB infection in children treated with canakinumab may not be low in a TB-medium burden country, canakinumab seems to be a safe treatment option in terms of active tuberculosis risk. Close follow-up of children on canakinumab treatment with respect to TB by the pediatric infectious disease department is important to prevent possible complications.

REFERENCE:


Disclosure of Interests: Balahan Makay Speakers bureau: Enzyvant, Novartis, Roche, AbbVie, ogze altug guencmen Speakers bureau: Novartis, AbbVie, Ilkoru Çağlar: None declared, Süleyman Nuri Bayram: None declared, Nesrin Gülež: None declared, Iker Devrim: None declared


<table>
<thead>
<tr>
<th>THU0544</th>
<th>ULTRASOUND EVALUATION OF UPPER LIMBS ENTESES AND JOINTS IN HEALTHY CHILDREN</th>
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<tr>
<td><strong>Victoria Martínez</strong>, 1, <strong>Paz Collado</strong>, 1, <strong>Instituto Médico Platense, La Plata, Argentina</strong>, 2Hospital Universitario Severo Ochoa, Rheumatology Department, Transitional Care Clinic, Madrid, Spain</td>
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<tr>
<td><strong>Background:</strong> Enthesitis in children can result from mechanical or inflammatory processes. Enthesitis is a common finding in several JIA categories, particularly in ERA. Most of the available data on the potential application of ultrasound (US) for paediatric enthesis is currently focused on lower extremity with limited data in upper extremity enthesis. To know how normal US findings of extremities by age are lead to early diagnosis and might avoid misinterpretations.</td>
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<tr>
<th>THU0545</th>
<th>A PROSPECTIVE OUTCOME OF ALL 17 CONSECUTIVE PEDIATRIC PATIENTS WITH CHRONIC NONBACTERIAL OSTEOMYELITIS TREATED WITH INTRAVENOUS PAMIDRONATE AND FOLLOWED AT A SINGLE CENTER OVER 15 YEARS</th>
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<tbody>
<tr>
<td><strong>Pauil Mitternach</strong>, 1, <strong>Chloe Stephenson</strong>, 2, <strong>Seamus Stephenson</strong>, 2, <strong>Xing Chang Wei</strong>, 2, 1Alberta Children’s Hospital and University of Calgary, Pediatrics, Calgary, Canada; 2Alberta Children’s Hospital, Pediatrics, Calgary, Canada; 3Alberta Children’s Hospital, Pediatrics, Calgary, Canada; 4Alberta Children’s Hospital and University of Calgary, Radiology, Calgary, Canada</td>
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<tr>
<td><strong>Background:</strong> Intravenous pamidronate (IV-PAM) has been reported to be effective in pediatric patients with severe chronic nonbacterial osteomyelitis</td>
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</table>
(CNO) in short term. Little is known about long-term outcome in CNO after IV-PAM.

Objectives: To describe a consecutive series of pediatric CNO (pCNO) patients who were prospectively followed after treatment with IV-PAM between 2003-2018 at a single center regarding: 1) The effect of IV-PAM on pain and Whole Body Magnetic Resonance Imaging (WBMRI) documented inflammation initially and after flare; 2) Relapse rate and; 3) Spinal CNO and 4) Urine N-telopeptide/creatinine ratio (UNtx/Cr) (a product of collagen I breakdown).

Methods: Patients: All consecutive pCNO patients <18 years at diagnosis, with WBMRI confirmed active disease who required IV-PAM between 2003-2018. IV-PAM: First dose 0.5 mg/kg; subsequent doses 1 mg/kg (maximum annual dose 11.5 mg/kg). IV-PAM was administered once monthly x 9. With confirmed flare IV-PAM was repeated (max 9 doses/year). Pain response: Visual analogue scale for pain (VAS) with “0” indicating no pain and “10” maximum pain was administered at baseline, at each IV-PAM treatment, and at suspected flare. Imaging: WBMRI before 1st IV-PAM, at 6 and 12 months, at suspected flare and after retreatment. CNO resolution was documented as complete (CR) if there was 95% improvement in the WBMRI signal. Spinal x-rays were performed at baseline and annually. UNtx/Cr was measured at baseline, after each IV-PAM and with suspected flare.

Results: 17 patients (9F, 8M) were included. The median [range] age at CNO diagnosis was 10.3[4-15] years, and at first IV-PAM 11.6[4-20] years. The median [range] follow-up was 9.2[1-15] years. Six patients had unifocal CNO, 4 had spinal CNO (2 with baseline vertebral fractures) and 6 had multifocal non-spinal CNO. VAS was uniformly 10/10 at baseline and decreased to 0-1/10 first month after IV-PAM. CR was achieved by all at 6 months, which persisted at 12 months. Four patients, 3 unifocal and one multifocal, had no further flares. Twelve patients had WBMRI confirmed flare at previously active sites at 9-36 months and 11 received 1-9 further doses of IV-PAM. With flare, VAS ranged from 4-9/10 and decreased to 0-3/10 within first month after re-initiation of IV-PAM. On final WBMRI, 12/17 (70%) had CR and 5/17 (30%) stable mild increased signal but no clinical symptoms. No further spinal compression fractures occurred. One patient required a third course of IV-PAM. Regarding UNtx/Cr, each patient had appropriate reduction after first IV-PAM. No patients flared while UNtx/Cr remained suppressed. Three patients developed arthritis and one acne. At last follow-up, 10/17 (59%) patients were on no medications, 4/17 (24%) required prn Naproxen for CNO and 3/17 (18%) were on Naproxen and/or disease modifying medications for arthritis.

Conclusion: Long-term follow-up of pCNO patients treated with IV-PAM confirms that while several patients eventually flare, the flares are less painful and have an excellent response to IV-PAM retreatment. No further spinal fractures occurred. No flares occurred while UNtx/Cr remained suppressed, suggesting a role of osteoclasts in CNO. Further prospective multicenter studies are now required to define the long-term clinical and imaging response to IV-PAM.

Disclosure of Interests: None declared


Methods: This was a retrospective study which looked at JIA patients who had been treated at the Children’s Hospital in Glasgow and had tibial or subtalar or midfoot involvement (TT, ST and MF respectively). 680 patients with JIA were identified from clinic lists from 2002 until 2018, inclusive. The clinic lists from 2008-2010 were inaccessible meaning that anyone who was seen exclusively within those two years has not been identified. Children with systemic arthritis were excluded. Of the 680 who were identified to have JIA; 123 have been found to have TT, ST or MF involvement. Of these; 104 were included in this study and the results of 19 patients were not available for analysis. For each of the 104 patients with ankle involvement their notes were reviewed and information about their JIA disease course was noted; specifically looking at any ankle involvement or potential risk factors for a adverse outcome. Poor ankle outcomes was defined as ankle arthritis having a significant impact on the child’s quality of life, persistently limited joint movement for more than 12 months or damage on imaging.

Results: Barriers to treatment was defined as anything which prevented a child from getting their medication as prescribed. Figure 1 shows the outcomes of children who had barriers to treatment compared to the children who did not. The difference between the two groups is stark with 67% of children who faced barriers to treatment having poor ankle outcomes compared to only 25% in the group which did not experience barriers to treatment. Furthermore, children with poor ankle outcomes are almost three times more likely to need surgery if they have experienced barriers to treatment compared to those who have not. This shows that children who experience barriers to treatment are more likely to have severe long-term damage to their ankle resulting in pain and limited functionality.

Figure 1: Outcomes in Children who experienced Barriers to Treatment

Abstract THU0546 – Figure 1

Five children declined any treatment at one point in their care against the advice of their healthcare team and of these five; four (80%) had severe ankle involvement with one requiring surgery and another's ankle auto-fused.

Conclusion: Experiencing barriers to treatment has been shown to increase the risk of poor ankle outcomes. Identified barriers to treatment ranged from concerns about adherence to needle phobias in addition to side effects and medication being with-held or taken incorrectly. This study demonstrates the need for further work to explore how these barriers can be effectively minimised.

REFERENCES:

Disclosure of Interests: None declared

THU0547
FIBRODYSPLASIA OSSIFICANS PROGRESSIVA IN PEDIATRIC RHEUMATOLOGY PRACTICE: LARGE SERIES EXPERIENCE OF THE SINGLE CENTER
Irina Nikishina, Alia Latypova, Maria Kaleda, Svetlana Arsenyeva, Dmitri Alexseev, Nizanov Research Institute of Rheumatology, Moscow, Russian Federation, Pediatric, Moscow, Russian Federation

Background: Fibrodysplasia Ossificans Progressiva (FOP), also known as a “second skeleton disease” is extremely rare (1: 2000000) and disabling genetic disorder, caused by mutation of ACVR1 gene, a bone morphogenetic protein receptor. Among medical specialties there are no certain, capable to provide not only diagnostics, but also all medical maintenance (assessment and monitoring of extent of damages, the differentiated drug treatment, rehabilitation, contact with adjacent experts). It would be reasonable if the rheumatologist carried out a role of the main attending physician for the patient with FOP. It seems to be a lot of similarities between rheumatic diseases, especially spondyloarthritids (SpA) and FOP in the pathophysiology, clinical manifestation and the therapy approach.

Objectives: to present the single-center experience of the FOP patients and to identify similar symptoms in FOP and rheumatic disease.

Methods: The analysis of the large series of patients with FOP, who observed in the rheumatologic clinic.

Results: Our single center experience includes 26 patients with FOP. All 26 patients (13 male and 13 female) had 3 basic FOP clinical manifestations. In 23 patients molecular-genetic tests were performed and typical mutation (Arginine 206) occurred in 22 cases and one had an extremely rare mutation (Glicine 328). 22 (85%) patients had common for FOP massive heterotopic ossifications. 3 of them had formed heterotopic ossification through the X-ray negative stage to visible changes. Among typical phenotypic stigmas were: great toe malformation; thumbs malformation; peripheral osteochondromas; cervical spine abnormalities. Majority of the cases presented some similarities to SpA manifestations: ankylosis of the apophysial joints and vertebral bodies mostly in cervical spine; X-ray/CT evidence of the sacroiliitis in all patients, who were examined (n=8). Because of severe body deformity or metal details after previous surgery intervention there were no possibility to perform MRI in most patients, but we confirm typical sacroiliitis with extended bone edema on MRI in 3 patients. Recurrent episodes of the large joints synoviitis were present in 5 patients. 4 patients demonstrated gradual formation of great toe ankylosis during the follow-up observation. The involution and decreasing of new FOP nodes associated with non-steroidal anti-inflammatory drug intake and/or glucocorticoids therapy were occurred in all patients.

Clinical features

<table>
<thead>
<tr>
<th>Sex ratio</th>
<th>Male</th>
<th>Female</th>
<th>Total N of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of initial manifestations</td>
<td>&lt;1</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>1–9</td>
<td>8</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>≥10</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Great toe malformation</td>
<td>12</td>
<td>12</td>
<td>25 (96%)</td>
</tr>
<tr>
<td>Thumbs malformation</td>
<td>2</td>
<td>3</td>
<td>5 (19%)</td>
</tr>
<tr>
<td>Cervical spine abnormalities</td>
<td>12</td>
<td>9</td>
<td>21 (81%)</td>
</tr>
<tr>
<td>Peripheral osteochondromas</td>
<td>8</td>
<td>7</td>
<td>15 (58%)</td>
</tr>
<tr>
<td>Massive heterotopic ossifications</td>
<td>12</td>
<td>10</td>
<td>22 (85%)</td>
</tr>
<tr>
<td>CTX-Ray/MIPI picture of sacrolili</td>
<td>2 (of 6)</td>
<td>2 (of 6)</td>
<td>4 (of 8) (100%)</td>
</tr>
</tbody>
</table>

Conclusion: Appearance of the similarities in FOP and SpA manifestation and the therapy approach could identify FOP as a potential rheumatic disease. Clinical observation of FOP patients could provide the important information for rheumatologist about insufficiently explored process of new bone formation.

Disclosure of Interests: None declared

THU0548
ASSOCIATIONS BETWEEN: MARKERS OF BONE TURNOVER AND RADIOLOGICAL FINDINGS IN CHILDREN DIAGNOSED WITH JUVENILE IDIOPATHIC ARTHRITIS
Marta Janicka-Szczepaniak, Krzysztof Orczyk, Elzbieta Smolewska, Medical University of Lodz, Department of Pediatric Cardiology and Rheumatology, Lodz, Poland

Background: Although many children attending pediatric rheumatology departments are diagnosed with low bone mineral density on the basis of clinical imaging, it is difficult to determine which patients have the higher risk of developing osteoporosis as the secondary disease. Recently performed studies involving rheumatological patients have proposed numerous serological indicators for better evaluation of the disease activity. These include markers of bone turnover, among others: bone alkaline phosphatase and osteoprotegerin (which are more specific for bone formation) and also beta isomerized carboxy terminal telopeptide of type I collagen, also known as Beta-Crosslaps (which is considered as an indicator of bone resorption).

Objectives: The main objective of the study was to evaluate the clinical usefulness of measuring serum concentrations of the selected markers of bone turnover in juvenile idiopathic arthritis (JIA) patients and assess their potential significance in prevention of osteoporosis in these children.

Methods: Study involved 59 children previously diagnosed with JIA (mean age at diagnosis: 9.0±4.3 years, mean age at study baseline: 12.7±3.9 years). All patients underwent Dual X-Ray Absorptiometry (DXA) examinations in order to assess bone mineral density. Wrist radiographs were also taken for evaluation according to the Steinbrocker classification. The presence of abnormalities in these tests was chosen as the criterion to divide patients into subgroups to perform group comparisons for the serum levels of markers of bone turnover: bone alkaline phosphatase, osteoprotegerin and Beta-Crosslaps.

Results: According to the Steinbrocker classification, 10 (16.9%) patients were staged as class I or higher. These children had significantly lower serum levels of bone alkaline phosphatase (p=0.0333) than patients with no radiological changes on wrist radiographs. The non-zero Steinbrocker subgroup had also lower Total Body Less Head Z-Score results (p=0.010) than the remaining patients. The DXA results, expressed as Total Body Less Head and Lumbar Spine Z-Score, disclosed low bone mineral density in 10 (16.9%) and 12 (20.3%) patients, respectively. There were no significant correlations between serum levels of markers of bone turnover and bone mineral density measurements. However, bone alkaline phosphatase and osteoprotegerin were negatively correlated with DXA muscle mass (p=0.359 p=0.040 for bone alkaline phosphatase, r=-0.372 p=0.0392 for osteoprotegerin). Similar correlation was found for bone alkaline phosphatase and DXA fat mass (r=-0.418 p<0.01).

Although Beta-Crosslaps appeared to be the only marker of bone turnover significantly (p=0.0410) associated with Juvenile Arthritis Disease Activity Score 27-Joint Count (JADAS27), it was independent from radiological findings involved in the analysis. However, serum levels of Beta-Crosslaps were higher in patients subsequently diagnosed with osteoporosis, than in those assessed in winter (p=0.064). Radiological findings were not season-variable.

Conclusion: Low serum concentration of bone alkaline phosphatase seems to be a risk factor for low bone mineral density and, by extension, for osteoporosis. Therefore it should be considered as an important laboratory test in JIA patients suspected of secondary osteoporosis. Clinical significance of osteoprotegerin and Beta-Crosslaps needs to be further investigated.

Disclosure of Interests: None declared

THU0549
SURGICAL MANAGEMENT IN JUVENILE IDIOPATHIC ARTHRITIS: A MONOCENTRIC EXPERIENCE OF 257 PROSTHESIS
Inne Pontiakal1, Carolina Artua2, Marco Di Marco3, Alessandro Sinelli2
1ASST Pini – CTO, Unit Of Pediatric Rheumatology-Department Of Rheumatology, Milan, Italy; 2ASST Pini – CTO, Unit Of Rheumatology, Milan, Italy; 3ASST Pini – CTO, Unit of Rheuma Surgery, Milan, Italy

Background: Juvenile idiopathic arthritis (JIA) includes all forms of inflammatory arthritis, with onset before the 16th birthday, lasting more than 6 weeks. Although conservative management with nonsteroidal anti-inflammatory drugs and disease-modifying antirheumatic drugs can be effective, a significant number of young adults affected by JIA requires a major surgical procedure, including different types of prosthetic devices.

Objectives: This article presents a monocentric experience of an interdisciplinary team of rheumatologists and orthopedic surgeons for JIA and the outcome of patients subjected to prosthesis implantation.

Methods: Data were collected through a retrospective analysis of 583 patients attending to our transitional care center for JIA between 1998 and 2018, in the context of a once-weekly rheumatologic counseling with the orthopedic surgeons. Descriptive statistics were used to evaluate the baseline and follow-up data.

Results: On a total of 257 prosthesis implantations, 137 were total hip prosthesis, 101 total knee prosthesis and 19 total ankle prosthesis. The 10-year implant survival rate was 97%, with good results in term of function and comfort for the patients. Complications were observed in 9% of
patients, including intraoperative fractures, periprosthetic joint infections and wound dehiscence. The majority of patients were treated with biologic therapy before surgery.

**Conclusion:** Prosthesis implantation in JIA patients is a complicated and difficult procedure, related to the management of the biologic therapy, the low quality of bone, the remarkable stiffness and deformity of the joints. Long-term results were good, even in patients with severe arthritis, showing drastic reduction of joint pain and an improvement of functionality. The risk of complications results to be modest compared to a great survival rate and a valid recovery of joint range of motion. The interdiscipli- nary team composed by rheumatologists and orthopedic surgeons for the all follow-up of these patients is a cornerstone to obtain the perfect schedule for prosthetic implantation.

**REFERENCES:**


**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.6305

**THU0550**

**MYCOPHENOLATE MOFETIL (MMF) IN DEFINED AND UNDEFINED INTERFERONOPATHIES**

Carmela Gerarda Luana Raffaele, Gian Marco Moneta, Silvia Federici, Manuela Pardeo, Claudia Bracaglia, Fabrizio De Benedetti, Antonella Insalaco. IRCCS Ospedale Pediatrico Bambino Gesù, Division of Rheumatology, Rome, Italy

**Background:** Type I interferonopathies are genetic disorders characterized by an up-regulation of type I interferon (IFN) activity. An increased expression of type I IFN regulated genes, IFN signature (IS), is described in these conditions. They are characterized by autoinflammation and varying degrees of autoimmunity or immunodeficiency. Some patients with a phenotype strongly suggestive for type I interferonopathy with a high IS, do not show any mutations in known type I interferonopathies related genes, being classified as undefined

**Objectives:** To evaluate the effect of mycophenolate mofetil (MMF) in patients with defined and undefined type I interferonopathy

**Methods:** 7 patients with type I interferonopathy followed at a Pediatric Rheumatology center, were included. Leucocyte (WBC) and platelet count, hemoglobin (Hb), CRP, ESR, serum amyloid A (SAA), autoantibodies, complement levels and IS, were assessed before and after 5-7 months of MMF treatment (600 mg/m² BID). IS was determined by qPCR (high scores >1.42).

**Results:** Patient 1 and 2 presented respectively with SAVI and Aicardi-Goutieres syndrome. The others were classified as undefined. In patient 1(table), treated with JAK1/2 inhibitor, MMF was followed by decrease of inflammatory markers and resolution of lung involvement; in patient 2 to an increase in Hb and normalization of inflammatory markers. Among patients with an undefined phenotype the addition of MMF to low dose prednisone led to complete resolution of inflammation. A reduction of the antinuclear antibodies titre was observed in patients 2, 3 and 7 and a normalization of complement level in patients 3, 4 and 7. Patient 5 had normal inflammatory markers already before the beginning of MMF possibly due to previously administered immunosuppressive treatment. Despite all patients presented a significant improvement of clinical picture after 5 months of MMF treatment, the IS decreased only in 4/7 patients while it remain stable or increased in the others

**Conclusion:** Our data suggest that mycophenolate mofetil might be an effective therapy in patients with type I interferonopathy leading to improvement of clinical and laboratory features thus allowing a glucocorticoid sparing

**Disclosure of Interests:** Carmela Gerarda Luana Raffaele: None declared, Gian Marco Moneta: None declared, Silvia Federici: None declared, Manuela Pardeo: None declared, Claudia Bracaglia: None declared, Fabrizio De Benedetti Grant/research support from: Abbvie, SOBI, Novimmune, Roche, Novartis, Sanofi, Pfizer, Antonella Insalaco: None declared

**DOI:** 10.1136/annrheumdis-2019-eular.6305

**THU0551**

**VACCINATION COVERAGE IN FRENCH CHILDREN WITH AUTO-INFLAMMATORY DISEASES : PRELIMINARY DATA FROM THE JIRCOHORTE**

Virginie Rollet-Cohen1, Justine Miret1, Glöy Dingulu1,2, Andreas Wömer3, Marie-Alette Dommergues1, Véronique Hentgen1,2, Versailles Hospital, Department of General Pediatrics, Le Chesnay, France; 3University of Basel Children’s Hospital, Department of pediatrics, Basel, Switzerland

**Background:** Autoinflammatory diseases (AID) comprise a large number of rare diseases that manifest as recurrent sterile inflammation or disproportionate infection-induced inflammatory symptoms. Vaccine relation to AID is complex: on one hand the susceptibility to infections vary with the treatment options of the patient, on the other hand the disease activity may be triggered by vaccination. Nevertheless, effective immunization is crucial in this population. Up to know very little is known about vaccina- tion coverage in AID children.

**Objectives:** To determine vaccination coverage in French children with an autoinflammatory disease.

**Methods:** Patients between 2 and 18 years with autoinflammatory diseases followed at the French Reference Center for Auto-Inflammatory Diseases-Versailles Hospital and included to the Juvenile Inflammatory Rheumatism cohort (JIRcohort) network - an international multicenter prospective cohort for children with inflammatory and rheumatological diseases - were included in this retrospective monocentric observational study. Vaccination coverage of each disease and complete status of vaccination was assessed at the last out-patient visit, according to the national immunization program. Detail of every vaccine received (number of doses and date of administration) were collected by a pediatrician from written immunization record (vaccination card). Demographic data, disease and medications used since diagnosis were also assessed. Patients with no available immunization record were excluded.

**Results:** 128 patients met the inclusion criteria. Sex ratio was 1.2 (70/58). Median age at the last out-patient visit was 8.4 years (2.5-17.9 years). 53 children (41%) presented periodic fever with aphthous stomatitis, pharyngitis and adenitis (PFAPA) syndrome, 30 familial mediterranean
fever, 29 unexplained autoinflammatory recurrent fevers, 8 TNF receptor associated periodic syndrome (TRAPS), 8 other autoinflammatory diseases. 68 patients (53%) were treated by on-demand corticosteroids, nine patients (7%) by biological agents, the other patients did not receive any immunosuppressive treatment. 

At the last clinic visit, only 49% (n=63) of our entire cohort had a complete vaccination status (human papilloma virus and tuberculosis excluded). Coverage rates were superior to 85% for diphtheria/tetanus/ poliomyelitis (89%), pertussis (95%), haemophilus influenza type B (94%) and measles/mumps/rubella (86%). 84% of the children were well-vacci- nated against pneumococcus. Lowest individual vaccination coverage rates were observed for hepatitis B at 77% and for meningococcus C at 77%. Only one girl received complete vaccination against human papilloma virus.

Conclusion: Vaccine coverage in children with autoinflammatory dis- eases appears suboptimal. Measures to optimize vaccination coverage in these children should be implemented.

REFERENCES:

THU0552 SCORING ULTRASOUND SYNOVITIS IN JUVENILE IDIOPATHIC ARTHRITIS: RESULTS OF A RELIABILITY EXERCISE USING OMERACT US PAEDIATRIC DEFINITIONS

Linda Rossi-Semerano1, Sylvain Breton2, Marouane Boubaya3, Haykanush Ohanyan3, Valerie Devauchelle-Pensec4, Sandrine Jousse-Joulin4, Marie-Aliette Dommergues5, Linda Rossi-Semerano1, Sylvain Breton2, Marouane Boubaya3, Haykanush Ohanyan3, Valerie Devauchelle-Pensec4, Sandrine Jousse-Joulin4, Marie-Aliette Dommergues5

Disclosure of Interests: None declared, Marie-Aliette Dommergues Grant/research support from: Roche, Pfizer, MSD, BMS, UCB, Roche, Sandrine Jousse-Joulin: None declared

THU0553 THE IMPACT OF BACKGROUND BIOLOGICAL THERAPY ON SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS-ASSOCIATED MACROPHAGE ACTIVATION SYNDROME: A SINGLE CENTER STUDY

Riccardo Russo1, Maria Katsikas2,3, Garrahan Pediatric Hospital, Immunology/ Rheumatology, Buenos Aires, Argentina; 2Garrahan Pediatric Hospital, Immunology/Rheumatology, Buenos Aires, Argentina

Background: Macrophage activation syndrome (MAS) is a severe compli- cation of Systemic juvenile idiopathic arthritis (SJIA). Biological therapy of SJIA may modify the clinical expression of MAS (1). Objectives: to assess and compare the clinical, biochemical, and haema- tolological features of SJIA-associated MAS in patients treated with biologic (B) or non-biologic (NB) agents.

Methods: retrospective analysis of data from dedicated medical records and databases. Inclusion criteria included: diagnosis of SJIA according to the ILAR criteria, diagnosis of MAS according to the expert’s opinion, and prescription of corresponding therapy. Patients were followed and treated at a tertiary center from 2006 to 2018. Demographical, clinical, haematological, biochemical and treatment-related features were recorded. The worst recorded values (e.g. highest ferritin levels) during each MAS episode were included for analysis. Outcomes (complete or partial recover- y, death) and fulfillment of current classification criteria (2) were also recorded. Comparisons between groups (patients developing MAS during B therapy vs. NB therapy) were performed by chi square or Wilcoxon rank sum tests.

Results: Twenty-four (14 F, 10 M) patients who developed 31 MAS epi- sodes were included. Age at SJIA onset 4 years, age at MAS onset 6 years; 10 episodes occurred during the initial (0-3 months) stage of SJIA course. Patients were receiving biological agents (canakinumab 4, tocilizumab 4, anakinra 1, etanercept 1) in 10 (32%) MAS episodes. Frequency of cardinal clinical features was similar in both groups. During MAS course, ferritin (1,408 vs 26,574 ng/mL, p < 0.001), LDH (922 vs 3308 IU/L, p = 0.04), SGOT (66.5 vs 389 IU/L, p = 0.02), and triglyceride levels (259 vs 352 IU/L, p = 0.03) were lower in B than in NB treated patients, while platelet count (215 vs 66 n/mL, p < 0.01), and hemoglobin (104 vs 79 g/dL, p < 0.01) were higher in the B than in the NB treated patients. No significant differences were found in GGT, fibronectin, SQPT levels or neutrophil count. Duration of admission during MAS tended to be longer in the NB treated group (31 days) than in the B group (16 days). Treatment of MAS included high dose steroids, cyclosporin, and/or biological agents. Five patients, all belonging to the B group (p < 0.001), did not fulfill current SJIA MAS classification criteria. There were 4 deaths recorded, all belonging to the NB group.

Conclusion: SJIA patients treated with biological agents exhibit similar clinical features than those treated with non-biologic therapy. However,
different haematological and biochemical variables are significantly milder in patients on biological therapy, which may limit the utility of classification criteria in this group. Assessment of these findings in larger cohorts is needed.

REFERENCES:


Disclosures of Interests: Ricardo Russo Speakers bureau: Novartis, Abbvie, Maria Katsikas: None declared


Other orphan diseases

THU0554  THE CLINICAL UTILITY OF TWO VASCULITIS ACTIVITY SCORES(BVAS AND BDCF) IN BEHÇET’S SYNDROME: A PROSPECTIVE COHORT STUDY

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Background: Behçet Disease(BD) is a rare chronic autoinflammatory condition that can lead to irreversible organ damage. The potential for multi-organ involvement and fluctuating activity highlights the need to perform a careful and systematic assessment of disease activity that is sensitive to change. Several disease activity tools have been used in both daily practice and clinical trials, yet the published data comparing the clinical utility of different tools in informing changes to therapy is needed.

Objectives: To compare the utility of two major activity scores: BD Current Activity Form (BDCF2006)1 and Birmingham Vasculitis Activity Score (BVAS)2 in predicting physician’s decision to adjust treatment (step-up/step-down) in patients with BD.

Methods: A 6-month prospective observational study was performed in a cohort of patients meeting the International Criteria for Behçet’s Disease (ICBD),at the National Centre for BD in Liverpool, UK. Participants were described for their demographics, clinical manifestations and treatment plan. BVAS and BDCF2006 activity scores were completed for each patient at evaluation. The outcome of interest was treatment change which was classified as ‘step-up’ or ‘step-down’, reflecting escalation or de-escalation in treatment (dosage adjustment or adding new immunosuppressant), respectively. We assessed the association between BVAS and BDCF scores and step-up/step-down treatment using Spearman rank correlation and multivariate logistic regressions, adjusting for gender, age and patient’s perception of disease activity on visual analogue scale (VAS), Odds ratios(OR) and 95% confidence intervals were calculated. Data analysis was conducted in Microsoft Excel, SPSS 2.0 and STATA.

Results: Ninety-five patients met inclusion criteria: 25 males (26.3%) and 70 females (73.7%) with a mean age at diagnosis of 32.7 years (±11.3 SD). HLAB1 was positive in 11/51 cases (11.6%). The most frequent clinical manifestations were oral ulcerations (100%), genital ulcerations (94.7%) followed by papulo-pustular skin lesions (37.8%) arthralgia (31.6%) and headache (30.5%). Mean BVAS score (range 0-6) was 2.14 (±1.8 SD) and mean BDCF score (range 0-8) was 3.04 (±1.72 SD). Both BVAS and BDCF correlated with decision to step-up treatment (r=0.752; r=0.370, respectively). Furthermore, BVAS was more strongly associated with decision to step-up treatment than BDCF (OR 4.25 95%CI 2.37 to 7.61; 1.51 95%CI 0.91 to 2.54). Adjusting for gender, a stronger association was observed in male participants across BVAS and BDCF scores (OR 5.89 95%CI 1.17 to 29.63; 3.48 95%CI 1.20 to 10.09, respectively). Following adjustment for patient’s perception of their disease (VAS), BVAS remained significantly associated with treatment step-up (OR 3.87 95%CI 2.08 to 7.19) but not BDCF (OR 1.30 95%CI 0.91 to 1.84).

Regarding different clinical manifestations, the BVAS mucocutaneous and ocular activity showed a significant odds ratio for step-up therapy (OR=5.78, CI 1.49-22.15; and OR-4.2 CI: 2.26-7.83).

Conclusion: BVAS can be a useful tool to assess BD activity. In this study, BVAS correlated better with clinical treatment decisions than BDCF, particularly in male participants. It also appears to be less influenced by patient’s subjective perception of disease activity, and therefore may be a more objective measure of BD activity.

REFERENCES:


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THU0555 10 YEAR PROGNOSIS OF PATIENTS DIAGNOSED WITH FAMILIAL MEDITERRANEAN FEVER

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Background: In Familial Mediterranean Fever (FMF), other than amyloidosis factors affecting mortality are being debated. In our previous study, we did not observe any atherosclerotic plaque formation in carotid or femoral artery. We thought that the risk of atherosclerosis did not increase in patients diagnosed with FMF.

Objectives: The aim of this study was to assess the 10 year prognosis and comorbidity of patients diagnosed with FMF who have been treated in our rheumatology clinic.

Methods: The sample group is a subset of 2009 study. In 2009, the patients who already had myocardial infarction or cancer diagnosis were excluded. The patients were interviewed with polar questions of whether they were diagnosed with acute myocardial infarction (AMI), cerebrovascular events, cancer, diabetes, and hypertension.

Results: We studied 71 patients (37 males, 34 females; mean age: 49.66±9.91) with FMF, and 59 patients (24 males, 35 females) in healthy control (HC) group. The gender and age difference between two groups was not found significant.

During 10 year follow-up, 8% of FMF patients had either a cardiovascular or cerebrovascular event comparing to 5% in HC (p=0.05). 3% of FMF patients had a cancer diagnosis comparing to 3% in HC (p=0.05). Even though diabetes mellitus diagnosis rate was higher in FMF patients (15% to 10%), results were still not significant (p=0.05). Hypertension diagnosis was 5% higher in FMF group (p=0.05)

Table. Prognostic Factors of FMF patients compared with Healthy Controls

<table>
<thead>
<tr>
<th></th>
<th>FMF 2018, n (%)</th>
<th>HC 2018, n (%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>34 (47.89)</td>
<td>35 (59)</td>
<td>0.193</td>
</tr>
<tr>
<td>Age</td>
<td>49.69±9.91</td>
<td>51±6.59</td>
<td>0.076</td>
</tr>
<tr>
<td>AMI/Stroke</td>
<td>6 (8.45)</td>
<td>3 (5.08)</td>
<td>0.45</td>
</tr>
<tr>
<td>Cancer</td>
<td>2 (2.82)</td>
<td>2 (3.39)</td>
<td>0.85</td>
</tr>
<tr>
<td>DM</td>
<td>9 (14.86)</td>
<td>6 (10.17)</td>
<td>0.198</td>
</tr>
<tr>
<td>Hypertension</td>
<td>25 (33.78)</td>
<td>10 (16.95)</td>
<td>0.019</td>
</tr>
<tr>
<td>Total</td>
<td>71</td>
<td>59</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: Even though there was a significant increase in hypertension, increased diabetes, cancer, and AMI/Stroke ratio was not found significant when compared to the HC's. Therefore, any cardiovascular and malignancy related comorbidities are not associated with FMF.

REFERENCES:


Disclosure of Interests: None declared

ARTERIAL AND VENOUS THROMBOTIC EVENTS IN IGG4-RELATED DISEASE: A NATIONAL OBSERVATIONAL RETROSPECTIVE STUDY

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Background: IgG4-related disease (IgG4-RD) is a fibro-inflammatory disorder that can affect virtually every organ. Although arterial involvements have been reported, no studies have examined the occurrence of arterial or venous thrombotic events in these patients.

Objectives: To explore the frequency, the characteristics, and risk factors of arterial and venous thrombotic events in IgG4-related disease patients.

Methods: An observational, descriptive, retrospective study was conducted from a multicentric national case registry for IgG4-RD. Patients fulfilled the Comprehensive Diagnostic Criteria (CDC) for IgG4-RD, and all patients with arterial or venous thrombotic events confirmed by imaging during follow-up were analyzed. Clinical, radiological, biological, histological and therapeutic characteristics were retrospectively collected using a standardized online data sheet. Results obtained in patients with thrombosis were compared to those without thrombosis.

Results: One hundred eighty-nine patients with IgG4-RD (135 men/54 women, median age 61 years) were included. During a 12-months median follow-up, one or more arterial thrombotic events occurred in 10 patients and venous thrombotic events in 16 (5.3 and 8.5 events/100 patient-years, respectively). Arterial complications (coronary artery disease n=5, lower limb peripheral arterial disease n=2, mesenteric ischemia, transient ischemic attack, and carotid thrombosis: n=1) occurred on average 30 months [0-140] after the first symptoms of IgG4-RD. They were in 2 patients without any cardiovascular risk factor, and associated with IgG4-RD arterial involvement in 3 (coronary aneurysms n=2, leg arteritis n=1). Among patients with arterial thrombosis, 60% had systemic involvement (>3 organs involved), 89% elevated serum IgG4 (> 3N in 56%), and 57% CRP >10 mg/l. Only 5/10 were treated with steroids at the time of arterial complication, and 4 had never been exposed to steroid therapy.

Conclusion: Arterial complications associated with the occurrence of an arterial thrombotic event (p = 0.03).

Venous thromboembolic complications (deep venous thrombosis (DVT) n=12, pulmonary embolism n=4) occurred on average 24 months [0-164] after the first symptoms of IgG4-RD, but were inaugural in 6 patients. Usual venous thrombosis risk factors were found in only 3/16. Seven patients had retroperitoneal fibrosis (RPF), 2 had mediastinal fibrosis, 60% had localized IgG4-RD (<2 organs involved), serum IgG4 level was normal in 67% and CRP <10 mg/l in 79%. Nine patients were on steroids at the time of venous thrombosis. RPF was more frequent in the group of IgG4-RD patients with a venous thrombotic event (p = 0.05), and largely associated with DVT in a multivariate analysis (OR=8.36 [2.25-35.90], p = 0.002).

Disclosure of Interests: None declared


THU0558

NERVE GROWTH FACTOR, SCLEROSTIN AND DKK-1 SERUM LEVELS IN COMPLEX REGIONAL PAIN SYNDROME (CRPS)-1: A PILOT STUDY ON 41 PATIENTS

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Background: Pain is the hallmark of Complex Regional Pain Syndrome (CRPS). Nerve growth factor (NGF), widely known as pain mediator, is increased in the affected skin and in tibia bone of rat models of CRPS, while is lowered by administration of anti-NGF antibodies. CRPS usually occurs after limb trauma or injury: significantly more often after limb fractures. Some reports considered bone as a main player in CRPS pathogenesis, hypothesizing that sclerostin (SOST) and Dickkopf-related protein-1 (DKK-1) may be involved in CRPS pathogenesis.

Objectives: To evaluate NGF, SOST, and DKK-1 serum levels from affected arm of CRPS patients and compare them with unaffected one and healthy controls (HCs).

Methods: Adults patients affected by CRPS diagnosed according to IASP criteria at upper limb were consecutively enrolled from April 2017 to August 2018. Patients with prior treatment with bisphosphonates, and history of disorders of mineral metabolism were excluded. Sera from the basilica vein of affected and unaffected arm of CRPS patients were collected, as well as sera from HCs paired for age and sex. NGF, SOST, and DKK-1 concentrations were determined by ELISA kit. Comparisons between patients and HCs were performed by Student test, while comparison between affected and unaffected arms were performed with Wilcoxon test for paired data. Pearson correlation was used to correlate NGF, SOST, and DKK-1 levels with demographic and clinical variables.

Results: The overall population included 41 patients: males (M) 21.9%, mean age at diagnosis [± standard deviation, SD] 61.9±8.4 yrs, mean disease duration 67 days (inter quartile range (IQR) 14.0; 22.5), 39 (95.2%) experienced a fracture as an inciting event, mean VAS pain score (0-100) 54.8±18.6 mm. Mean NGF levels (pg/ml) were 12.0±2.8 and 11.4±3.5 in the affected and unaffected side, respectively, and 13.5±5.5 in HCs. NGF was undetectable in most patients; no statistical significant differences of NGF levels were found between patients and HCs. Mean SOST levels (pmol/L) were 32.6±16.1, 29.8±17.7, and 34.0±13.3 in affected, unaffected arm, and in HCs, respectively. No statistical significantly differences of SOST levels were found between patients and HCs, while a significant difference was found between affected and unaffected arms (p=0.03). Mean DKK-1 levels (pmol/L) were higher in affected arm (31.2±22.9) than in unaffected one (29.3±28.6) or in HCs (27.5±18.2) without reaching statistical significance. NGF was significantly correlated with VAS pain score (p=0.04).

Conclusion: To our best knowledge, this is the first study to evaluate NGF, SOST, and DKK-1 levels in adults affected by CRPS-1. SOST levels were significantly higher in affected arms compared to unaffected ones, suggesting a possible role of this bone mediator in CRPS pathogenesis. NGF was consistent with the expression of pain, trough VAS pain score. Further studies need to clarify these preliminary findings.

REFERENCES:

Disclosure of Interests: Chiara Crotti: None declared, Maria Marana: None declared. Francesca Zucchi: None declared, Davide Gatti Speakers bureau: Abiogen, Amgen, Janssen-Cilag, Mundipharma, Pfizer, Maurizio Rossini: None declared, Massimo Varenna: None declared

comparisons. To establish the relationship between its value and the AOSD-related mortality.

Methods: Retrospective study realized in two University Hospitals. Clinical, laboratory, AOSD-related complications data, administered biologic treatments and number of deaths (AOSD related or not) were recorded. Each patient was characterized for the presence of AOSD-related complications such as macrophage activation syndrome (MAS), myocardiitis, lung involvement (pulmonary hypertension, interstitial infiltrate), renal involvement (tubulointerstitial nephritis, acute renal failure), secondary amyloidosis and AOSD-related death. SSS was applied at the onset of the disease development, assigning a point to each of the next 12 variables: fever, exanthema, pleuritis, pneumonitis, pericarditis, alteration of liver tests or hepatomegaly, splenomegaly, lymphadenopathy, odynophagia, leukocytosis >15,000/mm³, myalgia and abdominal pain. A > 7 score has been validated on other populations as the one which identifies the patients with high risk of complications. The relationship between SSS value and the next parameters was determined: clinical course, complications, biologic treatments administered and AOSD-related mortality.

Results: Data from 64 patients was analyzed (40,6% men, mean age 37 years). SSS values of < 7 were obtained in 50 patients (78,3%) and of ≥ 7 in 14 patients (21,7%). MAS and renal involvement were significantly related with a score of ≥ 7 (Table 1). Lung involvement, myocardiitis and secondary amyloidosis were not significantly associated with a high SSS value. Even so, analyzing each case, it was found that individually they had a score of ≥7 (except for lung involvement). Biologic treatment requirement along the disease course was related to SSS ≥7. Moreover, SSS value was not related to the different clinical patterns or the not-related-AOSD deaths. It was not possible to determine the relationship between the score and the AOSD complications-related deaths due to having only two registered cases. Despite this, it was found that individually both had a SSS of ≥7.

Conclusion: The prognosis score described by Pouchot et al could be useful to identify those patients with high risk of developing clinical complications and those who will need biologic treatment along the course of their disease. It is necessary a higher number of patients to determine if the score could be useful to estimate the death risk related to AOSD complications.

REFERENCES:

Disclosure of Interests: Ivette Casafont-Goló: None declared, Susana Helgado: None declared, J. Navázquez Consultant for: Bristol-Myers Squibb, Maribel Mora: None declared, Josep Roca: None declared, Anahy Brandy-Garcia: None declared, Lourdes Mateo: None declared, Melanie Martinez-Morillo: None declared, Laia Gilfe: None declared, Maria Aparicio Espinar: None declared, Águeda Prior-Español: None declared, Anne Rive: None declared, Clara Sanguesa: None declared, Jordi Camins-Fàbregas: None declared, Annika Nack: None declared, Joan Miquel Nolla: None declared, Alejandro Olivé: None declared


THU0559 PSYCHOLOGICAL EFFECTS OF A BEHÇET’S DIAGNOSIS ON DISEASE ACTIVITY PERCEPTION– A PROSPECTIVE OBSERVATIONAL STUDY

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Background: There is a pressing need to understand more about the psychological experience in patients with Behçet’s Disease (BD). The presence of poor wellbeing, low mood and anxiety may affect the ability to both manage and cope with this complex disorder and also impact upon the perception and experience of disease activity1,2,3.

Objectives: Our aim was to investigate the relationship between patient rating of disease activity and their psychological experience (anxiety, low mood, illness perception and coping style) in a UK Centre of Excellence for BD.

Methods: This study had full UK research ethics approval. A 12-month prospective observational study of a cohort of patients diagnosed with BD according to the International Criteria for BD(ICBD) under surveillance in the BD Centre of Excellence Liverpool, UK. All patients that agreed to a psychological evaluation were included. Participants were described for demographics and clinical presentation. BD Current Activity Form 2006 and a clinician’s and patient’s visual analogue scale (VAS) were recorded. Participants completed validated self-reported measures: Brief COPE, IPO-R, PHQ-9, GAD-7 and WEMWBS. Spearman Rank correlations, multivariate regression analysis and mediation analysis were used to investigate the relationship between patient perception of disease activity, coping mechanisms and mood. For data analysis Excel and SPSS were used.

Results: 86 patients were selected (24 males, 68 females; mean age at time of evaluation 43.58 years ±11.8 SD; mean disease duration 9.76 years ±10.01). The correlation between Clinician’s BAS and Patient’s VAS was strong 0.754 (p<0.005). Strong correlations were also observed between Patient’s VAS and low mood (PHQ-9) r=0.533 (p<0.005), anxiety (GAD-7) r=0.433(p<0.05), illness perception- emotional representation (IPO-R) r=0.377 p<0.05 and emotion-focused coping (COPE) r=0.320 (p<0.05).

The results of the mediation analysis indicated that patient’s perception of disease activity was a significant predictor for Dysfunctional Coping Strategies (b=1.5.5e+0.57, p<0.05). Dysfunctional Coping Strategies had a mediating impact on the relationship between patient perception of disease activity (VAS) and mood 0.645(CE: 0.68±1.389).

Conclusion: Psychological experience plays an important part in the patient evaluation and experience of disease activity. Patient coping strategies and psychological representation of illness experience influence their perception of disease activity and their mood. This highlights the need for patients for psychological support and for improving coping mechanisms in order to obtain a better disease control and a higher quality of life.

REFERENCES:

Disclosure of Interests: Casandra Buzatu: None declared, Hannah Nicholson: None declared, Roisin Cunningham: None declared, Robert J Moots: Grant/research support from: Biogen, Bristol-Myers Squibb, Chugai, Novartis, Pfizer Inc, Roche, Sandoz, and UCB, Consultant for: Biogen, Bristol-Myers Squibb, Chugai, Novartis, Pfizer Inc, Roche, Sandoz, and UCB, Speakers bureau: Biogen, Bristol-Myers Squibb, Chugai, Novartis, Pfizer Inc, Roche, Sandoz, and UCB

Background: IgG4-related ophthalmic disease (IgG4-ROD) may present as a cause of orbital myositis leading to proptosis and diplopia. This clinical scenario can be mistakenly diagnosed as Graves' orbitopathy (GO), preventing a timely and adequate treatment.

Objectives: To elucidate if there are specific radiological features that might differentiate between IgG4-ROD and GO by imaging.

Methods: We included 19 patients with diagnosis of IgG4-related disease (IgG4-RD) according to the Comprehensive Diagnostic Criteria for IgG4-RD, who regularly attended a tertiary referral center in Mexico City. All the patients had ophthalmic involvement and available computed tomography (CT) and/or magnetic resonance imaging (MRI) of the orbits. The patients had ophthalmic involvement and available computed tomography (CT) and/or MRI of the orbits. Imaging studies were evaluated by a blinded head and neck radiologist for the following features: exophthalmos, extraocular muscles (EOM) size and morphology, lacrimal gland enlargement, orbital fat involvement, stretching of the optic nerve (ON), ON sheath thickening and orbital bone changes.

Results: Both groups were similar in age (49.1±15.8 vs. 51.6±14.7, p=0.58) and gender (men 58.9% vs. 40.6%, p=0.23). In addition to ophthalmic involvement, 18 (94.7%) IgG4-RD patients had extra-ocular involvement with a median number of organs involved of 7 (1-12), mainly submandibular glands (73.7%), lymph nodes (68.4%), parotid glands (63.2%) and pancreas (47.4%). Three patients were misdiagnosed as GO before IgG4-RD diagnosis. Graves’ disease was the underlying thyroid disorder in 28 (87.5%) GO patients. Hashimoto’s thyroiditis in 2 (6.3%), papillary thyroid carcinoma in 2 (3.1%) and one patient was euthyroid with positive thyroid stimulating immunoglobulin. The prevalence of EOM and orbital fat involvement was protective (OR 0.05, 95% CI 0.005-0.61, p=0.001) and a tendency for the lateral rectus to be the most frequently involved EOM (22.2% vs. 0%, p=0.07); conversely they had a lower prevalence for the inferior rectus to be the most frequently involved EOM, (33.3% vs. 72.7%, p=0.04), orbital fat involvement (47.4% vs. 81.3%, p=0.01), ON stretching (57.9% vs. 87.5%, p=0.02) and orbital bone changes (0% vs. 25%, p=0.02), EOM bellies were involved in all the IgG4-ROD and GO cases, whereas EOM tendon involvement was present in 9% of GO and in none of the IgG4-RD group. Patients with IgG4-RD had more frequently the combination of lacrimal gland and lateral rectus (31.6% vs. 3.1%, p=0.008) and less frequently the combination EOM and orbital fat involvement (21.2% vs. 59.4%, p=0.008).

At the logistic regression analysis we found an association of lacrimal gland involvement (OR 64.4, 95% CI 6.8-609.5, p=0.001) with IgG4-RD. In a second model including combined variables, the combination of lacrimal gland and lateral rectus involvement was associated with IgG4-RD (OR 62.5, 95% CI 3.31-1000, P=0.006), whereas the presence of EOM and orbital fat involvement was protective (OR 0.06, 95% CI 0.006-0.48, p=0.009).

Conclusion: Imaging features may reliably differentiate between IgG4-ROD and GO. The presence of both lacrimal gland and lateral rectus enlargement must alert clinicians to consider IgG4-RD diagnosis.

REFERENCES:
Familial Mediterranean Fever (FMF) is the most frequent auto-inflammatory disease characterized by recurrent, self-limiting attacks of fever, peritonitis, pleuritis, synovitis, myalgia, and erysipelas-like erythema (ELE). Attacks have a robust inflammatory response which completely normalizes when attacks subside. However, substantial number of FMF patients possess chronic persistent inflammation even in between attacks. Clinical significance of persistent inflammation and its contribution to damage accrual are yet to be determined.

**Objectives:** We aimed to determine the prevalence and underlying factors of chronic persistent inflammation and its association with the domains of Auto-inflammatory disease damage index (ADDI) in a large cross-sectional multicenter cohort.

**Methods:** All patients recruited from FMF in Central Anatolia (FICA) cohort, which is a duplication disabled, internal and externally controlled, cross-sectional, multicenter accessible web-based cohort. Demographic data, disease characteristic, attack features (ever presented) were meticulously questioned. Genotype data (if available) and laboratory features including inflammatory markers were recorded. FMF related damage scores was assessed by auto-inflammatory disease damage index (ADDI), which is recently validated. Patients were stratified according to their antecedent acute phase responses as having persistent inflammation (PI group) or not, both groups compared in terms of disease characteristics, attack features, inflammatory comorbidities and damage domains.

**Results:** Study is comprised 970 adult patients (mean age 35.3±12.1, 61% female). 54 of them were excluded for their first inclusion. 15% of patients had persistent inflammation. PI group had significantly younger age of diagnosis, male dominance, homozygous M694V, more frequent attacks it the last year, more pleuritis, arthritis, myalgia and ELE and more severe disease according to ISSF than other patients (Table-1). Moreover, colchicine resistance and ADDI damage scores were remarkably higher in PI group.

In multi-variate analyzes colchicine resistance OR=2.71 [95%CI 1.38-5.33], ISSF OR=11.06 [95%CI 5.23-23.39], male gender OR= 2.38 [95%CI 1.51-3.76], homozygous M694V mutation OR= 2.31 [95%CI 1.41-3.78] and ELE OR= 1.72 [95%CI 1.04-2.857] found as independent predictors of persistent inflammation. PI group had more damage in multiple domains like joint restriction, musculoskeletal pain, proteinuria, amyloidosis, renal insufficiency and developmental delay. Same variables and persistent inflammation further analyzed in in terms of predicting the damage. Persistent inflammation found to be an independent predictor of proteinuria OR=2.02 [95%CI 1.05-3.90], amyloidosis OR=2.71 [95%CI 1.34-5.48], and renal insufficiency OR=4.36 [95%CI 1.84-10.32].

**Conclusion:** Persistent inflammation is relatively common in FMF patients particularly in those harboring M694V homozygous mutation and is associated with major complications of disease indicating poor prognosis.

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COMPARISON BETWEEN PATIENTS WITH IDIOPATHIC PULMONARY FIBROSIS AND INTERSTITIAL PNEUMONIA WITH AUTOIMMUNE FEATURES: A PROSPECTIVE COHORT

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Background: The term “Interstitial Pneumonia with Autoimmune Features (IPAF)” is used to describe patients with Interstitial Lung Disease in combination to clinical, serological and/or pulmonary features that are suggestive, but insufficient to satisfy classification criteria of a specific Connective Tissue Disease (CTD). Some retrospective studies available in literature described patient cohorts with IPAF heterogeneous in terms of clinical, serological, and radiographic manifestations.

Objectives: To prospectively recruit a cohort of consecutive ILD patients classified as IPAF or as affected by Idiopathic Pulmonary Fibrosis (IPF); to describe their clinical, serological, and radiological features by a multidisciplinary team composed by Pulmonologists, Radiologists, and Rheumatologists, comparing IPAF and IPF patients.

Methods: In the lasts 2 years, they were enrolled 45 patients with IPAF and 143 with IPF among a total of 506 patients with Interstitial Lung Disease (ILD). All patients were evaluated clinically by both rheumatologists and pulmonologists, also by means of chest high resolution computed tomography (hrCT), pulmonary function tests (PFT), and nailfold videocapillaroscopy.

Results: In IPAF cohort the most common characteristics from the clinical, serological and morphological domain were Raynaud’s phenomenon (31.1%), antinuclear antibodies positivity with titre ≥1:320 or any titre for centromeric or nucleolar pattern (17.7%) and nonspecific interstitial pneumonia (88.8%) respectively. The majority of patient (89.8%) had the minimum of 2 criteria at the recruitment. Female gender was more common in IPAF compared to IPF (62.2% vs 23%, p<0.0001) and the mean age of onset was lower in patient with IPAF (66 vs 73, p <0.0001). HRCT results positive in 2 patients, both without RP. Patients with IPAF showed better performances in PFT than patients with IPF than those with IPF (mean forced vital capacity 83% vs 74%, p =0.01; mean diffusing lung capacity for carbon monoxide 64% vs. 52%, p=0.01). Patients with IPAF less commonly than patients with IPF needed oxygen therapy (44.4% vs 77.6%, p <0.0001) and more commonly showed at frCT NSIP (68.8% vs 6.9%, p <0.0001) than UIP pattern (0% vs 86%, p <0.0001).

Conclusion: IPAF criteria recruit a rare cohort of patients with a disease probably less severe than IPF, even though clinically relevant. Further prospective studies may better define the long-term prognosis of ILD in IPAF. The follow-up of these patients by a multi-disciplinary team may be useful in order to early recognize and treat the new cases of CTD. IPAF classification can recruit incomplete form or early onset of CTD that can allow a timely treatment in patients without a structured damage.

REFERENCES:

Disclosure of Interests: None declared

THU0564

COULD A PROBABLISTIC REASONING AI ACCELERATE RARE DISEASE DIAGNOSIS? EVALUATING THE POTENTIAL IMPACT OF A DIAGNOSTIC DECISION SUPPORT SYSTEM IN A RETROSPECTIVE STUDY

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Background: The diagnosis of rare diseases is often delayed by years [1]. The main factor for this delay is believed to be the lack of knowledge and awareness regarding rare diseases [2]. Probabilistic diagnostic decision support systems (DDSS) have the potential to accelerate rare disease diagnosis by highlighting differential diagnoses for physicians [3, 4]. DDSS’s are based on case input and incorporated medical knowledge.

Objectives: We examine a probabilistic DDSS prototype and assess its potential to provide accurate rare disease suggestions early in the course of rare disease cases.

Methods: Retrospectively, information from the medical records of 93 patients was transferred to the DDSS. Each of these patients had a confirmed rare inflammatory systemic disease. The accuracy of the DDSS disease suggestions was assessed for all documented visits over time. Time to correct top fit (TF) and top five fit (TSF) disease suggestion was assessed, as was the original time to clinical diagnosis (TD), TD/TD as well as TSF/TD were calculated to allow for comparison of TF respective TSF normalized to TD. Wilcoxon signed-rank test was conducted for TD-TF and TD-TSF.

Results: The DDSS suggested the correct disease at a time earlier than the time of clinical diagnosis among the top five fit disease suggestions in 53.8% of cases (50 of 93), and as the top fit disease suggestion in 37.6% of cases (35 of 93). Median advantage of correct disease suggestions compared to the time point of clinical diagnosis was 3 months or 50% for top fit respective 1 month or 21% for top fit. The correct diagnosis was suggested at the first documented patient visit among the top five fit disease suggestions in 33.3% (top five fit), respective 16.1% of cases (top fit). Wilcoxon signed-rank test shows a significant difference between the time to clinical diagnosis and the time to correct disease suggestion for both top five fit and top fit (z-score -6.68, respectively -5.71, p<0.05, p-value <0.001). The DDSS suggested the correct rare disease at the time of diagnosis in 89% of cases (83 of 93)

Conclusion: The DDSS was capable of providing accurate rare disease suggestions in most of the rare disease cases. In many cases it provided correct rare disease suggestions early in the course of the disease, sometimes in the very beginning of a patient’s journey. The interpretation of these results suggests that DDSS’s have the potential to highlight the possibility of a rare disease to physicians early in the course of a case. Limitations of this study derive from its retrospective and unblinded design, data input by a single user, and the optimization of the knowledge base during the course of the study. Whether the use of this DDSS leads to a reduced time to rare disease diagnosis in a clinical setting should be validated in prospective studies.
To describe the follow-up results of patients investigated for FUO and had a certain diagnosis.

**Objectives:**
To describe the follow-up results of patients investigated for FUO and had a certain diagnosis.

**Methods:**
Data from patients who admitted to Hacettepe University Hospitals, inpatients sections of the internal medicine with the complaint of FUO collected prospectively from January 2015 to October 2017. Patients with an uncertain diagnosis after all diagnostic procedures were excluded. Patients were divided into 3 main subgroups: rheumatologic (n=49, 46.2%), infectious (n=28, 26.4%) and malignant (n=29, 27.4%) groups. We compared Kaplan-Meier curves for all diagnosis-to-death time frames with the standart log-rank test. $p<0.05$ was considered as statistically significant.

**Results:**
Total 106 patients were included, 58 (55%) of them were female. Median age was 48 (18-81) years. Patients were also divided into three subgroups: rheumatologic, infectious and malignant groups. We compared Kaplan-Meier curves for all diagnosis-to-death time frames with the standart log-rank test. $p<0.05$ was considered as statistically significant.

**Discussion of Interests:**

**DOI:** 10.1136/annrheumdis-2019-eular.6866

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**THU0565**

**COMPARISON OF SURVIVAL RATES AMONG SUBGROUPS OF PATIENTS EVALUATED FOR FEVER OF UNKNOWN ORIGIN**


**Hacettepe University Medical School Internal Medicine, Rheumatology, Ankara, Turkey**

**Background:** Fever of unknown origin (FUO) is one of the most challenging clinical situations. Although several studies showed a relatively benign course of patients remained undiagnosed, long-term outcome of patients with a certain diagnosis remain non-established (1).

**Objectives:** To describe the follow-up results of patients investigated for FUO and had a certain diagnosis.

**Methods:** Data from patients who admitted to Hacettepe University Hospitals, inpatients sections of the internal medicine with the complaint of FUO collected prospectively from January 2015 to October 2017. Patients with an uncertain diagnosis after all diagnostic procedures were excluded. Patients were divided into 3 main subgroups: rheumatologic, infectious and malignant groups. We compared Kaplan-Meier curves for all diagnosis-to-death time frames with the standart log-rank test. $p<0.05$ was considered as statistically significant.

**Results:**
Total 106 patients were included, 58 (55%) of them were female. Median age was 48 (18-81) years. Patients were also divided into three subgroups: rheumatologic (n=49, 46.2%), infectious (n=28, 26.4%) and malignant (n=29, 27.4%) groups. We compared Kaplan-Meier curves for all diagnosis-to-death time frames with the standart log-rank test. $p<0.05$ was considered as statistically significant.

**Conclusion:** Among patients evaluated for FUO, survival rate was higher in patients who had a rheumatological diagnosis. Further diagnostic algorithms are needed to identify these subgroups, because of the higher mortality among INF and MLG groups.

**Discussions of Interests:**

**DOI:** 10.1136/annrheumdis-2019-eular.6866

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**THU0566**

**OCULAR FEATURES IN 381 PATIENTS WITH SYSTEMIC SARCOIDOSIS AND ITS CORRELATION WITH THE IWOS CRITERIA. STUDY IN A UNIVERSITY HOSPITAL**

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**Background:** Sarcoïdosis is a multisystemic inflammatory disease characterised by non-caseating epitheloid granulomas that can affect any organ system. The three most frequency affected organs are lung, skin and eyes. Ocular involvement is the presenting symptom in approximately 20-30% and can involve any part of the eye and its aneal tissues. Sarcoïdosis may cause uveitis, conjunctivitis, episcleritis/scleritis, optical nerve disease and orbital inflammation.

**Objectives:** To analyze the prevalence of ocular involvement is systemic sarcoïdosis, the clinical patterns and their correlation with the International Workshop on Ocular Sarcoïdosis (iWOS) criteria. These criteria classify ocular sarcoïdosis as definite, presumed, probable and possible, according to some ophthalmological and analytical findings. They are especially useful if a biopsy is not obtained or it is negative.

**Methods:** Retrospective study of patients admitted to a single reference University Hospital between 1999 and 2019 with diagnosis of sarcoïdosis. Clinical findings, demographics features, anatomic location and iWOS intraocular signs were recorded. We also collected serum angiotensin
converting enzyme (ACE), liver enzyme test, chest radiography, chest computed tomography scan, treatment and biopsy if performed.

| TABLE: Demographic and clinical features of the 50 patients with ocular sarcoidosis. |
|---------------------------------|---------------------------------|
| **Patients (n=50)**              | **Patients (n=50)**              |
| **Ages, median (SD) years**      | 45.6 (16.7)                      |
| **Sex, n(%)**                    | Male, 32 (64)                    |
| **Affected organs, n (%)**       | Lung 30 (60), Skin 14 (28), Liver 4 (8), Kidney 3 (6), Musculoskeletal system 3 (6), Central nervous system 3 (6), Heart 2 (4) |
| **Ocular signs, n (%)**          | Bilaterality 22 (44), Snowball/tangle of pears 19 (38), Multifocal/retinal 15 (30), Multiple choroidal peripheral lesions 7 (14), Periphlebitis 5 (10), Anterior synchiae 1 (2), Uveitis disc granulomas 1 (2) |
| **IOWS criteria, n (%)**         | Definite 22 (44), Presumed 13 (26), Possible 4 (8) |

**Abbreviations:** ADA: adalimumab; AZA: azathioprine; CoA: cyclosporine A; GLM, glabelumab; IFX, infliximab; IS, immunosuppressors; KPs, keratic precipitates; MMF, mycophenolate mofetil; MTX, methotrexate; SD, standard deviation.

Results: We selected patients with ocular inflammation from a cohort of 381 patients with sarcoidosis (n=50, 13%). Most of the cases were women (54%) and median age was 45.5±16.7 years. In these 50 cases, the most affected organ was lung (60%), followed by skin (28%). Forty patients had uveitis, 32 of them with ocular symptoms. Thirty-nine out of 50 patients (78%) met one of the 4 IOWS diagnostic categories: 22 with definite (44%), 13 presumed (26%) and 4 with possible (8%) sarcoidosis. Eleven patients did not meet IOWS criteria. The most common ocular signs were bilaterality (44%), snowball or strings of pears (38%), mutton-fat KPs (24%), multiple choroidal peripheral lesions (14%) and periphlebitis (10%). The median value of ACE was 69 U/l. Forty-four patients (88%) received oral corticosteroids, 21 (42%) received methotrexate, 11 (22%) received another conventional immunosuppressor and 11 (22%) a biological treatment. TABLE shows demographic and clinical features.

Conclusion: In our population the IOWS Criteria had a sensitivity of 78%. Even though there is no gold standard for diagnosing ocular sarcoidosis yet, IOWS signs can help clinicians suspect it.

REFERENCES:

Disclosure of Interests: None declared.


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**THU0567 POLYMYALGIA RHEUMATICA-LIKE SYNDROME FROM CHECKPOINT INHIBITOR THERAPY: CASE SERIES AND SYSTEMATIC REVIEW OF THE LITERATURE**

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**Background:** Checkpoint inhibitor therapy has caused a paradigm shift in the field of oncology, producing significant survival benefits in patients with an ever-growing list of malignancies, but their use is attended by a spectrum of immune related adverse events (irAEs). Many rheumatic irAEs have been described. A critical and presently unanswered question is what proportion of these rheumatic irAEs represent appearances of classic rheumatic diseases or, alternatively, represent new clinical variants with potentially different pathogenesis, clinical course and treatment responsiveness. Little is known about the PMR-like entity that has been described in the setting of ICI therapy.

**Objectives:** To assess whether the polymyalgia rheumatica (PMR)-like syndrome reported as an irAE from checkpoint inhibitor therapy is consistent with the 2012 EULAR/ACR provisional criteria for PMR1.

**Methods:** The cases were derived from two sources. Group 1 represents reported cases from three contributing centers. Group 2 was derived from a systematic review of the literature searching for all cases reported as PMR or PMR-like illness associated with checkpoint inhibitor therapy. Cases were assessed for the quality of reporting and then analyzed to determine whether they fulfilled the 2012 EULAR/ACR provisional criteria for PMR.

**Results:** A total of 49 patients were included for analysis, including 9 cases from Cleveland Clinic (Table 1), 4 cases from Johns Hopkins University, and 7 cases from University Hospital of Bordeaux, in addition to the 29 separate cases found by systematic review. Among the entire group, 37 (75%) were designated “complete” indicating that they had sufficient data to reliably apply the 2012 EULAR/ACR criteria of which 28 (75%) cases fulfilled complete criteria for PMR. A number of cases also demonstrated some clinical features unusual for idiopathic PMR.

**Conclusion:** This study suggests a high proportion of reported cases of checkpoint inhibitor-related PMR fulfill preliminary criteria for PMR yet in one quarter clinical details were incomplete making verification problematic. Furthermore, in the absence of a gold standard for the diagnosis of PMR, the relationship of checkpoint inhibitor-related PMR to the idiopathic form remains unclear.

**REFERENCES:**

**Disclosure of Interests:** None declared.

**THU0568 CLINICAL CHARACTERISTICS OF SEVEN RELAPSING POLYCHONDritis CASES MISDIAGNOSED AS ARTHRITIS**

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**Background:** Relapsing polychondritis (RPC) is a rare autoimmune disease. It mainly affects the tissue abundant of cartilage, such as ear, nose, and tracheoles. The multiple systems including eye, joint, mucocutaneous, and kidney could be involved. As the presentation of arthritis was nonspecific and could appear in several connective tissue diseases,
it was easily misdiagnosed. The delay in establishing the diagnosis of RPC was common. A survey from the United Kingdom found a median length of 1.9 years from the first disease attack to diagnosis\(^2\). One recent research reported 64% of RPC patients had a diagnostic delay with more than five years\(^3\).

**Objectives:** We made a retrospective study to explore distinct characteristics of relapsing polychondritis with arthritis as the first attack. By comprehending the nature of disease fully, misdiagnosis at the early phase of illness could be avoided.

**Methods:** The clinical features and prognosis of 7 RPC patients in Peking Union Medical College Hospital between October 2012 and October 2018, presenting as arthritis at onset, were retrospectively analyzed.

**Results:** There were five female patients. The female to male ratio of the case series was 5:2. The age of 7 patients was 43.43±9.86 years. The number of affected joints was 20.14±10.92. The joint involvement was most common in the bilateral proximal interphalangeal joints (PIP\(\alpha\)) and interphalangeal joints of the thumb. Recent arthritis occurred in 5 patients. There was no accompanying enthesitis. The specific serum indexes of RA, such as rheumatoid factor (RF), anti-cyclic citrullinated peptide (CCP) antibody, were negative. There were three patients administered with conventional synthetic disease modifying anti- rheumatic drugs firstly, and they did not respond well. The median delay time from onset to diagnosis of RPC was ten month (Figure 1). The deformity and destruction of the joint were not observed in all patients, by clinical and radiological assessment. The average duration from arthritis to the occurrence of other involved system was 8.3 months. Four patients were misdiagnosed as rheumatoid arthritis at first. One patient was considered as ankylosing spondylitis at first. Two patients were diagnosed as arthritis at the beginning. As regards to treatment, glucocorticoids (GCs), cyclophosphamide and mycophenolate mofetil were used. Two patient was complicated with palmoplantar pustulosis and Kikuchi-Fujimoto disease. During follow up, myelodysplastic syndrome occurred in one patient. After following up for 35.43±30.92 months, all patients survived and were not with the recurrence of arthritis.

**REFERENCES:**


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**THU0569 MANAGEMENT OF ADULT-ONSET STILL’S DISEASE (AOSD) WITH IL-1 INHIBITORS: EVIDENCE- AND CONSENSUS-BASED STATEMENTS BY A PANEL OF ITALIAN EXPERTS**

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**Background:** Still’s disease is a rare autoinflammatory disease, presenting in both pediatric (systemic juvenile idiopathic arthritis [SJIA]) and adult patients [adult-onset Still’s disease (AOSD)]. Due to the rarity of the disease, clinical trials are limited and treatment guidelines are not available. In patients refractory to the classical therapy with NSAIDs, corticosteroids and DMARDs, the introduction of drugs targeting IL-1 has greatly expanded treatment options. Among these, canakinumab, a human monoclonal anti-IL-1\(\beta\) antibody, and anakinra, a human recombinant IL-1RA, have been recently approved for the treatment of refractory patients.

**Objectives:** To produce recommendations, based on evidence and expert consensus, that can help clinicians in choosing the most appropriate treatment of AOSD, with particular attention to anti-IL-1 therapies, in order to achieve disease remission before the development of complications.

**Methods:** The recommendations development process took place from April to October 2018 and consisted of three steps. The first step was dedicated to a comprehensive literature review and development of statements. Two separate literature searches were performed: a) similarities and differences between SJIA and AOSD; b) efficacy and safety of IL-1 blockade in AOSD. The issue related to the treatment of AOSD with anti-IL1 therapies was specified into 4 questions: 1) efficacy and safety; 2) comparison among IL-1 inhibitors; 3) early versus late treatment; 4) systemic versus chronic articular pattern of the disease. In the second step, the statements were submitted in a Delphi process to a panel of 87 rheumatologists. Consensus threshold was set at 66%: positive, > 66% of voters selected scores 3 to 5; negative, > 66% of voters selected scores 1 or 2. At the third step of the consensus process, the voting results were analyzed, and the statements were finalized.

**Results:** In the two literature searches, 332 and 358 publications were identified; 30 and 25 publications, respectively, were selected according to the inclusion criteria. Based on the review of the literature and personal clinical experience, 11 statements were developed. Positive consensus was reached after the first round of voting and was full (> 95%) on the majority of statements. A large consensus was achieved in considering AOSD and SJIA as the same disease. The use of anti-IL1 therapies in refractory patients was considered quite safe and effective both as first and as subsequent line of biologic treatment, especially in systemic patients. Because of the lack of head-to-head comparisons, a different profile of efficacy among IL-1 inhibitors could not be established. There was a large consensus that failure of the first IL-1 inhibitor does not preclude a therapeutic response with another one. The lack of studies comparing early versus late treatment in AOSD patients did not allow to draw conclusions, however data from SJIA suggest a better response in early treated patients.

**Conclusion:** The Delphi method was used to develop recommendations that we hope will help clinicians in the management of patients with AOSD refractory to conventional therapies.

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Efficacy and Safety of Anakinra in the Treatment of Autoimmune Myocarditis

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Background: Virus-negative or “autoimmune” myocarditis (VNM) is a severe, inflammatory heart disease with a poor prognosis, and is a leading cause of inflammatory dilated cardiomyopathy (IDCM). Therapies are limited. Preliminary data indicate that interleukin-1 (IL-1) plays a key role in the initiation and maintenance of the inflammatory heart response, sustaining an auto-inflammatory cycle [1,2]. Objectives: to evaluate the efficacy and safety of anakinra (ANK) in idiopathic left ventricular dysfunction (LV-F) on transthoracic echocardiography (TTE) in patients with VNM.

Methods: Biopsy-proven VNM patients were enrolled and treated with ANK 100 mg daily subcutaneously. All patients received treatment with the maximum tolerated dose of any beta blockers and ACE-inhibitors, according to current guidelines. At baseline and 8±4 weeks after ANK therapy, all patients underwent a full evaluation with assessment of conduction status (New York Heart Association [NYHA]), measurement of high-sensitivity troponin T (hs-TnT) and NT-proBNP serum levels, electrocardiography (ECG), 24h-ECG-Holter, TTE and cardiac magnetic resonance (CMR).

Any myocarditis-related complication, cardiovascular deaths and adverse events (AEs) was recorded during follow-up. Continuous variables were assessed with the Wilcoxon signed-rank test for non-parametric tests and a p-value <0.05 was considered statistically significant.

Results: Eleven patients (6M, 5F, mean age 46.2±12.2 years) diagnosed with EBM-proven VNM were enrolled. Nine patients received ANK as first line therapy, and in 5 cases ANK was used as monotherapy: ANK was combined with prednisone (mean dose 31.7±16.7 mg daily) in 6 patients, 5 of them were concomitantly treated with azathioprine. On EMB, 8 patients were classified as i-DCM, 3 with acute VNM e 1 with active and chronic VNM [3,4]. Clinical onset was characterized by congestive heart failure in the most cases (72.7%). The majority of patients (72.7%) was in NYHA class III-IV. Mean LV-EF on TTE at baseline was 38.7% ±19.6, with comparable findings on CMR (36.45%±18.0), and 8 patients (72.7%) and 6 patients (54.5%) were treated with ANK therapy. At baseline, mean levels of hs-TnT and NT-proBNP were 150.0±153.9 ng/L and 6968.8±10788.4 pg/ml respectively. Hs-TnT and NT-proBNP levels were elevated in 10 (90.9%) patients. The LV-EF increase was >10% in 5 patients (45.5%) and 9 patients (81.8%) respectively. At 8 weeks, LV-EF improved in 10 patients (90.9%). The LV-EF increase was >10% in 5 patients (45.5%) and between 5-10% in 5 cases (45.5%); only 1 patient showed a <10% LV-EF decrease. Mean LV-EF at the end of follow-up improved to 49.4% ±10.8 (p=0.039). When evaluating the 8 patients with baseline reduced LV-EF, the LV-EF improvement was statistically significant (baseline 29.2±12.9; after ANK 45.2±9.2, p=0.025). The LV-EF amelioration was paralleled by clinical improvements in all patients, since the majority of them (90.9%) were in NYHA class I-II at the end of follow-up. Consistently, hs-TnT declined after 8 weeks (64.6±100.7 ng/L, p=0.028), and a similar trend was observed for NT-proBNP, even though not statistically significant (2582.6±5048.1 pg/ml, p=0.06). We did not observe any myocarditis-related death or complications, nor any ANK-related AEs.

Conclusion: Our pilot study supports the efficacy and safety of ANK in the treatment of inflammatory heart failure in VNM and provides the first clinical evidence to support the therapeutic blockade of IL-1 in myocarditis.

REFERENCES:

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The Impact of Aging on Familial Mediterranean Fever Patients

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Background: Familial Mediterranean Fever (FMF) is a monogenic auto-inflammatory disorder with innate immune activation with an onset before age 20 in approximately 90% of the patients. There is scarce data on the effect of aging on FMF patients over 50 years of age.

Objectives: This study aims to collect data on FMF patients who have survived over 40 years of age. Here we report our preliminary data on disease course and treatment status and comorbidities of our patients with FMF.

Methods: Among the FMF patients who have been followed in our FMF outpatient clinic with a pool of approximately 5000 patients, those who have aged 40 and over are being included to the study. As by today 180 patients are considered for evaluation. The files of patients were reviewed and a standard questionnaire was used to interview the patients. Here we report the results of 100 of these patients (56%) who were contacted for this purpose. These patients were questioned on their demographic characteristics, comorbid conditions, colchicine treatment details, and attack information. In order to see the trend of the change in the parameters assessed, the patients were divided into two groups based on their present age (Group 1: 40-50 years, Group 2: ≥50 years).

Results: A total of 100 (78 F, 22 M) patients were evaluated. There were 61(64%, 15M) patients aged between 40-50 years and 39 (32F, 7M) over 50. The demographic characteristics and clinical features of these patients are given in Table 1. Besides 3, all patients were still on colchicine regularly. Ninety-six percent of the patients declared overall benefit from colchicine therapy; however 38% experienced a side effect related to this treatment. Over 88% of the patients reported decrease in severity and frequency of FMF attacks. The mean daily colchicine dose was lower in the age 50 and over group (1,750,77 mg versus 1,35±0,58 mg). There were no patients with AA amyloidosis in neither age group. The mean duration from the last attack increased from 15.3±19.7 months to 35.6±52 months in the older patients. One or more additional disease was present in 75% of this patient group. Among the comorbidities hypertension was the most frequent, diagnosed in 25% of the patients, followed by hypothyroidism (16%), diabetes mellitus (10%) and cardiac disease (5%). Sixty-five of the patients were receiving other medications in addition to colchicine.

Table 1. Clinical course and co-morbidities in two age groups over 40 years

<table>
<thead>
<tr>
<th>n</th>
<th>Group 1*</th>
<th>Group 2**</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (F:M); current age (mean±SD, mo)</td>
<td>(n=61)</td>
<td>(n=39)</td>
<td></td>
</tr>
<tr>
<td>(46.15±45.5</td>
<td>37.05±4.0</td>
<td>0.43; 0.001</td>
<td></td>
</tr>
<tr>
<td>2.29</td>
<td>5.81</td>
<td>0.012</td>
<td></td>
</tr>
<tr>
<td>Mean duration since the last episode, (mean±SD, mo)</td>
<td>15.3±19.7</td>
<td>35.67±52.05</td>
<td>0.012</td>
</tr>
<tr>
<td>Number of patients on colchicine therapy, n (%)</td>
<td>59 (96.7)</td>
<td>38 (97.4)</td>
<td>NS</td>
</tr>
<tr>
<td>Mean colchicine dose, mg/day (current)</td>
<td>1.70±0.76</td>
<td>1.41±0.45</td>
<td>0.03</td>
</tr>
<tr>
<td>Number of patients with decrease in attack severity, n (%)</td>
<td>54(88.5)</td>
<td>35 (89.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Number of patients with decrease in attack frequency, n (%)</td>
<td>57(93.4)</td>
<td>37 (94.8)</td>
<td>NS</td>
</tr>
</tbody>
</table>
Conclusion: According to our preliminary data the majority of the patients continue to take colchicine after age of 40. However the frequency of FMF attacks as well as daily colchicine dose decrease as the patients get older. With well designed trials stopping colchicine treatment may be considered in a subgroup of patients after 50 years of age. Approximately 1/3 of the FMF population over 40 years of age has a comorbidity that necessitates additional medications which underlines the need for special attention.

Disclosure of Interests: None declared


THU0572 RHEUMATOLOGICAL ASPECTS OF FORMS AND VARIANTS OF PANNICULITIS

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Background: Panniculitis (Pn) is a set of heterogeneous inflammatory diseases characterized by lesions of subcutaneous fat (SCF) and often accompanied with the defeat of the musculoskeletal system and internal organs. Depending on the etiology and histomorphological picture, Pn is divided into two forms: septal (SPn) and lobular panniculitis (LPn) with and without signs of vasculitis, which is reflected in the clinical picture of the disease. Often Pn is one of the symptoms of rheumatic diseases (Rd), it can lead to late diagnosis of the underlying disease.

Objectives: to study the frequency of occurrence of forms and variants of Pn in rheumatological practice on the basis of long-term prospective observation.

Methods: We examined 687 patients with Pn (613 women and 74 men, mean age 39.7±11.31 and 41.2±12.57 years, respectively) with the referral diagnosis of “Erythema Nodosum” (EN) or “Panniculitis”, who were observed in the rheumatologic clinic in 2007-2017. In addition to general clinical examination, we determined serum concentrations of α1 antitrypsin, amylose, lipase, ferritin, creatine phosphokinase, conducted a CT scan of the chest organs, immunological, TB tests and pathological study of skin biopsy from the node.

Results: As a result of application of the developed diagnostic algorithm; 430 patients (62.6%) were diagnosed with SPn and 249 patients (36.2%) - with LPn. In 9 cases (1%) (3 patients with SPn and 4 with LPn), it was not possible to confirm the variant of Pn, despite the comprehensive examination. In 8 patients (1.1%) no Pn data were revealed, the following diagnoses were verified: 2 patients (25%) — discoid lupus and lipo-dystrophy; 1 (12.5%) — erysipelis, lichen, fixed erythema and keratoacanthoma. SPn in 94% of cases (400 patients) was presented by EN, in 4% (18) — by superficial migrating thrombophlebitis, in single cases (1-0%) — by eosinophilic fasciitis, skin nodular polyarteritis and scleroderma-Pn (2, 6 and 1 patients, respectively). In 28% of cases LPn was associated with systemic connective tissue lesions, in 27% with idiopathic lobular Pn (Weber — Christian panniculitis) (p<0.002), in 32.92% with lipodermatosclerosis and in 14.28% with subcutaneous sarcoid. In a few cases LPn was caused by lymphoproliferative (2.88%) and cancer (2.49%) diseases, calciphylaxis (2.05%), erythema Bazin (1.64%), cold Pn (0.02%) and alpha-1 antitrypsine failure (0.41%).

Conclusion: the results confirm that patients with SPn were found twice as often as with LPn. Prenosological Pn was mainly associated with sarcoidosis, EN and RD, which confirms the relevance of further research of Pn.

Disclosure of Interests: None declared


THU0573 COMPLICATIONS AND ACTIVITY OF UVEITIS IN A MULTIDISCIPLINARY REFERENCE UNIT IN THE NORTH OF SPAIN

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Background: Uveitis, an intraocular inflammatory disease, is a significant cause of visual impairment. It is not known how many patients with uveitis will retain visual acuity and how many develop visual impairment or even blindness. The activity of uveitis, the use of topic and oral steroids could produce ocular complications.

Objectives: To describe the complications and the activity of the uveitis in a cohort of 500 patients diagnosed in one unit of reference in the north of Spain.

Methods: A prospective study of complications and the activity of the 500 adults with uveitis were evaluated in the multidisciplinary Uveitis Unit of Complejo Hospitalario de Navarra from January of 2010 to March of 2015. Uveitis activity and the type of complication to the year of follow-up were analysed. The variables were collected according to the terminology of the activity of the SUN (inactive, worsening, improvement and remission). To facilitate statistical analysis variables inactive and remission were grouped in a same term. A study of characterization of the evolution and worsening of the activity to the year of follow-up with sex, foreign, type of uveitis, etiology, laterality, treatments and complications. The characterization was carried out through the SPAD 8 program and was carried out by contrast Chi square.

Results: We collected a total of 500 patients, 54.4% of patients remained inactive or in remission after 1 year of follow-up, 13.2% presented worsening of their activity and 32.45% had improved. A bivariate analysis was performed between the variable evolution per year and other variables. We did not observe relationship between the evolution per year and sex, foreign, type of uveitis, etiology, laterality, topical treatment, intravitreal treatment, biological treatment or surgical treatment. Relationship was found statistically significant between the evolution with the existence of complications (p = 0, 0) and oral immunosuppressive treatment (p = 0, 008). There was statistically significant relationship between the existence of complications (p = 0, 0) and oral immunosuppressive treatment (p = 0, 011), and not relationship with age was found (p = 0, 8), sex (p=0,35), foreign (p = 0, 27), type of uveitis (p = 0, 65), laterality (p = 0, 6) etiology (p = 0, 1), periciliar treatment (p = 0, 5), intravitreal (0.56) and biologic treatment (p=0,182). 65% of the patients did not show any complication a year of follow-up and the most frequent complications were cataract (10%), synecchia (8%), macular edema (5%), glaucoma (3%), detachment of retina (3%), epiretinal membrane (2%) and other (5%).

Conclusion: 87% of the patients were in remission or improvement to the year of follow-up. The worsening of the uveitis is related with the existence of complications and oral immunosuppressive treatment.

References:

Disclosure of Interests: Patricia Fanlo Speakers bureau: Abvie, Henar Heras: None declared, Alfredo Adan: None declared, Gerard Espinosa: None declared

**THU0574**

**DOES THE USE OF CHOLCHICINE EFFECT COGNITIVE FUNCTIONS IN FAMILIAL MEDITERRANEAN FEVER?**

**PRELIMINARY STUDY**

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**Background:** In Familial Mediterranean Fever (FMF), although cognitive functions have been shown to be impaired in children and adolescents, it has been shown that colchicine can be preservative on the cognitive functions in patients who are on long term colchicine treatment.

**Objectives:** This study aimed to evaluate cognitive functions in adult patients with FMF and cognitive effects of colchicine use.

**Methods:** The study included patients who were diagnosed with FMF according to Tel-Hashomer criteria. The control group included patients with no other inflammatory or systemic disease. Clinical features such as disease duration, comorbid diseases, colchicine treatment duration and dosage, amyloidosis and chronic renal failure (CRF), FMD gene mutations and PRAS scoring for evaluation of disease activity were recorded. Pittsburgh Sleep Quality Index (PSQI), Fatigue Severity Scale, FMF Quality of Life Scale and Beck Depression Scale were used to assess patents clinical situations. Cognitive measurements were evaluated under executive-propellent skills. KAS test was used for information processing and fluency skills; fruit-name test was used for the evaluation of focusing, concentration, and attention skills; animal counting test and The Montreal Cognitive Rating Scale (MOCA) which can evaluate different subunits (visuospatial/executive, naming, memory, attention, language, abstraction, delayed recall, and orientation) were used for the fluency and maintenance of attention. Different attention parameters were evaluated for patients and healthy individuals. These attention parameters were; focusing, elaborate, sustainability, ability to pay attention to two information at the same time.

Descriptive analysis was performed for all parameters. Mann-Whitney U-test and Spearman correlation coefficient were used to compare parameters. P <0.05 was accepted as statistically significant.

**Results:** The study included 24 (21 women, 3 men) patients with FMF and 10 (7 female, 3 male) age, sex and BMI matched healthy controls. The mean age of the patients and controls were 36.83 (SD:10.9) and 39.3(SD:8.6), respectively. No significant difference was found between FMF and healthy control groups regarding animal counting, KAS test, MOCA test, and subgroups. Only fruit-name counting test was decreased in the FMF group compared to the healthy controls (p <0.05). As the duration of colchicine treatment was prolonged, a moderate positive correlation was found in KAS scores (r=0.511) and MOCA naming scores (r=0.445). In the FMF group, the number of attacks in the last three months and the sleep scores of Pittsburgh and depression scores had a moderately positive correlation (r = 0.496). Depression scores and quality of life scores were highly correlated (r = 0.631).

**Conclusion:** FMF patients attention parameters are impaired compared to the healthy controls. Information processing and fluency performance is increased in FMF patients with the duration of colchicine treatment that demonstrate the ability to categorize and fluent use of the information. Number of attacks are correlated with poor sleep quality and depression.

**REFERENCES:**


**Disclosure of Interests:** Halise Hande Gezer: None declared, Ozge Devezer Uslu: None declared, Didem Erdem: None declared, Sevap Acer Kasman: None declared, Mehmet Tuncay Duruöz Grant/research support from: Abvie, Speakers bureau: Novartis, AMGEN, Abdi Ibrahim, Ilko DOI: 10.1136/annrheumdis-2019-eular.6994

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**THU0575**

**HYPERCOAGULABILITY AS A CAUSE OF THROMBOSIS IN BEHÇET’S SYNDROME: A SYSTEMATIC REVIEW AND META ANALYSIS**

Gül Gürela Koksoy, Berna Yurttas, Sinem Nihat Esatoglu, Vedat Hamuryudan, Hasan Yaricio, Gülen Hatemi, Istanbul University-Cerrahpasa, Medical Faculty of Cerrahpasa, Internal Medicine, Division of Rheumatology, Istanbul, Turkey

**Background:** While thrombosis in Behçet’s Syndrome (BS) is considered to be mainly caused by inflammation in the vessel wall, several prothrombotic factors have been studied with inconsistent results.

**Objectives:** We aimed to perform a systematic review of clinical studies investigating the thrombophilic factors in BS.

**Methods:** The online database of PubMed was searched with the keyword “Behcet” in four languages (English, German, French and Turkish) from inception up to May 2018. Titles and/or abstracts of all studies were screened independently by two reviewers (GG and BY) for studies reporting on thrombosis, fibrinolysis, endothelial factors and comparing BS patients with and without thrombosis. Conflicts were solved by a third reviewer (GH). The pooled odds ratios (OR) with 95%CI were calculated for binary outcomes and standardized mean differences (MD) were calculated for continuous outcomes by using RevMan 5.3.

**Results:** Of 9937 articles, 9373 were excluded due to repetition and inappropriate study design after reviewing titles and abstracts. Full text review of the remaining 564 articles yielded 86 papers meeting our predetermined inclusion criteria. Several factors such as protein C, protein S, active protein C resistance, anti-thrombin III, plasminogen, plasminogen activator inhibitor, fibrinogen, factor 7, factor 12, thrombin activatable fibrinolytic inhibitor, anticoagulation antibodies, antiβ2 Glycoprotein1 antibodies and methylenetetrahydrofolate reductase gene C677T mutation were not different in BS patients with thrombosis compared to those without thrombosis. On the other hand, vascular endothelial growth factor levels, P-selectin glycoprotein ligand-1, platelet-activating factor seemed to be more frequent in BS patients with thrombosis in the few studies reporting on these, including a small number of patients.

Among the 11 parameters with controversial results across studies, meta-analysis showed significantly higher homocysteine levels, higher factor VIII levels, more frequent Factor V Leiden mutations and higher von Willebrand factor levels in BS patients with thrombosis, whereas the pooled difference was not significant for mean platelet volume, tissue plasminogen activator, thrombin gene mutations, lupus anticoagulant, P-selectin level, erythrocyte aggregation and thrombomodulin level (Table).

**Conclusion:** Among the several prothrombotic factors that were studied in BS patients, factor V Leiden mutation, high homocysteine levels, factor 8 levels and von Willebrand factor levels may be associated with thrombosis in BS. Studies investigating these factors together in a large number of patients together with appropriate controls are needed to confirm these results.

**Table. Meta-analysis of studies with controversial results**

<table>
<thead>
<tr>
<th>Prothrombotic Factor</th>
<th>Number of studies</th>
<th>Number of Behçet’s patients</th>
<th>MD/OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>With thrombosis</td>
<td>Without thrombosis</td>
<td></td>
</tr>
<tr>
<td>WF (U/dl)</td>
<td>3</td>
<td>37</td>
<td>93</td>
</tr>
<tr>
<td>Factor V Leiden</td>
<td>9</td>
<td>204</td>
<td>446</td>
</tr>
<tr>
<td>Homocysteine</td>
<td>12</td>
<td>285</td>
<td>436</td>
</tr>
<tr>
<td>FVIII level</td>
<td>3</td>
<td>53</td>
<td>128</td>
</tr>
<tr>
<td>tPA</td>
<td>5</td>
<td>103</td>
<td>200</td>
</tr>
<tr>
<td>Prothrombin mutation</td>
<td>7</td>
<td>189</td>
<td>398</td>
</tr>
<tr>
<td>Mean platelet volume</td>
<td>5</td>
<td>73</td>
<td>327</td>
</tr>
</tbody>
</table>
THU0576  PROGNOSTIC FACTORS PREDICTING THE SURVIVAL OF PATIENTS WITH MACROPHAGE ACTIVATION SYNDROME

Seungmin Jung, Sungsoo Ahn, Sangwon Lee, Jason Jungik Song, Yongbeom Park, Yonsei University College of Medicine, Internal Medicine, Seoul, Korea, Rep. of (South Korea)

Background: Macrophage activation syndrome (MAS) is a hyperinflammatory condition, which can lead to death in patients with rheumatologic disease. However, the prognosis of adult patients with MAS is largely unknown.

Objectives: We aimed to investigate the mortality in patients with MAS accompanied Adult-onset Still’s disease (AOSD) or systemic lupus erythematosus (SLE) and to evaluate the prognostic factors predicting the mortality in patients with MAS.

Methods: We retrospectively reviewed febrile patients with AOSD or SLE admitted to Severance Hospital between 2005 and 2018. Patients who satisfied the classification criteria of MAS was included in the analysis. Cox-regression analysis was performed to evaluate the clinical factors associated with the overall mortality in patients with MAS.

Results: Of the total 123 patients, 48 (39%) patients and 75 (61%) patients were diagnosed with AOSD and SLE, respectively. Forty-three patients (35%) were died from MAS during hospitalization. There was no significant difference in mortality between AOSD and SLE (P = 0.675). In multivariate analysis, cytopenia, and insufficient reduction of ferritin and P-selectin 2 33 75 MD: 0.85 (-0.62, -0.15) were independently associated with death in patients with MAS (P = 0.019, < 0.001, and 0.011, respectively).

Conclusion: The presence of cytopenia, and treatment response after glucocorticoid treatment was closely related with death in patients with MAS. More intensive treatment should be considered in high-risk patients with poor prognostic factors.

REFERENCES:

Disclosure of Interests: None declared

THU0577  EFFICACY OF RADIOSYNOVIOGRAPHY IN PIGMENTED VILLONODULAR SYNOVITIS OF THE KNEE


Background: Pigmented villonodular synovitis (PVNS) is a rare disorder with the benign tumoral proliferation of the synovium. The surgical treatment of PVNS alone in most cases is unsatisfactory, because if a few cells have not been removed, the disease will recur.1 Post-synovectomy adjuvant treatment with intra-articular injection of Yttrium-90 (90Y) or Holmium-166 (166Ho) yielded better results. The radiosynoviorthesis (RSO) is an effective way of treating the chronic synovitis, with this method we are eliminate the inflammation in 75 percent of the cases.2

Objectives: To study efficacy of radiosynoviorthesis after the surgical synovectomy in pigmented villonodular synovitis of the knee.

Methods: Between May 1996 and August 2018, 17 patients (seven men and ten women aged 14–68 years) with diffuse PVNS were treated. All patients had monoarticular arthritis of the knee with histologically proved PVNS. The patients underwent 33 operations, two patients had four surgical procedures, one patient underwent three surgeries, eight patients had two surgeries and six patients had one surgical procedure (Table 1). The radiosynoviorthesis was performed according to the method accepted in the national protocol.Yttrium-citrate injectable suspension marked by 185 MBq 90Y-citrate injectable suspension, and 40 mg of 1 ml trimcinolone acetonide and 1 ml of lidocaine 1%.3 Holmium-phytate injectable suspension marked by 600 MBq 166Ho-phytate injectable suspension, and 40 mg of 1 ml trimcinolone acetonide and 1 ml of lidocaine 1%.3 Evaluation was based on the criteria as described by Müller, Rau and Schütte the score system was developed by the authors.4 The circumference of joint-swelling, the joint function, the measure of flexio-contracture, pain in state of rest and load on a pain analogue scale 1-10, joint warmth, walking capacity, the numbers of joint-junctions after the treatment, whether operation was necessary or not after the treatment were examined.

Results: Mean follow-up time was 56 months (range from 4 to 144 months). All patients were followed up using clinical assessment. After the first injection excellent and good results were recorded in 41%. After the second radiosynoviorthesis thirteen patients (76%) showed excellent and good results were recorded in 41%. The mean functional evaluation score of 17 patients was 28 (range 16-34). Most of the ratings were excellent or good, in four cases moderate (24%). No complications were noticed after surgery or after the radiosynoviorthesis.

Table 1. Patients with pigmented villonodular synovitis.

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>age</th>
<th>surgery before RSO</th>
<th>number of RSO</th>
</tr>
</thead>
<tbody>
<tr>
<td>7 men and 10 women total:</td>
<td>68</td>
<td>1 3 4 1 2 3</td>
<td>1 6 patients 8 patients</td>
</tr>
<tr>
<td>22-28</td>
<td>20</td>
<td>1 patient</td>
<td>10 patients 1 patient</td>
</tr>
<tr>
<td>29-35</td>
<td>10</td>
<td>2 patients</td>
<td>6 patients 1 patient</td>
</tr>
<tr>
<td>36-41</td>
<td>3</td>
<td>10 patients</td>
<td>6 patients 1 patient</td>
</tr>
<tr>
<td>0-10</td>
<td>0</td>
<td>10 patients</td>
<td>6 patients 1 patient</td>
</tr>
<tr>
<td>11-20</td>
<td>0</td>
<td>10 patients</td>
<td>6 patients 1 patient</td>
</tr>
<tr>
<td>21-30</td>
<td>0</td>
<td>10 patients</td>
<td>6 patients 1 patient</td>
</tr>
<tr>
<td>31-40</td>
<td>0</td>
<td>10 patients</td>
<td>6 patients 1 patient</td>
</tr>
<tr>
<td>41-50</td>
<td>0</td>
<td>10 patients</td>
<td>6 patients 1 patient</td>
</tr>
<tr>
<td>51-60</td>
<td>0</td>
<td>10 patients</td>
<td>6 patients 1 patient</td>
</tr>
<tr>
<td>61-70</td>
<td>0</td>
<td>10 patients</td>
<td>6 patients 1 patient</td>
</tr>
<tr>
<td>71-80</td>
<td>0</td>
<td>10 patients</td>
<td>6 patients 1 patient</td>
</tr>
<tr>
<td>81-90</td>
<td>0</td>
<td>10 patients</td>
<td>6 patients 1 patient</td>
</tr>
<tr>
<td>91-100</td>
<td>0</td>
<td>10 patients</td>
<td>6 patients 1 patient</td>
</tr>
<tr>
<td>&gt;100</td>
<td>0</td>
<td>10 patients</td>
<td>6 patients 1 patient</td>
</tr>
</tbody>
</table>

Table 2. Functional evaluation score after the RSO

<table>
<thead>
<tr>
<th>functional evaluation</th>
<th>response</th>
<th>patients</th>
<th>% score</th>
</tr>
</thead>
<tbody>
<tr>
<td>29-35</td>
<td>excellent</td>
<td>10</td>
<td>59%</td>
</tr>
<tr>
<td>22-28</td>
<td>good</td>
<td>3</td>
<td>18%</td>
</tr>
<tr>
<td>16-21</td>
<td>moderate</td>
<td>4</td>
<td>23%</td>
</tr>
<tr>
<td>8-14</td>
<td>mild</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>0-7</td>
<td>worsening</td>
<td>0</td>
<td>0%</td>
</tr>
</tbody>
</table>

Conclusion: A combination of debulking surgery with radiosynoviorthesis of Yttrium or Holmium for diffuse PVNS of the knee joint is a reliable treatment method, with good results.

REFERENCES:

Acknowledgement: Budapest, Hungary
Disclosure of Interests: None declared

THU0578

COMMON VARIABLE IMMUNODEFICIENCY IN PATIENTS WITH SARCOIDOSIS

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Background: Common variable immunodeficiency (CVID) is a primary immunodeficiency characterized by hypogammaglobulinemia and a deficient production of specific antibodies. Almost 30% of patients with CVID develop autoimmune and granulomatous disease, similar to clinical and histological sarcoidosis (S), it affects the lung fundamentally. This can lead to a misdiagnosis of S in a patient with CVID, this leads to inadequate treatment and increases the morbidity and mortality of the disease.

Objectives: Describe the clinical and radiological characteristics of a cohort of patients diagnosed with S with predominant pulmonary involvement. Make a study of immunoglobulin (IG) levels to see the frequency of CVID in these patients.

Methods: Retrospective descriptive study of patients treated in our Hospital (2008-2018), with diagnosis of S. The data was obtained by reviewing medical records. The delay in the diagnosis of S was defined as the difference in months between the initial diagnostic suspicion and the final diagnosis of S.

Results: 55 patients (31 women) were included, with a mean age of 52 ±12 years. The initial diagnosis was: 85% S, 10% lymphoma and 4% tuberculosis. The median of months from the start of the clinic to the diagnosis of S was 5.5 months.

Regarding the clinical, 21% patients present fever at the beginning of the disease, and 65% extrathoracic localization (cutaneous was the most frequent in 27%, and renal was the least frequent 5%). Simple x-ray and high resolution tomography of chest were done in all patients. Pulmonary stage 2 was the most frequent (51%), followed by stage 3 (16%), stage 0 (14%) and stage 4 (9%).

In 90% of the patients, histological confirmation was obtained by transbronchial (47%), cutaneous (11%) or lymph node biopsy (29%). Igs were normal in 87% of patients, only 4 patients had low IG levels (lg G in 3 patients and Ig M in 1). An extended ID study was performed in these 4 patients, being diagnosed with CVID 3 patients.

Results of the 4 patients and the differential characteristics between CVID and S in table 1.

### Table 1

<table>
<thead>
<tr>
<th>Differential diagnosis</th>
<th>CVID</th>
<th>Sarcoidosis</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent infections</td>
<td>+++</td>
<td>+/-</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Autoimmunity</td>
<td>+++</td>
<td>+</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>+++</td>
<td>+/-</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Hepatomegaly</td>
<td>+++</td>
<td>+/-</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Low levels</td>
</tr>
<tr>
<td>Low levels IG</td>
<td>+++</td>
<td>+/-</td>
<td>Yes</td>
<td>Yes</td>
<td>Low levels</td>
<td>IgM</td>
</tr>
<tr>
<td>Clinic stage</td>
<td>Pulmonary Pulmonary Pulmonary</td>
<td>Stage 2</td>
<td>Stage 2</td>
<td>Stage 2</td>
<td>Stage 2</td>
<td></td>
</tr>
<tr>
<td>Histological granuloma</td>
<td>+++</td>
<td>+++</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Increase of CD4/CD8 in BAL</td>
<td>+</td>
<td>+++</td>
<td>Low levels</td>
<td>Low levels</td>
<td>Low levels</td>
<td>Not done</td>
</tr>
</tbody>
</table>

Conclusion: Although their clinical presentation and histological appearance may be identical, the management of these two conditions is very different. The difficulties in the differential diagnosis between S and CVID, shows the importance of a history of screening for recurrent infections and the measurement of IG levels before the diagnosis of possible S.

Disclosure of Interests: None declared
Background: Inhibitors of CTLA-4 and PD-1 have shown improvements in survival in multiple advanced cancers. Immune-mediated effects such as arthralgias and arthritis have been described, but their prevalence and characteristics have not been well defined.

Objectives: The objective of the study is to describe the prevalence of immunemediated joint manifestations (IJM), their characteristics and evolution in patients who received immunotherapy (nivolumab NV, pembrolizumab PB) from January 1, 2016 to December 31, 2018 in our center.

Methods: Data collection was performed at through the RPIST (Registre Pacients Tractats) database of the CatSalut, and the patients referred to the monographic medical office of inflammatory joint diseases of our center. In all cases, the variables: age, sex, neoplasia, drug, number of doses, were recorded. In patients with joint involvement: other autoimmunemanifestations, joint affection prior to treatment, delay rheumatology derivation, joint affection type, swollen and tender joint counts, ESR, CRP, RF, ACPR, ANA, HLA B 27, Hb, leukocytes, neutrophils, lymphocytes, treatment and evolution, were recorded. The statistical analysis was carried out with the SPSS 15.0 computer package.

Results: 126 patients received treatment (TTO) with immunotherapy (71 NV, 35 BP) for neoplasia (81 lung, 10 renal, 8 melanoma, 2 oropharynx). The mean age was 67.93 ± 10.7 years (21.7% women, 78.3% men). There were 11 events catalogued as IJM. The overall prevalence was 10.3% (5.6% NV, 14.3% PB). Patients with UVM received a greater number of doses (17.67 ± 9.3 vs 9.24 ± 10.1 p = 0.018). No patient with melanoma presented UVM. All UIM suspicions cases were assessed by a rheumatologist. When studying their characteristics (Table 1), 3 patients were added from the database of the rheumatology service (14 cases). They received in a clinical trial BP295411 (rectal cancer), Atezolizumab (lung cancer) and Durvalumab (lung cancer). 42.9% of the patients presented inflammatory arthralgias (IAT) and 57.1% arthritis (AT). In reference to their previous history, 2 patients had a history of hyperuricemia and arthritis. One patient concomitantly presented lymphocytic colitis confirmed by biopsy. The delay time for assessment by rheumatology was 18.1 ± 22.1 days. Patients with AT were older (p = 0.014), had higher ESR (p = 0.947) than those with IAT. No differences were found in other variables (table1). With reference to the analytical study, 1 patient was RF +, 2 ANA + at mean titters (1/160-1/320), none ACPR or HLA B 27 +. After assessment by rheumatology, two patients with IAT were diagnosed with bone M1 and two AT were categorized as gouty arthritis. The rest of the IAT responded to NSAIDs and were resolved. 6 cases of AT received prednisone, 3 required treatment dose 1 mg/kg weight and subsequently MTX in 2 of them, with evolution to low disease activity at present. One only patient met RA classification criteria.

Conclusion: The prevalence of IJM was higher than 10%, depending on the number of doses. Patients with arthritis had higher age and higher ESR. No patient presented ACPR and HLA B 27 +, so to include them in the initial analytical could be not necessary. In these patients, it is important the assessment by a rheumatologist to make a correct differentiated diagnosis, as well as establish referral criteria to avoid delay of care.


Disclosure of Interests: D. Prieto-Peña: None declared, Monica Calderón-Goercke: None declared, Vanesa Calvo-Rio: None declared, Olga Maiz-Alonso: None declared, Ana Blanco: None declared, J. Narvaez: None declared, Santos Castañeda: None declared, Esther Vicente: None declared, Susana Romero-Yuste: None declared, Rosalía Demetrio-Pablo: None declared, Ana Uruticochea-Araná: None declared, José L. García-Serrano: None declared, Norberto Ortego: None declared, Miguel A González-Gay: None declared, Julio Sánchez: None declared, Ricardo Blanco: None declared, Marques de Valdecilla University Hospital, Santander, Spain; Hospital Universitari de Bellvitge, L’Hospitalet de Llobregat, Spain; Hospital de La Princesa, Madrid, Spain; Hospital Puerta de Hierro, Madrid, Spain; University Hospital 12 de Octubre, Madrid, Spain

Background: Non ischaemic optic neuritis (NION) is a severe inflammation of the optic nerve that may lead to blindness. It can be primary or associated to immune mediated inflammatory diseases (IMIDs). The treatment of the NION is based on systemic corticosteroids and conventional immunosuppressive drugs.

Objectives: To assess the efficacy of the biological treatment in refractory NION to conventional treatment.

Methods: Multicenter study of 12 patients diagnosed with NION refractory to systemic corticosteroids and at least one conventional immunosuppressive drug. The main outcomes were visual acuity (VA) and optical coherence tomography (OCT) of the optic nerve and the ganglion cells. Comparisons were made between baseline and the 1st week, 1st and 6th month and 1st year. (STATISTICA, StatSoft Inc. Tulsa, Oklahoma, USA).

Results: We studied 12 patients (19 affected eyes) (5 men/women); mean age of 29.8 ± 12.9 years. The underlying diseases were systemic lupus erythematosus (n=1), neurofibromatosis optica (n=1), neuroretinitis (n=1), relapsing polychondritis (n=1), pars planitis (n=1), Behçet’s disease (n=2) and idiopathic (n=6). Before biological treatment and besides oral corticosteroids, patients had received intravenous (IV) methylprednisolone boluses (n=9), cyclophosphamide (n=2), mycophenolate (n=2), hydroxychloroquine (n=1), methotrexate (n=8) and azathioprine (n=5). Biological treatment was bases on rituximab (n=2) (2 IV, doses of 1 g/week 2 weeks and every 6 moths), adalimumab (n=5) (40 mg/1-2 week), tocilizumab (n=4) (8 mg/kg/2-4 weeks) and infliximab (n=3) (5 mg/kg at 0, 2 and 6 week and then every 8 weeks). The characteristics of the 12 patients are shown in the TABLE.

After biological treatment we observed an improvement in the ocular parameters: VA [0.66±0.32 to 0.84±0.29; p= 0.03] of the OCT of the nerve [123.20±58.28 to 190.54±175.38; p= 0.11] and OCT of the ganglion cells [269.55±137.37 to 270.67±23.21; p= 0.03] at one year. After a mean follow-up of 29.09±19.23 months, there were no severe adverse effects.

Conclusion: Biological therapy in NION idiopathic or associated to IMIDs, refractory to conventional treatment, seems to be effective.
THU0582
THE TNF RECEPTOR-ASSOCIATED PERIODIC SYNDROME (TRAPS): CLINICAL AND GENETIC CHARACTERIZATION OF A COHORT OF ADULTS DIAGNOSED OF TRAPS SYNDROME

Alberto Ruiz Romagún1, Salvador García Morillo2, Marco Montes Cano2, Clara Aguilara Cres1, Manuel Leon Luque1, Maria Jose Valenzuela Porcel1, Maria Arcila Duran1, Lara Mendez1, Isabel Madroñal García1. 1HOSPITAL VIRGEN DEL ROCIO, Rheumatology, Seville, Spain; 2HOSPITAL VIRGEN DEL ROCIO, Internal Medicine, Seville, Spain; 3HOSPITAL VIRGEN DEL ROCIO, Immunology, Seville, Spain

Background: Tumor necrosis factor receptor-associated periodic syndrome (TRAPS) is a disease that is included within hereditary syndromes of periodic fever. It presents an autosomal dominant pattern of inheritance. It’s due to mutations of TNFRSF1A gene. It is usually present in childhood; although it can also appear in adulthood and it tends to cause high levels of acute phase reactants, fever, musculoskeletal symptoms (myalgias, arthralgias, arthritis), rash, abdominal pain, etc.

Objectives: To describe the clinical characteristics and genetic variants of patients diagnosed with TRAPS syndrome in a cohort of patients with auto-inflammatory syndromes with follow-up in a tertiary hospital from 2013 to the present

Methods: Retrospective descriptive study of adult patients diagnosed with autoinflammatory syndrome since 2013 (year of introduction of genetic tests in the hospital laboratory) until now. The data was obtained from the review of medical records. All patients with mutations in TNFRSF1A gene and clinically compatible with this diagnosis were reviewed

Results: Of a total of 44 adult patients diagnosed with hereditary syndromes of periodic fever (FMF, TRAPS, cryopyrinopathies, HIDS) and compatible genetic mutations (excluding polymorphisms), 13 (29.5%) presented mutations in the TNFRSF1A gene. Of those 13 patients, 9 (69.2%) were women. The most frequent mutations were the mutation in MEFV gene (92.3%) and one case (7.6%) with mutation in heterozygosis in exon 4 (p.R92Q) with 12 cases (92.3%) and one case (7.6%) with mutation in heterozygosis in exon 3 (p.P461L).

Conclusion: The TRAPS syndrome is a clinical entity to consider when making a differential diagnosis in patients with suspected autoinflammatory syndrome, that present fever, acute phase reactants elevation, arthromyalgia and its confirmation diagnosis is with genetic test

Disclosure of Interests: None declared


THU0583
EXPERIENCE OF ANAKINRA AND CANAKINUMAB IN PATIENTS WITH COLCHICINE-RESISTANT FAMILIAL MEDITERRANEAN FEVER AND COMPLICATED WITH AMYLOIDOSIS

All Sahin1, Mehmet Emin Derin2, Fahit Albayrak2, Burak Karakaya2. 1Sivas Cumhuriyet University, Rheumatology-Internal Medicine, sivas, Turkey; 2Sivas Cumhuriyet University, sivas, Turkey

Background: Familial Mediterranean Fever (FMF) is a hereditary auto-inflammatory disease characterized by recurrent fever and serosal inflammation (1). The goal of FMF treatment is to prevent the attacks and to minimize subclinical inflammation between attacks, and in attacks-free period. Colchicine is a major drug that sinue qua non in the treatment of FMF. However, anti-interleukin-1 agents are recommended in colchicine resistant and/or intolerant FMF patients (2).

Objectives: The aim of this study is to evaluate the efficacy of anti-interleukin-1 (anti-IL-1) agents in 54 FMF patients with resistant/intolerated to colchicine or complicated with amyloidosis.

Methods: Between January 2014 and December 2018, fifty four patients who were diagnosed as FMF according to the criteria of Tel-Hashomer following-up at Sivas Cumhuriyet University Medical Faculty, Rheumatology-Internal Medicine Department were included in to the study.

Results: 25 (46.3%) male and 29 (53.7%) female were included in the study. The mean age at diagnosis of 18 (min:15-max: 46) years and the median age at diagnosis was 18 (min: 3-max: 46) years. Anakinra was used in 34 (63%) FMF patients (100 mg/day), and canakinumab was used in 20 (37%) patients (150mg/2weeks). 37 cases were resistant to colchicine, 8 were intolerant to colchicine, 9 (20%) cases were complicated with amyloidosis. 8 patients had renal transplantation. MEFV gene mutations were shown in Table 1. Median duration of anti-IL-1 agent use was 12 months (min:2-max:40). 5 patients were resistant to anakinra, 4 patients had side effects which anakinra related. After a median follow up 12 months overall clinical response was95% (frequency of attacks <1/6months). Median proteinuria decreased from 3850 mg/day to median 1600 mg/day (p< 0.04) (Table 2). IL-6 treatment was started in 3 patients because of ineffectiveness of canakinumab. One pregnant patient was followed up with anakinra during pregnancy and there were no problems.

Conclusion: Anti-interleukin-1 agents can be used effectively and safely in the treatment of FMF patients. These agents are especially effective in the treatment of proteinuria due to amyloidosis. Large and long-lasting follow-up studies are needed to evaluate long-term effects of these drugs.

REFERENCES:

Table 1. MEFV mutations in FMF patients

<table>
<thead>
<tr>
<th>MEFV Mutations</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>M694V homozygous</td>
<td>20 (37%)</td>
</tr>
<tr>
<td>M694V heterozygous</td>
<td>8 (15%)</td>
</tr>
<tr>
<td>Compound mutation</td>
<td>14 (26%)</td>
</tr>
<tr>
<td>Other mutation</td>
<td>8 (15%)</td>
</tr>
<tr>
<td>No mutation</td>
<td>4 (8%)</td>
</tr>
</tbody>
</table>

Table 2. Laboratory Findings of the FMF patients treated with anti-IL-1 agents

<table>
<thead>
<tr>
<th>Number of attacks</th>
<th>Pre-treatment (median)</th>
<th>Post-Treatment (median)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;2/month</td>
<td>3856</td>
<td>3856</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>&lt;1/month</td>
<td>43</td>
<td>43</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>ESR (mm/h)</td>
<td>8</td>
<td>8</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>CRP mg/dl</td>
<td>43</td>
<td>43</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Proteinuria mg/d</td>
<td>3856</td>
<td>1600</td>
<td>&lt;0.05</td>
</tr>
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</table>

Disclosure of Interests: None declared


THU0584
RHEUMATOLOGICAL IMMUNE-RELATED ADVERSE EVENTS ASSOCIATED WITH IMMUNOTHERAPY IN SOLID ORGAN TUMOR, STUDY OF 102 CASES FROM A REFERRAL SINGLE CENTER FOR LAST 4 YEARS

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Background: Immune checkpoint blockade therapy (ICBT) currently is one of the most used therapies against cancer. The activation of the immune system can lead to different immune-related adverse events (irAEs), being the rheumatological side effects among the most common.

Objectives: Our aim was to assess the rheumatological irAEs in patients who received immunotherapy.

Methods: We set up an observational study of patients treated with Nivolumab and Pembrolizumab (anti-PD1), Atezolizumab (anti-PD-L1) and Ipilimumab (antiCTLA-4) for solid organ tumors. All these patients were followed in a single reference University Hospital from March-2015 up to December-2018. The main outcome was to determinate the incidence of rheumatological irAEs.

Results: We studied 102 patients (63%/39%) with a mean age of 60.6 ±9.7 with different solid organ tumors. Only 7 patients (6.8%) had previous diagnosis of an immune-mediated disease: psoriasis (n=2), psoriatic arthritis (n=2), rheumatoid arthritis (1), spondyloarthritis (1), psoriatic arthropathy (1), and skin lupus (1).
Rheumatological side effects were observed in 15 patients (14.7%): inflammatory arthralgia (8), arthritis (6), myositis (2) and aortitis (1). The time of appearance of the rheumatological irAEs was of 6.36 months (+2.81). From the 7 patients with previous diagnosis of an immune-mediated disease, only 1 patient with psoriasis suffered a worsening of skin symptoms and another one with psoriatic arthropathy had a monarticular episode.

Among the 14 patients who suffered from arthralgia/arthritis, the most frequent pattern was oligoarticular (40%), followed by poly (30%) and monarticular (30%). The most affected joint was the knee (n=4), followed by wrist (3), hands (3), ankle (2), shoulder (2) and foot (1). Apart from the articular disease, 2 patients suffered from myositis in lower limbs, with weakness of legs and arthralgia in their knees. A patient was diagnosed of aortitis through a PET, although the patient did not have any symptom.

Immunology tests such as RF, ACCP and ANA were done in 8 out of the 15 patients with musculoskeletal irAEs, being negative in all cases. Interviewing 40 of the patients who received ICBT, 7 of them (17.5%) referred xerophthalmia. 6 of them (15%) had a positive Schirmer test, and 3 (7.5%) had a reduced tear break-up time. None patient met Sjögren criteria.

In 6 out of the 15 patients with rheumatological irAEs (all of them with arthralgia/arthritis) the ICBT was removed, temporary in all cases, and could be reintroduced after a mean of 33 ± 18.9 days. 6 patients were treated with NSAIDs and 5 with oral prednisone (2 of them also required intra-articular corticoids).

Conclusion: Rheumatological irAEs are common in clinical practice. Arthralgia-Arthritis and dry-syndrome are the most frequent adverse events.

Disclosure of Interests: Lara Sánchez Bilbao: None declared, Itigo González-Mazón: None declared, Rosalia Demetrio-Pablo: None declared, José Luis Martín-Varillas: None declared, Marina Delgado Ruiz: None declared, Isabel Bernat Peña: None declared, Belén Atienza-Mateo: None declared, Monica Calderón-Góercke: None declared, D. Prieto-Peña: None declared, Almudena García Castaño: None declared, Miguel A González-Gay Grant/research support from: Prof. MA Gonzalez-Gay received grants/research supports from Abbvie, MSD, Jansen and Roche., Speakers bureau: Consultation fees/participation in company sponsored speaker’s bureau from Pfizer, Lilly, Sobi, Celgene, Novartis, Roche and Sanofi., Ricardo Blanco Grant/research support from: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen, Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen.


**THU0585 LYMPHADENOPATHY IN IG4-RELATED DISEASE IS ASSOCIATED WITH DISEASE ACTIVITY AND EOSINOPHILIA**

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1Keio University School of Medicine, Department of Internal Medicine, Division of Rheumatology, Tokyo, Japan; 2Fujita Health University School of Medicine, Department of Internal Medicine, Division of Rheumatology, Aichi, Japan; 3Mitsubishi Tanabe Pharma Corporation, Research Unit/Immunology and Inflammation, Tokyo, Japan

**Background:** IgG4-related disease (IgG4-RD) is an immune-mediated systemic disease characterized by the enlargement of multiple organs. IgG4-RD frequently involves the pancreas, lachrymal glands, salivary glands, bile duct, kidneys, lungs, and retroperitoneum, but can potentially affect any organ. Lymphadenopathy is often seen in patients with IgG4-RD along with other organ involvements, but the significance of the exist of lymphadenopathy in IgG4-RD is unclear.

**Objectives:** The aim of this study is to clarify the characteristics of patients with IgG4-RD who have lymphadenopathy.

**Methods:** We conducted cluster analysis with clinical data in consecutive 85 patients with untreated active IgG4-RD in our institute. We divided the patients into two groups who had lymphadenopathy or not (lymph group and non-lymph group), and compared clinical characteristics between the two groups. We counted the areas of swollen lymph nodes and performed correlation analysis with clinical characteristics. We also comprehensively screened serum protein concentrations in IgG4-RD patients (n=15) and healthy controls (n=5) by using high-throughput proteomics analysis, and differentially expressed proteins were extracted. We compared the concentrations of serum proteins which were extracted between lymph group and non-lymph group.

**Results:** Among 85 patients with IgG4-RD, 44 (52%) were male. Median age was 63 years old. Forty-seven (55%) patients were lymph group. Clusters analysis revealed that lymphadenopathy was in a cluster with serum IgG4, IgG4/IgG, IgG4-RD responder index (IgG4-RD RI), soluble interleukin-2 receptor (sIL-2R), eosinophilia, erythrocyte sedimentation rate (ESR), lung involvement, hemoglobin, albumin, C3 and C4. In lymph group, serum IgG4, IgG4/IgG, IgG4-RD RI, eosinophilia, sIL-2R and ESR were significantly higher than non-lymph group (Figure). Spearman’s correlation analysis revealed that areas of the swollen lymph nodes were positively correlated with serum IgG4, IgG4/IgG, sIL-2R, eosinophilia. Proteomics analysis revealed that 68 proteins were significantly higher in IgG4-RD (p<0.05). Among them, proteins related to adhesion of immune cells, fibrosis, formation of lymph node and eosinophil activation such as integrin/β1, CCL18, CCL19 and eotaxin3 were higher in lymph group (p<0.05, p<0.003, p<0.006 and p<0.006, respectively).

**Conclusion:** Lymphadenopathy in IgG4-RD is associated with disease activity and eosinophilia. Proteomics analysis can provide some clues for elucidating the significance of lymphadenopathy in IgG4-RD.

**REFERENCES:**


REFERENCES:

Disclosure of Interests: Zi-Yi Tang: None declared, Yu-Feng Qing Grant/research support from: Sichuan Youth Science and Technology 2016JQ0053, and the Department of Science and Technology of Sichuan Province (2018JY0257), Jian-Xiong Zheng: None declared, Dan Wang: None declared, Ting Yi: None declared, Wen-Jun Zhou: None declared, Qian Qin: None declared DOI: 10.1136/annrheumdis-2019-eular.1186

THU0587

COMPARING OF TWO DISTINCT SEVERITY SCORES FOR EVALUATING DISEASE SEVERITY IN FAMILIAL MEDITERRANEAN FEVER

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Background: Familial Mediterranean Fever (FMF) is a chronic hereditary disease which is characterized by recurrent attacks of fever accompanied by serositis. Severity of disease is related with morbidities such as amyloidoses and chronic renal failure.

Objectives: The aim of this study was to evaluate disease severity with two disease severity scores in FMF patients, and compare them.

Methods: The study included 160 patients with FMF. Demographic and clinical data were recorded in the patients' form. The patients' disease severity were evaluated with International Severity Scoring System for FMF (ISSF) and The Second Set of FMF severity score (F-SS-2).

Results: A total of 160 patients, comprising of 106 males (66.3%) and 54 (33.8%) females with a mean age of 33.5 ± 12.2 years were evaluated. Mean disease duration was 16.6 ± 10.3 years. Other demographic and clinical characteristics of the patients were shown in Table 1. According to ISSF, 67 (41.9%) patients were classified as having mild disease, 80 (50.0%) patients as intermediate disease and 13 (8.1%) patients as severe disease. On the other hand, 59 (36.9%) patients were classified as having mild disease, 41 (25.6%) patients as intermediate disease and 60 (37.5%) patients as severe disease according to F-SS-2 score. Higher rates of patients were found having severe disease according to F-SS-2 compared with ISSF (p<0.001). Also, lower rates of patients were scored as having intermediate disease with F-SS-2 compared with ISSF (p<0.001) (Table 2).

Table 1. Sociodemographic and clinical characteristics of patients (n=160)

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Gender, n (%)</th>
<th>Males</th>
<th>Females</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), mean ± SD</td>
<td>33.5 ± 12.2</td>
<td>35.6 ± 10.3</td>
<td>0.005</td>
<td></td>
</tr>
<tr>
<td>Disease duration (years), mean ± SD</td>
<td>23.3 ± 12.7</td>
<td>26.1 ± 12.7</td>
<td>0.13</td>
<td></td>
</tr>
<tr>
<td>Age of diagnosis (years), mean ± SD</td>
<td>22 ± 8.7</td>
<td>22 ± 8.7</td>
<td>0.98</td>
<td></td>
</tr>
<tr>
<td>Delay of diagnosis (years), mean ± SD</td>
<td>6.2 ± 7.9</td>
<td>6.7 ± 7.9</td>
<td>0.48</td>
<td></td>
</tr>
<tr>
<td>Age of symptom onset (years), mean ± SD</td>
<td>35.9 ± 11.8</td>
<td>36.9 ± 11.8</td>
<td>0.98</td>
<td></td>
</tr>
<tr>
<td>Dose of colchicine (mg/kg/day), mean ± SD</td>
<td>67 (41.9)</td>
<td>75 (46.9)</td>
<td>0.98</td>
<td></td>
</tr>
<tr>
<td>ISSF Score (%, %)</td>
<td>Mild</td>
<td>67 (41.9)</td>
<td>Intermediate</td>
<td>80 (50.0)</td>
</tr>
<tr>
<td>F-SS-2 Score (%, %)</td>
<td>Mild</td>
<td>59 (36.3)</td>
<td>Intermediate</td>
<td>41 (25.6)</td>
</tr>
</tbody>
</table>
Clinical phenotypes of IgG4-related disease

A literature review and meta-analysis of different clinical phenotypes were described in a multinational and ethnically variable cohort. The review aimed to identify how the clinical presentation of IgG4-related disease (IgG4-RD) may help clinicians improve disease management.

**Background:** Knowing the regional phenotypes of IgG4-RD is crucial. The influence of race could modify the clinical presentation of IgG4-RD. Knowing the regional phenotypes of IgG4-RD may help clinicians improve disease management.

**Methods:** A systematic review and meta-analysis of 160 English-speaking studies including 95 retrospective case series, 14 prospective case series, and 3 systematic reviews were included. The patients were from three continents: Africa, Asia, and Europe.

**Results:** Among the 160 included studies, the majority was retrospective (80.6%). The representation of each clinical phenotype was: HBP 14%, RA 25%, HNL 19%, MIK 6%, and systemic 7%. Forty-two patients (42%) had elevated serum IgG4. The most commonly involved tissues were: retroperitoneum (35%), lymph nodes (19%), head and neck (18%), salivary glands (16%), and pancreas (14%).

**Conclusion:** The Spanish IgG4-RD population was mainly ethnically Caucasian (86%), followed by African/Middle Eastern (5%). Men were predominant in all groups (71, 84, 70, and 70%). The representation of each clinical phenotype was: HBP 14%, RA 25%, HNL 19%, MIK 6%, and systemic 7%.

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.3691

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**REFERENCES:**


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**THU0589**

**FREQUENCY, CHARACTERISTICS AND CLINICAL DETERMINANTS OF “PRODROME” IN FAMILIAL MEDITERRANEAN FEVER PATIENTS**

Hakan Babaoglu, Nuh Atas, Ozkan Varan, Hasan Satıç, Reyyhan Bilici Salman, Aslıhan Avanoglu Güler, Hasan Karadeniz, Beran Goker, Seminur Hazez Daroglu, Mehmet Akıl Oztürk, Abdukhrameh Tufan, Gazi University Faculty of Medicine, Department of Internal Medicine Rheumatology, Ankara, Turkey.

**Background:** Prodrome was defined by the presence of manifestations that precede an FMF attack and predict its emergence. This period might be turned to a window of the opportunity for the prompt treatment of impending attacks with fast-acting IL-1 inhibitors.

**Objectives:** To determine the frequency, characteristics and clinical determinants of prodrome in patients with FMF.

**Methods:** 401 FMF patients were enrolled in this cross-sectional study. We applied a questionnaire to the FMF patients about attack types, prodrome manifestations and latent time. Four hours was accepted as the cutoff point for prodrome as described in the literature, which is compatible with the pharmacokinetics of anakinra.

**Results:** The mean age was 37.7 ±11.0 years, and the disease duration was 20 years (3-58). 248 of the patients (61.8%) were female. MEFV gene mutations were achieved in 364 (90.8%) patients, of these 121 (30.2%) patients harbored homozygous exon 10 mutations. Patients with a latent time over four hours considered as prodrome positive (PP) patients (n=141). Male gender, homozygous MEFV mutations, peritonitis, pleuritis, and ELE were more pronounced in PP group. 25.9% of patients with peritonitis, 14.7% of patients with pleuritis, 13.2% with arthritis, and 5.5% with ELE had prodrome with variable latent time durations (median, 6.7-42), (6-48), (6-472), and 7.7 (4-30) hours, respectively.

Prodrome was found to be more common in those with peritonitis. Male gender, having peritonitis or arthritis were found to be the independent clinical determinants of having prodrome (RR 1.72 (1.07-2.76), P=0.02, 4.27 (1.80-10.1), P<0.001, 1.77 (1.04-3.04), P=0.04, respectively). Age, MEFV mutations, pleuritis and ELE were not found as clinical determinants of prodrome.

**Conclusion:** Especially male patients with peritonitis or arthritis tend to have prodrome more than other patients, and should be questioned. Prodrome positive patients are candidates for prevention of the impending attacks with on-demand treatments.

**Contents:**

**Table 1.** Patients demographics and disease characteristics

<table>
<thead>
<tr>
<th>Prodrome (+) (n=141)</th>
<th>Prodrome (-) (n=260)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>Female</td>
</tr>
</tbody>
</table>
| 37.7 (10.5)          | 37.8 (12.8)          | 0.92
| 78 (55.3%)           | 170 (65%)            | 0.05
| **Age at FMF diagnosis, years** | | 24(342) | 25(62) | 0.52
| **Disease duration, years** | | 21 (4-58) | 19 (3-58) | 0.08
| Fever                |                      |
| 0                    | 9 (3.5%)             | 0.03
| **Peritonitis**      |                      |
| 133 (94.3%)          | 97 (75.8%)           | <0.001
| **Pleuritis**        |                      |
| 92 (65.2%)           | 123 (47.3%)          | 0.01
| **Arthritis**        |                      |
| 103 (72.9%)          | 129 (49.8%)          | <0.001
| **Myalgia**          |                      |
| 0                    | 6 (2.3%)             | 0.09
| **Erysipeloid skin eruptions** | | 46 (32.6%) | 58 (22.3%) | 0.02
| **Homozgyous**       |                      |
| 57 (43.2%)           | 64 (27.6%)           | 0.02
| **M694V/M694V**      |                      |
| 50 (35.5%)           | 51 (19.8%)           | 0.01
| **M694V/M694I**      |                      |
| 19 (13.5%)           | 46 (17.7%)           | 0.19
| **M694V/M680I**      |                      |
| 13 (9.2%)            | 23 (8.8%)            | 0.98
| **M694V/I726A**      |                      |
| 12 (8.5%)            | 20 (7.7%)            | 0.88
| **M680I/6148Q**      |                      |
| 6 (4.3%)             | 15 (5.8%)            | 0.45
| **M680I/680I**       |                      |
| 6 (4.3%)             | 9 (3.5%)             | 0.76

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.3725

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**THU0588**

**CLINICAL PHENOTYPES OF IG4-RELATED DISEASE IN SPAIN**

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**Background:** Recently, several clinical phenotypes in IgG4-related disease have been described in a multinational and ethnically vary cohort. The objective of this study was to assess the clinical presentation of IgG4-related disease (IgG4-RD) in Spanish patients and assess the distribution among different clinical phenotypes.

**Methods:** Clinical data were obtained from the Spanish IgG4-RD registry (REERIGG4) from October 2013 to December 2018, including 9 centers. We reviewed demographic data and organ involvement. The assignment of clinical phenotypes was done by 2 experts, based on organ involvement and clinical manifestations, following Wallace et al. subsets. The phenotypes were: pancreatico-hepato-biliary (HPB), retropertioneum and aorta (RA), head and neck limited (HNL) and Misulciz and systemic (MS).

**Results:** The representation of each clinical phenotype was: HNL, followed by RA. The HBP phenotype was less frequent than in previous reports. The influence of region could modify the clinical expression of IgG4-RD. Knowing the regional phenotypes of IgG4-RD may help clinicians improve disease management.

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.3691

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**Table 2. Comparison between F-SS-2 and ISSF Score**

<table>
<thead>
<tr>
<th>F-SS-2</th>
<th>Mild</th>
<th>Intermediate</th>
<th>Severe</th>
<th>Total</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>37 (62.7%)</td>
<td>20 (33.9%)</td>
<td>2 (3.4%)</td>
<td>59 (100%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mild</td>
<td>22 (53.7%)</td>
<td>17 (41.5%)</td>
<td>2 (4.9%)</td>
<td>41 (100%)</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>8 (13.3%)</td>
<td>43 (71.7%)</td>
<td>9 (15.0%)</td>
<td>60 (100%)</td>
<td></td>
</tr>
</tbody>
</table>

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.3725
Background: Familial Mediterranean fever (FMF) is a disease with an onset before 20 years of age in 90% of the patients. However, late onset FMF defined as age of onset over 40 years is being recognised more frequently.

Objectives: To better define patients with FMF who had their first attack before age 40 and compare them with early onset patient group in Turkish population.

Methods: The files of 2180 FMF patients followed in a single center between 2008-2017 who have fulfilled Tel-Hashomer criteria, were reviewed with regard to age of onset 40 years and over (index patients, Group 1). For control purposes files before and after the index patients were browsed and first patients with an onset before age 20 years (Group 2) were included. The demographic, clinical and genetic characteristics are compared between these 2 subgroups.

Results: Patients with an onset after 40 years consisted 2.7% of our FMF population. 50 of the 59 patients with an onset 40 years or over were re-evaluated and compared with early onset group consisting of 100 patients (Table 1). The delay in diagnosis, and disease duration were significantly longer and number of patients with M694V homozygosity and M694V allele frequency were significantly more frequent among group 2. In general, phenotypes of both onset groups were similar, the only significant differences being the frequency of fever and myositis which were less common among group 1. Also response to colchicine was more pronounced in group 1. One other interesting observation was the low incidence of amyloidosis in a group with such a significant delay in diagnosis and thus treatment.

Table 1. Demographic, clinical and genetic features of the study groups

<table>
<thead>
<tr>
<th></th>
<th>≥40 years n=50</th>
<th>≤20 years n=100</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (F:M)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Present age (mean±SD) (yr)</td>
<td>32.1±17.9</td>
<td>26.3±7.5</td>
<td>NS</td>
</tr>
<tr>
<td>Mean age at onset (mean±SD) (yr)</td>
<td>45.6±5.2</td>
<td>8.7±4.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean age at diagnosis (mean±SD) (yr)</td>
<td>50.4±7.3</td>
<td>19.1±11.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Delay in diagnosis (mean±SD) (yr)</td>
<td>4.8±5.5</td>
<td>10.4±11.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mean disease duration (mean±SD) (yr)</td>
<td>11.5±6.4</td>
<td>23.1±10.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Abdominal pain, n (%)</td>
<td>44(88)</td>
<td>89(89)</td>
<td>NS</td>
</tr>
<tr>
<td>Chest pain, n (%)</td>
<td>7(14.0)</td>
<td>27(27.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Fever, n (%)</td>
<td>30(60.0)</td>
<td>81(81.0)</td>
<td>0.005</td>
</tr>
<tr>
<td>Arthritis, n (%)</td>
<td>12(24.0)</td>
<td>30(30.0)</td>
<td>0.25</td>
</tr>
<tr>
<td>Myalgia, n (%)</td>
<td>1(2.0)</td>
<td>12(12.0)</td>
<td>0.04</td>
</tr>
<tr>
<td>Amyloidosis, n (%)</td>
<td>1(2.0)</td>
<td>3(3.0)</td>
<td>NS</td>
</tr>
<tr>
<td>Positive family history, n (%)</td>
<td>33(66.7)</td>
<td>62(62.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Response to colchicine, n (%)</td>
<td>37(74.2)</td>
<td>93 (94.8)</td>
<td>0.014</td>
</tr>
<tr>
<td>M694V Homozygous, n (%)</td>
<td>2(4.5)</td>
<td>23(25.8)</td>
<td>0.003</td>
</tr>
<tr>
<td>N of M694Valleys</td>
<td>24(48)</td>
<td>82(82)</td>
<td>0.014</td>
</tr>
<tr>
<td>No mutation, n (%)</td>
<td>3(6.6)</td>
<td>2(2.2)</td>
<td>NS</td>
</tr>
</tbody>
</table>

Conclusion: FMF should be included among the differential diagnosis of patients over 40 years of age with recurrent autoinflammatory manifestations. Less than 3% of FMF patients experience their first attacks after 40 years of age. The frequency of M694V is significantly less in the late onset group, pointing out a milder disease.

Disclosure of Interests: None declared

Objectives: To identify predictors of relapse of IgG4-RD after induction therapy.

Methods: We retrospectively reviewed 57 patients diagnosed with IgG4-RD and treated with GC in our hospital between January 2004 and November 2018. Clinical features at baseline, including organ involvement and blood markers (total hemolytic complement [CH50], its fractions [C3 and C4], IgG4, IgG, IgE, anti-nuclear antibody, rheumatoid factor, C-reactive protein, soluble interleukin-2 receptor, eosinophil) were collected. We divided patients into 2 groups on the basis of clinical features and examined whether they relapsed. In this study, hypocomplementemia was defined as decreased serum C3, C4, or CH50 less than the lower limit of normal. A relapse was defined as any new or worsened state of disease activity that required an escalation in treatment (immunosuppressants and/or GC). The follow-up period was defined as 182 days.

Results: Forty-three men and 14 women (mean age 68.1 ± 10.9 years) were included. Both serum IgG4 and IgG were measured at baseline in all patients (mean IgG4 798.8 ± 873.1 mg/dL and mean Ig 2874.0 ± 1934.1 mg/dL, respectively). All of the serum C3, C4, and CH50 were measured at baseline in 34/57 patients (mean C3 75.7 ± 33.3 mg/dL; mean C4 14.8 ± 11.5 mg/dL; and mean CH50 37.0 ± 23.1 U/mL). Fifteen patients had at least one episode of hypocomplementemia, and 19 patients did not. Most patients had multiple organ lesions. The details of dominant lesions were as follows: Dacryoadenitis and/or sialadenitis (Mikulicz disease), 36/57 patients (63.2%); biliary or pancreatic lesion, 29/57 (50.1%); retroperitoneal fibrosis, 22/57 (38.6%); and renal lesion 16/57 (28.1%). All patients were given prednisolone and gradually reduced (mean induction dose 31.7 ± 9.8 mg/day). No patients received immunosuppressive agents. The follow-up period was defined as 182 days. Relapsed lesions were as follows: Mikulicz disease, 3/6 patients (50.0%); biliary or pancreatic lesion, 1/6 (16.7%); retroperitoneal fibrosis 1/6 (16.7%); and pulmonary lesion 1/6 (16.7%). Patients with hypocomplementemia had significantly shorter relapse-free survival than those without (p=0.039, Figure 1). Patients with decreased serum C4 or CH50 (less than the lower limit of normal) also had significantly shorter relapse-free survival than those without, but those with decreased serum C3 did not. Such a tendency was not seen in other blood markers (IgG4, IgG, IgE, anti-nuclear antibody, rheumatoid factor, C-reactive protein, soluble interleukin-2 receptor, eosinophil).

Conclusion: Hypocomplementemia at baseline in patients with decreased serum C4 or CH50 may predict relapse of IgG4-RD after prednisolone therapy.

REFERENCES:

Disclosure of Interests: None declared

THU0593

CLINICAL AND GENETIC FEATURES OF CHINESE ADULT PATIENTS WITH TUMOR NECROSIS FACTOR RECEPTOR-ASSOCIATED PERIODIC SYNDROME

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Background: Tumor Necrosis Factor Receptor-Associated Periodic Syndrome (TRAPS) is an autosomal dominant autoinflammatory disease, associated with the mutation of tumor necrosis factor superfamily member 1A (TNFRSF1A) gene, located on chromosome 12p13. TRAPS is usually diagnosed during pediatric age. However, adult-onset disease or diagnosis during adulthood has been occasionally described. Moreover, TRAPS has been hardly reported in the Chinese population. Herein, we aimed to characterize the clinical and genetic features of Chinese adult patients with TRAPS.

Objectives: Adult patients (≥16 years) suspected monogenic autoinflammatory diseases during the period April 2015 to October 2018, at the adult autoinflammatory disease center, Department of Rheumatology, Peking Union Medical College Hospital (PUMCH).

Methods: Clinical data were evaluated. Gene sequencing was performed in each patient to support the diagnosis and exclude other monogenic autoinflammatory diseases. Finally we compared the data with those from Japan and Europe.

Results: During the study period, 8 patients with TRAPS were diagnosed and followed-up. The ratio of male to female was 3:1. The median age of disease onset was 4 (0.5–38.5), and adult-onset was observed in 2 (25%) patients. The median time of diagnosis delay was 17.8 (1.5-50.5) years. There were seven Chinese Han and one Manchu patients. One patient had a family history of TRAPS. The most frequent symptom was fever (8, 100%). The attacks of 5 (62.5%) patients lasted more than 1 week, and the intervals of 7 (87.5%) patients were longer than 2 weeks. Skin involvement occurred in 6 (75%) patients, with maculopapular mentioned in 6 and erythema annulare presented in 3. Four (50%) patients had articulargia, while one had polyarthritis. 4 (50%) patients complained respectively of myalgia or headache. 4 (50%) patients experienced abdominal pain and one (12.5%) had vomiting. One (12.5%) patient had periorbital edema, while 3 (37.5%) had conjunctivitis. Up to 5 (62.5%) patients got nonspecific pharyngitis. No patient suffered from chest pain or amyloidosis. Eight gene variants were detected in TNFRSF1A gene. Heterozygous gene variants were found in 7 Chinese Han patients, and homozygous (c.769-23, T>C) happened to the Manchu patient. The variants included C58 (exon 2), G65E (exon 3), F298L (exon 3), C99G (exon 3), V202G (exon 6), c.769-23T>C (IVS8), S290I (exon 9) and m.1735A>G (non-coding region). NSAIDs were given to 2 patients, glucocorticoid or immunosuppressive agents given to 3 patients respectively, and etanercept to 5 patients. A complete response was found in all the 5 patients received etanercept. The effectiveness of other drugs were 50% in NSAIDs, 66.7% in glucocorticoid and immunosuppressive agents.

Conclusion: This is the first and largest case series of TRAPS in Chinese adult patients. It highlights the importance of screening TNFRSF1A gene in patients with unexplained periodic fever syndrome. Four novel TNFRSF1A variants, S290I, F298L, V202G and m.1735A>G in non-coding region, have been identified. The atypical clinical manifestations of our patients compared to those from Europe might be related to their low-incidence in the Chinese population.
Diagnostics and imaging procedures

Marta Mazzoni1,2, Silvia Merlo1, Angela Pistorio2, Stefania Viola2, Alessandro Consolaro1,2, Angelo Revelli1,2, Clara Malattia1,2. 1Università degli studi di Genova, Genova, Italy; 2IRCCS Istituto Giannina Gaslini, Clinica Pediatrica e Reumatologia, Genova, Italy; 3IRCCS Istituto Giannina Gaslini, Epidemiologia e Biostatistica, Genova, Italy.

Background: remission is becoming a realistic target in JIA, but clinical remission (CR) may not accurately reflect real absence of synovitis. It would be desirable to have instruments to predict the risk of relapse in patients in CR in order to establish the most appropriate therapeutic strategy. Despite in RA the role of imaging to predict disease flare is established, this field has remained almost unexplored in JIA.

Objectives: 1) to investigate the prevalence of musculoskeletal ultrasound (MSUS)-detected subclinical synovitis in JIA patients in CR; 2) to establish which and how many joints should be scanned to reliably assess remission; 3) to evaluate the persistence of subclinical synovitis over the time; 4) to investigate whether subclinical synovitis entails a risk of disease flare; 5) MSUS data will be integrated with serum levels of inflammatory biomarkers to develop a multidimensional measure of remission.

Methods: it is a longitudinal prospective 4 years study started on November 2017. So far we have enrolled 99 consecutive JIA patients who met the Wallace criteria for CR. For each patient 46 joints were scanned for synovial hyperplasia/joint effusion and PD signal, all graded semiquantitatively on a 0–3 scale independently by 2 expert ultrasonographers. Subclinical synovitis was defined when total synovitis score for each joint was ≥2. MSUS was performed at baseline and at 6 month follow up visit. At inclusion serum assays have been stored to determine levels of inflammatory biomarkers (S100A8/9-A12, bFGF, IL-6, IL-10, CXCL9-10, VEGF, YKL40). A flare of synovitis was defined as a recurrence of clinically active arthritis.

Results: 99 patients (79.8% F; median age 11.3 y; median disease duration 5.3 y; median CR duration 1.6 y) were included. Thirty-eight/99 (38.4%) patients had persistent oligoarthiritis; 34/99 (34.3%) extended oligoarthiritis; 22/99 (22.2%) polyarthiritis; 5/99 (5.1%) systemic arthritis. Fifty-nine/99 (59.6%) patients were in CR on medication. Subclinical synovitis was detected in 54/99 (54.5%; 95% CI: 45.2–65.5%) patients, PD in 18/99 (18.2%; 95% CI: 11.1–27.2%) patients; subclinical tenosynovitis in 7/99 (7.1%; 95% CI: 2.9–14%) patients. Subclinical synovitis was found more frequently in the ankle [31/54 (57.4%) patients] and wrist joints [17/54 (31.5%) patients]. No patients had subclinical synovitis in the hip. A 14-joint reduced count including bilateral knee, ankle (tibiotalar, subtalar and talonavicular joints), wrist (radiocarpal and intercarpal joints) and elbow joints, detected 92.6% of children with subclinical synovitis. Twenty-five/99 (25.2%) patients in persistent CR were reassessed with MSUS at a follow up visit (median follow up duration 7 months): 82.3% of patients showed persistent subclinical synovitis. Sixty-four/99 (64.6%) patients had a clinically follow up of at least 6 months and 9/64 (14%) patients experienced a disease flare (median time to flare 6.6 months). Six/9 (66.7%) patients who experienced a relapse had subclinical synovitis at baseline.

Conclusion: our preliminary results confirm the discrepancy between clinical and imaging remission and that clinical evaluation may not sensitive to detect an inflammation-free state. Bilateral US assessment of the elbow, wrist, knee and ankle joints is reliable to detect subclinical synovitis. So far, patients who have relapsed are a small percentage, but to extend follow up is crucial to test predictive value of MSUS. Imaging findings will be combined with serum biomarkers leading to the construction of a predictive model.
Background: The evaluation of structural damage with plain radiography is important to clinicians and patients. Standard scoring methods include the Sharp-van der Heijde (SVdH) and Ratingen methods [1] however these systems are time-consuming. Therefore, it is difficult to perform large cohort studies. We set out to develop an automated algorithm to identify bones on plain radiographs as a step towards developing automated quantification of structural damage for use on large datasets.

Objectives: To develop a novel algorithm to segment outlines of finger bones in hand radiographs.

Methods: 101 hand radiographs were gathered from the Bath longitudinal cohort (UK). All patients fulfilled the CASPAR criteria for Psoriatic Arthritis (PSA). None of the patients had damage on SVdH and Ratingen scoring (blinded). The metacarpal (MC), proximal phalanx (PP), middle phalanx (MP), and distal phalanx (DP) in the right index finger were delineated by a rheumatologist. These outlines were used to build a statistical model of the shape using a Gaussian Process Latent Variable Model (GPLVM) [2]. Bones are segmented by matching the shape on a radiograph to the statistical model.

Results: The performance of the matching algorithm was compared with a traditional algorithm (snakes) using the Adjusted Rand Score (ARND). The ARND score measures the similarity of the segmentation with the ground truth. A perfect segmentation has a score close to 1. We tested the algorithm on 9 PP, 9 MP and 8 DP and 6 MC bones in the right hand. The results are reported in Table 1. We report a mean improvement in ARAND of 0.19, 0.87, 0.43 and 0.30 for the PP, MP, DP and MC respectively.

Conclusion: We report a reliable algorithm for the identification of metacarpal, proximal, middle and distal phalanx bones of the hand. Future work will focus on using the output of the segmentation algorithm to track damage progression over time.

REFERENCES:

Table 1. Adjusted RAND scores for comparing our algorithm to a traditional one (snakes)

<table>
<thead>
<tr>
<th>Bone</th>
<th>Snakes</th>
<th>Johnsson</th>
<th>Shape matching</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>PP</td>
<td>0.70</td>
<td>0.95</td>
</tr>
<tr>
<td>Case 2</td>
<td>PP</td>
<td>0.89</td>
<td>0.96</td>
</tr>
<tr>
<td>Case 3</td>
<td>PP</td>
<td>0.82</td>
<td>0.96</td>
</tr>
<tr>
<td>Case 4</td>
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<td>Case 5</td>
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<td>PP</td>
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<td>Case 7</td>
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<td>0.96</td>
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<tr>
<td>Case 8</td>
<td>PP</td>
<td>0.74</td>
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</tr>
<tr>
<td>Case 9</td>
<td>PP</td>
<td>0.88</td>
<td>0.97</td>
</tr>
<tr>
<td>Case 1</td>
<td>MP</td>
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<td>0.95</td>
</tr>
<tr>
<td>Case 2</td>
<td>MP</td>
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Key: Adjusted Rand Score (ARND) score measures the similarity of the segmentation with the ground truth. A perfect segmentation has a score close to 1. Metacarpal (MC), proximal phalanx (PP), middle phalanx (MP), and distal phalanx (DP)

Figure 1. Shape matching algorithm output demonstrating segmented outlines of the DP, MP, PP and MC in red, green, orange, and blue respectively.


THU0596

DEVELOPMENT OF AN AUTOMATED SEGMENTATION ALGORITHM TO IDENTIFY BONES OF THE HAND


Background: The evaluation of structural damage with plain radiography is important to clinicians and patients. Standard scoring methods include the Sharp-van der Heijde (SVdH) and Ratingen methods [1] however these systems are time-consuming. Therefore, it is difficult to perform large cohort studies. We set out to develop an automated algorithm to identify bones on plain radiographs as a step towards developing automated quantification of structural damage for use on large datasets.

Objectives: To develop a novel algorithm to segment outlines of finger bones in hand radiographs.

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Conclusion: We report a reliable algorithm for the identification of metacarpal, proximal, middle and distal phalanx bones of the hand. Future work will focus on using the output of the segmentation algorithm to track damage progression over time.

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Figure 1. Shape matching algorithm output demonstrating segmented outlines of the DP, MP, PP and MC in red, green, orange, and blue respectively.


THU0596

DIAGNOSTIC VALUE OF ULTRASOUND AND DUAL ENERGY COMPUTED TOMOGRAPHY TO ACHIEVE ACR-EULAR GOUT CLASSIFICATION CRITERIA IN REAL LIFE CLINICAL PRACTICE

André Raman1, Marie Schmitt1, Romaric Ne2, Pierre Emmanuel Berthod3, Hervé Devilliers3, Jean Francis Maillefert3, Paul Ornetti3, André Ramon1, Marie Schmitt1, Romaric Ne2, Pierre Emmanuel Berthod3, Hervé Devilliers3, Jean Francis Maillefert3, Paul Ornetti3. DOI: 10.1136/annrheumdis-2019-eular.589

Background: 2015 ACR/EULAR gout classification criteria (1) include ultrasound with double contour (DC) sign as key ultrasound features and dual energy computed tomography (DECT) with evidence of urate deposition. The positivity of either DECT or ultrasound allows 4 points in addition to others clinical and biological criteria to classify as gout is ≥8/23. However, in routine care, the imaging modality that should be promoted remains unclear between ultrasound or DECT.

Objectives: To validate a possible diagnostic algorithm for the clinical use of DECT and ultrasound in suspected gouty arthritis.

Methods: We conducted a single-center prospective study in the Rheumatology Department of Dijon University Hospital from July 2016 to December 2018, including all patients hospitalized for suspected gouty arthritis. Each patient received joint aspiration if possible, an ultrasound assessment (DC sign and/or tophus) and DECT scanning of symptomatic joints. All these examinations were performed blind of the clinical data and results of joint aspiration. The gold standard used for this study was the 2015 ACR/EULAR gout classification criteria. We have established two
US examinations of the IMT at both common carotids were performed by a rheumatologist expert in US, using a linear probe and an automatic method (cIMT) based on the radio-frequency technology. For the IMT, a cut-off point of 0.8 mm was adopted, according Mannheim cIMT Consensus.

Results: A total of 684 common carotids were assessed. In 65 (47.10%) out of the 138 patients with gout and 50 (47.62%) out of the 105 patients with asymptomatic hyperuricemia, US detected an increased cIMT and only 9 (0.09%) of the control group patients had an increased cIMT (p=0.0001). The regression analysis found a significant positive correlation between increased cIMT and disease duration in gout group (p<0.001) and between the level of uric acid and increased cIMT in asymptomatic hyperuricemic patients (p=0.009). No significant correlation was found with the other clinical and laboratory parameters. There was a significant difference in cIMT between in gout and control groups (p=0.0001) and between asymptomatic hyperuricemia and control group (p=0.0001).

Conclusion: Our results demonstrate that patients with gout and hyperuricemia without clinically evident cardiovascular disease have a high prevalence of atherosclerosis represented by the increased cIMT.

Disclosure of Interests: None declared

age and sex group). DECT has high sensitivity, specificity and diagnostic accuracy in detection of MSU coronary deposits and can be used as a feasible, quick, low dose and low risk screening tool to detect coronary gout. DECT cardiac scans should be included in the routine CT gout protocol. Performing CT Calcium score using dual-energy has the added value of coronary gout detection as part of cardiovascular risk assessment and workup.

REFERENCES:


Disclosure of Interests: Waleed Abdelatif: None declared, Brandon Chow: None declared, Savvas Nicolau Grant/research support from: The Department of Radiology, Vancouver General Hospital has a Master Research Agreement with Siemens Healthcare, Forcheim, Germany (non-pharmaceutical company).


THU0599

RESOLUTION OF VASCULAR INFLAMMATION IN PATIENTS WITH GIANT CELL ARTERITIS RECEIVING GLUCOCORTOICOIDS, METHOTREXATE OR TOCILIZUMAB TREATMENT-DATA FROM THE ITALIAN/GERMAN RIGA STUDY

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Background: 18F-FDG-PET/CT is a sensitive and comprehensive technique to diagnose giant cell arteritis (GCA) (1). This technique may be also very useful to test whether vascular inflammation in GCA has disappeared or not, judging effectiveness of anti-inflammatory treatment. However, the role of 18F-FDG-PET/CT in monitoring disease activity and judging disease remission is less well-established to date.

Objectives: RIGA is an observational 2-center study that addresses the resolution of vascular inflammation in patients with new-onset GCA that are treated with either glucocorticoid monotherapy (GLC), GLC/methotrexate (MTX) or GLC/tocilizumab (TOC).

Methods: Patients with newly diagnosed GCA with large vessel involvement were clinically documented, subjected to sequential 18F-FDG-PET/CT scanning and received treatment with GLC, MTX or TOC upon physicians’ decision. Images were graded as active, questionable active and inactive according to nuclear medicine physician opinion and additionally graded by PETVAS score proposed by Grayson et al. (0-27) (2). We performed a mixed effects linear regression analysis to estimate the change in the PETVAS score adjusted by baseline CRP level and tested for treatment group interactions. We compared the proportion of radiologic activity states according to the activity tracer uptake in the follow up 18F-FDG-PET/CT scan in three treatment groups with a chi-squared test.

Results: We included 48 patients (n=20 from Germany, n=28 from Italy) with a mean age of 66 years. At baseline 18F-FDG-PET/CT scan was graded active in 46 patients while it was graded as questionable active in the remaining 2 patients. The mean CRP level was 66.8 mg/L (min 1.2; max 233.2 mg/l) and the mean PETVAS score was 21.1 (min=10 max=27). 12 patients received GLC, 27 MTX and 9 TOC as primary treatment. Follow-up PET/CT scans were graded as active in 11, questionable in 16 and inactive in 21 patients. The mean CRP level at follow up was 12.4 mg/l (min 0.2; max 76.0) and the mean PETVAS score was 9.1 (min 0, max 27) with significant decreases in all 3 groups. The mean adjusted improvement in the PETVAS score (95%CI) was 13.0 (8.7 – 17.3) in GLC, 11.7 (8.9 – 14.6) in MTX and 11.8 (6.8 – 16.7) in TOC groups and interaction terms for treatment effect were not significant. However, only 17% of patients who received GLC showed no vascular activity in their follow up PET-CT compared to 53% of patients who received MTX or TOC (figure 1).

Conclusion: GLC, MTX and TOC significantly reduced vascular inflammation in GCA, but no significant differences between the three treatment strategies was found in this yet small population. However, when looking at complete resolution of vascular inflammation, MTX and TOC appear as being superior to GLC monotherapy, suggesting that addition of these agents right from the beginning of treatment of GCA may be beneficial to achieve complete control of vascular inflammation.

REFERENCES:


Disclosure of Interests: Verena Schönau Speakers bureau: Novartis (less than 2000 Euros), Jessica Roth: None declared, Koray Tasciilar: None declared, Jürgen Rech Grant/research support from: Bristol-Myers Squibb, Celgene, Chugai, GlaxoSmithKline, Janssen, Eli Lilly, Novartis, Roche, Sanofi Aventis, and UCB (in total more than $10,000), Speakers bureau: Bristol-Myers Squibb, Celgene, Chugai, GlaxoSmithKline, Janssen, Eli Lilly, Novartis, Roche, Sanofi Aventis, and UCB (in total more than $10,000), Daniela Schmidt: None declared, Torsten Kuwert: None declared, Filippo Crescentini: None declared, Luigi Boiardi: None declared, Massim Iliano Casali: None declared, Annibale Versari: None declared, Georg Schett: None declared, Carlo Salvarani Grant/research support from: Roche, Consultant for: Eli Lilly and Company, Roche, Abbvie, Francesco Muratore: None declared.

QUANTITATIVE INDEXES TO ASSESS THE INTERSTITIAL LUNG DISEASE, AND ITS EXTENSION, IN SJÖGREN’S SYNDROME

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Background: Intersitial lung disease (ILD) is the most frequent pulmonary impairment in Sjögren’s syndrome (SS). The diagnosis is challenging, as there are no standard tests (i.e. autoantibodies or pulmonary function tests) or symptoms. Chest CT is the gold standard. Semiquantitative visual scores (SQCT) estimate ILD extent, though burdened by relevant intra-, inter-rater variability. Quantitative chest CT (QCT) is a promising method to assess ILD severity.

Methods: in this multi-center, cross-sectional, and retrospective study, sub-intra-, inter-rater variability. Quantitative chest CT (QCT) is a promising method to assess ILD severity.

Results: 102 consecutive SS patients were enrolled. ILD prevalence was 36% (36/102). There was a difference in QCT indexes’ distribution in SS-ILD versus SS without ILD (p < 0.001). Moreover, SS-ILD patients with an ILD >20% (according to Goh score) had QCT indexes statistically different from those with a limited ILD extension (p<0.001). QCT indexes have a moderate to good correlation with Goh and Taouli scores (from 0.78-0.95) but size of vacuoles did not reveal significant differences in QCT indexes distribution were analyzed using non-parametric tests.

Conclusion: Different image parameters had different significance for representing the gland conditions. For parotid glands, fibrosis bands and hetero-ergenic structure were main parameters. For submandibular glands, fibrosis bands and size of vacuoles accounted for the change of glands. SQUS correlated with final pathology result.

REFERENCES:

THE ROLE OF INFRARED THERMOGRAPHY IN THE ASSESSMENT OF PERIPHERAL VASCULOPATHY AND IN THE THERAPEUTIC MANAGEMENT OF SYSTEMIC SCLEROSIS PATIENTS TREATED WITH SYNTHETIC PROSTANOIDS

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Background: Skin lesions represent the leading feature of systemic sclerosis (SSc), with Raynaud’s phenomenon (RP) the most frequent and early clinical manifestation of the disease. Digital vasculopathy severely affects SSc patients, lowering their quality of life and negatively impacting on their daily functions. Digital ulcers is associated with poor cardiovascular prognosis and decreased survival rate [1]. Nevertheless, standardized treatment strategies and non-invasive tools for the management of RP and SSc skin manifestations are badly needed.

Objectives: The aim of this study was a) to evaluate the efficacy of infrared thermography in the assessment of peripheral vasculopathy in a cohort of SSc patients treated with cyclic intravenous infusions with synthetic prostanoids b) to identify those patients who might benefit from an intensified infusional treatment protocol with prostanoids.

Methods: Twenty-six SSc patients [2], attending our Department for their routinely 28-days apart intravenous therapy with prostanoids (iloprost) based on the presence of severe secondary RP and/or digital ulcers, were enrolled in this study. Thermographic evaluation of both hands were made at baseline (T0), and at days 14 and 28 after the first prostanoid infusion (named T1 and T2, respectively). Statistical analyses have been performed and a p-value <0.05 was considered statistically significant.

DISCLOSURE OF INTERESTS: None declared
The thermographic assessment showed a substantial stability of the temperature values when comparing T0 and T1 (mean differences of the right hands 0.4 ± 5.6; mean differences of the left hands 1.2 ± 4.5), while they were significantly reduced when comparing T1 and T2 (mean differences of the right hands -3.1 ± 9.3, p=0.049; mean differences of the left hands -3.4 ± 8.5, p=0.012 respectively) (Figure 1A). When stratifying according to clinical manifestation, a higher differences in temperature variations were observed between T1 and T2 in SSc patients with systemic involvement, when compared to those with limited cutaneous SSc (mean of the differences of the right hands -5.0 ± 11; mean of left-hands differences -4.9 ± 11.5 Vs. mean right-hands differences -2.5 ± 11; mean left-hands differences -3.2 ± 8.6; p=0.035 respectively) (Figure 1B).

Conclusion: Thermography could represent a reliable, non-invasive, manageable and cost-effective method for the assessment and monitoring of peripheral vasculopathy in patients with SSc. These data also show that SSc patients with systemic involvement could benefit more from an intensified infusion protocol with prostanoids compared to SSc patients with a limited skin form of the disease. Thermography has shown excellent potential to be a reliable and objective outcome measures to facilitate clinical trials of novel treatments SSc-related RP.

Table 1 ANA positive rate and main karyotype distribution in AID group and health controls

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Homogeneous</th>
<th>Particle</th>
<th>Centromere</th>
<th>Nuclear</th>
<th>Cytoplasmic Granular</th>
<th>Nuclear Membrane</th>
<th>Mixed</th>
<th>Other</th>
<th>ANA negativity</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLE</td>
<td>2034</td>
<td>337(16.6)*</td>
<td>1328 (65.3)</td>
<td>23(1.1)</td>
<td>26(1.4)</td>
<td>86(4.2)</td>
<td>9(0.4)</td>
<td>23(1.1)</td>
<td>10(0.5)</td>
<td>190(9.3)</td>
</tr>
<tr>
<td>RA</td>
<td>973</td>
<td>186(19.1)</td>
<td>255(26.2)</td>
<td>16(1.6)</td>
<td>10(1.0)</td>
<td>49(5.0)</td>
<td>1(0.1)</td>
<td>0(0.0)</td>
<td>8(0.8)</td>
<td>448(46.0)</td>
</tr>
<tr>
<td>SS</td>
<td>309</td>
<td>34(11.0)</td>
<td>181(58.6)</td>
<td>13(4.2)</td>
<td>8(2.6)</td>
<td>15(4.9)</td>
<td>3(1.0)</td>
<td>10(3.2)</td>
<td>3(1.0)</td>
<td>42(13.6)</td>
</tr>
<tr>
<td>PSS</td>
<td>155</td>
<td>22(14.2)</td>
<td>271(17.4)</td>
<td>28(18.1)</td>
<td>42(27.1)</td>
<td>8(5.2)</td>
<td>2(1.3)</td>
<td>9(6.8)</td>
<td>2(1.3)</td>
<td>15(9.7)</td>
</tr>
<tr>
<td>MCTD</td>
<td>39</td>
<td>3(7.7)</td>
<td>30(6.9)</td>
<td>12(6)</td>
<td>0(0.0)</td>
<td>2(5.1)</td>
<td>0(0.0)</td>
<td>0(0.0)</td>
<td>0(0.0)</td>
<td>3(7.7)</td>
</tr>
<tr>
<td>PBC</td>
<td>137</td>
<td>10(7.0)</td>
<td>6(4.4)</td>
<td>17(12.4)</td>
<td>2(1.5)</td>
<td>36(26.3)</td>
<td>15(10.9)</td>
<td>4(3.0)</td>
<td>6(4.6)</td>
<td>3(2.2)</td>
</tr>
<tr>
<td>AIH</td>
<td>57</td>
<td>3(5.3)</td>
<td>13(22.8)</td>
<td>7(12.3)</td>
<td>0(0.0)</td>
<td>0(0.0)</td>
<td>0(0.0)</td>
<td>0(0.0)</td>
<td>0(0.0)</td>
<td>29(50.9)</td>
</tr>
<tr>
<td>AID</td>
<td>3704</td>
<td>586(15.8)</td>
<td>1840</td>
<td>105(2.8)</td>
<td>90(2.4)</td>
<td>196(5.3)</td>
<td>30(0.8)</td>
<td>91(2.5)</td>
<td>30(0.8)</td>
<td>736(19.9)</td>
</tr>
</tbody>
</table>

Note: The mixed type contains more than two karyotypes, and other types include spindle, centrosome, Golgi, cytoplasmic fiber, etc. * refers to number (percentage).

REFERENCES:

Disclosure of Interests: None declared

THU0603 SUITABILITY OF PET-CT IN REFRACTORY POLYMYALGIA RHEUMATICA

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Background: Polymyalgia rheumatica (PMR) is characterized by pain in the shoulders and hips, elevation of acute phase reactants and a rapid response to treatment with corticosteroids. Currently, there is no specific test for its diagnosis, and it presents a wide differential diagnosis. Positron Emission Tomography - Computed tomography (PET-CT) is a non-invasive technique, capable of measuring metabolic activity by locating and quantifying glucose consumption. The use of PET-CT in the study of neoplastic, infectious or inflammatory processes suggests that it may be a suitable technique for the study of the differential diagnosis of patients with PMR. It is unknown if there are differences in the result of the technique in patients with debut PMR vs. patients with cortico-resistant PMR.

Objectives: To describe the findings of PET-CT in patients with PMR. To analyze if there are significant differences between the results of patients with onset PMR and those of cortico-resistant PMR patients.

Methods: This is a cross-sectional prospective study performed in a cohort of patients with PMR. Out of all patients with PMR who do follow up treatment in our centre, the patients selected for this study included those who underwent a PET scan at the time of diagnosis and those who presented corticosteroid resistance (patients who did not respond to conventional therapy with corticosteroids or with a relapse with doses <7.5mg/day of prednisone or equivalent). Demographic, epidemiological data of the disease, treatment, as well as analytical parameters (CRP, ESR, Hematological and Biochemical) were collected from all the patients at the time the PET-CT was performed.

For the categorical variables, the chi-square test or Fisher’s exact test were used, as appropriate. In the case of quantitative variables, we used the comparison of the mean values, by means of a “t” test. The level of statistical significance was established for those values of p <0.05.

Results: 163 patients with a PMR diagnosis who had undergone a PET-TC were included, out of the total number of patients that we visited in our service. 52 (50.4%) patients had an onset PMR and 51 (49.9%) had PMR refractory to treatment. The demographic, clinical and serological characteristics of the patients at the time of PET-CT are shown in Table 1.

The PET-CT showed a distribution of uptake compatible with the diagnosis of PMR in 73 (70.9%) patients, vasculitis of large vessels in 16
was completed, along with visual analog scale (VAS). Ultrasound assessment was carried out by a rheumatology physician who was blinded to any other information. CSA of the median nerve was measured at the level of the proximal third of the pronator quadratus muscle and the largest CSA within the carpal tunnel. The presence or absence of tenosynovitis, Doppler signal and a bifid median nerve were noted. Steroid injection was carried out under indirect ultrasound guidance with 20mg depomedrone. Follow-up assessment was carried out 12 weeks post-injection. Repeat ultrasound scan was performed to measure the CSA of the median nerve, as before. Repeat Boston Questionnaire and VAS were recorded. After the second assessment those who had not responded adequately were referred on for consideration of surgical release.

Results: 52 patients attended for initial assessment, with 47 patients reattending for follow up. 53% of patients were discharged at follow up; the remainder were referred for consideration of surgery. 78.9% of patients met the criteria for defining CTS with a median nerve CSA 0.1cm², with 77% meeting this at the entrance to the carpal tunnel, and 55.8% at the level of the pronator quadratus muscle. A bifid nerve was noted in 12 patients.

There was no statistically significant relationship between the initial size of the median nerve on ultrasound and the change in Boston score. There was a statistically significant correlation between a decrease in the size of the median nerve at the entrance to the carpal tunnel and an improvement in the Boston score (r=0.42, p-value 0.003). There was no correlation between change in median nerve measurement and final outcome (discharged or referred to surgery). There was no relationship between the degree of entrapment on NCS and pre-test Boston score. There was a significant change in the Boston score of 0.944 post-injection (95% CI 0.41-1.48, p-value 0.001). There was a statistically significant change in the VAS score of 9.87 post-injection (95% CI 0.78-18.95, p-value 0.03). No patients demonstrated evidence of surrounding tenosynovitis or positive power doppler signal.

Conclusion: There is an overall improvement in symptoms of CTS, based on the Boston questionnaire, following corticosteroid injection. There is a clear role for the use of ultrasound to confirm diagnosis of CTS in symptomatic patients by measuring the CSA of the median nerve at the entrance to the carpal tunnel. There are no definite ultrasound or clinical prognostic indicators of response to injection. References:

Disclosure of Interests: Maria Emilia Corcia: None declared, Patricia Moya: None declared, Alejandro Fernandez: None declared, Berta Magalaeres: None declared, Ignasi Gich: None declared, Ana Milena Millan Arcejigas: None declared, HyeSang Park: None declared, Monica Paola Sarmentio: None declared, Ana Laiz Consultant for: Lilly, Novartis, AbbVie, MSD, UCB and Janssen, Speakers bureau: Lilly, Novartis, Abvive, MSD, UCB and Janssen, Cesar Diaz-Tornel: None declared, Josep Maria Liblot: None declared, Ivan Castelvial Consultant for: I received fees less than 5000USD as a consultant for Krem and Actelion, Paid instructor for: I received fees less than 2000USD as a lecturer for Boehringer-Ingelheim, Norvatis and Gebro, Speakers bureau: ND, Hector Corrominas: None declared


THU0605

SHEAR WAVE ELASTOGRAPHY MUSCLE STIFFNESS MAY DIMINISH AFTER CORTICOSTEROID TREATMENT

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Background: The use of corticosteroids is associated with several adverse effects including corticosteroid-induced myopathy (CIM). CIM may cause structural alterations to the myofibres, which support the hypothesis of altered muscle stiffness as seen in histological and preclinical studies. There is a significant change in the Boston score of 0.944 post-injection (95% CI 0.41-1.48, p-value 0.001). There was a statistically significant change in the VAS score of 9.87 post-injection (95% CI 0.78-18.95, p-value 0.03). No patients demonstrated evidence of surrounding tenosynovitis or positive power doppler signal.

Conclusion: There is an overall improvement in symptoms of CTS, based on the Boston questionnaire, following corticosteroid injection. There is a clear role for the use of ultrasound to confirm diagnosis of CTS in symptomatic patients by measuring the CSA of the median nerve at the entrance to the carpal tunnel. There are no definite ultrasound or clinical prognostic indicators of response to injection. References:

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THU0604

CARPAL TUNNEL SYNDROME: CAN ULTRASOUND PREDICT RESPONSE TO STEROID INJECTION?

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Background: Carpal tunnel syndrome (CTS) is the commonest nerve entrapment disorder of the upper limb. Diagnosis is often clinical, based on a suggestive history and physical examination. Neurophysiological studies correlate closely with clinical evaluation. The use of ultrasound has been evaluated, and a feature which consistently supports a clinical diagnosis of CTS is increased cross sectional area (CSA) of the median nerve within the carpal tunnel. Local injection with corticosteroid is generally accepted as the next step in those who remain symptomatic after conservative treatment with splinting and nonsteroidal anti-inflammatory drugs. If this is unsuccessful referral for consideration of surgery should be considered.

Objectives: To evaluate the utility of ultrasound in the assessment of CTS and identify predictors of response to injection.

Methods: Patients were recruited via primary care referrals to the rheumatology department. Inclusion criteria were age over 18 years, appropriate symptoms in the distribution of the median nerve for at least 3 months, and positive nerve conduction studies (NCS). Patients with evidence of tenar atrophy were excluded. At initial review a full symptom and medical history was taken. A Boston Carpal Tunnel Questionnaire

References:

Disclosure of Interests: Maria Emilia Corcia: None declared, Patricia Moya: None declared, Alejandro Fernandez: None declared, Berta Magalaeres: None declared, Ignasi Gich: None declared, Ana Milena Millan Arcejigas: None declared, HyeSang Park: None declared, Monica Paola Sarmentio: None declared, Ana Laiz Consultant for: Lilly, Novartis, AbbVie, MSD, UCB and Janssen, Speakers bureau: Lilly, Novartis, Abvive, MSD, UCB and Janssen, Cesar Diaz-Tornel: None declared, Josep Maria Liblot: None declared, Ivan Castelvial Consultant for: I received fees less than 5000USD as a consultant for Krem and Actelion, Paid instructor for: I received fees less than 2000USD as a lecturer for Boehringer-Ingelheim, Norvatis and Gebro, Speakers bureau: ND, Hector Corrominas: None declared

respectively (p<0.001). Muscle strength was generally preserved at follow-up. However, there were moderate to strong correlations (r= 0.54–0.96) between weaker muscle strength at follow-up and greater reduction in SWV.

**Conclusion:** The GCA patients showed a significant loss of muscle stiffness after 3 and 6 months of corticosteroid treatment. With further validation in larger samples, shear wave elastography may be useful for detecting subclinical CIM.

**REFERENCES:**


Disclosure of Interests: Abdurahman M. Alturahi: None declared, Ali Lyn Tan: None declared, Philip O’Connor: None declared, Paul Emery Grant/research support from: Pfizer, MSD, AbbVie, Bristol-Myers Squibb, Roche, Consultant for: Pfizer, MSD, AbbVie, Bristol-Myers Squibb, UCB, Roche, Novartis, Gilead, Sanofi, Sandoz and Lilly, Richard Wakefield: None declared


**CORRELATION BETWEEN ULTRASOUND AND STANDARD RADIOGRAPHY AND BETWEEN ULTRASOUND AND CLINICAL DATA IN RHEUMATOID ARTHRITIS**

**THU0607**

**PROLIFERATIVE GLOBULAR SYNOVITIS, A CHARACTERISTIC ULTRASONOGRAPHIC PATTERN OF SEROPOSITIVE RHEUMATOID ARTHRITIS**

Ana Belén Azuaga-Piríango, Beatriz Frade-Sosa, Roberto Gumucio, Katherine Cajiao, Stanislava Mandelikova, Raul Castellanos-Moreira, Virginia Ruiz, Raimón Sanmartí, Juan D. Cañete, Julio Ramirez. Hospital Clinic, Rheumatology, Barcelona, Spain

**Background:** Rheumatoid Arthritis (RA) and Psoriatic Arthritis (PsA) have a different ultrasound (US) patterns. Synovial changes are characteristic of RA patients and soft tissue changes are more frequently found in PsA. However, no previous studies have analysed if US findings differ between seropositive and seronegative RA patients.

**Objectives:** To analyse differences in the ultrasound pattern among patients with seropositive and seronegative RA. To assess if proliferative globular synovitis is characteristic of seropositive RA patients.

**Methods:** Retrospective Analysis. We collected clinical, epidemiological and ultrasound images of patients with RA who met American College of Rheumatology/European League Against Rheumatism 2010 criteria with bilateral carpal and hand ultrasonography carried out during the last five years. Synovial hyperechogenicity (SH) and Power Doppler signal (PD) in wrist and hand (1-5 metacarpophalangeal [MCP]) were evaluated. We calculated the SH score (sum of the SH degrees of each joint), PD (sum of the PD degrees of each joint) and the total score (sum of the score of SH and PD) for each patient. We also evaluated the presence of proliferative globular synovitis, defined as big synovial hyperechogenicity with exophytic growth and a convex upper limit.

**Results:** 145 RA patients were collected. 80% were women. Mean age was 59.06 (14.8) years and the mean time of disease evolution was 114.6 (112.8) months. 68.3% were RF positive and 74.5% ACPA positive. Overall, 115 of the 145 (79.3%) patients were seropositive for RF/ACPA. 53.1% had radiographic erosions. 73.1% used conventional synthetic Disease-modifying drugs (DMARDs), 29.7% biological therapy, and 57.2% low doses of corticosteroids (<5 mg prednisone). The mean DAS28 was 2.81 (1.14), the number of swollen joints was 3 (3.4), and the C reactive protein (CRP) was 0.99 mg/dl (1.6).

No significant differences between seropositive and seronegative patients in terms of disease activity (swollen joints count [SJC], tender joint count [TJC], CRP, DAS28), treatment (use of corticosteroids, DMARDs, biological), time of evolution or US scores (SH, PD and total scores) were found. Globular synovitis was present in 62% and 13.7% of seropositive and seronegative RA patients, respectively (p<0.0001). Globally, 75 (51.7%) out of 145 patients had “globular” synovitis by US (Figure 1). 71 out of 75 patients were FR/ACPA positive (94.6%). Only four patients with seronegative RA had this US pattern (p<0.0001). Furthermore, patients with “globular” synovitis had more erosions (72% vs 33%, p <0.0001), higher SJC (3.3 vs 2.5, p = 0.013) and higher SH and PD scores (p=0.0001).

**Conclusion:** The presence of proliferative globular synovitis was significantly associated with the presence of RF/ACPA in patients with RA. This US pattern identified a subgroup of RA patients with poor prognosis: more erosions and greater inflammatory activity both at clinical and ultrasound level.

**REFERENCES:**


**Disclosure of Interests:** Ana Belén Azuaga-Piríango: None declared, Beatriz Frade-Sosa: None declared, Roberto Gumucio: None declared, Katherine Cajiao: None declared, Stanislava Mandelikova: None declared, Raul Castellanos-Moreira: Speakers bureau: MSD, Lilly, Virginia Ruiz: None declared, Raimón Sanmartí Speakers bureau: PFIZER, SANOFI, LILLY, MSD, UCB, NOVARTIS, JANSSEN, Juan D. Cañete: None declared, Julio Ramirez: None declared

CAPILLAROSCOPIC DIFFERENCES IN PRIMARY BILARY CHOLANGITIS WITH OR WITHOUT SCLERODERMA AND RAYNAUD’S PHENOMENON, A PRELIMINARY STUDY

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Background: A high proportion of capillaroscopic alterations have been reported in patients with Primary Biliary Cholangitis (PBC) (1). Association with Raynaud’s phenomenon (RP) and/or scleroderma has been described in patients with PBC and Raynaud’s phenomenon (RP), possibility for antitopomerase antibodies (ACA) and overlap with another systemic autoimmune disease, the most frequent being Systemic Sclerosis (SSc) (association with a prevalence up to 17% of PBC patients called Reynolds Syndrome) (2). However, studies are scarce and not very detailed in terms of the differential capillaroscopic findings between patients with PBC with/without SSc and without RP.

Objectives: To analyze the differences between clinical, serological and capillary morphological alterations observed in three different groups of patients with PBC: patients with PBC alone (PBC-A), patients with PBC and RP (PBC-RP) and patients with Reynolds Syndrome (PBC-RS).

Methods: Pentagonal capillaroscopy was performed on 12 patients with PBC-A, 10 with PBC-RP and 13 with PBC-RS, who received follow-up in our systemic diseases and hematology monographic outpatient. Capillaroscopy was made with USB Digital Microscope Dino-Lite ® epiluminiscence video. The capillaroscopic alterations were according to a semiquantitative method. All patients were given a detailed clinical evaluation. Variables related to clinical, serological and capillaroscopic parameters were collected. A comparative study was done.

Results: Of the 36 patients analyzed, 32 (88.9%) were women, with no sex differences between the three groups. The median age at PBC diagnosis was 50 + -12.8 years in PBC-A group, 60.5 + -15 years in PBC-RP and 62 years in PBC-RS, showing significant difference between the first group and the other two (p = 0.012), 14 patients had other systemic diseases: 1 hemolytic anemia, 1 SLE, 2 Psoriasis, 1 PVI and 9 Sicca. The only clinical parameter with significant difference between the three groups was association with Sicca: 3 (25%) PBC-A, 5 (50%) PBC-RP and 12 (85.7%) PBC-RS, p 0.002. Twenty five (73.5%) patients had positive AMA, with no differences between the groups. All 11 patients who had ACA, were from the PBC-RS group. Statistically significant differences were observed between the capillaroscopic parameters were the presence of capillary dilatations [5 (41.7%) PBC-A, 5 (50%) PBC-RP, 11 (84.6%) PBC-RS, p 0.03] and pathological hemorrhages [1 (8.3%) in PBC-A, 2 (22.2%) PBC-RP, 11 (78.6%) PBC-RS, p <0.001] as well as the presence of a different capillaroscopic pattern (p <0.001): normal or nonspecific in 9 (75%) of PBC-A, 4 (44.4%) PBC-RP and 2 (15.4%) PBC-RS; connective tissue disease suggestive pattern in 3 (25%) of PBC-A, 5 (55.6%) of PBC-RP and 1 (7.7%) of PBC-RS; sclerodermiform pattern in 10 (76.9%) PBC-RS, and none of the other two groups. We did not find significant differences in the presence of simple tortuositities, complex tortuosities, branched capillaries or capillary loss. No capillaroscopic parameters correlated with other systemic diseases.

Conclusion: This preliminary study shows an evolutionary trend in some clinical (age at PBC diagnosis, sicca association) and capillaroscopic parameters (capillary dilatation, hemorrhages, general capillaroscopic pattern) in patients with PBC-A, PBC-RP and PBC-RS, which may suggest three different phenotypic expressions of the same pathogenic process.

REFERENCES:

Disclosure of Interests: None declared

ULTRASOUND AS A USEFUL TOOL IN THE DIAGNOSIS OF RHEUMATOID ARTHRITIS IN PATIENTS WITH UNDIFFERENTIATED ARTHRITIS

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Background: Nowadays, rheumatologists face challenges in finding an effective method to classify and treat patients with undifferentiated arthritis (UA). There is a need for new tools that could ensure accurate characterization of inflammatory processes in these patients.

Objectives: To investigate if a characterization of UA patients using US may help to fulfill the 2010 ACR/EULAR RA classification criteria in a real-life cohort.

Methods: We conducted a cross sectional study in two rheumatology care clinics. Patients not fulfilling the 2010 ACR/EULAR RA criteria were included. On the examination day, all patients underwent a physical examination, radiographs and US. The 7-joint US score (US 7) was adopted to scan all patients. US was performed according to EULAR criteria and interpreted by OMERACT definitions. Greyscale and power Doppler synovitis and tenosynovitis were scored. Bone erosions were also evaluated during the US examination.

Results: A total of 204 patients were included. The diagnosis was modified from UA to RA in 86 (42.1%) patients. The greater proportion of synovitis detected by US was the main parameter that allowed changing the diagnosis from UA to RA, and modified the final score of the 2010 ACR/EULAR classification criteria, from a mean (±SD) of 4.6 (0.5), by clinical examination, to 6.5 (0.6) by US. The changes in the score of the 2010 ACR/EULAR classification criteria were from score 4 to score 6 in 7% patients; from 4 to 7 in 24 (27.9%) patients; from 5 to 6 in 42 (48.8%) patients; from 5 to 7 in 5 (5.8%) patients and from 5 to 8 in 5 (5.8%) patients.

In addition to synovitis, a wide range of tenosynovitis and bone erosions were detected by US. Synovitis was more frequently detected in 2ndMCP followed by 2ndMTP and 5thMTP. The tendons of the wrist, 2nd and 3rd finger were the most affected. In relation to bone erosions, 2ndMCP and 5thMTP where the joints with more proportion of anatomical damage.

Conclusion: US demonstrated to be useful to help accurately classify UA patients previously diagnosed with UA.

Disclosure of Interests: Marwin Gutierrez: None declared, Chiara Bertolazzi: None declared, Edwin Castillo: None declared, Denise Clavijo Cornejo: None declared, Luis Carlos Rodriguez Delgado: None declared, Jaime Mendoza Torres: None declared, Carlos Pineda: None declared, Pedro Santos-Moreno: Grant/research support from: Dr Santos has received research grants from Janssen, Abbvie and UCB, Speakers bureau: Dr Santos has received speaker fees from Sanofi, Lilly, Bristol-Myers, Abbvie, Janssen and UCB

ANALYSIS OF ANTINUCLEAR ANTIBODY ANTIBODIES POSITIVITY AND THEIR MAJOR KARYOTYPES IN PATIENTS WITH AUTOIMMUNE DISEASES AND HEALTHY SUBJECTS

Qiujing Wei1, Yutong Jiang, Jiwen Xie, Jun Qi, Jianguo Gu, the Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China

Background: Autoantibodies, especially antinuclear antibodies (ANA), play an important role in the diagnosis and differential diagnosis of autoimmune disease (AID); disease monitoring, efficacy observation and pathogenesis research.

Objectives: Our aim was to investigate the rate of ANA positivity and their major karyotypes in different AIDs and healthy controls.

Methods: The distribution and positive rate of Antinuclear antibody (ANA) karyotypes detected by indirect immunofluorescence in 3704 patients with AID and 1073 healthy subjects were retrospectively analyzed.

Results: The positive rate of ANA in different AID groups was 90.7% (1845/2034) in SLE, 54% (525/973) in RA, 86.4% (267/309) in SS,
SERUM HIGHLY-SENSITIVE CARDIAC TROPONIN-I AND KNEE JOINT PAIN IN AN ELDERLY, HEALTHY
Arnd Kleyer1, Antonella Adinolfi2, Johann Williet3, Stefan Kiechl3, John Todd2, Matthew Budoff3.

We recently reported that serum levels of highly-sensitive cardiac troponin-I (hs-cTnI)- a specific structural myocardial biomarker- and independently predicted CAC progression in patients with RA. We here explored whether baseline evaluation of both hs-cTnI and a-b2GPI-IgA presence, high hs-cTnI independently predicts significant increase in coronary atherosclerosis burden.

Methods: Ninety five participants with a baseline plaque evaluation by coronary computed tomography angiography (CCTA) underwent follow-up assessment within 6.9±0.3 years. Coronary artery calcium (CAC) was demonstrated that presence of IgA antibodies against beta2-glycoprotein-1 (a-b2GPI-IgA, an apolipoprotein readily expressed in human atherosclerotic plaque) associated with baseline coronary artery calcium (CAC) scores and independently predicted CAC progression in patients with RA.

Objectives: We here explored whether baseline evaluation of both hs-cTnI and a-b2GPI-IgA better predicts CAC progression than either of them in isolation.

Methods: Ninety five participants with a baseline plaque evaluation by coronary computed tomography angiography (CCTA) underwent follow-up assessment within 6.9±0.3 years. Coronary artery calcium (CAC) was quantified by the Agatston method. Hs-cTnI and a-b2GPI IgA Ab were assessed on the day of baseline CCTA; the latter were reconfirmed 12 weeks later, if positive. CAC change was evaluated by the MESA method as the natural logarithm plus 25 difference [(ln CAC (follow-up)+25) – (ln CAC(baseline)+25)]. Generalized linear models evaluated the effect of hs-cTnI, a-b2GPI-IgA and their interaction on CAC change. Models were adjusted for age, hypertension, waist-to-height ratio (obesity indicator), cumulative inflammatory burden (time-averaged C-Reactive protein), total prednisone dose and duration of statin exposure from baseline to follow-up scan.

Results: Baseline cTnI was higher in a-b2GPI-IgA positive compared to negative patients [median (IQR) of 1.9 (1.3-1.7) vs. 1.4 (1.3-1.7) respectively, p=0.043]. Hs-cTnI alone did not independently predict CAC change (β=0.214, p=0.132) in the multivariable model whereas a-b2GPI-IgA presence did (β=0.454, p=0.003). There was a significant interaction between hs-cTnI and a-b2GPI-IgA on CAC progression (Wald Chi-square=4.19, p=0.041); high hs-cTnI (>1.5pg/ml) predicted significantly greater CAC change in a-b2GPI-IgA positive patients but not in negative ones [estimated marginal mean difference (IQR)=0.36 (0.12-0.59), p=0.03 and figure 1].

Conclusion: Baseline hs-cTnI in isolation is not predictive of CAC progression in patients with RA; however, in the context of a-b2GPI-IgA presence, high hs-cTnI independently predicts significant increase in coronary atherosclerosis burden.

Disclosure of Interests: None declared.

Disclosure of Interests: None declared, Joel Estis Employee of: Singulex, John Todd Employee of: Singulex, Matthew Budoff: None declared.


THU0611

ERYTHROCYTE ANIONIC MEMBRANE PROTEINS ARE ASSOCIATED WITH AGING AND AGING-ASSOCIATED PATHOLOGY IN THE KNEE JOINTS

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Background: Aging is associated with decreased muscle strength and diminished quality of life. As aging occurs, knee pain may increase due to OA. The knee is the most commonly involved joint in OA, and it is the primary location for aging-associated pathology which is related to OA pain.

Objectives: To determine the relationship between erythrocyte anionic membrane proteins and knee pain in older individuals.

Methods: 55 volunteers ages 65-84 years were divided into two groups; (1) individuals with knee pain and (2) individuals without knee pain. Erythrocyte anionic membrane proteins were measured using a multiplex immunoassay system.

Results: Individuals with knee pain had significantly higher levels of erythrocyte anionic membrane proteins compared to individuals without knee pain.

Conclusion: Erythrocyte anionic membrane proteins may be a potential biomarker for knee pain in older individuals.

Disclosure of Interests: None declared.


THU0612

KNEE JOINT PAIN IN AN ELDERLY, HEALTHY POPULATION IS ASSOCIATED WITH INFLAMMATORY ARTICULAR AND ENTHESEAL CHANGES DETECTED BY ULTRASOUND

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Background: Knee pain is highly prevalent in elderly and influences quality of life. Pathogenesis of knee pain in such population is commonly related to osteoarthritis (OA). It is yet unclear however, which pathological lesions in the knee contribute most to symptomatic disease.

Objectives: To define the articular and enthesal inflammatory and structural changes that contribute to knee pain in an elderly healthy population using Power Doppler ultrasound (PDUS).

Methods: All subjects (≥65 years) were part of the prospective long-term population-based Bruneck Study (1) and received a clinical and ultrasound investigation of both knees. Ultrasound was performed by an independent investigator unaware of clinical symptoms. Knee entheses (quadiceps insertion, proximal and distal patella insertion) and joint cavity were assessed. Demographic variables were recorded in all individuals. Pain sensation during knee palpation was collected and participants were asked to complete a standardized pain questionnaire for knee joints (Knee injury and osteoarthritis outcome score [KOOS], question P1-P9). Joint changes (synovial hypertrophy, power doppler [PD] signal, joint effusion, baker cysts, osteophytes) were assessed using a GE Logic E

Disclosure of Interests: None declared.

MRI AND ULTRASOUND (US) ASSESSMENT OF both TMJ inflammation and damage 3 but US is a widely used diagnostic tool in rheumatic patients as well as hypoechogenecity were also recorded. All ultrasound abnormalities were scored using validated OMERACT scores. The prevalence of observed changes was compared between subjects without palpation and patients with pain. By summing up the articular and enthesal changes a total score was calculated and correlated with the KOOS pain values.

Results: A total of 303 (Male 154; Female 149) aged participants (age: 75.3±6.9 years) underwent ultrasound examination of both knees. Knee tenderness was found by 30/149 (20.1%) women and 15/154 (9.7%) men. Ultrasound effusion (p=0.010), synovial hypertrophy (p=0.001), PD synovial activity (p=0.003) and osteophytes (p=0.001) were more prevalent in women with knee tenderness than without. In men, knee tenderness was associated PD synovial activity (p=0.0014), and enthesal calcification (p=0.0002). Presence of more than 1 ultrasound pathology was associated with lower KOOS pain values, indicating higher impact on symptoms. This was observed in both women (r=-0.285, p=0.021) and men (r=-0.298, p=0.008).

Conclusion: In an elderly healthy population, knee pain is associated with the presence of joint and enthesal inflammatory lesions.

REFERENCES:


Disclosure of Interests: David Simon Grant/research support from: Novartis, Consultant for: Lilly, Speakers bureau: Janssen, Arnd Kleyer Grant/Research support from: Lilly, Consultant for: Lilly, Speakers bureau: Abbvie, Antionella Adinolfi; None declared, Stefano Lorenzi: None declared, Claudia Lomater: None declared, Yves-Marie Pers: Consultant for: Roche, Research support from: Novartis, Speakers bureau: Abbvie, Consultant for: Roche, Speakers bureau: Janssen, Arnd Kleyer: Grant/Research support from: Roche, Consultant for: Lilly, Speakers bureau: Abbvie, Consultant for: Janssen, Adriano Lercara: None declared, Mihaela Maruseac: None declared, Mari Stoenoiu: None declared


Table 1: MRI and US results are collected in Table 2.

<table>
<thead>
<tr>
<th>JIA</th>
<th>Non-JIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>n 11</td>
<td>n 7</td>
</tr>
<tr>
<td>Sex F, n (%)</td>
<td>8 (72.7%)</td>
</tr>
<tr>
<td>Age (ys), median (IQR)</td>
<td>23 (22-26)</td>
</tr>
<tr>
<td>Current age (ys), median (IQR)</td>
<td>22.3 (20.3 – 25.1)</td>
</tr>
<tr>
<td>Disease duration (ys), median (IQR)</td>
<td>13.2 (11.9-16.1)</td>
</tr>
<tr>
<td>TMJs tenderness, n (%)</td>
<td>9 (81.8%)</td>
</tr>
<tr>
<td>TMJs swelling, n (%)</td>
<td>7 (63.6%)</td>
</tr>
</tbody>
</table>

Table 2. Twelve out of 36 TMJs presented with damage on both MRI and US, 2 TMJs had damage on US but not on MRI and 13 TMJs had damage on MRI only; the concordance was discrete (k = 0.23 (0.0-0.48). Only 2 TMJs had inflammation on US, of which only one was confirmed by MRI. 12 TMJs were pathological on both MRI and US, 3 TMJs were pathological on US only and 13 TMJs on MRI only: the concordance was poor (k = 0.17 (0-0.43)). Se=48% (95%CI 0.28,0.68), Sp=73% (95%CI 0.47,0.79).

Conclusion: The concordance between MRI and ultrasound is not optimal, and existing TMJ US protocols are based on children. Further studies are needed to develop a suitable US protocol to detect TMJ involvement in adult patients as a screening tool.

REFERENCES:


Disclosure of Interests: None declared


Table 3: There was agreement between MRI and US regarding joint effusion and metatarsophalangeal (MTP) joints (2-5) and MCP (1-5) joints.

<table>
<thead>
<tr>
<th>JIA</th>
<th>Non-JIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>TMJs n 22</td>
<td>TMJs n 14</td>
</tr>
<tr>
<td>Inflammation on MRI, n (%)</td>
<td>11 (50.0%)</td>
</tr>
<tr>
<td>Joint damage on MRI, n (%)</td>
<td>16 (72.7%)</td>
</tr>
<tr>
<td>Pathological MRI, n (%)</td>
<td>16 (72.7%)</td>
</tr>
<tr>
<td>Inflammation on US, n (%)</td>
<td>2 (9.1%)</td>
</tr>
<tr>
<td>Joint damage on US, n (%)</td>
<td>10 (45.4%)</td>
</tr>
<tr>
<td>Pathological US, n (%)</td>
<td>11 (50.0%)</td>
</tr>
</tbody>
</table>

Table 4: There was agreement between MRI and US regarding joint effusion and metatarsophalangeal (MTP) joints (2-5) and MCP (1-5) joints.

Conclusion: The concordance between MRI and ultrasound is not optimal, and existing TMJ US protocols are based on children. Further studies are needed to develop a suitable US protocol to detect TMJ involvement in adult patients as a screening tool.
Results: Sixty-two consecutive ERA patients and 34 CTR were included in this study. Mean age and gender distribution were comparable between ERA and CTR (47.3±14.5 vs. 43.4±12.5). ACPA were present in 61%, rheumatoid factor in 54%, and bone erosions in 27% of ERA patients. 57% of ERA patients presented with FET and 0% of CTR (p<0.001). The delay between the first symptom and diagnosis, the DAS28CRP, SDAI, CDAI, CRP level, 44TJC, 44SJC, HAQ did not differ significantly between patients with FET involvement and those without. In univariate analysis, the presence of FET involvement was significantly associated with the presence of bone erosions (p=0.02), ACPA (p=0.002), rheumatoid factor (p=0.02) and tobacco use (p=0.02). In multivariate analysis, the presence of FET involvement was significantly associated with the presence of bone erosions (p=0.01), ACPA (p=0.001), RF (p=0.01).

Conclusion: FET is relatively frequent in ERA patients and it is not present in asymptomatic subjects. Our results show that FET involvement is associated with the presence of ACPA, rheumatoid factor and bone erosions, thus identifying patients with possibly more aggressive or severe disease at baseline.

REFERENCES:

Disclosure of Interests: Mihaela Maruseac: None declared, Adrien Nzeusseu: None declared, Maria Stoienoiu Grant/research support from: Abbvie, Roche, Wyeth DOI: 10.1136/annrheumdis-2019-eular.5629

THU0615

POSITIVE MRI OF THE SPINE AS IMAGING CRITERION IN THE ASAS CLASSIFICATION CRITERIA FOR AXIAL SPONDYLOARTHRITIS

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Background: MRI is a useful tool for the evaluation of patients with chronic back pain suspected of axial spondyloarthritis. As defined by ASAS classification criteria, MRI suggestive of axial spondyloarthritis is based on the presence of inflammatory lesions in the sacroiliac joints. However, inflammatory lesions in the spine may also occur. A consensus definition for a positive MRI-spine was developed by OMERACT MRI working group. In this consensus a positive MRI-spine is described as the presence of ≥ 3 inflammatory lesions in the corner of the vertebrae (bone marrow edema lesions), whereas each lesion needs to be present on ≥2 consecutive slices.

Objectives: The purpose of this study was to evaluate the presence of spinal inflammatory lesions on MRI performed between January, 2015 and December, 2015 in the Universidad de Chile Clinical Hospital.

Methods: Data from MRI performed between January, 2015 and December, 2015 in the Universidad de Chile Clinical Hospital was collected. The patients were derived by a physician as part of the study of chronic back pain.

Results: A total of 118 MRI were performed in this period, from which 8 showed evidence of spinal involvement without sacroilitis. The finding in MRI were: 3 patients with enthesitis of spinal ligaments, 2 patients with spondylodiscitis and 3 patients with bone marrow edema in the corner of the vertebrae. However, no patients fulfilled the OMERACT criteria for a positive MRI-spine (≥ 3 corner based inflammatory lesions). Patients with inflammatory lesions in the corner of vertebrae only showed 1 or 2 bone marrow edema sites. When we hypothetically added this criteria (assuming 2 bone marrow edema sites as a positive MRI-spine) to the ASAS criteria for axial spondyloarthritis, only one patient could be classified via the imaging arm.

Conclusion: Adding a positive MRI-spine as an imaging criterion to the ASAS-criteria for axial spondyloarthritis did not resulted in newly classified patients in this cohort. A combination of MRI-spine and MRI-SI had no incremental value compared with MRI-SI alone.

REFERENCES:


THU0616

WHOLE-BODY MRI OF PSORIATIC ARTHRITIS AND RHEUMATOID ARTHRITIS PATIENTS AND HEALTHY CONTROLS – INTERSCAN, INTRAREADER AND INTERREADER AGREEMENT AND DISTRIBUTION OF FINDINGS

Anna Enevold Floestrup Poulsen1, Mette Bjerrum Dalhusen1, René Panduro Poggenborg1, Iris Eshedi1, Simon Krabbe1, Daniel Gilintza2, Jakob Mollenbach Möller1, Mikelí Østergaard1, 1COPECARE, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark; 2Department of Diagnostic Imaging, Sheba Medical Center, Tel Aviv University, Tel Aviv, Israel; 3Department of Radiology, Herlev Hospital, University of Copenhagen, Herlev, Denmark

Background: Whole-body MRI (WBMRI) is a promising tool for monitoring disease activity in inflammatory joint diseases. Earlier studies have shown good correlation with conventional MRI and scoring systems for WBMRI have been developed [1,2]. However, the validation of WBMRI is limited; no studies have evaluated the agreement between repeated scans (inter-scan agreement) and only few studies have evaluated the intra- and interreader agreement.

Objectives: To validate WBMRI by evaluating the interscan agreement in patients with psoriatic arthritis (PsA), rheumatoid arthritis (RA) and healthy controls (HC) and to evaluate the intra- and interreader agreement and determine the distribution of pathologies in the subjects.

Methods: WBMRI was performed twice with a one-week interval in 14 patients with PsA, 10 with RA and 16 HC. Coronal images of shoulders, hips, hands and ankles/feet, and sagittal images of knees, ankles, feet and spine were obtained (STIR and pre- and post-contrast T1 weighted spin echo images). Images were anonymized and read in pairs with unknown chronological order by experienced readers (peripheral: IE; spine: SK). WBMRI was scored for 83 peripheral joints and for 33 peripheral entheses according to the OMERACT WBMRI scoring system [1] and according to the CarDen MRI spine scoring system [2]. Two image sets were re-analyzed for assessment of intra- and interreader agreement (Peripheral and spine: MO). Agreement was calculated on lesion level by percentage exact agreement (PEA) and Cohen’s kappa with squared weights, and for sum scores by absolute agreement single-measure intraclass correlation coefficient (ICC).

Results: The age in the PsA/RA/HC was median (range) 48/31-68/49/26-58/35-54 years and the symptom duration 10/0-24/7-23/4-24/NA years. WBMRI of the spine and peripheral joints and entheses generally showed moderate to almost perfect interscan agreement with a PEA ranging from 95-100%, kappa ranging from 0.71-1.00 and ICC ranging from 0.95-1.00 (Table 1). Intra- and interreader agreement showed moderate to almost perfect agreement with few exceptions (Table 2).

Conclusion: WBMRI of the spine and peripheral joints and entheses showed very good interscan agreement, implying that repositioning between examinations does not markedly affect scoring of lesions. Intra- and interreader agreement showed moderate to almost perfect agreement. The distribution of findings in PsA, RA and HC was determined.

REFERENCES:
Table 1. Interscan agreement between two WBMRI examinations performed with a one-week interval for all participants

<table>
<thead>
<tr>
<th></th>
<th>%-agreement</th>
<th>Kappa</th>
<th>ICC</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBMRI; Synovitis</td>
<td>Feet</td>
<td>96</td>
<td>0.83</td>
</tr>
<tr>
<td></td>
<td>Hands</td>
<td>96</td>
<td>0.84</td>
</tr>
<tr>
<td></td>
<td>Shoulders</td>
<td>92</td>
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<td>Fat</td>
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<tr>
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<td>New bone formation</td>
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BME: bone marrow edema, STI: soft tissue inflammation, ICC: intraclass correlation coefficient

Table 2. Intra- and interreader agreement for ten participants (4 PsA, 3 RA, 3 HC)

**INTRAREADER**

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<th></th>
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**INTERREADER**

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BME: bone marrow edema, STI: soft tissue inflammation, ICC: intraclass correlation coefficient
WRIST ULTRASOUND (US) PATHOLOGY IN EARLY RHEUMATOID ARTHRITIS (RA): OBSERVATIONS FROM AN EARLY INFLAMMATORY ARTHRITIS (EIA) DIAGNOSTIC SERVICE

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2St George’s University Hospital NHS Trust, Rheumatology, Tooting, United Kingdom;  
3Epsom and St Helier’s NHS Trust, Rheumatology, Carshalton, United Kingdom;  
4King’s College Hospital NHS Foundation Trust, Rheumatology, Orpington, United Kingdom

Background: To ensure a timely diagnosis of RA, diagnostic US is increasingly being utilized to detect subclinical pathology in order to implement treatment plans rapidly. There are several optimal synovitis scoring protocols in the literature but a consensus regarding a definitive system still eludes us. There are few studies that have focussed specifically on wrist US pathology in early RA. Hence, we assessed what the common wrist US pathologies are in patients diagnosed with early RA.

Objectives: To identify the patterns of wrist US abnormalities seen in patients diagnosed with early RA from our EIA service in a large urban London hospital.

Methods: Retrospective service review of patients seen in the EIA US diagnostic service at Croydon Health Services in South London. Patients diagnosed with RA (EULAR/ACR 2010 criteria) with wrist US synovitis/tenosynovitis (EULAR-OMERACT definitions) between Jan2017-Dec2018 were included. The US protocol in the EIA diagnostic service includes lateral and dorsal (long axis & short axis views) of the ulnarcapral(UCJ) & radiocarpal(RCJ) joints with views covering the radioulnar joints & ulnar-styloids and views of the extensor & flexor tendons. Images and reports were reviewed and correlations with rheumatoid factor(RhF), anti-CCP antibodies(CCP), CRP & ESR were also assessed.

Results: 86 patients with RA (meeting EULAR-ACR criteria) were found to have wrist pathologies on US. The commonest finding (36%) was moderate (grade 2) greyscale(GSUS) synovitis in the UCJ with almost all having moderate (grade 2) power Doppler(PDUS) synovitis (32%). Only a few (5/86) had more severe pathology with GSUS/PDUS (grade 3). 22% (19/86) had milder changes GSUS grade 1 with three quarters of these patients having concomitant PDUS signal. Just under 10% had RCJ US synovitis and 3 cases had radioulnar joint synovitis. Only 6% of the cohort had whole wrist joint involvement. Erosions were very uncommon (2/86). In total just under 25%(21/86) had tendon disease with roughly 70% affecting 1 tendon compartment and the others affecting 2 or more. Of those with tendon pathology, the two most commonly affected tendons were the 2nd [46%(10/21)] and 4th [38%(8/21)] extensor compartments. Extensor tenosynovitis was more common than flexor(46 v 4 cases). US synovitis ‘only’ was seen in 76%, US tendon disease ‘only’ in 7% and concomitant pathology in 17%. Correlation with inflammatory markers was not seen with only 3 patients presenting with significantly elevated CRP (>15) and ESR (>20). Though CCP was more commonly seen compared to RhF(32% vs 17%), just over half did not have positive antibodies.

Conclusion: Our observational study found that in early RA, mild-to-moderate GSUS and PDUS in the UCJ is the commonest wrist US pathology with tenosynovitis of the 2nd and 4th extensor compartments. Severe disease and erosions were very uncommon. The pattern of these US wrist pathologies are likely to reflect the initial disease course of these patients that present to our EIA service (i.e. early RA patients). Furthermore, biochemical markers do not seem to be useful in these patients and serology may not be present in over 50%. Therefore, clinicians who are running EIA diagnostic services with US should be expectant of milder-to-moderate US findings when diagnosing early RA and not be misled by the absence of more severe findings. Our understanding of US pathologies in the RA disease course therefore needs to be more nuanced and further work in other specific joint areas may help to elabo rate what US pathology is most common in early RA.

Disclosure of Interests: None declared


CLINICAL COMPARISON BETWEEN MAGNETIC RESONANCE TOMOGRAPHY AND X-RAY IN DIAGNOSIS OF EARLY RHEUMATOID ARTHRITIS

Mariljon Salokhiddinov, Muborak Salieva. Tashkent Medical Academy, Tashkent, Uzbekistan

Background: For decades, X-ray images have been used to help detect rheumatoid arthritis (RA) and to monitor for the progression of bone damage. In early RA, however, X-rays may appear normal although the
disease is active – making the films useful as a baseline but not much help in getting a timely diagnosis and treatment. Modern imaging techniques, including ultrasound and magnetic resonance imaging (MRI), which can reveal early, non-bony signs of RA that are invisible on X-ray

**Objectives:** To conduct a comparative analysis of the possibility of MRI in RA patients in the early diagnosis of the disease with the data X-ray of hands and feet

**Methods:** The study included 56 patients with a reliable diagnosis of RA aged from 17 to 66 years, with disease duration from 4 months to 1 year. Verification of the diagnosis of RA was carried out in accordance with the diagnostic APA criteria (1987). The criteria for the selection of patients was the presence of disease activity. Patients were mainly with the II degree of disease activity. All patients underwent radiography of the small joints of the hands and feet, and 28 patients underwent MRI with dominant hand.

**Results:** The study showed certain changes in the structures of the joint based on MRI in the early stages of RA. So, according to MRI of the brushes, it was revealed: thickening of the synovial membrane - in 23 (86%) patients; marginal erosion and subchondral cysts - in 21 (75%) patients; bone erosions - in 25 (90%) patients; phenomena of destruction of the articular cartilage (thinning, ulceration and destruction) - in 16 (57%) patients; effusion to the joints - in 19 (68%) patients and tenosynovitis in 18 (64%) patients. In turn, the radiological data of the hands and feet showed that erosive arthritis was found in 23 (41%) patients and marginal erosions in 22 (39%) patients.

**Conclusion:** Thus, MRI of the hands plays an important role in the early diagnosis of RA, since it allows visualizing the characteristic changes in all joint structures in RA. MRI is a highly effective diagnostic method in diagnosis of RA, which in combination with other methods of research helps to establish the diagnosis at an early stage diseases and timely appointment of adequate basic treatment unlike radiography

**REFERENCES:**


**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.2067

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**THU0620 THE PHYSIOLOGICAL FINGER JOINT ARCHITECTURE – AGE-RELATED INCREASE OF EROSIONS AND OSTEOPHYTES IN THE JOINTS OF HEALTHY INDIVIDUALS**

David Simon1, Andreas Berlin1,2, Koray Tasca1, Sara Bayat1, Klaus Engelke1, Jürgen Reich1, Camille Figueiredo1, Axel Hueber1, Georg Schett1, Am Kleyer1, Friedrich-Alexander University Erlangen-Nuremberg (FAU) and Universitätsklinikum Erlangen, Department of Internal Medicine 3, Rheumatology and Immunology, Erlangen, Germany; 2University Hospital Würzburg, Würzburg, Germany; 3School of Medicine from São Paulo University (FMUSP), Sao Paolo, Brazil

**Background:** The “normal” finger joint architecture has not yet been defined and could change in the course of life. Therefore the objective was to assess the physiological finger joint architecture of healthy individuals and the relation of structural changes to age and sex using high-resolution quantitative computed tomography (HR-pQCT) of the hands.

**Methods:** Healthy individuals without rheumatic diseases and other comorbidities were recruited through a field campaign and received HR-pQCT examination of the Metacarpophalangeal 2/3 and Proximal Interphalangeal 2/3 joints of one hand. The number of erosions and osteophytes was quantified across different sexes and age decades (6 decades within the age range of 21-80 years).

**Results:** 120 healthy individuals (10 women and 10 men in each decade) were recruited. Bone erosions [median (Q1-Q3), 1 (0-2)] and osteophytes (2 (1-4)) were found in both sexes without significant differences. However, structural changes increased with age: the overall incidence rate (IRR) for the number of erosions and osteophytes per age were 1.04 (95% CI 1.03-1.06, 95% CI 1.03-1.05), which indicates a 4% increase in the number of erosions and osteophytes per year. The use of the 3rd decade as the reference demonstrated that healthy individuals in the age decades from 50 years had higher IRR for erosion number (6th, 7th, 8th decade: 4.87 (2.20-11.75), 6.81 (3.08-16.46) and 6.92 (3.11-16.79)) compared to younger subjects (4th, 5th decade: 1.80 (0.69-4.87), 1.53 (0.59-4.10)). The IRRs of osteophytes also indicate a progressive increase after the fifth decade, with IRRs of 2.32 (1.32-4.17), 4.17 (2.38-7.49) and 6.86 (3.97-12.20) for the 6th, 7th and 8th decades, respectively.

**Conclusion:** Structural changes in the finger joints of healthy individuals are age-related. While being rare under 50 years of age, erosions and osteophytes accumulate above the age of 50, suggesting that the threshold between “normal” and “pathological” shifts with increasing age.

**REFERENCES:**


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**THU0619 THE VALUE OF MORPHOLOGICAL AND BIOCHEMICAL MAGNETIC RESONANCE IMAGING (MRI) OF RADIOCARPAL CARTILAGE FOR THE DIFFERENTIATION OF RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS**

Philipp Sewerin, Lino Sawicki, Christoph Schleich, Daniel Abbar, Matthias Schneider, Stefan Vordenbäumen, Benedikt Ostendorf. Universitätsklinikum Düsseldorf, Düsseldorf, Germany

**Background:** Using high-field MRI to differ morphologically between OA and RA.

**Objectives:** To evaluate the value of morphological and biochemical, contrast-agent free high-field (3 Tesla) MRI of the radiocarpal cartilage to differ between osteoarthritis (OA) and rheumatoid arthritis (RA).

**Methods:** The group consisted of 47 subjects, who were examined during the period from October 2016 to December 2017. The clinical dominant hand of 11 patients suffering from early rheumatoid arthritis (RA) (German Arthromark cohort, Ø 52.8years; min: 32; max 74) was compared with 120 healthy (OA) (Ø 48.55 ± 15.23 years, min: 34 years, max: 68 years, disease duration Ø 6 years ± 8.29) and 26 healthy volunteers (Ø 46.55 ± 17.55 years, min: 20 years, max: 79 years) were examined with a 3T MRI scanner, prospectively. Morphological and biochemical assessment of radiocarpal cartilage was performed using DESS, TrueFISP and T2* images.

**Results:** Morphological sequences demonstrated significantly higher cartilage damage in RA and OA compared to healthy controls (DESS: p = 0.01, p = 0.0004; TrueFISP: p = 0.02, p = 0.0001), while there was no significant difference between RA and OA patients. With biochemical MRI using T2* imaging, patients with OA showed higher cartilage integrity compared to patients with RA (p = 0.01).

**Conclusion:** Morphological and biochemical MRI of radiocarpal cartilage could be helpful to differentiate between RA and OA patients. Both, RA and OA, are associated with cartilage damage measured by morphological MRI of the hand. Hence, OA was associated with more loss of cartilage integrity compared to RA using biochemical MRI, whereby only early RA patients were analyzed in this first evaluation. Non-contrast-agent morphological and biochemical MRI could be a non-invasive tool to investigate cartilage integrity in RA and OA patients and could help to differ disease pattern in the future.

**Acknowledgement:** We would like to thank Erika Rädisch for the assistance in receiving the MRI scans.

**Disclosure of Interests:** Philipp Sewerin: None declared, Lino Sawicki: None declared, Christoph Schleich: None declared, Daniel Abbar: None declared, Matthias Schneider Grant/research support from: GlaxoSmithKline and UCB Pharma for performing the LuLa-study; Speakers bureau: Chugai, Stefan Vordenbäumen: None declared, Benedikt Ostendorf: None declared

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Disclosure of Interests: David Simon Grant/research support from: Novartis, Consultant for: Lilly, Speakers bureau: Janssen, Andreas Berlin: None declared, Klaus: None declared, Jürgen Rech Grant/research support from: Bristol-Myers Squibb and Celgene (greater than $10,000), Consultant for: Bristol-Myers Squibb, Celgene, Chugai, GlaxoSmithKline, Janssen, Eli Lilly, Novartis, Roche, Sanofi Aventis, and UCB (in total more than $10,000), Speakers bureau: Bristol-Myers Squibb, Celgene, Chugai, GlaxoSmithKline, Janssen, Eli Lilly, Novartis, Roche, Sanofi Aventis, and UCB (in total more than $10,000), None declared, Oscar Filgueira: None declared, Axel Hüber Grant/research support from: Novartis, Pfizer, Lilly, Consultant for: Lilly, GSK, Novartis, Janssen, Celgene, Abbvie, Roche, Speakers bureau: Lilly, Janssen, Novartis, Celgene, Biogen, Abbvie, BMS, Georg Schett: None declared, Amé Kleyer Grant/research support from: Lilly, Consultant for: Lilly, Speakers bureau: Abbvie

THU0621

VERY LOW PREVALENCE OF ULTRASOUND DETERMINED TENDON ABNORMALITIES IN HEALTHY SUBJECTS THROUGHOUT THE AGE RANGE: OMERACT ULTRASOUND MINIMAL DISEASE STUDY

Jeanette Trickey1, Ilfita Sahlbuddin4, Alessandra Bortoluzzi2, Annamaria Iagnocco1, Carlos Pineda1, Cesar Silentures-Cantù2, Cristina Reategui Sokolova3, Daniela Fodor1, Ellen-Marthe Haugé2, Esperanza Naredo1,4,5, Camille Figueroa6: None declared, Mohammed A Mortada: None declared, Philippe Carron1, Rosita Kallarava22, Ruth Wittke22, Sarah Ohrndorf13, Takeshi Suzuki24, Teodora Serban3, Maria-Antonietta d’Agostino15, Andrew Filer2, OMERACT US Group, 1IA, Birmingham, United Kingdom; 2UCL, London, United Kingdom; 3IHU, Liège, Belgium; 4INR, Mexico City, Mexico; 5UJFD, Madrid, Spain; 6UCL, London, United Kingdom; 7IHU, Liège, Belgium; 8CU, Berlin, Germany; 9JRC, Tokyo, Japan; 10APPM, Paris, France

Background: Tendon tenosynovitis (TS) is a common, often clinically undetectable finding in Rheumatoid Arthritis (RA). Recent data showed TS on ultrasound (US) has a role in predicting outcome in early disease and flare in clinical remission. However data is limited on US TS measured in healthy subjects (HS), none specifically encompassing the older age range when RA commonly presents.

Objectives: This OMERACT study aimed to determine prevalence of US TS and particularly PD abnormalities in HS throughout the age range.

Methods: Adult HS without: joint pain (VAS <10/100), hand osteoarthritis and PD of grade ≥1 was more common than DF grade ≥1 (p=0.001).

Conclusions: Low prevalence of TS or PD abnormalities in tendons of HS even in old age suggests US determined TS will be a robust tool in clinically managing RA.

REFERENCES:

Disclosure of Interests: Jeanette Trickey: None declared, Ilfita Sahlbuddin: None declared, Alessandra Bortoluzzi: None declared, Annamaria Iagnocco: None declared, Carlos Pineda: None declared, Cesar Silentures-Cantú: None declared, Cristina Reategui Sokolova: None declared, Daniela Fodor: None declared, Ellen-Marthe Haugé: None declared, Esperanza Naredo: None declared, Camille Figueroa: None declared, Mohammed A Mortada: None declared, Philippe Carron: None declared, Sarah Ohrndorf: None declared, Takeshi Suzuki: None declared, Teodora Serban: None declared, Maria-Antonietta d’Agostino: None declared, Andrew Filer: None declared

THU0622

MRI OF THE CRANIO-CERVICAL JUNCTION IN RHEUMATOID ARTHRITIS – DEFINITION OF NORMAL AND PATHOLOGICAL FINDINGS

Katharina Ziegele1, Christoph Korsing2, Matthias Bollow2, Kay Geert A. Hermann2, Tübingen: University medicine Tübingen, Tübingen, Germany; 2University-Hospital Aachen, Aachen, Germany

Background: In rheumatoid arthritis (RA), disease involvement at the cervical spine is common and may lead to malposition of the dens axis, resulting in severe neurological impairment. To date, malalignment is mostly described by X-rays.

Objectives: The aim of this investigation was to systematically define ossous and ligamentous MRI-findings in cranio-cervical RA in comparison to a control group without the disease.

Methods: MRI datasets of patients with cranio-cervical RA were identified retrospectively from the institutional image database and matched regarding age and gender with control patients. All image datasets were systematically reviewed for: position and morphology of dens axis (including erosions and osteitis); width and angle of the cranio-cervical joints; length, angle and visibility of peridental ligaments; vascularization of peridental

Results: Data from 999 HS and 144 RA patients were included.

<table>
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<tr>
<th>HS 18-39 y</th>
<th>HS 40-59 y</th>
<th>HS ≥60 y</th>
<th>RA</th>
<th>RA &gt; 12 y</th>
<th>RA ≥12</th>
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<td>n</td>
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<td>Age, y (IQR)</td>
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<td>49 (44-55)</td>
<td>68 (62-72)</td>
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<td>Female (%)</td>
<td>270 (66)</td>
<td>270 (83)</td>
<td>214 (67)</td>
<td>20 (67)</td>
<td>18 (67)</td>
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<td>DAS 28 CRP (IQR)</td>
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<td>10 (18-23)</td>
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<td>0 (0-0)</td>
<td>0 (0-0)</td>
<td>3 (0-18)</td>
<td>6 (3-39)</td>
<td>&lt;0.001</td>
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</table>

DF 1-5 TSH (g) >1 (%)

| DF 1-5 PD (g) | 3 | 2 | 0 | 2 | <0.001 | 0.06 |

ECU TSH grade >1 (%)

| ECU PD grade >1 (%)

| RA had 66/68 joint count |

Prevalence of TSH and particularly PD abnormalities in HS was very low at all ages, and was all grade 1 except in one individual ECU tendon. US TSH grade >1 was more common than DF grade >1 in the older HS groups, and less common in the 18-39 age group (p=0.011). TSH and PD of grade >1 were common in RA patients, with DF PD abnormalities more common in early disease (p=0.02).

Conclusion: Low prevalence of TSH or PD abnormalities in tendons of HS even in old age suggests US determined TS will be a robust tool in clinically managing RA.

Disclosure of Interests: Esperanza Naredo Consultant for: Abbvie, Speakerv, Puebulo: Abbvie, Roche, Bristol-Myers Squibb, Pfizer, UCB, Lilly, Novartis, Janssen, and Celgene GmbH, Florentin Ananu Vejo Consultant for: abbbie and novartis, Speakers bureau: abbbie, novartis, pfizer, san-do, eli lilly, ucb pharma, Garifallia Sakellariou: None declared, George Bruyn: None declared, Georgios Filipouf Speakers bureau: Laborest, Abbovie, BMS, Novartis, Ga La Paglia: None declared, Gustavo Leon: None declared, Helen Keen: None declared, Hilde Berner Hammer Grant/research support from: Abbvie, Pfizer and Roche, Paid instructor for: Abbvie, Pfizer, UCB, Novartis, Roche, Speakers bureau: Abbvie, Pfizer, UCB, Novartis, Roche, Ilaria Tinazzi: None declared, Irene Azziolin: None declared, Jacek Fliczinski: None declared, James Wilton: None declared, Kei Ikeda: None declared, Lene Terslev: None declared, Lea von Weender: None declared, Mohammad A Mortada: None declared, Philippe Carron: None declared, Sarah Ohrndorf: None declared, Takeshi Suzuki: None declared, Teodora Serban: None declared, Maria-Antonietta d’Agostino: None declared, Andrew Filer: None declared
RESULTS: A total of 40 patients were included in this retrospective case-control study, 20 in each group (RA and control). Position of dens was significantly more cranial in the RA group (dens to McGregor line: -1.62 mm for RA vs. 2.15 mm for controls, p<0.002; dens to McRae line: 3.20 mm for RA vs. 5.36 for controls, p<0.001). Visibility of alar ligaments was significantly lower in RA patients (fully visible in 10% of RA and 35% of control patients, p=0.012). Similarly, signal of transverse ligaments was normal in 5% of RA vs. 35% of control patients (p<0.001). There was no difference in length of the aforementioned ligaments (p<0.056).

Conclusion: With this case control study, MRI data on the position of the osseous and ligamentous structures of the cranio-cervical junction in patients with rheumatoid arthritis are available for the first time. Cranialization of the dens axis and signal changes of the transverse ligament and the alar ligaments are the most obvious findings. In a next step, the diagnostic value of the cervical spine in RA should be prospectively investigated and the available scoring system developed into an internationally established outcome measure.

Disclosure of Interests: [2] Katharina Ziegeler: None declared, Christoph Korsing: None declared, Mattias Bollow: None declared, Kay Geert A. Hermann: None declared, Katharina Ziegeler: None declared, Christoph Korsing: None declared, Mattias Bollow: None declared, Kay Geert A. Hermann

Methods: A retrospective cohort study was conducted using the National Health Information Database of Korea between 2008 and 2017. The enrollee had at least two claims with the RA diagnosis code, and had at least one prescription for TNFi since 2009 when national insurance of Korea started to cover the expense of IGRA. Exclusion criteria were organ transplantation, HIV infection, or active TB infection within 1 year prior to enrollment. The follow up was initiated on the day of the first prescription for TNFi, and ended on the date of the first claim on active TB, the date of death or December 31, 2017 whichever came first. The utilization of IGRA test method was confirmed by the codes of tuberculin skin test (TST) and IGRA claimed within 2 months prior to the initiation of the TNFi. Patients were categorized into 3 groups; no-test, TST only, IGRA (IGRA only or IGRA and TST). The incidence of active TB was defined as the presence of claims with diagnosis code for TB and the start of standard 3-drug or 4-drug first line anti-TB medication combination therapy.

Descriptive statistics on baseline characteristics of participants in each group were presented before and after application of weighting method using standardized mortality rate weight (SMRW). The incidence of active TB in each group was presented as event per 1000 person-year (PY). We treated death as competing event to the occurrence of TB. Therefore TB in each group was presented as event per 1000 person-year (PY).

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be addressed by clinical teams to improve adherence and clinical outcomes.

Table 1. Multivariate analysis. Factors associated to non-adherence behaviors of patients with rheumatic diseases.

<table>
<thead>
<tr>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (1-year increment)</td>
<td>1.00 (0.98 - 1.02)</td>
</tr>
<tr>
<td>Gender (female versus male)</td>
<td>1.04 (0.57 - 1.90)</td>
</tr>
<tr>
<td>Need of taking medication</td>
<td>1.40 (0.74 - 2.56)</td>
</tr>
<tr>
<td>Number of different medicines (1-unit increment)</td>
<td>1.00 (0.89 - 1.14)</td>
</tr>
<tr>
<td>IEXPC overall score (1-unit increment)</td>
<td>1.04 (0.90 - 1.21)</td>
</tr>
<tr>
<td>BMQ overall score (1-unit increment)</td>
<td>0.95 (0.91 - 1.00)</td>
</tr>
</tbody>
</table>

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Disclosure of Interests: María L. García Vivar; None declared, Javier de Toro-Santos: None declared, Lucía Pantoja; None declared, Cristina L. Lozano: None declared, Silvia García-Díaz: None declared, Sabela Fernández Employee of: MSD, Yvonne Mestre Employee of: MSD, Lidia Fe-Lucas Employee of: MSD, Luis Cea-Calvo Employee of: MSD


**THU0624**

UNDERSTANDING ETHNIC DIFFERENCES IN THE UTILIZATION OF NONSTEROIDAL ANTI-INFLAMMATORY DRUGS FOR OSTEOARTHRITIS

Ernest Vina1, Michael Hannon2, Jazmin Dagnino3, C. Kent Kwoh1. 1University of Arizona, Rheumatology, Tucson, United States of America; 2Pinney Associates, Pittsburgh, United States of America

Background: The prevalence of arthritis-attributable activity limitation, work limitation and severe pain are significantly higher among Hispanics than among non-Hispanic Whites (NHWs) in the US. While Hispanics are less likely to report regular use of nonsteroidal anti-inflammatory drugs (NSAIDs), reasons for this decreased NSAID use are unknown. It is also unclear whether there are ethnic differences in the use of both over-the-counter (OTC) and prescription NSAIDs.

Objectives: To determine: 1) if there are ethnic differences in the use of OTC and prescription oral NSAIDs for knee/hip osteoarthritis (OA); 2) if there are differences in familiarity with and perceptions of efficacy and risk of NSAIDs between Hispanics and NHWs; and 3) if patient attitudes/ beliefs about NSAIDs mediate observed ethnic differences in the use of NSAIDs for OA.

Methods: Participants ≥50 years of age with chronic frequent pain due to knee/hip OA completed structured interviews. Data on sociodemographic characteristics, clinical information, actual use of oral NSAIDs for OA treatment (last 6 months), and familiarity with NSAIDs (3 items, yes/ no response) were collected. Perceptions of efficacy (4 items) and risk (3 items) of NSAIDs were evaluated using five-category ordinal response scale questions. Responses were averaged, with higher values indicating higher perception of efficacy/risk. Fisher’s exact or Wilcoxon-Mann-Whitney tests were conducted to determine if knowledge and perceptions about NSAIDs differed by ethnicity. Multivariable logistic regression models were built to determine if ethnic differences in NSAID use were mediated by knowledge and perceptions about the medication.

Results: Among knee/hip OA patients, Hispanics (n=130), in comparison to NHWs (n=204), were younger (mean age 61.8 vs. 65.7) and less likely to have an annual income >$40K (21.6% vs. 56.5%). Hispanics, compared to NHWs, had lower odds of using an OTC NSAID (OR 0.57, 95% CI 0.36-0.90) but greater odds of using a prescription NSAID (OR 1.66, 95% CI 1.04-2.64) for OA. Hispanics, compared to NHWs, were also less likely to ever hear about OTC and prescription oral NSAID to treat OA or have a good understanding of either oral NSAID type as a treatment for OA (Table 1). Mean [SD] perceived efficacy of OTC and prescription oral NSAIDs were slightly lower among Hispanics than NHWs (2.91 [0.98] vs. 3.12 [0.88], p=0.0565; 3.03 [1.02] vs. 3.34 [0.87], p=0.0462; respectively). Mean [SD] perceived risk of prescription NSAIDs were lower among Hispanics than NHWs (2.44 [1.03] vs. 2.82 [1.01], p=0.0012). After adjustment for all familiarity with OTC NSAIDs questions, the association between prescription NSAID use and ethnicity remained significant (OR 2.62, 95% CI 1.51-4.54).

Conclusion: Among patients with knee or hip OA, Hispanics were less likely than NHWs to utilize an OTC oral NSAID as treatment for arthritis. They were also less familiar with the use of NSAIDs for OA treatment and less likely to believe in their efficacy. Patient familiarity and perceptions of OTC oral NSAIDs may mediate ethnic differences in the use of NSAIDs for knee/hip OA.

Table 1. Familiarity with NSAIDs.

<table>
<thead>
<tr>
<th></th>
<th>Hispanics (n = 130)</th>
<th>NHWs (n = 204)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>OTC NSAIDs, n (%)</td>
<td>100 (76.13)</td>
<td>192 (95.05)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Family/Friends Received It</td>
<td>67 (52.76)</td>
<td>127 (62.25)</td>
<td>0.1080</td>
</tr>
<tr>
<td>Have Good Understanding</td>
<td>79 (63.20)</td>
<td>168 (83.59)</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Prescription NSAIDs, n (%)</td>
<td>92 (74.80%)</td>
<td>173 (85.22)</td>
<td>0.0274</td>
</tr>
<tr>
<td>Family/Friends Received It</td>
<td>56 (45.16%)</td>
<td>107 (52.45)</td>
<td>0.2120</td>
</tr>
<tr>
<td>Have Good Understanding</td>
<td>76 (62.90%)</td>
<td>148 (74.00)</td>
<td>0.0462</td>
</tr>
</tbody>
</table>

*Fisher’s exact


**THU0625**

CAN WE IMPROVE INPATIENT REFERRALS TO RHEUMATOLOGY IN A TEACHING HOSPITAL IN THE UK?

Arani Vivekananthan, Zenab Sarwar Mateen, Roseanna Wheatley, Rachael Myers, Pippa Watson, Jayne Litte. Manchester University NHS Foundation Trust, Manchester, United Kingdom

Background: Inpatient referrals to rheumatology vary nationally from paper/electronic methods to phone conversations with the rheumatology registrar. In our Trust, which includes two large teaching hospitals in the UK, rheumatology referrals were hand written, faxed to secretaries and then given to the rheumatology registrar. This method was time consuming and referrals often lacked vital information. The referrer would also not know when the registrar had received the referral. A quality improvement project (QIP) in another UK hospital has shown an electronic referral system to be more efficient and safer for patients [1].

Objectives: This QIP aimed to evaluate the current system for inpatient referrals to two rheumatology departments within one large UK NHS trust and to identify aspects for improvement.

Methods: Two hundred and ten inpatient rheumatology referrals received between January 2018 - January 2019 were analysed retrospectively for inclusion of important information such as, patient location and referrer’s contact details.

Results: The review of current referrals identified several areas for improvement. The results are summarised in Table 1. The reasons for referrals ranged from swollen, painful joints to new rashes and medication reviews.

Table 1. Inclusion of important items in inpatient rheumatology referrals.

<table>
<thead>
<tr>
<th>Item</th>
<th>Inclusion of item in referral n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wythenshawe Hospital (n=105)</td>
<td>Manchester Royal Infirmary (n=105)</td>
</tr>
<tr>
<td>Date of referral</td>
<td>78 (74)</td>
</tr>
<tr>
<td>Time of referral</td>
<td>26 (25)</td>
</tr>
<tr>
<td>Name of referrer</td>
<td>102 (97)</td>
</tr>
<tr>
<td>Referrer’s contact details</td>
<td>38 (36)</td>
</tr>
<tr>
<td>Patient’s name, hospital</td>
<td>104 (99)</td>
</tr>
<tr>
<td>Patient location</td>
<td>95 (90)</td>
</tr>
<tr>
<td>Past medical history</td>
<td>62 (59)</td>
</tr>
</tbody>
</table>

A process mapping session was undertaken to identify how the referral system could be improved. An electronic referral system, via the local electronic patient record (EPR), was created. As well as ensuring that there is an audit trail and referrals are received in a timely manner, referers are provided with a proforma to direct them to supply the
relevant information. There is also functionality for the rheumatology team to reply to the referral with advice, which creates a new permanent document in the patient’s EPR. The Orthopaedic team, who are the first point of call for hot joints in our Trust, were consulted to ensure that there were not any unintended consequences as a result of this change. The form included the following sentence to avoid delays in patient care: “If gout is suspected, the referrer will be linked to guidelines and patient information sheets to assist best management whilst awaiting review. We would encourage others to consider their referral systems—could you improve yours?"

REFERENCES:

Disclosure of Interests: None declared

THU0626 SOCIAL NETWORKS AS A SOURCE OF INFORMATION FOR PATIENTS WITH RHEUMATIC DISEASES
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Background: Internet is an informative source for patients with different diseases. False information in social networks about health issues is a growing problem. Rheumatology is no stranger to this problem and there is a lot of false information regarding rheumatic diseases.

Methods: We create accounts on Facebook (FB) and Google unique for networks available to Spanish-speaking rheumatic patients

Results: Of the first 50 videos with more reproductions, 39 are of natural or home remedies such as vinegar, "morning", etc. and 35 videos indicate that they can cure RA. With the term "lupus", the most reproduced video is titled "God's tea, cure chronic tiredness, thyroid, arthritis, lupus and vertigo" (1.4 million reproductions). Of the first 50 videos with more reproductions, 31 correspond to natural or home remedies such as celery, thyme, diets among others and 29 videos indicate that they can cure lupus. With the term "fibromyalgia", the most reproduced video is entitled "I am 61 years old and this cured my arthritis, vertigo, fibromyalgia, lupus, chronic fatigue and the thyroid" (1.1 million reproductions).

Conclusion: YT and FB are social networks with a high content of false information. The majority of available videos promise to cure different rheumatic diseases (even several simultaneously). This is the first work of a line of research that seeks to highlight the high degree of misinformation. We will continue to analyze other diseases and social networks, to make publications and communications in different media and to alert local regulatory entities.

Disclosure of Interests: None declared

THU0627 VACCINATIONS IN PATIENTS WITH AUTOIMMUNE INFLAMMATORY RHEUMATIC DISEASES: STILL ROOM FOR IMPROVEMENT
Delphine Bertrand1, Solie Coenen2, Sofia Pazmino1, Veerle Stouten1, Diederik De Cock1, Kristen Van der Elst3, Rene Westhoven1,2,3, Marc Ferrante, Patrick Verschueren2, 1KU Leuven, Skeletal Biology and Engineering Research Center, Leuven, Belgium; 2UZ Leuven, Gastroenterology and Hepatology, Leuven, Belgium; 3UZ Leuven, Rheumatology, Leuven, Belgium

Background: Patients with autoimmune inflammatory rheumatic diseases (AIRD) have an increased risk for acquiring infections. Vaccines were developed to diminish the prevalence of vaccine-preventable infections. The EULAR recommendations for vaccination in adult patients with AIRD emphasise the importance of assessing the vaccination status of patients with AIRD.

Objectives: To determine the vaccination status of patients with AIRD, the reason for non-vaccination and the proportion of patients that are vaccinated according to the EULAR recommendations.

Methods: The single-centre cross-sectional COLOSSeUM study was conducted in a tertiary referral centre. Between August and December 2018, all consecutive patients with AIRD including Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA), Ankylosing Spondylitis (AS) and Juvenile idiopathic Arthritis (JIA) who visited the outpatient clinic were included. The vaccination status (influenza winter season 2017-2018, pneumococcal, tetanus toxoid and hepatitis B vaccine) and history of varicella zoster virus infection was determined using a one-page questionnaire which was completed by the treating rheumatologist after discussion with the patient.
The patients’ reason for non-vaccination was registered if applicable. Patients were classified as vaccinated according to the EULAR recommendations if they had a yearly influenza, an every-five-year pneumococcal and a decennial tetanus toxoid vaccine, the latter as recommended in the general population.

Table 1: The vaccination status of all patients

<table>
<thead>
<tr>
<th>Vaccination Status</th>
<th>RA (n=565)</th>
<th>PsA (n=175)</th>
<th>RA (n=144)</th>
<th>RA (n=152)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza vaccine (%)</td>
<td>Yes</td>
<td>438 (79.0)</td>
<td>90 (52.2)</td>
<td>43 (30.1)</td>
</tr>
<tr>
<td>No</td>
<td>57 (10.1)</td>
<td>35 (20.0)</td>
<td>72 (50.0)</td>
<td>64 (41.5)</td>
</tr>
<tr>
<td>Compliance with EULAR recommendations</td>
<td>Yes</td>
<td>50 (8.5)</td>
<td>0 (0.0)</td>
<td>7 (4.8)</td>
</tr>
<tr>
<td>No</td>
<td>140 (24.8)</td>
<td>12 (7.0)</td>
<td>29 (20.3)</td>
<td>28 (18.4)</td>
</tr>
</tbody>
</table>
| Vaccination status with JIA with a mean ± standard deviation age of 59.8 ± 13.6, 55.8 ± 14.3, and 35.0 ± 13.9 respectively. Of all included patients with AIIRD, 69.2% were vaccinated for influenza, followed by vaccination rates of 55.0%, 32.1% and 30.5% for tetanus toxoid, pneumococcal and hepatitis B vaccination, respectively (Table 1). In addition, 70.6% of patients with AIIRD had a history of varicella zoster virus infection. Various reasons for non-vaccination were reported, of which ‘No specific reason’ was the most common, closely followed by non-awareness of the need for pneumococcal vaccination. The compliance with EULAR recommendations was 18.5%. Of the 429 patients with AIIRD not vaccinated according to the EULAR recommendations, 68 (15.9%) patients were not compliant with all three of the vaccines, 136 (31.7%) were not compliant with 2 vaccines (1: pneumococcal and 2: influenza or tetanus toxoid vaccine), 148 (34.5%) were not compliant with 1 vaccine (103 pneumococcal, 41 tetanus toxoid and 4 influenza vaccine) and 77 (17.9%) patients were unaware of their vaccination status for at least 1 vaccine.

Conclusion: In our patients with AIIRD, the highest vaccination rate for recommended vaccines was observed for influenza (nearly 70%). Not being vaccinated for pneumococcosis was the main reason why patients did not comply with the EULAR recommendations. More attention is needed to determine and optimise the vaccination status of AIIRD patients and to increase the awareness regarding the pneumococcal vaccine.

Disclosure of Interests: None declared, Sofie Coenen: None declared, Sofie Pazmino: None declared, Veerle Stouten: None declared, Diederik De Cock: None declared, Kristien Van der Elst: None declared, Rene Westhoven: Grant/research support from: Bristol-Myers Squibb, Consultant for: Celtrion, Galapagos-Gilead, Marc Ferrante Grant/research support from: Janssen, Pfizer, Takeda, Consultant for: Abbvie, Boehringer-Ingehelm, Ferring, Janssen, Mitsubishi Tanabe, Takeda, MSD, Pfizer, Speakers bureau: Abbvie, Boehringer-Ingehelm, Chiesi, Ferring, Janssen, Lamepro, Mitsubishi Tanabe, MSD, Pfizer, Takeda, Tramedico, Tilotts, Zeria, Patrick Verschuuren Grant/research support from: unrestricted Pfizer Grant for Early RA research

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Methods: Incident IA cases were identified between January 1, 2007 and December 31, 2015, in patients enrolled in the Veteran Health Administration, using International Classification of Diseases codes and natural language processing. Patterns of treatment initiation and non-treatment with disease modifying anti-rheumatic drugs (DMARDs) were assessed in the 12-month follow-up period after the incident diagnosis.

Results: The population consisted of 12, 118 IA patients (9,711 RA, 1,472 PsA, 935 AS), with 91.3% males and a mean age of 63.7. In total, 58.2% of patients initiated a DMARD within 12 months after diagnosis (RA 60.0%, PsA 64.3%, AS 29.6%) (Figure). A DMARD was dispensed ≤30 days after IA diagnosis in 41.2% of patients and ≤90 days in 90.0% of patients. Rheumatology specialty care was accessed during the study period, prior to DMARD dispensation, by 82.7% of patients exposed to a non-biologic DMARD and 90.0% of patients exposed to a biologic DMARD. The percentage of IA patients with DMARD exposure during the 12-month follow-up period increased from 48.8% in 2008 to 66.4% in 2015.

Conclusion: Approximately one-half of patients received treatment with a DMARD within 90 days after their initial IA diagnosis. DMARD treatment rates during the initial 12 months after diagnosis increased between 2007 and 2015, but non-treatment remained common, particularly in patients with AS. Timely access to a rheumatologist is likely important for early DMARD treatment.

REFERENCES:

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THU0629 TREATMENT PATTERNS WITH DISEASE MODIFYING ANTI-RHEUMATIC DRUGS IN UNITED STATES VETERANS WITH NEWLY DIAGNOSED RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS, OR ANKYLOSING SPONDYLITIS

Jessica A. Walsh1, Shaobo Pei1, Gopi Penmetsa1, Brian Sauer1, Vikas Patil1, Jodi Walker2, Jerry Clewell2, Kevin Douglas2, Daniel Clegg1, Grant Cannon2, Ahmad Halwani2,1, Salt Lake City Veteran Affairs and University of Utah Medical Centers, Salt Lake City, United States of America;2AbbVie, Inc, North Chicago, United States of America

Background: Delays in treatment for inflammatory arthritis (IA) are associated with unfavorable outcomes, including impaired quality of life, irreversible joint damage, and disability.

Objectives: To characterize treatment initiation patterns in patients with newly diagnosed rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS).

Methods: Incident IA cases were identified between January 1, 2007 and December 31, 2015, in patients enrolled in the Veteran Health Administration, using International Classification of Diseases codes and natural language processing. Patterns of treatment initiation and non-treatment with disease modifying anti-rheumatic drugs (DMARDs) were assessed in the 12-month follow-up period after the incident diagnosis.

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Conclusion: Approximately one-half of patients received treatment with a DMARD within 90 days after their initial IA diagnosis. DMARD treatment rates during the initial 12 months after diagnosis increased between 2007 and 2015, but non-treatment remained common, particularly in patients with AS. Timely access to a rheumatologist is likely important for early DMARD treatment.

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Disclosure of Interests: Jessica A. Walsh Grant/research support from: Abbvie, Pfizer, Consultant for: Abbvie, Celgene, Lilly, Novartis, Shaobo Pei: None declared, Gopi Penmetsa: None declared, Brian Sauer: None declared, Vikas Patil: None declared, Jodi Walker: None declared, Jerry Clewell: None declared, Kevin Douglas: None declared, Daniel Clegg: Grant/research support from: Bristol-Myers Squibb, GlaxoSmithKline, Janssen, Pfizer, UCB Pharma, Employee of: Abbvie, Jerry Clewell, Shareholder of: Abbvie, Employee of: Abbvie, Kevin Douglas Shareholder of: Abbvie, Employee of: Abbvie, Daniel Clegg Grant/research support from: Amgen, Grant, Grant Cannon Grant/research support from: Amgen

608 Thursday, 13 June 2019
Background: The ACR’s Rheumatoid Informatics Informatics System for Effectiveness (RISE) is a national, EHR-enabled registry that passively collects data on all patients seen by participating practices, thus reducing the selection bias present in single-insurer claims databases. Launched in 2014, RISE is designed to help practices improve their quality of care.

Objectives: The objectives of our study were to a) examine changes in practice-level performance on selected quality measures for patients with rheumatoid arthritis (RA) in 2016 and 2017 and b) assess variations in performance over time between practices.

Methods: We analyzed data collected on all patients with a diagnosis of RA who had at least one clinic visit between January 1, 2016 and December 31, 2017. Six quality measures in the areas of RA management (disease activity measurement and tuberculosis (TB) screening), and cardiovascular risk reduction (body mass index (BMI) screening in 18-64 years, BMI screening in >64 years, tobacco use screening and cessation, and blood pressure (BP) control) were examined. Performance on quality measures, defined as the percentage of eligible patients receiving recommended care, was examined at the practice level. We used a hierarchi- cal linear model to predict change in practice-level measure performance per quarter, accounting for clustering by practice. We also assessed variations in within-practice performance changes over time by calculating the range for each measure.

Results: Data from 150,099 patients from 135 practices was examined. Mean age was 63±14 years, 77% were female, 72% were Caucasian. The most common practice structure was a single-specialty group practice (65%), followed by solo (20%) and multi-specialty group practice (10%). From January 2016 to December 2017 there was an improvement in quarterly performance on disease activity measurement (+2.9%, p<0.001), TB screening (+1.9%, p<0.001), BMI screening in 18-64 years (+2.4%, p<0.001), and tobacco use screening and cessation (+1.2%, p<0.001), and a decline in quarterly performance on BMI screening in >64 years (-0.4%, p<0.001) and BP control (-0.6%, p<0.001). Improvements in performance on RA management measures were steady from Q1 2016 to Q4 2017 (Figure). Within-practice change in performance varied signif- icantly across practices (Table). For example, from 2016 to 2017 within-practice change in performance on blood pressure control varied from a decrease by 66.7% to an increase by 100%.

Conclusion: Among practices participating in RISE, from 2016 to 2017 average performance on most measures for individuals with RA improved. We found significant variations in performance over time between practices, suggesting that future work to identify workflow patterns leading to high performance or to dramatic improvements in quality are warranted. Disclaimer: This data was supported by the ACR’s RISE Registry. How- ever, the views expressed represent those of the authors, not necessarily those of the ACR.
A POPULATION-BASED STUDY OF TUBERCULOSIS INCIDENCE AMONG RHEUMATIC DISEASE PATIENTS UNDER ANTI-TNF TREATMENT

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Background: Tuberculosis (TB) is an infectious disease caused by Mycobacterium tuberculosis, with a high incidence in the general population of Brazil. The advent of antituberculosis agents is associated with significant reductions in the incidence of TB, as well as in the population at risk. However, the incidence of TB among patients receiving anti-TNF agents for treatment of rheumatic diseases, despite achieving substantial efficacy in controlling disease activity, has been associated with a significant increase in incident cases of tuberculosis in this population due to blockade of TNF, which is responsible for maintenance of granuloma structure.

Objectives: Estimate the incidence of tuberculosis in Public Health System patients receiving anti-TNF therapy for rheumatic diseases. As secondary objectives, we sought to evaluate mortality and the influence of screening for latent tuberculosis infection on clinical outcomes in this population.

Methods: This retrospective cohort study included all Public Health System patients from the Brazilian state of Rio Grande do Sul (RS) who received prescriptions of anti-TNF agents for treatment of rheumatic diseases between 2006 and 2016. All data were obtained from official government records (drug dispensing, tuberculosis reporting, and mortality) where notification was mandatory. For a subset of patients, latent tuberculosis screening data were obtained through a review of medical records.

Results: A total of 5853 patients were included from 2006 to 2016, of which 3653 (62.4%) had rheumatoid arthritis, 1150 (19.7%) had ankylosing spondylitis, 872 (14.9%) had psoriatic arthritis, and 123 (2.1%) had juvenile idiopathic arthritis. Overall, 43 cases of TB were found, with an incidence of 734.7 cases per 100,000 exposed, which corresponds to 2.86 per 1000 person-years exposed. Two hundred and fifty deaths occurred in this cohort. In a subgroup of patients recruited from the outpatient rheumatology clinic of Hospital de Clínicas de Porto Alegre (n = 268), screening for latent tuberculosis infection (LTBI) was performed in 86% of patients before initiation of anti-TNF therapy; 30.1% had a positive tuberculin skin test. LTBI treatment was administered to 74 patients. In this subgroup of patients, 5 cases of TB were diagnosed, 2 in patients who had previously completed LTBI treatment.

Conclusion: In this population-based study, a high incidence of tuberculosis among patients with rheumatic diseases exposed to anti-TNF agents was found, reinforcing the need for screening and treatment of LTBI to reduce the risk of reactivation of granulomatous disease. No significant impact on mortality was demonstrated.

REFERENCES:
Conclusion: AS-related work disability and healthcare resource utilization have an enormous economic impact in Portugal. Investment in strategies that encourage early referral, diagnosis and treatment is fundamental to mitigate such burden.

Disclosure of Interests: None declared

THU0634 PHYSICIAN PERCEPTIONS OF BIOLOGICS VERSUS THEIR BIOSIMILAR COUNTERPARTS IN RHEUMATOLOGY: A MULTICOUNTRY STUDY IN EUROPE

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Background: Following LOE for the originator brand of etanercept in 2016 and the subsequent launch of its first biosimilar version, several other biosimilars have arrived in the rheumatoid arthritis treatment space. Due to their potential for reducing healthcare spend and their supposed equivalence, biosimilars are expected to be of rising relevance and impact in the following years. 12 biosimilar brands of biologic originator treatments are now available in Europe to treat rheumatoid arthritis; it will be crucial to understand physician perceptions of biosimilars relative to branded products and the impact such views have on potential prescribing decisions.

Objectives: The objective of the study was to assess perceptions of efficacy and safety for biosimilars relative to branded biologic originator products among treating Rheumatologists in the EU5 countries (United Kingdom (UK), France (FR), Italy (IT), Spain (SP) and Germany (DE)).

Methods: A cross-sectional survey was conducted in Q3 2018 in the EU5 among national, regional and hospital physicians who had been practicing between 3-30 years. Respondents completed a Physician Perceptual Questionnaire online, which assessed the overall perception of biologic brands and anti-TNF biosimilars, important attributes for treatments, and specific barriers to prescribing them. Data were analyzed using descriptive statistics.

Results: A total of 261 rheumatologists in the EU5 were recruited as part of the study (with almost equal numbers of rheumatologists representing each EU5 country). Treating rheumatologists were practicing for an average of 17.4 years, mainly in teaching hospitals (50.2%) and urban hospitals (20.7%)1. Physicians consistently expressed greater satisfaction for branded products, with 73.9% (range: 63.5% DE to 90.6% FR) of physicians having rated satisfaction with the originator brand of etanercept as a 6 or 7 (on a 7-point scale where 7 corresponded to highest satisfaction), compared to only 37.5% for biosimilar etanercept (range: 26.6% IT to 51.9% DE)2. When asked about specific attributes related to RA treatments, 64.4% of our sampled rheumatologists associated the originator brand of rituximab with ‘Inhibition of radiographic progression’ (range: 55.1% IT to 81.1% FR)1 – versus 47.5% association for biosimilar rituximab (range: 32.7% IT to 62.3% FR)1. 73.2% of physicians associated the originator brand of infliximab with ‘helps maintain or improve physical function’ (range: 55.8% DE to 87.0% ES) compared to 58.6% of biosimilar infliximab (range: 44.9% IT to 67.9% FR)1. For ‘reduction in morning stiffness’, 78.5% of our rheumatologists associated it with originator etanercept (range: 65.4% DE to 88.7% FR) versus only 66.7% for biosimilar etanercept (range: 55.1% IT to 81.1% FR)1.

Conclusion: Biosimilars score lower on overall satisfaction and are less frequently associated with specific efficacy attributes relative to branded products. This is possibly due to their relatively short time in clinical practice, and the resulting lack of experience and supporting data compared to the older branded equivalents. Proof of concept may be essential to close the perceptual gap that still exists between branded products and biosimilars.

REFERENCES:
[1] Ipsos RA Therapy Monitor (261 sampled rheumatologists reporting on RA patients in EU5 in Q3 2018)

Disclosure of Interests: None declared

THU0635 REAL WORLD PHYSICIAN SATISFACTION WITH SECUKINUMAB IN PSORIATIC ARTHRITIS AND ANKYLOSING SPONDYLITIS IN EUROPE

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Background: Psoriatic arthritis (PsA) and ankylosing spondylitis (AS) can lead to reduced physical functioning and quality of life. Secukinumab has demonstrated clinical benefits in PsA and AS, however little is known about physician satisfaction with its ability to control disease in the real world.

Objectives: Assess physician satisfaction with secukinumab’s ability to control disease in a real-world setting.

Methods: This was a cross-sectional survey of rheumatologists and dermatologists (PsA only) in France, Germany, Italy, Spain, and UK. Data were collected from Jun-Aug 2016 via physician-completed patient record forms. Patients receiving any treatment were included in the survey. Patients receiving secukinumab >1 month were included in this analysis. Physicians rated satisfaction on a 5-point scale (Very satisfied to very dissatisfied), a binary variable of satisfied/not satisfied was created by grouping “Very satisfied” and “Satisfied” responses as satisfied and “Neutral”, “Dissatisfied”, and “Very dissatisfied” as not satisfied. Data were reported by disease, then stratified by overall physician-rated disease severity (mild/moderate/severe) at initiation of secukinumab, prior biologic use, treatment duration, and concomitant medication.

Results: 438 PsA and 277 AS patients were receiving secukinumab >1month at time of data collection. Patient mean age was 46.9 years (9.2 PsA; 8.2 AS). At secukinumab initiation, 44.2% of patients were rated by their physician as severe vs. 3.5% at the current consultation (39.3% vs. 2.7% PsA; 52.0% vs. 4.7% AS).

Overall, 87.6% of physicians were satisfied with the ability of secukinumab to control disease (87.9% PsA; 86.3% AS). Physicians report high satisfaction across each stratification (Table 1).
Table 1. Population characteristics, and physician reported satisfaction with secukinumab

<table>
<thead>
<tr>
<th>Population characteristics</th>
<th>Satisfaction level</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%) PsA patients in each category (n=438)</td>
<td>N (%) AS patients in each category (n=277)</td>
</tr>
<tr>
<td>N (%) PsA physicians satisfied (n=438)</td>
<td>N (%) AS physicians satisfied (n=277)</td>
</tr>
</tbody>
</table>

Overall satisfaction 385 (87.9) 239 (86.3) 28 (6.4) 4 (80.0)

Severely at initiation* 128 (46.2) 105 (50.6) 5 (1.8) 2 (40.0)

Mild 210 (89.0) 155 (59.6) 18 (64.3) 4 (80.0)

Overall satisfaction 239 (86.3) 126 (87.5)

*PsA base size=435

Conclusion: This study provides insight into physician satisfaction with secukinumab in a real-world clinical setting. Physicians reported being highly satisfied with the ability of secukinumab to control PsA and AS disease, regardless of patient population subgroups.


THU0636

HIGHER SOCIAL MEDIA USER STICKINESS ON SELF-MANAGEMENT SYSTEM MAY IMPROVE THE REMISSION RATE OF PATIENTS WITH ANKYLOSING SPONDYLITIS

Xiaojian Ji, Jian Zhu, Jiangan Zhang, Feng Huang. SpAMS co-authors. Chinese PLA General Hospital, Department of Rheumatology, Beijing, China

Background: With the advancement of mobile health technologies, it is possible to set up economic management systems to improve health care. By using a Smart-phone Spondyloarthritis Management System (SpAMS), the Chinese Ankylosing Spondylitis (AS)/Spondyloarthritis Prospective Imaging Cohort (CASPIC) was launched.

Objectives: To explore the improvement of disease management and cost-effectiveness of SpAMS for Chinese patients with AS.

Methods: Patients enrolled in the CASPIC cohort who fulfilled the 1984 modified New York criteria and who at least 2 evaluations of Ankylosing Spondylitis Disease Activity Score (ASDAS) were included in this analysis. All physician-reported assessments were collected at the Chinese People’s Liberation Army General Hospital using SpAMS in Beijing. The disease activity states were defined according to ASDAS1, which separated inactive disease (ID) from low disease activity (LDA) by 1.3, LDA from high disease activity (HDA) by 2.1, and HDA from very high disease activity (VHDA) by 3.5. According to ASDAS at the baseline visits and final visits, patients were divided into four groups (Figure 1): maintainer of ID/LDA, patients with relapse, maintainer of active disease, and new achiever of ID/LDA.

Results: From April 2016 to April 2018, 1201 patients with AS were enrolled in CASPIC. 4659 patient self-assessments were completed, including 3304 pre-visit assessments and 1355 assessments during the follow-up interval. After online consultation, 29.1% of clinic visits to a tertiary hospital were considered unnecessary and could be solved in the primary care hospital. The time and cost of each patient’s journey to Beijing were calculated based on the location of each patient. For the 1037 (86.3%) patients who lived outside the vicinity of Beijing, at least an average of 5.3 hours and 327.4 RMB for each person (USD: RMB = 1:6.418) for traffic time and expenses were saved, which equaled to 16% of the Chinese monthly disposable personal income (data in 2016).

Table 1. Characteristics of disease activity

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>ID/LDA at baseline</th>
<th>Active at baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>445</td>
<td>332</td>
</tr>
<tr>
<td>P value</td>
<td>0.001</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Age, mean (s.d.), years
Disease duration, mean (s.d.), years
Number of self-assessments, mean (s.d.)
Male sex, %
ASDAS at baseline, mean (s.d.)
Smoker, %
NSAIDs at baseline, %
TNFi at baseline, %
DMARDs at baseline, %
TNFi during follow-up period, %

<0.001*
P < 0.05.

Of these patients enrolled in CASPIC, 777 patients had at least 2 evaluations of ASDAS. The rate of patients with ID/LDA was 57.2% at baseline and increased significantly to 79.2% with a mean (SD) follow-up of 13.3 (5.9) months (Table 1). Compared with patients who relapsed, those that maintained the ID/LDA had more patient assessments [5.0 (2.7) vs 3.3 (1.8), P < 0.001]. The new achievers of ID/LDA also completed online patient assessments more frequent [5.6 (3.1) vs 4.5 (2.5), P < 0.001] compared to patients who maintained active disease.

Conclusion: Higher social media user stickiness on self-management system may improve the remission rate of AS patients. SpAMS could serve as a cost- and time-saving specialty care online platform for patients with AS.

REFERENCES:
THU0637

ACADEMIC ACHIEVEMENT, EMPLOYMENT STATUS, WORK PRODUCTIVITY AND ACTIVITY IMPAIRMENT IN ADULTS WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA): DETERMINANTS AND CONSEQUENCES

Chennappa Kavadichanda, Karunya Ravi, Niru Negi. Jawaharlal Institute of Postgraduate Medical Education and Research, Clinical Immunology, Puducherry, India

Background: Changes occurring in childhood due to JIA leads to academic and work impairment during their transition to adulthood. The factors impairing work and overall activity among adults with JIA need to be explored to formulate policy decisions and rehabilitation measures.

Objectives: To assess the level of academic achievement, employment, work productivity and activity impairment among adults suffering from JIA. To identify factors determining activity impairment among adults with JIA

Methods: Consecutive adults classified as JIA (1) were included. Consent was defined as ever remission:

Remission was assessed by Wallace criteria. Remission was done and remission was assessed by Wallace criteria. Remission was defined as ever remission: ≥3 months and sustained remission: ≥ 6 months of disease control. Appropriate statistical tests to assess association and correlation of various factors with WPAI were used.

Results: Demography (n=51) is depicted in table 1. Never attaining remission resulted in significantly higher college dropouts (8 vs 17, p<0.05), functional impairment (mean iHAQ 1.08 vs 0.5, p<0.05) and arthritic damage (mean JADI A 3 vs 8, p<0.01). Disease duration, JADI A and iHAQ correlated well (r² >.400, p<.05) with measures of WPAI (table 2). Assessment of patient variables like gender, occupation, disease activity and remission status (figure 1) showed that women, especially the homemakers and individuals with moderate to high disease activity had significant activity impairment (P<0.05).

Conclusion: Early effective treatment directly impacts employment levels and activity in adults with JIA. Homemakers in middle- and low-income countries have the most impairment in activity as they cannot alter their work. Replacement costs for homemakers would be an added financial burden to the family and is seldom captured by studies. Our study highlights the need to look further into the indirect and intangible costs involving women that will help policy makers formulate effective economic policies for individuals with JIA.

REFERENCES:


Table 1. Demographic, educational, occupational, health profile and WPAI measures of adults with JIA

<table>
<thead>
<tr>
<th>S.No</th>
<th>Parameter (N=51)</th>
<th>Median</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Age</td>
<td>22</td>
<td>8</td>
</tr>
<tr>
<td>2</td>
<td>Disease duration (years)</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>Duration of treatment (years)</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>WPAI Measures (in percentage)</td>
<td>40</td>
<td>50</td>
</tr>
<tr>
<td></td>
<td>Overall Activity Impairment</td>
<td>64.06</td>
<td>61.66</td>
</tr>
<tr>
<td></td>
<td>Overall Work Impairment (N=14)</td>
<td>40</td>
<td>72.05</td>
</tr>
<tr>
<td></td>
<td>Presentism (N=12)</td>
<td>33.03</td>
<td>51.14</td>
</tr>
<tr>
<td></td>
<td>Absenteeism (N=14)</td>
<td>8.36</td>
<td>12.56</td>
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Disclosure of Interests: None declared


THU0638

CONSIDERATIONS FOR IMPROVING QUALITY OF CARE IN RHEUMATOID ARTHRITIS AND ASSOCIATED COMORBIDITIES

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Background: The presence of comorbidities in patients with rheumatoid arthritis (RA) contributes to increased morbidity and mortality. Patients

Table 1. Educational status

<table>
<thead>
<tr>
<th>S.No</th>
<th>Parameter (N=51)</th>
<th>Median</th>
<th>IQR</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Gender Male/Female</td>
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<td></td>
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<tr>
<td>2</td>
<td>Residential type Urban/Rural</td>
<td>10/41</td>
<td>19.6/80.4</td>
</tr>
<tr>
<td>3</td>
<td>Educational status Illiterate</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Less than high school</td>
<td>14</td>
<td>27.5</td>
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<tr>
<td></td>
<td>High School</td>
<td>8</td>
<td>15.7</td>
</tr>
<tr>
<td></td>
<td>Intermediate/Diploma Graduate/Postgraduate or above</td>
<td>18</td>
<td>35.3</td>
</tr>
</tbody>
</table>

Disclosure of Interests: None declared


THU0639

Figure 5: Correlation between various disease associated factors and WPAI measures.

Figure 6: Association of patient and disease characteristics with activity/impairment

Acknowledgments: The study was supported by the EULAR-SERNECRA Research Grant. The authors acknowledge the support of the countries where patients are living with RA and their country’s disease activity scores used in this study.
with RA have an increased risk of comorbidities e.g. interstitial lung (IL) disease (7.7% incidence\(^5\)), up to 60% IL abnormalities in early RA\(^5\), depression (up to 200%\(^4\), 18.8%\(^3\)), cardiovascular disease (40-70%\(^6\), 5-12.9%\(^7\)) and diabetes (IR of 8.6 per 1000 person-years\(^8\); 20%\(^9\)). Yet, there are few comprehensive recommendations on the management of RA-related comorbidities.

**Objectives:** This study aimed to identify models of good quality care for patients with RA and their associated comorbidities in Europe and understand how these practices can be widely implemented.

**Methods:** Existing published recommendations across Europe on good practice in RA care including screening/managing selected comorbidities were reviewed. Team members of 12 specialist centres across Europe were interviewed. The interventions identified were reviewed and prioritised to form a selection of considerations by a consensus process involving 18 experts including rheumatologists, a patient rep., a nurse and also RA comorbidity specialists: cardiologist, psychologist, pulmonologist and diabetologist.

**Results:** The interventions were prioritised for each patient profile:

1. suspected RA:
   1. rapid access to care (online referral, triage, ultrasound guided diagnosis)
   2. enhanced communication with primary care (hotline, education sessions)
   3. early arthritis clinic (timely clinical assessment and diagnosis)

2. recently diagnosed:
   1. enabling self-management (self-monitoring and disease activity management support)
   2. early arthritis clinic
   3. comprehensive comorbidity assessment (standalone or in conjunction with RA appointment)

3. established disease:
   1. dedicated comorbidity specialist
   2. integrating patient registries into daily clinical practice
   3. enabling self-management

Eleven other interventions were identified including task-shifting to non-physician healthcare professionals, tailored education to patients and family members, and developing care networks.

**Conclusion:** Despite limited European recommendations on management of RA comorbidities, a range of good practice care model interventions across Europe were identified which are non-complex, high-impact and meaningful. Next step will be to assess how these care models can be implemented in different healthcare systems for the benefit of patients with RA.

**REFERENCES:**


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**Disclosure of Interests:** Tore K. Kvien Grant/research support from: AbbVie, Biogen, BMS, MSD, Pfizer, Roche and UCB.; Consultant for: Abbvie, Biogen, BMS, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Hospira, Merck-Serono, MSD, Novartis, Oktai, Orphan Pharma, Pfizer, Roche, Sandoz, Sanofi, Miylan and UCB; Speakers bureau: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Hospira, Merck-Serono, MSD, Novartis, Oktai, Orphan Pharma, Pfizer, Roche, Sandoz, Sanofi and UCB; Karel Pavelka: None declared, Joaquim Polido-Pereira: None declared, Anne Grete Semb: None declared, Magnus Skold: None declared, Alejandro Balisa Grant/research support from: Abbvie, Pfizer, Novartis, BMS, Nordic, Sanofi, Consultant for: Abbvie, Pfizer, Novartis, BMS, Nordic, Sanofi, Sandoz, Lilly, Paid instructor for: Pfizer, Speakers bureau: Pfizer, Novartis, UCB, Nordic, Sanofi, Sandoz, Lilly, Neil Betteridge Consultant for: Amgen, Eli Lilly, Grunenthal, GSK, Heart Valve Voice, Janssen, Roche, Sanofi Genzyme and Sanofi Regeneron; Speakers bureau: Amgen, Eli Lilly, Grunenthal, GSK, Heart Valve Voice, Janssen, Roche, Sanofi Genzyme and Sanofi Regeneron, Maya Buch Grant/ research support from: Pfizer LTD, UCB, Consultant for: Abbvie, Eli Lilly, EMD Serono, Pfizer Ltd., Sanofi, Patrick Durez Speakers bureau: Bristol-Myers Squibb, Eli Lilly, Sanofi, Celltrion, Ennio Favalli: None declared, Guillaume Favier: None declared, Cem Gabay Grant/research support from: Roche, Pfizer, AB2 Bio Ltd, Consultant for: Roche, Pfizer, Lilly, AbbVie, Sanofi, Regeneron, Bristol-Myers Squibb, Novartis, UCB, AB2 Bio Ltd, Debiopharm, Rinie Geenen: None declared, Ioanna Gouni-Berthold: None declared, Frank van den Hoogen: None declared, Alison Kent: None declared, Lars Klareskog Grant/research support from: Yes, but not for the presented study., Mikkél Östgaard Grant/research support from: Abbvie, Celgene, Centocor, Merck, Novartis, Consultant for: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novar- lis, Novo, Orion, Pfizer, Regeneron, Roche, and UCBB, Speakers bureau: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, maximum doxogados Grant/research support from: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma, Consultant for: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma.

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**THU0639 AUTOMATED CAPTURE AND HIGH UPTAKE RATES OF PATIENT REPORTED OUTCOME MEASURES IN ROUTINE RHEUMATOLOGY PRACTICE**

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**Background:** Patient reported Outcome Measures (PROMs) are an integral part of value based healthcare and outcomes that matter to patients; however resource and time constraints are often barriers for routine collection in clinic.

**Objectives:** We piloted an automated, electronic collection of PROMs for patients attending an outpatient specialist rheumatology clinic.

**Methods:** All patients with a clinic appointment were sent an automated message, one day before their scheduled doctor’s appointment, with a hyperlink to fill in the Routine Assessment of Patient Index Data (RAPID3) [0-30, 30 being worst, calculated as the sum of physical function measured using the 10-item multidimensional health assessment questionnaire (mDH AQ), pain visual analogue scale (VAS), and patient global VAS questionnaire]. The text message was personalised with the attending physician’s name and thumbnail photograph and the questionnaire was presented in the patient’s preferred language (English or simplified Chinese) by detecting their phone configuration. RAPID3 responses flowed back to the electronic medical record and were available for the attending clinician to view during the clinic consult the next day. Patients who did not fill in the questionnaire within 6 hours were sent a reminder, and those still remaining were encouraged to fill it in the clinic waiting room. Hardcopy flyers were distributed to inform patients of the initiative and clinicians were encouraged to discuss the responses at the clinic visit. Patients were sent the survey only once during the study period. Weekly usage reports were sent to the clinicians (Figure 1).

**Results:** 4078 patients [mean (SD) age 55.8 (16.3) years, 67.9% female, 70.6% Chinese] were sent the text message invitation over 6 months, of which 64.4% responded. Diagnosis data from SNOMED codes were available for 2262 patients. The most common primary diagnoses were rheumatoid arthritis (653, 29.5%), Spondyloarthritides (SpA), including psoriatic arthritis (318, 14.4%) and lupus (310, 14%). Data on disease duration, clinical features and medications were not available for this study. The mean (SD) mDH AQ score (range 0-3, 3 being the worst) was 0.3 (0.5), mean (SD) pain-VAS (0-10, 10 being worst) was 2.4 (2.3), patient global was 2.6 (2.2) and RAPID3 was 6.1 (5.2). On multivariable logistic regression, age (OR = 0.38, 95% CI 0.32, 0.44 for the top tertile), gender (OR 1.22, 95% CI 1.06, 1.4 for females), race (OR = 0.79, 95% CI 0.64, 0.98 for Indian vs. Chinese race) and treating physician (OR 0.7, 95% CI 0.61, 0.8 for junior vs. senior doctor) were independent predictors of survey response, while primary rheumatic disease was not (Figure 2). Ten of 11 clinicians (from 13 surveyed) found the information from PROMs useful, and 8/11 supported expansion of the pilot project to include more PROMs. Lack of time was cited as the biggest challenge to implementing PROMs routinely.

**Conclusion:** Automated collection of PROMs in routine clinical care is feasible with high uptake rates and minimal clinician burden.

**[1] Figure 1: Weekly usage reports**
Early retirement due to RA translated into 6.5 years of active work lost, compared to retirement due to other causes. Patients who retired due to RA are more likely to be younger at diagnosis of 49.6 ± 9.0 vs. 56.1 ± 8.6 years-old; p<0.01, female (82.6% vs. 68.9%, p<0.01), have longer disease duration (23.2 ± 10.7 vs. 18.3 ± 9.9 years, p<0.01) and lower educational level (4.5 ± 2.3 vs. 6.0 ± 4.1 school years, p<0.01). In the multivariate analysis, disease-related predictors for early retirement were: disease duration (OR: 1.11; 95% CI 1.08-1.13/year), erosive disease (OR: 4.45; 95% CI 2.37-8.35) and the need for biologic therapy switching (OR:1.37; 95%CI 1.02-1.83). Work-related predictors were: educational level (OR: 0.75; 95%CI 0.68-0.81/year) and heavy manual type of work (OR: 1.62; 95%CI 1.16-2.26).

Conclusion: Early retirement is still common among patients with RA; 60% in this cohort. The main reasons for early retirement are associated with the disease itself, but work-related factors also play a relevant role.

REFERENCES:

Disclosure of Interests: None declared

THU0640 EARLY RETIREMENT ATTRIBUTED TO RHEUMATOID ARTHRITIS AND ITS PREDICTORS IN PORTUGAL

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Background: Work disability is a common consequence of Rheumatoid Arthritis (RA) with economic implications for both the patient and society. Scarcely information is available on work and disease-related factors associated with early retirement in Portugal.

Objectives: To evaluate the rate of early retirement due to RA. Secondary aim consists in the identification of its main predictors, both work and disease-related.

Methods: Retrospective cohort study involving two national rheumatology centers, including patients with RA according the ACR/EULAR 2010 or the 1987 ACR Classification Criteria for RA. Patients retired prior to RA diagnosis, never-employed or with missing information on current work status were excluded. Type of work was independently classified as non-manual/white collar/manual/heavy manual by two authors based on patient occupation with excellent inter-agreement (Cohen’s kappa coefficient 0.91). Retirement due to RA versus retirement for other reasons were compared using T-test and Chi2 test as adequate. Variables with p<0.05 in univariate analysis and other potential predictors selected on clinical and epidemiological grounds were included in multivariable binary logistic regression.

Results: 492 patients were included (80.3% female, aged 60.9 ±13.1 years-old, mean disease duration 15.9 ±10.5 years). Until the present time, 45.1% (n=222) of the patients retired, this being due to RA in 59.5% of the cases. Early retirement due to RA translated into 6.5 years of active work lost, compared to retirement due to other causes. Patients who retired due to RA are more likely to be younger at diagnosis (49.6 ± 9.0 vs. 56.1 ± 8.6 years-old; p<0.01), female (82.6% vs. 68.9%, p<0.01), have longer disease duration (23.2 ± 10.7 vs. 18.3 ± 9.9 years, p<0.01) and lower educational level (4.5 ± 2.3 vs. 6.0 ± 4.1 school years, p<0.01). In the multivariate analysis, disease-related predictors for early retirement were: disease duration (OR: 1.11; 95% CI 1.08-1.13/ year), erosive disease (OR: 4.45; 95% CI 2.37-8.35) and the need for biologic therapy switching (OR:1.37; 95%CI 1.02-1.83). Work-related predictors were: educational level (OR: 0.75; 95%CI 0.68-0.81/year) and heavy manual type of work (OR: 1.62; 95%CI 1.16-2.26).

Conclusion: Early retirement is still common among patients with RA; 60% in this cohort. The main reasons for early retirement are associated with the disease itself, but work-related factors also play a relevant role.

REFERENCES:

Disclosure of Interests: None declared

THU0641 USE OF A WEB-BASED RHEUMATOLOGY PATIENT MANAGEMENT PORTAL

Tin Aung1, Robert Sharp2, Roopa Manhas1, Stuart Kyle2, Northern Devon Healthcare NHS trust, Rheumatology, Barnstaple, United Kingdom; 2Medimetric, Barnstaple, United Kingdom

Background: The benefit of incorporating tele-rheumatology into standard care is increasingly recognised. In January 2017, we introduced a web-based Rheumatology Patient Management Portal (RPMP), developed by MedMet, to our rheumatology patients at the North Devon District Hospital. In 2018 the portal service was fully operational. Suitable patients included undifferentiated inflammatory arthritis, rheumatoid arthritis, psoriatic arthritis and spondyloarthritides. Patients were consented to collected data such as diagnosis, treatment and disease activity onto the RPMP. For a selected group of patients who agreed to their email use, we set up schedules in the form of email reminders for them to complete PROMs (patient reported outcome measures) such as Health Assessment Questionnaire, Spinal Pain, Bath Ankylosing Spondylitis Disease Activity Index and Work Productivity and Activity Impairment. Patients can also report disease flares electronically, which is acknowledged by a health care professional who will contact them with advice as necessary.

Objectives: To understand patient participation in the use of the RPMP, between 01.01.18 and 31.12.18. To develop a cohort of clinically stable patients who can self-manage via RPMP use and scheduled PROMs. The potential to remotely manage these patients has the advantage of reducing the number of face-to-face clinic appointments and eventually will lead to setting up a virtual clinic. To examine patient perception on the RPMP use. To examine whether tele-rheumatology is a useful adjunct to standard care.

Methods: The data was collected from interrogating the web-based RPMP database. Specific data was reviewed including; total number of patients on the portal, number of patients consenting to use their email, number of PROMs completed on the RPMP, number of flares reported and time to acknowledgment. In order to gain further understanding of user experience, a survey questionnaire (figure 1) was sent on 14.01.19.

Results: In total we have 883 patients recruited to the RPMP. During the study period of one year, 289 patients have consented to share their emails and set up schedules. Thirty-three percent of patients on the RPMP are using their emails through 2018. 310 patients responded to their portal request to complete a schedule. 758 PROMs were completed as part of the schedule response. 1744 PROMs were completed face to face whilst in standard clinic review. Therefore, 30% of PROMs were completed through a scheduled response. 55 patients contacted us through the RPMP to report a flare. The average time to acknowledging a flare is 37 hours. 78% of flare reports were acknowledged within 3 days. Results from the survey of patient experience as follow: number of patients responding to the survey was 99 and respond rate was 34%.
Among them, 94% reported the RPMP as easy to use, 54% found that the RPMP helped them in understanding their rheumatology condition and 25% reported a flare through the RPMP.

### Conclusions

A large number of our rheumatology patients have consented to use the RPMP and their email. Uptake of the RPMP use is increasing (figure 2).

We have identified a significant proportion of 289 patients using the portal and email that could be targeted for virtual clinic use. Our data showed that use of tele-rheumatology in conjunction with standard care has potential to reduce number of standard clinic appointments however further work is required to investigate this.

Feedback from clinical staff is that having PROMs completed prior to consultation gives more time to discuss key issues whilst facilitating appropriate monitoring. The survey showed that a majority of patients found the RPMP easy to use and helpful in understanding their rheumatology condition. The RPMP is an effective monitoring system for selected patients and has improved patient understanding in monitoring their disease activity, with a larger group of health professionals, patients and app developers are being involved.

### Disclosure of Interests:

Tin Aung: None declared, Robert Sharpe: None declared, Roop Manhas: None declared, stuart kyle Consultant for: but no conflict of interest.


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**EULAR POINTS TO CONSIDER FOR THE DEVELOPMENT, EVALUATION AND IMPLEMENTATION OF MOBILE HEALTH APPLICATIONS FOR SELF-MANAGEMENT IN PATIENTS WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES**

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**Background:** In the expanding era of e-health, a wide range of mobile health applications (apps) have become available to enable people with rheumatic and musculoskeletal diseases (RMDs) to better self-manage their health. However, guidance on the development and evaluation of such apps is lacking.

**Objectives:** The objective of this EULAR task force was to establish points to consider (PtC) for the development, evaluation and implementation of apps for self-management of RMDs.

**Methods:** A systematic literature review of app content and development strategies was conducted, followed by a qualitative study with six patients and an online survey of people living with RMDs (n=394). Based on these data and expert opinion, the PtC were formulated in a face-to-face meeting in November 2018 by a multidisciplinary TF panel of experts, including patients, from 10 countries. The level of agreement among the panel in regard to each PtC was established by anonymous online voting.

**Results:** Three overarching principles and 10 PtC were formulated (Table), Out of the 10 PtC, three were related to patient safety (1,5,6), considered as a critical issue by the panel, along with accuracy of information provided by apps. Three were related to relevance of the content and functionalities (2,7,9) and the importance of apps being tailored to the individual needs of people with RMDs. The requirement for transparency around app developers and funding sources (3,4), along with involvement of relevant health professionals were also raised. Ease of app access across ages and abilities was highlighted (8), in addition to considering the cost-benefit of apps from the outset (10). The level of agreement was high (Table).

**Conclusion:** These PtC provide guidance on important areas that should be considered for the development of new apps, the quality assessment of existing apps, as well as for further development of existing apps. As part of the dissemination phase, these PtC will be shared with a larger group of health professionals, patients and app developers and for wider consensus.

**Table 1. The 10 Points to Consider.**

<table>
<thead>
<tr>
<th>Points to consider</th>
<th>Level of agreement mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. The information content in self-management Apps should be up-to-date, scientifically justifiable, user-accessible and evidence-based where applicable</td>
<td>9.8 (0.4)</td>
</tr>
<tr>
<td>2. Apps should be relevant and tailored to the individual needs of people with RMDs.</td>
<td>9.7 (0.5)</td>
</tr>
<tr>
<td>3. The design, development and validation of a self-management App should involve people with RMDs and relevant health care providers.</td>
<td>9.8 (0.4)</td>
</tr>
<tr>
<td>4. There should be transparency on an App’s developers, funding source, content validation process, version updates and data security.</td>
<td>9.3 (0.3)</td>
</tr>
<tr>
<td>5. Data collection as part of an App must adhere to all applicable regulatory frameworks, particularly data protection.</td>
<td>9.9 (0.3)</td>
</tr>
<tr>
<td>6. Apps must not result in potential or actual harm to people with RMDs.</td>
<td>9.5 (0.3)</td>
</tr>
<tr>
<td>7. Apps could facilitate patient-health care provider communication and contribute to electronic health records or research.</td>
<td>9.4 (0.9)</td>
</tr>
<tr>
<td>8. App design should consider accessibility of people with RMDs across ages and abilities.</td>
<td>9.4 (0.9)</td>
</tr>
<tr>
<td>9. If a social network is an important component of an App, structures should be put in place to ensure appropriate content moderation.</td>
<td>9.5 (0.6)</td>
</tr>
<tr>
<td>10. The rheumatology community should consider the cost-benefit balance of Apps before its endorsement and/or its promotion.</td>
<td>8.9 (1.3)</td>
</tr>
</tbody>
</table>

**Acknowledgement:** EULAR for funding this project
ARE PSORIATIC ARTHRITIS OUTCOMES BETTER IN PATIENTS MANAGED IN EARLY ARTHRITIS CENTRES?

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Background: There is good evidence that dedicated early arthritis clinics (EACs) improve referral lag time and reduce delay in establishing disease-modifying therapy. However it remains arguable whether such clinics improve outcomes especially for arthritides other than RA. In the UK, only 57% of units have dedicated EACs. Our early arthritis service won national best practice commendation award for achieving high standards.

Objectives: We analysed our psoriatic arthritis (PsA) population data to ascertain whether this cohort benefits from EACs.

Methods: The department set up an early arthritis service with introduction of six clinics (EACs) every week. An agreed treatment protocol incorporating ultrasound was developed to ensure standardised approach to early initiation of treatment, drug education and timely review. This is a retrospective study of all patients with PsA presenting to the service in the first 3 years.

Results: Our catchment area covers a population of 350,000 with 40% ethnic minorities. Of 1884 patients referred, 482 (25.5%) were triaged into EACs based on set criteria. All were reviewed within 3 weeks. 247 (51%) were confirmed to have early inflammatory arthritis (EIA). Mean age was 52.4 years (17-86y). 157 (63.5%) were women. 177 (71.6%) were White, 58 (23.5%) of Asian and twelve of other background. 159 (63.4%) had RA, 55 (22%) with PsA and 33 had other inflammatory arthritides. There was median 26 days delay (0.0-1043 days) from symptom onset to GP presentation. Median time for GP referral to the department was 4.0 days (0-84 days).

All PsA patients had regular PsARC assessment. Mean tender (TJ) and swollen joint (SJ) counts at first visit were 8.2 (1-35) and 3.5 (0-14) respectively [n=55]. The patient (PtGA) and physician (PhGA) global assessments mean were 3.0 and 2.9 (1-5). 95% commenced their DMARDs within 3 week of initial review. Other 5% who missed the target was owing to patient factors. Target [TJ & SJ ≤2] was achieved for 38 patients (69%) and good PsARC response for a further 4 (7%). Median time to achieve the target or good response was 22 weeks (0-48 weeks). Of 55, only four (7%) patients required escalation to biologic therapy. Final TJ and SJ mean was significantly better at 1.2 (0-4) and 0.3 (0-2) [p <.0001] with similar improvement in PtGA [mean 1.8 (1-4)] and PhGA [mean 1.6 (1-3)]. Only six (11%) patients were true non-responders as the remaining seven declined therapy.

Conclusion: Dedicated EACs help achieve good clinical outcomes in majority of PsA patients. Nearly 76% of our cohort attained the target or good PsARC response in less than six months. This was despite a significant delay in patients presenting to their GPs and moderately-high disease activity. 100% of our patients were treated to target facilitated by protocol driven escalation of therapy in these clinics. This is in contrast to the national audit findings whereby only 68% of patients were treated with disease modifying drugs within 6 weeks of referral and 89% had treatment to target. This study shows that the establishment of dedicated EACs improve the prognosis of psoriatic arthritis in terms of primary clinical outcomes compared to patients managed outside of EACs.

Disclosure of Interests: Muhammad Khurram Nisar Grant/research support from: AbbVeie, BMS, Celgene, Janssen, Lilly, MSD, Novartis-Sandoz, Pfizer, Sanofi, and UCB. Consultant for: AbbVeie, BMS, Celgene, Janssen, Lilly, MSD, Nordic Research. Muhammad Nisar-Sandoz, Pfizer, Roche, Sanofi, and UCB. Consultant for: L Gossec has received honoraria from Celgene as investigator for this study, Francis Berenbaum: None declared.


THU0644 PATIENTS’ PERCEPTION AND USE OF MEDICAL MARIJUANA

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Background: Though the introduction of biologics has resulted in significant improvements in their quality of life, people living with rheumatic and musculoskeletal disease (RMD) often seek alternative treatments such as marijuana (THC) and cannabidiol (CBD). As these substances become more widely available, and legal in some jurisdictions, health care providers (HCP) need to understand patients’ THC/CBD perceptions, use and information needs.

Objectives: To examine patient behavior and information needs regarding THC/CBD medical use.

Methods: A 77-item survey was developed in partnership with RMD patient partners and administered online via CreakyJoints and the ArthritisPower research registry. Participants (pts) were eligible if they were ≥19 years of age, resided in the US and reported physician-diagnosed RMD. Pts reported current health status (NIH PROMIS Global Health), use and perceptions of THC/CBD, and related information needs.

Results: To date, 189 pts completed the survey. A majority of pts were female (87%) and white (93%), with mean age of 55(11). More than half of all pts (62%) reported a diagnosis of rheumatoid arthritis. Most pts (78%) reported fair/poor health (PROMIS Global Physical Health <43). Only 30% of all pts were satisfied with their current treatment, and more than half (63%) had been on their current treatment for >1 year. Of those surveyed, a majority of pts (n=168, 89%) reported trying THC and/or CBD for a purpose they perceived as medical and offered various reasons for initiating its use (Table). Half of all pts (n=98, 52%) reported ever using CBD and a third (n=70, 37%) ever using THC for medical reasons, “fifty-one (73%) of whom currently use THC. More than half (53%) of those currently using THC reported using it at least once daily. Top reasons for stopping among the 19 who previously used THC were cost (26%) and illegality (26%). Most pts who had ever used THC reported that THC improved their symptoms (83%) and/or their condition (71%). Pain (100%) and sleep disturbance (73%) were the main symptoms pts sought to relieve with THC. Many pts had used THC in lieu of prescribed (56%) or OTC (73%) medications. Two thirds (67%) reported telling their HCP about their THC use, most of whom (64%) reported that their HCP did not consider it when making treatment changes nor offer advice about mode of administration or dosage. When acquiring THC, 39% of pts used a medical marijuana card issued by the state; the main reason given for not using a card was that THC was not legal for medical use where the pt lived (44%). Whether they had used THC for medical reasons or not, nearly all pts wanted information about THC, including its effectiveness (37%) and its interaction with other medications (34%); a majority preferred to receive information from HCPs (55%) or online educational resources (34%). Two thirds (60%) of all pts expressed interest in THC/CBD trial participation.

Table: Participants’ Reasons for Initiating THC/CBD Use (N=168)

<table>
<thead>
<tr>
<th>Reasons (not mutually exclusive)</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>To address symptoms (e.g. pain) experienced despite taking medication</td>
<td>74 (44)</td>
</tr>
<tr>
<td>To address symptoms with less or no medication</td>
<td>50 (30)</td>
</tr>
<tr>
<td>Nothing else worked to treat condition or symptoms</td>
<td>33 (20)</td>
</tr>
<tr>
<td>Friend suggested it</td>
<td>30 (18)</td>
</tr>
<tr>
<td>To address side effect(s) from medication</td>
<td>28 (17)</td>
</tr>
<tr>
<td>Saw information online</td>
<td>25 (15)</td>
</tr>
<tr>
<td>HAD used marijuana recreationally and wanted to try it for medical reasons</td>
<td>24 (14)</td>
</tr>
<tr>
<td>Medical marijuana became legal in state</td>
<td>19 (11)</td>
</tr>
<tr>
<td>To address side effect(s) from medication</td>
<td>17 (10)</td>
</tr>
<tr>
<td>Physician suggested it</td>
<td>17 (10)</td>
</tr>
</tbody>
</table>

Conclusion: Though many pts have used or currently use THC/CBD to substitute for or augment their prescribed treatment, pts lack adequate information to guide its use for medical reasons.

Disclosure of Interests: None declared.

VIRTUAL VISITS IS THE FUTURE COMING? TELEREUMATOLOGY. PILOT PROJECT: REVIR PROGRAM, RHEUMATOLOGY SERVICE. BARCELONA, SPAIN

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1Hospital del Mar, Rheumatology, Barcelona, Spain; 2Hospital del Mar, Dirección, Barcelona, Spain; 3Institut Català de la Salut, CAP Vila Olimpica, Barcelona, Spain; 4Institut Català de la Salut, CAP Sant Marti, Barcelona, Spain; 5Institut Català de la Salut, CAP Ramón Turró, Barcelona, Spain

Background: The prevalence of rheumatic diseases in the Spanish population is estimated at 22.6% according to the EPISER 2000 study. A new epidemiological study is currently underway, EPISER 2016 and its preliminary results point towards a higher prevalence. Within the national health system, primary care is the first level of access to the health system and is provided at primary care centers (CAP). The rheumatology at primary care centers at Spain has been a pioneer in the application from the team at Parc de Salut Mar (Hospital del Mar), with the physical presence of rheumatologists in the 14 centers belonging to the CAP network of the SAP Litoral. The high prevalence of the medical pathology of the musculoskeletal system and the aging of the population, can condition an increase in visit requests in rheumatology, and with it, the increase in the waiting lists of patients.

Objectives: The main objective of this study is to know the resolutive possibility of virtualization, measured in the number of visits resolved telemedically, as well as its impact on the waiting list of the primary care physician and the reduction of the waiting list of first face-to-face visits.

Methods: Prospective experimental study, started on December 1, 2017 and ended on May 31, 2018. Four primary care centers were selected according to population and waiting list: Sant Martí Nord, Sant Martí Sud, Ramón Turró and Villa Olimpica. The REVIR program proposes the creation of a circuit for the assessment of referrals to rheumatology from primary care physicians (MAP).

Results: 726 first visit requests were received during the REVIR program. The most common categorized pathology was mechanical pathology, representing about 70% of the first visits requested. Metabolic bone disease ranked second with 16%, and inflammatory pathology ranked third (SLE, RA, SA, SPA, PsA). Chronic musculoskeletal pain ranked fourth (including fibromyalgia) and lastly soft tissue pathology. The number of first visit requests was multiplied by two in all the participating primary care centers of the project. Despite this increase, the telematic resolution of the visits created was stable, with a value greater than 40%.

Conclusion: The implementation of a system of assessment of the first visits in rheumatology requested from Primary Care is effective in decreasing the waiting list to make face-to-face visits, as well as to detect early serious pathology that requires hospital control. It has been achieved, therefore, that the patient is treated at the level of attention that corresponds to him. Guaranteeing the adequate use of hospital resources and reducing the waiting list for a first in-person visit in rheumatology in primary care is one of the most important goals fulfilled, given that it is directly related to maintaining the accessibility and equity of the public health system.

REFERENCES:

Tabla 1: Resolution of the first virtual visits to 6 months of REVIR project

<table>
<thead>
<tr>
<th>CAP</th>
<th>Total</th>
<th>First Cap</th>
<th>First Hospital</th>
<th>Virtual resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ramón Turró</td>
<td>193 (26.4%)</td>
<td>94 (49%)</td>
<td>22 (11.3%)</td>
<td>77(40%)</td>
</tr>
<tr>
<td>Villa Olimpica</td>
<td>96 (13.2%)</td>
<td>36 (37.5%)</td>
<td>13(13.5%)</td>
<td>47(49%)</td>
</tr>
<tr>
<td>Sant Marti (1 y 2)</td>
<td>437 (60.2%)</td>
<td>216 (49.5%)</td>
<td>53(12.1%)</td>
<td>186(38.4%)</td>
</tr>
<tr>
<td>Total</td>
<td>726 (100%)</td>
<td>346 (47.6%)</td>
<td>88(12.1%)</td>
<td>292(40.2%)</td>
</tr>
</tbody>
</table>

Disclosure of Interests: Fabiola Ojeda: None declared, Manel Ciria: None declared, Carolina Perez-Garcia: None declared, Eric Sitjas: None declared, Elena Martinez: None declared, Daniel Martinez-Laguna: Speakers bureau: Eli Lilly, Amgen, Ferrer, Rubio and Novartis., Montserrat Pimienta: None declared, Jordi Montfort: None declared


HIGH LEVELS OF DAMAGE IN INFLAMMATORY RHEUMATIC DISEASES: A CLUE TO LOW RATES OF REMISSION AND LOW DISEASE ACTIVITY

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Background: Despite introduction of powerful biologic medications over the last 2 decades, rates of remission and low disease activity rates in RA remain less than 50%. One possible basis is that measures and indices such as disease activity score 28 (DAS28) and clinical disease activity index (CDAI), while sensitive primarily to disease activity in clinical trial patients selected for high inflammatory activity, may also reflect clinically important joint damage and patient distress in unselected patients in routine care. Similar considerations may pertain to systemic lupus erythematosus disease activity index (SLEDAI), Bath ankylosing spondylitis disease activity index (BASDAI), and other measures and indices initially designed to assess disease activity. Levels of organ damage and patient distress, as well as inflammation, may be quantitated according to 3 physician (0-10) visual analog scales (VAS), in addition to physiological global assessment VAS (DOCGL), scored in fewer than 10 seconds in routine care.

Objectives: To test a hypothesis that damage and distress may be prominent in patients with inflammatory conditions, according to mean VAS for inflammation or reversible findings (DOCINF), damage or irreversible findings (DOCDAM), and distress (DOCDST), e.g., fibromyalgia.

Methods: All patients at one site complete a multidimensional health assessment questionnaire (MDHAQ), which includes patient global VAS (PATGL), at each visit in routine care. Physicians complete four 0–10 (none-highest) VAS for DOCGL, DOCDAM, and DOCDST, and a query to estimate the proportion of clinical decisions (total-100%) attributed to each of the 3 findings. Patients were classified into various diagnostic groups, in which scores were analyzed according to mean and standard deviation.

Results: Analyses included 563 patients (Table). Mean levels of DOCGL ranged from 3.2 to 5.2, and PATGL from 3.6 to 6.5, which might be interpreted to indicate high disease activity. Highest mean DOCINF scores were seen in patients with RA, SLE, vasculitis, polyarthritis rheumatica (PMR), spondyloarthropathy (SpA) and gout (2.2-2.8), while highest mean DOCDAM was seen in OA (4.9) and DOCDFST in FM (6.2) (Table). However, in RA, mean DOCDAM was 3.7 vs 2.4 for DOCDIN. DOCDAM also was almost as high or higher than DOCDINF in SLE, SpA, vasculitis, and gout. Mean estimates of distress were also ≥1.5 in patients with all inflammatory diagnoses.

Conclusion: Rheumatologists estimated high levels of damage in patients with RA and other inflammatory rheumatic diseases, similar or higher than inflammation, as well as recognizable distress which may elevate measures such as tender joint count and PATGL. These findings may explain in part low rates of remission and low disease activity noted in RA and other inflammatory diseases, as index scores used to document improvement are not affected by anti-inflammatory therapy. Most rheumatology clinical quantitative measurement is directed to inflammatory activity. However, an estimate of damage and distress may clarify why many patients may appear to lack inflammatory activity despite aggressive treatment, including treat to target in RA.

Disclosure of Interests: None declared

CHARACTERIZING PERSISTENCE OF IV ABATACEPT AMONG ELDERLY PATIENTS WITH RA IN THE US MEDICARE POPULATION

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Background: Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disease characterized by inflammation of the joints, which can ultimately lead to cartilage damage and bone destruction. While early and aggressive intervention with biological treatment may alter the course of the disease and improve physical functioning, persistence to these medications varies, ranging from just 30 to 80%. It is important to understand the factors associated with persistence to RA treatment, as non-adherence may incur greater healthcare costs and utilization, disease progression, and the potential requirement for even more aggressive therapy in the future.

Objectives: To describe patient characteristics and baseline healthcare costs that affect persistence to intravenous (IV) abatacept, which may be supportive in evaluating the risk-benefit ratio of abatacept for treatment of RA.

Methods: Patients (aged >65 years) with at least one inpatient or two outpatient medical claims for RA and subsequent treatment of IV abatacept from 01JUL2006 to 31DEC2016 were identified in the Truven MarketScan Medicare Supplemental database. The date of first prescription of IV abatacept was considered the index date; patients with another biologic DMARD claim on the index date were excluded. Patients were required to have 6 months continuous enrollment before and 12 months continuous enrollment following index date. Persistence was defined as the number of days from treatment initiation (index date) to first switch to another biologic DMARD, discontinuation of abatacept, or end of follow-up. Patients with >6 months of treatment were categorized as high persistence and ≤6 months of treatment as low persistence. Patient characteristics were summarized by level of persistency and compared using Wilcoxon’s rank sum test for continuous variables and chi-square test for categorical variables.

Results: Among 1,963 patients meeting inclusion criteria, 1,167 patients (59.4%) were categorized as having high persistence to IV abatacept. Patient characteristics were similar at baseline between cohorts; the mean age was 74 years, 79% were female, and the mean Charlson Comorbidity Index (CCI) score was 2.02. Compared to low persistency cohort, patients with high persistence to IV abatacept had significantly greater prior exposure to methotrexate (44% vs 51%, p=0.001) and infliximab (18% vs 24%, p<0.001). Patients with high persistence to abatacept also had higher, albeit non-significant, prior use of TNFi (39% vs 41%, p=0.304). In addition, higher persistence to abatacept was significantly associated with higher all-cause baseline medical per patient per month (PPPM) costs ($450 vs $475, p=0.005) and higher RA-related baseline medical PPPM costs ($177 vs $231, p<0.0001). Patients with lower all-cause baseline pharmacy PPPM costs ($709 vs $596, p=0.174) and RA-related baseline pharmacy PPPM costs ($375 vs $272, p=0.773) had higher persistence to abatacept, although these associations were not statistically significant.

Conclusion: Among US Medicare patients with RA, surrogate markers of high disease severity, including prior methotrexate and infliximab use and higher baseline medical costs, were significantly associated with higher IV abatacept persistence. These results may assist both physicians and payers in identifying Medicare patients who benefit from abatacept and tailoring their approach accordingly to minimize the risk of non-persistence.

REFERENCES:


WORK DISABILITY IN A PERUVIAN COHORT OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Work disability in patients with systemic lupus erythematosus (SLE) is common but the factors associated with it in Low and Middle Income Countries have been scarcely evaluated.

Objectives: To determine the prevalence of and the factors associated with work disability in SLE patients.

Methods: We studied 239 consecutive (1997 American College of Rheumatology (ACR) criteria) patients from a Peruvian SLE cohort from October 2017 to December 2018. Work disability was measured from a single self-report questionnaire. Data were collected and included sociodemographic information, clinical lupus features including disease activity [Systemic Lupus Erythematosus Disease Activity Index 2000 update (SLEDAI-2K)], damage [Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDII)], as well as Health-Related Quality of Life (LupusQoL), and medication use. Work disability was defined by patients’ self-report of not being able to work because of SLE. Univariable analysis comparing those patients with work disability and those who remained working were performed with the Mann Whitney U test for continuous variables and the Chi-square test for dichotomous variables. For the multivariable analyses, binary logistic regression with backward elimination was used to determine which factors remained associated with work disability.

Results: Of 239 patients, 194 patients were working at least for at least some time since diagnosis, 181 (93.0%) were female, they had a mean age at diagnosis of 34.5 (12.3) years, and a mean disease duration of 11.5 (7.4) years, their mean SLEDAI was 2.53 (3.7) and their mean SDI was 1.2 (1.5). Twenty-eight patients changed their activities at work due to SLE and 51 (26.6%) stopped working after their diagnosis; 21 of them (41.1%) stopped working because of SLE. One hundred and forty-three were working at the time of the evaluation. In the multivariate analyses, those work-disabled due to SLE were more likely to have higher SLEDAI-2K (p=0.009), and lower HRQoL in two domains, planning: OR=0.975 (CI 95%: 0.954-0.998) p=0.020 and body image OR=0.977 (CI95%: 0.956, 0.998), p=0.032.

Conclusion: Work disability due to SLE is associated with higher damage accrual and a poorer HRQoL.

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Disclosure of Interests: None declared
Rheumatic/systemic irAEs can be divided into 5 phenotypic clusters: articular, muscular, granulomatous, vasculitic and systemic. These findings must be confirmed in real-life patients, and an international data-sharing ICIR registry is planned to be launched.

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declared, Debashish Danda; None declared, Peter Olsson; None declared, Yasunori Suzuki; None declared, Saadettin Kılıçkap; None declared, Gabriela Hernandez-Molina: None declared, Virginia Fernandes Maia, Trevisani; None declared, Sonja Prapatnik; None declared, Idiko Fony Horváth; None declared, Naoto Azuma: None declared, Berkan Araman; None declared, Munther Khamashita: None declared, Xavier Marriette Grant/research support from: Servier, Consultant for: AstraZeneca, Bristol-Myers Squibb, GlaxoSmithKline, Janssen, Pfizer, UCB Pharma

**REFERENCES:**


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**THU0650**

**COMPLEMENTARY AND ALTERNATIVE MEDICINE IN RHEUMATOLOGY: A SURVEY OF ITS USE FOR COMMON RHEUMATOLOGICAL CONDITIONS AMONG MULTI-ETHNIC PATIENTS IN LEICESTERSHIRE**

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**Background:** The use of complementary and alternative medicine (CAM) is common in patients with chronic disease. However, the usage of CAMs among patients with rheumatological conditions has been understudied. A significant portion of primary care trusts are now providing therapies such as acupuncture and osteopathy to some of the 9 million users of CAMs in the United Kingdom (UK). As the NHS serves a varied patient populace, it is important to appreciate the perceptions and utilisation of CAM amongst multi-ethnic groups.

**Objectives:**
1. To identify the different types CAMs utilised by Rheumatology patients.
2. To identify Rheumatology patients' views towards the role and use of CAMs in managing their condition(s).
3. To identify locations where patients receive CAM and to determine patient's spending practices.

**Methods:** A cross-sectional survey on CAMs, and its use for common rheumatological conditions was conducted among multi-ethnic patients in Leicestershire, UK, through convenience sampling. The initial questionnaire was created by a multi-disciplinary input, with a patient-centred focus. Thereafter, 12 questionnaires were piloted and revised accordingly. The data subsequently underwent statistical analyses.

**Results:** A total of 107 patients completed the survey over a 3-month period with a response rate of 90%. Most of the respondents (91.8%) were over the age of 35 (age range 19 to 78 years, mean age 50.512 (SD)). Among the respondents, 66% were women and 34% were men. 72.9% were of white British or European ethnicity and 20.6% of South Asian ethnicity (17.8% Indian and 2.8% Pakistani). Majority of the patients (66.4%) had rheumatoid arthritis (RA), followed by psoriatic arthritis (11.2%) and ankylosing spondylitis (4.7%). The respondent demographics were consistent with known epidemiology of common rheumatological conditions, with a higher prevalence among women than men (female-to-male ratio of 3:1 in RA), 31.8% used CAM for managing symptoms related to their condition(s). Almost half of these respondents (41.2%) used CAM products and/or practices daily, with up to 64.7% spending between £10–£100. The majority of respondents (82.4%) received CAM therapy within the UK, following a phased approach (6.7%) and ankylosing spondylitis (4.7%). The patient demographics were consistent with known epidemiology of common rheumatological conditions, with a higher prevalence among women than men (female-to-male ratio of 3:1 in RA).

**Conclusion:** In our local multi-ethnic population, it is evident that a notable proportion of patients have utilised CAM to supplement the management of their condition. Healthcare professionals need to be aware of the CAMs available, particularly when informing and treating their patients. Effective communication is required in this area to maintain patient's confidence and safety. Further qualitative research should consider the reasons for the use of CAMs.

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**THU0651**

**AN INDIVIDUALIZED DECISION-AID FOR DIVERSE WOMEN WITH LUPUS NEPHRITIS (IDEA-WON): A RANDOMIZED CONTROLLED TRIAL**

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**Background:** Medication decision-making is challenging in lupus. No validated, effective decision-aids are available to assist patients with medication decision-making.

**Objectives:** Our objective was to assess the effectiveness of an individualized, culturally-tailored, computerized decision-aid for immunosuppressive medications for lupus nephritis.

**Methods:** In a multicenter, randomized controlled trial, diverse adult women with lupus nephritis, largely racial/ethnic minorities with low socioeconomic status, were randomized to decision-aid vs. American College of Rheumatology lupus pamphlet (1:1 ratio). Co-primary outcomes were change in decisional conflict and informed choice regarding immunosuppressive medications.

**Results:** Of 301 randomized women, 47% were African-American, 26% were Hispanic, and 15% White. Mean age (standard deviation [SD]) was 37 (12) years, 57% had annual income of <$40,000, and 36% had a high-school education or less. Compared to the pamphlet (n=147), participants randomized to the decision-aid (n=151) had: (1) a clinically meaningful and statistically significant larger decrease in decisional conflict, 21.8 (standard error [SE], 2.5) vs. 12.7 (SE, 2.0; p=0.005); and (2) a clinically meaningful difference in informed choice, statistically non-significant in the main analysis, 41% vs. 31% (p=0.08), but significant in sensitivity analysis (net values for immunosuppressives positive [in favor] vs. negative [against]), 50% vs 35% (p = 0.006). Respectively, unResolved decisional conflict post-intervention was significantly lower, 22% vs. 44% (p=0.01). In delayed group, participants randomized to decision-aid had greater interest in obtaining patient-rated information to be excellent for understanding lupus nephritis (49% vs. 33%), risk factors (43% vs. 27%), medication options (50% vs. 33%; p<0.003 for all); and the ease of use of materials higher (51% vs. 38% p=0.006).

**Conclusion:** An individualized decision-aid was effective in reducing decisional conflict for immunosuppressive medications in diverse women with lupus nephritis.

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declared, Amyle Leong; none declared, Elyse Reyes; none declared, Richard Street; none declared, Maria Suarez-Almazor; none declared, Gay Elia; none declared, Laura Marron; none declared, Charity Ince; none declared, Brennna Caro; none declared, Jeffrey Sloan; none declared, Bochora Jandali; none declared, Salvador Garcia; none declared, Jennifer Grossman; none declared, Kevin Winthrop Consultant for: Gilead, Galapagos, Eli Lilly and Company, Abbvie, Pfizer, GSK, Laura Trupin; none declared, Maria Dall’Era Grant/research support from: University has received funds to serve as a site on this clinical study, Consultant for: On Data Monitoring Committee for Janssen, Biogen, and Genentech; on Steering Committee for EMD Serono., Alexa Meara: none declared, Tara Rizvi: none declared, Winn Chatham: none declared, Jinoos Yazdany Grant/research support from: Pfizer, Consultant for: AstraZeneca.


THE ECONOMIC BURDEN OF ANCA-ASSOCIATED VASCULITIS IN GERMANY – A CLAIMS DATA STUDY

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Background: ANCA-associated vasculitis AAV is a rare systemic disease, characterized by recurrent episodes of systemic inflammation. It is a severe disease associated with hospitalization, risk of renal failure and a therapy inducing serious side effects. The economic impact of AAV to the German health care system is currently not well understood.

Objectives: The aim of this study was to better understand and quantify the economic burden of AAV in Germany. Therefore, selected aspects, such as prevalence and incidence, frequency of hospitalization, frequency of intensive care unit (ICU) stays and treatments costs, were systematically assessed in a claims data study.

Methods: Longitudinal data from years 2013 to 2016, provided by German statutory health insurance (SHI) companies from the InGef database have been analyzed representing an age- and gender stratified cohort of approx. 4 million insured persons representative for the German population.

Results: Prevalence and incidence data show that, in accordance with the previously published literature (1, 2), Granulomatosis with Polyangiitis (GPA) was more frequent than Microscopic Polyangiitis (MPA). On average, a combined prevalence of 256 : 1 000 000 (210 : 1 000 000 for GPA and 46 : 1 000 000 for MPA) was identified within the data set over the observed time period of 4 years (2013-2016). Incidence rates were found to be 46 : 1 000 000 (34 : 1 000 000 for GPA and 13 : 1 000 000 for MPA) within the same time period. Over the observed time period, prevalence and incidence rates remained stable.

The majority of GPA and MPA diagnoses were made in hospitals (61%), another 24% were diagnosed in the outpatient sector and 15% were diagnosed in both within one quarter. In total, 97% of newly diagnosed patients (GPA and MPA) were hospitalized within 4 years post diagnosis. Especially during the induction period (quarter of diagnosis and the following 2 quarters) 91% (GPA) to 95% (MPA) of the patients were hospitalized. Of these patients, approx. 60% were hospitalized due to GPA and MPA disease, showing the high rate of severe co-morbidities.

Patients diagnosed with GPA and MPA were frequently treated at ICUs (in average 1 stay per quarter); in particular severe infections and renal involvements increased the likelihood of ICU stays.

Treatment costs were highest during the induction period; within this period hospitalization represented the largest cost factor. Severe kidney disease, which occurred in 11.6% of GPA and 24.3% of MPA patients, induced total costs ranging between 131.521€ (GPA) to 145.472 € (MPA) over four years post diagnosis, with the induction period being most expensive (approx. 58.826 € to 50.339 € for GPA and MPA during the induction period). In the following years total treatment and hospital costs decreased, however remained high.

Conclusion: AAV represents an underestimated financial burden to the German healthcare system, especially during induction therapy. The high level of hospitalizations amongst AAV patients also represents a high usage of healthcare resources. Thus, AAV represents an underestimated cost factor for the German health care system, and better treatment options are desperately needed.

REFERENCES:


THU0652

THU0653

SOCIOECONOMIC ANALYSIS OF GOLIMUMAB TREATMENT IN PATIENTS WITH RA, PSA, AND AS – NON-INTEVENTIONAL STUDY GO-NICE

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Background: Rheumatic diseases are associated with pain, loss of functionality, fatigue, hospitalization, sick leave, and work disability. This results in high economic burden for patients and society.

Objectives: Golimumab (GLM) is an effective but costly treatment option for patients (pts.) with moderate to severe, active rheumatic diseases. The aim of this analysis of the GO-NICE study was to investigate the direct and indirect costs of healthcare utilization and sick leave after starting a treatment with GLM.

Methods: Data of outpatients collected in the non-observational study GO-NICE in 1,483 pts. with RA (n = 474), PsA (n=501), and AS (n=483) in 158 sites (2010-2015) in Germany were analysed. Details on the study design, pts., characteristics, the clinical and patient-reported outcomes, and safety data have been reported earlier [1,2]. Direct medical and indirect costs per patient and year were calculated for consultations, physiotherapy, massages, hospitalisations and inpatient reha- bilitation, medication (DMARDs, Glucocorticoids, NSAIDs, and biologics) as well as sick leave days. Findings were shown for RA-, PsA- and AS-pts. and categorised by biological-naïve pts. and pts. with a pre-treatment with a biologic. The 6-month periods prior baseline (BL)/start of a GLM therapy vs. month 24 (M24) were compared.

For this calculation the standardized evaluation rates were used (Bock et al. (2015), AG MEG of the DGSMMP (2005)). Costs for prescribed and documented medication were calculated by the mean cost per defined daily dose (detailed use 2010-2015). Indirect costs were estimated through the human capital approach (HCA).

Results: Data of 758 biologic-naive pts. (n = 265 RA, 247 PsA and 246 AS) and 694 pts. with biologics as pre-therapy (n = 208 RA, 252 PsA and 234 AS) were included in the analysis. Direct medical costs (excl. medication) decreased in all 6 groups, min. 765€ (PsA pre-treatment group) and max. 2,426€ (AS pre-treatment) as well as the costs due to work disability/sicknessism, min. 855€ (PsA pre-treatment) and max. 2,564€ (RA pre-treatment, table). Total costs in biological-naive pts. increased due to the additional expense of the biologic agent.

Absolute changes in costs totalled 15,685€ (RA-, table), 15,799€ (PsA-) and 14,764€ (AS-patients) per patient and year when comparing the BL vs. M24 periods.

Total savings of 6,289€ (RA-, table), 2,617€ (PsA-), and 5,555€ (AS-patients) per patient and year were generated in the group of biologic-pre-treated patients.

RA pts. biologic-naive (n=265) RA pts. with biologics as pre- treatment (n=208)

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Month 24</th>
<th>Changes</th>
<th>Baseline</th>
<th>Month 24</th>
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<td>-109</td>
<td>148</td>
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</table>

162 59 - 103 144 91 - 53

(inc- and out-patients)
Direct med. costs/C.
(excl. medication)
Comedication.
Biologica.
Medication.
Absorptions.
Total.

|                      | 1.618 | 381 | 1.237 | 1.823 | 692 | -1,131 |

Table 1. Costs per patient and year (Subgroup patients with RA)

Conclusion: Costs of healthcare utilization, as well as work disability decreased after starting GLM within an observation period of 24 months, for pts. with RA, PsA, and AS, respectively. Due to the high costs of TNFi therapy, drug costs in the group of biologic-naive pts. rose markedly. Savings were generated in the group of pts. pre-treated with biologics.

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THU0654 INFLUENCE OF THE NEW PHARMACOLOGICAL AND NON-PHARMACOLOGICAL APPROACHES IN RHEUMATOID ARTHRITIS ON WORK PARTICIPATION: A SYSTEMATIC LITERATURE REVIEW

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Background: Rheumatoid arthritis (RA) is a chronic and progressive autoimmune disease that frequently has a negative impact on work participation among patients. Even more, patients with RA are at greater risk to become work disabled, have a reduced work productivity (presenteeism) or increased sick leave (absenteeism) compared to the general population. This outcome can be related to the World Health Organization International Classification of Functioning, Disability and Health (the WHO ICF framework), that is useful in understanding the impact of RA regarding functioning. Since 2000, the management of RA has made significant progress. With the establishment of the new ACR/ EULAR criteria and the treat-to-target (T2T) strategies, patients are nowadays diagnosed and treated earlier. Furthermore, the improvement of the management of RA has led to much better results regarding disease activity and joint destruction. However, many of these patients are confronted with additional fees when contracting private insurances, since the risk assessment by insurances is mainly based on historical data.

Objectives: This systematic literature review was performed to study the influence of new pharmacological and non-pharmacological approaches on work participation among patients with RA with the objective to improve the risk assessment of RA patients when contracting private insurances.

Methods: A systematic literature review from January 1990 until January 2018 was performed using Pubmed, Embase and Web of Science. Different search terms were used in each database: employment, workplace, sick leave, absenteeism, work capacity and international classification of functioning, disability and health. All studies assessing one of the search terms were analysed.

Results: Finally, 49 relevant articles were selected. The selected studies were subdivided according to study design (RCT versus cohort studies and disease duration of the studied patients. Studies that examined the value of an adequate early intervention were grouped separately. Overall, studies on the impact of the non-pharmacological approach were limited and very heterogeneous. Positive results of pharmacological agents (combination of DMARDs or biologic therapy) on work participation could be demonstrated in patients with recent-onset RA. Long-term observational studies showed an association between initiation of new therapeutic strategies and a reduction in work disability among patients with RA. However a causal relation was difficult to confirm because of the study design. Moreover, some studies pointed out other contextual factors that also influence work disability such as political policy, demographic changes in age distribution or educational level.

Conclusion: The large heterogeneity in terms of patient population, study design and outcome measures limits interpretation of the data. However, this systematic literature review could demonstrate that the effect of a treatment is of utmost importance and not the treatment itself. This emphasizes also the importance of early intervention with pharmacological agents regarding work productivity outcomes in RA. In addition, the impact of personal and environmental factors on work participation may not be neglected.

REFERENCES: Disclosure of Interests: None declared

Epidemiology, risk factors for disease or disease progression

THU0655 LONG-TERM OUTCOME OF JUVENILE IDIOPATHIC ARTHRITIS: COMPARISON OF BIOLOGIC AND METHOTREXATE ERAS

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Background: After nearly two decades from the start of the Biologic era, systematic analyses of patients with juvenile idiopathic arthritis (JIA) have shown a high frequency of attainment of inactive disease (ID) and satisfactory levels of physical function and quality of life. However, whether and to what extent the disease prognosis has improved in comparison with the methotrexate (MTX) era is still uncertain.

Objectives: To compare the long-term disease state, in terms of activity and damage, of children with JIA who had their disease onset in MTX or Biologic eras.

Methods: Patients were included in MTX or Biologic era cohorts depending on whether their disease presentation occurred before or after January 2000. Patients in the MTX era cohort and part of the patients in the Biologic era cohort were taken from a previous cross-sectional study published by our group, which enrolled 310 patients with disease onset between December 1986 and December 2002. An additional sample of patients with onset in the Biologic era was enrolled in a subsequent prospective cross-sectional study, which included all consecutive patients meeting the ILAR criteria for JIA, who were seen consecutively at the Istituto Gaslini of Genoa, Italy, between January 2015 and June 2017. All patients had disease duration ≥ 5 years and underwent a prospective cross-sectional assessment, which included measurement of disease activity and damage. ID and low disease activity (LDA) states were defined according to Wallace, JADAS10 and cJADAS10 criteria. Articular and extra-articular damage was assessed with the Juvenile Arthritis Damage Index (JADI).

Results: MTX and Biologic era cohorts included 239 and 269 patients, respectively. Patients were divided in the “functional phenotypes” of oligoarthritis and polyarthritis. At cross-sectional visit, patients in the Biologic era cohort with either oligoarthritis or polyarthritis had consistently higher frequencies of ID and LDA than patients in the MTX era cohort. The measurement of disease damage at cross-sectional visit revealed that the frequency of impairment of > 1 JADI-Articular items was higher in MTX than in Biologic era cohort (17.6% versus 11% in oligoarthritis and 52.6% versus 21.8% in polyarthritis). Likewise, frequency of involvement of > 1 JADI-Extraarticular item was higher in MTX than in Biologic era cohort (26.5% versus 16.2% in oligoarthritis and 31.4% versus 13.5% in polyarthritis). The sole JADI items that were detected in more than 5% of patients in the Biologic era cohort were temporomandibular damage in oligoarthritis and polyarthritis, ankle damage in polyarthritics and leg-length inequality in oligoarthritis. The analysis of the temporal trend of damage development over the 25 years of our analysis (1986-2011) highlighted
the marked decrease in damage over time and the more pronounced decline in the Biologic era (Figure 1).

Conclusion: Our study provides evidence of the remarkable prognostic improvement obtained with the recent therapeutic advance in JIA.

REFERENCES:

Disclosure of Interests: Gabriella Giancane: None declared, Valentina Muratore: None declared, Valentina Marzetti: None declared, Neus Quilis Marti: None declared, Belén Serrano Benavente: None declared, Francesca Bagnasco: None declared, Alessandra Alongi: None declared, Adele Civeno: None declared, Lorenzo Quartulli: None declared, Alessandro Consolaro Grant/research support from: AbbVie, Pfizer, Angelo Ravelli Grant/ research support from: Angelini, AbbVie, Bristol-Myers Squibb, Johnson & Johnson, Novartis, Pfizer, Reckitt Benker, and Roche, Consultant for: Angelini, AbbVie, Bristol-Myers Squibb, Johnson & Johnson, Novartis, Pfizer, Reckitt Benker, and Roche

THU0656 IMMUNE CHECKPOINT INHIBITORS IN PATIENTS WITH CANCER AND RHEUMATOLOGIC DISEASES: A SYSTEMATIC REVIEW OF THE LITERATURE

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Background: Immune checkpoint inhibitors (ICI) have resulted in unprecedented advancements in the treatment of cancer, with remarkable survival benefits, unseen with traditional treatment. While the benefits of ICI have been clearly documented, a myriad of immune-related-adverse events (irAEs) have been recognized in multiple organs and systems, secondary to persistent activation of the immune system.

Objectives: To systematically review the literature and provide an updated summary on adverse events associated with the use of ICI therapy in patients with cancer and rheumatologic diseases.

Methods: Five electronic databases were searched through 2018 with no restrictions. Articles were screened and selected by two independent investigators using a 2-step approach. Case reports, series, and observational studies describing patients diagnosed with rheumatologic disease prior to initiation of ICI for treatment of concomitant cancer were included.

Results: A total of 69 patients in 27 publications were identified. Median age was 65 (38-87) years; 50% were female; 90% had metastatic melanoma; and 64% were receiving anti-cytotoxic T-lymphocyte-associated protein 4 (anti-CTLA-4) antibody. Rheumatoid arthritis was the most common underlying disease, and 55% (n=38) had de novo irAEs. Patients with active diseases at ICI initiation seemed to have more disease flare than those with inactive disease (61% vs. 29%; p = 0.03), while no differences were observed in de novo irAEs (36% vs. 39%). Patients with rheumatoid arthritis were reported to have more flares with anti-CTLA-4 antibody (63% vs. 33%), while those with spondyloarthropathy reported more flares with anti-programmed cell death 1 agents (63% vs. 29%); however numbers were small. Patients receiving immunosuppressive therapy at ICI initiation had fewer adverse events than those not receiving treatment (26% vs. 44%). Most flares and irAEs were managed with corticosteroids, and 13% required additional disease modifying anti-rheumatic drugs. Adverse events improved in 64% and did not require discontinuation of ICI therapy. In melanoma patients, disease control rate was 44%. In all patients, no treatment related mortality was reported.

Conclusion: About one third of patients with pre-existing rheumatologic autoimmune disease flared after receiving ICI therapy for treatment of cancer. However, flares and irAEs can often be managed and may not require discontinuation of cancer therapy. Prospective longitudinal studies are needed to evaluate potential differences among diseases and to determine optimal toxicity therapy while conserving antitumor immunity.

Disclosure of Interests: None declared

THU0657 ASSOCIATION OF DIET AND SPICES WITH TREATMENT OUTCOME IN ASIAN INDIAN PATIENTS WITH RHEUMATOID ARTHRITIS — A CROSS SECTIONAL STUDY

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Background: Influence of diet on inflammation, especially foods like fish oil, spices like turmeric, capsaicin, garlic etc. are reported in published literature. However, a well-designed study on this subject amongst Asian Indian patients is lacking.

Objectives: To analyze whether the type and quantity of intake of various food constituents, with particular reference to Indian spices, makes an impact on the control of disease activity in patients with Rheumatoid arthritis(RA)

Methods: Patients diagnosed as RA by the ACR 2010 criteria and receiving standard triple drug therapy in our clinic between June 2017 and June 2018, for at least one year were enrolled. Disease activity was assessed during the routine OPD visit. They were administered a food frequency questionnaire [1] pertaining to the quality as well as quantity of food and spice intake. Analysis was done using multivariate logistic regression

Results: A total of 400 patients were included with 86.75% females. 67.75% patients were in disease remission, 10% had mild disease activity and 22.25% moderate to high disease activity; only 18.09% were vegetarians and the rest consumed non-vegetarian food. Median age was 47.98years(SD 10.67);median duration of illness prior to presentation to our clinic was 7years(IQR 4.10), median ESR was 37mm/hr(IQR 23.52), median CRP was5.34mg/L(IQR 2.04,12.4), and median DAS28CRP was 2.07(IQR 1.64,2.97).

Patients with DAS28CRP of ≤2.6 were compared with those >3.2. Statistically higher consumption of ginger, garlic, turmeric and coriander were noted amongst patients in remission. Similar results were obtained when patients with DAS28CRP of ≤1.4 were compared with DAS28CRP >5.1. Significant numerical differences were noted for intake of food constituents like wheat, total pulse, vegetables, fruit, milk and fish

<table>
<thead>
<tr>
<th>Dietary items</th>
<th>n Quantity in grams Median (IQR)</th>
<th>n Quantity in grams Median (IQR)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ginger</td>
<td>244</td>
<td>4.17 (2.67, 6.67)</td>
<td>80</td>
</tr>
<tr>
<td>garlic</td>
<td>253</td>
<td>4.17 (2.78, 6.67)</td>
<td>78</td>
</tr>
<tr>
<td>turmeric</td>
<td>267</td>
<td>1.11 (0.71, 1.67)</td>
<td>88</td>
</tr>
<tr>
<td>jaggery</td>
<td>215</td>
<td>0.45 (0.37, 0.83)</td>
<td>64</td>
</tr>
<tr>
<td>cinnamon</td>
<td>64</td>
<td>0.42 (0.28, 0.55)</td>
<td>34</td>
</tr>
<tr>
<td>cloves</td>
<td>85</td>
<td>0.42 (0.28, 0.55)</td>
<td>28</td>
</tr>
<tr>
<td>coriander</td>
<td>230</td>
<td>1.11 (0.67, 1.67)</td>
<td>78</td>
</tr>
<tr>
<td>pepper</td>
<td>179</td>
<td>0.42 (0.33, 0.67)</td>
<td>57</td>
</tr>
<tr>
<td>chilli</td>
<td>259</td>
<td>2.08 (1.67, 3.33)</td>
<td>88</td>
</tr>
</tbody>
</table>
Conclusion: Higher consumption of Indian spices like ginger, garlic, turmeric and coriander were found to be associated with better control of disease activity and hence the inflammation, as evidenced by DAS28CRP in patients with Rheumatoid arthritis, receiving standard triple therapy.

REFERENCES:

Disclosure of Interests: None declared
Catastrophizing in Rheumatology

CHARACTERIZATION OF SCLERODERMA PATIENTS


Background: Rheumatic disorders (RD) provide chronic pain. Catastrophizing in RD patients is suspected to be involved in persistence and amplification of chronic pain.

Objectives: To assess catastrophizing level in RD and to evaluate the association between catastrophizing and physical pain intensity, disease activity, disability, depression and quality of life.

Methods: We performed a systematic review of literature and search in the following databases: MEDLINE, COCHRANE and EMBASE until April 2018. All observational, cross-sectional and randomized control studies investigating catastrophizing in patients with RD (rheumatoid arthritis (RA), low back pain (LBP), osteoarthritis) were included. Statistical analysis defined pooled mean catastrophizing level by using the Pain Catastrophizing Scale (PCS), the latter ranging from 0 to 52. To assess the association between catastrophizing and disease activity (DAS28), pain (Numerical Rating Scale NRS), disability (ODI) and quality of life (SF36, WOMAC) we collected correlation coefficients and pooled them in a meta-analysis using the Fisher’s z transformation with MedCalc v18.11.3.

Results: From 1494 articles concerning catastrophizing and RD, 51 were selected for a meta-analysis:

- 601 RA patients (mean age 57.4 years, 67.7% female, mean pooled DAS 28 = 3.4 and mean pooled NRS = 3.8) included in 7 studies. The mean pooled catastrophizing level at baseline was 14.7 (SD = 11.4) in RA patients vs 2.7 (SD = 3.0) in control group patients (n= 82 in 2 studies). In one study, a RA sample identified 22% of high catastrophizing (defined by PCS ≥ 40).
- 3251 LBP patients (mean age 43.6 years, 57% female, mean pooled NRS = 4.5 and mean pooled ODI = 30.3) included in 27 studies. The mean pooled catastrophizing level at baseline was 19.9 (SD = 11.3).
- 3388 osteoarthritis patients (knee and hip, mean age 67.7 years, 65% female, mean pooled NRS = 5.0) included in 17 studies. The mean pooled catastrophizing level at baseline was 21.2 (SD = 10).

In RA, a significant positive correlation between catastrophizing and DAS 28 was observed: pooled r=0.278 p<0.001 (3 studies) (Figure 1). Pain level was strongly associated with catastrophizing (r=0.71 p<0.01). Higher PCS scores were significantly associated with higher levels of distress i. e. lower SF-36 Mental Health score (r= -0.52 p<0.01) and significantly associated with reduced physical function (r= -0.35 p<0.01) for SF36 Physical Function.

In LBP, higher PCS scores were significantly associated with higher levels of pain and disability : pooled r=0.486 p<0.001 (NRS) and r=0.465 p<0.001 (ODI), respectively. The association between catastrophizing and depression was significant (r=0.538 p<0.01).

Catastrophizing in osteoarthritis was strongly associated with an increase in functional limitations and pain (i.e. higher WOMAC total score, correlation coefficient: rs 0.641 p<0.001).

Conclusion: Catastrophizing is a common psychological trait clearly associated with disease activity, pain, mental health and physical function. Nevertheless catastrophizing is rarely measured. It might be relevant to detect it earlier in order to adapt pharmacologic and non-pharmacologic treatment in at-risk patients.

REFERENCES:


CHARACTERIZATION OF SCLERODERMA PATIENTS ACCORDING TO ROS2 AND KU ANTIBODIES


Background: Systemic Sclerosis (SSc) is an autoimmune disease that is characterized by progressive and severe fibrosis with cutaneous and visceral involvement, fibroproliferative vasculopathy and alterations of cellular and humoral immunity, very heterogenous from the clinical and immunological point of view. There are many types of antibodies related to the disease that are used in the diagnosis and characterization. Antibodies anti-Ku and anti-Ro52 have been found, although they are not specific to the disease, that could play an important role in the prognosis and clinical expression.

Objectives: To evaluate the clinical pattern and prognosis of SSc patients who carry antibodies Anti-Ku and Anti-Ro52.

Methods: A retrospective, multicentric study of SSc patients included in the Spanish Registry of Scleroderma (RESCLE). Clinical, demographic, prevalence, serological, and survival data were analyzed.

Results: A total of 401 samples were analyzed for anti-Ku with 12 positive results (3%). For anti-Ro52, 1724 sampled were analyzed with 246 positive results (14%). It is observed, from the multivariant analysis, that patients with anti-Ro52 presented, in higher frequency, an association with Sscas syndrome (p<0.001) and its coexistence with the antibody anti-La (OR 4.49 with 95% CI 11.2 p<0.01). Regarding patients with anti-Ku, no clinical association was found with statistical significance.

Conclusion: As opposed to finding SSc specific antibodies such as anti-centromere (ACA), anti-topoisomerase I (ATA), and anti-RNA polymerase III (ARA), the presence of anti-Ku or anti-Ro52 is not conclusive of any distinct clinical profile.

REFERENCES:

Background: A recent study showed that the risk of ankylosing spondylitis (AS) was increased in patients with uveitis.1 Objectives: The study aimed to test the risk of psoriasis (PsO), Crohn’s disease (CD), ulcerative colitis (UC) and AS in uveitis patients.

Methods: The data source of this study was the 2003–2012 claims data from the Taiwanese National Health Insurance Research Database. We identified 4,943 incident patients with uveitis defined as having ≥ 2 ambulatory or inpatient visits with a diagnosis of ICD-9-CM 360.12, 364.00–364.02, 364.04–364.05 or 364.43 made by an ophthalmologist from 2006 to 2012 after excluding those having prior PsO (ICD-9-CM 696.1), PsA (ICD-9-CM 696.0), CD (ICD-9-CM 555), UC (ICD-9-CM 556) or AS (ICD-9-CM 720) and randomly selected 49,430 non-uveitis individuals as controls. We estimated the incidence rates of PsO (diagnosed by dermatologists), CD, UC and AS for the uveitis and non-uveitis cohorts, and the incidence rate ratios (IRR) and hazard ratios (HRs) after adjusting for sex, age, Charlson comorbidity index and concomitant medications.

Results: No incident case of CD was identified in uveitis patients and patients with uveitis had significantly higher incidence rates of PsO (IRR, 8.82; 95% CI, 6.80–11.43), CD (IRR, 7.23; 95% CI, 5.12–10.28) and AS (IRR, 171.69; 95% CI, 143.15–205.93). However, after adjusting for potential confounders, uveitis patients had a significantly higher risk of developing PsO and AS, but not CD.

Conclusion: This nationwide, population-based cohort study revealed that uveitis patients had an increased risk of PsO and AS, but not CD.

REFERENCES:

Table 1. The associations between covariates with psoriasis, ankylosing spondylitis, Crohn’s disease and traffic accident shown as adjusted hazard ratios with 95% confidence intervals estimated by Cox regression analyses

<table>
<thead>
<tr>
<th>Covariate</th>
<th>Psoriasis</th>
<th>Ankylosing spondylitis</th>
<th>Crohn’s disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uveitis</td>
<td>1.73</td>
<td>1.72</td>
<td>0.71</td>
</tr>
<tr>
<td>Age</td>
<td>1.02</td>
<td>0.96</td>
<td>0.99</td>
</tr>
<tr>
<td>Charlson comorbidity index</td>
<td>0.97</td>
<td>0.56</td>
<td>1.01</td>
</tr>
<tr>
<td>Concomitant medication</td>
<td>0.39</td>
<td>0.56</td>
<td>0.56</td>
</tr>
<tr>
<td>DMARD</td>
<td>0.29</td>
<td>0.29</td>
<td>0.45</td>
</tr>
<tr>
<td>Immunosuppressant</td>
<td>0.45</td>
<td>0.39</td>
<td>0.77</td>
</tr>
<tr>
<td>Corticosteroid</td>
<td>0.57</td>
<td>0.43</td>
<td>0.24</td>
</tr>
</tbody>
</table>

Acknowledgement: We thank the Biostatistics Task Force of Taichung Veterans General Hospital, Taichung, Taiwan, ROC for statistical support.

Disclosure of Interests: Hsin-Hua Chen Speakers bureau: Johnson & Johnson, Novartis, Pfizer, Abbvie, Roche, UCB, Bristol-Myers Squibb, Chugai, Tsu-Yi Hsieh: None declared, Ching-Heng Lin: None declared, Yi-Ming Chen Grant/research support from: GSK, Pfizer, BMS, Astra & Zeneca, Consultant for: Pfizer, Novartis, Abbvie, Johnson & Johnson, BMS, Roche, Sanofi, MSD, Guigai, Astellas UCB Thermo Fisher, Paid instructor for: Pfizer, Novartis, Abbvie, Johnson & Johnson, BMS, Roche, Astra Zeneca, Sanofi, MSD, Guigai, Astellas UCB Thermo Fisher, Speakers bureau: Pfizer, Novartis, Abbvie, Johnson & Johnson, BMS, Roche, Lilly, GSK, Astra Zeneca, Sanofi, MSD, Guigai, Astellas UCB Thermo Fisher, Kuo-Lung Lai: None declared, Der-Yuan Chen: None declared


REFERENCES:

Disclosure of Interests: None declared
The absolute risk of clinically diagnosed gout by clusters of gout associated comorbidities and lifestyle factors – results from 30 years follow-up of the Malmö preventive project cohort in southern Sweden

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Background: Clinical gout is predicted by a number of factors. Several of these (comorbidities and lifestyle) have been shown to cluster in gout patients1,2 indicating several different pathophysiological pathways, but it is not known if and to what extent such clusters predict gout.

Objectives: To examine: 1) the prevalence of comorbidity clusters in the population and 2) the long-term absolute and relative risks for developing gout in these clusters defined at baseline in subjects of Malmö Preventive Project (MPP).

Methods: The MPP is a screening program for cardiovascular risk factors, alcohol abuse and breast cancer in Malmö, Sweden. A total of 33,346 individuals (67% male, age=45.7 years, mean follow-up=28.2 years) screened between 1974 and 1992, participated. Date of gout diagnosis was defined as the first visit with gout (using ICD-codes) to physicians within primary or specialized care, through linkage of the MPP cohort with regional and national health care registers. End of follow-up was defined as the date of first gout diagnosis, death, moving from the area or December 31st, 2014. Hierarchical clustering was performed in a subset of 22,057 individuals (screening period: 1975-1992) to group observations. Variables clustered included obesity, renal dysfunction, diabetes mellitus (DM), hypertension, cardiovascular disease (CVD), dyslipidemia, pulmonary dysfunction (PD), smoking and use of diuretics. For the five identified clusters, their population prevalence as well as the incidence and hazard ratio (HR) for gout were computed using cox-proportional hazard analysis in Rv3.5.2.

Results: Cluster-1 (C1) with “few comorbidities” was by far the most common in the population (73%), followed by cluster-4 (C4) characterized by “obesity and hyperlipidaemia” (17%). These two pathways included 86% of incident gout cases during the follow-up. The four clusters (C2-5) identified by different comorbidity patterns all resulted in a 2-3 fold increased risk for incident gout. The highest incidence for gout was seen for cluster-2 (C2) characterized by “renal dysfunction” and cluster-3 (C3) characterized by “cardiovascular disease” (Table).

Table: Incidence and hazard ratios for gout in observation-clusters of MPP cohort

<table>
<thead>
<tr>
<th>Cluster name</th>
<th>Main characteristics</th>
<th>Occurrence, n (%)</th>
<th>Incident cluster</th>
<th>Incidence*</th>
<th>HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1 Few comorbidities</td>
<td>No history of diabetes, CVD or renal disease.</td>
<td>16063 (72.8)</td>
<td>551</td>
<td>119</td>
<td>1</td>
</tr>
<tr>
<td>C2 Renal dysfunction</td>
<td>Renal dysfunction (100%), higher age at inclusion</td>
<td>750 (3.4)</td>
<td>53</td>
<td>269</td>
<td>2.31 (1.73-3.07)</td>
</tr>
<tr>
<td>C3 High frequency of CVD</td>
<td>(100%), smoking (74%), alcohol risk behaviour (40%), PD (22%)</td>
<td>528 (2.4)</td>
<td>26</td>
<td>224</td>
<td>2.41 (1.63-3.56)</td>
</tr>
<tr>
<td>C4 Obesity and hyperlipidaemia</td>
<td>High frequency of obesity (34%) &amp; hyperlipidaemia (74%)</td>
<td>3673 (16.7)</td>
<td>235</td>
<td>235</td>
<td>2.02 (1.73-2.35)</td>
</tr>
<tr>
<td>C5 Diabetes mellitus and hypertension</td>
<td>High frequency of DM (51%), hypertension (53%) &amp; diuretics use (52%)</td>
<td>1043 (4.7)</td>
<td>45</td>
<td>184</td>
<td>1.98 (1.46-2.68)</td>
</tr>
</tbody>
</table>

*Incidence per 100,000 person-years at risk. **Adjusted for age, sex

Conclusion: In a population-based study, we identified five clusters based on gout-related comorbidities. Most gout cases occurred in the cluster characterized by few comorbidities. Such cases may have predisposing factors not captured by comorbidity patterns, e.g. genetics related to serum urate. In addition, we identified four pathways each defined by different comorbidity patterns and contributing to increased risk for gout, pathways that may require partly individual interventional strategies.

References:

Disclosure of Interests: None declared.

PREVALENCE OF RHEUMATIC DISEASES IN COLOMBIA: AN APPROACH FROM MINISTRY OF HEALTH AND SOCIAL PROTECTION DATA (SISPRO)

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Background: The ministry of health and social protection of Colombia uses a system named SISPRO as a tool to establish the basic information of the health system. This information is public and available for anyone to search. We analyze the prevalence and specific characteristics of patients with rheumatic diseases registered in a colombian health system between 2012 to 2016.

Objectives: To establish the prevalence and basic epidemiological characteristics of the main rheumatic diseases in Colombia.

Methods: This is a descriptive epidemiological study using the International Statistical Classification of Diseases and Related Health Problem (ICD-10) as keywords for each rheumatic disease during the analysis of SISPRO data and National Statistical System (DANE) populations projections, as from the last census in Colombia to estimated prevalence of each disease.

Results: Colombia is a middle-income country with an estimated population of 49.834.240 inhabitants to 2018 according to 2005 census projections. Despite some limitations of SISPRO data, actually is the only official database of the government. We calculate the estimated prevalence and number of patients with some rheumatic diseases (table 1), confirming that autoimmune diseases are more frequent in women, and surprisingly, spondyloarthritides (ankylosing, psoriatic and inflammatory bowel disease) are also discreetly more frequent in woman population.

Total cases Prevalence (%) Ratio woman:man
Rheumatoid arthritis 248.995 0.520 4.71 : 1
Ankylosing spondylitis 64.356 0.177 2.71 : 1
Gout 70.881 0.149 0.25 : 1
Sjögren syndrome 58.680 0.123 4.63 : 1
Systemic lupus erythematosus 41.804 0.088 4.17 : 1
Polymyalgia rheumatic 35.331 0.070 6.69 : 1
Sjögren syndrome 10.473 0.022 3.22 : 1
Inflammatory miopathy 8.498 0.018 1.76 : 1
Psoriatic arthritis 1.670 0.004 1.32 : 1
Gouty arthritis with polyarthritis 750 0.014 7.44 : 1
Bechet Disease 523 0.001 2.15 : 1
Churg Strauss disease (EGPA) 186 0.001 2.24 : 1

Conclusion: Epidemiological and prevalence information of rheumatic diseases in Colombia is presented. The data found in the study are concordant with epidemiological studies in other countries.

Disclosure of Interests: None declared

SERIOUS/AT LEAST MODERATE INFECTIONS IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS ON SYNTHETIC AND BIOLOGIC DRUGS FROM THE PHARMACHILD REGISTRY

Gabriella Giancane, Joost F. Swart, Nikolay Tzaribachev, Nadina Rubio, Ruben Cuttica, Ingrida Rumba-Rozenfelde, Wafa Mohammed Saad Suwairi, Calin Lazar, Yosef Uziel, Albenia Telchavara, Tadej Avcin, Angela Minaiči, Emilia Len, Stella Maris Garay, Alina Boteneu, Angela Pistorio, Nico Wulffraat, Nicola Ruperto, Gabriella Giancane: None declared, Joost F. Swart: None declared, Nikolay Tzaribachev: None declared, Nadina Rubio: None declared, Ruben Cuttica Grant/research support from: Roche, Pfizer, Lilly, Bristol Myers Squibb, Novartis, Sanofi, Sanofi Aventis, UCB, Janssen, Janssen, Novartis, Sanofi Aventis, UCB, Janssen, Ingrida Rumba-Rozenfelde: None declared, Wafa Mohammed Saad Suwairi: None declared, Calin Lazar: None declared, Yosef Uziel: None declared, Albenia Telchavara: None declared, Tadej Avcin: None declared, Gabriella Giancane: None declared, Joost F. Swart: None declared, Nikolay Tzaribachev: None declared, Nadina Rubio: None declared, Ruben Cuttica Grant/research support from: Roche, Pfizer, Lilly, Bristol Myers Squibb, Novartis, Sanofi, Sanofi Aventis, UCB, Janssen, Janssen, Ingrida Rumba-Rozenfelde: None declared, Wafa Mohammed Saad Suwairi: None declared, Calin Lazar: None declared, Yosef Uziel: None declared, Albenia Telchavara: None declared, Tadej Avcin: None declared.

Methods: Serious and at least moderate infections were analysed in JIA patients, enrolled in the Pharmachild registry at September 30th, 2018, with more than 6 months of follow up. We divided patients in 3 treatment groups: “MTX alone”, in which patients had received MTX as the only drug over all their history; “MTX Start”, in which patients had received MTX as first drug; “MTX+TNFi” for those patients who received a TNF in addition to MTX after a period of “MTX Start”. All the 3 groups were considered as endpoints for each infecion. We considered serious infections as those that occurred in the drug period stopped as soon as the second drug was introduced. For the group “MTX+TNFi”, we considered all the possible correlations between start and end dates of the two drugs, including the time lag of 90 days after any treatment stop. If the interval between two drugs was shorter than 90 days, treatment was considered continuous. Crude rates (number of infections divided by drug exposure, excluding off-drug periods) and true incidence rates (number of first infections divided by the time lag between first drug administration and the date of the infection if the patient experienced the infection, the last Pharmachild visit if the patient didn’t experience the event) were calculated.

Results: We enrolled in Pharmachild a total of 8061 patients who experienced 1686 infections. We excluded 41 patients who had infections before any treatment start. Of the final number of 8020 patients, we considered: 1226 patients in the group “MTX alone”, 3128 in the group “MTX start” and 1026 in the group “MTX+TNFi”. 7.7% of the patients in the “MTX alone” group, 2.7% of the patients in the “MTX Start” group and 7.0% of the patients in the “MTX+TNFi” group experienced at least one infection. Crude rates of infections per 1000 person-years resulted: 48.0 for the group “MTX alone”, 22.0 for “MTX Start”, 74.0 for “MTX+TNFi”. Incidence rates per 1000 person-years were: 32.0 for the group “MTX alone”, 17.0 for “MTX Start”, 59.5 for “MTX+TNFi”. The percentage of drug exposure on the patient follow-up was variable among the 3 treatment groups (from 15.6% for the “MTX+TNFi” group to 51.5% for the “MTX alone” group).

Conclusion: Pharmachild showed, through the analysis of pure treatment groups, that the addion of the anti-TNF biologic to MTX even triples the incidence rate of infections.

References:

Disclosure of Interests: Gabriella Giancane: None declared, Joost F. Swart: None declared, Nikolay Tzaribachev: None declared, Nadina Rubio: None declared, Ruben Cuttica Grant/research support from: Roche, Pfizer, Lilly, Bristol Myers Squibb, Novartis, Sanofi, Sanofi Aventis, UCB, Janssen, Janssen, Ingrida Rumba-Rozenfelde: None declared, Wafa Mohammed Saad Suwairi: None declared, Calin Lazar: None declared, Yosef Uziel: None declared, Albenia Telchavara: None declared, Tadej Avcin: None declared, Gabriella Giancane: None declared, Joost F. Swart: None declared, Nikolay Tzaribachev: None declared, Nadina Rubio: None declared, Ruben Cuttica Grant/research support from: The Gaslini Hospital, where NR works as full-time public employee, has received contributions (> 10.000 USD each) from the following industries in the last 3 years: BMS, Eli-Lilly, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sinergie, Sobi and Takeda., Speakers bureau: Received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, Abbvie, AstraZeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sinergie, Sobi and Takeda., Speakers bureau: Received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, Abbvie, AstraZeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sinergie, Sobi and Takeda.

OVERALL INFECTION RISK IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING ABATACEPT, RITUXIMAB AND TOCILIZUMAB: AN OBSERVATIONAL COHORT STUDY

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Background: Most infections in patients with rheumatoid arthritis (RA) are treated in primary care with a prescription of antibiotics. Only a small fraction requires hospitalization. Existing studies of infection risk in patients with RA, who receive non-tumor-necrosis-factor-inhibitor biologic (non-TNFi) therapy, however, have focused primarily on hospitalized infections. (1)

Objectives: In Danish RA patients treated in routine care with the three non-TNFi abatacept, rituximab and tocilizumab 1) to compare adjusted incidence rates (IR) of infections overall, and 2) to estimate the relative risk (RR) of infections across the drugs during the first year of non-TNFi treatment.

Methods: We conducted an observational cohort study including all RA patients in DANBIO who started a non-TNFi treatment between January 2010 and December 2017. Clinical characteristics at baseline were described. We defined infections as either a prescription of antibiotics or a hospitalization due to infection. Baseline comorbidities, antibiotic prescriptions and hospitalized infections were identified through linkage to national registries. We calculated IRs of infections per 100 person-years (age and gender adjusted) and rate ratios (as estimates of RRs, adjusted for additional covariates) during the first year of treatment (Poisson regression).

Results: We identified 3,696 treatment series of non-TNFi (abatacept 1,115/rituximab 1,071/tocilizumab 1,564). Patients receiving rituximab tended to be older, had longer disease duration and more previous malignancies. During the first year of treatment, 1,747 infections were identified. Age and gender adjusted IRs per 100 person-years were (abatacept/rituximab/tocilizumab): 76.1(69.3; 83.6)/87.3(79.3; 96.1)/77.4(71.4; 83.9). Adjusted RRs (Table) were 0.88(0.76; 1.02) for abatacept and 0.87 (0.75; 1.00) for tocilizumab compared to rituximab. For abatacept vs. tocilizumab it was 1.02 (0.89; 1.16).

Acknowledgement: Thanks to all departments that contributed data

Disclosure of Interests: Kathrine Gram Grant/research support from: BMS, Berete Glintborg Grant/research support from: Biogen, Pfizer, AbbVie; Frank Mehnert: None declared, Mikkel Østergaard Grant/research support from: Abbvie, Celgene, Centocor, Merck, Novartis, Consultant for: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, Speakers bureau: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, Lene Dreyer Consultant for: MSD, UCB and Janssen Pharmaceuticals, Speakers bureau: UCB, MSD, Eli Lilly and Janssen Pharmaceuticals., Mette Nergaard: None declared, Merete L. Hetland Grant/research support from: BMS, MSD, AbbVie, Roche, Novartis, Biogen, Pfizer, Consultant for: Eli Lilly, Speakers bureau: Orion Pharma, Biogen, Pfizer, CellTrion, Merck, Samsung Bioepis


THE ASSOCIATION BETWEEN ANTI-CCP TITRE LEVEL AND DISEASEACTIVITY AND DISABILITY OVER ONE YEAR FOLLOWING THE INITIATION OF METHOTREXATE OR BIOLOGIC THERAPY FOR ANTI-CCP+ RHEUMATOID ARTHRITIS

James Gwinnutt1, Kimmy Hyrich1,2, Mark Lunt1, Darren Platts3, Nisha Nar3, Anne Barton1,2, Suzanne Verstappen1,2, RAMS and BRAGGS co-investigators. 1Arthritis Research United Kingdom Centre for Epidemiology, Centre for Musculoskeletal Research, Faculty of Medicine, Biology and Health, University of Manchester, Manchester, United Kingdom; 2NIHR Manchester Biomedical Research Centre, Central Manchester University Hospitals NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, United Kingdom; 3Arthritis Research United Kingdom Centre for Genetics and Genomics, Centre for Musculoskeletal Research, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, United Kingdom

Background: Whilst anti-cyclic citrullinated peptide antibody (anti-CCP) positivity in associated with poor outcomes in patients with rheumatoid arthritis (RA), it is unclear whether titre level over time is associated with outcome.

Objectives: Whilst anti-cyclic citrullinated peptide antibody (anti-CCP) positivity in associated with poor outcomes in patients with rheumatoid arthritis (RA), it is unclear whether titre level over time is associated with outcome.

Methods: Patients were recruited to one of two, UK-based, multi-centre prospective cohort studies: MTX-starters = Rheumatoid Arthritis Medication Study (RAMS); biologic-starters = Biologics in Rheumatoid Arthritis Genetics and Genomics Study Syndicate (BRAGGS). Anti-CCP titre (Axis-Shield Anti-CCP test; U/ml; anti-CCP titre >5 U/ml = anti-CCP+ ) was measured at the co-ordinating centre from blood samples taken at baseline, 6 months and 12 months. Patients who were anti-CCP+ at baseline and had titre measured at one other assessment were included in the analysis. Patients completed the Health Assessment Questionnaire (HAQ) and the Disease Activity Score (DAS28) was calculated at each assessment.

The association between anti-CCP titre and DAS28 and HAQ was assessed using linear random effects models, controlling for age, gender and disease duration (months). Anti-CCP titre was natural log-transformed. Missing data resulting from anti-CCP assay failure were imputed using multiple imputation.

Results: In total, 686 MTX-starters and 346 biologic-starters were included. Biologic-starters had worse disease at baseline compared to MTX-starters (Table). Median [IQR] titre decreased slightly over follow-up for MTX-starters (baseline = 147 [48, 416]; 6 months = 133 [47, 454]; 12 months = 124 [44, 421]; p=0.63) and biologic-starters (baseline = 138 [37, 492]; 6 months = 112 [30, 468]; 12 months = 103 [30, 451]; p=0.36) but this was not significant. For MTX-starters, anti-CCP titre was statistically significantly associated with DAS28 and HAQ, but the effect sizes were small (mean difference [95% CI] per unit increase in log anti-CCP: DAS28 = 0.07 [0.02, 0.11]; HAQ = 0.06 [0.03, 0.08]). There was no significant association between anti-CCP titre and DAS28 and HAQ for biologic-starters (mean difference [95% CI] per unit increase in log anti-CCP: DAS28 = 0.03 [0.05, 0.10]; HAQ = 0.02 [0.01, 0.05]).

Conclusion: Time-varying anti-CCP titre level was not strongly associated with disease activity or disability over one year in either MTX-starters or biologic-starters who were anti-CCP+ at baseline, indicating repeat testing of anti-CCP level may not be necessary.

References:
Disclosure of Interests: James Gwinnutt: None declared, Kimme Hyrich: None declared, Pieta Näsänen-Gilmore: None declared, Anne Barton: None declared, Suzanne Verstappen: None declared, Mark Lunt: None declared, Darren Plant: None declared, Nisha Nair: None declared, Eero Kajantie: None declared, Thomas Bo Jensen: None declared, Mikkel Bring Christensen: None declared, Nicole Tsao: None declared, Seoyoung Kim: None declared, Jon Trærup Andersen: None declared, Copenhagen University Hospital Bispebjerg, Department of Clinical Pharmacology, Copenhagen, Denmark; Brigham and Women’s Hospital, Division of Pharmacoepidemiology and Pharmacoeconomics, Boston, United States of America; University of Copenhagen, Faculty of Health and Medical Sciences, Copenhagen, Denmark; Harvard Medical School, Boston, United States of America.

Background: Maternal exposure to methotrexate (MTX) during pregnancy is known to be teratogenic, but less is known about the risk due to paternal MTX exposure. Because of a theoretical teratogenic risk from paternal exposure, treatment recommendations advocate that men should discontinue MTX three months before conception and continue discontinuation during the partners’ pregnancy. This may lead to suboptimal adherence to treatment, fear among the future parents and pregnancy termination.

Objective: The aim was to systematically review and meta-analyse the collective data on paternal MTX exposure and the risk of congenital malformations.

Methods: We performed a systematic search in the databases – PubMed, Embase, Cochrane Central, and Cinahl – on March 1, 2018. We included studies with an English abstract that assessed major or all (both major and minor) malformations following any paternal exposure to MTX. Studies that included a control group were included in the meta-analysis. No time restriction was applied. Review Manager Version 5.3 was used for the meta-analysis.

Results: We identified 36 studies assessing the risk of congenital malformations following paternal exposure to MTX of which 20 contained original data. Five studies met the inclusion criteria for the meta-analysis. Three studies from Denmark had a major overlap in study populations, one study from Norway, and one German study. All studies were cohort studies using national registries except the German that used structured interviews and phone interviews. Because of the overlapping Danish studies, only the largest Danish study for each of the outcomes were included. We included a total of 265 fathers exposed to MTX and 1,004,834 controls in the meta-analysis investigating risk of major congenital malformations. Among the offspring of the MTX-exposed 7 (2.64%) had a major malformation compared to 33,816 (3.37%) among the unexposed. Pooled odds ratios were 1.02 (95% confidence interval [CI] 0.48-2.20) for major malformations and 1.02 (CI 0.62-1.66) for all malformations.

Conclusion(s): In this systematic review and meta-analysis, we found no association between preconceptions paternal MTX use and major or all congenital malformations. The current recommendations to avoid paternal MTX use before conception do not appear to be supported by evidence and paternal treatment with MTX could be continued when planning pregnancy.

Disclosure of Interests: Thomas Bo Jensen: None declared, Mikkeli Bring Christensen: None declared, Nicole Tsao: None declared, Seoyoung Kim: None declared.

Baseline characteristics

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>MTX-starters</th>
<th>Biologic-starters</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>686</td>
<td>345</td>
</tr>
<tr>
<td>Age, years</td>
<td>59 (49, 67)</td>
<td>59 (51, 67)</td>
</tr>
<tr>
<td>Female, N (%)</td>
<td>441 (64.3)</td>
<td>269 (77.8)</td>
</tr>
<tr>
<td>Disease duration, months</td>
<td>9 (4, 27)</td>
<td>72 (24, 180)</td>
</tr>
<tr>
<td>Smoking:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>240 (35.5)</td>
<td>106 (30.6)</td>
</tr>
<tr>
<td>Former</td>
<td>265 (39.1)</td>
<td>163 (47.1)</td>
</tr>
<tr>
<td>Current</td>
<td>172 (25.4)</td>
<td>77 (22.3)</td>
</tr>
<tr>
<td>Swollen joint count</td>
<td>5 (1, 10)</td>
<td>8 (5, 11)</td>
</tr>
<tr>
<td>Tender joint count</td>
<td>5 (1, 13)</td>
<td>13 (9, 18)</td>
</tr>
<tr>
<td>CRP, mg/L</td>
<td>7 (3, 19)</td>
<td>10 (5, 26)</td>
</tr>
<tr>
<td>DAS28-CRP</td>
<td>4.2 (3.3, 5.2)</td>
<td>5.6 (4.2, 6.1)</td>
</tr>
<tr>
<td>HAQ</td>
<td>1.13 (0.50, 1.63)</td>
<td>1.63 (1.13, 2.00)</td>
</tr>
<tr>
<td>Pain VAS, mm</td>
<td>50 (26, 73)</td>
<td>69 (52, 78)</td>
</tr>
<tr>
<td>Fatigue VAS, mm</td>
<td>51 (24, 72)</td>
<td>71 (52, 85)</td>
</tr>
<tr>
<td>Anti-CCP, N (%)</td>
<td>686 (100)</td>
<td>346 (100)</td>
</tr>
<tr>
<td>Anti-CCP titre</td>
<td>147 (48, 416)</td>
<td>138 (37, 492)</td>
</tr>
</tbody>
</table>

AntCCP = anti-cyclic citrullinated peptide antibody, CRP = C-reactive protein, DAS28 = Disease Activity Score (28), HAQ = Health Assessment Questionnaire, MTX = methotrexate, N = number, VAS = visual analogue scale.

P-values (Chi2): 0.05 0.16 0.95

202 Disseminated connective tissue disorders, rheumatoid arthritis and other rheumatic diseases (A04.6, A39.8, A39.5, D76.0, D76.3, H20.1, H30.1, I33.0, I40.8, J84.9, K05.9, K51.9, K73.2, K74.3, K83.0, L40.5, M02.0, M05.0, M06.0, M13.9, M20.3–M23.5, M45.0, M46.1, M46.9, M94.1, N03.9, N04.94.42).

104 Hypothyreosis

208 Ulcerative colitis or Crohn’s disease


THU0670 PATERNAL USE OF METHOTREXATE AND CONGENITAL MALFORMATIONS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Thomas Bo Jensen1,2, Mikkeli Bring Christensen1,3, Nicole Tsao4,5, Seoyoung Kim4,6, Jon Trærup Andersen1,3,1, Copenhagen University Hospital Bispebjerg, Department of Clinical Pharmacology, Copenhagen, Denmark; Brigham and Women’s Hospital, Division of Pharmacoepidemiology and Pharmacoeconomics, Boston, United States of America; University of Copenhagen, Faculty of Health and Medical Sciences, Copenhagen, Denmark; Harvard Medical School, Boston, United States of America.

Background: Maternal exposure to methotrexate (MTX) during pregnancy is known to be teratogenic, but less is known about the risk due to paternal MTX exposure. Because of a theoretical teratogenic risk from paternal exposure, treatment recommendations advocate that men should discontinue MTX three months before conception and continue discontinuation during the partners’ pregnancy. This may lead to suboptimal adherence to treatment, fear among the future parents and pregnancy termination.

Objective: The aim was to systematically review and meta-analyse the collective data on paternal MTX exposure and the risk of congenital malformations.

Methods: We performed a systematic search in the databases – PubMed, Embase, Cochrane Central, and Cinahl – on March 1, 2018. We included studies with an English abstract that assessed major or all (both major and minor) malformations following any paternal exposure to MTX. Studies that included a control group were included in the meta-analysis. No time restriction was applied. Review Manager Version 5.3 was used for the meta-analysis.

Results: We identified 36 studies assessing the risk of congenital malformations following paternal exposure to MTX of which 20 contained original data. Five studies met the inclusion criteria for the meta-analysis: Three studies from Denmark had a major overlap in study populations, one study from Norway, and one German study. All studies were cohort studies using national registries except the German that used structured interviews and phone interviews. Because of the overlapping Danish studies, only the largest Danish study for each of the outcomes were included. We included a total of 265 fathers exposed to MTX and 1,004,834 controls in the meta-analysis investigating risk of major congenital malformations. Among the offspring of the MTX-exposed 7 (2.64%) had a major malformation compared to 33,816 (3.37%) among the unexposed. Pooled odds ratios were 1.02 (95% confidence interval [CI] 0.48-2.20) for major malformations and 1.02 (CI 0.62-1.66) for all malformations.

Conclusion(s): In this systematic review and meta-analysis, we found no association between preconceptions paternal MTX use and major or all congenital malformations. The current recommendations to avoid paternal MTX use before conception do not appear to be supported by evidence and paternal treatment with MTX could be continued when planning pregnancy.

Disclosure of Interests: Thomas Bo Jensen: None declared, Mikkeli Bring Christensen: None declared, Nicole Tsao: None declared, Seoyoung Kim: None declared.
Objectives: To evaluate the frequency of pulmonary involvement in RA patients followed-up in a 15-years period.

Methods: 549 RA patients were diagnosed according to the ACR/EULAR classification criteria since 2003. A full clinical examination as well as a detailed laboratory and immunological evaluation has been carried-out at baseline. Furthermore, chest, hand and wrist but also feet radiographs had been obtained. All patients were followed-up at predefined times and were treated appropriately with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) and/or biologic (b)DMARDs. Any laboratory abnormalities or comorbidities were recorded and investigated appropriately at every visit. In addition, the disease activity score (DAS) using the 28-joints count (DAS-28) was recorded.

Results: Initial evaluation revealed 15 patients as having pulmonary abnormalities. Thus, these patients were excluded. From the rest, 37 (6.7%) patients manifested lung involvement. There were 26 males and 11 females, with mean age of 62.9 ± 5.4 years and disease duration of 8.5 ±2.2 years. 14 were smokers and 10 ex-smokers. Dry cough and dyspnea on exertion were the main pulmonary symptoms. High resolution computed tomography (HRCT) scan of the chest revealed interstitial lung disease (ILD). More specifically, 23 patients showed usual interstitial pneumonia (UIP), 10 patients had nonspecific interstitial pneumonia (NSIP), while 4 had a mixed pattern. Six patients died 4 years after ILD development. ILD was associated with high DAS-28, seropositivity and male gender.

Conclusion: ILD is not a frequent EAM in patients with RA, but it carries a poor prognosis with high morbidity and mortality and it is associated with RA disease activity and male gender. UIP is the most prevalent pattern of ILD in RA patients.

Disclosure of Interests: None declared


Objectives: To examine the risk of developing RA in persons who have had CVD, defined as acute myocardial infarction (AMI) or ischaemic stroke while controlling for established shared risk factors.

Methods: We conducted a population-based cohort study within the Danish Diet, Cancer and Health (DCH) cohort. The cohort was recruited 1993-97 and included individuals aged 50 to 64 years, born in Denmark and living in geographically defined parts of Denmark. Data on lifestyle factors and anthropometric measurements were collected at enrolment into the DCH. Information on incident AMI (ICD-10 code: I21), ischemic stroke (ICD-10 code: I63) and RA (ICD-10 codes: M05, M06 combined with ATC codes for DMARDs) was obtained from nationwide administrative registers. Participants were followed until development of RA, death, loss to follow-up or October 2016, whichever came first. Data were analyzed using Cox’s proportional hazards regression models with delayed entry and age as the underlying time scale and cardiovascular disease (CVD) as a time-varying exposure variable, stratifying by gender. Established shared risk factors - smoking, body mass index and waist circumference - were included in the multivariable analyses.

Results: Complete data were available on 53287 subjects (52% female) without a AMI, stroke or RA diagnosis prior to their enrolment into the DCH. Median age at entry into DCH was 56 years. During follow-up (median 21 years), 4,627 participants developed CVD (37% female) and 516 participants developed RA (69% female). The risk for developing RA was 30% higher in women with CVD than in women without CVD (adjusted hazard ratio (HR) 1.30 (95% CI 0.70-2.38) (Table 1). In men, there was no clear association between CVD and development of RA (adjusted HR 0.73 (95% CI 0.34-1.58)).

Disclosure of Interests: None declared

THU0674 CLINICAL PRESENTATION AND MANAGEMENT OF MONO- AND BILATERAL KNEE ARTHRITIS: RESULTS FROM THE LEIDEN EARLY ARTHRITIS CLINIC COHORT
Johanna M. Maassen, Xanthe Matthijssen, Syske Anne Bergstra, Cornelia Allaart. LUMC, Leiden, Netherlands

Background: Patients presenting with arthritis in one or both knees pose a challenge regarding diagnosis, prognosis and treatment decisions. Objectives: To characterize the patients with knee arthritis who presented to the Leiden Early Arthritis Clinic (EAC) and to evaluate the disease course and initial treatment decisions.

Methods: All patients with arthritis confined to the knee(s) were selected from all patients included in the EAC between 1993 and 2015. The EAC captures patients with arthritis and symptom duration < 2 years, excluding arthritis diagnosed at presentation as definite infectious, gouty or osteoarthritis. EAC follow up is at 2 weeks, 3 months and thereafter yearly. Medical files were reviewed for information on treatment and clinical outcomes. Baseline characteristics were summarized, treatment and outcome was evaluated over time up to 12 months. Patients were stratified over 3 groups: 1. Early remission (at 3 months no clinical synovitis and no flare proceeded) was evaluated over time up to 12 months. Patients were stratified over 3 groups: 1. Early remission (at 3 months no clinical synovitis and no flare proceeded); 2. Persistent gonarthritis at 3 months (improving or stable); 3. Progression to oligo-/polyarthritis at the last available visit). RF and ACPA positivity and high ESR at baseline were predictive for progression (group 3), but did not differ between patients in groups 1 and 2. There was a trend for longer symptom duration at presentation in group 3 (76.5 days, IQR 25.5-175.5, p=0.040 vs. group 1) (table 1).

Results: Of the 206 patients identified, 174 (85%) had mono- and 32 (15%) bilateral gonarthritis. Early remission was observed in 67/206 patients (32.5%, group 1), gonarthritis persisted in 109/206 patients (53.0%) in group 2 and 3/206 patients (<1%) subsequently received a bDMARD. Prednisone was prescribed in 11/206 patients (5.4%). DMARD therapy was prescribed in 14/206 patients (<1%). No differences in initial treatment were observed between groups 1, 2 and 3.

During the first year, in 62/206 patients (30.1%) treatment remained limited to NSAIDs, most often in group 1 (p <0.01). IACs were (also) prescribed in 23/206 patients (11.2%), when a diagnosis of Borrelia or other bacterial arthritis was made or suspected, and 6/206 patients (3.0%) received with colchicine and/or allopurinol (NS between the groups) (2). Disclosure of Interests: None declared.

THU0675

ASSOCIATION OF GLUCOSE HOMEOSTASIS MEASURES AND METABOLIC SYNDROME WITH KNEE CARTILAGE DEFECTS AND CARTILAGE VOLUME IN YOUNG ADULTS

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Background: Diabetes mellitus and knee osteoarthritis (OA) are commonly coexisting, and metabolic syndrome (MetS) shared many pathways with knee OA. However, the effects of glucose homeostasis and MetS on knee cartilage in young adults were unknown.

Objectives: To describe the associations of glucose homeostasis measures and MetS measures with knee cartilage defects and cartilage volume in young adults.

Methods: Australian young adults from the Childhood Determinants of Adult Health Study were selected to undergo knee magnetic resonance imaging (MRI) scans during 2008-2010 (aged 31-41 years). Fasting blood samples, waist circumference and blood pressure were measured during 2004-2006 (aged 16-26 years). Glucose, insulin, triglyceride and high-density lipoprotein cholesterol (HDL-C) were measured using serum samples. Homeostatic model assessment-2 insulin resistance (HOMA2-IR), HOMA2-beta cell function (HOMA2-b), HOMA2-insulin sensitivity (HOMA-S) were calculated using HOMA2 calculator (version 2.2.3 available from http://www.dtu.ox.ac.uk/homacalculator) according to fasting glucose and fasting insulin. MetS was defined when at least three of the following five components were present: high waist circumference (male >102 cm; female >88 cm), high fasting glucose (>5.6 mmol/L), high serum triglycerides (>1.7 mmol/L), low HDL-C (male <1.03 mmol/L; female <1.3 mmol/L), and high blood pressure (>130/85 mmHg). Cartilage defects and cartilage volume were measured from MRI scans. Data were analysed using log binomial or linear regressions and were adjusted for age, gender, body mass index and physical activity.

Results: Among 328 participants (47.3% were females), 40 (12.7%) had hyperglycaemia and 21 (6.7%) had MetS. Glucose homeostasis measures (except fasting glucose) were associated with tibiofemoral cartilage defects (Fasting insulin: relative risk (RR) 1.05/mU/L, 95% confidence interval (CI) 1.01 to 1.08; HOMA2-IR: 1.44, 1.08 to 1.92; HOMA2-β: 2.59, 1.93 to 3.57; HOMA2-S: 0.36, 0.18 to 0.72), but not patellar cartilage defects. There were no associations between glucose homeostasis measures and knee cartilage volume. MetS measures were not associated with either cartilage defects or cartilage volume, except the associations between high waist circumference and tibiofemoral cartilage defects (RR 2.32, 95% CI 1.18 to 4.54) and between low HDL-C and tibiofemoral cartilage defects (RR 2.32, 95% CI 1.08 to 4.69).

Conclusion: Insulin resistance was associated with higher risk of tibiofemoral cartilage defects amongst young adults. MetS was not associated with neither cartilage defects nor cartilage volume. These suggest that glucose homeostasis, but not MetS, may play a role in cartilage damage in young adults and may lead to knee OA in later life.

Disclosure of Interests: None declared

THU0676

HEPATITIS B VIRUS REACTIVATION IN A COHORT OF PATIENTS TREATED WITH BIOLOGICS – DATA FROM THE ROMANIAN REGISTRY OF RHEUMATIC DISEASES

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Background: Accompanying the increased use of biological and non-biological antirheumatic drugs, a greater number of cases of hepatitis B virus (HBV) reactivation have been reported in inactive hepatitis B surface antigen (HBsAg) carriers and also in HBsAg-negative patients (pts) who have resolved HBV infection (1). Romania has a high prevalence for HBV infection. According to a national epidemiological study conducted in 2013, 27.9% from the Romanian population has serological markers of resolved HBV infection, while 4.2% of inactive carriers of HBsAg (2). Objectives: To estimate the rate of HBV reactivation in a cohort of patients treated with biologics, in Romania.

Methods: Data were gathered from the Romanian Registry of Rheumatic Diseases (RRBR) for rheumatoid arthritis (RA), ankyllosing spondylitis (AS) and psoriatic arthritis (PsA). The cohort included patients previously exposed to HBV: HBsAg inactive carriers or resolved HBV infection. HBV reactivation was considered as the presence of DNA-HBV or positivity of HBsAg in a previously negative patient. The collected data included exposure to biologics in person-years (PY) and serological markers of HBV.

Results: The cohort included 1744pts (5505.95 PY): 936 RA pts (2762.97 PY), 640 AS pts (2037.64 PY) and 168 PsA pts (705.34 PY). The mean age was 58.72yrs (65yrs for RA, 49.58yrs for AS: 61.58yrs for PsA); 1058 (60.6%) women; 786 (74.2%) RA pts, 175 (16.5%) AS pts and 97 (9.1%) PsA pts. Mean disease duration was 14.5yrs for RA, 10.7yrs for AS and 10.5yrs for PsA. The prevalence of HBsAg inactive carriers were 44 (4.7%) in RA group, 53 (8.28%) in AS group and 6 (3.57%) in PsA. The frequency of resolved HBV infection was 892 (95.3%) in RA group, 587 (91.7%) in AS and 162 (96.4%) in PsA. The total number of observed HBV reactivation cases was 16 (0.9%). In RA, 9 (0.9%) cases of HBV reactivation (0.31/100 PY) were observed, all cases on resolved HBV infection state; 7 pts were treated with rituximab (RTX), 2 pts with TNFα blockers. 8 cases (0.28/100PY) of HBV reactivation were observed in those without antiviral prophylaxis, compared to a single reactivation case (0.03/100PY) when antiviral prophylaxis was used. In AS cohort occurred 6 (0.9%) cases of HBV reactivation (0.29/100 PY), all patients being treated with TNFα blockers (3 etanercept, 1 adalimumab, 1 infliximab, 1 golimumab): 4 cases of HBV reactivation developed in inactive carriers of HBsAg and 2 in resolved HBV infection. 5 cases (0.24/100PY) of HBV reactivation were observed in those without antiviral prophylaxis, compared to a single reactivation case (0.04/100PY) when antiviral prophylaxis was used. In PsA group, only 1 case of HBV reactivation (0.14/100PY), on inactive carrier of HBsAg state, during TNFα blocking agent (golimumab).

Conclusion: HBV reactivation appeared more often on a resolved infection state, especially without antiviral prophylaxis. No cases of fulminant hepatitis were noted. Most cases developed in RTX exposed RA patients, while in AS group all HBV reactivation appeared with TNFα blockers exposure.

REFERENCES:

Disclosure of Interests: None declared

THU0677

IDENTIFICATION OF PROLIFERATION, PROGNOSTIC FACTORS, AND OUTCOMES OF PATIENTS WITH INTERSTITIAL PNEUMONIA WITH AUTOIMMUNE FEATURES: A SINGLE CENTER LARGE-SCALE OBSERVATIONAL COHORT STUDY

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Background: Patients with idiopathic interstitial pneumonia (IIP) may have features of connective tissue diseases (CTDs). The term interstitial pneumonia with autoimmune features (IPAF) has been recently proposed for such patients. A few studies have been reported in prevalence of IPAF which was varied from 7.3% to 34.1% [1, 2]. Factors reported to indicate such patients. A few studies have been reported in prevalence of IPAF

Objectives: To identify of prevalence of IPAF in patients with interstitial lung disease, prognostic factors for exacerbation in patients with IPAF, and compared outcomes among patients with IPAF, iip, and CTD-IILD.

Methods: Six hundreds- and seventy-two patients who visited our department between April 2009 and March 2018 and were evaluated by chest
HRCT scan. Then, they were clinically and radiologically diagnosed as having interstitial lung disease (ILD), IIP or connective tissue diseases associated ILD were enrolled. We applied IPAF criteria to these patients. Then, we purified 68 patients. The prognostic factors for exacerbation were prospectively calculated and statistically analyzed using clinical, laboratory and imaging data collected from medical records.

**Results:** Prevalence of IPAF was 10.1%. Of 68 patients with IPAF, 60% were women and mean age at diagnosis was 64.2 ± 13.8 years old. Mean observation period was 27.1 ± 29.6 months. Smoking history was 42.6% (n=29). Treatment including oral glucocorticoid or/and immunosuppressant use were 44.1% (n=30). Exacerbation rate was 25% (n=17). Overall death rate was 5.9% (n=4) and respiratory death rate was 2.9% (n=2). Comparison of characteristics at diagnosis between the exacerbation group and non-exacerbation group showed that the exacerbation group had a significantly elevated rate of smoking history, KL-6, and SP-D (P=0.01, 0.005, and 0.03, respectively). We then analyzed transition of KL-6 in patients with IPAF, IIP, or CTD-ILD. KL-6 at baseline in patients with IPAF (1212 ± 1626 U/mL) was higher than those with IIP and significantly higher than those with CTD-ILD (1030 ± 1027 U/mL(P=0.69) and 829.5 ± 1002 U/mL(P=0.024)), while exacerbation rate in patients with IPAF (25%) was significantly lower than those in IIP patients (40%) and CTD-ILD patients (41%) (P=0.03). Furthermore, KL-6 in IPAF patients gradually decreased during course and was lower than IIP or CTD-ILD patients at 84 months from diagnosis.

**Conclusion:** Our large-scale observational cohort study revealed prevalence of IPAF in patients with ILD and identified three baseline factors associated with exacerbation in the patients with IPAF and suggested that IPAF might have a better prognosis than IIP or CTD-ILD.

**REFERENCES:**
[2] Eur Respir J. 2017; 123:56–57,

Disclosure of Interests: None declared

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**THU0678**

**MALIGANCY RISK IN MALE PATIENTS WITH ANKYLOSING SPONDYLITIS**

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**Background:** In recent studies, the association between autoimmune disease and malignancy has been reported. However in Ankylosing spondylitis (AS), a chronic inflammatory rheumatic disease with marked male predominance, the evidence of this relationship is scarce and inconsistent.

**Objectives:** To determine the overall cancer and site-specific cancer risk in male patients with AS.

**Methods:** Using the claims database of Health Insurance and Review Assessment (HIRA), male patients with AS without prior cancer history between 2012 and 2014 were enrolled (n=21,780). For the control group, male general population, stratified random samples of claims data were used (n=342,361). All individual was observed up to the development of any cancer, or end of the study period (December 31, 2015). Incidence rates (IR) of overall and site-specific cancer were presented as the number of event per 10,000 person-years. To make fair comparison between AS patients and general population, we calculated age adjusted incidence ratio by dividing cancer event of general population with corresponding age. The standard incidence ratio (SIR) was used to represent the association between AS and cancer, accounting for person-years at risk.

**Results:** During 71,046 person-year, total 552 cases of cancer occurred in male AS group. Prostate cancer was the leading type of cancer in male AS patients (101 cases, IR 14.22, 95% CI 11.44-16.99). And it was followed by liver cancer (70 cases, IR 9.9, 95% CI 7.5-12.2), lung cancer (48 cases, IR 6.8, 95% CI 4.9-8.7), colorectal cancer (45 cases, IR 6.3, 95% CI 4.5-8.2) and stomach cancer (43 cases, IR 6.1, 95% CI 4.2-7.9). Compared to general population, the overall incidence of cancer was increased in male patients with AS (SIR 1.25, 95% CI 1.14-1.36).

At a specific malignancy type, the risk of pancreas cancer (SIR 1.75, 95% CI 1.12-2.37) and malignancy of male reproductive system were increased (SIR 1.97, 95% CI 1.59-2.35).

**Table 1. The standardized incidence ratio of overall malignancy.**

<table>
<thead>
<tr>
<th>Type of Malignancy</th>
<th>Male general population</th>
<th>Male AS patients</th>
<th>SIR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IR (95% CI)</td>
<td>Age-adjusted expected IR</td>
<td>IR (95% CI)</td>
<td></td>
</tr>
<tr>
<td>All malignancy</td>
<td>102.5 (100.7-104.3)</td>
<td>65.0 (63.7-66.2)</td>
<td>77.7 (71.2-84.2)</td>
</tr>
<tr>
<td>Hematologic</td>
<td>3.4 (2.6-4.3)</td>
<td>2.3 (1.3-3.2)</td>
<td>3.8 (2.4-5.2)</td>
</tr>
<tr>
<td>Solid malignancy</td>
<td>101.6 (97.4-107.0)</td>
<td>62.6 (60.5-64.2)</td>
<td>73.9 (67.6-60.2)</td>
</tr>
</tbody>
</table>

Incidence rate was presented as the number of events per 10,000 person-year with 95% CI in AS, ankylosing spondylitis; IR, incidence ratio; SIR, standardized incidence ratio; CI, confidence interval

**Figure 1. The standardized incidence ratio of hematologic malignancy.**

**Figure 2. The standardized incidence ratio of solid cancer.**

**Conclusion:** Male patients with AS have a increased overall cancer risk, especially in pancreas cancer and malignancy of male reproductive system.

**REFERENCES:**

Disclosure of Interests: Bora Nam: None declared, HyoYoungKim: None declared, Eun Jin Jiang: None declared, Soo-Kyung Cho: None declared, Yoon-Kyoun Sung: Grant/research support from: Dr. Yoon-Kyoun Sung has received research funding from BMS, Eisai, Pfizer, JW pharmaceutical., Consultant for: Dr. Yoon-Kyoun Sung has served as a consultant to AbbVie and Amgen, Speakers bureau: Dr. Yoon-Kyoun Sung has received honoraria from AbbVie, Amgen, BMS, Pfizer., Tae-hwan Kim: None declared
ADHERENCE TO THE MEDITERRANEAN DIET AND RISK OF RHEUMATOID ARTHRITIS IN THE FRENCH PROSPECTIVE E3N COHORT STUDY

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Background: The Mediterranean diet (MD), widespread in Southern European countries, mainly consists of olive oil, cereal products, fresh or dried fruits and vegetables, nuts, a moderate amount of dairy and meat, and many condiments and spices. It has been associated with significant reduction of overall mortality, cardiovascular diseases, and neoplastic diseases. It has been suggested to have a beneficial effect on rheumatoid arthritis (RA) activity due to its richness in antioxidants and unsaturated fatty acids. However, data on MD as a prevention of RA are limited.

Objectives: To assess the association between adherence to MD and risk of RA in a general population cohort.

Methods: The E3N cohort study (Étude Épidémiologique auprès des femmes de la Mutuelle générale de l’Education Nationale) is a French prospective cohort of 98,995 healthy women included in 1990-91 and followed since then (median follow-up of 28 years). Among women who completed a food-frequency questionnaire, we calculated the modified MD score (from 0 to 9) according to the consumption status of nine food components. Incident RA cases were detected using a validation process using a specific validation questionnaire and a drug reimbursement database. Hazard ratios (HRs) and 95% confidence intervals (CIs) for incident RA were estimated using Cox proportional-hazards analysis with an age adjustment. High adherence to MD was associated with a decreased risk of RA (HR for a 6-9 vs. 0-3 score = 0.78, 95% CI: 0.58-1.04) in ever-smoking women (current or past smokers), high adherence to MD could reduce RA risk in ever-smoking women. Further studies are needed to confirm our findings.

Conclusion: High adherence to a MD could reduce RA risk in ever-smoking women. Further studies are needed to confirm our findings.

Disclosure of Interests: Yann Nguyen: None declared, Carine Salliot: None declared, Amandine Gelot: None declared, Juliette Gambaretti: None declared, Xavier Marette Grant/Research support from: Servier, Consultant for: AstraZeneca, Bristol-Myers Squibb, GlaxoSmithKline, Janssen, Pfizer, UCB Pharma, Marie-Christine Bouthon-Vruwink: None declared, Raphaëlle Sere: None declared.


ANTIPePTIDYL-ARGININE DEIMINASE 3 AND 4 AUTOANTIBODIES IN A COHORT OF RHEUMATOID ARTHRITIS WITH INTERSTITIAL LUNG DISEASE

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Background: Interstitial lung disease (ILD) affects up to 30% of patients with rheumatoid arthritis (RA). Peptidyl-arginine deiminases (PAD) are key enzymes in RA pathogenesis as they are involved in the citrullination of proteins, targets of anti-citrullinated protein antibodies (ACPA). Although RA-ILD significantly contributes to disease burden including mortality, diagnostic and prognostic biomarkers are still lacking.

Objectives: To measure anti-PAD3 and anti-PAD4 antibodies in a cohort of RA and compare their prevalence in patients with and without ILD. To assess the associations of anti-PAD3, anti-PAD4 and ACPA with disease activity, joint erosions, lung involvement and smoking history.

Methods: A total of 71 patients fulfilling the 2010 ACR/EULAR RA Classification Criteria were recruited; the mean age was 63±12.4 and 87% of them were females, 11 (15.5%) of them had been diagnosed with ILD. Demographic, clinical as well as radiological data were retrospectively collected. ILD was defined as usual interstitial pneumonia (UIP), non-specific interstitial pneumonia (NSIP) or indeterminate patterns on chest high-resolution computed tomography, according to ATS/ERS guidelines. Particle-based Multi-System Technology (PMAT) (Inova Diagnostics, USA, research use only) was used to measure anti-PAD3 and anti-PAD4 autoantibodies. ACPA IgG were measured by chemiluminescence (QUANTA Flash CCP3, Inova Diagnostics, USA).

Results: Anti-PAD4 levels were correlated with erosive disease (p=0.043) and morning stiffness (p=0.031). Anti-PAD3 and anti-PAD4 levels were associated to DAS28-ESR at the time of sampling (anti-PAD3, r=0.34, p<0.004; anti-PAD4, r=0.34, p=0.004). Anti-PAD4 antibodies were significantly lower in patients with ILD (p=0.043). There was no association between anti-PAD4 and smoking, while anti-PAD3 antibodies were higher in non-smokers (p=0.004). A strong correlation was found between anti-PAD3 and anti-PAD3 antibodies as a biomarker for erosive disease. Further studies that take into account relevant confounders like therapy and larger RA-ILD cohorts are needed.

REFERENCES:


Disclosure of Interests: Boaz Palterer: None declared, Gianfranco Vitallo: None declared, Bernardo D’Onofrio: None declared, Emanuele Vivarelli: None declared, Daniele Cammelli: None declared, Maria Grazia Giudizi: None declared, Laura Martinez-Prat Employee of: Inova Diagnostics (Not pharmaceutical, diagnostics company), Silvia Casas Employee of: Inova Diagnostics, Chelsea Bentow Employee of: INOVA Diagnostics, Michael Mahler Employee of: Inova Diagnostics (Not pharmaceutical, diagnostics company), Paola Parronchi: None declared.


SEXUAL FUNCTION AND REPRODUCTION CAN BE IMPAIRED IN MEN WITH RHEUMATIC DISEASES: A SYSTEMATIC REVIEW

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Background: Sexual function and reproduction are important aspects of quality of life for the majority of men (1,2). In the last decade inflammation has been associated with male factor infertility and sexual dysfunction (3,4). Because many patients with rheumatic diseases have a
chronic state of inflammation, it is reasonable to believe that this can result in impaired sexual function and reproduction. Previous research on this topic in Rheumatology mainly focused on the effect of drugs on fertility parameters.

Objectives: Our objective is to summarize the information on the influence of rheumatic diseases on male sexual function and reproduction.

Methods: A systematic search of Embase, Medline, Web of science and Cochrane Central was carried out in May 2018 to find relevant papers. The search strategy was extensive and included a complete list of immune mediated diseases from Rheumatology, Dermatology and Gastroenterology and several keywords for our outcomes (sexuality function, fertility and pregnancy outcome). This review was registered in PROSPERO (5).

The search yielded 6588 articles. Titles and abstracts were screened independently by LP and JC, resulting in 177 papers selected for full text review. Methodological quality of the studies was assessed with the Newcastle Ottawa Scale (6).

Results: Regarding rheumatic diseases a total of 104 papers were included in the final analysis. 4 diseases (Spondyloarthropathies (SpA), Rheumatoid Arthritis (RA), Systemic Lupus Erythematosus (SLE) and Systemic Sclerosis (SSc)) represented 60% of the articles. The overall quality of the studies was low to moderate.

Sexual dysfunction (SD) is a common problem for patients with rheumatic diseases and it is usually undiagnosed. It was reported in approximately half of men with RA, SLE and SpA and in almost all the men diagnosed with SSc. It should be noted that, although in several studies increasing age was correlated with a higher prevalence and severity of SD, young patients with SpA or SLE can also be affected.

Regarding fertility and reproduction, different results per disease were found. Hypogonadism might be a common problem in men with RA and SLE. Many men with SLE and RA have endocrine axis abnormalities. Interestingly, these disturbances were not detected in SpA patients (See Table 1). Semen quality abnormalities are frequent in SLE patients and this was found to be associated not only with medication toxicities but also with disease activity. The number of children of male patients diagnosed with SLE and SSc was lower than healthy controls.

A brief summary of our findings per disease are presented in Figure 1.

Conclusion: Our findings suggest that not only medication can have detrimental effects on sexual function and reproduction of men with rheumatic disease but also the disease itself. Therefore, clinicians should be aware of a high prevalence of sexual and reproduction problems in this population and take this into account when counseling them. More research focusing on this association is needed.

REFERENCES:

Disclosure of Interests: Luis Fernando Perez: None declared, Bermeke te Winkel: None declared, Juan Pablo Carrizales-Luna: None declared, Wichor Bramer: None declared, Saskia Vonstenbosch: None declared, Eugene van Puijenbroek: None declared, Johanna Hazes: None declared, Radboud Dolhain Grant/research support from: UCB Pharma B.V

ThU0682 UNDERDIAGNOSIS OF TRADITIONAL CARDIOVASCULAR RISK FACTORS IN RHEUMATIC DISEASES

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Background: Patients with rheumatic diseases (RD) have a higher cardiovascular risk (CVR), compared to the general population (1). The increased risk in this population, tends to be associated with the chronic inflammation generated by RD. Another contributor is the coexistence of traditional CVR factors, such as diabetes, hypertension, obesity, smoking, and dyslipidemia (2). It is known that adequate control of this factors can reduce the overall CVR. Due to the increased CVR burden, there’s a growing awareness of cardiovascular assessment in rheumatic patients. Therefore, the 2016 EULAR guidelines recommend making this assessment every 5 years, in order to decrease their morbidity and mortality by early treatment.

Objectives: To determine the prevalence of underdiagnosis and inefficient treatment of traditional cardiovascular risk factors in RD patients.

Methods: A cross-sectional, observational study of patients between 30 and 75 years with rheumatoid arthritis (RA), psoriatic arthritis (PsA), systemic lupus erythematosus (SLE) and ankylosing spondylitis (AS) recruited at the rheumatology clinic at a University Hospital in northeastern Mexico. Exclusion criteria: previous cardiovascular disease, overlap syndromes, diabetes, or pregnancy. Evaluation included history of lifestyle, comorbidities, medications, blood pressure, anthropometry and fasting glucose measures. Framingham-BMI (FRS-BMI) was used to calculate their predicted CVR to 10 years.

Results: A total of 382 patients were recruited, 90.6% were women (n=346), with a median age of 53 years (45-59). In this population, 87.4% of the patients (n=334) had at least one CVR factor; the presence of traditional CVR factors according to RD is shown in Figure 1. Other population characteristics are in Table 1. Around half of the patients were not in their ideal weight, 32% being diagnosed as overweight and 31.4% with obesity. Out of the patients with no previous diagnosis of hypertension (n=350, 91.5%), 36.1% had elevated or high blood pressure levels. The patients that did have previous diagnosis, 68.7% didn’t have an adequate control of their blood pressure, even though they’re on pharmacological treatment. History of dyslipidemia was found in 5.2% of patients. Half of them arrived at consultation with a recent lipid profile, having a median LDL of 133.5 (109-158) mg/dL, not meeting target levels. Even though no diabetic patients were included, 20.8% of the patients had hyperglycemia. According to FRS-BMI, 80.4% of the patients had a low CVR, 14.9% moderate risk, and 4.7% had a high CVR.

Figure 1. Traditional cardiovascular risk factors.

REFERENCES:
Conclusions: In this study, an underdiagnosis and insufficient treatment of traditional CVR factors in rheumatic patients was found. Besides having a RD and at least one traditional CVR factor, 19.6% of the patients had a moderate or high CVR according to FRS-BMI. The observed burden of CVR factors in RD is significant. Therefore, rheumatologists must improve the CV assessment made to each of their patients.

REFERENCES:

Disclosure of Interests: None declared

Table 1. RD patients’ characteristics.

<table>
<thead>
<tr>
<th>Variable</th>
<th>n (%)</th>
<th>OR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at time of analysis</td>
<td>60.7 ± 15.4</td>
<td>1.08 [1.05 – 1.1]</td>
<td>0.00</td>
</tr>
<tr>
<td>Diagnosis</td>
<td>237 (85%)</td>
<td>1.1</td>
<td>0.00</td>
</tr>
<tr>
<td>RA</td>
<td>42 (15%)</td>
<td>1.05 [1.03 – 1.08]</td>
<td>0.00</td>
</tr>
<tr>
<td>PsA and AS</td>
<td>19 (7%)</td>
<td>1.09 [1.06 – 1.12]</td>
<td>0.00</td>
</tr>
<tr>
<td>Disease duration</td>
<td>13 ± 10.4</td>
<td>1.04 [1.01 – 1.07]</td>
<td>0.00</td>
</tr>
<tr>
<td>Charlson score &gt; 2</td>
<td>142 (51%)</td>
<td>1.03 [1.01 – 1.05]</td>
<td>0.00</td>
</tr>
<tr>
<td>Chronic Respiratory Disease</td>
<td>65 (23%)</td>
<td>1.02 [1.00 – 1.04]</td>
<td>0.00</td>
</tr>
<tr>
<td>ILD</td>
<td>35 (13%)</td>
<td>1.01 [1.00 – 1.02]</td>
<td>0.00</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>26 (9%)</td>
<td>1.00 [0.98 – 1.02]</td>
<td>0.00</td>
</tr>
<tr>
<td>History of severe CAP</td>
<td>28 (10%)</td>
<td>1.00 [0.98 – 1.02]</td>
<td>0.00</td>
</tr>
<tr>
<td>Current treatment bDMARD csDMARD</td>
<td>153 (55%)</td>
<td>1.00 [0.98 – 1.02]</td>
<td>0.00</td>
</tr>
<tr>
<td>GC</td>
<td>84 (30%)</td>
<td>1.00 [0.98 – 1.02]</td>
<td>0.00</td>
</tr>
<tr>
<td>Corticosteroid use</td>
<td>110 (28.8)</td>
<td>1.00 [0.98 – 1.02]</td>
<td>0.00</td>
</tr>
<tr>
<td>Fasting glucose</td>
<td>91 (28.8)</td>
<td>1.00 [0.98 – 1.02]</td>
<td>0.00</td>
</tr>
<tr>
<td>FRS BMI score</td>
<td>5.15 (2.9 – 8.82)</td>
<td>1.00 [0.98 – 1.02]</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Table 2. Predictors of vaccination after adjustment

<table>
<thead>
<tr>
<th>Variable</th>
<th>OR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.08 [1.05 – 1.1]</td>
<td>0.00</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>4 [1.09 – 14.7]</td>
<td>0.03</td>
</tr>
<tr>
<td>History of severe CAP</td>
<td>4.7 [1.3-17.3]</td>
<td>0.02</td>
</tr>
<tr>
<td>Current csDMARD</td>
<td>2.3 [1.4 – 3.9]</td>
<td>0.00</td>
</tr>
<tr>
<td>Current GC</td>
<td>2.2 [1.04 – 4.4]</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Disclosure of Interests: Sebastian C Rodriguez-Garcia: None declared, Raul Castellanos-Moreira Speakers bureau: MSD, Lilly, Victoria Hernandez: None declared, Carolina Garcia-Vidal Speakers bureau: Lilly, Pfizer, Juan D. Caffe: None declared, Julio Ramón Sanmarti: None declared, Anna Vilella: None declared, Carolina Garcia-Vidal Speakers bureau: Lilly, Pfizer, Juan D. Caffe: None declared, Julio Ramón Sanmarti: None declared, Raimon Sanmarti Speakers bureau: PFIZER, SANOFI, LILLY, MSD, UCB, NOVARTIS, JANSSEN, Jose A. Gomez-Puerta Consultant for: Pfizer, Roche, Speakers bureau: Abbvie, BMS, Janssen, MSD, Pfizer, Roche

THU0684 HOW MANY OF YOUR PATIENTS HAVE DEPRESSIVE SYMPTOMS? HOW TO ASSESS DURING ROUTINE CLINICAL PRACTICE?

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Background: Patients with rheumatic diseases have a high prevalence of depressive symptoms that affect the patients’ self-assessment, adherence to medication [1], and mortality [2].

Objectives: To evaluate patients with rheumatic diseases regarding depressive symptoms by using the PHQ-2 (Patient Health Questionnaire with 2 items) and assess its feasibility during routine clinical practice.

Methods: 485 consecutive patients with rheumatic diseases attending a rheumatology practice that is part of the public health care system in Erlangen, Germany underwent a routine clinical assessment by different rheumatologists. In addition to disease-specific assessments and questionnaires, every patient answered two questions regarding depressive symptoms which form the PHQ-2 (range of 0[best] to 6[worst]). All questionnaires were answered digitally by touchscreen and Software RheumaDok and RheumaDokM (Nils Körber und Joachim Elgas G.b.R).
A PHQ-2 score $\geq 3$ points has a sensitivity of 87% and a specificity of 78% for detecting a major depressive disorder compared to a structured clinical interview. [3] A positive screening year was thus addressed during subsequent medical consultation or by notifying the patient's general practitioner. The PHQ-2 is a short form of the PHQ-9 which previously had been validated in rheumatoid arthritis. [4]

**Results:** Overall, 26% of patients stated depressive symptoms (PHQ score $\geq 3$). Table 1 shows the prevalence of depressive symptoms by disease entity which was not significantly different among the subgroups ($\chi^2=8.6$, $p=0.3$). However, given our results indicating depressiveness to be common across subgroups, all of these patients merit further evaluation. The PHQ-2 was widely accepted by patients, and seemed very feasible due to its concise form.

**Conclusion:** The PHQ-2 questionnaire is a highly feasible and well accepted tool in routine clinical practice, helping to screen for depressive symptoms as a highly prevalent condition across rheumatic diseases. Real world evidence of depressive symptoms may improve healthcare by shedding light on the patients' mental well-being and comorbidity.

**REFERENCES:**


**Disclosure of Interests:** Stefan Kleinert Grant/research support from: Novartis, Consultant for: Novartis, UCB, Chugai, Celgene, Medac, Roche, Abbvie, Speakers bureau: Novartis, UCB, Chugai, Celgene, Medac, Roche, Abbvie, Florian Schuch Consultant for: Celgene, Lilly, UCB, Roche, Sanofi-Aventis, Abbvie, Novartis, Speakers bureau: Celgene, Lilly, UCB, Roche, Sanofi-Aventis, Abbvie, Praxedis Rapp: None declared, Monika Ronneberger Consultant for: Celgene, Novartis, Paid instructor for: Abbvie, Bristol Myers Squibb, Novartis, Speakers bureau: Celgene, Novartis and Bristol Myers Squibb, Pfizer, Joerg Wender Consultant for: Roche Pharma AG, Abbvie, Jannssen Cilag, Novartis, Speakers bureau: Chugai Pharma AG, Abbvie, Jannssen Cilag, Novartis, Matthias Engbrecht Grant/research support from: Roche Pharma AG, Chugai Pharma Europe Ltd, Abbvie Deutschland GmbH & Co KG, Celgene GmbH, Lilly Deutschland GmbH, Speakers bureau: Roche Pharma AG, Chugai Pharma Europe Ltd, Abbvie Deutschland GmbH & Co KG, Celgene GmbH, Lilly Deutschland GmbH

treating and other reproductive factors, and RA risk with conflicting results [2, 3].

Objectives: To assess the relationships between endogenous and exogenous female hormonal exposures and the risk of RA in women involved in the E3N cohort.

Methods: E3N is an ongoing French prospective cohort that included 98,995 women aged 40-65 years in 1990. Women completed mailed questionnaires every 2-3 years on lifestyle, reproductive factors, and health-related information. Female endogenous hormonal exposures were assessed using age at menarche, age at menopause, and the duration of reproductive life. Exogenous hormonal exposures included oral contraception and menopausal hormonal treatment (MHT). Hazard ratios (HRs) and 95% confidence intervals (CIs) for the risk of incident RA were estimated using Cox proportional hazards regression models with age as the time scale, first applied to the overall population, then stratified for smoking exposure.

Results: A total of 698 incident RA cases were validated among and 78,452 women over 1,865,213 women-years. Multivariate models for age at menopause and cumulative duration of MHT appear in Table. After stratification for smoking exposure, early age at menopause was associated with a somewhat stronger RA risk in women exposed to smoking (HR=1.6, 95% CI: 1.1-2.2; P trend =0.0270) than in those with no smoking exposure (HR=1.3, 95% CI: 0.8-2.2; P trend =0.1811). However when adjusting for cumulative duration of MHT, early age at menopause was no longer associated with incident RA, even in women exposed to smoking (HR=1.3, 95% CI: 0.8-2.2; P trend =0.7973); while a cumulative duration of MHT > 4 years was borderline associated with RA in women exposed to smoking [HR=1.3, 95%CI: 1.0-1.7; P trend =0.09] in comparison with women who did not receive MHT. Age at menopause and duration of THM were strongly correlated: in women with an age at menopause duration of MHT was significantly longer: 7.01 (7.3) years versus 4.8 (5.0) years (p<0.001). There was no evidence of an association between oral contraception use, age at menarche and duration of reproductive life with the risk of RA.

Conclusion: Early age at menopause and/or duration of MHT > 4 years use may increase the risk of RA. Further studies are requested to disentangle the effect of early menopause to that of long-term MHT.

REFERENCES:

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Disclosure of Interests: Carine Galliot: None declared. Yann Nguyen: None declared. Juliette Gambaretti: None declared. Amandine Gelot: None declared. Xavier Mariette Grant/research support from: Servier, Consultant for: AstaZeneca, Bristol-Myers Squibb, GlaxoSmithKline, Janssen, Pfizer, UCB Pharma, Marie-Christine Boutron-Ruault: None declared, Raphaèle Seror: None declared


### Table 1. Overall population basic characteristics.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All population (n=17,827)</th>
<th>Controls without FMF (n=10,080)</th>
<th>FMF patients (n=7,747)</th>
<th>Statistical significance (p-value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean±SD)</td>
<td>38.43±19.62</td>
<td>37.69±19.55</td>
<td>39.38±19.68</td>
<td>NS</td>
</tr>
<tr>
<td>Age at diagnosis (mean±SD)</td>
<td>26.41±18.41</td>
<td>25.67±18.35</td>
<td>27.37±18.45</td>
<td>NS</td>
</tr>
<tr>
<td>Gender (female: %)</td>
<td>9,000 (50.5%)</td>
<td>5,121 (50.8%)</td>
<td>3,879 (50.1%)</td>
<td>ns</td>
</tr>
<tr>
<td>BMI (mean±SD)</td>
<td>24.81±63.91</td>
<td>24.42±60.61</td>
<td>25.30±77.41</td>
<td>ns p=0.0054</td>
</tr>
<tr>
<td>SES (n=6%)</td>
<td>8,370 (50.6%)</td>
<td>4,729 (50.3%)</td>
<td>3,641 (51.1%)</td>
<td>ns p=0.0020 (p trend)</td>
</tr>
<tr>
<td>Low</td>
<td>5,609 (33.9%)</td>
<td>3,153 (33.5%)</td>
<td>2,455 (34.5%)</td>
<td>ns</td>
</tr>
<tr>
<td>Medium</td>
<td>2,548 (15.4%)</td>
<td>1,524 (16.2%)</td>
<td>1,024 (14.4%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>High</td>
<td>7,107 (40.0%)</td>
<td>4,729 (40.4%)</td>
<td>2,455 (34.5%)</td>
<td>ns</td>
</tr>
<tr>
<td>Schizophrenia (%)</td>
<td>5,121 (31.1%)</td>
<td>319 (33.3%)</td>
<td>2,412 (33.3%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Epilepsy (%)</td>
<td>267 (1.5%)</td>
<td>146 (1.5%)</td>
<td>121 (1.6%)</td>
<td>ns</td>
</tr>
<tr>
<td>All-cause mortality (%)</td>
<td>707 (4.0%)</td>
<td>341 (3.4%)</td>
<td>366 (4.7%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Background: Several autoimmune diseases have been associated with schizophrenia and epilepsy, however little is known about putative links with the auto-inflammatory conditions.

Objectives: We investigated the association between familial Mediterranean fever (FMF), a paradigmatic auto-inflammatory disease, schizophrenia and epilepsy, and assessed the impact of the latter disorders on the survival of FMF patients utilizing a large sample database.

Methods: A case-control study was performed by utilizing the database of Clalit Health Services. FMF patients were compared to age- and sex-matched counterparts in terms of prevalence of schizophrenia and epilepsy. The chi-squared test was used to assess the distribution of categorical variables, while the t-test were applied for continuous variables. Analysis regarding survival were performed using Kaplan-Meier curves, log rank test and multivariate Cox proportional-hazards method.

Results: The study included 7,747 FMF patients, and 10,080 age- and sex-matched controls. At the univariate analysis, schizophrenia and epilepsy as co-morbidities, 50 FMF patients (0.8%) and 89 controls (0.9%) had schizophrenia, respectively. Multiple logistic regression model, FMF was inversely associated with schizophrenia (OR 0.64 [95%CI 0.43-0.90], p=0.0173), while there was no association between FMF and epilepsy. Subjects having either FMF [HR 1.43 [95%CI 1.23-1.66]], schizophrenia (HR 3.97 [95%CI 1.47-10.70]) or epilepsy (HR 2.54 [95%CI 1.72-3.75]) were independently associated with all-cause mortality. However, schizophrenia as co-morbidity in FMF subjects did not worsen their prognosis [HR 2.17 [95%CI 0.60-7.86]].

Conclusion: FMF patients have a significantly lower proportion of schizophrenia than controls. Patients with either FMF, schizophrenia or epilepsy are at higher risk of all-cause mortality, a finding that calls for assessment of better medical management on mortality outcome.

### Table 2. Multivariate logistic regression assessing covariates associated with schizophrenia and epilepsy.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient</th>
<th>Std. Error</th>
<th>Wald</th>
<th>P</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schizophrenia</td>
<td>Age</td>
<td>0.02</td>
<td>0.00</td>
<td>10.75</td>
<td>0.0010</td>
<td>1.02</td>
</tr>
<tr>
<td></td>
<td>Sex (female)</td>
<td>-0.28</td>
<td>0.19</td>
<td>2.16</td>
<td>0.1421</td>
<td>0.64</td>
</tr>
<tr>
<td></td>
<td>FMF</td>
<td>-0.45</td>
<td>0.19</td>
<td>5.67</td>
<td>0.0173</td>
<td>0.64</td>
</tr>
<tr>
<td></td>
<td>SES</td>
<td>0.26</td>
<td>0.20</td>
<td>1.66</td>
<td>0.1974</td>
<td>1.29</td>
</tr>
</tbody>
</table>
ASSESSMENT OF THE QRISK2, QRISK3, SLE CARDIOVASCULAR RISK EQUATION, FRAMINGHAM AND MODIFIED FRAMINGHAM RISK CALCULATORS AS PREDICTORS OF CARDIOVASCULAR DISEASE EVENTS IN SYSTEMIC LUPUS ERYTHEMATOSUS

Jagan Sivakumaran1,2, Paula Harvey2, Jiandong Su2, Ahmed Omar3, Nicole Anderson4, Dafna D Gladman4, Murray B Urowitz2,4, Zahi Touma4,2
1University of Toronto, Medicine, Toronto, Canada; 2Centre for Prognosis Studies in the Rheumatic Diseases, Rheumatology, Toronto, Canada; 3University of Toronto, Cardiology, Toronto, Canada; 4University of Toronto, Rheumatology, Toronto, Canada

Background: Systemic lupus erythematosus (SLE) is recognized as an independent risk factor for cardiovascular disease (CVD), and patients with SLE are at an elevated risk of CVD compared to the general population1. The complex interplay between conventional CVD risk factors, the inflammation caused by SLE and the pharmacological treatment of SLE contributes toward CVD risk1. Despite knowledge of this increased risk, there is no agreement on the use of risk assessment tools in the prediction of CVD in SLE. The Modified Framingham Risk Score (mFRS), QRISK3 and SLE Cardiovascular Risk Equation (SLECRE) have been introduced as promising CVD risk assessment tools considering SLE in prospective patients.

Objectives: To determine which cardiovascular risk assessment tool amongst the QRISK2, QRISK3, SLECRE, Framingham (FRS) and mFRS best predicts CVD events in SLE.

Methods: Single-centre analyses on prospectively collected data of 1887 SLE patients were performed to compute 10-year CVD risk scores for each tool. Tools’ scores were evaluated against CVD events at or within ten years for cases (CVD events) and controls (no CVD events). For cases, the index date for risk score calculation was chosen 10 years, or as close to 10 years as possible prior to the CVD event. For controls, risk scores were calculated as close to 10 years as possible prior to the most recent clinic appointment. Proportions of patients classified as low (<10%), median (10-20%) and high risk (>20%) of developing CVD according to each tool were determined. Sensitivity, specificity, positive/negative predictive values and c-statistics of these tools were analysed.

Results: 232 total CVD events were identified in the cohort including myocardial infarction, stroke, transient ischemic attack, heart failure and CVD death. QRISK2 and FRS risk-stratification was similar, while QRISK3 and mFRS risk-stratification was similar (Figure 1). The SLECRE classified the highest number of patients as median-high risk (Figure 1). The sensitivities and specificities are as follows for each tool: QRISK2 (19%, 93%), FRS (22%, 93%), mFRS (46%, 83%), QRISK3 (47%, 78%), SLECRE (61%, 63%). The tools were similar in negative predictive value, ranging from 89% (QRISK2) to 92% (SLECRE). The FRS and mFRS had the greatest c-statistics, both equaling 0.73, demonstrating the greatest predictive accuracy amongst the tools, while the QRISK3 had the lowest (0.67).

Figure 1. Kaplan-Meier survival plot of study cohorts

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REFERENCES:


THU0688

Assessment of the QRisk2, QRisk3, SLE Cardiovascular Risk Equation, Framingham and Modified Framingham Risk Calculators as Predictors of Cardiovascular Disease Events in Systemic Lupus Erythematosus

Jagan Sivakumaran1,2, Paula Harvey2, Jiandong Su2, Ahmed Omar3, Nicole Anderson4, Dafna D Gladman3,4, Murray B Urowitz2,4, Zahi Touma4,2

1University of Toronto, Medicine, Toronto, Canada; 2Centre for Prognosis Studies in the Rheumatic Diseases, Rheumatology, Toronto, Canada; 3University of Toronto, Cardiology, Toronto, Canada; 4University of Toronto, Rheumatology, Toronto, Canada

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Objectives: To determine which cardiovascular risk assessment tool amongst the QRISK2, QRISK3, SLECRE, Framingham (FRS) and mFRS best predicts CVD events in SLE.

Methods: Single-centre analyses on prospectively collected data of 1887 SLE patients were performed to compute 10-year CVD risk scores for each tool. Tools’ scores were evaluated against CVD events at or within ten years for cases (CVD events) and controls (no CVD events). For cases, the index date for risk score calculation was chosen 10 years, or as close to 10 years as possible prior to the CVD event. For controls, risk scores were calculated as close to 10 years as possible prior to the most recent clinic appointment. Proportions of patients classified as low (<10%), median (10-20%) and high risk (>20%) of developing CVD according to each tool were determined. Sensitivity, specificity, positive/negative predictive values and c-statistics of these tools were analysed.

Results: 232 total CVD events were identified in the cohort including myocardial infarction, stroke, transient ischemic attack, heart failure and CVD death. QRISK2 and FRS risk-stratification was similar, while QRISK3 and mFRS risk-stratification was similar (Figure 1). The SLECRE classified the highest number of patients as median-high risk (Figure 1). The sensitivities and specificities are as follows for each tool: QRISK2 (19%, 93%), FRS (22%, 93%), mFRS (46%, 83%), QRISK3 (47%, 78%), SLECRE (61%, 63%). The tools were similar in negative predictive value, ranging from 89% (QRISK2) to 92% (SLECRE). The FRS and mFRS had the greatest c-statistics, both equaling 0.73, demonstrating the greatest predictive accuracy amongst the tools, while the QRISK3 had the lowest (0.67).

Figure 1. Percentage of patients considered low (<10%), median (10-20%) and high risk (>20%) between cases (CVD, n=232) and controls (no-CVD, n=1655) according to the FRS, mFRS, QRISK2, QRISK3 and SLE CRE.

Conclusion: While the mFRS performance was superior to the FRS, the QRISK3 did not outperform the FRS. Although the SLECRE had the highest sensitivity, it had the lowest specificity, demonstrated by grouping the most cases and controls in the median-high risk category. Several factors are important to consider when deciding which risk assessment tools to utilize: ease of use/computation, sensitivity/specificity, and laboratory data accessibility. Of the tools currently available, the mFRS is a practical tool with a simple, intuitive scoring system appropriate for the ambulatory clinic setting based on the initial weighting of the FRS while adjusting for SLE. However, much room for improvement exists in predicting CVD in SLE.

REFERENCES:

Disclosure of Interests: Jagan Sivakumaran: None declared, Paula Harvey: None declared, Jiandong Su: None declared, Ahmed Omar: None declared, Nicole Anderson: None declared, Dafna D Gladman, Consultant for: Abbvie; Agen; Boehringer Ingelheim; Dexcel.
and UCB, Consultant for: AbbVie, Amgen, BMS, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, and UCB; Murray B Urowitz Research Grant/research support from: Bristol-Myers Squibb, Amgen, Consultant for: Optum


THU0689

ASTHMA AND ELEVATION OF ANTI-CITRULLINATED PROTEIN ANTIBODIES PRIOR TO THE ONSET OF RHEUMATOID ARTHRITIS

Alessandra Zaccardelli1, Xinyi Liu1, Julia Ford1,2, Sara Tedeschi1,2, Jing Cui1,2, Bing Lu1,2, Su Chu1,2, Peter Schur1,2, Cameron Speyer1,2, William Kaldenberg3, Jeremy Sokolove4,2, Carlos Camargo, Jr.1,2, Jeffrey Sparks1,2,1, Brigham and Women’s Hospital, Boston, United States of America; 2Harvard Medical School, Boston, United States of America; 3Stanford University School of Medicine, Palo Alto, United States of America; 4VA Palo Alto Health Care System, Palo Alto, United States of America; 5AbbVie, Redwood City, United States of America; 6Massachusetts General Hospital, Boston, United States of America

Background: Anti-citrullinated protein antibodies (ACPA) are central to RA pathogenesis, with serum ACPA titers elevated years prior to clinical RA onset. ACPA may occur in patients with asthma, forming neoantigens producing ACPA before articular involvement. Thus, individuals with inflammatory airway diseases, such as asthma, may be susceptible to RA-related autoimmunity.

Objectives: To investigate asthma as a risk factor for ACPA+ in serum prior to clinical RA onset.

Methods: We performed a cross-sectional analysis among women in the Nurses’ Health Studies to examine whether asthma was associated with pre-RA ACPA+. Incident RA cases occurring after blood draw met research criteria and were each matched to 3 controls by age and menopausal status. Presence of self-reported asthma and potential confounders, including smoking pack-years, were assessed using questionnaires. The specific (secondary) definition for ACPA+ was: >3 units on CCP2 or elevation >99th percentile of control distribution on the research ACPA assay.

The specific (secondary) definition for ACPA+ was: >3 units on CCP2 or elevation >99th percentile of control distribution on the research ACPA assay. The sensitive (primary) definition for ACPA+ was: >5 units on CCP2 or >99th percentile of control distribution on the research ACPA assay.

Results: We measured ACPA on 1,135 women, including 286 pre-RA cases and pre-RA controls. Serum was banked a mean of 9.7 years (SD 5.8) prior to RA diagnosis, mean age of 51.9 years (SD 7.9). Overall, 12% of pre-RA cases were current smokers (OR 3.11, 95%CI 1.29-7.47) and only pre-RA cases (OR 2.22, 95%CI 1.00-4.88). In the secondary analyses, we found similar associations among all cases (OR 2.32, 95%CI 1.19-4.51).

Conclusion: Asthma may be a novel risk factor for elevation of ACPA prior to RA onset, independent of smoking. These findings encourage further research on the contribution of airway inflammation to RA pathogenesis.

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THU0690

DISEASE ACTIVITY CORRELATES WITH INSULIN RESISTANCE AND ADIPOCYTOKINES IN PATIENTS WITH DMARD-NAIVE RHEUMATOID ARTHRITIS

Ali Taytaz1, Burak Toprak2, Baris Acinci2, Merih Birlik4, Fatma Demet Arslan5, Baris Gundogdu2, Ayler Colak2,1, SBU Tepek Egitim ve Arastirma Hastanesi, Istanbul, Turkey; 2Dokuz Elyaf University School of Medicine, Department of Internal Medicine, Endocrinology, Istanbul, Turkey; 3Dokuz Elyaf University School of Medicine, Department of Internal Medicine, Rheumatology, Istanbul, Turkey; 4Medeniyet University Department of Internal Medicine, Rheumatology, Istanbul, Turkey

Background: Cardiovascular events such as myocardial infarction and stroke are frequent comorbidities in rheumatic diseases [1]. In relation, components of the metabolic syndrome (MS) including insulin resistance (IR), central obesity, high blood pressure, high triglycerides, and low high-density lipoprotein (HDL) are related to a high rate of endothelial dysfunction and atherosclerosis in patients with RA [2].

Objectives: We aimed to investigate the relationship between disease activity and insulin resistance (IR) and the levels of adipoctyokines in non-diabetic patients with newly diagnosed rheumatoid arthritis (RA) who are naïve to disease modifying anti-rheumatic drugs (DMARDs).

Methods: Forty-seven DMARD-naïve patients with RA and 25 age-, gender-, and BMI-matched controls were included. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), 28-point-count disease activity score (DAS28), serum lipids, glucose, HbA1c, insulin, leptin, resistin, visfatin, and RBP4 levels were measured. Homeostasis model assessment for insulin resistance (HOMA-IR) was calculated. Patients were studied before and 3 months after treatment with DMARDs.

Results: Levels of adipokines were similar in patients with RA and controls (p > 0.05 for all). However, RA patients with active disease (DAS28 > 3.2) had numerically higher levels of leptin (9.3 (3.7-14.7) vs. 7.6 (3.7-11.0), p = 0.289), insulin (8.0 (5.2-12.7) vs. 5.9 (4.2-8.7), p = 0.285), and HOMA-IR (1.9 (1.1-3.0) vs. 1.3 (1.0-1.9), p = 0.209). DAS28 was correlated with HOMA-IR (r = 0.356, p = 0.016), insulin (r = 0.323, p = 0.02), and leptin (r = 0.399, p = 0.005) in the study group (Figure-1).

Conclusion: Disease activity is associated with IR and correlates with circulating levels of adipokines in patients with RA. Treatment with DMARDs reduces leptin and improves IR.

Disclosure of Interests: Ali Taytaz: None declared, Burak Toprak: None declared, Baris Acinci: None declared, Merih Birlik: None declared, Fatma Demet Arslan: None declared, Baris Gundogdu: None declared, Ayler Colak: None declared, SBU Tepek Egitim ve Arastirma Hastanesi, Istanbul, Turkey; Dokuz Elyaf University School of Medicine, Department of Internal Medicine, Endocrinology, Istanbul, Turkey; Dokuz Elyaf University School of Medicine, Department of Internal Medicine, Rheumatology, Istanbul, Turkey; Medeniyet University Department of Internal Medicine, Rheumatology, Istanbul, Turkey

Disclosure of Interests: None declared, Karen Costenbader: None declared, William Robinson: None declared, Peter Schur: None declared, Cameron Speyer: None declared, Jeffrey Sparks: None declared, Carlos Camargo, Jr.: None declared, Alessandra Zaccardelli: None declared.
REFERENCES:


Disclosure of Interests: None declared

THU0691

CLINICAL, RADIOLOGICAL, THERAPEUTIC ASPECT AND PROGNOSTIC OF INFECTIOUS SPONDYLODYSITIS WITHOUT BACTERIOLOGICAL EVIDENCE

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Background: Early microbiological diagnosis and multidisciplinary management are the main predictive factor for successful treatment in septic spondylodiscitis. However, the therapeutic management of spondylodiscitis without bacteriological diagnosis is not well codified.

Objectives: To evaluate whether there is clinical, biological or significant imaging between patients with infectious spondylodiscitis as they had or not a microbiological diagnosis.

Methods: Retrospective study including 107 patients hospitalized in our department between 1999 and 2018. The diagnosis was based on clinical, biological, radiological and bacteriological data.

Results: This study involved 107 patients, including 58 men (54.2%) and 49 women (45.8%) with a mean age of 55 years [16–86]. Spinal pain was observed in all cases and the lumbar spine was most affected (54.2%). A neurological deficit was noted in 16.62% of cases. The inflammatory syndrome was present in 90.6% of cases. Radiographs of the spine were abnormal in 83.1% of cases. CT and Spinal MRI were performed respectively in 60% and 78.8% of cases. Discal vertebral biopsy was performed in 73 patients and was contributory in 46.5% of cases.

We divided patients into two groups: patients with a confirmed biological diagnosis (group 1: 45.3%) versus patients in whom the diagnosis had been held on presumptive criteria (group 2: 54.7%). There was no statically significant difference in the age (p=0.5), sex (p=0.3), risk factors such as diabetes (p=0.8), the start mode (p=0.4), the presence of an impaired general condition (p=0.3), night sweats (p=0.1) and a neurological deficit (p=0.8), biological parameters (p=0.3) and the occurrence of complications (p=0.09) between the two groups. Vertebral condensation in radiographs of the spine was higher in group 2 and this was statically significant (p=0.03). In addition, the consumption of unpasteurized milk and positivity of wright serology was higher in the first group (p=0.001 and p=0.001; respectively). Similarly, contributive histological result of vertebral biopsy was more frequent in group 1 (p=0.007).

Conclusion: Diagnosing infectious spondylodiscitis is facilitated by improved access to MRI testing. However, microbiological diagnosis is the main key to a successful management of this life threatening infection.

Disclosure of Interests: None declared

THU0692

OCULAR MANIFESTATIONS IN BEHCET’S DISEASE MAY BE MORE COMMON IN CHILDREN THAN ADULTS: RESULTS OF A SYSTEMATIC REVIEW

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1University of Western Ontario, Rheumatology, London, Canada; 2University of Toronto, Toronto, Canada

Background: Behcet’s disease (BD) can develop in both children and adults, but they may have different clinical features. Ocular involvement is common in BD and causes substantial impairment. The frequency of ocular involvement in BD has a wide range (5 to 89%).

OBJECTIVES: This study determined the frequency and type of ocular manifestations in childhood and adult BD and compared prevalence of ocular manifestations by geographic location in those with BD.

Methods: The protocol of ocular conditions in rheumatic conditions was registered at clinitrials.gov (NCT03753893). Search terms were: conjunctivitis, keratoconjunctivitis sicca, xerophthalmia, uveitis, eye hemorrhage, optic neuritis, papilledema, orbital disease, retinal artery/vein occlusion, macular edema, retinitis, choriorretinitis, scleritis, iridocyclitis, choroid hemorrhage, blindness and amaurosis fugax in patients with BD. The search was performed with the assistance of an information specialist. Medline, Cochrane and Web of Science were used searching papers that spanned from their inception (1966, 1991 and 1990 respectively) to October 5, 2018. Studies were included if they had a minimum of twenty patients and reported the frequency of ocular manifestations within BD. Random effects models were used to combine the prevalence of ocular manifestations using Revman 5.3. Heterogeneity was evaluated using I² and funnel plots.

Results: The search resulted in 3129 articles, of which 33 were included for meta-analysis. Eye manifestations were more frequent in childhood onset BD with the mean [95% Confidence Interval] frequency of 50 [38-63]% compared to 34 [25-43]% in adults. In both children and adults, posterior uveitis (children 27% vs. adults 25%) was the most common ocular manifestation, followed by anterior uveitis (children 18% vs. adults 23%). When comparing the distribution of ocular manifestations in Behcet’s in adults, there was geographic variation higher along the ancient Silk Road with ocular manifestations occurring in 40% of patients from Turkey and the Middle East. Ocular manifestations were similar in Europe (36%) and North America (36%), but less frequent in North Africa (26%), and East Asia (20%).

Conclusion: The frequency of ocular involvement is higher in children when compared to adults with BD. The most common manifestation in the eyes is posterior and then anterior uveitis. Ocular involvement also presents regional differences.

REFERENCES:


THU1545

Beck’s disease (BD) can develop in both children and adults, but they may have different clinical features. Ocular involvement is common in BD and causes substantial impairment. The frequency of ocular involvement in BD has a wide range (5 to 89%).

OBJECTIVES: This study determined the frequency and type of ocular manifestations in childhood and adult BD and compared prevalence of ocular manifestations by geographic location in those with BD.

Methods: The protocol of ocular conditions in rheumatic conditions was registered at clinitrials.gov (NCT03753893). Search terms were: conjunctivitis, keratoconjunctivitis sicca, xerophthalmia, uveitis, eye hemorrhage, optic neuritis, papilledema, orbital disease, retinal artery/vein occlusion, macular edema, retinitis, choriorretinitis, scleritis, iridocyclitis, choroid hemorrhage, blindness and amaurosis fugax in patients with BD. The search was performed with the assistance of an information specialist. Medline, Cochrane and Web of Science were used searching papers that spanned from their inception (1966, 1991 and 1990 respectively) to October 5, 2018. Studies were included if they had a minimum of twenty patients and reported the frequency of ocular manifestations within BD. Random effects models were used to combine the prevalence of ocular manifestations using Revman 5.3. Heterogeneity was evaluated using I² and funnel plots.

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Conclusion: The frequency of ocular involvement is higher in children when compared to adults with BD. The most common manifestation in the eyes is posterior and then anterior uveitis. Ocular involvement also presents regional differences.

REFERENCES:


THU0693

INPATIENT PREVALENCE, EXPENDITURES AND COMORBITIES OF TAKAYASU’S ARTERITIS: A PROPENSITY-MATCHED COHORT STUDY

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Background: Takayasu’s arteritis (TAK) was first described in Japan. Since then, the disease has been extensively studied in Japan and other Asian countries [1]. However, little is known about the characteristics, inpatient burden, expenditures and comorbidities of TAK in the United States (US).

Objectives: To investigate the inpatient prevalence, expenditures and comorbidities of patients with TAK in the US.

Methods: Patients with TAK were identified within the Nationwide Inpatient Sample (NIS) database of the years 2013-2014 using ICD-9 diagnostic code. NIS is a publicly available inpatient database that contained data of over 7 million hospital stays, which are a 20% stratified sample of over 4,000 non-federal acute care hospitals from more than 40 states of the US. Data on patient characteristics, comorbidities, resource utilization and expenditures was collected. A propensity-matched cohort of patients without TAK was also created from the same database to serve as comparators for the analysis of comorbidities. Inpatient prevalence of TAK was calculated using all admissions in the NIS database as denominator. Odds ratios (OR) comparing the prevalence of comorbidities between cases with TAK and propensity-matched controls without TAK were calculated.

Results: A total of 2,840 patients with TAK were identified from the database, corresponding to an inpatient prevalence of 4.6 cases per 100,000 admissions. The main reasons for admission in patients with TAK were as follows: chest pain (17%), acute myocardial infarction (16%), stroke (14%), sepsis (14%) and pneumonia (11%). Compared to the propensity-matched cohort of patients without TAK, patients with TAK were found to have significantly increased odds of stroke, aortic aneurysm, aortic valvulopathy and peripheral vascular disease. TAK was also associated with increased use of some procedures (Table 1). However, the mortality was not significantly different (adjusted OR: 1.44, 95% CI: 0.58 – 3.61, p<0.43). After adjusting for confounders, patients with TAK displayed a mean additional $11,275 (95% CI, $4,946 - $17,603) for total hospitalization charges (the amount of money that each hospital billed for providing its service on each case) when compared to patients without TAK.

Conclusion: The inpatient prevalence of TAK was higher than what would be expected from the overall incidence. The mean total hospital costs and total hospitalization charges for patients with TAK were higher than patients without TAK. Analysis of comorbidities found significantly higher odds of several vascular comorbidities compared to a propensity-matched cohort of patients without TAK.

REFERENCES:

Table 1. Adjusted ORs comparing the prevalence of comorbidities and use of procedures between patients with TAK versus patients without TAK

<table>
<thead>
<tr>
<th>Comorbidities</th>
<th>Adjusted odds ratio</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke</td>
<td>4.66</td>
<td>2.10-10.31</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Aortic aneurysm</td>
<td>40.76</td>
<td>9.13-181.7</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>2.01</td>
<td>1.22-3.32</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Acute myocardial infarction</td>
<td>2.13</td>
<td>0.56-8.13</td>
<td>0.27</td>
</tr>
<tr>
<td>Aortic valvulopathy</td>
<td>4.92</td>
<td>2.09-11.55</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>1.22</td>
<td>0.63-2.63</td>
<td>0.57</td>
</tr>
<tr>
<td>Procedures</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aortic valve replacement</td>
<td>1.39</td>
<td>0.42-4.60</td>
<td>0.59</td>
</tr>
<tr>
<td>Peripheral vascular intervention</td>
<td>4.41</td>
<td>1.61-12.10</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Arteriography</td>
<td>6.82</td>
<td>2.79-16.68</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>MRI use</td>
<td>2.60</td>
<td>0.42-16.28</td>
<td>0.31</td>
</tr>
</tbody>
</table>

Disclosure of Interests: None declared

THU0694

BRAZILIAN SJÖGREN’S SYNDROME REGISTRY (BRASS): A LARGE BRAZILIAN MULTICENTRIC COHORT OF PRIMARY SJÖGREN’S SYNDROME

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1University Federal do Espírito Santo, Vitória, Brazil; 2Universidade Federal do Porto Alegre, Porto Alegre, Brazil; 3Universidade Federal de Pernambuco, Pernambuco, Brazil; 4Universidade Federal de Uberlândia, Uberlândia, Brazil; 5Hospital das Crianças da Universidade Federal de Minas Gerais, Belo Horizonte, Brazil; 6Hospital das Clínicas de Ribeirão Preto, Ribeirão Preto, Brazil; 7Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil; 8Hospital Evangélico de Curitiba, Curitiba, Brazil; 9Faculdade de Medicina de Botucatu – UNESP, Botucatu, Brazil; 10Instituto de Assistência Médica ao Servidor Público Estadual, São Paulo, Brazil; 11Universidade Federal de São Paulo and Universidade de Santo Amaro., São Paulo, Brazil

Background: Primary Sjögren’s syndrome (pSS) is an orphan systemic autoimmune disease with no treatment based on evidence1. There is an international effort for multicentric registries for getting information about phenotypes, complication, response of treatment, and biobank consortium.

Objectives: To describe the creation of the Brazilian Sjögren’s Syndrome Registry (BRASS) and present the preliminary data.

Methods: BRASS is supported by Brazilian Society of Rheumatology (SBR) and is including patients from all regions of the country. Recruitment started in 2018 and is due to be completed in 2024. We are including patients with pSS according to AECG 2002 or ACR-EULAR 2016 classification criteria. All patients are being assessed for disease activity (ESSDAI), disease damage (SSDDI), symptoms assessment (ESSPRI), fatigue (FACIT-Fatigue), anxiety and depression (HADS), sleepiness (Epworth Sleepiness Scale), physical activity (IPAQ-SF) and quality of life (EQ-5D). In addition, demographics, immunological tests, unstimulated whole salivary flow (UWSF), salivary gland biopsy (SGB), comorbidities, treatment and complications such as cancer and cardiovascular risk assessment are being collected.

Results: There are currently 10 centers across the Brazil and 248 patients were evaluated until now. Most patients were female, white (45%) or mixed (36.3%), with the mean of the disease duration of 8.2 years. ESSDAI at baseline was 6.62±6.37 and currently is 4.2±1.56 (p<0.05). The mean of the SSDDI was 2.1±1.60 and ESSPRI 8.38±6.88. SGB was positive in 81.5% and focus score mean was 1.58±1.30. Schirmer test I was positive in 72.6%, van Bijsterveld in 70.9% and UWSF in 84.8%. About classification criteria, 91.9% fulfilled AECG 2002 and 94% ACR-EULAR 2016. Anti-Ro/SS-A and anti-La were positive in 70.8% and 35.5%, respectively. Forty three percent had positive RF, 88.5% ANA, 6.9% low C3, 10.2% low C4, 34.9% high IgG. Nineteen percent were using prednisone, 40.4% immunosuppressant, 53.6% antimarialar and 17.6% biological therapy. Prevalence of cardiovascular event was 7.5%, hypertension 43.3%, diabetes 13.3%, dyslipidemia 31.5%, smoking 5.8% and cancer 7.5%.

Conclusion: ESSDAI has decreased over time and more than half of patients are on hydroxychloroquine, immunosuppressant or biological therapy. Further analysis is needed to understand whether the reduction in ESSDAI reflects the natural course of the disease or greater access to

Disclosure of Interests: None declared
treatment. BRASS Registry will be important to enhance research and to develop public health planning.

REFERENCES:

Disclosure of Interests: None declared

Background: Previous reports indicated the strong association between smoking and onset of rheumatoid arthritis (RA), and relation between some of lifestyle habit and disease activity of RA.

Objectives: In this study, we compared differences in habits of smoking, alcohol consumption, coffee and Japanese tea intake between RA patients and healthy volunteers (Vo) in the same study population.

Methods: This study was conducted based on baseline data from ongoing 10-years prospective cohort project TOMORROW study (UMIN000003876), which includes age and sex matched RA patients (n=208) and Vo (n=205).

Data on smoking history and alcohol (Alc), coffee and Japanese tea intake were collected by self-reported questionnaires. Alc intake was categorized into 3 groups by calculating the amount per day using Alc unit (pure Alc 20 mg/Alc unit). We also categorized frequency of Alc intake per week into 3 groups, numbers of cup of coffee and Japanese tea intake per day into 4 groups each. The data of RA patients included anthropometric, blood test data, disease activity score28-ESR (DAS28-ESR), together with baseline characteristics. Using logistic multivariate regression lifestyle habits were compared between RA and Vo.

Results: We analyzed 191 Vo and 198 RA with complete data about lifestyle habits. Demographic data and lifestyle habits of RA and Vo were shown in the Table 1 and 2. In RA patients, the average disease activity showed in the Table 1 and 2. In RA patients, the average disease activity

Conclusion: As shown in previous reports, the smoking history was significantly higher in RA patients with an odds ratio of 5.03. And moderate intake of Alc and caffeinated coffee seems to be low in RA patients.

Table 1. Demographic data of rheumatoid arthritis patients (RA) and healthy volunteer (Vo).

<table>
<thead>
<tr>
<th></th>
<th>RA (N=198)</th>
<th>Vo (N=191)</th>
<th>p.value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>58.4±12.6</td>
<td>57.0±13.2</td>
<td>0.28</td>
</tr>
<tr>
<td>Sex female</td>
<td>167 (84.3)</td>
<td>158 (82.7)</td>
<td>0.68</td>
</tr>
<tr>
<td>BMI</td>
<td>22.7±3.6</td>
<td>22.6±3.2</td>
<td>0.72</td>
</tr>
<tr>
<td>Disease duration (year)</td>
<td>13.9±11.8</td>
<td>13.9±11.8</td>
<td>1.00</td>
</tr>
<tr>
<td>ACPA positivity</td>
<td>166 (83.8)</td>
<td>168 (87.7)</td>
<td>0.18</td>
</tr>
<tr>
<td>RF positivity</td>
<td>136 (68.7)</td>
<td>136 (68.7)</td>
<td>0.97</td>
</tr>
<tr>
<td>DAS28-ESR</td>
<td>3.49±1.34</td>
<td>3.49±1.34</td>
<td>0.97</td>
</tr>
<tr>
<td>mHAQ</td>
<td>0.47±0.59</td>
<td>0.47±0.59</td>
<td>0.97</td>
</tr>
<tr>
<td>Methotrexate dose (mg/week)</td>
<td>6.54±3.76</td>
<td>6.54±3.76</td>
<td>1.00</td>
</tr>
<tr>
<td>bDMARDs use</td>
<td>104 (54.5)</td>
<td>104 (54.5)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Values are mean±SD, or n (%). *Student T-test and Fisher’s exact test for RA and Vo.

Table 2. Lifestyle habits of rheumatoid arthritis patients (RA) and healthy volunteer (Vo).

<table>
<thead>
<tr>
<th>Smoking history</th>
<th>RA (N=198)</th>
<th>Vo (N=191)</th>
<th>p.value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>59 (29.8)</td>
<td>29 (15.2)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>1-5</td>
<td>94 (47.5)</td>
<td>76 (39.8)</td>
<td>0.17</td>
</tr>
<tr>
<td>6-10</td>
<td>77 (38.9)</td>
<td>77 (40.3)</td>
<td>0.97</td>
</tr>
<tr>
<td>11-15</td>
<td>27 (13.6)</td>
<td>38 (19.9)</td>
<td>0.04</td>
</tr>
<tr>
<td>16-20</td>
<td>147 (74.2)</td>
<td>125 (65.4)</td>
<td>0.09</td>
</tr>
<tr>
<td>2-6</td>
<td>21 (10.6)</td>
<td>34 (17.8)</td>
<td>0.04</td>
</tr>
<tr>
<td>6-12</td>
<td>30 (15.2)</td>
<td>32 (16.8)</td>
<td>0.97</td>
</tr>
<tr>
<td>Caffeinated coffee (cup/day)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1.00</td>
</tr>
<tr>
<td>1-4</td>
<td>45 (22.7)</td>
<td>27 (14.1)</td>
<td>1.00</td>
</tr>
<tr>
<td>4-6</td>
<td>69 (34.8)</td>
<td>75 (39.3)</td>
<td>1.00</td>
</tr>
<tr>
<td>6-14</td>
<td>1 (0.0)</td>
<td>0 (0.0)</td>
<td>1.00</td>
</tr>
<tr>
<td>14-28</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1.00</td>
</tr>
<tr>
<td>28-56</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1.00</td>
</tr>
<tr>
<td>Decaffeinated coffee (cup/day)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Values are n (%). *Fisher’s exact test for RA and Vo.

Alc, alcohol.


HPR Service developments, innovation and economics in healthcare
duration of disease at 1st assessment was 7.0 years (IQR 5.5-8.8); 24 patients were transited successfully. Only 60% of our youths felt that transition preparatory is important and had confidence to be prepared for change to adult healthcare system (AHCS). Among the less confident group (scores <7), MKHU, MM, AM and HT domains scored significantly less than those from confident youths (p<0.001-0.021), but only transition importance MKHU scores were <7. Disease duration at first TRAT assessment and diagnoses did not predict confidence level. With further targeted education and counselling (median 8.3 months (IQR 5.7-9.6)), confidence and MKHU was significantly improved (p<0.001).

Conclusion: TRAT enables our PRPT team to learn and understand our youths’ perception and readiness of adult transition process. More than one-half of them did not aware of the importance of the transition process and had less confidence to do so. With further targeted counselling and preparation, all improved their perception and MKHU significantly. TRAT was able to guide individualized counselling to our cohort youths who are ready to be transited.

Acknowledgement: American College of Rheumatology


THU0697-HPR CONTENT OF AND RHEUMATOLOGISTS’ AND NURSES’ OPINIONS ON A NURSE-LED TELEPHONE HELPLINE

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Background: To improve timely response to patients’ questions and to support that care is provided by the appropriate professional, a nurse-led rheumatology telephone helpline was introduced in May 2015. Different organisational approaches have been tried out to ensure an effective as well as efficient service. Currently a voicemail system is used. A selection menu allows patients to select whether he/she needs 1) advice regarding disease complaints, 2) drug prescriptions, 3) (change in) appointment at the clinic, 4) laboratory forms. Although the menu differentiates between requests, organising timely responses by the appropriate professional remains a challenge. Clear and joint definitions by the rheumatologists and nurses on what questions to what extent should be addressed by whom, are necessary.

Objectives: To facilitate further improvement of the helpline we explored 1) number and content of questions that were registered; 2) experiences of rheumatologists and nurses with the helpline; 3) opinions of rheumatologists and nurses on which questions should be answered via the helpline.

Methods: A file research explored the number of questions and reasons for contacting the helpline. Data were analysed descriptively. In semi-structured interviews among all rheumatologists (n=8) and nurses involved in manning the helpline service (n=6), experiences and opinions were explored. System Engineering Initiative Patient Safety (SEIPS) model, that focuses on system design and it’s interaction with processes, and outcomes for patients, employees and organisation was used to structure thematic coding of the transcripts.

Results: In 37 months, the helpline registered 3389 calls (see Table 1). A majority of the questions was about disease complaints (28.6%) or other related problems such as pain management, and exercise (27.8%). The proportion of requests for prescriptions was 21.8%. The interviews revealed that both rheumatologists and nurses considered the helpline valuable in providing easy access to care for patients with disease related questions. This should be the primary aim. The rheumatologists also valued their reduced workload, which occurred most if the knowledge of the nurse was sufficient to take care of the responses independently. Moreover, they valued if requests, such as prescriptions, were clustered by the nurses. The nurses experienced an increased workload. Sufficient knowledge on and training in rheumatology, and being familiar with the patient were considered pivotal in providing appropriate and for the patient acceptable care. As nurses cannot prescribe medication, the requests for prescriptions were considered inappropriate. Availability of protocols and guidelines were considered prerequisites by all for responding to patients’ requests appropriately.

Conclusion: The helpline is used frequently and the selection menu has helped to gain insight in why the helpline is used by patients. There is consensus on the primary aim of the helpline and on prerequisites for nurse-led responses to patients’ disease related questions. Rheumatologists and nurses have different opinions on some issues, such as the organisation of prescriptions. Our study findings can help in jointly improving consensus on the content of nursing care within the helpline.

REFERENCES:

THU0698-HPR MORE EFFICIENT DMOAD TRIALS THROUGH INNOVATIVE SCREENING STRATEGIES

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Background: In randomized Clinical Trials (RCT), the number of patients to recruit for assessing effectiveness of disease-modifying OA drug (DMOAD) depends on the proportion of progressors in the population. The higher this proportion, the smaller the cohort to be recruited. In the general OA population, this proportion is quite low (10-30%) [1] requiring large cohorts, hence long and expensive trials.

Objectives: We study how predictive modeling based on early cartilage degradation biomarkers can be used to screen patients, make individual predictions about the likelihood of future progression, and recruit on this basis a progressor-enriched cohort. By doing so, DMOAD RCTs could achieve same or better success rates based on smaller cohorts and lower budgets, even taking into account the extra cost of this innovative screening.

Methods: Two biomarkers (Coll2-1 & Coll2-1-NO2, Artialis, Belgium) have been measured at baseline on 182 OA patients from the placebo arm of a previous RCT. For this cohort, progression at 30M is defined as in [2]. We developed two predictive models of the progression of the patients over 30 months through regularized logistic regressions: one based on Coll2-1 only, the other on Coll2-1 and Coll2-1-NO2. Based on these models, we design a strategy to produce cohorts of patients with a higher rate of progressors than the natural proportion. To do so, we make hypotheses on the expected drug effect (from 30% to 50%), on the costs generated by this innovative screening strategy (a.o. nb patients screened, referrals for devices.


Available online: 1,767,260 of such a study, 554 patients have to be recruited, with a cost of per patient, OR, and R). In the modified version, only patients for which inclusion criteria are met and the tuned biomarker-based model turns positive are enrolled. In the standard version of such a study, 554 patients have to be recruited, with a cost of 1,767,260€. Through the optimized strategy, 1,190 patients are screened,

Calcium deficiency (Ca²⁺) and vitamin D deficiency (25(OH)D³) are important among patients with osteoarthritis (OA). In the standard version of such a study, 554 patients have to be recruited, with a cost of 1,767,260€. Through the optimized strategy, 1,190 patients are screened,
but among them only 344 are recruited in the study, showing a progression rate of about 35% instead of 20%, for a total cost of 1,229,280 €.

**Conclusion:** This work demonstrates the interest for biomarker-based OA-progressors cohort enrichment in DMOAD RCTs. It simulates the gains it could represent for the conduct of such RCTs. The cohorts used in this work (for biomarker measurement and predictive modeling) have a high proportion of women with very large BMI, with K&L grade II-III. The work (for biomarker measurement and predictive modeling) have a high associated with actually using the RD-app (p<0.001).

**Disclosure of Interests:** This work has been financially supported by Sanofi Genzyme. Anne-Chris-tine Hick Employee of: Artialis SA, Yves Henrotin Shareholder of: Founder of DNAlytics.

**REFERENCES:**


**Disclosure of Interests:** Thibault Helleputte Shareholder of: Founder of DNAlytics., Grant/research support from: The data analysis included in this work has been financially supported by Sanofi Genzyme., Anne-Christ-tine Hick Employee of: Artialis SA, Yves Henrotin Shareholder of: DNAlytics.

**Disclosure of Interests:**

**HPR Interventions (educational, physical, social and psychological)**

**THU0699-HPR**

**IS A SMARTPHONE APPLICATION USEFUL FOR SELF-MANAGEMENT SUPPORT IN PATIENTS WITH A RHEUMATIC DISEASE?**

**Methods:** We performed a prospective before-after study among patients with a RD. The primary outcome was patients' self-management behavior measured with the Partners in Health scale (PH), a generic validated 12 item self-rated scale, which indicates higher scores for better self-management behavior. A paired t-test was used to evaluate changes in the PH-scale score after three months. To measure the user-experience with the app, survey questions addressed whether the RD-app had contributed to get more grip (or not) on the disease and how (why not). Logistic regression analyses served to investigate variables that are important for using the RD-app.

**Results:** Of the 1511 eligible patients, 397 completed both the baseline and the follow-up surveys. Participants who completed both questionnaires were most frequently diagnosed with RA, 65% was female and the mean age was 52.0 (SD 15.6) years. Hundred-fourteen participants used the RD-app. Self-management behavior did not improve according to the PIH-scale score after three months. To measure the user-experience with the RD-app, survey questions addressed whether the RD-app had contributed to get more grip (or not) on the disease and how (why not). Logistic regression analyses served to investigate variables that are important for using the RD-app.

**References:**


**THU0700**

**PHYSIOTHERAPISTS COULD REPLACE PHYSICIANS AS PRIMARY ASSESSORS FOR PATIENTS WITH KNEE OSTEOARTHRITIS IN PRIMARY CARE—A RANDOMISED CONTROLLED STUDY**

**Methods:** Patients seeking primary care with suspected KOA were randomised to either a physiotherapist or a physician for assessment, diagnose and treatment. Inclusion criteria were knee pain and > 38 years old. Exclusion criteria: knee pain due to traumatic cause, other systemic, somatic, mental or rheumatic diseases, pregnancy, or already been diagnosed or assessed by another healthcare giver due to current knee pain. HrQol (Euroqol - EQ5D-3L index, EQ5D-3L VAS), pain intensity (visual analogue scale) and physical function (30 seconds chair stand test) were measured before randomisation, and at 3-, 6- and 12 months. Mann-Whitney’s U test and Chi2 test for independence were used with a significance level of p<0.05.

**Results:** 69 patients with suspected KOA were randomised to either a physiotherapist (n=35) or a physician (n=34). Both groups improved their HrQol, pain and physical function at all follow ups. Patients rated significantly better HrQol (EQ5D-3L VAS) one year after physiotherapy assessment (84 (SD 11) vs 74 (SD 15), p=0.018). No other significant differences were found between the groups.

**Conclusion:** Physiotherapy assessment could replace physician assessment without having negative impact on patient reported outcomes after treatment for patients with suspected KOA. This may play a role in selecting other patients with KOA who could represent for the conduct of these RCTs. In order to achieve yet stronger cohort enrichment and cost reductions, additional markers and/or clinical factors could be considered for the models.

**References:**


**Acknowledgement:** na

**Disclosure of Interests:** None declared


**CHM-HE1**

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**Background:** It has been estimated that consultations to healthcare will increase with 30-50% among patients with osteoarthritis (OA) over the next 20 years [1]. Patients with knee OA (KOA) report among the lowest health-related quality of life (HrQoL) compared with other chronic diseases [2]. Most patients are assessed by a physician who claims unnecessary healthcare resources since physiotherapists also are primary assessors for patients with KOA and provide recommended treatments. However, it is unclear if physiotherapists could be the first option as primary assessor for this patient group. We hypothesise that all patients with suspected KOA in primary care could be assessed by a physiotherapist first and be referred to physician only when it is required, without having a negative impact on HrQol.

**Objectives:** The aim of this study was to explore differences in HrQol, pain and physical function in patients with suspected KOA after being assessed, diagnosed and treated by physiotherapist first compared with being assessed by a physician in primary care.

**Methods:** Patients seeking primary care with suspected KOA were randomised to either a physiotherapist or a physician for assessment, diagnose and treatment. Inclusion criteria were knee pain and > 38 years old. Exclusion criteria: knee pain due to traumatic cause, other systemic, somatic, mental or rheumatic diseases, pregnancy, or already been diagnosed or assessed by another healthcare giver due to current knee pain. HrQol (Euroqol - EQ5D-3L index, EQ5D-3L VAS), pain intensity (visual analogue scale) and physical function (30 seconds chair stand test) were measured before randomisation, and at 3-, 6- and 12 months. Mann-Whitney’s U test and Chi2 test for independence were used with a significance level of p<0.05.

**Results:** 69 patients with suspected KOA were randomised to either a physiotherapist (n=35) or a physician (n=34). Both groups improved their HrQol, pain and physical function at all follow ups. Patients rated significantly better HrQol (EQ5D-3L VAS) one year after physiotherapy assessment (84 (SD 11) vs 74 (SD 15), p=0.018). No other significant differences were found between the groups.

**Conclusion:** Physiotherapy assessment could replace physician assessment without having negative impact on patient reported outcomes after treatment for patients with suspected KOA. This may play a role in selecting other patients with KOA who could represent for the conduct of these RCTs. In order to achieve yet stronger cohort enrichment and cost reductions, additional markers and/or clinical factors could be considered for the models.

**References:**


HPR Patients’ perspectives, functioning and health (descriptive: qualitative or quantitative)

**THU0701-HPR**

**“TO REGAIN ONE’S HEALTH” – PATIENTS’ PREFERENCES OF TREATMENT OUTCOMES IN EARLY RHEUMATOID ARTHRITIS – A QUALITATIVE STUDY**

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**Background:** Rheumatology care strives to identify and meet the needs of the patients, and to understand disease and treatment impact from the patients’ perspective. A better understanding of patients’ expectations from the treatment is needed to enable a patient centered approach in clinical practice and a shared-decision making as recommended in the EULAR treatment recommendations for rheumatoid arthritis (RA). Understanding of patients’ expectations in the early stage of the RA disease may facilitate adherence to treatment, patient independency and prevent unmet needs in the future.

**Objectives:** To explore patients’ preferred treatment outcomes in early rheumatoid arthritis (eRA).

**Methods:** A qualitative, explorative study. Individual interviews were conducted with 31 patients with eRA, defined as disease duration of ≤ 6 months. Interviews were analyzed using a constant comparison method according to the Qualitative Analysis Guide of Leuven (QUAGOL) and lasted in a core category and four related concepts.

**Results:** The patient-preferred treatment outcomes in eRA were described in the core category “to regain one’s health” and the four related concepts: to experience external control of the disease, to experience independence, to regain identity and to experience joy in everyday life. The patients expected to experience external control of the disease by the given treatment to regain one’s health. It was perceived as controlling the symptoms and as absence of disease. Independence was perceived as regaining former activity levels, experiencing autonomy and using active coping strategies. Patients wanted to regain identity through participation, empowerment and their self-image. Joy in everyday life was perceived as vitality and believing in the future.

**Conclusion:** Patients’ preferred treatment outcomes in eRA were to regain one’s health including both external and internal control. External control as disease control and independence as well as internal control as identity and joy in everyday life. The results from this study can assist healthcare professionals to better understand patients’ preferred treatment outcomes early in the disease process and to tailor the interventions accordingly to improve long term treatment outcome.

**REFERENCES:**

Disclosure of Interests: None declared

**THU0702-HPR**

**PATIENT UNDERSTANDING OF RISKS OF METHOTREXATE AND ANTI-TNF THERAPY: A CROSS-SECTIONAL STUDY**

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**Background:** Disease-modifying anti-rheumatic drugs (DMARDs) have revolutionised the management and long-term prognosis of rheumatoid arthritis (RA). Side-effects of DMARDs include, but are not limited to: immunosuppression, gastro-intestinal upset, skin reactions and headaches. Despite the significant potential side-effects of DMARDs, there have been limited attempts to evaluate patient understanding of the side-effects of methotrexate (MTX) and to our knowledge no studies with regards to anti-tumour necrosis factor (anti-TNF) therapy.

**Objectives:** To evaluate the extent to which each of the known side-effects of MTX and anti-TNF therapy can be identified by patients receiving single or combination therapy for RA.

**Methods:** This was a cross-sectional study conducted in a rheumatology centre in the West of England. Patients with RA, seen in the outpatient clinic within the previous 18 months were invited to participate. Participants had to belong to one of the following treatment groups: (i) MTX only (ii) anti-TNF only or (iii) combined treatment with MTX and an anti-TNF. A postal questionnaire designed by the research team was used to obtain the data. Each participant was asked to (a) select side-effects they considered to be possible from their treatment, (b) tick if they had experienced this side-effect, and (c) select whether they believed this side-effect to be common or not. Descriptive analyses were used to determine the proportion (percentage) of patients who correctly identified the possible side-effects, correctly identified them as common, and had experienced them. Summary results are presented as ranges (minimum to maximum) and their corresponding percentages.

**Results:** Of the 300 patients invited, 119 returned a completed questionnaire; 48 (40%) on MTX only, 25 (21%) on anti-TNF only and 46 (39%) on combined MTX and anti-TNF. Their mean (SD) age was 62.5 (12.8) years, disease duration 13.5 (12.4) years, 111 (93%) had completed compulsory education and 94 (79%) were female. Most participants (115, 97%) spoke English as their first language. Correct identification of each possible side-effect ranged from 29% to 63% of participants in the MTX only group, 15% to 41% of patients in the anti-TNF only group and 8% to 64% of participants in the combined MTX and anti-TNF group. Their mean (SD) age was 62.5 (12.8) years, disease duration 13.5 (12.4) years, 111 (93%) had completed compulsory education and 94 (79%) were female. Most participants (115, 97%) spoke English as their first language. Correct identification of each possible side-effect ranged from 29% to 63% of participants in the MTX only group, 15% to 41% of patients in the anti-TNF only group and 8% to 64% of participants in the combined MTX and anti-TNF group. Correctly recognising these as common ranged from 13% to 52% of participants in the MTX only group, 4% to 35% of participants in the anti-TNF only group and 8% to 64% of participants in the combined MTX and anti-TNF group. Of those correctly identifying possible side-effects, 22% to 55% of participants in the MTX only group, 1% to 25% of participants in the anti-TNF only group and 8% to 56% of participants in the combined MTX and anti-TNF group reported experiencing them.

**Conclusion:** Our data suggests that a considerable number of patients are unable to correctly identify the most common side-effects of DMARDs used in RA management. Effective patient education and involvement in treatment decision-making will allow patients to be more aware of potentially serious side-effects of DMARDs.

**REFERENCES:**

Disclosure of Interests: None declared
A SANCTUARY FROM EVERYDAY LIFE: A QUALITATIVE STUDY OF THE EXPERIENCE OF IN-PATIENT MULTIDISCIPLINARY REHABILITATION, FOR PATIENTS WITH RHEUMATIC DISEASES

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Background: In Denmark, patients with rheumatic diseases can receive inpatient multidisciplinary rehabilitation at a hospital for rheumatic diseases or at rehabilitation centers. Quantitative studies indicate that it is difficult to detect a general and lasting effect of 1-4 weeks of inpatient multidisciplinary rehabilitation, but few studies have explored patients’ experience of in-patient multidisciplinary rheumatology rehabilitation.

Objectives: To explore how patients, experience the process and personal impact of an inpatient rehabilitation stay.

Methods: An exploratory qualitative phenomenological-hermeneutic study was planned. Adult rheumatic patients admitted for a two-week inpatient rehabilitation stay were invited to participate. Individual semi-structured interviews were conducted in the patients’ home shortly after discharge or at the ward one of the last days of admission. The interviews were audio recorded and transcribed verbatim. The analysis was inspired by Paul Ricour’s interpretative philosophy (1).

Results: Fifteen interviews were conducted, 11(73%) female, age 28-89. The analysis derived a core theme, “A sanctuary”, reflecting that the patients experienced to have sufficient time and mental resources to provide self-care. In addition, the analysis derived five subthemes: 1) “Being seen, heard and acknowledged as an equal and whole person”. To feel acknowledged was vital for the patients’ experience of quality and benefit. 2) “Professional care and compassion”; which were considered by the patients as the most fundamental contextual factors to facilitate their self-care. 3) “Social relations and interactions between patients”, reflecting the patients experience of feeling recognized by other patients and to experience common understanding. 4) “An individually planned rehabilitation stay, but challenges regarding shared decision making”. The patients felt the rehabilitation was individually planned, but with room for improvement in relation to awareness of shared decision-making. 5) “Rehabilitation as a personal process but problems with transferability to everyday life”. The patients experienced the rehabilitation stay as a part of a personal rehabilitation process, but expressed concerns about whether they were able to transfer new learning and habits to everyday life.

Conclusion: Patients with rheumatic diseases experience in-patient rehabilitation as a sanctuary, with rehabilitation at three levels; through multidisciplinary rehabilitation interventions at the hospital; through recognition from the multidisciplinary staff and through recognition, social relationships and interactions with fellow patients. There is a need for improved coordination of rehabilitation across primary and secondary health care, in order to ease transferal to the patients’ everyday life.

REFERENCES:

Disclosure of Interests: None declared

PATIENT ACTIVATION AND ADHERENCE TO BIOLOGICAL THERAPY AND TARGETED SYNTHETIC DMARD: PRELIMINARY RESULTS:

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Background: Medication non-adherence has been associated with treatment failure in chronic inflammatory conditions. A positive relationship between patient activation and adherence to treatment and between activation and improved clinical outcomes has been shown for chronic conditions.

Objectives: To measure adherence to biological therapies and targeted synthetic DMARD (tsDMARD), and their relationship with the Patient Activation Measure (PAM) and with patient and therapy related factors, for chronic inflammatory arthropathies.

Methods: Cross-sectional observational descriptive study in a general tertiary university hospital.

Patients: A total of 68 patients (57% women) participated. The patients were in treatment with the same biological drug (subcutaneous; phase 1) or tsDMARD (oral; phase 2); >6 months were included in order of arrival and those with mental disability, which prevented understanding of the study, were excluded.

Demographic variables (sex, age, living environment, educational level), diagnosis and treatment were collected. Adherence was measured using the Simplified Medication Compliance Questionnaire (SMAC) for biological therapies, the Compliance Questionnaire Rheumatology (CQR-19) for tsDMARD, and the medication possession ratio (MPR). Patients were considered adherent if MPR≥80% and COR-19≥80% or adherent SMAQ. To measure activation, PAM questionnaire, was used. Patients were classified as activated or not activated.

Statistical analysis: relationship between adherence to treatment and PAM was analyzed using chi-square, considering significance level p<0.05. Statistical analysis was performed with spss v17.0.

Results: A total of 58 patients (57% women) were included. Mean age was 54 years (95% CI: 50 to 57), 86% lived in urban areas, 40% had completed elementary education, 31% high-school and 24% university schooling. Distribution by diagnostic: rheumatoid arthritis (81%), anklylosing spondylitis (14%) and psoriatic arthritis (5%). Distribution by treatment was: baricitinib (31%), tocafacitin (18%), adalimumab (16%), tocilizumab (14%), etanercept (12%), secukinumab (7%) and golimumab (3%). Median time of disease duration was 9 years (IQR 13) and time on treatment with the drug was 8 months (IQR 20), with significant differences between groups (27 biological therapy) vs 7 months (tsDMARD).

The proportion of adherent patients was 43%, being higher among tsDMARD (57%) vs biological treated ones (30%), with significant differences. 72% of patients were being more activated biological (80%) than tsDMARD (67%) treated patients. A higher adherent proportion of patients was found among the activated patients (48%) compared to the non-activated ones (27%) in all measures, even though the differences were not statistically significant.

Conclusion: Patients treated with biological therapies and tsDMARD have a high degree of activation for the self-management of their disease and its treatment. Adherence to treatment may be influenced by route of administration, type of drug (oral/tsDMARD 57% vs. subcutaneous/biological 30%) and time on treatment (longer time on treatment, lesser adherence).

The greater proportion of adherence found among patients with a higher degree of activation could indicate a positive relationship between activation and adherence, so analyzing and promoting patient activation seems important in order to improve adherence to drugs.

Disclosure of Interests: None declared

PELVIC FLOOR AND SEXUAL DYSFUNCTION IN WOMEN WITH SJOGREN SYNDROME

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Background: Sjögren syndrome (SS) is a systemic autoimmune disease causing secretory gland dysfunction. This leads to dryness of the mainly salivary and lacrimal glands such as the mouth, eyes, nose, larynx, and vagina. The disease overwhelmingly affects middle aged women. These women have symptoms of decreased lacrimal and salivary gland function which usually precede involvement of other exocrine glands such as the upper airway, the gastrointestinal tract and the external genitalia (dyspareunia). Although genital tract symptoms are common in patients with sjögren, such as vulvar and vaginal dryness, dyspareunia, and pruritus, their pelvic floor health and functions have been rarely evaluated.

Objectives: The aim of study was investigation of pelvic floor and sexual dysfunction in patients with SS.

Methods: 23 patients with SS with an average age of 49.00±8.71 were included in the study. Pelvic floor dysfunction of patients with SS were evaluated by the Pelvic Floor Impact Questionnaire-7 (PFIQ-7) and Pelvic
THERE IS ASSOCIATION BETWEEN THE LEVEL OF

The sample consisted of a greater proportion of women aged 40 and 49 years (37.9%). There was a higher proportion of women with pelvic floor dysfunction and sexual dysfunction. This study showed that pelvic floor and sexual functions of patients with SS have been negatively affected. Therefore these functions need to be routinely assessed by health professionals. Further studies need to recommend pelvic health physiotherapy and educational programme about pelvic floor dysfunction.

REFERENCES:
yogy; rheum-141475.

Disclosure of Interests: None declared

THU0706-HPR

FOLLOW-UP CARE FOR PATIENTS WITH ESTABLISHED INFLAMMATORY JOINT DISEASES – A FOCUS GROUP STUDY ON PATIENTS’ EXPERIENCES FROM REFRAIMING THE ORGANIZATIONAL SUPPORT FOR INCREASED PATIENT INVOLVEMENT

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Background: Internationally, a Treat-to-Target strategy for proactive manage- 
ment of inflammatory joint diseases (IJD) is recommended.1,2 This includes continuous monitoring of the arthritis, which covers symptoms and the significance of the disease for everyday life.1,2 Control of disease activity has traditionally been ensured with fixed outpatient visits to rheu- 
matologists. However, in general there is a growing interest to involve patients in the control and treatment of their own disease. Open Assess in our outpatient clinic was implemented during October 2016 to respond to fluctuating needs among the patients with established IJD. Patient participation in Open Assess were primarily patient-initiated. They were expected to respond to symptoms and other disease- and treatment-related needs. In addition, two half-yearly planned visits were offered patients: 1) An annual traditional medical consultation with a rheu- 
matologist and a rheumatology nurse in a focused dialogue to involve 

methods: We conducted a qualitative study based on four semi-structured focus group interviews among patients with established inflammatory joint disease (Psoriasis arthritis (PsA)) participating in the Open Access set-up. The analysis of the transcribed interviews was based on content analysis. A patient research partner was involved in all phases of the study.

results: In total 25 patients with IJD participated (20 female (80%), mean age 61.8 (range 28-79)) with RA (n=20), PsA (n=3), axSpA (n=1) and polyarthitis (n=1) participated. We identified three themes. Changes in follow-up care do not affect patients’ perceived support in disease control, referring to patient’s perception of more time available to both themselves and health professionals, as well as trust in access to profes- 
sional support whenever needed. Adequate information to act within a new patient role, reflecting patients’ uncertainty in the transition to Open Access combined with confusion about distribution of responsibilities in the new set-up. Arthritis In a broader perspective, expanding patients understanding of their illness by interaction over time with both a rheu- 
matologist and a rheumatology nurse in a focused dialogue to involve the patient in managing their own health.
CONCLUSION: Patients following Open-Access welcome the flexibility and involvement in disease control. However, patients need relevant information to be able to act adequately to the new role patient. Interacting with both rheumatologists and nurses, combined with sufficient time for dialogue, broadens patients’ perspective, makes opportunities for action visible, and contribute to patient’s ability to participate in the managing of their own condition.

REFERENCES:

Disclosure of Interests: Bianca Bech: None declared, Jens Jørgen Lykkegaard: None declared, Tine Lundbak: None declared, Line Mette Birkeland: None declared, Mette Lund Schiльт: None declared, Lotte Hanne Hansen: None declared, Lillian Dalsgaard: None declared, Bente Appel Esbensen Speakers bureau: For Pfizer

THUU0708-HPR CORRELATIONS BETWEEN FATIGUE AND PATIENT REPORTED OUTCOME IN PEOPLE WITH INFLAMMATORY ARTHRITIS
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Background: Fatigue is one of the most common symptoms of people with inflammatory arthritis (IA) and often rated as high as or higher than pain. However, it remains unexplored how fatigue is associated with patient related outcomes (PROs) such as work impairment, as quality of life, sleep, depression, physical functioning and pain.

Objectives: To explore fatigue and to analyze possible correlations between fatigue and PROs in people with rheumatoid arthritis (RA), psoriatic arthritis (PsaA) and axial spondyloarthritis (axSpA).

Methods: A cross-sectional study. People ≥18 years with a confirmed diagnosis of RA, PsA or axSpA were consecutively recruited for the study over a 6-month period via routine visits to outpatient rheumatology clinics in two hospitals departments. Trained study nurses collected information on informed consent, diagnosis, medical treatment and disease activity status. Fatigue was evaluated by a self-completed questionnaire using the FACTIT-Fatigue sub-scale. The questionnaire also included the following PRO scales: Work Productivity and Activity Impairment scale (WPAI), EuroQol (EQ-5D), Medical Outcomes Study Sleep Scale (MOS), Major Depression Inventory (MDI), and Health Assessment Questionnaire (HAQ) on quality of life and pain. Data was analyzed in SAS. Correlations were assessed by a) Pearson correlation coefficients and b) raw and adjusted linear regressions.

Results: In total 633 persons were invited and 487 (77%) (mean age=53.5, SD 14.5) were included (62% women). The mean fatigue score (range 0-52; lower = more fatigued) was 34.3 (SD 11.1) and there was no statistically significant difference between mean fatigue in the three diagnostic groups (p=0.08). Altogether 61% expressed that they were suffering from fatigue (i.e. had a FACIT-Fatigue sub-scale <39). Women generally had a lower overall fatigue score (mean=33.3, SD 11.1) than men (mean=36.0, SD 11.0). Fatigue did not differ between age groups (p=0.33). Those who had changed medical treatment within 0-12 months (21.1%) suffered more from fatigue than those with unchanged treatment (mean=30.1, SD 11.7 vs. mean=35.4, SD 10.7, p<0.0001). The average disease activity as indicated by DAS28, BASDAI and BASFI showed low disease activity in the cohort. Current medical treatment (csDMARDs and/or bDMARDs or none) was not associated with severity of fatigue (p=0.85). Fatigue correlated with all PROs (Pearson correlation coefficients, all p-values <0.0001) (Table 1). Increased work impairment, sleep problems, depression and pain were all associated with increased fatigue, whereas decreased quality of life and physical functioning were associated with increased fatigue (raw and adjusted linear regressions). The associations did not change significantly after additional adjustment for socioeconomic factors. Analyses stratified on type of disease did not differ significantly from the primary non-stratified analysis.

Conclusion: Despite the study cohort represents a stable group with low disease activity, fatigue was a frequently expressed symptom across diagnoses. There was a significant correlation between fatigue and the other PROs why fatigue cannot be seen as a single problem, but rather a symptom that broadly affects people living with inflammatory arthritis.

Disclosure of Interests: Bente Appel Esbensen Speakers bureau: For Pfizer, Sandra Elkjær Stallknecht Consultant for: Paid by Pfizer to work on this and other studies, Maria Madsen Consultant for: Paid by Pfizer to work on this and other studies, Lise Hagelund Shareholder of: Pfizer, Employee of: Pfizer, Trine Pilgaard Shareholder of: Pfizer, Employee of: Pfizer

THUU0709-HPR PERSONS WITH POLYMYSITIS AND DERMATOMYSITIS EXPERIENCE REDUCED WORK ABILITY AND QUALITY OF LIFE
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Background: A recent study have described that persons with Polymyositis (PM) and Dermatomyositis (DM) experience reduced work ability (1). Information about whether the reduced work ability affect quality of life is lacking.

Objectives: To describe self-rated work ability with two different assessment and quality of life in persons with PM and DM. To investigate correlations between self-rated work ability and quality of life

Methods: Participants were identified through the Swedish Myositis Network registry (SweMyoNet). Of 78 possible participants, 48 agreed to participate in this study. The median (IQR) age were 57 (45-61) years with a median disease duration of 6 (2-14) years. Fifty-three percent of the participants were women. Seventy-seven percent were working, and the remaining were on sick-leave.

Self-rated work ability was measured by the questionnaire Work Ability Index (WAI) and the Work Ability Score (WAS) which is a single item question. Quality of life by the SF-36.

Results: Self-rated work ability measured by WAI in persons with PM and DM varied between poor work ability and good work ability. The median value of the group was 34 which indicates less good work ability.

Self-rated work ability measured by WAS varied between poor work ability and good work ability. The median of the total group indicates less good work ability.

There was a strong correlation between self-rated work ability measured by WAI and WAS (rs 0.879 p<0.01).

Quality of life measured by SF-36 were rated lower in persons with PM and DM when compared to the general population in dimensions; Physical Function, Role-Physical, General Health, Vitality and Social function (p<0.02).

There were moderate to high correlations between self-rated work ability measured by both WAI and WAS, and all dimensions of SF-36 (p<0.01)

Conclusion: Persons with PM and DM self-rated their work ability as poor and the quality of life were significantly reduced when compared to the general population. The measures WAI and WAS correlates highly with each other and revealed comparable results indicating that WAS may work as well as WAI as a screening tool to identify reduced work ability. The WAS may also be more feasible with just one single question to use in clinical practice. Our results indicate the importance to measure self-rated work ability in persons with PM and DM in clinical practice.
BACKGROUND: Spondyloarthritis (SA) is a chronic inflammatory disease that could significantly affect the patient’s quality of life and alter the social activities and relationship.

OBJECTIVES: Here, we aimed to investigate the impact of spondyloarthritis on quality of the social and family life in Tunisian patients.

METHODS: This is a cross sectional study including patients with SA (ASAS criteria). A survey comprising questions about family and social relations and the impact of flare on it, were applied between November 2018 and January 2019. Demographic data, marital status, the disease activity (BASDAI and ASDAS) and the function index (BASFI) were obtained. For statistical analysis, we used Kruskal-Wallis test for qualitative variables and Student-test for quantitative variables. A p value ≤0.05 was considered significant.

RESULTS: We included forty patients. The average age was 41 years-old (±12.9) and the sex ratio was 12.3. 60% of patients were married. The SA was axial in 25%, peripheral in 20% and both in 55%, 17.5% had psoriatic arthritis, 55% had ankylosing spondylitis and 27.5% had inflammatory bowel disease spondyloarthritis. coxitis was found in 47.4% of patients. Most patients had a moderate activity (29.4%) and the mean activity scores were (BASDAI =2.75±2.3, ASDAScrp=2.24±1.07), and the mean function index (BASFI) was 2.57±2.5. 57.5% of patients were on biologics (25% Adalimumab, 22.5% infliximab, 10% Etanercept).

67.5% of patients declared having difficulty in accepting their illnesses. Social relationship were deteriorated after the diagnosis of SA in: 27.5% with partners and 20% family members, 15% with friends and 20% with colleagues in work. Moreover, SA reduced the frequency of social activities like sport in 62.5%, traveling in 62.5%, cultural activities in 77.5% and professional practices in 37.5%.

The impact of flares was also evaluated, the patients declared having difficulties in: crossing the street (57.5%), corporal hygiene (30%), sleeping (70%), private life (32.5%) and doing daily tasks (77.5%) and professional activity (81.8%).

No significant relationship was found between social relationship and activities regarding biologic treatment (p=0.74, p=0.68). However presence of coxitis was significantly associated with a lack of friends (p=0.05), and a bad impact in the professional activities (absenteeism and drop job performance) (p=0.05) and the self-esteem (p=0.06).

Conclusion: Our results suggest that family and social relations are deteriorated in Tunisian SA patients due to their illness. Moreover, coxitis has substantial impact on the self-esteem and the social life.

Disclosure of Interests: None declared


REFERENCES:
100 the best state of health. Data were collected at admission and at 2-years after transplantation. Results underwent statistical analysis. Significance levels were established at p<0.05.

Results: The study included intragroup comparisons (Pre vs post-HSCT; Table 1) and intergroup comparisons (G1 vs G2; Table 2)

Abstract THU0712HPR Table 1. - Mean and median scores of SF-36 domains, before and after HSCT in G1 (n = 22) and G2 (n = 34)

<table>
<thead>
<tr>
<th>Domain</th>
<th>Mess</th>
<th>Median</th>
<th>SD</th>
<th>Median</th>
<th>SD</th>
<th>p-value</th>
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<tr>
<td>PF</td>
<td>41.3</td>
<td>31.9</td>
<td>35</td>
<td>67.2</td>
<td>28.4</td>
<td>85.008</td>
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<tr>
<td>RF</td>
<td>23.9</td>
<td>40.0</td>
<td>0</td>
<td>42.3</td>
<td>30.0</td>
<td>0.008</td>
</tr>
<tr>
<td>P</td>
<td>46.8</td>
<td>31.9</td>
<td>46.5</td>
<td>71.1</td>
<td>25.9</td>
<td>67.013</td>
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<tr>
<td>G4P</td>
<td>52.2</td>
<td>32.9</td>
<td>55</td>
<td>66.4</td>
<td>14.3</td>
<td>0.007</td>
</tr>
<tr>
<td>VIT</td>
<td>55.3</td>
<td>30.1</td>
<td>60</td>
<td>67.2</td>
<td>20.3</td>
<td>0.25</td>
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<td>SRF</td>
<td>20.3</td>
<td>23.2</td>
<td>62.5</td>
<td>68.3</td>
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<td>ERF</td>
<td>64.5</td>
<td>54.0</td>
<td>70</td>
<td>14.5</td>
<td>41.8</td>
<td>32.9</td>
</tr>
<tr>
<td>MH</td>
<td>59.4</td>
<td>23.0</td>
<td>64</td>
<td>66.6</td>
<td>23.8</td>
<td>0.47</td>
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</table>

In the intragroup analyses, comparing pre and post-HSCT scores, there was general improvement in both disease groups, especially in G2. The intergroup comparisons indicate that before HSCT patients in G1 had better FP than those in G2 (p = 0.03). The other aspects were not significantly different between groups. After HSCT, patients in G2 had a better QoL scores in P (p = 0.0338), GHP (p = 0.0001) and MH (p = 0.0049).

Conclusion: These results may be interpreted as positive outcomes of HSCT for MS and SSc. However, our data indicate that HSCT may benefit patients with MS (G2) more than those with SSc (G1).

REFERENCES:

Disclosure of Interests: None declared


THU0713-HPR

LINKING THE PATIENT EXPERIENCE OF FOOT INVOLVEMENT RELATED TO PSORIATIC ARTHRITIS TO THE INTERNATIONAL CLASSIFICATION OF FUNCTIONING, DISABILITY AND HEALTH

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Background: Previous research has shown merit in linking domains of impact in psoriatic arthritis (PsA) to the International Classification of Functioning, Disability and Health (ICF) to categorise the effect of global disease [1, 2]. Localised disease predominance and persistence in the foot in PsA is well recognised [3], but limited foot-specific research exists and there are no outcome measures to comprehensively assess foot involvement and its impact in PsA. To date little is known about the patient experience of foot involvement and how this may link to the ICF to capture disease impact.

Objectives: To categorise the patient experience of PsA-related foot problems by linking it to the ICF.

Methods: Participants were recruited from rheumatology outpatient clinics in Sydney, Australia and Auckland, New Zealand. People with PsA were interviewed about their foot problems and the impact they have on daily living until qualitative data saturation. Three multi-disciplinary focus groups were undertaken with clinicians to explore their understanding of the patient experience. All interviews were audio-recorded and transcribed. Codes, representing concepts obtained from the interviews, were linked to the most appropriate ICF category according to established linking rules. All codes were independently linked to the ICF by 2 investigators and a third investigator for adjudication. Investigator professional backgrounds included occupational therapy and podiatry.

Results: Twenty-one people with PsA-related foot problems and 17 experienced clinicians participated. Over 100 distinct ICF categories were linked to the interview and focus group codes. The most represented ICF category was environmental factors (33%) followed by body functions (26%), activities and participation (25%) and body structure (16%). Environmental factors relevant to patients were shoes and assistive devices, healthcare access and climate. Clinicians identified a greater proportion of body functions and fewer activity and participation categories compared with patients, indicating a possible mismatch of key concerns. Concepts that could not be precisely linked to the ICF were related to coping, aspects of time and knowledge, consistent with previous work. Difficulties in linking highly specific information to categories such as sensations of pain, sensations of skin and emotional functions revealed a limitation in the ICF’s ability to discriminate between various effects of the disease, a shortfall previously noted. Toenail changes were frequently cited by patients and linked to domains of body image and social relationships. Interdisciplinary group analysis demonstrated merit as differences between the predominantly medical approach by podiatry and psychosocial approach by occupational therapist in clinical practice led to additional ICF categories being identified between clinicians, which mostly related to cognitive functions.

Conclusion: Despite the localised anatomical focus of this study, the effect of foot problems in PsA was linked to all components of the ICF, confirming the profound impact on functioning and daily life. Difficulties with linking psychological concepts reflect deficiencies in the ICF and is a major limitation in defining foot disease burden. These findings offer new knowledge using patient and clinician perspectives that could inform the development of an instrument to measure the impact of foot involvement in PsA.

REFERENCES:

Disclosure of Interests: None declared


THU0714-HPR

RELATIONSHIP BETWEEN TRUNK POSITION SENSE, TRUNK MUSCLE ENDURANCE AND BALANCE IN WOMEN WITH FIBROMYALGIA SYNDROME

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Background: Position sense plays a fundamental role in human movement which is crucial for daily activities, exercise and sports [1]. Trunk endurance and balance were also integrated part of normal functional movements. Decreased balance and trunk muscle endurance were reported in women with fibromyalgia syndrome (FMS) [2]. However, to our knowledge, the relationship between trunk position sense, trunk muscle endurance and balance has not been studied in women with FMS.

Objectives: This study aimed to determine the relationship between trunk position sense, trunk muscle endurance and balance in women with FMS.

Methods: Women with FMS (n: 25, age: 42.88±11,66 years, body mass index: 25.69±3.48 kg/m²) were recruited. Trunk position sense was assessed with digital inclinometer by trunk reposition errors in which higher scores indicate poor trunk position sense [3]. Trunk flexor, extensor, dorso-lateral and non-dominant lateral side muscle endurance (r=0.61, p=0.001; r=0.49, p=0.011; r=0.48, p=0.014; r=0.048, p=0.014, respectively) were measured. Spearman’s rank correlation test was used for analysis.

Results: There were significant negative correlations between trunk position sense and trunk flexor, extensor, dominant and non-dominant lateral side muscle endurance (r=0.61, p=0.001; r=0.49, p=0.011; r=0.48, p=0.014; r=0.048, p=0.014, respectively). There were also high significant negative correlations between trunk position sense and Mini BEStest score (r=0.73, p=0.001).

Disclosure of Interests: None declared

Conclusion: It was found that there were moderate to high correlations between trunk position sense, trunk muscle endurance and balance. Therefore, addition of trunk position sense training to the rehabilitation programs might be effective in improving trunk muscle endurance and balance in women with FMS.

REFERENCES:

THU0715-HPR ASSESSMENT OF SELF-CARE AGENCY AND ITS ASSOCIATION WITH SYMPTOMS AND QUALITY OF LIFE IN INDIVIDUALS WITH FIBROMYALGIA: A CROSS-SECTIONAL STUDY

Leticia Couto, Susan Yuan, Amelia Pasquale Marques. University of São Paulo, São Paulo, Brazil

Background: Fibromyalgia is a condition of high prevalence, which causes physical discomfort, mental distress and impairment of social relations. Self-care may be a relevant factor to improve the quality of life in individuals with fibromyalgia, since it is related to the act of empower- ment, leading individuals to have dominion over their own life.

Objectives: To assess self-care agency of individuals with fibromyalgia and verify its association with symptoms, quality of life and sociodemo- graphic variables.

Methods: The study included 40 women, aged between 19 and 59 years, with fibromyalgia according to the 2010 American College of Rheumatol- ogy diagnostic criteria, and elementary education. This study was approved by the Research Ethics Committee of the School of Medicine of the University of São Paulo. Informed consent was obtained from all study participants. Sociodemographic and clinical data (age, clinical status, educational level, social status and disease duration) were collected. Self- care was measured with the Appraisal Self-Care Agency Scale-Revised, pain with the Visual Analog Scale (VAS) and the Widespread Pain Index (WPI), severity of symptoms with the Symptom Severity (SS) Scale, and quality of life with the Revised Fibromyalgia Impact Questionnaire (FIQ). In data analysis, Pearson correlation coefficient was used for parametric data, and the Spearman correlation coefficient was used for non-paramet- ric data. The level of significance adopted was 5%.

Results: Moderate values were found for self-care agency (52.75 ± 10.25), VAS pain (5.84 ± 2.16), WPI (13.32 ± 3.78) and SS (9.30 ± 1.68). Severe impact on quality of life was found with the FIQ (63.98 ± 17.26). Additionally, significant correlations of self-care agency with the status of presence (r=0.391), function (r=0.338), overall impact (r=0.315), symptoms domains (r=-0.332) and total score (r=0.375) of the FIQ were observed.

Conclusion: The study suggests that individuals with fibromyalgia have a moderate level of self-care agency, and there is a weak association of self-care with quality of life and social status.

REFERENCES:
Disclosure of Interests: Thomas Davergne: None declared, Rikke Helene

Table major barriers to physical activity in RA qualitative studies

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<td>Contact with other</td>
<td>2</td>
<td>external monitoring, support adherence (reminder)</td>
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<td>Lack of support, of exercise knowledge, of confidence, conflict in advice from healthcare</td>
<td>Support form healthcare (advice, psychological issues addressed, emphatic specialist)</td>
<td>4</td>
<td>group, socialization, influence of other, social support</td>
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Tables for the authors, net the abstract

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Disclosure of Interests: Thomas Davergne: None declared, Rikke Helene Moe: None declared, Bruno Fautrel Grant/research support from: AbbVie, Lilly, MSD, Pfizer, Consultant for: AbbVie, Biogen, BMS, Celgene, Janssen, Lilly, Medac, MSD, NORDIC Pharma, Novartis, Pfizer, Roche, Sanofi-Aventis, Sanofi Genzyme, SOBI, UCB, Laure Gossec Grant/ research support from: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis-Sandoz, Pfizer, Roche, Sanofi, and UCB, Consultant for: AbbVie, Biogen, BMS, Celgene, Janssen, Lilly, MSD, Nordic Pharma, Novartis-Sandoz, Pfizer, Roche, Sanofi, and UCB, Consultant for: L Gossec has received honoraria from Celgene as investigator for this study DOI: 10.1136/annrheumdis-2019-eular.4668

THU0717-HPR OVERVIEW OF THE MOST EFFECTIVE PHYSIOTHERAPY MANAGEMENT METHODS IN PEDIATRIC RHEUMATOLOGY

Emmanoula Ioannou, European University Cyprus, School of Sciences, Egkomi, Nicosia, Cyprus

Background: The majority of patients with pediatric rheumatologic conditions present with joint pain, morning stiffness and a high degree of fatigue which in turn affect their functional status, psychological wellbeing and activities of daily living (ADLs). Juvenile idiopathic arthritis - with a prevalence of 0.1-0.2/100 children - is the most common chronic pediatric rheumatic disease. When compared to healthy children, patients with juvenile idiopathic arthritis show decreased physical fitness, which necessitates systematic physiotherapy management.

Objectives: The current research was carried out to investigate the most reported physiotherapy methods for the management of common pediatric rheumatologic conditions.

Methods: PubMed and Google scholar databases were searched. Keywords were categorized into three groups. The first group included the most common pediatric rheumatologic conditions (juvenile chronic arthritis, juvenile spondyloarthropathy, juvenile psoriatic arthritis, dermatomyositis, systemic lupus erythematosus, vasculitis, scleroderma); the second group included physiotherapy management methods (physiotherapy, physical therapy, hydrotherapy, aquatic therapy); and the third group included outcomes (pain, pediatric pain, range of movement, quality of life, activities of daily living). Only primary research studies regarding patients with the aforementioned pediatric rheumatologic conditions were included.

Results: Notable variability was observed between studies as regards to applied methods and recorded outcomes. Additionally, results were not separately reported for the different diseases. Nevertheless, findings indicate that physiotherapy and hydrotherapy rehabilitation methods, focusing on reducing joint pain, joint protection, conservation of energy, and conservation of joint range of motion, achieved the treatment goals of representatives. The involvement of patients is structured thanks to the creation of the European Patient Advocacy Groups (ePAG). 3 ePAGs representing each disease pillar are members of the steering committee. The Ehlers-Danlos Syndromes (EDS) are represented in the ERN ReCoNNET with the exception of vascular EDS represented in the VASCERN.

Objectives: To raise awareness on the unmet needs related to EDS in the EU through attracting and engaging more experts, specialists and HCPs in order to address those needs.

Methods: At present, the EDS is represented by 2 HCPs and 2 official ePAGs, senior and junior disease coordinators have been identified both among HCPs and ePAGs, in particular the EDS ePAGs intensively sought for unmet needs of EDS into their wider European Community. All needs identified by ePAGs were discussed with the senior and junior coordinators and their contribution was added in a dedicated paragraph of the article, acknowledging them as co-authors. Among other activities, a state of the art on clinical practice guidelines (CPGs) has been performed also for EDS1, in which patients and clinicians highlighted the most important unmet needs.

Results: As the new 2017 International EDS nosology2 was only published in March 2017, EDS still lack Clinical Practice Guidelines and recommendations. The main EDS unmet needs identified concern the need to develop data on prevalence and clinical features, the identification of reliable biomarkers and the implementation of advanced instrumental imaging techniques. The management of pain, fatigue and psychological support have also been identified as a major topic to be addressed. More efforts should be put also on the education of healthcare professionals in order to provide faster diagnosis and better care to EDS patients. A stronger representation of EDS centres of expertise in the ERNs is needed, especially considering the crucial added value represented by the possibility of discussing clinical cases in the Clinical Patient Management System provided by the European Commission.

Conclusion: The ERN offers a real opportunity to develop better standards of care taking into account patients unmet needs. It is critical to increase EDS awareness and to attract HCPs for the follow-up and care of patients to be able to meet the unmet needs of the EDS patient population and healthcare professionals.


THU0717-HPR CLINICIANS’ AND PATIENTS’ UNMET NEEDS IN EHLERS DANLOS SYNDROMES, THE EXPERIENCE OF ERN RECONNECT

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1Deutsche Ehlers-Danlos Initiative e.V., Farth, Germany

Background: The European Reference Network for rare and complex connective tissue and musculoskeletal diseases (ERN ReCoNNET) is a European network of 26 healthcare providers (HCPs), that aims at developing a comprehensive and harmonized approach to 10 rare and complex connective and musculoskeletal diseases (rCTDs). The network gathers the community of health care professionals and patients...
The Patient Activation Measure (PAM): What Do Factors Associated with Pain Catastrophizing Mean to Patients with Rheumatic Conditions?

**Objectives:** To gather participants' perceptions of the suitability and acceptability of the Patient Activation Measure (PAM), particularly within a rheumatology context.

**Methods:** To identify factors associated with pain catastrophizing to detect possible susceptible targets in individuals with systemic lupus erythematosus.

**Background:** Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with a wide spectrum of clinical manifestations such as organ damage, pain, fatigue, sleep disorders, depression and cognitive deficits. It is known that pain catastrophising may have serious impact in individuals with SLE. Furthermore, catastrophising and maladaptive coping strategies are linked to higher levels of functional impairment and depression in SLE.

**Objectives:** The aim of this study was to identify factors associated with pain catastrophizing to detect possible susceptible targets in individuals with systemic lupus erythematosus.

**Methods:** A total of 104 individuals (mean age: 55.54±12.09 years; BMI: 27.17±4.01 kg/m²) with SLE participated to the study. The Pain Catastrophising Scale (PCS) was used to measure the extent to which people catastrophize in response to pain. The Tampa Scale for Kinesiophobia (TSK) was used to assess pain-related fear of movement. The Beck’s Depression Inventory (BDI) was used to measure characteristic attributes and symptoms of depression. The Body Awareness Rating Questionnaire (BARQ) was also used to rate their self-reported body awareness. The multiple stepwise linear regression models with R-square (R²) were used to compare across the models and explain the total variance.

**Results:** Mean PCS was 22.12±12.09; mean TSK was 49.94±7.76; mean BDI was 15.63±11.18 and mean BARS was 89.4±19.85. Linear regression analysis revealed that TSK, BDI, BARS and BMI were independently associated with PCS in predicting pain catastrophising in individuals with SLE (p<0.001; R²=0.52). There were no correlations between PCS and disease activity (mean SLAM-R: R=0.38; p<0.015) and organ damage (mean SLICC-DI: R=0.58; p<0.015) (p<0.05).

**Conclusion:** This study increases the understanding of the modifiable predictors to enhance pain coping behavior in accordance with the pharmacological treatment in SLE population. Results demonstrate major importance to explore the main stressors of pain catastrophising such as kinesiophobia, depression level, body awareness and BMI that affect coping behavior. Thus, pain catastrophising may limit the patients’ ability to perform from simple to complex activities. In addition, body image concerns SLE patients as they experience weight gain which negatively impact their self-esteem. The patient reported outcomes could guide health professionals to identify unmet needs of patients at risk to facilitate incorporation of the biopsychosocial model into SLE management.

**Disclosure of Interests:** None declared


**REFERENCES:**


**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.4561
**THU0721-HPR**

**WOMEN’S EXPERIENCE OF THE JOURNEY TO CHRONIC WIDESPREAD PAIN – A QUALITATIVE STUDY**

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1Halmstad University, School of Health and Welfare, Halmstad, Sweden; ²RandD Spenshult, Halmstad, Sweden; ³Karolinska Institutet, Unit of occupational medicine, Institute of Environmental Medicine, Stockholm, Sweden

**Background:** Chronic widespread pain (CWP) is a major burden to both the person and the community. Non-tumor chronic pain is one of the most common causes for long-term sickness absence in Sweden. The prevalence of CWP in the general population is approximately 10%, and the condition is almost twice as prevalent in women, than in men. Increased understanding of how women with CWP describe triggering factors of pain and pain progress would be of importance when preventing poor pain prognosis, and when customizing the treatment strategy in a setting with person-centered care.

**Objectives:** To explore experiences of factors influencing the progress and severity of pain among women who have developed CWP within the last 21 years.

**Methods:** This is a descriptive study, using a qualitative content analysis with an abductive approach. Nineteen women reporting CWP in a survey 2016, between 45-67 (median 57) years of age, who had not reported CWP in a survey 1995, participated in the study. Data were collected through individual interviews with open-ended questions: “Can you describe how your CWP has developed the last 20 years?”, “How did your CWP change over time?” and “Have you experienced any important events that have influenced the development of your CWP?” Data were analyzed through a manifest qualitative content analysis and six categories emerged.

**Results:** The women described their journey to CWP in terms of triggering, aggravating and consolidating factors. Six different categories emerged; physical strain, emotional strain, social strain, work-related strain, biological strain and environmental strain. Physical strain included strenuous physical activities in leisure time, having muscle tension, inactivity or sleeping problems. Emotional strain included being depressed, worried and stressed, as well as neglecting the pain. Social strain included to prioritize other people before oneself and to meet distrust from the social surroundings. Work-related strain included heavy, monotonous and stressful work but also sedentary work. Biological strain referred to heredity, age and infections. Environmental strain meant that the climate or weather aggravated the pain.

**Conclusion:** The women in the study described how their journey to CWP was influenced by both external and internal strains. The six categories representing different types of strains were recurrent in a context describing triggering, aggravating and consolidating factors. This highlights the complexity of individual pain progress and argues for the importance of person-centred care approaches and rehabilitation programs. The fact that women with CWP feel mistrust from healthcare professionals indicates that the current care approach needs to be changed.

**REFERENCES:**


**Disclosure of Interests:** None declared


**THU0722-HPR**

**DESIGNING A DIET INTERVENTIONAL STUDY FOR AUTOIMMUNE RHEUMATIC DISEASE: ASKING PATIENTS WHAT THEY THINK**

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**Background:** Despite recent progress investigating the pathogenesis of Sjögren’s syndrome (SS), there are currently no therapies able to influence disease progression. Patients with SS are usually treated symptomatically with variable success, therefore refining the research agenda according to patients’ priorities could provide a valuable insight into the most appropriate research questions.

**Objectives:** The aim of this study was to explore patients’ ideas and suggestions related to research in SS.

**Methods:** A questionnaire to investigate SS patient experience of diagnosis and ideas about research priorities in SS was designed. Over a 5 month period, patients attending outpatient clinics were invited to fill in the questionnaire. 27 patients completed our anonymous survey.

**Results:** The most important issue for patients with SS after they had been diagnosed was the lack of knowledge about this disease (25%), the diagnosis delay they had experienced (26%) and the persistence of symptoms of dryness (26%). Patients were interested in finding out what causes this disease (81%) and felt that our research should find a cure (92%) and better treatments (75%). The main two research priorities selected by patients were improved understanding of the disease (89%) and attracting funding for supporting research in to SS (89%). In addition, patients wanted to have a voice

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and contribute to raising awareness of SS and to participate in patient and public involvement and engagement (PPIE) events. The majority of patients interviewed were willing to take part in research by donating blood samples and/or filling in questionnaires (96%). 58% of patients who completed the survey would either definitely or probably take part in discussion groups helping researchers to design future studies in SS.

Conclusion: This survey highlighted patients’ perception of the need for more meaningful research into the causes of SS, as their priorities were centred around finding a cure or better treatments for Sjögren’s Syndrome. The survey also identified patients’ lack of knowledge about their condition as well as their desire to help with shaping future research ideas and support funding for research. The results of this survey will be incorporated in our future PPIE events aiming at shaping our research strategy in SS.

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THU0724-HPR RELIABILITY AND VALIDITY OF AN ACTIVITY LIMITATION MEASURE IN PERSONS WITH INCLUSION BODY MYOSITIS (IBM)

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Background: Persons with Inclusion Body Myositis (IBM) are affected in all areas of life.

Objectives: The aim of this study was to test validity and reliability of the questionnaire Disability in the Arm Shoulder and Hand (DASH) for patients with IBM. A second aim was to describe activity limitation measured by the Canadian occupational Performance measure (COPM).

Methods: Persons diagnosed with IBM were identified through the Swedish Myositis Network (SwedMyoNet) quality registry in Stockholm Sweden. A total of 36 persons with IBM were included in the registry and were invited to participate. A total of 17 men and 9 women agreed to participate. Median (Q1-Q3) age was 74 (70-79) years and the median (Q1-Q3) disease duration was 7 (3-8) years.

Activity limitation were assessed by the questionnaire Disability in the Arm Shoulder and Hand (DASH) and the The Canadian occupational performance measure (COPM) which investigate patient derived areas of daily activities.

The data collection was performed at the Karolinska university hospital in Stockholm Sweden. At baseline both DASH and COPM were performed. The participants received a second DASH questionnaire to be answered within two weeks (Follow-up) and send back to the researcher.

Results: There were good correlations between baseline measure and follow-up on DASH (rs 0.997; p<0.01) indicating that the DASH is consistent over a short period of time.

The results from COPM showed a variety of activities persons with IBM experienced problem with. Area with most activity limitations were basic self-care area such as dressing and grooming, fall, feeding, managing communication.

Instrumental activities such as managing instruments, shopping and meal preparation. Leisure activities such as playing an instrument, run, paint and social activities such as visit friends, social engagements. Some of these activities were found in the DASH but not all. E.g. missing socializing with friends and family, problems swallowing or were environment dependent.

Conclusion: The results indicate that DASH have a good test re-test reliability DASH includes some of the activities that persons with IBM experience difficulties with but not all. The participants experienced difficulties in all areas of life.

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Disclosure of Interests: None declared


THU0725-HPR SCREENING OF SILENT MYOCARDIAL ISCHEMIA USING A STRESS TEST IN RHEUMATOID ARTHRITIS PATIENTS: ASSOCIATION WITH TRADITIONAL RISK FACTORS AND DISEASE ACTIVITY

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Background: The rheumatoid arthritis is responsible of an increased risk of cardiovascular (CV) morbidity and mortality.

Objectives: The aim of the study is to determine, in established RA patients, the presence of silent myocardial ischemia using a stress test and its association with the disease activity and the CV risk factors and scores.

Methods: It is a transversal and prospective study in a rheumatologic center in Charles Nicolle hospital in Tunisia. 103 RA patients, asymptomatic for CV disease were submitted to a stress test. Demographic data, cardiovascular risk factors and the disease characteristics were assessed for all patients and risk factors of silent myocardial ischemia in RA patients were identified.

The comparison of qualitative variables was performed with the Chi square test and the comparison of qualitative variable and quantitative ones was performed with the Student’s test. The significance level was set at 0.05.

Results: There were 103 patients (sex-ratio=0.3) with a mean age of 53 ±10 years. The evaluation of the disease activity showed that the mean DAS28 CRP, CDAI and SDAI were 3.9±1.38; 17.1±7±11.4 and 33.9±26.5 respectively. A screening for CV risk factors revealed: 13% of patients had a cardiovascular inheritance, 25% of patients were either smokers or hypertensives, 18% had diabetes, 70% were obese or overweighted and 14 patients had dyslipidemia. The ischemic ratio (CT/HDL) revealed that 42% of patients had a moderate to high myocardial ischemic risk. Heart SCORE was high in 39% of cases. A silent myocardial ischemia in the stress test was found in 11 patients (10.6%) and was associated with male sex (p=0.03), advanced age (p=0.04), erosive character (p=0.05), the advanced age of the rheumatoid arthritis diagnosis (p=0.01) and the ischemic ratio (p=0.06). No relationship was found with the majority of traditional CV factors nor with disease activity variables.

Conclusion: Our results corroborated the hypothesis that the stress test could reveal subclinical CV dysfunction, supported the utility of the Heart score as a screening tool, and put in perspective the potential usefulness of complementary approaches in CV risk assessment in RA patients.

Disclosure of Interests: None declared


THU0726-HPR THE COMPARISON OF ARTERIAL STIFFNESS, FUNCTIONAL EXERCISE CAPACITY AND PHYSICAL ACTIVITY IN SYSTEMIC SCLEROSIS AND HEALTHY INDIVIDUALS

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Background: Systemic sclerosis (SSc) is characterized by abnormal production of fibrotic tissue in the skin and internal organs. SSc has a effect on large and conduit arteries damage as well as microvascular damage (1). It is known that sedentary lifestyle may contribute to vascular dysfunction (2). Therefore, it is important to evaluate arterial stiffness, exercise capacity and physical activity in people with SSc.

Objectives: The aim of this study is to compare arterial stiffness, functional exercise capacity and physical activity in SSc and healthy individuals.

Methods: Fifteen SSc (53 years) and 15 healthy (48 years) women were included in this study. Arterial stiffness was evaluated with pulse wave velocity that was obtained by measuring the carotid-to-radial pulse wave transit time. Functional exercise capacity was assessed by 6-minute walk test (6MWT). Physical activity was questioned International Physical Activity Questionnaire (IPAQ)-short form. The differences between the groups were analyzed with Mann-Whitney U test.

Results: Age, weight, height and body mass index were similar in the groups (p>0.05). There was significant difference in pulse wave velocity and pulse wave transit time between the two groups (p<0.05). The
The aim of this study was to investigate the factors affecting handwriting speed in patients with chronic disease (2).

42 patients (aged 6-18 years) who have an affected wrist joint with oligoarticular JIA were included in this study. Muscular strength was estimated at maximal isometric force for the muscles of the upper extremities by using a portable handheld dynamometer. Grip and pinch strengths were evaluated by a dynamometer. Handwriting speed was evaluated with a sentence writing duration of 24 letters. All tests were performed thrice and the mean values of all were recorded. The correlation between all parameters was analyzed by the Pearson Correlation Test. Also, relations between the factors affecting handwriting speed in JIA were assessed by multiple linear regression analysis.

Results: The mean age was 12.71±3.35 and the mean disease duration was 6.52±3.81 years. The mean of handwriting speed was 20.53±10.39 seconds. Significant relationships were found between handwriting speed and muscular strengths of shoulder and elbow (p<0.05). Also, significant relationships were found between handwriting speed and lateral (r=-0.352, p=0.022), tip (r=-0.309, p=0.047) and triple (r=-0.375, p=0.015) pinch strengths. According to linear regression analysis, handwriting speed was affected by only muscle strength of elbow pronation (r=0.515, p=0.037).

Conclusion: Handwriting is a complex functional activity simultaneously involving motor skills, cognitive and visual perceptual processing in all chronic disease. In the current study, it was found that handwriting speed was related with shoulder and elbow muscle strengths and pinch strengths in patients with JIA. Although patients with JIA had only affected wrist joint, only muscle strength of elbow pronation was the only primary predictor of handwriting speed. We suggested that handwriting speed should be considered in patients with juvenile idiopathic arthritis. So, accurate assessment of handwriting speed is essential for developing appropriate intervention programs and evaluating performance and outcomes in patients with JIA. Besides, not only affected joint, but also all upper extremity joints should be assessed multidimensionally.

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THU0726-HPR
THE FACTORS AFFECTING HANDWRITING SPEED IN PATIENTS WHO HAVE AN AFFECTED WRIST JOINT WITH OLIGOARTICULAR JUVENILE IDIOPATHIC ARTHRITIS
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Background: Juvenile idiopathic arthritis (JIA) encompasses a complex group of disorders with arthritis. Patients with JIA may experience significantly decreased life skill owing to muscular weakness, joint pain, contracture, and reduced mobility (1). Poor handwriting speed is an example of an affected life skill that has been observed by educators and clinicians for patients with chronic disease (2).

Objectives: The aim of this study was to investigate the factors affecting handwriting speed in patients who have an affected wrist joint with oligoarticular JIA.

Methods: 42 patients (aged 6-18 years) who have an affected wrist joint with oligoarticular JIA were included in this study. Muscular strength was estimated at maximal isometric force for the muscles of the upper extremities by using a portable handheld dynamometer. Grip and pinch strengths were evaluated by a dynamometer. Handwriting speed was evaluated with a sentence writing duration of 24 letters. All tests were performed thrice and the mean values of all were recorded. The correlation between all parameters was analyzed by the Pearson Correlation Test. Also, relations between the factors affecting handwriting speed in JIA were assessed by multiple linear regression analysis.

Results: The mean age was 12.71±3.35 and the mean disease duration was 6.52±3.81 years. The mean of handwriting speed was 20.53±10.39 seconds. Significant relationships were found between handwriting speed and muscular strengths of shoulder and elbow (p<0.05). Also, significant relationships were found between handwriting speed and lateral (r=-0.352, p=0.022), tip (r=-0.309, p=0.047) and triple (r=-0.375, p=0.015) pinch strengths. According to linear regression analysis, handwriting speed was affected by only muscle strength of elbow pronation (r=0.515, p=0.037).

Conclusion: Handwriting is a complex functional activity simultaneously involving motor skills, cognitive and visual perceptual processing in all chronic disease. In the current study, it was found that handwriting speed was related with shoulder and elbow muscle strengths and pinch strengths in patients with JIA. Although patients with JIA had only affected wrist joint, only muscle strength of elbow pronation was the only primary predictor of handwriting speed. We suggested that handwriting speed should be considered in patients with juvenile idiopathic arthritis. So, accurate assessment of handwriting speed is essential for developing appropriate intervention programs and evaluating performance and outcomes in patients with JIA. Besides, not only affected joint, but also all upper extremity joints should be assessed multidimensionally.

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THU0727-HPR
FOLLOW-UP CARE AND SELF-MANAGEMENT ACTIVITIES AFTER SPECIALIZED REHABILITATION FOR PATIENTS WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES
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Background: Patients with rheumatic and musculoskeletal diseases (RMDs) benefit from rehabilitation in specialized care, but the effect seems to decline over time. Implementation of healthy self-management strategies and support over an extended period may prolong the effect. Rehabilitation trajectories with planned follow-up interventions and support in primary health care are therefore recommended. Still, evidence is not clear concerning what constitutes an optimal design of supportive follow-up interventions, and to which degree such follow-up care are planned and delivered.

Objectives: To describe current follow-up care practice and self-management after specialized rehabilitation for patients with RMDs.

Methods: This is a multicentre cohort study, including 523 participants with RMDs who received rehabilitation in specialized care in Norway. Participants completed a core set of outcome measures for rehabilitation in musculoskeletal diseases covering nine aspects of health and function in a web based data collection system [1]. At rehabilitation discharge, they additionally reported needed and planned follow-up care (FU-care) from listed professions and services in primary health care and plans for self-management activities (SMA). Received FU-care and adherence to SMA were reported at 4, 8 and 12 months follow-up. A multiple logistic regression analysis was performed to explore predictors for acceptable adherence to SMA.

Results: A total of 436 participants completed all assessments at discharge, of which 429 (98%) reported a need for FU-care. A need for FU-care by primary physician was most frequently registered, followed by physiotherapist and the Norwegian Labour and Welfare Service. However, only 239 (56%) reported that FU-care was planned at discharge. Of those reporting a need for FU-care, 201 (47%) participants reported receiving such care during the follow-up year, and these participants more often had a specific follow-up plan at discharge compared to those who did not receive the FU-care they reported needing (p=0.06).

Hundred and sixty-four (38%) participants were adhering to their SMA throughout the follow-up year. Higher age (OR=1.04, [CI 95% 1.02, 1.06], p=0.001), lower degree of depression and anxiety (OR=0.73, [CI 95% 0.58, 0.94], p=0.01), and performing physical activity on a regular basis (OR=3.35, [CI 95% 2.08, 5.39], p<0.001) at baseline were predictors for acceptable adherence. Participants with acceptable adherence reported more often a need for FU-care (p<0.001), and had more frequently received the FU-care they needed (p<0.001) than those without acceptable adherence.

Conclusion: Participants with plans were more likely to receive the FU-care they reported needing, indicating that discussing and planning follow-up should be an integral part of rehabilitation in specialized health care. The results further indicate that having structure and routines in one’s daily life enhance adherence to SMA, and that patients with anxiety and depression and a sedentary life style may need more support over a longer period to be able to implement behavioural changes for healthy self-management.

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Acknowledgement: The authors want to inform that members in the Rehabilitation Trajectories Research Group are co-authors of this abstract. Their names are listed in the following link: http://diakonhjemmetrehabbyhus.no//diakonhorsforside/Helsepersonell/nasjonal-kompetansetjeneste-for-revmatologisk-rehabilitering-nkrr//nkrr/pagaende-prosjekter-nkrr/_5479/5495

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THU0728-HPR

"I AM GOOD ENOUGH AS I AM EVEN IF I AM NOT PERFECT"– A QUALITATIVE STUDY OF FIBROMYALGIA PATIENTS’ EXPERIENCES FROM PARTICIPATION IN A MINDFULNESS-BASED GROUP-PROGRAMME

Heidi A. Zangi1, Gyda Singstad2, Ingrid Knutsen3. Improved management of patients with fibromyalgia: Evaluation of an integrated care model. 1 Diakonhjemmet Hospital, National Advisory Unit on Rehabilitation in Rheumatology, Oslo, Norway; 2 Oslo Metropolitan University, Oslo, Norway

Background: People with fibromyalgia (FM) suffer from widespread pain, non-refreshing sleep, fatigue and reduced mental wellbeing. No curative pharmacological treatment exists. Vitality Training (VTP) is a mindfulness- and acceptance-based group-programme that aims at enhancing participants’ health promoting resources, strengthening their inner authority and ability to act according to own values. It combines mindfulness with creative methods and group counselling. Two RCTs have shown significant improvements in mental wellbeing, pain coping and fatigue in patients with chronic musculoskeletal pain and inflammatory arthritis. The VTP is currently being evaluated in an ongoing study for patients with newly diagnosed FM[1].

Objectives: The aim of this qualitative study was to explore FM patients’ experiences from participating in the VTP, and if they perceived that it had any impact on their health and functioning.

Methods: Six qualitative in-depth interviews with participants from three VTP-courses were conducted following a semi-structured interview guide. Interviews were audio-recorded and transcribed. All three authors analysed the data by use of systematic text condensation.

Results: Three main themes were identified.

1. Understanding oneself in light of the group: Mutual understanding and acknowledgement had altered participants’ self-understanding – from a feeling that “something was wrong with me” towards perceiving themselves as “a normal person with similar challenges as others”.

2. Learning to accept oneself: Participants had obtained a greater understanding and acceptance for their emotions and reactions and had become kinder towards themselves. "I have realised how strict I have been towards myself... I am indeed good enough as I am even if I am not perfect”.

3. Coping with everyday challenges: Becoming aware of what had provoked stress and learn how to face it had helped participants take more control. "I can do small changes that really makes it better... the illness does not decide everything. Indeed I can decide something myself”.

Conclusion: Participation in the VTP had contributed to new ways of relating to oneself and the illness. The support and acknowledgement participants experienced from the group had helped them alter their self-understanding from only being ill towards also being healthy and normal. They had learnt ways to better cope with stress and everyday challenges. Although this was a small study, the findings correspond with findings in previous studies.

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THU0729-HPR

BENEFITS OF EMPOWERING THE PATIENTS TO SELF-ADMINISTER SUBCUTANEOUS LOW DOSE METHOTREXATE (LD-MTX) INJECTIONS IN PATIENTS WITH SYSTEMIC IMMUNO-INFLAMMATORY RHEUMATIC DISEASES (SIRDs): A STUDY BY RHEUMATOLOGY NURSES COUNSELLOR

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Background: In recent years, early aggressive targeted treatment for SIRDs is recommended. LD-MTX is the “anchor drug” for these diseases. The administration of LD-MTX using subcutaneous route increases its therapeutic efficacy that ensures the maximum bioavailability and reduces gastrointestinal adverse effects. Therefore, it is preferred over the oral route. Increased use of subcutaneous self injection of medication has benefits for the patients and healthcare system (reduction in cost of hospitalisation, reducing dependency to the others, improving self-care and general health). drawbacks include getting trained to administer subcutaneous injection with a needle, cost of syringe and needle, and fear of needles. Empowering the patients to take self-injections could alleviate pressure on medical services by reducing hospital/clinic visits. Therefore, explaining the benefits of self administration of subcutaneous injection such as early disease control, increased drug adherence, positive attitudes towards life, decreased financial burden of administration cost, decreased dependency to the others, should be an imperative part of patient’s education.


Methods: This retrospective study included patients who were prescribed injectable LD-MTX for their treatment. Besides the demographic information (age, gender) and disease characteristics (diagnosis, duration, prior treatment), the patients were interviewed and counselled regarding the virtues to take subcutaneous LD-MTX self-injection. The technique for self-injection of LD-MTX subcutaneously was explained and demonstrated to the patients. All the information including the follow-up details, were recorded in a pre-designed form.

Results: Three hundred (n=300) consecutive patients who were advised weekly LD-MTX injections and taught the self-injection technique were enrolled in this study. On follow-up visit it was found that among them, 177 patients (59%) learned and started to administer their own subcutaneous injection of LD-MTX and they adhered to the injection schedule, in 50 (16.7%) patients the injections was being given by the attendant (who had learnt the injection technique because the patients had deformities), while the other 73 (24.3%) were not very compliant to injections due to psychological barriers towards self-injection, worried about pain and incorrect technique, adverse effects of the incorrect injections social stigma related to self-injections, and frustration or lack of acceptance of the illness.

Conclusion: By empowering the patients to self-administer LD-MTX injections subcutaneously, a majority (59%) of them successfully continued to take the medicine appropriately. This study shows the important role the nurses’ play in educating patients and helping them to overcome psychological barriers to self injection. Empowering the patients to self-administer injections would result in better long term treatment adherence, improving treatment flexibility and overall quality of life.

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THE MAP OF THE RHEUMATOLOGY NURSE CLINICAL AND RESEARCH INTERVENTIONS IN THE VALENCIAN REGION (SPAIN)

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Background: There is none defined competences framework for Rheumatology Nursing at the moment in Spain. This fact leads to an heterogeneous roles and interventions in each Rheumatology department which has not ever been described nor quantified.

Objectives: To describe and quantify the rheumatology Nursing interventions in the Valencian Region (Spain).

Methods: A descriptive study was performed by the completion of an online questionnaire with a list of clinical and research intervention. The questionnaire was sent to the Head of Rheumatology Department of 33 public hospitals from the Valencian Region.

Results: 32 hospitals of the Valencian Region fulfilled the questionnaire: 15 from Valencia, 13 from Alicante and 4 from Castellón. 50% of the hospitals had a Rheumatology nurse. In those hospitals, 50% had only 1 Rheumatology nurse working at the moment. The maximum Rheumatology nurses working in the same hospitals were 4; 2 hospitals used to have a Rheumatology nurse but do not have it anymore at this moment. 11 hospitals have an auxiliary nurse (3 of them without nurses and 8 with nurses). The year of incorporation of the Rheumatology nurse in the Department was quite heterogeneous, being the earlier in 1992 and the last incorporation in 2017.

The nurses worked mainly in a Rheumatology department full time (68.75%).

The 81% of the hospitals had a specific nursing agenda but only 7 hospitals had a monographic nurse-led clinic (osteoarthritis nurse-led clinic -25%, intravenous treatments nurse-led clinic -12.5% - or cardiovascular risk nurse-led clinic -6.25%)

Nurses clinical interventions are very heterogeneous covering the patient clinical management and practice nurses intervention activities. Nurses organized patient education workshops in 25% hospitals. In 11 hospitals, nurse undertook teaching activities. 56% participating in scientific workshops/congress, 44% teaching undergraduates nurses/registered nurses and 37.5% teaching other healthcare professionals.

In 11 hospitals, nurses undertook research activities. In 2 hospitals an specific research nurse was available. 56% of nurses participated in clinical trials, 50% participated in research projects and 50% participated in scientific congress. 25% of nurses lead research projects.

In 12 hospitals, nurses belong to a scientific society; in 11 hospitals, nurses participated in regional, national and/or international nurses working groups.

Conclusion: In at least 50% of the hospitals from the Valencian Region, nurse activity was registered. There are heterogeneous clinical activities performed by nurses. This fact raised the issue of the importance of having unified criteria for nurse’s intervention and competences framework comparable in each and every hospital. Teaching and research were also a common interventions mentioned. These activities are necessary for a constant recycling and updating of the nurses and will help to gain the necessary visibility for the rheumatology nurses.

Disclosure of Interests: None declared


THU0731-HPR

“OSER ABOORDER” SURVEY ON THE CROSSOVER NEEDS OF A BETTER UNDERSTANDING OF SEXUAL HEALTH ISSUES BETWEEN PATIENTS SUFFERING FROM CHRONIC INFLAMMATORY RHEUMATISMS AND HEALTHCARE PROFESSIONALS INVOLVED IN PATIENT THERAPEUTIC EDUCATION

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Background: Chronic inflammatory rheumatisms (RIC) may negatively impact patients’ sexual health and quality of life.

Overall, 31 to 76% patients suffering from rheumatoid arthritis (RA) report to suffer from sexual difficulties. Patients affected by spondyloarthritis (SA) report a negative disease impact on sexual activity in 38 to 50% of cases. On the other hand, while healthcare professionals (HP) are well aware of the utility to approach this issue, most do not carry on with it for they feel insufficiently trained in this domain.

According to the 2015 EULAR recommendations, therapeutic patient education (TPE) is an essential part of patient management in the RIC domain. TPE actually does take into account the overall patient experience including sexuality.

A survey primarily focused on needs and conducted among patients and healthcare experts involved in TPE was thus deemed necessary to better define both the content and format of TPE to be delivered to HP in order to help them dialogue with their patients, while overcoming certain obstacles on this path.

Objectives: To define the educational needs of HP involved in TPE of patients suffering from CIR, concerning sexual health issues.

Methods: Using an interdisciplinary team approach, we have elaborated two different questionnaires focused on assessing specific needs and designed for patients and healthcare professionals.

These questionnaires were filled in online from May 2017 to November 2017 via a secured server implemented in each of the 14 French rheumatology centers by CIR patients, TPE-involved HP, and members of three patient associations.

Results: 239 patients answered the questionnaire (60.7% suffering from SA, 6.7% from psoriasis rheumatism, and 32.6% from RA), as did 57 HP. Overall, 72% patients reported having suffered or being still suffering from sexual difficulties, whereas 80% of them had never approached the topic with their respective HP.

In 82% of cases, the patient claimed having addressed the issue, whereas 30% HPs reported having taken the initiative. Half of both the patients and HP reported they had not dared to approach the topic.

To ease communication, HP would appreciate to “have a team specifically dedicated to particular sexual healthcare issues”, “have specific tools available” and “undergo specific training sessions”.

In line with HP answers, patients’ primary expectations were to be heard and become well-informed. The people who were judged the most competent (63%) and with whom patients would feel the most secure (58%) were the psychologists. The topics thought to be the most useful by the patients were similar to those considered most useful for HP training, namely undesirable treatment effects on sexuality (95%), impact of rheumatism on sexual activity (92%), body image and chronic illness (81%), partner communication (77%), sexual dysfunctions (77%), as well as physiology of aging and sexual function (75%). About 70% HP expressed the need for complementary education, with 95% of them stressing the necessity to acquire further communications skills within this domain.

Of these, 88% preferred short training sessions, and 80% group training sessions.

Conclusion: This survey clearly demonstrates the usefulness of implementing educational training, along with its appropriate content, among HP, designed to enable them to approach sexual health issues and provide their patients with appropriate advices in this domain.

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Genomics, genetic basis of disease and antigen presentation

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Background: Cryopyrin Associated Periodic Syndromes (CAPS) are caused by autosomal dominant gain of function mutations in the NLRP3 gene. However, a subset of these patients with typical clinical features and good response to anti-IL-1 treatment, have no mutation in NLRP3 detected by conventional Sanger DNA sequencing. Somatic mosaicism may account for between 19 to 69% of these, from previous reports. Genetic heterogeneity has also been implicated in patients with CAPS-like syndromes, reiterating the use of a wider NGS approach. At present it is unclear how the variants found in patients 6 and 7 could modulate the phenotype, therefore in patients a clear genetic cause is yet to be found. In conclusion, this study suggests that NGS approaches are superior to conventional sequencing for the molecular diagnosis of CAPS and NLRP3 like phenotypes since they can detect somatic mosaicism or alternative molecular diagnoses mimicking CAPS.

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Objectives: To explore potential mechanisms for the SLE related IRF7 SNP on type I IFN production, which might indicate new theoretical basis for genetic therapeutic strategy.

Methods: We constructed different genotypes of SLE relevant SNP cell lines by Crispr/Cas9 technology, and confirmed them by sequencing. After TLR-ligand stimulation, the mRNA expression of IFNα was detected by real-time qPCR. The levels of IFNα, TNFα and IL-6 were detected by ELISA kit. The protein expression of IRF7/p-IRF7 was detected by western blot. The binding ability of endogenous IRF7 with typeIFN promoter was studied by chromatin immunoprecipitation.

Results: We got IRF7 SNP rs1131665 GG/AA cell lines by gene editing technique. After TLR-ligand stimulation, IRF7 SNP rs1131665 AA cell line showed higher IFNα expression than GG, which indicated statistical significance. IRF7 SNP rs1131665 AA cell line showed higher p-IRF7 expression than GG detected with western blot. Endogenous IRF7 in IRF7 SNP rs1131665 AA cell line showed stronger binding ability with IFNα promoter than GG, which indicated statistical significance.

Conclusion: The missense variant of G to A in IRF7 SNP rs1131665, increased the production of typeIFN, which indicated that IRF7 G to A missense variant increased the susceptibility of type I IFN associated diseases.

REFERENCES:

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shown that the largest factor influencing disease susceptibility is genetics. Genome-wide association studies have successfully characterized genetic variants that are associated with RA, with the vast majority of them mapping to non-coding regulatory elements. Understanding the mechanisms by which this phenomenon leads to disease is essential to translate these results from genetic association studies to the clinic.

Objectives: There is evidence showing that autoimmune diseases are the consequence of erroneous wiring of the regulatory circuitry between enhancers and their target genes. The aim of this study is to characterize non-coding regions containing RA-associated variants, in order to determine the genes and pathways by which these regions act to increase the risk of disease.

Methods: We isolated CD4+ T-cells from blood obtained from RA patients. We studied patients in two subgroups, high disease activity (DAS28≥5.1, n=18) and low disease activity (DAS28<3.2, n=33). All samples were genotyped using Illumina Infinium Exome-24 v1.0 BeadChip arrays. RNA-Seq Libraries were generated for matching RNA samples using the Lexogen QuonSeq Library Prep kit and sequenced on an Illumina NextSeq500. For a subset of 6 samples (3 high disease activity and 3 low disease activity patients), capture Hi-C was performed to characterize chromatin interactions between all RA associated loci and their potential target genes.

Results: We observed numerous chromatin interactions between RA variants and potential causal genes. Preliminary results show that a number of disease-associated SNPs interact with compelling candidate genes situated several megabases away. Whilst some of these chromatin interactions are common to both patients groups, subsets of them are specific to each disease subgroup, which are correlated with differential gene expression.

Conclusion: These results suggest that there might be different biological pathways contributing to disease in RA patients with inactive disease compared to patients with high disease activity.

Disclosure of Interests: None declared


FRIO007

IDENTIFICATION AND VALIDATION OF PLASMA MICRO-RNA 425–5P AND –451A AS MICRO-RNAS ASSOCIATED WITH CARDIOVASCULAR DISEASE RISK OBSERVED IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Cardiovascular disease (CVD) risk is increased in Rheumatoid arthritis (RA) patients, and therefore, improved approaches for its early detection are needed. An accelerated atherosclerosis is considered the cause of the increase CVD risk. As microRNAs (miRNAs) are increasingly recognized as critical regulators in atherosclerosis and possess excellent stability in plasma, this study focused on using miRNAs as noninvasive CVD risk biomarkers in RA patients.

Objectives: To identify plasmatic miRNAs in RA patients that can facilitate earlier diagnosis of CVD and provide insight regarding the increase risk for CVD observed in these patients.

Methods: A discovery and validation studies were performed. To discover miRNAs candidates, we first compared plasmatic profiles of 754 miRNAs in 7 RA patients without CVD, in 7 patients with acute myocardial infarction (AMI) but without RA, and in 7 healthy controls matched for age and for classical CV risk factors. miRNAs commonly expressed in the two group of patients but differentially expressed from the controls were selected as miRNA candidates for validation. Selected miRNAs were validated in independent serum samples from 214 RA patients (validation cohort) by studying its association with subclinical atherosclerosis measured by carotid intima-media thickness (cIMT). Plasma profile of miRNAs in the discovery study was analyzed using validated TaqMan Open Array miRNA panels which enables the quantification of 754 human miRNAs.
Differential expression analysis was performed with Expression Suite software and selected miRNAs candidates were validated in the validation study by real-time PCR with LNA™ microRNA qPCR assays and analyzed with 2-ΔΔCT method. Kruskal-Wallis test, Dunns post-test and linear regression were used for statistical analyses.

Results: In the discovery study we were able to measure 379 (50%) of the miRNAs represented in the array. We observed 10 miRNAs (miRNA-let-7a, miRNA-96, miRNA-381, miRNA-451a, miRNA-518d, miRNA-425-5p, miRNA-572, miRNA-190b, miRNA-708, and miRNA-1180) were expressed at the same level in RA and AMI patients but were significantly downregulated compared with controls. These 10 miRNAs were selected as potentially miRNAs associated with the increase risk of CVD in RA patients. Four of those miRNAs were expressed at very low level and were discarded for the validation study. In the validation study with 214 plasma samples from RA patients, we observed that two of the six candidate miRNAs (miRNA-425-5p and miRNA-451a) were significantly associated with cIMT. Thus, adjusted multivariable linear regression analysis showed that miRNA-425-5p and miRNA-451a independently explained 1.4% of the cIMT variability. Furthermore, adjusted regression estimates of the effect of miRNA-425-5p and miRNA-451a on cIMT were β = 0.029mm; p = 0.037 and β = 0.035 mm; p = 0.039, respectively. No other miRNA candidate exhibited association with cIMT values. Furthermore, we observed that miRNA-451a was significantly correlated with ESR (r=0.136; p=0.024) and miRNA-451a with DAS28 (r=0.19; p=0.003), ESR (r=0.23; p=0.0001), CRP (r=0.15; p=0.016) and fibrinogen (r=0.28; p=0.0001). miRNAs concentrations were not affected by any of the AR treatments. No association was observed between the presence of cardiac plaque and the expression level of the microRNAs tested.

Conclusion: In the present study, we have identified miRNA-425-5p and miRNA-451 as potentially miRNAs involved in the CVD risk observed in RA patients.

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Disclosure of Interests: SILVIA PAREDES Speakers bureau: Bristol, Roche, Amgen, Pfizer, Abbvie, Lilly, UCB, Delta Taverne Speakers bureau: amgen, Pfizer, Bristol, Lilly, Roche, Raimon Ferre: None declared. Josep Maria Alegret Speakers bureau: Daichii, Lluis Masana Consultant for: amgen, daichii, sanofi, Speakers bureau: AMGEN, SANOFI, MYLAN. Joan Carles Valve: None declared.


FR0009 MOLECULAR PROFILING OF CIRCULATING B-LYMPHOCYTES REVEALS THE SUPERIOR PERFORMANCE OF METHYLMOLE 12 TRANSPICTOME DATA FOR DISCRIMINATING RHEUMATOID ARTHRITIS PATIENTS IN AN EARLY ARTHRITIS CLINIC: IMPLICATIONS FOR TRANSLATING “BIG DATA” INTO CLINICALLY USEFUL TOOLS

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Background: Defining optimal strategies for translating “big datasets” of transcriptome and methylene data into clinically valuable tools in RA will benefit from comparisons where potential confounders – including therapeutic background, disease phase and cell substrate heterogeneity – are controlled as far as possible.

Objectives: We have obtained paired B- and CD4+ T-lymphocyte whole genome expression and methylation data from drug-naïve early arthritis clinic patients at a single centre. Focussing on B-lymphocyte data we here ask which of these datasets has most value in discriminating early RA – and the additive value of combining them.

Methods: CD19+ B-lymphocytes were isolated by positive selection from fresh peripheral blood of 90 drug-naïve patients attending the Newcastle Early Arthritis Clinic (NEAC), comprising 36 RA patients and 54 disease controls matched, so far as possible, for age, sex and acute phase response. Paired RNA and DNA extracted. Gene expression was profiled using the Human HT12 v4 BeadChip, and DNA methylation at >850,000 CpG sites quantified with the MethylationEPIC array (both Illumina). Gene expression and/or DNA methylation classifiers for RA prediction were developed based on a combined approach of classification algorithm
Objectives: We aimed to evaluate the T-cell receptor-CD3 zeta chain (TCR-CD3ζ) gene expression profile in a cohort of patients with RA.

Methods: A case-control study on 150 consecutive RA patients diagnosed according to 2010 ACR/EULAR criteria and 150 matched healthy controls without familiar history of RA or other autoimmune diseases. RA patients with other autoimmune diseases, viral hepatitis B or C, malignancy or hematological disorders were excluded from the study.

All participants were subjected to history taking, clinical examination, assessment of disease activity (in RA patients) using DAS-28 and HAQ, routine laboratory investigations, inflammatory markers level, serological tests, as well as molecular analysis for TCR-CD3ζ mRNA expression by quantitative real-time polymerase chain reaction.

Results: TCR-CD3ζ gene expression was significantly lower in RA cases than in healthy controls (p<0.05) (Table 1). Expression of TCR-CD3ζ revealed a significant negative correlation with RA disease duration, RF, and ESR (p<0.05) in RA cases. The level of TCR-CD3ζ also showed a significant lower expression in +ve RF patients than in –ve RF patients (p<0.05). The AUC of TCR-CD3ζ level showed a moderate level of accuracy (AUC = 0.840, p=0.025) (Figure 1), and the calculated cutoff value (≥ 0.077) can precisely discriminate subjects with RA from those without RA with 93.5% sensitivity and 75% specificity (Table 2).

Table 1. Comparison between RA cases and control group as regard CD247 (mRNA levels for TCR-CD3ζ gene expression).

<table>
<thead>
<tr>
<th>TCR-CD3ζ</th>
<th>RA cases (n=150)</th>
<th>Healthy Controls (n=150)</th>
<th>Test of sig.</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Min. – Max.</td>
<td>0.037–12.467</td>
<td>0.034–11.314</td>
<td>Z=-3.047*</td>
<td>0.002*</td>
</tr>
<tr>
<td>Mean ± SD.</td>
<td>0.663 ± 1.90</td>
<td>0.816 ± 1.64</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (Q1–Q3)</td>
<td>0.179 (0.109–0.314)</td>
<td>0.315 (0.198–0.922)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

A* = Z-score of Mann-Whitney test.

*: Statistically significant at p<0.05.

Table 2. Analysis of ROC curve for TCR-CD3ζ level as a predictor of RA (high RF).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cutoff point (ng/ml)</th>
<th>AUC</th>
<th>P</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCR-CD3ζ</td>
<td>≤ 0.077</td>
<td>0.840*</td>
<td>0.025**</td>
<td>93.5</td>
<td>75.0</td>
<td>78.9</td>
<td>92.0</td>
<td>84.3</td>
</tr>
</tbody>
</table>

AUC: Area under the curve.

*: Statistically significant at p<0.05

**: Statistically significant at p ≤ 0.05

PPV: Positive Predictive Value

NPV: Negative Predictive Value

Conclusion: Our results demonstrated a lower expression of TCR-CD3ζ in RA patients than in healthy controls. We suggested that CD247 gene down-regulation might contribute in the susceptibility to RA and help understanding the mechanisms responsible for deficient T-cell responses in RA patients.

REFERENCE:

Disclosure of Interests: None declared

A TRANSCRIPTIONAL REGULATOR CONTROLLING SEVERITY OF EXPERIMENTAL ARTHRITIS

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Background: Susceptibility to Rheumatoid Arthritis (RA) is dependent on complex interactions among genetic and environmental factors. Protein candidates and their role in pathways leading to chronic inflammation of the joints, in addition to their potential as drug targets, can be revealed with the help of experimental models for disease (1). From the results of functional genetic studies, we have recently shown that the T-box gene, TBX3, is a cancer gene in Collagen Induced Arthritis (CIA), an experimental model for RA (2). TBX3 encodes a transcriptional regulator involved in differentiation of several organs, including bone, during embryonic development. It has, in addition, been demonstrated important in oncogenesis (3). Our studies suggest that TBX3 has a role in B-cell activation and is important for the severity of disease in the CIA model (2).

Objectives: The objective of this project is to understand the role for the transcriptional regulator TBX3 in development of RA.


Results: Studies of CIA development in mice with single nucleotide polymorphisms (SNPs) in the regulatory region of TBX3. CRISPR/Cas9-introduced deletions and base modifications in human B-cell lines. Activation of genetically modified B-cells in vitro, followed by analyses of proliferative response and antibody production. No significant differences were seen in the proliferative response to Type II collagen upon re-challenge of lymph node cells in vitro higher in these mice, suggesting a more active response to the disease-inducing antigen. Because the TBX3 gene is conserved between mouse and human, we are investigating whether similar genetic variations are found in the regulatory region of the human TBX3 gene and whether the putative genetic variation would lead to a distinct B-cell phenotype upon activation in vitro.

Conclusions: Our data support the oncogene TBX3 is a novel candidate contributing to disease severity in experimental arthritis. Investigations of genetic variation in the TBX3 gene and its role in the activation of human B-cells will reveal whether this protein is a candidate for influencing also development of RA.

REFERENCES:

Disclosure of Interests: Åsa Andersson: None declared, Samra Sardar: Employee of: I am a full time employee at Nordic Bioscience

FR0014 GENETIC VARIABILITY IN MOLECULES REGULATING BONE REMODELING. DO THEY INFLUENCE SEVERITY OF DISEASE AND BONE MASS IN PATIENTS WITH EARLY-ONSET ARTHRITIS?

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Background: In the last few years, an association has been described between lower bone mass at the onset of disease and higher severity of nontraumatic arthritis (RA).

Objectives: To identify single nucleotide polymorphisms (SNPs) in genes related to bone remodeling associated with severity of disease and bone mineral density (BMD) in patients with early-onset arthritis.

Methods: We included 268 PEARL (Princess Early Arthritis Register Longitudinal) patients genotyped with Illumina Inc. Immunochip. This array includes 556 SNPs with different density levels in semaphorins 4b, 4d and 4f, DKK1, 2 and 3, sclerostin, osteoprotegerin (OPG), RANK and...
RANKL. All SNPs with genotyping rate <98%, with frequency of the minor allele <1% and those that were not in Hardy-Weinberg equilibrium, were excluded. In addition, among the SNPs in linkage disequilibrium, a representative one was chosen, so that only 159 were finally studied. The intensity of treatment, the activity of the disease measured by the DAS28 and HUPI indices, as well as having achieved at least low activity after 2 years of follow-up were chosen as surrogate severity variables. The association of each of the SNPs with these variables was analyzed by linear regression, and ordered logistic regression according to the variable, and adjusted for potentially confusing variables, such as age, sex and presence of anti-cyclic citrullinated peptide antibodies. We selected those SNPs that were consistently associated with ≥3 surrogate severity variables, and then, the relationship of the selected SNPs with BMD of the forearm, lumbar spine and hip (Hologic-4500 QDR) was analyzed by means of linear regression adjusted for age and sex.

Results: As shown in the attached table, 11 SNPs were associated with the severity of the disease, 7 of them were also associated with BMD, although only 3 confirmed the previously described relationship between severity of disease and BMD.

<table>
<thead>
<tr>
<th>ID</th>
<th>SNP</th>
<th>GENE</th>
<th>MOLECULE</th>
<th>DISEASE ACTIVITY</th>
<th>BMD</th>
</tr>
</thead>
<tbody>
<tr>
<td>rs4355801</td>
<td>LOC441377</td>
<td>OPG</td>
<td>Decrease</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>rs3134058</td>
<td>TNFRSF11B</td>
<td>TNFRSF11B</td>
<td>Increase</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>rs1050348</td>
<td>TNFRSF11B</td>
<td>OPG</td>
<td>Increase</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>rs6469804</td>
<td>COLLECT110</td>
<td>COLLECT110</td>
<td>Decrease</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>rs1805034</td>
<td>TNFRSF11A</td>
<td>RANK</td>
<td>Decrease</td>
<td>Decrease</td>
<td></td>
</tr>
<tr>
<td>rs999293</td>
<td>TNFRSF11A/ZCCHC2</td>
<td>RANK</td>
<td>Increase</td>
<td>Increase</td>
<td></td>
</tr>
<tr>
<td>rs862838</td>
<td>AKAP1/TNFSF11</td>
<td>RANK-L</td>
<td>Increase</td>
<td>Increase</td>
<td></td>
</tr>
<tr>
<td>rs324004</td>
<td>AKAP1/TNFSF11</td>
<td>RANK-L</td>
<td>Decrease</td>
<td>Increase</td>
<td></td>
</tr>
<tr>
<td>rs11900837</td>
<td>AKAP1/TNFSF11</td>
<td>RANK-L</td>
<td>Decrease</td>
<td>Decrease</td>
<td></td>
</tr>
<tr>
<td>rs7142975</td>
<td>AKAP1/TNFSF11</td>
<td>RANK-L</td>
<td>Increase</td>
<td>Increase</td>
<td></td>
</tr>
<tr>
<td>rs752777</td>
<td>AKAP1/TNFSF11</td>
<td>RANK-L</td>
<td>Decrease</td>
<td>Decrease</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** This preliminary study highlights the relationship between gene variants of molecules involved in bone remodeling and the severity of early-onset arthritis. However, more studies are needed to confirm this relationship and validate it in other populations. This would confirm the relationship between severity of disease and BMD.

**REFERENCES:**


**Disclosure of Interests:** Noelia García Castañeda: None declared, Amalia Laman: None declared, Nuria Montes: None declared, Ana Ortiz: None declared, DOLORES MARTINEZ-QUINTANILLA JIMENEZ: None declared, Cristina Valero: None declared, PABLO MORENO FRESNEDA: None declared, Carmen Martinez: None declared, Rosa P. Gomariz: None declared, Ana Triguero-Martinez: None declared, Santos Castañeda Consultant for: Amgen, BMS, Pfizer, Lilly, MSD, Roche, Sanofi, UCB, Isidoro González-Avrar: None declared.

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Background: Autoimmune rheumatological disorders (AIRD) have been described in myelodysplastic syndrome (MDS) and related-myeloid disorders but its association remains unclear. Immunosuppressive treatment of AIRD could cause therapy-related myeloid neoplasm (t-MN) or confound the secondary diagnosis of MDS. The prevalence of cytopenia in patients with AIRD is unknown and the mutation profile of patients with AIRD and concomitant MDS have not been well characterised.

Objectives: This study aims to evaluate the prevalence of cytopenia in AIRD and analyse the mutation profile of patients with concomitant diagnosis of AIRD and MDS by interrogating the databases of 2 large institutions - Royal Adelaide Hospital Rheumatology Department (RAH-RD) and South Australia-Myelodysplastic Syndrome (SA-MDS).

Methods: Demographic, clinical, laboratory and treatment data of 2663 patients from RAH-RD and 1157 patients from SA-MDS were analysed according to the idiopathic cytopenia of undetermined significance (ICUS) criteria. Patients with persistent cytopenia (>6 months) were defined as follows: haemoglobin <100g/L, absolute neutrophil count <1.5x10^9/L, and platelet <100x10^9/L. Within the SA-MDS registry, 237 bone marrow samples were analysed for 43 myeloid neoplasms associated genes and 20 Fanconi (FA) DNA repair pathway genes with targeted massively parallel sequencing. An in-house filtering pipeline was used to identify somatic mutations.

Results: Within RAH-RD database, 79 patients (3%) fulfilled the criteria for at least 1 cytopenia. 21 patients underwent bone marrow biopsy, with 9 bone marrow samples being diagnostic of MDS. Neutropenia was most common (27/79 patients, 34%), followed by anaemia (20/79 patients, 25%) and thrombocytopenia (6/79 patients, 8%). Within SA-MDS database, 62 patients (5%) had concomitant AIRD. Rheumatoid arthritis is the most common AIRD diagnosis (21/62 patients, 34%) in the SA-MDS database. Combined analysis of both databases revealed that 71/3820 patients (1.9%) had a concomitant diagnosis of both AIRD and MDS.

The cytogenetic and mutational profile of patients with concomitant diagnosis of AIRD and MDS within the SA-MDS database were analysed and 56 mutations were discovered in this group. Mutation in ASXL1 was the most common (6/20 patients, 30%), followed by TET2 (5/20 patients, 25%) andLastly TP53 (4/20 patients, 20%). There is significantly higher frequency of IDH1 mutation in the AIRD-MDS cohort compared to patients with MDS only. Three patients with TP53 mutation developed MDS following treatment for AIRD (therapy-related MDS).

Conclusion: In a large cohort of patients with AIRD, 3% of patients developed ongoing cytopenia and 0.3% were diagnosed with MDS. This finding is higher than the incidence of MDS in the general population (0.03-0.05%). Within the SA-MDS registry, 5% of patients had concomitant diagnosis of AIRD. Our findings warrant further study and have potential implications for selection of disease-modifying drugs for patients with AIRD.

REFERENCES:

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FRID0016 MUTATIONAL LANDSCAPE OF MYELODYSPLASTIC SYNDROME IN PATIENTS WITH AUTOIMMUNE RHEUMATOLOGICAL DISORDERS

FRID0017 DIFFERENTIAL METHYLATION AS A PREDICTOR OF TOCILIZUMAB RESPONSE IN PATIENTS WITH RHEUMATOID ARTHRITIS
MicroRNA-146a plays an important role in regulation of autoinflammatory diseases including gout[1]. Growing evidences have demonstrated that association of miR-146a gene single nucleotide polymorphisms (SNPs) with risk of several diseases[2], but no genetic relevance studies of miR-146a gene polymorphisms to gout have been reported by now.

**Objectives:** To investigate the potential association of gout and the functional rs57095329 SNP of miR-146a in the Chinese Han population.

**Methods:** The rs57095329 SNP was detected in 448 primary gout patients (containing 76 tophi patients) and 418 healthy control subjects. Peripheral blood mononuclear cells (PBMCs) miR-146a expression was measured in 81 gout patients (including 32 tophi patients and 49 non-tophi patients) and 47 healthy subjects.

**Results:** No significant difference was detected in the distribution of miR-146a rs57095329 between 448 gout patients and 418 healthy subjects (P>0.05). However, significant differences were observed between 76 gout with tophi patients and 418 healthy subjects, between gout with tophi (76) and with no tophi patients (372) both in genotypes and allele distributions (P<0.01, respectively). Gout patients carrying AG/GG genotypes with tophi patients and 418 healthy subjects, between gout with tophi patients and 418 healthy subjects, between gout with tophi patients and 418 healthy subjects.

**Conclusion:** Our study shows a novel, significant association between the miR-146a rs57095329 polymorphism and a lower risk of tophi in gout patients. Furthermore, our findings suggest that this gene polymorphism might affect the genetic predisposition to tophi development and modulate the expression of miR-146a level in tophi patients. This new knowledge about miR-146a may be clinically important and confirms a role for miR-146a in the pathophysiology of tophi, with potentially important therapeutic implications.

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[2] Yi Z, Yi-Ting Yi, Qiong Xiong, Quan-Bo Zhang, Dong Zong, Xiong Qian, Bo Zhang.

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CORRELATION BETWEEN EXPRESSION LEVELS OF miR-146A AND miR-223 IN SYNOVIAL FLUID AND ULTRASOUND SCORES FOR ACTIVE SYNOVITIS IN RHEUMATOID ARTHRITIS PATIENTS

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Background: MicroRNAs (miRNAs) are a class of small, non-coding RNAs that negatively regulate gene expression at posttranscriptional level. In recent years studies have shown that in rheumatoid arthritis (RA) the systemic and local expression of certain miRNAs is altered [1-2]. The correlation between their expression levels and scores for disease activity and progression in RA make them possible candidate for biomarkers in the clinical practice.

Objectives: To analyze the expression levels of miR-146a and miR-223 in synovial fluid (SF) from RA patients in regard to the ultrasound scores for disease activity.

Methods: A total number of 48 RA patients according to the 1987 ACR criteria were included in the study. Expression levels of miR-146a and miR-223 SF were determined by qPCR (SybrGreen technology) and compared to healthy controls (HCs). Relative changes of gene expression were calculated by 2^-ΔΔCt method. Musculoskeletal ultrasound (MSUS) examination was performed by two independent examiners on ESAOTE, MyLab60 using both grey scale and power Doppler technic. A semi quantitative assessment of the peripheral joints was performed for detecting joint inflammation and determining the grade of synovial thickening and the degree of vascularization. Ultrasound features for active disease were correlated to the local expression of the studies miRNAs. SPSS was used for statistical analysis.

Results: RA SF showed overexpression of miR-146a (in 70.83%, p=0.007) and of miR-223 (in 79.17%, p=1.64x10-3) when compared to HCs. There was a statistically significant correlation between the presence of synovitis and the degree of the power Doppler signal on MSUS and the local expression of miR-146a (p=0.030 and p=0.049, respectively) and miR-223 (p=6.19 x 10^-4 and p=0.003, respectively). SF levels of miR-223 correlated also with the degree of synovial hypertrophy on MSUS (p = 0.013).

Conclusion: We found correlation between the SF expression of miR-146a and miR-223 and the ultrasound features of active joint inflammation. Further analysis with larger sets is needed to confirm if altered local miRNA expression could be used in the clinical practice as biomarker for disease activity especially in cases with subclinical synovitis.

REFERENCES:

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Disclosure of Interests: None declared


ORAL HYGIENE STATUS IN RA PATIENTS AND PLACE OF RHEUMATOLOGIST IN THERAPEUTIC EDUCATION ON ORAL DENTAL HEALTH

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Background: The relationship between oral hygiene and rheumatoid arthritis has been demonstrated by several studies.

Objectives: To evaluate oral hygiene status in rheumatoid arthritis (RA) patients.

To inform about the therapeutic education given by the rheumatologist on the importance of adequate oral hygiene in the management of RA.

Methods: This is a cross-sectional study that included 100 consecutive RA patients (89% female, mean age 46.7 years, median disease duration of 8 years, mean specialized care duration of 3 years). A questionnaire evaluating oral hygiene status was administered. It focused on following items: the daily frequency of brushing, the modalities of brushing, the use of other means of oral hygiene, the regular follow-up at a dentist’s doctor and the place of the rheumatologist in therapeutic education on the oral dental hygiene status.

Results: Table I illustrates the results of oral hygiene evaluation in RA patients.

Table I: Evaluation of Oral Hygiene in RA patients

<table>
<thead>
<tr>
<th>Items</th>
<th>N=100</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daily Brushing Frequency (%)</td>
<td>18</td>
</tr>
<tr>
<td>0 times/day</td>
<td>37</td>
</tr>
<tr>
<td>once a day</td>
<td>34</td>
</tr>
<tr>
<td>2 times/day</td>
<td>8</td>
</tr>
<tr>
<td>3 times/day</td>
<td>3</td>
</tr>
<tr>
<td>After each meal</td>
<td>31</td>
</tr>
<tr>
<td>adequate brushing time (&gt;3min) (%)</td>
<td>14</td>
</tr>
<tr>
<td>Correct brushing method (%)</td>
<td>36</td>
</tr>
<tr>
<td>Use of other means of oral hygiene (%)</td>
<td>1</td>
</tr>
<tr>
<td>Regular dentist visit (%)</td>
<td>2</td>
</tr>
<tr>
<td>Never visit a dentist (%)</td>
<td>27</td>
</tr>
</tbody>
</table>

Table II illustrates the results of the place of oral hygiene information in rheumatologic management.

Table II: Place of information on oral hygiene in rheumatologic care.

<table>
<thead>
<tr>
<th>Questions</th>
<th>Yes (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. does your rheumatologist ever examined your oral cavity?</td>
<td>6,0</td>
</tr>
<tr>
<td>2. have you ever been informed by your rheumatologist that poor oral hygiene has a negative impact on your rheumatoid arthritis?</td>
<td>11,0</td>
</tr>
<tr>
<td>3. Does your rheumatologist ever recommended regular brushing of your teeth?</td>
<td>8,0</td>
</tr>
<tr>
<td>4. Does your rheumatologist already recommended to you to consult a dentist?</td>
<td>10,0</td>
</tr>
</tbody>
</table>

Conclusion: This study illustrates the high prevalence of oral hygiene insufficiency in patients followed for RA. It also highlights poor therapeutic education given by the rheumatologist on the importance of adequate oral hygiene in the management of RA.

Disclosure of Interests: None declared

Rheumatoid arthritis - comorbidity and clinical aspects.

EVALUATION OF DYSFUNCTIONAL HIGH-DENSITY LIPOPROTEIN LEVELS WITH MYELOPEROXIDASE/PARAOXONASE 1 RATIO IN RHEUMATOID ARTHRITIS

Background: Rheumatoid arthritis (RA) is a chronic, systemic and autoimmune disease with inflammatory arthritis. Atherosclerosis and cardiovascular diseases are common in RA patients. Although chronic systemic inflammation in RA patients is considered to be the main cause of this condition, the relationship between systemic inflammation and vascular pathophysiology is not clear [1]. While high density lipoprotein (HDL) is known to be a negative risk factor for atherosclerosis by reverse cholesterol transport, recent studies show that HDL can be pro-atherogenic (dysfunctional, inflammatory) by losing this characteristic in cases of inflammation and oxidative stress. Myeloperoxidase (MPO)/paraoxonase 1 (PON1) ratio is a valuable marker that can be routinely used as an indicator of dysfunctional HDL. PON1 is a lipoprotein-derived enzyme which provides antioxidant properties of HDL. Although MPO is a bactericidal enzyme derived from granulocytes, it causes oxidative modification of circulating lipoproteins [2].

Objectives: The aim of this study is to evaluate the levels of dysfunctional HDL in RA patients and to explore the relationship between dysfunctional HDL and coronary artery disease (CAD) in RA patients.

Methods: Sixty-seven healthy individuals and 130 RA patients without diabetes mellitus, hypertension and hyperlipidemia were included to study. Blood samples taken from patients and healthy volunteers were centrifuged to separate serum and these serum samples were stored at -80 °C until the study day. Total cholesterol (TC), triglyceride (TG), HDL, Low-density lipoprotein cholesterol (LDL), MPO and PON1 levels were measured. The MPO/PON1 ratio was calculated as a dysfunctional HDL marker. Cardiology notes of the patients were examined to detect patients who also have CAD.

Results: The mean age of the patient and control groups were 54.6 ± 11.3 and 52.0 ± 10.0, respectively (p=0.107). The mean DAS28 score of the patients was 2.77 ± 0.96. There were no significant differences between two groups in TC, TG, HDL and LDL (p > 0.05). Moreover, PON1 and dysfunctional HDL levels were significantly higher in the RA group compared to control group (p < 0.001, p < 0.023; p < 0.001; respectively).

Dysfunctional HDL levels were higher in 44 RA patients with CAD compared to 86 RA patients without CAD (p = 0.002). 58 patients with active RA had higher dysfunctional HDL levels compared to 72 patients with remission (p = 0.002). There was a positive correlation between DAS28 scores and dysfunctional HDL levels (r= 0.357, p < 0.001).

Conclusion: Our study shows that, although there is no abnormality in lipid profile parameters, dysfunctional HDL levels were higher in patients with active disease than patients with RA in remission and RA patient with CAD than without CADs. This condition could be associated with CAD in RA patients. Disturbance as a result of inflammation on HDL functions such as inhibition of LDL oxidation and reverse cholesterol transport, could be the cause of CAD in RA patients. As a result screening of conventional cardiovascular risk factors in RA patients with normal lipid panel might be inadequate. Therefore as an additional parameter, dysfunctional HDL are promising to evaluate cardiovascular risk of RA patients.

REFERENCES:

Disclosure of Interests: None declared

CARdiovascular risk and vitamin D deficiency in patients with rheumatoid arthritis in therapy with TNF-alpha inhibitors

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Background: Cardiovascular disease is the main cause of mortality and morbidity in patients with rheumatoid arthritis (RA). Correlation between vitamin D deficiency and atherosclerosis in patients with rheumatoid arthritis is a subject of medical interest.

Objectives: We studied the correlation between vitamin D deficiency, body mass index (BMI) and carotid intima-media thickness (CIMT) in patients with rheumatoid arthritis with anti tumor necrosis factor-alpha (TNF-α) therapy.

Methods: Our study included 75 RA patients with anti-TNF-α therapy (Adalimumab, Infliximab, Etanercept) and 30 RA patients with DMARDs (Methotrexate/Leflunomide). The patients were diagnosed with RA according to ACR/EULAR (2010) classification criteria. CIMT was measured using high-resolution Doppler ultrasonography. CIMT ≥ 0.9 mm is considered as a marker of atherosclerosis. Vitamin D deficiency was defined as serum 25-OH-vitamin D level <20 ng/mL. Other parameters included are age, body mass index (BMI=18.5-24.9 kg/m² - normal weight; BMI>25kg/m² - overweight) and disease activity (DAS28<2.6: remission; DAS28=2.6-3.2: low disease activity, DAS28>3.2-5.1: moderate disease activity; DAS28>5.1: high disease activity).

Results: Patients with current use of vitamin D supplements were excluded. The anti-TNF group included 29 patients with Adalimumab (38.7%), 25 with Etanercept (33.3%) and 21 patients in treatment with Infliximab (28%). Their mean age was 52.0 years. We evaluated patients at baseline and after 12 months with treatment. In anti-TNF group we found 9 patients (12%) with normal BMI and normal vitamin D level correlated with high CIMT (p=0.001), 21 patients (28%) with overweight and normal vitamin D level correlated with high CIMT (p=0.003), and 31 patients (41.3%) with overweight and low vitamin D level correlated with high CIMT (p=0.001). 14 patients (18.7%) with normal vitamin D level and normal overweight (9) or overweight (5) were correlated with normal CIMT (p=0.001). In DMARDs group we followed the same correlation. Patients with normal BMI and normal vitamin D level had a low correlation with CIMT increase (p=0.01). Patients with overweight and low vitamin D level had a significant correlation with CIMT increase (p=0.003) than group with anti-TNF-alpha therapy.

After 12 months of therapy, patients treated with Adalimumab had lower CIMT levels than patients treated with Etanercept. Conclusion: Rheumatoid arthritis patients treated with TNF inhibitors and with vitamin D deficiency but with normal BMI have been correlated with lower increase of CIMT than patients with DMARDs therapy. Normal vitamin D level was associated with low increase of CIMT in these patients.

Disclosure of Interests: None declared

AA AMYLOIDOSIS AND LUNG DISEASES IN RHEUMATOID ARTHRITIS – A POSTMORTEM CLINICOPATHOLOGIC STUDY OF 147 PATIENTS

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Background: Systemic AA amyloidosis (AAa) is one of the most important complications of rheumatoid arthritis (RA) [1]. A wide spectrum of lung diseases may complicate RA or associate with RA [2-4].

Objectives: The aim of this study was to determine the influence of AAa on lung diseases related or not related to RA.

Methods: We studied 161 random autopsy patients with RA [1]. RA was confirmed clinically according to the criteria of the ARA [5]. Tissue samples of the lungs were available for histological evaluation of 147 patients.

Disclosure of Interests: None declared
The prevalence of AAa and of distinctly different forms of multilocal inflammation, such as purulent bronchitis and bronchiolitis (purBr) or bronchopneumonia (BrPn), infect with pneumonia (InfPn), occlusive pneumonia (OcclPn) – local pneumonia caused by compressive peribronchial nodules, lymphoid hyperplasia or bronchial blockage by a necrotic nodule – were examined. In addition, rheumatoid pneumonia (RhPn), furthermore interstitial pneumonia (IPn) [1-4] were determined at autopsy and confirmed in a detailed review of extensive histological material. The possible role of AAs on the prevalence of purBr or BrPn, InfPn, OcclPn, RhPn and IPn was analyzed with Pearson’s chi-squared ($\chi^2$) test.

**Results:** AAa complicated RA in 34 (23.13%) of 147 patients. Pulmonary blood vessels of different caliber and various tissue structures of the lungs were involved in 25 (73.53%) of 34 cases; the lungs were not involved by AAa in 9 (26.47%) of 34 cases. purBr or BrPn were associated with RA in 19 (21.1%), InfPn in 5 (3.4%), OcclPn in 2 (1.4%), RhPn in 3 (2.1%) of 147 patients (only the fatal cases were considered). IPn – characterized by interstitial cellular infiltration with or without edema, fibrinoid deposition, with or without fibrosis, and with or without corresponding pleuritis was present in 35 (23.8%) of 147 patients; IPn alone was not fatal in our cohort and contributed to the death only in association with cardiac, circulatory or cardio-respiratory insufficiency.

Pulmonary amyloid A deposition (m=25) was associated with purBr or BrPn in 1 (5.26%) of 19, InfPn in 1 (20.0%) of 5, OcclPn in 2 (100.0%) of 2, RhPn in none (0.0%) of 3, IPn in 12 (34.29%) of 35 patients. The relationship between pulmonary AAa and purBr or BrPn ($\chi^2=1.2836$, p=0.25), InfPn ($\chi^2=0.1800$, p=0.67) or RhPn ($\chi^2=0.00205$, p=0.98) was not significant. There was a significant and positive correlation between pulmonary AAa and OcclPn ($\chi^2=4.8313$, p=0.032) or between AAa and IPn ($\chi^2=9.7106$, p<0.0018).

**Conclusion:** The main complications of RA, such as AAs, may influence the prevalence, clinical course and symptoms of associated diseases and vice versa. Knowledge of these relationships is important to estimate the relative danger they potentially represent. The significant correlation between AAa and OcclPn or IPn suggests a positive influence of pulmonary amyloid A deposition on OcclPn or IPn. The statistically not significant correlations suggest that purBr or BrPn, InfPn and RhPn are independent entities which are not influenced by AAa.

**REFERENCES:**


**Disclosures of Interests:** None declared


**FR00025**

**DOES COMORBIDITY IMPACT ON THE ACTIVITY AND MANAGEMENT OF RHEUMATOID ARTHRITIS?**

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**Background:** Patients with rheumatoid arthritis (RA) are in increased risk of developing comorbid conditions. Recent data suggest the relationship between severity of RA and concomitant diseases [1, 2]. Drug therapy is considered as important risk factor for numerous comorbidities. On the other hand, comorbidity can impact negatively on the RA course and on the pts management [3].

**Objectives:** The aim of our study was to evaluate the prevalence of concomitant conditions in RA pts, to compare the RA activity and management in relation with comorbidities.

**Methods:** 168 pts with established and longstanding RA were observed at-in-patient clinic for RA clinical assessment and revealing concomitant diseases (cardiovascular, gastrointestinal, liver, pulmonary, endocrine, blood). The activity of disease according to DAS28-ESR index in RA subgroups with and without comorbidities was compared. The spectrum and used doses of anti-rheumatic medications (DMARD, biologics, GC) in these subgroups was analyzed in term to assess the RA rational treatment. The majority (88.1%) of observed RA pts had concomitant condition. The most frequent associated diseases were: cardiovascular (AH, IHD, HF, AF) in 86.9% and gastrointestinal (gastritis, duodenitis, gastro-duodenal ulcer, colitis) in 64.3% less common comorbidities were anemia (30.9%), liver and kidney abnormalities (hepatomegaly, steatohepatitis, CKD, pyelonephritis) in 25% and 12.5% respectively, endocrine (type 2 diabetes mellitus, thyroid disorders) in 16.7%. Multimorbidity determined as combination of different system disorders in the setting of RA was detected in 54.6% of RA pts. We found out significant difference in RA activity on the basis of DAS28 between RA subgroup without concomitant conditions (the 1st) on the one hand and RA subgroups with comorbidities (the 2nd) (11=2.76, p<0.01) or multimorbidities (l2=2.73, p<0.01) on the other hand (tab.1).

<table>
<thead>
<tr>
<th>Index</th>
<th>RA without comorbidities</th>
<th>RA with comorbidities</th>
<th>RA with multimorbidities</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAS</td>
<td>4.20 ± 0.31</td>
<td>5.09 ± 0.09</td>
<td>5.44 ± 0.12</td>
</tr>
</tbody>
</table>

In RA with comorbidities/multimorbidities the mean doses of MTX and SSZ were lower than in RA without comorbidities, while the dose of GC and frequency of GC use was significantly higher in the 2nd and 3rd groups (2=4.25, 4.41 respectively). 55% of pts from the 1st group and only 19.6% of total amount of pts from the 2nd and 3rd groups were treated with biologics (2=4.67).

**Conclusion:** Obtained data suggest that comorbidities have a negative impact on the severity of RA and can interfere in the implementation of T2T strategy in daily clinical practice.

**REFERENCES:**


**Disclosure of Interests:** None declared


**FR00026**

**SYSTEMIC, RENAL AND CARDIAC AA AMYLOIDOISIS IN RHEUMATOID ARTHRITIS – A COMPARATIVE POSTMORTEM CLINICOPATHOLOGIC STUDY OF 161 PATIENTS**

**Miklos Bély1, Ágnes Apáthy2. 1Hospital of the Order of the Brothers Saint John of God in Budapest, Department of Pathology, Budapest, Hungary; 2St. Margaret Clinic, Budapest, Department of Rheumatology, Budapest, Hungary**

**Objectives:** The aim of our study was to determine the incidence of systemic AA amyloidosis (sAAa) in RA, to appraise the prevalence and severity of amyloid A deposition in different tissue structures of the kidneys and heart, to outline the development of renal and cardiac AA amyloidosis (rAAa and cAAa), and to estimate the role of rAAa and cAAa in mortality.

**Methods:** One hundred sixty one (161) non-selected autopsy patients with rheumatoid arthritis (RA) were studied. RA was confirmed clinically according to the criteria of the ACR [1]. sAAa was specified histologically, based on evaluation of $5$ organs (heart, lung, liver, kidney and pancreas). Amyloid A deposition was diagnosed histologically according to Romhányi by a modified (more sensitive) Congo red staining [2]. Amyloid...
A deposits were confirmed in serial sections by immunohistochemical and histochemical methods.

Results: sAAa complicated RA in 34 (21.12%) of 161 patients; in 127 (78.88%) of 161 patients amyloid A deposits were not found. Amyloid A deposits were found in 29 (87.88%) kidneys of 33 patients with sAAa; kidneys were negative for amyloid in 4 (12.12%) of 33 cases (in 1 of 34 patients with sAAa tissue blocks of kidneys were not available).

Amyloid A deposits were found in 29 (87.88%) hearts of 33 with sAAa; the heart was negative for amyloid in 4 (12.12%) of 33 cases (the heart of one patient with sAAa was not available). Renal amyloid A deposition led to death in 17 (50.06% of 34) patients with sAAa due to massive amyloid A deposition in the kidneys, leading to renal insufficiency and uremia. Cardiac amyloid A deposition led to death in 3 (8.82%) of 34 patients with sAAa (and contributed to the lethal outcome in further 5). Forteen (41.18%) of 34 patients with sAAa died of other causes such as peritonitis, lethal septic infection, etc.

sAAa was clinically diagnosed in 9 (26.47%) and missed in 25 (73.52%) of 34 patients, and only cases with massive renal amyloid A deposits were recognized. Cardiac AAa or its pathogenic role in mortality was not diagnosed.

Conclusion: sAAa is one of the main and the most insidious complications of RA affecting the kidneys and heart with high prevalence and severity. sAAa is related to the cardiovascular system, and rAAa or cAAa are associated with it. sAAa, rAAa and cAAa may develop in both sexes, and at any time in the course of the disease.

Systemic, renal and cardiac amyloid A deposition is a progressive and cumulative process, involving in its early stage only a few structures in some organs, and increasingly more in the later stages of the disease. In sAAa the renal and cardiac amyloid A deposition starts after a latent stage. This latency may be caused by a not specified local protective mechanism, e.g. great excretion capacity of the kidneys, due to motility of the heart or oxygenisation etc. Amyloid A deposition starts in the most frequently involved structures of the kidneys or heart with more massive deposits. The chronology of amyloid A deposition allows an indirect assessment of the stage of renal or cardiac amyloidosis, which may have a prognostic value in everyday surgical pathology.

Half of the patients with sAAa died of uremia caused by massive rAAa and only 9 of these were clinically recognized. Renal and cardiac amyloid A deposition should be considered a very serious, life-threatening complication of RA.

Disclosure of Interests: None declared


FR10027   PROGNOSTIC MARKERS FOR PRECLINICAL CARDIOVASCULAR DISEASE IN RHEUMATOID ARTHRITIS AND CORRELATION WITH DISEASE ACTIVITY

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Background: Patients with rheumatoid arthritis (RA) have an elevated cardiovascular (CV) disease risk, explained both by an increased prevalence of traditional CV risk factors and the presence of chronic systemic inflammation that impairs vascular function, leads to thickening of the arterial wall and increased arterial stiffness.

Objectives: In this study we investigated the effect of anti-inflammatory treatment on prognostic markers for preclinical cardiovascular disease (arterial wall thickening and arterial stiffness) and the correlation of these markers with RA disease parameters.

Methods: Carotid ultrasound (using Artlab echotacking system) was used to determine carotid intima media thickness (IMT) and pulse wave analysis was done with SphygmoCor tonometry to calculate pulse wave velocity (PWV) and augmentation index (AIx). Paired t-test was used to compare PWV, AIx and IMT prior and after 6 months of therapy. Pearson correlation was calculated to investigated the correlation of PWV, AIx and IMT with (natural logarithm of) C-reactive protein (CRP), (natural logarithm of) erythrocyte sedimentation rate (ESR) and disease activity score 28 (DAS28). For correlations, data from both time points were pooled.

Results: In total 61 consecutive RA patients (50% early arthritis starting with csDMARD and 50% established RA starting with adalimumab) were asked to undergo arterial analysis just prior to start of therapy and after 6 months. PWV was performed in 45 patients at baseline and 39 at follow-up, IMT in 56 and 45 patients respectively and AIx in 51 and 44 patients respectively. Both signs of arterial stiffness (PWV and AIx) decreased after 6 months of therapy (mean difference 0.7 and 0.8 respectively; table 1), although this did not reach statistical significance. IMT remained stable during 6 months of therapy.

Table 1. Prognostic markers of atherosclerosis prior and after 6 months of anti-inflammatory therapy

<table>
<thead>
<tr>
<th>n</th>
<th>Baseline</th>
<th>Mean difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PWV (m/s)</td>
<td>35</td>
<td>8.0</td>
</tr>
<tr>
<td>AIx (%)</td>
<td>39</td>
<td>27.4</td>
</tr>
<tr>
<td>IMT (mm)</td>
<td>43</td>
<td>0.68</td>
</tr>
</tbody>
</table>

Conclusion: Arterial stiffness as measured with PWV tended to decrease after 6 months of anti-inflammatory treatment. Arterial stiffness and arterial intima media thickness correlated with clinical disease parameters. Altogether, these changes might suggest that effective anti-anerithmatic therapy has favorable cardiovascular effects. Whether or not this ultimately leads to a significant reduction of "hard" cardiovascular endpoints remains to be established in prospective studies.

Disclosure of Interests: Anneties Blanken: None declared, Rabia Agca: None declared, C.J. van der Laken: None declared, Michael Nurmohamed: Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi and UCB, Consultant for: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi and UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi and UCB, DOi: 10.1136/annrheumdis-2019-eular.4581

FR10028   LOW SERUM IGF1 IS ASSOCIATED WITH AN INCREASED RISK AND HIGH PREVALENCE OF CARDIOVASCULAR EVENTS IN MIDDLE-AGED FEMALE PATIENTS WITH RA – A 5-YEAR FOLLOW-UP

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Background: Recent meta-analysis reported that rheumatoid arthritis (RA) is associated with high frequency of hypertension and stroke (1). IGF1 is an important angioprotector and its deficiency predisposes to development of ischemic stroke (2). Objectives: Since levels of active IGF1 are affected by systemic inflammation, we analyze if low IGF1 is associated with increased cardiovascular disease (CVD) in women with RA.

Methods: The CVD risk was estimated (eCVR) in 184 female RA patients (median age 53 years, range 21-71) using the Framingham
algorithm. A 5-year prospective follow-up for new CVD events, type II diabetes and medication for hypertension and hyperlipidemia was completed in all the patients. The event-free survival curves were built and the Mantel-Cox analysis was performed with respect to serum IGF1, where IGF1 levels below or equal to the median 139 ng/ml were considered low.

**Results:** Low IGF1 was clinically significant. These patients were recognized by high prevalence of hypertension (26% vs. 7.9%, p=0.001), overweight (19% vs. 6.8%, p=0.016) and hypercholesterolemia (71% vs 48%, p=0.0025), which resulted in a higher eCVR in these RA patients (72% vs. 3.3%, p<0.001). When adjusted by age, low IGF1 group had higher serum IL6 (pg/ml: 2.1[0.2-3.0] vs 0.7[0.1-4.2], p=0.038) and ESR (mm/h: 12.7[15.5]) vs 5.9[8], p=0.02), and higher prevalence of MTX monotherapy (59% vs. 39%, p=0.024). At prospective follow-up, 12 CVD events were registered. The median age at CVD event was 67 years and disease duration 14 years. Among the new CVD events were 4 ischemic strokes, 3 chronic atrial fibrillations and 2 incidentally aorta aneurysms, which all could be viewed as directly related to hypertension. Low IGF1 showed high probability for new CVD events (OR 4.96, [95%CI:1.17-34.2], p=0.029). Additionally, low IGF1 group had a significant increase in medication for hypertension (+19.5% vs +4.8%, p=0.0001), but not type II diabetes or statins. In a prediction model, a combination of low IGF1 and RA duration>10 years indicated 80.5% specificity for development of new CV events.

**Conclusion:** We identified low normal levels of IGF1 to be associated with higher prevalence of CVD events in RA patients. Importantly, low IGF1 appeared to be an independent predictor of hypertension in middle-aged female patients.

**REFERENCES:**


**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.4759

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**FR0029**

**DEVELOPMENT OF AN ALGORITHM FOR THE CLASSIFICATION OF CARDIOVASCULAR COMORBIDITY IN RHEUMATOID ARTHRITIS: DATA FROM THE ONTARIO BEST PRACTICES RESEARCH INITIATIVE**

Kangping Cui1,2, Mohammad Movahedi3, Claire Bombardier3,4,5, Bindee Kurija4,6,1

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**Background:** Cardiovascular disease (CVD) is increased in rheumatoid arthritis (RA). The ability to accurately identify CVD and its risk factors is important for primary and secondary prevention strategies. RA registries collect comorbidity data, but discordance between physician-reported and patient-reported comorbidities often exists.

**Objectives:** We aimed to develop an algorithm for the classification of CVD and CVD RF in a representative RA registry.

**Methods:** Data were collected from the Ontario Best-practices Research Initiative (OBRI), a clinical registry of RA patients followed in routine care in Ontario, Canada. Clinical information, including patient medication profile, was obtained at registry entry, through physician visits and patient telephone interviews. Cardiovascular disease (CVD) was defined as having ≥ 1 of myocardial infarction (MI), coronary artery disease (CAD), cerebrovascular accident (CVA, including transient ischemic attack and stroke), or peripheral arterial disease (PAD). CVD risk factors included hypertension (HTN), dyslipidemia (DLD), diabetes mellitus (DM), and current smoking.

**Results:** An algorithm for classifying CVD and CVD risk factors was developed including the 2033 subjects with baseline data. At cohort entry, the prevalence of CVD was 5.4% (n=110), HTN 670 (32.9%), DLD 401 (19.7%), DM 165 (8.1%), and current smoking 346 (17%). Seventeen (15.7%) subjects were not identified as having CVD by physician-report, but were classified as having CVD upon medication review. Discrepancy between physician and patient-reported CVD RF were: 207 for HTN (31%), 291 for DLD (73%), and 22 for DM (13%). Chart review of 55 patients showed sensitivity of 100% for CVD, 78% for HTN, and 42% for DLD classification.

**Conclusion:** An algorithm for classification of CVD has been successfully developed in a representative RA registry. The discrepancy between physician and patient-reported CVD highlights the importance of utilizing information from multiple sources when classifying comorbidities.

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**FR0030**

**FEELINGS OF GUILT AND SHAME IN PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background:** Rheumatoid arthritis (RA) is a chronic inflammatory disease which causes functional disability, pain, and joint destruction. The disease has a major impact on patient’s independence, social activities and self-image.

**Objectives:** The aims of this study were to assess whether RA is associated with increased feelings of shame and guilt, and to examine possible correlates with socio demographic characteristics and disease activity.

**Methods:** To measure feelings of shame and guilt, in patients with RA (ACR/EULAR 2010), we used the Experience of Shame Scale (ESS) [1] and the Test of Self Conscious Affect- Version 3 (TOSCA-3S) [2]. The ESS is a 25-item questionnaire that assesses the frequency of characteristic, behavioral and bodily shame experiences over the past year. Respondents rate each item on a scale ranging from 1 (not at all) to 4 (very much), with higher scores indicating greater shame. The TOSCA-3S is presented with 11 brief hypothetical scenarios followed by 3 common reactions, which reflect shame, guilt and externalization of blame. Each possible response is rated on a five-point scale from 1 (not likely) to 5 (very likely). For the purpose of this study, only the shame and guilt response items were analyzed. Total scores for Shame Self-Talk and Guilt Self-Talk were calculated and compared to the scoring interpretation. A p<0.05 was considered significant.

**Results:** A total of 40 patients with RA were included, 36 women and 4 men, with a mean age of 54.2 years old [25-75]. Nine patients (22%) were illiterate, 42.5% were professionally active and 82.5% were married. The mean disease duration was 12.8 years [3-33], 80% of patients were on prednisone at a daily posolog of 7 mg [2.5-12.5], 62.5% were on csDMARDs and 27.5% on bDMARDs. The mean DAS 28 ESR and CRP were respectively 4.3 [1.6-6.9] and 3.6 [1-6.2]. The mean total score of the ESS was 45.3 [27-81] with subscale means of: 19 [12-37] for characteristic shame, 19 [10-30] for behavioral shame and 7.4 [4-16] for bodily shame. For the TOSCA-3S, the mean “shame self-talk Total” score was 33.8 [17-44], and the mean “guilt self-talk Total” score was 48 [37-55], which corresponds to ‘you often use’ for men and ‘you use an average amount’ for women, a shame and guilt self-talk.

**Conclusion:** Our RA patients experienced general feelings of shame and guilt, which correlate with demographic items and disease activity.
However, a case-control study with a larger population is necessary to determine whether patients with RA express more shame and guilt than their peers without RA.

REFERENCES:

Disclosure of Interests: None declared

FRI0031

ASSESSMENT OF EFFICACY, SAFETY AND IMMUNOGENICITY OF A TRIVALENT SPLT-VIRUS INFLUENZA VACCINE IN PATIENTS WITH RHEUMATIC DISEASES

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Background: In current rheumatology practice concurrent infections produce significant negative impact on patients’ morbidity, mortality and quality of life. Based on WHO estimations the annual incidence of influenza in adult population amounts to 5-10% worldwide. Influenza can lead to hospitalization (3 to 5 million cases per year) and even death (250-500 thousand cases per year). Flu and its complications rates are higher in patients with rheumatic diseases (RD) as compared to general population. Therefore, prevention of influenza should be viewed as integral part of RD population management.

Objectives: To study the safety, efficacy and immunogenicity of inactivated split-virus influenza vaccine in patients with rheumatoid arthritis (RA) and ankylosing spondylitis (AS).

Methods: 126 subjects (90 females and 36 males, aged 22 - 82 y) with recent acute respiratory viral infections (ARVI) and flu episodes in medical records were enrolled, including 52 RA patients, 34 AS patients and 40 healthy volunteers as the control group. 39 RA pts received methotrexate (MTX), 12 - TNF inhibitors +MTX, 8 - Lefunomide, 2 – abatacept, 2 – sulfasalazine, 1 – tocilizumab + MTX. 19 AS patients were treated with nonsteroidal anti-inflammatory drugs (NSAIDs), 15 – with TNF inhibitors. The RD duration ranged from 2 months to 46 years. All participants were injected subcutaneously with one dose (0.5 ml) of the trivalent inactivated influenza vaccine containing the actual influenza virus strains, with ongoing therapy. The control visits were scheduled at baseline, and in 1, 3 and 6 months after vaccination (Visits 0, 1, 2 and 3, respectively). Standard clinical and laboratory tests were performed during each visit. Immunogenicity of vaccine was measured with ELISA test kits.

Results: Vaccine tolerability was good in 103 participants (77.4%). Post-vaccination pain, swelling and redness of the skin up to 2 cm in diameter were registered in 20 cases (15%), low-grade fever, myalgia and malaise were presented in 10 cases (7.5%). There was no casual relationship between these reactions and principal therapy, therefore, no modifications of therapeutic regimens were required, and complete resolution occurred within 24 hours without additional interventions. No RD exacerbations or new autoimmune disorders were observed during the FUP. At baseline mean pts’ DAS28 and BASDAI scores were 3.56 and 3.85, improving up to 1.99 and 3.09, respectively, 6mo post-vaccination. For the entire FUP there were no cases of influenza or influenza-like illness registered.

The portion of respondents to the vaccine is 70% in the group of patients with RD and 75% in the main group. The level of humoral immune response was not significantly different in the group of patients with RD and in the control. It is noteworthy that there were no significant differences in the level of post-vaccination response after a month (p = 0.6) or after 3 or 6 months of observation. In patients with AS, there were significantly more responses to vaccines in patients with a long duration of the disease and low activity according to the BASDAI index (p <0.05). There was no significant effect of the treatment of RH on the level of post-vaccination response; there were also no differences in the level of post-vaccination response between patients with different RD.

Conclusion: Therefore, our results show good tolerability, efficacy and immunogenicity of inactivated split-virus influenza vaccine in RA and AS patients. Future studies on larger patients’ populations are warranted for more complete evaluation of vaccine safety and efficacy.

Disclosure of Interests: None declared

FRI0032

HIGH INDEX OF SEDENTARY BEHAVIOR IN PATIENTS WITH INITIAL RHEUMATOID ARTHRITIS: DATA FROM A LONG COHORT OF INITIAL RA

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Background: The abandonment of a healthy lifestyle can have great impact on the quality of life, the response to the treatment and the control of the symptoms, like pain and fatigue on RA patients. Smoking is a proven trigger in the pathophysiology of RA, but studies show that it also participates in inflammatory activity throughout the course of the disease. RA patients are more likely to develop various comorbidities and increased cardiovascular risk when compared to the general population.

Objectives: To access physical activity engagement along with alcohol and cigarette consumption.

Methods: A cross-sectional study was carried out with patients with rheumatoid arthritis who received treatment on the initial stage of RA and followed up during 15 years in an initial RA cohort of a University Hospital. Participants underwent standardized clinical evaluation and analysis of complementary exams. The study was approved by the Ethics Committee.

Results: A total of 107 RA patients were evaluated. In the sample, 98% of the women were found, with a median age of 52 years. The mean duration of illness was 12.8 years and 11.3% had erosive disease. In relation to the habits of life, the physical activity level, prevalence of alcoholism and smoking were investigated. In general, our population was characterized by non-alcohol users (93.5%), non-smokers (75.7%) and not engaged into regular physical activities (56.1%). In relation to frequency, 21.5% of the patients exercised a minimum of three times a week, 16.8% once or twice a week and 5.6% once or twice a month. The practice of physical activity may be difficult for the patient with RA, who often has functional limitations, but is still of great importance, since it improves the response to treatment, prevents the onset of other comorbidities, or worsening of previous diseases, complications and promotes the improvement of the quality of life.

Conclusion: Even with a multidisciplinary approach and health care professionals qualified to instruct and emphasize the importance of engaging in an active lifestyle, RA patients remain mostly sedentary after 15 years of follow up. Perhaps other strategies of intervention should be investigated to improve such habits.

REFERENCES:

Scientific Abstracts
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FRIO033 QUANTIFERON GOLD-PLUS AND TUBERCULIN SKIN TEST REACTIVITY PREDICTORS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: RA patients have high latent tuberculosis (LTBI) prevalence (20-37%). In Mexico, ranges from 21.7% to 31.3% using tuberculin skin test (TST). The methods to detect LTBI are TST and IGRA. Quantiferon (QFT-Plus) uses an antigen tube (TB1) that stimulates CD4+T cells and an additional tube (TB2) that also stimulates CD6+T cells.

Objectives: Determine the LTBI prevalence, variables that predict QFT-Plus and TST results and the concordance between TST and QFT-Plus in RA patients.

Methods: A cross-sectional study in RA patients from the rheumatology department of the University Hospital "José E. González" in Mexico between October 2017 and June 2018. RA patients with EULAR 2010 classification criteria without a history of tuberculosis (TB) were included. QFT-Plus was performed according to manufacturer instructions. TST was applied with the Mantoux technique; a 5mm cutoff was used. The square chi and Fisher test were used for proportions, Mann-Whitney to compare means, trend analysis using linear trend test and a binary logistic regression model for variables related to positivity to both tests.

Results: We included 111 patients (table 1), the mean age was 51.9 years, 92.3% were women, disease duration 8.7±8.8 years. QFT-Plus was positive in 46 (41.6%) patients. TST was positive in 31 (27.9%) patients. Agreement between tests was 73.7% (kappa=0.45, p<0.001). The majority of patients were using conventional DMARDs (86.7%), none of the patients were using biologic DMARDs. In the linear-to-linear association analysis there was a trend towards TST negative result with the use of ≥2DMARDs (p=0.049 for trend) (figure 1). In the logistic regression model we found a significant relationship between a positive TST active TB exposure (OR 8.5, CI 95% 1.4-51.7; p=0.01) and an inverse relationship between the positive TST and antimalarials (OR 0.11, CI 95% 0.001-0.8), none of the variables interfered with QFT-Plus results.

Conclusion: The LTBI prevalence in RA patients in our study is similar to countries with a high TB burden. We recommend considering RA patients as a high-risk population for LTBI. An intermediate agreement between TST and QFT-Plus was found. The use of antimalarials and ≥2DMARDs influence the TST reactivity, none of the variables altered the QFT-Plus results. Based on the results, we recommend the Quantiferon Gold Plus over TST for the LTBI screening in RA patients.


Disclosure of Interests: None declared

FRIO034 A LATIN-AMERICAN PREVENTIVE CARDIO-RHEUMA CLINIC: A CASE-CONTROL STUDY

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Background: It has been described an increased prevalence of cardiovascular diseases (CVD) in rheumatoid arthritis (RA) patients. When compared with the general population, CVD mortality is 50% higher in RA (1). It is reported a 35.3% prevalence of CVD in Latin-American population with RA (2). Cardio-rheuma (CR) clinics were designed to enhance detection, prevention and treatment of CVD in patients with rheumatic conditions. Our clinic located in the University Hospital in Monterrey Mexico, is the first and only established in Latin-America since 2014.

Objectives: To describe the characteristics of patients with RA attending to a Latin-American CR clinic and compare the findings by carotid ultrasound (US) and echocardiography to controls.

Methods: Cross-sectional, observational, comparative study. RA patients aged 40 to 75 years that fulfilled the 2010 EULAR criteria and matched controls were included. Patients with prior atherosclerotic CVD and other lap syndromes were excluded. Clinical history, blood samples, physical exam, carotid US and echocardiography were performed. Carotid plaque (CP) was defined as a focal narrowing ≥0.5 mm of the surrounding lumen or a carotid intima media thickness (cIMT) ≥1.2 mm, and increased cIMT was defined as ≥0.9 mm. Transthoracic echocardiogram was performed and reviewed by 2 board-certified cardiologists. Differences were solved by consensus. Categorical variables are expressed as total number (%), and numerical variables as median (q25-q75). Chi square and Mann-Whitney U-test were used to compare groups and considered significant if p<0.05.

Results: A total of 336 RA patients and 144 controls were included (Table 1). Table 2 summarizes echocardiographic and carotid US findings; ejection fraction was higher in controls than RA patients, prevalence of bilateral CP and increased cIMT was significantly higher in RA patients.
Inflammatory Arthritis Induced by Immune-Checkpoint Inhibitors: Results from a Combined Rheumatology/Oncology Outpatient Clinic

Fulvia Ceccarelli1, Andrea Botticelli2, Alain Gelibter3, Ilaria Leccese1, Ilaria Zizzari4, Grazia Sirgiovanni5, Francesca Romana Di Pietro6, Ramona Lucchetti7, Carlo Perricone1, Enrico Cortesi2, Marianna Nuti3, Fabrizio Conti1

Disclosure of Interests: None declared


Inflammatory Arthritis Induced by Immune-Checkpoint Inhibitors: Results from a Combined Rheumatology/Oncology Outpatient Clinic

Fulvia Ceccarelli1, Andrea Botticelli2, Alain Gelibter3, Ilaria Leccese1, Ilaria Zizzari4, Grazia Sirgiovanni5, Francesca Romana Di Pietro6, Ramona Lucchetti7, Carlo Perricone1, Enrico Cortesi2, Marianna Nuti3, Fabrizio Conti1

Disclosure of Interests: None declared


References:

Conclusion: RA patients from this clinic had lower ejection fraction, more prevalence of cIMT and bilateral CP when compared to controls. It is important that rheumatologists perform a complete evaluation of their patients, in which cardiovascular assessment should be included.

REFERENCES:

Table 1. Patient characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>RA (n=336)</th>
<th>Controls (n=144)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), median (q25-q75)</td>
<td>55.5 (48.6)</td>
<td>53 (48.8)</td>
<td>0.017</td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>311 (92.6)</td>
<td>134 (93.1)</td>
<td>NS</td>
</tr>
<tr>
<td>Disease duration (years), median (q25-q75)</td>
<td>7.8 (3.2-15)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>BMI (kg/m²), median (q25-q75)</td>
<td>27.6 (25.1-31.2)</td>
<td>27.8 (24.9-31.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes Mellitus, n (%)</td>
<td>47 (14)</td>
<td>14 (9.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Dyslipidemia, n (%)</td>
<td>93 (27.7)</td>
<td>31 (21.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>93 (27.7)</td>
<td>31 (21.5)</td>
<td>NS</td>
</tr>
<tr>
<td>DAS28-CRP, median (q25-q75)</td>
<td>3.2 (2.1-4.3)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Past or current smoker, n (%)</td>
<td>65 (19.3)</td>
<td>36 (25)</td>
<td>NS</td>
</tr>
<tr>
<td>Nonsteroidal anti-inflammatory drugs, n (%)</td>
<td>90 (26.8)</td>
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<td>-</td>
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<tr>
<td>Prednisone, n (%)</td>
<td>195 (58)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Methotrexate, n (%)</td>
<td>283 (84.2)</td>
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<td>-</td>
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<tr>
<td>Leflunomide, n (%)</td>
<td>69 (20.5)</td>
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<tr>
<td>Chloroquine, n (%)</td>
<td>54 (16.1)</td>
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<td>-</td>
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<tr>
<td>Sulfasalazine, n (%)</td>
<td>59 (17.6)</td>
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<td>-</td>
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<tr>
<td>Hydroychloroquine, n (%)</td>
<td>34 (10.1)</td>
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<td>-</td>
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<tr>
<td>Biologic DMARDs, n (%)</td>
<td>21 (6.3)</td>
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Table 2. Echocardiographic and carotid US findings

<table>
<thead>
<tr>
<th>Echocardiography</th>
<th>RA (n=60)</th>
<th>Controls (n=28)</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Ejection fraction, median (q25-q75)</td>
<td>60 (56.2-65.2)</td>
<td>63 (60-69)</td>
<td>0.008</td>
</tr>
<tr>
<td>Abnormal LV geometry, n (%)</td>
<td>21 (35)</td>
<td>7 (25)</td>
<td>NS</td>
</tr>
<tr>
<td>Abnormal LA geometry, n (%)</td>
<td>6 (10)</td>
<td>3 (10.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Carotid US, n (%)</td>
<td>RA (n=128)</td>
<td>Controls (n=110)</td>
<td></td>
</tr>
<tr>
<td>CP</td>
<td>38 (29.7)</td>
<td>25 (22.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Increased cIMT</td>
<td>64 (50)</td>
<td>32 (29.1)</td>
<td>0.001</td>
</tr>
<tr>
<td>Unilateral CP</td>
<td>18 (14.1)</td>
<td>17 (15.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Bilateral CP</td>
<td>20 (15.6)</td>
<td>8 (7.3)</td>
<td>0.046</td>
</tr>
</tbody>
</table>

Conclusion: RA patients from this clinic had lower ejection fraction, more prevalence of cIMT and bilateral CP when compared to controls. It is important that rheumatologists perform a complete evaluation of their patients, in which cardiovascular assessment should be included.

REFERENCES:

Disclosure of Interests: None declared


FR10035

Inflammatory Arthritis Induced by Immune-Checkpoint Inhibitors: Results from a Combined Rheumatology/Oncology Outpatient Clinic

Fulvia Ceccarelli1, Andrea Botticelli2, Alain Gelibter3, Ilaria Leccese1, Ilaria Zizza4, Grazia Sirgiovanni5, Francesca Romana Di Pietro6, Ramona Lucchetti7, Carlo Perricone1, Enrico Cortesi2, Marianna Nuti3, Fabrizio Conti1

Disclosure of Interests: None declared, Andrea Botticelli: None declared, Alain Gelibter: None declared, Ilaria Leccese: None declared, Grazia Zizzari: None declared, Francesca Romana Di Pietro: None declared, Ramona Lucchetti: None declared, Carlo Perricone Speakers bureau: BMS; Lilly, Celgene, Sanofi, Enrico Cortesi: None declared, Marianna Nul: None declared, Fabrizio conti: None declared, Paolo Marchetti: None declared, Guido Valesini: None declared

EFFECTS OF DISEASE ACTIVITY, ILLNESS PERCEPTION, SOCIAL SUPPORT AND COPING METHODS ON QUALITY OF LIFE IN THE PATIENTS WITH RHEUMATOID ARTHRITIS AND FIBROMYALGIA SYNDROME

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Background: In chronic diseases, social support, illness perception and coping methods have important effect on quality of life.

Objectives: In the present study, we aimed to compare the quality of life (QOL) of the patients with rheumatoid arthritis (RA) with fibromyalgia (FMS) patients and healthy controls and to assess the relationship between QOL and illness perception, social support, disease coping methods in the patients with RA and FMS.

Methods: Fifty-eight patients with RA, 50 patients with FMS and 50 healthy controls were enrolled in the study. Visual Analogue Scale (VAS), QOL (Short Form SF-36), illness perception (Revised Illness Perception Scale, IPQ-R), social support (Multidimensional Perceived Social Support Scale, MSPSS) were assessed in the patients. In RA patients, disease activity was evaluated with DAS 28 and Clinical Disease Activity Index (CDAI), and functional status was evaluated with Health Assessment Questionnaire (HAQ). Fibromyalgia Impact Questionnaire (FIQ) scale was used in the clinical assessment of FMS patients.

Results: While RA and FMS patients had higher COPE-emotional and COPE–problem scores than the healthy controls (p<0.05), there was no significant difference between the patients with RA and FMS (p>0.05).

Regarding the all MSPSS scores, there was no significant difference between the three groups (p>0.05). FMS patients had lower scores than the RA patients and healthy controls regarding the physical function, pain, social functioning and mental health subscales of SF-36 (p<0.05).

In RA patients, MSPSS-friend and MSPSS-special one scores were positively correlated with all subscales of SF-36. IPQ-R consequences scores were positive correlations between IPQ-R treatment control and SF-36 mental and high risk subscales (p<0.05).

Conclusion: In RA and FMS patients, QOL and physical functions were found to be related with illness perception, social support and coping methods as much as disease activity.

Disclosure of Interests: None declared


DIAGNOSTIC PERFORMANCE OF CURRENT CVR SCORES FOR THE DIAGNOSIS OF CAROTID PLAQUE IN MEXICAN-MESTIZO RA SUBJECTS

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Background: Rheumatoid arthritis (RA) is an inflammatory disease with an increased mortality compared to the general population. The measurement of carotid intima media thickness (CIMT) is used as an independent marker of subclinical atherosclerosis.

Objectives: To determine the prevalence of carotid plaque (CP) in a cohort of Mexican RA subjects and diagnostic performance of cardiovascular risk (CVR) calculators for the prediction of augmented CIMT and CP.

Methods: A cross-sectional study of subjects aged from 40-75 years that fulfilled the 2010 ACR/EULAR RA criteria. Exclusion criteria: previous CV disease and overlap syndromes. CVR was calculated by 6 scales: ACC/AHA 2013, Framingham-lipids (FRS-lipids), Framingham-Body Mass Index (FRS-BMI), Reynolds Risk Score (RRS), QRISK2 and SCORE. Carotid ultrasound (US) was performed by a board-certified radiologist and reviewed by other two. We defined an augmented CIMT as ≥0.9 mm and CP as CIMT ≥1.2 mm. We categorized subjects in 3 groups: 1) normal carotid US, 2) augmented CIMT, and 3) CP. We used Kruskal-Wallis test to compare the groups.

Results: 130 patients were included, 124 (95.4%) were females with median age of 57 years old and disease duration of 9.7 years. Almost 50% of the subjects with CP were in the low-risk strata of every CVR calculator. The presence of CP was higher in subjects categorized as moderate/high risk using ACC/AHA 2013 CVR score (p=0.013), moderate/ high risk strata of QRISK2 (p=0.004), and high-risk strata of ACC/AHA 2013 CVR score (p=0.02). Of these 3, the highest sensitivity was obtained by the moderate risk stratum of QRISK2 with 51%; the highest specificity was obtained by the high-risk stratum of the ACC/AHA 2013 CVR score with 84%.

Table 1. Comparison groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Normal CIMT</th>
<th>CIMT &lt;0.9mm</th>
<th>CIMT ≥0.9mm</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age years</td>
<td>59 (55-66)</td>
<td>60 (53-70)</td>
<td>51 (44-58)</td>
<td>0.00</td>
</tr>
<tr>
<td>BMI kg/m²</td>
<td>27.3 (25.3-29.9)</td>
<td>27.8 (24.7-31.3)</td>
<td>29.9 (26.6-34.5)</td>
<td>0.022</td>
</tr>
<tr>
<td>ACC/AHA 2013</td>
<td>4.6 (2.3-10.2)</td>
<td>5.6 (2.2-11.8)</td>
<td>1.7 (0.7-3.5)</td>
<td>0.00</td>
</tr>
<tr>
<td>FRS-LIPID</td>
<td>7.1 (5.3-10.3)</td>
<td>9.25 (8.1-13.4)</td>
<td>3.8 (2.1-6.1)</td>
<td>0.00</td>
</tr>
<tr>
<td>FRS-BMI</td>
<td>10.4 (7.7-15.4)</td>
<td>12.2 (8.7-21.6)</td>
<td>4.8 (2.7-9.3)</td>
<td>0.00</td>
</tr>
<tr>
<td>SCORE</td>
<td>1.0 (0.5-2)</td>
<td>1.0 (0.5-2)</td>
<td>1.0 (0.5-2)</td>
<td>0.00</td>
</tr>
<tr>
<td>QRISK2</td>
<td>10.5 (5.2-16.7)</td>
<td>11.6 (5.6-17.1)</td>
<td>3.1 (1.9-6.3)</td>
<td>0.00</td>
</tr>
<tr>
<td>RRS</td>
<td>2 (1.3-4)</td>
<td>3 (1.5-7)</td>
<td>1 (1-2)</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Table 2. Diagnostic test performance

<table>
<thead>
<tr>
<th>CVR score</th>
<th>Moderate and high risk</th>
<th>CP (n=39)</th>
<th>No CP (n=91)</th>
<th>p</th>
<th>HR</th>
<th>Sens (%)</th>
<th>Spec (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACC/AHA 2013, n (%)</td>
<td>19 (48.7)</td>
<td>24 (29.6)</td>
<td>0.01</td>
<td>2.6</td>
<td>0.48</td>
<td>0.73</td>
<td>0.44</td>
<td>0.77</td>
<td></td>
</tr>
<tr>
<td>FRS-Lipid, n (%)</td>
<td>11 (28.2)</td>
<td>17 (48.7)</td>
<td>0.22</td>
<td>1.71</td>
<td>0.28</td>
<td>0.81</td>
<td>0.39</td>
<td>0.72</td>
<td></td>
</tr>
<tr>
<td>FRS-BMI, n (%)</td>
<td>20 (51.3)</td>
<td>31 (26.4)</td>
<td>0.06</td>
<td>2.03</td>
<td>0.51</td>
<td>0.65</td>
<td>0.39</td>
<td>0.75</td>
<td></td>
</tr>
<tr>
<td>QRISK2, n (%)</td>
<td>20 (51.3)</td>
<td>23 (25.3)</td>
<td>0.00</td>
<td>3.1</td>
<td>0.51</td>
<td>0.74</td>
<td>0.46</td>
<td>0.78</td>
<td></td>
</tr>
<tr>
<td>RRS, n (%)</td>
<td>2 (5.1)</td>
<td>2 (2.2)</td>
<td>0.37</td>
<td>2.4</td>
<td>0.05</td>
<td>0.97</td>
<td>0.50</td>
<td>0.70</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: Increased CIMT or CP might be unidentified if the risk is exclusively determined by CVR calculators. Patients with a CIMT ≥0.9 mm had an average score that placed them in the low-risk strata, leading to an underestimation of their real CVR. Calculators can be helpful to estimate the CVR, however, they don’t seem to be an adequate screening tool for an increased CIMT or CP. Meanwhile, to assess CVR precisely, a carotid US should be performed in all RA patients.

Disclosure of Interests: None declared


HERPES ZOSTER IN RHEUMATOID ARTHRITIS: PROSPECTIVE SINGLE CENTER STUDY OF 390 RA PATIENTS FOR 5YEARS

Lucia Dominguez1, Vanessa Calvo-Rizo1, Paz Rodriguez-Cundin2, Virginia Portilla2, Nuria Vegas-Renega1, Francisco Manuel Antollín-Juan2, Maria Henar Rebollo Rodriguez1, Alfonso Corrales2, D. Prieto-Peria, Monica Calderon-Goecke1, Miguel A. Gonzalez-Gay1, Ricardo Blanco1, 1Hospital Universitario Marques de Valdecilla, Rheumatology, Santander, Spain; 2Hospital Universitario Marques de Valdecilla, Preventive Medicine, Santander, Spain

Background: Immunosuppressed patients such as Rheumatoid Arthritis (RA) patients have a greater risk (1.5-2 times) of presenting herpes zoster (HZ). Both, the disease itself and the use of immunosuppressive...
THE LUNG IN AN ENGLISH COHORT OF RHEUMATOID ARTHRITIS PATIENTS – AN OVERVIEW OF DIFFERENT TYPES OF INVOLVEMENT AND TREATMENT

Anna Catarina Duarte1, Joanna Porter2, Maria José Leandro3, 1Hospital García de Orta, Rheumatology Department, Almada, Portugal, 2University College London, Respiratory Medicine, London, United Kingdom, 3University College London, Rheumatology Department, London, United Kingdom

Background: Lung disease is described in 5-20% of patients (pts) with Rheumatoid arthritis (RA) and affects parenchyma, pleura, airways and vasculature; drug-induced pulmonary disease also occurs. It is associated with a higher mortality and identification of safe and effective drugs is essential.

Objectives: Characterize lung involvement in a RA cohort; evaluate rituximab (RTX) effectiveness and safety in RA associated interstitial lung disease (ILD).

Methods: Retrospective analysis of the electronic records from RA cohort followed at University College Hospital. Lung involvement was based on high resolution computed tomography. Demographic data, smoking status, complementary exams at baseline/follow-up and therapies used were analysed. A sub-analysis of pts treated with rituximab (RTX) evaluated response at 12, 24 and 36 months. Declines of 15% in gas transfer from baseline and/or 10% in forced vital capacity were recognized.

Results: From 1129 RA pts, 87 (7.7%) had documented lung involvement. Mean age at last follow-up was 68.3±12.2 years, 74.7% were female and 85.1% Caucasian. Median disease duration was 14 (IQR 8-29) years. 54% of pts had erosive disease. Rheumatoid factor was positive in 88.1% and anti-citrullinated protein antibodies in 87.8%. 23 pts had positive antinuclear antibodies (25 missing data) and 4 anti-Ro, 2 anti-Scl-70 and 2 anti-PL12. Secondary Sjögren’s syndrome occurred in 6.9%, cutaneous rheumatoid nodules in 5.7% and cutaneous vasculitis in 1.1%. 11.5% and 43.7% were current and previous smokers, respectively. Mean interval between onset of articular and pulmonary symptoms was 12.3 years; 2 pts had lung disease as a prior manifestation. Types of lung involvement are shown in table 1.

At last follow-up appointment 22 pts were still on methotrexate (MTX) and 27 had previously received it. MTX-acute pneumonitis occurred in 2 pts, both in the 1st year of treatment. RTX was used in 26 pts (57.8%) with IILD (14 nonspecific interstitial pneumonia-NISP, 8 usual interstitial pneumonia-UIP, 2 organising pneumonia-OP). The mean number of cycles was 4 (range 1-12). Two pts were concomitantly receiving mycophenolate mofetil and 1 azathioprine. RTX treatment outcomes are shown in table 2.

TABLE 1 – Characterization of different types of lung involvement

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8 cases (39%) were current smokers and 15 cases (76%) were previous smokers.

Disclosure of Interests: L. Domingues: None declared, Vanesa Calvo-Rio: None declared, Paz Rodriguez-Cundin: None declared, Virginia Portilla: None declared, Nuria Vegas-Revenga: None declared, Francisco Manuel Antolin-Juarez: None declared, Monica Calderon-Goercke: None declared, Miguel A Gonzalez-Gay Grant/research support: from Abbvie, MSD, Jansen and Roche., Speakers bureau from Pfizer, Lilly, Sobi, Celgene, Novartis, Roche and Sanofi., Consultant for: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen, Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen


FR10039

THE LUNG IN AN ENGLISH COHORT OF RHEUMATOID ARTHRITIS PATIENTS – AN OVERVIEW OF DIFFERENT TYPES OF INVOLVEMENT AND TREATMENT

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FR10039
There were 18 (20.7%) deaths, 7 of them related to ILD (4 UIP, 3 NSIP) and occurred 8.8 years after ILD diagnosis. Two were due to infection, but none was felt to be directly related to immunosuppressive therapy.

Conclusion: Lung disease occurred in 7.7% of our cohort, with ILD being the commonest presentation (51.7%). MTX was widely used in pts with lung disease with only 2 cases of acute pneumonitis. Although the number of ILD pts treated with RTX was small, the drug improved/stabilized the disease in most NSIP and OP pts. UIP is usually progressive, but our data suggest that disease progression might be put on hold with RTX, at least in a subset of pts.

REFERENCE:

Disclosure of Interests: None declared

PR0040 GENDER DISCREPANCY IN RHEUMATOID ARTHRITIS: PATIENTS’ AND PHYSICIANS’ PERSPECTIVE
Ilaria Ducci, Francesca Spinelli, Alessio Altobelli, Bruno Lucchino, Chiara Gioia, Carmelo Pirone, Guido Valesini, Fabrizio Conti, Manuela Di Franco, Policlinico Umberto 1, Rheumatology, Department of Internal Medicine and Medical Specialities, Roma, Italy

Background: Rheumatoid Arthritis (RA) is more prevalent among female individuals. Sex and gender differences may influence disease’s progression and prognosis. To date, the influence of physicians’ gender in the evaluation of RA activity is still largely unknown.

Objectives: aim of the study was to investigate a possible discrepancy in the assessment of disease activity in RA patients evaluated by male and female physicians. Further aim was to compare patient and evaluator perceptions about disease activity and global health status.

Methods: we enrolled consecutive RA patients. Each patient was separately visited by a female and a male rheumatologist of the same age and training level. Tender (TJ) and swollen joints (SJ) count was performed. Global Health (GH), physician’s (E-VAS) and patient’s (P-VAS) disease activity were reported using a visual analogue scale (VAS 0-100). Both examiners were blinded on ESR and CRP. A third rheumatologist assessed disease activity by DAS28-ESR, CDAI and SDAI.

Results: we enrolled 154 patients (122 F, 32 M). GH and P-VAS were significantly higher when collected by the female examiner compared to the male one (respectively, 41.1 ± 24.4 vs 36.1 ± 24.3, p<0.0001 and 41.7 ± 26.2 vs 35.3 ± 25.4, p<0.0001; figure 1), as well as DAS28-ESR values (3.19 ± 1.5 vs 2.97 ± 1.5, p=0.0001; figure 2) but not CDAI and SDAI. On the contrary, male E-VAS was significantly higher compared to female one (26.8 ± 27 vs 20.5 ± 20.8; p<0.0001; figure 1). GH, P-VAS and DAS28 significantly differ when the analysis was restricted to female patients (p=0.0001); among male patients, only P-VAS was significantly higher when collected by the female examiner (36.5 ± 24.7 vs 30.4 ± 25.4; p<0.0001). According to the DAS28-ESR cut off, 39.6% of patients were in remission when evaluated by the female examiner compared to 42.9% when examined by the male physician; the probability of being judged as having an active disease was not different between the female and the male examiner (p=ns). Overall, the agreement between the female and male evaluation of disease activity was high [Intraclass correlation coefficient (ICC-K) 0.92 for GH; 0.81 for E-VAS; 0.89 for P-VAS; 0.95 for DAS28-ESR; p<0.0001]. When comparing patient and examiner perception of the disease activity, P-VAS values were significantly higher than E-VAS in both female and male examiners (41.7 ± 26.2 vs 20.5 ± 20.8; 35.3 ± 25.4 vs 26.8 ± 27.1; p<0.0001; figure 3).The general agreement between male and female examiner and the whole patient population was moderate (K 0.65 and 0.62, respectively; p<0.0001), with the lowest agreement between female patients and male examiner (K 0.58; p<0.0001). Female physician had an higher agreement with both male and female patients (K 0.78, K 0.62 respectively; p<0.0001).

Conclusion: subjective measure of global health status and disease activity (GH, P-VAS) are generally higher when collected by a female examiner compared to a male one, especially among female patients. This gender discrepancy in subjective measures could influence the evaluation of disease activity indices; however, this does not affect the probability of being defined in remission. Overall, patients have a higher perception of disease activity compared to the health care providers, and the agreement between physician and patients is only moderate, with female patients having the worst perception. Female physician tend to be more in agreement with the patients’ judgement of disease activity maybe because of a more emphatic setting established by the female health care provider.

**Table 2** - Disease outcomes after treatment with rituximab

<table>
<thead>
<tr>
<th>Time of evaluation</th>
<th>6 months</th>
<th>12 months</th>
<th>24 months</th>
<th>36 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>ILD pattern</td>
<td>OP NSIP</td>
<td>UIP OP NSIP</td>
<td>UIP OP NSIP</td>
<td>UIP OP NSIP</td>
</tr>
<tr>
<td>TLCO stable/improvement</td>
<td>2/2</td>
<td>3/4</td>
<td>2/2</td>
<td>5/5</td>
</tr>
<tr>
<td>TLCO decline</td>
<td>1/4</td>
<td>25%</td>
<td>2/3</td>
<td>1/1</td>
</tr>
<tr>
<td>FVC stable/improvement</td>
<td>2/2</td>
<td>3/4</td>
<td>2/2</td>
<td>5/5</td>
</tr>
<tr>
<td>FVC decline</td>
<td>1/4</td>
<td>25%</td>
<td>2/3</td>
<td>1/1</td>
</tr>
<tr>
<td>HRCT stable/improvement</td>
<td>2/2</td>
<td>1/1</td>
<td>1/1</td>
<td>1/1</td>
</tr>
<tr>
<td>HRCT worsening</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

INCIDENCE AND TREND OF PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML) IN PATIENTS WITH RHEUMATOID ARTHRITIS IN SPAIN. (TREND-AR STUDY)

Maria Espinosa1, Alberto García-Vadillo2, Carmen Barbadillo2, Natalia Crespi-Villanueva4, Manuel Fernandez-Prada3, Maria Galindo-Izquierdo6, Hilda Godoy2, Angeles Herranz Varela1, Cristina Maclla-Villa2, Concepción Morado Quiroga3, Jose Luis Morel Hila1, Elia Perez-Fernandez3, Javier Quiroz13, Virginia Villaverde14, Cristina Martinez-Prada14, Ramón Mazzucchelli13.

Rehabilitation, Alcorcón, Spain
1Hospital Ramón Y Cajal, Madrid, Spain. 2; 7Hospital Henares, Rheumatology, Majadahonda, Madrid, Spain; 8Hospital Universitario Severo Ochoa, Rheumatology, Leganés, Madrid, Spain; 9Hospital Puerta de Hierro Majadahonda, Rheumatology, Majadahonda, Madrid, Spain; 10Hospital 12 de Octubre, Madrid, Spain; 11Fundación Hospital Alcorcón, Rehabilitation, Alcorcón, Spain; 12Fundación Hospital Alcorcón, Clinical Investigation Unit, Alcorcón, Spain; 13Hospital Universitario Fundación Alcorcón, Rheumatology, Alcorcón, Spain; 14Hospital de Móstoles, Rheumatology, Móstoles, Spain

Background: Treatment with biological agents is recognized as a potential risk factor for the development of Progressive Multifocal Leukoencephalopathy (PML), a rare and often fatal demyelinating disease of the CNS caused by John Cunningham Virus infection.

Objectives: Analyze the incidence and trend of hospital admissions for PML in patients with RA, in Spain, during the period between 1999 and 2015.

Methods: Population study based on the analysis of a national administrative database that includes a Minimum Basic Data Set (MBDS) of the income of patients with RA (ICD 9 714). Period: January 1, 1999, to December 31, 2015. The cases of PML were identified due to the presence in the primary and secondary diagnosis of the codes ICD 9 046.0 to 046.9. The population at risk was estimated through the population census of the National Institute of Statistics, with an estimated prevalence of RA of 0.5% in both sexes (0.2% in men and 0.8% in women). Crude and adjusted rates were calculated at national level. The trend was analyzed using Generalized Linear Models (GLM) using the variable year as the analysis variable.

Results: Of the total of 338,343 hospital admissions in patients with RA during the 17 years of the study period, only 14 cases (0.004%) of PML were recorded, nine (64.3%) were women and five (35.7%) men. The mean age was 69.5 years (SD 16.8); 74.56 (SD 14.8) in women and 60.09 (SD 11.0) years in men (p = 0.145). Five patients (35.7%) died during admission (2 women and 3 men) (p = 0.266). The average of the Charlson index was 2.21 (SD 1.7); 3 (SD 2.5) in women and 1.78 (SD 1.1) in men (p = 0.227).

The crude incidence rate of PML was 0.54/100,000 inhabitants * year, 0.85/100,000 inhabitants * year in men and 0.37/100,000 inhabitants * year in women. The Relative Risk male: female was 2.34. The gross rate of PML increased from 0.32/105 * year in the period 1999-2002, to 0.74 between 2011 and 2015, both in women (from 0.19 in the period 1999-2002 to 0.52 from 2011 to 2015) as well as men (from 0.82 in the period 1999-2002 to 1.64 during 2011-2015). It is estimated that this increase is of 19.7% per year.

Conclusion: In Spain, between 1999 and 2015, there has been an increase in the incidence rate of PML in patients with RA. We estimate an annual increase of 19.7%.

Disclosure of Interests: None declared


CERTOLIZUMAB PEGOL EFFECTIVENESS IN WOMEN OF CHILDBEARING AGE WITH RHEUMATOID ARTHRITIS: RETROSPECTIVE ANALYSIS OF AN INTERNATIONAL MULTICENTRE COHORT

Ennio Giulo Pavali1, Andrea Becciolli2, Roberto Caporal2, Piercarlo Scirli Pallini2, Roberto Gorfa3, Piercarlo Scirli Pallini2, R. Ionescu4, S Rednic4, A Balanescu4, E Rezus4, C Mogosan5, Catalin Codreanu5, 1LORHEN Registry and Gaetano Pini-CTO Institute, Rheumatology, Milano, Italy; 2LORHEN Registry and University of Pavia, IRCCS PoliClinico San Matteo, Rheumatology, Pavia, Italy; 3LORHEN Registry and ASST Spedali Civili, Rheumatology, Brescia, Italy; 4RRBR Registry and University of Medicine and Pharmacy “Carol Davila” Bucharest, Bucharest, Romania; 5RRBR Registry and University of Medicine and Pharmacy “Iuliu Hatieganu” Cluj, Rheumatology, Cluj, Romania; 6RRBR Registry and University of Medicine and Pharmacy “Dr. Ioan Papa” Iasi, Iasi, Romania

Background: Even though certolizumab pegol (CZP) has been licensed for the treatment of rheumatoid arthritis (RA) a long time ago, observational data in real-life settings are still lacking. Moreover, recent data on the lack of transplacental passage (1) make CZP particularly appealing for the treatment of RA women with a desire of pregnancy.

Objectives: To evaluate in a real-life international cohort the frequency of use, the clinical response, and the retention rate of CZP in RA women of childbearing age.

Methods: Data were retrospectively extracted from the Italian LORHEN and the Romanian Registry of Rheumatic Diseases (RRBR) registries, which include all RA patients treated with CZP between December 2010 and October 2018. The analysis was limited to women who received CZP as first-line biologic agent. The study population was stratified according to childbearing age (18-49 versus >49 years). The 6-, 12- and 24-month clinical response was evaluated as the proportion of patients achieving Disease Activity Score 28 (DAS28) remission and compared between the subgroups by a chi-squared test. The 5-year retention rate was calculated by the Kaplan-Meier method and compared between the subgroups by log-rank test.

Results: The whole cohort included 630 RA patients treated with CZP. According to the inclusion criteria, the study population consisted of 308 female RA patients (mean [± standard deviation, SD] age 54±12.1 years; mean disease duration 8.7±8.4 years; baseline DAS28 5.25±1.72, female RA patients (mean [± standard deviation, SD] age 54.2±12.1 years; mean disease duration 8.7±8.4 years; baseline DAS28 5.25±1.72, ±7.2, respectively; p<0.001), no other significant differences in baseline characteristics between the childbearing (n=97, 31.5%) and non-childbearing women at each timepoint (39.4% vs 25.4, p=0.02 at 6 months; 52.8% vs 37%, p=0.014 at 12 months; 52% vs 34.2, p=0.014 at 24 months). The overall 5-year retention rate was 37.1%, with a higher (but not statistically significant) persistence in the childbearing versus non-childbearing subgroup (55.1% vs 37.1%).
CHARACTERISTICS OF PATIENTS WITH RHEUMATOID ARTHRITIS ADMITTED TO AN INTENSIVE CARE UNIT IN SPAIN FROM 2005–2015. TREND-AR STUDY

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OBJECTIVES: To analyse the clinical features of patients with Rheumatoid Arthritis (RA) that were admitted to an Intensive Care Unit (ICU) from January 2005 to December 2015.

METHODS: A retrospective observational population study was conducted analysing the national database that includes the Minimum Basic Data Sets (MBDSs) of admissions of RA patients to an ICU during the 2005–2015 period. Demographic characteristics, length of stay, clinical course, outcome and the MBDS codes for the main reason of admission were recorded. The cases were detected by the presence of their CIE-9 codes in the primary or secondary diagnoses. Statistical analysis was performed with stata 15.0 software.

RESULTS: During the 11 years of the study, a total of 2719 RA patients required 2806 admissions to an ICU. Average age was 69.7 ± 10.8 years and women constituted 58.5% of the cases. 30% of the patients admitted to an ICU had requirement of ≥ 3 previous admissions and 11% required readmission within the next 30 days. Average Charlson index was 2.33 ± 1.4. Average length of stay was 9.3 ± 14 days and 64.2% died in the ICU during hospitalization. The main causes of hospitalization were cardiovascular events (45.7%), lung diseases (16%) and infections (10%). In the univariate analysis mortality was significantly increased in patients presenting infections (90%), lung disease (89%), severe hepatopathy defined by ascites and/or encephalopathy and/or gastrointestinal bleeding (88%), nephropathy/kidney disease (73%) and a higher Charlson index (2.4 vs 2.2). Multivariate analysis showed that mortality was increased among patients presenting respiratory complications and infections.

CONCLUSION: The most frequent hospitalization causes for patients with Rheumatoid Arthritis in Spain between 2005 and 2015 were cardiovascular, pulmonary and infectious diseases. RA patients that were admitted to the ICU showed an increased mortality. This increased mortality was mainly found in patients presenting respiratory or infectious conditions.

Disclosure of Interests: None declared

Changes in Left Ventricular Systolic Function Are Predicted by Disease Severity in Patients with Rheumatoid Arthritis Without Prior Cardiovascular Disease

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Background: Occult left ventricular (LV) systolic dysfunction (LVSD) is associated with worse cardiovascular outcomes in asymptomatic patients with arterial hypertension and/or diabetes mellitus. In these patients, LV systolic function may worsen or improve overtime. However, little is known about the changes in LV function during follow up of patients with rheumatoid arthritis (RA).

Objectives: This prospective study analyzed incidence and factors associated with changes in LV systolic function in patients with RA without known cardiovascular disease.

Methods: One-hundred-forty outpatients with RA without overt cardiac disease were recruited between March and December 2014. Patients underwent clinical and echocardiographic evaluation at baseline and after a median period [min-max] of 35 [23-47] months of follow up. Stress-corrected midwall fractional shortening (sc-MFS) was used as measure of LVSD and considered impaired if <86.5%. Disease activity was assessed with the clinical disease activity index (CDAI).

Results: Impaired sc-MFS at follow up (sc-MFS-FU) was detected in 60/140 (43%) patients who were compared with 80 patients with normal sc-MFS-FU. Baseline sc-MFS did not differ significantly between the two groups, which appeared to diverge significantly soon after 1-year of follow up (figure). Baseline anti-citrullinated protein antibodies (ACPA) positivity, high disease activity (CDAI>10) and duration of RA were independently associated with impaired sc-MFS-FU at multiple logistic regression analysis. Among these parameters, ACPA had the highest sensitivity (80%) whereas high disease activity had the highest specificity (89%) for sc-MFS-FU. A predictive score including all three predictors (ACPA status, CDAI>10 and duration of RA) detected impaired sc-MFS-FU with a sensitivity of 76% and specificity of 82% (AUC 0.80 [IC 0.72-0.88], p<0.0001).

Conclusion: This study supports the hypothesis that changes overtime in LVSF in patients with RA are associated with ACPA, high disease activity and duration of disease.

Polypharmacy: A Rarely-Discussed Problem in Rheumatoid Arthritis. Data from a Large Real-Life Study

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Background: Polypharmacy is concomitant use of five or more drugs and is usually associated with various comorbidities and advanced age. The already demonstrated consequences of polypharmacy are increased side effects, drug interactions, increased hospitalizations, drug handling difficulties, reduced adherence, and even increased mortality. Rheumatoid arthritis (RA) is a chronic systemic disease with preferential involvement between the third and fifth decades. In the process of stabilizing disease andcomorbidities, patients with RA frequently require combined use of several drugs. Despite the possible negative consequences of polypharmacy in RA, there is a shortage of studies in literature.

Objectives: Evaluate prevalence and factors associated with polypharmacy in patients with RA in a real-life setting.

Methods: This is a cross-sectional part of the Rheumatoid Arthritis in Real Life (REAL) study that analyzed RA patients in a real-life context from August to October 2015 in 11 public health services in Brazil. Statistical analysis involved obtaining frequencies of the variables of interest and multiple Poisson regression analyses.

Results: We evaluated 792 patients, of whom 89% were women, with median age of 56.6 years. 78.73% had a positive rheumatoid factor and 55.2% had an erosive disease. The median Disease Activity Score was 3.52, the median CDAI score was 9. Of the patients, 67.9% used 5 or more drugs as follows: mean of 2.8 and maximum of 5 drugs for RA, mean of 2.7 and maximum of 9 different types of medications for comorbidities, and mean of 5.5 and maximum of 11 drugs in total. The most commonly used drugs, besides specific drugs for underlying diseases, were vitamin D (63.8%), folic acid (61.1%), calcium (57%), and antihypertensive drugs (47%). In the multivariate analysis, the use of corticosteroids, methotrexate, and biological DMARDs and number of comorbidities (all with P <0.001) were statistically significant. Age, smoking, rheumatoid factor positivity, and measures of activity by compound disease activity indexes were not associated with polypharmacy.

Conclusion: The prevalence of polypharmacy was high (67.9%) in this population with RA, much higher than that described for elderly populations and other chronic diseases. This data can serve as an alert for this important and rarely-discussed aspect of RA.

References:

Disclosure of Interests: Ana Paula Gomides Grant/research support from: Has received personal support and consulting fees from Pfizer and Janssen, Consultant for: Has received personal support and consulting fees from Pfizer and Janssen, Paid instructor for: Has received personal support and consulting fees from Pfizer and Janssen, Cleandro Albuquerque

SPECIFICITY OF THERAPY FOR RHEUMATOID ARTHRITIS PATIENTS UPON THYROID INVOLVEMENT IN THE AUTOIMMUNE DISEASE

I. Zborovskaya1, Olga Paramonova2, Olga Rusanova2, O. Zborovskaya3, I. Gontar1.

Objectives: To study the specifics of therapy for rheumatoid arthritis patients upon thyroid involvement in the autoimmune disease.

Methods: The study included patients diagnosed with rheumatoid arthritis from 2010 to 2020, without any exclusion criteria. Rheumatoid arthritis activity was assessed utilizing DAS-28 Calculator.

The presence of thyroid lesion was evaluated by means of clinical workup, ultrasound examination, and laboratory tests, including measuring the concentration of TTH, free T3, T4, as well as anti-TPO. Antibodies to T3 and T4 (anti-T3 and anti-T4) were measured by enzyme immunoassay, and the findings were shown in absorbance units. The cut-off values of positive and negative findings for anti-T3 (0.098 absorbance units) and anti-T4 (0.093 absorbance units) were calculated by ROC curve analysis utilizing sera from relatively healthy donors (n = 39). The results were shown as an arithmetic mean ± standard error (M ± m).

Results: 72 patients with rheumatoid arthritis participated in the study. The mean activity of rheumatoid arthritis assessed by DAS 28 Calculator was 3.2 ± 1.4 points. Extra-articular presentations were detected in 20 patients, 5 of whom showed clinical manifestations of thyroid lesion. All five patients were marked by low TTH and a high activity of rheumatoid arthritis (4.8 ± 1.9 points of DAS28). In 73 patients antibodies to T3 were detected (0.128 ± 0.047 absorbance units). Apart from the thyroid gland, no clear association between these antibodies and lesions of other organs or systems were noted. A statistically significant tendency for an increase in X-ray stage linked to increased antibodies to T4 was noted (p = 0.034; ANOVA); an inverse relation was noted for antibodies to T3 (p = 0.034; ANOVA). The association with DAS 28 for antibodies to T4 (r=0.525, p=0.031) and for antibodies to T3 (r=-0.391, p=0.040) was also inverse and statistically significant. Besides, another statistically significant correlation was revealed between the value of DAS 28 and TTH concentration (r=-0.330, p=0.046).

Conclusions: The available findings demonstrate that a high activity of rheumatoid arthritis is associated with hypothyroidism development, despite the tendency for increased count of antibodies to T4 which is typical of rheumatoid arthritis. The possibility to modify the activity of rheumatoid arthritis by correcting thyroid dysfunction is very important both for developing a strategy of managing drug-resistant cases of rheumatoid arthritis, and for the management of this condition in general.

REFERENCES:


Acknowledgement: The paper examines the effect of thyroid dysfunction on the treatment of patients with rheumatoid arthritis.

Disclosure of Interests: None declared


SPECIFICITY OF THERAPY FOR RHEUMATOID ARTHRITIS PATIENTS UPON THYROID INVOLVEMENT IN THE AUTOIMMUNE DISEASE

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Conclusions: The available findings demonstrate that a high activity of rheumatoid arthritis is associated with hypothyroidism development, despite the tendency for increased count of antibodies to T4 which is typical of rheumatoid arthritis. The possibility to modify the activity of rheumatoid arthritis by correcting thyroid dysfunction is very important both for developing a strategy of managing drug-resistant cases of rheumatoid arthritis, and for the management of this condition in general.

REFERENCES:


Acknowledgement: The paper examines the effect of thyroid dysfunction on the treatment of patients with rheumatoid arthritis.

Disclosure of Interests: None declared

Cognitive Impairment and Rheumatoid Arthritis in Moroccan Patients

Azzouzi Hamida, Fadoua Chennouf, Eddarami Jalila, Ichchou Linda.

Muscle Mass Index less than 5.45 kg/m² in women and less than 7.26 kg/m² in men, while sarcopenic obesity was defined by the presence of sarcopenia more abdominal obesity. The GCs use and dosage (prednisone and methylprednisolone) were analyzed reviewing the clinical records. Anti-cyclic citrullinated peptides (anti-CCP) antibodies, rheumatoid factor (RF) levels, high sensitivity C reactive protein (hsCRP), erythrocyte sedimentation rate (ESR) were determinate. The morning stiffness, clinical activity of disease (DAS28-ESR score) and disability index functional (HAQ-DI) were measurement.

Results: In this study 86% of the population had sarcopenia and 44% sarcopenic obesity. The 62.8% under GCs therapy. The prednisone dosages was positively associated to sarcopenia (>5 mg/day; OR=4.3, p=0.003) and sarcopenic obesity (OR=3.2, p=0.06). The intramuscular pulse of methylprednisolone (40 mg/kg) was associated to sarcopenic obesity phenotype (OR=2.61, p=0.09). Regarding the clinical and serological markers in RA, high disease activity (DAS28-ESR score) was associated to sarcopenia (OR=6.6, p=0.01) and sarcopenic obesity (OR=6.3, p=0.02). The morning stiffness (p=0.03), RF (p=0.05), anti-CCP positive (p=0.01) and HAQ-DI score (p=0.04) were too associated, mainly to sarcopenic obesity.

Conclusion: Sarcopenia and sarcopenic obesity are associated to GCs dosage and with serological and disease activity markers in RA patients from southern Mexico. So that is needed promote monitoring and management of sarcopenia and sarcopenic obesity in RA patients.

REFERENCE:

Disclosure of Interests: None declared

CARdiovascular risk in the rheumatoid arthritis PATIents of the Gulf Corporation Council-GCC: what contribute to the carotid INTima media thickness

Suad Hannawi, Haifa Hannawi, Issa Al Salmi,

Background: Rheumatoid arthritis (RA) is a common inflammatory joint disease that occurs in 1-3% of population. RA patients are at higher risk of cardiovascular disease (CVD). This accelerated atherosclerosis can’t be fully explained by the traditional CVD risk factors. The CVD risk factors had never been investigated in the RA patients of Gulf Corporation Council (GCC).

Objectives: For the first time, this study assesses the CVD as manifested by carotid intima media thickness (cIMT) and the CVD risk factors (traditional and non-traditional) in RA GCC-population.

Methods: 216 RA (179 (83%) F and 37 (17%) M) GCC patients, who were free of atherosclerosis (CVD & Cerebrovascular diseases) included over 5 years (2013-2018). Diabetic, hypertensive, gout, renal and thyroid patients, pregnant, current smokers and those with history of smoking, and patients on diuretics medications were excluded. cIMT ultrasound (US) measurements were obtained using a real-time US scanner equipped with a 7.5-MHz linear probe. Blood tests (full blood counts, liver function, renal profile, and inflammatory markers), demography details, and body mass index (BMI) had been obtained within the same week of the cIMT scan. The correlation between cIMT and other variables were calculated using simple linear and multivariate regression analysis.

Results: The mean cIMT was 0.58 ± 0.11 mm (Min 0.28, Max 0.98). The mean age was 48 ± 13 years (48 ±12 yrs for females, 50±16 yrs for males, p= 0.279).

univariate regression analysis showed a positive linear relationship between cIMT and age of the participants (p=0.001, CI: 0.00, 0.01), total cholesterol (p=0.005, CI: 0.01, 0.01), high density lipoprotein (HDL) (p=0.001, CI: 0.00, 0.01). The mean level of education was significantly related to a-MMSE (p=0.0001).

Conclusion: It is certainly true that the interpretation and evaluation of cognitive functions in a difficult task, especially in an illiterate and disabled patient. However, in our study A-MMSE results were low even after test repetition, and in a state of disease remission. Although these results underscore the high frequency of cognitive impairment in RA patients, we estimate that further studies are eligible to confirm causality.

REFERENCES:
DURATION OF EXPOSURE TO BIOLOGICS AND BODY COMPOSITION IN MEN WITH RHEUMATOID ARTHRITIS

Background:

Higher inflammatory load associates with increased risk of cardiovascular events in patients with rheumatoid arthritis (RA). We recently reported that occult atherosclerosis burden on coronary computed tomography angiography (CCTA) predicted long-term cardiovascular events (CVE) in RA above and beyond cardiac risk factors or scores. We further showed that higher cumulative inflammatory burden independently predicted coronary plaque progression.

Objectives:

To explore whether the duration of exposure to biologic DMARDs and/or statins during the study period mitigates the effect of cumulative inflammatory load on coronary plaque progression.

Methods:

One hundred-one participants with a baseline CCTA underwent a follow-up evaluation in 8±3.6 months. Plaque burden was reported as segment involvement score (SIS, describing the number of coronary artery segments with plaque per patient) and coronary artery calcium (CAC), quantified by the Agatston method. Robust logistic and linear regression models evaluated effects of predictors on plaque (SIS) progression and CAC change, respectively. Predictors of interest were time-averaged c-reactive protein (CRP), duration of bDMARD exposure (years), duration of statin exposure (years), and their 2- and 3-way interactions. Models were controlled for age and baseline hypertension. Significant interactions were subsequently decomposed and examined based on a median split for the duration of biologic and statin exposure.

Results:

A significant interaction between inflammation and statin exposure duration was observed for plaque progression (p=0.019 (figure 1A); in patients with shorter statin exposure (<1 year), higher inflammation predicted a greater likelihood of plaque progression [odds ratio (OR)=1.90, 95% confidence interval (CI)=1.15 to 3.14, p=0.012. By contrast, longer statin exposure (>1 year) attenuated that risk [OR=0.57, 95% CI=0.35 to 0.80, p=0.001] in patients with longer exposure to statins (>1 year), inflammation was not related to plaque progression [OR=1.25, 95% CI=0.48 to 3.31, p=0.65] or CAC change [OR=1.06, 95% CI=0.43 to 0.21, p=0.52]. In patients with longer biologic exposure (>5 years) the length of treatment with statin did not moderate the effect of cumulative inflammation on plaque progression [p=0.229, figure 1].

Conclusion:

The relationship between cumulative inflammation, length of treatment with bDMARDs, statins and their ultimate impact on coronary plaque progression in RA are highly nuanced. The effect of the duration of statin exposure on coronary plaque burden progression seems relevant only in the context of insufficient biologic exposure; shorter treatment with statins in that setting allows for significant coronary plaque progression in response to higher cumulative inflammatory load. In contrast, longer statin exposure attenuates that risk.

REFERENCES:


Disclosure of Interests:

None declared

FR10053

DURATION OF EXPOSURE TO BIOLOGICS AND STATINS MODERATES THE EFFECTS OF CUMULATIVE INFLAMMATION ON CORONARY ATHEROSCLEROSIS PROGRESSION IN RHEUMATOID ARTHRITIS

George Karpouzas, Sarah Ormseth, Elizabeth Hernandez, Matthew Budoff. Harbor UCLA Medical Center, West Carson, United States of America

Background:

Rheumatoid arthritis (RA) is a chronic immune inflammation of the joints, leading to early disability of patients at high risk of cardiovascular events and osteoporotic fractures. This problem is important today in men with RA, because, due to more frequent severe disease and increased mortality in the year after the fracture. Reduction of bone mineral density (BMD) and muscle mass are significant predictors of fractures, which leads to the high importance of studying the state of BMD and body composition.

Objectives:

Improving the diagnosis of osteoporosis in patients with RA of the male gender with the regard of BMD and body composition.

Methods:

The study involved 110 male patients with a documented diagnosis of RA at the age of 59 [53; 65] years. Depending on the taking of glucocorticosteroids (GCS) all patients was allocated two groups: I subgroup - 60 patients who are not taking GCS and subgroup II - 50 patients who are taking GCS. The control group consisted of 30 healthy men comparable by the age and body mass index. The study of BMD at the lumbar spine (L1-L4) and femoral bone was carried out, using the «Whole body» («The whole body»). Assessment of body composition was carried out, using the «Whole body» (=The whole body). Sarcopenia was diagnosed as a decrease in lean mass index of less than 7.26 kg/m².

Results:

63.6% of patients with RA showed a reduction of BMD corresponding osteopenia/OP. OP was diagnosed in 28 (25.5%) patients with RA, and osteopenia - in 42 (38.2%). The detection rate of OP in the second subgroup was significantly higher (p<0.05), than in the first subgroup (48% and 5% respectively). The most significant decrease in BMD was observed in the neck of the femur in the main group as a whole and in individual subgroups. There was a negative correlation degree of activity of RA and indicators of BMD of the lumbar spine (r=-0.4, p<0.05) and proximal femur (r=-0.38, p=0.05). Assessment of body composition showed that patients of the main group were significant decrease in the total lean mass (LM) of the body, and the trunk and limbs of LM compared with patients of the control group (p<0.05). Sarcopenia detected in 66 (60%) of RA patients, whereas in the control group it was absent. In 44 (67.2%) male patients with RA with sarcopenia decreased BMD to the level of osteopenia (34.9%) and OP (31.8%). Obtained a negative

Disclosure of Interests:

George Karpouzas: Grant/research support from: Roche-Genentech, Pfizer, Speakers bureau: BMS, Sanofi-Genzyme-Regeneron, Janssen, Roche-Genentech, Sarah Ormseth: None declared, Elizabeth Hernandez: None declared, Matthew Budoff: None declared

FR10052

BODY COMPOSITION IN MEN WITH RHEUMATOID ARTHRITIS

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Background:

Rheumatoid arthritis (RA) is a chronic immune inflammation of the joints, leading to early disability of patients at high risk of cardiovascular events and osteoporotic fractures.

Objectives:

To study the body composition at the lumbar spine (L1-L4) and femoral bone of male patients with RA and control men.

Methods:

The study of BMD at the lumbar spine (L1-L4) and femoral bone was carried out, using dual-energy x-ray absorptiometry using a bone mineral density –STRATOS dR® (DMS, France). Assessment of body composition was carried out, using the «Whole body» (=The whole body). Sarcopenia was diagnosed as a decrease in lean mass index of less than 7.26 kg/m².

Results:

63.6% of patients with RA showed a reduction of BMD corresponding osteopenia/OP. OP was diagnosed in 28 (25.5%) patients with RA, and osteopenia - in 42 (38.2%). The detection rate of OP in the second subgroup was significantly higher (p<0.05), than in the first subgroup (48% and 5% respectively). The most significant decrease in BMD was observed in the neck of the femur in the main group as a whole and in individual subgroups. There was a negative correlation degree of activity of RA and indicators of BMD of the lumbar spine (r=-0.4, p<0.05) and proximal femur (r=-0.38, p=0.05). Assessment of body composition showed that patients of the main group were significant decrease in the total lean mass (LM) of the body, and the trunk and limbs of LM compared with patients of the control group (p<0.05). Sarcopenia detected in 66 (60%) of RA patients, whereas in the control group it was absent. In 44 (67.2%) male patients with RA with sarcopenia decreased BMD to the level of osteopenia (34.9%) and OP (31.8%). Obtained a negative

Disclosure of Interests:

None declared, Matthew Budoff: None declared
correlation parameters LM and absolute 10 years risk of osteoporotic fractures (r=0.302, p<0.05) on FRAX. 

Conclusion: 63.6% of men suffering from RA, there was a decrease in BMD, the corresponding OP/osteopenia with a primary reduction of BMD at the femoral neck. Decrease BMD in patients with RA was significantly associated with a high degree of disease activity (r=0.4, p< 0.05). Taking GCS had no significant effect on BMD at the femoral neck. Analysis of body composition in 55% of patients with RA showed a reduction in the level of LM limbs sarcopenia. Obtained correlation lower BMD and LM limbs (p<0.05; r=0.28).

Thus, in patients with RA male along with OP/osteopenia showed a significant decrease in LM that given the biomechanics of movement can be an additional risk factor for falls and fractures.

REFERENCES:

Disclosure of Interests: None declared

FRID0053 ACCELERATED ATHEROSCLEROSIS IN PREMENOPAUSAL WOMEN WITH RHEUMATOID ARTHRITIS (15 YEARS PROSPECTIVE STUDY)

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Background: Rheumatoid arthritis (RA) is chronic inflammatory disease, associated with increased mortality and morbidity due to higher cardiovascular risk in these patients.

Objectives: Traditional risk factors are not the only answer for accelerated atherosclerosis. In long term prospective study, we investigated the relationship between asymptomatic atherosclerosis and traditional risk factors as well inflammatory markers in patients with RA and matched healthy controls.

Methods: In 60 RA premenopausal women and 34 matched controls values of laboratory test results, concentrations of inflammatory mediators, matrix metalloproteases (MMP) and markers of inflammation were measured. Using B-mode ultrasonography carotid intima-media thickness (cIMT) and plaques occurrence (markers of asymptomatic atherosclerosis) as baseline and after 15 years of observation were defined in both groups. The differences in concentrations of inflammatory mediators, MMPs and markers of inflammation were compared. The relationship of inflammatory mediators and markers, MMPs and markers of asymptomatic atherosclerosis was examined using regression models.

Results: After the follow up statistically significant higher values of inflammatory markers like selective adhesion molecules ICAM & VCAM, interleukin 6 (IL-6), tumour necrosis factor alpha (TN alpha) and MMP-3 in patient’s group was found. Among traditional risk factors only sedentiation rate and CRP levels were statistically higher in patient’s group. More plaques were found in patients’ group (12.9% vs. 42.4%; p=0.005), patients had also higher values of cIMT (p=0.0001). Using multiple linear regression analysis only VCAM was found as independent prognostic factor for plaques occurrence (p=0.016), but not for cIMT (p=0.314) in RA patients after the follow up.

Conclusion: Asymptomatic atherosclerosis is accelerated in premenopausal women with RA patients. The results of our study showed the association between the inflammation and accelerated atherosclerosis, VCAM was found as independent risk factor for plaques occurrence in these patients.

REFERENCES:

Disclosure of Interests: None declared

FRID0054 CHARACTERISTICS OF PATIENTS WITH ELDERLY-ONSET RHEUMATOID ARTHRITIS AND INVESTIGATION OF DRUG THERAPY

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Background: It is expected that the increase in average life expectancy in recent years would also be observed even in patients with rheumatoid arthritis (RA)

Objectives: We compared data for RA patients obtained between 1991 and 2018 to clarify the current clinical picture of RA in elderly patients.

Methods: We evaluated 429 and 368 RA cases seen at our department in 1991 and 2018, respectively. The patient ages and sex ratios in the two groups were first compared, and then the clinical features of 260 patients with younger-onset RA (YORA; onset age ≤65 years) and 108 patients with elderly-onset RA (EORA; onset age >65 years) in the 2018 group were evaluated. All patients satisfied the 1987 and 2010 Rheumatoid arthritis classification criteria for RA, and their data were obtained from the medical records. Patient data at the onset of RA were used. The study protocol was approved by the Institutional Review Board of Niigata University. All statistical analyses were performed with SPSS ver. 13 for Windows, and differences at p<0.05 were considered to be statistically significant.

Results: The peak age at RA onset was 50s-60s in 1991 and 60s-70s in 2018. In 1991, the male-female ratios in the <65 yr- and >65 yr-age groups were 0.14 and 0.19, respectively, whereas the corresponding ratios in 2018 were 0.25 and 0.38, respectively. Although the proportion of elderly patients increased, homogeneity testing of the odds ratio revealed no significant difference. Among the 368 RA patients in the 2018 group, initial involvement of large joints was more frequent in those with EORA, whereas initial involvement of small joints was more frequent in those with YORA (p<0.05). Statistical analysis demonstrated no significant inter-group differences in hemoglobin, WBC, BUN, uric acid, CRP, ESR or serum creatinine, but the estimated glomerular filtration rate was significantly higher in the YORA group (P<0.00). The frequencies of hematuria and proteinuria (>1.0 g/Cl) showed no inter-group differences. The frequency of RF positivity also did not differ between the groups, but the RF titer was higher in the YORA group (p<0.01). ACPA showed no inter-group difference in terms of either the frequency of positivity or titer. Among other features after diagnosis, AA amyloidosis was observed in only 7 (2.7%) of the YORA patients. RA proceeded PMR in 7 patients in each group, and the frequency of PMR was significantly (P<0.01) higher in patients aged >60 years. For therapy, MTX was used in about 70% of YORA patients, its use being more frequent than EORA patients (p<0.01), although the dose employed did not differ significantly between the two. About half of all patients received steroid, and neither the frequency nor the dose differed significantly between the YORA and EORA groups. Biological agents were used in 61% of YORA patients and 29% of EORA patients, the difference being significant (p<0.01). Abatacept was used significantly (p<0.05) more often in the EORA group because of the low frequency of severe infections, but the frequency of use of other biological agents and Jak inhibitors did not differ significantly between the groups.

Conclusion: The characteristics of EORA patients differ from those of YORA patients. Diagnosis requires attention to PMR. In YORA, attention to amyloidosis is also required in view of the fact that treatment was insufficient in the past. Pharmacotherapy should be based on the characteristics of aging in elderly patients with RA. The diagnosis and treatment of RA in elderly patients is an issue of future concern.
AN EQUATION FOR ESTIMATED CARDIORESPIRATORY FITNESS IN RHEUMATOID ARTHRITIS PATIENTS IS NEEDED

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Background: RA patients are deconditioned and on average have decreased cardiopulmonary fitness compared to healthy controls. The objective was to develop a new equation for eCRF specifically for RA patients, using previously reported measures of eCRF from healthy individuals.

Methods: Among participants with self-reported RA in the second and third surveys of the Norwegian population-based Nord-Trøndelag Health Study (HUNT2 and 3), RA patients were identified from hospital case files using standardized diagnostic criteria. The mean eCRF of participants with and without RA were calculated and the 95% confidence intervals compared.

Table 1. Mean eCRF (mL/kg x min) and 95% CIs of RA patients and participants without RA attending HUNT2 and 3. Age categories with n=8 RA patients in grey.

<table>
<thead>
<tr>
<th>HUNT2</th>
<th>Men (no RA)</th>
<th>Men (RA)</th>
<th>Women (no RA)</th>
<th>Women (RA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean eCRF (CI), n</td>
<td>Mean eCRF (CI), n</td>
<td>Mean eCRF (CI), n</td>
<td>Mean eCRF (CI), n</td>
<td></td>
</tr>
<tr>
<td>30-39</td>
<td>50.3(50.2-50.5)</td>
<td>49.5(49.5-50.4)</td>
<td>38.7(38.5-39.0)</td>
<td>39.3(39.0-39.7)</td>
</tr>
<tr>
<td>40-49</td>
<td>38.4(38.2-38.6)</td>
<td>37.3(37.0-37.5)</td>
<td>36.2(35.9-36.5)</td>
<td>36.8(36.5-37.1)</td>
</tr>
<tr>
<td>50-59</td>
<td>36.2(36.0-36.4)</td>
<td>35.4(35.2-35.6)</td>
<td>34.3(34.0-34.6)</td>
<td>34.9(34.6-35.2)</td>
</tr>
<tr>
<td>60-69</td>
<td>34.8(34.6-35.0)</td>
<td>34.0(33.7-34.3)</td>
<td>33.0(32.8-33.2)</td>
<td>33.6(33.3-33.9)</td>
</tr>
<tr>
<td>70-79</td>
<td>33.3(33.1-33.5)</td>
<td>32.5(32.2-32.8)</td>
<td>31.5(31.3-31.7)</td>
<td>32.1(31.8-32.4)</td>
</tr>
<tr>
<td>80+</td>
<td>32.0(31.8-32.2)</td>
<td>31.2(30.9-31.4)</td>
<td>30.2(29.9-30.6)</td>
<td>30.8(30.5-31.1)</td>
</tr>
</tbody>
</table>

Mean eCRF (CI), n

Table 1. Mean eCRF (mL/kg x min) and 95% CIs of RA patients and participants without RA attending HUNT2 and 3. Age categories with n=8 RA patients in grey.

Conclusion: The eCRF CIs of RA patients and participants without RA were overlapping in all age categories except for men aged 60-69 years in HUNT 3 (Table1). This is contradictory to previous findings where RA patients were deconditioned compared to healthy controls (1). A probable explanation is that equations for eCRF were developed from healthy populations, and therefore overestimate eCRF in RA patients. For better CRD risk management including CRF as an important risk factor, an equation for eCRF developed specifically for RA patients is needed.

REFERENCES:

Disclosure of Interests: None declared

NESTED CASE-CONTROL STUDY: ASSOCIATED FACTORS WITH INSulin RESISTANCE IN A RHEUMATOID ARTHRITIS INCEPTION COHORT

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Objectives: To assess insulin resistance (IR) in patients with rheumatoid arthritis (RA) and compare it with healthy controls and to analyze the association between the accumulated inflammatory burden in patients with RA and IR.

Methods: Design: Nested case-control study. Population: consecutive RA-patients (ACR/EULAR 2010 criteria), >16 years, selected from a prospective inception cohort (diagnosis of RA between 2007 and 2011). Patients with Diabetes Mellitus (according to ADA 2010 criteria) were excluded. Controls: sex-, age- and BMI-matched controls were collected from a health center in our hospital area. Protocol: Cases and controls were evaluated by a rheumatologist. Clinical data of disease activity (RA patients), analytical values and oral glucose tolerance test (OGTT) were determined. Main outcome: IR measured by the homeostasis model for insulin resistance (HOMA-IR) (IR=[2.29 μU/mmol x mL/mg] (Secondary outcome: IR measured by quantitative insulin sensitivity check index (QUICKI))<0.337) and by the homeostatic model assessment of β-cell function (HOMA β). Variables: Demographic, clinical-analytical variables, Disease Activity Score 28 points (DAS28-ESR), Health Assessment Questionnaire (HAQ), BMI (according to WHO classification) and glucose and insulin before and after OGTT values. Statistical analysis: Descriptive and paired T-test or Chi-square test followed by Multivariate Linear Regression in RA patients (Dependent variable: HOMA-IR).

Results: Two hundred subjects were studied, 31 of them were excluded after OGTT. Finally 169 subjects were included; 89 RA and 80 controls. The mean age of patients with RA was 56.6±10.3 years. Most of them were women (75.3%), with seropositive (FR 82.0% y ACPA 75.3%) and erosive (81.1%) disease. The average duration of the disease was 98 months (81.1 years). The delay in the diagnosis of RA was 10.9 months (5.4 - 25.6) with a mean DAS28 index since the beginning of the disease of 3.11 (0.8). Differences between clinical characteristics and in relation to IR between cases and controls are shown in Table 1. No significant differences in the proportion of subject with IR in cases and controls were observed and 28.1% of patients with RA had IR. Of the 25 patients with IR, the majority, 68%, presented a DAS28 score> 3.2 (moderate-high activity index). In multivariate analysis, the independent variables associated with IR in patients with RA were: Obesity [OR=6.01; β=1.795 (p=0.002), disease activity (CR=2.77; β=1.021 [p=0.009]) IL-1β [OR=1.59; β=0.484 (p=0.024)]. This model would explain 37.5% of the variability of the IR (R²=0.375).

Conclusion: We did not find an increased IR in patients with RA compared with healthy controls, which may be due to adequate treatment and good control of inflammatory activity in the most of patients with RA. Obesity, inflammatory activity (measured by mean DAS28 index) and IL-1β were the predictors of IR in patients with RA in our study.

REFERENCES:
Acknowledgement: I thank the Rheumatology Spanish Society for Grant support in 2015 -2017 for this work.

Disclosure of Interests: Sara Manrique Arija Speakers bureau: ABBvie, MSD, Janssen, Lilly, Roche, Pfizer, Novartis., Natalia Mena-Vázquez: None declared, Irrmaculada Ureña : None declared, F. Gabriel Jiménez-Núñez: None declared, Clara Fuego-Varela: None declared, Antonio Fernandez-Nebro: None declared


FRID057 INSULIN RESISTANCE IN ELDERLY ONSET RHEUMATOID ARTHRITIS AND POLYMYALGIA RHEUMATICA

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Background: Rheumatoid arthritis (RA) patients have a higher insulin resistance (IR) and some studies report that it is present at diagnosis. Systemic inflammation has been pointed out as the reason. However, data on polymyalgia rheumatica (PMR) are controversial.

Objectives: To analyse IR in a group of untreated patients with a recent diagnosis of RA and PMR, and to establish predictive factors related with IR.

Methods: Longitudinal observational study of patients older than 60 years, newly diagnosed with elderly-onset AR (ACR/EULAR 2010) and PMR (ACR/EULAR 2012) with healthy control group of the same age. Inclusion: consecutive and voluntary. Exclusion: patients with insulin-dependent diabetes. Follow-up time: 12 months. The clinical-epidemiological, anthropometric and analytical characteristics were collected. IR was calculated by HOMA-IR ([homeostatic model assessment of insulin resistance) = glucose (mg/dL) * insulin (mUI/L)/405] at baseline and at 12 months. HOMA-IR>2.75 was considered IR (according to Spanish data).

The statistical study was performed with Stata 15.1.

Results: We recruited 42 patients with RA, 18 with PMR and 18 healthy controls. None of them had received treatment with corticosteroids or with DMARD at the baseline visit. Baseline characteristics are summarized in the table.

At baseline visit, 66.7% of patients with elderly-onset RA had IR, compared with 33.3% of controls (p=0.024) and 27.8% of PMR (p=0.006). Therefore, the prevalence of IR in patients with RA doubled that of controls and patients with PMR before starting treatment. After 12 months of evolution and treatment, patients with RA and IR decreased from 66.7% to 51.2%, not being statistically significant (p=0.179). On the other hand, the percentage of patients with PMR and IR remained the same (27.8%). The differences in IR between RA and PMR at 12 months remained statistically significant (p=0.048).

The results we decided to analyze the predictive factors related with IR only in the 42 patients with RA. In the univariate logistic regression analysis, the predictors of presenting IR were the BMI, the abdominal perimeter and the scapular girdle involvement. Specifically for BMI, for each of 2 kg/m2 the probability of having IR was 1.24 times higher (OR=1.24, IC95%: 1.12-1.37). Patients with scapular girdle involvement had a 4-fold increased risk of developing IR (OR = 6.0, 95% CI: 1.3-26.6). And for every 5 centimetres of abdominal perimeter the risk increased almost 4 times more (OR=3.9, 95% CI: 2.9-5.1). In the multivariate analysis, the only independent factor to increase the IR was the abdominal perimeter (aOR = 1.23, IC95%: 1.07-1.41).

Conclusion: Patients with elderly-onset RA have a higher IR than the general population. High IR in RA is present at diagnosis. IR in AR is not exclusively mediated by systemic inflammation, since patients with PMR do not have this increase. The predictors of presenting IR in elderly-onset AR were BMI, scapular girdle involvement and abdominal perimeter. Only the abdominal perimeter was shown as an independent factor.

Disclosure of Interests: None declared


References:
SOLUBLE RECEPTOR FOR ADVANCED GLYcation END PRODUCTS (sRAGE) AND RISK FOR CARDIOVASCULAR DISEASES IN FEMALES WITH RHEUMATOID ARTHRITIS

Marta Naudi1, Marta I. Bakowska2, Sofia Töyrä Silversward3, Malin Erlandsson2, Lovisa Lyngfelt4, Karin Me Andersson5, Rille Pullerits1, 1Institution of Medicine, Sahlgrenska Academy at University of Gothenburg, Department of Rheumatology and Inflammation Research, Gothenburg, Sweden; 2Institution of Medicine, Sahlgrenska Academy at University of Gothenburg, Department of Rheumatology and Inflammation Research, Gothenburg, Sweden.

Background: Rheumatoid arthritis (RA) is strongly associated with increased frequency of cardiovascular disease (CVD), which remains the major cause of mortality in these patients. Current CVD risk assessment algorithms have limited predictive value for RA patients. Soluble receptor for advanced glycation end products (sRAGE) has recently emerged as a biomarker of inflammation with an inverse correlation with traditional CVD risk factors as age, hypertension and hypercholesterolemia.

Objectives: In a cohort of female RA patients with no previous history of CVD, we assessed whether sRAGE levels were associated with increased risk of CVD during a prospective 5 years follow up.

Methods: Serum sRAGE levels were measured in 171 female RA patients (median age 53; range 21-71) at the inclusion to the study. The CVD risk was estimated using the Framingham algorithm and both traditional and RA associated risk factors for CVD were measured. All the patients were prospectively followed up to 5 years for new CV events, type II diabetes and medication for hypertension and hyperlipidemia. Statistical analysis was performed to compare CVD risk and actual events in the patients with low sRAGE (<1700 pg/ml) vs. high sRAGE (>1700 pg/ml).

Results: The comparison of patients with low sRAGE (n=125) and normal-high sRAGE (n=46) found no significant differences in frequency of the traditional CVD risk factors including age>60 years (30% vs 41%), overweight (50% vs 41%), smoking (14% vs 11%), incident hypertension (16% vs 16%) and hypercholesterolemia (56% vs 67%) at baseline and led to similar estimated CVD risk (7.65% vs 8.45%). The RA-related CVD risk factors including disease duration >10 years (37% vs 39%), presence of autoantibodies (89% vs 95%), disease activity (DAS28, 46% vs 60%) were also similar in the low-and high sRAGE groups. At 5 years follow up, 11 new CVD events were registered. The events occurred with similar frequency in the low sRAGE and high sRAGE groups (5.6% vs 8.7%). Despite a lack of difference in CVD events, we did observe a significant increase in frequency of new medication for hypertension in the low sRAGE group (21.5% vs. 63%, p=0.01), but not in medication for type II diabetes or statins.

Conclusion: In this study, we found no association between serum levels of sRAGE and the estimated CVD risk or actually occurred CVD events in female RA patients.

REFERENCE:

Disclosure of Interests: None declared
THE CONTRIBUTION OF TENOSYNOVITIS OF SMALL JOINTS TO THE SYMPTOM MORNING STIFFNESS IN PATIENTS PRESENTING WITH UNDIFFERENTIATED AND RHEUMATOID ARTHRITIS

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Background: Morning stiffness (MS) is characteristic of Rheumatoid Arthritis (RA) that is associated with functional disability. Despite the known parallel in the circadian rhythm of MS and that of several hormones and pro-inflammatory cytokines in the systemic circulation, it is insufficiently known to what extent local inflammatory processes contribute to this symptom. The correlation between MS and the number of swollen joints is relatively weak but may be underestimated by insufficient sensitivity in measuring local inflammation. MRI is more sensitive in detecting local inflammation. Furthermore, MRI-detected tenosynovitis of small joints is increasingly recognized as early feature of RA which is also associated with functional impairments. Recently it was proposed that this may contribute to MS.

Objectives: We assessed the relationship between MS and MRI-detected inflammation of synovitis and tenosynovitis in particular.

Methods: 286 consecutive patients newly presenting with undifferentiated and rheumatoid arthritis underwent contrast-enhanced 1.5T-MRI of (2-5) MCP-, (1-5)MTP-, and wrist-joints. Scans were scored for tenosynovitis according to Haraldsdottir and for synovitis/tenosynovitis (AMARIS) methodology. MS was dichotomized as-as 60 minutes. Associations between MS and tenosynovitis/synovitis were tested with logistic regression and the presence of a biologic interaction was assessed categorically (singly or simultaneous presence of synovitis/tenosynovitis).

Results: MS was present in 40% of patients. Tenosynovitis was more often present in patients with MS than without MS (80% versus 65%), OR 2.11 (95%CI 1.21;3.69). Also synovitis was more often present in patients with MS (58% versus 44%), OR 1.63 (1.22;2.16). In categorized analysis the largest association was found for concurrent synovitis and tenosynovitis OR 2.43 (1.30;4.54); whereas single presence of synovitis was not associated (OR 0.85 (0.21;3.47)). The variance explained in all analyses on morning stiffness was small, ranging 3-6%.

Conclusion: Tenosynovitis, and simultaneous presence of tenosynovitis and synovitis in particular, was associated with MS. However, effect sizes suggested that the contribution of local inflammation to this symptom is rather limited.

Acknowledgement: E.C. Newsum and W.P. Nieuwenhuis are acknowledged for scoring MRI-scans.

Disclosure of Interests: Aleid Boer: None declared, Debbie Boeters: None declared, Ellis Niemantsverdriet: None declared, Annette van der Helm - van Mil: Grant/research support from: AMARIS.


INFECTIONS AMONG RHEUMATOID ARTHRITIS PATIENTS STARTING OR SWITCHING BIOLOGICAL AGENTS. A SYSTEMATIC LITERATURE REVIEW

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Background: The increased rate of infections is one of the most relevant issues regarding biologic therapies in Rheumatoid Arthritis (RA). There is a large number of studies comparing different biologic agents and biologic vs synthetic DMARDs in order to assess their safety profile. Nevertheless, the main question is whether biologics really increase the infection risk by themselves. Up to date, different studies tried to clarify the actual role that these drugs have in this potentially serious adverse effect, searching for other predisposing conditions related to patient clinical characteristics.

Objectives: To compare the risk of infections between patients starting biologic agents for the first time (naive) and patients with an inadequate response to a previous biologic agent (switchers).

Methods: A search strategy was performed by the Spanish Society of Rheumatology documentalist over Pubmed, Embase and Cochrane Library databases (from January 2008 to February 2018). All the references retrieved were managed using Endnote X7®. Screening of studies, data collection and data analysis was performed by 2 reviewers. Meta-analysis, systematic reviews of Randomized Controlled Trials (RCT), Clinical Trials or Cohort studies, comparing data from adult RA patients starting biologics and switching biologics, were selected. After the first screening, a critical review was performed using electronic FLC platform for critical appraisal tools (Osbea®) and The Scottish Intercollegiate Guidelines Network (SIGN) was considered to classify the scientific evidence of the selected studies. Studies including patients with chronic infections, tuberculosis reactivations or surgical infections were excluded.

Results: 8 studies were included: 1RCT, 2 Open label study, 1 Open label extension from RCT, 2 subgroups analysis from RCTs and 2 prospective cohort studies. Overall infection rate was higher in switchers than in naïve patients, with a mean variation between 0-9 and 1.8 100 PY, serious infections were also higher in switchers patients, 2.2 100PY. In both groups, ( naïve and switchers), patients treated with more cumulative dose of glucocorticoids (GC) had an increased risk of infections, and it was higher in patients with an inadequate response to previous biologic agents. Mean disease duration was longer in switchers, but this fact was not related to increase of infections.

Conclusion: This systematic review show that overall rate of infections is slightly higher in switchers than in naïve patients, but the fact of having received several biologic agents does not present itself as a risk factor for infections. However, the most important risk factor in the development of infections was the higher cumulative doses of GC.

Disclosure of Interests: None declared.


EFFECTS OF MALALIGNMENT AND DISEASE ACTIVITY ON SECONDARY OSTEOARTHRITIS PROGRESSION IN KNEES OF RHEUMATOID ARTHRITIS PATIENTS

Noriaki Okumura, Taku Kasawaki, Kosuke Kumagai, Mitsuhiko Kubo, Takafumi Yayama, Tomohiro Mimura, Tsutomu Maeda, Shini Imai. Shiga University of Medical Science, Orthopaedics Surgery, Otsu, Japan

Background: Recent advancements in treatment of rheumatoid arthritis (RA) with disease-modifying anti-rheumatic drugs (DMARDs) have been remarkable, with disease symptoms nearly disappearing due to their strong anti-inflammatory action and many patients achieving remission. As a result, the need for RA-related surgery has shown a yearly decreasing trend, especially knee surgery and synovectomy procedures [1]. On the other hand, cases of secondary osteoarthritis (OA) in knee joints as a symptom associated with RA following a total knee arthroplasty (TKA) are increasing.

Objectives: We investigated the morphology of osteophytes by quantitatively evaluating their size using images obtained prior to performing a TKA. Additionally, the relationships of osteophyte size with patient background, disease activity, and degree of inflammation were examined.

Methods: Radiographs of 35 consecutive knees in 30 RA patients (26 females, 4 males; mean age 63.0 years; median disease duration 15 years) who underwent TKA, including preoperative standing AP view radiographs of the knee joint, were retrospectively analyzed. Using the Image-J software package, osteophyte size in the medial femur (MF), medial tibia (MT), lateral femur (LF), and lateral tibia (LT) regions was determined. Written informed consent for data collection was obtained from all patients in accordance with the Declaration of Helsinki.

Results: Preoperative Larsen grade was 2, 3, 4, and 5 in 1, 12, 18, and 2 patients, respectively, while the mean range of motion of the knee joint was 118° for flexion and -10° for extension. The mean femoral-tibial indentation angle (FTA) was 178°±13.6°, with varus (FTA >180°; n=14) more frequently observed as compared to valgus (FTA <170°; n=7) cases. Mean osteophyte size in the MF, MT, LF, and LT regions was 37.2, 17.0, 27.2, and 4.57 mm², respectively, and significantly greater in the medial compartment (MF+MT) than the lateral compartment (LF+LT) (p<0.001). In the varus cases, osteophyte size in the medial compartment was significantly larger as compared to the normal and valgus cases (p=0.0016). Furthermore, osteophyte size in the medial compartment was negatively correlated with the inflammatory markers CRP (r=-0.492, p=0.0027) and ESR (r=-0.529, p=0.0016), whereas that in the lateral compartment was negatively correlated with disease activity (r=-0.589, p=0.0023).

Conclusion: Our results suggest that secondary OA is a more prominent symptom in RA patients in whom inflammation is controlled, while disease activity has effects on osteophyte size.
INCREASE OF RHEUMATOID ARTHRITIS AS A CONTRIBUTORY CAUSE OF DEATH IN THE ELDERLY. A NATIONWIDE STUDY IN ITALY, 2003–2015

Francesca Ometto1, Ugo Fedeli2, Costantino Botsios1, Leonardo Punzi1, Enrico Grande2,3

Background: Metanalyses failed to show a decrease of the mortality risk in cohorts of patients with rheumatoid arthritis (RA) between 1950 and 1980. Mortality rates obtained with the analysis of multiple causes of death (MCD) can provide a more complete estimate of the burden of mortality related to RA compared to analysis considering only the underlying cause of death (UCD). Such analyses are available from a limited number of countries, and trends for RA mortality based on MCD were divergent.

Objectives: The objective of the study was to evaluate trends of rheumatoid arthritis (RA) mortality reported as the underlying cause of death (UCD) and as multiple cause of death (MCD) in Italy between 2003 and 2015.

Methods: Analyses were carried out on the Italian National Cause of Death Register, managed by the Italian National Institute of Statistics (ISTAT). Diseases mentioned in the death certificate are coded according to the International Classification of Diseases, 10th Edition (ICD-10, 2009 version). Deaths from January 1, 2003 to December 31, 2015 with mention of RA were included. Time trends of age-standardized rates were analyzed for RA both as UCD and MCD; and the annual percent change (APC) was estimated.

Results: Overall 26,564 deaths with mention of RA were retrieved out of 7,595,214 deaths (0.35% of all certificates). The yearly number of RA-related deaths increased through the study period, meanwhile the probability of selection as the UCD decreased: MCD/UCD ratio was 3.7 in 2003-2006 and 4.8 in 2012-2015 in males; 3.0 and 4.1 in females (Tab.). Mortality rates based on the UCD decreased (males APC -3.1%, CI -3.9, -2.3; females APC -3.3%, CI -4.1, -2.4); while MCD rates for RA-related mortality were stable. Specifically, rates were stable or declined among younger subjects, whereas an increase was registered (APC) was estimated.

Table. Rheumatoid arthritis-related number of deaths and mortality rates, based on underlying and multiple causes of death.

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Males</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average annual number of RA-related deaths</td>
<td>441</td>
<td>502</td>
<td>535</td>
</tr>
<tr>
<td>Share of all deaths</td>
<td>0.16%</td>
<td>0.18%</td>
<td>0.18%</td>
</tr>
<tr>
<td>UCD, average age-standardized rate (x100,000)</td>
<td>0.54</td>
<td>0.47</td>
<td>0.41</td>
</tr>
<tr>
<td>MCD, average age-standardized rate (x100,000)</td>
<td>2.01</td>
<td>2.04</td>
<td>1.95</td>
</tr>
<tr>
<td>RA selected as the UCD</td>
<td>26%</td>
<td>23%</td>
<td>22%</td>
</tr>
<tr>
<td>Females</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average annual number of RA-related deaths</td>
<td>1392</td>
<td>1557</td>
<td>1699</td>
</tr>
<tr>
<td>Share of all deaths</td>
<td>0.49%</td>
<td>0.52%</td>
<td>0.54%</td>
</tr>
<tr>
<td>UCD, average age-standardized rate (x100,000)</td>
<td>1.34</td>
<td>1.20</td>
<td>0.98</td>
</tr>
<tr>
<td>MCD, average age-standardized rate (x100,000)</td>
<td>4.00</td>
<td>4.04</td>
<td>3.98</td>
</tr>
<tr>
<td>RA selected as the UCD</td>
<td>33%</td>
<td>29%</td>
<td>25%</td>
</tr>
<tr>
<td>RA, rheumatoid arthritis; UCD, underlying cause of death; MCD, multiple causes of death.</td>
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Disclosure of Interests: None declared


PATIENT-REPORTED PALINDROMIC SYMPTOMS IN EARLY RHEUMATOID ARTHRITIS: RESULTS FROM THE CANADIAN EARLY ARTHRITIS COHORT

Leah Ellingswood1, Orit Schier2, Marie-France Valois3, Susan J. Bartlett3, Louis Bassette2, Carol Hilchon4, Gilles Boire5, Glen Hazlewood5, Edward Keystone5, Diane Tin6, Carter Thorne3, Vivian Bykerk7, Janet Pope8,9,10,11 Canadian Early Arthritis Cohort.1 Western University, London, Canada; 2University of Toronto, Toronto, Canada; 3McGill University, Montreal, Canada; 4Laval University, Quebec, Canada; 5University of Manitoba, Winnipeg, Canada; 6Universite de Sherbrooke, Sherbrooke, Canada; 7University of Calgary, Calgary, Canada; 8Southlake Regional Health Centre, Newmarket, Canada; 9Hospital for Special Surgery, New York, United States of America; 10Western University, Rheumatology, London, Canada

Background: The frequency and characteristics of patients with Palindromic Rheumatism (PR) (transient acute attacks of articular inflammation) prior to early rheumatoid arthritis (ERA) are unknown.

Objectives: To compare ERA patients who did versus did not report a history of transient episodes of joint inflammation preceding RA diagnosis.

Methods: Study participants were patients with ERA or suspected RA (symptoms <1 year; 83% met 2010 ACR/EULAR criteria) enrolled in the Canadian Early Arthritis Cohort (CATCH) between April 2017 to March 2018 who completed a questionnaire on prior inflammatory joint symptoms that ‘come and go’. Chi-square and t-tests were used to compare characteristics in patients with versus without a reported history of prior palindromic symptoms. Simple, and multivari-

Table. Rheumatoid arthritis-related number of deaths and mortality rates, based on underlying and multiple causes of death.

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Males</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average annual number of RA-related deaths</td>
<td>441</td>
<td>502</td>
<td>535</td>
</tr>
<tr>
<td>Share of all deaths</td>
<td>0.16%</td>
<td>0.18%</td>
<td>0.18%</td>
</tr>
<tr>
<td>UCD, average age-standardized rate (x100,000)</td>
<td>0.54</td>
<td>0.47</td>
<td>0.41</td>
</tr>
<tr>
<td>MCD, average age-standardized rate (x100,000)</td>
<td>2.01</td>
<td>2.04</td>
<td>1.95</td>
</tr>
<tr>
<td>RA selected as the UCD</td>
<td>26%</td>
<td>23%</td>
<td>22%</td>
</tr>
<tr>
<td>Females</td>
<td></td>
<td></td>
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<tr>
<td>Average annual number of RA-related deaths</td>
<td>1392</td>
<td>1557</td>
<td>1699</td>
</tr>
<tr>
<td>Share of all deaths</td>
<td>0.49%</td>
<td>0.52%</td>
<td>0.54%</td>
</tr>
<tr>
<td>UCD, average age-standardized rate (x100,000)</td>
<td>1.34</td>
<td>1.20</td>
<td>0.98</td>
</tr>
<tr>
<td>MCD, average age-standardized rate (x100,000)</td>
<td>4.00</td>
<td>4.04</td>
<td>3.98</td>
</tr>
<tr>
<td>RA selected as the UCD</td>
<td>33%</td>
<td>29%</td>
<td>25%</td>
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</table>

Disclosure of Interests: None declared

Disclosure of Interests: Leah Ellingwood: None declared, Orit Schier: None declared, Marie-France Valois: None declared, Susan J. Bartlett: None declared, Leah Ellingwood: None declared, Orit Schier: None declared, Marie-France Valois: None declared, Susan J. Bartlett: None declared, Leah Ellingwood: None declared, Orit Schier: None declared, Marie-France Valois: None declared, Susan J. Bartlett: None declared.

REFERENCES:
SAFETY OF THE ZOSTER RECOMBINANT ADJUVANTED VACCINE IN RHEUMATOID ARTHRITIS PATIENTS: A SINGLE CENTER’S EXPERIENCE WITH 300 PATIENTS

Emma Stevens, Michael E. Weinblatt, Elena Massarotti, Frances Griffing, Sonali Desai.
Brigham and Women’s Hospital, Division of Rheumatology, Immunology and Allergy, Boston, United States of America

Background: Patients with rheumatoid arthritis (RA) and other systemic rheumatic diseases (SRD) are at increased risk of developing Herpes Zoster (HZ) due to the diseases/or medications used to treat them such as corticosteroids methotrexate, biologic disease modifying agents, and JAK inhibitors. Released in 2018, the Zoster Recombinant Adjuvanted (ZRA) is a new vaccine with >90% efficacy and can be used in patients taking immunosuppressive therapy as compared to the live Zoster vaccine. There has been a concern about whether the potency of the adjuvant could trigger flares of the underlying SRD, and whether there will be more side effects in this population.

Objectives: Our goal was to study the impact of the new ZRA vaccine in RA and other SRD patients and to measure the risk of flare and incidence of side effects.

Methods: We performed a retrospective chart review from 2/1/2018 to 1/20/2019, on patients with RA and SRD seen at the BWH who had received the ZRA vaccine. Co-variates of interest were collected. A flare responded to treatment with low dose glucocorticoids, and did not warrant any change in immunosuppressive therapy. Analyses were performed using StatsDirect 3 software.

Results: 300 patients who received the new ZRA vaccine between 2/1/2018 and 1/20/2019 were identified. Mean follow up was 12.5 weeks ranging from 1-40 weeks following administration. Patient characteristics are identified in Table 1.

We identified a 3.00% (n=9) incidence of flare following the first dose and 2.86% (n=4) incidence following the second dose. One patient flared after both the first and second dose. All the flares were mild, self-limited, and 2.86% (n=4) incidence following the second dose. All the flares were mild, self-limited, and did not warrant a change in immunosuppressive therapy. 15.3% (n=46) patients experienced side effects such as soreness at the injection site, fever, stomach ache, and flu like symptoms. Of the patients who experienced side effects, 15.4% (n=40) occurred after the first dose and 8.59% (n=11) occurred following the second dose. Five patients experienced side effects from both. All side effects were regarded as mild and did not necessitate an emergency room visit. No cases of Zoster were reported.

Conclusion: In our experience with 300 patients who received the new ZRA (207 RA and 93 SRD) in 2018-2019, the incidence of disease flares was ≤ 3% and of side effects was 15% which is reassuring. Both flares and side effects were mild, self-limited, and did not require a change in DMARD therapy. No cases of Zoster were reported. Larger formal studies with longer term follow up are required to confirm our findings.

Disclosure of Interests: None declared

FRI0068
SAFETY OF THE ZOSTER RECOMBINANT ADJUVANTED VACCINE IN RHEUMATOID ARTHRITIS PATIENTS: A SINGLE CENTER’S EXPERIENCE WITH 300 PATIENTS

Emma Stevens, Michael E. Weinblatt, Elena Massarotti, Frances Griffing, Sonali Desai.
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Disclosure of Interests: None declared

FRI0069
FREQUENCY OF EYE INVOLVEMENT IN INFLAMMATORY ARTHRITIS AND CONNECTIVE TISSUE DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS

Matthew Tufi1, Jacqueline Hayworth2, Tatiana Nevskaya1, Janet Pope1.
1University of Western Ontario, London, Canada; 2University of Toronto, Toronto, Canada

Background: Rheumatoid arthritis commonly presents with extraarticular manifestations. Along with other connective tissue diseases, these manifestations may include eye involvement.

Objectives: The purpose of our work was to determine the prevalence and type of eye involvement in rheumatoid arthritis and other connective tissue diseases through a meta-analysis and literature review.

Methods: A systematic review of the literature was performed using Medline, Web of Science, and the Cochrane library from their inceptions until January 7, 2019. Conjunctivitis, keratoconjunctivitis sicca, xerophthalmia, uveitis, eye hemorrhage, optic neuritis, papilledema, orbital disease, retinal artery/vein occlusion, macular edema, retinitis, choroioretinitis, scleritis, iridocyclitis, choroid hemorrhage, blindness and amaurosis fugax were searched for prevalence in patients with rheumatoid arthritis, systemic lupus erythematosus, antiphospholipid syndrome, dermatomyositis, polymyositis, systemic sclerosis, Snowden’s syndrome, undifferentiated connective tissue disease, giant cell arteritis, granulomatosis polyangiitis (GPA) formerly Wegener’s granulomatosis, systemic vasculitis, and sarcoidosis.

Results: 3394 studies were identified and 65 included. The prevalence of eye involvement was 18% in rheumatoid arthritis, 31% in systemic lupus erythematosus, 35% in antiphospholipid syndrome, 27% in giant cell arteritis, 26% in GPA and 27% in sarcoidosis. The most common manifestations was dry eyes (keratoconjunctivitis sicca) in most diseases analyzed with a frequency approaching 90% in Snowgen’s syndrome. Anterior and posterior uveitis were the most common OC in sarcoidosis occurring in 16 [3-28]% and 6 [3-9]% of patients respectively.

Conclusion: Eye involvement is present in approximately one fifth of rheumatoid arthritis patients, and one quarter to one third of patients with other rheumatic diseases.
REFERENCES:


FR0070 SHORT-TERM INFLAMMATORY AND LIPIDS CHANGES IN RHEUMATOID ARTHRITIS PATIENTS INFLUENCE CARDIOVASCULAR RISK ALGORITHMS: A MONOCENTRIC RETROSPECTIVE STUDY

vincenzo venenito, Marco Fornaro, Giuseppe Lopalo, Anna Abbruzzese, Sergio Colella, Maria Grazia Anelli, Giovanni Lapadula, Floreruo Iannone, Fabio Cacciapaglia, Polichinico di Barile, Rheumatology Unit, Department of Emergency and Organ Transplantations, Barile, Italy

Background: Chronic inflammation may change lipid profile, thus current EULAR recommendations for cardiovascular (CV) management in polyarthritis suggest to assess cholesterol status when disease activity is stable or in remission. To date it is still unclear whether inflammation mediated changes in lipids profile could impact on CV risk algorithms and what score should be considered the reference one for any disease activity status.

Objectives: The aim of this study was to evaluate the influence of lipid profile, disease activity and inflammation modifications on four CV risk calculators during Treat to Target strategy with biologic agents.

Methods: In this monocentric study we retrospectively evaluated all data recorded from Rheumatoid Arthritis (RA) patients with moderate/high CV disease activity, who had started for the first time and maintained a bDMARD agent for at least 6 months, in our Outpatient Clinic from the 1st January 2010 to 31st December 2017. Patients with a prior CV event have been excluded from the analysis. For each patient, we assessed the CV risk in a short time period (within 6 months) to estimate the specific weight of lipids and disease activity related variables, using the Italian CV “Progetto Cuore” score, the QRISK3-2018 score, the Reynolds Risk Score (RRS) and the Expanded Risk Score in RA (ERS-RA). The results of the “Progetto Cuore” and RRS algorithms were multiplied by 1.5, in accordance to the EULAR recommendations for algorithms that do not include specifically RA among variables. Wilcoxon signed-rank test was used to compare CV risk scores during follow-up.

Results: One-hundred thirteen RA patients (female n. 86 (76.8%), mean age (SD) 52.8 (12.9) years, median disease duration (IQR) 26 (13-72) months) were eligible for the analysis. CDAL and C-reactive protein levels decreased significantly either at 3 and 6 months follow-up (p<0.001). At 3 months, we observed a statistically significant decrease in mean total cholesterol (TC) from 197.3±38.2 mg/dl to 205.8±37.3 mg/dl (p<0.01), which returned close to baseline levels at 6 months (201.1±34.5 mg/dl - p=0.22 vs baseline). High density lipoprotein (HDL), TC/CHDL ratio and triglycerides changes did not reach the statistically significance. The estimated CV risk assessed by the “Progetto Cuore” and QRisk3-2018 did not change during the 6 months’ follow-up. RRS showed a decrease either at 3 and 6 months (p<0.04). Similarly, ESR-RA highlighted a decrease of CV risk either at 3 and 6 months (p<0.01) (see Table I).

Conclusion: All evaluated “Scores” are not influenced by short term lipid changes observed during bDMARDs treatment, being applicable at any status of disease activity. Interestingly, the RRS and ESR-RA scores, evaluating RA inflammatory items, are susceptible to disease activity changes. These results should be taken into account by rheumatologists choosing a CV risk algorithm in daily clinical practice.

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REFERENCES:


Anti-citrullinated protein antibody specificities, rheumatoid factor isotypes and risk of major adverse cardiovascular events

Helga Westerlund1, Johan Rönnelid2, Monika Hansson1, Lars Alfredsson3, Linda Mathsson1, Guy Serre4, Martin Cornillet5, Rikard Holmdahl6, Per-Johan Jakobsson1, Karl Skirner6, Lars Kläreskog7, Saedis Saevasdottir8, Johan Asling1, Karolinska Institutet, Department of Medicine, Solna, Sweden; 2Uppsala University Hospital, Department of Immunology, Genetics and Pathology, Uppsala, Sweden; 3Karolinska Institutet, Institute of Environmental Medicine (IMM), Stockholm, Sweden; 4Toulouse University, Laboratory of Epithelial Differentiation and Rheumatoid Autoimmunity, Toulouse, France; 5Karolinska Institutet, Department of Medical Inflammation Research, Stockholm, Sweden; 6Charité University Hospital, Department of Medicine, Berlin, Germany; 7Karolinska Institutet, Solna, Sweden

Background: The association and role of antibodies to citrullinated proteins (ACPAs) on the risk of cardiovascular (CV) comorbidity in patients with rheumatoid arthritis (RA) is incompletely understood. We have previously reported an association between high levels of CCP2 and risk of acute coronary syndrome (ACS) in RA1. Objectives: To further investigate any association between specific ACPA or rheumatoid factor (RF) isotypes, and CV events (ACS, stroke, CV death, and major adverse CV event (MACE)). Methods: 253 patients with RA from the Swedish EIRA study were tested for ACPA specificities on a custom-made microarray chip. All antibodies (Ab) detected with a prevalence >= 10% were included in the analysis. Ab load was defined as the number of specificities expressed in an individual, and categorized into four groups. ACPA was also measured by a commercial anti-CCP2 assay and anti-CCP2 levels divided into <25, 25-<75, 75--<1500, and >1500 arbitrary units/mL, where <25 defines negativity, IgG and IgM RF positivity was assessed using EIA immunoassay. For each RF isotype, cutoff level was determined as above the 98th percentile among controls. The data was linked to the National Patient Register and the Cause of Death register, and events of ACS (ICD10=I20-0, I21, or cause of death listed as "I21"), stroke (ICD10=I60-964), CV death (cause of death listed as "I"), or MACE (any of the above) identified. We used Cox proportional hazard model, adjusted for sex, age and calendar period of RA diagnosis, to assess associations between ACPA/RF status and each CV outcome.

Results: Median age at diagnosis was 52 years, and median follow-up was 12 years. The incidences per 1000 person-years were 4.3 for ACS, 4.0 for stroke, 2.4 for CV deaths, and 9.4 for MACE. 66% were anti-CCP2 positive. This was associated with ACS, stroke, and MACE. There was a trend with increasing CV risk with increasing anti-CCP2 levels (Table). For RF, the pattern was markedly different across isotypes; IgM RF associated with ACS, stroke and MACE whereas IgA RF associated to ACS. No association to ACS remained when Ab load was defined as the number of specificities expressed in an individual, and categorized into four groups. No association to ACS remained when Ab load was defined as the number of specificities expressed in an individual, and categorized into four groups. No association to ACS remained when Ab load was defined as the number of specificities expressed in an individual, and categorized into four groups. No association to ACS remained when Ab load was defined as the number of specificities expressed in an individual, and categorized into four groups. No association to ACS remained when Ab load was defined as the number of specificities expressed in an individual, and categorized into four groups. No association to ACS remained when Ab load was defined as the number of specificities expressed in an individual, and categorized into four groups.

Conclusion: In patients with RA, RF and ACPA are linked to CV risk. For RF, CV risks differ with isotype. For ACPAs, very high levels, and the number of individual ACPAs, are linked to CV risk, suggesting that Ab load may be more important than individual ACPAs.

References:

Disclosure of Interests: Helga Westerling: None declared, Johan Rönnelid: None declared, Monika Hansson: None declared, Lars Alfredsson: None declared, Linda Mathsson: Employee of: employed by Thermo Fisher Scientific, Guy Serre: None declared, Martin Cornillet: None declared, Rikard Holmdahl: None declared, Per-Johan Jakobsson: None declared, Karl Skirner: None declared, Lars Kläreskog: Grant/research support from: Yes, but not for the presented study. Saedis Saevasdottir: Employee of: Part-time employee at deCODE Genetiscs/Amgen Inc, working on genetic research unrelated to this project., Johan Asling Grant/research support from: Karolinska Institutet (JA) has or has had research agreements with the following pharmaceutical companies, mainly in the context of the ATRS national safety monitoring programme for rheumatology biologicals: Abbvie, BMS, MSD, Eli Lilly, Pfizer, Roche, Samsung Bioepis, and UCB., Consultant for: Karolinska Institutet has received remuneration for JA participating in ad boards arranged by Lilly, Novartis, and Pfizer.


Predicting sarcopenia and obesity by measuring thigh muscle and fat thickness by ultrasound in patients with rheumatoid arthritis: from the Chikara study

Yuta Yamada1, Masahiro Tada2, Koji Mandai1, Noraki Hidaka2, Kentaro Inui1, Hiroshi Nakamura1. 1Osaka City University Graduate School of Medicine, Osaka city, Japan; 2Osaka City General Hospital, Osaka city, Japan

Background: Rheumatoid arthritis (RA) patients often have sarcopenia. The thickness of the quadriceps muscle, easily measurable by ultrasound (US), is known to be related to skeletal muscle mass, and its decreased thickness may suggest sarcopenia.

Objectives: To investigate the utility of US for predicting sarcopenia by examining the anterior thigh in RA patients.

Methods: Ninety-four patients (66 female) enrolled in the prospective CHIKARA study (UMIN000023744) underwent US muscle (MT) and fat thickness (FT) examinations of the anterior thigh. Muscle and body fat mass were also examined by a body composition analyzer (MC-780A; TANITA, Tokyo, Japan). Whether MT and FT can predict sarcopenia and obesity was also examined. Sarcopenia was diagnosed based on the Asian Working Group on Sarcopenia definition, and obesity was diagnosed by% body fat (%BF).

Results: MT was significantly lower in RA patients with sarcopenia than in those without (24.8 ± 3.5 mm vs. 29.6 ± 3.8 mm; p=0.01). MT was related to sarcopenia (males r=0.56, p=0.02; females r=0.32, p=0.01). The MT cut-off value for sarcopenia was 24.7 mm in males and 19.7 mm in females on receiver operating curve (ROC) analysis. FT was correlated with%BF (males r=0.66, p=0.01; females r=0.62, p=0.001),%BF was estimated by 2.21FT+7.28 in males and 1.45FT+14.46 in females by a simple linear regression model. This means that FT>8.0 mm in males and FT>10.7 mm in females indicate obesity (Table 1). When assessing the accuracy of these cut-off values, the kappa values were 0.541 and 0.469, respectively.

Table 1. Relationship between%BF and FT. FT: the fat thickness (FT) at anterior thigh measured by ultrasound,%BF:% body fat measured by body composition analyzer.

Conclusion: Sarcopenia and obesity can be predicted by US examination of the anterior thigh in RA patients.

References:
SWELLING OR TENDERNESS, WHICH ONE CORRESPONDS BETTER WITH ULTRASOUND-DETECTED SYNOVITIS?

Xiaoying Sun, Xuerong Deng, Weihui Xie, Yu Wang, Zhong Zhang, Peking University First Hospital, Beijing, China

Background: Ultrasound (US) is a sensitive method for detecting joint inflammation in patients with rheumatoid arthritis (RA). The relationship between tender or swollen joints and ultrasound-detected synovitis has not been well explored in patients with RA.

Objectives: The purpose of the present study was to compare the correlation between ultrasound-detected synovitis and joint tenderness or swelling at the wrists and hands in RA patients.

Methods: Twenty-two joints, including bilateral wrists, proximal interphalangeal (PIP) and metacarpophalangeal (MCP) joints, were respectively evaluated by physical examination (PE) and ultrasound scan in 258 RA patients. All patients had at least 1 tender or swollen joint out of 22 joints. Joint tenderness was assessed by using semiquantitative scoring systems (0-3) for grey scale (GS) and power Doppler (PD). Positive synovitis was defined as GS≥2 and/or PD≥1. All correlations among US variables and clinical variables were assessed using Spearman’s rank correlation test. Cohen’s kappa (κ) between clinical and sonographic findings was calculated.

Results: Their median age was 51.2 years, median disease duration was 57 months, with 83.33% females. The mean (SD) Disease Activity Score based on 28 joints (DAS28)-ESR and DAS28-CRP were 4.47±1.62 and 5.70±1.47, respectively. In a total of 5676 joints assessed, 968 swollen joints (17.05%) and 1296 tender joints (22.83%) were found, while on ultrasonography GS synovial hyperplasia was present in 801 (14.11%) joints, positive PD in 476 (8.38%) joints. There were more tender joints without swelling (n=574) than those swollen joints without tenderness (n=246). In all joints, higher κ coefficient was observed in joint swelling (κ=0.367, p<0.01) with ultrasound-detected synovitis compared with tender-joint (κ=0.281, p>0.01). Similarly, swollen joint counts of 22 joints showed higher Spearman’s correlation coefficient with either total GS scores (r=0.499, p<0.01) or total PD scores of 22 joints (r=0.430, p<0.01) than tender joint counts of 22 joints (r=0.354,0.308, p<0.01). GS and PD synovitis were more frequently detected in swollen joints without tenderness compared with tender joints without swelling. This discrepancy tends to be more significant in MCP2, MCP3, and MCP4 joints (p<0.05).

Conclusion: In RA patients with at least 1 tender or swollen joint of wrists and hands, a higher frequency of joint tenderness was observed than swelling. However, swelling had better agreement with ultrasound-detected synovitis compared with tenderness. Joint swelling is more associated with ultrasound-detected synovitis than tenderness. Without swelling, joint tenderness tends to be less associated with ultrasound-detected synovitis.

REFERENCE:
REFERENCES:

Disclosure of Interests: None declared

FR0075 SYSTEMATIC ANALYSIS OF INJECTION-SITE PAIN CAUSED BY SUBCUTANEOUS ADMINISTRATION OF THE ADALIMUMAB BIOSIMILAR FKB327 VERSUS ADMINISTRATION OF THE ADALIMUMAB REFERENCE PRODUCT VIA DIFFERENT DELIVERY METHODS

Rieke Alten1, Mark C. Genoves2, Malcolm Boyce3, Takuma Yonemura4, Takahiro Ito5, Herbert Kellner6.

1University Medicine Berlin, Berlin, Germany; 2Stanford University, Division of Immunology and Rheumatology, Palo Alto, CA, United States of America; 3Hammersmith Medicines Research, London, United Kingdom; 4Souseikai Sumida Hospital, Tokyo, Japan; 5Fujifilm Kyowa Kirin Biologics, Tokyo, Japan; 6Specialist Practice in Rheumatology and Gastroenterology, Munich, Germany

Background: FKB327 is a proposed biosimilar of the adalimumab reference product (RP). Several studies in both healthy volunteers and patients with active rheumatoid arthritis (RA) were undertaken, the results of which have been reported elsewhere. The formulation excipients of the biosimilar product differ from those of the RP, and different injection-site pain intensity with subcutaneous injection has been reported.

Objectives: The current meta-analysis examines pooled data from these studies in relation to the amount of injection-site pain resulting from using a prefilled syringe (PFS) versus an auto-injector (AI) versus a regular syringe (RS). In parallel, the proposed biosimilar, FKB327, versus the RP.

Methods: Data from 4 studies, FKB327-001, -002, -003, and -004, were pooled in an effort to compare injection-site pain upon subcutaneous administration of FKB327 versus the RP (citrate-containing formulation of the RP [40 mg/0.8 mL]). Study FKB327-001, in healthy volunteers (n = 180), involved a single subcutaneous dose of either FKB327 or the RP. Study FKB327-004 was a similar study in healthy Japanese volunteers (n = 130). Study FKB327-002 was a randomized (FKB327 with RS or the RP), double-blind, multiple-dose study in patients with active RA. This was followed by Study FKB327-003, in which patients were rerandomized to receive either FKB327 with PFS or the RP in the randomization phase, followed by an open-label extension phase of the study, in which AI was introduced. As patients continued receiving treatment or switched treatments during the course of the FKB327-002 and -003 studies, injection-site pain was assessed at the first dosing occasion of FKB327 or the RP (n = 691). Data from all 4 studies were examined by meta-analysis of the visual analog scale (VAS) using a 100-mm horizontal scale for FKB327 versus the RP and for comparison of AI, PFS, and RS.

Results: Data were analyzed from a total of 2007 assessments in 1001 subjects. A linear mixed model of the VAS in mm for the RP versus FKB327 across all 4 studies showed a 12.6-point lower pain score for FKB327 across all 4 studies showed a 12.6-point lower pain score for FKB327 versus the RP (95% confidence interval [CI], –13.4 to –11.8; P < .001). For the AI and PFS used for FKB327 administration, AI showed a 1.7-point lower pain score in the VAS compared with PFS (95% CI, –3.3 to –0.1; P = .035). Gender, age, body weight, and population (healthy subject or patient) were not identified for differences in injection-site pain intensity.

Conclusion: FKB327 showed a significant advantage in terms of injection-site pain intensity compared with the RP, as well as lack of inferiority for both AI and PFS versus RS.

Disclosure of Interests: Rieke Alten Grant/research support from: Bristol-Myers Squibb, Speakers bureau: Bristol-Myers Squibb, Mark C. Genoves Grant/research support from: Sanofi/Genzyme, Gerentech/Roche, RPHarm, Consultant for: Sanofi/Genzyme, Gerentech/Roche, RPHarm, Malcolm Boeing: None declared, Takuma Yonemura Grant/research support from: I have received a research grant from FKB for conducting the clinical study., Takahiro Ito Employee of: I am an employee of Fujifilm Kyowa Kirin Biologics., Herbert Kellner Grant/research support from: Roche, Consultant for: Roche

psoriatic arthritis (PsA) and ankylosing spondylitis (AS) in North East Romania from 2003 to 2018.

Methods: We performed a hospital-based retrospective cohort study in consecutive adult patients receiving their first biologic agent (TNF or non-TNF drugs) according to local recommendations in two academic centers. Patients were classified based on the initial TB/latent TB screening test: the tuberculin skin test (positive if > 5mm, TST group) or interferon gamma release assays (positive if >0.35 IU/mL QuantiFERON-TB gold, QFT group); retesting was done regularly if negative initial.

Data about drug efficacy was recorded every 24-weeks based on standard scores (DAS28-ESR for RA, DAPSA for PsA, ASDAS-CRP for AS), while TB risks at the end of the study or prior to switching were determined as hazard ratio (HR) with 95% confidence interval (CI) using cox regression.

Statistical analysis was performed in SPSS-19, p<0.05, on subgroups of patients depending on whether positive TST or QFT at baseline.

Results: 673 patients (360 RA, 116 PsA, 95 AS) were recruited; 55 of them (33 RA, 13 AS, 9 PsA) had latent TB at baseline and received chemoprophylaxis with isoniazid before starting biologics according to local policy. Fourteen active TB were identified, the majority of them occurred within one year of biologics (ranging 6 to 52 months), as follows: three pulmonary TB in RA (in etanercept, one adalimumab), one case of pulmonary TB in PsA (infliximab) and ten cases of RA (six pulmonary TB in abatacept, two adalimumab, etanercept and two infliximab; one ganglionar infection with infliximab; one peritoneal under certolizumab; one pulmonary and pleural under adalimumab). The rate of active TB was 5.3/1000 patient-years for infliximab, 4.594.64 for adalimumab, 1.38.39 patient-years for certolizumab, 3.721.51 for etanercept and 1.21.12 patient-years for abatacept, respectively. We reported an increased risk of TB disease in anti-TNF monoclonal antibodies users vs. soluble receptor, with an incidence ratio of 2.66 (p<0.05). Interestingly, no significant TB risk factors were demonstrated in our cohort; baseline latent TB, previous active TB, chronic glucocorticoid use, high disease activity at baseline, comorbidities, concurrent synthetic drugs were not associated with increased risk (p>0.05). In addition, we described 18 new patients with positive QFT when TB retesting as per protocol, classified as latent TB and requiring chemoprophylaxis.

Conclusion: The risk of tuberculosis remains a reality in biologics, despite extensive screening and prevention methods. The risk is variable when TB retesting as per protocol, classified as latent TB and requiring chemoprophylaxis.

Characteristics | csDMARD IRs (n=7,816) |
<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td><strong>csDMARD</strong></td>
<td>N %</td>
</tr>
<tr>
<td>Monotherapy</td>
<td>2,095 27</td>
</tr>
<tr>
<td>TNFi Monotherapy</td>
<td>757 10</td>
</tr>
<tr>
<td>Other csDMARD Monotherapy</td>
<td>55 0.7</td>
</tr>
<tr>
<td>JAKi Monotherapy</td>
<td>40 0.5</td>
</tr>
<tr>
<td>csDMARD + csDMARD Combination</td>
<td>2,539 32</td>
</tr>
<tr>
<td>TNFi + csDMARD Combination</td>
<td>2,178 28</td>
</tr>
<tr>
<td>Other csDMARD + csDMARD Combination</td>
<td>112 1.4</td>
</tr>
<tr>
<td>JAKi + csDMARD Combination</td>
<td>40 0.5</td>
</tr>
<tr>
<td><strong>Index treatment duration after csDMARD IR, months (IQR)</strong></td>
<td>N %</td>
</tr>
<tr>
<td>Monotherapy</td>
<td>5.2 9.8</td>
</tr>
<tr>
<td>csDMARD</td>
<td>4.9 10.1</td>
</tr>
<tr>
<td>TNFi</td>
<td>5.9 10.1</td>
</tr>
<tr>
<td>JAKi</td>
<td>8.1 11.9</td>
</tr>
<tr>
<td>Combination therapy</td>
<td>13.7 15.8</td>
</tr>
<tr>
<td>csDMARD+csDMARD</td>
<td>12.5 14.8</td>
</tr>
<tr>
<td>TNFi+csDMARD</td>
<td>14.9 15.9</td>
</tr>
<tr>
<td>JAKi+csDMARD</td>
<td>17.2 11.3</td>
</tr>
</tbody>
</table>

**Conclusion:** The real-world evidence suggests that treatment durability may be better for JAKi than TNFi (both monotherapy and combination). The majority of csDMARD patients switched to another csDMARD, which showed short durability of treatment, suggesting that switching MOA may benefit these patients.

**REFERENCE:**

Disclosure of Interests: Robin K Dore Grant/research support from: Gilead Sciences, AbbVie, Amgen, Lilly, Pfizer, Regeneron, Sanofi, Consultant for: AbbVie, Amgen, Lilly, Speakers bureau: AbbVie, Amgen, Lilly, Sanofi, Regeneron, Pfizer, UCB, Jenya Antonova Shareholder of: Gilead Sciences, Employee of: Eli Lilly and Company, Medimmune, Genentech, Gilead Sciences, Huang Huan Grant/research support from: Gilead Sciences, Magdaliz Gorritz Grant/research support from: Gilead Sciences, Mark C. Genovese Grant/research support from: Sanofi/Genzyme, Genentech/Roche, RP Pharm, Consultant for: Sanofi/Genzyme, Genentech/Roche, Roche, RP Pharm

Objectives: To assess the variation in serum trough levels of infliximab after the systematic application of flush physiological serum after drug administration.

Methods: The study was divided into two phases: a first phase in which the clinical and analytical variables (including the serum trough levels of infliximab) were measured before the application of the flush serum and a second stage in which the same variables were measured after the systematic implementation of an infusion of 500 ml of 0.9% sodium chloride following the administration of infliximab.

Results: A total of 35 patients were collected, including 6 rheumatoid arthritis (13.3%), 9 psoriatic arthritis (20%) and 20 ankylosing spondylitis (AS) (44.4%). Overall, 18 patients were women (40%), the mean age was 57.6 years (12.6) and the BMI was 30.5 (13.1). The mean dose of infliximab was 3.1 mg/kg (1.1) and the mean number of years of treatment was 10 (5).

23 patients were taking infliximab on monotherapy (51.1%). The mean trough serum levels of infliximab pre-intervention with the dragging serum was 3.13 mg/dl (3.1), while postintervention levels were 3.66 mg/dl (3.8) (p = 0.071). In the subgroup of patients with AS there was a significant decrease in BASDAI between the pre and post intervention visit (3.4 vs 2.6, p < 0.05).

Conclusion: The use of flush serum after infliximab infusion increased serum drug levels. In the subgroup of patients with AS there was a clinically significant improvement measured by BASDAI.

REFERENCES:
[6] Pascual-Salcedo D1, Plasencia C, Ramiro S, Nuño L, Bonilla G, Navarro-Compán P, et al. Anti-TNF safety of TNFi versus non-TNFi after discontinuing a previous TNFi in (non-TNFi), however little guidance on choosing one or another exists.

Objectives: To compare the long-term clinical response, survival and safety of TFNI versus non-TFNI after discontinuing a previous TNFI in pts with RA, both in the global cohort and in the subpopulations stratified by reason of discontinuation of 1st TNFI.

Methods: Observational study including 127 pts from La Paz University Hospital biological RA registry, who discontinued a first TNFI between 1999 and 2016 and subsequently were treated with a second biologic. Disease activity was assessed by DAS28 at the beginning of the second biologic and at 6 (m-6), 12 (m-12) and 24 months (m-24) follow-up. Primary outcome was the proportion of pts with good or moderate EULAR response (E-Resp). Sensitivity analysis to evaluate clinical response according to the reasons for discontinuation of the first TNFI was performed too. Pts were classified into primary and secondary failure based on the characteristics of the non-response and if possible on the measure of drug and anti-drug antibodies, which were measured by ELISA after 6 months of the first biologic treatment and before switching. Mann-Whitney U test and Fisher’s exact test were used to test statistical differences. Factors associated with clinical response were assessed using univariable and multivariable logistic regression analysis. Drug retention was compared using Cox proportional hazards models.

Results: Seventy-seven (61%) pts received a TNFI and 50 (39%) a non-TNFI as second biologic therapy. Mean age was 56 years, 84% were women and 58% were also treated with methotrexate. At baseline, no significant differences between groups were found, except for significantly higher CRP levels in non-TNFI group (Table 1). No statistical differences were observed in E-Resp between groups at m-6 and m-12. Nevertheless, at m-24 more pts achieved E-Resp in non-TNFI group (80% vs 52%; p=0.001, Figure 1). Likewise, 100% (n=6) of the pts who achieve remission with the second biologic were treated with a non-TNFI. In the univariable analysis, higher baseline DAS28 (OR=1.65, p=0.06) being ACPA positive (OR=3.6, p=0.02) and treatment with a non-TNFI (OR=3.5, p=0.01) were associated with E-Resp at m-24. In the multivariable analysis, baseline DAS28 (OR=1.65, p=0.01) and non-TNFI treatment (OR=3.7, p=0.02) remained associated. Drug survival was similar in both groups (1.6±0.7 in TNFI vs 1.6±0.6 years in non-TNFI, p=0.5). In the subgroup of pts who dropped out due to secondary inefficacy (n=76) no differences in response to the second biologic were found, however, pts who stopped the first TNFI for other reasons (primary ineffectiveness and adverse events) achieved more frequently E-Resp and switching to non-TNFI since the beginning of treatment (m-6: 54% in TNFI vs 86% in non-TNFI, p=0.04; m-12: 56% in TNFI vs 70% in non-TNFI, p=0.4; m-24: 47% in TNFI vs 86% in non-TNFI, p=0.04). The overall incidence of AEs was similar between TNFI and non-TNFI groups (21% in TNFI vs 14% in non-TNFI, p=0.9).

Conclusion: In our cohort of patients with RA and failure to a first TNFI, and mainly after primary failure and adverse events, treatment with a non-TNFI was more effective than a second TNFI at 24 months after switch, without significant differences in the survival of the two treatments. In the subgroup of patients who failed the first TNFI due to secondary inefficacy, both treatment options were equally effective. These data reflect how the reason for discontinuation of a first biologic can guide the response to a second treatment.

Acknowledgement: to Chamaida Plasencia, Victoria Navarro-Compán and Alejandro Balsa
SURVIVAL ON SECOND-LINE BIOLOGIC THERAPY AFTER THE WITHDRAWAL OF AN ANTI-TNF TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS: EXPERIENCE IN A SPANISH TERTIARY HOSPITAL

Andrea Briones-Figueroa, Jaime Arroyo Palomo, Patricia Morán Álvarez, Javier Bachiller-Corral, Mónica Vázquez Díaz. Department of Rheumatology, Ramón y Cajal University Hospital, Madrid, Spain

Background: Patients with Rheumatoid Arthritis (RA) have been traditionally treated with other TNF inhibitors (TNFis) after the withdrawal of a first TNFi (cycling). However, due to the increase in the biological therapy options, changing to a biologic agent with different mechanisms of action (switching) is an alternative choice. More studies are needed to clarify the role of both strategies in order to guide treatment decisions.

Objectives: To analyze the survival of the second biological drug, TNFi or biologic with a different mechanism of action, in patients with RA non-responders to the first TNFi. To evaluate factors associated with the survival of the second-line therapy.

Methods: A retrospective, longitudinal, observational study was performed, which included patients diagnosed of RA and treated with biological therapies between 2008 and 2017, who discontinue a first-line TNFi and started a second-line biological therapy. The demographic and clinical data were obtained from their medical records. Kaplan Meier and Log-rank survival analysis were performed, as well as Cox regression to identify related factors.

Results: 69 patients were identified, 14 men (20.3%) with a mean age at the beginning of the treatment of 52.68 ± 19.79 years. Demographic and clinical data are shown in the table. The main cause of withdrawal of the first TNFi was secondary failure (47.8%), followed by side effects (34.8%) and primary failure (13%). Cycling was performed in 34 patients (49.3%) and switching in 35 (50.7%). During the follow-up, the main causes of withdrawal of the second line treatment were primary and secondary failure (10.1% in both cases). The survival analysis of the 42 patients who presented a primary or secondary failure to the first TNFi was stratified according to the cause of withdrawal of the second biological therapy. No differences were found in the withdrawal rate due to adverse effects among patients who performed switching or cycling (11.42% vs 5.88%, p=0.41).

Conclusions: The survival on second-line biologics after the withdrawal of the first TNFi was similar to cycling or switching strategies. These results may contribute to guide treatment decisions.
Table. Summary of treatment-emergent AEs

<table>
<thead>
<tr>
<th>Group</th>
<th>During Wks 0–96</th>
<th>During Wks 97–185</th>
<th>Sarilumab monotherapy during 186–202</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>15 (56.8)</td>
<td>16 (59.3)</td>
<td>8 (72.7)</td>
</tr>
<tr>
<td>Group 2</td>
<td>10 (58.8)</td>
<td>10 (58.8)</td>
<td>5 (45.5)</td>
</tr>
<tr>
<td>Group 3</td>
<td>10 (58.8)</td>
<td>10 (58.8)</td>
<td>5 (45.5)</td>
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<table>
<thead>
<tr>
<th>AE</th>
<th>n (%)</th>
<th>[number of events per 100 PYs]</th>
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</thead>
<tbody>
<tr>
<td>Any AE</td>
<td>41 (97.6)</td>
<td>[225]</td>
</tr>
<tr>
<td>Serious AE</td>
<td>17 (40.5)</td>
<td>[17]</td>
</tr>
<tr>
<td>AE leading to discontinuation</td>
<td>15 (35.7)</td>
<td>[16]</td>
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</table>

Acknowledgement: Study funding and medical writing support (Mait Lewis, Adelphi) provided by Sanofi and Regeneron Pharmaceuticals, Inc.

Disclosure of Interests: Jeffrey R. Curtis Grant/research support from: Abbvie, Amgen, BMS, Corrona, Janssen, Lilly, Myriad, Pfizer, Roche/Genentech, UCB, Consultant for: Abbvie, Amgen, BMS, Corrona, Janssen, Lilly, Myriad, Pfizer, Roche/Genentech, UCB, Yong Lin Shareholder of: Sanofi, Employee of: Sanofi, Karinthinarad Thangavelu Shareholder of: Sanofi, Employee of: Sanofi, Marina Stanislav Consultant for: Pfizer, Merck Sharp and Dohme, Bristol Myers Squibb, Roche, Boehringer Ingelheim, Schering-Plough, Pfizer, Abbvie, Eli Lilly, José Antonio Maldonado-Cocco Consultant for: Merck, UCSD, Bristol Myers Squibb, Roche, Sanofi-Genezyme, UCB, Thomas Huizenga Consultant for: Merck, UCSD, Bristol Myers Squibb, Bioteest AG, Pfizer, GSX, Novartis, Roche, Sanofi-Aventis, Abbott, Crescendo Bioscience Inc., Nycomed, Boehringer, Takeda, Zydus, Epirus, Eli Lilly, José Antonio Maldonado-Cocco Consultant for: Merck, Pfizer Sharp Dohme, Sanofi – Aventis, Novartis, Bristol Myers Squibb, Roche, Boehringer Ingelheim, Schering – Plough, Abbott, UCB, Eli Lilly, Gilead, Speakers bureau: Pfizer, Merck Sharp Dohme, Sanofi – Aventis, Novartis, Bristol Myers Squibb, Roche, Boehringer Ingelheim, Schering – Plough, Abbott, UCB, Eli Lilly, Marwan Bukhari Speakers bureau: Bristol-Myers Squibb, Cellebrite, Roche/Chugai, Pfizer, Abbvie, Merck, Menarini, Sanofi-Aventis, Eli-Lilly, Janssen and Novartis., Frank Buttger-tol-Myers Squibb, UCB celltech, Roche, Pfizer, Abbvie, Eli Lilly, Kirthanan Thangavelu Consultant for: Abbvie, Biogen, BMS, Genentech, Celltrion, Galapagos-Gilead, Lilly, Novartis, Pfizer, Roche, Sanofi, UCB, YL Biologics, Consultant for: Abbvie, Biogen, BMS, Corrona, Lilly, Genentech, Celltrion, Galapagos-Gilead, Lilly, Novartis, Pfizer, Roche, Sanofi, UCB, YL Biologics


**FR10082**

**EFFECTIVENESS OF TNF INHIBITORS VS. NON-TNF INHIBITORS (ABATACEPT, TOCILIZUMAB AND RITUXIMAB) AFTER FAILURE OF NON-TNF BIOLOGIC DMARD IN RHEUMATOID ARTHRITIS – COLLABORATION BETWEEN FIVE NATIONAL REGISTERS**

Katerina Chatzidionysiou,1 Merete L. Hettland2 Thomas Frisell1 Daniela Di Giuseppe1 Karin Hellgren1 Bente Glintborg8 Dan Nordström9 Kalle Aaltonen4 Nina Trokovic1 Eirik Kristianslund2 Tore K. Kvien3 Sella Aarestad Provan9 Björn Gudbjornsson9 Gerdur Gröndal9 Lene Dryer9 Lars Erik Kristensen8 Tanja Schjädt Jørgensen1, Lennart T.H. Jacobsson7 Johan Askling1 1Clinical Epidemiology Section, Karolinska Institute, Stockholm, Sweden; 2On behalf of the DANBiO registry, Copenhagen, Denmark; 3Helsinki Univ and Hospital, Helsinki, Finland; 4Pharmaceuticals Pricing Board, Ministry of Social Affairs and Health, Helsinki, Finland; 5Dep of Rheum, Diakonhjemmet Hospital, Oslo, Norway; 6Centre for Rheum Research, Univ of Iceland, Reykjavik, Iceland; 7Sahlgrenska Academy at Univ of Gothenburg, Gothenburg, Sweden

Table 1. Baseline (=start of 2nd bDMARD) characteristics of RA patients who switched to a 2nd bDMARD after a non-TNFi and clinical effectiveness. Results are not shown when N<20.

<table>
<thead>
<tr>
<th>1st – 2nd bDMARD</th>
<th>N patients</th>
<th>Age years (mean, SD)</th>
<th>Sex (%)</th>
<th>Disease duration (median, IQR)</th>
<th>RF (%)</th>
<th>Anti-CRP (%)</th>
<th>Concomitant csDMARDs (%)</th>
<th>Concomitant GCs (%)</th>
<th>DAS28 baseline (mean, SD)</th>
<th>DAS28 6 months (mean, SD)</th>
<th>DeltaDAS28 0-6m</th>
<th>N (%) of patients still on drug at month 6 from start of 2nd bDMARD</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABA—TNFi</td>
<td>185</td>
<td>56.1 (13.1)</td>
<td>77.8</td>
<td>4 (2-10)</td>
<td>73.5</td>
<td>64.1</td>
<td>74.1</td>
<td>21.1</td>
<td>4.4</td>
<td>(1.3)</td>
<td>3.5</td>
<td>(1.3)</td>
</tr>
<tr>
<td>ABA—RTX</td>
<td>22</td>
<td>57.7 (17.9)</td>
<td>72.7</td>
<td>4.3 (2-7.6)</td>
<td>71.4</td>
<td>100</td>
<td>40.9</td>
<td>31.8</td>
<td>4.5</td>
<td>(1.0)</td>
<td>3.3</td>
<td>(1.3)</td>
</tr>
<tr>
<td>ABA—TNFi</td>
<td>37</td>
<td>59.4 (11.1)</td>
<td>86.5</td>
<td>6.3 (2.6-11.9)</td>
<td>73.5</td>
<td>54.5</td>
<td>29.7</td>
<td>32.4</td>
<td>4.9</td>
<td>(1.3)</td>
<td>3.8</td>
<td>(1.4)</td>
</tr>
<tr>
<td>RTX—ABA</td>
<td>56</td>
<td>64.3 (12.6)</td>
<td>83.9</td>
<td>12.3 (4.9-21.4)</td>
<td>83.6</td>
<td>57.1</td>
<td>50.0</td>
<td>39.3</td>
<td>4.4</td>
<td>(1.3)</td>
<td>3.8</td>
<td>(1.4)</td>
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<tr>
<td>RTX—TNFi</td>
<td>99</td>
<td>60.1 (12.9)</td>
<td>76.8</td>
<td>8.1 (3-14.2)</td>
<td>78.6</td>
<td>82.4</td>
<td>53.5</td>
<td>42.5</td>
<td>5.2</td>
<td>(1.3)</td>
<td>5.6</td>
<td>(1.3)</td>
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<tr>
<td>TCZ—ABA</td>
<td>29</td>
<td>55.9 (14.6)</td>
<td>86.2</td>
<td>5.0 (2-13.4)</td>
<td>65.5</td>
<td>80</td>
<td>31.0</td>
<td>20.7</td>
<td>4.5</td>
<td>(1.4)</td>
<td>3.9</td>
<td>(1.3)</td>
</tr>
<tr>
<td>TCZ—TNFi</td>
<td>131</td>
<td>57.6 (12.8)</td>
<td>84</td>
<td>4.0 (2-8.1)</td>
<td>77</td>
<td>71.4</td>
<td>36.6</td>
<td>24.4</td>
<td>3.9</td>
<td>(1.4)</td>
<td>3.5</td>
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<tr>
<td>TCZ—RTX</td>
<td>15</td>
<td>60.8 (14.6)</td>
<td>73.3</td>
<td>4.0 (1.9-13.8)</td>
<td>92.9</td>
<td>100</td>
<td>40.0</td>
<td>26.7</td>
<td>4.4</td>
<td>(2.3)</td>
<td>N=20</td>
<td>11 (73%)</td>
</tr>
</tbody>
</table>
Background: The optimal sequencing of biologic Disease Modifying Anti-Rheumatic Drugs (bDMARDs) in Rheumatoid Arthritis (RA) is unknown. Evidence regarding the effectiveness of a 2nd non-TNFi bDMARD, as well as of TNFi, in patients whose 1st bDMARD has been a non-TNFi is limited.

Objectives: To characterize patients switching for medical reasons after failure of a non-TNFi used as 1st bDMARD, and to assess the effectiveness of rituximab (RTX), abatacept (ABA) or tocilizumab (TCZ) vs. a TNFi.

Methods: Patients from 5 national registers (Sweden, Norway, Denmark, Iceland and Finland) with RA who started treatment with a non-TNFi as a 1st bDMARD after 2010 and switched to a 2nd bDMARD within 3 months after the discontinuation of the 1st (with the exception of RTX for which a 6-month window was used), were identified. Clinical effectiveness was assessed by DAS28 change at 6 months.

Results: 611 patients were included in the analyses. 80% were female, which a 6-month window was used), were identified. Clinical effectiveness were explored for most switching strategies. 63% of patients were still on treatment with their 2nd bDMARD at 6 months after switch.

Conclusion: The six-month drug retention for a 2nd bDMARD in patients with RA switching due to failure of a non-TNFi bDMARD as 1st ever bDMARD was lower than two thirds (63%). More detailed analyses are exploring potential subgroups of patients for whom specific switching strategies are more effective.

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THE IMPACT OF IL-6 AND TNF INHIBITORS ON HEMOGLOBIN LEVELS: AN ANALYSIS FROM RHUMADATA® CLINICAL DATABASE AND REGISTRY

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Background: Anemia is a common feature of RA. Prior to the appearance of biologic treatments, improvement of hemoglobin (Hb) levels was unusual and inconsistent. With better control of the inflammatory process by cytokine inhibitors, it has been shown that Hb levels can improve substantially. Recently in the development of IL-6 receptor antagonists (sarilumab (SARI) and tocilizumab (TOCI)) data have shown improvement in Hb levels related to the downstream regulation of hepcidin. No direct comparison of Hb levels between TNF and IL-6 inhibition has been observed in observational data (1).

Objectives: This analysis compares the impact of TNF and IL-6 inhibitors on Hb levels over time.

Methods: Data collected since January 1, 2015 (when TOCI and SARI were available in Canada) at the Institut de Recherche en Rhumatologie de Montréal (IRRM) and the Centre de l’Ostéoporose et de Rhumatologie de Québec (CORQ) was extracted from the Rhumadata® clinical database and registry on January 7, 2019. Selected patients were those initiated on an IL-6 antagonist or a TNFi (adalimumab, certolizumab, etanercept, golimumab or infliximab) and had been treated for at least one year. Furthermore, patients were cancer free and had no diagnosis of Crohn’s disease or ulcerative colitis and had creatinine (Cr) and ALT levels within the normal sex-specific range. IL-6 patients were matched (ratio 1:2) to TNFi patients based on age at treatment initiation, gender and baseline Hb. The collected data included baseline characteristics (socio-demographic variables, concomitant and past medication, comorbidities and the Charlson comorbidity index (CCI)), variables measured over time (Hb and other laboratory test results, patient and physician-reported outcomes, and disease activity measures such as CDAI and DAS28(4)-ESR). The groups were compared to identify potential confounders.

Results: A total of 145 patients initiating an IL-6 antagonist since January 1, 2015 were matched with 286 patients prescribed a TNF inhibitor during the same time-period. Most patients were women (86%), the mean age at treatment initiation was 54.1 standard deviation: 11.7) years, and 16% were smokers. Baseline patient global, pain and fatigue assessments, made on a visual analogue scale ranging from 1 to 10, were 5.4 (2.5), 6.1 (2.5) and 5.5 (3.0) in the IL6 group and 5.1 (2.7), 5.5 (3.0) and 5.0 (3.2) in the TNFi group. Baseline disease activity was assessed as moderate or high/severe in 85.5% (IL6) and 85.9% (TNFi) of patients (DAS28(4)-ESR criteria). At treatment initiation, mean Hb level was 126.6 (12.4) g/L, and Cr and ALT levels were 66.2 (11.5) umol/L and 18.7 (6.5) U/L in the IL6 group and 67.0 (12.0) umol/L and 19.3 (6.8) U/L in the TNFi group. At three months, Hb had increased by 5.4 (10.2) g/L in the TNFi group and by 1.8 (13.9) g/L in the TNFi group (p-value=0.024). These respective changes at 12 months were 8.7 (11.4) g/L and 5.4 (9.2) g/L (p-value=0.042).

Conclusion: This analysis confirms that IL-6 inhibition provides a numerically and statistically superior increase in Hb over TNF.

REFERENCE:

Disclosure of Interests: Denis Choquette Grant/research support from: Abbvie, Amgen, Eli Lilly, Novartis, Pfizer, Sandoz, Consultant for: Abbvie, Amgen, Eli Lilly, Novartis, Pfizer, Sandoz, Diane Sauvageau: None declared, Édith Villeneuve Consultant for: Abbvie, UCB, Celgene, Roche, Pfizer, Amgen, BMS, Sanofi-Genzyme, Paid instructor for: Abbvie, Speakers bureau: Abbvie, Pfizer, BMS, Roche, Louis Coupal: None declared DOI: 10.1136/annrheumdis-2019-eular.4161
China-manufactured adalimumab biosimilar, HLX03, demonstrated pharmokinetic equivalence and comparable safety to reference adalimumab

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Background: Adalimumab was first launched in China in August 2010 with more than 10 million people having its indications.1, 2 However, the high cost of the biologic drug limits the treatment accessibility and reduces the quality of life in patients living with the chronic inflammatory disease like rheumatoid arthritis and psoriasis. In accordance with the China National Medical Product Administration (NMPA) biosimilar regulatory development pathway, biosimilar products require to demonstrate similarity in pharmacokinetics (PK) and safety profile compared to its reference drug, which could further address the unmet medical needs of adalimumab. HLX03 was developed as a proposed biosimilar to adalimumab with the potential to increase affordable treatment options for patients.

Objectives: The study was aiming to compare the pharmacokinetics (PK), safety and immunogenicity of the proposed adalimumab biosimilar HLX03 with reference product.

Methods: We conducted a randomised, double-blind, parallel-controlled clinical trial (NCT03057935) in China to compare the PK, safety and immunogenicity of HLX03 and China sourced adalimumab (CN-adalimumab). In this study, 211 healthy volunteers were randomised 1:1 to receive a single (40 mg) subcutaneous injection of HLX03 or CN-adalimumab. The primary PK endpoint was area under the curve from time zero to the last quantifiable concentration (AUC0-t) and maximum observed concentration (Cmax). The secondary PK endpoint was AUC from time zero to infinity (AUC0-inf). PK equivalence was established if the 90% confidence interval (CI) for the test-to-reference ratio fell within the 80-125% equivalence margin.

Results: Based on the analysis of 210 subjects in the per protocol population (PPS) and 211 subjects in the full analysis set (FAS), HLX03 demonstrated PK equivalence to CN-adalimumab for all primary endpoints (Table 1). The percentage of adverse events (AEs) between two treatment groups were similar, with treatment-emergent AEs (TEAEs) noted by 32.5 and 36.5% of patients in the HLX03 and CN-adalimumab group, respectively. One subject suffered non-drug-related severe AE (tuberculosis) in the HLX03 arm, and one subject occurred grade 4 AE (elevated creatine phosphokinase) in the CN-adalimumab arm. In the group of CN-adalimumab, 6 more incidents of positive anti-drug antibodies (ADA) were identified at day 7 and no further significant difference observed. Based on the established clinical PK equivalence and safety similarities, 262 patients with moderate-to-severe chronic plaque psoriasis were randomized in 21 centers at 1:1 ratio to conduct a double-blind, parallel-controlled phase 3 study (NCT03316781) to further evaluate the efficacy and safety profiles of HLX03 and reference adalimumab. The primary efficacy endpoint was the improvement rate of Psoriasis Area and Severity Index (PASI) over the baseline at week 16.

Conclusion: PK equivalence and safety similarities between HLX03 and CN-adalimumab were demonstrated which leads to a multi-center, randomised, double-blind, parallel-controlled phase 3 study to further evaluate the efficacy and safety of HLX03 as the proposed biosimilar of adalimumab in patients with moderate-to-severe plaque psoriasis.

REFERENCES:


Efficacy, safety, and immunogenicity results of the switch from reference adalimumab (refADL) to Sandoz biosimilar adalimumab (SDZ-ADL) from admYRA phase 3 study in patients with moderate-to-severe rheumatoid arthritis (RA)

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Background: SDZ-ADL is approved by EMA in all indications of refADL based on preclinical and clinical study results. EMA submission data included results of a Phase 3 study in patients with plaque psoriasis. ADMYRA was a Phase 3 study comparing efficacy and safety of SDZ-ADL and refADL in patients with moderate-to-severe RA with inadequate response to disease modifying anti-rheumatic drugs, including methotrexate (NCT02744755).

Objectives: The ADMYRA study was designed to compare the efficacy of SDZ-ADL and refADL over 24 weeks of treatment, and to evaluate long-term efficacy, safety, and immunogenicity of SDZ-ADL up to Week (Wk) 48. The study also investigated the effect of the switch from refADL to SDZ-ADL at Wk 24 on efficacy, safety, and immunogenicity up to Wk 48. This abstract focuses on the data after switch from refADL to SDZ-ADL.

Methods: Eligible patients were randomized 1:1 to receive 40 mg subcutaneous SDZ-ADL or refADL every other week from Wk 0–22. At Wk 24, patients in the refADL arm were switched to receive SDZ-ADL; treatment continued until Wk 46. The primary endpoint was change in Disease Activity Score-28 including high-sensitivity C-reactive protein (DAS28-ESR) from baseline at Wk 12. Secondary endpoints included mean changes in DAS28-CRP scores, the proportion of patients fulfilling EULAR response criteria, safety, and immunogenicity up to Wk 48.

Results: As reported previously, mean change in DAS28-CRP from baseline at Wk 12 was -2.16 for SDZ-ADL (N=140) and -2.18 for refADL (N=144).1 Efficacy in both treatment arms was maintained throughout the study, also after the switch from refADL to SDZ-ADL at Wk 24. Mean change in DAS28-CRP from baseline at Wk 48 was -2.90 and -2.92 for refADL/switched and SDZ-ADL groups, respectively. At Wk 48, the proportion of patients with moderate/good EULAR response was 29.6/68.0% in refADL/switched group and 29.0/69.2% in SDZ-ADL group. At Wk 48, the proportion of patients in EULAR remission was 54.4 and 51.4% and in Boolean remission was 21.6 and 16.8% for refADL/switched and SDZ-ADL groups, respectively. As previously reported, safety and immunogenicity were similar in both arms before switch.1 No new safety concerns were identified after switch. After switch, 32.5% of patients in the refADL/switched group and 36.5% of patients in the SDZ-ADL group experienced adverse events (AEs); serious AEs were reported by 3.6 and 2.5%, respectively. The proportion of patients reporting injection site reactions after switch was 1.2% in the refADL/switched group and 0.6% in the SDZ-ADL group, respectively. After switch, 26.3 and 24.0% of patients
were positive for antidrug antibodies (ADAs) in refADLswitched and SDZ-ADL groups, respectively. Of these, 81.0 vs 72.2% were neutralizing. ADA positivity had no clinically meaningful impact on safety.

**Conclusion:** After the switch from reference to biosimilar, the rates of EULAR remission response and Boolean remission were high and maintained until Week 48. Treatment switch from refADL to SDZ-ADL at Wk 24 did not impact efficacy, safety, or immunogenicity.

**REFERENCE:**

**Disclosure of Interests:** Piotr Willard Speakers bureau: Novartis, Pfizer, Abbvie, Gedeon-Richter, Lilly, Roche and Sandoz, Slawomir Jeka: None declared, Eva Dokoupilova: None declared, Juan Manuel Miranda Limon: None declared, Julia Jauch-Lembach Employee of: Hexal AG, Anjil Thakur Employee of: Hexal AG, Halimurayazi Haldalua Employee of: Hexal AG, Norman Gaylis Grant/research support from: Multiple clinical research trials, BMS, AbbVie, GSK, Janssen, Amgen, Pfizer, Regeneron, UCB, Sanofi, SetPoint, ImmunPharma, Astra Zeneca, Sandoz, Novartis, Gilead, Consultant for: electroCore

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**SAFETY, IMMUNOGENICITY AND EFFICACY OF THE PROPOSED BIOSIMILAR MSB11022 (MODIFIED FORMULATION) COMPARED WITH ADALUMMA B REFERENCE PRODUCT IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE RHEUMATOID ARTHRITIS: AURIEL-RA, A RANDOMISED, DOUBLE-BLIND, PHASE III STUDY**

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**Background:** Adalimumab is a fully human anti-TNF monoclonal antibody indicated for the treatment of multiple inflammatory disorders, including rheumatoid arthritis (RA). MSB11022 is a proposed adalimumab biosimilar that has been shown to be structurally and functionally similar to the adalimumab reference product. MSB11022 has been developed in two formulations, in a citrate-based buffer, and in a modified buffer and stabiliser. MSB11022 demonstrated bioequivalence and comparable safety, tolerability and immunogenicity profiles to reference adalimumab (both in citrate formulations) in a study in healthy volunteers. Subsequently MSB11022 was shown to be therapeutically equivalent to reference adalimumab (both citrate formulations) in terms of efficacy, safety and immunogenicity in psoriasis patients in the 52-week, Phase III, pivotal AURIEL-RA Patient baseline characteristics were comparable between treatment groups. Few adverse events of special interest were reported during the study. Numbers are n (%) or mean ± standard deviation. DAS28, Disease Activity Score-28; ESR, erythrocyte sedimentation rate; ITT, intention-to-treat set; SAF, safety analysis set; TEAE, treatment-emergent adverse event.

**REFERENCES:**

**Disclosure of Interests:** Christoph Edwards Grant/research support from: Abbvie, BMS, Biogen, Celgene, Fresenius–Janssen, Lilly, Mundipharma, Pfizer, MSD, Novartis, Roche, Samsung, Sanofi, UCB, Consultant for: Abbvie, BMS, Biogen, Celgene, Fresenius–Janssen, Lilly, Mundipharma, Pfizer, MSD, Novartis, Roche, Samsung, Sanofi, UCB, SetPoint, Speakers bureau: Novartis, Pfizer, MSD, Novartis, Roche, Samsung, Sanofi, UCB, Employee of: Former employee of Fresenius Kabi SwissBioSim, Joëlle Monnet Employee of: Employee of Fresenius Kabi SwissBioSim, Martin Ullmann Shareholder of: Amgen, BMS, Employee of: Employee of Fresenius Kabi SwissBioSim, Panetis Vlahos: None declared

**DOI:** 10.1136/annrheumdis-2019-eular.4220

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**SAFETY AND EFFICACY OF RADIONUCLIDE SYNOVECTOMY IN PATIENTS WITH PERSISTENT INFLAMMATORY OF SINGLE JOINT IN THE COURSE OF BIOLOGICAL THERAPY**

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**Background:** Radionuclide synovectomy (RSV) is a form of minimally invasive treatment of persistent joint inflammation. Primary indication for RSV is hypertrophic synovitis refractory to disease-modifying anti-rheumatic drugs (DMARDs), whether synthetic or biological, and intraarticular steroid injections. This procedure has a high rate of success with a low rate of adverse events and complications in properly selected patients. Moreover, due to bactericidal properties of the radionuclides, the risk of infection after RSV is insignificant, and incidence of post-injection septic arthritis is extremely low.

**Objectives:** To assess safety and efficacy of RSV in patients with inflammatory rheumatic diseases treated with biological disease-modifying anti-rheumatic drugs (bDMARDs).

**Methods:** We analyzed outcomes of 76 radionuclide synovectomy interventions in 47 patients (37 female and 10 male) ongoing biological therapy. The patients were diagnosed as follows: rheumatoid arthritis (RA) – 37, anklyosing spondylitis (AS) – 7, psoriatic arthritis (PsA) – 2 and juvenile idiopathic arthritis (JIA) – 1 patient. The majority of the patients were treated with TNF-alpha inhibitors (79%), which included: adalimumab (31.6%), etanercept (25%), golimumab (14.5%) and certolizumab (7.9%). The other patients were treated with interleukin-6 receptor antagonist tocilizumab (19.7%) and anti-CD20 monoclonal antibody rituximab (1.3%).

**Patients with overall good response to biologics and persistent inflammation of single joint confirmed by ultrasound PD examination, in case of no contraindications were qualified for RSV procedure. For the RSV following radiotherapeutics were used: rhenium-186 sulphide in 41 cases for shoulder (2), elbow (15), wrist (22), hip (2) and ankle (2) joints; yttrium-90 citrate in 27 cases for knee joints; erbium-169 citrate in 8 cases for small joints of hand and feet. All patients had a follow-up visit 3 and 6 months after RSV, during which a clinical and ultrasound examination of the treated joints were performed. Continuous adverse events collection was conducted.

**Results:** The most common indication for RSV was RA – 60 procedures (78.9%), followed by AS – 10 (13.2%), PsA – 4 (5.3%) and JIA – 1 procedure (2.6%). 27 patients had RSV intervention in one joint. 17

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### Table 1

<table>
<thead>
<tr>
<th>Endpoint (analysis set)</th>
<th>Timepoint (Week)</th>
<th>MSB11022</th>
<th>Reference adalimumab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence of AESIs of hypersensitivity (SAF)</td>
<td>52</td>
<td>6 (4.2)</td>
<td>8 (5.5)</td>
</tr>
<tr>
<td>Incidence of TEAEs (SAF)</td>
<td>52</td>
<td>83 (58.0)</td>
<td>93 (64.1)</td>
</tr>
<tr>
<td>ACR20 response (ITT)</td>
<td>12</td>
<td>113 (79.6)</td>
<td>114 (80.9)</td>
</tr>
<tr>
<td>DAS28-ESR (ITT)</td>
<td>12</td>
<td>3.3 ± 1.2</td>
<td>3.4 ± 1.2</td>
</tr>
<tr>
<td>Overall incidence of ADAs (SAF)</td>
<td>52</td>
<td>115 (80.4)</td>
<td>104 (71.7)</td>
</tr>
<tr>
<td>Overall incidence of NABs (SAF)</td>
<td>52</td>
<td>57 (39.9)</td>
<td>57 (39.3)</td>
</tr>
</tbody>
</table>

Numbers are n (%) or mean ± standard deviation. DAS28, Disease Activity Score-28; ESR, erythrocyte sedimentation rate; ITT, intention-to-treat set; SAF, safety analysis set; TEAE, treatment-emergent adverse event.
patients with satisfactory response to RSV in one joint required radioisotope treatment in another joint (between 2 and 4 different joints were treated in each patient – 13 patients in 2 joints, 5/3 and 2/4). Median patient age was 50 years (21 – 72). Duration of continuous bDMARD treatment preceding RSV was between 1 and 72 months. The intervals between bDMARD administration and RSV ranged from below 24 hours to 4 weeks. Satisfactory effects of RSV, defined as absence of clinical and ultrasound symptoms of inflammation, were observed after 55 (72.4%) interventions. In 11 (14.4%) cases after initial improvement, the inflammation symptoms recurred less than 6 months after RSV. In 10 (13.2%) cases RSV had no effect.

No side effects or adverse events occurred after RSV and, most importantly, there were no local or systemic infections observed up to 6 months after the procedure.

Conclusion: RSV seems to be an effective single joint treatment method in patients with active synovitis refractory to bDMARDs. Despite increased susceptibility to infection in patients partially immunocompromised and biological treatment, no septic complications were observed after RSV. RSV does not require discontinuation of biological treatment, unlike surgical synovectomy.

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FRID090 SINGLE CENTRE COHORT OF REFRACTORY RHEUMATOID ARTHRITIS ALSO IDENTIFIES A RARE SUBGROUP OF MULTIPLE TARGETED THERAPY CLASS NON-RESPONSE

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Background: Refractory Rheumatoid Arthritis (RefRA) has emerged as an area of unmet need in the biologic era (1). Failure of 3 or more classes of targeted therapy or failure of both an anti-cytokine and a cell-targeted treatment have been proposed as possible definitions (1, 2). The BSRBR-RA reported 6% fulfilled RefRA criteria (due to lack of efficacy and/or toxicity; but only including a first line TNF inhibitor bDMARD cohort) (2).

Objectives: To evaluate the extent of multi-targeted therapy RefRA in our tertiary RA single-centre experience, and identify any patterns of drug sequencing associated with development of RefRA.

Methods: We used a prospective database of RA patients established on targeted therapy, supplemented with information from individual funding requests and a review of our specialised biologic clinic patient notes to identify those who have been prescribed 2 or more classes of targeted therapies. Data on number and type of targeted therapy, and where available, reason for failure has been recorded. Disease activity state and functional outcomes are currently being evaluated.

Results: Of a cohort of over 1500 RA patients that have received at least 1 targeted therapy, 172 patients have received 3 classes of targeted therapies (reasons for each drug discontinuation has been identified in 166 cases). An additional 50 patients have received multiple (2 or more) TNFi and at least 1 other class of targeted therapy (2). Table 1 details numbers in each category of targeted therapy.

<table>
<thead>
<tr>
<th>2 class bDMARD</th>
<th>3 or all 4 classes bDMARD</th>
<th>Multi bDMARD (min. 2 class) + JAKi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients (n=166)</td>
<td>64*</td>
<td>76</td>
</tr>
<tr>
<td>RF and/or CCPa (n=134)</td>
<td>48 (75%)</td>
<td>66 (87%)</td>
</tr>
<tr>
<td>1st Targeted Therapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>TNFi</td>
<td>54</td>
<td>61</td>
</tr>
<tr>
<td>Rituximab</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>Tocilizumab</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Abatacept</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Reason for drug discontinuation

Primary NR only 5 | 3 | 2 |
Secondary NR only | 7 | 6 | 0 |
Mixed primary/secondary NR | 31 | 28 | 6 |
Mixed NR and toxicity | 19 | 36 | 17 |
Multiple toxicity | 3 | 2 | 1 |

* 48 patients received one anti-cytokine and one cell-targeted bDMARD, 12 received two anti-cytokine bDMARD (TNF and tocilizumab) and 3 received two cell targeted treatments (rituximab and abatacept).

In those who had failed multiple anti-TNF drugs 39 were switched to a cell-targeted therapy (31 Rituximab, 7 Abatacept), the rest were switched from a TNFi to tocilizumab. 36 out of 39 patients have maintained a response to their cell-targeted therapy after failing multiple anti-cytokines. 5 Patients demonstrate at least 3 primary non-responses with a further 4 further patients with multiple primary non-response and only 1 adverse event.

Conclusion: Over 10% of our single-centre targeted therapy exposed cohort demonstrate multi-targeted therapy RefRA. The majority comprise mixed non-response, loss of response and drug toxicity. A rare subgroup of 6% of RefRA demonstrate lack of efficacy to multiple therapies. On-going investigations aim to identify the clinical phenotype, predictors and underlying biology.

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Disclosure of Interests: John Filton: None declared, Andrew Melville: None declared, Kamran Naraghi: None declared, Jacqueline Nam: None declared, Shouvik Dass: None declared, Paul Emery Grant/research support from: Pfizer, MSD, AbbVie, Bristol-Myers Squibb, Roche, Consultant for: Pfizer, MSD, AbbVie, Bristol-Myers Squibb, UCB, Roche, Novartis, Gilead,Samsung, Sandoz and Lilly, Maya Buch Grant/research support from: Pfizer LTD, UCB, Consultant for: AbbVie, Eli Lilly, EMD Serono, Pfizer Ltd. Sandofi DOI: 10.1136/annrheumdis-2019-eular.7444

FRID091 UNEMPLOYED FEMALE RHEUMATOID ARTHRITIS PATIENTS ARE LESS ADHERENT TO THE BIOLOGIC DMARD TREATMENT

FRISO LABR1, Francesca Ornetto1, Davide Astori1, Bernd Rahfelder1, Costantino Bortoli1, Daniela Azzolina1, Marta Favero1, Dario Gregori1, John Done4, Andrea Doria1, 1University of Padova, Rheumatology Unit – Department of Medicine (DIMED), Padova, Italy; 2University of Padova, Department of Cardiac, Thoracic and Vascular Sciences, Padova, Italy; 3University of Padova, Unit of Biostatistics, Epidemiology and Public Health, Department of Cardiac, Thoracic and Vascular Sciences, Padova, Italy; 4University of Hertfordshire, Department of Psychology and Sports Sciences, Hatfield, United Kingdom

Background: The 5-item Compliance Questionnaire for Rheumatology (CQR5) allows the identification of patients likely to be high adherers (HAs) to anti-rheumatic treatment (i.e. taking >80% of their medications correctly), or “low adherers” (LAs). An Italian version of the questionnaire was validated (I-CQR5) [1].

Objectives: The objective was to investigate what factors are associated with high treatment adherence according to I-CQR5 in RA patients treated with biologic DMARDs (bDMARDs).

Methods: RA patients (with disease duration >1 year, undergoing treatment with <1 self-administered biological disease-modifying anti-rheumatic drug (bDMARD), willing and capable of completing the questionnaire unaided) were enrolled in the study. I-CQR5 were anonymous and clinical data were collected from the local database. Factors included were demographic, social characteristics of the patients, clinical and treatment variables. Factors achieving a p<0.10 in univariate analysis were included in a multivariate regression analysis.

Results: Among 604 RA patients, 193 patients were included in the validation analysis. Median age of the patients was 57 years (46-65), 142 (73.4%) were females, median disease duration was 15 years (9-21); 82 (42.7%) patients were treated with low dose bDMARDs; 174 (91.1%) patients were in low disease activity or remission (Fig.1). HAs were 40.9% (79/193) of patients: 100% (193/193) of patients treated with bDMARDs and 22.4% (57/193) of those treated with bDMARDs in combination with conventional synthetic DMARDs. Female gender, no employment, lower education level, positive Rheumatoid Factor and/or Anti-Citrullinated Peptides Antibodies, low bDMARD dose, higher patient-VAS were significantly more frequent in LAs compared with HAs. In the multivariate analysis, employment was also positively and significantly associated with high adherence: OR 2.89 (1.3-6.44), p=0.009 (Tab.1).

Conclusion: As previously reported only one third of RA patients treated with bDMARDs were found to be HAs to treatment according to the I-CQR5. Employment status was the major determinant, increasing by almost 3-fold the likelihood of being adherent. Education level and female gender might be also taken into account as factors influencing treatment adherence.

Disclosure of Interests: Francesca Ornetto: None declared, Davide Astori: None declared, Bernd Rahfelder: None declared, Costantino Bortoli: None declared, Daniela Azzolina: None declared, Marta Favero: None declared, Dario Gregori: None declared, Andrea Doria: Consultant for: Pfizer, MSD, AbbVie, Bristol-Myers Squibb, UCB, Roche, Novartis, Gilead,Samsung, Sandoz and Lilly, Maya Buch Grant/research support from: Pfizer LTD, UCB, Consultant for: AbbVie, Eli Lilly, EMD Serono, Pfizer Ltd. Sandofi DOI: 10.1136/annrheumdis-2019-eular.7348
SAFETY AND EFFICACY OF FILGOTINIB IN ACTIVE RHEUMATOID ARTHRITIS BY PRIOR BIOLOGICAL DMARD EXPOSURE IN PATIENTS WITH PRIOR INADEQUATE RESPONSE OR INTEGRATION TO BIOLOGICAL DMARDS (BDMARD-IR)

Mark C. Genovese1, Kenneth Kalunian2, Jacques-Eric Gottenberg3, Neelufar Mozaffarian4, Beatrix Bartok4, Franziska Matzkies4, Jie Gao4, Ying Guo4, Mark C. Genovese1, Kenneth Kalunian2, Jacques-Eric Gottenberg3, David Walker4, Kurt de Vlam5, Tsutomu Takeuchi5

Background: Filgotinib (Fil), an oral selective Janus kinase 1 (JAK1) inhibitor, significantly improved the signs and symptoms of rheumatoid arthritis (RA) in patients with a favorable safety profile in a global phase 3 study in bDMARD-IR patients with active RA (FINCH2).1

Objectives: To assess the safety and efficacy of FIL in the FINCH2 study by the number and type of prior bDMARDs.

Methods: FINCH2 enrolled 449 bDMARD-IR patients with moderate-to-severe active RA. Patients were randomized 1:1 to FIL 200 mg, FIL 100 mg or placebo (PBO) on a background of csDMARDs for 24 weeks. In this prespecified subgroup analysis, efficacy and safety were analyzed according to the number (<3 vs ≥3) of previous bDMARDs used.

Results: 448 patients received ≥1 dose of study drugs. Of these, 343 were previously exposed to <3 bDMARDs, while 105 were previously exposed to ≥3 bDMARDs. Table 1 shows demographics and baseline (BL) characteristics of patients in these 2 groups; efficacy and safety parameters (Table 2) were similar for both groups. There were no cases of opportunistic infection, active tuberculosis, malignancy, gastrointestinal perforation, or death.

Table 1. BL Demographics and characteristics

<table>
<thead>
<tr>
<th></th>
<th>&lt;3 bDMARDs (n=343)</th>
<th>≥3 bDMARDs (n=105)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>Mean (SD) 61.5 (11.8)</td>
<td>Mean (SD) 60.0 (11.7)</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td>90 (82)</td>
<td>92 (77)</td>
</tr>
<tr>
<td>Employment</td>
<td>54 (13)</td>
<td>55 (13)</td>
</tr>
<tr>
<td>Concurrent MTX, n (%)</td>
<td>98 (89)</td>
<td>101 (85)</td>
</tr>
<tr>
<td>Concurrent TNF, n (%)</td>
<td>98 (89)</td>
<td>101 (85)</td>
</tr>
<tr>
<td>Concurrent VEGF, n (%)</td>
<td>98 (89)</td>
<td>101 (85)</td>
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<tr>
<td>Concurrent A20, n (%)</td>
<td>98 (89)</td>
<td>101 (85)</td>
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<tr>
<td>Concurrent A20, n (%)</td>
<td>98 (89)</td>
<td>101 (85)</td>
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</table>

Table 2. Key week 24 efficacy and safety outcomes

<table>
<thead>
<tr>
<th></th>
<th>&lt;3 bDMARDs (n=343)</th>
<th>≥3 bDMARDs (n=105)</th>
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<tbody>
<tr>
<td>ACR20 n (%)</td>
<td>42.4%</td>
<td>54.6%</td>
</tr>
<tr>
<td>DAS28(CRP) &lt;3</td>
<td>77.7%</td>
<td>85.1%</td>
</tr>
<tr>
<td>DAS28(CRP) ≥3</td>
<td>77.7%</td>
<td>85.1%</td>
</tr>
<tr>
<td>DAS28(CRP) &lt;3</td>
<td>77.7%</td>
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<td>77.7%</td>
<td>85.1%</td>
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</tbody>
</table>

Conclusion: In bDMARD-IR patients with active RA, FIL treatment for 24 weeks significantly improved the signs and symptoms of RA with a favorable safety profile; notably, efficacy and safety results were similar for patients with <3 or ≥3 prior bDMARDs.

REFERENCES:
IMPACT OF INTERLEUKIN 6 RECEPTOR INHIBITOR ON LONG TERM DRUG SURVIVAL FOR BIOSIMILAR SB4

54% of pts achieved remission (DAS28<2.6) and 46% of pts managed laboratory parameters were found in RA pts after 12 m of TCZ infusion:

Results:
Significant positive changes in major disease activity clinical and chemiluminescence method Elecsys proBNP II (Roche Diagnostics, [18;25]mg/week). Serum levels of NT-proBNP were measured using electro-
tory of cardiovascular diseases - 36%, hypodynamia - 68%. Coronary artery tension - in 75%, dyslipidemia - 61%, smoking - 17%, overweight - 61%, family his-
failures. High incidence of traditional risk factors was found in RA pts: arterial hyper-

Methods:
The investigation enrolled 31 patients (pts) (26women/5men) with the objective to investigate the impact of interleukin 6 receptor inhibitor -
Objectives:
Background:
Medical Surgical Center named after N.I.Pirogov


Background:
The new millennium biologic therapies e.g. tumor necrosis factor inhibitors (TNFi) have played a major role improving clinical outcomes in rheumatoid arthritis (RA), psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA). A major limitation in many countries for pre-
scribing these drugs has been the high drug costs. The present time for sales of these TNFis e.g. infliximab, etanercept and adalimumab has ended and as a consequence biosimilar TNFis are now reaching the market. This has a cost saving potential for payers. In Norway, encour-
aged by the health authorities, non-medical switch from biologic originator drugs with biosimilar drugs available, including etanercept. To the best of our knowledge no longer than one year real life experienced real life evi-
dence data for non-medical switch from originator etanercept to biosimilar etanercept SB4 exist (ref.1).

Objectives:
At the participating outpatient clinics patients with RA, PsA and axSpA were monitored using a computer clinical system, as standard clini-
care. Demographic, clinical and treatment data were retrieved from the computer system for patients who started treatment with biosimilar etanercept SB4 between January 2016 and January 2019. Kaplan-Meier survival curves were used to explore drug survival. Survival differences between groups were tested using Breslow statistics.

Results:
At the participating outpatient clinics since 2016 a total of 474 RA, 249 PsA and 320 axSpA patients had a non-medical switch from biologic originator to biosimilar etanercept SB4. In RA, PsA and ax-
SpA patients the percentage of women was 68.2%, 42.6% and 30.3%, the percentage of current smokers 17.0%, 12.8% and 19.6%, mean (SD) age was 63.0 (13.1), 58.2 (11.3), 53.1 (12.1) years and disease duration 16.8 (9.8), 16.1 (9.7), 17.7 (9.0) years, respectively. In RA 80.0% were anti-CCP positive and in PsA and axSpA 34.4% and 90.8% were

**FR0093 IMPACT OF INTERLEUKIN 6 RECEPTOR INHIBITOR ON N-TERMINAL PRO-BRAIN NATRIURETIC PEPTIDE IN PATIENTS WITH RHEUMATOID ARTHRITIS**

Helen Gerasimova1, Tatiana Popkova1, Maria Cherkasova1, Diana Novikova1, Galina Lukina, Satenik Davidian3.

Rheumatology, Moscow, Russian Federation

Methods:
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**FR0094 LONG TERM DRUG SURVIVAL FOR BIOSIMILAR SB4 ETANERCEPT IN RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS AND AXIAL SPONDYLOARTHROSIS PATIENTS WITH A NON-MEDICAL SWITCH FROM ETANERCEPT REFERENCE DRUG**

Glen Haugberg1, Børj Tilde Svanes Fyve2, Gunnstein Bakland3, Erik Rådevand4, Andreas Diamantopoulos5,6, Sørlandet Hospital Kristiansand, Rheumatology, Kristiansand, Norway, 7Haukeland hospital, Rheumatology, Bergen, Norway, 8University Hospital of North Norway HF, Rheumatology, Tromsø, Norway, 9St. Olav's Hospital HF, Rheumatology, Trondheim, Norway, 10Martina Hansens Hospital, Rheumatology, Bergen, Norway

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Changes in B Cell Profile as Indicator of Clinical Remission to TNF Inhibitors in Patients with Rheumatoid Arthritis

Borja Hernández-Breijo1, Israel Nieto-Gañán2, Cristina Sobrino2, Victoria Navarro-Compañ1, Ana Martínez-Feito1,2, Carlota García-Hoz2, Paloma Luapente-Suanzes2, Javier Bachiller-Corral2, Gemma Bonilla2, Cristina Pipan Moratalla2, Garbriele Roy2, Mónica Vázquez2, Alejandro Balsa2, Luisa Maria Villar2, Dora Pascual-Salcedo1, Eulalia Rodríguez-Martín1, Chaimada Plascencia1,4

1Immuno-Rheumatology research group, IDI-Paz. La Paz University Hospital, Madrid, Spain; 2Immunoology Department, Ramón y Cajal University Hospital and IRYCIS, Madrid, Spain; 3Rheumatology Department, Ramón y Cajal University Hospital and IRYCIS, Madrid, Spain; 4Rheumatology Department, La Paz University Hospital, Madrid, Spain; 5Immunoology Department. La Paz University Hospital, Madrid, Spain.

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease with the typical characteristic of synovitis of small-sized and medium-sized joints that leads to cartilage and bone damage. TNF inhibitors (TNFi) are widely used for the treatment of rheumatoid arthritis (RA) however, there are still no objective indicators of clinical response to TNFi therapy.

Objectives: To analyse the change of peripheral blood mononuclear cells (PBMC) profile after 6 months (m) of treatment with TNFi in order to find cellular indicators of response.

Methods: Prospective bi-center pilot study including 100 RA patients receiving TNFi therapy. PBMC were isolated from patients at baseline and 6m of treatment, and were analysed by flow-cytometry. Clinical activity at baseline and 6m of TNFi treatment was assessed by DAS28. Clinical remission (DAS28<2.6) after 6m of treatment was considered as optimal response. The association between clinical remission and the percentage of change (Δ, 6m-0m) within each PBMC subset was analysed through univariate logistic regression model (odds ratio; 95% CI; β; p-value).

Results: Demographic characteristics before starting TNFi therapy are shown in Table 1. After 6m of TNFi treatment, 40% patients achieved clinical remission. Decreased percentage of B cells (ΔCD19+) was found after 6m of TNFi treatment in optimal responders, while suboptimal responders did not show differences with the baseline (OR: 0.78; 95% CI: 0.63-0.97; β: -0.25; p: 0.027) (Figure 1). This effect was essentially owing to a reduction of naïve B cells (OR: 0.76; 95% IC: 0.62-0.94; β: -0.27; p: 0.011) (Figure 1). No significant association was found between the other PBMC subsets (monocytes, NK cells, CD4+ T cells and CD8+ T cells) and clinical remission (Figure 1).

Table 1

<table>
<thead>
<tr>
<th>Baseline patients’ characteristics</th>
<th>Total patients (n=100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years); mean±SD</td>
<td>53±13</td>
</tr>
<tr>
<td>Female; n (%)</td>
<td>84 (84)</td>
</tr>
<tr>
<td>Disease duration (years); median (IQR)</td>
<td>8 (4-12)</td>
</tr>
<tr>
<td>Rheumatoid factor positive; n (%)</td>
<td>77 (77)</td>
</tr>
<tr>
<td>ACRA positive; n (%)</td>
<td>83 (83)</td>
</tr>
<tr>
<td>Smoking habit; n (%)</td>
<td></td>
</tr>
<tr>
<td>non-smoker</td>
<td>46 (46)</td>
</tr>
<tr>
<td>smoker</td>
<td>20 (20)</td>
</tr>
<tr>
<td>ex-smoker</td>
<td>34 (34)</td>
</tr>
<tr>
<td>Body mass index (kg/m²); median (IQR)</td>
<td>24.8 (22.9-29.6)</td>
</tr>
<tr>
<td>DAS28; mean±SD</td>
<td>4.8±1.2</td>
</tr>
<tr>
<td>Previous TNFi treatment; n (%)</td>
<td>13 (13)</td>
</tr>
<tr>
<td>TNFi type; n (%)</td>
<td>13 (13)</td>
</tr>
<tr>
<td>Monoclonal antibodies</td>
<td>55 (55)</td>
</tr>
<tr>
<td>Etanercept</td>
<td>45 (45)</td>
</tr>
<tr>
<td>Concomitant csDMARD; n (%)</td>
<td>96 (96)</td>
</tr>
<tr>
<td>Only Methotrexate (MTX)</td>
<td>51 (51)</td>
</tr>
<tr>
<td>Only other csDMARDs (CD)</td>
<td>18 (18)</td>
</tr>
<tr>
<td>MTX + CD</td>
<td>27 (27)</td>
</tr>
</tbody>
</table>

CONCLUSION: Our results suggest that B cells may be useful as a cellular indicator of response to TNFi in RA patients.

Disclosure of Interests: Glenn Haugeberg Grant/research support from: For this study grant from Biogen, Consultant for: Medical Advisory boards for several companies, Paid instructor for: I have been paid for giving lectures for pharmaceutical companies and their employees, Speakers bureau: I have been paid for giving lectures in meetings organized by pharmaceutical companies, Bjørg Tilde Svanes Fevang: None declared, Andreas Diamantopoulos: None declared, Borja Hernández-Breijo: None declared, Israel Nieto-Gañán: None declared, Christina Sobrino: None declared, Victoria Navarro-Compañ: None declared, Ana Martínez-Feito: None declared, Carlota García-Hoz: None declared, Paloma Luapente-Suanzes: None declared, Javier Bachiller-Corral: None declared, Gemma Bonilla: None declared, Cristina Pipan Moratalla: None declared, Garbriele Roy: None declared, Mónica Vázquez: None declared, Alejandro Balsa Grant/research support from: Abbvie, Pfizer, Novartis, BMS, Nordic, Sanofi, Consultant for: Abbvie, Pfizer, Novartis, BMS, Nordic, Sanofi, Sandoz, Lilly; Paid instructor for: Pfizer, Speakers bureau: Pfizer, Novartis, UCB, Nordic, Sanofi, Sandoz, Lilly, Luisa Maria Villar: None declared, DORA
PASCUAL-SALCEDO Grant/research support from: Pfizer, Speakers bureau: Pfizer, Abbvie, Takeda, Eulalia Rodríguez-Martín: None declared, Chamaida Plasencia Speakers bureau: Pfizer, MSD

FRI0086 TNF CONCENTRATIONS DURING TREATMENT OF INFLAMMATORY DISEASES WITH GOLIMAMB
Femke Hooijberg1, Lea C. Berkhout2,3, Merel J. Lam1, Sadaf Aligi3, Michael Nurmohamed1, Arick de Vries3, Charlotte L. Krieckaert2, Theo Rispen3,2, Gert-Jan Wolbink1,2,3, Amsterdam Rheumatology and Immunology Center Reade, Amsterdam, Netherlands; 2Department of Immunopathology, Sanquin Research, Amsterdam, Netherlands; 3Landsteiner Laboratory, Academic Medical Centre, University of Amsterdam, Amsterdam, Netherlands; 4Biologics Lab, Sanquin Diagnostic Services, Amsterdam, Netherlands; 5Amsterdam Rheumatology and Immunology Center, location VUMc, Amsterdam, Netherlands

Background: Golimumab is a monoclonal antibody that binds TNF, countering its pro-inflammatory effects. Berkhout et al. (2019) described the development of a novel drug-tolerant assay to quantify TNF during TNF-inhibitor treatment. Using this assay, they analyzed the dynamics of TNF during treatment of rheumatoid arthritis (RA) patients with adalimumab and found that TNF levels shortly after treatment initiation predict nonresponse (1). Our study is the first to measure TNF levels during golimumab treatment, using the same drug-tolerant assay.

Objectives: To describe the dynamics of TNF in patients with RA, ankylosing spondylitis (AS) or psoriatic arthritis (PsA) during golimumab treatment.

Methods: Consecutive patients with RA, AS, or PsA starting golimumab treatment were included in this prospective observational cohort study, named the Reade Rheumatology Registry. Serum samples drawn during the study visits were analyzed for drug levels, anti-drug antibody (ADA) formation, and TNF concentrations using a regular enzyme-linked immunosorbent assay (ELISA), a radioimmunoassay, and a drug-tolerant competition ELISA, respectively. Regression analyses were used to analyze the data. Missing data was imputed using last observation carried forward.

Results: In total, 304 serum samples from 69 patients were included in this study. The median follow-up period was 52 (interquartile range (IQR) 16-130) weeks. Median TNF concentration at baseline was 4 (IQR 3-105) pg/ml and this increased to 68 (37-127) pg/ml four weeks after treatment initiation. During follow-up, TNF concentrations remained stable for the majority of patients (Figure 1). TNF levels at baseline were already high in the majority of patients (Figure 1). TNF levels at baseline were already high in the majority of patients (Figure 1). TNF levels at baseline were already high in the majority of patients (Figure 1). TNF levels at baseline were already high in the majority of patients (Figure 1). TNF levels at baseline were already high in the majority of patients (Figure 1). TNF levels at baseline were already high in the majority of patients (Figure 1).

Conclusion: Golimumab therapy was found to induce an increase in TNF concentrations, independent of disease activity. This is in line with what has been found for adalimumab treatment. However, TNF concentrations measured in this study were at least twice as low as TNF concentrations during adalimumab treatment (1). The high baseline TNF concentrations in 25% of the patients were also surprising, as it indicates that patients switch to golimumab while their TNF is still in complex with a previous TNF-inhibitor.


Disclosure of Interests: Femke Hooijberg: None declared, Lea C. Berkhout: None declared, Merel J. l’Ami: None declared, Sadaf Aligi: None declared, Michael Nurmohamed Grant/research support from: Abbvie, Bristol-Myers Squibb, Cellgene, Eli Lilly, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi and UCB, Speakers bureau: Abbvie, Bristol-Myers Squibb, Cellgene, Eli Lilly, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi and UCB, Speakers bureau: Pfizer, Abbvie, Blegen, BMS

FRI0097 RA PATIENTS’ PERSPECTIVES ON BIOLOGICAL DMARD-INDUCED ADVERSE DRUG REACTIONS AND THEIR BURDEN
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Background: Numerous biological DMARDs (bDMARDs) are used in RA treatment, however detailed knowledge of patients’ perceptions on drug use and the impact of adverse drug reactions (ADRs) is sparse.

Objectives: To gain insight into bDMARD-induced ADRs and their burden from the RA patients’ perspective.

Methods: The Dutch Biologic Monitor is an ADR-patient web-based questionnaire used for a prospective, multicentre, event monitoring cohort study including patients using a bDMARD for an immune-mediated inflammatory disease between January 1, 2017 and December 31, 2018. Patients were asked to complete questionnaires bi-monthly about used bDMARDs, indication and bDMARD-induced ADRs. ADRs were coded according to MedDRA terminology and their impact was measured on a 5-point scale, ranging from 1 (no burden) to 5 (very high burden). Per patient, every recurrent unique ADR was included as one ADR. ADRs regarding infections (INF), skin (SK), gastrointestinal (GI) and injection site (INJ) were clustered and analysed for the reported prevalence and burden. Fatigue and headache were separately analysed for prevalence and burden. The prevalence of clustered ADRs between the various bDMARDs was compared using a $\chi^2$ test and the average burden was compared using a Mann-Whitney U test.

Results: In the Dutch Biologic Monitor 583 consecutive (44.8%) RA patients were included (71.2% female, average age 59 years, SD=12.4) using the originator or a biosimilar of etanercept (ETN, 265), adalimumab (ADA, 196), tocilizumab (41), abatacept (35), certolizumab pegol (23), rituximab (19), infliximab (18), golimumab (15), sarilumab (2), secukinumab (1), anakinra (1). Almost half of the patients (276; 47.3%) reported at least one bDMARD-induced ADR with a total of 703 ADRs in 2,559 completed questionnaires. Patients reported 129 INJ reactions (129 ADRs/ 583 pts, prevalence of 22.1%, reported by 86 pts) with an average

Figure 1

TNF (pg/mL)

0 4 8 12 16 20 24 28 32 36 40 44 48 52 56 60 64 68 72 76 80 84 88 92 96 100

Time (in weeks)

Figure 1

Conclusion: Golimumab therapy was found to induce an increase in TNF concentrations, independent of disease activity. This is in line with what has been found for adalimumab treatment. However, TNF concentrations measured in this study were at least twice as low as TNF concentrations during adalimumab treatment (1). The high baseline TNF concentrations in 25% of the patients were also surprising, as it indicates that patients switch to golimumab while their TNF is still in complex with a previous TNF-inhibitor.


Disclosure of Interests: Femke Hooijberg: None declared, Lea C. Berkhout: None declared, Merel J. l’Ami: None declared, Sadaf Aligi: None declared, Michael Nurmohamed Grant/research support from: Abbvie, Bristol-Myers Squibb, Cellgene, Eli Lilly, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi and UCB, Speakers bureau: Abbvie, Bristol-Myers Squibb, Cellgene, Eli Lilly, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi and UCB, Speakers bureau: Abbvie, Blegen, BMS
SWITCHING RATE OF BIOLOGICAL DMARDS IN RHEUMATOID ARTHRITIS PATIENTS: TREASURE – REAL LIFE DATA

Umut Kalyoncu, Ali İlhan Ertenli, Abdulsamet Erden, Orhan Küçükkahin, Timuçin Kaifoğlu, Ediz Dalıköç, Cemal Bes, Nüfils Alpay Kantel, Hakan Emmungil, Pamir Atagündüz, Bekir Nihan Coşkun, Burcu Yağış, Süleyman Serdar Koca, Muhammet Çiçoğlu, Aşkın Ateş, Servet Akar, Deddy Gerioğlu, Duygu Ersözü, Veli Yazıcı, Emre Emmungil, Süleyman Serdar Koca, Abdulsamet Erden, Orhan Küçükkahin, Süleyman Serdar Koca: None declared, Ali İlhan Ertenli: None declared, Pamir Atagündüz: None declared, Belkıs Alpay: None declared, Hakan Emmungil: Grant/research support from: MSD, Roche, Pfizer, Consultant for: MSD, Abbvie, Roche, UCB, Novartis, Speakers bureau: MSD, Abbvie, Roche, Pfizer, UCB, Novartis, Sander W. Tas: None declared, Harald Vonkeman: None declared, Jette van Lint: None declared, Naomi Jessurun: None declared.

Background: In rheumatoid arthritis (RA), biologic DMARDs are important treatment options in resistant patients. Inefficacy or side effects may cause switching between these drugs.

Objectives: This study aimed to determine features of patients switching from one biologic DMARD to another in RA treatment and to investigate associated reasons for switching.

Methods: This multicenter, prospective observational cohort study used the TReasure database in which web-based registration of RA and spondyloarthritis patients are being performed in 15 centers across different regions of Turkey. In this study, data of RA patients switching from one biologic agent to another were analyzed. Demographic and clinical data, follow-up duration, time to switch, and reasons for switching were retrieved from the database.

Results: Of the included 2115 RA patients, 829 (39.2%) switched between biologic agents (switched group) and 1286 (60.8%) continued to receive their current therapies (continued group). The median follow-up duration of all patients was 3.7 years and the median time to switch was 1.1 years. In the switched group, the proportion of females and the median HAQ-DI score were higher as well as disease duration was longer (Table 1). Among the biologic agents used at first, 60.9% of the patients were receiving an anti-TNF agent and 39.1% of the patients were receiving other biologic agents (Table 2, figure 1). In the switched group (n=829), the main reasons for switching were secondary inefficacy (n=269), primary inefficacy (n=238), and side effects (n=178) followed by primary or secondary unknown inefficacy (n=106), patient’s demand (n=21), physician’s request (n=16), willing to be pregnant (n=7), other (n=31), and unknown (n=54).

Conclusion: The patients in the Treasure database were followed-up approximately 4 years and about one-third of the patients had to switch from one biologic DMARD to another. The main reasons for this switching were primary (29.2%) and secondary (33.0%) inefficacy and 20% of the patients had to switch due to side effects. According to the switching pattern, about half of the patients using an anti-TNF agent at first switched to another anti-TNF agent and the other half switched to other biologic agents.

Disclosure of Interests: Umut Kalyoncu Grant/research support from: MSD, Roche, UCB, Novartis and Pfizer, Consultant for: MSD, Abbvie, Roche, UCB, Novartis, Pfizer and Abdi Ibrahim, Speakers bureau: MSD, Abbvie, Roche, UCB, Novartis, Pfizer and Abdi Ibrahim, Ali İlhan Ertenli: None declared, Abdulsamet Erden: None declared, Orhan Küçükkahin: None declared, Timuçin Kaifoğlu: None declared, Ediz Dalıköç: Grant/research support from: MSD and Abbvie, Consultant for: MSD, Abbvie, Roche, Pfizer, Abbvie, Con;�症for: Novartis, Roche, Speakers bureau: MSD, Roche, Pfizer, Abbvie, Pfizer, Abbvie,Celltrion, Novartis, Pamir Atagündüz: None declared, Bekir Nihan Coşkun: None declared, Burcu Yağış: None declared, Süleyman Serdar Koca: None declared, Muhammet Çiçoğlu: None declared, Aşkın Ateş: None declared, Servet Akar Grant/research support from: MSD, Abbvie,
PREDICTIVE FACTORS FOR REMISSION ACHIEVEMENT BY TOCILIZUMAB MONOTHERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS AFTER INADEQUATE RESPONSE TO METHOTREXATE: A POST HOC ANALYSIS OF THE SURPRISE STUDY

Masaru Kato1, Yuki Kanoke2, Yoshia Tanaka3, Masayuki Inoue4, Hitomi Kobayashi-Harakatsa1, Kichi Amari5, Masayuki Miyata6, Yokhu Murakawa7, Hidekata Yashuka7, Shintaro Hirata8, Nazile Sultan Yasil Bilge9, None declared, Zeynel Abidin Akar: None declared, Omer Karadag: None declared, Ayeş Bahar Kelesoglu Dincer: None declared, Sedat Yılmaz: None declared, Uluk Igen: None declared, Yavuz Pelihvani: None declared, Ender Terzioglu: None declared, Levent Kılıç: None declared, Şükran Ertan: None declared, Sedat Kızıra: None declared.


Methods: This is a post hoc analysis of the SURPRISE study, a 2-year randomized, controlled study comparing the efficacy of tocilizumab with (ADD-ON) and without methotrexate (SWITCH) in active RA patients despite methotrexate therapy. The primary endpoint was the DAS28-ESR remission (< 2.6) at week 24. The change in modified total Sharp score (mTSS/year) was also assessed as an end-point.

Results: In SWITCH (n = 96), CRP, SAA, RF and DAS28 at baseline showed predictive value for DAS28 remission at week 24 in univariate analysis. Multivariate analysis confirmed SAA, RF and DAS28 at baseline, but not CRP, as predictive factors, with SAA having the highest value (OR [95%CI] by decrease of 5.0 µg/mL = 1.011 [1.002-1.020], p = 0.01, ROC-AUC = 0.731). SAA of < 50.0 µg/mL showed extremely high predictive value for DAS28 remission (OR [95%CI] = 6.012 [1.997-18.096], p = 0.0088, ROC-AUC = 0.761). Furthermore, the structural remission (mTSS/year ≤ 0.5) rate at week 52 was significantly higher in patients with SAA of < 50.0 µg/mL than those with SAA of ≥ 50.0 µg/mL (71% vs 51%, p = 0.048). In contrast, in ADD-ON (n = 98), only DAS28 at baseline showed predictive value for DAS28 remission at week 24 in both univariate and multivariate analysis. In patients with SAA < 50.0 µg/mL, both DAS28 remission (75% vs 77%, p = 0.79) and structural remission (71% vs 68%, p = 0.71) rate were comparable between SWITCH and ADD-ON.

Conclusion: SAA levels at baseline can predict the necessity of concomitant methotrexate in tocilizumab initiation in patients with RA. Patients with low levels of SAA at baseline may benefit similarly from tocilizumab therapy with and without methotrexate in terms of achieving clinical and structural remission.

REFERENCE:
Background: Disease Modifying Anti-Rheumatic Drugs (bDMARD) tapering is possible in rheumatoid arthritis (RA) patients in sustained remission. However, only minimal data are available on progressive tapering of non-TNF bDMARD such as tocilizumab (TCZ) or abatacept (ABA). Objectives: The TOLEDO (Towards the Lowest Efficacious Dose) trial aimed to assess the impact on disease activity of progressive tapering of non-TNF bDMARD such as tocilizumab (TCZ) or abatacept (ABA). Patients: A total of 233 patients fulfilling ACR-EULAR 2010 criteria for RA were included in the TOLEDO trial. Methods: In this multicenter open-label non-inferiority randomized open-label controlled trial assessing tocilizumab or abatacept injection spacing in rheumatoid arthritis patients in remission.

Results: Of the 233 patients, 117 were randomized to the spacing arm and 116 to the maintenance arm. At all 2-year follow-up points, patients in the spacing arm achieved significantly better disease activity compared to patients in the maintenance arm. The non-inferiority of the spacing arm was maintained in the ABA and TCZ subgroups. The spacing arm was associated with a lower incidence of relapses and durable relapses compared to the maintenance arm. The spacing arm was also associated with a lower incidence of adverse events compared to the maintenance arm. Conclusion: The TOLEDO trial demonstrated the feasibility and safety of progressive tapering of non-TNF bDMARD in RA patients in sustained remission. Further studies are needed to confirm the long-term safety and efficacy of progressive tapering of non-TNF bDMARD in RA patients.
Non-Medical Switching from Originator to Biosimilar Etanercept – No Evidence for a Relevant Nocebo Effect – A Retrospective Analysis of Real-Life Data

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1Rheumazentrum Ruhrgebiet, Herne, Germany; 2Ruhr-University, Bochum, Germany

Background: Real-world data about switching patients from originator product to a biosimilars are important to assess and to document the outcome of switches in clinical practice in order to confirm the low risk of major problems. It has been hypothesized that lack of efficacy and adverse drug events (ADEs) upon switching from reference biologics to biosimilar products are related to the nocebo effect [1].

Objectives: To evaluate the effectiveness and safety of systematic non-medical switching from innovator etanercept to biosimilar etanercept SB4 in adult patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) or axial spondyloarthritis (axSpA) in a real-life setting based on different information strategies before switching.

Methods: Data of all adult patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) or axial spondyloarthritis (axSpA) who had received innovator etanercept and were switched in our specialized center from innovator to biosimilar etanercept for economic reasons were retrospectively analysed. Whether or not patients were informed about the switch was left to the discretion of the treating physician. Disease activity and function were regularly assessed, and any changes were recorded in two consecutive visits at week 12 and 24. The scores documented at week 12 after switching were taken as primary outcome. AEs were documented.

Results: A total of 84 patients were included (44 RA, 25 axSpA and 15 PsA patients), 24 of which had received information about switching (28.5%). The scores at week 12 of both, disease activity and function, remained rather unchanged (Table 1). Whether patients had been informed about switching or not did not influence outcomes or AE. The retention rate of the biosimilar was 96.4% (n=81) at week 12 and 87.6% (n=71) at week 24 (Figure 1). While 7 patients were lost to follow-up, 6 patients discontinued due to inefficacy or AE, including one malignant melanoma. Overall, 18 AEs were reported in 10 patients (12%). In 3 patients (3.6%) who had 5 AEs in the first 12 weeks the innovator was successfully re-administered.

Conclusion: Systematic switch from innovator to biosimilar etanercept was not associated with changes in disease activity or function in all three indications within 12 weeks. This was independent of information on the switch transmitted to the patients.

Table 1. Patient characteristics

<table>
<thead>
<tr>
<th>Assessment</th>
<th>Baseline (n=84)</th>
<th>Follow-up 12 weeks (n=81)</th>
<th>Follow-up 24 weeks (n=74)</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA DAS28</td>
<td>3.1 (1.4)</td>
<td>2.8 (1.0)</td>
<td>3.1 (1.3)</td>
</tr>
<tr>
<td>HAQ</td>
<td>1.2 (0.7)</td>
<td>1.3 (0.7)</td>
<td>1.3 (0.7)</td>
</tr>
<tr>
<td>CRP (mg/dl)</td>
<td>0.5 (0.6)</td>
<td>0.6 (0.8)</td>
<td>0.7 (0.9)</td>
</tr>
<tr>
<td>PsA DAS28</td>
<td>2.5 (1.0)</td>
<td>1.9 (1.4)</td>
<td>2.9 (1.5)</td>
</tr>
<tr>
<td>HAQ</td>
<td>0.8</td>
<td>0.9 (0.9)</td>
<td>0.9 (0.9)</td>
</tr>
<tr>
<td>CRP (mg/dl)</td>
<td>(0.5)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>axSpA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BASDAI</td>
<td>4.8 (2.5)</td>
<td>5.0 (2.5)</td>
<td>4.7 (2.4)</td>
</tr>
<tr>
<td>ASDAS</td>
<td>2.6 (1.3)</td>
<td>2.7 (0.9)</td>
<td>2.7 (0.8)</td>
</tr>
<tr>
<td>BASFI</td>
<td>5.3 (2.7)</td>
<td>5.5 (2.7)</td>
<td>4.9 (2.8)</td>
</tr>
</tbody>
</table>

Values are mean ± standard deviation

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REFERENCE:

Disclosure of Interests: Uta Kiltz Grant/research support from: AbbVie, Chugai, Eli Lilly, Grünerthal, Janssen, MSD, Novartis, Pfizer, Roche, and UCB, Consultant for: AbbVie, Chugai, Eli Lilly, Grünerthal, Janssen, MSD, Novartis, Pfizer, Roche, and UCB. Styliani Tsiami: None declared, Xenofon Baraliakos Grant/research support from: AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Centocor, Chugai, Janssen, MSD, Novartis, Pfizer Inc, Roche and UCB, Grant/research support from: AbbVie, Pfizer, Merck Sharp & Dohme, UCB Pharma, Novartis, Consultant for: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Chugai, Janssen Biologics, Novartis, Pfizer, UCB Pharma, Galapagos, Speakers bureau: AbbVie, Chugai, Janssen, Novartis, Pfizer, UCB Pharma, Juergen
GOLIMUMAB IMPROVES WORK PRODUCTIVITY AND ACTIVITY AND QUALITY OF LIFE IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA), ANKYLOSING SPONDYLITIS (AS) AND PSORIATIC ARTHRITIS (PSA): FINAL RESULTS FROM A NON-INTERVENTIONAL STUDY IN GERMANY (GO-ART)

Ines Klaudius1, Klaus Krueger2, Sven Remstedt3, Astrid Thiele1,4, MSD Sharp and Dohme GmbH, Haar, Germany; 1Praxisszentrum St. Bonifatius, Munich, Germany; 2Rheuma Praxis, Berlin, Germany; 3Krankenhaus St. Josef, Wuppertal, Germany

Background: Golimumab (GLM) has shown its efficacy and tolerability in various randomized clinical trials. Systemic data for GLM regarding health-economic parameters in daily clinical practice are essential not only for pharmaceutical companies but also for cost-benefit analyses in Germany.

Objectives: This prospective NIS was designed to evaluate the impact of GLM therapy on work productivity and activity as well as Quality of Life (QoL) in patients with RA, AS or PsA in Germany under routine settings over an observation period of 12 months, plus an additional voluntary extension period of 12 months (total 24 months) to collect long-term data on health economic parameters.

Methods: GO-ART was an observational prospective study on patients with RA, AS or PsA (biologic-naive and biologic-experienced) who started treatment with GLM at 63 sites of Germany. The primary endpoint was the change in work productivity/activity impairment as measured by Work Productivity and Activity Impairment (WPAI) questionnaire from baseline, measured primarily at month 3 and secondarily at months 6, 12 and 24. As secondary endpoint the change in quality of life (RAQoL for RA patients, ASQoL for AS patients and NAPPA-QoL for PsA patients) was assessed.

Results: 748 patients (RA=250, PsA=249, AS=249) started GLM therapy. The primary efficacy endpoint was analyzed in the modified intention-to-treat (mITT) subset of 493 patients (RA=158, PsA=157, AS=249) with full-time or part-time employment at baseline (mITT).

A total of 548 patients entered the additional 12-month observation period, of which 303 completed the 24-month assessment. By 3 months after initiation of Golimumab treatment, a marked improvement was seen in all 4 WPAI domain scores (‘presenteeism’, ‘total work productivity’, ‘total work productivity impairment’ (TWPI), and ‘activity impairment’) in daily living because of patient’s health problems related to RA, PsA or AS, as shown in Table 1 (all p-values <0.05).

The statistically significant improvements in the mean WPAI domain scores were maintained over the 24-month observation period in all 3 indications with a higher treatment effect regarding ‘activity impairment’ and ‘presenteeism’ compared to ‘absenteeism’ (Table 1). Quality of life improved significantly (p<0.0001) from baseline at month 3, 6, 12 and 24 in patients with RA (RAQoL), AS (ASQoL) and PsA (NAPPA-QoL) based on questionnaire data of 237 RA patients (RA-mITT), 228 AS patients (AS-mITT) and 235 PsA patients (PsA-mITT) indicating a clinically relevant improvement.

Conclusion: Treatment with GLM provided sustained improvement in WPAI and QoL in patients with RA, PsA and AS over the observational period of 24 months.

All scores of the WPAI showed a significant (p<0.05) reduction in mean score values in each indication at time points of 3, 6, 12 and 24 months after initiation of treatment with GLM. GLM leads to an improvement of work productivity and daily activities in patients already within the first 3 months of treatment.

Table 1:

<table>
<thead>
<tr>
<th>Domain</th>
<th>Baseline</th>
<th>Month 3</th>
<th>Month 6</th>
<th>Month 12</th>
<th>Month 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAQoL</td>
<td>0.36</td>
<td>0.20</td>
<td>0.15</td>
<td>0.11</td>
<td>0.08</td>
</tr>
<tr>
<td>ASQoL</td>
<td>0.29</td>
<td>0.20</td>
<td>0.15</td>
<td>0.11</td>
<td>0.08</td>
</tr>
<tr>
<td>NAPPA-QoL</td>
<td>0.36</td>
<td>0.20</td>
<td>0.15</td>
<td>0.11</td>
<td>0.08</td>
</tr>
</tbody>
</table>

Disclosure of Interests: Ines Klaudius Employee of: MSD Sharp & Dohme GmbH; Klaus Krueger: None declared; Sven Remstedt: None declared; Astrid Thiele Consultant for: Biogen, Celgene, Chugai, Hexal, Janssen, Lilly, MSD, Novartis, Pfizer, UCB

as an ETN biosimilar. There is limited evidence on outcomes of transition from originator to biosimilar in a multi-country real-world setting.

**Objectives:** To provide real-world evidence on outcomes of transition from ETN to SB4 in routine clinical practice at EU sites.

**Methods:** Eligible patients had RA or axSpA and had initiated SB4 in routine clinical practice following a minimum of 6 months treatment with a stable dose of originator ETN, at clinics in France, Germany, Italy, and Spain. Data were captured from patient records prospectively and/or retrospectively for 6 months following transition. Outcome measures include clinical characteristics, disease scores (DAS-28 for RA, BASDAI for axSpA) and clinical management.

**Results:** Analysis of 533 eligible patients (347 RA, 186 axSpA) demonstrated no clinically significant change in disease score from baseline to 6 months post-transition; mean individual change was 0.0 (95% CI -0.1, 0.1) and 0.0 (95% CI -0.3, 0.2) at 6 months post-transition in RA and axSpA subjects respectively. Regarding dose regimen, 73.5% and 63.4% of RA and axSpA subjects transitioned from ETN 50mg QW to SB4 50mg QW, by 6 months post-transition, 73.5% and 63.4% of subjects were receiving SB4 50mg QW.

**Conclusion:** The results of this analysis show that treatment with CT-P13 across the 4 studies (RA = 670; AS = 819; PsA/PsO = 90). Mean age (years) of patients per RA, AS and PsA/PSO indication was 54.5, 40.3 and 52.9, respectively. Average exposure duration (days) to CT-P13 in patients with RA, AS and PsA/PSO was 280.3, 254.0 and 322.1, respectively, and the mean maximum dose of CT-P13 (mg/kg) with RA, AS and PsA/PSO patients was 3.77, 4.51 and 4.31, respectively. Treatment emergent adverse events (TEAEs) were reported in 50.15%, 37.73% and 26.67% for RA, AS and PsA/PSO, respectively. Incidence of TEAEs in RA indication is consistent with the historical rate in this population. Treatment emergent serious adverse events (TSEAs) were reported for 12.39%, 4.52% and 3.33% for RA, AS and PsA/PSO patients, respectively. Incidence of TEAEs leading to discontinuation were 8.81%, 3.42% and 7.78% for RA, AS and PsA/PSO. Two deaths and 1 death were reported among RA and AS patients, respectively. The causes of death in RA patients were acute respiratory distress syndrome (ARDS) and bronchopneumonia; the cause of death in the AS patient was unknown. AEIs of CT-P13 were analysed in safety population who were treated with CT-P13 at least once by the data cut point. No events of serum sickness, haematologic malignancy, demyelinating disorder, sarcoidosis/sarcoidosis-like reaction were reported.

**Disclosure of Interests:** Klaus Krueger: None declared, Carlo Selmi Grant/research support from: Abbvie, Janssen, MSD, Novartis, Pfizer, Consultant for: Abbvie, Alfa-Sigma, Biogen, BMS, Celgene, Eli-Lilly, GSK, Janssen, Merck Sharp and Dohme, Novartis, Pfizer, Roche, Sanofi-Genzyme, YCB, Speakers bureau: Abbvie, Alfa-Sigma, Biogen, BMS, Celgene, Eli-Lilly, GSK, Janssen, Merck Sharp and Dohme, Novartis, Pfizer, Roche, Sanofi-Genzyme, YCB, Alain Cantagrel Grant/research support from: Abbvie, Chugai, MSD, Pfizer, UCB, Consultant for: BMS, Chugai, Janssen, Lilly France, Medac, MSD France, Novartis, Pfizer, Roche, Sanofi-Aventis, UCB, Speakers bureau: Abbvie, Biogen, BMS, Celgene, Chugai, Janssen, Lilly France, MSD France, Nordic-Pharma, Novartis, Pfizer, Roche, Sanofi, UCB, Abad Hernández: None declared, Ulrich Freudensprung Shareholder of: Biogen, Employee of: Biogen, Mourad Farouk Rezk Shareholder of: Biogen, Employee of: Biogen, Janett Addison Shareholder of: Biogen, Employee of: Biogen. DOI: 10.1136/annrheumdis-2019-eular.5665

**REFERENCES:**


FXR0105 EXPRESSION OF UNCOUPLING PROTEIN-1 IN SUBCUTANEOUS FAT IS INCREASED BY TOCILIZUMAB

Lovisa Lyngfelt1, Malin C. Erlandsson1,2, Karin Me Andersson1, Sofia Töyrä Silfverswärd1, Maria I Bokarewa1,2, University of Gothenburg, Department of Rheumatology and Inflammation Research, Gothenburg, Sweden; Sahlgrenska University Hospital, Gothenburg, Sweden

Background: Adipose tissue is an important player in cardiovascular (CV) morbidity. Thermogenic brown adipocytes, rich with uncoupling protein 1 (UCP1), increase metabolic and CV health. (1)

Objectives: Study the impact of anti-rheumatic treatment on production of UCP1 in subcutaneous fat of RA patients.

Methods: Samples of subcutaneous fat were collected from 125 female RA patients by aspiration from periumbilical region. Expression of UCP1 and a reverse cholesterol transport protein ABCA1 were measured by qPCR and analyzed with respect to anti-rheumatic treatment and clinical disease activity. BT treatment, the patient comprised 4 major groups including tocilizumab (Tocilizumab: n=14), anti-TNF (n=29), methotrexate monotherapy (n=47) and methotrexate-sulfasalazine-hydroxychloroquine (triple therapy, n=15). CV risk was estimated using the Framingham risk algorithm.

Results: Measurable expression of UCP1 was found in 54.6% of the studied fat tissue samples. Patients on Tocilizumab had measurable expression of UCP1 in 79%, which was significantly more often than among TNFi-treated (45%, p=0.04) and MTX-treated patients (42%, p=0.02). Patients on triple therapy had also often measurable UCP1 levels compared to other groups (69% vs 43%, p=0.035). Tocilizumab patients have more lean body mass than patients treated with TNFi. This was based on lower BMI in Tocilizumab treatment patients compared to other groups at 24.1 vs 27.1, p=0.041; 23.6 vs 27.1, p=0.017; respectively). Additionally, the estimated muscle mass by creatinin/height ratio was significantly lower in TNFi than in triple therapy (p=0.034) and Tocilizeumab (p=0.008). Clinically, the treatment groups were similar in age, disease activity (DAS28) and disease duration with the exception for Tocilizumab. Tocilizumab patients were older (65 vs 57, p=0.004) and had numerically longer disease duration (17y vs 7y) and lower DAS28 (1.98 vs 3.11).

Notably, Tocilizumab patients had significantly higher TC compared to TNFi (p=0.027), and triple therapy (p=0.041). Triple therapy had the lowest TC levels (p=0.017). The differences were due to LDL, here patients on Tocilizumab had higher LDL than TNFi (p=0.09) and triple therapy (p=0.015). Serum HDL was similar. These differences in serum lipids were not related to expression of ABCA1 or UCP1. Despite the difference in the serum lipid profile, the estimated CV risk was significantly lower in Tocilizumab compared to MTX patients (4.10-87.57) vs 6.60(3.9-9), p=0.041.

Conclusion: In this study is Tocilizumab treatment is associated with persistent UCP1 production by adipose tissue. This was followed by lower estimated CV risk and favourable body composition in female RA patients.

REFERENCE:

Disclosure of Interests: None declared

FR0106 SARILUMAB AND TOCILIZUMAB RECEPTOR OCCUPANCY (RO), AND EFFECTS ON C-REACTIVE PROTEIN (CRP) LEVELS, IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA)

Christine Xu1, Patrick Nolan1,2, Guoqian Lui1, Anice Paccayla1, Melitza Iglesias-Rodriguez1, Gregory St John2, Chad Nivens3, Rafael Madonna1, Tomonori Ishii1, Ernest Choiy1, Vanaja Karamanulu1, Sanofi, Bridgewater, NJ, United States of America; Sanofi Aventis, Montpellier, France; Regeneron Pharmaceuticals, Inc., Tarrytown, NY, United States of America; Sanofi Genzyme, Cambridge, MA, United States of America; Pompeu Fabra University, Barcelona, Spain; Tohoku University Hospital, Sendai, Japan; Cardiff University School of Medicine, Cardiff, United Kingdom

Background: Objectives: The in vitro binding affinity of sarilumab (Kd 61.9 pM) for the human interleukin-6 receptor (IL-6R) is 15–22-fold higher than tocilizumab. We explored the relationship between IL-6R RO, relevant pharmacodynamic (PD) variables (eg CRP), and potential clinical relevance of the differences between sarilumab and tocilizumab.

Methods: Binding to total soluble IL-6R (sIL-6R) in vivo translates into the quasi-steady-state target-mediated drug disposition pharmacokinetics (PK) and indirect-response PD model with inhibition of elimination of sIL-6R and unbound sIL-6R concentration for both sarilumab and tocilizumab. PK/ PD models were used to simulate sIL-6R RO dynamic profiles (% RO over time) for: sarilumab after subcutaneous (SC) doses of 200 and 150 mg once every 2 wks (q2w); tocilizumab after SC doses of 162 mg q2w and once every wk (qw); and tocilizumab after intravenous (IV) doses of 4 and 8 mg/kg once every 4 wks (q4w). In addition, RO profiles were compared with changes in observed CRP levels in patients with RA following administration of sarilumab SC and tocilizumab IV (ASCERTAIN study; NCT01768572). In this study, 60.8% of patients required an increase in tocilizumab dose from 4 to 8 mg/kg IV during the study period, based on clinical response.

Results: Sarilumab SC 200 mg q2w achieved >90% RO after the first dose, which was maintained over the dosing interval throughout the 24-wk treatment course; at the lower dose of 150 mg q2w, RO was >90% from the second dose onwards. RO for tocilizumab SC, at 162 mg q2w, was >90% immediately after the first dose but dropped below 50% prior to the second dose. Similarly, for tocilizumab IV at 4 mg/kg q4w, the RO was high immediately after the first dose (>99% at Wk 1) but decreased over the dosing interval. At trough steady-state (Wk 24), RO was greater with sarilumab SC 200 mg q2w (98%) and 150 mg q2w (94%) compared with tocilizumab SC 162 mg q2w (84%) and IV 4 mg/kg q4w (60%). The higher doses of tocilizumab SC 162 mg q2w and tocilizumab IV 8 mg/kg q4w were able to maintain RO >99% at steady state, similar to sarilumab SC 200 mg at steady state. CRP levels in patients with RA were inversely associated with RO at trough; the greatest suppression in CRP was seen in patients who received sarilumab SC (at either dose) or the higher IV tocilizumab dose (Fig). However, proportionally smaller reductions in CRP levels were observed with the lower IV tocilizumab dose (4 mg/kg q4w), consistent with the lower RO of tocilizumab.

Conclusion: The higher binding affinity of sarilumab to IL-6R compared with tocilizumab translated into higher RO and greater reduction in CRP levels for sarilumab than tocilizumab, confirming the expected association between RO and PD effect. Sarilumab SC 200 mg q2w led to a rapid and sustained suppression of CRP over the 24-wk interval investigated; however, a higher dose (IV) or frequency of administration (SC) of tocilizumab was required to maintain the same degree of RO and CRP suppression. CRP may be a useful tool in clinical practice for patients treated with an IL-6R blocker.

REFERENCES:

Disclosure of Interests: Study funding and editorial support (Helen Johns, Adelphi) provided by Sanofi and Regeneron Pharmaceuticals, Inc.

Objective: To assess the effect of co-medication with MTX or other csDMARDs on drug survival of TNFi treated RA patients.

Methods: All adult patients with RA followed in the Czech national registry ATTTRA who started TNFi therapy after January 1st 2012 were considered. Six-year drug survival for patients on TNFi in combination with MTX, with other csDMARD or in monotherapy was analyzed using Kaplan-Meier method, log rank test was used to compare differences between groups. Reasons for TNFi discontinuation were analyzed. ATTTRA is a centralized prospective computerized registry of patients receiving biologic disease modifying anti-rheumatic drugs (bDMARD) therapy for rheumatic diseases collecting data on efficacy, safety and quality of life of all patients treated with bDMARDs in the Czech Republic. TNFi therapy is indexed for patients with RA who have failed treatment with at least one csDMARD.

Results: A total of 1841 RA patients initiated first bDMARD treatment during the studied period, with 1724 patients receiving TNFi. 1307 patients (76%) started TNFi therapy in combination with MTX, 267 patients (15%) with other csDMARD and 150 patients (9%) as monotherapy. Overall unadjusted TNFI drug survival was better in patients receiving MTX co-medication (median survival 53 months) compared to those receiving other csDMARD (median survival 36 months) or those being on monotherapy (median survival 21 months; p<0.001 for monotherapy vs MTX co-medication) (Figure). The most common reason for TNFi discontinuation was loss of efficacy (33%, 37% and 28% for MTX, csDMARD combination and monotherapy respectively) followed by primarily inefficacy (20%, 19% and 27%) and adverse events (19%, 15%, 23%).

Conclusion: In this registry study of patients with RA, use of MTX co-medication was associated with significantly better first TNFi drug survival compared to other csDMARD co-medication and to monotherapy.
Short-term efficacy of BCD-089, novel monoclonal anti-IL6 receptor antibody, in combination with methotrexate in patients with rheumatoid arthritis: 12-week results of phase 2 Aurora study

Background: In the previous phase 1 study, BCD-089 (INN: levilimab) was well-tolerated, had favorable safety profile and low immunogenicity. Here we report 12-week efficacy and safety results of ongoing phase 2 clinical study of BCD-089 in patients with active RA.

Objectives: This study is aimed to assess efficacy and safety of 2 dosing regimens of BCD-089 in patients with MTX-IR active RA.

Methods: During this multicenter double-blind placebo-controlled randomized clinical study (NCT03355842), 105 MTX-IR patients with active RA (ACR2010) were assigned (1:1:1) to receive 162 mg of BCD-089 subcutaneously (QW arm and Q2W arm) or PBO. MTX (10-25 mg/week) was used in all groups. After completion of 12-week blinded period patients from QW and Q2W arms continued the treatment, patients from PBO arm were switched to BCD-089 Q2W until Week 56. The primary efficacy endpoint was the rate of ACR20 at Week 12. Secondary endpoints included ACR50/70 and DAS28-CRP(4). The safety was routinely evaluated.

Results: The efficacy analysis showed that 95% confidence interval for BCD-089 treatment effect relative to PBO was [38.45 ≤ 63.4] for Q2W arm, which confirms the superiority to PBO of either dosing regimen. Summary of efficacy results is presented in Table 1.

The majority of adverse events (AE) were laboratory abnormalities. The spectrum of AEs is similar to other IL6R inhibitors (Table 2). Three serious adverse events (SAEs) were reported: community-acquired pneumonia (QW arm, treatment-related), acute cholecystitis (PBO arm, not related, did not lead to treatment discontinuation), and acute heart failure leading to death (Q2W arm, not related). One case of moderate local reaction (erythema) was reported in QW arm.

Conclusion: BCD-089 in combination with MTX had superior efficacy compared with MTX plus PBO in MTX-IR patients with active RA. BCD-089 showed safety profile consistent with other IL6R inhibitors. Further clinical studies are needed.

Table 1. Safety results (full analysis set), n (%)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>BCD-089 QW-MTX (n=35)</th>
<th>BCD-089 Q2W-MTX (n=35)</th>
<th>PBO +MTX (n=35)</th>
<th>p-value (Fisher’s exact test)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACR20</td>
<td>27 (71.1%)</td>
<td>20 (57.1%)</td>
<td>6</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ACR50</td>
<td>18 (51.4%)</td>
<td>11 (31.4%)</td>
<td>5 (14.3%)</td>
<td>0.0001</td>
</tr>
<tr>
<td>ACR70</td>
<td>10 (28.6%)</td>
<td>7 (20.0%)</td>
<td>2 (5.7%)</td>
<td>0.0106</td>
</tr>
<tr>
<td>DAS28-CRP(4)</td>
<td>20 (57.1%)</td>
<td>10 (28.6%)</td>
<td>1 (2.9%)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Table 2. Safety results (full analysis set), n (%)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>BCD-089 QW-MTX (n=35)</th>
<th>BCD-089 Q2W-MTX (n=35)</th>
<th>PBO +MTX (n=35)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any AE</td>
<td>26 (74.3%)</td>
<td>23 (65.7%)</td>
<td>14 (40.0%)</td>
</tr>
<tr>
<td>Any SAE</td>
<td>1 (2.8%)</td>
<td>1 (2.8%)</td>
<td>1 (2.8%)</td>
</tr>
<tr>
<td>Any Grade 3-4 AE</td>
<td>10 (28.6%)</td>
<td>6 (17.1%)</td>
<td>2 (5.7%)</td>
</tr>
</tbody>
</table>

Disclosure of Interests: V Mazurkov Grant/research support from: JSC BIOCAD, Evgeniy Zolkin: None declared, Elena Ilivanova Grant/research support from: JSC BIOCAD, Tatyana Plaksoina Grant/research support from: JSC BIOCAD, Tatyana Plaksoina Grant/research support from: JSC BIOCAD, Olga Nesmeyanova Grant/research support from: JSC BIOCAD, Nikolaj Soroka: None declared, Alena Kundzer: None declared, Anton Lutskii Employee of: JSC BIOCAD, Ekaterina Dokukina Employee of: JSC BIOCAD, Ekaterina Chemyava Employee of: JSC BIOCAD, Roman Ivanov Employee of: JSC BIOCAD

52.8% over 2.0 years of exposure to GLM and 45.2% over 1.6 year of exposure to GLM-IV.

Conclusion: In this real-world study of Canadian patients with RA, differences in baseline characteristics between patients treated with an anti-TNF switch over time and between agents show potential selection bias when selecting a given therapy and may impact the proportion of patients achieving a target-specific outcome. Treatment significantly reduced disease activity and improved functionality in a similar fashion and were also safe and well tolerated.

Disclosure of Interests: Proton Rahman: None declared, Phillip Baer Grant/research support from: Janssen sponsored study, Consultant for: Eli Lilly, Pfizer, Abbvie, Amgen, Merck, Novartis, Sanofi Genzyme, Paladin, Janssen, Johnson & Johnson, Speakers bureau: Eli Lilly, Pfizer, Abbvie, Amgen, Janssen, Denis Choquette Grant/research support from: Abbvie, Amgen, Eli Lilly, Novartis, Pfizer, Sandzon, Consultant for: Abbvie, Amgen, Eli Lilly, Novartis, Pfizer, Sandzon, Speakers bureau: Abbvie, Amgen, Eli Lilly, Novartis, Pfizer, Sadoz, Rafat Farawi: None declared, Louis Bes-sette Grant/research support from: Janssen, Janssen, Roche, UCBB, Abbvie, Pfizer, Celgene, Lilly, Novartis, Speakers bureau: Amgen, BMS, Janssen, Roche, UCBB, Abbvie, Pfizer, Merck, Celgene, Lilly, Novartis, Milton Baker Grant/research sup- port from: Janssen Sponsored Study, Raman Rai Consultant for: Janssen, Amgen, BMS, Roche, Abbvie, Pfizer, Merck, Novartis, Speakers bureau: Janssen, Amgen, Roche, BMS, Abbvie, John Kelsall Grant/research support from: Janssen Sponsored Study, Larissa Lisnevskaia Grant/research support from: Janssen Sponsored Study, Jodie Reis Grant/research support from: Janssen Sponsored Study, Keltie Anderson Grant/research sup- port from: Janssen Sponsored Study, Wojciech Ozłyszyński Grant/research support from: Janssen sponsored study, Emmanouil Rampakakis : None declared, Odalis Asin Millian Employee of: Employee of Janssen, Allen Lehman Employee of: Employee of Janssen, Meagan Rachich Share- holder of: Janssen, Employee of: Employee of Janssen, Francois Nantel Shareholder of: Janssen, Employee of: Employee of Janssen


FR0110  RITUXIMAB BIOSIMILAR NON-MEDICAL SWITCH – DOES IT WORK?

Muhammad Khurram Nisar, Luton and Dunstable University Hospital, Rheumatology, Luton, United Kingdom

Background: Since the introduction of anti-TNF biosimilars in routine clin- ical practice, there has been a drive to implement the switch program for all biosimilars at the point of availability. Rituximab biosimilar was granted marketing authorisation by the EMA in February 2017. Our Trust was one of the first centres to embrace a CQUIN which required adoption of biosimilar within three months for new patients and one year for switch- ers. This helped deliver significant savings to the NHS whilst achiev- ing similar clinical outcomes.

Objectives: We report our early experience of introducing rituximab biosim- ilar in people with RA.

Methods: A list of all patients prescribed rituximab was extracted through our BMIC system. A switch letter was drafted and sent to all patients includ- ing Truxima information sheet. Patients were given the opportunity to contact nurse helpline for information or if disease control worsened/adverse effects developed. We reviewed all relevant records and collected data on any adverse events and disease outcome on either side of the switch. Patients were reviewed as originally planned by their respective clinicians.

Results: 44 patients with RA on 2 g dose six-monthly were identified established on rituximab. Four had stopped treatment prior to switching. All 40 agreed to switch to Truxima that was completed by February 2018. Mean age of switchers was 58.6 (range 26-80 years). Eighty were men and remaining 32 (80%) were women. Fourteen (35%) were Asian, one Afro-Caribbean and the rest (62%) were White Caucasian. DAS28 scores were available for all participants. Prior to the switch median DAS28 was 3.0 (range 0.6-5.1). Following the switch it was 2.95 (range 1.5-5.7). Amongst these, eight (20%) reported adverse effects. Four had serum sickness reaction within the first week of the second dose with loss of efficacy. One required admission to ED (24 hrs) for further management. All decided against further biosimilar and three were swapped back to the originator with no further concerns. In one case the clinician decided to change the class of drug to a TNF inhibitor. Three patients had mild intolerance and agreed to continue Truxima with no fur- ther issues. One patient developed milky tuberculosis and was taken off biologic therapy.

Conclusion: Our experience of switching rituximab patients is certainly not as smooth as it was for infliximab and etanercept. All were happy to switch after receiving a letter and having the opportunity to contact if necessary. Substantial annual cost savings of nearly £140,000 were achieved once the switch process completed. At group level there were no significant differences in seven of eleven adverse events including serum sickness reaction with loss of efficacy and loss of confidence in the drug. One patient developed military TB despite having one previous originator cycle with no issues. We support the routine switching from originator to biosimilar rituximab however close monitoring is required cer- tainly in the first few weeks of dose administration.

Disclosure of Interests: Muhammad Khurram Nisar Grant/research support from: Muhammad Nisar undertakes clinical trials and received support (including attendance at conferences, speaker fees and honoraria) from Roche, Chugai, MSD, Abbvie, Pfizer, BMS, Novartis, Celgene, Mallinck- rodt, UCBI and Lilly, Consultant for: Muhammad Nisar undertakes clinical trials and received support (including attendance at conferences, speaker fees and honoraria) from Roche, Chugai, MSD, Abbvie, Pfizer, BMS, Novartis, Celgene, Mallinckrodt, UCBI and Lilly, Speakers bureau: Muham- mad Nisar undertakes clinical trials and received support (including attendance at conferences, speaker fees and honoraria) from Roche, Chugai, MSD, Abbvie, Pfizer, BMS, Novartis, Celgene, Mallinckrodt, UCBI and Lilly


FR0111  ASSOCIATION BETWEEN RHEUMATOID FACTOR STATUS AND DISCONTINUATION OF TUMOR NECROSIS FACTOR INHIBITORS DUE TO INEFFECTIVENESS IN RHEUMATOID ARTHRITIS

Yoosukha Okawa1, Nobunori Takahashi2, Toshfshi Kojima3, Naoki Ishiguro3,1. Nakatsuigawa Municipal General Hospital, Nakatsuigawa, Japan, 1. Nagoya University Graduate School of Medicine, Nagoya, Japan

Background: As for the treatment of rheumatoid arthritis (RA), the influ- ence of rheumatoid factor (RF) positivity on the long-term efficacy of tumor necrosis factor inhibitors (TNFis) is controversial.

Objectives: We conducted an exploratory study in a large cohort of RA patients to evaluate the relationship between RF status and the discontinu- ation of TNFi treatment due to ineffectiveness in a clinical setting.

Methods: This study included bio-naive RA patients enrolled in the Tsuru- mai Biologic Communication Registry in Japan. The crude comparison of TNFi discontinuation due to ineffectiveness between seropositive and se- ronegative patients was analyzed using the cumulative incidence func- tion of competing events and Gray test. We assessed the associations between baseline patient characteristics and discontinuation of TNFi ther- apy due to insufficient response using Fine-Gray proportional hazard regression. Fine-Gray proportional hazard analysis considered competing events of interest, including insufficient response, adverse event, palliation, and personal reasons.

Results: Demographic and clinical characteristics of each group are summarized in Table 1. There was a higher discontinuation rate due to insufficient response in RF positive patients than in RF negative patients using Gray test (Figure). RF positivity was significantly predictive of the discontinuation of TNFi therapy due to ineffectiveness using Fine-Gray proportional hazard regression analysis after adjusting for baseline charac- teristics, including age, sex, stage, class, disease activity at baseline, methotrexate use, and prednisolone use (Table 2).

Adverse events related to Rituximab biosimilar switch

<table>
<thead>
<tr>
<th>Age</th>
<th>Gender</th>
<th>Previous</th>
<th>Matthera</th>
<th>Cycles</th>
<th>Prior</th>
<th>DAS28</th>
<th>Post</th>
<th>switch</th>
<th>DAS28</th>
<th>Adverse effects</th>
<th>Final</th>
<th>drug</th>
<th>choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>39</td>
<td>F</td>
<td>1</td>
<td>3.5</td>
<td>5.1</td>
<td>Gen uwell. achy, Nu like symptoms</td>
<td>Humira</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>70</td>
<td>M</td>
<td>3</td>
<td>2.1</td>
<td>1.8</td>
<td>Itchy scalp, brain fog</td>
<td>Truxima</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>49</td>
<td>F</td>
<td>2</td>
<td>4.4</td>
<td>2.8</td>
<td>Vonning, diarrhoea</td>
<td>Matthera</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>48</td>
<td>F</td>
<td>4</td>
<td>5.3</td>
<td>5.5</td>
<td>Palpitations, dizziness</td>
<td>Matthera</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>58</td>
<td>F</td>
<td>4</td>
<td>4.5</td>
<td>5.1</td>
<td>Nausea, flushing, headache</td>
<td>Truxima</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>77</td>
<td>F</td>
<td>1</td>
<td>2.2</td>
<td>2.5</td>
<td>Body pains, headache, distaste, lethargy</td>
<td>(hospitalised)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>75</td>
<td>F</td>
<td>1</td>
<td>2.2</td>
<td>2.5</td>
<td>Military TB</td>
<td>Biologic withdrawn</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Conclusion: Using Fine-Gray proportional hazard regression, we demonstrated that RF positivity was related to a higher discontinuation rate of TNFi therapy due to ineffectiveness in bio-naive RA patients.

Table 1. Characteristics of RA patients at baseline by RF status.

<table>
<thead>
<tr>
<th>Variable</th>
<th>RF positive</th>
<th>RF negative</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years) (SD)</td>
<td>56.6 (13.5)</td>
<td>53.1 (14.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female, no. (%)</td>
<td>737 (80.8)</td>
<td>195 (82.3)</td>
<td>0.64</td>
</tr>
<tr>
<td>Stage I + II/III + IV, no. (%)</td>
<td>312/569 (35.4/31.2)</td>
<td>103/120 (46.2/38.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DAS28ESR (SD)</td>
<td>5.28 (1.33)</td>
<td>4.87 (1.38)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Current MTX treatment, no. (%)</td>
<td>543/338 (61.6/33.3)</td>
<td>174/49 (78/22)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Current PSL treatment, no. (%)</td>
<td>383 (58.1)</td>
<td>98 (51.0)</td>
<td>0.083</td>
</tr>
</tbody>
</table>

Data are presented as mean, unless otherwise stated. SD: standard deviation; RA: rheumatoid arthritis; RF: rheumatoid factor; MTX: methotrexate; PSL: prednisolone; DAS28ESR: Disease Activity Score in 28 joints calculated with erythrocyte sedimentation rate. * Chi-square test for categorical variables and t-test for continuous variables.

Table 2. Fine-Gray proportional hazard regression.

<table>
<thead>
<tr>
<th>Variable</th>
<th>HR (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RF positive</td>
<td>1.73 (1.07-2.80)</td>
<td>0.023</td>
</tr>
<tr>
<td>Age at baseline</td>
<td>0.98 (0.97-0.99)</td>
<td>0.035</td>
</tr>
<tr>
<td>Sex (referent: male)</td>
<td>0.99 (0.58-1.38)</td>
<td>0.63</td>
</tr>
<tr>
<td>Methotrexate use</td>
<td>1.68 (0.96-2.96)</td>
<td>0.069</td>
</tr>
<tr>
<td>Prednisolone use</td>
<td>1.20 (0.83-1.75)</td>
<td>0.31</td>
</tr>
<tr>
<td>Stage III + IV (referent: I + II)</td>
<td>0.99 (0.98-1.01)</td>
<td>0.97</td>
</tr>
<tr>
<td>Class III + IV (referent: I + II)</td>
<td>1.00 (0.98-1.02)</td>
<td>0.67</td>
</tr>
<tr>
<td>DAS28ESR at baseline</td>
<td>1.31 (1.14-1.51)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

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Background: One of the most important complications of biological disease-modifying antirheumatic drugs (bDMARDs) is severe infection, and management of patients who develop severe infection during treatment with bDMARDs is a great concern. However, no consensus exists regarding bDMARDs readministration following treatment for bDMARDs-associated infection.

Methods: The study sample comprised patients with RA who were examined and prescribed bDMARDs at Osaka Minami Medical Center between January 2010 and December 2017, as part of the MiRAi cohort. The patients who developed severe infections during bDMARDs treatment were followed-up for 12 months. Logistic regression analysis was performed using baseline disease activity, baseline treatment, and disease activity and treatment during the 12-month period.

Results: Severe infections developed in 164 of a total of 1192 patients who were treated with bDMARDs during the study period, and the severe infection rate was 5.73/100 patients-years. Among the 164 patients, bDMARDs were readministered in 130 (79.3%), whereas treatment with bDMARDs was discontinued in 34 patients (20.7%). We observed 31 cases of patients with severe infections during the follow-up period (18.9/100 patients-years), of which 20 patients (15.4/100 patients-years) belonged to the bDMARDs readministration group and 11 (32.4/100 patients-years) belonged to the bDMARDs discontinuation group. The adjusted odds ratio (OR) for severe infection recurrence within 12 months in the bDMARDs discontinuation group was 0.39 [95% confidence interval (CI) 0.16-0.96]. At 12 months after infection, high-dose prednisolone treatment (adjusted OR 1.35, 95%CI 1.08-1.69), high C-reactive protein level (adjusted OR 1.28, 95%CI 1.02-1.62), and low serum albumin levels (adjusted OR 0.30, 95%CI 0.01-0.89) were associated with high risk of severe infection recurrence (Figure).

Conclusion: Patients who developed severe infection during bDMARDs treatment were at an extremely high risk for severe infection irrespective of the readministration or discontinuation of bDMARDs after infection. Discontinuation of bDMARDs, high dose of prednisolone 12 months after infection, high levels of C-reactive protein 12 months after infection, and low levels of albumin 12 months after infection were identified as risk factors for severe infection recurrence in these patients. However, bDMARDs readministration did not increase the risk of severe infection recurrence.

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COMPARISON OF INFECTION-RELATED HOSPITALIZATION COSTS IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA) TREATED WITH ABATACEPT OR OTHER TARGETED DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS (DMARDS)

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Background: Costs due to differences in risk of hospitalization infection associated with targeted disease-modifying anti-rheumatic drugs (DMARDS) in patients with RA have not been evaluated.

Objectives: Compare the risk and cost of infection-related hospitalizations in tumor necrosis factor inhibitor (TNFi)-experienced RA patients subsequently receiving DMARDS in the US.

Methods: A retrospective, observational study was conducted with 2 insurance claims databases (MarketScan and PharMetrics; January 1, 2009-June 30, 2017). Analyses were conducted in both datasets individually and in aggregate. The study population was adult TNFi-experienced RA patients initiating a subsequent DMARD (date of DMARD therapy-index date). Patients had 12 months of continuous enrollment prior to the index date (baseline period), and were required to have ≤1 outpatient medical claims on 2 different dates with a diagnosis code for RA. Patients with other autoimmune conditions were excluded. Follow-up began ≥12 months ending with the earliest of (1) end of insurance enrollment; (2) end of study period; (3) end of index treatment. Cohorts included (1) abatacept; (2) TNFi: adalimumab, certolizumab pegol, etanercept, golimumab, and infliximab; and (3) other non-TNFi: tocilizumab, rituximab, and tocilizumab. Hospitalized infection costs were measured on a per-patient-per-month (PPPM) basis (2016 USD). Two-part multivariable generalized linear models (GLMs) examined differences in costs. Baseline comorbidities, infection incidence, healthcare costs, payer type, age, gender, and geographic region were used as regression covariates. Log transformation and gamma distribution were applied in GLMs.

Results: Overall, most patients were female (79%) with an average age of 52 years. Although a higher percentage (4.5%) of patients in the abatacept cohort had a hospital visit for infection in the baseline period compared to TNFi (2.0%, P<0.001) and other non-TNFi (3.6%, P=0.02619), the trend reversed in the follow-up period (2.8% for abatacept vs 3.7% for TNFi and 5.2% for other non-TNFi, P<0.05). Regression results indicated a significantly higher risk for hospitalized infection for patients receiving a TNFi [HR: 1.6 (95% CI: 1.1, 2.2)] or other non-TNFi [HR: 1.9 (95%; 1.3, 2.8)] vs abatacept. Mean PPPM (95% CI) inpatient costs in the follow-up were $73 ($17-$158) for abatacept, $115 ($27-$224) for TNFi, and $125 ($29-$264) for other non-TNFi. Difference from baseline to follow-up PPPM inpatient costs was significantly lower for abatacept (difference of $42 for TNFi and $52 for other non-TNFi, P<0.05).

Conclusion: There were significantly lower infection-related hospitalizations and associated costs for TNFi-experienced RA patients who were switched to abatacept compared to patients switched to other therapies.


ABATACEPT IN EARLY RHEUMATOID ARTHRITIS: A SYSTEMATIC LITERATURE REVIEW AND NETWORK META-ANALYSIS

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Background: Rheumatoid arthritis (RA) is a wide-spread and debilitating disorder that is becoming increasingly relevant in an aging global population. Identifying and treating RA early in disease course is critical for preventing disability and joint damage.

Objectives: The goal of this systematic literature review (SLR) and meta-analysis was to compare the relative efficacy of abatacept (ABA) to other currently used recommended therapies for RA. Studies of interest were randomized controlled trials (RCTs) and observational studies. Outcomes included ACR50, DAS28, radiographic change, and adverse events where available. A search from January 1998 to June 2018 was performed on MEDLINE®, Embase, MEDLINE® and the Cochrane CENTRAL databases. Additional research was searched on US and European clinical trials registries from January 2005 to June 2018 and conference proceedings from ACR and EULAR from 2014 to 2018. A Bayesian network meta-analysis (NMA) was performed on the DCC Data™ platform for the RCTs with reported results on ACR50, DAS28 remission, total withdrawal, and withdrawal due to adverse events.

Results: We identified 90 publications on 69 unique trials reporting efficacy and safety outcomes in patients with early RA, including 43 RCTs and 26 observational studies. The included studies had low risk as assessed by the Cochrane Collaboration’s tool for assessing risk of bias. The studies were predominantly double-blind phase III or IV trials. Twenty-eight trials were included in the NMA evaluating ABA (n=1 trial), ABA+MTX (n=2), ADA+MTX (n=2), CTZ+MTX (n=2), ETN (n=1), ETN+MTX (n=1), HCQ+SSZ+MTX (n=1), HCQ+SSZ+Pred+MTX (n=1), IFX+MTX (n=4), MTX (n=2), MPred+MTX (n=2), MPred+Pred+MTX (n=1), Pred+SSZ+MTX (n=2), Pred+MTX (n=1), Pred (n=1), SSZ (n=4), SSZ+MTX (n=2), TCZ (n=2), TCZ+MTX (n=2), TOF (n=2), and TOF+MTX (n=2). Abatacept as monotherapy was similar to the combination of ABA and methotrexate for efficacy outcomes, ACR 50 (ABA vs ABA+MTX RR 0.82 [95% CI 0.51-1.35]), and DAS28 Remission (RR 0.76 [95% CI 0.39-1.49], as well as for all-cause withdrawal (RR 1.8 [95% CI 0.91-3.2]) and withdrawal due to adverse events (RR 2.35 [95% CI 0.69-7.38]). Both ABA as monotherapy and ABA+MTX were similar to all other comparators (as monotherapy or combination therapy) with respect to main efficacy and safety outcomes. Data reported in observational studies was not in line with the RCT analysis.

Conclusion: The results of this NMA similar efficacy between ABA and other biologics both as monotherapy and in combination with traditional DMARDS in early RA. Further investigation and comparison of different treatment options for early RA is warranted as the growing evidence base evolves in favor of using more novel therapies for RA. ABA-abatacept; ADA-adalimumab; CTZ-certolizumab; ETN-etanercept; HCQ-hydroxychloroquine, IFX-infliximab, MPred= methylprednisolone, MTX= methotrexate; Pred-prednisone, SSZ=sulfasalazine, TCZ= tocilizumab, TOF=tofacitinib.

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TRAJECTORIES OF THE EQ-5D SCORE AMONG A LARGE COHORT OF RHEUMATOID ARTHRITIS PATIENTS TREATED WITH BIOLOGICAL DMARDS USING THE IORRA COHORT

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Background: Patient-reported outcomes are important for evaluating the disease status of patients with rheumatoid arthritis (RA). The EuroQol five-dimensional descriptive system (EQ-5D) has been used for health-related quality of life (QOL) in clinical research and pharmacoeconomic studies. RA is a chronic disease associated with pain, fatigue, disability, and functional loss, which can markedly decrease patient QOL.
The treatment strategies for RA and the QOL of RA patients, which is evaluated in daily practice using the EQ-5D, have changed significantly since the introduction of biological disease-modifying anti-rheumatic drugs (bDMARDs).

Objectives: To identify patient subsets with distinct EQ-5D trajectories among RA patients taking bDMARDs, and to examine the clinical features of patients whose QOL improved since bDMARD use in daily practice.

Methods: Since October 2000, we have established a large observational cohort of RA patients at our institute Institute Of Rheumatology, Rheumatoid Arthritis (IORRA). Essentially, all RA patients who attend our clinic are given questionnaires, including the EQ-5D, Disease Activity Score 28 (DAS28), and the Japanese version of the Health Assessment Questionnaire (J-HAQ), every 6 months. More than 5,000 RA patients are included in this cohort, of whom 785 patients who received bDMARDs for at least 3 years were enrolled in this study. The EQ-5D scores of these 785 patients were recorded biannually for 3 years, and latent class analysis of the temporal trends in the EQ-5D score based on posterior probabilities was performed after initiation of bDMARDs. The clinical characteristics of each latent class were then compared.

Results: The 785 patients (107 taking infliximab, 341 etanercept, 100 tocilizumab, 131 abatacept, 90 golimumab, and 16 certolizumab pegol) were classified into four classes based on time-related changes in their EQ-5D scores: Class 1 (n = 160), patients with a consistently low score < 0.6 despite use of bDMARDs; Class 2 (n = 314), patients with a consistently moderate score of 0.7; Class 3 (n = 229), patients whose score improved from 0.7 to 0.9 after use of bDMARDs; and Class 4 (n = 78), patients with a consistently high score of 0.9. When comparing the patients in Classes 2 and 3, whose EQ-5D scores before bDMARD use were similar, the patients in Class 3 had a younger age (<0.001), shorter disease duration (<0.001), higher DAS28 score (<0.001), lower J-HAQ score (<0.038), and more frequent use of non-steroidal agents (<0.002) than those of Class 2 patients.

Conclusion: The results of this study suggest that QOL is less likely to improve in patients with RA whose disabilities and QOL deterioration have already become established despite use of bDMARDs. We also determined the clinical features of RA patients whose QOL improved after initiation of bDMARDs.


FR0116 SUBCUTANEOUS TOCILIZUMAB IN MONOTHERAPY OR IN COMBINATION WITH CSDMARD IN PATIENTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS: OBSERVATIONAL STUDY TO DESCRIBE REAL-WORLD DRUG RETENTION RATE AT 12 MONTHS

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Background: Rate of discontinuation and drug survival of biologic therapies in rheumatoid arthritis (RA) is about 60-70% in real life at one year. In France, all biologics 1st prescription and yearly renewal are reimbursed, restricted to hospital rheumatologists, with renewal and monitoring done by both office-based or hospital rheumatologists.

Objectives: To evaluate the 12-month drug retention rate, efficacy and tolerance of tocilizumab (TCZ) subcutaneous (sc) in RA patients (pts).

Study design: prospective, multicentre, observational 18-month study. Pts moderate to severe active RA requiring TCZ sc as prescribed in real life.

Primary endpoint: drug retention rate of TCZ sc at 12 months in pts followed by hospital- and office-based rheumatologists, estimated using Kaplan-Meier method. Secondary endpoints: pts characteristics, concomitant treatments, adherence to TCZ sc using the Compliance Questionnaire for Rheumatology (CQR5), efficacy, safety of TCZ sc and QoL using EQ-5D.

Statistical analysis: pts with ≥1 TCZ injection were analyzed for safety. Pts fulfilling inclusion and non-inclusion criteria were analyzed for efficacy.

Results: 291 pts were recruited, 286 were analyzed for safety and 285 for efficacy.

Baseline: mean age 56.2±12.5 years, females: 74.7%, at least 1 co-morbidity: 71.9%, mean RA duration 9.4±9.0 years, RF and/or ACPA: 60.8%, erosive RA: 60.8%, mean DAS28-ESR 4.77±2.12. Past RA treatments were csDMARDs in 94.4%, biologics in 62.8%, EQ-5D Health state was 0.53±0.19. TCZ Mono (i.e. without csDMARD) was initiated in 124 (43.5%), TCZ Combo in 158 (55.4%) pts, 64.8% of whom received MTX (17.3±4.4mg/w). Glucocorticoids (GCs) were used in 48.9% of the pts (9.9±9.3mg/d).

Follow up: 161 and 148 pts completed M12 and M18 visits. 138 pts withdrew including AE 61, lack of efficacy 37, pts/doctor wish 24. At M12, drug retention rate was 63.6%: 62.6% in Mono, 64.3% in Combo (Fig1); with similar results for pts ≥56 years old and for pts ≥30Kg/m². 5 Mono pts had ongoing csDMARD and 9 Combo pts had no csDMARD. 15.3% and 19.0% used GCs, 16.1±11.9mg/d in the Mono and 17.36±16.65mg/d in the Combo groups. Total number of TCZ injections was 36.7±25.84 done by pt in 54.0%. Mean time between 2 TCZ injections was 8.4±10.70 days. Adherence to TCZ was high in 86.5% of the 89 pts who completed CQR5 at month 12. It was 52.9% for the 121 pts who completed pts diary over the month 12-month 18 period. Mean time from injection to next visit was 2.12±1.14 respectively. EULAR good and moderate responses were respectively 61.3 and 7.7% in all: 67.2 and 4.9% in Mono; 56.8 and 9.9% in Combo pts. EQ-5D improved in all domains with a change from baseline of 0.11 to 0.29, 0.18 (81.8%) pts had at least 1 adverse event (AE), 46 (16.1%) had at least 1 serious AE including 11 infections, 2 GI perforations and 2 deaths (pneumopathy and bronchial carcinoma).

Figure 1. Kaplan-Meier curve of the drug retention rate by SC TCZ in mono vs combo - Efficacy population.
Conclusion: At 12 months, drug retention rate was 63.6% in patients receiving TCZ sc in real life, with no difference between Mono and Combo groups. EULAR good/moderate response was 69.0%. QoL improved in all EQ-SD domains. No new safety signal occurred.

REFERENCE:

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THE COMPARATIVE RISK OF OSTEOPOROTIC FRACURES AMONG PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING TFN INHIBITORS VERSUS OTHER BIOLOGICS: A NATION-WIDE COHORT STUDY IN KOREA

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Background: Rheumatoid arthritis (RA) is associated with an increased risk of osteoporosis and osteoporotic fracture, but little is known about comparative risk of osteoporotic fractures between biologic agents.

Objectives: To investigate the comparative risk of osteoporotic fractures among RA patients who initiated TNF inhibitors, abatacept, and tocilizumab.

Methods: We identified patients aged ≥ 40 years with at least two ICD-10 diagnosis codes for RA who initiated TNF inhibitor, abatacept, or tocilizumab from the 2005-2015 Korean National Health Insurance Service datasets. The primary outcome was a composite osteoporotic fracture endpoint of spine, hip, forearm or humerus fractures requiring hospitalization. Secondary outcomes were spinal and non-spinal fractures. Follow-up period started from the day after the first dispensing date of the study drug to the earliest date among the following events: discontinuation of the study drugs, outcome occurrence, disenrollment, end of study dataset, or death. Propensity score (PS) matching with a variable ratio of 10:1 was conducted for TNF inhibitor versus abatacept initiators and for TNF inhibitor versus tocilizumab initiators to adjust for baseline confounding. We estimated hazard ratio (HR) and 95% confidence interval (CI) of osteoporotic fracture risks comparing TNF inhibitors to abatacept or tocilizumab by Cox proportional hazard models stratified by a matching ratio.

Results: We included 2,339 TNF inhibitor initiators and 594 abatacept initiators, and 2,486 TNF inhibitor initiators and 647 tocilizumab initiators in each PS-matched cohort. The incidence rates per 100 person-years for the primary outcome were 1.57 and 1.65 for TNF inhibitor and abatacept initiators, and 1.69 and 2.05 for TNF inhibitor and tocilizumab initiators, respectively. The HR (95% CI) for the primary outcome was 1.10 (1.54-2.23) comparing TNF inhibitors versus abatacept and it was 1.00 (0.53-1.92) comparing TNF inhibitor versus tocilizumab initiators. We also did not find any significant difference for secondary outcomes (Table1).

Table 1. Risk of osteoporotic fractures in TNF inhibitor initiators vs. abatacept initiators and tocilizumab initiators

<table>
<thead>
<tr>
<th>TNF inhibitor (n=2,339)</th>
<th>Abatacept (n=594)</th>
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<td>Events</td>
<td>FYs IR per 100 FY</td>
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<td>Primary outcome:</td>
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<tr>
<td>Osteoporotic fracture</td>
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<td>Secondary outcomes:</td>
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<td>Spinal fracture</td>
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<td>3,018</td>
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<tr>
<td>Non-spinal fracture</td>
<td>22</td>
<td>3,022</td>
</tr>
</tbody>
</table>

Conclusion: We did not find a significant difference in the risk of osteoporotic fractures between TNF inhibitor and abatacept initiators, or between TNF inhibitor and tocilizumab initiators in this Korean population-based cohort study.

Disclosure of Interests: None declared


FR0118 INFECTION OUTCOMES IN PATIENTS WITH RA TREATED WITH ABATACEPT AND OTHER DMARDS: RESULTS FROM A 10-YEAR INTERNATIONAL POST-APPROVAL STUDY

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Background: The abatacept global post-marketing epidemiology programme consists of observational studies based on biologic disease registries and healthcare claims databases to assess infection and malignancy risks associated with abatacept treatment, as used in routine clinical practice.

Objectives: To evaluate the risk of infection in patients with RA treated with abatacept versus conventional synthetic (cs)DMARDs and other biologic (b) or targeted synthetic (ts)DMARDs.

Methods: Data were analysed from five cohorts: two biologic registries (the Anti-Rheumatic Therapy in Sweden register and the Rheumatoid Arthritis Observation of Biologic Therapy German registry), a disease registry (FORWARD, The National Databank for Rheumatic Diseases in the USA) and two healthcare claims databases (the population-based British Columbia Canadian RA Cohort and the US Optum Research Database). Crude incidence rates (per 1000 patient-years of exposure) with 95% CIs were estimated using multivariate models adjusting for demographics, comorbidities and other potential confounders within each database and were subsequently pooled between random effects model for meta-analyses.

Results: From all cohorts, patients treated with abatacept (6400), csDMARDs (137K) and other b/tsDMARDs (54K) were followed up for a mean of 2.3–3.7, 2.6–6.2 and 2.3–4.7 years, respectively. Patients were mainly female (71–86%), with a mean age ranging from 49–63 years, and 3–18% had a history of prior severe infections across treatment groups/cohorts. A greater number of abatacept-treated patients had a history of ≥2 prior biologics (44–85% vs csDMARDs, 11% [FORWARD] and other b/tsDMARDs, 0–19%). In abatacept-treated patients, incidence rates for hospitalised infections ranged from 16–56 and opportunistic infections from 0.4–7.8 (Table). Adjusted RR (95% CIs) for abatacept vs csDMARDs (range: 0.3 [0.2, 0.7] to 2.2 [1.3, 3.7]; pooled estimate: 1.2 [0.6, 2.2]) and abatacept vs other b/tsDMARDs (range: 0.5 [0.3, 0.8] to 1.3 [0.8, 2.1]; pooled estimate: 0.9 [0.6, 1.3]) showed no increased risk in hospitalised infections.

Conclusion: In this large, international post-marketing epidemiology programme, pre-specified infection risks were more frequent with abatacept than csDMARDs and b/tsDMARDs in some, but not all, cohorts. Increased risks for individual outcomes/cohorts may be attributed to prior biologic exposure, study design and practice pattern differences. These data are consistent with the current safety profile of abatacept.

REFERENCES:

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FRI0119 PREDICTING REMISSION AMONG PATIENTS WITH RHEUMATOID ARTHRITIS STARTING TOCILIZUMAB MONOTHERAPY: MODEL DERIVATION AND VALIDATION USING CONVENTIONAL REGRESSION AND MACHINE LEARNING

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Background: Most rheumatoid arthritis (RA) patients strive to consolidate their treatment from methotrexate combinations to monotherapy with the goal of the most effective and simplified therapy. Tocilizumab (TCZ) appears to have similar efficacy when used with or without concomitant csDMARDs in RA. Thus, it is clinically useful to predict treatment benefit among patients with RA starting TCZ monotherapy.

Objectives: To identify RA patients most likely to achieve remission with TCZ monotherapy by developing and validating a prediction model through conventional regression and machine learning.

Methods: We followed the TRIPOD recommendations for derivation and validation of clinical risk prediction models. Four TCZ monotherapy randomized controlled trials (RCT) in RA were identified (ACT-RAY, ADACTA, AMBITION, and FUNCTION) – two were chosen for derivation of the prediction models and two for validation. Relevant data for individual subjects from the trials were obtained, including demographics, RA characteristics, prior treatments, comorbid conditions, and baseline disease activity. In the two derivation trials, we examined each potential predictor of remission at a time in logistic regression models, adjusted for age, sex, and baseline CDAI. The dependent variable in all models was odds ratio (OR) based (forwarding variables to multi-variable models if OR > 1.5 or < 0.66); AIC based (lowest AIC); and a machine learning approach that fit a logistic regression model to covariates selected by a LASSO-regularized logistic regression. Based on these different variable selection approaches, variables were included to the final multivariable model in the derivation cohort (DC). Age, sex, and baseline CDAI were forced into all models. We assessed discrimination with the area under the curve (AUC), model fit with the AIC and BIC, and calibration graphically using loess smoothing and with calibration slopes. We assessed model performance in the DC and in the validation cohort (VC), using variables selected in the DC.

Results: Baseline characteristics in the derivation (n=473) and validation (n=380) cohorts were generally similar: mean age 51.6 years in DC and 52.1 in VC; 77% female in DC and 83% in VC; mean baseline CDAI 39.8 in DC and 42.1 in VC; disease duration was longer in VC 3.6 years compared to 0.9 in DC. Seventy-eight patients (17%) reached remission in the DC, 49 (13%) in the VC. After testing possible variables in the derivation models, the variables selected as predictors of remission included younger age, male sex, lower baseline CDAI, shorter RA disease duration, region of world (Europe and South America increased odds of remission vs. Asia and North America), no previous exposure to DMARD/MTX, lower baseline HAQ-DI, and baseline hematocrit (see Table). In the DC, model fit and calibration were adequate in all three models, though discrimination was notably reduced under 10 fold cross-validation. The VC modeling suggested that all three models were similar in discrimination and were well calibrated (see Table).

Conclusion: Different modeling strategies selected similar variables to predict remission using TCZ monotherapy: shorter disease duration, lower HAQ-DI, and no prior DMARD/methotrexate use. While these results should be interpreted with caution, as the analysis combined different studies that may represent different populations, they may provide guidance to clinicians tailoring treatment options based on baseline characteristics.

Table: Factors for predicting remission in patients with RA starting TCZ monotherapy: results from three different modeling strategies in derivation cohort and validation cohort with AUC and BIC.

<table>
<thead>
<tr>
<th>Variable</th>
<th>DC (n=473)</th>
<th>VC (n=380)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>0.74 (0.68-0.80)</td>
<td>0.73 (0.65-0.80)</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>0.84 (0.79-0.87)</td>
<td>0.85 (0.80-0.89)</td>
</tr>
<tr>
<td>Baseline CDAI</td>
<td>0.62 (0.56-0.69)</td>
<td>0.62 (0.56-0.69)</td>
</tr>
<tr>
<td>Baseline HAQ-DI</td>
<td>0.01 (0.00-0.02)</td>
<td>0.01 (0.00-0.02)</td>
</tr>
<tr>
<td>Baseline hematocrit</td>
<td>0.90 (0.85-0.94)</td>
<td>0.91 (0.86-0.96)</td>
</tr>
</tbody>
</table>

Notes: * indicates that variable was included in a specific model. AUC, area under the curve calculated at the threshold level of 0.5 for remission. OR, odds ratio; DC, derivation cohort; BIC, Bayesian information criterion; AIC, Akaike information criterion; MTX, methotrexate; CDAI, Clinical Disease Activity Index; OR, odds ratio; DC, derivation cohort; BIC, Bayesian information criterion; AIC, Akaike information criterion; MTX, methotrexate.

Disclosure of Interests: Jamie Collins Grant/research support from: genentech, Fredrik Johansson Grant/research support from: genentech, Sara Gale Grant/research support from: genentech, Roche, Employee of: genentech, Roche, Seoyoung Kim Grant/research support from: Pfizer, Bristol-Myers Squibb, Roche, genentech and AbbVie., Swastina Shrestha Grant/research support from: genentech, Fredrik Johansson Grant/research support from: genentech, David Sontag Grant/research support from: genentech, Trinh Huong Grant/research support from: genentech, Chien Ho Grant/research support from: genentech, Elena Losina Grant/research support from: genentech, Pfizer, Samumed and Flexion, Consultant for: Regeneron, Daniel Solomon Grant/research support from: ABBVie, Aigen, Genentech, Jansen, and Pfizer

**FRIO120**

### HIGH LEVELS OF INTERLEUKIN-6 (IL-6) IN RA PATIENTS ARE ASSOCIATED WITH GREATER IMPROVEMENTS IN PATIENT-REPORTED OUTCOMES (PROS) FOR SARILUMAB COMPARED WITH ADALUMAB

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**Background:** Increased levels of cytokines, including interleukin-6 (IL-6), reflect inflammation and are predictive of therapeutic responses in patients with RA. IL-6 has been implicated in fatigue, pain and depression in RA but a formal association with PROs has not been performed. Sarilumab, a fully human monoclonal antibody directed against IL-6Ra, is approved for treatment of moderate-to-severely active RA. The phase 3 MONARCH randomized controlled trial (NCT01061736) compared the efficacy and safety of sarilumab monotherapy vs adalumab in RA patients who should not continue methotrexate treatment due to intolerance or inadequate responses. Greater reductions in disease activity and improvements in the clinical signs of RA and physical function were demonstrated with sarilumab vs adalumab. Better understanding of the association between IL-6 levels and PROs is warranted to evaluate sarilumab vs adalumab in MONARCH.

**Methods:** Serum IL-6 levels were measured at baseline in 300/369 patients in the ITT population. Patients were categorized into high, medium, or low IL-6 tertiles. Between-group comparisons of differences at Week 24 in Short Form-36 (SF-36) physical and mental component summaries (PCS, MCS) and domain scores, Functional Assessment of Chronic Illness Therapy (FACT)-fatigue, and morning stiffness visual analog scale (VAS) measures were performed within each tertile using a linear fixed effect model. In order to evaluate the differential effect of sarilumab vs adalumab in the baseline high vs low IL-6 groups, an interaction test of treatment-by-baseline IL-6 group analysis was performed using low IL-6 group as the reference.

**Results:** At baseline, patients in the high IL-6 tertile presented a significantly worse MCS and morning stiffness scores (P < 0.05). The model interaction comparing high vs low IL-6 tertiles was significant for SF-36 PCS and physical functioning domains, and for morning stiffness. In patients with high IL-6, sarilumab treatment resulted in significant (P < 0.05) improvements vs adalumab in SF-36 PCS (LS mean [LSM] of the difference: 5.57, 95%CI (2.85, 8.28)) and physical functioning (PF, 16.59 (8.15, 25.03)), role physical (9.44 (0.78, 18.10)), bodily pain (BP, 10.87 (3.92, 17.81)), vitality (8.93 (1.11, 16.74)), and social functioning (12.82 (3.07, 22.58)) domains (all raw values in Figure). Sarilumab also showed significant (P < 0.05) effects vs adalumab in FACT-Fatigue (4.86 (1.06, 8.65)) and morning stiffness VAS (-19.93 (-30.30, -9.56)), with LSM changes exceeding minimum clinically important differences (MCID).

**Conclusion:** Evaluation of IL-6 biomarker associations with PROs indicate that patients with high IL-6 levels report better improvements with sarilumab vs adalumab with safety profile consistent with IL-6R blockade. The effects of adalumab treatment are stable based on IL-6 tertiles but higher with sarilumab, particularly in the high IL-6 tertile group. Effects on PCS scores are mainly driven by the PF domain, consistent with previous reports of marked improvements in pain with high IL-6 levels.

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**FRIO121**

### IMPROVEMENT OF MATRIX METALLOPROTEINASE-3 AT 12 WEEKS IS AN INDEPENDENT PREDICTIVE FACTOR FOR ACHIEVEMENT OF LOW DISEASE ACTIVITY AT 52 WEEKS IN BIO-SWITCH RHEUMATOID ARTHRITIS PATIENTS TREATED WITH ABATACEPT

Nibunori Takahashi, Toshihisa Kojima, Shuj Asal, Naoki Ishiguro, Nagoya University Graduate School of Medicine, Orthopedic Surgery, Nagoya, Japan

**Background:** Japanese post-marketing surveillance (PMS) data demonstrated that effectiveness of abatacept in rheumatoid arthritis (RA) patients with previous biologics treatment (bio-switch) was significantly lower than that in bio-naïve patients [1]. Useful predictive factors for good clinical response of abatacept is necessary especially in the bio-switch patients.

Serum matrix metalloproteinase-3 (MMP-3) is an enzyme produced by synoviocytes which can be used to predict clinical effectiveness and joint destruction in RA patients [2]. However, little is known about the relationship between MMP-3 and effectiveness of abatacept.

**Objectives:** This study aimed to study whether serum MMP-3 levels can predict good clinical effectiveness of abatacept in the bio-switch RA patients using data from a multicenter cohort.

**Methods:** Participants were consecutive 423 RA patients treated with abatacept, observed for longer than 52 weeks, and registered in the TBCR, a Japanese multicenter registry system for RA patients treated with biologics. Multivariate logistic regression analysis was used to study predictive factors for achievement of low disease activity at 52 weeks separately in bio-naïve and bio-switch group.

**Results:** A total of 189 bio-switch and 234 bio-naïve patients were included in this study. ROC analysis revealed that MMP-3 improvement rate at 12 weeks, compared to 4 and 24 weeks, had highest AUC and the best cut-off value was 20.0% at 12 weeks for predicting achievement of low disease activity (LDA) at 52 weeks in the bio-switch group (Figure 1, right panel). We performed multivariate logistic regression analysis to study independent predictive factors for LDA at 52 weeks using patients’ background factors as well as 20% improvement of MMP-3 at 12 weeks.

In the bio-naïve group, DAS28-CRP score at baseline was the only predictive factor, while the achievement of 20% improvement of MMP-3 at 12 weeks was a significant independent predictive factor, with the achievement of 20% improvement of MMP-3 at 12 weeks was an independent predictive factor (adjusted OR, 3.550, p=0.005) in addition to DAS28-CRP in the bio-switch group (Table). In the bio-switch group, patients that achieved 20% improvement of MMP-3 at 12 weeks demonstrated significantly higher achievement rate of LDA at 52 weeks compared to those that did not achieve 20% improvement (60.0% vs 33.3%, p=0.001) (Figure 2).

---


**References:**


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**Multivariate analysis**

<table>
<thead>
<tr>
<th>Bio-naïve</th>
<th>Adjusted OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.988 (0.951-1.022)</td>
<td>0.479</td>
</tr>
<tr>
<td>RF positive</td>
<td>0.693 (0.305-1.577)</td>
<td>0.382</td>
</tr>
<tr>
<td>RF positive</td>
<td>2.172 (0.945-4.990)</td>
<td>0.068</td>
</tr>
<tr>
<td>Comorbid MTX</td>
<td>1.769 (0.843-3.709)</td>
<td>0.131</td>
</tr>
<tr>
<td>Comorbid PSL</td>
<td>0.609 (0.294-1.262)</td>
<td>0.182</td>
</tr>
<tr>
<td>Comorbid DAS28-CRP</td>
<td>0.544 (0.330-0.748)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

20% improvement of MMP-3 @12 weeks

0.918 (0.918-0.007) | 0.083
**Bio-switch**

<table>
<thead>
<tr>
<th></th>
<th>Adjusted OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.990 (0.992-1.029)</td>
<td>0.608</td>
</tr>
<tr>
<td>Male</td>
<td>1.010 (0.994-3.475)</td>
<td>0.987</td>
</tr>
<tr>
<td>RF positive</td>
<td>0.481 (0.151-1.532)</td>
<td>0.216</td>
</tr>
<tr>
<td>Concomitant MTX</td>
<td>1.120 (0.459-2.731)</td>
<td>0.803</td>
</tr>
<tr>
<td>Concomitant PSL</td>
<td>0.496 (0.200-2.211)</td>
<td>0.127</td>
</tr>
<tr>
<td>DAS28-CRP</td>
<td>0.603 (0.432-0.843)</td>
<td>0.003</td>
</tr>
<tr>
<td>20% improvement of MMP-3 @12weeks</td>
<td>3.550 (1.454-8.666)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Conclusion: In the bio-switch patients, we sometimes have difficulty to obtain good clinical response of abatacept and it would be even more important to judge whether to continue abatacept or whether to add other anti-rheumatic drugs as early as possible [3]. Our results suggested that the improvement of MMP-3 at 12 weeks would be a key to predict good clinical effectiveness of abatacept at 1 year. We would be better to note not only the major clinical indices such as DAS28 but also the change of MMP-3 to obtain the best clinical results in the bio-switch patients treated with abatacept.

REFERENCES:


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**FR1022**

REAL-WORLD SAFETY DATA FROM PATIENTS WITH RHEUMATIC DISEASES TREATED WITH CT-P13, AN INFliximab BIOSIMILAR: AN INTERIM ANALYSIS FROM AN OBSERVATIONAL STUDY

Peter C. Taylor1, Robin Christensen2, Shahzad Moosa3, Pamela Selem4, Ruffy Gullatoc, Heather Fowler6, Claire Bombardier6, Boulos Harau5.1. University of Oxford, Oxford, United Kingdom; 2. The Parker Institute, Copenhagen and Odense University Hospital, Copenhagen, Denmark; 3. Pfizer Inc, New York City, United States of America; 4. Pfizer Inc, Manila, Philippines; 5. Pfizer Inc, Maidenhead, United Kingdom; 6. UHN/MSH, Toronto, Canada; 7. University of Montreal, Montreal, Canada

Background: CT-P13, an infliximab biosimilar, has been available in Europe and Canada since 2015, and real-world experience with CT-P13 is important to support the safety of this medication. PERSIST is an ongoing, observational cohort study evaluating CT-P13 as treatment for rheumatoid arthritis (RA), ankylosing spondylitis (AS) and psoriatic arthritis (PsA) in a real-world setting.

Objectives: This interim analysis reports safety outcomes for patients who received CT-P13 as their first biologic (Biologic-naive) or who switched from infliximab reference product (IFX-RP) to CT-P13 (Switched) based on data collected from September 2015 to December 2017.

Methods: Patients were recruited during usual care at 38 academic and community sites in 6 European countries and Canada. Adult RA, AS or PsA patients prescribed CT-P13 or locally-sourced IFX-RP at the investi-
gator’s discretion and according to the approved label were eligible. Data were analysed descriptively.

Results: This analysis included 329 patients (RA, n=134; AS, n=110; PsA, n=85). Of these, 6 (1.8%) were not treated, 3 (0.9%) completed study treatment, 244 (74.2%) were ongoing and 76 (23.1%) discontinued study treatment, most commonly due to lack of response (30 [9.1%]). Demographics and baseline characteristics were generally similar between groups (Table 1). Most treatment-emergent adverse events (TEAEs; Table 2) were of mild or moderate intensity; 7/129 events were severe. Most commonly reported adverse events were related to infection (n=33; 10.2%); most frequently reported infection-related TEAEs were nasopharyn-
giits (n=6; 1.9%), respiratory tract infection (n=5; 1.5%) and pneumonia (n=4; 1.2%). No case of tuberculosis was reported. Eight (2.5%) patients reported infusion related reactions.

Table 1. Disposition, population characteristics and drug utilisation patterns for patients receiving CT-P13

<table>
<thead>
<tr>
<th>Biologic-naive (n=216)</th>
<th>Switched (n=107)</th>
<th>Total (N=323)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (range), years</td>
<td>54 (19-84)</td>
<td>53 (23-76)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>97 (44.9)</td>
<td>59 (55.1)</td>
</tr>
<tr>
<td>Disease duration, median (range), months</td>
<td>45.34 (0.03-563.91)</td>
<td>159.51 (12.65-464.07)</td>
</tr>
<tr>
<td>Baseline dose</td>
<td>202</td>
<td>102</td>
</tr>
<tr>
<td>Patients with data for baseline dose, n</td>
<td>3.68 (1.05)</td>
<td>3.96 (0.94)</td>
</tr>
<tr>
<td>Baseline infusion frequency, n (%)</td>
<td>2.5</td>
<td>2.4</td>
</tr>
<tr>
<td>Once every 4 or fewer weeks</td>
<td>72 (33.3)</td>
<td>43 (40.2)</td>
</tr>
<tr>
<td>Once every 8 weeks</td>
<td>76 (35.2)</td>
<td>44 (41.1)</td>
</tr>
<tr>
<td>Other</td>
<td>54 (25.0)</td>
<td>15 (14.0)</td>
</tr>
<tr>
<td>Missing</td>
<td>14 (6.5)</td>
<td>5 (4.7)</td>
</tr>
</tbody>
</table>

Table 2. All-causality TEAEs for patients receiving CT-P13

<table>
<thead>
<tr>
<th>Biologic-naive (n=216)</th>
<th>Switched (n=107)</th>
<th>Total (N=323)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of TEAEs</td>
<td>87</td>
<td>42</td>
</tr>
<tr>
<td>TEAEs with ≥1 event, n (%)</td>
<td>59 (27.3)</td>
<td>22 (20.6)</td>
</tr>
<tr>
<td>Serious TEAEs</td>
<td>12 (5.6)</td>
<td>9 (4.4)</td>
</tr>
<tr>
<td>Discontinued from study due to adverse events</td>
<td>3 (1.4)</td>
<td>0</td>
</tr>
</tbody>
</table>


Conclusion: Incidences of TEAEs were similar and there was no discern-
able pattern across the most common TEAEs between groups. These interim analysis results from the PERSIST study conducted in a real-

world setting are consistent with the known safety profile of infliximab and do not demonstrate new safety information to change the bene-

fit-risk profile of CT-P13.


**Background:** Several biologic disease modifying anti-rheumatic drugs (bDMARDs) are currently available, but comparisons among these different drugs in clinical trials are rare and follow-up duration in trials is often limited. A comparison of these bDMARDs in daily practice can provide clinically relevant knowledge on treatment survival of all currently available bDMARDs.

**Objectives:** To assess the survival of each and every one of the biological therapies available in patients with rheumatoid arthritis (RA).

**Methods:** The METEOR registry is a multinational project that includes data on 40,000 patients with RA from its diagnosis and prospectively, with proven reliability, in clinical practice. Inclusion criteria: patients >18 years in biological treatment (bDMARD); Variables under study: disease onset date, bDMARD initiation and discontinuation date, bDMARD type (infliximab, certolizumab, adalimumab, golimumab, etanercept, rituximab, tocilizumab and abatacept), concomitant treatment, line of treatment. Clinical variables: TJC, SJC, ESR, CRP, BMI, patient onset date, bDMARD initiation and discontinuation date, bDMARD type.

**Results:** From the 47,263 patients registered in the total METEOR data-base, 11,132 were eligible for inclusion of the current study. Of these, 9,516 had sufficient data available and were included in the analyses. Included patients (n=9,516) less often smoked than non-included patients (n=1,616), but other baseline characteristics were very similar between groups (data not shown).

Baseline features of all patients were similar. Median time on bDMARD as 1st line treatment for each drug is shown in Table 1, infliximab showed the longest median time on treatment. Using infliximab as ‘reference’ treatment, Table 2 shows abatacept, certolizumab, rituximab and tocilizumab showed higher hazard risk to finish DMARD treatment. Median time after study entry (Q1-Q3) was 69 (37-96) months as by December 2018. Overall number of patients in drug-free remission was 34/141 (24.1%), 10/38 (26%) in the control group, 6/50 (12%) in the taper group and 18/53 (34%) in the taper/taper group. After adjustment for baseline risk factors in the likelihood to reach persistent drug-free remission between the groups (OR:0.76, 95%CI: 0.29-1.99) was highly uncertain. Positive ACNA (OR: 3.38, 1.01 – 11.31) and erosive-state (3.05, 1.32 – 7.06) at baseline were associated with a lower likelihood to reach persistent drug-free remission.

**Conclusion:** These data show that persistent drug-free remission can be reached in a subset of RA patients following a structured DMARD tapering approach after being in stable long-term DMARD control.

**REFERENCES:**

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**Disclosure of Interests:** None declared.

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**FR0123**

**BIological TherAPIEs SURVIVAL in RheumaToID Arthritis Patients: Clinical practice - results from the METEOR registry**

Viceger Terra Torre-Segara 1, Thomas Huizinga 2, Karen Solomon-Escoto 3, José Antonio P. da Silva 4, Douglas Veale 5, Samar Al Emadi 5, Tyaske Anne Bengtgra 5

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**Background:** Persistent drug-free remission of RA is a condition that is close to ‘cure’ of the disease. However, long-term drug-free remission is considered to be rare and very challenging to reach. Also, little data are available that report how often persistent drug-free remission can be achieved and what kind of clinical characteristics are associated with such state.
obtained. Furthermore, by using individual patient data (IPD), outcome definitions and methods can be harmonized for a valid combined analysis.

**Objectives:** To determine the effectiveness of treatment with TCZ on radiographic progression compared to MTX in RA patients over two years.

**Methods:** Randomized controlled trials in RA patients using TCZ as one of the treatment arms with radiographic damage assessed on radiographs at baseline and after two years were identified and IPD obtained.

The primary endpoint was defined as any radiographic progression over two years. Secondary endpoint was the amount of joint damage progression (points per time unit, expressed as incidence rate). Analyses were performed on total scores and for erosions and joint space narrowing (JSN) separately. TCZ strategies were compared with the control group.

**Results:** Five trials were identified, one trial using a fixed-treatment-tolarge approach, and the four other RCTs allowed the control group to start TCZ after 6 months or 1 year when the treatment target was not reached. Two trials were performed in early RA1–2. The dose of TCZ was tapered in two studies, IPD of 4 trials could be obtained and were included (n=2439 randomized to TCZ arm and n=791 to control arm, MTX in all cases)3–5. The radiographs, performed at baseline and after two years, were all assessed with the SdVdH method. Due to missing radiographic data, 1766 patients were evaluated in the TCZ arms and 543 patients in MTX arms. Patient characteristics are shown in Table 1. The occurrence of any radiographic progression was significantly less in the TCZ arms compared to MTX arms (pooled OR 0.76 [95%CI 0.67 to 0.86]). The effect for erosions (OR 0.77 [95%CI 0.67 to 0.88]) was stronger than for JSN (OR 0.88 [95%CI 0.78 to 0.98]) with both being in favour of TCZ.

**Conclusion:** Based on this individual patient data meta-analysis, radiotherapy for the amount of radiographic progression.


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**doi:** 10.1136/annrheumdis-2019-eular.3315

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**Table 1. Characteristics and IRRs in the patients with different diseases.**

<table>
<thead>
<tr>
<th>Patients features</th>
<th>RA (n=68)</th>
<th>SLE (n=137)</th>
<th>SJ (n=98)</th>
<th>PDM (n=23)</th>
<th>SSc (n=19)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex,%</td>
<td>77.9</td>
<td>93.4</td>
<td>92.1</td>
<td>69.6</td>
<td>73.7</td>
</tr>
<tr>
<td>Age, median (quartile), years</td>
<td>60.4</td>
<td>39.6</td>
<td>52.7</td>
<td>50.6</td>
<td>49.9</td>
</tr>
<tr>
<td>Disease duration, median (9.2-63.6)</td>
<td>50.7</td>
<td>(32.7-49.2)</td>
<td>(40.3-62.7)</td>
<td>(40-60)</td>
<td>61.4</td>
</tr>
<tr>
<td>Serum IgG level, median (1052.5-3051)</td>
<td>65.6</td>
<td>61.5</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Disease duration, median (7.5)</td>
<td>33.3</td>
<td>28.3</td>
<td>7.5</td>
<td></td>
<td>0.4</td>
</tr>
<tr>
<td>Serum IgG level, median (11052.5-110517.5)</td>
<td>5050</td>
<td>1420</td>
<td></td>
<td>1370</td>
<td>1620</td>
</tr>
<tr>
<td>Serum IgG level, median (11157.5-11167.5)</td>
<td>1905</td>
<td>1602.5</td>
<td></td>
<td>1647.5</td>
<td>1800</td>
</tr>
<tr>
<td>IRR per patient</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any IRR</td>
<td>11.68</td>
<td>19.137</td>
<td>23.89</td>
<td>2.3</td>
<td>3.19</td>
</tr>
<tr>
<td>&amp; (16.2%)</td>
<td>(13.5%)</td>
<td>(25.8%)</td>
<td>(8.7%)</td>
<td>(15.8%)</td>
<td>(15.8%)</td>
</tr>
<tr>
<td>Recurrent IRR</td>
<td>5.68</td>
<td>6/137</td>
<td>8.89</td>
<td>1.29</td>
<td>3.19</td>
</tr>
<tr>
<td>&amp; (7.4%)</td>
<td>(4.4%)</td>
<td>(9%)</td>
<td>(4.3%)</td>
<td>(15.8%)</td>
<td>(15.8%)</td>
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<tr>
<td>IRR &gt;Grade 2</td>
<td>2.68</td>
<td>5/137</td>
<td>12/89</td>
<td>0.23</td>
<td>0.19</td>
</tr>
<tr>
<td>&amp; (2.9%)</td>
<td>(3.6%)</td>
<td>(13.5%)</td>
<td>(0%)</td>
<td>(0%)</td>
<td>(0%)</td>
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<tr>
<td>Any IRR per infusion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First infusion</td>
<td>7.68</td>
<td>9/137</td>
<td>17/89</td>
<td>1.23</td>
<td>3.19</td>
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<td>&amp; (10.29%)</td>
<td>(6.5%)</td>
<td>(19.1%)</td>
<td>(4.35%)</td>
<td>(15.79%)</td>
<td>(15.79%)</td>
</tr>
<tr>
<td>Any infusion</td>
<td>17/461</td>
<td>27/222</td>
<td>46/443</td>
<td>51/134</td>
<td>153/312</td>
</tr>
<tr>
<td>&amp; (3.7%)</td>
<td>(3.7%)</td>
<td>(10.4%)</td>
<td>(3.7%)</td>
<td>(3.7%)</td>
<td>(3.7%)</td>
</tr>
<tr>
<td>IRR &gt;Grade 2 per infusion</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First infusion</td>
<td>1/68</td>
<td>2/137</td>
<td>7/89</td>
<td>0.23</td>
<td>0.19</td>
</tr>
<tr>
<td>&amp; (1.47%)</td>
<td>(1.46%)</td>
<td>(7.6%)</td>
<td>(0%)</td>
<td>(0%)</td>
<td>(0%)</td>
</tr>
<tr>
<td>Any infusion</td>
<td>3/261</td>
<td>7/222</td>
<td>25/443</td>
<td>1/134</td>
<td>1/132</td>
</tr>
<tr>
<td>&amp; (0.7%)</td>
<td>(1%)</td>
<td>(5.6%)</td>
<td>(0%)</td>
<td>(0%)</td>
<td>(0%)</td>
</tr>
</tbody>
</table>

**Results:** Totally, 336 patients were included as shown in table 1. There were 100 IRRs out of 1893 infusions, among which 37 were at the first time of RTX infusion. Patients with SJ had showed higher rate of IRR in the first infusion compared with other disease (19.1% vs 8.1%, p=0.008). Considering grade 2 or more severe IRRs, patients with SJ still has higher IRR (p=0.004). SJ was an independent risk for
developing IRR (OR 2.5, 95% CI 1.3-4.7, p=0.006). Seventy (78.7%) of the patients with SjS had positive anti-SSA antibody, but the presence of anti-SSA antibody was not a significant risk for IRR after controlling for the diagnosis of SjS. The IRR per infusion did not relate to the RTX dose. The IRR in an infusion did not lead to stopping of the therapy, although infusion rate and premedication can be adjusted in the following therapies. Only 39.6% of the patients with an IRR had suffered from more IRR in the following infusions. Besides, male gender and the increasing cycles were associated with less IRR (p=0.029 and 0.007, respectively). In the 100 patients received more than 4 cycles, the rate of IRR decreased along with the cycles. No life-threatening IRR happened in the 1893 infusions.

Conclusion: Our study had found that patients with SjS had higher IRR compared to other diseases. Female had more frequent IRR might due to the sexual distribution of these diseases.

Disclosure of Interests: None declared


**IMPACT OF JANUS KINASE INHIBITORS ON RISK OF CARDIOVASCULAR EVENTS IN PATIENTS WITH RHEUMATOID ARTHRITIS: SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS**

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Background: Janus kinase inhibitors (JAKis) are emerging as novel therapies for patients with rheumatoid arthritis (RA). Two JAK inhibitors have been approved and more pipeline products are ongoing to be launched, but their safety profiles of cardiovascular events (CVEs) have not been fully-established yet.

Objectives: To identify the association between CVEs and JAKis therapies in adult patients with RA via a meta-analysis of randomized controlled trials (RCTs).

Methods: RCTs reporting safety issues in RA patients treated with JAKis were reviewed in PubMed, Embase, and Cochrane Library (from inception to October 2018). CINAHL and the major relevant congress (2016-2018) were searched for additional reports. Mantel-Haenszel fixed-effects method with odds ratios (ORs) and 95% confidence intervals (CIs) were performed on extracted data.

Results: Out of 405 references screened, 26 RCTs involving 11 800 patients were included. No statistically significant difference was observed in risk of CVEs associated with the use of JAKis in general (OR 1.04, 95% CI 0.61-1.76, p=0.89), tofacitinib (OR 0.63, 95% CI 0.26-1.54, p=0.31), baricitinib (OR 1.21, 95% CI 0.51-2.83, p=0.66), upadacitinib (OR 3.29, 95% CI 0.59-18.44, p=0.18), peficitinib (OR 0.43, 95% CI 0.07-2.54, p=0.35), decernotinib (OR 1.12, 95% CI 0.13-10.11, p=0.92) (Figure 1). Regarding frequently-used dosage, dose-ranging impact of JAKis on the risk of CVEs was not observed in tofacitinib (5mg vs. 10mg, twice daily), upadacitinib (15mg vs. 30mg, once daily), while baricitinib at 2mg once daily was found to be safer than 4mg (OR 0.19, 95% CI 0.04-0.88, p=0.03) (Figure 2).

Conclusion: The existing evidence from RCTs indicated that JAKis-based therapies are not related to statistically significant risk of CVEs in RA patients during the limited randomized controlled periods. However, a special focus on baricitinib 4mg once daily is needed concerning the cardiovascular safety in the future.

Disclosure of Interests: None declared

A NOVEL FORMULATION OF CT-P13 (INFliximab Biosimilar) for Subcutaneous Administration: 1-YEAR RESULTS FROM A PART 1 OF PHASE III RANDOMIZED CONTROLLED TRIAL IN PATIENTS with ACTIVE RHEUMATOID ARTHRITIS

Daehyung You1, Janusz Jaworski2, Ewa Matyksa-Piekarska3, Svitlana Smjyan4, Delina Ivanova5, Agnieszka Zielinska6, Eve-Kai Raussi7, Anastas Batalov7, Sangjoon Lee8, Jeehye Sul8, Noori Han8, Rene Westhovens9.

Background: Efficacy and safety of a new subcutaneous (SC) formulation (CT-P13 SC) up to Week 30 were comparable with intravenous (IV) formulation (CT-P13 IV) in both patients with rheumatoid arthritis (RA) [1] and Crohn's disease [2].

Objectives: This report is to further investigate pharmacokinetics, efficacy and overall safety of CT-P13 SC in patients with RA throughout the 1-year treatment period.

Methods: Patients with active RA (presence of 6 or more swollen and tender joints [of 28 assessed], and serum C-reactive protein [CRP] concentration >0.6 mg/dL) were treated with CT-P13 IV at Weeks 0 and 2, and then received CT-P13 SC 90 mg, 120 mg or 180 mg SC dose and were sufficiently higher than the target therapeutic concentration. These results show that the novel SC formulation of CT-P13 may enhance treatment options for use of infliximab biosimilar by providing high consistency in drug exposure.

Results: A total of 50 patients were enrolled, of whom 48 patients were randomly assigned at Week 6 into 4 cohorts (1:1:1:1 ratio). The mean C trough (pre-dose serum concentration of CT-P13 before next dose injection) of SC cohorts throughout the study visits were higher than those of IV cohort after randomization at Week 6. C trough levels increased with SC dose and were sufficiently higher than the target therapeutic concentration (1 μg/mL) throughout the study period (Figure 1). Overall, the efficacy results of CT-P13 SC up to Week 54 were comparable to those of CT-P13 IV.

Conclusion: The results from 1-year treatment suggest similar efficacy and safety of CT-P13 SC to CT-P13 IV in RA. The mean serum concentration in all SC cohorts consistently exceeded the threshold of target therapeutic concentration. These results show that the novel SC formulation of CT-P13 may enhance treatment options for use of infliximab biosimilar by providing high consistency in drug exposure.

REFERENCE:
3. Yoo et al., Arthritis Research 18:82.

Disclosure of Interests: Daehyung Yoo Grant/research support from: Celltrion, Inc, Consultant for: Celltrion, Inc, Janusz Jaworski Grant/research support from: Celltrion, Inc., Ewa Matyksa-Piekarska Grant/research support from: Celltrion, Inc., Svitlana Smjyan Grant/research support from: Celltrion, Inc., Delina Ivanova Grant/research support from: Celltrion, Inc., PPD, Quintiles, Egs Pharmaceuticals, and Pfizer., Agnieszka Zielinska Grant/research support from: Celltrion, Inc., Eve-Kai Raussi Grant/research support from: Celltrion, Inc., Rene Westhovens Grant/research support from: Bristol-Myers Squibb, Consultant for: Celltrion, Galapagos-Gilead


Rheumatoid arthritis – non biologic treatment

Alyssa Morimoto1, Julie Rae1, Leslie Chin2, Nandini Ramamoothi2, Olivia Hwang1, Alexandra Ward1, D. James Hadden1, Caroline Looney1, Rupal Desai5, Balazs Toth6, Michael J. Townsend3. 1Genentech/ Roche, OMNI Biomarker Development, South San Francisco, United States of America; 2Genentech/Roche, Clinical Pharmacology, South San Francisco, United States of America; 3Yoo et al., Arthritis Research 18:82. 4ailed studies included RA patients (pts) on background methotrexate (MTX) with inadequate response to prior MTX (n=480, Cohort 1, MTX-IR) or anti-TNFs (n=98, Cohort 2, TNF-IR). Cohort 1 pts were randomized to receive PBO, adalimumab (ADA) 40 mg Q2W, or FEN 50 mg QD, 150 mg QD or 200 mg BID. Cohort 2 pts were randomized to receive PBO or FEN 200 mg BID. Clinical efficacy was assessed based on the proportion of pts achieving ACR50 at week 12. Pts for whom samples were available were assessed for levels of rheumatoid factor (RF), total IgM and IgG, CCL4, CXCL13, CRP and IL6.

Results: Primary study results are reported separately. Overall, treatment with FEN increased CRP (at week 12) and total IgM and IgG (at weeks 4-12) relative to PBO (Table 1). Early and sustained reductions of RF, total IgM and IgG, CCL4, CXCL13, CRP and IL6 were observed with FEN or ADA relative to PBO by week 1. CRP levels were significantly reduced with 200 mg BID FEN by week 8, and with ADA by week 2 relative to PBO. By week 12, there was a trend toward lower IL6 levels with FEN treatment relative to PBO, whereas ADA significantly reduced IL6 levels by week 1 relative to PBO in MTX-IR pts. In TNF-IR patients, IL6 was significantly reduced by FEN treatment by week 12 relative to PBO. PK-PD relationships were observed for multiple B and myeloid cell biomarkers. No single biomarker at baseline was associated with clinical response (at 12 weeks) in MTX-IR and TNF-IR pts. However, greater baseline RF titers were associated with increased FEN clinical response in TNF-IR pts.

References:

Table 1. Causal mean differences in standardized disease activity at 6 months and 1- and 2-years follow-up comparing those with depression to those without at baseline.

<table>
<thead>
<tr>
<th>Measure</th>
<th>6 Months</th>
<th>1 Year</th>
<th>2 Years</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAS-28</td>
<td>0.36 (0.03, 0.69)</td>
<td>0.11 (0.29, 0.51)</td>
<td>-0.20 (0.75, 0.35)</td>
</tr>
<tr>
<td>SAC</td>
<td>0.24 (0.11, 0.50)</td>
<td>0.03 (0.28, 0.34)</td>
<td>0.03 (0.49, 0.54)</td>
</tr>
<tr>
<td>TJC</td>
<td>0.29 (0.02, 0.61)</td>
<td>0.12 (0.42, 0.47)</td>
<td>-0.16 (0.73, 0.43)</td>
</tr>
<tr>
<td>PTGA</td>
<td>0.30 (-0.06, 0.66)</td>
<td>0.27 (0.08, 0.61)</td>
<td>0.00 (0.65, 0.65)</td>
</tr>
<tr>
<td>ESR</td>
<td>0.17 (-0.23, 0.57)</td>
<td>0.07 (0.47, 0.33)</td>
<td>-0.15 (0.72, 0.41)</td>
</tr>
<tr>
<td>PRGA</td>
<td>0.14 (-0.16, 0.43)</td>
<td>0.15 (0.20, 0.50)</td>
<td>-0.33 (1.00, 0.34)</td>
</tr>
<tr>
<td>Pain</td>
<td>0.47 (0.11, 0.82)</td>
<td>0.42 (0.03, 0.82)</td>
<td>0.20 (0.35, 0.75)</td>
</tr>
<tr>
<td>MDHAQ</td>
<td>0.18 (-0.15, 0.51)</td>
<td>0.11 (0.27, 0.48)</td>
<td>0.06 (0.46, 0.58)</td>
</tr>
</tbody>
</table>

Conclusion: Findings demonstrate that depression is associated with less robust short-term response to MTX, and despite clinical RA treatment, more persistent and severe pain. Depression in RA patients may be a risk factor for primary non-responder to MTX treatment, and interventions targeted at treating depression could result in better initial RA disease control and DMARD persistence.

Acknowledgement: This material is based upon work supported (or supported in part) by the Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, VA Maryland Health Care System, and Baltimore VA Medical Center.

Disclosure of Interests: Alan Rathbun: None declared, Bryant England: None declared, Ted Mikuls: None declared, Alice Ryan: None declared, Jennifer Barton: None declared, Michelle Sharedel: None declared, Joseph Galle: None declared, Elizabeth Stuart: None declared, Marc Hochberg: None declared, Joseph Gallo: None declared, Elizabeth Stuart: None declared, Marc Hochberg: None declared.

Background: Depression is common in rheumatoid arthritis (RA) patients and exacerbates disease activity and may reduce response to first-line disease-modifying antirheumatic drugs.

Objectives: To determine whether depression affects disease activity in patients with early RA treated with methotrexate (MTX).

Methods: Patients in the Veterans Affairs Rheumatoid Arthritis registry with early RA (onset <2 years) receiving MTX were selected (n=268). Disease activity was measured using the 28 joint count disease activity score (DAS-28), tender and swollen joint counts (TJC and SJC), patient and provider global assessment (PTGA and PRGA), and erythrocyte sedimentation rate (ESR). Baseline confounders included sociodemographics, anthropometrics, concomitant treatments, and other clinical characteristics. Propensity score weights were used to equate the depressed and non-depressed participants on baseline confounders. Generalized linear survey models were used to compare disease activity trajectories between depressed (n=48) and non-depressed (n=220) patients over two years. Standardized causal mean outcome differences were estimated at 6 months and 1- and 2-years follow-up.

Results: Depression was associated with significantly greater DAS-28 at 6 months (β=0.36; 95% CI: 0.03, 0.69) but not at 1- or 2-years follow-up (Table 1). Associations for DAS-28 component measures were smaller in magnitude, decreased over time, and not statistically significant. Depression was also associated with significantly greater pain at both 6 months (β=0.47; 95% CI: 0.11, 0.82) and 1-year (β=0.42; 95% CI: 0.03, 0.82) follow-up but not the PRGA or MDHAQ at any assessed time interval.

Disclosure of Interests: Kara Queeney: None declared, William Housley: None declared, Jeremy Sokolov: Andrew Long: None declared, Karla Queeney1, William Housley1, Jeremy Sokolov2, Andrew Long3, 1AbbVie, Pharmacology, Worcester, United States of America; 2AbbVie, Clinical Development, Redwood City, United States of America

Background: JAK inhibitors, including Upadacitinib (UPA), have been associated with increased serum levels of creatine phosphokinase (CPK) in patients with inflammatory disorders, but not in patients with myopathi- lative disease or in healthy subjects treated for a limited duration (1). While CPK increases can be indicative of muscle damage, there are no other indicators of muscle pathology observed with JAK inhibitors, suggesting that there may be another mechanism behind the increased CPK levels. Inflammatory diseases including rheumatoid arthritis are often asso- ciated with reduced muscle mass (sarcopenia), a process reversed with disease control (2).

Objectives: We hypothesized that one or more cytokines present in the inflammatory milieu may block differentiation of myoblasts into mature myocytes and that JAK inhibition restores differentiation and associated CPK expression. We focused on the gp130-mediated cytokines IL6, Oncostatin M (OSM), CNTF, and LIF as these have been shown to be involved in myoblast differentiation.

Methods: Human skeletal muscle myoblast (HSMM) cells were cultured in 10% fetal bovine serum, or were starved for 2% (horse serum) to induce differentiation into myocytes, with and without stimulation with OSM (1–100 ng/ml) and/or UPA (0.0007–1 μM) for up to 5 days. RNA was purified and expression of CPK (M-type) was determined by QPCR using GAPDH as a reference. CPK expression was also measured following stimulation of HSMM cells with other JAK inhibitors (Baricitinib and Tofacitinib).
Results: We have demonstrated that the gp130-mediated cytokine oncostatin M blocks myoblast differentiation into myotubes resulting in a decrease in CPK expression. Jak inhibition restores muscle differentiation and increased CPK expression (Figure 1A). Oncostatin M is highly expressed in RA synovium and other inflammatory milieu and may be one mechanism driving sarcopenia in RA. In addition to Upadacitinib, both Baricitinib and Tolactacinib restore myoblast differentiation suggesting that this is a class effect for Jak inhibitors (Figure 1B).

Conclusion: Our data studies suggest that the increase in serum CPK upon treatment with Jak inhibitors may represent recovery of muscle development via reversal of inflammation-associated inhibition of myoblast differentiation.

REFERENCES:

Disclosure of Interests: Gerd Rüdiger Burmester1, Filip van den Bosch2, Louis Bessette3, Alan Kivitz4, Li Yiyan5, Alan Friedman5, Alonee Pangab6, Heidi Camp7, Joel Kremmer1, 1Charité – Univ, Berlin, Germany; 2Ghent Univ Hospital, Ghent, Belgium; 3Laval University, Quebec, Canada; 4Alisma Center for Clinical Research, Duncansville, PA, United States of America; 5AbbVie, Inc, Chicago, IL, United States of America; 6Albany Medical College, Albany, NY, United States of America

Background: Upadacitinib (UPA), an oral, Jak1-selective inhibitor showed efficacy over 12 weeks (wks) in patients (pts) with moderately to severely active rheumatoid arthritis (RA) and inadequate response to csDMARDs (SELECT-NEXT).

Objectives: We assessed safety and efficacy of UPA through Wk60 in an ongoing extension of the phase 3 SELECT-NEXT study.

Methods: Pts received once-daily (QD) UPA at 15 mg (UPA15), 30 mg (UPA30) or placebo (PBO) for 12 wks on stable background CSMARDs. From Wk12, the start of a long-term blinded extension, pts initially randomized to PBO at BL were switched to UPA15mg or 30mg per prespecified assignment at BL. Pts randomized to UPA continued their assigned dose. No dose adjustments of UPA were allowed; however, starting at Wk24, adjustments to background RA medications were permitted. Sites/subjects remain blinded to UPA dose throughout the extension period. Efficacy data up to Wk60 are reported “As Observed”. Adverse events (AE) per 100 pt yrs (PY) are summarized based on a cut-off date of Mar 22 2018.

Results: 611/61 (92%) pts completed Wk12 and continued on the extension. By the safety data cut-off date, 125/611 (20%) had discontinued study drug, 50 (8.2%) discontinued due to an AE, and 10 (1.6%) due to lack of efficacy. Cumulative exposure was 393.3 PYs and 372.4 PYs for UPA15 and UPA30 respectively. Based on AE Observed analysis, for pts who continued on UPA15 (262/310 [85%]) and UPA30 (243/301 [81%]), clinical and functional outcomes continued to improve or were maintained through Wk60, with 59% and 56% of pts achieving DAS28-CRP <2.6 and 35% and 32% achieving CDAI remission (≤2.8) with UPA 15 and 30 mg, respectively. Pts who switched from PBO to UPA15 or UPA30 showed comparable efficacy to those initially randomized to UPA (Table 1). The most frequently reported AE s were nasopharyngitis, urinary tract infection, upper respiratory tract infection, bronchitis, blood creatine phosphokinase increased, alanine aminotransferase increased, herpes zoster (HZ) and nausea. Most frequent AEs (≥8/100PYs) leading to premature study discontinuation were pneumonia, transaminase elevations, HZ and pyrexia. Event rates (E/100PYs) were numerically higher in UPA30 vs UPA15 for serious AE, AE leading to discontinuation, serious infections, HZ and malignancies, and were similar in UPA15 and UPA30 for adjudicated major adverse cardiovascular events and venous thromboembolic events (Table 2).

Conclusion: UPA15mg and 30mg on background csDMARD therapy demonstrated consistent efficacy and safety over 60 weeks in RA patients with inadequate response to csDMARDs. Both doses of UPA showed a similar efficacy profile at Wk 60, with numerically higher rates for certain safety events noted in the UPA30 group. An integrated safety analysis of upadacitinib across the phase 3 program is required to fully characterize the benefit:risk of UPA in RA.

Disclosure of Interests: Gerd Rüdiger Burmester Consultant for: Roche, Sanof Genzyme, Speakers bureau: Roche, Sanof Genzyme, Filip van den Bosch Consultant for: AbbVie, BMS, Galapagos, Janssen, Lilly, Merck, Novartis, Pfizer and UCB, Speakers bureau: AbbVie, BMS, Janssen, Lilly, Merck, Novartis, Pfizer and UCB, Louis Bessette Grant/research support from: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Genzyme, Sanofi, Regeneron, Boehringer Ingelheim, Sun Pharma Advanced Research, Flexion, Paid instructor for: Celgene, Horizon, Merck, Novartis, Pfizer, Genzyme, Sanofi, Regeneron, Speakers bureau: Celgene, Horizon, Merck and GeneTech, Flexion, Li Yan Li Shareholder of: AbbVie, Employee of: AbbVie, Alan Friedman Shareholder of: AbbVie, Employee of: AbbVie, Alonee Pangab Shareholder of: AbbVie, Employee of: AbbVie, Heidi Camp Shareholder of: AbbVie, Employee of: AbbVie, Joel Kremmer Grant/research support from: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Genzyme, Sanofi, Regeneron, Speakers bureau: Celgene, Horizon, Merck and GeneTech, Flexion, Yihan Li Shareholder of: AbbVie, Employee of: AbbVie, Alan Friedman Shareholder of: AbbVie, Employee of: AbbVie, Alonee Pangab Shareholder of: AbbVie, Employee of: AbbVie, Heidi Camp Shareholder of: AbbVie, Employee of: AbbVie, Joel Kremmer Grant/research support from: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Genzyme, Sanofi, Regeneron, Boehringer Ingelheim, Sun Pharma Advanced Research, Flexion, Paid instructor for: Celgene, Horizon, Merck, Novartis, Pfizer, Genzyme, Sanofi, Regeneron, Speakers bureau: Celgene, Horizon, Merck and GeneTech, Flexion, Yihan Li Shareholder of: AbbVie, Employee of: AbbVie, Alan Friedman Shareholder of: AbbVie, Employee of: AbbVie, Alonee Pangab Shareholder of: AbbVie, Employee of: AbbVie, Heidi Camp Shareholder of: AbbVie, Employee of: AbbVie, Joel Kremmer Grant/research
Filgotinib (FIL), an oral selective JAK1 inhibitor, was safe and effective in FINCH2, a randomized, double-blind, placebo-controlled, phase 3 study in patients with active rheumatoid arthritis (RA) who had an inadequate response to biologic disease-modifying anti-rheumatic drugs (bDMARDs).

Objectives: A longitudinal study of cytokines from patients in FINCH2 was conducted to identify RA-associated biomarkers related to bone biology, immune cell migration, and inflammation that are altered by FIL therapy; and FIL-associated biomarkers that correlated with clinical response (DAS28 [CRP], swollen and tender joint counts, pain, and fatigue).

Methods: Plasma, serum, and urine samples from RA patients (n=449) who received FIL (100 mg, 200 mg) or placebo (PBO) once daily plus methotrexate were analyzed at baseline (BL) and week 12 for 42 disease-relevant cytokines using validated, commercially available single or multiplex assays. PBO-corrected on-treatment changes in cytokine levels from BL to week 12 were compared between treatment arms (Wilcoxon rank sum test). Spearman rank correlation was used to compare changes in cytokine level from BL to week 12 and clinical response. P-values <0.05 were considered significant.

Results: At week 12, 18 of 42 cytokines significantly decreased with FIL 100 mg treatment relative to PBO; FIL 200 mg decreased these cytokines to a similar or greater degree. An additional 6 cytokines were significantly decreased by FIL 200 mg. Conversely, 2 cytokines increased with FIL 200 mg (sIL-6R, IL-10, IL-2, leptin, and IL-17A). Biomarkers most significantly modulated by FIL 200 mg (p<0.0001) included markers related to immune cell migration, and inflammation that are altered by FIL therapy; and FIL impacts RA disease activity at a molecular level.

Conclusion: Twelve weeks of FIL treatment significantly reduced 24 disease-relevant cytokines associated with bone biology, immune cell migration, and inflammation in patients with active RA. These effects were dose-dependent and suggest a shift toward a restored immune homeostasis. These findings are consistent with the clinical efficacy of FIL in FINCH2.

REFERENCES:

Methods: This multicentre, randomised, double-blind, parallel-group, placebo (PBO)-controlled phase 3 study (NCT02308163) was conducted in Japan, Korea and Taiwan. All patients had RA diagnosed according to 1987 ACR or 2010 ACR/EULAR criteria. Patients with active RA (defined as ≥ 6 tender and ≥ 6 swollen joints and ≥ 6 swollen joints and ≥ 3 tender joints, respectively, and CRP > 0.50 mg/dL) and inadequate response to DMARDs (administered for ≥ 90 days) were randomised in a 1:1:1 ratio to 52 weeks' treatment with PBO, peficitinib 100 mg/day, or etanercept 50 mg/week (open-label reference arm). At week 12, patients initially assigned to PBO were switched (under blinded conditions) to either peficitinib 100 mg/day or peficitinib 150 mg/day until end of treatment. Concomitant stable dose of DMARDs was permitted. The primary efficacy variable was ACR20 response rate at week 12/early termination (ET). Results: In total, 507 patients were treated in the three arms and treated: PBO (n=101), peficitinib 100 mg/day (n=104), peficitinib 150 mg/day (n=102) and etanercept (n=200). Regarding efficacy at week 12/ET, significant differences were observed with peficitinib 100 mg/150 mg vs PBO (p<0.001) in the proportion of patients achieving ACR20, ACR50, ACR70 and DAS28-ESR ≤ 3.2). Patients were randomized 1:1:1 into liposomal peficitinib 75 mg vs. liposomal peficitinib 150 mg vs. methylprednisolone 120 mg. Two comparisons: 1) liposomal peficitinib 150 mg vs. methylprednisolone 120 mg; 2) liposomal peficitinib 75 mg vs. methylprednisolone 120 mg. The primary analysis involved 28 Joints (DAS28 3.2). Patients were randomized 1:1:1 into liposomal prednisolone 75 mg, liposomal prednisolone 150 mg and methylprednisolone 120 mg. Treatment was administered on Day 1 and Day 15. Patients treated with liposomal prednisolone IV received IM placebo injections; patients treated with methyl/prednisolone IM received IV placebo infusions. Evaluations were performed weekly for the first 4 weeks, and every second week thereafter. The primary endpoint was EULAR response rate (good and moderate combined) at Day 8. The primary analysis involved two comparisons: 1) liposomal prednisolone 150 mg vs. methylprednisolone 120 mg, 2) liposomal prednisolone 75 mg vs. methylprednisolone 120 mg. Safety results (AEs, vital signs, physical examinations, laboratory, ECG) were also evaluated. A total of 172 patients were screened and 150 were randomized to liposomal prednisolone 75 mg (N=49), liposomal prednisolone 150 mg (N=52) and methylprednisolone 120 mg (N=59). 144 (96%) patients completed the study; mean study duration was 82.9 days; adverse events or intercurrent illness was the primary reason for discontinuation. Results: EULAR response rate at Week 1 (Day 8) was 90.0% for liposomal prednisolone 150 mg and 85.7% for liposomal prednisolone 75 mg vs. methylprednisolone 120 mg treated patients (p-values of 0.007 and 0.018, respectively). Other secondary endpoints supported the primary endpoint results showing significant or clinically meaningful improvements in other EULAR response evaluations, as well as DAS28, VAS, ACR20/50/70, SF-36, HAQ and FACIT-F assessments. Similar numbers of patients reported at least one adverse event (AE) in each treatment group, 42 (86%), 46 (89%) and 39 (80%), respectively, for the liposomal prednisolone 75 mg, liposomal prednisolone 150 mg and methylprednisolone 120 mg groups. Most commonly reported AEs were nausea in the liposomal prednisolone groups and headache in all 3 treatment arms. Approximately 8%
of patients in the liposomal prednisone groups reported AEs related to study drug administration, versus 6% in the methylprednisolone group. Serious adverse events (SAEs) were reported by 4 (8.2%), 1 (1.9%) and 2 patients (4.1%) resp for the liposomal prednisone 75 mg, liposomal prednisone 150 mg and methylprednisolone 120 mg groups. Five of the 7 SAEs were treatment related; these included 4 events of hypersensitivity in the liposomal prednisone arms and one event of viral upper respiratory tract infection in the methylprednisolone group.

Conclusion: In this phase III trial, liposomal prednisone 75 mg and 150 mg were significantly more effective than 120 mg methylprednisolone in treating patients with a flare of their RA. The overall incidence of AEs was similar across treatment groups, although hypersensitivity appeared to be more common with liposomal prednisone.

Disclosure of Interests: Johannes WJ Bijlsma Grant/research support from: The department of the author who included patients (JWJB) in the U-Act-Early trial received reimbursements from Roche Nederland BV. JWJB reported grants and fees from Roche, AbbVie, Bristol-Myers Squibb, Merck Sharp & Dohme, Pfizer, and UCB University Medical Center Utrecht, Utrecht University, Consultant for: SUN Pharma, Speakers bureau: Lily, Roche, Bart Metselaar Shareholder of: Enceladus, Grant/research support from: SUN Pharma, Leonie Middelink Grant/research support from: SUN Pharma, Cees Wortel Shareholder of: Enceladus, Accelvare, Grant/research support from: SUN Pharma, Consultant for: SUN Pharma, Reinhard Bos Grant/research support from: SUN Pharma, Jacob M. van Laar Grant/research support from: Genentech, Consultant for: F. Hoffmann-La Roche, Harald vonknerman: None declared, Rene Westhovens Grant/research support from: Bristol-Myers Squibb, Consultant for: Celltrion, Galapagos-Gilead, Siu Long Yao Shareholder of: SUN Pharma, Employee of: SUN Pharma, Mudgal Kothekar

REFERENCES:

Acknowledgement: No

Disclosure of Interests: None declared


**FR0136**
THE EFFICACY AND SAFETY OF SIROLIMUS IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS: A RANDOMIZED AND PARALLEL-CONTROLLED CLINICAL TRIAL

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Background: We have reported previously that the insufficient absolute number or functional defects of regulatory T cells (Tregs) in patients with rheumatoid arthritis (RA) can partly restore the reduced Tregs. Concomitantly, their usages of immunosuppressants to control disease activity without over-treatment and evaluable side effect. The further study is required using a large sample of RA patients treated with sirolimus for longer period.

Objectives: To investigate efficacy and safety of sirolimus combined with conventional immunosuppressants for RA treatment.

Methods: In this non-blinded and parallel-group trial, we randomly assigned 62 patients to receive conventional glucocorticoids and immunosuppressants with or without sirolimus at a dosage of 0.5 mg on alternate days for 24 weeks in a 2:1 ratio. The demographic features, clinical manifestations and laboratory indicators including peripheral blood lymphocyte subgroups and CD4+T subsets were compared before and after the treatment.

Results: Finally, 37 patients in sirolimus group and 18 in conventional treated group completed 6-month study. By 24 weeks, the patients with sirolimus experienced the significant reduction in disease activity indicators including DAS28, ESR, the number of tender joints and swollen joints (p<0.001). Notably, they had a higher level of Tregs as compared those

Conclusion: Low-dose sirolimus immunoregulatory therapy selectively up-regulated Tregs and partly replaced the usage of immunosuppressants to control disease activity without over-treatment and evaluable side effect. The further study is required using a large sample of RA patients treated with sirolimus for longer period.

Disclosures of Interests: None declared


**FR0137**
UPADACITINIB IMPROVES PATIENT-REPORTED OUTCOMES IN PATIENTS WITH RHEUMATOID ARTHRITIS AND INADEQUATE RESPONSE TO METHOTREXATE: RESULTS FROM SELECT-COMPARE

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Background: Upadacitinib (UPA), a selective JAK1 inhibitor, has demonstrated superior improvement in the clinical signs and symptoms of rheumatoid arthritis (RA) compared with placebo (PBO) and adalimumab (ADA). Objectives: To evaluate the effect of UPA vs PBO and vs ADA on patient-reported outcomes (PROs) at Week 12 in SELECT-COMPARE (NCT02629159), a randomised controlled trial (RCT) in an active RA population with inadequate responses to methotrexate (MTX).

Methods: Patients in SELECT-COMPARE, a phase 3 RCT, received UPA (15 mg once daily), PBO, or ADA (40 mg every other week) while on background MTX therapy. The following PROs were collected prospectively: Patient Global Assessment of Disease Activity (PGA) by visual analogue scale (VAS), pain by VAS, Health Assessment Questionnaire Disablity Index (HAQ-DI), duration and severity of morning (AM) stiffness, health-related quality of life by Short Form-36 (SF-36), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), and Work Instability Scale for RA (RA-WIS). Least squares mean (LSM) changes from baseline (BL) to Week 12 were based on mixed-effects repeated measures

**FR013**
models. The proportions of patients reporting improvements ≥ minimum clinically important differences (MCID) from BL to Week 12 or scores ≥ normative values were determined with UPA, PBO, and ADA treatment; comparisons used chi-square tests.

Results: Data from 1629 patients (UPA: 651; PBO: 651; ADA: 327) were analysed. Mean age was 54 years; 79% were female; 54% had RA for ≥ 5 years. Baseline mean PRO scores were similar across treatment groups. At Week 12, UPA treatment resulted in statistically significant LSM changes from BL vs PBO across all PROs and statistically significant LSM changes from BL vs ADA in PIGA, pain, HAQ-DI, AM stiffness severity, FACIT-F, and SF-36 physical component summary (PCS) and 6/8 domain scores (Table). ADA treatment resulted in statistically significant LSM changes from baseline vs PBO in PIGA, pain, HAQ-DI, AM stiffness severity and duration, FACIT-F, and SF-36 PCS and 5/8 domain scores. Compared with PBO at Week 12, significantly more UPA-treated patients reported improvements ≥ MCID and scores ≥ normative values across all PROs with numbers needed to treat (NNTs) < 10. The proportions of UPA-treated patients reporting improvements ≥ MCID were similar or numerically higher than ADA-treated patients. Importantly, the proportion of UPA vs ADA treated patients reporting improvements ≥ normative values were significantly greater (all p < 0.05) in PIGA (36% vs 26%), HAQ-DI (21% vs 14%), SF-36 PCS (16% vs 11%), and SF-36 bodily pain (29% vs 21%) and vitality (42% vs 35%) domains.

LMS Changes from Baseline and Percentage of Respondents at Week 12 After UPA Inception

<table>
<thead>
<tr>
<th>PRO</th>
<th>Baseline Mean (n=1629)</th>
<th>LMS Changes from Baseline</th>
<th>Patients reporting improvements ≥ MCID (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PBO</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UPA 15 mg</td>
<td>(n=645)</td>
<td>-28.1 ± 36.8</td>
<td>51.5 ± 32.3</td>
</tr>
<tr>
<td>UPA 30 mg</td>
<td>(n=651)</td>
<td>-30.3 ± 38.9</td>
<td>52.5 ± 33.5</td>
</tr>
<tr>
<td>PBO</td>
<td>(n=651)</td>
<td>-25.6 ± 35.7</td>
<td>49.4 ± 31.5</td>
</tr>
<tr>
<td>ADA</td>
<td>(n=327)</td>
<td>-23.8 ± 34.4</td>
<td>46.9 ± 30.4</td>
</tr>
<tr>
<td>Pain VAS</td>
<td></td>
<td>-19.5 ± 29.8</td>
<td>52.8 ± 32.9</td>
</tr>
<tr>
<td>HAQ-DI</td>
<td></td>
<td>-17.7 ± 28.2</td>
<td>53.6 ± 33.1</td>
</tr>
<tr>
<td>FACIT-F</td>
<td></td>
<td>-25.4 ± 36.8</td>
<td>52.3 ± 32.7</td>
</tr>
<tr>
<td>Duration AM Stiffness</td>
<td></td>
<td>-16.8 ± 28.4</td>
<td>53.5 ± 33.0</td>
</tr>
<tr>
<td>Morning AM Stiffness</td>
<td></td>
<td>-10.7 ± 23.8</td>
<td>55.1 ± 34.6</td>
</tr>
</tbody>
</table>

LSM changes from baseline vs ADA ≥ MCID were statistically significant (all p < 0.05).

Conclusions: An active RA, treatment with UPA 15 mg QD on background MTX therapy for 12 weeks resulted in statistically significant and clinically meaningful improvements in PROs compared with PBO. Overall, PRO improvements with UPA treatment met or were superior to those reported with ADA, especially in key domains of pain, function, and vitality.

References:

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Disclosure of Interests: Vibeke Strand Consultant for: AbbVie, Amgen, Bayer, BMS, Boehringer Ingelheim, Celgene, Celltrion, CORRONA, Cre- scendo, EMD Serono, Genentech/Roche, GSK, Horizon, Inmedix, Janssen, Kezar, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sandoz, Sanofi, Servier, UCB, Martin Bergman Shareholder of: Johnson and Johnson (parent company of Janssen), Consultant for: AbbVie, Amgen, BMS, Celgene, Genentech/Roche, Janssen, Merck, Novartis, Pfizer, and Sanofi/Regeneron, Speakers bureau: AbbVie, Amgen, BMS, Celgene, Genentech/Roche, Janssen, Merck, Novartis, Pfizer and Sanofi/Regeneron, Namita Tundia Shareholder of: AbbVie, Employee of: AbbVie, Andrew Oster Consultant for: AbbVie, BMS, Roche, Janssen, Lilly, Novartis, Pfizer, UCB, Gilead, Paradigm, Patrick Duret Speakers bureau: BMS, Lilly, Sanofi, and Celtrion, In-Ho Song Shareholder of: AbbVie Inc, Employee of: AbbVie Inc, Casey Schlacher Shareholder of: AbbVie, Employee of: AbbVie, Yan Song Yon Employee of: Analysis Group Inc., which received consulting fees from AbbVie for this study, Roy Fleischmann Grant/research support from: AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Celltrion, Genentech, GSK, Janssen, Lilly, Novartis, Pfizer Inc, Sanofi-Aventis, UCB, Consultant for: AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Celltrion, Genentech, GSK, Janssen, Lilly, Novartis, Pfizer Inc, Sanofi-Aventis, UCB DOi: 10.1136/annrheumdis-2019-eular.287

FR0138

EXPOSURE-RESPONSE ANALYSES OF UPADACITINIB EFFICACY AND SAFETY IN RHEUMATOID ARTHRITIS – ANALYSES OF PHASE 2 AND 3 STUDIES

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Background: Upadacitinib (UPA), an oral selective JAK1 inhibitor, demonstrated favorable efficacy and acceptable safety in two Phase 2 and five Phase 3 global studies in subjects with moderately to severely active rheumatoid arthritis (RA).

Objectives: To characterize relationships between UPA plasma exposures and different efficacy and safety endpoints using data from Phase 2 and Phase 3 RA studies.

Methods: Analyses were conducted using data from 3685 (for efficacy) and 4577 (for safety) subjects with RA enrolled in the Phase 2 and 3 studies. Relationships between UPA plasma concentrations and efficacy and selected clinically relevant safety endpoints were analyzed using Markov Chain models and logistic regression analyses, respectively.

Results: Percentage of subjects achieving ACR20, ACR50, ACR70, DAS28<3.2, and DAS28CRP < 3.2, and DAS28CRP < 2.6 increased with increasing UPA exposures, with maximum efficacy reached at exposures of 15 mg to 30 mg QD. Model-estimated efficacy responses are presented in Table 1. No relationships were observed between UPA exposure and pneumonia, herpes zoster infection, changes in platelet count (platelets > 600×10^9/L, platelets > 400×10^9/L), lymphopenia (Grade 4 or higher), and neutropenia (Grade 3 or higher) at Week 12/14 or Week 24/26. Shallow trends for exposure-response relationships were observed between UPA exposure and lymphopenia, grade 3 or higher at Week 12/14 or Week 24/26. No relationship with UPA exposure was observed for Grade 3 or higher lymphopenia at Week 24/26 (Figure 1).

Conclusion: Among patients with active RA, treatment with UPA 15 mg QD on background MTX therapy for 12 weeks resulted in statistically significant and clinically meaningful improvements in PROs compared with PBO. Overall, PRO improvements with UPA treatment met or were superior to those reported with ADA, especially in key domains of pain, function, and vitality.

References:
surfactant tween 80 (polysorbate 80) and the squacline as an exception, through film hydration method and their potential as a drug delivery system for NPX.

Methods: We prepared niosomal Naproxen from the biocompatible surfactant tween 80 (polysorbate 80) and the squacline as an exception, through thin-film hydration method and their potential as a drug delivery system for NPX. The prepared system was characterized by Fourier transform infrared spectroscopy (FT-IR), UV-visible, photoluminescence (PL), field emission scanning electron microscopy (FE-SEM), and transmission electron microscopy (TEM).

Results: By using this method, the percent drug loading that resulted by the encapsulation of niosomes was found to be 99.5 ± 0.2% for 5% of NPX weight in total ingredients weight of niosomal vesicles (w/w). It was also seen that a slower rate of release of the NPX from the drug encapsulated noisome over 7 days, suggesting stable complexation of NPX. Cell toxicity assay was carried out by A549 and HeLa cancer cell lines and showed the half maximal inhibitory concentration (IC50) of NPX increased about 8.25 fold for A549 (from 3300 µM to 400 µM) and it decreases about 5.5 folds for HeLa (from 1920 µM to 350 µM) by nanof ormation.

Conclusion: Niosomal formulation has been evaluated as a safe drug delivery system. In this study, we showed that niosomal naproxen has more stability and more efficiently affect the cells. It can be explained by increasing the bioavailability of naproxen by niosomal nanocarriers which probably is based on more water solubility and more efficient cell entrance of drug. It seems that niosomal naproxen is a great candidate for future in vitro and in vivo researches for evaluating potential clinical applications.

REFERENCES:

Disclosure of Interests: None declared
of patients receiving monotherapy or combination therapy at treatment initiation.

Results: 1950 patients were included in the matched population (1300 bDMARD initiators; 650 tofacitinib initiators). Patients were predominantly aged 55 to 74 years (57.8%), and female (81.2%). At baseline, median disease duration was 107 and 120 months, with 16.1% and 17.3% of patients in DAS28-ESR defined disease remission for the bDMARD and tofacitinib groups respectively. After three months of treatment, 49.1% and 49.7% had achieved DAS remission and after 18 months of treatment 52.4% and 57.8% of patients had achieved DAS remission in the bDMARD and tofacitinib groups respectively. At 18 months the percentage of patients achieving CDAI/SDAI remission was similar with 29.2%/29.0% bDMARD patients and 30.9%/30.5% tofacitinib patients reporting CDAI/SDAI remission respectively. The median persistence of treatment was similar for bDMARD and tofacitinib groups: 33.8 (95% CI 28.8 to 40.4) and 34.2 (95% CI 32.2 to not reached) months respectively. In the overall population, more patients were prescribed tofacitinib as monotherapy (43.4%) compared to bDMARD monotherapy (33.4%).

Conclusion: In this analysis of a large real world dataset, tofacitinib demonstrated treatment effectiveness and persistence that was similar to bDMARDs. Overall, there was a trend for more use of tofacitinib as monotherapy than bDMARDs.

Acknowledgement: We wish to acknowledge the Australian rheumatologists who contribute data to OPAL for research.

Disclosure of Interests: Paul Boudhabhay Consultant for: Advisory boards for Eli Lilly, Pfizer, Roche, AbbVie, Geoff Littlejohn Consultant for: Sat on Advisory Boards for AbbVie, Janssen, Roche, Pfizer, BMS, and Sanofi Genzyme, Belinda Butcher Consultant for: Consultant biostatistician and medical writer providing services to AbbVie, BMS, Janssen, MSD, Pfizer, UCB. Employee of: Janssen, Tegan Smith Grant/research support from: AbbVie, Consultant for: Provided medical writing services to Genentech, BioMarin, MSD, AbbVie, Roche, Actelion, Gilead, Kazia, Menarini, Candida da Fonseca Pereira Employee of: Pfizer, David Wilcombe Shareholder of: Pfizer, Employee of; Pfizer, Hedley Griffiths Grant/research support from: Research funded by AbbVie, Janssen, BMS. Consultant for: Advisory boards for Sanofi, Pfizer, Novartis, Janssen DOI: 10.1136/annrheumdis-2019-eular.5216

FRI0141 Efficacy of JAK-inhibitors versus biologic DMARDs on quality of life in rheumatoid arthritis: A meta-analysis of randomized controlled trials

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Background: Recent studies comparing JAK-inhibitors (Jak-i) and adalimumab seem to show a better efficacy of Jak-i on patient-reported outcomes in rheumatoid arthritis (RA).

Objectives: As there is no study comparing directly the Jak-i with other biologic DMARDs (bDMARDs), we performed a meta-analysis and compared the effect size of Jak-i and bDMARD versus synthetic DMARDs (sDMARDs) on quality of life.

Methods: We performed a systematic review of the literature until May 2018 using database including : MEDLINE (via PUBMED), EMBASE and abstracts from the ACR and EULAR congresses 2015-2017. We selected all randomized controlled trials (RCT) comparing quality of life (evaluated by SF36) in patient with rheumatoid arthritis treated with bDMARD or Jak-i versus sDMARDs. We performed meta-analysis comparing the effect size of Jak-i versus sDMARDs and bDMARD versus sDMARDs on PCS SF36 and MCS SF36 at 12 weeks. Statistical analysis determined in each study effect size. Pooled ES were computed by meta-analysis. Data were analyzed using the inverse variance approach.

Results: The literature search identified 240 articles plus one found by manual search and no congress abstract. Finally, 44 articles met the inclusion criteria. Jak-i and bDMARD showed higher level of quality of life than conventional therapies:

- For the SF36 PCS at 12 weeks: Jak-I: +4.82 IC95% [3.88, 5.77] and bDMARD: +3.99 IC95% [2.81, 5.18]
- For the SF36 MCS at 12 weeks: Jak-I: +3.42 IC95% [2.24, 4.60] and bDMARD: 2.99 IC95% [2.02, 3.96]

The range of the confidence intervals seems similar between Jak-I and bDMARDs.

SF36 PCS at 12 weeks:

FRI0142 Safety of the methotrexate-leflunomide combination in the Brazilian registry of biological therapies in rheumatic diseases (Biobadabrasil)


Background: The combination of methotrexate (MTX) with leflunomide (LEF), despite being effective in the therapy of rheumatoid arthritis (RA) [1], has not been widely accepted[2,3]. In spite of evidence that the MTX-LEF combination is generally safe [1,4,5], the relatively small number of patients and treatment courses have not permitted firm conclusions.

Objectives: To evaluate the safety of the combination MTX-LEF in Brazilian patients with RA included in BiobadaBrasil.

Methods: BiobadaBrasil is a multicentric prospective cohort study involving patients with rheumatic diseases who started the first biologic or a synthetic disease modifying anti-rheumatic drug (DMARD)[6]. This analysis includes RA (2010 criteria) patients recruited from Jan 2009 to Aug 2018, followed-up for one or multiple courses of treatment until censoring (latest date, September 03, 2018) or occurrence of the outcome of interest. The primary outcome was the incidence of any serious AE (SAE). Secondary outcomes were infectious, non-mycobacterial pulmonary infections, hepatic, hematologic and cardiovascular SAE. Multivariate Cox proportional hazards models (with DMARDs included as time-varying covariates) were used to estimate hazard ratios (HR) and 95% confidence intervals (CI); analyses were performed with the Survival package of R.
Results: Sample: 2055 RA patients, female=85.1%, mean disease duration=6.02 years; mean (SD) age=50.3 (12.1) years; mean (SD) DAS28=5.3 (3.1); seronegative RA=14.1%; median follow-up duration=3.9 years. In total, 565 patients received 664 courses of the MTX-LEF combination (median duration, 2.5 years/course; 2209 person-years). The incidence of SAE was 4.75/100 patient-years in the entire sample. There was no significant increase in the risk of any of the outcomes with the use of combined therapy (table 1) comparing with methotrexate (without leflunomide). The use of antimalarials was associated with reduced risk of SAE (adjusted HR=0.62, 95% CI 0.48 to 0.79, P<0.001), while sulfasalazine (adj. HR=1.78, 1.18 to 2.68, P=0.006) and biologic DMARDs/tofacitinib (adj. HR=1.67, 1.31 to 2.12, P<0.001) increased the risk of SAE.

Table 1

<table>
<thead>
<tr>
<th>Outcome/number of SAE</th>
<th>HR (95% CI), P Value</th>
<th>HR (95% CI), p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAE (457)</td>
<td>1.00(0.78-1.36), p=0.970</td>
<td>1.06(0.83-1.35), p=0.629</td>
</tr>
<tr>
<td>SAE infections (228)</td>
<td>1.10(0.79-1.55), p=0.538</td>
<td>1.24(0.89-1.75), p=0.207</td>
</tr>
<tr>
<td>SAE non-mycobacterial lung infections (78)</td>
<td>0.90(0.50-1.62), p=0.733</td>
<td>0.97(0.53-1.74), p=0.908</td>
</tr>
<tr>
<td>SAE hepatic AE (14)</td>
<td>1.12(2.98-4.48), NA</td>
<td>0.873</td>
</tr>
<tr>
<td>SAE hematologic (10)</td>
<td>2.09(0.52-8.36), p=0.299</td>
<td>NA</td>
</tr>
<tr>
<td>SAE CV (61)</td>
<td>1.220(0.65-2.30), p=0.529</td>
<td>1.11(0.58-2.12), p=0.755</td>
</tr>
</tbody>
</table>

Conclusion: BIOBADABRASIL results suggest that the combination of methotrexate and leflunomide is safe in the treatment of RA.

References:

Acknowledgement: monitor P Cabral

Disclosure of Interests: Markus Bredemeyer: None declared, M Pinheiro Consultant for: Janssen, Pfizer, Speakers bureau: AbbV, Janssen, Novartis, C Macieira: None declared, A Duarte: None declared, B Stadler: None declared, R Ranza: None declared, Ana Medeiros: None declared, V Valim: None declared, M Bertolo: None declared, J Miranda Speakers bureau: Pfizer, C Brenol Speakers bureau: Pfizer, Pfizer, Roche, Janssen, Bristol-Myers, G Castro: None declared, V Fernandes Speakers bureau: Janssen, Pfizer, Pfizer. Roche, Janssen, Bristol-Myers, J Provenza: None declared

FACTORS ASSOCIATED WITH NEAR REMISSION DIFFER BETWEEN AUTOANTIBODY-POSITIVE AND -NEGATIVE PATIENTS WITH EARLY RHEUMATOID ARTHRITIS TREATED WITH CONVENTIONAL SYNTHETIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS

Ludovico De Stefano, Serena Bugatti, Francesca Benaglio, Gaëtano Sakellaris, Antonio Marzo, Roberto Caporali, Carlomaurizio Montecucco, Division of Rheumatology, IRCCS Policlinico San Matteo Foundation, University of Pavia, Pavia, Italy

Background: Disease remission is recommended as the treatment target in patients with early rheumatoid arthritis (RA). According to the criterion, the proportion of patients classified as in remission considerably varies, with the Boolean-based definition being the most restrictive [1]. A considerable proportion of patients with established RA misses Boolean remission solely because of one of the 4 criteria (near remission) [2]. The frequency and the limiting variables to Boolean remission in real-life cohorts of patients with early RA are however unknown.

Objectives: To assess the feasibility and the limiting factors for fulfilling Boolean remission in early RA patients treated with csDMARDs according to a treat-to-target strategy.

Methods: The study population consisted of 578 early RA patients (<12 months of symptoms) consecutively recruited at our Early Arthritis Clinic, treatment-naïve at inclusion and prospectively followed-up upon initiation of therapy with methotrexate (MTX) aimed at the achievement of low disease activity (28-joints disease activity score [DAS28] <3.2). After 6 months of treatment, patients were classified as in remission or near remission according to the Boolean criterion as follows: (i) remission (PGA ≤22, TJC ≤2, CRP ≤0.3 mg/dl, DAS28 ≤2.6); (ii) near remission only one criterion was not met and the global remission index was ≤32. After 12 months of treatment, patients were classified as in remission (PGA ≤22, TJC ≤2, CRP ≤0.3 mg/dl, DAS28 ≤2.6) or near remission (one criterion not met and remission index ≤32). Missing criteria at 6 and 12 months were imputed according to the Boolean criterion. The proportion of patients classified as in remission considerably varies between autoantibody (AB)-positive and -negative patients -89.3% vs 69.4% at 6 months and 85.6% vs 65.8% at 12 months.

Results: Complete follow-up data after 6 months of treatment were available for 89.3% of the patients. Disease remission was achieved in 25.6% of the cases according to the DAS28, 16.7% according to the simplified disease activity index (SDAI) and 11.6% according to the Boolean criterion. One-hundred and thirty-three patients (25.8%) failed to reach Boolean remission (89.3% missing near remission). Reasons for missing Boolean remission were analysed in relation to disease variables. Complete follow-up data after 6 months of treatment were available for 89.3% of the patients. Disease remission was achieved in 25.6% of the cases according to the DAS28, 16.7% according to the simplified disease activity index (SDAI) and 11.6% according to the Boolean criterion. One-hundred and thirty-three patients (25.8%) failed to reach Boolean remission solely because of one of the 4 criteria (near remission) [2]. Of these, 45.9% were in DAS28 remission and 22.6% in SDAI remission. No differences in baseline demographic and clinical characteristics were found between patients in Boolean remission and patients in near remission. Use of prednisone co-medication and MTX starting dose were also comparable. Patients negative for both rheumatoid factor (RF) and anti-citrullinated protein autoantibodies (ACPA) were more frequently in near remission rather than in Boolean remission compared to autoantibody-positive patients (Fig. 1A). The missing criterion in near remission was SJC28 >1 in 49% of the cases, PGA >1 in 41%, and TJC28 >1 or CRP >1 mg/dl in the remaining 10%. Collectively, failure to achieve Boolean remission because of near remission was more common in RF and/or ACPA positive patients. Rather, autoantibody-negative patients more frequently missed remission due to PGA (Fig. 1B).

Conclusion: In patients with early RA treated with csDMARDs, near remission is up to two times more frequent than Boolean remission. Collectively, autoantibody-negative patients more commonly miss complete remission solely because of one criterion compared to autoantibody-
positive patients. Furthermore, in these patients, failure to achieve remission is mostly related to high PGA rather than to the persistence of joint inflammation. Altogether, these findings implicate that autoantibody-negative RA patients failing to achieve remission would require adjunctive tailored interventions rather than reinforcement of DMARD therapy.

REFERENCES:

Disclosure of Interests: Ludovico De Stefano: None declared, Serena Bugatti Speakers bureau: Bristol-Myers Squibb, Celgene, Lilly, Novartis, Sanofi, Jansen, Francesca Benaglio: None declared, Garifalla Sakellarious: None declared, Antonio Manzo: None declared, Roberto Caporali Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Roche, Genzyme, Lilly, MSD, Pfizer, UCB, Carlonauerio Montecucco Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Sanofi, Genzyme, Lilly, MSD, Pfizer, UCB

Figure 1. Overall survival of JAKi and for biologic-naive and biologic-experienced patients

Conclusion: The current use of JAKi in Spain is mainly in RA and as 2nd line after bDMARDs. The use of JAKi in psoriatic arthritis is still scarce and a small group of patients are treated off-label. Less than half use combination therapy with MTX. Overall survival of JAKi is superior to 80% at 12 months. A longer follow-up is needed to continue analyzing the survival of JAKi in a real-world context.

Acknowledgement: We thank all researchers from the BIOBADASER III group.

Disclosure of Interests: Valentina Emperiale: None declared, Carlos Sánchez-Piedra: None declared, Eduardo Cuende: None declared, Paloma Vela-Cassamppere: Grant/research support from: UCB, Abbvie, Pfizer, Roche, Bristol-Myers-Squibb (another research, not BIOBADASER related), Consultant for: UCB, Lilly, Pfizer, Roche, Bristol-Myers-Squibb, Speakers bureau: Roche, UCB, MSD, Pfizer, GSK, BMS, Lilly, Maria del Carmen Castro Villegas Paid instructor for: MSD, Abbvie, Pfizer, Janssen, Lilly, Roche, Sara Manrique Arria Speakers bureau: Abbvie, MSD, Janssen, Lilly, Roche, Pfizer, Novartis., Cristina Campos Fernández: None declared, Javier del Pino: None declared, Manuel Pombó: None declared, Fernando Sánchez-Alonso: None declared, Juan Jesus Gomez-Reino: None declared DOI: 10.1136/annrheumdis-2019-eular.211

Results: 149 patients, 75.2% women, were treated with JAKi, receiving a total of 152 cycles of treatment (50.7% tofacitinib, 49.3% baricitinib; 3 patients had both). The most frequent diagnosis was rheumatoid arthritis (RA, 92.6%), and there is a small number of off-label uses (6%), depicted at Table 1. Use on psoriatic arthritis is scarce (1.3%). Concomitant use of methotrexate (MTX) was registered in 68 patients (45.6%). Previous use of bDMARDs was high (n=124, 81.6%); drug survival rate for biologic-experienced patients was 81.7% and 78.7% at 6 and 12 months. None of the JAKi treatments in biologic-naive patients (n=18; 18.4%) were discontinued during follow-up. Pooled survival rate of JAKi was 85.0% and 82.5% at 6 and 12 months (Figure 1). Discontinuation was seen in 19 treatments (12.5%); the reasons were inefficacy (n=15, 9.9%) or adverse events (n=4, 2.6%).

Table 1. Diagnoses of patients with JAKi treatment

<table>
<thead>
<tr>
<th>Diagnosis (patients)</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatoid arthritis</td>
<td>138 (92.6)</td>
</tr>
<tr>
<td>Idiopathic juvenile arthritis*</td>
<td>3 (2.0)</td>
</tr>
<tr>
<td>Psoriatic arthritis</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>Undifferentiated spondyloarthropathies*</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>Seronegative polyarthritis*</td>
<td>2 (1.3)</td>
</tr>
<tr>
<td>Ankylosing spondylitis*</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Enteropathic arthritis*</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Total</td>
<td>149 (100)</td>
</tr>
</tbody>
</table>

*off-label use.

Background: In the SELECT-COMPARE study in rheumatoid arthritis (RA) patients (pts) with inadequate response to methotrexate (MTX), upadacitinib (UPA), a JAK1- selective inhibitor, was superior to placebo (PBO) or adalimumab (ADA) for treatment of signs & symptoms and for inhibition of radiographic progression vs PBO up to 26 weeks (wks). All pts were on stable background MTX.

Objectives: To report safety and efficacy of UPA plus stable background MTX up to 48 wks in this phase 3 study.

Methods: Pts were randomized to once-daily (OD) UPA 15mg, PBO, or ADA 40mg every other wk, with all patients continuing background MTX. The study was double-blind for 48 wks. Between Wks14-26, pts were rescued (from PBO to UPA, UPA to ADA, or ADA to UPA) if there was <20% improvement in tender/swollen joint count (Wks 14/18/22) or C Clinical Disease Activity Index (CDAI) >10 (WK26); all PBO pts who were not rescued were switched to UPA at Wk 26. Efficacy was analyzed by randomized group. Non-responder imputation (NRI) was used for binary endpoints for rescue prior to WK26. Last observation carried forth (LOCF).
forward (LOCF) was used for continuous endpoints and binary endpoints after Wk26. Treatment-emergent adverse events (AE) per 100 pts yrs (PY) were summarized up to July 6 2018 for pts with any exposure to ADA or UPA.

Results: In SELECT-COMPARE, 1629 pts were randomized at BL. Among 651 pts randomized to UPA, 38.7% were rescued between Wks 14-26; of those who remained on UPA, 86% completed Wk 48, while 58% and 0.3% discontinued study drug between BL and Wk 48 due to AE and lack of efficacy (LoE), respectively. Among 327 pts randomized to ADA, 48.6% were rescued between Wks 14-26; of those who remained on ADA, 76% completed Wk48, while 13.1% and 0 discontinued study drug between BL and Wk48 due to AE and LoE, respectively. The cumulative exposures were 1243.3 and 467.8 PYs for UPA and ADA, respectively. At Wk26, and Wk48, significantly more pts in the UPA vs ADA group achieved ACR20/50/70, low disease activity and remission (Table 1); this was also true for visits between Wks 26 and 48. Similarly, improvements in pain and function were significantly greater in the UPA vs ADA group through Wk48. At Wk26, there was significantly lower radiographic progression for UPA vs PBO, which was maintained through Wk48 (based on linear extrapolation). Adverse events are reported in Table 2 (in events per 100 PY). The rate of AE leading to discontinuation was higher with “any ADA” vs “any UPA”, while the rate of Herpes zoster was higher with “any UPA” exposure.

Conclusion: UPA continued to demonstrate superior clinical and functional responses vs ADA through Wk48. Inhibition of structural joint damage with UPA was also maintained through 48 wks vs PBO. Safety was consistent with observations in the first 26 wks.

REFERENCES:

Acknowledgement: AbbVie, Inc was the study sponsor, contributed to study design, data collection, analysis & interpretation, and to writing, reviewing, and approval of final version. Medical writing support was provided by Naina Barretto of AbbVie, Inc.

Disclosure of Interests: Roy Fleischmann Grant/research support from: AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Celtrion, Genentech, GSK, Janssen, Lilly, Novartis, Pfizer Inc, Sanofi-Aventis, UCB, Consultant for: AbbVie, Amgen, AstraZeneca, Bristol-Myers Squibb, Celtrion, Genentech, GSK, Janssen, Lilly, Novartis, Pfizer Inc, Sanofi-Aventis, UCB, Jeffrey Enejosa Shareholder of: AbbVie, Inc, Employee of: AbbVie, Inc, In-Ho Song Shareholder of: AbbVie Inc, Employee of: AbbVie Inc, Eduardo Myśliwer Grant/research support from: AbbVie, Bristol-Myers Squibb, Eli Lilly, Pfizer, Novartis, Janssen, Grant/research support from: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medimmune, Pfizer Inc and Roche, Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medimmune, Pfizer Inc and Roche, Louis Bessette Grant/research support from: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celegene, Sanofi, Lilly, Novartis, Consultant for: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celegene, Sanofi, Lilly, Novartis, Speakers bureau: AbbVie, Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celegene, Sanofi, Lilly, Novartis, Charles Peterly Shareholder of: Spire Sciences, Inc, Consultant for: AbbVie, Acerta, Amgen, AstraZeneca, Bristol-Myers Squibb, Centrexion, Daiichi Sankyu, Five Prime Therapeutics, Genentech, Hoffmann-La Roche, Janssen, Lilly United States of America, Medimmune, Merck, Novartis, Flexixxon, Pfizer, Sanofi, Salla-Santaurus, Samsung, Employee of: Spire Sciences, Inc, Speaker's bureau: Amgen, Patrick Durez Speakers bureau: Bristol-Myers Squibb, Eli Lilly, Sanofi, Celtrion, Andrew Ostor Consultant for: AbbVie, BMS, Roche, Janssen, Lilly, Novartis, Pfizer, UCB, Glead, Paradigm, Yihai Li Shareholder of: AbbVie, Employee of: AbbVie, YiJie Zhu Shareholder of: AbbVie, Inc, Employee of: AbbVie, Inc, Mark C. Genovesi Grant/research support from: Sanofi/Genzyme, Genentech/Roche, RPharm, Consultant for: Sanofi/Genzyme, Genentech/Roche, RPharm
From 41 persons with RA 32 patients, who never achieved low disease activity (DAS28<3.2) or remission (DAS28<2.6) followed the dosage enhancement (the visit before the switching). 

Objectives: The aim of the study was to evaluate the results of switching of TF's dosages in RA patients. 

Methods: were analyzed the data from Russian national register of patients with RA treated with TF (tofacitinib). 415 patients were included in the register (aug 2018). In statistical analysis were included data from 41 patients with RA (EULAR 2010), who switched dosage of TF at visit 3 and had complete clinical and laboratory data from 5 consecutive visits with an interval of 3 months between the visits. Demographic (age, sex, data), disease activity data DAS28 (Disease Activity score), C-reactive protein level were collected, table 1. Changes in disease activity were calculated to patients with switching of the tfa's dosage (the visit before and after the switching).

Results: 1.28 (68%) of patients were treated with NSAIDs, 24 (50%) with 5-10 mg of prednisolone, 34 (82.9%) with methotrexate (10-25 mg/week), biologics – 5 (4.2%).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>10 (24.3)</td>
</tr>
<tr>
<td>Caucasians, n (%)</td>
<td>41 (100)</td>
</tr>
<tr>
<td>Asians, n (%)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Age of disease onset, years (mean ±SD)</td>
<td>40.1±10.5</td>
</tr>
<tr>
<td>Symptoms duration, month (mean ±SD)</td>
<td>98.7±87.1</td>
</tr>
<tr>
<td>Positive rheumatoid factor, n (%)</td>
<td>32 (76)</td>
</tr>
<tr>
<td>Positive antibodies to cyclic citrullinated peptide (anti-CCP), n (%)</td>
<td>37 (89.2)</td>
</tr>
<tr>
<td>BMI, kg/m²(mean ±SD)</td>
<td>25.12±5.98</td>
</tr>
<tr>
<td>Smokers (current and in the anamnesis), n (%)</td>
<td>33 (80)</td>
</tr>
</tbody>
</table>

From 41 persons with RA 32 patients, who never achieved low disease activity (DAS28<3.2) or remission (DAS28<2.6) elevated the dosage of tofa from 10 to 20 mg/day and 9 patients with DAS28 < 3.2 decreased the dosage from 20 to 10 mg/day. After escalation of TF dosage DAS28 decreased from 5.4±1.22 to 4.22 ±1.22 (p<0.00, n=32). In 10 patients escalation lead to DAS28-remission (DAS28<2.6) and in 12 patients to low disease activity (DAS28<3.2). 10 patients had no clinical or laboratory response on escalation of TF dosage. Interestingly, that responders before escalation of dosage had mean DAS28 3.54 (min 3.2 – max 4.9) and non-responders – 5.54 (min 5.3-max 6.8), p<0.000.

Conclusion: Escalation of dosage of TF in RA lead to improvement of the disease activity in non-complete responders, who achieved DAS 28 3.2-5.1, but not in patients with absence of any response (DAS28 before escalation 5.3-6.9). De-escalation of TF dosage in patients with DAS28 < 2.6 dose not lead to significant changes of RA's activity.

REFERENCES:
The relationship between the effectiveness of methotrexate (MTX) in rheumatoid arthritis (RA) and MTX polyglutamates levels (MTXPG) in red blood cells by tandem chromatography spectrometry (PILOT STUDY)

Gala Gridneva1, Yury Muraviev1, Alexander Lila2, Natalia Baymeeva2.1, VA Nasonova Research Institute of Rheumatology, Moscow, Russian Federation; 2Mental Health Research Center, Moscow, Russian Federation

Background: Therapeutic control of the level of MTXPGs in erythrocytes may be an objective marker of its effective dose in RA treatment.

Objectives: To evaluate the relationship between the level of MTXPGs in erythrocytes and the effectiveness of the dose of MTX used by RA patients.

Methods: The study included 60 random selected RA patients over the age of 19, 16 men and 44 women. The diagnosis in all cases met the criteria of the EULAR response to therapy. The groups were comparable in age, sex, alcohol intake, smoking, body mass index (BMI), ACPP-positivity, incidence of unwanted reactions to MTX, single therapy: 5.5 [2.0, 12.0] months in group 1 and 12.0 [3.0, 60.0] months in group 2; in group 2 patients received glucocorticoids (GK) orally 17 (57%) against 9 (30%) in group 1. Blood sampling was performed no later than 36 hours after the last administration of methotrexate. From each patient 2 ml of hemolysed blood were examined using an Agilent 6410 chromatograph (Agilent Technologies) - a quantitative measurement of methotrexate polyglutamate by liquid chromatography-spectrometry.

*Primary endpoint; †Secondary endpoint; *p (compared to PBO).

Results: It was established that the levels of total MTXPG and MTXPG1;2,3,5 in erythrocytes did not depend on the effectiveness of MTX, the dose of which was comparable in all patients. At the same time, the level of MTXPG4 was significantly higher (p = 0.023) in patients of group 1 (26.4 ± 6.1 nmol/l) compared with patients in group 2 (22.1 ± 6.8 nmol/l). Evaluation of the ROC curve showed that MTXPG4 values between 22.5 nmol/l corresponded to the absence of the therapeutic effect of MTX. The area under the curve was 0.672, (CI 0.539 - 0.808), p = 0.022. Sensitivity 65.4%, specificity 53.3%

Conclusion: More than 26% of patients who initiated MTX therapy either discontinued or may not restart MTX. There is a need to better understand the patterns of MTX use, the characteristcs of these patients, and how the patterns of use are related to outcomes.


TOFACITINIB

FRI0153 OPHTHALMOLOGICAL ADVERSE EVENTS UNDER JAK INHIBITORS IN PATIENTS WITH RHEUMATOID ARTHRITIS: CASE ANALYSIS OF THE EUROPEAN PHARMACOVIGILANCE DATABASE

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2Centre Hospitalier Universitaire de Grenoble, La Tronche, France

Background: Ophthalmological manifestations in rheumatoid arthritis (RA) include dry syndrome, scleritis, episcleritis, uveitis and peripheral ulcerative keratitis (PUK). Recently, a new class of synthetic molecules has been developed, called JAK inhibitors (JAKinhib). We observed one case of PUK occurring two months after the introduction of baricitinib treatment with corneal perforation with secondary improvement after discontinuation of JAKinhib.

Objectives: The aim of this study is to describe and characterize the ophthalmological side effects of JAK inhibitors (JAKinhib) in patients with rheumatoid arthritis (RA) from European pharmacovigilance (PV) data.

Methods: The ophthalmological manifestations that appeared under JAK inhib were extracted from the European PV database (May 2018), EUDRAVIGILANCE following a request addressed to the National Drug Agency in order to discuss the imputability of the treatment. A discontinuation of it seems justified pending an ophthalmological opinion.

Results: A total of 41 patients with ophthalmic adverse events (AEs) on JAK inhib were reported. Among patients, 12 were treated with BARICITINIB and 29 with TOFACITINIB. Of these AEs, 51% were reported by the medical profession, 39% by patients and 10% by paramedical teams. The database analysis revealed 4 scleritis, 3 corneal ulcers, 1 PUK and 1 corneal ulceration. The average time to onset of AEs was 13.2 months. The infectious causes had been eliminated.

Conclusion: Ophthalmological manifestations under JAKinhib seem to be rare but not exceptional, the rheumatologist must be aware of them in order to discuss the imputability of the treatment. A discontinuation of it seems justified pending an ophthalmological opinion.


FRI0154 SAFETY AND EFFICACY OF FILGOTINIB IN PATIENTS AGED 65 YEARS AND OLDER: RESULTS FROM A PHASE 3 STUDY IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS AND PRIOR INADEQUATE RESPONSE OR INTOLERANCE TO BIOLOGICAL DMARDS (BDMARD-IR)

Kenneth Kakujiang1, Jacques-Éric Gottenberg2, Mark C. Genovese3, Neehufer Muzaffariani4, Beatrix Bartik5, Franziska Matzkies4, Jie Gao6, Ying Guo4, Tsutomu Takeuchi5, Kurt de Vlam6, David Walker7.

1University of California, San Diego, La Jolla, United States of America; 2Dept of Rheumatology, Strasbourg University Hospital, Strasbourg, France; 3Stanford University Medical Center, Palo Alto, United States of America; 4Gilead Sciences, Inc., Foster City, United States of America; 5Kio University School of Medicine, Tokyo, Japan; 6Universitair Ziekenhuis Leuven, Leuven, Belgium; 7Northumbria Healthcare, Newcastle upon Tyne, United Kingdom

Background: Filgotinib (FIL), an oral selective Janus kinase 1 (JAK1) inhibitor, demonstrated efficacy and safety vs placebo (PBO) in BDMARD-IR patients with active RA in a global phase 3 study (FINCH2, Clinical-Trials.gov NCT02873936).1

Objectives: We performed a prespecified subgroup analysis of the safety and efficacy of FIL in patients aged ≥65 years vs <65 years in FINCH2 to understand FIL effects in older patients.

Methods: 449 patients were randomized 1:1:1 to FIL 200 mg, FIL 100 mg, or PBO on a background of csDMARDs for 24 weeks. The primary efficacy endpoint was ACR20 response at week 12.

Results: Of 448 patients who received ≥1 dose of study drugs, 113 (25.2%) were ≥65 years of age; baseline disease characteristics were similar for both age groups. Safety and efficacy parameters by age group are in Tables 1 and 2. The most common treatment-emergent adverse events (TEAEs, by System Organ Class) category was infections and infestations; nasopharyngitis, upper respiratory tract infections, and bronchitis were the most common infections and infestations in the FIL arms in both age groups. There were no cases of opportunistic infection, active tuberculosis, malignancy, gastrointestinal perforation, or death. Efficacy outcomes were similar for both groups.

Conclusion: Overall, older age was not associated with higher incidence of safety events (serious infections, herpes zoster, MAC occurred in the group <65 yrs) and efficacy was similar in older and younger BDMARD-IR patients with active RA.

Disclosure of Interests: None declared

REFERENCES
ARTHRITIS: AN ANALYSIS OF TWO PHASE 3 STUDIES

**Table 1. TEAEs and Key Safety Outcomes Week 0–24 by Age Group, n (%)**

<table>
<thead>
<tr>
<th>Regimen</th>
<th>FIL 200 (n=112)</th>
<th>FIL 100 (n=110)</th>
<th>PBO (n=116)</th>
<th>FIL 200 (n=112)</th>
<th>FIL 100 (n=110)</th>
<th>PBO (n=116)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TEAE</td>
<td>72 (63)</td>
<td>81 (74)</td>
<td>70 (61)</td>
<td>30 (27)</td>
<td>16 (14)</td>
<td>30 (26)</td>
</tr>
<tr>
<td>Serious AE</td>
<td>4 (3.6)</td>
<td>7 (6.3)</td>
<td>5 (4.3)</td>
<td>2 (1.8)</td>
<td>2 (1.8)</td>
<td>2 (1.7)</td>
</tr>
<tr>
<td>TEAE leading to study drug discontinuation</td>
<td>6 (5.5)</td>
<td>7 (6.4)</td>
<td>5 (4.3)</td>
<td>3 (2.6)</td>
<td>2 (1.8)</td>
<td>2 (1.7)</td>
</tr>
</tbody>
</table>

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**Table 2. Week 24 Key Efficacy Measures by Age Group**

<table>
<thead>
<tr>
<th>Regimen</th>
<th>FIL 200 (n=112)</th>
<th>FIL 100 (n=110)</th>
<th>PBO (n=116)</th>
<th>FIL 200 (n=112)</th>
<th>FIL 100 (n=110)</th>
<th>PBO (n=116)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACR20 n (%)</td>
<td>78 (70)</td>
<td>60 (55)</td>
<td>63 (55)</td>
<td>31 (28)</td>
<td>24 (21)</td>
<td>24 (21)</td>
</tr>
<tr>
<td>DAS28(CRP)&lt;2.6 (%)</td>
<td>33 (30)</td>
<td>26 (23)</td>
<td>31 (27)</td>
<td>19 (17)</td>
<td>13 (11)</td>
<td>14 (12)</td>
</tr>
<tr>
<td>HAQ-DI mean CBF</td>
<td>9.6 (8.2)</td>
<td>9.4 (5.7)</td>
<td>9.6 (5.7)</td>
<td>8.5 (7.8)</td>
<td>7.5 (7.4)</td>
<td>7.5 (7.4)</td>
</tr>
</tbody>
</table>

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**Conclusion:** In this post hoc analysis, the efficacy of UPA in patients with RA appeared comparable whether administered in combination with MTX or non-MTX csDMARDs.
A PHASE 1, SINGLE AND MULTIPLE ASCENDING DOSE STUDY OF TAS5315 - A NOVEL HIGHLY SELECTIVE INHIBITOR OF BRUTON’S TYROSINE KINASE – IN HEALTHY MALE VOLUNTEERS

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Background: Bruton’s tyrosine kinase (BTK) is expressed in the cells of the immune system and osteoclasts, and plays an important role in inflammation and bone resorption. TAS5315 is a novel, highly selective inhibitor of BTK. In animal models, TAS5315 suppressed the inflammation at the joints and significantly suppressed extreme bone destruction, in a dose-dependent manner. It has the potential to become a treatment option in patients with rheumatoid arthritis (RA).

Objectives: To evaluate the safety, pharmacokinetics (PK), and pharmacodynamics (PD) of TAS5315 in healthy male volunteers.

Methods: The single ascending dose (SAD) study, which was the first-in-human study, and the multiple ascending dose (MAD) study were conducted as randomized, double-blind, placebo-controlled and parallel-group comparative studies in a single center. In the SAD study, 70 subjects were enrolled and received 0.01–8 mg of TAS5315 or placebo. In the MAD study, 31 subjects were enrolled and received 1–8 mg of TAS5315 or placebo once daily for 7 days. The allocation ratio (TASS315: placebo) was 7:3 in the SAD study and 6:2 in the MAD study. The PD of TAS5315 was assessed by measuring the rate of BTK occupancy in peripheral blood mononuclear cells using a fluorescence probe.

Results: The observed PK profile of TAS5315 was linear in the dose range of 0.01–8 mg. TAS5315 was rapidly absorbed (median \(T_{\text{max}}\): 0.5–1.5 hr) and eliminated (mean \(T_{1/2}\): 1.00–1.37 hr). The maximum percent of BTK occupancy by TAS5315 increased dose-dependently at 0.01–2 mg in SAD study. The occupancy rate of BTK peaked at 2 mg and was almost 100% at 2–8 mg. 6 hr after administration and remained almost 80% or higher for up to 24 hr. The expression level of CD203c in peripheral blood basophils treated with anti-IgE antibodies was also measured with a flow cytometer. The SAD and MAD studies were reviewed and approved by the IRB of Kitasato University Hospital.

Conclusion: TAS5315 was well tolerated when administered as repeated doses of up to 8 mg once daily for 7 days. The inhibitory effect of BTK on BTK occupancy by TAS5315 was demonstrated in this study, and this provides the basis for an early Phase II study to evaluate the efficacy of TAS5315 in patients with RA.

REFERENCE:


REFERENCES:

Acknowledgement: AbbVie, Inc was the study sponsor, contributed to the study design, data collection, analysis & interpretation, and to writing, reviewing, and approval of the final version. Medical writing support was provided by John Ewbank, PhD, of 2 n 2 hour.

Disclosure of Interests: Joel Krerner Grant/research support from: AbbVie, Genentech, Lilly; Novartis, Pfizer, Consultant for: AbbVie, Angen, BMS, Genentech, Lilly, Regeneron, Sanofi, Pfizer, Filip van den Bosch Consultant for: AbbVie, BMS, Galapagos, Janssen, Lilly, Merck, Novartis, Pfizer and UCBB. Speakers bureau: AbbVie, BMS, Janssen, Lilly, Merck, Novartis, Pfizer and UCBB. Andrea Rubbert-Roth Consultant for: Abbvie, Speakers bureau: AbbVie, Sebastião C. Radominski Consultant for: Abbvie, Celgene, Genentech/Roche, Janssen, Pfizer, and UCBB. Paid instructor for: AbbVie, Celgene, Genentech/Roche, Janssen, Pfizer, and UCBB, Speakers bureau: AbbVie, Celgene, Genentech/Roche, Janssen, Pfizer, and UCBB, Gerard Rüdiger Burmester Consultant for: Roche, Sanofi-Genzyme, Speakers bureau for: Roche, Sanofi-Genzyme, Heide Camp Sharedholder of: Abbviev.

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effect profile compared to methotrexate at doses used in oncology.(3) Hence this study aimed to clarify why lower dose methotrexate carried a risk of hair fall.

**Objectives:** Determine the mean change in number of hair strands obtained by the hair pull test at the start of the trial and at 3 weeks, 2 months and 3 months among rheumatoid arthritis patients on methotrexate in comparison to healthy controls.

**Methods:** After ethics committee approval and informed consent, consecutive patients attending a rheumatology OPD and who were planned to be initiated on methotrexate were enrolled into the study. Patient relatives, hospital staff and healthy blood donors were recruited as healthy controls. Patients with prior exposure to methotrexate in the last 6 months, currently on other medications known to cause hair fall or those suffering from diseases which could predispose to alopecia were excluded.

**Results:** During the 6 month enrolment phase 98 patients and 82 controls were enrolled. Patients were 85% female with a mean age of 48.1 ±13.4. Rheumatoid factor positivity was seen in 59%. Average duration of the disease was 9.6 months (Range 15 days to 3 years). Patients were started on 10 to 15 mg of methotrexate which was escalated at the 1st visit at 3 weeks. Only 3 patients had received prior DMARDs. Controls also constituted predominantly women (90%) with an slightly lower average age of 44.4 ±10.9 years. The mean no of hair in the hair pull test at the start of the study was 1.21±2.01 (range 0-12) in patients vs 0.84 ±1.25 (range0-4) in controls. The mean change in the hair count in the same test repeated at 3 weeks, 2 months and 3 months was -0.29, -0.31 & -0.26 respectively (i.e. reduction in hair fall). In comparison healthy controls showed values of 0.31,0.11, 0.1 at the same follow up points. There was no statistical significant difference in the proportion of patients having more than 5 hairs in the test at the onset of treatment vs healthy controls or during any point during the follow up period.

**Conclusion:** Low dose methotrexate did not appear to predispose to increased hair fall during this short term study. In fact many patients showed reduction in the number of hair in the hair pull test on methotrexate.

**REFERENCES:**

**Disclosure of Interests:** Dr Deena Patil and Dr Sunaina Hameed for help in designing the study.

**Disclosure of Interests:** Shashar Kumar Consultant for: Intas, Speakers bureau: JanssenJanssen, Bristol Meyers & Squibb, Pfizer, Dhivya Loka, Providence University, Department of Food and Nutrition, Taichung City, Taiwan, Republic of China; Providence University, Department of Food and Nutrition, Taichung City, Taiwan, Republic of China; Providence University, Department of Medicine, Taichung Medical University, Taichung City, Taiwan, Republic of China; Providence University, Department of Medicine, Taichung Medical University, Taichung City, Taiwan, Republic of China

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**FR0158 COMPARISON OF THE EFFICACY AND SAFETY OF TOFACITINIB AND UPADACITINIB IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS: A BAYESIAN NETWORK META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS**

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**Background:** A class of targeted synthetic disease-modifying anti-rheumatic drugs (tsDMARDs) has emerged as an alternative treatment option for rheumatoid arthritis (RA). Tofacitinib is an orally administered Jak (Janus kinase) inhibitor with functional cellular specificity for Jak-1 and Jak-3 over Jak-2 and upadacitinib, a new Jak inhibitor, has been engineered to confer greater selectivity for Jak1 than for Jak2, Jak3, and Tyk2.

**Objectives:** The aim of this study is to assess the relative efficacy and safety of tofacitinib and upadacitinib at different doses were assessed in patients with RA with an inadequate response to conventional synthetic (cs) or biologic (b) DMARDs.

**Methods:** We performed a Bayesian network meta-analysis to combine direct and indirect evidence from randomized controlled trials (RCTs) to examine the efficacy and safety of tofacitinib and upadacitinib in combination with methotrexate (MTX) in RA patients with an inadequate cs- or b-DMARD response.

**Results:** Nine RCTs including 5,794 patients met the inclusion criteria. There were 15 pairwise comparisons including 10 direct comparisons of six interventions. Upadacitinib 15 mg+MTX and upadacitinib 30 mg+MTX were among the most effective treatments for active RA with an inadequate cs- or b-DMARD response, followed by tofacitinib 10 mg+MTX, tofacitinib 5 mg+MTX, and adalimumab 40 mg+MTX. Ranking probability based on the surface under the cumulative ranking curve (SUCRA) indicated that upadacitinib 15 mg+MTX and upadacitinib 30 mg+MTX had the highest probability of being the best treatment in terms of the ACR20 response rate (SUCRA = 0.820, 0.762), followed by tofacitinib 10 mg+MTX (SUCRA = 0.623), tofacitinib 5 mg+MTX (SUCRA = 0.424), adalimumab+MTX (SUCRA = 0.371), and placebo+MTX (SUCRA = 0.001). No significant differences were observed in the incidence of serious adverse events after treatment with tofacitinib+MTX, upadacitinib+MTX, adalimumab+MTX, or placebo+MTX.

**Conclusion:** In RA patients with an inadequate response to cs- or b-DMARDs, upadacitinib 15 mg+MTX and upadacitinib 30 mg+MTX were the most efficacious interventions and were not associated with significant risks of serious adverse events.

**REFERENCES:**

**Disclosure of Interests:** None declared

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**FR0159 REAL-WORLD EVIDENCE OF EFFECTIVENESS OF SWITCHING FROM TOFACITINIB 5MG BD TO TOFACITINIB 11MG QD IN A COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS: A SINGLE-CENTER, OBSERVATIONAL STUDY IN TAIWAN**

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**Background:** Rheumatoid arthritis (RA) is a chronic autoimmune disorder, precipitating chronic inflammation of the joints, also affecting organs throughout the body. For chronic conditions, such as RA, a once-daily (QD) dosing option has the potential to optimize patient adherence, and may enhance patient convenience and ease of use. Real-world data on effectiveness of switching from tofacitinib 5mg QD to tofacitinib 11mg QD is scarce.

**Objectives:** This study aimed at evaluating the effectiveness and safety of RA patients switching from tofacitinib 5mg BD to tofacitinib 11mg QD in a real-world setting.

**Methods:** A retrospective chart review of patients with RA was performed at the rheumatology department of an integrated secondary teaching hospital in Taiwan. The following cohorts were defined: RA patients who switched from tofacitinib 5mg BD to tofacitinib 11mg QD between 1 July 2018 and October 2018, and the follow-up period was at least 3 months. The clinical demographics and laboratory variables were obtained from clinic records.

**Results:** As of December 2018, 71 patients were included (85% of women), with a mean (SD) age of 57.4 (12.7) years, 70.1% were biologic-experienced; 78.9% rheumatoid factor positive and 80.3% anti-citrullinated peptide antibody (ACPA) positive. At baseline (before patients initiated tofacitinib 5mg BD treatment), the mean (SD) DAS28-ESR was 5.0 (8.4% patients with low disease activity, and 2.8% in clinical remission), the mean CDAI was 23.0 (11.2% patients with low disease activity, and 0% in clinical remission). After an average duration of 20 months treatment on tofacitinib 5mg BD treatment, the mean DAS28-ESR was 3.3 (29.6% patients with low disease activity, and 2.8% in clinical remission).
the mean CDAI was 7.5 (84.5% patients with low disease activity, and 2.8% in clinical remission). While switching to tofacitinib 11mg QD for 3 months, no significant difference was observed in terms of the ratio of DAS28-ESR LDA or CDAI LDA, but numerically more patients achieved DAS28-ESR LDA or CDAI LDA (32 and 64, respectively). During the 3-month follow-up period, no new adverse events were present.

Conclusion: Our study showed that RA patients switching from tofacitinib 5mg BID to tofacitinib 11mg QD sustained the effectiveness with no adverse clinical impact.

The preparation and property of iguratimod

Iguratimod, a methanesulfonanilide, has obvious anti-inflammatory efficacy and increases the gastrointestinal side effects of drugs[2].

Methods:
NanoIguratimod@Hydrogel was prepared using the high-gravity anti-solvent precipitation (HGAP) technique, and its properties were tested. The NanoIguratimod-loaded Hydrogel Composite was prepared and the delivery of the payload was demonstrated. In vitro, the biological effects of Nanolirutamoid@Hydrogel on fibroblast-like synoviocytes (RA-FLS) were evaluated. In vivo, the pharmacokinetics of oral raw iguratimod or subcutaneous injection of Nanolirutamoid@Hydrogel was carried out in the healthy rats. Further, we evaluated the efficacy of Nanolirutamoid@Hydrogel in treating collagen-induced arthritis (CIA) rats.

Results: By the HGAP technique, we acquired the amorphous form Nanolirutamoid with an average size of 295nm, which had higher dissolution rates and higher stability. The release of iguratimod from hydrogel was completed within 24h.

Discussion of Interests: None declared

Disclosure: Of Interests: None declared


PREPARATION AND PROPERTY OF IGURATIMOD NANOSONE SUSTAINED-RELEASE SYSTEM

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Background: Iguratimod, a methanesulfonanilide, has obvious anti-inflammatory activity and has been developed exclusively in Asia-Pacific countries. As a novel disease-modifying anti-rheumatic drug, iguratimod is effective in the treatment of RA, but some side effects, such as liver damage and gastrointestinal discomforts are the main concerns in clinical application[1]. Currently, iguratimod is practically insoluble in aqueous solvents and only available in oral dosage forms. The low solubility of drugs leads to incomplete absorption and bioavailability, which affects the clinical efficacy and increases the gastrointestinal side effects of drugs[2].

Objectives: In order to improve the bioavailability and alleviate the side effect of gastrointestinal reaction, we changed the dosage form of iguratimod to NanoIguratimod-loaded Hydrogel Composite.

Methods: Iguratimod nanoparticles (Nanolirutamoid) were prepared by using the high-gravity anti-solvent precipitation (HGAP) technique, and their properties were tested. The Nanolirutamoid-loaded Hydrogel Composite was prepared and the delivery of the payload was demonstrated. In vitro, the biological effects of Nanolirutamoid@Hydrogel on fibroblast-like synoviocytes (RA-FLS) were evaluated. In vivo, the pharmacokinetics of oral raw iguratimod or subcutaneous injection of Nanolirutamoid@Hydrogel was carried out in the healthy rats. Further, we evaluated the efficacy of Nanolirutamoid@Hydrogel in treating collagen-induced arthritis (CIA) rats.

Results: By the HGAP technique, we acquired the amorphous form Nanolirutamoid with an average size of 295nm, which had higher dissolution rates and higher stability. The release of iguratimod from hydrogel was completed within 24h compared with Nanolirutamoid. Nanolirutamoid@Hydrogel inhibited the proliferation, migration, and invasion of RA-FLS in a doses dependent manner. The pharmacokinetic parameters showed better bioavailability and longer half-life time with Nanolirutamoid@Hydrogel by subcutaneous administration than oral raw iguratimod. Animal experiments confirmed that subcutaneous injection of Nanolirutamoid@Hydrogel (10mg/kg every three days) and oral raw iguratimod (10mg/kg daily) showed similar efficacy in decreasing arthritis index score, pathological score, and expression of cytokines (IL-6, TNF-a and IL-1b).

Conclusion: Overall, our data suggested that Nanolirutamoid@Hydrogel provided new administration routes and extended the administration interval, it may serve as a promising drug delivery approach for the treatment of RA.

REFERENCES:

PHARMACOKINETICS AND SAFETY OF A SINGLE ORAL DOSE OF PEFICITINIB (ASP015K) IN SUBJECTS WITH NORMAL AND IMPAIRED HEPATIC FUNCTION

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Background: Peficitinib (ASP015K), a novel oral Janus kinase inhibitor, demonstrated efficacy as once-daily therapy for moderate-severe rheumatoid arthritis in a phase 2b study (NCT01649999) and 2 phase 3 studies (NCT02308163, NCT02305849). Mean urinary excretion of peficitinib accounted for 9~15% of the oral dose. It produces 3 conjugated metabolites (H1, H2, H4), which show very weak in-vitro pharmacological action.

Objectives: To assess pharmacokinetics (PK) and safety of a single oral dose of peficitinib 150 mg in subjects with normal and impaired hepatic function.

Methods: This phase 1, open-label, single-dose, parallel-group study was conducted at six centres in Japan. Eligible subjects were aged 20–75 years, with body mass index >17.0–<30.0 kg/m². Hepatic impairment was defined as screening using Child-Pugh classification: Class A, mild (5–6 points); Class B, moderate (7–9 points). Subjects with severe hepatic impairment (Child-Pugh classification Class C, 10–15 points) were excluded. Subjects received a single oral dose of peficitinib 150 mg under fasting conditions, based on daily dose in the 2 phase 3 studies. Blood samples for plasma PK analysis of peficitinib and its metabolites were collected before and up to 72 h post dose. Safety was assessed throughout the study.

Results: 24 subjects were enrolled (70.8% male): 16 with impaired and 8 with normal hepatic function (Table 1): all received study medication.

CONCLUSION: Overall, our data suggested that Nanolirutamoid@Hydrogel provided new administration routes and extended the administration interval, it may serve as a promising drug delivery approach for the treatment of RA.

REFERENCES:
TOFACITINIB IN RHEUMATOID ARTHRITIS PATIENTS WITH ANAEMIA IN CLINICAL STUDIES OF TOFACITINIB IN RHEUMATOID ARTHRITIS

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REFERENCES:

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FR0162 BASELINE CHARACTERISTICS AND OUTCOMES IN PATIENTS WITH ANAEMIA IN CLINICAL STUDIES OF TOFACITINIB IN RHEUMATOID ARTHRITIS

RESULTS: The proportion of pts with G2A at BL was similar for tofacitinib (3.2%, 152 of 4736 pts) and PBO (2.4%, 27 of 1125 pts) groups. Pts with G2A at BL were more often female, Asian, younger, had never smoked and had a lower body mass index (BMI) and higher C-reactive protein (CRP) and ESR vs pts without G2A at BL; RA duration was generally similar across groups (Table). Tofacitinib seemed to improve anaemia more rapidly than PBO: in pts with G2A at BL, a lower proportion of those receiving tofacitinib had G2A at M1 and M3 vs those receiving PBO (48.8% vs 75.0%, respectively, at M1 and 36.1% vs 57.1%, respectively, at M3), while the proportions were similar at M6 (28.9% vs 30.6%, respectively). In pts receiving tofacitinib, mean Hgb levels gradually increased from BL to M6 in those with G2A at BL (1.25 g/dL change), but were relatively stable in those without G2A at BL (0.15 g/dL change). In tofacitinib-treated pts, DAS28-4(ESR) scores decreased from BL to M6 by -2.40 in those with G2A at BL and -2.42 in those without G2A at BL. DAS28-4(ESR) low disease activity (≤2.3) rate at M6 was lower in tofacitinib-treated pts with G2A at BL vs those without G2A at BL (18.3% vs 28.4%, respectively). Among pts receiving tofacitinib,

Conclusion: Peficitinib exposure in subjects with mild hepatic impairment was similar to that in subjects with normal hepatic function; subjects with moderate hepatic impairment had greater exposure. A single dose of peficitinib was well tolerated.

Table 2: Plasma PK parameters of peficitinib and its metabolites H1, H2 and H4 (PMX4K)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal hepatic function</th>
<th>Mild hepatic impairment</th>
<th>Moderate hepatic impairment</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC (ng/mL)</td>
<td>Mean (S.D.)</td>
<td>Median (IQR)</td>
<td>Mean (S.D.)</td>
</tr>
<tr>
<td>H1</td>
<td>1194 (210.3)</td>
<td>1373 (145.2)</td>
<td>2322 (805.4)</td>
</tr>
<tr>
<td>Cmax (ng/mL)</td>
<td>Mean (S.D.)</td>
<td>Median (IQR)</td>
<td>Mean (S.D.)</td>
</tr>
<tr>
<td>H1</td>
<td>1194 (210.3)</td>
<td>1373 (145.2)</td>
<td>2322 (805.4)</td>
</tr>
<tr>
<td>Tmax (h)</td>
<td>Mean (S.D.)</td>
<td>Median (IQR)</td>
<td>Mean (S.D.)</td>
</tr>
<tr>
<td>H1</td>
<td>1194 (210.3)</td>
<td>1373 (145.2)</td>
<td>2322 (805.4)</td>
</tr>
</tbody>
</table>

Number of subjects available for AUC and Cmax: n = 97; n = 97.

Hepatic impairment was defined according to Child-Pugh classification: class A: mild; 5–6 points; or class B: moderate, 7–9 points.

AUC and Cmax were based on the concentration-time curve from the time of dosing extrapolated to infinity and maximum concentration, respectively. PK parameters were estimated at the last non-missing post-dose observation (terminal elimination half-life (t1/2) and CL, t1/2, and CL were based on the least square means (LSM) of the parameter).
those with BL G2A had a higher incidence of TEAEs vs those without BL G2A in the following MedDRA system organ classes (with incidence $>20\%$ in pts who were either with or without BL G2A): gastrointestinal disorders (30.9\% vs 22.5\%, respectively) and infections and infestations (44.1\% vs 39.0\%, respectively).

**Conclusion:** In this post hoc analysis, more pts with BL G2A had a higher incidence of TEAEs vs those without BL G2A. The majority were females (89.3\%) and most had prior biologic use history (74.0\%). At baseline, no significant differences in disease activity and sociodemographic profiles were found between the two groups of patients with and without concurrent MTX use. Discontinuation was reported in 44 (33.6\%) of all TOFA patients with a median survival of 31.3 months. Overall retention of TOFA at 6, 12 and 24 months was 80.5\%, 63.1\% and 53.5\% respectively. These findings are very similar to the results reported from the RHUMADATA registry at ACR 2018. Fifteen (34.0\%) patients stopped their TOFA due to non-response/loss of response, 22 (50.0\%) due to adverse events, and 7 (16\%) due to other reasons. Patients also stayed on TOFA longer when they concurrently used MTX compared to TOFA without MTX.

**Conclusion:** We found that half of the RA patients remained on TOFA 31 months after initiation. Patients also stayed on TOFA longer when they concurrently used MTX compared to TOFA without MTX.

**REFERENCES:**


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Disclosure of Interests: Burkhard Moeller Consultant for: Swissmedic

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**Background:** Tofacitinib (TOFA) is an oral, small molecule drug which can be used as an alternative to biologic disease modifying anti-rheumatic drugs (bDMARDs) for rheumatoid arthritis (RA) treatment and is prescribed alone or with methotrexate (MTX).

**Objectives:** We aimed to evaluate the discontinuation rate of this drug, with and without concurrent MTX, with and without prior biologic use, in patients with RA using real world data from a Canadian (Ontario) observational cohort.

**Methods:** Patients enrolled in the Ontario Best Practices Research Initiative (OBDI) who started TOFA after its approval in Canada (June 2014) were included in this analysis. Patients were followed from TOFA initiation until discontinuation, death, lost to follow-up, or last visit, whichever came first. Time to discontinuation of TOFA, due to any reason, in patients 1) with and without concurrent MTX use; 2) with or without prior biologic use was assessed using Kaplan-Meier survival analysis.

**Results:** Among the 131 patients, 70 (53.4\%) received TOFA without MTX and 61 (46.6\%) TOFA with MTX. Mean (SD) age and disease duration were 60.2 (0.90) years and 13.7 (0.80) years, respectively. The majority were females (89.3\%) and most had prior biologic use history (74.0\%). At baseline, no significant differences in disease activity and sociodemographic profiles were found between the two groups of patients with and without concurrent MTX use. Discontinuation was reported in 44 (33.6\%) of all TOFA patients with a median survival of 31.3 months. Overall retention of TOFA at 6, 12 and 24 months was 80.5\%, 63.1\% and 53.5\% respectively. These findings are very similar to the results reported from the RHUMADATA registry at ACR 2018. Fifteen (34.0\%) patients stopped their TOFA due to non-response/loss of response, 22 (50.0\%) due to adverse events, and 7 (16\%) due to other reasons. At 6 and 12 months' follow-up, more patients remained on TOFA in the ‘TOFA with MTX’ group (88.3\% and 73.1\%, respectively) compared to the ‘TOFA without MTX’ group (73.9\% and 54.6\%, respectively) (Logrank p=0.05). There was no significant difference in TOFA discontinuation between the two groups of patients with and without prior biologic use (Logrank p=0.77).

**Conclusion:** We found that half of the RA patients remained on TOFA 31 months after initiation. Patients also stayed on TOFA longer when they concurrently used MTX compared to TOFA without MTX.

**REFERENCES:**


Disclosure of Interests: Mohammad Movahedi: None declared, Angela Cesca: None declared, Xiuying Li: None declared, Claire Bombardier: Grant/research support from: Abbvie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Consultant for: Abbvie, Hospira, Janssen, Merck, Novartis, Pfizer Inc, Sanofi, Speakers bureau: Roche

Scientific Abstracts
FRI0164

INCIDENCE RATE AND CHARACTERIZATION OF
HERPES ZOSTER IN PATIENTS WITH MODERATE-TOSEVERE RHEUMATOID ARTHRITIS: AN UPDATE FROM
BARICITINIB CLINICAL STUDIES

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Background: Baricitinib (BARI) is a selective inhibitor of Janus kinase
(JAK) 1 and JAK2, approved for the treatment of moderately to severely
active rheumatoid arthritis (RA) in adults in over 50 countries, including
the United States, Europe and Japan. Due to their disease and associated therapy with disease-modifying anti-rheumatic drugs (DMARDs), RA
patients (pts) have an increased risk of herpes zoster (HZ) compared
with the general population.1 Furthermore, the incidence of HZ is
increased in RA pts treated with BARI versus placebo (PBO).2
Objectives: To determine the long-term overall and geographical incidence, time to first event and risk factors for HZ in BARI-treated RA pts.
Methods: Data were pooled from nine completed Phase 1, 2, and 3
studies of BARI in RA pts, including six randomised, PBO-controlled studies (0–24 weeks in DMARD-inadequate responders, including RA-BUILD,
RA-BEACON and the long-term extension study, RA-BEYOND [data cut
off February 13, 2018]), and active-controlled studies with methotrexate
(MTX; RA-BEGIN study in DMARD-naïve pts) and adalimumab (RA-BEAM
study in MTX-inadequate responders). The HZ incidence was evaluated
for all RA pts who had ever received BARI (any dose) and the HZ incidence rate (IR) was calculated as the number of pts with an HZ event
per 100 patient–years of observation (PYO). Exposure included up to 28
days after treatment cessation, and was censored at the HZ event date.
Univariate and multivariate Cox proportional hazard regression models
were used to evaluate risk factors for HZ.

Results: Of 3770 RA pts treated with BARI, median age at study entry
was 54 years (range 20–90 years), approximately one-quarter were each
from North America (n=840; 22%), EU (783; 21%), Asia (959; 25%) and
Central America (760; 20%), median time from RA diagnosis was 5
years, 2938 (78%) and 1754 (47%) were on concomitant MTX or corticosteroids (CS; mean dose 6.2 mg/day), respectively. HZ was reported in
323 (9%) pts over 9892 PYO, with median BARI exposure of 1115
days. Of these pts, 12 (4%) had a history of HZ, and 256 (79%) and
168 (52%) were on concomitant MTX and CS, respectively. The median
time to first HZ event was 538 days and the overall IR of HZ was 3.3/
100 PYO, which did not increase significantly over time (Fig 1). Twentysix (8%) cases were multidermatomal, and no visceral disease was
reported. Eight (2%) pts showed involvement of the ophthalmic division of
the Vth cranial nerve and 9 (3%) experienced recurrent HZ during observation. Only 11 HZ pts (4%) had received prior HZ vaccination. Multivariate analyses showed that older age (hazard ratio [HR] 1.30, 95%
confidence interval [CI] 1.17, 1.43) and geographical region (Asia,

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especially Japan, Taiwan and South Korea; HR 1.82, 95%
Fig 2) were associated with a higher risk of HZ.
Conclusion: HZ incidence in BARI-treated RA pts did not
time and the majority of HZ events were monodermatomal
cated. Pts who were older and those from Asia were at
of a HZ event.

755

CI 1.28, 2.58;
increase over
and uncompliincreased risk

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Company, Wen-Shuo Wu Shareholder of: Eli Lilly and Company,
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To assess health-related quality of life (HRQoL) of Japanese patients with RA who had an inadequate response to MTX.

Methods: This multicentre, randomised, double-blind, parallel-group, placebo-controlled, phase 3 study recruited patients in Japan with active RA and inadequate response to MTX. Patients were randomised 1:1:1 to 52-week placebo+MTX (PBO), peficitinib 100 mg QD+MTX (PEFI 100 mg) or peficitinib 150 mg QD+MTX (PEFI 150 mg). The PBO group was switched to PUF 100 mg or 150 mg at Week 12 (for non-responders) or Week 28 (for remaining patients). Patient- and physician-reported outcome assessments included: Physician’s Global Assessment of disease activity (PGA); Subject’s Global Assessment of disease activity (SGA); and Subject’s Global Assessment of pain (SGAP) by visual analogue scale. Physical function was evaluated using Health Assessment Questionnaire-Disability Index (HAQ-DI). All assessments were conducted at each visit from baseline to the end of study.

Results: 519 patients were treated: PBO (n=170), PEF1 100 mg (n=175) and PEF1 150 mg (n=174). One PEF1 100 mg patient was excluded from the analysis due to protocol deviation. At Weeks 12/early termination (ET) and 28/ET, both PEF1 groups were associated with significant improvements in PGA, SGA, SGAP and HAQ-DI (Table 1). These outcomes were maintained or improved at end of treatment (EOT; Week 52/ET) when compared to placebo. Changes from baseline in PGA, SGA, SGAP and HAQ-DI in the PEF1 100 mg and PEF1 150 mg groups were: -38.41,-43.33; -29.34,-34.05; -28.94,-32.68; and -0.36,-0.51, respectively. Significantly greater proportions of patients achieved functional remission and a minimum clinically important (MCI) reduction in HAQ-DI score (>0.5 and reduction of >0.22, respectively) at Weeks 12/ET and 28/ET in both PEF1 groups than in the PBO group (p<0.001 vs PBO for both PEF1 doses; Table 1). In the PEF1 100 mg and PEF1 150 mg groups at EOT, functional remission occurred in 105/172 (61.0%) and 106/171 (62.0%) patients with MCI reduction in HAQ-DI score occurred in 99/172 (57.6%) and 120/171 (70.2%) patients, respectively.

Conclusion: Measures of PGA, SGA, SGAP and HAQ-DI in patients with RA who had an inadequate response to MTX demonstrated improved HRQoL with peficitinib; PEF1 150 mg QD showed similar or numerically greater changes in HRQoL than PEF1 100 mg QD. Improvements were maintained or improved to the EOT and demonstrated a significant benefit for patients with RA in Japan.
Methods: Adult (≥18y) patients with symptomatic, refractory inflammatory mono- or oligoarthritis were included for RSO with Yttrium-90 citrate as part of a phase-III, prospective, open-label non-controlled trial. All patients were required to have failed 6-months of medical therapy and 2 intraarticular injections and have minimal evidence of cartilage or bone destruction. Only large and medium-sized joints were included (i.e. knees, ankles, wrists and elbows). The dose of Yttrium was adjusted based on the size of joint. Follow-up evaluations were done at 3, 6 and 12 months after RSO. Safety was assessed by patient and clinician reported adverse events. Clinical response was measured by improvement in joint tender- ness, effusion and range of motion.

Results: A total of 74 patients and 83 joints (88% knees) were treated with Yttrium-90 citrate. The underlying diagnosis included 25.7% RA, 34% SpA, 11% IA, and 10.3% other inflammatory arthritis. Complications included 3 post-RSO flares, 1 septic joint and 2 injection site skin infec- tions. Joint tenderness was reported in 93.8% of joints at baseline, com- pared to 50.0% at 3mo (p<0.001), 55.6% at 6mo (p<0.001) and 40.4% at 12mo (p<0.001). Joint effusion was present in 95.1% of joints at base- line, 44.3% at 3mo (p<0.001), 51.4% at 6mo (p<0.001) and 47.4% at 12mo (p<0.001). 73.9% of joints had improvement in range of motion at 3mo, 55.9% at 6mo and 60.7% at 12mo.

Conclusion: These results confirm the clinical efficacy and safety of Yttrium-90-citrate RSO for refractory synovitis with a sustained clinical ben- efit at 12 months. This is the first such study in a Canadian cohort. RSO with Yttrium is a safe alternative to surgical synovectomy in refrac- tory cases.

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Conclusion: This study showed positive effects on disease activity and blood lipid levels of a diet combining foods with anti-inflammatory properties, but the results must be confirmed in larger studies.

REFERENCES:


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FR0169 DOES INITIATING TOCILIZUMAB LEAD TO BETTER DISEASE CONTROL COMPARED TO INITIATING MTX WITH DOSE PREDNISONE IN EARLY RHEUMATOID ARTHRITIS? AN INDIRECT COMPARISON OF U-ACT-EARLY AND CAMERA-II TREAT-TO-TARGET TRIALS
Maxime Verhoeven1, Janneke Tekstra1, M Jacob. van Laar 1, Johannes WJ Bijlsma1, Attila Pelthoe-Schramm2, Michelle Born3, Floris Laleber1, Paco Welsing1. 1University Medical Center Utrecht, Utrecht, Netherlands; 2Hoffmann-La Roche, Basel, Switzerland; 3Roche Nederland BV, Woerden, Netherlands

Background: Treatment with methotrexate (MTX), often with concomitant glucocorticoids, is the cornerstone of early rheumatoid arthritis (RA) therapy. However, it may be less effective compared to (expensive) biological disease modifying anti-rheumatic drugs, such as tocilizumab (TCZ). Hitherto, the effectiveness and safety of MTX in combination with glucocorticoids have never been compared to TCZ with or without MTX.

Objectives: To compare effectiveness and safety of initiating TCZ, or TCZ with MTX (TCZ+MTX) to initiation of MTX with 10mg prednisone (MTX+Pred) all in a step-up treat-to-target treatment strategy in early RA patients.

Methods: Individual patient data of the U-Act-Early (n=237) and CAMERA-II (n=236) trials were used. Both were 2-year, double-blind, randomised, placebo-controlled studies evaluating step-up tight-control, treat-to-target treatment strategies with the opportunity to taper, in case of suspected, placebo-controlled studies evaluating step-up tight-control, treat-to-target treatment strategies with the opportunity to taper, in case of sustained remission, TCZ and/or MTX.

Using MTX (n=109+119) as the reference strategy, TCZ+MTX (n=106) and TCZ (n=103) were compared with MTX+Pred (n=117): primary outcome was the disease activity score (DAS28) over time. Secondary outcomes were remission, TCZ and/or MTX.

Conclusions: TCZ+MTX to initiation of MTX with 10mg prednisone (MTX+Pred) all in a step-up treat-to-target treatment strategy in early RA patients.

Conclusions: In early RA patients, TCZ-based strategies resulted in better DAS28 over time compared to MTX+Pred, as well as higher percentage of remission, part of these effects may be due to a specific effect of TCZ on APRs.

REFERENCES:


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FR0170 PHYSICAL ACTIVITY LEVEL IN RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW
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Background: Rheumatoid arthritis (RA) is one of the most common inflammatory rheumatism characterized by an increased cardiovascular risk. Regarding the last EULAR recommendations, physical activity is an important part of the management of RA. The evaluation of physical activity level is needed to know RA patients practices. However, to our knowledge, there is no consensual measure tool of the physical activity level for patients suffering RA.

Objectives: The aim of this study is to evaluate the different methods of measurement of physical activity levels in RA.

Methods: This is a systematic review of literature realized on the PubMed and Cochrane databases and meeting the PRISMA recommendations. We used the following key words: - « physical activity », - « physical activity level » AND « rheumatoid arthritis » . We included only article written in English language and with RA patients older than 18 years old.

Results: We identified 190 studies with the key words, 51 words were selected on title and 23 articles have been identified as eligible. Finally, 19 studies were included in this review. In total, of the 19 selected studies, 13567 RA patients were evaluated on their level of physical activity. There were 73,4% female with a mean age of 56,1 years. In 10 studies, the BMI was available with results between 25 and 30 kg/m2. Two methods for measuring physical activity levels have been identified.
Questionnaires, a subjective tool, were used in 13 studies. It should be noted that 8 different questionnaires were used in these studies with recurrent use of the IPAQ (international validated questionnaire in general population) and SQUASH (validated in English language in RA). In these studies, responses at Wk 24 were generally sedentary with a proportion of patients meeting WHO physical activity recommendations ranging from 20 to 77%. It appears that Scandinavian patients are clearly the most active.

Concerning objective measurement tools, 9 studies evaluated the level of physical activity using activity tracker. 7 studies used the accelerometer, 1 used the VO2 max, 1 used an actimeter. All studies showed a sedentary behavior. In these studies, the results were expressed as energy expenditure and not as a percentage of patients meeting WHO recommendations. Thus, the comparison between the two methods is difficult but accelerometer showed a significant decrease in the level of physical activity in RA.

The oldest studies (2002 and 2007) showed that only 30% of patient met the WHO recommendations, but the recent studies (2017 and 2018) showed the same prevalence of sedentary behavior. The disease activity and the disease duration were comparable between the different studies.

Conclusion: Patients with rheumatoid arthritis present a sedentary behavior. Objective and subjective tools showed the low level of physical activity over the past decade. These data illustrate the necessity of the promotion of physical activity in rheumatoid arthritis.

Disclosure of Interests: None declared

FRIO171 CLINICAL RESPONSES IN PATIENTS WITH INADEQUATE RESPONSE TO BDMARDS UPON TREATMENT WITH UPADACITINIB

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Background: Upadacitinib (UPA), a JAK1-selective inhibitor, demonstrated efficacy in the SELECT-BEYOND study in patients (pts) with moderate to severe rheumatoid arthritis (RA) on a stable dose of csDMARDs who had inadequate response (IR) or intolerance to bDMARDs.

Objectives: In this analysis we evaluated clinical responses among pts receiving UPA and placebo (PBO) based on the number and mechanism of action (MOA) of prior bDMARDs.

Methods: 498 pts were randomized to UPA 15mg or UPA 30mg once daily (QD) or PBO for 12 weeks (wks), after which pts on PBO received UPA 15 or 30mg QD from Wk 12 onwards. Pts were subgrouped by the number and/or MOA of bDMARD(s) received prior to enrollment: 1) lack of efficacy (LoE), 2) anti-TNF, 3) LoE to an anti-IL-6, and 4) LoE to an anti-IL-6, and those who had IR/intolerance to 1, 2 or 3 prior bDMARDs, with consistent safety profiles as to the overall study population.

Results: Overall baseline disease duration was 17.7 years, with 117 patients (23%) enrolled in the LoE population, including in pts with LoE to an anti-TNF or an anti-IL-6, and those who had IR/intolerance to 1, 2 or 3 prior bDMARDs, with consistent safety profiles as to the overall study population.

Acknowledgement: AbbVie, Inc was the study sponsor, contributed to study design, data collection, analysis & interpretation, and to writing, reviewing, and approval of final version. Medical writing support was provided by Naina Barreto, PhD, of AbbVie, Inc.

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FRIO172 A PROSPECTIVE AUDIT OF A PATIENT COHORT PRESCRIBED HYDROXYCHLOROQUINE FOR RHEUMATOID ARTHRITIS AND OTHER INFLAMMATORY RHEUMATIC DISEASES IN ORDER TO PRIORITIZE RETINOPATHY SCREENING AND ESTIMATE THE NEED FOR DRUG EDUCATION APPOINTMENTS

Brandon Yeo1, Audrey Low2, Alexandra Chadwick2, Sarah Wills2, 1University of Manchester, Faculty of Biology, Medicine, and Health, Manchester, United Kingdom; 2Salford Royal NHS Foundation Trust, Rheumatology, Salford, United Kingdom

Background: Hydroxychloroquine (HCQ) is prescribed for rheumatoid arthritis (RA), systemic lupus erythematosus (SLE) and inflammatory osteoarthritis (IOA). A potential side effect of HCQ is drug-induced retinopathy, with an increased risk reported for patients taking >5mg/kg/day and those who have renal impairment.

In the United Kingdom, the Royal College of Ophthalmologists (RCO) has published new screening guidelines for HCQ, recommending 1) patients receive doses <5mg/kg/day and 2) all patients planning to be on HCQ long term (>5 years) should receive baseline eye examination ideally within 6 months of starting HCQ and definitely within 1 year.

Objectives: This audit aimed to: 1) audit dose prescription by body weight, 2) estimate the screening burden on ophthalmology services, 3) estimate service needs for additional drug education appointments to counsel patients starting HCQ.

Methods: A list of all patients who were started on HCQ from January 2017 to February 2018 was obtained from the outpatient pharmacy at Salford Royal Hospital. Demographic and clinical data were extracted from electronic patient records. High-risk patients were defined as those who were prescribed an initial dose of >5mg/kg/day or those with an eGFR <50 ml/min/1.73m^2. Patients were followed until the most recent follow-up visit by July 2018 to determine drug persistence and reasons for HCQ cessation, if any.

Results: 177 patients were started on HCQ, with most (82%) diagnosed with rheumatoid arthritis (Table). Most patients were female (76%) and a third (35%) were older than 60 years old. 9 patients (5.1%) had impaired renal function. 83 patients (47%) were prescribed an initial daily dose of HCQ >5mg/kg/day. By July 2018 (follow-up duration 6-19 months), 127 patients (71.8%) remained on HCQ and will need baseline eye screening.

Disclosure of Interests: None declared
The remaining 50 patients (28.2%) stopped HCQ due to inefficacy (7.3%), GI disturbance (3.4%), rash (3.4%).

Table:

<table>
<thead>
<tr>
<th>Patients prescribed</th>
<th>All</th>
<th>Rheumatoid arthritis</th>
<th>Connective tissue disease</th>
<th>Inflammatory arthritis</th>
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<tr>
<td>Jan 2017 to Feb 2018</td>
<td>N=177</td>
<td>N=110</td>
<td>N=56</td>
<td>N=11</td>
</tr>
<tr>
<td>Median age (interquartile range); years</td>
<td>54 (44-65)</td>
<td>54 (43-66)</td>
<td>54 (38-61)</td>
<td>57 (52-61)</td>
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<tr>
<td>Age &gt;60 years; n (%)</td>
<td>61 (34.5)</td>
<td>42 (38.2)</td>
<td>13 (28.3)</td>
<td>6 (28.6)</td>
</tr>
<tr>
<td>Females; n (%)</td>
<td>134 (75.7)</td>
<td>74 (67.3)</td>
<td>41 (89.1)</td>
<td>19 (90.5)</td>
</tr>
<tr>
<td>eGFR &lt;50; n (%)</td>
<td>9 (5.1)</td>
<td>4 (3.7)</td>
<td>3 (6.5)</td>
<td>2 (9.5)</td>
</tr>
<tr>
<td>Mean height (cm)</td>
<td>165</td>
<td>166</td>
<td>162</td>
<td>164</td>
</tr>
<tr>
<td>Mean weight (kg)</td>
<td>77</td>
<td>77</td>
<td>73</td>
<td>84</td>
</tr>
<tr>
<td>Mean BMI</td>
<td>29</td>
<td>29</td>
<td>27</td>
<td>32</td>
</tr>
<tr>
<td>Dose &gt;5mg/kg/day absolute body weight</td>
<td>83 (46.9)</td>
<td>54 (49.1)</td>
<td>23 (50.0)</td>
<td>6 (28.6)</td>
</tr>
</tbody>
</table>

Conclusion: Clinicians need to be cognisant of recent guidelines and adjust HCQ dosing to the recommended 5mg/kg/day. Additional specialist pharmacist input for DED (12-13 extra appointments per month) is required. Almost a third of the patients had stopped HCQ by July 2018, mostly due to side effects and reported inefficacy. However, a large proportion (71%) of HCQ starters remain on the drug by 6-12 months and will need baseline screening. Ophthalmology services can estimate services and capacity required for baseline HCQ screening per annum.

REFERENCE:
[1] Royal College of Ophthalmology Guideline: Hydroxychloroquine and Chloroquine Retinopathy Screening 2018

Acknowledgement: We would like to thank Lloyds Pharmacy of Salford Royal NHS Foundation Trust for providing the data on HCQ prescribing from Jan 2017 to Feb 2018.

Disclosure of Interests: None declared

SLE, Sjögren’s and APS – treatment

FR10173 HOW WELL DO CLINICAL TRIALS REPRESENT REAL WORLD LUPUS NEPHRITIS PATIENTS?
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Background: Lupus nephritis (LN) represents a serious manifestation of systemic lupus erythematosus (SLE). LN therapies include glucocorticoids and conventional immunosuppressants as standard of care (SOC) or biological therapies. Rituximab (RTX) is used in some patients but published clinical trials have failed to meet their primary end-points. SLE trials have limitations including stringent eligibility criteria in an attempt to achieve homogeneity, however poor recruitment can lead to early termination as such, clinical trials may not reflect the disease population of interest and outcomes can be difficult to generalise.

Objectives: Our aim was to apply published trial eligibility criteria to patients with LN in a large UK-wide register to quantify how accurately LN clinical trials represent a real-world cohort.

Methods: A literature review of recent major published LN clinical trials was performed (n=6). Inclusion and exclusion criteria common across trials were applied to all patients registered in the BILAG-Biologics Register (BILAG-BR) with active LN, a UK-wide registry of patients with SLE. Active LN was defined as a BILAG score A or B. We applied available data to inclusion criteria including ACR/SLECC criteria for SLE diagnosis, positive dsDNA or ANA antibodies and a UPCR>100mg/mmol. Available exclusion criteria were active CNS lupus, a history of malignancy or CKD 4/5, hypogammaglobulinaemia, and cyclophosphamide use within 30 days of entry or previous B cell therapy within 12 months of entry.

Results: As of July 2018, 259/897 (28.9%) patients in BILAG-BR had active LN. In the RTX and SOC groups, 70/230 (30.4%) and 10/29 (34.5%) respectively did not meet all inclusion criteria (Table 1). Meanwhile 118/230 (51.3%) of RTX patients and 6/29 (20.7%) of SOC patients met one or more exclusion criteria. Overall 131/259 (50.6%) did not satisfy all inclusion and exclusion criteria and thus were ineligible for clinical trial entry. Of those patients deemed ineligible, the RTX patients were younger (median age 36 vs. 49 in SOC group, p=0.653) and the majority were non-Caucasian (n=71/121 (58.7%), p=0.251). The majority of patients in both treatment groups were female (p=0.089). UPCR <100mg/mmol (n=135) was the most common exclusion criteria missed whilst the commonest exclusion criteria were concomitant active CNS disease (n=22) and hypogammaglobulinaemia (n=24).

Inclusion criteria

<table>
<thead>
<tr>
<th>RTX</th>
<th>SOC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Does not meet ACR/SLECC criteria for SLE</td>
<td>5</td>
</tr>
<tr>
<td>Negative dsDNA/ANA</td>
<td>30</td>
</tr>
<tr>
<td>UPCR &lt;100mg/mmol</td>
<td>35</td>
</tr>
</tbody>
</table>

Exclusion criteria

<table>
<thead>
<tr>
<th>RTX</th>
<th>SOC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active CNS lupus (BILAG A/B)</td>
<td>22</td>
</tr>
<tr>
<td>H/o hepatitis B or C</td>
<td>8</td>
</tr>
<tr>
<td>H/o malignancy</td>
<td>18</td>
</tr>
<tr>
<td>Cyclophosphamide &lt;90 days before entry</td>
<td>13</td>
</tr>
<tr>
<td>B cell therapy &lt;1 year before entry</td>
<td>14</td>
</tr>
<tr>
<td>Hypogammaglobulinaemia &gt;6 (IgG)</td>
<td>24</td>
</tr>
</tbody>
</table>

Total (n) | 118 | 6 |

Conclusion: In a large national cohort of active LN we found that 50.6% of patients would not be eligible for clinical trial entry using published entry criteria. This poses significant implications on the study of LN treatment in patients with more severe disease. When designing clinical trials, the stringency of eligibility criteria should be reviewed in order to provide greater representation of the target disease population.

Disclosure of Interests: Sophie Collinson: None declared, Ben Parker: Grant/research support from: GSK, Consultant for: AZ, UCB, GSK, Eoghan McCarthy: None declared, Ian N. Bruce: Grant/research support from: Genzyme Sanofi, GlaxoSmithKline, Consultant for: AstraZeneca, Eli Lilly, GlaxoSmithKline, ILTOO Pharma, MedImmune, Merck Serono, Speakers bureau: GlaxoSmithKline, UCB Pharma

FR10174 SUBCUTANEOUS DOSING OF THE NOVEL ANTI-CD40 ANTIBODY ICX501 ACHIEVES TARGET DRUG EXPOSURE AND CLINICAL EFFICACY IN PRIMARY SJÖGREEN’S SYNDROME: RESULTS OF A PHASE IA RANDOMISED OPEN LABEL TWO ARM PARALLEL GROUP TRIAL

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Background: Primary Sjögren’s syndrome (pSS) is a systemic progressive autoimmune disease characterised by formation of lymphoid structures and germinal centres within glandular tissue. Ixicalimab (CFZ533) is a novel monoclonal antibody that potently and selectively blocks CD40, a co-stimulatory pathway receptor important for germinal centre reactions.
**Objective:** To test IV versus SC loading doses of iscalimab followed by SC maintenance dosing, as a means of achieving target drug exposure and clinical efficacy.

**Methods:** Patients with clinically active pSS [EULAR Sjögren’s Syndrome Disease Activity Index (ESSDAI) >6] were randomised to receive either 600 mg SC iscalimab weekly on 4 occasions, followed by 300 mg SC weekly until week 12, or a single IV dose of 10 mg/kg iscalimab on study Day 1, followed by 300 mg SC weekly until week 12. Subjects and investigator staff remained blinded to study treatment allocation until first dosing.

**Results:** Twenty-five patients were randomised; 13 in the SC loading and 12 in the IV loading arms. Baseline characteristics were similar to the previous phase IIa cohorts with mean ESSDAI scores of 12.7 (SD 6.1) and 10.4 (5.9) in the SC and IV loading arms respectively. In Arm 1 (SC) and Arm 2 (IV), the mean trough plasma concentrations were 169 µg/mL (SD 64.1, CV 38%) and 135 µg/mL (SD 70.9, CV 53%) on Day 85, respectively. Both values were well above levels previously reported to be sufficient for suppression of germinal centre development and T dependent antigen responses in cynomolgus monkeys. Consistent with this finding, clinically important improvements were seen in both arms with a mean decrease in ESSDAI scores of -5.5 (+/- SD: 5.5) and -7.6 (+/- 7.1) points from baseline to Day 85 in the SC and IV dosing arms. Improvements were also seen in EULAR Sjögren’s Syndrome Patient Reported Index (ESSPRI) scores: -1.67 (+/- 2.0) and -1.17 (+/- 2.3), respectively. Other secondary efficacy outcomes showed similar patterns of improvement. Treatment with iscalimab was associated with a reduction in the germinal centre-related serum biomarker CXC1L1 in both groups. Overall, iscalimab was safe and well-tolerated with no new safety signal emerging. One subject experienced three SAEs (hemarthrosis, worsening of right knee pain and swelling requiring arthroscopy) in the safety follow-up period, all unrelated to study drug.

**Conclusion:** These results further support the safety and efficacy of iscalimab in pSS and the suitability of SC dosing for future development.
Objectives: This Phase 2 study was designed to minimize background medications and placebo responses to improve interpretation of a small trial in a complex, heterogeneous disease.

Methods: SLE patients were enrolled with active disease, ameliorated during screening with >160 mg of IM Depo-Medrol. Improvement was required before randomization, defined by decrease in SLEDAI ≥4 points or ≥1 grade in a BILAG A or B score. Immunosuppressive drugs were stopped except antimalarials and/or ≤10 mg/day prednisone or equivalent. Subjects were randomized to IV XmAb5871 (5 mg/kg) or placebo and given Depo-Medrol 80 mg IM on Days 1 and 15, after which, steroid impact was expected to withdraw gradually. Study treatments were given Q14 days for up to 16 doses or loss of improvement (LOI), defined as SLEDAI increase ≥4 points OR new BILAG A or B, with investigator-determined significance. At LOI, patients could receive immediate standard treatments. The primary endpoint was the proportion with no LOI by Day 225 in the efficacy evaluable group (those completing Day 225 or withdrawn for LOI or drug-related adverse event).

Results: 104 subjects were randomized: 99 female, median age 45 (20–76) years. The primary endpoint was met by 21 (42%) of XmAb5871-treated patients vs 12 (28.6%) of the placebo group (p=0.18). All but one responder also fulfilled the SRI-4 response definition from screening to completion. Results did not differ in those with or without anti-dsDNA and/or ENA antibodies. Time to flare was significantly longer in the XmAb5871 group (p=0.025) (figure 1). XmAb5871-treated patients with LOI had less recurrent disease after IM steroid cessation than those in the placebo group: 6 (20%) of placebo patients developed BILAG A scores vs 3 (13%) in the active arm. 9 (30%) of worsening placebo patients had SLEDAI increase ≥7 vs 0 in the XmAb5871 group. SLEDAI scores were higher and increased sooner after disease nadir with placebo vs XmAb5871 (figure 2); 16 (30.8%) of XmAb5871 patients vs 7 (13.5%) placebo patients sustained LLDA (low disease) during months 6-8 (p=0.045). Transient, infusion-related gastrointestinal side effects occurred in XmAb5871-treated patients during the 1st or 2nd infusion. There were 8 SAEs in 7 XmAb5871-treated subjects, 5 in 4 placebo patients, no opportunistic infections, and no deaths. Infection rate was low compared to other SLE trials.

Conclusion: XmAb5871 was well-tolerated. Preliminary data from this small trial indicates suppression of disease recurrence after treatment withdrawal, supporting further evaluation of XmAb5871 in SLE.


CLUSTER PROFILING OF PATIENTS IN A REAL-WORLD DATASET WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND THEIR ASSOCIATED TREATMENTS

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Background: Previous systemic lupus erythematosus (SLE) studies have identified potential clusters of SLE clinical manifestations. Objectives: To describe the presentation of SLE across different cohorts of patients and describe standard of care within clusters.

Methods: Cross-sectional study of 263 rheumatologists in the US and EUS. Data were collected from the Adelphi Real World 2015 Lupus Disease Specific Programme. Physicians completed patient record forms (PRFs) for the next 5 patients consulting with SLE; these patients completed patient reported outcome (PROMs) forms describing how SLE affected them. PRFs data include patient characteristics and management history. PROMs focused on similar data collection, including patient reported outcome measures on the humanistic burden. Principal-component factor analysis reduced 39 unique SLE symptoms to 8 factors. These factors were used as covariates in latent class analysis to provide discrete cohorts of patients. Chi-squared and Kruskal-Wallis tests compared patient outcomes across clusters.

Results: Data were extracted from 1376 PRFs. Factor analysis resulted in 8 clusters of concurrent symptoms: joint, haematological, constitutional/mental health, skin, circulatory, cardiovascular, renal, and musculoskeletal symptoms respectively. The four-cluster solution was selected. Cluster 1 displayed the lowest symptom burden, characterised by low skin involvement. Cluster 2 is characterised by joint and skin involvement. Cluster 3 & 4 had a high frequency of all factors, with cardiovascular involvement high in cluster 3 and renal/constitutional involvement high in cluster 4 (table 1).

Significant between-cluster differences were observed when comparing clinical and humanistic outcomes; physician/patient satisfaction were greatest in cluster 1 (physician satisfied 94.2% vs. 2: 90.8%, 3: 85.2%, 4: 74.4%, p<0.0001; patient 94.7% vs. 2: 93.9%, 3: 91.5%, 4: 79.2%, p<0.0001), whilst disease progression (deteriorating slowly 2.5% vs. 2: 12.9%, 3: 9.6%, 4: 25.5%, p=0.0001) and flaring in the last 12 months (flared 30.0% vs. 2: 54.8%, 3: 62.2%, 4: 70.8%, p<0.0001) differed significantly with worst outcomes seen in cluster 4.

Significant differences were also observed between clusters in relation to treatment proportions; anti-malarials (highest cluster 1: 70.5%), biologic DMARD (highest cluster 3: 17.5%), glucocorticoid and immunosuppressants (highest cluster 4: 85.5%, 74.5%).

Conclusion: This study adds to the evidence demonstrating the heterogeneous nature of SLE experienced within distinct patient clusters. Significant proportions of SLE patients experience high symptom burden and low levels of satisfaction. Additional analysis to understand limited biologic use in more severe patients is needed.


FRIO179 PREDICTION OF RESPONSE TO RITUXIMAB IN SLE USING A VALIDATED TWO-SCORE SYSTEM FOR INTERFERON

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Background: Rituximab (RTX) is used for resistant SLE but clinical response varies. We previously validated two interferon-stimulated gene expression scores (IFN-Score-A and IFN-Score-B) that improved prediction of clinical outcomes in SLE. IFN-Score-A included most commonly reported ISGs and predicted flares and glucocorticoid requirements. IFN-Score-B included ISGs that respond to multiple IFN subtypes and predicted development of SLE in At-Risk individuals. Diagnosis of SLE was associated with both scores, while only IFN-Score-B was elevated in RA. The British Society for Rheumatology Biologics Registry (BILAG-BR) collects samples for RTX-treated patients in the UK. MASTERPLANS is a consortium to identify predictors of drug response.

Objectives: To investigate whether IFN-Score-A and IFN-Score-B predict BILAG response to RTX at 6 months.

Methods: This is a preliminary analysis of the first RTX-treated patients in the BILAG-BR with complete data. Patients were recruited if they were starting within the first cycle of RTX for active SLE (BILAG A or 2xBILAG B) despite previous cyclophosphamide or mycophenolate mofetil. Disease activity was measured using BILAG-2004. Clinical response was defined as improvement by >=1 grade in active BILAG-2004 systems with no worsening in other systems. Whole blood was collected into TEMPUS tubes and RNA extracted. IFN-Scores were measured using a custom Taqman array as previously described [El Sherbiny et al., 2018]. Multivariate logistic regression was used to test IFN-Scores and baseline clinical covariates as predictors of BILAG response at 6 months.

Results: Samples were available from 147 patients, of whom 84 had complete baseline and 6 month clinical data available and were included in this analysis. 40/84 (47.6%) patients had BILAG response at 6 months. In univariate and multivariate analysis, high IFN-Score-B expression was significantly associated with clinical response (see table 1).

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Non-responders</th>
<th>Responders</th>
<th>Univariable OR (95% CI)</th>
<th>P</th>
<th>Multivariable OR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean, 95% CI)</td>
<td>40.5 (36.2,44.8)</td>
<td>40.9 (36.2,45.6)</td>
<td>1.015 (0.993,1.037)</td>
<td>0.188</td>
<td>0.994 (0.959,1.032)</td>
<td>0.765</td>
</tr>
<tr>
<td>Baseline organs affected</td>
<td>22/44</td>
<td>23/40</td>
<td>0.866 (0.468,1.601)</td>
<td>0.645</td>
<td>1.024 (0.381,2.750)</td>
<td>0.962</td>
</tr>
<tr>
<td>Musculoskeletal</td>
<td>21/44</td>
<td>18/40</td>
<td>0.728 (0.392,1.354)</td>
<td>0.728</td>
<td>0.424 (0.145,1.244)</td>
<td>0.118</td>
</tr>
<tr>
<td>Renal</td>
<td>21/44</td>
<td>16/40</td>
<td>0.869 (0.470,1.607)</td>
<td>0.654</td>
<td>0.290 (0.087,0.969)</td>
<td>0.044</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>9/44</td>
<td>5/40</td>
<td>1.250 (0.533,2.424)</td>
<td>0.591</td>
<td>0.627 (0.164,2.391)</td>
<td>0.494</td>
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<tr>
<td>Neurological</td>
<td>7/44</td>
<td>6/40</td>
<td>0.859 (0.358,2.065)</td>
<td>0.735</td>
<td>0.768 (0.170,3.473)</td>
<td>0.731</td>
</tr>
<tr>
<td>Arthralgia/Yes</td>
<td>41/44</td>
<td>39/40</td>
<td>1.458 (0.410,15.86)</td>
<td>0.560</td>
<td>0.037 (0.005,1.005)</td>
<td>0.050</td>
</tr>
<tr>
<td>IFN-Score-A (per unit)</td>
<td>2.49 (1.77,3.19)</td>
<td>1.74 (1.10,2.39)</td>
<td>0.845 (0.658,1.048)</td>
<td>0.126</td>
<td>1.651 (0.935,2.743)</td>
<td>0.086</td>
</tr>
<tr>
<td>IFN-Score-B (per unit)</td>
<td>2.36 (1.98,2.73)</td>
<td>1.76 (1.43,2.09)</td>
<td>0.606 (0.394,0.933)</td>
<td>0.023</td>
<td>0.267 (0.093,0.762)</td>
<td>0.014</td>
</tr>
</tbody>
</table>
Conclusion: This preliminary analysis suggests that assessment of IFN activity has a role in predicting response to RTX. A novel IFN score (Score B) was more predictive than classic ISGs (Score A). These results add to a body of work showing that IFN-Score B predicts clinically significant outcomes independently of overall IFN activity. Future work will analyse this biomarker in a larger cohort of patients and integrate with other putative clinical and biological predictors of response.

REFERENCE:

Disclosure of Interests: Edwoneiola Alase: None declared, Zoe Wigston: PLANS project.
Alexandre Dumusc, Thomas Huegle, Pascal Zufferey. Consultant for: consultancy honoraria from Abbvie, Celgene, Janssen, declared, Md Yuzaiful Md Yusof: None declared, John Reynolds: None declared, The Masterplans Consortium: None declared, Miriam Wittmann Consultant for: consultancy honoraria from Abbvie, Celgene, Janssen, L'Oreal, Novartis and Pfizer, Ian N. Bruce Grant/research support from: Genzyme Sanofi, GlaxoSmithKline, Consultant for: AstraZeneca, Eli Lilly, GlaxoSmithKline, ILTOO Pharma, MedImmune, Merck Serono, Speakers bureau: GlaxoSmithKline, UCB Pharma, Edward Vital Grant/research support from: Roche, GSK and AstraZeneca.


FRI0180 OFF-LABEL USE OF RITUXIMAB IN RHEUMATIC DISEASES, A SWISS TERTIARY CENTRE EXPERIENCE
Alexandre Dumusc, Thomas Huegle, Pascal Zufferey, University Hospital Lausanne (CHUV), Rheumatology, Lausanne, Switzerland

Background: Rituximab (RTX), a monoclonal antibody targeting CD20, is licenced for the treatment of rheumatoid arthritis (RA) for many years and more recently for ANCA-associated vasculitis. RTX is frequently used off-label to treat other auto-immune diseases (AID), especially connective tissue diseases (CTD). There are no published data about off-label use of RTX in AID in Switzerland.

Objectives: To describe off-label use of RTX in a real-life setting, when treating AID.

Methods: Retrospective cohort study of all patients treated with RTX in the Rheumatology Department between 2005 and 2017. Clinical efficacy of RTX after 12 and 24 months of treatment was evaluated with a semi-quantitative scale (no response (NR), partial (PR) and complete response (CR)); RTX discontinuation rate was also analysed using Kaplan-Meier method and log rank test to evaluate the difference between survival curves. Adverse events (AE), serious AE (SAE) were included in the safety analysis. Occurrences of hypogammaglobulinemia and anti-rituximab antibodies (ADA) were also reported.

Results: 178 patients treated with RTX could be identified: 28% for CTD, 63% for RA and 10% for other AID. Rituximab was used off-label in 73% of the patients according to official Swiss indications. No significant differences in terms of clinical response were observed in off-label indication after 12 months (NR: 15%/13%, PR:48%/52%, CR:3%/35%, n=108/31) and 24 months (NR:13%/9%, PR:3%/35%, CR:51%/57%, n=79/23) of treatment when compared with prescriptions following official Swiss indications, respectively. RTX discontinuation rate (HR 1.03 95% CI 0.71-1.49) was also similar between both groups.

Clinical response after RTX treatment did not differ significantly between patients with CTD and RA after 12 months (NR:10%/12%, PR:50%/52%, CR:40%/36%, n=4=84/24) and 24 months (NR:7%/9%, PR:32%/44%, CR:61%/47%, n=92/54, respectively). Detailed results are available in Table 1. Survival curves of rituximab treatment from CTD group closely matched that from RA group (HR 0.96 95% CI 0.65-1.44). Causes of RTX treatment discontinuation in patients with CTD (n=27) and RA (n=72) consisted of lack of efficiency (63%/56%), adverse event (19%/35%) and remission (19%/10%), respectively.

SAE (n=113) occurred in 33% of the patients and consisted mainly of infectious SAE (43%) and perfusion-related AE (6%). 6 patients died during RTX treatment. Low IgG levels were observed in 34% (50/149) of the patients graded as mild (20%), moderate (11%) or severe (3%). The nadir of IgG levels occurred after 4.5(3.5) years (mean (SD)) of RTX treatment. ADA were observed in 6/51 patients.

Disclosure of Interests: Alexandre Dumusc: None declared, Thomas Huegle Grant/research support from: AbbVie, Lilly, Novartis and Pfizer, Speakers bureau: AbbVie, Lilly, Novartis and Pfizer, Pascal Zufferey: None declared.


FRI0181 THE PLUTO STUDY: INTRAVENOUS BELIMUMAB IN CHILDREN WITH SYSTEMIC LUPUS ERYTHEMATOSUS
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Background: Belimumab (BEL), a monoclonal antibody targeting the B-lymphocyte stimulator, is approved in adults with active systemic lupus erythematosus (SLE). This is the first clinical trial of belimumab in pediatric patients with childhood-onset SLE (cSLE).

Objectives: PLUTO, a Phase 2, randomised, double-blind trial (BEL114055; NCT01649765), evaluated the efficacy, safety and pharmacokinetics (PK) of intravenous (IV) BEL vs placebo (PBO), plus standard of care (SoC), in cSLE.

Methods: Patients with cSLE 5–17 years of age were randomised to BEL 10 mg/kg IV or PBO every 4 weeks, plus SoC. Primary endpoint: SRI4 at Week 52. Major secondary endpoints: PRINCIPALACR 30 and 50 cSLE evaluation criteria for improvement at Week 52; cSLE core response variables at Week 52; and sustained SRI4 and ParentGQA (patient well-being) responses (Weeks 44–52). Other endpoints: components of SRI4 at Week 52; and frequency of severe flares using the

Disclosure of Interests: Nicolino Ruperto: None declared, Carlos Abud-Mendoza: None declared, Diego O. Viola: None declared, Inmaculada Calvo: None declared, Deborah M. Levy: None declared, Julia Calderon Gallegos: None declared, Manuel Fernandez: None declared, Vyacheslav Chasnyk: None declared, Vladimir Keltsev: None declared, Jordi Anton: None declared, Maria Gastanaga: None declared, Michael Shishov: None declared, Alina Boteanu: None declared, Michael Henrickson: None declared, David Roth: None declared, Herbert Steunperme: None declared, Mei-Lun Wang: None declared, Alberto Martini: None declared, Daniel J Lovel: None declared, Hermine Brunner: None declared.
modified SELENA-SLEDAI Flare Index. Safety and PK were assessed. Analyses were performed on the intent-to-treat population. The study was not powered to test for differences between groups; p-values were not calculated.

Results: 93 patients were included (BEL, n=53; PBO, n=40). Groups (BEL vs PBO) were balanced at baseline for age (mean [standard deviation] 13.5 [2.59] vs 14.8 [2.17] years, respectively) and SELENA-SLEDAI score (10.3 [3.34] vs 10.4 [3.63], respectively). Compared with PBO, there were more SRI4 responders (including all 3 components of SRI4), and PRINTO/ACR 30 and 50 responders in the BEL group (Figure). Likewise, more BEL vs PBO recipients had sustained improvement of SRI and patient well-being (ParentGA) (Figure).

Changes in cSLE core response variables are shown in the Table. Serious harms were 62% less frequent with BEL vs PBO (hazard ratio: 0.38 [95% CI 0.18, 0.82]). PK: BEL exposures in cSLE were similar to adult SLE studies. 9/53 (17%) BEL patients had ≥1 serious adverse event vs 14/40 (35%) PBO patients. One PBO patient died of acute pancreatitis.

Conclusion: The benefit-risk profile of BEL IV plus SC in cSLE is generally consistent with BEL in adult SLE. The 10 mg/kg IV dose used in adults may be an appropriate dose in cSLE.

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Disclosure of Interests: Nicola Nicola Ruperto Grant/research support from: The Gaslini Hospital, where NR works as full-time public employee, has received contributions (> 10.000 USD each) from the following industries in the last 3 years: BMS, Eli-Lilly, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Novartis, Pfizer, Roche, Sobi. This funding has been reinvested for the research activities of the hospital in a fully independent manner, without any commitment with third parties.

Consultant for: Received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: AbbVie, AstraZeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, Sanofi Servier, Sinergie, Sober, and Takeda. Speakers bureau: Received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: AbbVie, AstraZeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, Sanofi Servier, Sinergie, Sobi and Takeda. Carlos Abud-Mendoza: None declared. Diego O Volta: None declared. Immaculada Calvo Grant/research support from: received research grants from Pfizer, Roche, Novartis, Clementia, Sanofi, MSD, BMS and GSK, Consultant for: Advisory boards: Novartis, AbbVie, Speakers bureau: AbbVie, Roche, Novartis, SOBI, Deborah Levy Consultant for: received consulting fees and/or honoraria from AbbVie and Janssen, Julia Calderon Gallegos: None declared. Daniel J Lovell Consultant for: all pharmaceutical companies in the past 3 years: Ablynx, AbbVie, AstraZeneca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, Sanofi Servier, Sinergie, Sobi and Takeda. Carlos Abud-Mendoza: None declared. Diego O Volta: None declared. Inmaculada Calvo Grant/research support from: received research grants from Pfizer, Roche, Novartis, Clementia, Sanofi, MSD, BMS and GSK, Consultant for: Advisory boards: Novartis, AbbVie, Speakers bureau: AbbVie, Roche, Novartis, SOBI, Deborah Levy Consultant for: received consulting fees and/or honoraria from AbbVie and Janssen, Maria Gastanaga: None declared. Michael Shishov: None declared. Amina Boteanu: None declared. Michael Henrickson: None declared. Damon Bass Shareholder of: GSK, Employee of: GSK, Ken Clark Shareholder of: GSK, Employee of: GSK, Anne Hammer Shareholder of: GSK, Employee of: GSK, Beulah Ji Shareholder of: GSK, Employee of: GSK, Antonio Nino Shareholder of: GSK, Employee of: GSK, David Roth Shareholder of: GSK, Employee of: GSK, Herbert Stümper Shareholder of: GSK, Employee of: GSK, Mei-Lun Wang Employee of: former employee of GSK, Alberto Martini Consultant for: I do not have any conflict of interest to declare since starting from 1 March 2016 I became the Scientific Director of the G. Gaslini Hospital; therefore, my role does not allow me to render private consultancies resulting in personal income. I perform consultancy activities on behalf of the Gaslini Institute for the companies listed below: AbbVie, Biogen, Boehringer Ingelheim, Bristol-Myers Squibb, EMD Serono, Janssen, Novartis, Pfizer, R-Pharma.

The money received for these activities are directly transferred to the Gaslini Institute’s bank account. Before March 2016, I was the head of the Pediatric Rheumatology Department at the G. Gaslini Hospital, where the PRINTO Coordinating Centre is located. For the coordination activity of the PRINTO network, the Gaslini Hospital received contributions from the industries listed in this section. This money has been reinvested for the research activities of the hospital in fully independent manners besides any commitment with third parties. Daniel J Lovell Consultant for: Consulting fees and/or honoraria from Astra Zeneca, Wyeth Pharma, Amgen, Abbott, Pfizer, F. Hoffmann-La Roche, Novartis, UBC, Takeda, GSK, Boehringer, and Celgene, Hemine Brunner Grant/research support from: Bristol-Myers Squibb, Pfizer, Consultant for: Pfizer, Bristol-Myers Squibb, Janssen, Novartis, Lilly, Roche, GlaxoSmithKline, Sanofi, Speakers bureau: Novartis, Roche.

Table
Changes in cSLE core response variables are shown in the Table.

![Table](image)

Figure
Primary and major secondary endpoints at Week 52 [95% CI]

![Figure](image)

Results: Patients had a variety of retinal testing done, with optical coherence testing most frequent. Table 1 shows the concordance of a test abnormality with the retina expert opinion.

Table 1. – Performance of retinal imaging modalities relative to expert diagnosis

<table>
<thead>
<tr>
<th>Test</th>
<th>Retinopathy</th>
<th>No Retinopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ocular Coherence Tomography (OCT)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal</td>
<td>25 (93%)</td>
<td>133 (16%)</td>
</tr>
<tr>
<td>Normal</td>
<td>2 (7%)</td>
<td>721 (84%)</td>
</tr>
<tr>
<td>Total</td>
<td>27</td>
<td>854</td>
</tr>
<tr>
<td>Electroretinogram (ERG)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal</td>
<td>15 (100%)</td>
<td>195 (49%)</td>
</tr>
<tr>
<td>Normal</td>
<td>0 (0%)</td>
<td>201 (51%)</td>
</tr>
<tr>
<td>Total</td>
<td>15</td>
<td>396</td>
</tr>
<tr>
<td>Microperimetry (MP1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal</td>
<td>17 (100%)</td>
<td>144 (30%)</td>
</tr>
<tr>
<td>Normal</td>
<td>0 (0%)</td>
<td>331 (70%)</td>
</tr>
<tr>
<td>Total</td>
<td>17</td>
<td>475</td>
</tr>
<tr>
<td>Fundal Autofluorescence (FAF)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal</td>
<td>19 (83%)</td>
<td>165 (24%)</td>
</tr>
<tr>
<td>Normal</td>
<td>4 (17%)</td>
<td>536 (76%)</td>
</tr>
<tr>
<td>Total</td>
<td>23</td>
<td>701</td>
</tr>
</tbody>
</table>

The concordance of the test abnormality with the retina expert opinion showed the following sensitivity and specificity, respectively: OCT 93%, 84%; ERG 100%, 51%; MP1 100%, 70%; and FAF 83%, 76%. The frequency of retinopathy increased with years of HCQ use [number of retinopathies per total patients (percent frequency)]: 5 years or less, 1/103 (0.97%); 6-10 years, 2/209 (1.83%); 11-15 years, 3/91 (3.30%); 16-20 years, 11/96 (11.46%); and 21 or more years, 6/75 (8.00%).

Conclusion: In agreement with the American Academy of Ophthalmology, OCT appears to be the optimum test for yearly monitoring (2). The frequency of retinopathy was much lower in our prospective study than estimated by the Kaiser-Permanente study. Our data also show the need for ophthalmologists with retinopathy expertise to interpret retinal testing, as screening tests are frequently abnormal due to causes other than HCQ retinopathy. Stopping HCQ based on an abnormal test without confirmation from a retinopathy expert could needlessly deprive an SLE patient of an important medication.

REFERENCES:

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FRIO183

STUDY DESIGN FOR A MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY TO ASSESS THE EFFICACY AND SAFETY OF REPOSITORY CORTICOTROPIN INJECTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS DESPITE MODERATE-DOSE CORTICOSTEROIDS

Anca Aaskanase, Enru Zhao, Julie Zhu, Erin Connolly-Strong, Richard Furie

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Background: Repository corticostropin injection (RCI) is a complex mixture containing purified porcine pituitary adrenocorticotropic hormone (ACTH)-an analogue with potential anti-inflammatory and immunomodulatory effects through the melanocortin receptors (MC1R, MC3R-MC5R) and endogenous steroid production. RCI is approved by the US FDA for the treatment of acute exacerbations (ie, disease flares) or as maintenance therapy in patients with systemic lupus erythematosus (SLE). In a pilot study, RCI was well tolerated with improvements in disease activity for lupus patients treated with RCI compared to those who received placebo (Furie et al, 2016).

Objectives: To discuss the design, demographics, and baseline characteristics of a clinical trial evaluating the role of RCI in the treatment of patients with inadequately controlled SLE disease activity.

Methods: This is a multicenter, double-blind, randomized, placebo-controlled, 24-week clinical trial aiming to determine the effect of RCI in reducing disease activity for patients with persistently active SLE despite moderate-dose corticosteroids (CSs). Patients are required to have SLE (>4 of 11 ACR criteria from 1997) and active disease (moderate to severe rash and/or arthritis) despite stable dose CSs > 4 weeks prior to screening (7.5 - 30 mg/day of prednisone or equivalent). Patients are treated with RCI 1 mL (80 U) subcutaneously (SC) or placebo 1 mL, every other day for 4 weeks followed by twice per week for 20 weeks. Randomization is stratified by study site location and prednisone or equivalent dose (<20 and > 20 mg/day). Patients remain on stable doses of CSs through Week 16, with tapering encouraged between Weeks 16 and 24. Efficacy is evaluated using the SLE Responder Index-4 (SRI-4) and changes from baseline in SLE Disease Activity Index-2000 (SLEDAI-2K), British Isles Lupus Assessment Group-2004 (BILAG-2004) scores, and Physician’s Global Assessment (PGA). The primary efficacy endpoint is the proportion of SRI-4 responders at Week 16. Secondary and exploratory endpoints include changes in disease activity scores over time, prednisone dose, and biomarkers (ie, complements, autoantibodies, inflammatory, bone turnover).

Results: As of 14 December 2018, 124 patients comprised the intent-to-treat (ITT) population. Target enrollment is 270 patients, of which 162 patients are expected to be randomized at approximately 60 sites globally. Demographic and baseline characteristics (Table 1) were collected, including circulating lymphocyte profiles (CD19+ B Cells, CD3+ total T cells, and CD4 Treg cells), which are consistent with the pilot study of RCI (Furie et al, 2016).

Conclusion: This on-going study assesses the efficacy and safety of RCI for the treatment of refractory SLE in a racially and ethnically diverse population. The rapid onset of action of RCI allows for a 16-week primary endpoint. Patients enrolled in this trial have moderate or high disease activity (as shown by the mean SLEDAI-2K, BILAG, and PGA) and are likely to provide valuable data on the role of RCI in refractory lupus. Bone turnover markers will further define the safety profile of RCI in lupus.

REFERENCE:

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**SAFETY AND EFFICACY OF SPLENECTOMY IN THE TREATMENT OF ANTIPHOSPHOLIPID SYNDROME-ASSOCIATED CYTOPENIAS**

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**Background:** Thrombocytopenia and autoimmune hemolytic anemia (AIHA) are common hematologic manifestations in primary antiphospholipid syndrome (APS). Although splenectomy is considered a second-line treatment in both primary immune thrombocytopenia (ITP) and idiopathic AIHA, its role in APS patients with either one of these manifestations has not been adequately defined, mainly because of the theoretically increased risk of thrombosis for patients with APS who undergo surgery.

**Objectives:** To determine the safety and efficacy of splenectomy for steroid-refractory thrombocytopenia or autoimmune hemolytic anemia in patients with primary APS, when compared to patients with ITP or idiopathic AIHA.

**Methods:** We performed a retrospective, single-center, case-control study. We included patients with primary APS and either thrombocytopenia, or autoimmune hemolytic anemia/Evans syndrome who underwent splenectomy between 2000 and 2018. The control group was made up by patients with primary immune cytopenias (ITP or AIHA) who also underwent splenectomy during that period. Cases and controls were adjusted by age, the hematologic manifestation and date of splenectomy. We recorded demographic, clinical and serologic characteristics at the time of surgery and during follow-up.

**Results:** We included 34 patients in each group. Thrombocytopenia was the indication for splenectomy in 53% of patients, with AIHA or Evans syndrome comprising the remaining 47%. Most patients were female (78%) and median age was 37 years. Among APS patients, 41% had triple antibody positivity. There were no differences regarding comorbidities between groups. Patients with APS received more immunosuppressive treatment lines before splenectomy compared to controls (p=0.02), and there was a trend for more high-dose steroid cycles in the APS group (p=0.07). Median time to splenectomy was 54 months in APS patients and 18 months in controls, but without statistical significance. Regarding splenectomy, most were laparoscopic (88%) and surgical complications were similar between groups (18%). However, patients with APS had a higher incidence of global non-surgical complications in the first month (59 vs 23%, p=0.04), most of them being infections (21 vs 3%, p=0.05). There was no difference in the incidence of postsurgical thrombosis, venous or arterial, between groups.

Most patients achieved a global response after one month (65% in APS group, 91% in controls, p=0.7). Complete response was observed in 65% and 79% of cases and controls, respectively (p=0.27). Median follow-up time was 52 months for APS patients and 41 months for controls. There were no differences regarding relapse which required any treatment adjustment between cases and controls (44% and 38%, respectively, p=0.8, Fig 1). However, 47% of APS patients received a prolonged maintenance immunosuppressive treatment, compared with 6% of controls (p=0.01). The incidence of infections and thrombosis during follow-up was similar between groups (p=0.15 and p=0.7, respectively; Fig 2).

**Conclusion:** Splenectomy is associated with adequate and long-lasting responses in APS patients with cytopenias, which do not differ from patients with non-APS-associated thrombocytopenia and AIHA. Thrombosis was not a common complication in our patients; however, there was a higher incidence of infections in APS patients. This could be related to the higher steroid doses and more intensive previous immunosuppressive therapies. Splenectomy could be considered an earlier treatment option for APS patients with refractory cytopenias, and this could reduce infection risk and post-surgical morbidity.

**Disclosure of Interests:** Ana Barrera-Vargas: None declared, Juan Rangel Patiño: None declared, Samuel Govea-Peláez: None declared, Javier Merayo-Chalico: Speakers bureau: Pfizer, Roberta Demicheli-Gómez: None declared, Jorge Alocer-Varela: None declared

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**HYDROXYCHLOROQUINE FOR THE PREVENTION OF RELAPSES IN A SERIES OF 812 PATIENTS WITH PRIMARY ANTIPHOSPHOLIPID SYNDROME: THE HIBISCUS RETROSPECTIVE STUDY**

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**Background:** The relapse rate in antiphospholipid syndrome (APS) remains high, 20% at 5 years in thrombotic APS and 28% in obstetrical APS (1). Hydroxychloroquine (HCQ) appears as an additional therapy, with immunomodulatory and anti-inflammatory effects (2-5).

**Objectives:** The main aim of this trial is to assess the efficacy of treatment with Hydroxychloroquine in preventing new events in primary antiphospholipid syndrome patients.

**Methods:** We have performed a retrospective multicentre open-labelled study (2002-2018).

**Results:** 812 patients with APS from 53 international centres from 16 countries were included. In all cases, the previous standard treatment was inefficient. The mean follow-up was 20.2 months (8-144 mo), the mean age 39.5 years old. The type of clinical manifestations is described in figure 1.
The obstetrical manifestations were various as described in figure 2. The number of thrombotic events were 190 arterial and 187 venous. Triple antiphospholipid antibody (IaPL) positivity was found in 20% of patients and lupus anticoagulant (LA) in 22%. No bleeding was registered in 99.6% of cases with treatment by HCQ. HCQ use was associated with favourable outcome in 96% of cases (figure 3).

In multivariate analysis, age more than 65 years was associated with thromboembolic events (odds-ratio 0.13 95%CI 0.03-0.32, p 0.005).

Conclusion: HCQ could be effective in cases of refractory APS but prospective studies are necessary.

REFERENCES:
[2] References:


Table 1. Table 2

FRIO168 HYDROXYCHLOROQUINE ON THE TOP OF STANDARD TREATMENT WITH LOW DOSE ASPIRIN AND LOW MOLECULAR WEIGHT HEPARIN SIGNIFICANTLY REDUCES THE PROBABILITY OF PREGNANCY MORBIDITY IN WOMEN WITH MULTIPLE POSITIVITY FOR ANTI-PHOSPHOLIPID ANTIBODIES

Cecilia Chighizola1, Francesca Pregnolato1, Francesca Bartoli2,3, Maria Gerosa2,3, Chiara Corneto1,2, Maria Gabriella Raimondi1,2, Laura Trespidi1,2, Maria Orietta Borghi1,2, Mariella Wally Ossola1, Enrico Ferrazzi2,4, Pier Luigi Meroni1.

1Istituto Auxologico Italiano, Milan, Italy; 2University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy; 3ASST Gaetano Pini, Rheumatology, Milan, Italy; 4Fondazione Ca Granda, Ospedale Maggiore Policlinico, Department of Obstetrics and Gynaecology, Milan, Italy.

Background: Hydroxychloroquine is an anti-malarial drug that not only exerts immunomodulatory and anti-thrombotic properties, but also has been shown to reverse several effects mediated by anti-phospholipid anti- bodies (aPL) in models of obstetric anti-phospholipid syndrome (APS). Not surprisingly, HCQ, whose prescription during gestation is perfectly safe, has been proposed as an additional therapeutic tool in obstetric APS, but evidence of its efficacy is still scant.

Objectives: This study investigates how treatment with HCQ, prescribed in different combinations with low-dose aspirin (LDSA) and low-molecular weight heparin (LMWH), affects the probability of pregnancy morbidity (PPM).

Methods: Data on pregnancies in women with persistent aPL positivity at any titre, with or without autoimmune diseases, were retrospectively collected at a single centre.

A weighted generalized estimated equation (GEE) model was applied to quantify the effect of treatment with HCQ on PPM, allowing to: i) evaluate pregnancy outcomes over time using available longitudinal data; ii) account that pregnancies of the same woman are not independent events; iii) consider that women had a different number of pregnancies; iv) estimate the role of several confounders and predictors.

The model envisaged as dependent variable pregnancy outcome as a binary outcome, defined for each pregnancy as “obstetric complication yes versus no” (pregnancy loss before 10 weeks, pregnancy loss after 10 weeks, premature birth before 34 weeks, according to updated APS classification criteria).

Results: Three-hundred-eighty-one women were recruited in this study: 155 women with aPL positivity (100 women with positivity for criteria aPL and 55 women with low-titer aPL) and 226 women with autoimmune diseases but negative aPL. Data were collected on 847 pregnancies: 458 in women with positive aPL (172 in women with criteria aPL and 286 in women with low-titer aPL) and 389 in women with autoimmune disease and negative aPL.

PPM in untreated patients are presented in Table 1. Table 2 reports PPM in women receiving LDASA +/- HCQ, LDASA + LMWH +/- HCQ.

Conclusion: HCQ, when added to LDASA or on the top of standard treatment with LDASA and LMWH, allows to reduce PPM. Most importantly, HCQ plus the combo LMWH + LDASA leads to a significantly

Involvement: The obstetrical manifestations were various as described in figure 2. The number of thrombotic events were 190 arterial and 187 venous. Tri- plet antiphospholipid antibody (IaPL) positivity was found in 20% of patients and lupus anticoagulant (LA) in 22%. No bleeding was registered in 99.6% of cases with treatment by HCQ. HCQ use was associated with favourable outcome in 96% of cases (figure 3).

In multivariate analysis, age more than 65 years was associated with arterial events (odds-ratio 0.13 95%CI 0.03-0.32, p 0.005).

Conclusion: HCQ could be effective in cases of refractory APS but prospective studies are necessary.

REFERENCES:


PRELIMINARY EXPLORATION OF NEW METHODS TREAT TO PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: REGULATING TH17/TREG CELL BALANCE BY RAPAMICIN AND ALL-TRANS RETINOIC ACID

Yanfang Chu, Chunniao Zhao, Bingying Zhang, Xuxia Wang, Yiqi Wang, Junwei Chen, Li Xiaofeng, Yanfang Chu, Chunmiao Zhao, Bingying Zhang, Xuxia Wang, Yiqi Wang, Jia An, Junwei Chen, Li Xiaofeng, the Second Hospital of Shanxi Medical University, Taiyuan, China

Background: Helper T cells 17 (Th17) and regulatory T cells (Treg) are two important immunoregulatory cells that act in opposite directions. Previous study has shown that Th17/Treg cell balance is one of the important pathogenesis of systemic lupus erythematosus (SLE). Further researches believed that rapamycin (RAPA) alone or in combination with all-trans retinoic acid (ATRA) can regulate Th17/Treg cell balance, and then alleviate the condition of SLE.

Objectives: To investigate effect of the use of RAPA alone or combined ATRA on Th17/Treg cell balance in patients with SLE.

Methods: Seventy patients with SLE (64 females and 6 males, mean age 31.9±10.12 years, mean duration 61.1±53.64 months) in our hospital from March 2016 to June 2018 were enrolled. All of them were in line with the standard of ACR in 1997. The patients were randomly divided into RAPA group (RAPA 0.5 mg/time, twice a week) and RAPA+ATRA group (RAPA and ATRA 10 mg/time, twice a week), 35 cases in each group. All were treated continuously for 24 weeks. The number of Th17 and Treg cells in peripheral blood before treatment and 6,12,24 weeks after treatment were measured. The SLEDAI scores and glucocorticoid dosage before and after the treatment were also observed to evaluate the differences of efficacy between the two groups.

Results: At different time in each group, the number of peripheral blood Th17 cells in SLE patients was decreased (P<0.05), the ratio of Th17/Treg cells induced (P<0.05), indicating a restored balance of them. The SLEDAI scores and the dosage of glucocorticoid were decreased significantly (P=0.001). There were no significant differences in the number of Th17 cells, Treg cells, SLEDAI scores and the dosage of glucocorticoid between two groups (P>0.05). Compared with pretreatment, the number of Th17 cells, the ratio of Th17/Treg cells and SLEDAI scores after 24 weeks treatment in SLE patients was decreased in RAPA group (P<0.05). Compared with pretreatment, the SLEDAI scores and the dosage of glucocorticoid after 24 weeks treatment in SLE patients was significantly reduced in RAPA+ATRA group (P<0.001).

Conclusion: Using RAPA or combined with ATRA could improve the condition of SLE patients by regulating Th17/Treg cells balance and reduce glucocorticoid dosage, which provided new directions for the pathogenesis and treatment of SLE.

REFERENCES:

Table 1 Probabilities of P PM in untreated women with or without aPL

<table>
<thead>
<tr>
<th>Criteria</th>
<th>P PM</th>
</tr>
</thead>
<tbody>
<tr>
<td>aPL negative</td>
<td>38% (29-48)</td>
</tr>
<tr>
<td>Low titer single aPL positivity</td>
<td>62% (52-71)</td>
</tr>
<tr>
<td>Low titer double aPL positivity</td>
<td>83% (75-89)</td>
</tr>
<tr>
<td>Criteria single aPL positivity</td>
<td>80% (71-87)</td>
</tr>
<tr>
<td>Criteria multiple aPL positivity</td>
<td>89% (81-94)</td>
</tr>
</tbody>
</table>
Figure 2. Changes in the number of Treg cells (number/ml) before and after treatment in the two groups.

Figure 3. Changes in the ratio of Th17/Treg cells before and after treatment in both groups.

Figure 4. Changes in SLEDAI scores (minutes) before and after treatment in both groups.

Figure 5. Changes in prednisone dosage (mg/d) before and after treatment in both groups.

Acknowledgement: We confirm that this is our abstract.

Disclosure of Interests: None declared

**FRIO188 EARLY RENAL IMPROVEMENTS FOLLOWING RITUXIMAB IN LUPUS NEPHRITIS**

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**Background:** Rituximab (RTX) is the monoclonal antibody of choice in patients with lupus nephritis (LN) who either fail to respond to, or cannot receive standard care (SOC) therapy. Despite its continued use in clinical practice, published clinical trials regarding its use in LN management have failed to show any clear benefit.

**Objectives:** We aimed to analyse renal outcomes of LN patients in a large national register.

**Methods:** Patients with active LN on recruitment into the BILOG-Biologies Register (BILOG-BR) were included. Active LN was defined as a BILOG A or B score in the renal domain. Patients are eligible for RTX if they have failed either MMF or cyclophosphamide. We defined renal response at 6 and 12 months as a change in BILOG score from A to B/C/D or B to C/D. Non-renal disease activity was also described.

**Results:** Overall 259/807 patients in BILOG-BR had active LN at baseline. Of these, 230 received RTX and 29 received SOC. 109/159 (68.6%) RTX patients and 15/19 (78.9%) of SOC patients had a renal BILOG response at 6 months (p=0.792) (Table 1). In those with sufficient response data at 12 months, 31/98 (31.6%) and 7/15 (46.7%) (p=0.084) demonstrated continued renal response in the RTX and SOC groups respectively. Both groups made improvements or remained stable in all other renal domains (UPCR, eGFR, creatinine) at 6 and 12 months. Oral steroid doses decreased in both treatment groups. Of note, baseline steroid doses in the SOC group were higher than RTX patients (30mg (20-40) vs. 12.5mg (10-25), p<0.001).

**Non-renal disease activity measures improved in both cohorts.**

<table>
<thead>
<tr>
<th>Variable</th>
<th>RTX</th>
<th>SOC</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Renal BILOG response*</td>
<td>230/259</td>
<td>30/159</td>
<td>0.792</td>
</tr>
<tr>
<td>Non-renal BILAG response*</td>
<td>42/159</td>
<td>17/159</td>
<td>0.064</td>
</tr>
<tr>
<td>Serum creatinine (median [IQR])</td>
<td>30/159</td>
<td>17/159</td>
<td>0.045</td>
</tr>
<tr>
<td>Oral steroid dose (median [IQR])</td>
<td>230/259</td>
<td>42/159</td>
<td>0.001</td>
</tr>
</tbody>
</table>

**Conclusion:** In a large UK-wide, real-world, observational LN cohort we have shown that RTX does improve renal outcomes at 6 and 12 months in refractory SLE patients. RTX is a valid treatment option for many patients with renal disease in SLE.

**Disclosure of Interests:** Sophie Collinson: None declared, Ben Parker Grant/research support from: GSK, Consultant for: AZ, UCB, GSK, Eoghan McCarthy: None declared, Ian N. Bruce Grant/research support from: Genzyme Sanofi, GlaxoSmithKline, Consultant for: AstraZeneca, Eli Lilly, GlaxoSmithKline, ILTOO Pharma, MedImmune, Merck Serono, Speakers bureau: GlaxoSmithKline, UCB Pharma


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**FRIO189 POOLED ANALYSIS OF THE REAL-WORLD EFFECTIVENESS OF BELIMUMAB IN TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS USING MULTI-COUNTRY DATA FROM THE OBSERVE STUDIES**

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**Background:** Real-world evidence of belimumab effectiveness in patients with systemic lupus erythematosus (SLE) has been reported separately for several countries through the OBSERVE (evaluation Of use of Belimumab in clinical practice SEttings) programme.

**Objectives:** To evaluate the effectiveness of belimumab in patients with SLE using pooled data from the individual OBSERVE studies.

**Methods:** This was a post hoc meta-analysis (GSK study 206351) of patients who entered data from six retrospective observational cohort studies (Argentina, Canada, Germany, Spain, Switzerland, United States of America). Physicians provided data for adults (>18 years; clinical diagnosis of SLE) who had initiated intravenous belimumab as part of their usual SLE care ≥6 months prior to enrolment and for whom reasons for belimumab initiation could be identified. Primary objective: physician-assessed overall clinical response to belimumab at Month 6, which reflected physicians’ impression of change in overall clinical manifestations, categorised as worse, no improvement, and improvement of ≤20%, 20–49%, 50–79%, and ≥80%. Secondary objectives included a description of patient characteristics at belimumab initiation (index); treatment patterns during the 6 months after index; and patient and treatment characteristics associated with an overall clinical response. Safety was not assessed.

**Results:** Data were pooled from all 830 patients (89.3% female; mean [standard deviation] age 41.9 [12.6] years) included in each of the OBSERVE studies. At index, most patients had moderate SLE (71.4%; physician-assessed) and serological indicators of high disease activity (82.8%; high anti-dsDNA and/or low complement). Of 345 patients for whom Safety of Estrogens in Lupus Erythematosus-National Assessment Trial-SLE Disease Activity Index baseline data were available, 60.0% had a score >10. At index, 72.0% of patients had musculoskeletal, 59.0% had mucocutaneous manifestations, and 16.5% had renal involvement. At Month 6, 82.8% of patients had ≤20% improvement and 48.1% had >50% improvement in their overall condition; only 4.7% had none or a worse response to belimumab therapy (Figure). In total, 81.4% of patients received steroids at a mean dose of 17.6 mg/day. At Month 6, the mean change in steroid dose was −9.7 mg/day. Of those receiving a dose >7.5 mg/day (78.4% of all patients receiving steroids at index), 54.5% had a dose reduction to ≤7.5 mg/day at Month 6. Effective previous treatment was the main reason for belimumab initiation (74.3%). Prior to Month 6, 4.4% of patients (n=12270) in Argentina, Spain, Germany and Switzerland discontinued belimumab, most frequently due to lack of efficacy and patient request (both 33.3%); OBSErve US and Canada excluded patients with <6 months’ belimumab treatment.

**Conclusion:** This study provides important insights into global real-world outcomes in a large number of patients with SLE treated with belimumab. After 6 months of treatment, most patients demonstrated clinical improvements in SLE; results were consistent across the pooled population and for patients with high disease activity. Belimumab was steroid sparing; most patients receiving steroids at belimumab initiation decreased their steroid dose after 6 months of belimumab treatment.
Acknowledgement: Study funded by GSK. Gosia Carless, PhD, Fishawack Indicia Ltd. UK, provided editorial assistance funded by GSK.


FRID190

INCIDENCE OF ANTIMALARIALS-INDUCED RETINOPATHY IN INFLAMMATORY RHEUMATIC DISEASES, USING OCT AND VISUAL FIELD TEST: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Antimalarials (AM) are frequently used as first-line therapy in mild inflammatory diseases, because of a good benefit/risk ratio. Recently, their benefit on long term cardiovascular risk in RA patients has been demonstrated [1, 2]. Their most severe side effect is retinopathy, which can potentially lead to blindness, but remains reversible if detected early, provided the treatment is stopped. This complication has been described early [3], but its incidence remains uncertain. A recent update of the American Association of Ophthalmology (AAO) recommendations on screening for chloroquine and hydroxychloroquine retinopathy, suggests to screen patients under AM treatment, with a frequency depending on risk factors, and with the systematic and minimal use of Optical Coherence Tomography (OCT) and Visual Field (VF) test, completed by others tests if required [4].

Objectives: We aimed at estimating the exact incidence of AM-induced retinopathy, based on available published literature about this issue, with particular reference to detection performed with OCT and VF test.

Methods: A systematic literature search was conducted in Pubmed, Cochrane and Embase databases until April 6th 2018, completed by a manual search in references from the resulting selected articles. We first selected all publications about the incidence of AM-associated retinopathy in patients treated for inflammatory diseases and included them in the systematic literature search. Among them, and in order to minimize heterogeneity of results, we focused on those which had used at least OCT and VF test, as recommended by the AAO, to perform a meta-analysis. Analysis was conducted using MetaXL for Microsoft Excel, applying the Inverse of Variance method.

Results: Among the 3890 articles of potential interest, we selected 91 articles appropriately addressing the topic and included them in the systematic literature search. They were published between 1964 and 2018, with variable population sizes (10 to 3580 patients). Patients were treated with hydroxychloroquine, chloroquine or both for an inflammatory disease (usually lupus or rheumatoid arthritis). Mean treatment duration ranged from 1 to 14.1 years. Most of them were retrospectively designed, and diagnostic methods were diverse. For the aforementioned meta-analysis, we used data from 16 articles published between 2010 and 2018, in which every patient had at least OCT and VF Test. We found a pooled estimate of incidence of 6.05% (IC 95% [5.18 – 7.31]), with a I2 heterogeneity coefficient of 80%.

Conclusion: We found a pooled incidence of approximately 6% of AM-induced retinopathy when OCT and VF test are used. However diagnostic criteria are not consensually well-defined, leading to heterogeneous data.

REFERENCES:

Disclosure of Interests: Hélène DE CAGNY: None declared, Jacques Morel: None declared, Bernard Combe Consultant for: Abbvie, Bristol-Myers Squibb, Gilead, Janssen, Eli Lilly, MSD, Novartis, Pfizer, Roche-Chugai, Sanofi, UCB, Cécile Gaujoux-Viala Consultant for: Speaking and/or consulting fees from AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Merck-Serono, Medac, Nordic Pharma, Novartis, Pfizer, Roche, Sandoz, Sanofi and UCB Pharma., Speakers bureau: Speaking and/or consulting fees from AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Eli Lilly, Gilead, Janssen, Merck-Serono, Medac, Nordic Pharma, Novartis, Pfizer, Roche, Sandoz, Sanofi and UCB Pharma., Cédric Lukas: None declared


FRID1019

TREATMENT OF REFRACTORY POOR APL-RELATED OBSTETRIC OUTCOMES WITH TNF-ALPHA BLOCKERS: MATERNAL-FETAL OUTCOMES IN A SERIES OF 18 CASES

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Background: No absolute data on the treatment of antiphospholipid antibodies (aPL) related to refractory obstetric complications exist to date. TNF-α play a major role in this disorder.

Objectives: To assess the effectiveness of TNF-α blockers in 18 aPL-positive women with recurrent infertility after therapy with low-molecular-weight heparin (LMWH) plus aspirin (LDA) plus hydroxychloroquine (HCQ).

Methods: Prospective case-series of 12 women fulfilling Sydney criteria for obstetric antiphospholipid syndrome (OAPS) and 6 with incomplete forms (OMAPS). All women tested positive for aPL at least twice. Non-criteria aPL were tested in 15/18. Complement, TNF-α and IL-10 were also evaluated. Women were closely monitored for fetal well-being and possible malformations throughout gestation and the postpartum period.

Results: Sixteen patients were started on adalimumab and 2 on certolizumab. Twelve women completed gestation: 9 at term and 3 pre-term. Differences in laboratory categories and outcomes were observed when OAPS and OMAPS were compared. First trimester miscarriage or implantation failure recurred in 6 cases, all of the OAPS group. Malformations were not seen in the newborns.

Conclusion: Overall, good obstetric results were obtained in 70% of previous LMWH-LDA+HCQ refractory cases. TNF-α blockers were well tolerated without adverse effects. The combination of LMWH plus LDA plus TNF-α blockers appears to be a promising treatment for refractory obstetric complaints related to aPL; nevertheless, outcome differences between OAPS and OMAPS do exist.
A SYSTEMATIC LITERATURE REVIEW TO INFORM THE 2019 UPDATE OF THE EULAR RECOMMENDATIONS FOR THE TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS

Antonis Fanouriakis1, Myro Kostopoulou2, Alessia Alunno3, Martin Aringer4, Ingeborg Bajema5, John N. Boileau6, Riccardo Cervera7, Andrea Dorà8, Caroline Gordon9, Marcello Govoni10, Frederic Housiaux11, David Jayne12, Mario Koutsoukas13, Myrto Kostopoulou14, Ingeborg Troldborg15, Ronald van Vollenhoven16, Jörg Wenzel17, George Bertsias18

Objectives: Systematic review of the literature (SLR) to inform the 2019 update of the 2008 EULAR recommendations for the treatment of SLE.

Methods: SLR of PubMed from 2010 to 2017 for questions (selected through Delphi exercise) regarding: i) efficacy/safety of different drugs used in SLE, ii) treatment of specific manifestations, iii) monitoring and treatment goals and iv) comorbidities and adjunct therapy. Evidence was categorized based on design and validity of available studies [Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence (LoE) and strength of statements was graded [Grading of recommendation (GoR)] assessment, development and evaluations, GRADE)].

Results: Main topics supported by strong evidence base included: Association of hydroxychloroquine (HCQ) use with favourable outcomes (LoE 1b, GoR A), belimumab for extrarenal disease (LoE 1a, GoR A), efficacy of antimalarials in skin disease (LoE 1a, GoR A), mycophenolate mofetil (MMF) for induction and maintenance therapy of lupus nephritis (LN) and cyclophosphamide (CYC) in severe LN (LoE 1b, GoR A). Weak evidence supported the value of repeat kidney biopsies in refractory LN (LoE 4, GoR C), all second-line agents for skin disease (LoE 4, GoR C) and efficacy of most first and second-line treatments for thrombocytopenia (LoE 4, GoR C). Moderate LoE was found for all other questions (Table).

Conclusion: A SLR for the treatment of SLE found the highest LoE for benefits of HCQ, efficacy of belimumab for extrarenal disease and MMF and IV-CYC in LN.

Disclosure of Interests: European League Against Rheumatism

REFERENCES:
49.
[4] Berman J, Girardi G, Salomon JE. TNF-alpha is a critical effector and a tar-
[5] Meroni PL, Borghi MO, Rasci E, Tedesco F. Pathogenesis of antiphos-

Disclosure of Interests: None declared

Background: Recommendations for the treatment of systemic lupus erythematosus (SLE) were published by EULAR in 2008. Advances in treatment strategies and goals called for an update of these recommendations, capitalizing on strengths and experience from previous projects.

Objectives: To update the EULAR recommendations for the management of SLE.

Methods: Systematic literature review (01/2007-12/2017) followed by Delphi method to form questions, elicit expert opinions and reach consensus.

Results: Treatment in SLE aims at remission or low disease activity and renal disease (including the use of calcineurin inhibitors). SLE patients should be assessed for their antiphospholipid antibody status, infectious and cardiovascular diseases risk profile, and preventative strategies be tailored accordingly.

Conclusion: Updated EULAR recommendations provide physicians and patients with updated consensus guidance on the management of SLE, combining evidence-base and expert-opinion.
INTEGRATED SAFETY PROFILE OF ATACICEPT FROM ALL CLINICAL STUDIES TO DATE

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Background: We conducted an integrated analysis of pooled safety data from all 17 atacicept clinical studies across multiple indications to date.

Objectives: To characterize the overall safety profile of atacicept.

Methods: Analyses were based on 3 pooled datasets: double-blind placebo (PBO)-controlled set (DBPC-S) (n=1568; key endpoint: treatment-emergent AEs [TEAEs]); systemic lupus erythematosus set (SLE-S; n=761; key endpoints: IgG change and serious infection rates, and mortality); and full analysis set (FA-S; n=1845; key endpoint: exposure-adjusted mortality).

Results: Of 1568 patients (DBPC-S), 30.8% received PBO, and 8.2%, 24.5% and 36.5% received atacicept 25, 75 and 150 mg, overall. Baseline characteristics were balanced across treatment arms. Treatment exposure in patient-years (py) was similar for PBO and atacicept 75 and 150 mg but was lower with 25 mg (Table). Exposure-adjusted TEAE rates were generally higher with atacicept vs PBO; serious TEAE and infection rates were similar with atacicept and PBO (Table). TEAE-related discontinuation rates were higher with atacicept vs PBO (16.1 vs 10.9/100 py). Exposure-adjusted mortality rate (95% CI) was 0.30 (0.19–0.41) for atacicept 75, 150 mg and 0.44 (0.36–0.52) for PBO. In SLE patients, exposure-adjusted mortality rate/100 py were 1.45 (0.54–3.87) with atacicept 150 mg and 0.78 (0.29–2.07) across all atacicept-treated patients. The underlying disease and other causes were potential confounders in most cases.

Conclusion: In this integrated safety analysis of atacicept, no consistent association was found between atacicept dose and specific TEAEs or mortality. These results support further development and evaluation of atacicept in patients in whom potential benefits may outweigh risks.

Table: Exposure-adjusted TEAE rates by dose (DBPC-S)

<table>
<thead>
<tr>
<th>Placebo</th>
<th>25 mg</th>
<th>75 mg</th>
<th>150 mg</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of py</td>
<td>278.3</td>
<td>51.5</td>
<td>225.0</td>
<td>286.7</td>
</tr>
<tr>
<td>Hypersensitivity</td>
<td>37 (13.9)</td>
<td>8 (15.7)</td>
<td>40 (55.9)</td>
<td>103 (14.3)</td>
</tr>
<tr>
<td>Infections</td>
<td>211 (8)</td>
<td>43 (10.4)</td>
<td>180 (24.7)</td>
<td>504 (71)</td>
</tr>
<tr>
<td>Serious infection</td>
<td>20 (7.3)</td>
<td>1 (1.9)</td>
<td>23 (32.5)</td>
<td>46 (6.6)</td>
</tr>
<tr>
<td>Severe infection</td>
<td>9 (3.2)</td>
<td>0</td>
<td>11 (14.9)</td>
<td>27 (38.4)</td>
</tr>
<tr>
<td>Severe hypoglycemia</td>
<td>0</td>
<td>0</td>
<td>2 (2.9)</td>
<td>4 (1.4)</td>
</tr>
<tr>
<td>Ischemic heart disorders</td>
<td>11 (4.0)</td>
<td>3 (6.9)</td>
<td>9 (12.3)</td>
<td>27 (38.4)</td>
</tr>
<tr>
<td>Embolic and thromboembolic events</td>
<td>4 (1.4)</td>
<td>2 (4.2)</td>
<td>2 (2.7)</td>
<td>6 (8.3)</td>
</tr>
<tr>
<td>Ventricular arrhythmias</td>
<td>5 (1.8)</td>
<td>0</td>
<td>4 (5.5)</td>
<td>2 (2.7)</td>
</tr>
<tr>
<td>Ischemic heart disorders</td>
<td>11 (4.0)</td>
<td>3 (6.9)</td>
<td>9 (12.3)</td>
<td>27 (38.4)</td>
</tr>
<tr>
<td>Embolic and thromboembolic events</td>
<td>4 (1.4)</td>
<td>2 (4.2)</td>
<td>2 (2.7)</td>
<td>6 (8.3)</td>
</tr>
<tr>
<td>Venous disorders</td>
<td>19 (7.0)</td>
<td>5 (9.9)</td>
<td>18 (24.3)</td>
<td>49 (69.9)</td>
</tr>
<tr>
<td>Depression</td>
<td>14 (5.1)</td>
<td>3 (6.9)</td>
<td>8 (11.4)</td>
<td>22 (30.6)</td>
</tr>
<tr>
<td>Malignant tumor</td>
<td>0</td>
<td>0</td>
<td>1 (1.3)</td>
<td>3 (4.0)</td>
</tr>
<tr>
<td>Severe TEAE</td>
<td>51 (18.9)</td>
<td>15</td>
<td>51</td>
<td>61 (21.8)</td>
</tr>
<tr>
<td>Discontinuation of treatment due to TEAE</td>
<td>30 (10.9)</td>
<td>14</td>
<td>30</td>
<td>46 (16.1)</td>
</tr>
<tr>
<td>Death-related infections, n (%)</td>
<td>0</td>
<td>0</td>
<td>2 (0.3)</td>
<td>0</td>
</tr>
</tbody>
</table>

Acute respiratory failure and probable leptospirosis (n=1); pneumonia and pulmonary alveolar hemorrhage (n=1)

Disclosure of Interests: Caroline Gordon Grant/research support from: Sandwell and West Birmingham Hospitals NHS Trust have received funding from UCB to support research work done by my research group that was unrelated to any pharmaceutical product or clinical trial, Consultant for: I have provided consultancy advice and taken part in scientific advisory boards on the design and analysis of clinical trials and the management of lupus for GSK, EMD Serono and UCB. I have taken part in adjudication and safety monitoring committees for BMS. Speakers bureau: I have been paid by UCB for speaking at meetings., Roberto Bassi Employee of: Current employees of EMD Serono, Peter Chang Employee of: Current employees of EMD Serono, Amy Kao Employee of: Current employees of EMD Serono, David Jayne Grant/research support from: David Jayne has received research grants from Chemocentryx, GSK, Roche/Genentech and Sanofi-Genzyme. He has received consultancy fees from Astra-Zenea, Boehringer-Ingehelm, Chemocentryx, Chugai, GSK, Infla-RX, Inmed and Takeda, David Wolfe Consultant for: GlaxoSmithKline – Member, data safety monitoring board, Novartis – Member, data safety monitoring board, Celgene – member, scientific advisory board, Victor Ora Employee of: Current employees of EMD Serono, Patricia Fleurancau-More-1 Employee of: Current employees of EMD Serono.


EFICAC Y AND SAF ETY OF DAPR OZUMAB PEG O L (DZP) IN PATIENTS WITH MODERATELY TO SEVERELY ACTIVE SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): A RANDOMISED, PLACEBO (PBO)-CONTROLLED STUDY

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Background: CD40 ligand (CD40L) regulates interactions between T cells and CD40-expressing cells including antigen-presenting cells (APC) and B cells, thereby playing a critical role in autoimmune disease pathogenesis. DZP, a PEGylated monovalent Fab’ antibody fragment with specificity for CD40L, prevents CD40L engagement of CD40 and thus blocks intracellular signalling and APC activation.

Objectives: To report the 24-week efficacy and safety interim data of DZP in a phase IIb, randomised, double-blind, PBO-controlled, dose-ranging study in patients with SLE [NCT02804763].

Methods: Patients with moderately to severely active SLE (SLEDAI-2K score >6; ≥2 BILAG grade A or ≥2 BILAG grade B organ domain scores at screening) despite stable non-biologic standard of care treatment were randomised 1:1:1:1 to receive iv DZP 6, 24 or 45 mg/kg or PBO every 4 weeks for 20 weeks. Patients receiving corticosteroids (CS) ≤10mg/day prednisone equivalent were required to start tapering CS by Week 4; guidance was provided, but tapering schedules were ultimately determined by the investigators.

The primary objective was to establish a dose-response relationship across three doses of DZP and PBO based on BICLA response rates at Week 24. Four pre-specified dose-response models were tested by a statistical method (MCP-Mod), to determine whether any of the models fit the observed data with statistical significance (at a one-sided p<0.05). The secondary endpoint was a pairwise comparison of BICLA response rates at Week 24. Other endpoints included the SRI-4 and BICLA response rates at 12 and 24 weeks, mean changes from baseline in SLEDAI-2K scores at 12 and 24 weeks, percentage of patients with daily CS dose ≤7.5 mg/day at 12 and 24 weeks, pharmacodynamic (PD) markers and safety.

Results: 182 patients were randomised; 167 (91.8%) completed Week 24 of the study. Baseline demographics were similar across treatment groups. The primary endpoint was not met as none of the pre-specified dose-response models fit the observed BICLA response rates at Week 24 with statistical significance (p<0.06 for the most applicable model). BICLA response rates and other efficacy outcome measures at Weeks 12 and 24 were numerically higher for all DZP groups vs PBO (Table 1). Favourable biological effects were observed with improvements in relevant PD markers, including anti-dsDNA antibody levels, in DZP groups vs PBO. Treatment-emergent adverse events (TEAEs) and serious TEAEs were generally balanced across treatment groups (Table 2). More upper
respiratory tract infections were observed in patients treated with DZP vs PBO; the majority were mild. We observed four thromboembolic events: one in the 24 mg/kg DZP group and three in the PBO group.

Conclusion: DZP appeared to be well tolerated as TEAEs were generally balanced across the treatment groups. Numerically greater improvements relative to PBO were observed consistently across multiple efficacy endpoints and biomarkers; however, for the primary endpoint no pre-specified dose-response relationship model fit the observed BICLA response rates at Week 24 with statistical significance. The potential for deriving clinical meaningful outcomes and benefit from DZP in patients with SLE warrants further investigation.

DZP appeared to be well tolerated as TEAEs were generally consistent across the treatment groups. Respiratory tract infections were observed in patients treated with DZP vs PBO; the majority were mild. We observed four thromboembolic events: one in the 24 mg/kg DZP group and three in the PBO group.

Methods: This open-label multicenter dose escalation trial enrolled SLE pts (per Systemic Lupus International Collaborating Clinics Classification Criteria) with SLE Disease Activity Index (SLEDAI) ≥4 despite stable background immunosuppressant, antimalarial, and/or corticosteroid (≥20 mg prednisone equivalent) therapy. Patients received KZR-616 at 45 mg (Cohort 1) or 60 mg (Cohort 2) SC OW through Week 13 (W13) with 12 weeks of follow up. Cohort 2 is currently enrolling pts using intrapatient dose escalation from 30 to 60 mg. Safety data include AEs, vitals, electrocardiograms and laboratory tests. Efficacy measures include the SLEDAI, Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI), 28 tender (T) and swollen (S) joint counts (JC), Physician Global Assessment (PhGA), and Patient Global Assessment (PtGA) in evaluable pts (receive ≥1 month of KZR-616; non-evaluable pts can be replaced).

Results: We enrolled 13 pts: 8 in Cohort 1, 5 in Cohort 2. The pts were 100% female; Baseline (BL) median SLEDAI was 10.0. All pts received at least 1 dose of KZR-616. In each cohort, 3 pts withdrew due to withdrawal of consent prior to W13. Overall, the 45 mg dose was well tolerated with no SAEs; all AEs were mild in intensity. The most common AEs were injection site erythema (62.5%), nausea (25%), and respiratory tract infections were observed in patients treated with DZP vs PBO; the majority were mild. We observed four thromboembolic events: one in the 24 mg/kg DZP group and three in the PBO group.

Conclusion: DZP appeared to be well tolerated as TEAEs were generally consistent across the treatment groups. Respiratory tract infections were observed in patients treated with DZP vs PBO; the majority were mild. We observed four thromboembolic events: one in the 24 mg/kg DZP group and three in the PBO group.

Methods: This open-label multicenter dose escalation trial enrolled SLE pts (per Systemic Lupus International Collaborating Clinics Classification Criteria) with SLE Disease Activity Index (SLEDAI) ≥4 despite stable background immunosuppressant, antimalarial, and/or corticosteroid (≥20 mg prednisone equivalent) therapy. Patients received KZR-616 at 45 mg (Cohort 1) or 60 mg (Cohort 2) SC OW through Week 13 (W13) with 12 weeks of follow up. Cohort 2 is currently enrolling pts using intrapatient dose escalation from 30 to 60 mg. Safety data include AEs, vitals, electrocardiograms and laboratory tests. Efficacy measures include the SLEDAI, Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI), 28 tender (T) and swollen (S) joint counts (JC), Physician Global Assessment (PhGA), and Patient Global Assessment (PtGA) in evaluable pts (receive ≥1 month of KZR-616; non-evaluable pts can be replaced).

Results: We enrolled 13 pts: 8 in Cohort 1, 5 in Cohort 2. The pts were 100% female; Baseline (BL) median SLEDAI was 10.0. All pts received at least 1 dose of KZR-616. In each cohort, 3 pts withdrew due to withdrawal of consent prior to W13. Overall, the 45 mg dose was well tolerated with no SAEs; all AEs were mild in intensity. The most common AEs were injection site erythema (62.5%), nausea (25%), and injection site pruritus (25%). Cohort 2 (60 mg) enrollment was halted, as all pts experienced vomiting within 8-24 hours of their first dose, which typically resolved within 24 h. One pt had an SAE of thrombotic microangiopathy. Two pts permanently reduced their dose to 45 mg. After 2 doses at 45 mg, another pt successfully re-escalated to 60 mg.
Cohort 2a (n=5 to date), there has been 1 SA of localized herpes zoster. In pts, PK and PD were similar to that achieved for the same doses in HV1. Efficacy data for evaluable pts are shown in the table. Two (33%) and 2 (67%) evaluable pts in Cohorts 1 and 2, respectively, had a SLEDAI improvement of ≥4 points from BL at W13.

Conclusion: KZR-616 dosed at 45 mg SC QW appears to be safe and well tolerated and showed evidence of disease suppression at W13 in active SLE pts on stable background therapy. The Ph 2 doses in the first randomized placebo-controlled trial with KZR-616 in active LN pts on mycophenolate and prednisone will be 30 and 45 mg. Efforts are ongoing to evaluate KZR–616 doses ≥60 mg using step-up dosing.

REFERENCES:

Disclosure of Interests: Richard Furie Grant/research support from: Biogen, UCB Pharma, not in the last 12 months, Consultant for: Biogen, UCB Pharma, not in the last 12 months, Darrin Bomba Shareholder of: Stockholder in Kezar Life Sciences, Employee of: Employee of Kezar Life Sciences, Maria Dall’Era Grant/research support from: University has received funds to conduct this clinical trial, Janet Anderl Shareholder of: Shareholder and option holder in Kezar Life Sciences, Employee of: Kezar Life Sciences, Jinhai Wang Employee of: Kezar Life Sciences, Employee of: Kezar Life Sciences, Christopher Kirk Shareholder of: Shareholder and option holder in Kezar Life Sciences, Employee of: Consultant for: Amsgen, Employee of: Employee of Kezar Life Sciences, Nil Gøel Shareholder of: Own stock options in Kezar Life Sciences, Employee of: Corporate officer of Kezar Life Sciences.


FR0197 Efficacy data of MC2-03 (ciclosporin 0.03% and 0.06% eyedrops) in sjogren’s patients with severe keratitis: outcomes of the northern lights phase 2b trial
Frederic Gomez1, Johan Selmer1, Morten Praestegaard1, Miguel Teus2, Luis Pablo2, Maite Sainz de la Maza2, Steffen Heegaard2, MC2 Therapeutics, Horsholm, Denmark;1University of Alcalá, Madrid, Spain;2University Hospital Miguel Servet, Zaragoza, Spain; 1Institute Clinic of Ophthalmology, Hospital Clinic of Barcelona, Barcelona, Spain; 2Department of Ophthalmology/University Hospital Rigshospitalet, Copenhagen, Denmark

Background: Sjögren’s syndrome is one of the most common rheumatic autoimmune disorders (1). It is a chronic systemic autoimmune disease in which immunmediated inflammation, characterized by lymphocytic infiltration of exocrine glands and epithelia, causes secretory gland dysfunction leading to dryness of the main mucosal surfaces (2) including dry eye with severe keratitis. Ciclosporin is a well-known immunosuppressant with a long record in the treatment of various autoimmune disorders (2) including dry eye. The aim of this study was to evaluate the safety and efficacy of MC2-03 in the treatment of severe keratitis in Sjögren’s syndrome patients.

Objectives: To report the clinical efficacy of MC2-03 (ciclosporin 0.03% and 0.06% eyedrops) in Sjogren’s patients with severe keratitis from a 6-month clinical trial.

Methods: The NORTHERN LIGHTS trial is a randomized, double masked, controlled multicentre European trial that assessed MC2-03 0.03%, MC2-03 0.06%, vehicle and best-standard-of-care (BSC) for the treatment of moderate-to-severe dry eye disease (patients having baseline corneal fluorescein staining (CFS) score ≥4). The full analysis set consisted of a total of 255 patients with 66 patients having a documented history of Sjögren’s syndrome. The objective of the trial was to evaluate safety and efficacy of MC2-03 after treatment once daily for 6 months followed by a 3 month safety follow-up. The primary efficacy endpoint was the proportion of patients achieving ≥2-grade improvement in CFS. CFS was evaluated using the modified Oxford grading system: a 7-point ordinal scale (0, 0.5, and 1 to 5), where grade 0 represents complete corneal clearing (absence of staining dots).

Results: The 66 patients with documented history of Sjögren’s syndrome constituted 25.9% of the trial population with 90.9% of the patients being females (n=60). Among the Sjögren patients, 58% (n=38) had severe dry eye (CFS 4) at baseline. Data analyzed for observed cases showed that the proportion of Sjögren’s patients achieving 2-grade improvement of CFS (baseline CFS 3 and CFS 4) was higher in MC2-03 groups compared to the control groups (Table 1). When patients treated with any active were compared to patients treated with any control, a 2-grade improvement of the CFS was observed in 51.9% patients in the combined active group vs. 26.7% for the combined control group (p=0.0620).

Table 1. SJ patients with 2-grade reduction in CFS

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Combined active</th>
<th>Combined control</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>MC2-03</td>
<td>9/14 (64.3%)</td>
<td>3/15 (20.0%)</td>
<td>p=0.0286</td>
</tr>
<tr>
<td>BSC</td>
<td>3/14 (21.4%)</td>
<td>6/15 (40.0%)</td>
<td></td>
</tr>
</tbody>
</table>

Using the same approach, the most severe patients, having CFS 4 at baseline, had a statistically significantly higher responder rate of 64.3% in the combined active group versus 21.1% in the combined control group (p=0.0286).

Table 2. Severe Sjögren patients with 2-grade reduction in CFS

<table>
<thead>
<tr>
<th>Combined active</th>
<th>Combined control</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>12/14 (85.7%)</td>
<td>3/15 (20.0%)</td>
<td>p=0.0286</td>
</tr>
<tr>
<td>BSC</td>
<td>3/14 (21.4%)</td>
<td>6/15 (40.0%)</td>
</tr>
</tbody>
</table>

Conclusion: Data from the NORTHERN LIGHTS trial show that MC2-03 ciclosporin eyedrops has the potential to be a safe, well-tolerated and efficient treatment in Sjögren’s patients.

REFERENCES:


FR0198 Antimalarial agents diminish while methotrexate, azathioprine and mycophenolic acid increase BaFF levels in systemic lupus erythematosus
Boris Hernández-Breijo1, Alvaro Gomez2,3, Sofia Soukka2,3, Petter Johansson2,3, Ioannis Parodis2,3, La Paz University Hospital, Immuno-Rheumatology Research Group, IDiPaz, Madrid, Spain; 1Karolinska Institutet, Division of Rheumatology, Department of Medicine, Stockholm, Sweden; 2Karolinska University Hospital, Rheumatology, Stockholm, Sweden

Background: Elevated levels of the B cell activating cytokine BAFF (also known as BLYS) have been associated with active systemic lupus erythematosus (SLE), and the anti-BAFF monoclonal antibody belimumab has been approved as an add-on to standard-of-care SLE treatment, the latter mainly comprising glucocorticoids, antimalarial agents (AMA) and other immunosuppressive treatments.

Objectives: To investigate the effect of AMA and three other commonly used in SLE immunosuppressive agents (methotrexate, azathioprine, mycophenolate mofetil/sodium) on serum BAFF levels.

Methods: Access to data from the phase III clinical trials of belimumab BLISS-52 (n=865; NCT00424476) and BLISS-76 (n=819; NCT00410384) was granted by GlaxoSmithKline (Uxbridge, UK); a total of 1684 SLE patients were analysed. Serum samples obtained prior to belimumab initiation of patients achieving 2-grade improvement in CFS was evaluated using the modified Oxford grading system: a 7-point ordinal scale (0, 0.5, and 1 to 5), where grade 0 represents complete corneal clearing (absence of staining dots).

Results: The 66 patients with documented history of Sjögren’s syndrome constituted 25.9% of the trial population with 90.9% of the patients being females (n=60). Among the Sjögren patients, 58% (n=38) had severe dry eye (CFS 4) at baseline. Data analyzed for observed cases showed that the proportion of Sjögren’s patients achieving 2-grade improvement of CFS (baseline CFS 3 and CFS 4) was higher in MC2-03 groups compared to the control groups (Table 1). When patients treated with any active were compared to patients treated with any control, a 2-grade improvement of the CFS was observed in 51.9% patients in the combined active group vs. 26.7% for the combined control group (p=0.0620).
EFFECTIVENESS AND SAFETY OF BELIMUMAB IN PATIENTSWITH ACTIVE SYSTEMIC LUPUS
ERYTHEMATOSUS: RESULTS FROM A LARGE, PAN-NATIONAL, MULTICENTRIC STUDY
Luca Iaccarino1, Francesca Saccon1, Alessandro Matheiu2, Matteo Piga3, Angela Canbelli4, Carlo Selini5, Paolo Cardinali6, Armando Gabrielli7, Andrea Doria8, Francesca Sebastiani9, Rosetta De Angelis10, Paola Faggioni11, Antonella Laria12, Micaela Fredi13, Francesca Regola14, Laura Andreoli15, Giulia Pazzola16, Carlo Salvarani17, Maurizio Rossini18, Giovanni Orsolini19, Mariele Gatto20, Salvatore Scarpato21, Salvatore De Vita22, Alessandra Bortoluzzi23, Marcello Govoni24, Angela Ceribelli25, Carlo Selmi26, Paolo Cardinaletti27, Armando Gabrielli28, Andrea Doria29.

1University of Padova, Rheumatology, Department of Medicine, Padua, Italy; 2University of Genova, Genova, Italy; 3University of Bari, Bari, Italy; 4Catholic University of Sacred Heart, Rome, Italy; 5Hospital Gaeleano Pin, University of Milano, Milano, Italy; 6Hospital San Raffaele, Milano, Italy; 7San Raffaele Hospital, Milano, Italy; 8University of Pavia, Pavia, Italy; 9University of Genova, Genoa, Italy; 10University of Bari, Bari, Italy; 11University of Firenze, Firenze, Italy; 12University of Roma, Rome, Italy; 13University of Perugia, Perugia, Italy; 14University of Napoli, Napoli, Italy; 15University of Udine, Udine, Italy; 16University of Ferrara, Ferrara, Italy; 17University of Pisa, Pisa, Italy; 18University of Verona, Verona, Italy; 19Hospital of Scafati, Scafati (SA), Italy; 20Humanitas Hospital, Milano, Italy; 21University of Campania Vanvitelli, Napoli, Italy; 22Hospital of Scafati, Scafati (SA), Italy; 23University of Firenze, Firenze, Italy; 24University of Firenze, Firenze, Italy; 25University of Firenze, Firenze, Italy.

Background: Belimumab is the unique biologic therapy available for patients with SLE.

Objectives: To investigate effectiveness and safety of belimumab in SLE patients in clinical practice.

Methods: 458 active SLE patients (ACR criteria) from 24 Italian Centers, mean±SD age 43.5±11.3 years; mean±SD disease duration 12.3±8.7 years, were treated with belimumab (10 mg/kg day 0, 14, 28 and then every 28 days), as add-on therapy.

Results: BAFF levels (mean, SD; pg/mL) were higher in patients receiving methotrexate (1835, 1617; n=212; P=0.001), azathioprine (1901, 1472; n=364; P<0.001) or mycophenolate mofetil/sodium (1994, 1544; n=175; P<0.001) and no immunosuppressive treatment other than the one investigated compared with patients receiving no immunosuppressive treatment (1593, 1929; n=860); AMA were allowed in both groups, in all comparisons. In contrast, patients on AMA displayed lower BAFF levels (1654, 1318; n=1085) compared with patients who did not use AMA (1942, 2408; n=1942; P=0.002). In linear regression, AMA use showed a consistent and independent association with lower BAFF levels in all models, whereas use of each one of methotrexate, azathioprine and mycophenolic acid was associated with higher BAFF levels. All models were adjusted for the use of immunosuppressive agents other than the one investigated.

Conclusion: Our data imply differential effects of antimalarial agents and other immunosuppressive treatments on BAFF levels; AMA diminished while methotrexate, azathioprine and mycophenolic acid increased BAFF levels. It is worth noting that methotrexate and mycophenolic acid are not approved for the treatment of SLE. Considering the importance of BAFF in B cell homeostasis and SLE pathogenesis, exploration of the biological significance of the differential effects of different immunosuppressive agents on BAFF levels is anticipated.

Acknowledgement: The authors would like to thank GlaxoSmithKline (Uxbridge, UK) for granting access to the data from the BLISS-76 and BLISS-52 trials (ClinicalTrials.gov identifiers NCT00424476 and NCT00410384, respectively) through the Clinical Study Data Request (CSDR) consortium.


FR1020

REVIEW OF HYDROXYCHLOROQUINE USE AND DEVELOPMENT OF A REGIONAL STRATEGY TO MINIMISE RETINAL TOXICITY

Ursula Laverty1, Gerard Reid2, Julie Silvestri2, Adrian Pendleton1. 1Musgrave Park Hospital, Belfast, United Kingdom; 2Royal Victoria Hospital, Belfast, United Kingdom

Background: Guidelines from the Royal College of Ophthalmologists in February 2018 were developed for retinal screening for patients on hydroxychloroquine, as recent evidence suggests the risk of retinal toxicity is higher than previously reported. The prevalence of retinal toxicity in long term use appears to be 7.5% and depending on dose and duration of therapy can increase to 20-50% after 20 years of therapy. Risk is increased for patients taking more than 5mg per kg per day of hydroxychloroquine, patients on Tamoxifen and those with renal impairment. The guidelines recommend the use of a standardised referral proforma to help identify patients who are high risk.

Objectives: 1. Audit of Hydroxychloroquine use and retinal screening in the Belfast Health and Social Care Trust (BHSCST)
2. Develop a regional referral proforma and screening service for retinal toxicity

Methods: Patients who were treated with hydroxychloroquine, under the care of a consultant rheumatologist were identified on the database. A proforma was used to aid data collection and patients’ electronic records were reviewed. We audited the use of hydroxychloroquine and retinal screening against current Royal College of Ophthalmology (RCO) guidelines. We designed a standardised referral proforma and regional screening strategy in conjunction with ophthalmology colleagues.

Results: There were 151 patients identified on hydroxychloroquine on the database. 40 of these patients had stopped hydroxychloroquine, 2 of which had retinal toxicity. Therefore the rate of retinal toxicity in this sample was 1.3% (2/151).

There were 111 patients who remained on hydroxychloroquine treatment with a female: male ratio of 9:1. Age range was from 22 to 84, with a mean age of 55. There were 44% of patients on hydroxychloroquine for rheumatoid arthritis, 25% had systemic lupus erythematosus, 8% had Sjogren syndrome, 6% had panniculitis rheumatoid arthritis and 13% had other connective tissue diseases. The majority (79%) of patients were on 200mg hydroxychloroquine daily and 19% were on 400mg daily. 6% of patients had an eGFR<60. No patients were on tamoxifen. 72% of patients were on hydroxychloroquine treatment for over 5 years. Retinal screening was overdue in 64% of patients.

Conclusion: In this sample, only 1.3% of patients had evidence of retinal toxicity, although 64% of patients were overdue retinal screening. We developed a referral proforma and a regional screening strategy in line with RCO guidelines. In order to meet the RCO guidelines, we recognise the need for substantial investment in regional ophthalmology services.

REFERENCES:

Disclosure of Interests: None declared


FR10201

REAL WORLD MEDICATION USE IN INCIDENT SYSTEMIC LUPUS ERYTHEMATOSUS AND LUPUS NEPHRITIS PATIENTS

Lin Xi1, Furaha Karubuyo1, Jarni Sahl1, Jennifer H. Lockhart2, Lj Nari3, 1STATinMED Research, Ann Arbor, United States of America; 2Janssen Global Commercial Strategic Organization, Horsham, United States of America; 3Janssen Research and Development, LLC, Horsham, United States of America

Background: Systemic lupus erythematosus (SLE) is an autoimmune disease that causes inflammation in connective tissues and can involve multiple organs systems. Lupus nephritis (LN) is an inflammatory kidney disease caused by SLE. There is a gap in the literature regarding the standard of care in SLE and LN patients.

Objectives: This study generated real world medication use among SLE and LN patients.

Methods: This retrospective study used data from two large administrative databases in the US: Truven Health MarketScan® and Optum® databases to identify adult patients (≥18 years of age) with ≥2 medical claims on different dates for SLE or LN diagnoses from 01JAN2013-31DEC2015. SLE was identified using the International Classification of Diseases, 9th and 10th Revision, Clinical Modification [ICD-9-CM] codes (710.0) OR ICD-10-CM (M32.10-M32.19, 32.8, 32.9). LN was captured as a subset of SLE using [ICD-9-CM: 710.0 AND (581.81 or 582.81 or 583.81); OR ICD-10-CM-M32.14)]. The first SLE or LN diagnosis was designated as the index date. Patients were required to have continuous health plan enrollment for 1 year pre-index date (baseline period) and 1 year post-index date (follow-up period) and no prior SLE/LN diagnosis claims or belimumab medical/prescription claim during the baseline period to ensure incident patients were captured. The Truven Health MarketScan® and Optum® databases were pooled together and duplicates were identified and retained in MarketScan® only. Patient demographics and clinical characteristics during the baseline period were assessed. SLE treatment used during the follow-up period was evaluated and the proportion of patients that used SLE medications and average number of medical/prescription claims (#Rx) for each medication were provided.

Results: A total of 31,345 patients were identified including 30,086 SLE and 1,259 LN patients. Key results are shown in Table 1. The mean age was 52.7 years for SLE and 48.3 years for LN patients. Over 80% of the patients were female, with a mean Charlson Comorbidity Index (CCI) score of 1.1 and 1.8 for SLE and LN patients respectively. The most common comorbidities at baseline were hypertension and infections. Corticosteroids (SLE=58.3%, #Rx=4.5; LN=66.2%, #Rx=6.5) and hydroxychloroquine (SLE=43.4%, #Rx=5.8; LN=40.7% #Rx=6.2) were the most commonly used SLE medications during 1-year follow up period. Approximately 2% of patients used biologics including belimumab (SLE=1.1%, #Rx=8.8; LN=1.4%, #Rx=8.3) and rituximab (SLE=0.9%, #Rx=4.2; LN=2.1%, #Rx=4.0).

Disclosure of Interests: None declared

THERAPY IN REFRACTORY SKIN LUPUS LESIONS

Table 1: SLE Medications during 1 year of follow-up

<table>
<thead>
<tr>
<th>SLE Medications, N (%)</th>
<th>Systemic Lupus Erythematosus (n=216)</th>
<th>Lupus Nephritis (n=2,251)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corticosteroids, N (%)</td>
<td>172/3 (85.3)</td>
<td>634 (55.9)</td>
</tr>
<tr>
<td>Number of prescriptions, Mean (SD)</td>
<td>6.5 (3.9)</td>
<td>6.5 (3.6)</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>10/6 (49.0)</td>
<td>174 (15.4)</td>
</tr>
<tr>
<td>Number of prescriptions, Mean (SD)</td>
<td>5.0 (2.4)</td>
<td>5.0 (2.4)</td>
</tr>
<tr>
<td>Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)</td>
<td>33/14 (72.7)</td>
<td>278 (24.5)</td>
</tr>
<tr>
<td>Number of prescriptions, Mean (SD)</td>
<td>3.6 (5.0)</td>
<td>3.0 (5.3)</td>
</tr>
<tr>
<td>Angiotensin Converting Enzyme Inhibitors (ACEI)</td>
<td>27/7 (67.2)</td>
<td>409 (36.5)</td>
</tr>
<tr>
<td>Number of prescriptions, Mean (SD)</td>
<td>5.4 (3.1)</td>
<td>5.4 (3.1)</td>
</tr>
<tr>
<td>Angiotensin II Receptor Blockers (ARB)</td>
<td>1/1 (100)</td>
<td>1/1 (100)</td>
</tr>
<tr>
<td>Number of prescriptions, Mean (SD)</td>
<td>5.8 (1.7)</td>
<td>5.8 (1.7)</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>28/8 (96.4)</td>
<td>62 (5.5)</td>
</tr>
<tr>
<td>Number of prescriptions, Mean (SD)</td>
<td>5.5 (4.1)</td>
<td>5.5 (4.1)</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>2/2 (100)</td>
<td>40 (3.5)</td>
</tr>
<tr>
<td>Number of prescriptions, Mean (SD)</td>
<td>2.7 (2.6)</td>
<td>2.7 (2.6)</td>
</tr>
<tr>
<td>Mycophenolate Mofetil</td>
<td>9/5 (85.7)</td>
<td>397 (34.5)</td>
</tr>
<tr>
<td>Number of prescriptions, Mean (SD)</td>
<td>5.1 (2.7)</td>
<td>5.1 (2.7)</td>
</tr>
<tr>
<td>Leflunomide</td>
<td>5/5 (100)</td>
<td>351 (30.5)</td>
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<td>Number of prescriptions, Mean (SD)</td>
<td>4.5 (3.1)</td>
<td>4.5 (3.1)</td>
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<td>Bellinomide</td>
<td>3/3 (100)</td>
<td>37 (3.2)</td>
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<td>Number of prescriptions, Mean (SD)</td>
<td>8.8 (5.0)</td>
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<td>Rituximab</td>
<td>1/1 (100)</td>
<td>62 (5.3)</td>
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<td>Number of prescriptions, Mean (SD)</td>
<td>2.7 (2.0)</td>
<td>2.7 (2.0)</td>
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<tr>
<td>Cyclophosphamide</td>
<td>1/1 (100)</td>
<td>67 (5.8)</td>
</tr>
<tr>
<td>Number of prescriptions, Mean (SD)</td>
<td>5.0 (5.0)</td>
<td>5.0 (5.0)</td>
</tr>
</tbody>
</table>

Table:

Conclusion: Our findings indicate a nominal use of biologics (2%) among SLE and LN patients. Corticosteroids and hydroxychloroquine were the most commonly used SLE treatments. These data reveal an unmet need for availability of advanced therapy to treat SLE and LN. Future studies are warranted to understand the underlying causes.

Disclosure of Interests: José Luis Martín-Vanillas: None declared, Belén Alcena-Mateo: None declared, J. Loricer: None declared, Susana Armesto: None declared, Eduardo Cuende: None declared, Juanjo Alegre-Sancho: None declared, Clara Moriano: None declared, Vanessa Calvo-Rio: None declared, Monica Calderón-Goercke: None declared, D. Prieto-Peña: None declared, Lara Sánchez Bilbao: None declared, Iñigo González-Mázon: None declared, C. González-Vela: None declared, J. Luis Hernández: None declared, Santos Castañeda: Consultant for: Amgen, BMS, Pfizer, Lilly, MSD, Roche, Sanofi, UCB, Miguel A González-Gay: Grant/research support from: Prof. MA Gonzalez-Gay received grants/research supports from Abbvie, MSD, Jansen and Roche., Speakers bureau: Consultation fees/participation in company sponsored speaker’s bureau from Pfizer, Lilly, Solab, Cellgene, Novartis, Roche and Sanofi., Ricardo Blanco: Grant/research support from: Abbvie, MSD, Roche, Consultant for: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen, Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen

References:

1. Mucke J, Duesing C, Chehab G, Schneider M. The definition of an accurate target for a treat to target (T2T) approach in SLE has been challenging over the past years. Recently four definitions of remission were presented by the international DORIS task force. The aim of this study was to evaluate the frequency of remission in our outpatient SLE cohort and to assess feasibility and concordance of the remission definitions with the treating physician’s opinion regarding the patient’s state.

Disclosure of Interests: Jos captures the essence of the findings from a clinical study focusing on the treatment of refractory skin lupus lesions. The study was conducted at a tertiary center and included 216 patients with systemic lupus erythematosus (SLE) and 2,251 patients with lupus nephritis. The study aimed to evaluate the frequency of remission according to four different definitions proposed by the DORIS task force. The results showed that the definition of remission based on the treating physician’s opinion had the highest concordance rate among the four definitions. However, the study faced challenges in assessing the feasibility of implementing these definitions in clinical practice. The findings highlight the need for further research to improve the definition of remission in SLE and optimize treatment strategies.

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Results: A total of 233 patients were included (87.6% female). 88 (37.8%) patients fulfilled any of the four DORIS remission definitions, while 129 patients were in remission according to their physician’s judgement. Of the 88 in DORIS remission, 17 were in complete remission, 20 in clinical remission, 16 in complete remission on treatment (ROT) and 35 in clinical ROT. In most cases the treating physician agreed on their patient being in remission (94.1% for complete remission, 90.0% for clinical remission, 81.3% for complete ROT, 88.6% for clinical ROT). A total of 145 patient were not in any DORIS remission. We observed discordance in the assessment of remission in 58 patients (24.9%). 10/88 being not in remission according to their treating physician despite fulfilling the DORIS remission definition and 48/145 were considered in remission though not in DORIS remission. Reasons for failing DORIS remission in the patients with attested physician’s remission was an elevated cSLE-DAl Score (n=22), elevated (n=24) or missing (n=1) physician global assessment, and prednisolone dosage >5 mg (n=9).

Conclusion: DORIS remission proved an achievable target in our outpatient clinic. Still we found discordance regarding DORIS remission and the treating physician’s judgement with a greater number of patients considered in remission by their physicians. Main reasons were a cSLE-DAl>0 and physician global assessment >0.5. Further analyses are needed to better characterize cases of disagreement and to address the question, if the rather strict DORIS criteria are needed to improve long-term outcome.

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Disclosure of Interests: Johanna Mucke: None declared, Christina Duesing: None declared, Gamal Chehab Grant/research support from: GlaxoSmitKline and UCB Pharma for performing the LuLa-study., Matthias Schneider Grant/research support from: GlaxoSmitKline and UCB Pharma for performing the LuLa-study., Speakers bureau: Chugai.

FrHO204 SAFETY, TOLERABILITY, PHARMACOKINETIC AND PHARMACODYNAMIC EFFECT OF BIIB059, A MONOCLONAL ANTIBODY TARGETING BDCA2 FOLLOWING ADMINISTRATION OF SUBCUTANEOUS SINGLE DOESES IN JAPANESE HEALTHY VOLUNTEERS

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Background: BDCA2 is a plasmacytoid dendritic cell (pDC)-specific receptor that, when ligated inhibits the production of inflammatory media tors. BIIB059 is a fully humanized, IgG1 monoclonal antibody (mAb) which targets BDCA2. This study was performed to evaluate the safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of BIIB059 in Japanese healthy volunteers.

Objectives: This phase 1 study evaluated the safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of BIIB059 in Japanese individuals (NCT02847598).

Methods: A total of 32 subjects from Japan were enrolled into 4 cohorts (8 BIIB059: 2 Placebo) to receive a single subcutaneous (SC) injection of 20-, 50-, 150- or 450 mg of BIIB059 or placebo. Blood samples were obtained to characterize PK and PD profiles and establish PK-PD relationships for BIIB059.

Results: BIIB059 was generally well tolerated; no SAEs were observed. Adverse events were reported by 9 subjects (37.5%) and none (0.0%) in the BIIB059- and placebo-treated subjects, respectively. Overall, 95.8% and 4.2% subjects reported AEs that were mild or moderate in severity, respectively. Three subjects (12.5%) experienced AEs considered related to study drug and mild in severity. All AEs resolved without treatment. There were no clinically significant findings on laboratory or physical examination. Following single SC BIIB059 administration, Cmax and AUC (0-inf) increased in a dose-proportional manner. Mean t1/2 ranged from 10 to 27 days. Eleven subjects (45.8%) treated with BIIB059 tested positive for anti-BIIB059 antibodies at ≥ 1 postdose timepoint (ADA).

FrHO2025 ANTIMALARIAL AGENTS IMPROVE PHYSICAL FUNCTIONING IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Patients with systemic lupus erythematosus (SLE) suffer an impaired health-related quality of life (HRQoL), and the majority of them experience fatigue as a major problem. Traditionally, treatment of SLE has been symptomatic, and antimalarial agents (AMA) are considered a cornerstone of SLE treatment. In previous literature, results regarding the effect of antimalarial agents on HRQoL have been conflicting.

Objectives: In this study, we aimed at investigating the potential influence of AMA on SLE patients’ self-perception of HRQoL aspects.

Methods: We utilised pooled baseline data from the BLISS-52 and BLISS-76 clinical trials of belimumab (n=1684). Access to data was granted by GlaxoSmitKline. The patients’ HRQoL and fatigue were self-reported using the Medical Outcomes Study (MOS) short form 36 (SF-36) health survey, the functional assessment of chronic illness therapy (FACT)-Fatigue scale and the three-level EuroQual-5 Dimension (EQ-SD) questionnaire. Minimal clinically important difference (MCID) was set to ≥ 5.0 points for SF-36 scales, ≥ 2.5 points for SF-36 component summary scores, and ≥ 4 points for FACT-Fatigue scores. High disease activity was defined as a SELENA-SLEDAI score ≥10. Organ damage was assessed using the SLICC/ACR Damage Index (SDI). The non-parametric Mann-Whitney U test was used for comparisons between AMA users and non-users. Linear regression models were next used in order to adjust for possible confounding factors; these included age, sex, ethnic origin, SLE disease activity, SLE duration, organ damage, corticosteroid use and use of other immunosuppressive agents.

Results: Results are presented as mean values ± standard deviation. Patients receiving AMA (n=1098) performed better than patients who did not receive AMA (n=586) with regard to SF-36 physical component summary (PCS) scores (39.6 ± 9.5 versus 38.1 ± 9.9; P=0.001), physical
functioning (61.1 ± 24.9 versus 55.0 ± 26.5; P<0.001), role physical (53.2 ± 26.9 versus 50.3 ± 27.7; P=0.036), bodily pain (49.5 ± 23.8 versus 47.1 ± 25.3; P=0.016), FACIT–Fatigue scores (30.5 ± 11.8 versus 29.3 ± 11.9; P=0.046), EQ-5D scores (0.75 ± 0.18 versus 0.72 ± 0.19; P=0.004), and EQ-5D visual analogue scale (VAS) scores (64.6 ± 19.4 versus 61.7 ± 18.6; P=0.001). The difference in SF-36 physical functioning was the greatest one among the SF-36 parameters, exceeding the corresponding MCID (≥50 points). The association between AMA use and better physical functioning was still significant after adjusting for potential confounding factors (standardised coefficient, β=0.08; P=0.001).

In this analysis, Asian patients performed better in physical functioning (β=0.07; P=0.004) while African/African American patients performed worse (β=0.07; P=0.033). High disease activity (β=−0.09; P=0.001) and organ damage (β=−0.01; P=0.001) were also independent factors of worse physical functioning, whereas corticosteroid use independently improved the outcome (β=0.06; P=0.022).

Conclusion: AMA use contributes to better physical functioning in patients with SLE, independently of other factors.

Acknowledgement: The authors would like to thank GlaxoSmithKline (Uxbridge, UK) for granting access to the data from the BLISS-SC and BLISS-SD trials (ClinicalTrials.gov identifiers NCT01424476 and NCT00410394, respectively) through the Clinical Study Data Request (CSDR) consortium.

Disclosure of Interests: None declared


**FRIO206**

HYDROXYCHLOROQUINE BLOOD LEVELS PREDICT RETINOPATHY IN SLE

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Background: Hydroxychloroquine (HCQ) retinopathy after 10 years or more of use is more frequent than previously appreciated. This led to new ophthalmology guidelines that changed the recommended dosing from 6.5 mg/kg to 5 mg/kg (1).

Methods: We analyzed data on 537 SLE patients from a clinical cohort who had repeated assessments of HCQ blood concentrations, and were evaluated one or more times for retinopathy (300 single retinopathy exam, 149 two and 88 three or more assessments). The patients were 92% female and 42% Caucasian. Hydroxychloroquine blood levels were performed as previously described. In our analysis, HCQ toxicity was defined dichotomously by a retina expert: all those with a value of “No” or “Possible” were categorized as not having HCQ toxicity, and those who had a “Yes” were categorized as having it. Mean and maximum HCQ blood concentration over all cohort visits prior to the final retinopathy assessment were calculated. Risk of HCQ toxicity was then assessed in tertiles defined by these variables.

Results: Our data show that the risk of HCQ retinopathy is higher in men and Caucasians. As expected, it is higher in older patients and with greater duration. We also found that BMI and hypertension were predictive of HCQ retinopathy. For the first time, our data show the utility of HCQ blood levels in predicting retinopathy. This would allow clinicians to either decrease dose or increase monitoring in those with high blood levels.

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**FRIO207**

BASELINE LEVELS OF BAFF, APRIL AND CD8+ EFFECTOR MEMORY CELLS AS PREDICTORS OF SLEDAI RESPONSE TO BELIMUMAB THERAPY

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Background: Systemic lupus erythematosus (SLE) patients show high circulating levels of BLyS (B lymphocyte stimulator, also known as BAFF) and of other cytokines belonging to the tumor necrosis factor (TNF) superfamily [1]. Belimumab is a monoclonal antibody against soluble BLyS used for treatment of refractory SLE. Although B cells are the main target of this therapy, a BLyS-dependent T cell activation pathway has also been demonstrated [2]. Clinical studies showed that high levels of anti-DNA antibodies and low complement at baseline are predictors of response to Belimumab treatment.

Objectives: Our study aims at exploring the role of biomarkers belonging to the TNF superfamily and of effector T-lymphocytes as predictors of response.

Methods: Twenty-one patients with SLE received Belimumab. Clinical evaluation and laboratory test were performed at baseline and after six and twenty months of therapy. Biomarkers belonging to the TNF superfamily (BAFF, APRIL, sBCMA, sCD40L, sTACI, TWEAK) were tested by high-sensitivity ELISA in all patients and lymphocyte immunophenotyping was performed by flow cytometry in ten subjects. SLE-disease activity was assessed by SLEDAI-2K score.

Results: BAFF and APRIL baseline serum levels and the number of CD3+CD8+ effector memory T cells were correlated positively with SLEDAI-2K improvement after 12 months of treatment (Pearson correlation=0.535 (p=0.015), 0.504 (p=0.023) and 0.654 (p=0.040)). After backwards exclusion of linear regression analysis including SLEDAI-2K, effector T cell relative number and BAFF or APRIL at baseline, only APRIL remained as significant independent predictor of SLEDAI-2K improvement after 12 months of therapy (adjusted R square=0.649, p=0.025). Moreover, after controlling TNF-family members serum levels and SLEDAI-2K at baseline, only BAFF showed the best predictive value (adjusted R 0.564, p<0.001).
Conclusion: In our cohort of SLE patients, baseline serum level of APRIL, together with percentage of CD3+CD8+ effector memory cells, or BAFF serum level alone resulted as best predictors of response to Belimumab. Considering that immunophenotyping is often not done in clinical practice, BAFF baseline serum levels alone could be used routinely as a good predictor of response to therapy, as suggested by post-hoc analyses of the BLISS study and shown by a recent “real-life” observational study [3].

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Disclosure of Interests:

References: Francesco Regola: None declared, Silvia Piantoni: None declared, Laura Andreoli: None declared, Torsten Lownin: None declared, Rajesh Kumar : None declared, Paolo Arinó: None declared, Franco Franceschini: None declared, Angela Tincani Consultant for: UCB, Pfizer, Abbvie, BMS, Sanofi, Roche, GSK, AlphaSigma, Lilly, Janninen, Cellgene, Novartis, Georg Pongratz : None declared


FRIO208 IDENTIFYING LUPUS PATIENT SUBSETS AND SPECIFIC PHARMACODYNAMIC CHANGES THROUGH IMMUNE CELL DECONVOLUTION OF GENE EXPRESSION DATA IN ATACICEPT-TREATED PATIENTS IN THE APRIL-SLE STUDY

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Background: The Phase 2/3 APRIL-SLE study evaluated the safety and efficacy of atacicept, a dual inhibitor of the B lymphocyte stimulator (BLyS) and a proliferation-inducing ligand (APRIL), in systemic lupus erythematosus (SLE).

Objectives: The goal of this post-hoc analysis was to use cell-based gene signatures on gene expression data from the APRIL-SLE study to identify clusters of patients with potential to flare and to assess clusters for differences in treatment effects of atacicept vs placebo.

Methods: A published immune cell deconvolution algorithm (Abbas et al. 2009) was applied to whole-blood gene expression data from APRIL-SLE patients to identify relative proportions of 17 immune cell types. Patients were then grouped into clusters based on these immune cell profiles using a k-medoid clustering algorithm and were compared to each other based on patient characteristics, biomarkers and clinical efficacy. In addition, baseline expression and change in expression of putative APRIL-responder genes were compared among clusters. APRIL-responder genes were identified by combining differential expression results from the APRIL-SLE study (Week 52 vs Day 1 randomization) and tabalumab (targets BLyS) Phase 3 studies (Week 52 vs baseline; GSE88887).

Results: Patient gene expression data (N=105; placebo, n=30; atacicept 75 mg, n=40; atacicept 150 mg, n=35) were used to group patients into five main clusters (P1-P5) by predominant characteristic cells: P1, T helper cells; P2, plasma cells; P3, neutrophils and B cells; P4, B cells; P5, activated dendritic cells. Patients in P2 and P5 were more likely to have positive anti-dsDNA antibodies (≥30 IU/ml), elevated BLyS; ≥1.6 ng/ml, and high interferon gene signature in the blood than other those in other clusters. Patients in P2 were most likely to have low complement C3 and C4 levels. Placebo-group flare rates in P2 (100%), P4 (100%) and P5 (83%) were markedly higher than in P1 (33%) and P3 (29%). In P2, P4, and P5 the median time-to-flare was much lower with placebo (85, 98.5, and 115.5 days, respectively) than with atacicept 150 mg (over 364 days for all three clusters). A comparison of differentially-expressed genes from clinical studies of SLE patients treated with atacicept and tabalumab revealed possible APRIL-responder genes: SDC1, PARM1 and MZB1. These genes had a higher baseline expression in P2 and P4 compared with other clusters. SDC1 was reduced from baseline more in P2, P4, and P5 after atacicept treatment, while PARM1 and MZB1 decreased after atacicept treatment in P2 and P4.

Conclusion: These post-hoc analyses revealed different subsets of SLE patients based on their molecular profiles. Atacicept may have different treatment effects in the identified patient subsets vs placebo, providing insights into potential mechanisms of flare in SLE.

REFERENCES:


FRIO209 LOW-DOSE GLUCOCORTICOID COULD AFFECT ADVERSE PREGNANCY OUTCOMES, ESPECIALLY IN PRETERM BIRTH, LIGHT-FOR-DATE NEWBORNs, PRETERM PREMATURE RUPTURE OF MEMBRANE IN CONNECTIVE TISSUE DISEASE PATIENTS

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Background: Connective tissue disease (CTD) often occurs in women of child-bearing age, and flare-ups during pregnancy. Therefore, it is important to manage their disease activities with the treatment which have no influence on fetal growth and development. Among the treatment during pregnancy glucocorticoid is most often used for maintain or control to flare-ups of CTD disease activities. However, prolonged use of glucocorticoid during pregnancy is considered to increase the risk of adverse pregnancy outcomes (APOs) including preterm birth, intrauterine growth restriction, and premature rupture of membrane (PROM) (1, 2).

Objectives: The aim of this study is to reveal the dose of glucocorticoid which influences on APOs.

Methods: We investigated 164 pregnant patients complicated with CTD from March 2006 to January 2019. All these patients were managed their disease activities throughout pregnancy in our institute. APOs including preterm birth, light-for-date (LFD) newborns, PROMs in these pregnant patients were examined retrospectively. We analyzed the association between APOs and the incidence or mean dose of glucocorticoid use during pregnancy.

Results: Underlying CTD is Systemic lupus erythematosus (25.3%), Sjögren’s syndrome (24.9%), rheumatoid arthritis (18.1%), Antiphospholipid syndrome (6.8%), mixed connective tissue disease (6.7%), and others. Glucocorticoid was administered in 96 cases, which tended to be earlier gestational week at delivery (37.5±3.0 vs. 38.9±1.5, P<0.01) and lower birth weight of newborns (2601.9±603.0 vs. 3019.0±480.8, P<0.01) significantly. Compared with full-term birth, the cases of preterm birth had higher dose of glucocorticoid during pregnancy significantly (P<0.01). Logistic regression analysis for preterm birth revealed the cut-off value of mean prednisolone dose as 7.5 mg per day (Figure 1). Similarly, the
patients who delivered LFD newborns had higher dose of prednisolone (P=0.04), and logistic regression analysis revealed cut-off value as 6.7 mg per day (Figure 2). The cases with preterm PROM also had higher dose of prednisolone (P=0.01), and logistic analysis revealed cut-off value as 5.0 mg per day (Figure 3).

**Conclusion:** Glucocorticoid is often used for CTD patients during pregnancy, however, CTD patients who were treated with continuing high dose of glucocorticoid during pregnancy had high risks for APOs such as preterm birth, low birth weight of newborns, preterm PROM. Our data indicated that the cut-off dose of prednisolone values of preterm birth, LFD, preterm PROM was 7.5 mg, 6.7 mg, 5.0 mg per day respectively. It is important for rheumatologists to pay much attention for these risk of glucocorticoid use to CTD patients who hope to conceive and to manage the disease activity with appropriate dose of glucocorticoid. Recently, many immunosuppressants including biologics have been reported to be available for the safety use during pregnancy, and might be helpful to reduce the risk of APOs by glucocorticoid use.

**REFERENCES:**


**Disclosure of Interests:** None declared

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**Figure 1.** Logistic regression analysis for preterm birth (AUC=0.750, P=0.01, cut-off value=7.5mg/day)

**Figure 2.** Logistic regression analysis for preterm birth (AUC=0.644, P=0.05, cut-off value=6.7mg/day)

**Figure 3.** Logistic regression analysis for preterm birth (AUC=0.728, P=0.04, cut-off value=5.0mg/day)

**REFERENCES:**


**Disclosure of Interests:** None declared

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A LOW AND PROMPTLY TAPERED STEROID REGIMEN CAN ACHIEVE EXCELLENT RESULTS IN LUPUS NEPHRITIS, WITH LESS ADVERSE EVENTS

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Background: The optimal use of glucocorticoids (GC) in lupus nephritis (LN) remains a topic of debate, especially the tapering protocol and the duration of treatment. To date, only one randomized controlled trial, MyLupus, has compared two oral prednisolone (P) regimens in LN (0.5 mg/kg/d) with fewer side-effects in the 0.5 mg/kg/d group. Importantly, Herpes zoster infections were only observed in the higher P dose group, with a lower number of non-responders. The one-year renal response was defined by achieving a proteinuria target <0.8g/d.

Methods: Data from the last 30 consecutive proliferative LN patients diagnosed at the Louvain Lupus Clinic (between 2015 and 2018) were reviewed retrospectively. In these patients, the 10 last consecutive patients received a low fixed dose of P (20mg/d) for 4 weeks, rapidly tapered as follows: 15mg/d for 2 weeks, 12.5mg/d for 2 weeks, 10mg for 2 weeks, 5mg/d from for 2 weeks and 2.5mg/d for 6 months. GC were withdrawn at week 52. The baseline and the follow-up data of these 10 patients were compared to the 20 previous consecutive LN patients followed in the same center but given a standardized P dose of 0.5 mg/kg/d. Both groups of patients received 750 mg methylprednisolone IV pulses on 3 consecutive days at baseline. The one-year renal response was defined by achieving a proteinuria target <0.8g/d.

Results: Clinical (BMI, gender, age, mean serum creatinine, mean proteinuria, SLEDAI-2K, non-steroid immunosuppressants) and pathological (ISN/RPS class) characteristics did not differ at baseline between the two groups. As illustrated in the Table, the mean uPCR ratios measured at one year were similar, as were the percentages of patients who achieved the proteinuria target. Importantly, Herpes zoster infections were only observed in the higher P dose group, with the difference reaching almost statistical significance.

Conclusion: In patients suffering from proliferative LN, an induction protocol with a low and rapidly tapered dose of P may be as effective as higher dose regimen to achieve the proteinuria target at one year, with fewer Herpes zoster episodes. These results deserve to be confirmed in a controlled trial.

REFERENCE:
HQC: hydroxychloroquine; 1R: p=0.005 versus Group C; 2R: p=0.0005 versus A and B Groups; other p values were non-significant; p values were calculated by unpaired t-tests and Fisher’s exact tests, as appropriate.

Disclosure of Interests: None declared
At the same time, the use of anti-B-cell drugs in combination therapy resulted in a significant decrease of the reciprocal response

Disclosure of Interests: None declared


FRIO213 RANDOMIZED PLACEBO CONTROLLED TRIAL OF ABATACET FOR NON-ORGAN THREATENING SYSTEMIC LUPUS WITH BACKGROUND MEDICATIONS WITHDRAWN

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Background: Abatacept (ABA) is a fusion protein of the extracellular domain of CTLA4 and the Fc domain of human IgG1, constructed to inhibit B/T cell co-stimulation. Previous studies of ABA in lupus failed to show benefit in overall disease activity, but improvement in arthritis was suggested.

Objectives: This 6-month randomized, double-blind, placebo-controlled (PBO) study withdrew background medications to facilitate the assessment of the effect of treatment in SLE patients with SLE arthritis.

Methods: Patients were entered with moderate to severe arthritis [BILAG A or B with ≥3 swollen and ≥3 tender joints (28 joint count)]. All DMARDs except prednisone (up to 20mg daily) were withdrawn by baseline and patients were randomized 1:1 to weekly sc ABA or PBO. One or more DepoMedrol injections (≥320mg total) was allowed by end of Month 2. Additional steroids or immune suppressants (IMS) at any time, or more DepoMedrol injections were allowed, but designated non-response. The primary endpoint was BICLA response at Month 6 compared to screening. Secondary objectives included SRI-4, SLEDAI 4-point improvement, SLEDAI arthritis resolution, BILAG A/B musculoskeletal (MSK) improvement, as well as low disease activity defined by either SLEDAI 2 or Lupus Low Disease Activity State (LLDAS) at Month 6. Flares were evaluated by the modified SELENA-SLEDAI flare index (1) in patients followed after baseline.

Results: 66 patients were randomized and received at least one dose of the study drug, 31 ABA and 35 PBO. 7 withdrew prior to Month 6. Flares were evaluable in 64 patients (31 on ABA, 33 on PBO). 14 (45%) patients on ABA vs. 18 (55%) on PBO had a moderate/severe flare by Month 6. 22 (71%) patients on ABA vs. 23 (70%) on PBO had experienced flare by Month 6. Rates of flare and treatment failure by Month 6 did not differ between groups (Log-Rank test, p=0.688 and p=0.631, respectively). The safety profile of ABA was consistent with known effects of the treatment.

Conclusion: ABA did not demonstrate improvement vs placebo in controlling disease activity or flare in SLE patients in a protocol that mandated IMS withdrawal. Placebo response rates of ≥23% support the validity of these results. Since some evidence suggests potential efficacy of ABA for certain biologic subsets of SLE (2), immunophenotyping may prove helpful.

REFERENCES:

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FRIO214 EFFICACY OF RITUXIMAB AND CYCLOPHOSPHAMIDE TREATMENT IN PATIENTS WITH PRIMARY SJOGREN’S SYNDROME AND PAROTID GLAND MALT LYMPHOMA

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Background: Mucosa-associated lymphoid tissue (MALT) lymphoma occurred in a higher frequency and at an earlier age in primary Sjögren’s syndrome (pSS) than reported for MALT lymphoma in the general population. The optimal treatment of MALT lymphoma in pSS has not been defined.

Objectives: to analyze retrospectively the long-term clinical course of pSS in patients with MALT lymphoma.

Methods: 63 SS patients with MALT lymphoma were retrieved from our SSS database. Most of the 63 pSS-lymphoma patients were female (n=60; 95%), pSS was diagnosed at a mean age of 51 (43-58) years and lymphoma at a mean of 7 (2-10) years later. Total mean follow-up was 5 years (2-8). 14 patients received immunomodulator agents for SS before the development of lymphoma (low doses of prednisone - 8 patients, chlorambucil – 7, cyclophosphamide – 3 patients). In 43 patients, the diagnosis of SS and MALT - lymphoma were established simultaneously. Clinical features and treatment outcome of MALT - lymphoma as well as SS activity was evaluated.

All patients had features of autoimmune disease (ANA-100%, RF-90%, anti-Ro/o/anti-La antibodies-94%) and met the diagnostic criteria of the Association of Rheumatologists of Russia for primary Sjögren’s syndrome: salivary gland involvement (stimulated parotid flow rate ≤ 2 ml in 5 min, parotid sialography showing the presence of diffuse punctuate or globular shadows with a diameter > 1mm, histopathology: a focus score>2 per 4mm2 in minor salivary gland biopsy), keratoconjunctivitis sicca (stimulated Schirmer’s test ≤10mm in 5 min, tear break-up time < 10 seconds, rose Bengal test or fluorescent test >1+), presence of abnormal concentrations of at least one of the serum autoantibodies (anti-Ro/o, anti-La, anticardiolipin antibodies, IgM-rheumatoid factor). The histology and immunohistochemical diagnosis of lymphoma was performed with B-cell clonality determination in salivary gland tissue.

Patients were treated with RTX (25 patients) or RTX+CPH (38 patients). Patients received 2 1g intravenous infusions of RTX 2 weeks apart, then 375 mg every 3 months for 2 years. Cyclophosphamide 1000 mg was administered every two weeks for a period of 12 weeks.

Results: MALT lymphoma was localized in parotid glands in 60 cases, submandibular salivary glands – in 2 cases, lacrimal gland – in 1 case. Eleven patients showed systemic features (7-purpura, 1-ocular, 3 – nephritis). Blood serum and urine examination revealed monoclonal secretion in 16/56 patients (7- lgM, 4- lgG and IgA, 2-lgA and 3 - BJK). Nineteen of 56 (34%) patients had cryoglobulinaemia. After follow-up of 24 mo, complete clinical remission (CR) of MALT lymphoma (normalization of salivary gland size, disappearance of lymphadenopathy and cytopenia) was obtained in 25 (72%) in the group of RTX and 35 (92%) in the group of RTX+CPH (p=0.005). An erosion biopsy of the parotid gland before and after therapy was made in 21 patients. Complete disappearance of histological pattern of MALT lymphoma was shown in 50% of the RTX treated patients and in 66% patients with combined therapy. B-cell clonality in parotid glands disappeared in 1/5 cases after RTX monotherapy and in 1/4 cases after RTX with CPH therapy. Cryoglobulinaemia disappeared in 33% patients in group of RTX and 46% in group of RTX+CPH (p=0.6).

Conclusion: Complete clinical remission of the lymphomas was achieved significantly more often in the group treated with RTX plus cyclostatic agent in comparison with patients who had RTX monotherapy.

Disclosure of Interests: None declared

Background: Autoimmune thrombocytopenia (AITP) is common in systemic lupus erythematosus (SLE) patients and may be refractory to conventional therapies. SLE related thrombocytopenia (SLE-TP) patients have T-cell dysfunction that was reported to be associated with the activation of the mammalian target of rapamycin (mTOR). Rapamycin (RAPA) inhibits antigen-induced T-cell proliferation and has been developed as a medication named sirolimus.

Objectives: We assessed safety, tolerance, and efficacy of sirolimus in a prospective, open-label clinical trial.

Methods: We did a single-arm, open-label study of sirolimus in patients with refractory SLE-TP unresponsive to, or intolerant of, conventional medications at Peking Union Medical College Hospital (PUMCH, Beijing, China). We enrolled refractory TP patients (aged ≥18 years) with systemic lupus erythematosus (SLE) who visited our referral center since September 2017. We excluded patients with allergy or intolerance to sirolimus, patients with life-threatening manifestations of lupus, such as RPN, NPLE or PAH and patients with uncur ed infection. All eligible participants had signed informed consents. Patients received oral sirolimus at a starting dose of 2 mg per day for 3 days and a sequential dose of 1 mg per day, with dose adjustment according to tolerance and to maintain a therapeutic range of 6–15 ng/mL. Patients were treated with sirolimus for 6 months. Safety outcomes included tolerance as assessed by the occurrence of common side-effects. The primary efficacy endpoint was complete remission rate and partial remission rate at the sixth month. The secondary efficacy endpoint was treatment remission rates at the third month. The efficacy endpoints were assessed in all patients who completed 3 or more months of treatment, and all patients who received at least one dose of treatment were included in the safety analyses.

Results: Between September 2017 and November 2018, 12 lupus patients (1 male and 11 female) were enrolled with an average age of 33.3y, average disease duration of 8.4 years. All patients have achieved remission with front-line therapy, including corticosteroids, intravenous immunoglobulin and immunomodulatory agents, such as azathioprine, FK506, mycophenolate mofetil, and cyclosporine. After sirolimus therapy (2 weeks to 6 months), 5 of 12 patients achieved CR, 11 patients have finished 4 months’ assessment, and 9 of them achieved CR.

Conclusion: Sirolimus is effective for the treatment of refractory SLE-TP and can be a choice of the second-line treatment. Further prospective studies are needed to evaluate sirolimus as a therapeutic option for SLE-TP and to monitor for potential long-term side effects.

REFERENCES:

Acknowledgement: None

Disclosure of Interests: None declared

weeks), with 4 having CR and 6 PR. The median response duration (MRD) was 12 weeks.

**Conclusion:** Our study provided preliminary but promising clinical evidence for iガリトム in treating refractory LN patients. A large randomized clinical trial is needed to establish its safety and efficacy for refractory LN.

**REFERENCES:**


**Disclosure of Interests:** None declared

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**RESULTS:**

**Conclusions:** Our study highlights that pharmacological inhibition of IRAK4 response can reverse two key components of lupus nephritis; the inflammatory and the fibrotic response.

**REFERENCES:**


**Disclosure of Interests:** Dania Rabah Shareholder of: Employee and shareholder of Biogen, Employee of: Biogen, Ramon Bonegio2, Agnes Gardel1, Holly Legault1, Ian Rifkin2, Ti Wang1, Chris Roberts1, Jeffery Vessels1, Norm Alliare3, Andrea Bertolotti-Ciarlet4, Kevin Guckian1. Biogen, Cambridge, United States of America, 1Boston University, Boston, United States of America; 2Cystic Fibrosis Foundation Therapeutics, Lexington, United States of America; 3Takeda, Cambridge, United States of America

**Background:** IRAK4 is an important signaling mediator of the innate immune system. IRAK4 regulates MyD88-dependent signaling from most TLRs and from IL-1R, resulting in downstream production of pro-inflammatory cytokines.

**Objectives:** Inhibition of IRAK4 kinase activity is a promising therapeutic approach for the treatment of autoinflammatory diseases, such as lupus. To this end, we identified a potent and highly selective inhibitor of IRAK4 kinase activity, BIIB-IRAK4i.

**Methods:** Recombinant kinase assays and DiscoveRx kinomescan were used to measure BIIB-IRAK4i kinase inhibition and selectivity, respectively. BIIB-IRAK4i-mediated proximal and distal pharmacodynamics effects (PD) were measured in both cell lines and whole blood assays. The ability of BIIB-IRAK4i to inhibit cytokine production induced by TLR ligands was measured in vitro and in vivo. Acute antibody-mediated lupus nephritis mouse model, which is a TLR-7 dependent and characterized by severe glomerular proliferative lesions with crescent formation, was used to determine the efficacy of BIIB-IRAK4i.

**Results:** BIIB-IRAK4i displayed equipotent proximal inhibition of MyD88 signaling and distal inhibition of cytokine production in vitro. BIIB-IRAK4i led to potent inhibition of cytokine production in whole blood assays stimulated with various synthetic TLR ligands as well as more physiologically relevant stimuli such as immune complexes, a hallmark of lupus pathogenesis. BIIB-IRAK4i inhibited TLR9-mediated cytokine production with similar potency in vitro and in vivo. In addition, BIIB-IRAK4i decreased both inflammation and fibrosis in an acute antibody-mediated lupus nephritis mouse model. BIIB-IRAK4i inhibited crescent formation as well as markers of tubulointerstitial fibrosis., which are both associated with decreased survival and adverse outcomes in human lupus nephritis.

**Conclusion:** Our study highlights that pharmacological inhibition of IRAK4 response can reverse two key components of lupus nephritis; the inflammatory and the fibrotic response.

**REFERENCES:**

[1] Phansenee, S., Sekararithi, R., Jatavan, P., & Tongsong, T. (2018). Prevention of immune flare may be life-threatening, and some of the medications that are used to treat SLE adversely affect fetus.[]

**Objectives:** To evaluate the pregnancy outcome in SLE patients and to determine the predictive factors for adverse fetal and maternal outcomes.

**Methods:** The study was conducted on the pregnant SLE patients attending the Rheumatology department, Zagazig University hospital in the period from January 2013 to January 2018. The data was collected retrospectively; demographically, laboratory and serological data on all patients, age at the onset of SLE, disease duration, systems affected, their disease activity using the Systemic Lupus Erythematous Disease Activity Index (SLEDAI), treatment received immunosuppressive regimen (dose and duration) before and during pregnancy, SLE flare during pregnancy, the fetal and the maternal outcomes.

**Results:** Fifty-four pregnancies were observed in 49 SLE patients with mean age of (27.5±5.6), mean SLE disease duration (3.7±2.2) and mean SLEDAI (5.4±6.1). 39 (75%) pregnancies with successful live births and 13(25%) fetal losses were observed. 36 of the live births (92.3%) were full-term and 3 (7.7%) were preterm births. Fetal losses included six spontaneous abortions, 3 stillbirths and 4 therapeutic abortions; 2 of them due to observed fetal anomalies and one due to life threatening lupus flare. We found SLEDAI significantly higher in patients with lost pregnancies (p=0.0001) than successful pregnancies. Proteinuria during pregnancy was a predictive factor for adverse fetal outcomes (odds ratio [OR] 19.7; P < 0.0001), also the presence of antiphospholipid antibodies (OR 15.3; P<0.0001), low C3 and C4 (OR 15.3; P=0.0001), anti-RO antibodies (OR 11.1; P=0.02), anti-LA (OR 4.7; P=0.03), chronic hypertension (OR 54.8; p=0.0001) and SLE flares (OR 32; P=0.0003). SLE flares occurred in 10 pregnancies (19.2%), mostly during the second trimester (60%). Renal involvement (70%) was the most common SLE flare during pregnancy. SLE flares during pregnancy were highly associated by nephritis prior to pregnancy (adjusted OR 9; P = 0.04) and the presence of antiphospholipid antibodies (adjusted OR 12; p=0.01).

**Conclusion:** Favorable pregnancy outcome was observed in Egyptian SLE patients; particularly in those with longer period of remission. Planned pregnancy is very important to reduce undesirable fetal and maternal outcomes in SLE patients. The presence of lupus nephritis, chronic hypertension, antiphospholipid syndrome, active disease at the onset of pregnancy, and proteinuria were highly associated with bad outcome.

**REFERENCES:**

[1] Yan Q, Du F, Huang X, Fu Q, Chen S, Dai D, et al. Prevention of immune flare may be life-threatening, and some of the medications that are used to treat SLE adversely affect fetus.[]
Objectives: Our objective here was to analyse a clinically well-phenotyped patients using a suite of immune assessments and identify inter-relationships between these features as well as subgroups of patients who may differ in response to therapy.

Methods: 143 SLE patients were evaluated for clinical phenotype using BILAG-2004, autoantibodies using radioimmunoprecipitation (IP, University of Bath), two interferon scores (IFN-Score-A and IFN-Score-B), flow cytometry for major circulating immune cell subsets, as well as the surface protein expression of tetherin on each subset, a cell-specific assay for IFN response.

Unsupervised hierarchical clustering was used to define autoantibody subgroups. IFN scores (reflected dCT) were compared between the groups using multivariate models. Other variables were compared using Kruskal-Wallis test with pairwise comparisons.

Results: Using IP, 141 patients could be divided into five subgroups: U1RNP/Sm only (n=23), Ro60+ only (n=8), U1RNP/Sm+Ro60+ (n=6), Ro60+Ro52+La (n=11), Ro52+ (n=16) and other ANA (n=77). Antibody subgroups was strongly associated with IFN-Score-A (F=4.39, p=0.001). Expression was lowest for “other ANA”, intermediate for single antibody groups, and highest with multiple positive antibodies. Multivariate linear regression, including interaction terms between antibody types, revealed that Ro60 and U1RNP/Sm were the independent predictors of IFN-Score-A level (p=0.051 and 0.009 respectively). There was no association between autoantibody status and IFN-Score-B (F=0.973, p=0.438).

In flow cytometry, the U1RNP/Sm group was notable for significantly lower numbers of CD4+T-cells and memory-B-cells. Memory B-cells were also lower in antibody-positive groups compared to “other ANA”. Tetherin expression was increased in antibody positive groups, but to a similar extent on most cell subsets. Memory B cell tetherin was significantly higher in the groups with multiple positive antibodies.

U1RNP/Sm+ was associated with renal involvement (p=0.004). Multicollinearity was greater in the Ro60+Ro52+La group (p=0.037).

Conclusion: This cohort revealed relationships between immune features. U1RNP/Sm antibody was notable for defining a group of patients with a cluster of immune abnormalities, including the greatest elevation of IFN activity, greater abnormalities on flow cytometry and clinical renal involvement. This was independent to the IFN-Score-B high status that predicts better clinical response to rituximab (presented elsewhere at this conference).

Future work in MASTERPLANS will investigate the significance of these subgroups for response to therapy.

Disclosure of Interests: Marta Aguilar-Zamora: None declared, Hui Lu: None declared, Zoe Betteridge: None declared, Katie Dutton: None declared, Md Yuzaful Md Yusof: None declared, Antonios Psarras: None declared, The MASTERPLANS Consortium: None declared, Edward Vital Grant/research support from: He McHugh: None declared, Brenda Roxana Vázquez Fuentes: None declared, Dignacio Angel Galara-Delgado: None declared, Cassandra Michele Skinner Taylor: None declared, Karim Mohamed Noriega: None declared, César Alejandro Fernández de Luna: None declared, Fernando Morales Wong: None declared, Hospital Universitario Dr. José Eletteno Gonzalez, Department of Rheumatology and Clinical Immunology, Monterrey, Nuevo León, Mexico: None declared.

Background: In Sjögren’s Syndrome (SS), ocular damage is mediated by inflammation induced by antibodies, enzymes, and other effectors that could be used as clinical indicators of the ocular surface damage. There is evidence suggesting that increased activity of matrix metalloproteinases (MMPs) is correlated with an increased ocular damage because of its potential inflammatory activity and could be used as a potential therapeutic target for dry eye.1,2 Very few studies have addressed the role between the ocular MMPs and the clinical parameters of SS.

Objectives: To determine the level of correlation between the serological profile of autoantibodies with ophthalmological parameters at the cornea level.

Methods: Cross-sectional, observational, and descriptive study. Sixty patients with a diagnosis of primary Sjögren’s syndrome (pSS) classified according to the ACR/EULAR 2016 criteria were included. The following measurements were made: Schirmer test, lacrimal osmolality, ocular staining score (OSS), and ocular surface disease index (OSDI) and metalloproteinase-9 (MMP-9) in tear and antibodies were measured in peripheral blood serum: RF isotypes (IgA, IgG, IgM), anti-SSA/Ro and anti-SSB/La proteinase-9 (MMP-9) in tear and antibodies were measured in peripheral serum: RF isotypes (IgA, IgG, IgM), anti-SSA/Ro and anti-SSB/La.

Results: Fifty-eight women participated (96.7%) with an average age of 53 years (±13.01) (Table 1). We found a positive correlation between OSS and RF-IgM (r=0.385 P<0.002), RF-IgA (r=0.256 P=0.049), and anti-Ro/SSA (r=0.302 P=0.019). We found a statistically significant association between the seropositivity of the Anti-SSA/Ro antibody and the presence of MMP-9 in tears (OR 4.38, CI 95% 0.877-21.92, P=0.057). A

References:

Disclosure of Interests: None declared


FRI0220

OCULAR SURFACE INFLAMMATORY MARKERS CORRELATED WITH IMMUNOLOGICAL PARAMETERS IN PRIMARY SJÖGREN’S SYNDROME

Nicolás Añorga1, Janett Carmen Rieglores2, Cesar Vidal Solís1, David Vega Morales1, Brenda Roxana Vázquez Fuentes1, Díncio Angél Galara-Delgado1, Cassandra Michele Skinner Taylor3, Mario Alberto Garza Elizondo1, Karim Mohamed Noriega1, Jesús Mohamed Noriega1, César Alejandro Fernández de Luna1, Fernando Morales Wong1,2 Hospital Universitario Dr. José Eletteno Gonzalez, Department of Rheumatology and Clinical Immunology, Monterrey, Nuevo León, México.1Hospital Universitario Dr. José Eletteno Gonzalez, Department of Ophthalmology, Monterrey, Nuevo León, Mexico.

Background: In Sjögren’s Syndrome (SS), ocular damage is mediated by inflammation induced by antibodies, enzymes, and other effectors that could be used as clinical indicators of the ocular surface damage. There is evidence suggesting that increased activity of matrix metalloproteinases (MMPs) is correlated with an increased ocular damage because of its potential inflammatory activity and could be used as a potential therapeutic target for dry eye.1,2 Very few studies have addressed the role between the ocular MMPs and the clinical parameters of SS.

Objectives: To determine the level of correlation between the serological profile of autoantibodies with ophthalmological parameters at the cornea level.

Methods: Cross-sectional, observational, and descriptive study. Sixty patients with a diagnosis of primary Sjögren’s syndrome (pSS) classified according to the ACR/EULAR 2016 criteria were included. The following measurements were made: Schirmer test, lacrimal osmolality, ocular staining score (OSS), and ocular surface disease index (OSDI) and metalloproteinase-9 (MMP-9) in tear and antibodies were measured in peripheral blood serum: RF isotypes (IgA, IgG, IgM), anti-SSA/Ro and anti-SSB/La.

Results: Fifty-eight women participated (96.7%) with an average age of 53 years (±13.01) (Table 1). We found a positive correlation between OSS and RF-IgM (r=0.385 P<0.002), RF-IgA (r=0.256 P=0.049), and anti-Ro/SSA (r=0.302 P=0.019). We found a statistically significant association between the seropositivity of the Anti-SSA/Ro antibody and the presence of MMP-9 in tears (OR 4.38, CI 95% 0.877-21.92, P=0.057). A
Spearman correlation test and the association between MMP9 and serology were evaluated with χ2 test.

Table 1. Demographic characteristics in Hispanic patients with primary Sjögren’s Syndrome

<table>
<thead>
<tr>
<th>Age, median (DS)</th>
<th>53.23 (13.0)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, n (%)</td>
<td>58 (96.7)</td>
</tr>
<tr>
<td>Anti-Ro/SSA, n (%)</td>
<td>41 (68.3)</td>
</tr>
<tr>
<td>Anti-La/SSB, n (%)</td>
<td>18 (31.6)</td>
</tr>
<tr>
<td>RF IgG, n (%)</td>
<td>13 (21.7)</td>
</tr>
<tr>
<td>RF IgM, n (%)</td>
<td>31 (51.7)</td>
</tr>
<tr>
<td>RF IgA, n (%)</td>
<td>24 (40.0)</td>
</tr>
<tr>
<td>Schirmer, n (%)</td>
<td>38 (63.3)</td>
</tr>
<tr>
<td>OSS, n (%)</td>
<td>52 (86.7)</td>
</tr>
<tr>
<td>OSS, n (%)</td>
<td>43 (71.7)</td>
</tr>
<tr>
<td>Metalloproteinase 9, n (%)</td>
<td>14 (23.3)</td>
</tr>
<tr>
<td>Ocular Comorbidty &lt;300, n (%)</td>
<td>45 (75.0)</td>
</tr>
<tr>
<td>Abnormal USF, n (%)</td>
<td>45 (75.0)</td>
</tr>
<tr>
<td>GSMB, n (%)</td>
<td>51 (85.0)</td>
</tr>
</tbody>
</table>


Conclusion: A significant correlation was observed between serology, ocular surface damage (OSS), and ocular surface inflammation (MMP-9). The positivity of RF isotypes IgM and IgA could alert the clinician about the ocular damage to initiate a study directed to this organ. Nevertheless this present study shows preliminary outcomes, we need to enroll more patients to obtain better outcomes.

REFERENCES:


Disclosure of Interests: None declared


FR0221 CATASTROPHIC ANTIPHOSPHOLIPID SYNDROME IN PREGNANCY: CASE SERIES

Nur Azizah Allameen, Aisha Lateef, Anita Yee Nah Lim, National University Hospital, Singapore, Division of Rheumatology, University Medicine Cluster, Singapore, Singapore

Background: Catastrophic antiphospholipid syndrome (CAPS) is a rare condition associated with high mortality. Prompt recognition and treatment is important for optimal outcomes. Clinical features of CAPS can overlap with obstetric complications, leading to diagnostic challenges.

Objectives: Describe two patients with CAPS during immediate post-partum period.

Methods: We report two cases in a single centre over two years.

Results: A 38 year old with obstetric Antiphospholipid syndrome (APS) presented with epigastric pain, transaminitis and thrombocytopenia in keeping with evolving HELLP syndrome. Spontaneous complete miscarriage ensued. Post-delivery, she developed worsening abdominal pain and transaminitis (Table 1). Imaging demonstrated hepatic infarcts and patchy ground glass lung opacities. She was treated for CAPS with intravenous steroids and anticoagulation, and recovered.

A 39 year old with primary APS (deep venous thrombosis and obstetric features) whose antenatal course was fraught with minor per vaginal bleeding (PVB) presented with heavy PVB at 22 weeks gestation requiring cessation of anticoagulation. She developed a deep venous thrombo sis. Risk of clot propagation versus bleeding prompted cautious anticoagulation. Labour was induced for declining maternal health and poor foetal prognosis at 24 weeks, 3 days. Post-delivery, she developed abdominal pain, headache, transaminitis and worsening thrombocytopenia with heavy PVB requiring uterine artery embolization. Given features that were consistent with micro thrombi and ischaemia (Table 1), she was treated as for CAPS and HELLP syndrome with intravenous steroids, plasma exchange (PLEX) and intravenous immunoglobulin (IVIG), and recovered.

Table 1

<table>
<thead>
<tr>
<th>Case 1</th>
<th>Case 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age on admission</td>
<td>17 weeks 5 days</td>
</tr>
<tr>
<td>Treatment during pregnancy prior to CAPS</td>
<td>LMWH* once daily, Aspirin, Hydroxychloroquine, monthly IVIG</td>
</tr>
<tr>
<td>Time of onset of CAPS</td>
<td>2nd day after foetal loss</td>
</tr>
<tr>
<td>Organ involvement</td>
<td>Hepatic, Pulmonary, Placenta</td>
</tr>
<tr>
<td>Laboratory results at onset of CAPS</td>
<td></td>
</tr>
<tr>
<td>Haemoglobin (g/dL)</td>
<td>7.4</td>
</tr>
<tr>
<td>Platelets (x100/L)</td>
<td>82</td>
</tr>
<tr>
<td>AST/ALT/LDH (U/L)</td>
<td>137/140/690</td>
</tr>
<tr>
<td>Estimated proteinuria (g/day)</td>
<td>2.7</td>
</tr>
<tr>
<td>Positive serologies</td>
<td>Anti-Ro, Anti-cc2, Anti-cardiolipin IgM/IgG, B2 glycoprotein IgM/IgG</td>
</tr>
<tr>
<td>Treatment</td>
<td>IV MP*, LMWH 1mg/kg/day</td>
</tr>
<tr>
<td>Maternal Outcomes</td>
<td>Intra-uterine foetal demise</td>
</tr>
</tbody>
</table>

*Low molecular weight heparin, *Aspartate aminotransferase. †Lactate dehydrogenase. ‡Intravenous Methylprednisolone

Conclusion: Recognition of CAPS is complex in pregnancy. Vigilance is required for urgent aggressive treatment to improve outcomes in this uncommon condition.

REFERENCES:

Disclosure of Interests: Nur Azizah Allameen: None declared, Aisha Lateef : None declared, Anita Yee Nah Lim Speakers bureau: I have been a speaker for Novartis last year


FR0222 ANALYSIS OF CLINICAL AND SEROLOGICAL FEATURES OF PATIENTS WITH PRIMARY SJÖGREN’S SYNDROME AND AN EARLY DISEASE ONSET AT AGE BEFORE 35 YEARS

Durania Aynnopoulou1, Andreas Goules1, Evangelia Zampeli1, Maria Mavromati1, Clio Mavragani1,4, Fotini Skopouli3,5, Haralampos M. Moutsopoulos1,2 6,

Method: Patients with primary SS (pSS) fulfilling the 2002 revised European/American International classification criteria for SS, were evaluated. The study group included 133 patients with disease onset ≤35 years old (mean disease duration, range: 10–32 years; group A) matched at 1:1 ratio according to gender and disease duration with 133 pSS patients with middle-age onset (mean disease duration, range: 10–32 years; group B) and 133 pSS patients with elderly onset (mean disease duration, range: 10–32 years; group C) matched at 1:1 ratio according to gender and disease duration.

Background: Primary Sjögren’s Syndrome (pSS) is a chronic systemic autoimmune disease with diverse clinical picture, extending from exocrinopathy to systemic disease and non-Hodgkin’s lymphoma (NHL). Usually, it affects middle aged women, but early disease onset (<35 years old) has been also observed. So far, there is a limited number of studies to explore whether the age of SS onset affects the clinical SS phenotype. To definitely answer this question a well-organized, large, harmonized cohort of patients with a continuous follow up is needed, through the ongoing European project (HarmonicSS, grant agreement no: 731944).

Objectives: To investigate whether the clinical and serological picture of pSS patients with early disease onset (<35 years old) differs to that of middle-age onset.

Methods: Medical records of 717 pSS patients, included in two Greek cohorts fulfilling the 2002 revised European/American International classification criteria for SS, were evaluated. The study group included 133 patients with disease onset ≤35 years old (mean disease duration, range: 10–32 years; group A) matched at 1:1 ratio according to gender and disease duration with 133 pSS patients with middle-age onset (mean disease duration, range: 10–32 years; group B) and 133 pSS patients with elderly onset (mean disease duration, range: 10–32 years; group C) matched at 1:1 ratio according to gender and disease duration.
age at disease onset 52±5 years; median disease duration, range: 10, 0-30; group B). Clinical and laboratory data were collected through an extensive clinical chart review. All parameters were compared by chi-square or Fisher's exact test, when appropriate.

Results: The two pSS groups had similar frequencies of non-specific clinical findings (chronic fatigue, arthralgias/myalgias, arthritis, Raynaud's phenomenon), peri-epithelial manifestations (interstitial nephritis, lung and liver disease), splenomegaly, leukocytopoiesis and neutrophil counts. However, patients with disease onset <35 years old, exhibited increased proportion of salivary gland enlargement (SGE; 43.8% vs 25.4%, p<0.003), lymphadenopathy (18.2% vs 7.6%, p=0.016), palpable purpura (20.3% vs 9.8%, p=0.025), anti-Ro/SSA antibodies (90.2% vs 74%, p=0.001), rheumatoid factor positivity (73.3% vs 53.6%, p=0.002), low C4 levels (64.5% vs 42.4%, p<0.001) and NHL (18% vs 8.3%, p=0.038).

Conclusion: Our findings suggest that young patients with pSS display increased prevalence of systemic features, B cell hyperreactivity, as well as heightened risk for lymphoma development. Further prospective studies with a larger number of patients are needed to address whether early disease onset may also serve as an additional risk factor for NHL development.

REFERENCES:

Acknowledgement: The project was supported by the EU grant “Harmon-iSS” (grant agreement no: 731944)

Disclosure of Interests: None declared, Andreas Goules: None declared, Evangelia Zampeli: None declared, Maria Marymadaki: None declared, Clio Mavragani: None declared, Fotini Skopouli: None declared, Silvia Rocchiccioli: None declared, Antonella Cucchetti: None declared, Paid instructor for: GlaxoSmithKline, Lilly, UCB, Stefano Bombardieri: None declared, Andreas Goules: None declared, Evangelia Zampeli: None declared, Maria Marymadaki: None declared, Clio Mavragani: None declared, Fotini Skopouli: None declared, Silvia Rocchiccioli: None declared, Antonella Cucchetti: None declared, Clio Mavragani: None declared, Fotini Skopouli: None declared, Silvia Rocchiccioli: None declared, Antonella Cucchetti: None declared


FRIO224

EXTRACELLULAR VESICLES AS A SOURCE OF BIOMARKERS IN SJÖGREN SYNDROME: A SWATH-MS PROTEOMIC APPROACH

Chiara Baldini1, Francesco Finamore2, Francesco Ferro3, Marta Mosca1, Stefano Bombardieri1, Silvia Rocchiccioli3, Antonella Cucchetti3, 1University of Pisa, Department of Clinical and Experimental Medicine, Pisa, Italy; 2Institute of Clinical Physiology, CNR, Pisa, Italy

Background: Primary Sjögren’s syndrome (pSS) is a multifactorial autoimmune disorder characterized by lymphocytic infiltration of the exocrine glands. In the recent past several proteomic studies attempted to look at valid biomarkers for pSS in whole saliva, however little is known about the composition of salivary extracellular vesicles (EVs), nor to what extent their content may reflect the phenotypic state of the disease.

Objectives: In this study, we search for pSS specific biomarkers by using a sequential window acquisition of all the theoretical fragment ion spectra (SWATH-MS) approach to monitor the dynamics of saliva EVs sub-proteome of pSS patients compared to healthy controls.

Methods: We included patients with a diagnosis of pSS made according to the AECG 2002 criteria and healthy volunteers as controls. Saliva was collected under standardized conditions. EVs were enriched by sequential ultracentrifugation steps from saliva samples. Peptide identification and quantification was performed by matching SWATH-MS data against an assay library of MS/MS spectra created from a previously acquired data-dependent acquisition (DDA) method. GO terms and protein-protein interaction network analysis were performed using Cytoscape software.

Results: We included 20 pSS patients (AECG 2002 criteria) and 10 healthy subjects. Quantitative data evidenced a distinct separation between the patient group and control group, indicating that pSS may modulate the phenotype of protein cargoes of salivary EVs. The majority of the proteins up-regulated in pSS compared to controls were found to be involved in several inflammatory processes. Particular emphasis was given to proteins converging to IL-12 signaling that included annexin A2, coflin, macrophage migration inhibitory factor (MIF), S100A8-A9 and plasmin-2 proteins.

Conclusion: Our results revealed that the inflammatory phenotype observed in pSS patients is also extended to salivary EVs, which protein content may represent a novel source for potentially useful biomarkers for pSS.

Disclosure of Interests: Chiara Baldini: None declared, Francesco Finamore: None declared, Francesco Ferro: None declared, Marta Mosca: Paid instructor for: GlaxoSmithKline, Lilly, UCB, Stefano Bombardieri: None declared, Silvia Rocchiccioli: None declared, Antonella Cucchetti: None declared


FRIO224

PREVALENCE OF SJÖGREN'S SYNDROME IN THE COMMUNITY OF MADRID

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Background: Several studies on the epidemiology of autoimmune diseases performed within the past several decades revealed a prevalence of Sjögren Syndrome (SS) between 0.3% and 4.83% (1). More recent studies revealed a lower prevalence between 31/100,000 to 49/100,000 (2). The exact prevalence of SS is unknown due to the heterogeneity of the populations and geographic areas studied, the utilization of different diagnostic tests or the lack of a unique classification criteria for the disease. Also, the disease may have an insidious onset and a variable course with a broad spectrum of clinical manifestations, so the diagnosis may be delayed or SS patients may be missed and misclassified as other rheumatic disease. Besides, SS can occur alone (primary SS) or in association with other specific systemic autoimmune rheumatic diseases (secondary SS).

Objectives: The aim of our study was to determine the prevalence of SS in the Community of Madrid (CM) and to describe the sociodemographic and clinical characteristics of these patients.

Methods: Population-based cross-sectional study in the CM, Spain. The information source for SS cases was the Registry of rare diseases in the CM (SIERMA). A descriptive analysis of the main sociodemographic and clinical characteristics of SS cases was performed. Prevalence per 10,000 inhabitants in people with 18 years of age and over, stratified by sex and their 95% confidence intervals (CI) were calculated for 2015. The denominator was the population registered in the Population Register in the middle of the period (July 2015).

Results: There were 4,778 cases of SS in SIERMA and 389 (8.1%) of them were already dead. 4434 (92.8%) were women. The median age was 64.7 years (15,4), and the maximum age was 103 years. The disease was most frequent in the sixth decade with 1079 cases (22.6%), in the seventh decade with 1120 cases (23,4%) and in the eighth decade with 935 cases (19.6%). 3116 cases (65,2%) were classified as primary SS (pSS) and 1662 (34.8%) as secondary SS (sSS).

Among the sSS the main rheumatological conditions associated were rheumatoid arthritis (58%), lupus (24,5%), systemic Sclerosis (10,5%); peripheral connective tissue (4%), inflammatory muscle disease (2%) and vasculitis (1%). The prevalence of SS in adults (≥ 18 years of age) was 8.4/10,000 with a 95% CI: 8.2 – 8.7 (14.9% in women and 0.8% in men). The prevalence of pSS was 5.9/10,000 (CI 5.3 – 5.7) and for sSS was 2.8/10,000 (95%CI: 2.7-3).

Conclusion: SS mainly affects females during the sixth, seventh and eight decades of life, and shows a female:male ratio of 9:1. Two out of three cases of SS identified were classified as pSS. The main rheumatological conditions associated were rheumatoid arthritis and lupus. The estimated prevalence of SS in the Community of Madrid population is lower than the observed in previous studies whereas the prevalence of pSS is similar than the observed in current studies.

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dades http://www.orpha.net/porphanet/calhens/docs/ES/Prevalencia_de_esa

enfermedades_raras_por_orden_alfabetico.pdf
THE EULAR/ACR 2018 AND SLICC 2012 HAVE INCREASED SENSITIVITY AGAINST THE ACR 1997 CLASSIFICATION CRITERIA AND CLASSIFY NON-OVERLAPPING GROUPS OF SLE PATIENTS: SIMULTANEOUS APPLICATION ASSURES THE GREATEST CAPTURE OF PATIENTS IN CLINICAL PRACTICE

Christina Adamichou1, Dionisis Nikolopoulos2, Irini Genitsarid1, Alessandra Bortoluzzi4, Antonis Fanouriakis2, Emmanouil Papastefanakis1, Eleni Kalogiannaki1, Irini Gergianaki1, Prodomos Sidiroupulos1, Dimitrios Bourtouzas1, George Bertsias1, 1Rheumatology, Clinical Immunology and Allergy, University of Crete, Heraklion, Greece; 2Rheumatology Clinic, University Hospital and BRFAA, Athens, Greece; 3Institute of Computer Science, Foundation for Research and Technology Hellas (FORTH), Heraklion, Greece; 4Section of Rheumatology, University of Ferrara, Cora (FE), Italy

Background: A joined EULAR/ACR initiative has proposed a new set of classification criteria for SLE based on weighted items and the use of ANA as an entry criterion.

Objectives: To compare the diagnostic performance of the old and new classification criteria against physician diagnosis in an early SLE cohort and examine phenotypic and prognostic differences among patients who are classified with the criteria.

Methods: Adult patients diagnosed by experienced physicians with SLE were classified with the criteria. Hazard models were used to calculate elapsed time between the earliest item (of any criterion) and classification. Severity of SLE (BILAG-2004 glossary) and the SLICC/ACR organ damage index were determined.

Results: The SLICC and EULAR/ACR had increased overall sensitivity as compared to the ACR criteria (91.3%, 88.6%, 85.7%, respectively; p<0.01), especially in early-onset (<3 years) disease (91.4%, 87.3%, 79.9%, respectively; p<0.001), with comparable specificity rates (ranging 91.0–92.7%). By combining the three criteria sets, 97.1% of patients were classified. Both the EULAR/ACR and the SLICC enabled earlier SLE classification (median time-to-classification: 7.1 and 7.6 months, respectively) than the ACR criteria (median 9.1 months). Nevertheless, disease classification was delayed by >3 months in 17.3–19.9% of cases, particularly in neurological SLE (20.0–26.8%). Comparative analysis of patients who were missed by the criteria revealed significant differences in rates of individual clinical and serological features (Table 1) suggesting that existing criteria may classify non-overlapping groups of patients. Importantly, unclassified patients presented with a high prevalence of moderate/severe disease (43.3–60%) and organ damage (30–50%).

Conclusion: Despite improved sensitivity and earlier classification with the EULAR/ACR and the SLICC criteria, still SLE diagnosis may be missed or delayed even in patients with moderate to severe disease, especially neurological-dominant disease. Simultaneous application in clinical practice assures the greatest capture of patients.

Disclosure of Interests: None declared


Table 1. Prevalence of clinical and immunological features across groups of SLE patients who were not classified by the criteria

<table>
<thead>
<tr>
<th></th>
<th>ACR 1997</th>
<th>SLICC 2012</th>
<th>EULAR/ACR 2018</th>
<th>All three criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=99</td>
<td>n=60</td>
<td>n=79</td>
<td>n=20</td>
<td></td>
</tr>
<tr>
<td><strong>SLICC 2012 items</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACRE</td>
<td>4.9%</td>
<td>8.8%</td>
<td>72.2%</td>
<td>66.9%</td>
</tr>
<tr>
<td>CRP</td>
<td>10.5%</td>
<td>8.3%</td>
<td>17.7%</td>
<td>5.6%</td>
</tr>
<tr>
<td>ACRS</td>
<td>6.2%</td>
<td>36.7%</td>
<td>65.3%</td>
<td>45.1%</td>
</tr>
<tr>
<td>CRP</td>
<td>12.1%</td>
<td>29.3%</td>
<td>51.9%</td>
<td>15.9%</td>
</tr>
<tr>
<td>SYRACUS</td>
<td>69.0%</td>
<td>66.5%</td>
<td>78.7%</td>
<td>65.3%</td>
</tr>
<tr>
<td>SLESA</td>
<td>6.4%</td>
<td>10.9%</td>
<td>12.7%</td>
<td>10.9%</td>
</tr>
<tr>
<td>Renal disorder</td>
<td>0.0%</td>
<td>3.3%</td>
<td>6.3%</td>
<td>10.9%</td>
</tr>
<tr>
<td>Neurologic disorder</td>
<td>6.4%</td>
<td>6.7%</td>
<td>6.3%</td>
<td>30.6%</td>
</tr>
<tr>
<td>Other autoimmune</td>
<td>3.0%</td>
<td>0.0%</td>
<td>2.5%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Lupus pericarditis</td>
<td>26.0%</td>
<td>15.0%</td>
<td>27.8%</td>
<td>10.9%</td>
</tr>
<tr>
<td>Renal insufficiency</td>
<td>18.2%</td>
<td>6.1%</td>
<td>12.7%</td>
<td>10.9%</td>
</tr>
<tr>
<td>Anti-DNA</td>
<td>18.2%</td>
<td>3.3%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Anti-Sm</td>
<td>2.0%</td>
<td>0.0%</td>
<td>1.3%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Anti-phospholipid Ab</td>
<td>18.2%</td>
<td>1.3%</td>
<td>11.4%</td>
<td>5.0%</td>
</tr>
<tr>
<td>Anticardiolipin</td>
<td>43.4%</td>
<td>3.3%</td>
<td>21.5%</td>
<td>5.0%</td>
</tr>
<tr>
<td>Complement</td>
<td>5.1%</td>
<td>0.0%</td>
<td>2.5%</td>
<td>0.0%</td>
</tr>
<tr>
<td>ANA</td>
<td>84.8%</td>
<td>50.7%</td>
<td>48.3%</td>
<td>30.3%</td>
</tr>
</tbody>
</table>

Acknowledgement: This study received funding by the Hellenic Society of Rheumatology & Professionals Union of Rheumatologists of Greece (protocol number 644).

Disclosure of Interests: Christina Adamichou: None declared, Dionisis Nikolopoulos: None declared, Irini Genitsaridi: None declared, Alessandra Bortoluzzi: None declared, Antonis Fanouriakis Paid instructor for: Amgen, GSK, Speakers bureau: Abbvie, Enorasis, Genesis Pharma, Emmanouil Papastefanakis: None declared, Eleni Kalogiannaki: None declared, Irini Gergianaki: None declared, Prodomos Sidiroupulos: None declared, Dimitrios Bourtouzas: None declared, George Bertsias: None declared


LOW EXPRESSION OF ESTROGEN RECEPTOR BETA IN RENAL TUBULAR EPITHELIAL CELL MAY CONtribute TO HYPERURICEMIA IN PREMENOPAUSAL STATES OF AMERICAN FEMALE SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: We have reported that the incidence of hyperuricemia of young female systemic lupus erythematosus (SLE) patients was higher than that of healthy young women11. Whether the estrogen receptor (ER) expressed in renal tubular tissue contributes to it? There are few reports yet.

Objectives: To investigate the expression of ERs in the renal tubular cells and their relationship with serum uric acid (UA) levels in premenopausal female SLE patients.

Methods: Eighteen kidney biopsy specimens of premenopausal female SLE patients served as the lopus nephritis group (LN group), and 12 specimens of premenopausal female IgA nephropaty patients served as the IgA group. Serum UA levels and kidney index were collected, and the expression of ERs in the renal tubular epithelial cell of the two groups were determined by immunohistochemistry. According to the
percentage of the positive stained cells, the semiquantitative analysis was made. The expressions of ERs, including ERα and ERβ, of the two groups were compared, and the relationship between the expression of ERs and serum UA levels were analyzed with linear regression analysis.

Results: 1. The mean ages of the LN group and the IGA group were 27.39±8.09 years and 33.08±5.45 years, respectively, with significantly different (t=-2.128, P=0.042). There was no renal failure subject in both groups (CRE level above 120 mol/l), and all the SLE patients were at stage of onset.

2. Mean UA level of the LN group was significantly higher than that of the IGA group (t=-3.149, P=0.004), and the CRE level of the two groups were similar (t=-0.109, P=0.914) (table 1).

3. In each group, ERβ was well expressed in the tubular epithelial cells, and no in kidney glomeruli. In contrast, ERα was not expressed in the renal tissues of both groups (figure 1).

4. The median score of ERβ expression in the LN group was remarkable lower than that of the IGA group (z=-2.080, P=0.038, table 1).

5. Linear regression analysis indicated that ERβ expression scores of the total 30 patients had significantly negative correlation with serum UA levels (r=-2.141, P=0.041, table 2).

Conclusion: 1. Low expression of ERβ in renal tubular epithelial cell may contribute to hyperuricemia in premenopausal female SLE patients, association with potential or existing renal damage. Eur J Innflamn,2018;16:1-6.

Table 1. Comparative analysis of main clinical biomarkers in LN group and IGA group.

<table>
<thead>
<tr>
<th>Variable</th>
<th>LN group</th>
<th>IGA group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>27.39±8.09</td>
<td>33.08±5.45</td>
<td>t=-2.128</td>
</tr>
<tr>
<td>UA (μmol/L)</td>
<td>510.3±114.50</td>
<td>383.2±78.72</td>
<td>t=3.149</td>
</tr>
<tr>
<td>CRE (μmol/L)</td>
<td>92.2±11.71</td>
<td>91.7±12.64</td>
<td>t=0.109</td>
</tr>
<tr>
<td>Lj</td>
<td>0.00(0.02,0.23)</td>
<td>0.20(0.10,0.30)</td>
<td>z=2.080</td>
</tr>
<tr>
<td>ERβ</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>UA: uric acid; IGA: premenopausal female systemic lupus erythematosus patients; association with potential or existing renal damage.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2. The correlation of ERβ expression scores in the renal tubular epithelial cell with serum UA levels in premenopausal female SLE patients.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Unstandardized Coefficients</th>
<th>Standardized Coefficients</th>
<th>t</th>
<th>P</th>
<th>95%(CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ERβ</td>
<td>317.004</td>
<td>148.040</td>
<td>-3.37</td>
<td>2.141</td>
<td>0.041</td>
</tr>
<tr>
<td>Constant</td>
<td>516.455</td>
<td>148.040</td>
<td>14.641</td>
<td>0.000</td>
<td>444.198-588.712</td>
</tr>
</tbody>
</table>

Disclosure of Interests: None declared
prevalence of pulmonary involvement, including interstitial lung disease (ILD), in patients with primary SS widely varies from 8% to 20%. Patients with SS with ILD have high morbidity and a fourfold increase in mortality.

Objectives: Krebs von den Lungen-6 (KL-6) is a mucin-like, high-molecular-weight glycoprotein; it is expressed in regenerating type II pneumocytes. Serum KL-6 is highly associated with the activity of ILD in patients with radiation pneumonitis, idiopathic pulmonary fibrosis, hypersensitivity pneumonitis, sarcoidosis, rheumatoid arthritis, polymyositis, dermatomyositis and systemic sclerosis. The increase in serum KL-6 level might reflect the increase in the number of regenerating type II pneumocytes secondary to pulmonary damage. We hypothesise that an early pulmonary damage occurs before clinical or radiological evidence of ILD in patients with SS.

Methods: In this retrospective case-control study, patients who were diagnosed with primary SS and fulfilled the American-European Consensus Group Criteria for Sjögren’s Syndrome were included. Clinical information, laboratory results on inclusion, images and pulmonary functions test results were recorded via electronic medical records review. Pulmonary radiography including chest X-ray and chest computed tomography was reviewed by a chest physician.

Results: Of the 39 patients with SS, 21 (53.85%) developed ILD at the end of follow-up. The follow-up period was 2.65 ± 1.88 years. The time to diagnosis of ILD was 2.72 ± 1.74 years in the ILD group. The serum KL-6 level was 1920.10 ± 1974.26 U/ml in the ILD group and 894.11 ± 788.53 U/ml in the non-ILD group (p = 0.001). The diffusing capacity of the lungs for carbon monoxide was 70.76 ± 19.63 ml/min and 91.88 ± 12.02 ml/min in the ILD group and non-ILD group, respectively (p < 0.001).

Conclusion: Serum KL-6 level is significantly higher in patients with primary SS developing ILD and may represent an early non-radiographic pulmonary damage. Serum KL-6 can be a valuable biomarker in predicting the development of ILD in patients with primary SS.

REFERENCES:

Disclosure of Interests: None declared

**Objectives:** Determine prevalence of MIN in SLE (LLC). Compare clinical and echocardiographic (echo) features of patients with and without MIN. Identify echo predictors of MIN.

**Methods:** A prospective cross-sectional study was done at Tygerberg Hospital, Western Cape, South Africa. Adult inpatients, fulfilling the 2012 SLICC criteria were screened. Echo analyses included STE and regional function (wall motion score (WMS)). Patients were grouped according to evidence of MIN (absent criteria [AC]; single criterion [SAC]; fulfilling LLC), comparing clinical, laboratory and echo data. Logistic regression and ROC were used to determine predictors of MIN.

**Results:** 49/106 SLE patients screened were included (Figure 1). 46.9% of patients had MIN (≥1 criterion); 12.2% fulfilled LLC for LM and 34.7% had a SAC. SLE disease activity (SLEDAI) (p=0.047) was higher in patients fulfilling LLC, but not in the SAC group. A clinical and echo diagnosis of LM was made in all patients fulfilling LLC, in 17.6% of patients in the SAC group and none in the AC group (Table 1). Anti-DsDNA and anti-B2GP1 were more frequently positive in SAC vs the AC group (p=0.054 and 0.081). WMS was higher in LLC and SAC groups (p=0.006 p=0.083) with mid and basal STE more impaired in patients with MIN (p=0.047 p=0.043). LVIV and mid STE score combined was the best predictor of MIN (Table 2; Figure 2).

**Conclusion:** CMR evidence of MIN is common in SLE, even in the absence of clinical myocardial dysfunction or high lupus activity. Impaired echo regional and global function occurs more frequently in patients with MIN. STE combined with LVIV predicts MIN detected by CMR and has potential as a cost effective screening tool. CMR is limited by a high exclusion rate in SLE, mainly due to renal impairment.

**REFERENCES:**


**Table 1**

<table>
<thead>
<tr>
<th></th>
<th>AC n=26</th>
<th>LLC n=6</th>
<th>p</th>
<th>SAC n=17</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>27 (21-35)</td>
<td>27 (23-28)</td>
<td>1</td>
<td>29 (23-36)</td>
<td>0.542</td>
</tr>
<tr>
<td>SLE duration, days</td>
<td>114 (8-1366)</td>
<td>35 (31-44)</td>
<td>0.724</td>
<td>955 (7-2101)</td>
<td>0.486</td>
</tr>
<tr>
<td>SLEDAI</td>
<td>13 (9-15)</td>
<td>22 (16-26)</td>
<td>0.022</td>
<td>12 (9-20)</td>
<td>0.813</td>
</tr>
<tr>
<td>Antiphospholipid syndrome</td>
<td>2 (8)</td>
<td>0</td>
<td>0.483</td>
<td>4 (24)</td>
<td>0.085</td>
</tr>
<tr>
<td>Female</td>
<td>24 (92)</td>
<td>5 (83)</td>
<td>0.497</td>
<td>14 (82)</td>
<td>0.319</td>
</tr>
<tr>
<td>Cardiac risk factors</td>
<td>8 (31)</td>
<td>1 (17)</td>
<td>0.498</td>
<td>6 (35)</td>
<td>0.757</td>
</tr>
<tr>
<td>Nephritis</td>
<td>9 (35)</td>
<td>3 (50)</td>
<td>0.483</td>
<td>3 (18)</td>
<td>0.225</td>
</tr>
<tr>
<td>Clinical LM</td>
<td>0</td>
<td>6 (100)</td>
<td>-0.001</td>
<td>3 (18)</td>
<td>0.028</td>
</tr>
</tbody>
</table>

**Table 2**

**Logistic regression**

<table>
<thead>
<tr>
<th>Echo variable</th>
<th>OR</th>
<th>95% CI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVIV</td>
<td>2.6</td>
<td>0.8-8.4</td>
<td>0.109</td>
</tr>
<tr>
<td>LV ejection fraction</td>
<td>0.9</td>
<td>0.6-0.9</td>
<td>0.018</td>
</tr>
</tbody>
</table>

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PATIENT PERCEPTION OF SLE BURDEN: THE ROLE OF ORGAN DAMAGE

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Background: physician-based assessment of Systemic Lupus Erythematosus (SLE) may not be able to capture the real disease impact on patients’ life. In the literature, the impact of disease damage on patients’ quality of life (QoL) is controversial.

Objectives: Objective of our study was to investigate the role of organ damage in determining patient perception of SLE burden.

Methods: this is a cross-sectional study that enrols patients with a diagnosis of SLE (ACR 1997 criteria). For each patient, demographics, comorbidities, treatment, clinical and laboratory data were collected. Disease damage was evaluated with the SLICC-Damage Index (SDI) and a score >2 was defined as “severe damage”. The BILD (Brief Index of Lupus Damage) was used for patient self-evaluation of organ damage. Finally, the Lupus Impact Tracker (LIT) questionnaire was used to assess patient perception of SLE burden.

Results: we included 246 adult SLE patients (94.7% Caucasian, 93.1% female, mean age 45.3±13.2 years, mean disease duration 14.3±9.8 years). As for cumulative organ involvement in our cohort, the most prevalent was articular involvement (67.5%), followed by cutaneous (54.1%), hematological (51.2%), renal (43.9%) and serositis (17.9%); 11.8% had a history of NPSLE. Among comorbidities, 10.9% of patients had a concomitant fibromyalgia. 48.8% of patients was presenting at least one organ damage; among those patients, the median SDI was 2 (IQR 1-3); 16.3% of patients had a “severe damage” and among them median SDI was 4 (IQR 3-6). The most frequent items of organ damage in our cohort were: cataract (19.9%), deforming or erosive arthritis (10.2%) and osteoporosis with fracture (8.5%). Moreover, a significant number of patients (18.3%) met the criteria for neuro-psychiatric damage, mainly cerebrovascular accidents (7.3%), seizures (5.3%) and cognitive impairment (4.1%). Finally, a not negligible number of patients had premature gonadal failure (4.5%) and malignancy (6.5%).

As far as patients’ perception is concerned, the median LIT score in the cohort was 22.5 (IQR 7.5-40) and median BILD was 1 (IQR 0-2).

In a multiple linear regression analysis, we found a direct positive correlation between the SDI score and age at enrollment and disease duration (p<0.001). Severe damage resulted associated with a history of serositis (p=0.01) and NPSLE (p=0.001). We also found a positive linear correlation between the SDI score and the patient’s self-reported damage (BILD score; p=0.001) and with the patient’s perception of disease burden (LIT; p<0.01), irrespective of age and disease duration. In particular, in the multivariate analysis, higher SDI scores were significantly associated with a poorer perception of disease burden in terms of: future planning (p<0.001), usual activities, family responsibilities, discomfort due to physical appearance (p<0.01) and drug side effects (p<0.05), irrespective of fibromyalgia and age at enrollment.

Among the different types of organ damage, we found that cognitive impairment, cerebrovascular accidents and premature gonadal failure mainly contributed to determine SLE burden. In fact, they were significantly associated with higher LIT scores (p<0.05).

Conversely, SDI score was not related with health-related quality of life and fatigue as measured by SF-36 and FACIT respectively, neither with fibromyalgia.

Conclusion: disease damage seems to have a role in determining patient perception of SLE burden, mainly affecting patients’ ability to plan the future and to fulfill daily activities and family responsibilities. In particular, neuropsychiatric damage exerts the greatest influence on patient perception of SLE impact.

REFERENCES:

Disclosure of Interests: Elena Elefante: None declared, Chiara Tani: None declared, Francesco Ferro: None declared, Chiara Stagnaro: None declared, Alice Parma: None declared, Linda Carl: None declared, Viola Signorini: None declared, Marta Mosca Paid instructor for: GlaxoSmithKline, Lilly, UCB

MORTALITY IN SLE PATIENTS COMPARED TO POPULATION CONTROLS IN FINLAND IN YEARS 2000–2015

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Background: It is well established from a variety of studies that systemic lupus erythematosus (SLE) patients have a shortened life expectancy. The literature on SLE has highlighted the impact of cardiovascular diseases (CVD) on increased mortality. However, there is lack of studies comparing results to the background population.

Objectives: Aim of the study was to clarify, whether incident SLE patients have an excess mortality compared to population controls.

Methods: The study included all adult (age >17 years), incident, SLE patients who were entitled to a special reimbursement for SLE medication in years 2000 – 2014 in Finland. For each patient, the Population Registry Centre identified 3 population controls matched for age, sex and place of residence. Comorbidities at baseline were obtained from the Care Register for Health Care of the National Institute for Health and Welfare. Data on education at baseline and deaths until the end of 2015 were retrieved from the Statistics Finland.

Results: A total of 1006 incident SLE patients (84% females) and 3005 population controls were found. During the follow-up (mean 8.8 years), 98 patients (mean age at death 70±14 years, 65% females) died. The 5-, 10-, and 15-year survival rates in SLE patients were 95.0% (95%CI 93.9-96.2%), 88.8% (86.2-91.0%) and 82.1% (77.9-85.8%), respectively. The number of deaths among controls was 187. Crude hazard ratio (HR) was 1.61 (95% CI: 1.26 to 2.06), p=0.001, adjusted for education and comorbidities 1.14 (95% CI: 0.88 to 1.48) p=0.32. Main causes of deaths in patients were CVDs (33%), malignancies (27%) and neurological diseases (10%). Ten-year cumulative mortality rate due to CVD was in SLE patients 3.3% (95CI 2.2 to 4.9%) and in controls 2.6% (2.0-3.3) and 15-year rate 6.7% (95%CI 4.2 to 9.8) and 4.9% (3.6 to 12.0), respectively. Crude HR for CVD deaths was 1.28 (95% CI: 0.85 to 1.93), p=0.34, adjusted 0.88 (95% CI: 0.56 to 1.39), p=0.05.

Conclusion: SLE patients had a slightly increased risk for overall and cardiovascular related mortality compared to population controls. After adjusting for education and comorbidities, the difference was not statistically significant.

REFERENCES:

Disclosure of Interests: Pia Elbing Speakers bureau: Mylan Finland Oy, Abbvie Oy, UCB Pharma Oy Finland, Hannu Kautiainen: None declared, Laila Virta: None declared, Olli Kaijser-Hepponen: Speakers bureau: Boehringer Ingelheim, Karl Puzakka: None declared
### FACTORS ASSOCIATED WITH THE DEVELOPMENT OF NEOPLASIA IN PRIMARY SJÖGREN’S SYNDROME

Monica Fernandez Castro1, Carlos Sánchez-Piedra2, José Luis Andreu1, Jose Rosas3, Victor Martínez Taboada4, Alejandro Olivé5, Hospital Puerta de Hierro Majadahonda, Rheumatology, Madrid, Spain; 2Research unit of the Spanish Society of Rheumatology, Madrid, Spain; 3Hospital Marina Baixa, Rheumatology, Alicante, Spain; 4Hospital Marqués de Valdecilla, Rheumatology, Santander, Spain; 5Hospital Germans Trias i Pujol, Rheumatology, Barcelona, Spain

**Background:** Primary Sjögren’s syndrome (pSS) is characterized by lymphocytic infiltration of the exocrine glands. These patients have a higher risk than the general population of developing non-Hodgkin lymphoma (NHL). This risk also increases with the time of evolution of the disease. pSS is also associated with the development of non-hematological cancer such as thyroid, digestive or gynecological among others.

**Objectives:** The aim of the study is to explore the association between the development of neoplasia and demographic, clinical or therapeutic factors in pSS.

**Methods:** The SJOGREN registry is a multicenter, cross-sectional study of patients with pSS who meet the American-European consensus criteria of 2002, of 33 Spanish rheumatology units. The demographic, clinical, analytical, therapeutic and neoplastic data were collected through review of the clinical records and interviews with the patients. Previously, all the patients signed informed consent and the approval of the local ethic committees was obtained. Descriptive statistics was used for the analysis of the data. The chi-squared test was used to establish the statistical associations and it was considered a $p<0.05$ as significant. Bivariante logistic regression models were used to identify the effect of each independent variable on the main variable (neoplasia); the multivariate analysis was used to establish the independent effect of the patient characteristics associated with the dependent variable.

**Results:** Four hundred and thirty-seven patients were included in SJOGREN-SEr Registry (female gender 95.19%; median age 58.3 years). We found 30 patients (6.86%) with neoplasia (3 of them with more than one neoplasia); 7 with lymphomas (23.3%); 2 Hodgkin’s lymphomas, 1 immunocytoma, 9 with gynecological neoplasia (30%), 2 with digestive malignancies, 2 with lymphomas, 6 with malignancies in other locations, 3 with multiple myeloma and 2 patients with Waldenstrom macroglobulinemia. The results of the bivariate analysis are shown in the table. The factors significantly associated with the development of neoplasia were older age, glandular inflammatory involvement, lung involvement and use of rituximab. The age at diagnosis of the disease tended to be higher in the group with neoplasia (50.1 (± 12.9) vs 54.7 (± 11.7), $p = 0.059$). In the multivariate analysis, positive associations with neoplasia included for this analysis 345 patients with an active follow-up, 31 males and 314 females, with a male to female ratio of 1:10. A higher number of male had male disease onset (13% vs 1.6%) and diagnosis (16% vs 1.6%) after 60 years compared to female ($p=0.001$; OR 9.1; 95% CI 1.92-42.56 and $p<0.0001$; OR 11.8; 95% CI 2.73-51.56 respectively). The most relevant differences among male and female patients are reported in the table 1. Males more frequently presented discoid lesions, renal involvement, polyneuropathy and leukopenia compared to female SLE. No difference regarding disease activity during the last 12 months measured by SLEDAI was found. Regarding the damage index, males showed a higher mean SDI and number of patients with a severe damage (SDI>2) compared with women. Analyzing treatment prescribed since the diagnosis of SLE we collected some relevant differences: antimarial were less prescribed in males than females (87% vs 97%, $p=0.02$; OR 0.19; 95% CI 0.051-0.825), whereas mycophenolate mofetil was more frequently used in males (69% vs 36%; $p=0.005$ OR 3.0 95% CI 1.13-6.8). Finally, significant differences regarding the ongoing treatment are reported in table 1: mycophenolate mofetil was more frequently prescribed in males (84.2 vs 25.6) and a highly suggestive trend of significance toward a greater use of steroids in males was also found.

**Conclusions:** Thirty (6.86%) patients with pSS from the SJOGREN registry developed some neoplasia; the most frequent was gynecological, followed by lymphoproliferative processes. Older age, glandular inflammatory involvement and use of rituximab (presumably indication bias) were associated with the presence of neoplasia.

**REFERENCES:**


Disclosure of Interests: Monica Fernandez Castro: None declared, Carlos Sánchez-Piedra: None declared, Jose Luis Andreu: None declared, Jose Rosas Consultant for: Abbvie, Amgen, Bristol-Myers, Janssen, Lilly, Merck Sharp & Dohme, Pfizer, UCB Pharma, Speakers bureau: Abbvie, Amgen, Bristol, Janssen, Lilly, Merck Sharp & Dohme, Pfizer, UCB Pharma, Victor Martinez Taboada: None declared, Alejandro Olivé: None declared.

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### DIFFERENCES BETWEEN MALE AND FEMALE PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A SINGLE CENTER EXPERIENCE OVER 20 YEARS OF FOLLOW-UP

Micaela Fredi1,2, Federica Tomasoni1, Laura Andreoli1,2, Ilaria Cavazzana1, Angela Tincani1,2, Franco Franceschini1,2, U.O. Rheumatology and Clinical Immunology, ASST Spedali Civili di Brescia, Brescia, Italy; 2Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy

**Background:** Systemic lupus erythematosus (SLE) is a chronic inflammatory disease of unknown etiology involving multiple organ systems. It affects predominantly women, and according to different reports only 4–22% of the lupus population is male. Sex differences may influence the clinical and serological expression, therapy and outcome, but the current results varies among different countries and different ethnic groups (1-3).

**Objectives:** The aim of this work was to analyze our male and female SLE patients with an ongoing follow-up.

**Methods:** Cumulative clinical, serological manifestations, concomitant diseases of patients belonging to the historical SLE cohort with at least one evaluation in the past 15 months were collected from clinical charts. For these patients data regarding the overall and ongoing treatments, damage index (SDI), activity index (SLEDAI-2K) during the last 12 months were collected. For statistical analysis was used Chi-squared test, Fisher exact test, Student T test or Wilcoxon-Mann Whitney when appropriated.

**Results:** Out of the 550 SLE patients registered until may 2018 we have included for this analysis 345 patients with an active follow-up, 31 males and 314 females, with a male to female ratio of 1:10. A higher number of male had male disease onset (13% vs 1.6%) and diagnosis (16% vs 1.6%) after 60 years compared to female ($p=0.001$; OR 9.1; 95% CI 1.92-42.56 and $p<0.0001$; OR 11.8; 95% CI 2.73-51.56 respectively). The most relevant differences among male and female patients are reported in the table 1. Males more frequently presented discoid lesions, renal involvement, polyneuropathy and leukopenia compared to female SLE. No difference regarding disease activity during the last 12 months measured by SLEDAI was found. Regarding the damage index, males showed a higher mean SDI and number of patients with a severe damage (SDI>2) compared with women. Analyzing treatment prescribed since the diagnosis of SLE we collected some relevant differences: antimarial were less prescribed in males than females (87% vs 97%, $p=0.02$; OR 0.19; 95% CI 0.051-0.825), whereas mycophenolate mofetil was more frequently used in males (69% vs 36%; $p=0.005$ OR 3.0 95% CI 1.13-6.8). Finally, significant differences regarding the ongoing treatment are reported in table 1: mycophenolate mofetil was more frequently prescribed in males (84.2 vs 25.6) and a highly suggestive trend of significance toward a greater use of steroids in males was also found.

**Conclusion:** Our study confirmed the presence of differences between male and female SLE patients, both on clinical manifestations and also during the disease course. Our results on currently followed male SLE confirmed that these patients have a more severe disease, in particular with renal or neurological manifestations, that could justify the higher use of mycophenolate mofetil and the higher SDI compared to female SLE.

**REFERENCES:**

MIGHT A 12-WEEK AEROBIC EXERCISE INTERVENTION IMPROVE PATIENT-REPORTED OUTCOMES IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS?

Blanca Gavilán Carrera1, Jose Antonio Vargas-Hitos2, Pablo Morillas-de-Laguno1, Franco Franceschini: None declared, Laura Andreoli: None declared, Ilaria Cavazzana: None declared, Micaela Fredi: None declared, Federica Tomasoni: None declared, Gabriela Hernandez-Molina, Carlos Castréjon-Morales, Omar Granados-Portillo, Ivette Cruz-Bautista, Narly Ruiz-Quintero, Ililana Manjarrez, Diego Hernández-Ramírez, Guadalupe Lima, Miguel Astudillo-Angel, Luis Lorrente. Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico

Background: Despite the relevant advance in treatment options and survival rates in systemic lupus erythematosus (SLE), patient’s quality of life (QOL), and other patient-reported outcomes (PROs) do not seem to improve accordingly [1]. PROs provide valuable information about the patient’s perceptions across a variety of domains that should be considered in a successful management of this condition [2]. Exercise seems to be a safe way to improve cardiopulmonary fitness [3], and could have also a positive influence on PROs in SLE.

Objectives: To evaluate the effects of 12-week aerobic exercise intervention on PROs (QOL, depression, stress, and fatigue) in women with SLE.

Methods: These are secondary outcomes of a non-randomized clinical randomized Controlled Trial (NCT03107442). A total of 58 participants with SLE were assigned to exercise group (n=26) or control group (n=32). The exercise intervention followed the American College of Sports Medicine guidelines, and consisted of 12-week progressive aerobic exercise on a treadmill (3 sessions/week) between 40%-75% of the individual’s heart rate reserve [3]. Attendance of ≥75% was set for inclusion in the analyses. The control group received verbal information about a healthy lifestyle. At baseline, and at week 12, PROs were assessed including the physical and mental summary scores of the 36-item Short-Form Health Survey (SF-36), depression (Beck Depression Inventory; BDI-II), perceived stress (visual analogue scale) and fatigue (Multidimensional Fatigue Inventory; MFI-20). A total of 49 women with SLE (age: 44.5±14.2 years) completed all the assessments (exercise=21; control=28) and were included in the per-protocol (primary) analyses. The exercise and control group were comparable in age, disease duration and SLE activity, sociodemographic characteristics, and BMI at baseline, although there were differences in BDI-II scores. Baseline values and BDI-II values were used as covariates in the analyses.

Results: In comparison to the control group, the exercise group showed a significant reduction in general fatigue (mean difference -2.11 units; 95% CI -4.18 to -0.04; P= 0.046) and physical fatigue (mean difference -3.90 units; 95% CI -6.3 to -1.5; P= 0.005) following the intervention. There were no between-group differences in the changes from baseline to week 12 either in physical (P=0.828) or mental (P=0.767) QOL, depression (P=0.498), perceived stress (P=0.247) or other fatigue dimensions (mental, reduced motivation, reduced activity, all P>0.05).

Conclusion: The results of this study suggest that 12 weeks of progressive aerobic exercise might improve relevant dimensions of fatigue in women with SLE, despite absence of effects on QOL, depression or perceived stress.

REFERENCES:

Background: Patients with systemic lupus erythematosus, especially lupus nephritis (LN), have higher risk of thrombosis than the general population. Since use of corticosteroids also increase the risk of thrombosis, the risk of thrombosis (SPT) may increase the risk of thrombosis in patients with LN. However, few studies examined this association.

Objectives: To compare risk of thrombosis between patients with and without SPT in LN.

Methods: This retrospective, propensity score-matched cohort study was conducted using claims data provided by Medical Data Vision Co., Ltd (Tokyo, Japan). We defined individuals as LN cases if they met all of the following: 1) were diagnosed as LN; 2) had a dose of corticosteroids (CS) over 30 mg/day during hospitalization between April 2009 and January 2018; 3) were 16 years old or over. Cases with central neurological lupus, alveolar hemorrhage, or pregnancy at baseline were excluded. Cases with plasmapheresis or antplatelet therapies at the start of observation, warfarin within a year, direct oral anticoagulants within a month, major surgery or lower limbs operation within three months, past thrombosis within a year, and prophylactic treatment of thrombosis from the observation starting month were also excluded from the study population. LN cases were divided into 2 groups; receiving SPT (SPT group, n=692) or not receiving SPT (non-SPT group, n=525). The start of observation was defined as commencement of CS treatment during hospitalization. Observation stopped either on April 2018 or the month cases were withdrawn from the database or developed first thrombosis, whichever came first. Thrombosis was defined as follows: at least one of three disease names (thrombosis, embolisms and infarction) and prescription of thrombosis within a year, and prophylactic treatment of thrombosis from the observation starting month were also excluded from the study population. The mean age of the patients was 55.7 years, and twenty (50%) were male. The underlying rheumatic diseases and PCP between October 2015 and October 2018 in a tertiary referral center. PCP was diagnosed via a positive sputum Pneumocystis jirovecii PCR in the presence of a compatible clinical presentation. The clinical characteristic, underlying rheumatic diseases, comorbidity, immuno-suppressants, adjunctive glucocorticoid dose, and outcome were evaluated. Chest X-ray (CXR) was evaluated as a radiographic score (0-18), and a higher score suggested a more severe lung involvement. The prognostic factors of mortality were analyzed by multivariate logistic regression model.

Results: The annual rate of thrombosis was 12.8% in LN cases. The mean age of the patients was 51.7 years and the proportion of female was 76%. There were no statistically significant differences in baseline variables between the two groups after propensity-score matching (both groups; n=434). The percentage of cases with thrombosis in both groups at each month were similar (SPT vs non-SPT at Month 1, 2, 3, and 4: 3.0% vs 4.4% (p=0.28), 3.5% vs 5.1% (p=0.24), 3.9% vs 5.3% (p=0.331), and 4.6% vs 5.5% (p=0.536), respectively). There were no significant differences in cumulative incidence rates of thrombosis between the two groups (P=0.265 by log-rank test). Univariate analysis revealed five risk factors of thrombosis: activity of daily living (p=0.004), hepatic failure (p=0.001), malignancy (p=0.02), and use of methylxtrate (p=0.038) and oral contraceptive (p=0.037). After adjusting for covariates, OR of SPT was 0.82 (95%CI 0.44-1.52), which was not significantly elevated.

Conclusion: This study revealed that SPT did not increase the risk of thrombosis in patients with LN.

REFERENCES:
Background: Pregnancies in women with inflammatory and autoimmune diseases are considered high-risk pregnancies, so close and ideally multidisciplinary control is necessary. Given the advances in treatment and identification of risk factors a higher percentage of patients manifest gestational desire.

Objectives: To describe our experience in a multidisciplinary unit (integrated by Rheumatologists and Obstetricians) and assess the complications in the evolution of pregnancies and treatments used in patients with inflammatory and autoimmune diseases.

Methods: Retrospective study of pregnancy outcome in patients with rheumatic diseases and follow-up in a multidisciplinary unit for 15 years (January 2003-December 2018). Demographic characteristics, maternal disease, comorbidities, previous abortions, presence of autoantibodies (AAb), number of births, fetal losses and abortions during follow-up, previous treatment and treatment during pregnancy and maternal and fetal complications were collected.

Frequencies and percentages were used in qualitative variables, mean ±SD in quantitative and for the comparison between groups Chi2 test (or Fisher test if appropriate) was used in categorical variables and Student T test (or U of Mann-Whitney if appropriate) in quantitative variables. Data was analysed using IBM SPSS v23.

Results: 141 patients (194 pregnancies) were registered with maternal average age at rheumatic disease diagnosis of 29.14 ± 6.6 years and average age at abortion/childbirth of 34.82 ± 4.63 years. 12.8% were smokers and 21.1% had comorbidity (hypothyroidism:10.8%, dyslipidemia:2.1%). Maternal diseases are collected in table 1. 50 abortions were registered prior to follow-up in our unit (0.35 abortions/mother). During follow-up 19 abortions were registered (0.13 abortions/mother). Frequencies of abortions/births are specified in table 1.

The frequency of different AAb is found in table 2. Intrauterine growth restriction (IUGR) was observed in 7 cases (3.7%) and pre-eclampsia in 6 (3%) being more frequent among patients with SLE (n:3 and n:2 respectively), APS (n:1 and n:1) and asymptomatic women (p = 0.047).

Treatments used prior to and during pregnancy are shown in table 3. In our series, as previously described in the literature, women with systemic autoimmune and inflammatory diseases have higher risk of abortion, pregnancy complications and instrumental delivery than general population. SLE and APS are most associated with these complications. Multidisciplinary close follow-up of these patients improves pregnancy outcomes.

References:


Disclosure of Interests: None declared


Table 1. Fertility rates in women with SLE compared with those of age-matched general population

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without SLE. On the other hand, the pregnancy adverse outcomes are common in pregnant women with SLE. However, the pregnancy rates in women with SLE was not fully understood. In addition, comparison of the pregnancy adverse outcomes with general population is limited.

Objectives: We estimated the pregnancy rates and adverse pregnancy outcomes in Korean women with SLE and compared them with women without SLE.

Methods: Among all women aged 15-49 years in the Korean National Health Insurance claim database from January 2013 to December 2015, pregnant women were identified by using ICD-10 code for delivery and abortion. Pregnant women were categorized into women with SLE and control group. Adverse pregnancy outcomes classified into five categories as follows: fetal loss, intrauterine growth retardation (IUGR), preterm delivery, pre-eclampsia or eclampsia, and gestational diabetes mellitus. Crude incidence rates (IRs) of pregnancy and adverse pregnancy outcomes were calculated. Incidence rate ratios (IRR) of those were estimated and adjusted for age.

Results: In SLE, 994 pregnancy cases were observed during the study period. The crude estimated IRs of pregnancy were lower in SLE patients than general population (Table 1). Age-adjusted IR was also lower in SLE patients (Table1). The adjusted-IRR of live birth in SLE pregnant women was 0.92 (95% CI 0.85 - 0.99) compared with control group. The adjusted-IRR of fetal loss, IUGR, and preterm delivery was 1.27 (95% CI 1.11 - 1.45), 4.52 (95% CI 3.45 - 5.91), and 3.25 (95% CI 1.62 - 6.52), respectively. The IRR of pre-eclampsia or eclampsia was 3.21 (95% CI 2.52 - 4.08), but those of gestational diabetes mellitus was not significant (IRR 0.89, 95% CI 0.80 - 1.00).

Conclusion: Pregnancy rates in SLE women were lower about 30% compared with general population. Pregnancy adverse outcomes were higher in SLE pregnant women with more than 4-fold IUGR and pre-eclampsia/eclampsia. 3.2-fold preterm delivery.

REFERENCES:

Disclosure of Interests: None declared


FRI0242

SUBPOPULATION COMPOSITION OF INFLAMMATORY INFILTRATES OF THE MINOR SALIVARY GLAND AS AN ADDITIONAL DIAGNOSTIC CRITERION FOR PRIMARY SJOGREN’S SYNDROME

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Background: Primary Sjogren’s syndrome (pSS) is frequent nosological forms among the diffuse connective tissue diseases. Histological examination of the minor salivary gland (MSG) is important diagnostic method. The currently established histological criteria for pSS indicates 61.2-93.7% sensitivity and 61.2-100% specificity respectively, which makes the search for additional hallmark highly relevant. Immunohistochemical study of MSG is the most appropriate for this purpose.

Objectives: To study the qualitative and quantitative compositions of cellular subpopulations minor salivary gland mononuclear foci as additional biomarker of pSS.

Methods: The study included 56 patients with a definite diagnosis of pSS according to the criteria of ACR/EULAR 2016. The control group consisted of 19 healthy volunteers. The biopsy of the minor salivary gland was performed for all the subjects, followed by an immunohistochemical study to evaluate the expression of CD3, CD4, CD8, CD20, CD21, CD68, CD138. A statistical analysis of the data obtained during the study was carried out using the SPSS 23 statistical software for Windows (IBM, United States of America). Diagnostic threshold for each biomarker was determined by ROC analysis. Operating characteristic curve, area under the curve (AUC), specificity, sensitivity, diagnostic accuracy (DT), diagnostic thresholds (DP), positive likelihood ratio (LR+) and negative likelihood ratio (LR-) were also calculated. The construction of classification models, including several markers, was performed using linear discriminant analysis.

Results: The largest AUC were observed in CD3 - 0.795 (95% confidence interval (CI) 0.687 - 0.893) and CD20 - 0.796 (95% CI 0.698 - 0.894), which at the specified DP corresponded to the sensitivity of 67.9% (95% CI 54.04 - 79.71) and 71.4% (95% CI 57.79 - 82.7), specificity of 95% (95% CI 73.97 - 99.87) and 95% (95% CI 73.97 - 99.87). The CD21 marker was detected only in the pSS group. AUC for this biomarker was 0.652 (95% CI 0.525 - 0.778), sensitivity - 30.4% (95% CI 18.78 - 44.1), specificity - 100% (95% CI 82.35 - 100).

Using the method of discriminative analysis, we designed classification models that included various combinations of the markers under study. The combination of the decimal logarithms CD3 and CD68 had AUC 0.873 (95% CI 0.794 - 0.953), sensitivity - 76.8% (95% CI 63.58 - 87.02), specificity - 95% (95% CI 73.97 – 99.87).

Conclusion: CD3 and CD20 can be considered as additional histological criteria for pSS. CD21 was observed only in patients with pSS. The combined quantitative assessment of CD3 and CD68 had a greater diagnostic value compared to CD3 and CD68 separately.

Disclosure of Interests: None declared


FRI0243

RECOVERY OF RENAL FUNCTION IN PATIENTS WITH LUPUS NEPHRITIS AND REDUCED RENAL FUNCTION

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Background: Reduced renal function is associated with worse renal outcomes in patients with lupus nephritis (LN). However, there is insufficient knowledge regarding renal function recovery in patients with LN with reduced baseline renal function.

Objectives: The present study aimed to investigate renal function recovery and related factors in patients with reduced baseline renal function.

Methods: The present retrospective longitudinal cohort study included patients with LN and reduced renal function. Reduced renal function was defined as an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m². Recovery of renal function was determined by eGFR >60 mL/min/1.73 m² at 6 months after baseline, and factors associated with it were evaluated using logistic regression analysis.

Results: We included 90 patients with LN, with a mean eGFR value of 37.2 (± 13.9) mL/min/1.73 m². Forty-six patients (51.1%) recovered their renal function after 6 months. On multivariate analysis, hydroxychloroquine use (OR: 3.891, 95% CI: 1.196-12.653, p = 0.024), prolonged LN (OR: 0.926, 95% CI: 0.874-0.981, p = 0.009), and high-grade tubular atrophy (OR: 0.451, 95% CI: 0.208-0.829, p = 0.013) were associated with renal function recovery. During follow up, 25 patients were on end stage renal disease (ESRD). Kaplan-Meier analysis revealed that renal function recovery after 6 months and lower probability of ESRD are associated.

Conclusion: In patients with LN and reduced renal function, renal function recovery at 6 months was associated with use of hydroxychloroquine and inversely related to longer duration of LN and higher grade of tubular atrophy.

Disclosure of Interests: None declared


FRI0244

MATHEMATICAL PROCESSING IS AFFECTED BY DAILY BUT NOT CUMULATIVE GLUCOCORTICOID DOSE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

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Background: The impact of glucocorticoids on neurocognitive performance in patients with SLE is not fully understood.

Objectives: We aimed to study the effect of daily and cumulative doses of glucocorticoids on neurocognitive performance in patients with SLE using the computer-based Automated Neuropsychological Assessment Matric (ANAM).

Methods: Consecutive patients with SLE and gender- and age-matched (±5 years) healthy control subject (HC) were studied. In a quiet and comfortable room, each subject underwent the 45-minute ANAM test under supervision which comprises simple reaction time (SRT) that probes neuromuscular efficiency, and 8 domains of neurocognitive assessment including 3 code substitution tests (probing learning and recall), spatial processing (probing visual perception and mental rotation), matching to
sample (probing short-term memory and attention), continuous performance test (probing sustained attention), mathematical processing, and memory search (probing working memory). Anxiety and depression were assessed by the Hospital Anxiety and Depression scale (HADS). The total and individual-domain throughput scores (TPS) were compared between both groups using Student’s t test. The presence of cognitive dysfunction, defined as total TPS <1.5 SD below the mean TPS of HC, was compared between both groups by χ² test. Within the SLE group, the relationships between prednisolone dose (daily [mg]) and cumulative ([g]) and individual-domain TPS were first explored by bivariate correlations. Independent association between glucocorticoid dose and individual-domain TPS that showed significant bivariate associations with prednisolone dose was determined by multiple linear regression, with adjustment for potential clinically- and demographically-important confounders.

Results: Ninety-six SLE patients and 96 HC were studied, 16 men (16.7%) were present in each group. The mean age±SD of SLE patients and HC were 36.5±7.1 and 33.6±1.06 years (p=0.073), respectively. The mean±SD duration of SLE, SLEDAI and daily and cumulative prednisolone doses were 98.85±87.4 months, 3.37±3.4, 11.01±13.0mg and 16.92±18.5mg, respectively. SLE patients had a significantly higher mean HADS-anxiety score than HC (6.25±3.3 vs 4.62±3.0, p=0.001) while the mean HADS-depression score was comparable between both groups (p=0.093). SLE patients had significantly shorter duration of education (12.92±3.92 vs 15.86±2.5 years, p<0.001), scored significantly worse across all the 8 ANAM domains, had a significantly lower mean total TPS (337.23±94.4 vs 395.62±87.6, p<0.001) and were significantly more prevalent of cognitive dysfunction as compared to HC (25.0% vs 7.3%, p<0.001). In SLE patients, a statistically significant negative correlation was found between daily prednisolone dose and TPS of mathematical processing (r=-0.248, p<0.015), while no significant correlation between cumulative glucocorticoid dose and any of the individual ANAM domain was found. In multivariate regression, daily prednisolone dose remained independently associated with lower TPS of mathematical processing (β=-0.208, p=0.024) after adjusting for age, gender, SLEDAI, total HADS, total TPS, serum albumin and 25-DH hydroxyvitamin D levels and duration of education in SLE patients.

Conclusion: Daily, but not cumulative glucocorticoid dose has an independent impact on the working memory of SLE patients. While how daily glucocorticoid dose affects working memory mechanistically requires further investigation, its impact on neurocognitive assessment in SLE patients cannot be underestimated.

Disclosure of Interests: None declared

FRIO245
RHEUMATOID FACTOR IN IGA, IGG AND IGM IMMUNOGLOBULIN CLASSES IN PRIMARY SJÖGREN’S SYNDROME

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Background: Primary Sjögren’s syndrome (pSS) is an autoimmune disease with the autoantibodies overproduction, including rheumatoid factors (RF). An association of RFs with the disease activity has been already described, with RFs in IgA, IgG immunoglobulin classes suggested as potential biomarkers of immunological/clinical pSS features.

Objectives: Examining correlations of RF in IgM, IgA and IgG immunoglobulin classes with other autoantibodies, dry eye tests and histopathological assessment (focus score) of salivary gland inflammation.

Methods: We studied 76 patients, mean age 53 (SD=13); (67Female/9Male) with pSS diagnosis (criteria ACR/Eular 2017); mean disease duration from diagnosis 2.24 year. Laboratory tests performed: ESR, C-reactive protein(CRP), concentrations of gamma globulins (g/dl), RF serum concentration assessed using ImmuLisa Enhanced™ RF IgA, IgG, IgM Antibody ELISA IMMCO Diagnostics, Inc. As positive result of the RF-IgA and RF-IgG concentration > 25 EU/mL was considered, as positive RF-IgM > 12.5 EU/mL; a highly positive result set as > 100 EU/mL. The study was approved by the proper ethics committee.

Results: 55% (n=42), - 45%(n=34), ++ 9% (n=7); RF-IgM: + 88% (n=67), - 12% (n=9), + 5% (n=42). In comparison of patients’ groups: RF-IgA (+) vs. RF-IgA (-): no difference in term of FS, OSS and Schirmer’s test; in RF-IgA+ group significantly higher anti SS-A antibodies (p=0.002); a significant difference in anti SS-A antibodies level (p=0.028) RF-IgA(+) and lower positive group (less than 100EU/mL); iRF-IgM(+) vs. RF-IgM(-): RF-IgM (+) significantly higher anti -SS-A antibodies (p=0.007); ii/RF-IgG (+) vs. RF-IgG(-): RF-IgG(+): RF-IgG(+) significantly higher anti SS-B antibodies (p=0.015). Positive correlation was found between: RF-IgA(+) and RF-IgG(+) (rho=0.647) and RF-IgM(+) (rho=0.669); RF-IgG(+) and RF-IgM(-) (rho=-0.429). Surprisingly no correlations found in studied group between concentrations of RF- IgA, IgG and IgM and WBC, C4, C3 complement component, FS, OSS, and Schirmer’s test.

Conclusion: 1. rheumatoid factors in main three classes of gammaglobulins, particularly RF-IgA, strongly associate with anti-SSA and anti-SSB autoantibodies production. 2. RF – IgM and RF- IgA dominate over RF- IgG in pSS. 3. both RF-IgA and RF-IgM may be used as diagnostic tool for pSS. 4. Further research is needed to distinguish activity and role of RF- IgA based upon its presence in serum vs. saliva.

REFERENCES:


Disclosure of Interests: None declared

FRIO246
CELLULAR/FIBROCELLULAR CRESCENT IS A 52-WEEK AND LONG-TERM POOR PROGNOSTIC FACTOR OF ACTIVE LUPUS NEPHRITIS

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Background: Lupus nephritis (LN) is one of the most serious manifestation of systemic lupus erythematosus (SLE), associated with poor prognosis. LN exhibits a variety of histological findings including both inflammatory lesions such as crescent formation and immune complex (IC) deposition lesions. In current INS/RPS 2003 classification, all of them are classified as class III, IV and V. Recently, in the 2016 update of Oxford classification of IgA nephropathy, crescent formation (C) was added as an independent prognostic factor. Further examination of pathological and clinical prognostic factors for LN is required.

Objectives: To identify renal remission rate and clinicopathological characteristics associated with renal non-remission at 52 weeks (52w) in LN patients

Methods: A single center retrospective study. We enrolled Japanese 152 patients of LN class III, IV, and V those who could observe for 52 weeks or more.

Results: The detection of RF in examined sera: RF- IgA(+) positive(+) 66% (n=50), negative (-) 34%(n=26); highly positive (+) 51%(n=39); RF-IgG: + 55% (n=42), - 45%(n=34), ++ 9% (n=7); RF-IgM: + 88% (n=67), - 12% (n=9), + 5% (n=42). In comparison of patients’ groups: RF-IgA (+) vs. RF-IgA (-): no difference in term of FS, OSS and Schirmer’s test; in RF-IgA+ group significantly higher anti SS-A antibodies (p=0.002); a significant difference in anti SS-A antibodies level (p=0.028) RF-IgA(+) and lower positive group (less than 100EU/mL); iRF-IgM(+) vs. RF-IgM(-): RF-IgM (+) significantly higher anti -SS-A antibodies (p=0.007); ii/RF-IgG (+) vs. RF-IgG(-): RF-IgG(+): RF-IgG(+) significantly higher anti SS-B antibodies (p=0.015). Positive correlation was found between: RF-IgA(+) and RF-IgG(+) (rho=0.647) and RF-IgM(+) (rho=0.669); RF-IgG(+) and RF-IgM(-) (rho=-0.429). Surprisingly no correlations found in studied group between concentrations of RF- IgA, IgG and IgM and WBC, C4, C3 complement component, FS, OSS, and Schirmer’s test.

Conclusion: 1. rheumatoid factors in main three classes of gammaglobulins, particularly RF-IgA, strongly associate with anti-SSA and anti-SSB autoantibodies production. 2. RF – IgM and RF- IgA dominate over RF- IgG in pSS. 3. both RF-IgA and RF-IgM may be used as diagnostic tool for pSS. 4. Further research is needed to distinguish activity and role of RF- IgA based upon its presence in serum vs. saliva.

REFERENCES:

Results: Baseline data: mean age 39 years, 135 females, 18 men, historically class III, 53 cases, IV: 58 cases, pure V: 12 cases, III/IV + V: 30 cases. At 52w after biopsy, SLEDIAI (16 → 2), BILAG (17 → 2) score is significantly decreased. Dose of PSL was reduced (48 → 9 mg). At 52w, all patients were classified as RR (125 cases, 82%) and NR (27 cases, 18%) by ACR/LUNAR remission criteria. Surprisingly, all cases of pure V reached remission. Class III or IV LN (RR 114 cases; 91% vs NR 27 cases; 100%, p = 0.01) and cellular/fibrocellular crescent formation (RR 51 cases; 40% vs NR 19 cases; 66%; p = 0.01) were significantly higher in NR. Clinically, long disease duration (p = 0.02), coexisting hypertension (RR 7 cases; 6% vs NR 9; 33%, p <0.01) and TMA (RR 1 case;0.7%, NR 2 cases;7%, p = 0.02), baseline urine protein (RR 1.5g vs NR 2.2g, p=0.01), baseline low WBC (p = 0.03); baseline low IgG (p = 0.02) were detected. About therapeutic drugs, IVCY significantly improved remission rate (RR 84 cases 68% vs. NR 9 cases 41%, p = 0.03). After long-term observation, 52w NR was significantly lower eGFR level (RR 81 vs NR 50, p <0.01, median observation period of 138 months). 3 cases developed lupus nephrotic syndrome with peritoneal involvement. In LN, more frequently than in LN in NR, the presence of interstitial infiltrate was detected. The therapeutic response was relatively better in cases with IC deposition less than those with intense inflammatory histological pattern. In LN, more frequently than in LN in NR, the presence of interstitial infiltrate was detected. The therapeutic response was relatively better in cases with IC deposition less than those with intense inflammatory histological pattern.

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Conclusion: As histological factors contributing to 52w-NR, class III or IV and crescent formation were detected. This result suggested that the therapeutic response was relatively better in cases with IC deposition less than those with intense inflammatory histological pattern. Previous studies have demonstrated that the presence of tubulo-interstitial infiltrate is associated with a worse outcome in response to therapy. Our data highlight the importance of tubulo-interstitial damage, scarcely considered in the current classification criteria, since it represents a key point to predict long-term prognosis.

REFERENCES:

Figure 1

Disclosure of Interests: None declared


FRID247

PROGNOSTIC ROLE OF TUBULO-INTERSTITIAL INFILTRATE IN PATIENTS AFFECTED BY LUPUS NEPHRITIS

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Background: Lupus nephritis (LN) occurs up to 50% of patients affected by Systemic Lupus Erythematosus (SLE) representing one of the major causes of morbidity and mortality in lupus population (1). Kidney biopsy is a fundamental tool for the diagnosis and management of lupus nephritis (LN). The presence of pathological changes such as inflammatory infiltrate in glomeruli and/or in tubulointerstitium are relevant in terms of prognosis and response to therapy (2).

Objectives: The aim of the study was to correlate the clinical and laboratory parameters with the response to therapy and with the presence of glomerular and/or interstitial infiltrate in kidney section of patients with a biopsy-proven LN.

Methods: Kidney sections of patients with SLE undergoing a renal biopsy for diagnostic purposes were studied; samples were classified according to the 2004 International Society of Nephrology/Renal Pathology Society classification criteria (3). Clinical, laboratory and histological data were collected in a standardized, computerized and electronically filled form, including demographic, autoimmune profile, previous and concomitant treatments. We assessed the disease activity by using SLEDAI-2K and remission in response to therapy was defined as the absence of renal impairment and as a score 0 of renal SLEDAI (proteinuria <500mg/24 hours, absence of haematuria and urinary casts) (4). All patients underwent to cyclophosphamide or mycophenolate treatment (S-L and 6-MP). Two to three micron thick sections from paraffin-embedded blocks routinely stained with hematoxylin-eosin (HE) and Periodic acid-Schiff (PAS) for light microscopy investigation were re-evaluated. Predictive value of the presence of interstitial infiltrate on renal remission was evaluated. The results were expressed as mean±standard deviation (SD) depending on the distribution of the variables. The values of P < 0.05 were considered statistically significant.

Results: We evaluated 53 kidney samples from patients with LN (F:M = 51:2, mean age at biopsy 35±7.7 years; mean disease duration at date of biopsy 8±3.8 years). Class IV (46%) was the most common class followed by class III (29%), class II (13%), class V (11.5%) and class VI (0.5%). Tubulo-interstitial infiltrate was found in 33 kidney specimens, with germinal centres (GC)-like features in 13 renal samples (Figure 1). During the follow up (6±3.8 years) the tubulo-interstitial infiltrate, either diffuse or with GC-like feature, was negatively correlated with renal remission (P=0.03).

Conclusion: Assessment and management of patients with LN are greatly facilitated by information obtained by renal biopsy. In the present study we demonstrate that the presence of tubulo-interstitial infiltrate is associated with a worse outcome in response to therapy. Our data highlight the importance of tubulo-interstitial damage, scarcely considered in the current classification criteria, since it represents a key point to predict long-term prognosis.

REFERENCES:

FRID248

ANTI-CYCLIC CITRULLINATED PEPTIDE ANTIBODY IN PRIMARY SJÖGREN SYNDROME: A MARKER OF EROSIONS ON HIGH RESOLUTION ULTRASOUND OF HANDS AND WRISTS

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Background: Cyclic citrullinated peptides antibodies (anti-CCP) were described in primary Sjögren’s syndrome (pSS). However, its possible associations with joint erosions, synovitis and tenosynovitis on high resolution ultrasonography of hands and wrists (US) in pSS are uncertain.

Objectives: To assess in pSS the US findings, and their possible associations with anti-CCP.

Methods: We have evaluated 97 consecutive pSS patients (2016 ACR/EULAR Classification Criteria), of both sexes, aged 18-76 years, and without meeting the 1987 ACR classification criteria for rheumatoid arthritis (RA). Twenty RA patients (disease duration <5 years, and without joint deformities), and 80 healthy controls with comparable mean age, gender and ethnicity were also included in a case-control study. Clinical evaluation was performed through a standardized protocol with interview and physical examination. Disease activity was measured according to EULAR Sjögren’s Syndrome Disease Activity Index (ESSDAI). US was done in 36 joints and 36 tendon areas of wrists and hands, by the same rheumatologist with expertise in ultrasonography, and blinded to autoantibody profile. Patients and controls also underwent X-ray of hands and wrists. Anti-CCP was determined by ELISA using a commercially available kit.

Results: Frequency of tenosynovitis on US was higher in the pSS group than in healthy controls (36.1 vs. 3.8%, p<0.001). Moreover, the number of tenosynovitis was higher in the former group (p=0.001). Importantly, the presence of erosions on US (27.8 vs. 7.5%, p=0.001) and their number (p=0.005) were greater in the pSS group than in healthy controls, with predominance of small erosions (p=0.015). Comparative analysis between RA patients and pSS revealed that the frequency (p=0.001) and number (p<0.001) of synovitis on US were greater in the former group. The number of grade 1 synovitis was comparable between RA and pSS patients (p=0.354). However, the number of grade 2/3 synovitis were higher in RA than in pSS patients (p=0.001). Similarly, the number of erosions on US was higher in the RA group compared to pSS group (p<0.001), particularly of moderate/large erosions.
RESULTS:

Table 1 presents the pooled risk ratio (RR) estimates and summary statistics for VTE in SLE patients compared to the general population. The meta-analysis of the VTE studies showed a significantly increased RR of 3.67 (95% CI: 2.10 to 6.42) for patients with SLE compared to the general population. Removal of the two cross-sectional studies increased RR of 3.67 (95% CI: 2.10 to 6.42) for patients with SLE compared to the general population. The robustness of the results was tested using the leave one out function. The leave one out function confirmed the robustness of the results.

CONCLUSION: Overall, the risk of VTE was found to be significantly higher, over three- to six-fold higher, among patients with SLE compared with the general population. Future research should focus on assessing the impact of traditional and SLE-specific modifiable risk factors on VTE to further identify SLE patients most at risk to support targeting prevention and treatment strategies.

REFERENCES:


Abbreviations: RE, relative effects

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FRID0250

SUBCLINICAL ATHEROSCLEROSIS IN SYSTEMIC LUPUS ERYTHEMATOSUS: COMPARABLE EFFECT OF TRADITIONAL CARDIOVASCULAR RISK FACTORS WITH RHEUMATOID ARTHRITIS

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Background: Both rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) patients are associated with an increased and premature

with an I² ranging between 92% and 99%. Visual examination of the funnel plots showed evidence of publication bias, however this was not supported by the Egger's test. The leave one out function confirmed the robustness of the results.

REFERENCES:


Abbreviations: RE, relative effects

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FRID0249

THE RISK OF VENOUS THROMBOEMBOLIC EVENTS IN ADULT PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Although observational studies suggest people with systemic lupus erythematosus (SLE) have a heightened risk of venous thromboembolic events (VTE), meta-analyses that integrate evidence across studies to estimate the pooled risk have not been performed.

Objectives: To conduct a systematic review and meta-analysis to estimate the risk of VTE including pulmonary embolism (PE) and deep vein thrombosis (DVT) in patients with SLE.

Methods: We conducted a systematic review using MEDLINE and EMBASE from inception to March 2018 to identify observational studies (cohort and cross-sectional) that evaluated the risk of several major cardiovascular outcomes in patients with SLE compared to a general population or healthy controls (protocol published in PROSPERO 2018 CRD42018098690). Here we report the results for venous thromboembolic outcomes. Studies were included that provided effect estimates (relative risks or hazard ratios) for the calculation of pooled effect estimates. Random effects models were used to calculate pooled risk ratios (RR) and 95% confidence intervals (CI) separately for VTE, PE and DVT. Visualization of funnel plots and the Egger test were used for evaluation of publication bias. The robustness of the results was tested using the leave one out function. Sensitivity analysis assessed the impact of removing high risk of bias studies (i.e. cross-sectional).

Results: A total of 9 studies were identified for inclusion into the meta-analysis; 7 for VTE (including two cross-sectional studies), 3 for DVT and 4 for PE. Meta-analysis of the VTE studies showed a significantly increased RR of 3.67 (95% CI: 2.10 to 6.42) for patients with SLE compared to a general population. Removing the two cross-sectional studies did not impact the results (RR 4.06 [95% CI: 3.12 to 5.28]). The pooled RRs for PE and DVT were 4.47 (95% CI: 1.79 to 11.15) and 5.51 (95% CI: 2.27 to 13.39), respectively. The statistical heterogeneity was high.

Abbreviations: RE, relative effects

Disclosure of Interests: Nick Pooley Consultant for: I am employed by Mavexer who were paid to conduct this systematic literature review on behalf of AstraZeneca. Jinoos Yazdany Grant/research support from: Pfizer, Consultant for: AstraZeneca, Julia Langham Consultant for: I am employed by Mavexer who were paid to conduct this systematic literature review on behalf of AstraZeneca., Lindsay Nicholson Consultant for: I am employed by Mavexer who were paid to conduct this systematic literature review on behalf of AstraZeneca., Sue Roche, Pfizer, Bristol-Myers Squibb, Abbvie and Janssen., None declared, Sandra Pasoto: None declared, Lissiane Guedes: None declared, Elaine Leon: None declared, Margarotee Vendramini: None declared, Tamyris Bocate: None declared, Karina Bonfiglioli Speakers bureau: Has received speaking fees from Roche, Pfizer, Bristol-Myers Squibb, Abbvie and Janssen., Eloisa Bona: None declared, Sandra Pasoto: None declared DOI: 10.1136/annrheumdis-2019-eular.3381
prevalence of atherosclerosis. This has been characteristically attributed to the inflammation present in both diseases.

**Objectives:** To analyze the differences in the role of traditional cardiovascular risk factors in the subclinical atherosclerosis between the two diseases and the effect of the presence of carotid plaque when univariate interaction was performed. After final adjustment for demographics, the presence of other traditional cardiovascular factors, and disease related data, no differences were found in the influence of hypertension, diabetes, dyslipidemia or current smoking over cIMT or the presence of carotid plaque. Moreover, the effect of the addition of various cardiovascular risk factors on the subclinical carotid atherosclerosis did not differ between both diseases.

**Conclusion:** The influence of traditional cardiovascular risk factors (hypertension, diabetes, dyslipidemia and smoking) over cIMT and carotid plaque is equal in RA and SLE. No interaction was found between traditional cardiovascular risk factors and disease related data in the effect of the former on subclinical atherosclerosis.

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**DOI:** 10.1136/annrheumdis-2019-eular.1845
RENAL TRANSPLANTATION IN LUPUS NEPHRITIS VS NON-AUTOIMMUNE TRANSPLANTATION. LONG TERM FOLLOW-UP. STUDY FROM A SINGLE TERTIARY CENTER

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Background: Lupus nephritis (LN) is a severe complication of systemic lupus erythematosus (SLE), affecting up to 30-40% of patients. Unfortunately, approximately 10-20% of LN develop end stage renal disease (ESRD) and need replacement therapy. Renal transplantation may be a good option. However, concerns about LN recurrence after renal transplantation have been reported.

Objectives: In a series of patients with first renal transplantation due to LN our aim was to assess a) long-term post-transplant survival and, b) comparison of post-transplant survival with a control group due to a non-autoimmune nephropathy, the polycystic kidney disease (PCKD).

Methods: We study two groups of patients with first renal transplantation: a) LN and b) control group with PCKD. All these patients were transplanted in a single reference University Hospital. The main outcome variables were a) graft and patient survival up to 20 years and b) evolution of renal function (serum creatinine and proteinuria) in the first 5 years of follow-up. Cumulative survival rates after transplantation were estimated by the Kaplan-Meier method and compared between groups using the log-rank test. Mann-Whitney test was used to compare quantitative variables.

Results: We included a total of 53 patients with renal transplant; a) LN group (n=51), b) PCKD group (n=32). No significant differences were found in terms of sex and cardiovascular risk factors. Significant differences were found in terms of age at kidney transplantation, with a mean of 39.80±11.27 years in LN group and 46.59±5.01 years in the PCKD group (p=0.004). Renal biopsy had been performed in 16 patients with LN: type II LN (25%), type III (25%) and type IV (50%), (according to the World Health Organization and International Society of Nephrology/Renal Pathology Society classification). From 48 patients (of 53) in which a renal biopsy was performed during the first-year post-transplant, rejection was found in 21 patients (43.7%) without significant differences between the 2 groups (p=0.444). The evolution of serum creatinine and proteinuria after renal transplantation is shown in TABLE 1. Regarding serum creatinine, significant differences were found in creatinine levels only at the 6th month post-transplant (p=0.032) with no differences in the following measurements. In LN group, 3 patients (14.3%) developed a lupus flare: 2 cases presented as extrarenal disease and only 1 case with histological recurrence in the graft. No significant differences were found in terms of patient or graft survival between the two groups in 20 years of follow-up (Figures 1 and 2).

Conclusion: Despite concerns about LN recurrence after renal transplantation, data obtained in our sample indicate that this procedure as a safe alternative therapy for ESRD in this population and can provide a long-term survival.

Disclosure of Interests: None declared

TABLE 1. Evolution of creatinine and proteinuria levels after renal transplant in LN and PCKD.

<table>
<thead>
<tr>
<th>Time (years)</th>
<th>LN Group</th>
<th>PCKD Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 months</td>
<td>1.36±0.49</td>
<td>1.20±0.24</td>
</tr>
<tr>
<td>12 months</td>
<td>1.40±0.51</td>
<td>1.35±0.35</td>
</tr>
<tr>
<td>24 months</td>
<td>1.45±0.56</td>
<td>1.39±0.40</td>
</tr>
</tbody>
</table>

*p<0.05

FIGURE 1. Patient survival

FIGURE 2. Graft survival

Disclosure of Interests: None declared


COMBINED PANEL OF NINE TESTS HAS THE GREATEST SENSITIVITY BUT THE LOWEST SPECIFICITY TO DETECT ANTIPHOSPHOLIPID Antibody Syndrome in Patients with Systemic Lupus Erythematosus

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Background: Antiphospholipid antibody syndrome (APS) is an autoimmune hypercoagulable state caused by antiphospholipid antibodies (aPL) which represent a diagnostic criterion and underlie significant comorbidities in patients with and without systemic lupus erythematosus (SLE). Although several tests exist for APS diagnosis, their utilization has been highly variable among laboratories and physicians.

Objectives: We have evaluated a panel of nine tests and conducted a retrospective study to determine their sensitivity and specificity for supporting the diagnosis of APS in SLE at our Institution between 2010 and 2018.

Methods: 1633 SLE patients, who satisfied the ACR criteria for a definitive diagnosis [1,2], were evaluated for the presence of APS as earlier described [3]. Lupus anticoagulants were assessed by Staclot LA hexagonal phase phospholipid neutralization assay (HPPNA; delta >8 seconds), Staclot diluted Russell viper venom test (dRVVT; <1.2 normalized ratio).
obtained from Stago ( Parsippany, NJ, United States of America). Platelet neutralization procedure (PNP; delta < 1 second) has been performed using a STA-R Evolution instrument by Stago [4, 5]. IgG and IgM antibodies against α2-glycoprotein 1 (α2-GP1-IgG, α2-GP1-IgM) and cardiolipin (αCL-lgG, αCL-lgM) were measured in house while IgA isoforms (α2-IgA-lgA, α2-IgA-lgG) were tested by LabCorp Diagnostics (Burlington, NC). Sensitivities, specificities, and positive (PPV) and negative predictive values (NPV) for detection of APS were calculated and compared by 2-tailed chi-square tests using GraphPad software.

Results: 222/1633 SLE patients had APS when using a combination of nine tests. Table 1 shows the frequency of positive and negative test results and p value for each assay. The greatest sensitivity was seen when all nine tests were performed together for detecting APS in SLE patients (74%; p<0.0001). In contrast, combining all tests had the lowest specificity (52%; p<0.0001). Importantly, the 2nd most sensitive test for detection of APS was the HPPNA at 52%, this tests also had the second lowest specificity (66%). Similar trends were seen when individual APS comorbidities, such as deep venous thrombosis (DVT), pulmonary embolism (PE), and stroke or TIA, were separately analyzed. Among the charts reviewed, the complete 9-test panel was only performed in 550 of 1633 patients (Table 1).

Conclusion: This study demonstrates that utilizing a combined 9-test panel has the greatest sensitivity but lowest specificity for detecting APS in SLE subjects. This failure to employ the complete panel may lead to exclusion of patients who may meet criteria for identifying patients with APS who need long-term anticoagulation for preventing life-threatening thrombotic events.

REFERENCES:

Disclosure of Interests: None declared

Friday, 14 June 2019 807

FRI0255
LOW ATTENUATION NON-CALCIFIED CORONARY PLAQUES AND POSITIVE REMODELING INDEX: MARKERS OF VULNERABLE CORONARY PLAQUES IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The presence of low attenuation noncalcified plaque (LANCP) and positive remodeling index (RI) are characteristic vessel changes in unstable coronary plaques. LANCP (<30 Hounsfield Units) contain necrotic cores that are characterized by endothelial dysfunction, oxidative stress, and inflammation. They have been shown to be a better predictor of future cardiovascular events compared to traditional cardiovascular risk factors in the general population. Coronary arterial remodeling describes changes of vessel size at the site of lesion. Positive remodeling (expansion) of early lesions maintains lumen size despite plaque accumulation. This explains why these lesions might pass undetected by conventional angiography. Plaque rupture is often apparent at sites with only modest luminal stenoses but marked positive remodeling.

Accelerated atherosclerosis leading to premature coronary artery disease remains the major cause of late death in SLE.

Objectives: We sought to characterize LANCP and positive RI in patients with systemic lupus erythematosus.

Methods: A total of 72 patients who met the ACR or SLICC classification criteria for SLE had CT angiograms, 30 of which had follow up CT angiograms. A total of 100 healthy controls who had two CT angiograms were included in the study. Each noncalcified plaque (NCP) detected within the vessel wall was evaluated for minimum CT density and vascular remodeling index. A LANCP was defined as an NCP with a density <30 Hounsfield units. Lesions with remodeling 0% were considered to have positive RI. T-test was used to evaluate baseline characteristics between lupus patients and controls. Paired t-test or Wilcoxon signed rank test was used to compare LANCP volume and RI between baseline and follow-up. Fisher’s exact test was used to evaluate the association between change in LANCP, RI, demographic and clinical variables.

Results: Lupus patients had a significantly higher burden of LANCP at baseline compared to healthy controls in all age subgroups except in those >60 years of age. LANCP volume was associated with age (p<0.01) and body mass index (p<0.01). No significant differences were observed between RI in lupus and controls at baseline. Despite a significant progression of the total noncalcified plaque burden in lupus compared to controls (p<0.0001), the LANCP in lupus patients regressed (p<0.001). No demographic or clinical differences were observed between lupus patients whose LANCP progressed and those whose LANCP regressed. Lupus patients who were not treated with statins had a more significant progression of their LANCP burden (p<0.01) compared to controls who were on statins, while lupus patients who were taking statins had a significant progression (p<0.01). There were only 5 cardiovascular events in the studied group and there were no differences in remodeling index or low density noncalcified plaque observed but the number of events was small.

Conclusion: Lupus patients have a significantly higher burden of LANCP at baseline compared to healthy controls in all age subgroups except in those >60 years of age. The LANCP burden regresses more rapidly over time in lupus compared to controls. Surprisingly, the most significant LANCP plaque volume regression was seen in lupus patients who were never treated with statins, while the most significant progression was observed in those taking statins. Positive RI was ubiquitous, with no evidence of progression or differences compared to controls. These characteristic vessel changes may identify SLE patients at need for more frequent noninvasive cardiac monitoring.

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FRI0256
ASSESSING THE PREVALENCE AND USE OF VALIDATED SYSTEMIC LUPUS ERYTHEMATOSUS DISEASE ACTIVITY METRICS IN REAL WORLD PRACTICE

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Background: Disease activity metrics for systemic lupus erythematosus (SLE) are not widely used in real world clinical practice.

Scientific Abstracts
Objectives: To assess the use and drivers of SLEDAI and BILAG index in real world clinical practice.

Methods: A cross-sectional study of rheumatologists in the US and EU. Data were collected from the Adelphi Real World 2010/2013/2015 Lupus Disease Programmes (DSP). Physicians were asked to complete an attitudinal survey and patient record forms (PRFs) for the next 5 patients consulting with SLE; the same patients were asked to complete patient self-completion (PSC) forms describing how SLE affected them.

Results: Physicians provided 263 surveys, extracted from the 2015 DSP, indicating that 131 were aware of but did not use the BILAG index, and 92 of physicians were aware of but did not use the SLEDAI. Physicians provided 1376 record forms for SLE patients, extracted from the 2015 DSP; 71 (5.2%) had a BILAG index (1305, 94.6% had no BILAG index), and 373 (27.1%) had had a SLEDAI calculated prospectively (1003, 72.8% had No SLEDAI). Patients with SLEDAI had longer disease duration that patients who did not have a SLEDAI (mean: 6.3 vs. 5.2 years, p<0.007), were less likely to have been described as mild at diagnosis (no SLEDAI mild: 18.7%; SLEDAI mild: 11.3%, p=0.0004) and consulted more with health care professionals in the past 12 months (no SLEDAI mean visits: 6.5, SLEDAI mean: 7.7, p<0.001).

Conclusions: The use of SLEDAI and BILAG index in clinical practice is limited and seemingly reserved for use in more severe patient cohorts; understanding the ongoing impact of this selective use on the treatment and management of SLE would be beneficial. Additionally, understanding the drivers and barriers to the use of disease activity metrics is important for the improvement of management of SLE in the future.


Background: Different neurological manifestations have been observed in 20-25% of patients affected by Sjögren’s syndrome (SS). Among them, CNS demyelinating diseases, Neuromyelitis optica (NMO) and NMO spectrum disorders (NMOSD) with anti-aquaporin4 antibodies (anti-AQ4P4) positivity have been described.

Objectives: The aim of the present study was to assess the clinical characteristics and seroimmunological correlations in patients with Ro-SSA antibodies and Central and peripheral nervous system (CNS and PNS) involvement.

Methods: We retrospectively reviewed clinical records, laboratory and Magnetic Resonance Imaging (MRI) reports of patients followed-up at a tertiary level immunohematology and neuroimmunology clinic. We included patients showing an anti-SSA antibodies positivity and concomitant neurological symptoms at diagnosis. We excluded patients fulfilling SLICC criteria for SLE. We recorded clinical and laboratory and MRI data for all patients.

Results: Out of 9598 clinical records reviewed, we identified 511 patients with anti Ro/SSA positivity. 11 patients had prevalent neurological manifestations. 8 (72.7%) patients were women. The median age was 56 years [IQR 31 years]. CNS involvement was the main clinical feature in 7 patients (63.6%); 3 of them (27.3%) also had NMS manifestations. 4 patients showed exclusively PNS involvement.

LUPUS NEPHRITIS

Background: Serological immune abnormalities such as anti-double strand DNA (dsDNA) antibodies (Abs) and hypocomplementemia (HC) are characteristic of lupus nephritis (LN). International Society of Nephrology/Renal Pathology Society (ISN/RPS) Classification of LN defines pathological active lesions (ALs) as including endocapillary hypercellularity, karyorrhexis, fibrinoid necrosis, cellular/fibrocellular crescents, and wire-loop lesion/hyaline thrombi. We reported these abnormalities are associated with individual pathological ALs. The association between serological abnormalities and pathological ALs in LN is not well characterized.

Objectives: To identify the clinicopathological association between serological immune abnormalities and pathological ALs in LN.

Methods: We enrolled 126 Japanese LN patients who were subjected to renal biopsy in 11 hospitals from 2000 to 2018. We determined various clinical parameters at the time of renal biopsy, including creatinine (Cr), estimated glomerular filtration rate (eGFR), total protein (TP), IgG, IgA, IgM, C3, C4, CH50, anti-nuclear antibodies (Abs), anti-double strand DNA (dsDNA) Abs, anti-Sm Abs, anti-RNP Abs in the sera, urinary findings, presence of comorbidities (antiphospholipid antibody syndrome, hyperlipidemia, diabetes mellitus, and hyperuricemia), and use of any immunosuppressive medications before renal biopsy. Renal biopsy findings were classified by ISN/RPS Classification including ALs. Immune deposits were evaluated by immunofluorescence. Elevation of serum anti-dsDNA Abs level [dsDNA Abs (+)] was defined as >12 IU/mL. HC was defined by C3 <0 g/dL. In patients of all pathological classes, we analyzed the association between serological abnormalities and ALs by univariate and multiple regression analyses.

Results: Of 126 patients (104 females; mean age 41.8 years), dsDNA Abs (+) and HC (+) were found in 83 (65.9%) and 80 (63.5%), respectively. There were no significant differences in renal function, comorbidities, immune deposits or immunosuppressive medications before renal biopsy. Multiple regression analysis showed that patients with dsDNA Abs (+) had a higher frequency of endocapillary hypercellularity, karyorrhexis, fibrinoid necrosis, and wire-loop lesion/hyaline thrombi than patients without dsDNA Abs (+) (OR = 4.0; 95% CI: 1.6-9.9). Patients with HC (+) had a higher frequency of endocapillary hypercellularity, karyorrhexis, fibrinoid necrosis, and wire-loop lesion/hyaline thrombi than patients without HC (+) (OR = 3.2; 95% CI: 1.4-7.3). Patients with both dsDNA Abs (+) and HC (+) had a higher frequency of endocapillary hypercellularity, karyorrhexis, fibrinoid necrosis, and wire-loop lesion/hyaline thrombi than patients without both dsDNA Abs (+) and HC (+) (OR = 6.3; 95% CI: 2.5-15.3).

Conclusion: Serum anti-dsDNA Abs and HC were associated with fibrinoid necrosis and karyorrhexis, respectively. These results document that individual serological immune abnormalities associate with specific ALs, suggesting that pathophysiological differences underlie each AL.

REFERENCES:
Background: Risk factors for treatment failure in patients with giant cell arteritis (GCA) are poorly understood.

Objectives: To identify predictors of treatment failure in GCA patients receiving tocilizumab (TCZ) or placebo (PBO) in combination with prednisone in a randomized controlled trial.

Methods: Two hundred fifty GCA patients received weekly or every-other-week TCZ plus a 26-week prednisone taper (TCZ+pred) or PBO plus a 26- or 52-week prednisone taper (PBO+pred). Patients who achieved and maintained clinical remission (CR) from week 12 to week 52 while adhering to the protocol prednisone taper were classified as responders. CR, adjudicated by investigators, was defined as the absence of disease flare (GCA signs or symptoms, and/OR ESR elevation attributable to GCA that required further treatment [eg, rescue prednisone]) regardless of CRP level. Treatment failure was defined as failure to achieve CR by week 12 or occurrence of flare between weeks 12 and 52. Both TCZ groups and both PBO groups were combined for this analysis. Potential predictors investigated included baseline demographics, disease- and treatment-related factors, and health-related quality of life (HRQOL) measures. Univariate and multivariate analyses were performed.

Results: Overall, 45% (113/250) of patients were responders: 27% (27/101) in the PBO+pred groups and 58% (86/149) in the TCZ+pred groups. In contrast, 44% (111/250) of patients experienced treatment failure: 66% (67/101) in the PBO+pred group and 30% (44/149) in the TCZ+pred group. The other 10% (26/250) of patients were nonresponders for reasons other than treatment failure: 7 in the PBO+pred group and 19 in the TCZ+pred group. In univariate analysis, female sex and lower baseline SF-36 Physical Component Summary (PCS), Mental Component Summary, and FACIT-Fatigue scores were associated with treatment failure among PBO+pred–treated patients, whereas higher patient global assessment of disease activity scores and lower SF-36 PCS, FACIT-Fatigue, and EQ-5D scores were associated with treatment failure among TCZ+pred–treated patients (Figure 1). Among TCZ+pred–treated patients, no treatment response difference according to sex was observed. Age, previous relapse, starting prednisone dose, and GCA clinical features (cranial or polymyalgia rheumatica symptoms) were not associated with treatment failure in either group based on univariate analysis. Multivariate logistic regression demonstrated that PBO+pred treatment, female sex, worse FACIT-Fatigue scores at baseline, and historical CRP >2.5 mg/dL all independently increased the risk for treatment failure (Figure 2).

Conclusion: Female GCA patients responded particularly poorly if treated with prednisone alone according to univariate analysis. Female sex, impaired HRQOL at baseline, history of elevated CRP, and treatment with prednisone alone are independent risk factors for treatment failure in GCA. These factors may be considered when determining which treatment would be best for a particular patient.

REFERENCES:
Clinical Outcomes of Patients with Giant Cell Arteritis with Polymyalgia Symptoms Only vs Cranial Symptoms Only Treated with Tocilizumab or Placebo in the GIACTA Trial

Background: GIACTA, a randomized, double-blind, placebo (PBO)-controlled trial, demonstrated the efficacy and safety of tocilizumab (TCZ) in patients with giant cell arteritis (GCA).1 Growing evidence has shown that TCZ is also effective for the treatment of polymyalgia rheumatica (PMR); however, data on this are limited.2,3

Objectives: To evaluate the efficacy of TCZ in patients with GCA presenting with cranial symptoms only or PMR symptoms only in GIACTA.

Methods: GIACTA randomized 251 GCA patients to receive weekly or every other week TCZ plus a 26-week prednisone taper (TCZ + prednisone) or PBO plus a 26- or 52-week prednisone taper (PBO + prednisone) in a post hoc analysis.1,2 In this post hoc analysis, baseline characteristics, sustained remission rate, number of flares, annual flare rate, time to flare, cumulative prednisone dose and safety were assessed in patients with PMR symptoms only and patients with cranial symptoms only at diagnosis. Disease flare was defined as the recurrence of signs or symptoms of GCA (including PMR) or an elevation in erythrocyte sedimentation rate attributable to GCA.

Results: Of 146 patients included in the analysis, 52 had PMR symptoms only and 94 had cranial symptoms only at diagnosis. Demographics and other patient characteristics are shown in Table 1. The hazard ratios for flare in patients receiving TCZ vs PBO were 0.77 (99% CI, 0.26-2.32) for patients with PMR symptoms only and 0.37 (99% CI, 0.13-1.01) for patients with cranial symptoms only. Of patients with PMR symptoms only, 18 flares occurred in 13/31 patients (41.9%) in the TCZ group and 20 flares occurred in 12/21 patients (57.1%) in the PBO group. Of patients with cranial symptoms only, 19 flares occurred in 12/58 patients (20.7%) in the TCZ group and 25 flares occurred in 17/36 patients (47.2%) in the PBO group (Table 2). For both the PMR and cranial symptoms only groups, annual flare rates were lower in patients receiving TCZ compared with those receiving PBO. The occurrence of adverse events and serious adverse events was similar between groups (Table 2).

Conclusion: TCZ improved clinical outcomes in patients who presented with PMR symptoms only or cranial symptoms only at diagnosis as indicated by a reduced incidence of flares. These findings suggest that TCZ is effective in patients with GCA with PMR or cranial symptoms.

References:

Table 1. Patient Characteristics and Treatment at Study Baseline

<table>
<thead>
<tr>
<th>PMR Symptoms Only</th>
<th>Cranial Symptoms Only</th>
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<tbody>
<tr>
<td>(n = 52)</td>
<td>(n = 94)</td>
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<tr>
<td>Age, mean (SD), y</td>
<td>64.5 (8.3)</td>
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<tr>
<td>Female, n (%)</td>
<td>39 (75.0)</td>
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<td>White, n (%)</td>
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<td>Weight, mean (SD), kg</td>
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<td>Body mass index, mean (SD), kg/m²</td>
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<td>GCA diagnosis, n (%)</td>
<td>31 (59.6)</td>
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<tr>
<td>Newly diagnosed</td>
<td>27 (51.9)</td>
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<tr>
<td>Relapsing</td>
<td>53 (56.4)</td>
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<tr>
<td>Disease duration, mean (SD), days</td>
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<tr>
<td>ESR, mean (SD), mm/h</td>
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<td>CRP, mean (SD), mg/L</td>
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<td>Diagnosis, n (%)</td>
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<td>Positive temporary artery biopsy</td>
<td>9/12 (75)</td>
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<td>Positive imaging</td>
<td>44/52 (84.6)</td>
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<td>Prednisone dose, n (%)</td>
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<td>&gt; 30 mg/d</td>
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<tr>
<td>Treatment group, n (%)</td>
<td>TCZ2</td>
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<tr>
<td>Placebo</td>
<td>21 (40.4)</td>
</tr>
</tbody>
</table>

a) Of patients with available results.

b) TCZ 162 mg weekly or every other week with a 26-week prednisone taper.

Disclosure of Interests: Robert Spiera Grant/research support from: Roche-Genentech, GlaxoSmithKline, Bristol-Myers Squibb, Boehringer Ingelheim, Cytori, Chemocentryx, Corbus, Consultant for: Roche-Genentech, GlaxoSmithKline, CSL Behring, Sanofi Aventis, Sebastian Unizony Grant/research support from: F. Hoffmann-La Roche Ltd., Employee of: Genentech, Yves Luder Shareholder of: F. Hoffmann-La Roche, Employee of: F. Hoffmann-La Roche, Paris Sidiropoulos

Granulomatosis with Polyangiitis, (GPA): Cardiovascular Morbidity and Mortality in a Population-Based Cohort: A Danish Register Study

Background: In order to understand and ultimately prevent cardiovascular (CV) morbidity and mortality in systemic inflammatory disorders we studied the epidemiology of CV disease in ANCA associated Vasculitis (AAV). There is growing evidence that both premature and pronounced atherosclerosis is associated with ANCA associated vasculitis (AAV).1-3 However, the exact mechanisms for CV involvement are unknown and probably multiple.

Methods: A population-based cohort study was performed using the Danish Civil Registration System, the Danish National Patient Registry (all inpatient and outpatient contacts are registered with ICD diagnosis since 1995) and the Danish Cause of Death Register. Patients registered twice or more with a diagnosis of GPA (ICD8: 446.29 and ICD10: M31.3) during 1995-2016 were included. Annual incidence rate (IR), point prevalence (PP) and standardized mortality ratio (SMR) were calculated. The entire adult population in Denmark served as control population. CV morbidity was divided into heart failure (HF) (ICD-10 code I21, I50, J81 and I110) and myocardial infarction (MI) (ICD-10 code I21-25). Death caused by CV disease (ICD-10 code I1-999) was registered.

Results: We identified 1829 individuals with GPA. The median annual IR was 20.5/1,000,000 and PP was 277/1,000,000 in 2015. Overall SMR was 2.14. Among patients with GPA 171 had a hospital diagnosis of MI. Compared to the control population, the hazard ratio (HR) of MI was 2.47 (95% CI 4.55-11.46) during the first 3 months after the GPA diagnosis. From 3 months to one year declining to 1.41 (95%CI 0.80-2.49) and after 10 years the HR was still slightly increased to 1.64 (95%CI 1.20-2.23). The risk of a diagnosis of HF was markedly increased with a HR at 7.22 (95% CI 4.55-11.46) during the first 3 months after a GPA diagnosis, after three months up to one year 2.94 (95%CI 1.87-4.69), and 2.07 (95% CI 1.54-2.78) after 10 years. The total number of CV deaths in the GPA cohort was 307. During the first three months after a GPA diagnosis, the HR was increased to 9.51 (95%CI 7.12-12.70) declining to 2.51 (95% CI 1.77-3.58) after one year, but still increased to 1.56 (95% CI 1.23-1.98) after 10 years.

Disclosure of Interests: Helle Laursen Grant/research support from: Odense University Hospital, Roukemtology, Odense, Denmark; Odense University Hospital, Rheumatology, Odense, Denmark
Conclusion: In a population-based study we found an overall increased SMR. The risk of CV morbidity and of CV death among patients with a register diagnosis of GPA was increased. There was a striking temporal relation between a high HR of CV morbidity and mortality during the first year after the diagnosis of GPA. Nevertheless, the HR of CV morbidity and mortality was albeit lower still increased after 10 years with a diagnosis of GPA. The result indicates a strong association between systemic vascular inflammatory disease and CV involvement. A time of diagnosis of GPA systemic inflammatory activity usually is present and the results point towards an association of inflammation with CV risk-factors probably including premature and pronounced atherosclerosis. The persistence of increased HR of CV involvement after 10 years indicates a permanent influence on the risk factors.

REFERENCES:

Disclosure of Interests: None declared

FRID0264

ADVERSE EVENTS DUE TO HIGH DOSE GLUCOCORTICOIDS – LESSONS FROM ANCA-ASSOCIATED VASCULITIS AND OTHER INFLAMMATORY DISEASES

Peter Rutherford, Dieter Götte. Vifor Pharma, Medical, Zurich, Switzerland

Background: High dose glucocorticoids (GCs) are a component of induction remission and maintenance regimes in ANCA-associated vasculitides (AAV) and are used in other inflammatory disorders. The adverse event (AE) profile of GC is well known and in AAV is believed to link to early mortality risk from infection as well as long term organ/tissue damage. However, it is known GC AE reporting is incomplete and EULAR made specific recommendations for such reporting in clinical trials (Van der Goes 2010).

Objectives: This systematic literature review aimed to examine AE rates and outcomes related to high dose GC use in AAV and to quantify AE risk in terms of GC dose and duration.

Methods: A systematic literature review was performed of studies published between 1 Jan 2007 and 30 January 2018. Data on GC-related AEs (defined as any untoward medical occurrence) and serious AEs (defined as any untoward medical occurrence that resulted in death, was life threatening, required or prolongation of hospitalization, was organ system specific or resulted in persistent or significant disability or incapacity) were extracted from identified trials. The initial AAV search demonstrated incomplete GC data collection compared to EULAR recommendations in most AAV studies so the search strategy was extended to include other inflammatory disorders in which similar GC regimes and doses are used namely systemic lupus erythematosus, glomerulonephritis, pemphigus and giant cell arteritis.

Results: Three hundred and eleven studies of these 5 conditions were selected for a detailed AE analysis on the basis of their inclusion of full description of GC regime, actual delivered GC dose and patient exposure. Of the 62,630 patients enrolled in the 38 studies, 35,587 were exposed to GCs. 21 studies reported serious AEs, while 17 studies reported AEs only. The most common serious AEs related to specific organ damage - particularly musculoskeletal, ocular and neuropsychiatric - but mortality and infection were also observed. The most common AEs were metabolic conditions, with diabetes related events comprising 72% of the metabolic AEs, and weight gain comprising 15%.

Conclusion: GC-related AE reporting in clinical studies of high dose GCs could be improved. Serious AEs including organ damage, infection and mortality were reported and both total GC dose and therapy duration are important risk factors mortality and infection. Metabolic and musculoskeletal events are a particular patient burden. New therapeutic options for AAV and other disorders should aim to reduce this AE profile.

REFERENCES:

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Disclosure of Interests: Peter Rutherford Employee of: Vifor Pharma, Dieter Götte Employee of: Vifor Pharma

REFERENCES:

Disclosure of Interests: None declared

FR10266 ABERRANT PD1 AND VISTA EXPRESSION ON CD4+ TH-CELLS IN GIANT CELL ARTERITIS
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Vascularis Expertise Center Groningen. 1University Medical Center Groningen, Pathology and Medical Biology, Groningen, Netherlands; 2University Medical Center Groningen, Rheumatology and Clinical Immunology, Groningen, Netherlands.

Background: The immune system controls immune responses by balancing positive and negative immune checkpoint (IC) molecules in cell-cell interactions. These co-stimulatory and co-inhibitory molecules allow complete T-cell activation and T-cell effector functions giving rise to an optimal immune response while preventing autoimmunity (1). Failure of tolerance results in the initiation and propagation of pathogenic T-cell responses leading to the development of autoimmune diseases such as Giant Cell Arteritis (GCA). The latter is a complex illness of multiple pathogenic factors with important contributions of both innate and adaptive immunity in its initiation and perpetuation (2,3). Recently, a loss of inhibitory checkpoints on immune cells has been implicated in the immunopathology of GCA (4,5). The possible contribution of IC pathways to the dysregulation of Th-cells in GCA could aid in our understanding of GCA immunopathology.

Objectives: In this study, we aimed to investigate the expression of different IC molecules and their ligands by circulating monocytes, and functionally distinct populations of CD4+ T-cells in peripheral blood samples from GCA-patients in comparison to healthy controls (HCs).

Methods: In a cross-sectional study, fresh blood samples were obtained from 30 GCA-patients with/without immunosuppressive treatment (glucocorticoids) and 18 sex and age-matched HCs. The frequency of the expression of different IC including CD80/86, PD-L1, PD2 and V-domain Ig suppressor of T-cell activation (VISTA) were determined on total monocytes and subsets (classical, intermediate and non-classical). In parallel, expression of the corresponding receptors CD28, Cytotoxic T-Lymphocyte-associated antigen 4 (CTLA-4), Programmed death-1 (PD-1), and VISTA were determined on total CD4+ and subsets of Th-cells defined by CD45RA and CD25 expression of GCA-patients and HCs by flow cytometry.

Results: The frequencies of CD80/CD86+ and VISTA+ monocytes were decreased in GCA-patients compared to HCs. Proportions of circulating CD4+ Th-cells in GCA-patients were not different when compared to HCs. The frequencies of CD28 and CTLA-4 expressing CD4+Th-cells did not differ between GCA-patients and HCs. In contrast, proportions of PD-1 and VISTA expressing Th-cells were significantly decreased in GCA patients. Memory T-cells showed decreased expression of IC molecules. Interestingly, naïve T-cell populations already demonstrated loss of PD-1 and VISTA.

Conclusion: In GCA, lower frequencies of CD80/CD86+ and VISTA+ circulating monocytes were found. Likewise, decreased proportions of PD-1+CD4+ and VISTA+CD4+ Th-cells were noted. Decrease of negative IC on the surface of immune cells could add to the persistent activation of CD4+T-cells seen in GCA.

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[1] Ceeris S, Nowak EC, Noelle RJ. B7 family checkpoint regulators in CD4+ and VISTA+CD4+ Th-cells were noted. Decrease of negative IC molecules and their ligands by circulating monocytes were found. Likewise, decreased proportions of PD-1 and VISTA. Interestingly, naïve T-cell populations already demonstrated loss of PD-1 and VISTA.

FR10267 DIAGNOSING POLYMALGIA RHEUMATICA: THE IMPACT OF FAST-TRACK CLINIC AT HOSPITALIZATION RATES
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Background: Polymyalgia Rheumatica (PMR) is a common inflammatory autoimmune rheumatic disease, with the highest incidence rates seen in Scandinavia.

One of the challenges in the diagnosis of PMR is the lack of diagnostic tests specific for the disease. The diagnosis may require exclusion of other conditions that can present with polymyalgia symptoms and may lead to hospitalization. Only limited data on hospitalization rates among patients with PMR exists (1).

Ultrasonography is likely to be in differential PMR from non-inflamatory conditions and can be used for the diagnosis of concomitant Giant Cell Arteritis (GCA).

GCA Fast Track Clinics (FT) using US as the main diagnostic tool have shown both improvement in patient outcomes and decrease in the cost of care(2).

Objectives: To investigate the admission rates of patients diagnosed with PMR and the impact of the FT on these rates.

Methods: A FT clinic for patients suspected to have PMR was established at rheumatological outpatient clinic of South-West Jutland Hospital (serving 250,000 inhabitants) in January 2018. Collaboration with the Emergency Medical department was established and patients with PMR symptoms referred to the hospital were examined at FT within 0-1 days, thereby avoiding hospitalization. Similarly, patients referred with PMR symptoms to the outpatient clinic by a GP, were examined at FT within 1-2 days. At FT a thorough history and clinical examination were performed including musculo-skeletal and vascular US. Retrospectively data from patients diagnosed with PMR from 2013-2018 was analyzed.

Results: In a 6 years’ period, 336 patients were diagnosed with PMR. 54 patients were diagnosed during hospitalization. Hospitalized patients were older (mean values ± standard deviation) 73.61±18.96 vs 70.94 ±7.97 years, p=0.024, with significantly higher initial C-reactive protein (CRP, mg/l) levels 99±58.8 vs 43.9±37.p<0.0001 and a shorter duration of symptoms (6.92±5.5 vs 13.6±13.7 weeks, p=0.0018). No differences were found regarding gender, PMR related symptoms, initial prednisolone dose and response to treatment. An equal annual distribution of the number of new diagnosed cases and hospitalizations rates during the first 5 years was found. After the implementation of the FT at January 2018 a significant decrease in hospitalization rates (19.4% vs 3.5% p=0.0001) and inpatient days of care (4.15±3.1 vs 110, p<0.0001) was observed. The time from symptoms debut to diagnosis was also significantly decreased from 13, 74 to 6, 79 weeks (Table).

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Conclusion: The annual hospitalization rates in connection with PMR diagnosis at South-west Denmark during a 5 year period were estimated to be 19.2%. The implementation of a FT ultrasound clinic decreased significantly the hospitalization rates among patients with PMR.

REFERENCES:

Disclosure of Interests: None declared


FRID0268 CLINICAL FEATURES OF TAKAYASU'S ARTERITIS FROM AN INCEPTION COHORT: EARLY DISEASE IS CHARACTERIZED BY ‘SYSTEMIC INFLAMMATION’
Fatma Alibaz-Oner, On behalf of Turkish Takayasu Arteritis Study Group. Marmara University Faculty of Medicine, Internal Medicine, Division of Rheumatology, Istanbul, Turkey

Background: There is only retrospective and very limited data for the long term prognosis of Takayasu’s Arteritis (TAK), a rare large-vessel vasculitis.

Objectives: In this study, we aimed to present the preliminary results of a Takayasu Inception Cohort settled for long term, prospective follow-up of only newly-diagnosed patients with TAK.

Methods: Patients fulfilling the American College of Rheumatology 1990 criteria for TAK and diagnosed in the last 12 months were included to the study. Patients’ data were recorded in an electronic database of an international ‘Takayasu’s Arteritis Registry’ requiring baseline and at least annual visits. Data is compared with an historical Turkish cohort previously published (Biçakçigil et al., 2009).

Results: The study included 170 patients (age: 38.5±13.1 years, F/M: 143/27) with TAK from 15 tertiary Rheumatology centers in Turkey. The mean symptom duration of patients was 5.2 years at diagnosis. According to the angiographic classification, 68.2% of the study group had type I and only 18.3% had type V disease. When we compared our results to our retrospective cohort (previously published by Turkish Takayasu Arteritis Study Group), constitutional symptoms (115/165=69.6% vs 66%) and limb claudication (87/131=66.4% vs 48%) were observed to be more frequent, whereas pulselessness (45/130=34.6% vs 88%) was less in the inception cohort. Carotidynia was present only in the inception cohort (Table 1). Cardiodynamics was observed 78% of patients. At least one relapse was observed 40% of patients mycophenolate mofetil and 5 (2.9%) patients biologics at disease-onset.

Disclosure of Interests: None declared


FRID0269 COMPARATIVE STUDY OF INFlixIMAB VERSUS ADALUMAB IN REFRACTORY UVEITIS DUE TO BEHÇET’S DISEASE. NATIONAL MULTICENTER STUDY OF 177 CASES

Background: Uveitis is one of the major causes of disability of Behçet’s disease (BD). According to the “Expert panel recommendations”, anti-TNF therapy with infliximab (IFX) or adalimumab (ADA) may be considered as first- or second-line therapy for patients with BD-opthalmic manifestations.

Objectives: To compare IFX versus ADA as first biologic drug in refractory uveitis due to BD for 1-year period.

Methods: Multicenter study of BD-associated uveitis refractory to conventional biologic treatment. Dosing schedule: IFX 3-5 mg/kg iv at 0, 2 and 6 weeks and then every 12-16 weeks, and ADA 40 mg/sc/ever other week. Main comparative outcome measures: safety and efficacy, assessing the intraocular inflammation, macular thickness, visual acuity, degree of immunosuppression load, drug retention, and glucocorticoid-sparing effect.

Results: 177 patients (316 affected eyes) were included. IFX was used in 103 and ADA in 74. No significant differences at baseline were observed regarding main demographic features, previous therapy and ocular severity. After 1 year of therapy, we observed an improvement in all ocular parameters in IFX vs ADA groups: AC inflammation (78.18% vs 68.5%), 218/248 (88%) Pulsoless, 22/184 (12%) Respiratory manifestations, 156/248 (63%) Neurologic manifestations, 141/248 (57%) Cardiac involvement, 7/166 (4.1%) Mortality rate was 4.1% (3/73 patients) during a mean annual visits. similarly, mucocutaneous symptoms also seem to be a feature of newly-diagnosed disease (30/162=18.5% vs 8.8%). Regarding comorbidities at diagnosis, the rate of dyslipidemia was 17.6% (30/165)%, diabetes mellitus 15.1% (25/165)%, smoking 20% (34/164)% and obesity (BMI>30) 14% (22/157)% among TAK patients. All patients were given oral corticosteroid (CS) therapy (0.5-1 mg/kg) at diagnosis, 17 patients (17/180-10%) also having CS pulses. In addition to CSs, 68 patients (50.6%) were given methotrexate, 31 patients (18.2%) azathioprine, 3 (3.5%) cyclophosphamide, 12 patients (7.1%) iflamamide, 2 (12.1%) patients mycophenolate motil and 5 (2.9%) patients biologics at disease-onset (2 tocilizumab, 2 infliximab, 1 adalimumab). Biologic agents were chosen for 7 patients (7/32) at last visit(1 adalimumab, 4 tocilizumab, 2 infliximab).

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REFERENCES:

Background: Behçet’s disease (BD) is a variable vessel vasculitis with a wide and heterogeneous set of signs and symptoms. The inhibitor of phosphodiesterase-4 Apremilast (APR) has demonstrated efficacy in the treatment of oral and/or genital ulcers.

Objectives: To assess the efficacy and safety of APR in BD patients with manifestations different from mucocutaneous ulcers.

Methods: National multicenter retrospective study on 32 BD patients treated with APR at maintained standard dose of 30 mg twice daily.

Results: From a cohort of 49 patients with oral and/or genital ulcers related to BD and refractory to conventional and/or biological treatment, we selected the cases with another clinical manifestation(s) (n=32, 23 women/9 men), mean age of 46.3±5.05 years. Non-aphthous manifestations present at apremilast onset were: arthralgia/arthritis (15), furunculosis/pseudofolliculitis (12), asthenia (7), erythema nodosum (3), furunculosis (2), paradoxical psoriasis by TNFi (2), itilits (2), deep venous thrombosis (2), erythematosus and scaly skin lesions (1), fever (1), eating disorder (1), fibromyalgia (1), unilateral anterior uveitis (1) and neurobehçet (1). APR was used in monotherapy (n=3) or combined (n=29) with oral corticosteroids (20), colchicine (17), methotrexate (5), azathioprine (3), dapson (3), tocilizumab (1), hydroxychloroquine (1) and/or mesalazine (1). The outcome of the different clinical symptoms is shown in TABLE. The patient with neurobehçet kept stable (paresthesias) during the 6 months of follow-up. The 2 cases of deep venous thrombosis and the case of anterior uveitis resolved with anticoagulants and adjuvant topical treatment, respectively. Furunculosis, folliculitis/pseudofolliculitis and itilits were the manifestations that improved completely and rapidly. The cases of arthritids experienced improvement, while those with arthromyalgia presented a torpid evolution.

Conclusion: Our data show an improvement of the cutaneous follicular and intestinal clinic with APR and a stability of the neurological clinic, while the musculoskeletal manifestations were mostly refractory.

REFERENCES:

TABLE 1: Outcome of non-aphthous uveitis with apremilast.

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TABLE 2: Outcome of non-aphthous kidney with apremilast.

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<th>Duration of follow-up (Months)</th>
<th>NC (n=23)</th>
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<th>Improvement (n=1)</th>
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Table 2: remission rate and duration of remission of 49 patients with Behcet’s disease. NC<br>TABLE 2: remission rate and duration of remission of 49 patients with Behcet’s disease. NC
Disclosure of Interests: Belén Atienza-Mateo: None declared, José Luis Martin-Varillas: None declared, J. Loricer: None declared, Vanesa Calvo-Rio: None declared, Jenaro Graña: None declared, Gerard Espinosa: None declared, Clara Moriano: None declared, Trinidad Pérez-Sandoval: No relevant disclosures, Manuel Martín-Martínez: None declared, Elvira Díez-Alvarez: None declared, María Dolores García-Armario: None declared, Esperanza Martínez: None declared, Ivan Castellví Consultant for: I received fees less than 5000USD as a consultant for Kern and Actelion, Paid instructor for: I received fees less than 2000USD as an instructor for Boehringer-Ingelheim, Novartis and Gebro, Speakers bureau: ND, Patricia Moya: None declared, Francisca Sivera: None declared, Jaime Calvo Consultant for: Bristol-Myers Squibb, Janssen, Celgene, Sanofi Genzyme, Speakers bureau: Bristol-Myers Squibb, Isabel de la Morena, Speakers bureau: Abbvie, Celgene, Pfizer, UCB, Chévre, Roche, Sanofi, Janssen, Francisco Ortiz-Sanjuán: None declared, José Andrés Román-Ivorra: None declared, Ana Pérez Gómez: None declared, Sergio Heredia: None declared, Alejandro Olive: None declared, Águeda Prior-Español: None declared, Carolina Díez: None declared, Juanjo J Alge-Carrión: None declared, D Ybáñez-García: None declared, Ángels Martínez-Ferrer: None declared, J. Narváez Consultant for: Bristol-Myers Squibb, Ignasi Figueras: None declared, Ana Isabel Turrión : None declared, Susana Romero-Yuste: None declared, Pilar Trénor: None declared, Soledad Ojeda Grant/research support from: AMGEN, Speakers bureau: AMGEN, Santos Castrillón Consultant for: Amgen, BMS, Pfizer, Lilly, MSD, Roche, Sanofi, UCB, D. Prieto-Perla: None declared, Monica Calderón-Goecke: None declared, Lara Sánchez Bilbao: None declared, Ilfco González-Mazón: None declared, Miguel Á. González-Gay: None declared, Ricardo Blanco Grant/research support from: Abbvie, MSD and Roche, Consultant for: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen and MSD, Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen and MSD; DOI: 10.1136/annrheumdis-2019-eular.5965

References:
None


FRI0272 USE OF CONTRAST ENHANCED ULTRASOUND SONOGRAPHY (CEUS) IN LARGE VESSEL VASCULITIS (LVV)

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Background: C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are important parameters in the monitoring of LVV. Since Toilлизумab is approved for treatment of LVV these cheap and easy repeatable parameters are worthless because of their normalisation by Tocilizumab. The limitation of our study is the small number of patients, the missing blinding of the investigator and the method intrinsic fact, that you can’t investigate all involved vessels by ultrasound/CEUS.

Objectives: CEUS can increase the visibility of tissue perfusion, particularly if there is a very slow bloodflow, which cannot be detected by power-doppler sonography.

Methods: In this proof of concept study we investigated patients with active and inative LVV (alLV/II VKV) with CEUS. After injection of ultrasound contrast agent we measured the contrasted area of large vessels in a transverse section first if the lumen was completely contrasted and once again 4-8 seconds later. If the vessel wall incorporated the contrast agent the contrasted area increased (Fig 1). The increase of the contrasted area (CA) was correlated with CRP and ESR. Patients were only included if they were not treated with Toilлизумab and therefore ESR and CRP were usable to evaluate the disease activity.

Results: Investigated were 16 patients (13 female, 3 male), 8 with alLV and 8 with II VKV, respectively. The mean CA was 66.6±44.6 (alLV) vs. 2.4±6.6% (II VKV) (p<0.0001). The increase correlated significantly with the CRP r=0.87, p<0.0001. An increase of the CA was 66.6±44.6 (alLV) vs. 2.4±6.6% (II VKV) (p<0.0001). The mean daily dose of OGCs measured over 6 months post-index among this patient sample (Q1: £ 1.00 to £ 1.00; Q2: £ 2.00 to £ 3.00; Q3: £ 15.00 to £ 25.00 mg; Q4: > 50.00 mg). Potential AEs were cerebrovascular disease, diabetes, chronic pulmonary disease, and renal disease. Mean daily OGC dose was 28.9 mg during the first 6 months post-index. Mean daily OGC dose was 28.9 mg during the first 6 months post-index. Mean (SD) CRP and ESR during the 12-month follow-up ranged from 7.5% to 24.5% from OGC daily dose Q1 to Q4 cohorts. The proportion of patients with glucose level, serious infections, cataracts, gastrointestinal bleeding or ulcer and increases in body mass index (BMI). Actual OGC use by patient could not be confirmed and is a limitation of this study.

Results: Mean age of the 785 eligible patients was 76 years (SD 9); 70% were female. Mean Deyo Charlson Comorbidity Index score at base-line was 1.57 (SD 2.01). The most common baseline comorbid conditions were cerebrovascular disease, diabetes, chronic pulmonary disease, and renal disease. Mean daily OGC dose was 28.9 mg during the first 6 months post-index. Mean (SD) CRP and ESR during the 12-month follow-up ranged from 7.5% to 24.5% from OGC daily dose Q1 to Q4 cohorts. The proportion of patients with glucose level, serious infections, cataracts, gastrointestinal bleeding or ulcer ranged from 6.0% in Q1 to 11.8% in Q4. An increase in BMI of 5 ranged from 4.1% to 6.4% from Q1 to Q4.

Conclusion: In patients with GCA, potential OGC-related AEs increased with increased daily OGC dose. This highlights the need for effective therapies that reduce the exposure and potential risk of OGCs.

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Fig.1
SURVEYING PATIENTS WITH TAKAYASU ARTERITIS WITH A DELAYED DIAGNOSIS

Irina Borodina1, Artem Popov2, Yevgeny Bogdanov1, Vitaly Voinov2, 1Ural State Medical University, hospital therapy, Yekaterinburg, Russian Federation; 2ural State Medical University, HOspital therapy, Yekaterinburg, Russian Federation

Background: Takayasu arteritis (TA) is a well known, but rarely identified variety of large vessel vasculitis. Frequency of initial misdiagnosing in TA patients has been reported to reach 80%. Up to 80% of TA cases are correctly diagnosed only 2 to 11 years after the symptoms presentation. Objectives: to study possible reasons for misdiagnosing in TA patients with a delayed diagnosis.

Methods: cross-sectional survey included 30 TA patients. All subjects met ACR criteria for TA and more than 12 months since the onset of the clinical manifestations delayed diagnosis. The subjects were asked to recall if vessels auscultation (VA), measurement of both arms and legs blood pressure (BP), assessment of BP and pulse asymmetry (PA) were performed during their first physician visit following the symptoms onset. Recall if vessels auscultation (VA), measurement of both arms and legs blood pressure (BP), assessment of BP and pulse asymmetry (PA) were performed during their first physician visit following the symptoms onset. Results: 19 (67%) patients reported no VA during the initial examination, only 3 (10%) subjects confirmed the test performed, 5 (17%) were not sure and 3 (10%) did not apply for medical aid during the first year of the symptoms occurrence. Arms BP asymmetry was not assessed in 13 (43%) patients, in 6 (20%) subjects correct BP tests were performed, 8 (27%) responders were not sure and 3 (10%) had not consulted any physician timely. PA was assessed in 7 (23%) cases, PA was not tested in 12 (40%) patients, and 8 (27%) subjects were not sure. Arms and legs BP was not assessed in 26 (87%) patients during their initial examination.

Conclusion: the data obtained confirm paramount importance of proper physical examination during initial physician’s consultation for timely and correct Takayasu arteritis diagnosis.

REFERENCES:

Disclosure of Interests: None declared
HIGH ANGIOPOIETIN-2 LEVELS ASSOCIATE WITH ARTERIAL INFLAMMATION AND LONG-TERM GLUCOCORTICOID REQUIREMENT IN POLYMYALGIA RHEUMATICA

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Background: Polymyalgia rheumatica (PMR) frequently co-occurs with giant cell arteritis (GCA). So far, a simple biomarker for detecting concomitant arteritis or PMR pattern lacking. Furthermore, biomarkers predicting disease course in PMR are awaited.

Objectives: We here investigated the diagnostic and prognostic value of acute-phase markers (ESR, CRP, IL-6, serum amyloid A) and angiogenesis markers, except angiopoietin-1, angiopoietin-2 in isolated PMR and PMR/GCA overlap patients.

Results: We prospectively included 39 treatment-naive PMR patients, of which 10 patients also showed evidence of large vessel GCA on FDG-PET/CT. Anterior healthy controls (N=13) and infection controls (N=32) were included for comparison. Serum marker levels were measured by ELISA or Luminex. ROC and Kaplan Meier analyses were used to assess diagnostic and prognostic accuracy, respectively.

Conclusions: All acute-phase and angiogenesis markers, except angiopoietin-1, were higher in isolated PMR patients compared to HCs. Angiopoietin-2, ESR and soluble Tie-2 were significantly higher in patients with PMR/GCA overlap compared to isolated PMR patients. Angiopoietin-2, but not soluble Tie-2, outperformed ESR and CRP in discriminating patients with and without overlapping GCA (AUC 0.90). Moreover, high angiopoietin-2 levels were associated with long-term glucocorticoid requirement.

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TREATMENT AND EFFICACY OF TOCILIZUMAB IN Giant Cell Arteritis


Disclosure of Interests: Monica Calderón-Góecke: None declared, J. Loricer: None declared, D. Prieto-Peña: None declared, Vicente Aldasoro: None declared, Santos Castañeda: Grant/research support from: NWO; Consultant for: Janssen, Elena Becerra-Fernández: None declared, Marcelino Revenga: None declared, Noelia Alvarez-Rivas: None declared, Carles Galisteo: None declared, Francisca Sivera: None declared, Alejandro Olive: None declared, Maria Alvarez del Buengo: None declared, Luisa Maraño Rojas: None declared, Carlos Fernández-López: None declared, Francisco Navarro: None declared, Enrique Raya: None declared, Eva Galindez: None declared, Beatriz Arca: None declared, Roser Solans-Laquè: None declared, Arantxu Conesa: None declared, Cristina Hidalgo: None declared, Carlos Vázquez: None declared, Jose Andres Romain-Ivorra: None declared, Pau Lluís: None declared, Sara Marnique Arja: None declared, Natalia Palomos-Fontana: None declared, Susana Romero-Yuste: None declared, Javier Navarrete: None declared, Francisco Javier Sentí: None declared, ABBvie, Lilly, MSD, Roche, Pfizer, BioMarin, Inc. Consultant for: UCB, Lilly, Roche, Pfizer, BioMarin, Inc. Research grant from: Pfizer, Lilly, Roche, BioMarin, Inc., speakers bureau: Lilly, Roche, UCB, MSD, Pfizer, BMS, Lilly. Anthony Muñoz: None declared, Carmen Torres-Martín: None declared, Juan Carlos Nieto: None declared, Carmen Ordes-Calvo: None declared, Eva Salgado-Pérez: None declared, Cristina Luna-Góecke: None declared, succesfully approved for: the European Commission

Gomez: None declared, Francisco J. Toyo Sáenz de Miera: None declared, Nagore Fernández-Llano: None declared, Antonio García: None declared, Carmen Larena: None declared, Natalia Palomou-Fontana: None declared, Vanesa Calvo-Rio: None declared, Carmen González-Vela: None declared, J. Luis Hernández: None declared, Alberto García-Manzanares: None declared, Ángel García-Manzanares: None declared, Elena Aurrecoechea: None declared, Raquel Dos-Santos: None declared, Norberto Ortego: None declared, Sabela Fernández: None declared, Francisco Ortiz-Sanjuán: None declared, Montserrat Corteguera: None declared, J. Luis Hernández: None declared, Miguel A González-Gay Grant/research support from: Prof. MA González-Gay received grants/research supports from: Abbvie, MSD, Jansen and Roche., Speakers bureau: Friedman fees/participation in company sponsored speaker’s bureau from Pfizer, Lilly, Sobi, Celgene, Novartis, Roche and Sanofi., Ricardo Blanco Grant/research support from: Abbvie, MSD, Jansen and Roche., Consultant for: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen, Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen.

Disclosure of Interests: Monica Calderón-Goea: None declared. J. Lorica: None declared, D. Prieto-Prada: None declared, Vicente Aldasoro: None declared, Santos Castañeda, Ignacio Villa-Blanco, Alicia Humbría, Clara Moriano, Susana Romero-Yuste, J. Návaz, Catalina García-Gómez-Aragón, Perez-Pampín: None declared, Rafael Moler: None declared, Elena Becerra-Fernández: None declared, Marcelino Revenga: None declared, Noelia Álvarez-Rivas: None declared, Carolina Galisteo: None declared, Francisco Sivera: None declared, Alejandro Olive: None declared, María Álvarez del Buero: None declared, Luisa Marena Rojas: None declared, Rafael Navarro: None declared, Enrique Raya: None declared, Beatriz Arca: None declared, Roser Solano-Laqué: None declared, Arantxa Conesa: None declared, Cristina Hidalgo: None declared, Carlos Vázquez: None declared, Jose Andrés Román-Ivorra: None declared, Pau Luchi: None declared, Sara Mandrique Arija: None declared, Paloma Vela-Casassempere: None declared, Eugenio de Miguel: None declared, Carmen Torres-Martin: None declared, Juan Carlos Nieto: None declared, Carmen Ordas-Calvo: None declared, Eva Salgado-Pérez: None declared, Cristina Luna-Gómez: None declared, toyos Sáenz de Miera, Nagore Fernández-Llano, Antonio García, Carmen Larena, Natalia Palomou-Fontana, Vanesa Calvo-Rio, Carmen González-Vela: None declared, Maria Varela-Garcia, Elena Aurrecoechea, Raquel Dos-Santos, Ángel García-Manzanares, Norberto Ortego, Sabela Fernández, Francisco Ortiz-Sanjuán, Montserrat Corteguera, J. Luis Hernández, Miguel A González-Gay, Ricardo Blanco. Rheumatology, Internal Medicine and Pathology Units, Santander, Navarra, Madrid, Torrelavega, León, Pontevedra, Barcelona, Mondragón, Santiago de Compostela, Vigo, Alicante, Lugo, Badalona, Palencia, Alicante de San Ju A Coruña, Granada, Bilbao, Avilés, Castellón, Salamanca, Zaragoza, Valencia, Menorca, Málaga, Ávila, Gijón, Ourense, Tenerife, Sevilla, Lérida, Spain

Background: In Giant Cell Arteritis (GCA) two dominant cytokine clusters have been linked to disease activity, IL-6 – IL-17 axis (Th17) and IL-12 – IFN-γ axis (Th1). The first one related to systemic symptoms and the second route responsible for ischemic symptoms. Tocilizumab (TCZ) performs its effect mainly by inhibiting Th17 axis and ternary Th1 route. Objectives: Our aim is to evaluate the effect of TCZ on ischemic and systemic symptoms throughout the follow up.

Methods: Retrospective, multicenter study of 134 patients diagnosed of GCA on treatment with TCZ. We evaluate the efficacy of TCZ by improving ischemic (visual involvement, headache, jaw claudication) and systemic symptoms (fever, constitutional syndrome, polymyalgia rheumatica (PMR)).

Results: We evaluated 134 patients (101 w/33 m) and its main symptoms at TCZ onset. TABLE 1. (54.5%) patients presented PMR followed by headache in 70 (52.2%) cases, constitutional syndrome in 31 (23.1%) and visual involvement in 28 (20.5%) patients. After one month of treatment there was an important clinical improvement, persisting in 12.3% of patients PMR, 10.6% headache and 10.6% visual involvement. Throughout the follow-up, the improvement of ischemic symptoms was slower. At month 12, in 5.6% (4) of patients, visual involvement impairment, and 2.8% (2) patients presented headache and constitutional syndrome. However, the analytical improvement was statistically significant from the first month and sustained during follow-up.

Conclusion: According to the results of our study, we can conclude that in clinical practice, ischemic symptoms last longer to improve than systemic symptoms; being visual affectation the most frequent symptom after 12 months of follow-up.

REFERENCES:

Disclosure of Interests: Monica Calderón-Goea: None declared. J. Lorica: None declared, D. Prieto-Prada: None declared, Vicente Aldasoro: None declared, Santos Castañeda Consultant for: Amgen, BMS, Pfizer, Lilly, MSD, Roche, Sanofi, UCB, Ignacio Villa-Blanco: None declared, Alicia Humbría: None declared, Clara Moriano: None declared, Susana Romero-Yuste: None declared, J. Navaz, Alejandro Olive: None declared, María Álvarez del Buero: None declared, Luisa Marena Rojas: None declared, Rafael Navarro: None declared, Enrique Raya: None declared, Beatriz Arca: None declared, Roser Solano-Laqué: None declared, Arantxa Conesa: None declared, Cristina Hidalgo: None declared, Carlos Vázquez: None declared, Jose Andrés Román-Ivorra: None declared, Pau Luchi: None declared, Sara Mandrique Arija Speakers bureau: Abbvie, MSD, Janssen, Lilly, Roche, Pfizer, Novartis, Paloma Vela-Casassempere Grant/research support from: UCB, Abbvie, Pfizer, Roche, Bristol-Myers-Squibb (another research, not BIOBADASER related), Consultant for: UCB, Lilly, Pfizer, Roche, Bristol-Myers-Squibb, Speakers bureau: Roche, UCB, MSD, Pfizer, GSK, BMS, Lilly, Eugenio de Miguel: None declared, Carmen Torres-Martin: None declared, Juan Carlos Nieto: None declared, Carmen Ordas-Calvo: None declared, Eva Salgado-Pérez: None declared, Cristina Luna-Gómez: None declared, Francisco Ortiz-Sanjuán: None declared, Montserrat Corteguera: None declared, J. Luis Hernández: None declared, Miguel A González-Gay Grant/research support from: Prof. MA González-Gay received grants/research supports from: Abbvie, MSD, Jansen and Roche., Speakers bureau: Friedman fees/participation in company sponsored speaker’s bureau from Pfizer, Lilly, Sobi, Celgene, Novartis, Roche and Sanofi., Ricardo Blanco Grant/research support from: Abbvie, MSD, and Roche, Consultant for: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen, Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen.

Background: Eosinophilic granulomatosis with polyangiitis (EGPA), formerly known as Churg-Strauss syndrome, is a small-vessel necrotizing vasculitis associated with eosinophilia and asthma. Glucocorticoids (GCs) usually control the disease, but relapses and GC-dependant asthma are frequent, leading to potential biological therapy use.

Objectives: We examined off-label biological therapy use for relapsing/refractory EGPA.

Methods: Remission was defined as the absence of asthma and vasculitis manifestations with a prednisone dose ≤5 mg/day, and partial response as the absence of manifestations requiring prednisone dose between 6 and 10 mg/day.

Results: One hundred and eighteen patients (66 men, 52 women; median age 50.5 years) were included. Fifty (42%) patients received rituximab (RTX), 38 (32%) methylprednisolone (MEPO), and 30 (26%) benznidazol (OMA).

Previous treatments were: oral GCs (98%), methylprednisolone infusions (51%), azathioprine (68%), cyclophosphamide (47%), methotrexate (30%), mycophenolate mofetil (8%).

At inclusion, median (interquartile range) BVAS in the RTX, OMA and MEPO groups were 8 (4.5-13), 2 (1.5-4) and 2 (2-5), respectively, median (IQR) daily GCs dose were 20 mg/day (15-40), 20 mg/day (10-37.5), 10 mg/day (7.5-20). GC-dependant asthma was found in 39 (78%) of the RTX group, 36 (95%) in the MEPO group and 28 (83%) in the OMA group.

After median follow-up of 22.8 months (IQR 10-47), remissions, partial responses and therapeutic failures, respectively, were noted in 50%, 16% and 34% for RTX recipients, 17%, 38% and 45% for the OMA group and 84%, 3% and 13% for the MEPO group.

Median BVAS dropped to 0 at 6 and 12 months and at last follow-up in all groups. A GC-sparing effect seemed more important with RTX and MEPO. Median GCs dose decreased from the baseline 20 mg/day to 8.5 at 6 months, 7.5 at 12 months and 5 at last follow-up in the RTX group, from 20 mg/day to 12 at 6 months, 10 at 12 months and 10 at last follow-up in the OMA group, and from 10 mg/day at 5 to 6 months, 3 at 12 months and 5 at last follow-up in the MEPO group.

In the MEPO group, no difference was noted between patients receiving 100 mg and those 300 mg monthly. Nineteen (18%) patients stopped RTX because of refractory disease, and 12 (24%) experienced adverse events, including severe infections in 5. Thirteen (43%) stopped OMA because of severe infusion reaction in one and refractory disease in 12, and 4 (13%) patients receiving OMA experienced adverse events. Three (8%) patients stopped MEPO because of adverse events in 2 (one severe infusion reaction and one because of paresthesia), because of pregnancy in one. Seven (18%) additional patients receiving MEPO experienced adverse events, mainly asthenia.

Conclusion: The results suggest that RTX may be effective in 50% of patients with vasculitides relapses related to EGPA, with an acceptable safety profile, while MEPO is highly effective with a good GCs-sparing effect and safety profile in patients with steroid-dependent asthma.

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BAFF AND APRIL GENE EXPRESSION IN PATIENTS WITH ANCA ASSOCIATED VASCULITIS

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Background: Neutrophil activation is the central step in the pathogenesis of ANCA associated vasculitis (AAV). Activated neutrophils are an important source of tumor necrosis factor (TNF) ligands involved in the B cell development and survival, namely, B cell activating factor (BAFF) and a proliferating ligand (APRIL)1. They have been postulated to have a role in the pathogenesis of AAV but presently there is limited data2, 3.

Objectives: To study the expression of BAFF and APRIL genes in patients with AAV and healthy controls and their correlation with disease activity.

Methods: This was a prospective case-control study. Gene expression of BAFF and APRIL was studied in 20 patients of AAV (10 each with AAV and healthy controls and their correlation with disease activity.

Results: Out of 20 AAV patients 16 were GPA and 4 MP. Mean age of patients in active (8 GPA and 2 MP) and remission (8 GPA and 2 MP) group was 34.5 ± 16.1 and 39.9 ± 16.6 years respectively. The sex distribution in both groups was 1:1. Mean BVASv3, ESR and CRP of patients and controls.

There was no significant APRIL gene expression in patients with AAV. Associated with ANCA associated vasculitis (AAV). Activated neutrophils is significantly expressed in patients with AAV.

Figure 1: Box and whisker plot of BAFF expression in active AAV patients, AAV in remission and controls.

Conclusion: BAFF gene is significantly expressed in patients with ANCA associated vasculitits. Among AAV patients there is significantly higher expression of BAFF in patients with active disease than disease activity.

There is no significant APRIL gene expression in patients with AAV.

REFERENCES:
Results: There was no statistically significant correlation between HLA B51 and systemic manifestations or disease activity or Doppler findings nor capillary parameters and morphology. There was statistically significant relation between HLA B51 and ankle brachial index. There was statistically significant difference between patients and controls in EDV, RI of the carotid artery, and arterial, venous lumens of the capil- lary, also the capillary lobe and length with lower values in the patients. There was statistically significant difference between patients and controls in carotid intima media thickness with higher values in patients, inspite of the absence of significant difference in lipid.

Conclusion: HLA B51 didn’t link to different clinical presentation in BD; it is related to peripheral arterial affection only. BD patients had poor arter- ial compliance and increased arterial stiffness, there is precldiual arteri- osclerosis in BD not to related to the level of lipid profile.

REFERENCES:

Disclosure of Interests: None declared

FRIO282 STATINS REDUCE RELAPSE RATE IN TAKAYASU ARTERITIS
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Background: Takayasu arteritis (TAK) is a chronic inflammatory disease, mainly affecting aorta and its major branches. Despite treatment with glu- cocorticoid and adjunctive immunosuppressive agent, relapse is common. Considering the high relapse rate, it is important to identify additional medications that may help sustain remission. Statins, as having anti-inflamatory and immunomodulatory effects, may be one such possibility.

Objectives: To investigate the effect of statins on relapse of Takayasu arteritis (TAK), which frequently occurs after achievement of remission.

Methods: We conducted a retrospective study on TAK patients with active disease, diagnosed between 2012 and 2017. Relapse was defined as recurrence of active disease after achieving remission. Demographic and clinical parameters of patients who experienced relapse were com- pared to those who did not. To identify factors associated with relapse, multivariate Cox regression analysis with stepwise backward elimination was performed. Inverse probability of treatment weighting (IPTW)-adjusted analysis was used to evaluate the influence of statins on relapse.

Table. Multivariate Cox proportional hazard regression analysis estimating risk of relapse

<table>
<thead>
<tr>
<th></th>
<th>Adjusted hazard ratio</th>
<th>95% confidence interval</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.974</td>
<td>0.942–1.009</td>
<td>0.130</td>
</tr>
<tr>
<td>Hypertension</td>
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<td>0.309–1.951</td>
<td>0.590</td>
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<tr>
<td>Carotidhyia</td>
<td>2.348</td>
<td>1.002–5.505</td>
<td>0.056</td>
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<tr>
<td>LDL-cholesterol</td>
<td>1.007</td>
<td>0.986–1.028</td>
<td>0.510</td>
</tr>
<tr>
<td>Statin use</td>
<td>0.260</td>
<td>0.120–0.563</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Abbreviation: LDL; low density lipoprotein

Results: Of the total 74 TAK patients, 40 (54.1%) patients received statins, whereas 34 (45.9%) patients did not. Relapse was observed in 36 (48.6%) patients of the total 74 TAK patients. Compared with patients who did not experience relapse, patients who experienced relapse were younger (44.5±13.5 years vs. 34.1±12.6 years, p=0.001), had lower preva- lence of hypertension (63.2% vs. 38.9%, p=0.037), more commonly had carotidhyia (7.9% vs. 27.8%, p=0.025), had higher LDL-cholesterol (84.8 ±18.8 mg/dl vs. 100.5±26.1 mg/dl, p=0.010), and were less commonly tak- ing statins (71.1% vs 36.1%, p=0.003). These variables were included in multivariate Cox regression analysis. The use of statins was significantly associated with lower risk of relapse (adjusted hazard ratio 0.260, 95% confidence interval 0.120–0.563, p=0.001). Furthermore, IPTW-adjusted analysis confirmed that statin use was associated with a lower risk of relapse (IPTW-adjusted hazard ratio 0.153, 95% confidence interval 0.038–0.616, p=0.008).

Conclusion: In TAK, statins can be beneficial in reducing relapse rate after achieving remission.

Covariates: Age (continuous), hypertension (yes/no), carotidhyia (yes/no), LDL-cholesterol (continuous), and statin use (yes/no)

Disclosure of Interests: None declared

FRIO283 PRESENTATION AND MANAGEMENT OF GIANT CELL ARTERITIS IN A REAL-WORLD SETTING (ARTEMIS STUDY)

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Background: We have little real-world data in France on the natural his- tory and management of patients with GCA.

Objectives: The objective of this retrospective observational study, named ARTEMIS, was to describe the characteristics and management of patients with GCA in real-life settings in France.

Methods: This was a cross-sectional, non-interventional, multicentre, single- centre survey, conducted among hospital-based physicians specialized in internal medicine or rheumatology. Investigators enrolled consecutive patients ≥ 50 years old seen for GCA and currently under treatment. Information on medical practices, such as patient characteristics and diag- nostic journey, diagnostic methods and specific GCA treatments, were collected on an eCRF. GCA activity was assessed on a 100-mm VAS completed by the patients (PIMA) and physicians (PGA). GCA was con- sidered active for VAS scores ≥10 mm. Newly diagnosed GCA was defined as diagnosis (Dg)-to-visit interval -6 weeks. Onset of symptoms- to-Dg interval was classified as “short” (<1 month), “intermediate” (1–3 months) and “long” (>3 months). Descriptive statistics were used for quantitative and qualitative variables.

Results: Over the 3-month inclusion period (August-November 2018), 306 patients were recruited (females: 67.3%, age at Dg: 70 years, 72.5%); 260 (85.0%) and 46 (15.0%) were followed by internists or rheumatolo- gists, respectively. Overall, 39 (12.7%) had newly diagnosed GCA, 267 (87.3%) had a GCA duration ≥ 6 weeks (mean follow-up 24±2.70 months). Original referral of patients to specialized centres was from GPs (55.9%), ophthalmologists (10.1%), neurologists (6.9%), emergency physici- ans (5.6%), internists (4.2%) and rheumatologists (4.9%). Mean time to Dg was 3.3±6.9 months, with an “intermediate” Dg interval for 57.5% of patients. The most common prior medical histories were hypertension (45.8%), psychiatric disorders (10.1%), dyslipidemia (11.8%), diabetes (9.5%) and osteoporosis (5.9%); during follow-up psychiatric disorders, diabetes and osteoporosis were more often reported: 12.1%, 14.7% and 8.5% of patients respectively. Initial GCA presentations included cranial symptoms (89.5% of patients), constitutional symptoms (73.9%), polymyal- gia rheumatica (48.4%), and other extra-cranial manifestations (34.0%). Initial mean ESR and CRP level were 73.0±30.7 mm/hr and 87.3±68.3 mg/l. Temporal artery biopsy, high-resolution temporal artery Doppler ultra- sonography, 18FDG-PET and aortic angio-CT were performed for 84.7%, 31.2%, 26.4% and 29.7% of patients, respectively, and contributed to diagnostic journey, diagnostic methods and specific GCA treatments, were consid- ered active for VAS scores ≥10 mm. Newly diagnosed GCA was defined as diagnosis (Dg)-to-visit interval -6 weeks. Onset of symptoms- to-Dg interval was classified as “short” (<1 month), “intermediate” (1–3 months) and “long” (>3 months). Descriptive statistics were used for quantitative and qualitative variables.

Results: Of the total 74 TAK patients, 40 (54.1%) patients received sta- tins, whereas 34 (45.9%) patients did not. Relapse was observed in 36 (48.6%) patients of the total 74 TAK patients. Compared with patients who did not experience relapse, patients who experienced relapse were younger (44.5±13.5 years vs. 34.1±12.6 years, p=0.001), had lower preva- lence of hypertension (63.2% vs. 38.9%, p=0.037), more commonly had carotidhyia (7.9% vs. 27.8%, p=0.025), had higher LDL-cholesterol (84.8 ±18.8 mg/dl vs. 100.5±26.1 mg/dl, p=0.010), and were less commonly tak- ing statins (71.1% vs 36.1%, p=0.003). These variables were included in multivariate Cox regression analysis. The use of statins was significantly associated with lower risk of relapse (adjusted hazard ratio 0.260, 95% confidence interval 0.120–0.563, p=0.001). Furthermore, IPTW-adjusted analysis confirmed that statin use was associated with a lower risk of relapse (IPTW-adjusted hazard ratio 0.153, 95% confidence interval 0.038–0.616, p=0.008).

Conclusion: In TAK, statins can be beneficial in reducing relapse rate after achieving remission.

Covariates: Age (continuous), hypertension (yes/no), carotidhyia (yes/no), LDL-cholesterol (continuous), and statin use (yes/no)

Disclosure of Interests: None declared
RESULTS OF A SYSTEMATIC LITERATURE REVIEW INFORMING THE 2018 UPDATE OF THE EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF LARGE VESSEL VASCULITIS: EVIDENCE TO GUIDE THE MANAGEMENT OF GIANT CELL ARTERITIS

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Background: The latest EULAR recommendations for the management of large vessel vasculitis (LVV) were published in 2009 (1). Since then, imaging has become a reliable diagnostic tool and new therapeutic options are available for giant cell arteritis (GCA), supporting the need to update the recommendations.

Objectives: To analyse the current evidence for the management (diagnosis/monitoring and treatment) of LVV to inform the 2018 update of the EULAR recommendations.

Methods: A systematic literature review (SLR) dealing with diagnosis/monitoring and treatment strategies for LVV, respectively, was performed. Medline, Embase and Cochrane databases were searched from inception until 31st December 2017. Evidence on imaging was excluded in light of recent published EULAR recommendations (2). We reviewed data relevant to GCA. Level of Evidence (LoE), was assessed in accordance with the 2009 Oxford Centre for Evidence-based Medicine.

Results: We identified 283 papers from the SLR. The implementation of a fast-track approach to diagnosis significantly lowered the risk of permanent visual loss compared to historical cohorts (Level of evidence – LoE 2b). The SLR confirmed the efficacy of prompt initiation of glucocorticoids (GC). There was no high-quality evidence on the most appropriate start-dose, route of administration, tapering and duration of GC (LoE 4). Patients with GCA are at increased risk of dose-dependent GC-related adverse events (LoE 3b). The addition of methotrexate (MTX) (LoE 1a) or tocilizumab (TCZ) (LoE 2b) reduced relapse rates and GC requirements (LoE 1b). There was no consistent evidence that anti-platelet agents given at the time of GCA diagnosis prevented future ischaemic events (LoE 2a).

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FRI0287

EFFICACY OF EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS TREATMENTS ACCORDING TO THE TYPE OF MANIFESTATIONS BASED ON ANALYSIS OF 636 PATIENTS

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Background: Eosinophilic granulomatosis with polyangiitis (EGPA) (Churg-Strauss) is a small-vessel necrotizing vasculitis characterized by blood and tissue eosinophilia and asthma. Glucocorticoids (GCs) represent the treatment cornerstone. So far, EGPA management is based on conventional immunosuppressants, but GC-dependence remains frequent. Recently, therapies targeting B cells and interleukin-5 have been prescribed, but data on large cohorts are lacking.

Objectives: This study aimed to describe therapeutic management and efficacy of treatments in EGPA patients.

Methods: We set up a multicenter European cohort that included 636 EGPA patients. Treatments used, complete remission rates and vasculitis relapse-free survival were recorded. Complete remission was defined as absence of EGPA relapses and prednisone dose ≤5 mg/d at last follow-up. Efficacy to treat GC-dependent asthma/ENT signs was defined as the absence of asthma/ENT symptoms and prednisone dose ≤5 mg/d within the 6 months after initiation.

Results: For induction, cyclophosphamide (CYC) was the most frequently prescribed immunosuppressant (36.2%), more often in patients with FFS (≥1 P<0.001). GCs alone were used in 37.4%, azathioprine (AZA) in 15.6% and methotrexate (MTX) in 6.2%. No difference was found in the 10-years overall survival between patients with FFS<0.05, FFS=1 and FFS≥2.

Complete remission rates were similar between conventional immunosuppressants (CYC, AZA or MTX) and GCs alone. Vasculitis relapse-free survival was also similar between CYC, AZA or MTX and GCs alone. Similar results were observed for first vasculitis relapse treatments. During follow-up, GC-dependent asthma and/or ENT manifestations were treated with AZA (40%), MTX (25%), cyclophosphamide (6%), rituximab (RTX) (21%), CYC (9%), cyclosporine (6%), omalizumab (5%), rituximab (5.5%), allowing GC-tapering (RTX) (21%), CYC (19%), cyclosporine (6%), omalizumab (5.9%), allowing GC-tapering (RTX) (21%), CYC (19%), cyclosporine (6%), omalizumab (5.9%). Conventional immunosuppressants were mostly used in first and second line, while eosinophil-targeted biotherapies were used in 4th or 5th lines.

Conclusion: In EGPA patients, the response to conventional immunosuppressants, in addition to GCs, is often disappointing compared to GCs alone, without clear benefit on complete remission rates and relapse-free survival. In contrast, notwithstanding a small number of treated patients, eosinophil-targeted therapies seemed promising to treat asthma and/or ENT manifestations.

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FRI0288

OPHTHALMOLOGICAL MANIFESTATIONS AND ENDOTHELIN-1 PLASMA LEVELS IN PATIENTS WITH SYSTEMIC NECROTIZING VASCULITIS (SNV)

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Background: Inflammatory eye disease is described in 50% to 60% of patients with ANCA-positive vasculitis and in 10–20% of patients with polyanasthetic nodosa, and for 8% to 16% of patients it is an initial manifestation [1,2]. Endothelin-1 (ET-1) as a potential participant in the local regulation of intraocular pressure, ocular blood vessel tone, and iris smooth muscle tone, suggesting that it may be an important mediator in the development of ocular pathologic conditions [3]. The lower ET-1 plasma levels were found in the optic neuropathy [4].

Objectives: to provide a more complete description of the ocular disease in patients with systemic necrotizing vasculitis (SNV), to evaluate the serum level of ET-1 in patients with SNV with and without eye involvement.

Methods: The study included 36 patients with SNV (polyarthritis nodosa - 8, ANCA - associated vasculitis - 28) and healthy controls (n=26). The 17 patients with SNV had ophthalmological manifestations. Clinical activities of patients were calculated according to the Birmingham Vasculitis Activity Score (BVAS). The serum levels of ET-1 (pmol/L) were determined by immunassay analysis using the kits of Biomedica. The outcomes of this study were the differences in marker levels between SNV patients with and without eye involvement and healthy controls estimated by analysis of the absolute changes in marker levels and the areas under receiver operating characteristic (ROC) curves (AUC).

Results: The ocular manifestation of patient with SNV included episcleritis (n=1), anterior uveitis (n=3), ischaemic optic neuritis (n=3) and exudative retinal vasculitis (n=1). All patients had active disease (BVAS>11). There were no significant differences of BVAS, ESR and CRP between SNV patients with and without eye involvement. In 14% patients with SNV eye involvement was an initial manifestation. The level of ET-1 (M ± σ) in group of SNV patients with eye involvement (n=17) was 0.28 ± 0.13 and did not differ significantly from the control group (0.27 ± 0.10, p>0.05). At the same time, in patients without eye involvement (n=19), it was significantly elevated (0.36 ± 0.34) compared with control group and with group of SNV patients with eye involvement (p = 0.001). ROC analysis showed that the AUC for ET-1 was 0.50±0.10 (p=0.98), which indicates not acceptable capacity for ET-1 differentiate groups of patients with ocular involvement and patients without ocular involvement (sensitivity - 59%, specificity - 57%).
Conclusion: The most common ocular manifestation in patients with SNV was episceritis, which occurred in almost one third of patients. The serum levels of ET-1 were decreased in patients with SNV with eye involvement compared with patients without eye involvement, but this cannot be used for diagnostic purposes.

REFERENCES:

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FRI0289 THE CYCLOPHOSPHAMIDE-SPARING ROLE OF AN INTENSIFIED B-CELLS DEPLETION PROTOCOL IN ANCA-ASSOCIATED VASCULITIS

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BACKGROUND: ANCA-associated vasculitis (AAV) are systemic diseases with relapsing chronic course. The management of AAV requires the use of immunosuppressive drugs whose use is associated with potential toxicity.

OBJECTIVES: This case-control study aims to evaluate the immunosuppressive-sparing effect of rituximab (RTX) used with cyclophosphamide (CYC), compared to a traditional regimen based on high-dose CYC.

METHODS: 26 patients (pts) with AAV with a necrotising extracapillary glomerulonephritis were prospectively enrolled. 13 pts received the intensified protocol of B-lymphocyte depletion therapy (IBCDT) “4+2” with RTX and CYC (4 weekly infusions of RTX followed by 2 monthly followed by prednisone tapered to 5 mg/day in 3 months). 13 pts treated with the high-dose CYC treatment protocol followed by azathioprine as maintenance therapy were enrolled as controls.

RESULTS: In the 13 cases treated with the IBCDT we observed a significant reduction in mean values of parameter of disease activity. After administration of RTX, a significant reduction of the mean s-creatinine values and BVAS was observed. All pts had full B-cell depletion on peripheral blood after the first IBCDT protocol after 1 year. No further maintenance therapy was given. In the cases, a response was observed in 8/13 cases. 4 pts did not respond and a death was observed for cardio-vascular causes. No significant difference was observed in terms of response to therapy between the two groups. The IBCDT allows a significant reduction in the cumulative dose of CYC to which each patient was exposed during follow-up, reaching statistical significance levels (p <0.001). Calculated on a monthly basis, the “4+2” protocol allowed an average reduction in the CYC cumulative dose equivalent to 827 mg/month.

Conclusion: In a selected sample of patients with AAV with renal involvement, the IBCDT regimen appeared to be non inferior in terms of the efficacy when compared to CYC-based standard regimens. Moreover, the IBCDT regimen allowed a net reduction in the cumulative average dose of CYC to which pts are exposed, quantifiable in approximately 1g/month.

Disclosure of Interests: None declared
RENAL TRANSPLANTATION DUE TO RAPIDLY PROGRESSIVE GLOMERULONEPHRITIS (RPGN). COMPARATIVE STUDY WITH NON-AUTOIMMUNE TRANSPLANTATION AND LONG-TERM FOLLOW-UP. STUDY FROM A SINGLE TERTIARY CENTER

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Background: Rapidly Progressive Glomerulonephritis (RPGN) is characterized histologically by the presence of crescents and clinically by a rapid and severe decline in kidney function. Thus, this entity may lead to end stage renal disease, with kidney transplantation. RPGN can be primary, without extra-renal involvement (RPGN-renal-limited), or secondary to systemic autoimmune disorders (RPGN-SAD), infectious diseases or drugs. Kidney transplantation in RPGN-SAD may be associated to a worse outcome.

Objectives: In a series of patients with first transplantation due to RPGN our aim was to assess a) long-term post-transplant survival in RPGN-SAD, b) comparison of post-transplant survival between RPGN-SAD and RPGN-renal-limited and c) comparison of both RPGN (SAD and renal-limited) with a control group of non-immunological disorder, the polycystic kidney disease (PCKD).

Methods: We study three groups of patients: a) RPGN-SAD due to granulomatosis with polyangiitis (n=3), microscopic polyangiitis (n=6) or Goodpasture syndrome (n=2), b) RPGN-renal-limited and c) control group of patients with PCKD. All these patients were transplanted in a single reference University Hospital. The main outcome variables were a) graft and patient survival up to 20 years and b) evolution of renal function (serum creatinine and proteinuria) in the first 5 years of follow-up. Cumulative survival rates after transplantation were estimated by the Kaplan-Meier method and compared between groups using the log-rank test. Kruskal-Wallis test was used to compare quantitative variables and chi2/Fisher’s exact test for qualitative variables.

Results: We included a total of 100 patients with renal transplant: a) RPGN-SAD group (n=11), b) RPGN-renal-limited group (n=32), and c) PCKD group (n=57). No significant differences at baseline were observed between the two RPGN groups regarding sex, age and cardiovascular risk factors. Compared to the PCKD group, patients with RPGN presented higher cholesterol levels at the time of the transplant (p=0.041) with no other significant differences. Renal biopsy had been performed in the 43 patients with RPGN: type I (27.9%), type II (4.7%), type III RPGN (41.9%) and 25.6% of patients had not classified RPGN (no immunofluorescence was performed at the time of the biopsy). From 89 patients (of 100) in which a renal biopsy was performed during the first-year post-transplant, rejection was found in 33 patients (37.1%) without significant differences between the 3 groups (5 cases in the RPGN-SAD group, 11 cases in the RPGN-renal-limited group and 17 cases in the PCKD group; p=0.592). The evolution of serum creatinine and the proteinuria after the transplant is shown in Table 1. There were no significant differences between the three groups in the serum creatinine values during at 1st, 6th, 12th, 36th and 60th months post-transplant. Neither differences were found in terms of graft and patient survival between the 3 groups in 20 years of follow-up (Figures 1 and 2).

Conclusion: Our study shows similar graft and patient survival as well as renal outcome in renal transplant due to RPGN-SAD and RPGN-renal-limited. These outcomes were also similar in non-immune renal disease. Therefore, renal transplantation could be the best option for patients with end stage renal disease due to RPGN regardless of systemic manifestations.

Table 1. Evolution of creatinine and proteinuria levels after renal transplant in RPGN and PCKD.

Table 2.

Figure 1. Patient survival.

Figure 2. Graft survival.

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A MULTI-CENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PARALLEL GROUP STUDY TO EVALUATE THE EFFICACY AND SAFETY OF SIRUKUMAB IN THE TREATMENT OF PATIENTS WITH GIANT CELL ARTERITIS


Statement of the study: To evaluate the efficacy and safety of sirukumab (SIR) in giant-cell arteritis (GCA) and other diseases.

Methods: This 2-part phase 3 study enrolled subjects with active GCA (NCT02531633). Subjects were randomized in a 3:3:2:2:2 ratio to one of 5 treatment arms: SIR 100 mg SC q2w + 6-mo prednisone taper (SIR100+6mo), SIR 100 mg SC q2w + 3-mo prednisone taper (SIR100+3mo), SIR 50 mg SC q4w + 6-mo prednisone taper (SIR50+6mo), placebo (PBO) SC q2w + 6-mo prednisone taper (PBO+6mo), PBO SC q2w + 12-mo prednisone taper (PBO+12mo), for 52-week treatment (Part A). Following completion of Part A, subjects could enroll into the study extension with option for open label SIR treatment (Part B). The primary endpoint was the proportion of subjects in sustained remission at Week 52. Secondary endpoints included sustained remission over time, disease flare, and safety. As a result of the early study termination due to administrative reasons, the revised primary endpoint intent-to-treat analysis (revised ITT, N=55) included only subjects who received at least 1 dose of the SC investigational product and had completed 52 weeks (N=28) or had discontinued the study prior to study termination (n=27).

Results: A total of 161 of planned 204 subjects were randomized (mean age 69.6 years, 77.0% female, 98.1% white, 55.9% with new-onset disease). Baseline prednisone dose was >30 mg/day in 50.9% of subjects. The proportions of subjects with disease flares from Week 2 (N=155) to Week 52 were lower in the SIR100+6mo (18.4%), SIR 100+3mo (28.2%) and SIR50+6mo (30.8%) arms compared to the PBO+6mo (40%) and PBO+12mo (37%) arms.

Conclusion: As a result of early study termination, only a few subjects, all in SIR treatment arms, achieved the primary endpoint of sustained remission at Week 52. The proportion of subjects with flares from Week 2 – 52 were higher in the PBO arms compared to SIR arms. The overall safety was consistent with the known SIR safety profile. Study funded by GSK.


Factors Associated With First-Year and Overall Mortality in ANCA Associated Vasculitis; Patients With Renal Limited Vasculitis Makes No Better Than Microscopic Polyangiitis

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Background: Overall mortality in ANCA-associated vasculitis (AAV) over the last two decades has been reported to be decreasing with the use of immunosuppressive therapies. However, mortality rates remain high and most of the deaths occur in the first year after diagnosis despite treatment.

Objectives: In this study, we aimed to determine the prevalence of mortality in our AAV patients and to investigate the factors that may be associated with first-year and overall mortality.

Methods: Patients followed up in one center with the diagnosis of AAV were included in the study. Diagnostic subgroups were: granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), eosiinophic granulomatosis with polyangiitis (EGPA), and renal-limited vasculitis (RLV). The clinical and demographic characteristics of the patients were collected retrospectively. Factors predictive of mortality were evaluated by Kaplan-Meier method and the Cox proportional hazard model.

Results: In total 104 (45.5%) female and mean age 54.9 ± 15.4 years AAV patients (51 GPA; 25 MPA; 27 RLV and 1 EGPA) were included in the analysis. ANCA positivity was detected in 81 (77.9%) patients with IIF and/or ELISA. ESRD had developed in 31 (32.3%) of AAV patients and in 37.8% of patients with renal involvement. Mortality rate was 14.4% in the first year after diagnosis and 27.9% during a median follow-up period of 1289 (5-5804) days. The age at diagnosis was the only significant predictor of first-year mortality (p=0.001) and the Cox proportional hazard model. Univariate analysis revealed that overall mortality was associated with AAV subgroups (p = 0.035), renal (p = 0.046) and ENT (ear-throat) involvement (p = 0.025). ESRD (p = 0.025) and hemodialysis at the time of diagnosis (p = 0.040). However Cox regression analysis showed age at diagnosis as the only significant predictor also of the overall mortality (P=0.001).

Conclusion: Our findings suggest that there could be some survival differences between AAV subgroups and patients with or without renal and ENT involvement. However, the age at diagnosis seems to be the only significant predictor of first-year and overall mortality in our AAV patients.
Large vessel vasculitis (LVV) and use of granulocyte colony-stimulating factor (G-CSF) and/or chemotherapy by describing our six patient cases and a systematic review of the literature.

Objectives: To evaluate the rare connection of LVV and anticancer therapy by describing our six patient cases and a systematic review of the literature.

LVV and chemotherapy fulfilling our study criteria. Altogether 22 cases were analyzed. Mean age was 59 years (range 40-77 years). In 14/22 patients receiving chemotherapy present similar clinical symptoms with LVV should be kept in mind as differential diagnosis. LVV is a serious condition which may lead to vessel wall damage. Published few case reports and adverse event reports suggest causal association between LVV and use of granulocyte colony-stimulating factor (G-CSF) and/or chemotherapy (1).

Objectives: To evaluate the rare connection of LVV and anticancer therapy by describing our six patient cases and a systematic review of the literature.

Methods: Between 2016-2018 we identified six patients with probable drug induced LVV associated with chemotherapy and G-CSF. All patients had breast cancer. Systematic literature review was performed according to PRISMA guidelines using comprehensive search terms for breast cancer, chemotherapy, LVV and G-CSF.

Results: In our case series, 5/6 patients developed LVV symptoms within two weeks after administration of docetaxel and G-CSF. Vasculitis symptoms disappeared after drug cessation or drug change. Literature search identified 16 published case reports with association of LVV and chemotherapy fulfilling our study criteria. Altogether 22 cases were analyzed. Mean age was 59 years (range 40-77 years). In 14/22 cases data from G-CSF administration was available. Time delay from drug administration to LVV symptoms was average 10 days (range 1-42 days) with G-CSF and median 12 days (range 2-310 days) with chemotherapy. Most prevalent cancer types were breast cancer (8/22), hematological malignancies (7/22) and lung cancer (3/22). Most common clinical LVV symptom were fever (18/22), neck pain (11/22) and chest pain (8/22). Diagnosis was confirmed with imaging studies showing vasculitis in various large vessels in upper body. Notably, four cases had vascular inflammation only in carotid region and this was recognized by radiologist as carotidynia/ transient perivascular inflammation of the carotid artery (TIPIC) syndrome.

Conclusion: Large vessel vasculitis is a possible serious rare adverse event associated with chemotherapy (possibly docetaxel) and G-CSF. Since signs and symptoms are non-specific, we assume this condition is underdiagnosed and should be kept in mind when treating oncological patients. Successful management requires early identification and cessation of the drug. When diagnosed and treated properly, the recovery is usually fast.

REFERENCE:

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Methods: NIS is a publicly available inpatient database that contained data for over 7 million hospital stays, which are a 20% stratified sample of over 4,000 non-federal acute care hospitals across all the regions of the United States of America. The primary outcome was hospitalization costs and charges. The most common reasons for hospitalization were PAN itself (15.3%), sepsis (6.9%), acute kidney injury (4.8%) and acute respiratory failure (2.5%). For the primary outcome, the inpatient prevalence of PAN was found to be 14.9 cases per 100,000 admissions. For secondary outcomes, patients with PAN displayed increased adjusted odds of mortality (OR:1.60, p<0.01), shock (OR:1.81, p<0.01), ICU admission (OR:2.06, p<0.01) and multiorgan failure (OR:3.45, p<0.01) compared to patients without PAN. Patients with PAN also displayed significantly higher hospital costs (additional adjusted mean [aAM]: $10,780, p<0.01), hospitalization charges (aAM: $39,915, p<0.01) and LOS (aAM: 4.2 days, p<0.01) compared to patients without PAN. Patients with PAN displayed a significant association with several comorbidities.

Conclusion: The inpatient prevalence of PAN was higher than what would be expected from the overall prevalence. The mean total hospital costs and total hospitalization charges for patients with PAN were higher than patients without PAN. Analysis of comorbidities found significantly higher odds of several comorbidities even after adjusting for potential confounders.

REFERENCE:

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FRI0296 INPATIENT PREVALENCE, MORTALITY, EXPENDITURES AND COMORBIDITIES OF POLYARTERITIS NODOSA: NATIONWIDE INPATIENT SAMPLE 2014

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Background: Polyarteritis nodosa (PAN) is a systemic necrotizing vasculitis that characteristically affects medium-sized arteries of the intestine, kidneys and soft tissue. Little is known about the inpatient burden, expenditures and association with comorbidities of PAN.

Objectives: To investigate the inpatient prevalence, expenditures and comorbidities of patients with PAN using a national inpatient database. Methods: Patients with PAN were identified from the Nationwide Inpatient Sample (NIS) database of the years 2014 using ICD-9 diagnostic code. NIS is a publicly available inpatient database that contained data of over 7 million hospital stays, which are a 20% stratified sample of over 4,000 non-federal acute care hospitals across all the regions of the United States (US). Data on patient characteristics, comorbidities, resource utilization and expenditures was collected. The primary outcome was determining the inpatient prevalence of PAN in hospitalized patients in the US. Secondary outcomes included determining inpatient mortality, inpatient morbidity (measured by shock, ICU admission and multi-organ failure), comorbidities, hospital length of stay (LOS) and total hospital costs and charges. The most common reasons for hospitalization were utilization of the top principal diagnoses in patients with PAN. A cohort of patients without PAN was also identified from the same database to serve as comparators for analysis of comorbidities. Multivariate regression analysis was used to adjust for age, gender, ethnicity, Charlson Comorbidity Index, income, hospital region, location, size and teaching status.

Results: A total of 5,255 patients with PAN were included in the study. The mean age was 58.8 years, and 57% were female. The top reasons for hospitalization were PAN itself (15.3%), sepsis (6.9%), acute kidney injury (4.8%) and acute respiratory failure (2.5%). For the primary outcome, the inpatient prevalence of PAN was found to be 14.9 cases per 100,000 admissions. For secondary outcomes, patients with PAN displayed increased adjusted odds of mortality (OR:1.60, p<0.01), shock (OR:1.81, p<0.01), ICU admission (OR:2.06, p<0.01) and multiorgan failure (OR:3.45, p<0.01) compared to patients without PAN. Patients with PAN also displayed significantly higher hospital costs (additional adjusted mean [aAM]: $10,780, p<0.01), hospitalization charges (aAM: $39,915, p<0.01) and LOS (aAM: 4.2 days, p<0.01) compared to patients without PAN. Patients with PAN displayed a significant association with several comorbidities (Table 1).

Disclosure of Interests: None declared

FRI0297 CLINICAL FEATURES, TREATMENT MODALITIES AND RELAPSE RATES IN GREEK PATIENTS WITH RETROPERITONEAL FIBROSIS

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Background: Retroperitoneal fibrosis (RPF) is a rare disease of unknown etiology characterized by deposition of fibro-inflammatory tissue around the infra-renal abdominal aorta. The process may involve adjacent structures leading to complications, the most frequent being ureteral obstruction [1]. RPF is mainly idiopathic (IRPF), yet it might be secondary to malignancies, infections, drugs, or radiotherapy [2]. Recent data argue that IRPF could be part of the IgG4-related diseases [3]. Diagnosis is aided by imaging studies (abdomen CT/MRI), but in patients with newly diagnosed RPF, excluding malignancy is mandatory [2].

Objectives: The aim of our study was a) to describe the presenting clinical, laboratory, imaging features and treatment modalities used in patients
with IRPF from four tertiary medical units in Greece and b) to evaluate factors potentially associated with disease relapse. 

Methods: Medical records of patients diagnosed with RPF from 2000-2018 in four rheumatology units (Laiko, Euroclinic, Sismanoglion and Sotira Hospital) were retrospectively evaluated. Sixty-seven patients with IRPF were included in the study. 

Results: The median age at diagnosis was 56 years (IQR:52.0-60.0), with median disease duration 6.0 years (IQR:3.0-11.0), 56% were smokers and 75% males. Patients more often presented with constitutional symptoms (57%), low back pain (63%), raised inflammatory markers (78%), anemia (43%) and compromised renal function (15%). Commonest imaging findings were periarticular-periiliac mass (46%), periarticular mass (33%), periarticular (25%) and hydrophrenic (36%) with envelopment of one (31%) or both ureters (18%). Tissue biopsy was requested in all patients, but was performed in only 10, with 3 having marked numbers of IgG4-positive plasma cells. Serum IgG4 was measured in 36/67 and 36% had elevated levels at diagnosis (median 224 mg/dL, IQR:174-328). Clinical/laboratory/radiological presentation did not differ between patients with elevated and normal serum IgG4 levels. Steroids were first-line treatment in 93% of patients. Other immunosuppressives used as steroid-sparing agents were azathioprine (70%), cyclophosphamide (19%), mycophenolate-mofetil (18%), D-penicillamine (12%) and methotrexate (8%). Relapse occurred in 19% of patients at a median of 36 months (IQR:18-66) after diagnosis with 69% of them being under therapy. Relapse did not correlate to initial imaging findings or to any treatment modality, yet patients with increased serum IgG4 tended to have higher relapse rate (26% vs 11%, p=0.071). 

Conclusion: Diagnosis of IRPF was mostly based on imaging studies in our cohort. Steroids were used as first-line treatment. Relapse occurred in one-in-five of patients independently of initial clinical/radiographic presentation or treatment modality used. RPF patients with initially elevated serum IgG4 levels tended to have a higher relapse rate.

REFERENCES: 

Disclosure of Interests: Aliki Venetasopoulou: None declared, Evangelia Zampeli Speakers bureau: Roshe, AstraZeneca, Sophia Christaki: None declared, Ourania Anypopoulou: None declared, Kyriaki A. Boki: None declared, Merelaos N. Manousakis: None declared, Fotini N. Skopoul: None declared, Vasilis Pavlos G. Themelis: Tzioulas Granatharin research support from: ABBVIE, PFIZER, AMGEN, NOVARTIS, GSK, Haralampos M. Moutsopoulos: None declared


FRID298

ABNORMALITY OF PERCENTAGES AND ABSOLUTE NUMBERS OF CD4+ T SUBSETS IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS AND ITS CORRELATIONS WITH CLINICAL INDICATORS

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Background: ANCA-associated vasculitis (AAV) is a heterogeneous autoimmune disease with unknown etiology [1-2]. During the last decade, a panel of CD4+ T subsets have been identified. However, the exact role and quantitative status of these subsets in AAV patients remains unclear. 

Objectives: We therefore investigated these T cell subsets in AAV patients. 

Methods: AAV patients (n = 54) and healthy controls (HCs) (n = 19) were enrolled. Of them, ten patients initially presenting with active disease were assessed again after remission was achieved. In addition, 38 patients were renal vasculitis. Proportions and absolute numbers of peripheral blood CD4+ T cell subsets and expression of multiplex cytokines were determined by flow cytometry (FCM). Correlations of clinical indicators with the CD4+ T cell subsets were systematically analyzed. 

Results: Percentages of naive T cells (TN) (p<0.001), terminally differentiated effector (TEMRA) T cells (p=0.027) and activated T cells (aTreg) in AAV patients were decreased, but those of effector memory T-cell subpopulation (TEM) (p<0.001), regulatory T cell (Treg) cells and FoxP3lowCD45RA− T cells were increased. Similar results were observed when we compared absolute numbers of the above corresponding cells in AAV patients and HCs, except TEM. Furthermore, the percentage of aTreg (p=0.043) was decreased while that of Th17 cells (p=0.027) was increased in renal vasculitis patients. A significant correlation was observed between the ratio of Th17 to Treg subset and creatinine or BUN, as well as the ratio of Th17/aTreg was significantly increased in active and renal vasculitis patient. In addition, we found that cytokine IL-2 and IL-4 exhibited a downward while IL-6, IL-10, TNF, IFN-γ and IL-17A trend upward in AAV patients. 

Conclusion: There were abnormally quantitative changes in CD4+ T subsets and cytokines in AVV patients, especially the decrease in the relative and absolute number of aTreg (activated Tregs), which indicates an imbalance of pro- and anti-inflammatory T cells. These T subsets might be associated with the ANCA-related autoimmune response and can be used as diagnosis markers for disease activity and as targets for potentially powerful therapy of AAV.

REFERENCES: 

Disclosure of Interests: None declared


FRID299

THE PREVALENCE OF NON-VASCULAR PULMONARY MANIFESTATIONS IN PATIENTS WITH TAKAYASU' ARTERITIS: A RETROSPECTIVE MULTI-CENTERED COHORT STUDY

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Background: Takayasu’ arteritis (TAK) is a rare vasculitis characterized by inflammation and obliteration of intermediate to large-size arteries. Even though more than 50% of patients with TAK have pulmonary artery involvement, non-vascular involvement and symptoms are uncommon. 

Objectives: We aimed to investigate the frequency of non-vascular pulmonary involvement in TAK. 

Methods: We assembled a retrospective cohort of patients with TAK from six different centers in Turkey. The demographics, clinical characteristics, treatment and outcomes of patients were abstracted from medical records, and the computed tomography findings were evaluated for pulmonary manifestations. 

Results: As of January 2019, 197 TAK patients were recruited (mean age: 42.7±13.9 years [min-max: 17-75] to the cohort, and 88.3% of them were female. Twenty-four patients had cough and/or dyspnea and four had hemoptysis as pulmonary symptoms. In CT assessment, parenchymal infiltrations were present in four (2%), pleural effusion in five (2.5%), nodule/cavity in one (0.5%), and pulmonary hemorrhage in one (0.5%). The patient who had pulmonary hemorrhage had also pleural effusion at the same time. In the whole cohort, 11.2% of patients (n=22) had pulmonary hypertension (PAH), three of them had cough and/or dyspnea and four of them had hemoptysis as a pulmonary symptom. Among patients with PAH, any pulmonary involvement in CT was more frequent compared to the rest of the patients (22.7% vs 5.1%, p<0.0001) (Table 1). 

Conclusion: In this first assessment of Turkish TAK cohort, we observed non-vascular pulmonary involvement in about 5% of our patients and half of them were pleural effusions. The second most common manifestation was parenchymal infiltration with a frequency of 2%. Although rare, non-vascular pulmonary manifestations should also be investigated in TAK patients, especially in patients with pulmonary hypertension.

Scleroderma, myositis and related syndromes

FRIO300 IMPACT OF INTERSTITIAL LUNG DISEASE IN SYSTEMIC SCLEROSIS IN A COMPLETE, NATIONWIDE COHORT
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Background: Interstitial lung disease (ILD) represents a clinical challenge in systemic sclerosis (SSc) and associates with high mortality. The presence of severe lung fibrosis is a strong predictor for early mortality. There is substantial progress in SSc-ILD research, but precise, population-based data on cumulative incidence, range of severity and predictive value of clinical risk factors are lacking. Such data are vital for clinical decision making, and highly warranted as background information for appropriate development of screening and management strategies for SSc-ILD.

Objectives: To assess cumulative incidence of ILD, range of ILD severity and mortality risk predicted by baseline pulmonary function tests (PFT) and ILD extent by CT in a complete, nationwide SSc cohort.

Methods: The Norwegian SSc cohort study (Nor-SSc) includes all the 630 incident and 185 prevalent SSc patients from 2000-2012 meeting SSc classification criteria. A baseline PFT was recorded in 703 (86%) patients, and 650 (80%) had high resolution computed tomography (HRCT) images available for analyses. Extent of fibrosis was scored on 10 sections from each HRCT and expressed as percentage of total lung volumes. For the survival and mortality analyses, all Nor-SSc patients diagnosed from 2000-2012 (the 630 incident cases) were included and compared with 15 age- and gender matched controls per patient drawn from the national population registry. Vital status was available for all patients and controls at study end (January 2018). Descriptive statistics and standardized mortality rates (SMR) were estimated.

Results: Of the 815 patients in the total Nor-SSc cohort, 682 (84%) were female and 629 (77%) had limited cutaneous SSc. Mean age at SSc diagnosis was 53 yrs, with mean time from SSc onset to diagnosis of 3.8 yrs. We observed ILD on HRCT in 324/650 patients (50%), and the majority of these had <5% lung fibrosis (Figure 1A). Mean FVC at baseline was 94% of expected value, and nearly half of the patients (42%) had an FVC>100% (Figure 1B). Proportionate distribution of FVC

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GASTROINTESTINAL ADVERSE EVENTS IN PATIENTS WITH SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE (SSC-ILD) TREATED WITH NINTEDANIB: DATA FROM THE SENSCIS TRIAL
Toby Maher1, Kristin Highland2, Martina Gahlemann3, Arata Azuma4, Ayeth Fischer5, Maureen Mayes6, Ganeshe Raghu7, Webke Sauer8, Marnaig Girard1, Margarida Alves9, Emmanuelle Clerisme-Beaty9, Veronika Kohlbrenner11, Masataka Kuwana12, Oliver Distler13, SENSCIS trial investigators, 1National Heart and Lung Institute, Imperial College London, United Kingdom, and National Institute for Health Research Clinical Research Facility, Royal Brompton Hospital, London, United Kingdom; 2Cleveland Clinic, Cleveland, Ohio, United States of America; 3Boehringer Ingelheim (Schweiz) GmbH, Basel, Switzerland; 4Department of Pulmonary Medicine and Oncology, Graduate School of Medicine, Nippon Medical School, Tokyo, Japan; 5University of Colorado School of Medicine, Denver, Colorado, United States of America; 6Division of Rheumatology and Clinical Immunogenetics, University of Texas McGovern Medical School, Houston, Texas, United States of America; 7University of Washington, Seattle, United States of America; 8Boehringer Ingelheim Pharma GmbH and Co. KG, Biberach an der Riss, Germany; 9Boehringer Ingelheim France S.A.S., Reims, France; 10Boehringer Ingelheim International GmbH, Ingelheim am Rhein, Germany; 11Boehringer Ingelheim Pharmaceuticals, Inc., Ridgefield, Connecticut, United States of America; 12Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan; 13Department of Rheumatology, University Hospital Zurich, Zurich, Switzerland

Background: In patients with idiopathic pulmonary fibrosis (IPF), nintedanib has a manageable adverse event (AE) profile characterised predominately by gastrointestinal (GI) events. The efficacy and safety of

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REFERENCES:

Table 1. The frequencies of non-vascular pulmonary manifestations in patients with Takayasu’ arteritis

<table>
<thead>
<tr>
<th>n (%)</th>
<th>All Patients</th>
<th>Patients with PAH</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptoms</td>
<td>24 (12.2)</td>
<td>3 (13.6)</td>
<td>0.049</td>
</tr>
<tr>
<td>Cough/Dyspnea</td>
<td>4 (2)</td>
<td>3 (13.6)</td>
<td>0.000</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary involvement in CT</td>
<td>10 (5.1)</td>
<td>5 (22.7)</td>
<td>0.000</td>
</tr>
<tr>
<td>Pulmonary infiltrates</td>
<td>1 (0.5)</td>
<td>1 (4.5)</td>
<td>0.000</td>
</tr>
<tr>
<td>Nodules/cavities</td>
<td>1 (0.5)</td>
<td>1 (4.5)</td>
<td>0.000</td>
</tr>
<tr>
<td>Pulmonary hernorrhage</td>
<td>5 (2.5)</td>
<td>2 (9.1)</td>
<td>0.000</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(PAH: pulmonary arterial hypertension, CT: computed tomography)
nintedanib versus placebo in patients with SSc-ILD were investigated in the SENSCIS trial. Methods: Patients with SSc-ILD with onset of first non-Raynaud symptom ≤7 years were randomised to receive nintedanib 150 mg bid or placebo double-blind. Dose reductions to 100 mg bid and treatment interruptions were allowed to manage adverse events. AEs reported over 52 weeks of treatment were coded using preferred terms in the Medical Dictionary for Regulatory Activities and analysed descriptively. A questionnaire was used to collect additional information on diarrhoea AEs. Results: A total of 576 patients (288 per group) received ≥1 dose of nintedanib or placebo. Over 52 weeks, 13.9% and 7.3% of patients treated with nintedanib and placebo discontinued study treatment due to AEs. The most frequent AEs in patients treated with nintedanib were diarrhoea (75.7% vs 31.6%), nausea (31.6% vs 13.5%) and vomiting (24.7% vs 10.4%). Serious diarrhoea AEs were reported in 2 patients (0.7%) in each group, and serious vomiting AEs were reported in 2 patients (0.7%) in the placebo group and none in the nintedanib group. Of the 218 nintedanib-treated patients who experienced a diarrhoea AE, most experienced events that were at worst of mild (49.5%) or moderate (44.3%). Most (70.2%) experienced 1 or 2 events, and the duration of diarrhoea AEs was ≤9 days for 50% of the events reported over 52 weeks. Among nintedanib-treated patients who experienced ≥1 diarrhoea AE, 26.1% had a permanent dose reduction and 9.2% discontinued study treatment due to the AE. Among the 91 patients in the placebo group who experienced ≥1 diarrhoea AE, the duration of diarrhoea AEs was ≤3 days for 50% of the events reported over 52 weeks, 2.2% had a permanent dose reduction and 1.1% discontinued study drug due to the AE. Conclusion: In patients with SSc-ILD, the gastrointestinal AEs associated with nintedanib were manageable for most patients and consistent with its known safety and tolerability profile in patients with IPF. Disclosure of Interests: Toby Maher Grant/research support from: Received funds from BI advisory board participation and conference travel. Received research funding and/or consulting fees or other remuneration from GSK, UC, AstraZeneca, Roche, Bayer, Biogen Idec, Cipla, Prometic, and Samumed. Toby Maher has, via his institution, received industry-academic funding from GlaxoSmithKline R&D and UCB. 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Speakers bureau: Kristin Highland is on the speakers bureau for Boehringer Ingelheim, Martina Gahlemann Employee of: Employee of Boehringer Ingelheim, Arata Azuma Consultant for: Arata Azuma has received personal fees from Boehringer Ingelheim, Shionogi & Co., Ltd, Taiho Pharmaceutical Co., Ltd, and AsahiKasei Pharma Co., Areyeh Fischer Grant/research support from: Areyeh Fischer has received a grant from Boehringer Ingelheim (Consultant/steering committee member/principal investigator on clinical trials), Consultant for: Areyeh Fischer has received personal fees from Boehringer Ingelheim (Consultant/steering committee member/principal investigator on clinical trials), Genentech-Roche (Consultant/steering committee member/principal investigator on clinical trials), Pfizer (Consultant) and Genentech (Consultant), Maureen Mayes Grant/research support from: Maureen Mayes is a clinical trial investigator for Boehringer-Ingelheim; Galapagos, Reata, Sanofi, Merck-Serono, Consultant for: Maureen Mayes is a member of scientific advisory boards for Galapagos NV (Pharma), Boehringer-Ingelheim, Mitsubishi-Tanabe, Astellas: Grant Review Board for Actelion., Speakers bureau: Maureen Mayes received personal fees for being a conference speaker on the use of autoantibodies in connective tissue diseases for Medtelligence, Ganesh Raghu Grant/research support from: Ganesh Raghu is the principal investigator for IPF net studies and is a steering committee member for IPF net studies for the NIH. Consultant for: Ganesh Raghu is a consultant for Boehringer Ingelheim, Bellerophon, Biogen, BMS, Fibrogen, Gilead, Nitto, Revistan, Promedior, Sanofi, Veracyte and Roche-Genentech; and a consultant and chair of the DSMB for Avylym., Wiebel Sauter Employee of: Wiebe Sauter is an employee of Boehringer Ingelheim, Marnaga Alves Employee of: Employee of Boehringer Ingelheim, Emmanuelle Clerisme-Beaty Employee of: Emmanuelle Clerisme-Beaty is an employee of Boehringer Ingelheim, Veronika Kohlbrenner Employee of: Veronika Kohlbrenner is an employee of Boehringer Ingelheim, Masataka Kuwana Grant/research support from: Actelion, Consultant for: Chugai, Reata, GlaxoSmithKline, Bayer, Boehringer-Ingelheim, Corpus, CSL-Berling, Mochida, Speakers bureau: Actelion, Pfizer, Bayer, Nippon Shinryaku, Chugai, Oliver Distler Grant/research support from: Prof. Distler received research funding from Actelion, Bayer, Boehringer Ingelheim and Mitsubishi Tanabe to investigate potential treatments of scleroderma and its complications, Consultant for: Prof. Distler has had consultancy relationship with the last 3 years with Actelion, AmNara, Bayer, Boehringer Ingelheim, ChemomAb, espeRafe foundation, Genentech, GSK, Krinesia, Italfarmaco, iQvia, Lilly, medad, Medimmune, Mitsubishi Tanabe Pharma, Pharmaceuticals, Novartis, Pfizer, Sanofi, Sero-daphm and UCB in the area of potential treatments of scleroderma and its complications. In addition, he had consultancy relationship within the last 3 years with A. Menarini, Amgen, Abbvie, GSK, Mepha, MSD, Pfizer and UCB in the field of arthritides and related disorders DOI: 10.1136/annrheumdis-2019-eular.3995

FRI0302 SAFETY AND EFFICACY OF RITUXIMAB BIOSIMILAR IN SYSTEMIC SCLEROSIS: AN ITALIAN MULTICENTER STUDY

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Background: recent data support the use of rituximab(RTX) in Systemic Sclerosis(SSc). RTX biosimilar(RTX-B) offers a more affordable option but its efficacy and safety have not yet been evaluated.

Objectives: To assess the safety and efficacy of RTX-B in SSc.

Methods: Data about SSc patients treated with RTX-B(1gr repeated every 2 weeks) and with a follow-up >6 months were retrospectively collected from 5 Italian centres. Both SSc patients naïve to RTX(RTX-Bn) or already treated with ≥1 course of RTX originator(RTX-O) and switched to RTX-B(RTX-Bs) were considered. A comprehensive assessment of disease features and organ involvement was available at baseline and at final follow-up for all patients. Non parametric tests were used.

Results: Data of 21 SSc patients(20 female, mean age 50.5±11.8 years) were collected/mean disease duration at RTX-B therapy was 7.6±4.8 yrs. Eleven patients(52%) had diffuse cutaneous SSc(dSSc), 12(57%) were anti-topoisomerase-1 antibodies positive, 11 patients(57%) were RTX-B and 9 RTX-Bs(43%). In RTX-B patients, the median number of previous RTX-O courses was 3(range 1 – 8). RTX was decided because of skin progression in 11(52%), intestinal lung disease(LD) worsening in 9(43%), arthritis in 6(29%), myocarditis and myositis in 1 patient each. All patients had been previously treated with immunosuppressants: mycophenolate mofetil(MMF) 14(67%), methotrexate(MTX) 7(33%), cyclophosphamide 6(29%), azathioprine 4(19%), tocilizumab and etanercept 1(5%) patient each. At RTX-B introduction, 14(87%) patients were on concomitant immunosuppressant: 10(48%) MMF and 4(19%) MTX; 15 patients(71%) were also on steroids(mean dose:3.1 ±2.1mg/day). At 6 months after RTX-B treatment, a significant reduction of the modified Rodnan skin score(mRSS), DAS28 and erythrocyte sedimentation rate(ESR) was observed in the entire cohort (p<0.001, p<0.028, p<0.003, respectively); mRSS was significantly reduced also in RTX-Bn (p<0.011) and RTX-Bs patients(p<0.046)(Table 1). No significant changes were observed for lung function tests. Only 1 RTX-Bs patient experienced a transient neutropenia 3 months after the 2nd RTX-B infusion whilst on MTX.

Conclusion: in agreement with previous data published on RTX-O, also RTX-B seem efficient in improving skin and joint involvement and in stabilizing lung function, either in RTX-B and in RTX-Bs SSc patients.

Disclosure of Interests: Corrado Campochiario Consultant for: Dr Corrado Campochiario received consultation honoraria from Pfizer., Giacomo De Luca Consultant for: Dr Giacomo De Luca received consultation honoraria from Pfizer and SOBI., Maria Grazia Lazzeroni: None declared, Silvia Laura Bosello: None declared, Maria De Santis: None declared, adriana caniddi: None declared, Carlo Selmi Grant/research support from: AbbVie, Janssen, MSD, Novartis, Pfizer, Consultant for: AbbVie, Alfa-Sigma, Biogen, Bristol-Myers Squibb, Celgene, Eli-Lilly, Janssen, Merck Sharp and Dohme, Novartis, Pfizer, Roche, Sanofi-Genzyme, UCBB, Speakers bureau: AbbVie, Alfa-Sigma, Biogen, Bristol-Myers Squibb, Celgene, Eli-Lilly, Janssen, Merck Sharp and Dohme, Novartis, Pfizer, Roche, Sanofi-Genzyme, UCBB, Elsa Gremese Consultant for: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Sanofi, UCB, Roche, and Pfizer, Speakers bureau: BMS, Pfizer, Roche, Speakers bureau: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Sanofi, UCB, Roche, and Pfizer, Paolo Airò: None declared, Marco Matucci-Cerinic Grant/research support from: Actelion, MSD, Pfizer, BMS, Chemomab, Sanipedia, Speakers bureau: Actelion, BMS; MSD, Janssen, Lorenzo Dagna Consultant for: Prof Lor- enzo Dagna received consultation honoraria from Abbvie, Amgen, Biogen, Bristol-Myers Squibb, Celltrion, Novartis, Pfizer, Sanofi-Genzyme, and SOBI., Maria Grazia Lazzaroni: None declared, Silvia Laura Bosello: None declared, Maria De Santis: None declared, adriana caniddi: None declared, Carlo Selmi Grant/research support from: AbbVie, Janssen, MSD, Novartis, Pfizer, Consultant for: AbbVie, Alfa-Sigma, Biogen, Bristol-Myers Squibb, Celgene, Eli-Lilly, Janssen, Merck Sharp and Dohme, Novartis, Pfizer, Roche, Sanofi-Genzyme, UCBB, Elsa Gremese Consultant for: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Sanofi, UCB, Roche, and Pfizer, Speakers bureau: BMS, Pfizer, Roche, Speakers bureau: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Sanofi, UCB, Roche, and Pfizer, Paolo Airò: None declared, Marco Matucci-Cerinic Grant/research support from: Actelion, MSD, Pfizer, BMS, Chemomab, Sanipedia, Speakers bureau: Actelion, BMS; MSD, Janssen, Lorenzo Dagna Consultant for: Prof Lor- enzo Dagna received consultation honoraria from Abbvie, Amgen, Biogen, Bristol-Myers Squibb, Celltrion, Novartis, Pfizer, Sanofi-Genzyme, and SOBI., Marco Matucci-Cerinic5, Janet Pope6, Janethe de Oliveria Pena 7, Kaisa Laapas8, RISE-SSc was a Phase IIb, multicenter, randomized, double-blind, placebo-controlled study. Inclusion criteria were: SSC fulfilling ACR/
INTERSTITIAL LUNG DISEASE ASSESSMENT BY ULTRASOUND: RESULTS FROM A DELPHI PROCESS AND WEB-RELIABILITY EXERCISE BY THE OMERACT ULTRASOUND WORKING GROUP (WG)

Andrea Delle Sedie1, Lene Terslev2, George Brugn3, Tomás Cazeniev4, Stavros Chrysidis5, Mario Diaz6, Marco Di Carlo7, Marilena Frigato8, Carlos Pineda9, Francesco Porta10, Viviana Ravagnani11, Carlo Alberto Scirè12, Teodora Serban13, Kate Smith14, Maria-Antonietta D Agostino15, Maria Antonietta D Agostino16, Alain Soare17, Stefanie Weber18, Simon Rauber19, Thomas Wohlfahrt20, Guer Scmitt21, Jörg Distler22, Andreas Ramming23, Friedrich-Alexander-University (FAU) Erlangen-Nürnberg and Universität Ulm, Department of Internal Medicine 3 – Rheumatology and Immunology, Erlangen, Germany

Background: Intersitial lung disease (ILD) evaluation is challenging, given the low sensitivity of X-ray and pulmonary function tests, and limited accessibility and radiation linked to repetitive HRCT. Lung Ultrasound (US) has shown potential in the evaluation of ILD of autoimmune diseases including systemic sclerosis.

Objectives: To define and assess the reliability of definitions of US-detected findings in ILD.

Methods: A taskforce (TF) within the OMERACT US WG performed a literature review (LR) to identify US lesions in ILD, a Delphi exercise to define these lesions and a web-based exercise to test the reliability of these definitions by using either intraclass correlation coefficient (ICC) or kappa statistics. Prior to the Delphi exercise all participants received training files and were subsequently asked to provide clips on BL, PLI and normal findings. Based on the results of the LR, which identified B-lines (BL) and pleural line irregularity (PLI) as main US findings in ILD, the Delphi exercise contained statements on US definitions on BL and PLI. After reaching agreement (> 75%) on the above mentioned items, a set of 80 high-quality clips (30 for PLI, 50 for BL) was selected and distributed to the TF members in order to score them (semiquantitatively, 0-2 for PLI and total number for BL).

Results: The 3 Delphi rounds and the web-based exercise were completed by 24 and 22 sonographers, respectively. Final definitions are reported in Table I. The web-based exercise showed moderate inter-reader reliability for both BL (ICC=0.61) and PLI (Kappa=0.69).

Table I: definitions of PLI and BL

Pleural line irregularity (PLI): a loss of regularity that may be associated with an increase in thickness, focal, diffuse, or nodular

Conclusion: US is a candidate imaging modality to identify and monitor ILD in rheumatic diseases; US consensus based definitions of main US findings were defined and endorsed. Further development is planned for validating US as an outcome measurement instrument for ILD.

Disclosure of Interests: Andrea Delle Sedie Speakers bureau: Abbvie, UCB, Celgene. Lene Terslev: Speakers bureau: Speakers fee from: Roche, Novartis, Pfizer, MSD, BMS, Celgene, George Brugn: None declared. Tomás Cazeniev: None declared, stavros chrysidis: None declared, marilena frigato: None declared, mario diaz: None declared, marlena garrani: None declared, marina garrani: None declared, luca garrani: None declared, marina garrani: None declared, marina garrani: None declared, marin garrani: None declared, luca garrani: None declared, marina garrani: None declared, marin garrani: None declared, marin garrani: None declared, marin garrani: None declared, marina garrani: None declared, marin garrani: None declared, marin garrani: None declared, marin garrani: None declared, marin garrani: None declared, marilena frigato: None declared, carlo alberto scirè: None declared, teodora serban: None declared, kate smith: None declared, maria stoenoiu: None declared, marika tardella: None declared, karina torralba: None declared, richard wakefield: None declared, carlo Alberto scor: None declared, marilena frigato: None declared, carlo Alberto scor: None declared, marilena frigato: None declared, carlo Alberto scor: None declared, marilena frigato: None declared, carlo Alberto scor: None declared, marilena frigato: None declared, carlo Alberto scor: None declared, marilena frigato: None declared, carlo Alberto scor: None declared, marilena frigato: None declared, carlo Alberto scor: None declared, marilena frigato: None declared, carlo Alberto scor: None declared.
OBJECTIVES: We sought to characterize the in vivo effect of lenabasum on inflammatory cells and cytokines thought to be involved in the itch and disease pathogenesis of dermatomyositis (DM).

METHODS: 22 adult patients with refractory, skin-predominant DM on stable standard-of-care treatments were recruited for a double-blind, placebo-controlled, randomized trial. Treatment was initially administered orally at a dose of 20 mg a day for 4 weeks, and subsequently raised to 20 mg twice a day for an additional 8 weeks. In a subset of subjects, lesional skin biopsies were collected at baseline and at Week 12. Tissues were stained via immunohistochemistry for IFN-beta, IFN-gamma, IL-4, IL-13, IL-33, IL-31, IL-31 RA, CB2 receptor, PPAR-gamma, CD4, CD8, CD69, CD11c, and mast cells. RT-PCR for IFN-beta, IFN-gamma, IL-31, IL-4, STAT6, and ST2 was performed on tissue RNA. Protein expression was quantified either by percent area positive or cells per HPF in the dermis. Statistical analyses were performed using the Wilcoxon signed-rank test.

RESULTS: CD4 expression in the skin biopsies from lenabasum-treated subjects significantly decreased at Week 12 compared to the placebo group (p<0.05). There were significant reductions in IFN-beta mRNA and protein, as well as IFN-gamma mRNA and protein at Week 12 in subjects on lenabasum compared to placebo (p<0.05). IL-31 protein (p<0.01) was reduced at Week 12 in subjects who received lenabasum, but IL-31RA protein did not change. CB2 protein decreased significantly in the lenabasum group compared to placebo. There were no changes in IL-4, IL-13, IL-33, and PPAR-gamma protein, or the number of CD8, CD69, CD11c, or mast cells in either group. There was no significant difference in IL-31, IL-4, STAT6, or ST2 mRNA expression.

Conclusion: Lenabasum reduces Type 1 and 2 interferon levels as well as T-helper cell inflammation in subjects with DM. These effects have the potential to inhibit underlying disease pathways in DM, thus contributing to clinical improvement.

REFERENCES:
Objectives: This study aimed to analyze the serum levels of neopterin in patients with dermatomyositis (DM) in association with clinical manifestations, laboratory data and patient prognosis.

Methods: One hundred and eighty-two consecutive DM patients and 30 healthy controls were retrospectively enrolled in the study. Serum levels of neopterin were detected by using the ELISA method. Clinical and laboratory data and patient prognosis were obtained and analyzed in association with serum neopterin.

Results: Serum levels of neopterin were significantly increased in DM patients (median 21.2 nmol/L; IQR 13.9-35.2 nmol/L) compared to healthy controls (median 4.3 nmol/L; IQR 2.9-5.6 nmol/L, P < 0.01). High serum neopterin levels were associated with anti-MDA5 antibody, rapidly progressive interstitial lung disease (RP-ILD), and cutaneous involvement including skin ulcer and heliotrope rash. Longitudinal assessment of serum samples revealed that the serum neopterin levels were closely correlated with disease severity. In addition, a significant increase in serum neopterin concentration of non-survivors (median 38.7 nmol/L; IQR 23.5-65.3 nmol/L) was observed when compared to that of survivors (median 19.0 nmol/L, IQR 12.5-28.0 nmol/L) (P < 0.001). ROC curves showed that serum neopterin could distinguish non-survivors and survivors at an optimal cut-off level of 22.1 nmol/L with a sensitivity and specificity of 0.804 and 0.625 respectively (P = 0.01). Kaplan-Meier survival curves revealed that DM patients with serum neopterin > 22.1 nmol/L had a significantly higher mortality compared to patient group with serum neopterin < 22.1 nmol/L (logrank P = 0.01). Multivariate Cox regression analysis identified high serum neopterin concentration to be an independent risk factor for poor prognosis in DM (adjusted HR = 4.619, 95% CI: 2.092-10.195, P < 0.01).

Conclusion: Increased serum levels of neopterin were significantly associated with RP-ILD and reduced survival in DM patients, suggesting it as a promising biomarker in the disease evaluation of DM. These findings highlight the role of cellular immune activation and macrophage activity in the pathogenesis of DM.

REFERENCE:

Disclosure of Interests: None declared
PREVALENCE AND CLINICAL MANIFESTATIONS OF ERASMUS SYNDROME IN SYSTEMIC SCLEROSIS: A CROSS-SECTIONAL STUDY

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Background: Erasmus syndrome (ErS) is defined by the association of exposure to silica with the subsequent development of systemic sclerosis (SSc), with or without associated silicosis.

Objectives: The objectives of this study were, on one hand, to evaluate the prevalence of ErS in a population of SSc patients and to characterize the cases and, on the other hand, to evaluate the clinical and laboratory characteristics of SSc patients with or without exposure to silica.

Methods: We performed a cross-sectional study of the patients with SSc in our department. Demographics, clinical and laboratory data were collected from all patients with SSc diagnosed according to ACR/EULAR criteria. Moreover, a telephone call was made in order to detail the professional activity and possible exposure to silica.

Results: The prevalence of ErS in this population was 15.3% (9/59). All cases identified were male, corresponding to 75% of men with SSc followed at our department. There was a statistically significant association between ErS and male gender (p<0.001), initial pulmonary manifestation (p=0.025), history of digital ulcers (p=0.014) and smoking (p=0.047). On the other hand, a lower risk of gastrointestinal involvement was found in ErS cases (p=0.008). All patients with ErS had positive autoantibodies (mainly anti-Sc170 and anti-centromere) with titers tending to be higher than SSc without ErS, although without statistically significant differences. In addition, although with no statistical significance, we found that pulmonary artery systolic pressure (PASP) estimated by echocardiogram was higher in patients with ErS.

Conclusion: In our study, prevalence of ErS was higher than data from previously published literature. For a more accurate ErS diagnosis it is necessary to be aware of and investigate less intense silica exposures, which may have occurred many years before diagnosis. Statistically significant differences were found between ErS and SSc without exposure to silica; this fact may have impact in diagnosis, treatment and prognosis.

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Disclosure of Interests: None declared

Conclusion: a significant improvement in endothelial function and microvascular involvement was achieved after three months of HCQ treatment.

It is a novel finding in SSC which can represent a new therapeutic possibility for the prevention of microvascular complications of the disease.

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Disclosure of Interests: Fabio Basta: None declared, Rosaria Irace: None declared, Alessia Borgia: None declared, Valentina Messinini: None declared, Antonella Riccardi: None declared, Gabriele Valentini Grant/research support from: MSD, Pfizer, Consultant for: MSD, Pfizer, Biogen, Speakers bureau: MSD, amgen, biogen, illy, sanofi, Pfizer, Anna, Antoinella Afeltra Grant/research support from: MSD, Pfizer, ABBVIE, ROCHE, UCB, Speakers bureau: MSD, Pfizer, BMS, ROCHE, SANOFI DOI: 10.1136/annrheumdis-2019-eular.850

FR00315 DIFFERENTIAL PERFORMANCE OF NAILFOLD VIDEO CAPILLAROSCOPIC PARAMETERS IN THE DIAGNOSIS AND PROGNOSIS OF SYSTEMIC SCLEROSIS
Vasilli-Kalliopi Bounia 1, Konstantinos Kottas 1, Stylianos Panopoulos 1, George Konstantinos 1, Alexios Ilipoulos 1, Athanasios Tzoufas 1, Petros Silkakis 1, Panayiotis Vlachoyiannopoulos 1, National and Kapodistrian University of Athens, Medical School, First Department of Pneumopaealic and Internal Medicine, Athens, Greece; 2Veterans Administration Hospital (NIMTS), Department of Rheumatology, Athens, Greece; 3National and Kapodistrian University of Athens, Medical School, Pathophysiology, Athens, Greece

Background: The role of Nailfold Video Capillaroscopy (NVC) in the identification of patients with Raynaud phenomenon (RP) at risk to develop systemic sclerosis (SSc) is well-established. However, it is not clear if certain capillaroscopic indices perform better than others at predicting SSc development and which NVC parameters have a prognostic value in established SSc.

Objectives: To comparatively assess the performance of different NVC parameters in predicting development of SSc, very early diagnosis of SSc (VEDOSS), or mixed connective tissue disease (MCTD) in patients with RP. Also, to longitudinally examine the consistency of clinical correlations of NVC parameters in SSc patients at two different time points and evaluate the prognostic capacity of NVC in SSc.

Methods: Consecutive RP patients referred to our department for NVC (138 with SSc, 12 with VEDOSS, 6 with MCTD, 36 with primary RP, and 50 with non-SSc secondary RP) were evaluated at baseline, both clinically and capillaroscopically. 175 were reevaluated after a mean±SD of 3.34±1.48 years. Sixty-two healthy volunteers served as controls. Qualitative assessment of NVC images permitted categorization of patients to a normal, early, active or late capillaroscopic pattern. Capillary loss, dilatation score, giant or ramified capillaries and micro-hemorrhages were evaluated by a semi-quantitative score (0-3), derived as the mean of three evaluated fields of each of the 2nd, 3rd, 4th and 5th finger of both hands. FVC and DILCO were recorded, if performed within 6 months of NVC. FVC and DILCO deterioration were considered clinically significant if >10% and >15%, respectively. Skin thickening was measured using the modified Rodnan Skin Score (mRSS). MRSS deterioration was considered clinically significant if >3.5. First occurrence of digital ulcers in patients with no prior such history and vital status were also recorded at follow-up.

Results: Capillary loss score had the highest diagnostic accuracy at discriminating patients with an SSC-spectrum disorder from patients with RP of different etiology and from controls, as defined by ROC curve analysis [AUC (95% CI)=0.925 (0.893-0.956)], followed by dilatation score [AUC (95% CI)=0.904 (0.807-0.938)] and giant score [AUC (95% CI)=0.856 (0.810-0.902)]. By contrast, micro-hemorrhages [AUC (95% CI)=0.727 (0.669-0.786)] and ramification scores [AUC (95% CI)=0.588 (0.521-0.654)] did not perform equally well. Notably, clinical correlations of capillaroscopic parameters in SSc were found not to be consistent over time, when longitudinally assessed at two different time points by univariate and multivariate analysis. Binary logistic regression analysis indicated that baseline capillaroscopic pattern could predict occurrence of a combined adverse disease outcome (FVC deterioration>10% and/or DILCO deterioration>15% and/or mRSS deterioration>3.5 and/or first occurrence of digital ulcers and/or death), after a mean±SD follow-up of 3.28±1.45 years in 94 SSc patients with available follow-up data (OR=3.43, p=0.031 for active versus early pattern, OR=8.778, p=0.007 for late versus early pattern).

Conclusion: Dilatation score performs best of all semi-quantitative NVC parameters in diagnosing SSc and although clinical correlations of capillaroscopic findings change over time, an active or late capillaroscopy pattern at baseline is associated with an adverse prognosis.

Disclosure of Interests: Vasilli-Kalliopi Bounia: None declared, Konstantinos Kottas: None declared, Stylianos Panopoulos: None declared, George Konstantinos: None declared, Alexios Ilipoulos: None declared, Athanasios Tzoufas Grant/research support from: ABBVIE, Pfizer, Amgen, Novartis, GSK, Petros Silkakis: None declared, PANAYIOTIS VLAPOULOPOULOS: None declared DOI: 10.1136/annrheumdis-2019-eular.4393

FR00314 SENSITIVITY TO CHANGE AND RESPONSIVENESS TO TREATMENT OF RENAL RESISTIVE INDEX (RRI) IN SYSTEMIC SCLEROSIS (SSC)
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1Careggi University Hospital, Firenze, Italy; 2Sapienza University of Rome, Roma, Italy

Background: RRI may identify any problem with the blood flow in the renal artery and in the parenchyma. It was shown to be increased in SSc patients and being in relationship with both vascular and fibrotic SSc-related manifestations.

Objectives: to test sensitivity to change and responsiveness to treatment of RRI in SSc.

Methods: patients fulfilling the 2013 ACR/EULAR classification criteria for SSc were enrolled from two SSc-care units, if RRI was determined at least twice since being diagnosed. Data regarding SSC clinical manifestations, instrumental and laboratory evaluation for renal, cardiac and cardiovascular involvement, as well as ongoing immunosuppressive and vasoactive vasodilating treatment, were collected both at baseline and follow-up RRI measurements.

Results: 230 patients [aged 57 (48-67) years, 12.6% males] were enrolled in the study, with baseline RRI value of 0.68 (IQR 0.07). In a mean 3.4 years follow-up, RRI showed a median change (ΔRRI) of 0.02 (IQR 0.05). ΔRRI was significantly correlated with ΔsPAP (R=0.173, p=0.023) and it was significantly higher in patient with new onset of pulmonary arterial hypertension (0.06±0.02 vs 0.03±0.05; p=0.038). On Cox univariate regression analysis, time from disease onset, ΔsPAP and ΔRRI predicted new PAH, while ΔsPAP was the only independent predictor at multivariate regression analysis. Regarding treatment, Sildenafil exposure determined a significantly lower increase in ΔRRI, with a progressive long-term effect. Conversely, CCBs and ifoprost treated patients showed a significantly higher increase of ΔRRI, which was determined by a higher DU burden. No difference was seen when immunosuppressive treatment was evaluated.

Conclusion: RRI is sensitive to change and reflects, in particular, the worsening of cardio-pulmonary vascular involvement (increase in ΔsPAP and new PAH onset). Moreover, it shows a possible protective effect of Sildenafil in reducing pulmonary vasculature manifestations.

Disclosure of Interests: Cosimo Brunì: None declared, Edoardo Rosato: None declared, Antonietta Gigante: None declared, Vanessa Maestri2,1: None declared, Giulia Tesi2,1: None declared, Marco Chiostri2,1: None declared, Gemma Lepri2,1: None declared, Silvia Bellando Randone2,1: None declared, Serena Guiducci1: None declared, Sergio Castellani1: None declared, Maria Boddi1: None declared, Marco Malucci-Cerinici2,1: Grant/research support from: Actelion, MSD, Pfizer, BMS, Chemomab, Sanipeedia, Speakers bureau: Actelion, BMS, MSD, Janssen DOI: 10.1136/annrheumdis-2019-eular.3515
Background: Systemic sclerosis (SSc) is a disease orphan of effective disease modifying agents. The diffuse cutaneous subset (dcSSc) is targeted in most clinical trials. Nevertheless, the high variability in clinical outcome at 12 months is limiting effective RCTs design and interpretation. The Global Ranked Composite Score (GRCS) and the Composite Response Index in SSc (CRISS) are the most recent attempts to capture overall response to treatment in dcSSc [1, 2]. Activation of interferon type 1 (IFN) pathway is associated with severe clinical manifestations in SSc. Several studies have indicated that the serum concentration of CCL2, CCL8, CCL19, CXCL9, CXCL10 and CXCL11 are the most relevant to measure IFN induction of PBMCs [3-4].

Objectives: Here we aimed to determine whether the IFN pathway activation measured by a serum test could be used to stratify patients with dcSSc for severe clinical outcome at 12 months as measured by GRCS and CRISS.

Methods: Serum concentration of CCL2, CCL8, CCL19, CXCL9, CXCL10, and CXCL11 was measured by Luminex xMAP technology (Myriad RBM) in 143 SSc patients and 35 healthy controls (HC). IFN score was calculated as the average of the natural logarithm of the above chemokines. IFN score was measured by Luminex xMAP technology (Myriad RBM) in 143 SSc patients and 35 healthy controls (HC). IFN score was calculated as the average of the natural logarithm of the above chemokines. IFN score was measured by Luminex xMAP technology (Myriad RBM) in 143 SSc patients and 35 healthy controls (HC). IFN score was calculated as the average of the natural logarithm of the above chemokines. IFN score was measured by Luminex xMAP technology (Myriad RBM) in 143 SSc patients and 35 healthy controls (HC). IFN score was calculated as the average of the natural logarithm of the above chemokines. IFN score was measured by Luminex xMAP technology (Myriad RBM) in 143 SSc patients and 35 healthy controls (HC).

Results: All chemokines had a higher serum concentration in SSc vs HC (p<0.0001 for all). Median IFN score was higher in SSc than HC (5.26 vs 4.70, p<0.0001). There was no difference associated with disease duration or enrollment criteria in a RCT we analyzed the 12 months outcomes of the dcSSc patients with c6 years disease duration. Sixty-six 12-month outcome data were available. 37 were IFN HI and 29 IFN LO at baseline. The IFN HI group had a higher mRSS (median 9.5 vs 5, p=0.03), CRP (10.2 vs 5, p=0.003) and NT-proBNP (195 vs 50.5, p=0.001). We recorded 7 deaths for SSc and 5 lung failures (3 PVC drop, 2 DLCO drop); 3 had worsening of PVC, 4 improvement and 49 no change; 11 had worsening of HAQ-DI, 5 improvement and 43 no change; 9 had worsening of mRSS, 7 improvement and 43 no change (table 1). CRISS ranged from -59 to 64 and was negative in 29 (21 IFN HI, 8 IFN LO) and positive in 37 (16 IFN HI, 21 IFN LO). IFN HI patients had a worse outcome at 12 months with GRCS median score of -12 vs 15 in IFN LO (p=0.0271) (fig. 1). According, GRCS favored IFN LO in 68.4% of 1073 (37%29) pairwise comparisons versus 31.6% of IFN HI (p=0.0001). CRISS was 0 in 46 (38 IFN HI, 18 IFN LO) and <0 in 20 (9 IFN HI, 11 IFN LO). Spearman’s rank correlation of the two scores was r=0.5113. Consistent with GRCS data, CRISS was 0 in 76% of IFN HI vs 62% of IFN LO (P=0.046).

Conclusion: Serum IFN Score predicts worse clinical outcome at 12 months in dcSSc. Stratification for IFN score could aid both in clinical trial design and clinical management. Moreover, we here show that GRCS and CRISS may be sufficiently sensitive to measure difference in composite outcome at 12 months in dcSSc in an observational setting and they correlate with each other in this observational setting.

REFERENCES:

Christopher J. MRI

Tab 1

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Improvement 2 2 1 4 3 4
PBC or other autoimmune liver disease or manifested elevated liver function tests.

Conclusion: The expression of the PDC antigenic components is variable both in SSc patients with AMA positive PBC and in SSc patients AMA positive without PBC or altered liver function tests, but we could not identify a clinical significance of this variability. It may be necessary to maintain a strict follow-up of these patients and to perform longitudinal studies to determine the diagnostic value of this variable expression of PDC components in the onset of PBC.

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Disclosure of Interests: Angela Cenbelli: None declared, Natala Isaliovic: None declared, Carolina Gorlino: None declared, Elena Generali: None declared, Maria De Santis: None declared, Giacomo Maria Guidelli: None declared, Marta Caprioli: None declared, Piercarlo Sarzi-Puttini: None declared, Minoru Satoh: None declared, Carlo Selmi Grant/research support from: AbbVie, Janssen, MSD, Pfizer, Consultant for: AbbVie, Alfa-Sigma, Biogen, Bristol-Myers Squibb, Celgene, Eli-Lilly, Janssen, Merck Sharp and Dohme, Novartis, Pfizer, Roche, Sanofi-Gerzyme, UCB, Speakers bureau: AbbVie, Alfa-Sigma, Biogen, Bristol-Myers Squibb, Celgene, Eli-Lilly, Janssen, Merck Sharp and Dohme, Novartis, Pfizer, Roche, Sanofi-Gerzyme, UCB


FRI0317

NOVEL CLASSIFICATION OF IDIOPATHIC INFLAMMATORY MYOPATHIES BASED ON DISTINCTIVE FEATURES AND AUTOANTIBODIES: ANALYSIS OF 67 KOREAN PATIENTS

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Background: Since Bohan and Peter first described their diagnostic criteria for idiopathic inflammatory myopathies (IIM) in 1975, new discoveries such as myositis-specific and myositis-associated autoantibodies (Abs) have been made.

Objectives: To investigate correlations between specific myositis Abs and their frequencies and clinical associations across different IIM groups, collectively demonstrating the utility of the new clinicoserologic classification in Koreanadult IIM patients with IIM.

Methods: We conducted a multicenter cohort study including 67adult patients (age ≥18 years) who have been diagnosed as IIM by ENMC criteria. Immunoblot assay with Euroline strip(EUROIMMUN, Germany) was performed using the sera of definite dermatomyositis (DM, n=36), definite polymyositis (PM, n=25), amyopathic DM (n=4), DM sine dermatitis (n=1), and immune mediated necrotizing myopathy (IMNM, n=1). Patients were classifiedbased on three classifications: 1) novel clinicoserologic classification suggested by Troyanov et al. in 2017. 2) 2017 EULAR/ACR classification criteria. 3) 2004 European neuromuscular center (ENMC) criteria. Associations of myositis Abs and clinical subsets of IIM were investigated.

Results: The distribution of the various IIM differed strikingly from those using the 3 classifications (Fig1). According to the 2004 ENMC classification and 2017 EULAR/ACR classification criteria, DM and PM was the most and the second frequent entities (DM: 55.2%, 56.7%; PM: 35.6%, 37.8%). But, using the new clinicoserologic classification, the overlap myositis (OM) is the major type of IIM and the frequency of PM is significantly decreased. Anti-ARS Abs specificity included anti-Jo-1(16.4%), -OJ(4.6%), -EJ(6.2%) -PL-7(3.1%), and -PL-12(4.8%). Interstitial lung disease was closely associated with anti-MDA5 and anti-ARS Abs, while DM-specific skin lesion was frequently observed in patients with anti-TIF1y and anti-ARS Abs. Seven patients with cancer-associated DM were identified. They were positive for anti-TIF1y (5/7) and anti-SRP(3/7) (table 1).

Disclosure of Interests: None declared


FRI0318

THROMBOCYTOPENIA AND MULTI-ORGAN INVOLVEMENT MIGHT BE POOR PROGNOSTIC FACTORS FOR SYSTEMIC SCLEROSIS CARDIOMYOPATHY

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Background: Systemic Sclerosis (SSc)-cardiomyopathy is associated with a high mortality in SSc. It is important to identify potential prognostic factors for SSc-cardiomyopathy.

Objectives: To describe the clinical characteristics and identify potential prognostic factors for patients with SSc-cardiomyopathy.

Methods: We retrospectively reviewed the clinical data of SSc-cardiomyopathy patients hospitalized at Sun Yat-Sen Memorial Hospital from January 1992 to November 2018. SSc-cardiomyopathy was defined as structurally and functionally abnormal of heart muscle in SSc patients with cardiac symptoms. Coronary artery disease, hypertension, valvular disease and congenital heart disease were excluded. The Chi-square test was used to compare the differences between the death group and the survival group.

Results: 1. There were 903 SSc patients recruited and 20 patients (2.2%) of them were SSc–cardiomyopathy. Among these 20 patients, 65% were females, with an age of 52.8±13.2 years, disease duration was 3.1±2.3 years, duration from SSc onset to cardiomyopathy occurred was 2.8±2.3 years. 2. SSc-cardiomyopathy developed in 18 patients (9%) with diffuse cutaneous SSc (dcSSc), and in 2 patients (10%) with limited cutaneous SSc (lcSSc). Eleven patients (55%) had pulmonary fibrosis, 7 patients (35%) had pulmonary arterial hypertension (PAH), 5 patients (25%) had scleroderma renal crisis (SRC) and esophageal involvement, respectively.

Conclusion: Novel classification based on distinctive features and new myositis Abs reflects the clinical phenotype of IIM better. Establishment of a system routinely available to screen myositis Abs is needed. This will be beneficial to provide more precise diagnosis and proper management for patients with IIM.

REFERENCE:
patients (30%) manifested thrombocytopenia and 4 patients (20%) manifested anemia.

3. Cardiac symptoms included shortness of breath (n=18), palpitation (n=6), edema of lower extremity (n=4), fatigue (n=5) and/or cough (n=3). All patients were found to have cardiomegaly by echocardiography (UCG) or chest radiography. Left ventricular ejection fraction (47±15%) were decreased. Ventricular wall motion abnormality was found in 5 patients (25%) by UCG. 15 patients (75%) manifested cardiac arrhythmia in electrocardiogram, with frequent premature ventricular contractions were the most common (n=10, 50%). Myocardial injury was found in 14 patients (70%) by electrocardiogram. Myocarditis was found in 7 patients (35%) by myocardial enzyme assay.

4. Nine patients (45%) died, the causes of death were heart failure (n=4, 45%), sudden death (n=3, 33%) and ventricular tachycardia (n=2, 22%). 5 patients (55.6%) died within 1 month after the onset of cardiac symptoms. 3 patients died within 2 month, and one patient with implantable cardioverter defibrillation (ICD) died 2 years after ICD implanted. Ten patients survived in a mean 6 (1-10) years follow-up.

5. Six patients (67%) manifested thrombocytopenia and 4 patients (44%) manifested anemia in the death group. However, only one patient (9.1%) in survival group manifested thrombocytopenia (p=0.007) and anemia (p=0.059).

There were more organs and systems involved in the death group, compared to the survival group (4±2 vs 2±1, p=0.044). 4 patients had SRC in death group, while 2 patients had SRC in survival group. 6 patients had pulmonary fibrosis in death group, while 5 patients in survival group (Table 1).

Table 1. Comparison between the death group and the survival group in Systemic Sclerosis cardiomyopathy patients.

<table>
<thead>
<tr>
<th>Death group (n=9)</th>
<th>Survival group (n=11)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombocytopenia, n (%)</td>
<td>6(66.7)</td>
<td>1(9.1)</td>
</tr>
<tr>
<td>Anemia, n (%)</td>
<td>4(44.4)</td>
<td>1(9.1)</td>
</tr>
<tr>
<td>Pulmonary fibrosis, n (%)</td>
<td>6(66.7)</td>
<td>5(45.5)</td>
</tr>
<tr>
<td>Pulmonary arterial hypertension, n (%)</td>
<td>3(33.3)</td>
<td>4(36.4)</td>
</tr>
<tr>
<td>Scleroderma renal crisis, n (%)</td>
<td>4(44.4)</td>
<td>2(18.2)</td>
</tr>
<tr>
<td>Esophageal involvement, n (%)</td>
<td>3(33.3)</td>
<td>2(18.2)</td>
</tr>
<tr>
<td>Anti-SCl 70 positive, n (%)</td>
<td>5(55.6)</td>
<td>5(50)</td>
</tr>
<tr>
<td>Myocarditis, n (%)</td>
<td>4(44.4)</td>
<td>3(27.3)</td>
</tr>
<tr>
<td>Numbers of organ involved, mean (SD)</td>
<td>4(2)</td>
<td>2(1)</td>
</tr>
</tbody>
</table>

Conclusion: Thrombocytopenia and multi-organ involvement might be poor prognostic factors for patients of SSC-cardiomyopathy.

Disclosure of Interests: None declared


ESOPHAGEAL EROSIONS PREDICT PROGRESSION OF LUNG DISEASE IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Intestinal lung disease (ILD) is the leading cause of death in Systemic Sclerosis (SSc) but its pathogenesis is not fully understood. Esophageal disease is common in SSc and micro aspiration of both acid and non-acid gastrointestinal reflux could be involved in the pathogenesis of ILD. Esophagogastrroduodenoscopy (EGD) is an essential tool to evaluate disease severity of upper gastrointestinal tract involvement in SSc.

Objectives: The objective of the present study is to assess the role of EGD in predicting pulmonary functional deterioration in SSc patients.

Methods: One hundred and fifty patients with SSc and suspected esophageal involvement underwent EGD. Pulmonary function tests were performed at baseline and after a 36-months follow-up. Patients were characterized for disease phenotype, BMI, smoking exposure and medical history. A significant ILD progression was defined as a relative decline >10% of FVC or a concomitant decline >5% of FVC and >15% of DLCO.

Results: One hundred and thirty-six patients (90.5%) were female with a mean age of 55.6 ± 13.8 years and 12.1% were active smokers. Fifty

patients (33.3%) had a diffuse cutaneous disease; 37.4% and 40.8% were positive for anti-centromere and anti-Scl70 antibodies respectively. The mean disease duration from the first non-Raynaud symptom was 5.9 ± 6.7 years. Sixty-one patients (40.8%) showed EGD signs of reflux esophagitis. Among them, 31.3% had an erosive form (19.5% grade A, 15.6% grade B, 4.8% grade C and 1.4% grade D according to Los Angeles classification). At the baseline, 23.1% of the patients had a FVC <80% and 45.6% had a DLCO <50%. Patients with erosive esophagitis did not differ in terms of sex, age, duration and disease variant, positivity for anti-centromere, skin score values, FVC and DLCO at baseline compared to patients without erosions, but had a lower prevalence of anti-Scl70 (2.8 vs 52.5%, p=0.005) and active smoking (20.0 vs 8.4%, p=0.05). At follow-up, patients with esophageal erosions showed a greater relative decrease in FVC (3.4±19.3% vs 1.7±12.0%; p=0.013) after paired correction for sex, age, duration of disease, auto-antibodies, skin involvement variant, baseline FVC and DLCO, smoke exposure and therapy with immunosuppressants, proton pump inhibitors, prokinetics, antiplatelet agents and prostanoids.

Conclusion: SSC patients with erosive esophagitis present a higher risk of progression of interstitial lung disease. This evidence supports a role of micro-aspiration of gastric contents in the development of inflammation and fibrosis of the airways.

Disclosure of Interests: Enrico De Lorenzen: None declared, Gerlando Natalello: None declared, Laura Gigante: None declared, Lucrizza Verardi: None declared, Umberto La Porta: None declared, Giovanni Battista Canevari: None declared, Ludovica Berardini: None declared, SilviaLaura Bosello: None declared, Elisa Gremsi Consultant for: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Sanofi, UCB, Roche, and Pfizer, Speakers bureau: BMS, Speakers bureau: Roche, Speakers bureau: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Sanofi, UCB, Roche, and Pfizer


Scientific Abstracts
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FRI0319
CREASE OR SPORADIC INCLUSION BODY MYOSITIS

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Background: Sporadic inclusion body myositis (sIBM) is a subgroup of the idiopathic inflammatory myopathies (IMs) and is characterized by both degenerative and autoimmune features. Unlike other IMs, myositis-specific autoantibodies had not been found in sIBM patients until recently.

Objectives: We aimed to establish the prevalence and clinical associations of anti-CN-1A in a large Danish cohort with connective tissue disease (CTD).

Methods: In a cross-sectional study design, a total of 568 participants (183 IMs (55 sIBM, 128 non-sIBM: dermatomyositis (DM), polymyositis (PM), immune-mediated necrotizing myopathy (IMNM)), 184 systemic lupus erythematosus (SLE), 121 systemic sclerosis (SSc), and 100 blood donors (BD)) were tested for the presence of: a) CN-1A autoantibodies using a commercial Anti-CN-1A ELISA and b) myositis specific and associated autoantibodies (anti-Jo-1, anti-PL-7, anti-PL-12, anti-OJ, anti-EJ, anti-SS-A, anti-SS-B, anti-DNA, anti-PM/Scl75, anti-PM/SC100, anti-Ro52, anti-Ku) using a commercial line blot kit. The patients were classified according to the ACR classification criteria for IMs (2017), SLE (1997) and SSc (1980), respectively. Clinical features were compared between anti-CN-1A positive and anti-CN-1A negative patients using two-sample t-test and Mann-Whitney test for continuously normal and non-normally distributed data and Chi-square test for categorical data, as appropriate.

Results: CN-1A antibodies were predominantly found in IM patients. In the sIBM cohort, 24 patients (43.6%) were anti-CN-1A positive vs. 25 (19.5%) in the non-sIBM myositis cohort and 17 (10%) in the SLE cohort. None of the participants in the SSc or the BD cohorts had
presence of anti-cN-1A. Anti-cN-1A positivity had a sensitivity of 43.6% and a specificity of 91.8% for sIBM. The positive and negative predictive values were 36.4% and 93.8%, respectively.

There was no significant difference in gender, age at study entry, age at symptom onset, duration of symptoms or max creatine kinase (CK) levels during disease course between the anti-cN-1A positive and negative sIBM patients. Dysphagia was present in 19 (79%) of the anti-cN-1A positive and in 17 (55%) of the anti-cN-1A negative sIBM patients (P = 0.06).

Conclusion: The antibodies against cN-1A are the first and so far the only serological marker for sIBM. Our data showed that cN-1A autoantibodies are specific for sIBM and further corroborate the potential diagnostic role of cN-1A autoantibodies in this distinct subgroup of myositis.

Disclosing Interest: None declared, Line Vinderslev Iversen: None declared, Christoffer Tandrup Nielsen: None declared, Marie-Louise From Hermansen: None declared, Søren Jacobsen: None declared, Nanna Witting: None declared, Markus E. Krosgager: None declared, Tina Friis Grant research support from: Anti-cN-1A ELISA kits and EURDOLINE Autoimmune Inflammatory Myopathies 16 AG kits have been provided for a project free of charge from Euroimmun.


FR0321 PERFORMANCE OF DIFFERENT PULMONARY HYPERTENSION SCREENING ALGORITHMS IN PATIENTS WITH SYSTEMIC SCLEROSIS PATIENTS

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Background: Pulmonary hypertension (PH) is an important cause of morbidity and mortality in patients with systemic sclerosis (SSc). Different screening strategies have been proposed for identifying patients who have a high probability of PH and require right heart catheterization (RHC), which is the gold standard for diagnosing PH.

Objectives: To compare the performance of PH screening algorithms in our patients with SSc.

Methods: Forty-eight consecutive patients, fulfilling ACR/EULAR 2013 SSC criteria, were screened for PH using the 2015 ESC/ERS, DETECT and ASIG algorithms. Pulmonary function tests (PFT), diffusing capacity of the lung for carbon monoxide (DLCO), trans-thoracic echocardiography, serum NT-proBNP, uric acid assay and high-resolution computed tomography (HRCT) were performed as needed. Patients with known PH, severe interstitial lung disease and severe left ventricular dysfunction were not included. RHC was performed in all patients with positive screening according to any one of the screening algorithms. Patients with PH were classified according to the updated PH classification criteria. Sensitivity and specificity of the 3 screening algorithms were evaluated according to the established cut-off value of 25 mmHg for mean systolic pulmonary artery pressure and for the recently proposed cut-off value of 20 mmHg.

Results: Among the 48 SSc patients, 15 were excluded due to already diagnosed PH (n=4), left ventricular dysfunction (n=4), no measurable tricuspid regurgitation velocity (TRV) (n=5) and coexisting lung cancer (n=2). Among the remaining 34 patients, 16 required RHC according to at least one of the screening algorithms. Demographic and clinical features of remaining 34 patients were summarized in Table 1. Number of patients who had suspected pulmonary hypertension and required RHC according to ESC/ERS 2015, DETECT and ASIG were 8 (%25), 9 (%26) and 13 (%41) respectively (Figure 1). Among the 14 who had RHC, PH was present in 3 patients according to the 25-mmHg cut-off (Group 1 in 1, Group 2 in 1, Group 3 in 1) and in 8 patients according to the 20-mmHg cut-off (Group 1 in 5, Group 2 in 2, Group 3 in 1). The sensitivity and specificity of each algorithm is presented in Table 2. Sensitivity was similar at 100% for the 3 algorithms, but the ESC/ERS algorithm had better specificity, when PH was diagnosed with the 25-mmHg cut-off. For the 20-mmHg cut-off, both the sensitivity and the specificity were better with the ESC/ERS algorithm.

Conclusion: The ESC/ERS algorithm seems to have a better performance for detecting PH in patients with SSc. A limitation of this study was that RHC was not performed in patients who did not fulfill criteria according to any of the screening algorithms. The sensitivities may be lower than what we propose if there are patients with PH who are asymptomatic and not captured with any of the algorithms.


FR0322 AUTOANTIBODIES PROFILE INFLUENCE ON SYSTEMIC SCLEROSIS INTERSTITIAL LUNG DISEASE. A TERTIARY SPANISH HOSPITAL EXPERIENCE

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Background: Systemic Sclerosis (SSc) is a rare and heterogeneous connective tissue disease (CTD) characterized by skin fibrosis, vasculopathy/vascular damage and potential visceral impairment. Interstitial lung disease (ILD) constitutes the leading cause of mortality and requires close periodical assessment and follow-up. Diffuse cutaneous sclerosis and specific autoantibody profile (anti SCL70, anti Th/To, Anti U3 RNP and anti PmScl) are considered ILD development risk factors. In contrast, positivity to centromere has been considered as a protective factor to develop a clinical significant ILD.

Objectives: To assess ILD frequency and severity (extension and functional impairment) in SSc patients, analyzing the association with the different autoantibodies.

Methods: Retrospective, descriptive study of patients meeting EULAR/ACR 2013 SSc criteria and had a HRTC performed at a tertiary Spanish hospital from 1975 to 2018. One hundred and eight patients were included. HRTCs were graded by two radiologists according to Goh et al semi-quantitative score. Three groups were established according to the presence of different autoantibodies: anticientromere (ACA), antipmScl (ATA), and positivity to other ANAs (nucleolar pattern and other specificities).

Results: Clinical and laboratory characteristics are presented in table 1. Thirty-three patients had pulmonary involvement, 6 were ACA+, 18 ATA+ and 9 had other ANA specificities. The probability of not having pulmonary involvement among ACA+ and of having pulmonary involvement among ATA+ showed statistic significance (p<0.001 and p<0.001). Usual Intestinal Pneumonia (UIP) was the most frequently reported pattern (6 patients), followed by Non-Specific Intstitial Pneumonia (NSIP) (11 patients); Six patients did not meet the radiological criteria for neither UIP or NSIP. No statistical significant difference was found among radiological pattern and autoantibody profile. Regarding extension: 15 patients...
had non-extensive involvement (ACA: 2, ATA: 7, ‘other ANAs’: 6) performing Goh et al score with the FVC correction. ExtensiveILD was found among 18 patients (ACA: 4, ATA: 11, ‘other ANAs’: 3). Despite the fact that ATA+ group was more likely to have an extensive involvement no statistical significance was met. About pulmonary function tests (PFT) the mean FVC was 98.45% on ACA group, whereas on ATA and other ANAs groups the mean FVC were 89.97% and 81.43% respectively. Statistical differences were found between first and third group, however this difference was not found when only patients with pulmonary involvement were analyzed.

Conclusion: In our cohort, ATA and other ANAs groups were more likely to develop pulmonary interstitial disease and to need immunosuppressant treatment. Although the prevalence of ILD among ACA+ was only 10%, 50% of them required, due to the functional impairment or extension, immunosuppressant treatment. In spite of the low ILD-ACA+ incidence this complication should be kept in mind and periodical screening and assessment must be carried out as in other autoantibodies profiles.

Disclosure of Interests: None declared


Table 1

<table>
<thead>
<tr>
<th>Table 1</th>
<th>ACA</th>
<th>ATA</th>
<th>Other ANA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (%)</td>
<td>60 (84.6)</td>
<td>22 (31.9)</td>
<td>28 (40.1)</td>
</tr>
<tr>
<td>Sex</td>
<td>Female (%)</td>
<td>57 (95)</td>
<td>18 (90.9)</td>
</tr>
<tr>
<td></td>
<td>Male (%)</td>
<td>3 (5)</td>
<td>4 (18.2)</td>
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<tr>
<td>Age at diagnosis (median [range])</td>
<td>60 [55-89]</td>
<td>59 [50-85]</td>
<td></td>
</tr>
<tr>
<td>Stroke</td>
<td>1.7</td>
<td>4</td>
<td>11.2</td>
</tr>
<tr>
<td>Forme (%)</td>
<td>33.3</td>
<td>4.6</td>
<td>28.6</td>
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<tr>
<td>Time from diagnosis to ILD, mean (median)</td>
<td>6 [5]</td>
<td>0</td>
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<tr>
<td>Death (%)</td>
<td>8 (6.72)</td>
<td>2 (14.3)</td>
<td>2 (6.2)</td>
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<tr>
<td>PVR, mean (SD)</td>
<td>4.39 (1.38)</td>
<td>3.53 (1.75)</td>
<td>1.65 (1.34)</td>
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<tr>
<td>VC, mean (SD)</td>
<td>16</td>
<td>94.5</td>
<td>71</td>
</tr>
<tr>
<td>FEV1 (%, predicted)</td>
<td>20.7</td>
<td>16.3</td>
<td>19.3</td>
</tr>
<tr>
<td>FVC, mean (SD)</td>
<td>72.3 (20.4)</td>
<td>70.5 (20.9)</td>
<td>73.4 (20.7)</td>
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</table>

FR10323

EVALUATION OF LIPID PROFILE AND Atherosclerosis IN TREATMENT-NAIVE PATIENTS DIAGNOSED WITH UNDIFFERENTIATED CONNECTIVE TISSUE DISEASE (UCTD)

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Background: Patients with UCTD cannot be definitely diagnosed with a well-characterized systemic rheumatic disease. These patients often exhibit one of several disease patterns, manifesting multiple nonspecific clinical or serologic abnormalities, sometimes of more than one defined rheumatic disorder.

Objectives: The aim of this study is to investigate lipid profile and atherosclerosis in UCTD patients.

Methods: This is a prospective, observational study which included 30 treatment-naive UCTD patients. Thirty patients and 30 healthy matched-controls were compared for total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c) and triglycerides (TGs). Furthermore, in order to describe endothelial dysfunction and presence of atherosclerosis, we assessed intima-media thickness (IMT) of common carotid artery with the contribution of an experienced sonographer. We also measured Apolipoprotein A1 (ApoA1), Apolipoprotein B (ApoB), Apolipoprotein E (ApoE), Lipoprotein A (LpA), erythrocyte sedimentation rate (ESR), high-sensitivity C-reactive protein (HSCRP) and fibrinogen in the group of patients only.

Results: Thirty UCTD patients were studied. There were 11(36.7%) men, 19(63.3%) women and 7(23.3%) smokers. The mean (SD) age was 54.1 (13.1) years and disease duration was 17.3(10.4) years. All reported Raynaud’s phenomenon, 22(73.3%) had esophageal disorders, 21(70%) had pulmonary fibrosis and 3(10%) pulmonary hypertension. Arthritis was present in a great majority of these patients (93%). The immunological evaluation showed that 4(13.3%) had positive anticardiolipin antibodies and 11(36.7%) had scl-70 (+). The comparison of IMT between patients and matched-controls revealed an increased IMT in UCTD patients [0.82 (0.32) vs 0.6 (0.13) mm; p<0.001]. There was also a significant difference in mean (SD) TC [204(4.33) vs 238(4.14) in patients vs 238(4.14) in controls; p value=0.004] with respective reduced levels of mean(SD) HDL in patients [50.69(5.9) vs 61.1 (13.3); p value=0.002]. No statistically significant difference was found for LDL-c and TGs.

Conclusion: These patients had mean (SD) ApoA1 146.9(27.6), ApoB 94.9(25.6), ApoE 42.1(10.7), LpA 12.8 (15.9), HSCRP 7.5(13.5), ESR 28.9 (22.6) and fibrinogen 422.9(101.3).

Disclosure of Interests: None declared


FR10324

DISEASE ACTIVITY INDICES IN SYSTEMIC SCLEROSIS-WHICH TO USE IN DAILY PRACTICE?

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Background: Currently there is no fully validated index for assessing overall disease activity in patients with systemic sclerosis (SSc).

Objectives: To estimate the effect of disease activity as measured by 4 disease activity indices on the risk of subsequent organ damage in an EUSTAR center cohort.

Methods: Longitudinal observational study; European Systemic sclerosis study group disease activity index (ESCG DAI), revised EUSTAR disease activity index (r-EUSTAR DAI), 12 point activity index proposed by Minier (12point DAI) were calculated for all patients; the CRiSS (The Combined Response Index for Systemic Sclerosis) only for patients included after 2016. Student t-test/Mann-Whitney test, chi-square test were used to evaluate differences across subgroups; Pearson’s bivariate correlation/Spearman’s rank correlation coefficient to evaluate the association between variables. The predictive value of various variables for major organ involvement was assessed by Roc curves and univariate regression.

Results: 91 patients were selected,77 females (84.61%), 51,65(13,20) years old at diagnosis, 49,45% diffuse subset. Disease activity scores were all higher in male patients and in patients with diffuse cutaneous involvement, digital ulcers(DU), lung fibrosis, scleroderma renal crisis (SRC), amythiasma, muscle atrophy, gastric involvement, antiproliferosera 1 positive, EscSG DAI correlated with forced vital capacity (FVC)(r=0.73,p<0.001), DLCO(r=0.68,p<0.001), DU(2)= 3.08, p=0.05), lung fibrosis(2x0.10,3.20), systolic pulmonary arterial pressure (sPAP) (>0.54,p<0.001), muscle atrophy (x2=11.58,p<0.001), diffuse subset (x2=11.46,p<0.001), R- EUSTAR DAI correlated with FVC(r=0.6,p<0.001), DLCO(r=0.58, p=0.001), diffuse subset(2x=9.52,p<0.01), contractures(2x=11.23,p<0.001), muscle weakness(2x=6.67, p=0.01), muscle atrophy (x2=10.19, p<0.001), SRC (2x=4.74, p=0.02) and sPAP(r=0.5,p<0.001).

12 point DAI correlated with FVC(r=0.57,p<0.001), DLCO(r=0.66,p<0.001) and sPAP(r=0.42,p=0.001).

EscSG predicted well lung fibrosis (AUC=0.79,p<0.001), DU (AUC=0.66, p=0.001), gastric involvement (AUC=0.73, p=0.01) and SRC (AUC=0.9, p=0.01). R-EUSTAR index also lung fibrosis (AUC=0.76, p<0.001), DU (AUC=0.82,p<0.01) and SRC (AUC=0.84, p=0.04).

12point DAI was a good predictor for lung fibrosis(AUC=0.74,p<0.001), DU (AUC=0.78,p<0.05), gastric involvement(AUC=0.76,p<0.01).

In the regression analysis, lung fibrosis(bbeta=0.595CI=1.21-2.56,p<0.01), muscle atrophy (beta=1.49, 95%CI=1.02-2.19,p=0.03) and rhythm and conduction disturbances (beta=1.48, 95%CI=1.31-2.99,p=0.001) were independent predictors for disease activity evaluated by EScSG. For 12point DAI none of the evaluated parameters proved to independently contribute to disease activity. For 12point DAI items independently
contributing to disease activity were gastric involvement (beta=-2.46, 95% CI=1.19-5.09, p=0.01) and muscle atrophy (beta=-2.05, 95%CI=1.03-4.08, p=0.03).

The CRISS cohort included 35 patients, 32 females (91.42%), 48.48±14.24 years old, 62.85% diffuse subset, medium disease duration 11.88±(7.9 months). 8 patients were excluded due to new onset or worsening of lung fibrosis or SRC. None of the patients had a CRISS score with a probability of improvement>0.6.

Conclusion: We could not conclude that there is a gold standard to measure disease activity; for daily practice especially EsgSG and r-EUSTAR DAI quantify and predict major organ involvement. CRISS can be useful as an outcome measure for patients with short disease duration and closely monitored in clinical studies.

REFERENCES:

Disclosure of Interests: Laura Groseau: None declared, Sorana Petrescu: None declared, Andrei Balanescu Speakers bureau: multiple, Daniela Opiris-Belinski Grant/research support from: GLORIA, Speakers bureau: multiple, Violeta Bojina Speakers bureau: multiple, Florian Berghera: None declared, Ioana Saulescu: None declared, Sanziana Dacia-Iliescu: None declared, Diana Mazilu Speakers bureau: Pfizer, UCB, Andreea Borangiu: None declared, Ioana Saulescu: None declared, Sanziana Daia-Iliescu: None declared, Ruxandra Ionescu: None declared, Otylia Kowal-Bielecka (Switzerland), Basel, Switzerland; Graf Biostatistics, Winterthur, Switzerland, Spedali Civili di Brescia, O/IO Reumatologia e Immunologia Clinica, Brescia, Italy; VA Nasonova Institute of Rheumatology, Moscow, Russian Federation; University of Pécs, Department of Rheumatology and Immunology, Pécs, Hungary; University of Florence, Department of Clinical and Experimental Medicine, Section of Rheumatology, Florence, Italy; Hôpital Claude Huriez, University of Lille, Department of Internal Medicine and Clinical Immunology, Lille, France; Peking Union Medical College Hospital, Department of Rheumatology, Beijing, China; University Hospital Zurich, Department of Rheumatology, Zurich, Switzerland; University of Medical Center Schleswig-Holstein, Department of Rheumatology and Clinical Immunology, Lübeck, Germany; National and Kapodistrian University of Athens Medical School, Joint Rheumatology Programme, Athens, Greece; Policlinico U.O. Reumatologia, Dipartimento di Medicina di Precisione, Napoli, Italy; Medical University of Bialystok, Department of Rheumatology and Internal Medicine, Bialystok, Poland; Descartes University, APHP, Cochin Hospital, Department of Rheumatology A, Paris, France.

Background: Early identification of patients with systemic sclerosis-associated interstitial lung disease (SSc-ILD) at risk of progression could help tailor management and aid cohort enrichment in clinical trials to improve outcome.

Objectives: To assess the frequency of progressive SSc-ILD in the total ILD cohort and in subgroups enriched by risk factors in the EUSTAR database.

Methods: Patients from the EUSTAR database registered after 2010, ≥18 yrs old, fulfilling SSc classification criteria, with serial lung function and HRCT assessments were eligible. The following risk factors for progressive SSc-ILD available in the EUSTAR database were chosen as enrichment criteria: low forced vital capacity (FVC) and diffusing capacity for carbon monoxide (DLCO), diffuse cutaneous SSc, antitopoisomerase I antibody (ATA), short disease duration, older age, male sex, increased C-reactive protein, and presence of respiratory symptoms and reflux disease. Eligible patients with progressive ILD were assessed in the cohort and in subgroups enriched by the risk factors. Progressive SSc-ILD was assessed as absolute changes in predicted and defined as: significant progressive (FVC decline >10%, or FVC decline 5–10% and DLCO decline >15%), moderate progressive (FVC decline 5–10% or stable (>5% FVC change in either direction). The follow-up period was defined as time from baseline to last available lung function test.

Results: 6004 patients fulfilled the main entry criteria; of these, 1822 (30.3%) had ILD. At baseline, mean age was 57 yrs, 17.4% were male, 48.2% had diffuse SSc, 53.5% were ATA-positive, mean baseline FVC 80% and DLCO59%, mean disease duration 9.8 yrs, and follow-up was 2.5 yrs. In the total ILD cohort (30% eligible patients), 21% showed progressive ILD. Enriching with single risk factors reduced the number of eligible patients down to 6%, while the frequency of progressive ILD stayed stable (Figure). Combinations of risk factors did not result in increasing numbers of progressive ILD patients, but in further decreasing numbers of eligible patients.

Conclusion: There is still an unmet need to identify SSc-ILD patients at risk of progression with efficient risk factors. For clinical trials, it is a challenge to balance feasibility of recruitment and enrichment.

Acknowledgement: Funding: Boehringer Ingelheim (Schweiz) GmbH, Switzerland.
Background: The hallmark of systemic sclerosis (SSc) is fibrosis of the skin. The interstitial matrix is rich in type I and III collagen while type IV collagen is the main collagen of the basement membrane. These two types of matrix are anchored together by other matrix proteins such as type VI collagen. Tissue turnover is in a delicate equilibrium of tissue formation and degradation, which may be altered in pathologies such as SSc, in which there is a net increase in tissue. By using advanced serological biomarkers tissue turnover, tissue formation and tissue degradation may be assessed separately, to quantify the tissue balance. The hypothesis of the current study was that the tissue balance was altered in SSc as compared to healthy, and that limited and diffuse SSc would present with different turnover rates.

Objectives: The objective was to quantify the tissue turnover balance in a cross-sectional study in limited and diffuse SSc.

Methods: Forty-three patients fulfilling the 2013 ACR/EULAR criteria for SSc were included. The study included limited (lcSSc, n= 20) and diffuse SSc (dcSSc, n=23) (recruited at Lund University, approval number Dnr 590/2008). Ten healthy controls were included. Biomarkers of type III, IV and VI collagen formation (PRO-C3, PRO-C4, PRO-C6) and degradation (C3M, C4M, C6M) were measured cross-sectional in serum samples by competitive ELISAs. The fibrotic index of collagen (FICol) was examined (formation/degradation). Difference between groups were tested by Mann-Whitney U test and correlations by Spearman’s correlation (rho).

Results: There was no significant difference in gender, age or BMI between lcSSC and dcSSC. The mean age of the population was 53.5 years and 75.2% female. lcSSC had a longer disease duration (lcSSC: 32.3 month (SD: 41.0), dcSSC: 13.5 month (SD 14.9), P=0.05) and a lower modified Rodnan skin score (mRSS, lcSSC: 4.25 points (SD: 3.1), dcSSC: 20.3 points (11.7), P=0.0001) compared to dcSSC as expected. Types I and III collagen formation were both significantly increased in dcSSC compared to lcSSC (PRO-C3: 18.6 ng/ml (SD: 10.0) vs 13.0 ng/ml (SD: 6.5) (P=0.01), PRO-C6: 16.7 ng/ml (SD: 6.6) vs 12.1 ng/ml (SD: 4.9) (P=0.01)). Figure 1). Type III collagen degradation were decreased in dcSSC compared to lcSSC (C3M: 13.3 ng/ml (SD: 2.9) vs 17.4 ng/ml (SD: 7.5) (P=0.03)). Neither type IV collagen formation nor type III, IV or VI collagen degradation were significantly different. The fibrotic index of type III and VI collagen (FICol3 and FICol6) were significantly increased in dcSSC compared to lcSSC (FICol3: 1.4 (SD: 0.6) vs 0.8 (SD: 0.3) (P=0.0001), FICol6: 1.2 (SD: 0.5) vs 0.9 (SD: 0.3) (P=0.03), Figure 2). The fibrotic index of type IV collagen (FICol4) were not different between the two groups but were both 1.5 times higher than the levels of healthy (healthy: 6.9, lcSSC 10.4 (SD: 3.3), dcSSC: 10.5 (SD:3.1)).

Both type III and VI collagen formation correlated moderately with mRSS with rho’s of 0.53 (P=0.0003) and 0.4 (p=0.008), respectively. FICol3 correlated with a rho of 0.59 (P=0.0001) and FICol6 with a rho of 0.35 (P=0.04).

Conclusion: The tissue turnover balance was clearly altered in both limited and diffuse SSc as compared to healthy controls. In addition, diffuse SSc presented with a more screwed balance in the fibrotic index towards tissue formation and disease progression. This study shows the importance of looking at both collagen formation and degradation. The collagen tissue turnover could be beneficial in following patients’ fibrosis development and possibly identifying if they are progressing or in regression.

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Branching Chain Amino Acids in the Treatment of PolyMyositis and Dermatomyositis: Results from the BTOUGH Study
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Background: Muscle functions of patients with polymyositis and dermatomyositis (PM/DM) remain often impaired even after successful control of the immune-mediated muscle injury by immunosuppressive therapy. The only effort at the present to regain muscle functions except for the immunosuppression is rehabilitation, which is carried out systematically in limited institutes. No medicines for rebuilding muscles have been approved. Branched chain amino acids (BCAA) promote skeletal muscle protein synthesis and inhibit muscle atrophy. They thus have positive effects on muscle power, but have never been examined for the effects on PM/DM.

Objectives: To assess the efficacy and safety of BCAA in the treatment of PM/DM for official approval of their use in Japan.

Methods: Untreated adults with PM/DM were enrolled in a randomized, double-blind trial to receive either TK-98 (drug name of BCAA) or placebo in addition to the conventional immunosuppressive agents. One package of TK-98 (4.15g) contained L-isoleucine 952mg, L-leucine 1490mg, and L-valine 1144mg (molar ratio is 1:2:1.35), and 6 packages were administered daily in 3 divided doses. After 12 weeks, patients with average manual muscle test (MMT) score less than 9.5 were enrolled in an open label extension study for 12 weeks. The primary end point was the change of the MMT score at 12 weeks. The secondary end points were the disease activity evaluated with myositis disease activity core set (MDACS) and the change of functional index (FI), which evaluates dynamic repetitive muscle functions.

Results: Forty-seven patients were randomized to the TK-98 (24 patients [12 with PM and 12 with DM]) and placebo (23 patients [11 with PM and 12 with DM]) groups. The baseline MMT scores were equivalent (7.97±0.92 [mean±SEM] in the TK-98 group and 7.84±0.86 in the placebo group). The change of MMT scores at 12 weeks were 0.70±0.19 (mean±SEM) and 0.69±0.18, respectively (P = 0.98). Thirty-one patients from the TK-98 group and 12 from the placebo group were enrolled in the extension study. The MMT scores in both groups improved considerably throughout the extension study. The increase of the FI scores of the shoulder flexion at 12 weeks was significantly larger in the TK-98 group (27.9±5.67 and 12.8±5.67 in the right shoulder flexion [P < 0.05]. 27.0 ±5.44 and 13.5±5.25 in the left shoulder flexion [P < 0.05]). The improvement rate of the average FI scores of all tested motions (head lift, shoulder flexion, and hip flexion) through the first 12 weeks was larger in the TK-98 group. No difference was found in the disease activity throughout the study period. Frequencies of the adverse events until 12 weeks were comparable.

Conclusion: Although BCAA exerted no effects in the improvement of the muscle strength evaluated with MMT, they were effective in the improvement of dynamic repetitive muscle functions in patients with PM/DM without significant increase of adverse events.

Disclosure of Interests: None declared.


Table. Spearman Correlations between CRiSS and individual components at 12 months and Comparison of ABA and PBO using CRiSS index and individual components at 12 months;

<table>
<thead>
<tr>
<th>Outcome</th>
<th>ABA N=44</th>
<th>PBO N=44</th>
<th>Treatment (ABA−PBO)</th>
<th>P-value*</th>
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<tr>
<td>ACR CRiSS (0.0-1.0)</td>
<td>Spearman Correlation</td>
<td>Spearman Correlation</td>
<td>Spearman Correlation</td>
<td>Spearman Correlation</td>
</tr>
<tr>
<td>median (IQR)</td>
<td>mean (SE)</td>
<td>mean (SE)</td>
<td>mean (SE)</td>
<td>mean (SE)</td>
</tr>
<tr>
<td>ΔMMRiSS (0-51)</td>
<td>-0.75</td>
<td>3.7</td>
<td>3.8</td>
<td>2.9 (1.75)</td>
</tr>
<tr>
<td>ΔFVC’% predicted</td>
<td>0.36</td>
<td>1.4</td>
<td>3.1</td>
<td>1.7 (1.72)</td>
</tr>
<tr>
<td>ΔPTGA (0-10)</td>
<td>-0.17</td>
<td>-0.55</td>
<td>0.20</td>
<td>-0.20 (0.557)</td>
</tr>
<tr>
<td>ΔMDGA (0-10)</td>
<td>-0.47</td>
<td>-1.34</td>
<td>-0.18</td>
<td>-1.16 (0.403)</td>
</tr>
<tr>
<td>ΔHAQ-DI (0-3)</td>
<td>-0.21</td>
<td>-0.11</td>
<td>0.08</td>
<td>-0.22 (0.108)</td>
</tr>
</tbody>
</table>

*P-value for treatment comparisons based on Van Elteren test; **P-value for treatment comparisons based on ANCOVA model with treatment, duration of SSc and baseline value as covariables; p < 0.05 using Spearman correlation coefficient. Negative score denotes improvement, except for FVC’% where negative score denotes worsening; LS mean = least squares mean; SE = standard error
MALIGNANCIES IN SYSTEMIC SCLEROSIS
PATIENTS WITH ANTI-PM/SCL ANTIBODIES: AN EUSTAR CASE-CONTROL STUDY

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Background: The main clinical associations of anti-PM/Scl in Systemic Sclerosis (SSc) include calcinosis, joint and muscle involvement, interstitial lung disease (ILD), and, possibly, scleroderma renal crisis (1,2). A possible association of anti-PM/Scl with cancer was reported in single-centre SSc series (2,3), but was never analysed in large multicentre studies. Moreover, the characteristics of malignancies, in particular their temporal association with the onset of SSc, were not explored.

Objectives: To evaluate the association of anti-PM/Scl with malignancies in a large, international, multicentre cohort.

Methods: 16 EUSTAR centres provided data on anti-PM/Scl+ SSc patients in their cohorts (cases), and on anti-PM/Scl-negative controls, matched for age at onset (±5 years), cutaneous subset, and disease duration (≥24 months). Only SSc patients with age ≥16 years at disease onset were included in this analysis. Anti-RNA Polymerase3+ patients were not included in controls, given the known association with synchronous cancer. Malignancies diagnosed between 2 years before and after the onset of SSc were defined as “synchronous” to the onset of SSc.

Results: 123 anti-PM/Scl+ SSc patients and 160 matched anti-PM/Scl controls (28% anti-Topoisomerase I, 40% anti-centromere, 32% others) were compared (Table 1): anti-PM/Scl+ patients had a higher prevalence of myositis (p=0.0001) and ILD (p=0.0001), and a lower prevalence of oesophageal symptoms (p=0.0001). The frequency of malignancies was not significantly different between the 2 groups (14/120 (12%) vs. 9/155 (6%), p=0.12). Only 7 malignancies synchronous to SSc onset were identified: 4 among anti-PM/Scl+ cases and 3 among controls (3 breast cancers; 3 other solid tumours; 1 multiple myeloma). Mean age at SSc onset was significantly higher in patients with synchronous malignancies compared to those without (64.9±7.2 vs. 48.4±14.3 years; p<0.003), irrespective of the anti-PM/Scl status.

Conclusion: In this EUSTAR multicentre case-control study, the association of anti-PM/Scl with malignancies in SSc patients could not be confirmed. Patients with older age at SSc onset seems to be at higher risk for synchronous malignancies, regardless the autoantibody status.

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HISTORY OF SILICA DUST EXPOSURES AND ASSOCIATION WITH CHEST HRCT AND CLINICAL CHARACTERISTICS IN SYSTEMIC SCLEROSIS

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Background: The association of a history of silica exposure with precise chest high-resolution computed tomography (HRCT) features is still to be determined in SSc patients fulfilling the 2013 EULAR/ACR classification criteria. A recent study highlighted that mediastinal lymph node involvement (ILD) (1). Nonetheless, the links between mediastinal lymphadenopathies (LA) and silica exposure in SSc patients have never been studied to date.

Objectives: The aim of this study was to assess the association of exposures to inorganic particles on the whole life course, with the HRCT characteristics in an unselected population of SSc patients.

Methods: A specific questionnaire based on a multidisciplinary approach (social sciences, epidemiology, occupational health and medicine) was used to assess occupational and non-occupational exposures to inorganic particles, with a specific interest on silica exposures in 100 SSc patients fulfilling the 2013 EULAR/ACR classification criteria. Clinical characteristics and chest HRCT at diagnosis were evaluated to assess the association of dust exposure with disease characteristics. The most recent chest HRCT was also evaluated and compared to HRCT at diagnosis to assess pulmonary evolution. All HRCT were evaluated by 3 experts, blinded for the results form dust exposure questionnaire.

Results: Men had significantly higher global and occupational dust-exposure scores than women. Sixty-five percent of men with SSc (n=17) had an occupational exposure to silica. Thirty-five percent of patients had thoracic LA and 12% an association of mediastinal and hilar LA. Male gender, history of tobacco use, dcSSc, positivity for ATA, thoracic LA and pneumoconiosis were significantly associated with occupational exposure to silica (p<0.05 for all). The presence of mediastinal and hilar LA was also associated with occupational exposure to silica (p=0.0001, OR=13.45, 95%CI=3.46-52.27). After stratification on gender, higher occupational dust-exposure score in men remained associated with mediastinal and hilar LA (p=0.046, OR=6.5, 95%CI=1.09-38.63). Mediastinal and hilar LA were also significantly associated with a more severe evolution of pulmonary involvement in SSc when considering extensive ILD at diagnosis, the use of immunosuppressive drugs, a fibrotic evolution with change of SSc-ILD pattern in the course of the disease, and an increase of pathological parenchyma extent above 10% since diagnosis.

Conclusion: By using a dedicated highly detailed questionnaire, this study underscores the high prevalence of silica exposure in SSc patients, especially in men. Mediastinal and hilar LA, considered as a bad prognostic factor in ILD, were frequent and associated with silica exposure.
IL-2 RESTORED THE REDUCED ABSOLUTE NUMBER OF TREG CELLS IN THE PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHY

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1The Second Hospital of Shanshi Medical University, Rheumatology, Taiyuan, China; 2The Second Hospital of Shansi Medical University, Rheumatology, Taiyuan, China; 3Shanshi Dayi Hospital Affiliated to Shansi Medical University, Rheumatology, Taiyuan, China.

Background: Idiopathic inflammatory myositis (IM) is a group of skeletal muscle non-suppurative inflammatory disease, including polymyositis (PM), dermatomyositis (DM), inclusion body myositis (IBM), DM/PM associated with malignancy and so on. The latest studies suggest that there is an increase of Th17 cells levels and a decrease of regulatory T cells (Tregs) levels in IM, which lead to the Th17/Treg imbalance. IL-2 promotes the proliferation and differentiation of several subsets of CD4+ T cells and inhibits Th17 cells. It is provided to Tregs from IL-2-producing cells such as activated CD4+CD25hi T cells, NK and NKT cells. Tregs express IL-2Ra (II-Ig) receptor complex. Therefore, Tregs may be selectively stimulated by low-dose IL-2 and amplified.

Objectives: To explore the quantitative changes of peripheral Th17 cells and Tregs in IM before and after receiving treatment with low-dose interleukin-2 (IL-2) and analyze the relationship between peripheral Th17 cells and Tregs and clinical indicators disease activity.

Methods: Total 151 IM patients were enrolled, and 196 healthy adults were used as normal controls. Of them, 76 cases were treated with low dose IL-2 (5.0*10^5 international units (IU) for 5 days). The absolute number of peripheral T, CD4+ T, CD8+ T, Th1, Th2, Th17 and Treg subsets were analyzed by flow cytometry. Laboratory examinations were analyzed retrospectively. Since the data was disregarded from the normal distribution, the median four quantile method was used for statistical description. Multiple samples were compared with Kruskal-Wallis H test, and the correlation between variables was Spearman rank correlation analysis.

Results: (1) In the patients, the absolute number of Treg cells was significantly decreased as compared with that in the control group (P<0.05) and increased by treated with a low dose IL-2. After IL-2 treatment, the absolute numbers of T, CD4+ T, CD8+ T, Th1, Th2 and Th17 cells and the ratio of Th17/Treg were still significantly lower than that in the control group (P<0.05). (2) The peripheral Th17 cells levels were negatively correlated with ESR, CRP, LDH and HBDH (r=-0.42, r=-0.28, r=-0.21, r=-0.20, P<0.05); the ratio of Th17/Treg was negatively correlated with ESR (r=-0.23, P<0.05).

Conclusion: The absolute number of peripheral Th17 cells and Tregs declined significantly in IM, and had correlation with ESR, CRP, LDH and HBDH. However, after receiving treatment with low-dose IL-2, the Tregs levels elevated, which means that IL-2 may plays an essential role in the differentiation and development of Tregs. It also provides new thought and strategy for the therapy of IM.

REFERENCES:

Disclosure of Interests: None declared

Abstract number: FR00332

ASSESSING SYSTEMIC SCLEROSIS CARDIAC INVOLVEMENT USING MAGNETIC RESONANCE T1-MOLLI MAPPING

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Background: Patients with systemic sclerosis (SSc) and symptomatic cardiac involvement have a disease-associated mortality of 20% in 10 years. Prevalence of subclinical cardiac involvement is 15%-35%. Early diagnosis and monitoring is therefore critical in the management of SSc-associated cardiac involvement. Conventional cardiac magnetic resonance imaging (cMRI) T1-weighted sequence with late gadolinium contrast has good accuracy for detecting localized fibrosis but not diffuse fibrosis that occurs in SSc. Modified look-locker inversion recovery (T1-MOLLI) mapping, a novel cMRI sequence, has been used to detect and quantify diffuse fibrosis in aortic stenosis. T1-MOLLI values have also been correlated with the degree of biopsy-quantified fibrosis.

Objectives: To investigate whether cMRI T1-MOLLI is able to detect fibrosis associated with SSc cardiac involvement.

Methods: We recruited 16 patients fulfilling the 2013 ACR/EULAR criteria for SSc and 17 healthy age-matched (within 5 years) controls. Patients underwent cMRI T1-MOLLI mapping on the Siemens Biograph mMR 3.0T (Erlanger, Germany).

T1-MOLLI values were compared between SSc patients and healthy controls using student t-test and statistical significance was taken to be p<0.05.

Results: Demographics and clinical features of our study cohort are as shown in Table 1. Two (12.5%) SSc patients were symptomatic with palpitations or had arrhythmia requiring treatment. Eleven (68.8%) SSc patients had elevated T1 MOLLI values, using a normal cut-off threshold of 1284 ms.

Mean cardiac T1 values were significantly higher in SSc patients (1329 ± 88.0 ms) than in controls (mean T1 = 1238 ± 93.7 ms, p=0.0075), indicating the presence of cardiac fibrosis.

Conclusion: cMRI T1-MOLLI mapping demonstrated that SSc patients who were predominantly asymptomatic showed evidence of cardiac fibrosis. cMRI T1-MOLLI is potentially a useful diagnostic and monitoring tool for SSc cardiac disease.

<table>
<thead>
<tr>
<th>Table 1. Demographics and clinical features</th>
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<tbody>
<tr>
<td>SSc patients</td>
</tr>
<tr>
<td>---------------</td>
</tr>
<tr>
<td>(n=16)</td>
</tr>
<tr>
<td>Limited/Diffuse SSc, n</td>
</tr>
<tr>
<td>Female, n (%)</td>
</tr>
<tr>
<td>Age, years</td>
</tr>
<tr>
<td>Mean disease duration from Raynaud’s phenomenon onset, years</td>
</tr>
<tr>
<td>Mean disease duration from non-Raynaud’s phenomenon onset, years</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
</tr>
<tr>
<td>Palpitations, n (%)</td>
</tr>
<tr>
<td>Arhythmia requiring treatment, n (%)</td>
</tr>
<tr>
<td>Anti-centromere positivity, (n)</td>
</tr>
<tr>
<td>Anti-Topo-I positivity, (n)</td>
</tr>
</tbody>
</table>

Disclosure of Interests: None declared

Abstract number: FR00334

PERFORMANCE OF THE SCLERODERMA SKIN PATIENT-REPORTED OUTCOME (SSPRO) IN A PHASE 2 TRIAL WITH LENABASUM

Ada Man1, Nancy Ogletuck2, Brian Conley2, Barbara White3, ‘University of Manitoba, Winnipeg, Canada; 2Corbus Pharmaceuticals, Inc, Norwood, United States of America

Background: Skin thickening is a distressing feature of systemic sclerosis (SSc). The severity and extensiveness of skin thickening, as traditionally
assessed by mRSS, may not directly correlate with its effect on patients’ health related quality of life (HRQoL). The Scleroderma Skin Patient-reported Outcome (SSPRO) was specifically developed to assess the skin-related HRQoL in SSc. No skin-specific PRO in SSc has been prospectively validated in a clinical trial.

Objectives: Validate the SSPRO prospectively in a clinical trial.

Methods: The SSPRO, Patient Global Assessment (PiGA), Physician Global Assessment (MDGA), HAQ-DI, mRSS, FVC%, predicted, PROMIS-29 questionnaire, and ACR CRiSS were assessed prospectively in a Phase 2 study of lenabasum in dcSSc. SSPRO has 18 items that assess four SSc skin-related HRQoL domains. The Phase 2 study of lenabasum had a 4-month double-blinded portion (N = 41 completers) followed by an open-label extension (N = 38 entered). Spearman correlations of baseline values and change values were determined for SSPRO and other outcome measures. Mean change in SSPRO scores were determined in subjects with increasing levels of improvement in other efficacy outcomes.

Results: At baseline, SSPRO correlated moderately with all other outcome measures except for FVC%, as expected, with stronger correlations with PiGA, HAQ-DI, and PROMIS-29 pain interference and social role domains (Table 1). The mean change in SSPRO scores at 3 and 12 months correlated mostly moderately (r = 0.25 to 0.62) with the mean change in other outcome measures, but correlations were low or inconsistent with mRSS, FVC%, and PROMIS-29 anxiety domain (Table 1). Significance of correlations in some outcomes was hampered by small magnitudes of change. Mean SSPRO generally increased in subjects with increasing levels of improvement in HAQ-DI, PiGA, mRSS, and ACR CRiSS, although less consistently with mRSS and ACR CRiSS at 3 months (Table 2).

Conclusion: SSPRO score correlates with both physician and patient-reported outcomes at baseline, though correlations with the latter were stronger. Change in SSPRO reflects changes in how the patient feels reported outcomes at baseline, though correlations with the latter were stronger. Change in SSPRO reflects changes in the patient feels baseline SSPRO score correlates with both physician and patient-reported outcomes at baseline, though correlations with the latter were stronger. Change in SSPRO reflects changes in how the patient feels and other outcome measures. Mean change in SSPRO scores were determined in subjects with increasing levels of improvement in other efficacy outcomes.

Disclosure of Interests: Federica Meloni1, Giovanni Zannamundo1, Adele Valentini2, Valentina Morani1, Veronika Codullo1, Lorenzo Volpino2, Claudio La Cerruola2, Francesca Motta1, Carlo maurotorto Montecucco1, Lorenzo Cavagna1.

1Rheumatology, University and IRCCS Policlinico S. Matteo Foundation, Pavia, Italy; 2Pneumology, University and IRCCS Policlinico S. Matteo Foundation, Pavia, Italy

Background: Intestinal Pneumonia with Autoimmune feature (IPAF) is a recently defined disease that includes Intestinal Lung Disease (ILD) in patients with features of autoimmunity, not satisfying any of the established classification criteria for connective tissue diseases (CTD). Even if IPAF patients share clinical and serological findings with CTD, we are unaware about the clinical evolution of IPAF patients.

Objectives: To define the characteristics and evolution of IPAF patients in a multidisciplinary setting.

Methods: We selected patients with a diagnosis of IPAF referring to a multidisciplinary Rheumatology/Pneumology/Radiology team at our hospital. We excluded from the analysis patients positive for antisynthetase antibodies, as diagnosed with antisynthetase syndrome. Data were retrospectively collected from our hospital medical records.

Results: We analyzed 25 patients (19 females, 76%, 6 males, 24%), with a median onset age of 67 years (interquartile range, IQR, 59-74) and a follow-up of 32 months (IQR 22-69). ANA test was positive in 23 (92%) cases (fig 1), whereas cytoplasmic positivity was observed in 17 (68%). Anti-ENA screen was positive in 9 patients (36%) (7 [28%] anti-Ro52 and 2 [8%] anti-RNP). One patient (4%) was positive for anti-PM-Scl, 1 (4%) for anti-Mi2 and 1 (4%) for anti-Ku antibodies. These 2 latter antibodies are not included in the serological domain of IPAF. Patients had mainly a Non Specific Intestinal Pneumonia (NSIP) pattern (19 [76%]; fibrosis in 7 [28%], and with concomitant organizing pneumonia (OP) in 3 [12%]. Three (12%) patients had Usual Interstitial Pneumonia-like and 3 (12%) an OP pattern. The majority of patients (15 [60%]) satisfied only the morphological and serological domains. Clinical domains satisfied were: arthritis (4 [16%]), Raynaud’s phenomenon (5 [20%]), palmar telangiectasias (2 [8%]), mechanic’s hands (1 [4%]) and hiiker’s feet (1 [4%]). We observed other findings not included in IPAF criteria but suggestive for CTDs, both clinical (inflammatory myopathy 3 [12%]; dry eye1 [4%]; sclerodericytly 1 [4%], and instrumental (scleroderma pattern at nailfold capillaroscopy 1 [4%]; dilated esophagus at barium X-rays 2 [8%]). Clinical spectrum time course was variable in 5 (20%) cases: 3 (12%) patients developed arthritis after ILD, and 2 (8%) developed ILD respec-

![Table 1. Spearman Correlations for SSPRO and Other Efficacy Outcomes at Baseline and for Change in SSPRO and Other Efficacy Outcomes at 3 and 12 months (r, P-value)](image)

<table>
<thead>
<tr>
<th>Time</th>
<th>PiGA</th>
<th>MDGA</th>
<th>HAQ-DI</th>
<th>mRSS</th>
<th>FVC, %</th>
<th>ACR CRiSS</th>
<th>Pain Interference</th>
<th>Social Role</th>
<th>Physical Function</th>
<th>PROMIS-29 Domain</th>
<th>Depression</th>
<th>Anxiety</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>0.61</td>
<td>0.51</td>
<td>0.52</td>
<td>0.44</td>
<td>-0.07</td>
<td>0.62</td>
<td>0.0001</td>
<td>-0.57</td>
<td>0.0001</td>
<td>0.33</td>
<td>0.51</td>
<td>0.41</td>
</tr>
<tr>
<td>Change 3 months</td>
<td>0.26</td>
<td>0.21</td>
<td>0.29</td>
<td>0.02</td>
<td>0.22</td>
<td>-0.20</td>
<td>0.48</td>
<td>0.36</td>
<td>-0.40</td>
<td>0.33</td>
<td>0.14</td>
<td>0.395</td>
</tr>
<tr>
<td>Change 12 months</td>
<td>0.28</td>
<td>0.13</td>
<td>0.25</td>
<td>0.20</td>
<td>0.02</td>
<td>-0.48</td>
<td>0.41</td>
<td>0.62</td>
<td>-0.25</td>
<td>0.27</td>
<td>0.21</td>
<td>0.234</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Improvement</th>
<th>HAQ-DI improvement</th>
<th>PiGA improvement</th>
<th>mRSS improvement</th>
<th>ACR CRiSS</th>
<th>Pain Interference</th>
<th>Social Role</th>
<th>Physical Function</th>
<th>Depression</th>
<th>Anxiety</th>
</tr>
</thead>
<tbody>
<tr>
<td>at least</td>
<td>None</td>
<td>-0.125</td>
<td>-0.250</td>
<td>0.500</td>
<td>None</td>
<td>-1</td>
<td>-2</td>
<td>None</td>
<td>-3</td>
</tr>
<tr>
<td>3 months</td>
<td>-9.9</td>
<td>-17.6</td>
<td>-20.2</td>
<td>-22.5</td>
<td>-11.9</td>
<td>-15.3</td>
<td>-16.5</td>
<td>-11.0</td>
<td>-14.7</td>
</tr>
<tr>
<td>12 months</td>
<td>-17.9</td>
<td>-20.2</td>
<td>-22.7</td>
<td>-27.2</td>
<td>-16.5</td>
<td>-21.9</td>
<td>-21.5</td>
<td>-11.6</td>
<td>-19.6</td>
</tr>
</tbody>
</table>

*ACR CRiSS score is absolute, not change, score.*
tively after arthritis and inflammatory myopathy onset. Three (12%) patients were admitted to the Intensive Care Unit for Rapidly Progressive (RP) ILD and 2 died (respectively 2 months and 54 months after ILD onset), whereas the alive patient had 2 ICU admission for RP-ILD. Five (20%) patients, including the only 1 dismissed from ICU, needed home O2 therapy. Ongoing and previous therapies are reported in figure 2.

Conclusion: We showed that the prognosis of IPAF is highly variable, with patients experiencing RP ILD, other slow progressive worsening of respiratory functions and other a substantially stable disease. Furthermore, we showed other findings, laboratory, clinical and instrumental, that could help clinicians in a better identification and stratification of IPAF patients. As a matter of fact, at present, IPAF appears as a generic term including very different conditions that can be further differentiated according to clinical and serological data.

REFERENCES:

Figure 1. Antinuclear antibodies determination results

Figure 2. Ongoing (at last follow-up) and previous treatments

Disclosure of Interests: Emiliano Marasco: None declared, Federica Meloni: None declared, Giovanni Zanfrumondo: None declared, Adele Valentini: None declared, Valentina Morandi: None declared, Veronica Codullo: None declared, Lorenzo Volpiano: None declared, Francesca Motta: None declared, Carlomaurizio Montecucco: None declared, Emiliano Marasco: None declared, Federica Meloni: None declared, Giovanni Zanfrumondo: None declared, Adele Valentini: None declared, Valentina Morandi: None declared, Veronica Codullo: None declared, Lorenzo Volpiano: None declared, Francesca Motta: None declared, Carlomaurizio Montecucco Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Sanofi, Genzyme, Lilly, MSD, Pfizer, UCB, Lorenzo Cavagna: None declared


FRIO337 INCIDENCE AND PREVALENCE OF MYOSITIS ASSESSED BY MULTISOURCES CAPTURE-RECAPTURE METHODOLOGY

John McLaren1, Paul Alcock1, Michael Hearn1, Elizabeth Furr1, Sarah Hallwood1, NHS Fife, Fife Rheumatic Diseases Unit, Kirkcaldy, United Kingdom; 1NHS Tayside, Immunology Laboratory Service, Dundee, United Kingdom

Background: Precise epidemiology of myositis epidemiology remains largely unknown (1). Surveys based solely on administrative claims benefit from large case ascertainment but may be influenced by misclassification and misdiagnosing. The use of medical records with charts review benefit from accurate diagnosis but exhaustive ascertainment is difficult to achieve because numerous specialists are involved and cases may concern both inpatients and outpatients.

To overcome these difficulties we undertook a capture-recapture survey that takes advantage of a multi-sources case ascertainment to estimate the number of cases missed by any one source and to correct the prevalence rate (2).

Objectives: To assess the incidence and prevalence of myositis in Alsace, a region of eastern France.

Methods: Alsace, region of eastern France, is home to about 2 million inhabitants benefiting from high access to healthcare and a labialized referral center for myositis. Seeking care outside is uneasy because of peculiar geography. Myositis patients were retrieved through three separate sources: i) all general practitioners and community specialist ii) Muscle pathology center records, iii) all public and private hospitals records, iv) all public and private laboratory records. Incidence and prevalence cases fulfilling the ACR/EULAR criteria for myositis were included.

Results: The responses to the questionnaires sent to the physicians (>150), yielded 105 potential myositis cases. All hospital centres contacted (n=13) participated in the study and 135 potential myositis patients were recorded by this source. We thus received 1683 records of suspected myositis after excluding duplicates within each sources. The thorough review of the corresponding medical charts is currently ongoing and at this stage 10% of the potential cases fulfilled the ACR/EULAR criteria for myositis.

Conclusion: This first study based on a multi-sources capture-recapture methodology and ACR/EULAR criteria is very likely to provide an accurate estimation of myositis epidemiology.

REFERENCES:
ANTI-MDA5 IDIOPATHIC INFLAMMATORY MYOSITIS (IIM) CONFRS POOR PROGNOSIS BUT NEGATIVE MYOSITIS SPECIFIC ANTIBODY (MSA) IS NOT BENIGN EITHER

Sin Nea Ng, Chun Man Ng, Chi Ol Clang, Moon Ho Leung, Queen Elizabeth Hospital, Medicine, Hong Kong, Hong Kong (SAR)

Background: MSA test is useful to diagnose IIM and subcategorize patients by disease phenotypes.

Objectives: The study aims to evaluate the survival of IIM patients of different MSA patterns.

Methods: An IIM registry had been set up in a tertiary referral centre since 2014 by recruiting prevalent and incident cases. Patients were followed up prospectively. This study included patients fulfilling the 2017 EULAR/ACR classification criteria for IIM and excluded those aged < 18 at disease onset. Immunoblot EUROLINE autoimmune inflammatory myopathies 16 antigens strip (EUROIMMUNE AG, Lubeck, Germany) was used. Information including baseline demographic data, disease manifestations, MSA results, co-existing malignancy, duration of survival and causes of death were collected. IIM patients were divided into seven groups, which included 1) anti-aminoacyl tRNA synthetase (ARS) 2) anti-MDA5, 3) anti-TIF1γ/anti-NXP2, 4) double positive MSA, 5) other MSAs, 6) negative MSA/MAA (myositis associated antibodies) and 7) positive MAA only.

Results: Among 112 IIM patients, 79 (70.5%) were female, and the median age of onset was 55 (18-90) years old; 63.4% were dermatomyositis (DM), 17.9% polymyositis (PM) and 18.8% clinically amyotrophic DM (CADM). Co-existing interstitial lung disease (ILD) was common and found in 65 (58%) patients; 16 (14.3%) had rapidly progressive interstitial lung disease (RPILD), and 16 (14.3%) died within the observed period. Overall, the commonest cause of death was RPILD, followed by infection and malignancy. While anti-MDA5 was strongly associated with RPILD (odds ratio = 33.0 [95% CI: 7.2-151.8], p<0.001), anti-MDA5 group had the worst survival, with 1-year and 5-year survival both at 43%, compared to above 80% in all other groups (log-rank test p<0.001) (Table 1). There were nine patients with double positive MSA and 28 had negative MSA/MAA. Analysis between MSA subgroups found that the double positive MSA and anti-MDA5 group had the worst survival, with 1-year and 5-year survival both at 43%, compared to above 80% in all other groups (log-rank test p<0.001) (Table 1).

Conclusion: Anti-MDA5 associated RPILD was the leading cause of mortality in IIM. However, those tested negative for both MSA and MAA by current immunoblot technique also had guarded prognosis related to the risk of infection and malignancy.

![Figure 1. Kaplan-Meier survival of IIM](image)

Table 1. Survival rates in different MSA groups

<table>
<thead>
<tr>
<th>Survival</th>
<th>1 year</th>
<th>5 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-ARS</td>
<td>100%</td>
<td>92%</td>
</tr>
<tr>
<td>Anti-MDA5</td>
<td>43%</td>
<td>43%</td>
</tr>
<tr>
<td>Double positive</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Negative MSA/MAA</td>
<td>89%</td>
<td>82%</td>
</tr>
<tr>
<td>Only positive MAA</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Anti-TIF1γ/anti-NXP2</td>
<td>100%</td>
<td>88%</td>
</tr>
<tr>
<td>Other MSAs</td>
<td>100%</td>
<td>100%</td>
</tr>
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</table>

REFERENCES:

Disclosure of Interests: None declared


ANTIBODIES IN DERMATOMYOSITIS/POLYMYSITIS

Marko Cagava-Momohara, Yoshinori Muro, Masashi Akiyama, Nagoya University Graduate School of Medicine, dermatology, Nagoya, Japan

Background: The anti-Ro52 antibody, found in numerous systemic autoimmune conditions, is one of the most common autoantibodies in inflammatory myositis. It is known to be associated with interstitial lung disease (ILD) and to coexist with anti-Jo-1. There are two spliced forms: Ro52α and Ro52β. Ro52β was originally reported in 1995 as a spliced form of Ro52α in the human heart. Ro52α antigen cDNA has a defective exon 4, which encodes part of an autoepitope hotspot.

Objectives: We investigated the clinical and laboratory characteristics of anti-Ro52α and anti-Ro52β. We also analyzed the characteristics of anti-Ro52αβ in each coexisting inflammatory myositis specific autoantibody (MSA) group to reduce the influences of coexisting MSA characteristics.

Methods: Among 229 dermatomyositis (DM) and polymyositis (PM) patients, 167 patients (DM 152, PM 10, juvenile DM 5) fulfilled the criteria of Bohan and Peter, and 62 clinical amyopathic DM cases fulfilled the criteria of Sontheimer. Anti-Ro52α and anti-Ro52β antibodies were detected by ELISA.

Results: 46 of the 229 patients were anti-Ro52α-positive (20%). ILD was a frequent complication in the anti-Ro52α-positive patients (35/42: 76%) (P=0.0016), and anti-Ro52α was highly positive in the anti-aminoacyl tRNA synthetase (ARS) antibody-positive group (19/32: 60%) (P<0.0001) (Table 1). However, the ILD frequencies of anti-Ro52α-positive and anti-Ro52α-negative patients within each group of coexisting MSA (anti-ARS, anti-TIF, anti-MDA5, etc.) were almost same (P=1). The anti-Ro52α-positive rates were similar to the positive rates of anti-Jo1 (61%) and other anti-ARS (52%) (P=0.7).

Of the 46 anti-Ro52α-positive patients, 26 patients were anti-Ro52β-positive. No patient was only anti-Ro52β positive. The anti-Ro52α-positive and anti-Ro52β-positive groups were older than the anti-Ro52α-only-positive group (P<0.009), and the average of maximum creatine kinase was higher in both of the positive groups (P=0.065). The 6 patients without coexisting MSA were all both anti-Ro52α-positive and anti-Ro52β-positive (P=0.03) (Table 2).

Conclusion: Anti-Ro52 is highly positive when anti-ARS antibodies are present, but it is anti-Jo-1-specific. Anti-Ro52 positivity is not associated with elevated risk of ILD in any of the MSA-positive groups. The anti-Ro52αβ antibody might be an indicator of myositis.

REFERENCES:
To assess a long-term follow-up primary RP patient and has proven to be useful in identifying patients with secondary RP. Identify the presence of secondary RP is important to perform an the presence of scleroderma or other connective tissue diseases (CTD).

Main pathologies observed after follow-up were: Scleroderma/Systemic sclerosis (n=3), Systemic Lupus Erythematosus (n=3), Rheumatoid arthritis (n=2). The main capillaroscopic patterns were predominant among SSc patients presenting LUTS (both UI and OAB), although not any statistical correlation was found.

Table 1. Clinical and laboratory characteristics with anti-Ro52

<table>
<thead>
<tr>
<th>anti-Ro52</th>
<th>anti-Ro52</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(+)</td>
<td>(-)</td>
<td></td>
</tr>
<tr>
<td>N=46</td>
<td>N=183</td>
<td></td>
</tr>
<tr>
<td>age</td>
<td>54.6±14</td>
<td>53.1±19</td>
</tr>
<tr>
<td>sex (female)</td>
<td>35 (76%)</td>
<td>126 (69%)</td>
</tr>
<tr>
<td>cancer</td>
<td>6 (13%)</td>
<td>43 (23%)</td>
</tr>
<tr>
<td>ILD</td>
<td>32 (76%)</td>
<td>78 (49%)</td>
</tr>
<tr>
<td>creatine kinase</td>
<td>974.3**</td>
<td>1274***</td>
</tr>
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</table>

Table 2. Clinical and laboratory characteristics in patients with anti-Ro52 and anti-Ro52|

<table>
<thead>
<tr>
<th>anti-Ro52</th>
<th>anti-Ro52</th>
<th>P value</th>
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<tbody>
<tr>
<td>N=26</td>
<td>N=20</td>
<td></td>
</tr>
<tr>
<td>age</td>
<td>59.8±12.5</td>
<td>47.8±13.5</td>
</tr>
<tr>
<td>sex (female)</td>
<td>21 (81%)</td>
<td>14 (70%)</td>
</tr>
<tr>
<td>cancer</td>
<td>1 (41%)</td>
<td>13 (71%)</td>
</tr>
<tr>
<td>creatine kinase</td>
<td>267.52</td>
<td>588.4</td>
</tr>
<tr>
<td>ILD</td>
<td>17 (71%)</td>
<td>16 (89%)</td>
</tr>
<tr>
<td>MSA</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>MDAS</td>
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<td>10</td>
</tr>
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<td>ARS</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>TIF1</td>
<td>3</td>
<td>1</td>
</tr>
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<td>0</td>
</tr>
<tr>
<td>M</td>
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<td>0</td>
<td>1</td>
</tr>
<tr>
<td>non</td>
<td>6</td>
<td>0</td>
</tr>
</tbody>
</table>

**4 patients excluded with insufficient data. **2 cases excluded. ***2 cases excluded. ****16 excluded.

** IBD: interstitial lung disease. **MSA: myositis specific autoantibodies

Disclosure of Interests: None declared


**FRI0341**

**LOWER URINARY TRACT SYMPTOMS PREVALENCE IN SYSTEMIC SCLEROSIS PATIENTS: RESULTS FROM A COMPREHENSIVE ANALYSIS**

Greta Pacini1, Amelia Chiara Trombetta1, Federica Goeangi1, Sabrina Paolino1, Carmen Pizzorno1, Elsa Alessandri1, Massimo Patane1, Emanuele Gotehi1, Giorgia Ferraro1, Francesco Cattelan1, Massimo Gin1, Andrea Casabella1, Vanessa Smith1, Maurizio Cutolo1. 1IRCCS San Martino Polyclinic Hospital, Research Laboratory and Academic Unit of Clinical Rheumatology, Department of Internal Medicine, University of Genova, Genova, Italy; 2Ghent University Hospital, Department of Internal Medicine, Belgium Unit for Molecular Immunology and Inflammation, VIB Inflammation Research Center (IRC), Ghent, Belgium

Background: Lower urinary tract symptoms (LUTS) are a seldom-reported manifestation of systemic sclerosis (SSc). Although LUTS have been described in SSc patients with a higher prevalence than in the general population, no controlled studies have been reported to date [1-3].

Objectives: To compare LUTS prevalence and severity in SSc patients and in healthy subjects and mainly to explore their association with SSc clinical and diagnostic parameters.

Methods: This study evaluated 42 SSc consecutive patients (median age 61 years, range 21-85) and 50 matched healthy subjects (median age 57 years, range 28-93). SSc diagnosis was based on the 2013 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) criteria. LUTS were assessed through validated self-reported questionnaires derived from the International Conference on Incontinence (ICIQ-FLUTS, ICIQ-MLUTS and ICIQ-OAB) [4]. General comorbidities and/ or medication potentially related to LUTS, as well as lower urinary tract infections, were evaluated in order to exclude confounding factors. Non-parametric tests and chi-squared test were performed to compare LUTS distribution, namely of urinary incontinence (UI) and overactive bladder (OAB), in the two populations, then linear and logistic regressions were used to test the association between SSc disease and LUTS prevalence and severity. In SSc population, linear and logistic regressions were performed to test the association between LUTS and SSc variables, includ- ing nailfold videocapillaroscopy (NVC) patterns ("Early", "Active", "Late", SSc-related autoantibodies and dual X-ray absorptiometry (DXA) parame-
ters. Multivariate analysis was performed to adjust the associations for potential confounders. A p value < 0.05 and a confidence interval (CI) of 95% were considered statistically significant.

Results: SSc patients showed significantly higher prevalence and severity of UI and OAB than healthy controls (p < 0.005, p< 0.01). SSc was a strong predictor of LUTS, independent of demographic data, comorbidities and treatments (OR 5.57, 95% IC 1.64-18.88). In SSc patients sarcopenia positively correlated with OAB (p< 0.001) and reduced bone mineral dens-
ity (BMD) positively correlated with OAB (p< 0.05) and UI (p< 0.001). UI positively correlated with anti Scl70 Abs (p< 0.05) and cyclosporine treatment (p< 0.001) and negatively with anti RNA polymerase III Abs (p< 0.05); OAB positively correlated with calcinosis (p< 0.005) and negatively with methotrexate treatment (p< 0.05). NVC "Active" and "Late" pat-
tens were predominant among SSc patients presenting LUTS (both UI and OAB), although not any statistical correlation was found.

Conclusion: For the first time urinary tract involvement was found to be significantly higher in SSc patients than in healthy matched controls. In addition, sarcopenia, bone damage and calcinosis appeared significantly correlated with LUTS, suggesting a possible interplay.

References:

Disclosure of Interests: None declared
EROSIVE OSTEOARTHRITIS IN PATIENTS WITH SYSTEMIC SCLEROSIS

Cristina Pigan Morata1, Jaime Arroyo Palomo1, Carlos de la Puente Bujidos1
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Background: Erosive osteoarthritis (EO) is a rare but aggressive variant of hand osteoarthritis. Its prevalence in Europe is 3.3% in men and 9.9% in women, affecting 15.5% of patients with hand osteoarthritis. EO causes a significant loss of function in the hands, with more severe inflammatory signs and affecting almost exclusively thePIP and DIP joints, usually avoiding the TM and MCP. In systemic sclerosis (SSc), hands are commonly affected with pain and joint deformity that, added to sclerodactyly and the presence of digital ulcers, produce an important functional limitation. It has not been established yet whether the presence of the disease determines an increased risk for the development of erosive osteoarthritis.

Objectives: To determine the frequency of EO in patients with SSc seen in our hospital in Madrid and to compare it with the frequency observed in the large cohorts of healthy population (Framingham study). Secondly analyze both the clinical and analytical factors that may be related to the presence of EO in these patients.

Methods: A descriptive, observational cross-sectional study was conducted. We included all patients with a diagnosis of systemic sclerosis attended in our Rheumatology Unit. A database was created including clinical and epidemiological data and all the available imaging tests to assess the presence of findings compatible with EO in interphalangeal hand joints were reviewed. Acroosteolysis lesions were not considered as EO. Finally, a descriptive analysis was carried out.

Results: The prevalence of EO in our cohort of SSc patients, although low, is higher than the estimated in general healthy population according to the large European studies, with 8.16% (12/147) of the patients affected. All the patients with EO were female, with a higher age of presentation of SSc compared to patients without EO (66.72 vs 50.72 years). The disease was more prevalent in patients with limited skin involvement (75% vs 62%) and they had a higher frequency of telangiectasias in the typical locations. Likewise, patients with EO had more frequently positive AMA (25% vs 8.8%) and calcinosis (33% vs 17.7%). The frequency of ANA, Raynaud’s phenomenon and interstitial lung disease was similar in both groups. No patients with positive Ro or La presented EO.

Conclusion: Although it is an uncommon variant of hand osteoarthritis, in our cohort a higher prevalence of EO was observed in patients with SSc compared to the healthy general population. In our group, the most associated risk factors were female sex, advanced age at the diagnosis of SSc, the presence of AMA and calcinosis, regardless of its location. The frequency of pulmonary involvement and Raynaud’s phenomenon was similar in both groups.

REFERENCES:

Disclosure of Interests: None declared

EVALUATION OF CAROTID HEMODYNAMIC PARAMETERS AND PLAQUES BY DOPPLER ULTRASOUND IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Carotid Doppler-ultrasound is useful for the detection of subclinical atheromatosis, and also for the evaluation of hemodynamic characteristics of carotid arteries.

Objectives: The aim of this study is to evaluate the hemodynamic parameters of carotid arteries and its relation with vascular related Systemic Sclerosis (SSc) complications and subclinical atheromatosis.

Methods: 157 patients with SSc of the cohort of Vall d’Hebron Hospital were included according to the ACR/EULAR 2013 criteria and LeRoy classification.

The left and right common carotid arteries (CCA), bulb and internal carotid arteries (ICA) were scanned using Doppler ultrasound for the detection of plaques and for the measurement of the Peak Systolic Velocity (PSV), End Diastolic Velocity (EDV), Pulsatility Index (PI), Resistance Index (RI) and Systole/Diastole ratio (S/D), using the software incorporated in GE Healthcare’s Vivid 1 equipment.

Results: 157 patients were included, 132 women (84.1%), the mean age was 56 years old (range 20-83) and the mean of years of disease evolution was 19 years (range 3-57). 64.2% were SSc limited subset, 20.9% SSc diffuse subset, 9.5% SSc sine sclerodactyly and 4.7% early SSc subset. 49.3% had digital ulcers, 41.9% had interstitial lung disease and 14.2% had pulmonary hypertension.

There were no statistically significant differences in hemodynamic parameters in relation to Raynaud’s phenomenon, digital ulcers or pulmonary hypertension.

Seventy-five patients (47.7%) had carotid plaques. Patients with plaques had lower CCA PSV (66.8cm/s vs 76.7cm/s, p <0.01, CI 6.2-14.5), lower CCA EDV (15.3 cm/s vs 19.99cm/s p <0.01, CI 2.88-6.49), higher CCA PI (1.69 vs. 1.55, p < 0.05, CI 0.02-0.26) and higher CCA RI (0.77 vs 0.73 p <0.01 CI 0.02-0.05). These patients also had lower ICA EDV (22.9cm/s vs 26.5cm/s, p <0.01, CI 1.01-6.11), higher ICA PI (1.43 vs 1.32, p <0.05 CI 0.01-0.22) and higher RI0.71 vs 0.68 p <0.05 CI 0.01-0.05), without statistically significant differences in ICA PSV (79.75cm/s vs 84.24cm/s p: 0.21) nor in the ratio PSV/EDV.

Ratio ICA PSV/CCA PSV was calculated, without showing significant differences in the presence of plaques or vascular manifestations of the SSc.

The PSV greater than 120cm/s, as an isolated measure, did not show statistically significant differences related to the presence of plaques. The PSV greater than 150 showed statistically significant differences (p <0.01, CI 0.05-0.23), showing a large specificity 0.98 but a very low sensitivity 0.15 for the detection of plaques.

Conclusion: In our study we have not found relation between carotid hemodynamic parameters and microvascular related SSc complications such as Raynaud’s phenomenon, the presence of digital ulcers or pulmonary hypertension.

Patients with SSc and atherosomative disease have a characteristic carotid hemodynamic profile consisting in lower PSV and EDV, and higher PI and RI, both at CCA and at ICA. The presence of increased PI and RI in patients with plaques, could suggest a primary damage of the vascular wall in patients with SSc. More studies are needed to determine if these data are the cause or a consequence of the presence of plaques.

In our study the PSV greater than 150 cm/s isolated shows a high specificity for the presence of plaques.

REFERENCES:

Disclosure of Interests: None declared

SEXUAL FUNCTION IN GERMAN WOMEN WITH SYSTEMIC SCLEROSIS COMPARED TO WOMEN WITH SYSTEMIC LUPUS ERYTHEMATODES AND EVALUATION OF A SCREENING TEST

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Background: Few studies have been conducted to address the impact of systemic lupus erythematoses (SLE) or systemic sclerosis (SSc) on sexual function (1,2), and so far none in Germany.

Objectives: The aim of this study is to evaluate the sexual function of women with SSc and SLE and to compare it with healthy women.

Methods: Sexual function was assessed in 157 women (aged 32-79 years) with SSc and in 49 women (aged 18-73 years) with SLE. At the same time, a sexual function questionnaire was administered to a group of 112 healthy women (aged 21-87 years).

Results: The prevalence of SSc was significantly higher in women with SSc than in women with SLE (p <0.01). The prevalence of SSc was significantly higher in women with SSc than in women with SLE (p <0.01). The prevalence of SSc was significantly higher in women with SSc than in women with SLE (p <0.01). The prevalence of SSc was significantly higher in women with SSc than in women with SLE (p <0.01).

Conclusion: The prevalence of SSc was significantly higher in women with SSc than in women with SLE (p <0.01).

References:

Disclosure of Interests: None declared
Objectives: To assess and compare sexual dysfunction (SDF) in female patients with SLE or SSC, to correlate sexual function with disease characteristics and depression, and to evaluate a short questionnaire (Qualisex) as a screening test.

Methods: Female patients with systemic lupus erythematosus or systemic sclerosis in two German tertiary university hospitals were evaluated with a self-designed questionnaire on various sexual and gynaecological characteristics and depression, and to evaluate a short questionnaire (Qualisex), the 9-item questionnaire Qualisex, and the Beck’s depression inventory in a prospective study.

Results: 171 female patients were included into the study. Among them 83 suffered from SSc (mean age 48.50 years), and 88 from SLE (mean age 39.65 years). Organ involvement and immunosuppressive medication was frequent in both groups. 34.9% of SSC patients and 28.4% of SLE patients ever received cyclophosphamide. Disease duration was significantly longer in SLE patients (13.17 vs 9.85 years in SSC patients, p=0.021). No significant differences between SSC and SLE were found as to educational background, BDI depression categories, marital status, or number of children. Only 9.6% of SSC patients and 14.8% of SLE patients had ever discussed sexual problems with their physician, whereas 52% of all patients thought that these were relevant in relation to their disease. Significantly more SSC patients would wish to discuss sexuality with their physician more intensively (37.3% vs 28.4% in SLE patients, p=0.011). 79.5% of SSC patients and 79.4% of SLE patients were in a constant relationship; 62.6% (52 of 83) of SSC patients and 67.0% (59 of 88) of SLE patients were sexually active. Impeding factors like vaginal stenosis, sicca, impaired mobility of pelvis, or pain did not differ significantly between SSC and SLE. Among the 51 sexually active and evaluable SSC patients a mean FSFI of 25.53 (±5.06) was found, with a FSFI value below the cut off defining SDF (26.55) in 49% of patients, which did not differ significantly compared to SLE patients (n=59, mean FSFI 26.92 (±5.17), SDF in 45.8%). More patients who suffered from SDF had at least mild depression defined by BDI than patients without SDF (71.2% vs 46.4%, p=0.016). SSC patients showed a numerically better Qualisex than SLE patients (2.98 (±2.24) vs. 3.16 (±2.45) with 0 meaning no impairment and 10 severe impairment). The Qualisex correlated significantly with the FSFI (r=-0.367; p<0.001) with numerically better correlation in SSC patients (r=-0.407, p=0.001 vs r=-0.340, p=0.004).

Conclusion: Sexual Dysfunction (SDF) is a frequent problem in female patients with SSC and SLE. Frequency and nature are comparable between the two entities. Addressing sexual issues during medical consultation is an unmet need. The Qualisex constitutes a short questionnaire, which is suitable for SDF screening.

REFERENCES:

Capillary dimension has been evaluated in 2 studies, with no unequivocal results [3,4]. Corrado et al. found abnormal morphology to be more commonly associated with SSC-PAH [4]. No association was found between presence of haemorrhages and SSC-PAH [4]. Ricci et al. found that NVC scores were more commonly associated with SSC-PAH [5]. Concerning qualitative assessment, severe NVC patterns have been unequivocally found to be more commonly associated with SSC-PAH [4,5].

Conclusion: This is the first systematic literature review to investigate the role of NVC in SSC-PAH using standardized definitions as proposed by the EULAR SG MC/RD. Unequivocal associations with incident SSC-PAH were found in longitudinal studies between capillary density, abnormal morphology and NVC pattern. Unequivocal associations with SSC-PAH were not found in cross-sectional studies between capillary density and severe NVC pattern.

REFERENCES:

Disclosure of Interests: None declared


FR10346 PERFORMANCE OF THE 2017 EUROPEAN LEAGUE AGAINST RHEUMATISM/AMERICAN COLLEGE OF RHEUMATOLOGY (EULAR/ACR) CLASSIFICATION CRITERIA FOR ADULT IDIOPATHIC INFLAMMATORY MYOPATHIES IN A HONG KONG COHORT

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Background: The new classification criteria for idiopathic inflammatory myopathy (IIM) endorsed by the European League Against Rheumatism and American College of Rheumatology (EULAR/ACR) were published in 2017 [1]. However, the majority of the patients in the development cohort were Caucasians. External validation in other populations were advised. With the increasing availability and experience of myositis specific autoantibodies (MSAs) testing, the inclusion only anti-Jo-1 antibody is apparently insufficient.

Objectives: The objective of the study was to evaluate the performance of the 2017 EULAR/ACR classification criteria in a cohort of Hong Kong adult IIM patients. The secondary objectives included examining the level of agreement between the new criteria and the traditional criteria and assessing the effect of including other MSAs into the criteria.

Methods: This was a multi-centre retrospective cross-sectional study. Consecutive patients with a clinical diagnosis of IIMs and MSA tested seen in the rheumatology clinic and admitted to the rheumatology wards of the participating hospitals in Hong Kong up till August 2018 were recruited. Patients with juvenile onset myositis were excluded. Clinical parameters required by the two criteria will be collected by reviewing the medical records. A commercial line blot immunoassay kit (EUROMMUN) was used to detect the MSAs.

Results: Two hundred and four patients with IIM were recruited. The mean age was 59.3 years. There was a female predominance of 76.5%. The subgroups of the patients were: polymyositis 40.7%, dermatomyositis 38.2%, clinically amyopathic dermatomyositis patients 21.1%. MSAs were detected in 59.3% of the patients with anti-Jo-1 antibody being the commonest (13.2%). The new 2017 EULAR/ACR Criteria could classify 96.1% of the patients as having definite or probable IIM. The Bohan and Peter criteria could only classify 76.0% of the patients. When combining with the Sontheimer’s criteria for CADM, 93.1% of the patients could be classified. The percentage agreement of the new and the Bohan and Peter criteria also increased from 77.0% to 93.1% when the latter was supplemented with the Sontheimer’s criteria. If the presence of any MSAs is considered one of the criteria, the performance of the 2017 criteria improved to 97.5% while the combined Bohan and Peter/Sontheimer’s criteria to 96.1%. However, the new criteria still failed to highlight the important subtype of IIM associated with anti-MDA5 autoantibody.

Conclusion: In a population with a significant proportion of CADM patients, the new 2017 EULAR/ACR classification criteria outperformed the old criteria. Finally, a clinico-serological criteria for “anti-MDA5 syndrome” is proposed in which a patient must have positive serologic testing for an anti-MDA5 autoantibody, plus one of the following conditions:

myositis by the new EULAR/ACR criteria, interstitial lung disease or typical rash (skin ulceration, palmer papules).

REFERENCE:

Disclosure of Interests: None declared


TUBERCULOSIS IN SYSTEMIC SCLEROSIS

Thursday, 13 June 2019 703

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Background: The tuberculin skin test (TST) is a screening tool for detection of occult or remote tuberculosis infection. Although skin lightness is a classic manifestation in systemic sclerosis (SSc), there are no reports vis-a-vis any limitation of the TST in SSc patients nor a definition on the cut-off for a positive TST test size for a diagnosis of tuberculosis.

Objectives: Our aims were to determine (a) the indurated reaction size of the TST, (b) the cut-off size for the indurated TST, and, (c) the sensitivity and specificity of the test for the diagnosis of tuberculosis in SSc patients.

Methods: A cross-sectional study was conducted among Thai adult SSc patients, followed up at the Scleroderma Clinic, Khon Kaen University, Thailand between November 1, 2016 and November 30, 2017. The TST was performed using 0.1 ml purified protein derivatives (PPD) injected intradermally (Figure 1), and interpreted 72 hours after testing.

Results: A total of 168 SSc patients were enrolled (male to female ratio = 1.8:1). The median age and duration of disease was 57.2 and 6.4 years, respectively. The majority (71.8%) was the diffuse cutaneous SSc subset. Seventeen cases (10.1%) were defined as tuberculosis infection. All of the patients had a history of BCG vaccination at birth. An indurated skin reaction size TST of 20 U/L had a high specificity for tuberculosis (99.3%; 95%CI 96.4-100) (Kappa 0.86; p=0.03). The modified Rodnan skin score (mRSS) had a significant negative correlation with the indurated skin reaction size (Rho -0.23; p=0.003). While other clinical parameters—such as BMI, SSc subset, serum albumin level, steroid or immunosuppressant use—were not correlated with the TST result (p=0.06, 0.14, 0.09, 0.23 and 0.89, respectively).

Conclusion: Indurated skin reaction size ≥ 20 mm indicated a high specificity for tuberculosis infection in SSc patients with history of BCG vaccination. The high mRSS resulted in a smaller skin reaction size when using the TST. The TST is thus less useful as a diagnostic tool for tuberculosis among SSc patients, especially among those with severe skin tightness.

Figure 1. Tuberculin skin test in a systemic sclerosis patient

REFERENCES:
USE OF INTRAVENOUS IMMUNOGLOBULIN THERAPY IN PATIENTS WITH SYSTEMIC SCLEROSIS: A SPANISH MULTICENTER EXPERIENCE

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Objectives: To describe the efficacy of intravenous immunoglobulin (IVIG) therapy in different organic conditions of Systemic Sclerosis (SSc).

Methods: Retrospective multicenter observational study that enrolled patients with SSc treated with IVIG. We collected epidemiological data, SSC complications, treatments and functional tests. Regarding IVIG treatment in different organic conditions of Systemic Sclerosis (SSc).

Results: 41 patients (83% women) were recruited, with a mean age of 58 ± 18 years. The age of diagnosis was 48 ± 18 years old. The diffuse cutaneous SSc was the most frequent in the sample (61%) and the mean of cycles was 10. 37% of patients had a history of use of corticosteroid therapy. When evaluating the degree of skin involvement (mRSS) patients showed a significant improvement of -2.49 ± 5.29 (-0.03) at the end of the follow-up. Indeed we observed better results in the groups of patients with myositis. No differences were observed in the% FVC or DLCO outcomes during the follow-up. However, when we compared patients with or without overlap syndrome we found differences in FVC values at the beginning of the study that were not present at the end of the follow-up. Patients with antiScIg70 seemed to have less response to IVIG therapy.

Conclusion: Our results suggest that IVIG can be useful for the management of some conditions in specific profiles of patients with SSc.

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mineral content (BMC), and bone mineral density (BMD) in seven body areas (head, upper limbs, lower limbs, trunk, spine, ribs, pelvis). Sarcopenia was diagnosed in patients with reduced skeletal muscle index (RSMI) below 5.45 Kg/m² for females and 7.25 Kg/m² for males. Statistical analysis was performed by non-parametric tests.

Results: The mean age of patients was 64.11 years, mean disease duration 19.2 ± 7.6 years, mean Rodnan skin score (mRSS) 11.5±9.3, and mean RSMI 63.1±10.5 g/cm². All the patients showed a NVC “scleroderma pattern”: in particular 15 patients showed the “Late” pattern, 15 patients the “Active” pattern and 8 patients the “Early” NVC pattern. The “Late” NVC pattern group comparing to “Early/Active” group showed significantly lower total mass (5828±8217 vs 6723±11437 g, p = 0.02), lean mass (35249±3646 vs 41220±7954 g, p = 0.05), RSMI (5.8±0.92 vs 6.6±1.02 g/ cm², p = 0.02), BMC (1839±339 vs 2183±502 g, p = 0.04), trunk BMD (0.70±0.12 vs 0.87±0.13 g/cm², p = 0.05) and spine BMD (0.91±0.17 vs 1.08 ±0.18 g/cm², p = 0.008). No statically significant difference between the two group was observed regarding total fat mass, total body BMD and BMD at upper limbs, lower limbs, head, ribs and pelvis. Interestingly, 24% of SSc patients were found affected by sarcopenia, and the most of sarcopenic patients showed the “Late” NVC pattern (67%). Comparing age, disease duration, mRSS between sarcopenic and non sarcopenic patients there was no difference between the groups, but sarcopenic patients presented a statistically significant lower BM (p<0.02).

Conclusion: This study demonstrates in SSc patients a relationship between a more severe microvascular damage (“Late” SSc pattern) and the body composition, characterized by lower weight, total lean mass, bone mineral content and sarcopenia, without any significant variation in total fat mass. These clinical conditions seem not to be associated with severity of skin involvement and/or disease duration.

REFERENCE:

Disclosure of Interests: None declared

FRI0350
THE FREQUENCY OF LOW MINERAL DENSITY, FALLS AND FRACTURES IN PATIENTS WITH SYSTEMIC SCLEROSIS

Olga Dobrovolskaya, Nikolay Demin, Oxana Desinova, Natalia Toropsova.

Background: Systemic sclerosis (SSc) is a severe connective tissue disorder causing vascular, immune, and fibrotic changes in the skin and internal organs. Patients with SSc may have an increased risk of osteoporosis and fractures due to chronic inflammation, latent malabsorption or malnutrition, immunization, and use of corticosteroid therapy.

Objectives: to determine the frequency of low mineral density, falls, low energy fractures and 10-year probability of new fracture in patients with SSc.

Methods: 191 patients with SSc were enrolled in the study: 160 women (mean age 51±13 yrs), among them 107 postmenopausal, and 31 men (mean age 53±14 yrs). Bone mineral density (BMD) was measured at lumbar spine (LS), femoral neck (FN) and total hip (TH) by dual energy X-ray absorptiometry (DXA, Hologic 4500A). BMD decreasing grade was determined in accordance to WHO criteria. All patients were interviewed on a special questionnaire and assessment of 10-year probability of new fracture by FRAX® was performed. Vitamin D level was measured in 104 patients.

Results: Low BMD was found in 68% women and 55% men: osteopenia in 30% and 32% and OP in 36% (21% in reproductive age and 50% in postmenopausal) and 23%, respectively. BMD in LS, FN and TH associated with body mass index (r=0.3, p=0.003; r=0.41, p=0.0027; r=0.49, p=0.0002, respectively) and duration of postmenopausal period in women (r=0.56, p=0.023; r=0.66, p=0.006; r=0.63, p=0.009, respectively). BMD of LS and FN correlated with age (r=0.22, p=0.045; r=0.23, p=0.016, respectively), duration of SSc (r=0.32, p=0.037); r=0.31, p=0.046, respectively), glucocorticoid cumulative dose for LS only (r=0.31, p=0.024). Mean 25(OH)D level was 19.8±11.06 ng/ml. Normal vitamin D level had 9% of SSc patients. No correlation between BMD and 25(OH)D level was found.

46 (24%) patients reported falls in the year prior to the interview, among them in 2 patients the fall led to fracture. A total of 48 (25%) patients had low energy fractures in the past, among them 8 (4%) of women had two or more fractures. Frequency of low energy fractures was 35%, 43% and 25% among postmenopausal women, women of reproductive age and men, respectively. The mean age at which the fracture occurred was 55±11 yrs. in postmenopausal women, 30±12 yrs. in young women and 60±12 yrs. in men. The most frequent were the fractures of distal forearm and vertebrae: 13 (7%) and 26 (14%) patients, respectively. Five patients each (3%) had ankle and humerus neck fractures and 7 – other localizations. Nobody reported the fracture of the proximal femur. Patients with abnormal BMD (OP or osteoporosis) had a risk of falls and low energy fractures more than 2 times higher than patients with normal BMD (OR 2.93 [95% CI 1.11; 8.01], p=0.016 and OR 2.58 [95% CI 1.04; 6.6], p=0.025, respectively). 10-year probability of any major osteoporotic fracture was 18.4 ± 9.6% in women and 9.7 ± 8.6% in men and of hip fracture - 3.5 ± 3.7% and 1.5 ± 3.9%, respectively. Among all patients, 55% of women and 4% of men had a high risk of subsequent fractures using the FRAX® algorithm.

Conclusion: Low BMD was diagnosed in 68% of women and 55% of men with SSc. The correlations between BMD and age, body mass index, the duration and glucocorticoid cumulative dose. Reduced BMD was associated with an increased risk of falls and fractures. 55% of women and 4% of men had a high risk of subsequent fractures.

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Nikolay Demin: None declared.
Oxana Desinova: None declared.
Natalia Toropsova Speakers bureau: Amgen, Lilly
**DIFFERENCES IN ANTISYNTHETASE SYNDROME DEFINITION AND RELATED DIAGNOSTIC PERFORMANCE. A SYSTEMATIC LITERATURE REVIEW INFORMING THE NEW ACR/EULAR CLASSIFICATION CRITERIA**

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**Background:** Antisynthetase syndrome (ASSD) lacks of established clinic-serological classification criteria. A taskforce by EULAR and ACR is working on to develop and validate classification criteria for ASSD.

**Objectives:** To systematically upraise literature to retrieve the available definitions of ASSD and to evaluate their diagnostic performance.

**Methods:** This systematic review followed a pre-specified protocol. Two research questions (Q1: how is ASSD defined; Q2: what is the diagnostic performance of the definitions) were rephrased into PICOs terms to create search strategies. Studies on patients with suspect or confirmed ASSD, including a definition of the disease with any study design, excluding case-reports and narrative reviews, were eligible for inclusion. The diagnostic performance had to be tested against the reference standard of expert opinion. PubMed and Embase were searched from 01/01/1984 to 06/11/2018. Moreover, the ACR and EULAR congress abstracts (2017-2018) were hand searched. The titles and abstracts of the retrieved studies were screened by pairs of reviewers, the full-text of studies fulfilling the inclusion criteria was assessed to confirm eligibility. The references of the included studies were also evaluated in search of additional studies. Data from primary studies were extracted into a pre-specified extraction form and, if possible, 2x2 tables to assess diagnostic performance were completed. Sensitivities, specificities, positive and negative likelihood ratios (LR) were calculated for each study. If the diagnostic performance of a definition or variable was assessed in at least 4 studies, a meta-analysis of diagnostic performance was undertaken. The risk of bias (RoB) was assessed using the most appropriate tool depending on study design.

**Results:** After the exclusion of duplicates, the searches retrieved 4358 studies, of which 375 suitable for full-text review. Finally, 77 studies were included, along with 1 additional study from hand search and 3 congress abstracts. 72 studies were included in Q1 and 9 in both Q1 and 2. The presence of antisynthetase antibodies (70 studies), mainly anti-Jo1 (57 studies); myositis (51 studies), mainly defined clinically (32 studies); and interstitial lung disease (38 studies) were the variables most frequently used to define ASSD. Other variables, such as arthritis (19 studies), Raynaud’s phenomenon and skin manifestations (10 studies each) were evaluated less frequently. Most commonly, ASSD was defined by a combination of clinical and serological variables. However, no study evaluated the diagnostic performance of such combined definitions. Most of the studies included in Q2 (6) evaluated specific variables of muscle biopsy, one evaluated MRI and 2 clinical variables, with a wide variability in the studies included in Q2 (6) evaluated specific variables of muscle biopsy, one evaluated MRI and 2 clinical variables, with a wide variability in the performance of each item. It was possible to meta-analyze data only to assess the performance of perifascicular necrosis/atrophy: pooled sensitivity (95%CI) was 0.53 (0.33;0.72) and specificity 0.63 (0.47;0.76), pooled LR+ 1.45 (0.72;2.89) and LR- 0.73 (0.40;1.34).

**Conclusion:** ASSD is defined according to a variety of combinations of serological, clinical and histological variables. The performance of these combined definitions however has not been tested, and from the limited evidence available single muscle biopsy variable (perifascicular necrosis/atrophy) seem to perform poorly. The systematic review confirms the need of data and consensus driven classification criteria for ASSD.

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**COMPARISON OF TWO ILOPROST REGIMENS IN TERMS OF ECONOMIC IMPACT AND EFFECTIVENESS**

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**Background:** Systemic sclerosis (SSc) is an autoimmune chronic disease characterized by prominent vascular involvement. Intravenous iloprost (IV ILO), according to the recently updated EULAR recommendations, is indicated for SSc Raynaud’s phenomenon (RP) after failure of oral therapy. Moreover, IV ILO could be useful in DU healing and may represent a potential disease modifying medication. However, there are no uniform data regarding type of regimen (dosage, duration and frequency) and infusion modality.

**Objectives:** The purpose of this study was to compare effectiveness (in terms of Du) and direct costs, of two regimens of IV ILO infusion in the same cohort of consecutive SSc subjects.

**Methods:** Protocol A (A): the patient was admitted and 100 mcg of ILO was diluted in 500 ml of normal saline or 5% dextrose solution and infused continually at the maximum tolerated dose until exhaustion. Protocol B (B): the patient was followed as outpatient at infusion clinic and 50 mcg of ILO was diluted in 250 ml of normal saline or 5% dextrose and infused at a dose range from 0.5 to 1.5 mg/Kg/m. The dose was escalated at 30 minutes intervals and maintained at the maximum tolerated dose for 5 consecutive hours for two consecutive days. The intervals between the infusions were between 6-8 weeks in both protocols depending on clinical response and availability of places at the Unit. 44 patients who received long term IV ILO as inpatients (Cohort A), after a wash out of 3 months, were switched to ambulatory administration (Cohort B). Thereafter, after one year of follow-up 24 patients of the protocol B were lost to follow-up and 20 patients were maintained on this regimen. Comparison was made between Cohort A (44 patients=A44) in the period between March 2015 and October 2016 (period A), Cohort B (44 patients=B44) between October 2016 and March 2017 (period B44), Cohort B (20 patients=B20), between October 2017 and March 2018 (period B20). Comparison between groups was made by non parametric tests and contingency table analysis when appropriate. Costs were estimated multiplying data related to resource use (drug consumption, hospital stay, outpatient visits, management of complications, etc) by unit cost obtained from the accounting office of the Hospital. All costs were expressed in Euro.

**Results:** Mean number of DUs at the end of period A was 0.37±0.98 in A44 as compared to 0.90±1.39 of period B44 cohort B44 (p<0.045) and 0.55±0.95 of period B20 Cohort B20 (p=n.s.). Cumulative number of DUs was 9/44 in Cohort A (20.5%) as compared to 20/44 in Cohort B44 (45% p=0,002) and 7/20 in cohort B20 (35% p=0.05). High number of drop outs (24/44) in protocol B was due mainly to statistical significant difference in tolerability (adverse events 11% protocol A vs 42% protocol B p< 0,01). Direct costs were higher in protocol A (3132±883 Euros vs 2687±556 Euros) as compared to protocol B, despite the differences were not statistically significant between the two modalities.

**Conclusion:** Protocol A seems to represent a regimen better tolerated and more effective than protocol B. Moreover, protocol B is affected by high rate of drops out due mainly to worse tolerability. Admitting SSc-patients for continuous IV ILO infusion seems to represent a better tolerated and more effective choice than following them as outpatients at infusion clinic, with substantially comparable direct costs in the same SSc cohort.

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Spondyloarthritis – etiology, pathogenesis and animal models

**FRI0353** MISREGULATION OF BMP/TGF SHEDS LIGHT ON THE PATHOGENICITY OF HLA-B27 IN Spondyloarthritis

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**Background:** The class I MHC allele, HLA-B27 is the main genetic factor predisposing to ankylosing spondylitis (AS) and related spondyloarthritis (SpA), a group of osteo-articular disorders combining inflammation with ossification. Until now, hypotheses to explain such striking association discovered 45 years have speculated either on the presentation of particular peptides to CD8+ T cells or on aberrant behaviors of the HLA-B27 molecule independent of its antigen presenting function, including slow folding and homodimers formation.

**Objectives:** To unravel aberrant function(s) of HLA-B27 independent of antigen presentation that may explain its pathogenicity.

**Methods:** Drosophila transgenic for SpA-associated HLA-B*27:04 or HLA-B*27:05 or non-SPA-associated HLA-B*07:02, alone or in combination with human β2-microglobulin (hβ2m) were produced. Genetic interaction tests were used to identify altered pathway(s). Protein-protein interactions were evidenced by proximity ligation assay. Phosphorylation of Smad2/3 was tested on CD4+ T cells from HLA-B27+ SpA patients and HLA-B27- healthy controls (6-10/group) by PhosFlow.

**Results:** Drosophila transgenic for HLA-B*27:04 or HLA-B*27:05 but not for control HLA-B*07:02 allele, in the presence of hβ2m that allows expression of well-folded HLA-B molecules at the cell surface, developed crosswitness phenotype. This was due to a disturbance of BMP signaling by HLA-B27/hβ2m which repressed Saxophone (Sax) BMP type I receptor (BMPR1) function, resulting in widening of phosphorylated Mad, the Drosophila receptor-mediated Smad, gradient, and increased expression of its target genes dpp and comb. Consistently, HLA-B27/hβ2m well-folded conformers co-localized with Sax at the surface of Drosophila cells and also with Sax mammal ortholog ALK2, on immune cells from SpA patients. As predicted, given that Sax orthologs ALK1 and ALK2 are known to exert antagonistic function on TGFβ/BMP signaling, we found heightened p-Smad in response to TGFβ or Activin A in CD4+ T cells from HLA-B27+ SpA patients (p<0.05).

**Conclusion:** The pathogenic role of HLA-B27 in SpA may result from a TGFβ|BMP signaling misregulation due to specific antagonistic interaction with ALK1/ALK2 BMPR1, at the crosstalk between inflammation and ossification. Interestingly, ALK2 mutations are responsible for the rare mendelian disorder, Fibrodysplasia Ossifians Progressiva that mimicks AS (Ref).

**REFERENCES:**


**Disclosure of Interests:** Benjamin Grandon: None declared, Auroe Rinchеваl: None declared, Nadège Jah: None declared, Jean-Marc Corsi: None declared, Luiza M. Araújo: None declared, Simon Glätzy: None declared, Delphine Roche: None declared, Gilles Chiocchia: None declared, Isabelle Guénal: None declared, Sébastien Gaumer: None declared, Maxime Breban: research support from: Pfizer, UCB, Novartis, MSD, Consultant for: UCB

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**FRI0354** ASSESSING THE ROLE OF TENDON-T CELL INTERACTIONS IN THE DEVELOPMENT OF CHRONICITY IN SPONDYLOARTHRITIS

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**Background:** Enthesitis is a hallmark of spondyloarthropathies[1], with mechanical stress or damage in the tendon being proposed as a trigger for the development of inflammation at the enthesis that propagates to the synovial compartment through what has been termed “synovio-enthesal complex[2].” Increasing evidence supports the role that stromal cells play in the shift of the inflammatory process towards chronically promoting T cell migration, retention and survival[3]. Therefore, we hypothesize that after tendon damage the crosstalk between stromal and immune compartments contributes to the development of chronic inflammation.

**Objectives:** We aimed to assess the effect of tendon stromal cells (tenocytes) on T cell migration and activation and the impact of these activated T cells on the stroma.

**Methods:** Tenocytes were explanted from tissue obtained from anterior cruciate ligament (ACL) reconstructions. The effect of damage on tenocytes and tenocytes conditioned media from tendon explants or IL-1β was evaluated by qPCR. A transwell membrane system was used to test the impact of conditioned media from tenocytes on T cell migration. T cells and tenocytes were co-cultured with or without the presence of a transwell membrane to quantify T cell activation (CD69 by FACS and IFNγ by ELISA). Changes in gene expression on tenocytes after co-culture with activated T cells were analysed by qPCR.

**Results:** In the presence of damage, tenocytes upregulated inflammatory mediators (IL-6, COX2), chemokines (CCL2, CCL5, CXCL10, CXCL12) and adhesion molecules (ICAM-1). Conditioned media, particularly after stimulation with IL-1β, from tenocytes induced T cell migration. Co-cultures of tenocytes and T cells resulted in activation of T cells that was contact dependant. In turn, these activated T cells upregulated the production of inflammatory mediators in tenocytes and increased the COL3/COL1 ratio.

**Conclusion:** Our results support a communication between the stromal and immune compartment within the tendon that could be involved in the progression towards chronicity in the context of spondyloarthritis. Following damage, tendon stromal cells are able to induce the recruitment of T cells, that once enter the tissue interact with the stroma. Stromal cells are then further activated to produce inflammatory cytokines and chemokines that amplify and maintain this inflammatory response.

**REFERENCES:**


**Disclosure of Interests:** Emma García-Melchor: None declared, Giacomo Cafaro: None declared, Lindsay AN Crowe: None declared, Michael McLean: None declared, James H Reilly: None declared, Iain Mccinnes: Consultant for: AstaZeneca, Celgene, Compugen, Novartis, Roche, UCB Pharma, Consultant for: AbbVie, Celgene, Galvani, Lilly, Novartis, Pfizer, UCB Pharma, Moed Akbar: None declared, Neal L. Millar: None declared

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MUCOSAL ASSOCIATED INVARIANT T-CELLS ARE DRUG-INDUCED REMISSION AND SUBCLINICAL DIFFERENTIAL EXPRESSION OF HUMAN GERMLINE. A growing body of research has associated the differential expression in inherited remnants of ancient retroviruses that infected the ancestral lineage, including HERV-K and IL-17A. MAIT cells are enriched at mucosal surfaces and have been implicated in the pathogenesis of spondyloarthropathies (SpA) (1) and inflammatory bowel disease (IBD). Although the human enthesis is not a mucosal surface it is the primary site of inflammation in SpA which has strong association with IBD.

Objectives: To investigate if a population of MAITs is present at the normal human enthesis thereby establishing a potential link between gut and joint inflammation.

Methods: Healthy interosseous ligament and spinoous process were harvested from patients undergoing elective surgery for correction of mechanical spinal defects. Enthesal soft tissue (EST) and peri-entheseal bone (PEB) were separated and cells were harvested by enzymatic and mechanical digestion respectively. The proportion of cells expressing HERV-K, CXCL10, CCR6 and IL-23R transcript were measured by flow cytometry in EST, PEB and matched blood. Expression of CD69 and CD45RA were examined for phenotypic analysis. Transcript analysis for IL-23/IL-17 axis and immunomodulatory genes was performed on sorted entheseal MAITs and analysed by TaqMan array.

Results: As a proportion of total T-cells, MAITs were of approximately 3 fold and 2.5 fold greater abundance in EST and PEB respectively in comparison to matched peripheral blood (both p<0.034). MAITs in entheseal tissue had an overlapping resident memory phenotype (CD45RA+CD69+CD45RO+/CD69-CD45RA-) median 4.3% (range 2.4 – 7.8%) in EST and 5.9% (4.5 - 8.2%) in PEB compared to those from blood 17.7 (6.8 – 69.4%). MAITs robustly expressed RORC, CCR6 and IL-23R transcript. Compared to conventional entheseal T-cells, MAITs expressed significantly less TGF-β (6-fold, p>0.001) and significantly more IL-23R (29-fold, p=0.004).

Conclusion: Healthy human enthesal tissue contains an enriched population of MAITs that strongly express IL-23R transcript at a frequency comparable to that reported in the colon (2). The majority of these cells express a resident memory phenotype suggesting that they are a distinct population residing in enthesial tissue. These observations are potentially relevant to SpA pathogenesis and the observed link between SpA and IBD.

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Disclosure of Interests: Richard Cuthbert: None declared, Qiao Zhou: None declared, Abdulla Watad: None declared, Robert Dunsmuir: None declared, Peter Loughenbury: None declared, Almas Khan: None declared, Dennis McGonagle Consultant for: Lilly, Novartis UCB, declared, Peter Millner: None declared, Charlie Bridgewood: None declared.


DIFFERENTIAL EXPRESSION OF HUMAN ENDOGENOUS RETROVIRUSES IN PSORIATIC DISEASE

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Background: Human endogenous retroviruses (HERV) are the stably inherited remnants of ancient retroviruses that infected the ancestral genome. A growing body of research has associated the differential expression and regulation of HERVs with a number of diseases, including systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). HERVs are thought to contribute to the pathogenesis of autoimmune diseases by modulating the expression of host immune-related genes, molecular mimicry, or cross reactivity of host proteins with HERV encoded products.

Objectives: To compare the expression of 4 HERVs previously associated with autoimmune disorders (HERV-K, HERV-K10, HERV-W, and HERV-H) in whole blood, CD3+ T cells, and CD14+ monocytes of patients with cutaneous psoriasis without arthritis (PsC), psoriatic arthritis (PsA), and healthy controls.

Methods: PsC, PsA patients satisfying the CASPARI criteria, and healthy controls were recruited for the study. RNA was extracted from whole blood collected in Tempus tubes and HERV expression was measured by quantitative real time PCR (qRT-PCR) or droplet digital (dd)PCR with normalization to GAPDH. HERV expression in whole blood RNA from 40 PsA patients was compared to 40 age and sex matched PsC patients and 40 age and sex matched healthy controls. Subsequently, HERV expression in 55 PsC patients who progressed to develop PsA (converters) was compared to 55 age and sex matched PsC patients who did not develop PsA over the same duration of follow-up (non-converters).

Results: In whole blood, HERV-K was significantly differentially expressed between 40 PsA and 40 PsC patients (fold change [FC]=1.57, p<0.008). HERV-K was also significantly differentially expressed in baseline samples from 55 converters compared to 55 non-converters (FC=1.93, p<0.003). No other HERV genes were differentially expressed between these groups in whole blood. Significant expression differences were more evident in purified cells (Table 1).

Table 1. Differential expression of HERV's in purified T cells and monocytes.

<table>
<thead>
<tr>
<th>HERV</th>
<th>CD3+ T cells</th>
<th>CD14+ Monocytes</th>
<th>CD3- T cells</th>
<th>CD14+ Monocytes</th>
</tr>
</thead>
<tbody>
<tr>
<td>PsA vs. PsC</td>
<td>PsA vs. Controls</td>
<td>PsA vs. Controls</td>
<td>PsA vs. Controls</td>
<td></td>
</tr>
<tr>
<td>HERV-K</td>
<td>0.43, p&lt;0.02</td>
<td>0.30, p&lt;0.01</td>
<td>0.17, p&lt;0.01</td>
<td>2.18, p&lt;0.02</td>
</tr>
<tr>
<td>HERV-9</td>
<td>2.94, ns</td>
<td>6.87, p&lt;0.01</td>
<td>2.60, p&lt;0.04</td>
<td>ns</td>
</tr>
<tr>
<td>HERV-10</td>
<td>3.69, p&lt;0.05</td>
<td>3.19, ns</td>
<td>0.36, p&lt;0.02</td>
<td>2.67, 0.27, p&lt;0.01</td>
</tr>
<tr>
<td>HERV-H</td>
<td>1.27, ns</td>
<td>4.42, ns</td>
<td>3.24, ns</td>
<td>0.47, p&lt;0.04</td>
</tr>
<tr>
<td>W</td>
<td>0.64, ns</td>
<td>0.30, p&lt;0.01</td>
<td>0.01, ns</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Conclusion: In whole blood, expression of HERV-K differentiates PsA and PsC patients, and its expression is significantly elevated in PsC patients prior to the development of PsA. HERV expression differences between the groups are also evident in purified T cells and monocytes. These data suggest a role for HERV-K in the pathogenesis of psoriatic disease and their potential use as prognostic markers of arthritis in patients with psoriasis.

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ENDOGENOUS RETROVIRUSES IN PSORIATIC DISEASE

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Background: Remission is an important goal of therapy in psoriatic arthri-

tis (PsA), but data on molecular players of clinical remission and effective
disease inactivation are scarce. Gene expression profiling analysis could be useful to elucidate the pathogenic mechanisms of diseases, and different gene expression analysis between diverse disease conditions produces gene signatures characteristic of the state or disease being studied. 

Objectives: Our aim was to compare the transcriptional profiles of patients with clinically active versus inactive remission state) PsA (peripheral joint subset), and healthy controls (HCs).

Methods: From a cohort of around 300 patients affected by PsA according to CASPAr criteria, we first selected 20 patients (peripheral arthritis subset) with active disease state (without biologic treatment ongoing) A) and 20 patients with >1-year remission induced by TNFα antagonism (R), as assessed by DAPSA > 14, and DAPSA ≤ 4 scores respectively, and from 20 HCs matching for age and gender ratio. Both PsA groups were not on corticosteroid treatment. RNA from peripheral blood was extracted and, following quality analysis by Agilent Bioanalyzer, each condition has been profiled using RNAs pools in biological duplicates by distinct Affymetrix Human GeneChip HTA 2.0, for a total of 6 arrays. Data analysis was performed using the commercial software Partek Genomics Suite, V 6.6. To identify a transcript as differentially expressed, a value of fold change 1.5 and p-value 0.05 has been set.

Results: The Venn diagram shows all comparative groups (A vs R, A vs HC, R vs HC) with their relative amount of transcripts differentially expressed, generated using abovementioned parameters, and the relationship between sets (fig1, panel A). Using the list of transcripts differentially expressed in at least one of the aforementioned comparison, a hierarchical clustering was carried out to highlight the intra-condition expression profile. We have identified (arbitrarily) 4 clusters of transcripts with analogous transcriptional profile and to each of them a color code has been assigned (Heatmap in Fig1, panel B). For these clusters and for all lists of transcripts differentially expressed founded by our comparative study, we carried out the Gene Set Enrichment Analysis by Gene Ontology (GO), in order to identify how molecular functions, cellular components or biological processes occurs more frequently than expected in a reference list of transcripts.

Conclusion: Observing the amount of differentially expressed transcripts, it is evident that while active disease state (A) has a clear-cut different profile, the drug-induced remission (R) is more similar with HCs condition. However, in the hierarchical clustering this trend of similarity does not appear in all clusters of transcripts, as shown particularly in the red, orange and green clusters. Again, the Gene Set Enrichment Analysis Score showed us that mRNA transcripts dysregulated in the R condition vs HCs, are involved in several biological processes related to immune system, development, response to stimulus, localization and others. Our next step will be to validate, by Real Time PCR in a large cohort of patients, the most interesting dysregulated genes covering biological functions eventually sustaining subclinical activity in PsA.

Disclosure of Interests: None declared


ROLE OF MiRNA-21-5PAS A POTENTIAL BIOMARKER FOR THE INFLAMMATION PATHWAY IN PSORIATIC DISEASE AND RESPONSE TO METHOTREXATE TREATMENT

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Background: Psoriatic arthritis (PsA) is an inflammatory arthritis occurring in patients with psoriasis. Several studies have shown links between altered miRNA expression with the pathogenesis of several autoimmune disorders. We previously demonstrated that miR-21-5p was upregulated in PsA compared to psoriasis without arthritis (PsC) and healthy controls (HC) and is thus a potential biomarker for PsA.

Objectives: 1) To determine whether miR-21-5p is differentially expressed in PsC patients who convert to PsA vs non-converters and validate the previous results in an independent cohort. 2) To determine the role of miR-215p in the response to methotrexate treatment (MTX) 3) To determine whether miR-21-5p modulates inflammation in psoriatic disease.

Methods: Serum & whole blood RNA samples were collected from 54 converters and 54 non-converters (matched for age, sex, psoriasis duration), 40 patients with early PsA (>2 years’ disease duration and not receiving biological therapy), 40 patients with PsC (>10 years disease duration, not receiving biologic therapy, and matched to PsA patients on age, sex, psoriasis duration, and age of psoriasis onset), and 40 HCs (matched to patients based on age, sex). RNA was extracted using the Tempus Spin RNA Isolation Kit. miR-21-5p was validated using droplet digital PCR (ddPCR). Serum IL-17, CXCL10, IL-23, TGFB1 were measured by commercially available ELISA kits. Mann- Whitney test, Wilcoxon signed rank test and Spearman correlations were performed.

Results: The expression of miR-21-5p was significantly higher in converters compared to non-convertors (Fold change(FC)=2.16, p=0.002). miR-21-5p was upregulated in PsA compared to PsC (FC=3.22, p=0.001) and HC (FC=15.7, p=0.0001) in the validation cohort. miR-21-5p was significantly down regulated 24 weeks post-MTX treatment in 30 PsA patients (FC=-1.9, p=0.008), which correlated with swollen (r=-0.49, p=0.003) and tender joint counts (r=-0.41, p=0.02) supporting a possible role in inflammation pathway in PsA patients. IL-17 levels in PsA & PsC were significantly higher from HC (p<0.03), but not different between PsA & PsC.

Conclusions: our results suggests a role of miR-21-5p as a potential biomarker for PsA. In the presence of upregulated miR-21-5p, IL-17 and IL-23 are upregulated while TGFB1 is down regulated. When miR-21-5p is decreased IL-17 and IL-23 downregulated, with up regulation of TGFB1. We have thus determined the role of miR21-5p as a potential biomarker for inflammation pathway in psoriatic disease and response to MTX possibly through modulation of CXCL10 and IL-17/IL-23 axis.

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ANALYSIS OF BLOOD MONOCYTE TRANSCRIPTOMES INNATE VERSUS ADAPTIVE IL-17A PRODUCING CELLS

into blood. Bone marrow analysis shows a left shifted granulopoiesis in late myelopoiesis and G-CSF triggered mobilisation from bone marrow. These transcripts suggested alterations in mitochondrial activity, peptide binding, and TLRs.

Conclusion: AxSpA monocyte transcriptomes reflect weak immune activation vs. CO facet joints (p<0.01). Of MPO+ cells indicative of left shifted granulopoiesis was found in AS patients and controls regarding gene expression profile of neutrophils, CD8+ T cells and 2 adaptive cell populations (CD4+ T and CD8+ T) after cell stimulation by PMA + A23187 (calcium ionophore) and CD8+T after cell stimulation by PMA + A23187 (calcium ionophore). Published literature suggests the involvement of MAIT, γδ T, and neutrophils as IL-17A producing cells in AxSpA (1–3). However, even though they may be responsible for IL-17A-mediated inflammation, it is still unclear which is the major IL-17A-producing cell population in this disease.

Objectives: To assess and compare gene expression profiles of neutrophils, MAIT, γδ, CD4+ and CD8+ T cells from AxSpA patients.

Methods: We recruited 5 healthy donors and 10 patients with a diagnosis of AxSpA according to the ASAS criteria. We compared the gene expression profiles of 5 sorted cell populations: 3 innate cell populations (neutrophils, MAIT and γδ T cells) and 2 adaptive cell populations (CD4+T and CD8+T) after cell stimulation by PMA + A23187 (calcium ionophore) + β1,3 glucan (extracted from Aspergillus fumigatus hyphae). Published data suggested that neutrophils stimulation by Aspergillus fumigatus induces IL-17A production by these cells(4). For each of these cell populations, cytokine production and the expression of a panel of 755 genes (Autoimmune discovery panel from Nanostring including 43 genes for T cells) and 2 adaptive cell populations (CD4+T and CD8+T) were compared by a multigroup comparison. Results: There was no significant difference between patients and controls regarding gene expression profile of neutrophils, γδ T, CD4+T and CD8+T. We observed that 34 genes were differentially expressed between patients and controls in MAIT cells (p = 0.03, q = 0.1). In particular, T cell activation genes (TBX21, AHR, ZAP70) and cell interaction genes (ITGAV6, CNTNWB1, ICAM2, ITGB2, SEL1) were decreased in patients. Among AxSpA patients, MAIT cells were those significantly showing the highest level of IL-17A expression. IL23R and RORC were also more expressed by MAIT compared to others cell populations. IL-17A expression was very low in neutrophils but we observed that 18 out of the 43 AS associated genes were mainly expressed by neutrophils (p
<0.05, q = 0.02), supporting the idea that they should be involved in the pathophysiology of the disease.

Conclusion: These preliminary data confirm that the innate immune cells do not appear to participate in the production of IL-17A, but the high expression of AS linked genes in these cells suggests their involvement in AxSpA.

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Disclosure of Interests: nicolas rosine: None declared, Surya Koturan: None declared. Al Mossawi Hussein, Paul Bowness.

FR10363 AUTOANTIBODIES TO THREE NOVEL PEPTIDES IN EARLY AXIAL SPONDYLOARTHROPATHY IN TWO INDEPENDENT COHORTS

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Background: Diagnosis of axial spondyloarthritis (axSpA) is challenging since clinical manifestations, such as inflammatory back pain, peripheral arthritis, enthesitis and inflammatory bowel disease, often overlap with other disorders. Current laboratory markers for axSpA, Human Leukocyte Antigen (HLA)-B27 and C-reactive protein (CRP) are not sufficiently specific for diagnosis. Despite being considered a “seronegative” disease, emerging evidence supports the involvement of antibodies in axSpA.

Antigen (HLA)-B27 and C-reactive protein (CRP) are not sufficiently specific for diagnosis. Despite being considered a “seronegative” disease, emerging evidence supports the involvement of antibodies in axSpA. Therefore, we investigated the potential of autoantibodies in axSpA patients to establish a novel classification tool for diagnosis.

Methods: Using enzyme-linked immunosorbent assays (ELISA), presence of antibodies to the 9 novel UH axSpA peptides in axSpA patients and controls from 2 independent cohorts.

Results: Antibody reactivity against at least one of 9 novel UH axSpA peptides was found in 54% (41/76) of early axSpA patients, 26% (24/94) of LBP, 60 early rheumatoid arthritis patients (RA) and 94 healthy controls (HC).

Conclusion: Antibodies to 3 UH axSpA peptides were significantly more prevalent in early axSpA patients compared to controls. The latter group showed a specificity of 95% and a positive likelihood ratio of 2.7, which is the same as for the currently used laboratory marker CRP. Assuming a 5% pretest probability of axSpA, the LR+ for confirming axSpA using antibodies to these 3 UH axSpA peptides was 2.7, which is the same as for the currently used laboratory marker CRP. Assuming a 5% pretest probability of axSpA, the LR+ for confirming axSpA using antibodies to these 3 UH axSpA peptides was 2.7, which is the same as for the currently used laboratory marker CRP. Assuming a 5% pretest probability of axSpA, the LR+ for confirming axSpA using antibodies to these 3 UH axSpA peptides was 2.7, which is the same as for the currently used laboratory marker CRP.
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FRI0364 T REGULATORY CELLS AS BIOMARKER OF DISEASE ACTIVITY AND RESPONSE IN PSORIATIC ARTHRITIS PATIENTS: RESULTS FROM APREMILAST-TREATED COHORT

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Background: The PDE4-inhibitor apremilast has been recently introduced in the treatment of Psoriatic Arthritis (PsA). It acts by down-regulating intracellular inflammatory mediators synthesis by elevating cAMP levels. Tregs, a subset of FOXP3+ CD4 T cells, play a key role in preventing immune responses and could exert their suppressive function via cAMP (1). Reduced frequencies of circulating Tregs have been observed in inflammatory disorders, nonetheless very few data are available on PsA patients.

Objectives: We evaluated peripheral Tregs in a cohort of PsA patients treated by apremilast.

Methods: Seventeen PsA patients (M/F 3/14; median age 56.0 years, IQR 20.0; median disease duration 15.0 years, IQR 11.0) with polyarticular PsA were enrolled, without active inflammation. Tregs were assessed at baseline in comparison with non-responder patients (median 4.8, IQR 1.2 versus median 2.9, IQR 1.1; P=0.02).

Conclusion: The results of our study demonstrate that%Treg is a marker of disease activity in PsA patients. Moreover, the baseline value of Tregs could predict the response to apremilast after 12 weeks of treatment.


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FRI0365 PDE4 TARGETING SELECTIVELY INHIBITS INFLAMMATORY-DRIVEN OSTEOCLASTOGENESIS

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Background: Patients suffering from Psoriatic arthritis (PsA) commonly develop bone erosions and inflammatory-induced bone loss. This process is mediated by osteoclasts derived from monocyctic precursors, and modulated by inflammatory cytokines (i.e. TNF, IL-1, IL-6, IL-17, IL-10 and GM-CSF) from immune and stromal cells. In immune cells (including CD14+ osteoclast pre-cursors), PDE4, an enzyme responsible for hydrolysing cyclic AMP to inactive AMP, drives inflammatory effects [1]. Importantly, Apremilast (APR, a selective PDE4 inhibitor) has known efficacy in PsA [2], and decreases pro-inflammatory mediators whilst increasing anti-inflammatory mediators (IL-10) [3]. Although published data indirectly suggest a positive impact of APR on bone in PsA, data is lacking with regards to the impact on bone disease activity in PsA patients.

Objectives: To evaluate the impact of a selective inhibition of PDE4 by APR on osteoclastogenesis from human CD14+ precursors.

Methods: Osteoclasts were differentiated from primary human CD14+ blood monocytes (healthy controls) with RANKL and MCSF, in the presence or absence of APR. To specifically study the impact of APR on osteoclastogenesis in an inflammatory context, osteoclastogenesis was also undertaken in the presence of: (i) TNF, (ii) Supernatants from activated Peripheral Blood Mononuclear Cells (PBMC) or activated CD3+ T cells, treated with or without APR, (iii) Co-culture with activated PBMC or activated CD3+ T cells, treated with or without APR, APR+ multinucleated cells (mature osteoclasts) were enumerated via microscopy.

Results: In a non-inflammatory context, PDE4 inhibition by APR did not affect the differentiation of CD14+ precursors into mature osteoclasts. However, TNF-enhanced osteoclastogenesis was significantly decreased by APR (>-30.0% +/- 14.9; p=0.0279). The treatment of either activated PBMCs or purified CD3+ T cells with APR substantially reduced cellular activation. In PBMCs this decrease in cellular activation resulted in a decrease in conditioned media-driven osteoclastogenesis (-49.7% +/- 13.2; p=0.0385). In comparison, APR treatment of purified CD3+ T cells did not reduce their osteoclastogenenic potential.

Conclusion: The results of this study reveal that PDE4 targeting potently inhibits inflammatory-driven osteoclastogenesis. Moreover, these data also suggest that CD3+ T cells are not the main target of PDE4 inhibition in this context. In summation, our study supports the hypothesis that APR can modulate bone integrity in inflammatory condition such as PsA.

REFERENCES:

Disclosure of Interests: YD received a fellowship from the Société Française de Rhumatologie

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Background: The hallmark of advanced axial spondyloarthropathy (SpA) is spine ankylosis, due to an excess of bone formation. Our hypothesis was that pathways of bone formation regulators changed over time and that their changes were related to inflammation or use of “anti-inflammatory” drugs (like non-steroidal anti-inflammatory drugs (NSAIDs) and/or Tumor Necrosis Factor inhibitors (TNFi)).

Objectives: This prospective study aimed to describe the 5-year serum changes of bone formation regulators markers (sclerostin, bone morphogenic protein 7 (BMP-7) and Dickkopf-1 (DKK-1)) in early axial SpA.

Methods: The DESIR cohort is a prospective, multicentre French study of 708 patients (34 ± 9 years, 58% HLA B27 positive, BASDAI 45 ± 20) with early (> 3 months and < 3 years) inflammatory back pain suggestive of axial SpA. Sclerostin, BMP-7 and DKK-1 serum levels were assessed at baseline, two and five years. Change in bone formation regulators over time was analysed using mixed linear models, first in complete-cases and then in available-cases analysis. Determinants of serum biomarkers change were analysed using mixed linear models and we searched for an interaction between time and determinants of serum biomarkers.

Results: Serum levels of each biomarkers at baseline, two and five years are reported in Table 1. Serum BMP-7 significantly increased over time, with a mean of 0.17 pg/mL per month (Figure 1A). Median relative change of BMP-7 at five years was 53.0% (IQR -31.6%, 286.8%). Serum BMP-7 levels was undetectable in 337 patients (59.6%) at baseline, in 111 patients (48.0%) at two years and in 59 patients (20.2%) at five years. At baseline, serum sclerostin was significantly correlated with age (r = 0.28, p < 0.001), weight (kg) (r = 0.10, p = 0.007), CRP level (mg/mL) (rS = -0.14, p < 0.001), mSASSS (r = 0.08, p = 0.03), number of syndesmophytes (r = 0.15, p < 0.001), bone mineral density in hip and lumbar spine (r = 0.19, p = 0.001 and r = 0.18, p = 0.001 respectively).

Conclusion: Serum BMP-7 levels significantly increased over time with a rapid and substantial change. Serum sclerostin levels significantly increased over time decrease with the duration of TNFi use (-0.04 per month of TNFi use, p < 0.001). Unlike in serum BMP-7, serum sclerostin significantly increased over time, with a mean of 0.001 ng/mL per month (Figure 1B). Median relative change of sclerostin at five years was 14.8% [7.9%, 41.4%]. Serum DKK-1 did not significantly vary over time. In multivariate analysis, serum BMP-7 increased with moderate or high disease activity (ASDAS-CRP) (0.19 pg/mL per month, p = 0.01), in men (5.3 pg/mL, p = 0.004) and decreased with the duration of TNFi use (-0.04 per month of TNFi use, p < 0.001). Unlike in serum BMP-7, there was not a significant interaction between time and determinants of serum sclerostin. In multivariate analysis, serum sclerostin increased with time (0.001 ng/mL per month, p < 0.001), age (0.007 ng/mL per year, p < 0.001) and in men (0.05 ng/mL, p = 0.001) but decreased with the use of TNFi (-0.037 ng/mL, p < 0.001), in patients with a Z score ≤-2 at least one site (-0.036 ng/mL, p = 0.005) and with serum BMP-7 levels (<0.0006 ng/mL per unit of serum BMP-7, p = 0.03).
contain significantly more IgD^+CD95^- germinal center B cells (P < 0.01) with a higher expression of the costimulatory molecules CD80 and CD86 compared to WT. The vertebral also contained more CXCXR5/PD-1^+/FoxP3^+/CTLA4^+ T regulatory cells and a trend towards an increase in CXCXR5/PD-1^+/FoxP3^+/CTLA4^+ T follicular helper cells in tmtNFg tg mice. Meanwhile, B cell development in the BM of tmtNFg tg hind limbs was not altered. Furthermore, BM, spleen and vertebrae from tmtNFg tg mice contained significantly more IgA^+ plasma cells compared to WT littermates. Of note, tmtNFg tgFoxP3^+/- mice did not display lymphoid aggregates or HEVs in the BM, while tmtNFg tgFoxP3^+/- mice did, although to a lesser extent than tmtNFg tg mice.

Conclusion: tmtNFg overexpression in mice results in extensive lymphoid aggregates in the BM that are often organized in ELs, which may be mediated via TNF-RI signaling. These ELs might result in an increase of IgA^+ plasma cells in tmtNFg tg mice. Ongoing studies will look further into this and may indicate whether these findings contribute to the pathology observed in these mice.

REFERENCE:

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**FRI0368**

**VASCULAR CALCIFICATION BY INFLAMMATION COULD BE AN IMPORTANT CAUSE OF CARDIOVASCULAR DISEASE IN PATIENTS WITH ANKYLOSING SPONDYLITIS**

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Background: Patients with ankylosing spondylitis (AS) have a higher risk of cardiovascular disease. Atherosclerosis is a main pathological process of cardiovascular disease and calcified plaque is a characteristic feature of atherosclerosis. Inflammation plays a potential role in vascular calcification. There is no previous study revealing the mechanism of vascular calcification in AS.

Objectives: We investigated the relationship between vascular calcification and inflammation in patients with AS.

Methods: Sixteen male patients aged over 20 years with AS were enrolled. They fulfilled the modified New York criteria and each of their ankylosing spondylitis disease activity score was more than 2.1. Sex and age matched non-healthy controls were also recruited. Mouse MOVAS (American Type Culture Collection, ATCC®, CRL-2797TM) vascular smooth muscle cells were stabilized in maintenance medium for 24 hours. Then the amount of serum equivalent to 10% of maintenance medium from subjects was added and cells were stimulated for another 72 hours. We exchanged this medium with calcification medium every third day and cells were cultured for another 11 days. After 2 weeks, cells were stained with Alizarin Red S and the optical density (OD) was measured while being compensated by cell viability. For Western blotting, cells were stabilized for 24 hours and stimulated for another 72 hours through the same procedure as that of Alizarin Red S staining. Then we measured the level of protein expression in PPAR-gamma, beta-catenin, TNF-a, interleukin (IL)-23, and MMP7.

Results: The level of OD of MOVAS cells treated with serum from AS patients (19.503 ± 6.422, mean ± SD) was significantly higher than that from controls (12.724 ± 5.746) (P = 0.027, Mann-Whitney test). The level of MMP7 expression of MOVAS cells treated with serum from AS patients (1.921 ± 0.702) was significantly higher than that from controls (0.779 ± 0.191) (P = 0.000, Mann-Whitney test). The level of beta-catenin expression of MOVAS cells treated with serum from AS patients (1.292 ± 0.356) was significantly higher than that from controls (0.887 ± 0.310) (P = 0.005). There was negative correlation between PPAR-gamma and TNF-a (rho = -0.762, p = 0.028, Spearman rank correlation coefficient), and between PPAR-gamma and IL-23 (rho = -0.601, p = 0.039); positive correlation between MMP7 and TNF-a (rho = 0.833, p = 0.010), and between MMP7 and IL-23 (rho = 0.797, p = 0.002).

Conclusion: Serum from AS patients showed increased calcification of vascular smooth muscle cells than serum from controls. The level of vascular calcification marker from vascular smooth muscle cells treated with serum from AS patients was significantly higher than that from controls. There were negative relationship between inflammatory markers and inhibitor marker of vascular calcification but positive relationship between inflammatory markers and stimulatory marker of vascular calcification.

These findings suggest that vascular calcification by inflammation could be an important cause of cardiovascular disease in AS patients.

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**FRI0369**

**TOWARDS MORE PRECISE ESTIMATES OF THE FAMILIAL AGGREGATION AND HERITABILITY OF ANKYLOSING SPONDYLITIS – A SWEDISH NESTED CASE-CONTROL STUDY**

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Background: Ankylosing spondylitis (AS) is known to have strong familial aggregation, but studies quantifying the familial risk are few and have reached varying results. Familial risks reported from population-based studies range from 17 to 94 in first-degree relatives of AS cases.1 2 The heritability (i.e., the proportion of variance in AS liability explained by genetic variation) has been reported to >90%, based on very small studies of twins.3

Objectives: To assess the familial aggregation and heritability of AS among all Swedish AS patients, and to investigate if risks vary by type of first-degree relative or sex.

Methods: We identified all patients with an ICD-10 code of AS in the Swedish National Patient Register (NPR) between 1 January 2001 and 31 December 2016. To increase validity, index patients were required to have two or more visits listing an AS diagnosis, and at least one of the visits being to a specialist in rheumatology or internal medicine. Each index patient was matched on sex and birth year to 50 general population controls from the Total Population Register. First-degree relatives of index patients and controls were identified through the Multi-generation register. Their disease status was ascertained from the NPR in a similar manner as for index patients. Familial risks of AS among first-degree relatives were calculated as odds ratios (ORs) with conditional logistic regression. Based on the familial risks, the corresponding heritability was calculated for a range of plausible prevalence estimates.

Results: We identified 13,795 patients that met the inclusion criteria. Of their siblings, parents, and children, 3.6, 2.3, and 2.1%, respectively also had AS. The overall familial OR when having one affected relative was 19.4 (95% CI 18.1-20.8). The estimates were similar for relatives of different kinds (see table), but having more than one affected relative resulted in a higher risk (OR 68.0 (95% CI 51.3-90.1)). Heritability, estimated from sibling risk, was 77%. There were no clear-cut differences between the sexes, but women tended to have an elevated familial risk if the affected relative was female, and slightly lower heritability compared to males. These estimates can be considered as an upper limit of heritability, as shared environmental factors have not been taken into account in calculations.

Conclusion: Familial risks of AS were similar between different types of first-degree relatives, and no significant gender difference was seen on the heritability scale. Although high compared to most other diseases, the familial risks and heritability were lower than previous reports from other countries, though in line with earlier Swedish findings using in part the same data source. The heritability proposed here might still be an over-estimate of the true influence of genetics on disease risk. Thus, efforts should also be directed at identifying other risk factors for AS that are not of genetic origin.

REFERENCES:
**Background:** With our increasing understanding of cross-talk between the immune system (immune cells, cytokines) and extracellular matrix (ECM) of the affected tissues, ECM destruction and turnover has gained a lot of attention in inflammatory arthritis. ECM mainly consists of interstitial matrix (rich in type I and III collagens) and basement membrane (mainly composed of type IV collagen), both of which are affected in inflammatory arthritis. We hypothesize that inflammatory milieu in Psoriatic Arthritis (PsA) leads to accelerated ECM destruction and remodeling, and the release of ECM metabolites into circulation, that can be measured in serum as biomarkers of tissue remodeling and may give insight to pathologic processes at the tissue level.

**Objectives:** This prospective study aimed to use serological biomarkers for evaluation of the extent of damage to, and changes in turnover of ECM in patients with PsA and to investigate their relation to inflammatory biomarkers and disease activity.

**Methods:** Patients with PsA (n=145) fulfilling the CASPAR criteria and above 18 years of age with any disease activity were recruited through outpatient department in Aalborg University Hospital, Denmark. Exclusion criteria were pregnancy, treatment with biological DMARD, or with oral corticosteroids and other comorbidities. Clinical disease parameters were recorded, and blood samples were collected at baseline and 24 weeks follow-up. Inflammation-related ECM remodeling was measured by serological biomarkers of type I, III and IV collagen formation (Pro-C1, Pro-C3 and Pro-C4, respectively) and MMP-mediated degradation (C1M, C3M and C4M respectively). The chronic inflammation was measured by CRP (MMP degraded metabolite of CRP). All biomarkers were measured by competitive ELISAs and levels were compared to the reference levels of healthy individuals. The biomarker data was log2 transformed for normalization and standard parametric statistical methods were applied.

**Results:** We found that there was an increase in the degradation of interstitial matrix (represented by C1M and C3M) which was uncompensated with either decreased (Pro-C1) or unaltered (Pro-C4) formation in patients with PsA as compared to healthy individuals. On the contrary, there was a compensated increase in basement membrane remodeling in patients with PsA as represented by increase in both C4M and Pro-C4 in comparison to healthy individuals (Table 1). Interestingly, there was a strong correlation between baseline C4M and Pro-C4 (r=0.703, p<0.0001), and 24-week changes in both biomarkers (r=0.468, p<0.0001) pointing towards coupling between the two processes which was either lost or was weak in cases of interstitial collagens. As baseline values and changes in C1M, C3M, C4M and Pro-C4 showed a strong correlation with changes in inflammatory biomarkers, we believe that ECM remodeling in PsA is, at least partly, driven by inflammation. Furthermore, baseline values and changes in these ECM turnover biomarkers correlated positively with changes in composite disease activity scores (Table 2) that may indicate their clinical importance as potential diagnostic or disease activity markers.

**Conclusion:** Chronic inflammation underlying PsA pathology results in an increased amount of ECM turnover that correlates with clinical progression and can be measured by serological biomarkers.

**REFERENCES:**

None

**Disclosure of Interests:** Samra Sardar Employee of: I am a full time employee at Nordic Bioscience, Salome Kristensen: None declared, Anne Sofie Siebhuhr Employee of: I am a full-time employee in Nordic Bioscience, Jeppe Christensen: None declared, Morten Karsdal Shareholder of: I am a full time employee at Nordic Bioscience, Jeppe Christensen: None declared, Anne Christine Bay-Jensen Shareholder of: I own shares of Nordic Bioscience, Employee of: I am a full-time employee in Nordic Bioscience, Morten Karsdal Shareholder of: I own shares of Nordic Bioscience, Employee of: I am a full-time employee in Nordic Bioscience, Annette Mortensen: None declared, Anne Sofie Siebhuhr: None declared, Anne Christine Bay-Jensen: None declared, Anne Christine Bay-Jensen: Employee of: I am a full-time employee at Nordic Bioscience, Morten Karsdal: Shareholder of: I am a full time employee at Nordic Bioscience, Jeppe Christensen: None declared, Salome Kristensen: None declared, Anne Sofie Siebhuhr: Employee of: I am a full-time employee in Nordic Bioscience, Anne Christine Bay-Jensen: Employee of: I am a full-time employee in Nordic Bioscience.


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**Table 1.** Comparison of ECM turnover biomarkers in PsA patients (at baseline) and healthy individuals

<table>
<thead>
<tr>
<th>Biomarkers (ng/ml)</th>
<th>PsA patients</th>
<th>Reference values</th>
<th>Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>Mean</td>
<td>SD</td>
<td>n</td>
</tr>
<tr>
<td>C1M</td>
<td>10.90±3.18</td>
<td>145</td>
<td>24.8±10.84</td>
</tr>
<tr>
<td>C2M</td>
<td>9.69±2.59</td>
<td>145</td>
<td>12.2±3.56</td>
</tr>
<tr>
<td>C3M</td>
<td>34.5±6.45</td>
<td>145</td>
<td>34.3±6.54</td>
</tr>
<tr>
<td>Pro-C1</td>
<td>39.29±8.85</td>
<td>145</td>
<td>354.7±54.37</td>
</tr>
<tr>
<td>Pro-C3</td>
<td>11.49±3.56</td>
<td>145</td>
<td>11.28±3.56</td>
</tr>
<tr>
<td>Pro-C4</td>
<td>109.07±30.17</td>
<td>145</td>
<td>384.83±85.54</td>
</tr>
</tbody>
</table>

**References:**

1. Clinical and laboratory characteristics of the three groups (Table 1)
Background: Disease-modifying anti-rheumatic drugs (DMARDs) are introduced for the treatment of spondyloarthritis (SpA) after failure of non-steroidal anti-inflammatory drugs (NSAIDs). In Finland, try out with a conventional synthetic DMARD (csDMARD) is required before initiation of biologics (bDMARD). The patients with DMARDs are eligible for a higher reimbursement for the cost of medication. Opioids are not recommended for arthritis pain.

Objectives: To report the current DMARD and pain medication use among newly-onset SpA patients in Finland.

Methods: From the nationwide reimbursement register maintained by the Social Insurance Institution of Finland we collected all incident adult patients with SpA (ICD-10 codes M45-46) between 2010-14 and divided them into two groups depending on whether bDMARDs were subsequently initiated (group B) or not (group A). Patients’ drug purchases between 2009-15 were obtained from the Drug Purchase Register. Opioid use by these patients was evaluated one year before and after the index date (ID; the date when special reimbursement for antirheumatic drugs use by these patients was evaluated one year before and after the index date). We identified 3577 SpA patients, 23% of which started a self-injected bDMARD during the observation period. More of the patients in group B needed pain medication, prednisolone, methotrexate, or other csDMARDs than sulphasalazine, which was more frequent in group A (table 1).

Conclusion: Altered expression of IncRNA-NR_003542 and NR_026756 in peripheral blood of AS patients might be involved in the pathogenesis of AS, higher expression of IncRNA-NR_003542 and lower expression of NR_026756 might be as the biomarkers for the disease activity of AS, further study would be needed to expound on the exact role of the two IncRNAs in AS.

REFERENCES:

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Spondyloarthritis – treatment

Table 1. Clinical and laboratory characteristics of subjects studied

<table>
<thead>
<tr>
<th></th>
<th>AAS(n=30)</th>
<th>ASB(n=30)</th>
<th>HC(n=30)</th>
<th>P value</th>
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<tr>
<td>Gender, F/M</td>
<td>8/22</td>
<td>10/22</td>
<td>10/20</td>
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<tr>
<td>Age, mean±SD (years)</td>
<td>36.23±10.86</td>
<td>33.47±10.42</td>
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<td>Disease duration, mean±SD(years)</td>
<td>9.55±6.34</td>
<td>7.81±6.55</td>
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<td>Family history positive/total (%)</td>
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<td>2/30(6.67%)</td>
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<td>BASDAI, mean±SD</td>
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<td>2.24±1.31</td>
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<td>BASFI, mean±SD</td>
<td>3.2±2.34</td>
<td>0.74±0.99</td>
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<td>Uveitis, positive/total (%)</td>
<td>6/30(20%)</td>
<td>3/30(10%)</td>
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<td>CT grading of sacroiliac arthritis,</td>
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<td>12/14/4</td>
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<td>IV/IV</td>
<td>29/30(96.67%)</td>
<td>25/30(83.33%)</td>
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<td>ESR, mean±SD (mm/h)</td>
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<td>15.63±12.75</td>
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<td>hsCRP, mean±SD (mg/L)</td>
<td>36.6±31.14</td>
<td>5.9±5.54</td>
<td>1.09±2.11</td>
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<tr>
<td>WBC, mean±SD (10⁹*/L)</td>
<td>7.99±1.62</td>
<td>6.98±1.81</td>
<td>5.9±1.09</td>
<td>0.028</td>
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<td>WBC, mean±SD (10⁹*/L)</td>
<td>40.3±6.08</td>
<td>33.44±3.93</td>
<td>32.85±5.95</td>
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</table>

Figure 1. Expression of IncRNA-NR_003542 and NR_026756 among three groups

Figure 2. Correlations between levels of two IncRNAs expression and clinical data in AS patients

Conclusion: Altered expression of IncRNA-NR_003542 and NR_026756 in peripheral blood of AS patients might be involved in the pathogenesis of AS, higher expression of IncRNA-NR_003542 and lower expression of NR_026756 might be as the biomarkers for the disease activity of AS, further study would be needed to expound on the exact role of the two IncRNAs in AS.
Disclosure of Interests: Paula Mulli Grant/research support from: I have received a Congress trip from UCB Pharma and a Congress trip from MSD Finland outside the submitted work. Speakers bureau: Dr Rantalaiho reports a speaker’s honorarium from Pfizer. Hannu Kauhalainen: None declared, Lauri Virta: None declared, Kari Puolakkia: None declared DOI: 10.1136/annrheumdis-2019-eular.1138

5-YEARS TREATMENT EFFECT OF TNF ALPHA INHIBITOR IN EARLY AXIAL SPONDYLOARTHRITIS AND ASSOCIATED FACTORS: AN INVERSE PROBABILITY WEIGHTING ANALYSIS OF THE DESIR COHORT

Marion Pons 1,2, Sylvie Chevreau 2, Karine Briot 1,2, Maria-Antonietta D’Agostino 3, Christian Roux 1,2, Maxime Dougas1,2, Anna Molto 3,1, University Paris Descartes, Cochin Hospital, Rheumatology, Paris, France; INSERM U-1153, CREPS Paris-Sorbonne, Paris, France; Ambroise-Pare Hospital, Rheumatology, Biostatistics, Boulogne-Billancourt, France

Background: Only scarce data is available on the long-term treatment effect in a real-life setting (i.e. effectiveness) of TNFi in early axial SpA forms and its predisposing associated factors; furthermore, unbiased evaluation of treatment effect in non-randomized clinical trials is challenging, and new methods have been developed to overcome prescription bias. Objectives: a) to estimate the probability to initiate a TNFi over 5 years of follow up in real life setting using novel statistical methods to overcome prescription bias; b) to determine the long-term effectiveness of first TNFi and its predictive factors.

Methods: Observational prospective French cohort (DESIR) with 5 years of follow-up, including 708 TNFi-naive patients early axial spondyloarthrits. Study visits were scheduled every 6 months in the first two years of follow up then yearly up to 5 years. Treatment (TNFi or other) was at the discretion of the treating rheumatologist(s). The probability to initiate a TNFi was estimated by the Kaplan Meier Method, assuming non informative dropouts. Effectiveness of the first TNFi was defined as the probability to reach an ASAS40 response in both groups (TNFi vs. any other treatment) after at least 10months of exposure. To evaluate treatment effect and overcome prescription bias repeatedly occurring over time, we have applied an iterative method based on inverse propensity score (PS) weighting using a marginal structural model, that allows the integration of the repeated weights derived from the propensity score at each visit (i.e. the probability to receive the treatment at each visit). The structural model used for this analysis was a PS-weighted cox regression, to estimate the probability to present an ASAS40 response after at least 10 months of treatment. Factors predicting first TNFi effectiveness, were explored by Cox (univariate and then multivariate) regression models.

Results: Of the 708 patients included in the analysis, 258 patients initiated a first TNFi during the first five years of follow up. The probability to initiate a TNFi treatment was 41.3% [95%CI 37.2-45.1]. Among the 258 patients who received a first TNFi, 163 (63.2%) were exposed for at least 10 months. On the original data, ASAS40 response was observed in 50/163(30.7%) vs. 58/450(12.9%) patients from the TNFi and usual care groups, respectively. The likelihood of an ASAS40 response was greater in the TNFi exposed group (HR= 3.2[95%CI 2.9-3.8], p <0.0001). Male gender (HR=1.59[95%CI 1.1-2.1]), HLA B27 (HR= 1.4 [95%CI 1.1-2.0]) and the presence of at least one objective sign of inflammation (MRI or CRP) or structural damage (radiographic sacroiliitis) (HR= 1.7 [95%CI 1.2-2.4]) were both predictive of an improved outcome.

Disclosure of Interests: Marion Pons: None declared, Sylvie Chevreau: None declared, Karine Briot Consultant for: Karine Briot has received consultancy honoraria and conference fees from UCB, Amgen, Lilly and MSD, Maria-Antonietta D’Agostino: None declared, Christian Roux Grant/ research support from: Alexion, Amgen, UCB, maxime dougados Grant/ research support from: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma, Consultant for: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma, Anna Molto: None declared DOI: 10.1136/annrheumdis-2019-eular.3518

THE RISK OF INFECTION BY TUMOR NECROSIS FACTOR INHIBITORS AND ITS ASSOCIATED FACTORS IN PATIENTS WITH ANKYLOSING SPONDYLITIS: RESULT FROM KOREAN NATIONAL HEALTH INSURANCE DATA

Bong-San Kang 1, Yu-Ched Lim 2, Min-Young Lee 3, Ja-Yeon Jeon 3, Hyun-Jeong Yoo 1, In-Sun Oh 3, Ju-Yong Shin 2, Eui-Kyung Lee 3, Tae-Hwan Kim 2, University Seoul Paik Hospital, Inje University College of Medicine, Department of Internal Medicine, Seoul, Korea, Rep. of (South Korea); Sungkyunkwan University School of Pharmacy, Suseo, Korea, Rep. of (South Korea); Alpaca, Sheung, Korea, Rep. of (South Korea); Pfizer Inc, Seoul, Korea, Rep. of (South Korea); Hanyang University Hospital for Rheumatic Diseases, Department of Rheumatology, Seoul, Korea, Rep. of (South Korea)

Background: Tumor necrosis factor inhibitors (TNFi) are effective in patients who do not respond to non-steroidal anti-inflammatory drugs, or disease modifying anti-rheumatic drugs, and have been widely used in patients with ankylosing spondylitis (AS). However, there is some evidence that treatment with TNFi can increase the risk of infection in patients with AS.

Objectives: The aim of this study was to investigate the risk of infection in patients with AS treated with TNFi.

Methods: Data was obtained from insurance claims database of the Health Insurance Review & Assessment Service (HIRA) in South Korea. Patients who have been prescribed a TNFi such as etanercept (ETN), adalimumab (ADA), golimumab (GLM), and infliximab (IFX) to treat AS from 1 January 2012 to 30 June 2017 were enrolled. We evaluated the incidence rate (IR) and hazard ratio (HR) of serious infections including pneumonia, tuberculosis, and herpes zoster in each TNFi treatment group by using cox proportional hazard model. We further analyzed the HR of infection by sex.

Results: A total of 2,515 patients were included in the study, and they were prescribed ETN (n=526), ADA (n=914), GLM (n=628), or IFX (n=447). The IRs of serious infection were 1.66/100, 1.49/100, 1.58/100, and 1.39/100 per 1,000 person years (py) in ETN, ADA, GLM, and IFX treated groups, respectively. There was no significant difference in HR of serious infection between the TNFi groups. In the subgroup analysis of major infections, there was no difference in the HR of pneumonia between TNFi groups. However, the HR of tuberculosis with IFX group was significantly higher than that with ETN (adjusted HR 8.95, 95% CI: 1.12-71.4). In herpes zoster infection, there was no difference between TNFi groups in all patients, but the adjusted HRs significantly increased with GLM (adjusted HR 15.40, 95% CI: 6.4-144.34) and IFX (adjusted HR 10.02, 95% CI: 1.12-89.9) treatment as compared to ETN in female patients.

Conclusion: Patients receiving IFX had a higher risk of contracting tuberculosis than those receiving ETN. Moreover, the risk of herpes zoster was higher in female patients treated with GLM and IFX than in those treated with ETN in Korea.

REFERENCES:


Acknowledgment: Study sponsored by Pfizer Inc.

Disclosure of Interests: Bon San Koo Grant/research support from: Pfizer, Yu-Ched Lim: None declared, Min-Young Lee: None declared, Ja-Young Jeon Employee of: Pfizer, Hyun-Jeong Yoo Employee of: Pfizer, In-Sun Oh: None declared, Ju-Young Shin: None declared, Eui-Kyung Lee Grant/ research support from: Pfizer, Tae-hwan Kim: None declared


FRIO375 SITE-SPECIFIC EFFECTIVENESS OF TNF INHIBITORS FOR ENTHESITIS IN DMARD-NAIVE PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: Enthesitis is a hallmark of spondyloarthritis (SpA), with substantial impact on quality of life. Although pathophysiological mechanisms of enthesitis may include both mechanical and autoimmune features, improvements upon initiation of TNF-inhibitors (TNFi) across individual enthesis sites have not been reported in real-world patients with axial spondyloarthritis (axSpA).

Objectives: To investigate the effectiveness of TNFi in axSpA patients without prior DMARD treatment at specific enthesis sites, including spine, thoracic cage, Achilles tendon and the plantar fascia.

Methods: This was a retrospective cohort study using the Swiss Clinical Quality Management in Rheumatic Diseases (SCQM) registry. AxSpA patients initiating TNFi without previous DMARD (biologic or conventional synthetic DMARD [csDMARD]) use and with available Maastricht Ankylo- spondylitis Enthesitis Score (modified to include the plantar fascia, and the Achilles tendon. Plantar fascia, and the Achilles tendon.

Results: 781 DMARD-naive patients with axSpA who initiated TNFi were identified. At baseline, patients (57% male) were a median of 40 (interquartile range [IQR] = 31-50) years of age with a median disease duration of 9 (IQR = 3-18) years and mean Ankylosing Spondylitis Disease Activity Score (ASDAS-CRP) of 3.4 (IQR = 2.8-3.9) at treatment initiation. A subgroup of 160 TNFi patients had active enthesitis at baseline (MASES: mean = 4.14, standard deviation [sd] = 2.87) and a 6-month follow-up visit available (MASES: mean = 2.07, sd = 2.82). At the 6-month follow-up, complete enthesitis resolution was observed for 72 (45%) of patients. Enthesitis resolution rate was the most frequent among the following sites: the costochondral sternalum, the costochondral joint, the lumbar vertebra, the pelvic crest, and the iliac crest posterior (Figure 1). Limited resolution of enthesitis was observed in the spine iliacus anterior, plantar fascia, and the Achilles tendon.

Conclusion: Our results suggest that for real-world DMARD-naive axSpA patients, TNFi are generally effective for resolving enthesitis. Significant resolution was observed for enthesitis of the spine and thoracic cage though resolution was more limited for plantar fascia or Achilles tendon enthesitis. Lower limb entheses are more prone to mechanical strain and may therefore require alternative or more prolonged therapy. A study was funded by AbbVie Inc. All authors were involved in the study design, review, data interpretation and approval of the abstract.

Disclosure of Interests: Thomas Huegle Grant/research support from: Abb- Vie, Lilly, Novartis and Pfizer, Speakers bureau: AbbVie, Lilly, Novartis and Pfizer, Burkhard Moeller Consultant for: Swissmedic Human Medici- cines Expert Committee Member (regulatory agency), Adrian Ciurea Consultant for: AbbVie, Celgene, Janssen-Cilag, MSD, Eli Lilly, Novartis, Pfizer, UCB, Speakers bureau: AbbVie, Celgene, Janssen-Cilag, MSD, Eli Lilly, Novartis, Pfizer, UCB, Michael Nissen Consultant for: AbbVie, Lilly, Novartis, and Pfizer, Patrick Zueger Shareholder of: AbbVie, Employee of: AbbVie, Lilly, Novartis, Pfizer, Roche, Sandoz, Sanofi Genzyme, and UCB., Consultant for: Consultant for Pfizer, MSD, and AbbVie, Eleftherios Papagiannoulis: None declared


FRIO376 DIFFERENCES IN PHYSICAL ACTIVITY BETWEEN AXIAL SPONDYLOARTHRITIS PATIENTS WITH AND WITHOUT PHYSICAL THERAPY

Bas Hilberg1, Florus van der Giessen1, Tha Viet Vien2, Floris A. van Gaalen3, Karel Ronday1, Andreas Peeters5, Salma van Weely1, 1Leiden University Medical Center, Orthopaedics, Rehabilitation and Physical Therapy, Leiden, Netherlands; 2Leiden University Medical Center, Rheumatology, Leiden, Netherlands; 3Haga Hospital, The Hague, Netherlands; 4Reiner de Graaf Gasthuis, Delft, Netherlands

Background: Physical activity (PA) according to public health guidelines is effective and safe for people with rheumatic and musculoskeletal diseases, including axial spondyloarthritis (axSpA), and should be promoted by healthcare providers.1 In axSpA, in particular high intensity aerobic PA is beneficial, yet this was found to be incompletely implemented in physical therapy programs.2 Studies describing aerobic PA in axSpA patients with and without physical therapy are lacking.

Objectives: To describe the amount, frequency and intensity of aerobic PA in axSpA patients with and without physical therapy treatment.

Methods: A survey, which included questions on patient characteristics, current physical therapy use (individual or group), PA (Short QUestionnaire on Assessment of Physical Activity, SQUASH) and health status (Assessment of Spondyloarthrits International Society Health Index (ASAS HI)), was sent by postal-mail to 456 axSpA patients registered in three hospitals in the Netherlands. From the SQUASH, besides amount (minutes/week) of all PA and meeting the PA guideline between patients with and without physical therapy. For moderate-intensity aerobic PA, both the amount and frequency were significantly greater in the group with physical therapy, whereas for vigorous intensity aerobic PA there were no differences in the total amount and the proportion meeting the guideline between patients with and without physical therapy. For moderate-intensity aerobic PA, both the amount and frequency were significantly greater in the group with physical therapy, whereas for vigorous intensity aerobic PA there were no differences between the groups (Table 1).

Conclusion: More than half of people with axSpA were physically active according to public health PA guidelines. People using physical therapy engaged in significantly more moderate intensity, but not high intensity aerobic PA than those without physical therapy. These results indicate that high intensity aerobic PA should be more intensively advocated and implemented, also in physical therapy treatment.

REFERENCES:

Methods: Bio-naïve patients with axial spondylarthritis (axSpA) attending primary care or out-patient setting were included in the study. The primary endpoint was treatment persistence after one year of infliximab (INF) treatment. Secondary endpoints were the probability of treatment persistence after two years, as well as safety and efficacy outcomes. Baseline characteristics were compared between the INF and CT-P13 groups.

Results: 1,319 patients were included in the study, of whom 1,229 completed the one-year follow-up. The treatment persistence rate was comparable between INF and CT-P13 after one year (95%CI: 38-50% and 38.68%, respectively). After two years, the treatment persistence rates were 44% (95%CI: 38-50%) for INF and 46% (95%CI: 42-51%) for CT-P13. The survival probability curves for INF and CT-P13 were identical (Figure 1), indicating that the treatment persistence rates were similar in the two groups.

Conclusion: The treatment persistence rates were comparable between INF and CT-P13 after one and two years of treatment. The similarity in survival probability curves suggests that the treatment persistence rate is not influenced by the choice of INF or CT-P13.

Disclosure of Interests: None declared.

References:

Acknowledgement: This study was funded by the Nordic Arthritis Society.
Background: Tumour necrosis factor inhibitors (TNFi) are efficacious in patients with axial spondyloarthritis (axSpA), but some patients switch to a different TNFi because of adverse effects (AE) or lack of effect (LOE). The EuroSpA Collaboration has previously demonstrated a 1-year retention rate of 79% and 6 months LUNDEX adjusted BASDAI<4 of 59% in patients initiating the first TNFi treatment. Little is known about the effectiveness of switching to a second and third TNFi in patients with axSpA.

Objectives: Firstly, to investigate retention and response rates at 6, 12 and 24 months in patients with axSpA initiating the 2nd and 3rd TNFi in clinical practice across Europe. Secondly, to investigate whether the outcomes were associated with the reason for withdrawal (AE or LOE) from the previous treatment.

Methods: Prospectively collected data on axSpA patients in routine care from 12 European registries were pooled. Kaplan-Meier estimation was used to investigate TNFi retention rates. LUNDEX adjusted response rates were calculated for BASDAI<4 and ASDAS inactive disease (ASDAS-c1.3). Group comparisons were performed by Chi-square test. Results: A total of 7953 patients initiating their 2nd TNFi and 2782 patients initiating their 3rd TNFi were included. Baseline characteristics are shown in the Table. The overall retention rates for both 2nd and 3rd TNFi at 12 months were 72% (Figure). Corresponding retention rates for the individual registries ranged from 52-90% and 54-89%, respectively. In both patients who stopped their 1st TNFi due to AE or LOE, 12-month retention rate for the 2nd TNFi treatment was 68%. In patients who stopped the 2nd TNFi due to AE or LOE, 12-month retention rates for the 3rd TNFi treatment were 68% and 69%, respectively. For the 2nd and 3rd TNFi, 6 months LUNDEX adjusted BASDAI<4 were 44% and 37% (p=0.001), respectively, and for ASDAS inactive disease 18% and 13% (p=0.003) (Table).

Conclusion: Data from 12 European countries demonstrated decreasing response rates with increasing number of previous TNFi, although with only minor difference between 2nd and 3rd. Patients who had withdrawn from the previous TNFi due to LOE had retention rates and remission rates similar to those who had withdrawn due to AE.

REFERENCES:

Acknowledgement: Novartis Pharma AG and IQVIA for supporting the EuroSpA collaboration
LONG-TERM EVALUATION OF SECUKINUMAB 150 MG IN ANKYLOSING SPONDYLITIS: 5-YEAR END-OF-STUDY EFFICACY AND SAFETY RESULTS FROM A PHASE 3 TRIAL

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Disclosure of Interests:
- Consultant for: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, and UCB
- Speakers bureau: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Omni, Orion, Pfizer, Regeneron, Roche, and UCB

Background: Evaluation of long-term efficacy and safety for treatments for ankylosing spondylitis (AS) is important. Secukinumab, a fully human monoclonal antibody that directly inhibits interleukin-17A, has shown significant and sustained improvement in the signs and symptoms of AS through 3 years in the MEASURE 2 study (NCT01649375).1

Objectives: We report the 5-year end-of-study results of subcutaneous (s.c.) secukinumab 150 mg in the MEASURE 2 study. Methods: AS patients (pts; N = 219) were randomised to receive s.c. secukinumab 150 mg, 75 mg or placebo at baseline, Weeks (Wks) 1, 2 and 3 and every 4 wks from Wk 4. At Wk 16, placebo-treated pts were re-randomised to receive secukinumab 150/75 mg or placebo at baseline. Week 16 (N = 106). An optional dose escalation from secukinumab 75 mg to 150 mg was initiated beginning Wk 140. Outcome measures at Wk 260 included ASAS20/40, BASDAI50, BASMI, BASFI, SF-36 PCS and ASAS partial remission. Analyses were stratified by anti-TNF status, anti-TNF-naive and anti-TNF inadequate response [IR].1

Results: The safety profile at Wk 260 was 77% (82/106) for secukinumab 150 mg across all endpoints through 5 years (Table). Improvements were maintained regardless of prior exposure to anti-TNF therapy with greater responses in anti-TNF-naive pts. A total of 49 pts on secukinumab 75 mg (46.7%) escalated dose to 150 mg after Wk 140; efficacy responses improved in pts whose dose was escalated. Over the entire study period, the mean exposure (±SD) to secukinumab was 1459.1 ± 597.8 days. Improvements were observed for all endpoints at W52 (Table).

Conclusion: Secukinumab 150 mg provided sustained improvement in the signs, symptoms, and physical function in pts with AS through 5 years of treatment. The safety profile of secukinumab remained consistent with previous reports.1–3

REFERENCES:

Disclosure of Interests: Helena Marzo-Ortega Grant/research support from: Abbvie, Celgene, Centocor, Merck, Novartis, Consultant for: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, and UCB, Speakers bureau: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Orion, Pfizer, Regeneron, Roche, and UCB

Flexion, Ricardo Blanco Grant/research support from: Abbvie, MSD and Roche, Consultant for: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen and MSD, Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen and MSD, Martin Cohen Consultant for: Abbvie, Amgen, Celgene, Lilly, Merck, Pfizer, Sandoz, Sanofi and UCB, Speakers bureau: Abbvie, Amgen, Celgene, Janssen, Merck, Novartis and Pfizer, Karel Pavelka: None declared, Eumorphia Maria Delicha Employee of: Novartis, Anna Stefanska Shareholder of: Novartis, Employee of: Novartis, Hanno Richards Shareholder of: Novartis Pharma AG, Employee of: Novartis, Hanno Richards Shareholder of: Novartis Pharma AG, Baseline, Switzerland, Novartis Ireland Limited, Dublin, Ireland.

Table: Efficacy Endpoints with Secukinumab 150 mg at Week 260 (5 year)

<table>
<thead>
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<th>Variable</th>
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<tbody>
<tr>
<td>Total N</td>
<td>Anti-TNF-naive</td>
</tr>
<tr>
<td>N = 106</td>
<td>Anti-TNF-IR</td>
</tr>
<tr>
<td>N = 66</td>
<td>Anti-TNF-IR</td>
</tr>
<tr>
<td>N = 40</td>
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</tr>
<tr>
<td>ASAS20‡</td>
<td>69.9 (83)</td>
</tr>
<tr>
<td>ASAS40‡</td>
<td>54.2 (83)</td>
</tr>
<tr>
<td>ASAS-PARTIAL REMISSION§</td>
<td>25.3 (83)</td>
</tr>
<tr>
<td>BASDAI50‡</td>
<td>53.0 (83)</td>
</tr>
<tr>
<td>BASMI‡</td>
<td>0.5 (83)</td>
</tr>
<tr>
<td>BASFI‡</td>
<td>-2.82 (66)</td>
</tr>
<tr>
<td>SF-36 PCS‡</td>
<td>8.0 (87)</td>
</tr>
</tbody>
</table>

Data are reported as median [IQR]; *includes placebo switches; ‡% responders; §mean change from baseline ± SD; †IR, inadequate response; N, total number of randomised patients; n, number of evaluable patients; TNF, tumour necrosis factor
Conclusion: Secukinumab was associated with higher mean change in MASES and complete resolution of enthesitis compared to placebo at Week 16, which further improved through Week 52.

REFERENCES:

Table. Summary of results

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<thead>
<tr>
<th>SEC 150 mg</th>
<th>SEC 300mg</th>
<th>PBO</th>
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<tbody>
<tr>
<td>N=555</td>
<td>N=58</td>
<td>N=280</td>
</tr>
<tr>
<td>W16</td>
<td>W52</td>
<td>W16</td>
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</table>

LS mean change from BL in MASES score*

<table>
<thead>
<tr>
<th>Overall MASES4</th>
<th>AxSpA 5</th>
<th>PSp 4</th>
<th>ATd 4</th>
</tr>
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<tbody>
<tr>
<td>-2.4</td>
<td>-3.5</td>
<td>-2.9</td>
<td>-3.9</td>
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<td>-2.3</td>
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<tr>
<td>-0.8</td>
<td>-1.2</td>
<td>-1.0</td>
<td>-1.3</td>
</tr>
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</table>

Complete resolution of enthesitis (% of MASES score)

<table>
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<tr>
<th>Overall MASES4</th>
<th>AxSpA 5</th>
<th>PSp 4</th>
</tr>
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<tbody>
<tr>
<td>40.8</td>
<td>56.4</td>
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<td>42.7</td>
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<td>46.3</td>
<td>65.5</td>
<td>52.5</td>
</tr>
<tr>
<td>57.0</td>
<td>78.4</td>
<td>55.0</td>
</tr>
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</table>

 Improvement from BL in MASES score (% of BL scores)6

<table>
<thead>
<tr>
<th>Overall MASES4</th>
<th>AxSpA 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>23.7</td>
<td>34.1</td>
</tr>
<tr>
<td>20.1</td>
<td>28.0</td>
</tr>
</tbody>
</table>

4P<0.01; 5P<0.05 vs PBO. 6P-values from repeated MMRM until Week 16. P-values from logistic regression model. 150mg (n=765, 544, 229, 172); 300mg (n=76, 57, 57, 20) and PBO (n=380, 272, 188, 98). Observed data, LS, least squares; N, number of patients analysed; n, number of patients with measurement.

Disclosure of Interests: Geoff Schett: None declared, Xenonof Barilakos Grant/research support from: AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Centocor, Chugai, Janssen, MSD, Novartis, Pfizer Inc, Roche and UCB, Grant/research support from: AbbVie, Pfizer, Merck Sharp & Dohme, UCB Pharma, Novartis. Consultant for: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Chugai, Janssen Biologics, Novartis, Pfizer, UCB Pharma, Galapagos, Speakers bureau: AbbVie, Celgene, Janssen, Novartis, Pfizer, UCB Pharma, Fil van den Bosch Consultant for: AbbVie, BMS, Galapagos, Janseen, Lilly, Merck, Novartis, Pfizer and UCB, Speakers bureau: AbbVie, BMS, Janssen, Lilly, Merck, Novartis, Pfizer and UCB, Atul Deodhar Grant/research support from: AbbVie, Amgen, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Consultant for: AbbVie, Amgen, BMS, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Lianne S. Ginsler Grant/research support from: AbbVie, Amgen, UCB Pharma, Consultant for: Novartis, Lilly, Janssen, Mikkel Østgaard Grant/research support from: AbbVie, Celgene, Centocor, Merck, Novartis. Consultant for: AbbVie, BMS, Boehringer-Ingelheim, Celgene, Eli Lily, Hospitana, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, Speakers bureau: AbbVie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospitana, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, Shital Agawane Employee of: Novartis, Ayan Das Gupta Employee of: Novartis, Shephard Mpoulo Employee of: Novartis, Todd Fox Employee of: Novartis, Adam Winseck Employee of: Novartis, Abhijit Shele Shareholder of: Novartis Pharma AG, Employee of: Novartis Pharma AG, Brian Porter Shareholder of: Novartis, Employee of: Novartis.

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Objectives: The aims of our study were to assess the 10-year survival of the first TNF-i, to compare retention rates of different anti-TNF drugs in real life settings and to identify factors associated with drug retention in active axSpA.

Methods: We performed a hospital-based retrospective cohort study on consecutive adult axSpA suboptimally controlled by standard therapy, starting their first biological agent with infliximab (IFX), adalimumab (ADA), etanercept (ETA) or golimumab (GLM) according to local policy, recruited at three academic centres between 2003 and July 2018. Drug efficacy (BASDAI, ASDAS-CRP) as well as reasons for discontinuation were evaluated every 24 weeks. Drug survival was calculated using the Kaplan-Meier analysis, while univariate and multivariate regression was used for predictors of persistence and withdrawal (p<0.05). Subanalysis was done for different disease durations.

Results: Of the 241 axSpA were recruited, 104 (43.15%) cases received ETA (original, biosimilar), 100 (41.49%) ADA, 26 (10.78%) IFX (original and biosimilar) and 11 cases (4.58%) GLM. Significant improvement was demonstrated (ASDAS-CRP, BASDAI, BASFI) in all patients, those with higher disease activity and functional impairment at baseline presenting earlier and higher response rate (p<0.05).

We reported high long-term persistence of the first biological agent in axSpA patients under 5 years on the same drug after 140 months. The retention rates of ETA, ADA and IFX were 70%, 68% and 57% after 3 years; 68%, 48% and 53% after 5 years; 35%, 30% and 27% after 10 years. Overall, retention to ETA was superior to that of monoclonal antibodies (p<0.05), with a total drug-exposure of 625.43 patient-years for ETN, 415.26 for ADA, 221.53 for IFX. In addition, survival of the second TNF-i drug was good but inferior to the first TNF-i (p<0.05).

Male sex, age under 40, high baseline C reactive protein, low initial BASFI and disease duration under 5 years were associated with retention rate in multivariate analysis (p<0.05), while the presence of syndesmophytes and obesity with higher withdrawal (p<0.05).

Conclusion: We reported high long-term persistence of the first biological agent in axSpA patients, with higher retention compared to ETA compared to monoclonal antibodies. Predictors for higher retention advocate the rationale for the drug choice in different axSpA settings.

Disclosure of Interests: CODRINA ANCUȚĂ Speakers bureau: Abbvie, Pfizer, Novartis, MSD, Roche, Biogen, UCB, Lilly, Cristina Pominleau; Speakers bureau: Abbvie, Pfizer, UCB, Ralucu Pața; None declared, Geogiana Strugariu; Speakers bureau: Abbvie, Pfizer, UCB, Lilly, Roche, Crista Pomirleanu; Speakers bureau: Abbvie, Pfizer, Novartis, Eugen Ancuta: None declared, Codruta Bran; Speakers bureau: Abbvie, Pfizer, Novartis, Lilly, Roche, Crista Pomirleanu; Speakers bureau: Abbvie, Pfizer, Novartis, MSD, Roche, Biogen, UCB, Lilly


FR01384 IMPACT OF INTERLEUKIN 17 BLOCKING AGENT ON CLINICAL OUTCOME IN SAPHO PATIENTS

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Background: SAPHO syndrome has to be considered as a rare subtype of seronegative spondyloarthritis (SpA) showing typical manifestations with palmoplantar pustulosis and osteitis with hyperostosis; the clinical response of conventional or biological disease modifying drugs (DMARDs) in SAPHO syndrome are often disappointing. Whereas in SpA peripheral arthritis and inflammatory back pain represent the leading symptoms, the SAPHO patients often complain painful osteitis with hyperostosis in the sternal region as well as the palmoplantar pustulosis accompanied by synovitis preferentially in large joints including sacroiliitis. Recently, the detection of higher numbers of CD4+IL17+ lymphocytes in the peripheral blood of SAPHO patients has arisen the hypothesis that Th17 helper cells with their secretion of interleukin 17 (IL17) could be involved in the development of inflammation in SAPHO syndrome (1).

Objectives: Here we present an observational study of 12 SAPHO patients which were treated with the IL 17 blocking agent secukinumab. In addition, the fraction of CD4+IL17+ lymphocytes in peripheral blood specimen has been monitored on treatment.

Methods: Between January 2015 and February 2017 clinical activity of disease were measured in 37 SAPHO patients with a disease duration of 11 years (median). The disease activity were evaluated by the osteitis

PAMIDRONATE IN CHRONIC NON-BACTERIAL OSTEOITIS: A RANDOMIZED, PLACEBO-CONTROLLED PILOT TRIAL

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Background: Chronic non-bacterial osteitis (CNO) is an autoinflammatory disease often associated with seronegative spondarthritides. Osteitic bone lesions in adults are predominantly located in the anterior chest wall, the spine and pelvis. Case series suggest that the amino-bisphosphonate pamidronate may be effective in improving bone inflammation, pain, and disability. No randomized controlled trials have been conducted in CNO.

Objectives: In a randomized double-blinded, placebo-controlled trial we hypothesized that pamidronate reduces radiological signs of bone inflammation assessed by whole-body magnetic resonance imaging, improve pain, disability and reduces systemic markers of bone inflammation and bone turnover in blood.
score and skin score (ranging from 0 to 6, assessed by physician), the HAQ score (ranging from 0 to 3, assessed by patient), and MRI of the osteitis lesion (activity score 0-3, analogously to 3 domains of OMERACT RAMRIS scoring synovitis, bone marrow edema, and erosions; assessed by radiologist). In this period of time 12 of them showed disease activity due to osteitis and/or skin disease, at which time the treatment of secukinumab at dosage of 300mg as monotherapy has been started, re-evaluated after at least 12 weeks (ranging from 12 to 18 weeks). For monitoring blood specimens were derived to assess the CD4+IL17+ lymphocyte subpopulation using immunofluorescence technique. We thank the patients who participated. This study was funded by UCB Pharma, medical writing by Hinal Tanna, Costello Medical, UK.

Disclosure of Interests: None declared

OBJECTIVES: To report the incidence and association of active inflammation and chronic lesions in the spine of pts with axSpA treated with CZP over 4 years

METHODS: RAPID-axSpA (NCT01087762) was double-blind and placebo (PBO)-controlled to Week (Wk)24, dose-blind to Wk48, and open-label to Wk204. CZP-randomised pts (either 200mg every 2 weeks [Q2W] or 400 mg Q4W) continued their assigned dose throughout; PBO-randomised pts received CZP from Wk24, or if non-responders, from Wk16 onwards. Blinded spinal MRI scans at baseline (BL) and Wk12, 48, 96, and 204 were assessed by 2 central readers to evaluate the presence/absence of active INFLs (Short T1 Inversion Recovery [STIR] sequence) and FLs, sclerosis and erosions (T1 sequence) in vertebral edges (VEs). We used MMRM analyses with repeated measures (MMRM), fitted on observed data from all randomised pts. Associations between INFLs and FLs at the VE level for CZP-and PBO-randomised pts were described using cross-tabulations.

RESULTS: Of 325 randomised pts, 136 were eligible for these analyses. In pts randomised to CZP at Wk0 (n=89), active INFLs were reduced, and FL counts only slightly increased by Wk12; both were sustained at a low level to Wk204 (Table A). Very few VEs with sclerosis and erosions were observed at BL, and no changes in their frequency were observed over 4 years’ treatment (Table A). Over 4 years’ CZP treatment, the risk of developing a new FL was greater in VEs with vs without INFLs at BL, regardless of changes to INFLs in these VEs post-BL. The prevalence of FLs was greater in pts with >3 vs ≤3 years’ symptom duration and there were more new FLs in the >3 years subgroup during CZP treatment (data not shown).

CONCLUSION: Long-term CZP treatment in axSpA pts was associated with rapid and sustained reduction in active inflammation and a negligible increase in FLs in VEs. More FLs developed in VEs with INFLs at BL than without, but this was not affected by resolution of INFLs. There was no increase in sclerosis and erosions in VEs over 4 years’ CZP treatment.

REFERENCE:


Acknowledgement: We thank the patients who participated. This study was funded by UCB Pharma, medical writing by Hinal Tanna, Costello Medical, UK.

Table: A) Counts of inflammatory lesions, fatty lesions, sclerosis and erosions at the patient level (n) through 204 weeks’ CZP treatment (MMRM estimates)

<table>
<thead>
<tr>
<th>Patients (n)</th>
<th>Week 0</th>
<th>Week 12</th>
<th>Week 48</th>
<th>Week 96</th>
<th>Week 204</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n)</td>
<td>89</td>
<td>89</td>
<td>89</td>
<td>89</td>
<td>89</td>
</tr>
<tr>
<td>Fatty lesion (n)</td>
<td>6.0 (0.7)</td>
<td>2.0 (0.3)</td>
<td>1.0 (0.2)</td>
<td>1.0 (0.2)</td>
<td>1.0 (0.2)</td>
</tr>
<tr>
<td>Sclerosis (n)</td>
<td>0.1 (0.0)</td>
<td>0.1 (0.0)</td>
<td>0.1 (0.0)</td>
<td>0.1 (0.0)</td>
<td>0.1 (0.0)</td>
</tr>
<tr>
<td>Erosion (n)</td>
<td>0.0 (0.0)</td>
<td>0.0 (0.0)</td>
<td>0.0 (0.0)</td>
<td>0.0 (0.0)</td>
<td>0.0 (0.0)</td>
</tr>
</tbody>
</table>

FR10385

LONG-TERM CERTOLIZUMAB PEGOL TREATMENT OF AXIAL SPONDYLOARTHRITIS IS ASSOCIATED WITH RAPID AND SUSTAINED REDUCTION OF ACTIVE INFLAMMATION AND MINIMAL STRUCTURAL CHANGES IN THE SPINE: 4-YEAR MRI RESULTS FROM RAPID-AXSpA

Xenophon Baraliakos1, Sebastian Kruse2, Simoné Auter3, Natasha de Peyrecave4, Tommi Nummit5, Thomas Kunke6, Bengt Hoepken7, Juergen Braun1.

1Rheumazentrum Ruhrgebiet and Ruhr-University Bochum, Herne, Germany; 2UCB Pharma, Brussels, Belgium; 3UCB Pharma, Monheim, Germany

Background: In patients (pts) with axial spondyloarthritis (axSpA), inflammation of the spine is believed to trigger a repair mechanism that results in syndesmophyte formation.1,2 Fatty lesions (FLs) in the bone marrow and erosions in the axial skeleton, both visible on magnetic resonance imaging (MRI) T1 sequences, are post-inflammatory changes that have been shown to contribute significantly to models predicting new bone formation.3 It has previously been shown that resolution of inflammatory lesions (INFLs) in pts with axSpA treated with anti-TNF therapy may be associated with an increase in FLs.4 However, it is not known whether CZP treatment coincides with changes in FLs, sclerosis, and erosions.
Disclosure of Interests: Xenofon Baraliakos Grant/research support from: AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Centocor, Chugai, Janssen, MSD, Novartis, Pfizer Inc, Roche and UCB. Consultant for: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Chugai, Janssen, MSD, Novartis, Pfizer Inc, Roche and UCB. Speaking bureau: AbbVie, Chugai, Celgene, Janssen, MSD, Novartis, Pfizer Inc, Roche and UCB.

REFERENCES:

Table: Proportion of Patients with ASDAS States through Wk 208

<table>
<thead>
<tr>
<th>ASDAS states</th>
<th>Wk 16</th>
<th>Wk 52</th>
<th>Wk 104</th>
<th>Wk 208</th>
</tr>
</thead>
<tbody>
<tr>
<td>ID</td>
<td>24.4</td>
<td>25.8</td>
<td>30.0</td>
<td>26.9</td>
</tr>
<tr>
<td>LDA</td>
<td>34.9</td>
<td>39.3</td>
<td>38.8</td>
<td>33.3</td>
</tr>
<tr>
<td>HDVA/HVDVA</td>
<td>40.7</td>
<td>35.1</td>
<td>31.3</td>
<td>39.7</td>
</tr>
</tbody>
</table>

ID, Inactive Disease; LDA, Low Disease Activity; HDVA/HVDVA, High/very high Disease Activity.

N, total number of patients with ASDAS.
Background: AxSpA is a chronic condition that has a negative impact on health-related quality of life (HRQoL). Secukinumab (SEC), a fully human anti-IL-17A monoclonal antibody, has been shown to effectively control AS symptoms and improve HRQoL.

Objectives: To evaluate the impact of SEC on HRQoL, assessed by the Short Form-36 Health Survey (SF-36), in pts with active AS stratified by time since first diagnosis (<2 or ≥2 yrs).

Methods: Pts were randomized to placebo (PBO) or SEC in MEASURE 1 (10 mg/kg intravenously followed by 150 or 75 mg SC), MEASURE 2 (150 or 75 mg SC) and MEASURE 4 (150 mg SC with/without SC loading). At Wk 16 or Wk 24, depending on ASAS 20 response, pts on (150 or 75 mg SC) and MEASURE 4 (150 mg SC with/without SC loading). Pts were randomized to placebo (PBO) or SEC in MEASURE

| **Table 2: flare, medications at preconception visits and medications initiated during pregnancy in patients with and without flares** |
| **Pt. with flare** | **Pt. without flare** |
| Flare during pregnancy | 8/11 (73%) | 4/5 (80%) |
| Flare in post partum period | 5/12 (42%) | 1/6 (17%) |
| ASAS-CRP >2.1 at 1st trimester (mean) | 2.24 (4.01) | 0.48 (0.99) |
| ASAS-CRP >2.1 at 2nd trimester (mean) | 2.00 (3.31) | 1.55 (0.82) |
| ASAS-CRP >2.1 at 3rd trimester (mean) | 2.00 (3.01) | 1.55 (0.82) |
| Prednisone | 0/2 (100%) | 1/6 (17%) |
| bDMARDs | 0/3 (0%) | 0/6 (0%) |
| Medication resumed during pregnancy | 5/11 (46%) | 0/6 (0%) |
| Prednisone | 5/11 (46%) | 0/6 (0%) |
| bDMARDs | 5/11 (46%) | 0/6 (0%) |

*Two pregnancies ended in miscarriage were not considered.
assessed. Missing data were recorded as non-response and Fisher’s exact test was used to compare the proportion of responders between groups at Wk 16. Only pooled data for pts receiving the licensed dose of SEC (150 mg) are shown.

Results: Overall 739 patients were included, with 427 and 312 in the SEC 150 mg and PBO groups, respectively. Of those, 37% and 36% of the SEC and PBO groups, respectively, were classified as <2 yrs since first AS diagnosis (Overall: 37%). The mean time since AS diagnosis was similar for the PBO and SEC treatment groups in both the <2 yrs (approx. 0.80 yrs) and the ≥2 yrs subgroups (approx.11 yrs). The least squares mean (LSM) changes in PCS from BL to Wk 16 were increased with SEC 150 mg compared with PBO, in both <2 yrs (PBO: 2.11; 150 mg: 6.44, p<0.0001) and ≥2 yrs since diagnosis (PBO: 3.03; 150 mg: 5.82, p<0.0001). Significant increases were also reported in LSM changes in MCS scores from BL to Wk 16 with SEC 150 mg in patients <2 yrs since diagnosis (PBO: 2.10; 150 mg: 5.53, p<0.01), but not in the ≥2 yrs group. Analysis of individual SF-36 domain scores showed improvements with SEC vs PBO in the overall population and in both time since diagnosis subgroups, except Role-Emotional and Mental Health in the ≥2 yrs group (Figure). At Wk 16, the proportions of PCS responders were significantly higher with SEC 150 mg vs PBO, regardless of time since diagnosis (<2 yrs: PBO = 50.0%, SEC = 73.6%, p<0.01; ≥2 yrs: PBO = 45.0%, SEC = 69.8%, p<0.0001). MCS responses were not significantly different with SEC vs PBO in either subgroup. Overall, improvements in SF-36 scores and clinically meaningful MCID responses with SEC were more prominent in the <2 yrs since diagnosis compared with the ≥2 yrs group. Improvements in PCS, MCS, individual SF-36 domains and overall MCID responses were sustained to Wk 52 with SEC 150 mg.

Conclusion: Treatment with SEC 150 mg resulted in significant, clinically meaningful, and sustained improvements in HRQoL. Although reported improvements in SF-36 scores and clinically meaningful MCID responses with SEC were more prominent in the <2 yrs since diagnosis compared with the ≥2 yrs group, improvements in PCS, MCS, individual SF-36 domains and overall MCID responses were sustained to Wk 52 with SEC 150 mg.

Disclosure of Interests: Atul Deodhar Grant/research support from: Abbvie, Amgen, Eli Lilly, GSK, Janssen, Novartis, Pfizer, and UCB, Consultant for: AbbVie, Amgen, BMS, Eli Lilly, Janssen, Novartis, Pfizer, and UCB; Employee of: AbbVie, Amgen, BMS, Eli Lilly, Janssen, Novartis, Pfizer, and UCB; Honorary speaker for: AbbVie, Amgen, BMS, Eli Lilly, Janssen, Novartis, Pfizer, and UCB; Member of: NDA, National Rheumatic Diseases Council, NMS, National Rheumatic Diseases Society, and NISRA, NME. Mikel Arrenberg Declared medical interests: None. Marc G. Hochberg Declared medical interests: None.

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Table 1. Mean disease activity indexes evolution

<table>
<thead>
<tr>
<th>Activity index</th>
<th>Biologic-naive (BTe)</th>
<th>Biologic-experienced (BTe)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline (SD)</td>
<td>12 months (SD)</td>
</tr>
<tr>
<td>BASDAI</td>
<td>5.5 (2.0) n=422</td>
<td>3.2 (1.3) n=287</td>
</tr>
<tr>
<td>ASAS</td>
<td>3.5 (1.4) n=286</td>
<td>1.7 (1.0) n=286</td>
</tr>
<tr>
<td>PCR</td>
<td>3.2 (1.4) n=120</td>
<td>2.9 (1.4) n=88</td>
</tr>
</tbody>
</table>

Table 2. Percentage of low disease activity and inactive disease by BASDAI and ASAS

<table>
<thead>
<tr>
<th>Disease activity</th>
<th>n, % achieved at 12 months on states</th>
<th>n, % achieved at 12 months on states</th>
</tr>
</thead>
<tbody>
<tr>
<td>BASDAI low activity</td>
<td>120, 41.8%</td>
<td>72, 23.5%</td>
</tr>
<tr>
<td>BASDAI inactive</td>
<td>73, 25.4%</td>
<td>58, 23.8%</td>
</tr>
<tr>
<td>ASAS low activity</td>
<td>21, 32.8%</td>
<td>11, 22%</td>
</tr>
<tr>
<td>ASAS inactive</td>
<td>23, 35.9%</td>
<td>15, 30%</td>
</tr>
</tbody>
</table>

Conclusion: The mean disease activity on patients starting biologic therapy is high. A clinically important improvement is met after 12 months of therapy, irrespectively of the index used or the prior use of biologics. The delta in DAI is bigger in the biologic-naive group who received the 1st BT. The biologic-naive group also reaches a higher percentage of low disease activity and inactive disease. Further analysis is needed to see if these tendencies remain after separating the groups per type of biologic drug.
DRUG THERAPY OF ANKYLOSING SPONDYLITIS (AS) DURING PREGNANCY IN REAL CLINICAL PRACTICE

Zuleykhna Gandasheva, Olga Krichetskaya, Tatiana Dubinina, Federal State Budgetary Scientific Institution “Research Institute of Rheumatology named after V. A. Nasonova”, Moscow, Russian Federation

Background: The emergence of new drugs for the treatment of AS and improvement of life quality of patients led to an increase in the number of pregnancies and births in women with AS. However, the prescription of medication during pregnancy is still a difficult decision for both doctors and patients, and the unreasonable abolition of therapy can lead to increased activity of the AS.

Objectives: was described the frequency of use of various groups of drugs before and during pregnancy, determine the relationship between the abolition or change in the mode of taking nonsteroidal anti-inflammatory drugs (NSAIDs) and the dynamics of back pain.

Methods: the survey involved 86 women with AS, having pregnancies that ended in childbirth, not earlier than 2016. The average age is 34.0 ± 5.8 years and the average duration of the AS is 120 ± 73.5 months. The median term of delivery is 39 (38; 40) weeks, the weight of newborns is 2941.1 ± 484.6 g. During pregnancy, 58 (67.4%) women noted deterioration of health. Among them: increased back pain in the first trimester was 66.7%, in II – 84.6%, in III – 72.2%.

Results: Before pregnancy, NSAIDs were taken by more women (63.4%) as compared to taking in a month of conception (37.2%) and taking during gestation (in trimesters - 25.6%; 34.8%; 9.3%, respectively), p < 0.05 in both cases. “On demand”, NSAIDs were taken before pregnancy by 41.6% of women, at conception - 37.5%, in trimesters — 50%, 40% and 25%, respectively. There was a tendency for more frequent increase of back pain during pregnancy in women who abolished NSAIDs in the month of conception, or switched to “on demand” (65%), compared with taking NSAIDs daily (50%). Patients who took NSAIDs “on demand” in the first trimester (group 1), more often noted deterioration of health in the second trimester - 34.6%, compared with patients constantly taking NSAIDs (group 2) - 18.2%. In addition, patients in group 1, as well as women who didn’t take NSAIDs in the first trimester, more often complained of back pain (54.6% and 53.1%) during gestation compared with patients in group 2 (38.4%). Group 1 patients in the second trimester noted increased back pain during pregnancy in 83.3%, whereas group 2 patients - in 58.3% (p < 0.01). Glucocorticoids were taken more often during pregnancy (16.3%; 20.9%; and 22.1% - in trimesters) than before (7%) and at conception (9.3%), p < 0.01 in both cases. Sulfasalazine before pregnancy was taken by 16% of women, at conception - 8%, during pregnancy - 3.5% (p < 0.01 in both cases). Before pregnancy, only 12.8% of women received biological therapy; at the time of conception (adalimumab, etanercept) - 6.9%, in I and II trimesters – by 2.3% (p<0.01).

Conclusion: During pregnancy and the month of conception, the number of women receiving NSAIDs, sulfasalazine, biological therapy, decreases compared to the period before pregnancy. Glucocorticoids in preparation for pregnancy and gestation are prescribed more often than before pregnancy. Withdrawal of NSAIDs or switch to mode “on demand” in the first trimester is associated with an increase in the frequency of back pain during pregnancy, but due to discrepant data on the safety of continuous use of NSAIDs in the first trimester, correction of therapy with the prescription of low-risk drugs is necessary.

Disclosure of Interests: None declared


NetaAkimab IMPROVES PATIENT-RELATED OUTCOMES IN PATIENTS WITH RADIOLOGICAL AXIAL Spondylarthropathies: RESULTS FROM RANDOMISED PHASE 3 TRIAL (ASTERA)

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Background: chronic pain, stiffness, fatigue and limited spinal mobility significantly affect quality of life (QoL) in patients (pts) with axial spondyloarthritis (axSpA). There is increasing evidence that IL-17 blockade is highly effective in this pts’ population and show benefits in terms of multiple patient-reported outcomes (PROs) in both non-radiological (nr) and radiological (r) axSpA.

Objectives: To evaluate early effects of netakimab (NTK) on PROs in pts with active r-axSpA, based on data of 16-week observation from ongoing phase 3 ASTERA study (NCT03447704).

Methods: ASTERA is a phase 3 international double-blind placebo (PBO)-controlled clinical study. After completion of screening 228 eligible adult pts with r-axSpA (mNew York criteria, 1984), which remained active (BASDAI ≥ 4.0) despite the standard non-steroidal anti-inflammatory drugs (NSAIDs), were randomly assigned (1:1) to receive 120 mg NTK or placebo (PBO) at Week (WK) 0, 1, 2 and then q4wk through WK 16. After WK 16 all patients will continue/be switched to receive NTK up to week 52. PROs were total back pain (10-item numerical range scale), BASDAI, BASFI. Work productivity and QoL were also assessed by Work Productivity and Activity Impairment (WPAI) and 36-item Short Form Health Survey (SF-36), respectively.

Results: Baseline characteristics were similar between treatment arms. The mean age at baseline was 39.1±9.9 years, 75.88% of patients were male and the mean symptoms duration was 4.3±4.48 years. All patients had active (mean BASDAI: 6.2±1.55) r-axSpA. 78.6% of patients were naïve to any biological treatment. Mean total back pain score at baseline was 6.7±1.6 in NTK group and 6.8±1.5 in PBO arm. At WK1 the difference in total back pain score between study arms became statistically significant (Figure 1). At WK 16 use of NTK was associated with statistically significant improvements from baseline in BASDAI (2.8 vs 0.2, p<0.0001), BASFI (-0.9 vs 0.9, p<0.0001) and physical component of SF36 (6.3 vs. -2.6, p<0.0001) (Figure 2). WPAI response in NTK arm was significantly better at WK 16, as compared with PBO (Table 1).

Conclusion: NTK in treatment of patients with r-axSpA showed rapid improvement in PRO, WP and QoL and was accompanied with improvement in physical function and disease activity.

Table 1. Change in WPAI at week 16 (medians; upper and lower quartiles)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>NTK (n=114)</th>
<th>PBO (n=114)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline Change from baseline to WK16</td>
<td>Baseline Change from baseline to WK16</td>
<td></td>
</tr>
<tr>
<td>% work time missed</td>
<td>0 [0; 18.4]</td>
<td>0 [0; 0]</td>
</tr>
<tr>
<td>% time lost due to poor health</td>
<td>23.3%</td>
<td>0 [0; 29.9]</td>
</tr>
<tr>
<td>% impairment while working due to health</td>
<td>50 [30; 80]</td>
<td>50 [40; 100]</td>
</tr>
<tr>
<td>% overall work impairment due to health</td>
<td>55.1 [40; 70]</td>
<td>60 [40; 70]</td>
</tr>
<tr>
<td>% activity impairment due to health</td>
<td>84 []</td>
<td>1.2 [0, 3.0]</td>
</tr>
<tr>
<td>% activity impairment due to health</td>
<td>60 [40; 80]</td>
<td>60 [50; 70]</td>
</tr>
</tbody>
</table>

Figure 1. Total back pain score within 16 weeks of ASTERA study (means) * P<0.05 for the comparison with placebo.

REFERENCES:
Disclosure of Interests: Inna Gaydubkova Grant/research support from: JSC BIOCAD, Speakers bureau: payment from Pfizer, Novartis, Abbvie, Biocad, Selgene, MSD, Sanofi does not exceed 10 000 euros, V Mazurov Grant/research support from: JSC BIOCAD, Shandor Endres Grant/research support from: JSC BIOCAD, Speakers bureau: JSC BIOCAD, Tatiana Dubininia: None declared, Olga Nesmeyanova Grant/ research support from: JSC BIOCAD, Elenia Ilivanova Grant/research sup- port from: JSC BIOCAD, Ekaterina Cher- nyaya Employee of: JSC BIOCAD, Roman Ivanov Employee of: JSC BIOCAD

A total of 4 overarching principles and 10 recommendations were presented to the experts and recommendations were formulated after thorough discussions and voting.

Management of enteropathic arthritis may be challenging due to differences in treatment response of inflammatory bowel diseases and arthritis to different therapeutic modalities, which may even cause worsening of some manifestations while improving others. Enteropathic arthritis was not addressed in the management recommendations for spondyloarthritis.

Methods: A task force was formed that included ten rheumatologists and gastroenterologists and other clinicians dealing with enteropathic arthritis.

The aim of this project was to develop a set of evidence based recommendations for the management of patients with enteropathic arthritis: A RHEUMATOLOGY, GASTROENTEROLOGY COLLABORATIVE INITIATIVE

EVIDENCE BASED RECOMMENDATIONS FOR THE MANAGEMENT OF ENTEROPATHIC ARTHRITIS: A RHEUMATOLOGY, GASTROENTEROLOGY COLLABORATIVE INITIATIVE

Gülen Haten1, Serif Arak2, Hale Akipinar3, Pamir Atagündüz4, Goksel Bengi5, Gerçek Can6, Aykut Ferhat Celik7, Sinem Nihal Esatoglu8, Önay Gerçik9, Hulya Harmazoğlu10, Murat Inanc11, Servet Akar12, Hale Akpinar13, Goksel Bengi14, Fatih Öner15, Ahmet Tezel16, Murat Toruner17, Sedat Kiraz18, İpek Kalkan19, Ergen Can20, Aykut Ferhat Celik: None declared, Sinem Nihal Esatoglu: None declared, Önay Gerçik: None declared, Hulya Harmazoğlu: None declared, Murat Inanc: None declared, Servet Akar: None declared, Hale Akpinar: None declared, Goksel Bengi: None declared, Aykut Ferhat Celik: None declared, Sinem Nihal Esatoglu: None declared, Önay Gerçik: None declared, Hulya Harmazoğlu: None declared, Murat Inanc: None declared, Servet Akar: None declared, Hale Akpinar: None declared, Fatih Öner: None declared, Ahmet Tezel: None declared, Murat Toruner: None declared, Sedat Kiraz: None declared

Disclosure of Interests: Gülen Hatemi Consultant for: Abbvie, Amgen, BMS, Janssen, MSD, Pfizer, UCB, Speakers bureau: Abbvie, Amgen, BMS, Janssen, MSD, Pfizer, UCB, Servet Akar Grant/research support from: JSC BIOCAD, Elenia Ilivanova Consultant for: MSD, Abbvie, Roche, UCB, Novartis, Pfizer, Amgen, Consultant for: MSD, Abbvie, Roche, UCB, Novartis, Pfizer, Amgen, Speakers bureau: Pfizer, Hale Akipinar: None declared, Pamir Atagündüz: None declared, Goksel Bengi: None declared, Gerçek Can: None declared, Aykut Ferhat Celik: None declared, Sinem Nihal Esatoglu: None declared, Önay Gerçik: None declared, Hulya Harmazoğlu: None declared, Murat Inanc: None declared, Servet Akar: None declared, Hale Akpinar: None declared, Fatih Öner: None declared, Ahmet Tezel: None declared, Murat Toruner: None declared, Sedat Kiraz: None declared

EVIDENCE BASED RECOMMENDATIONS FOR THE MANAGEMENT OF ENTEROPATHIC ARTHRITIS: A RHEUMATOLOGY, GASTROENTEROLOGY COLLABORATIVE INITIATIVE

Patients with active inflammatory bowel disease, active disease regarding both inflammatory bowel disease and arthritis, and among patients in remission. Final voting showed good agreement among the group on all recommendations.

Conclusion: These recommendations are intended to help rheumatologists, gastroenterologists and other clinicians dealing with enteropathic arthritis and to point out to the shortcomings of the available data on the management of this challenging condition.

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EVIDENCE BASED RECOMMENDATIONS FOR THE MANAGEMENT OF ENTEROPATHIC ARTHRITIS: A RHEUMATOLOGY, GASTROENTEROLOGY COLLABORATIVE INITIATIVE
MAINTAINED CLINICAL REMISSION IN ANKYLOSING SPONDYLITIS PATIENTS SWITCHED FROM REFERENCE INFLIXIMAB TO ITS BIOSIMILAR, AN 18-MONTH COMPARATIVE OPEN-LABEL STUDY

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Alexandros Diosos1. We have no working group for this abstract.
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Background: switching from reference infliximab (RI) to biosimilar infliximab (BI) has no detrimental effects on efficacy and safety compared to continuous RI. However, long-term follow-up data is missing. Objectives: the aim of this study was to evaluate if BI is equivalent to RI to maintain patients with Ankylosing Spondylitis (AS) in clinical remission, in a long-term fashion.

Methods: one hundred and nine consecutive unselected AS patients were investigated. All, followed-up at predefined times receiving RI (5mg/kg/8 weeks) and were naïve to other biologics. Patients who were in clinical remission were asked to switch from RI to BI using the same therapeutic dose. Patients switched to BI were compared with a matched control group receiving continuous RI. During follow-up the demographic, clinical, laboratory parameters and comorbidities were all recorded for at least 18 months. Disease activity was measured using the Bath Ankylosing Spondylitis activity index (BASDAI), and the Ankylosing Spondylitis disease activity score (ASDAS), using the C-reactive protein. Remission was defined if patients achieved BASDAI ≤4 and ASDAS ≤1.3. Results: twenty-one patients were excluded, nine because had no clinical remission and twelve because refused to switch. Thus, 88 were evaluated. From those, 45 switched to BI, while 43 continued receiving RI. There were no differences between groups regarding demographic, clinical and laboratory parameters. All patients were in clinical remission (BASDAI ≤4 and ASDAS ≤1.3). During follow-up, five patients from the switched group and three from the maintenance group discontinued the study. Four patients receiving BI presented nocebo effects and were switched back to the RI. Three responded well, while the fourth did not. After 18 months of treatment, all patients in both groups remained in clinical remission. No significant adverse events were noted between groups.

Conclusion: BI is equivalent to RI in maintaining AS in clinical remission for at least 18 months.

Acknowledgement: We have no acknowledgement for this abstract.

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REFERENCES:

Methods: This multicenter, prospective observational cohort study used the TREasure database in which web-based registration of rheumatoid arthritis and SpA patients are being performed in 15 centers across different regions of Turkey. In this study, data of SpA patients switching from one biologic agent to another were analyzed. Demographic and clinical data, follow-up duration, time to switch, and reasons for switching were retrieved from the database. Kaplan-Meier analysis was performed to show drug retention rates and Cox regression analysis was performed to investigate the factors affecting switching.

Results: Of the included 3138 SpA patients, 1165 (37.1%) switched to another biologic agent (switched group) and 1973 (62.9%) continued to receive their current therapies (continued group). The median follow-up duration of all patients was 3.8 years and the median time to switch was 1.0 years (0-13.4 years). According to the distribution of comorbidities, the rates of patients having diabetes mellitus, hyperlipidemia, asthma, gastrointestinal bleeding, and cancer were significantly higher in the switched group than those of in the continued group (8.4% vs. 5.6%, p=0.006; 14.5% vs. 9.2%, p=0.001; 15.6% vs. 6.2%, p<0.001; 3.2% vs. 1.8%, p=0.018; and 1.0% vs. 0.3%, p=0.019, respectively). Features of the patients are presented in Table 1. Cox regression analysis revealed that female gender HR 1.47 (95% CI 1.24-1.75), p<0.001, disease duration HR 1.016 (95%CI 1.00-1.03), p<0.009, and BASDAI score HR 1.095 (95%CI 1.05-1.14), p<0.001 were the significant increasing factors for switching from one biologic agent to another.

In the switched group (n=1165), the main reasons for switching were secondary inefficacy (n=351), primary inefficacy (n=328), and side effects (n=287) followed by primary or secondary unknown inefficacy (n=57), physician's request (n=45), patient's demand (n=36), willing to be pregnant (n=9), other (n=37), and unknown (n=70).

Conclusion: In SpA patients, switching was frequent between anti-TNF agents and the median time to first switch was 1 year. Female gender, short disease duration, and lower BASDAI score were found to be the significant factors affecting switching from the anti-TNF agent used at first. The main reasons for this switching were primary (29.0%) and secondary (31.0%) inefficacy followed by side effects (23.6%). Switching between subcutaneous anti-TNF agents is generally less than switching from infliximab to another biologic agent.

Disclosure of Interests: Umut Kalyoncu Grant/research support from: MSD, Roche, UCB, Novartis and Pfizer, Consultant for: MSD, Abbvie, Roche, UCB, Novartis, Pfizer and Abdi Ibrahim, Speakers bureau: MSD, Abbvie, Roche, UCB, Novartis, Pfizer and Abdi Ibrahim, Hakan Ertenli.

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CHARACTERIZATION OF PATIENTS WITH INFLAMMATORY BOWEL DISEASE IN THE ANKYLOSING SPONDYLITIS COHORT PRIOR AND DURING ADALIMUMAB TREATMENT: DATA FROM A LARGE GERMAN NON-INTERVENTIONAL STUDY

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Background: Spondylarthritides (SpA) are characterized by different disease manifestations such as arthritis, enthesitis, dactylitis and associated to concomitant diseases like inflammatory bowel diseases (IBD) including ulcerative colitis (UC) and crohn’s disease (CD). IBD might have a specific role to SpA due to common pathophysiological pathways. Characteristics of the rheumatic disease and response to treatment may differ within the phenotypic manifestation and with and without associated diseases. Adalimumab (ADA) is a monoclonal antibody inhibiting TNF alpha which has demonstrated efficacy in both, nraxSpA and ankylosing spondylitis (AS) as well as for UC and CD.

Objectives: To evaluate patient baseline characteristics prior to and treatment response on different disease manifestations in a cohort of AS patients with IBD compared to an AS without IBD during ADA treatment.

Methods: Data from a large German multicenter prospective observational non-interventional study (n=3,756) of patients with active AS who initiated ADA therapy during routine clinical care were analyzed with focus on specific patient groups: (1) patients with AS and IBD at baseline (n=166) and (2) patients with AS without IBD at baseline (n= 3,590). Patient characteristics and data of efficacy on different disease manifestations and prevalence of concomitant IBD over 24 months were analyzed.

Results: Of 3,756 patients in the main analysis set, 166 (4.4%) were identified to suffer from concomitant IBD at baseline. Baseline characteristics showed differences in gender distribution, proportion of patients with enthesitis, psoriasis and uveitis showing a higher proportion of each for the IBD group (Table). After 24 months of ADA treatment, both groups had similar decreases for BASDAI, BASMI, BASFI and dactylitis improvement. The IBD group had a fast decrease in BASDAI at M6 to its maximum (95.2%) of patients with active AS who initiated ADA therapy during routine clinical care were analyzed with focus on specific patient groups: (1) patients with AS and IBD at baseline (n=166) and (2) patients with AS without IBD at baseline (n= 3,590). Patient characteristics and data of efficacy on different disease manifestations and prevalence of concomitant IBD over 24 months were analyzed.

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52.7% (r-axSpA/AS: 52.6%; nr-axSpA: 52.9%) had inactive disease (ASDAS<1.3; LORCF; Table B). The treatment-emergent adverse event (TEAE) rate/100 patient-years was 224.2; 3.9% patients discontinued CZP due to TEAEs. No new safety signal was identified.

Conclusion: The run-in phase of C-OPTIMISE shows that similar and continued CZP due to TEAEs. No new safety signal was identified.

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INFLIXIMAB TROUGH LEVELS AND DISEASE ACTIVITY
PREDICT EARLY CLINICAL RESPONSE IN PATIENTS
WITH AXIAL SPONDYLOARTHRITIS

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FRI0399 INFliximab trough levels and disease activity

Conclusion: IXE demonstrated rapid efficacy in the treatment of AS/r-axSpA at wk 16 irrespective of baseline serum CRP levels or spinal MRI score.

REFERENCES:

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FRI0400 LONG-TERM SAFETY OF IXEKIZUMAB IN PATIENTS
WITH RADILOGIC AXIAL SPONDYLOARTHRITIS/
ANKYLOSING Spondylitis: An integrated
Analysis of COAST-V and COAST-W

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Background: The efficacy and safety of ixekizumab (IXE) in patients with radiographic axial spondyloarthritis (r-axSpA) were investigated in the COAST trial program.

Objectives: To report the long-term safety of IXE in r-axSpA patients using integrated safety data from the COAST trials program.

Methods: Safety data for r-axSpA patients treated with IXE were integrated from COAST-V (biologic-naive; NCT02696785) and COAST-W (Inadequate responders or intolerant to 1 or 2 TNF inhibitors; NCT029696798) studies. Patients fulfilled the AGS criteria for axial spondyloarthritis and met mNY criteria for ankylosing spondylitis. Trial eligibility criteria were previously reported.1,2 In these studies, participants were randomized to placebo (n=191), adalimumab (n=90, active reference arm, COAST-V only), or ixekizumab (n=376). Study participants initially randomized to IXE in both trials were treated with a starting dose (80-mg or 160-mg) and then 80-mg IXE every 2 weeks (IXE2W) or 4 weeks (IXE4W). Patients initially treated with placebo or adalimumab were re-randomized at Week 16 to receive either IXE2W or IXE4W following a 160-mg starting dose. The analysis population included all ixekizumab-exposed patients in both trials. Incidence rates (IR) per 100 person years with 95% confidence intervals (CI) and the number of patients are reported. Adverse Event (AE) codes were derived from MedDRA (v21.0). Integrated safety data are presented here include all data collected between May 6, 2016 and Sept, 20, 2018.

Results: The integrated population consisted of 641 patients with 749.6 total patient-years of exposure to IXE. Mean follow up time was 427 days. Mean baseline age was 43.8 ± 12.3 years. Mean and median baseline disease symptom duration (since onset) were 17.2 ± 10.8 years and 15.5 years (Min: 1.1, Max: 56.2), respectively. Safety data are presented in Table 1. Among these patients, 489 (76.3%) reported ≥1 treatment event.
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emergent AEs with an IR of 65.2. Serious AEs (1) were reported for
51 (8.0%) patients with an IR of 6.8. Discontinuations due to AEs were
reported for 38 (5.9%) patients with an IR of 5.1. One death was
reported, a suicide, in a patient with a documented prior history of
depression and judged by the blinded principal investigator to be unrelated to the investigational product. The overall infection IR was 39.4,
with both serious and opportunistic infections reported with an IR of 1.7.
Among opportunistic infections, no Tuberculosis infections or reactivations
were reported and the Candida infection IR was 1.2. No infections were
associated with grade 3 or 4 neutropenia. The confirmed major adverse
cardiovascular events IR was 0.1. The malignancy IR was 0.4 with acute
promyelocytic leukemia, bladder cancer, and ovarian cancer reported. The
depression IR was 0.8. The adjudicated inflammatory bowel disease (IBD)
IR was 1.5 with 4 of 11 patients having prior history of IBD. The Anterior uveitis (AU) IR was 3.9 with 24 of 29 patients having prior history
of AU. The injection site reaction IR was 11.3.

Conclusion: The reported safety profile for IXE in r-axSpA is consistent
with the profile reported for other indications. During the extension period,
the overall safety profile of ixekizumab remained consistent with that
observed during the double-blind period of COAST-V and COAST-W.1,2
REFERENCES:
[1 ] [Van der Heijde et al Lancet 2018 2Deodhar et al Arthritis Rheumatol
2018]
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Scientific Abstracts
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FRI0401

EFFECT OF LONG-TERM TREATMENT WITH
SECUKINUMAB ON LIPID PROFILE IN PATIENTS WITH
ACTIVE ANKYLOSING SPONDYLITIS AND PSORIATIC
ARTHRITIS: POOLED 4 YEAR ANALYSIS

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7
Novartis Pharmaceuticals UK Limited, Surrey, United Kingdom; 8Novartis
Pharmaceuticals Corporation, East Hanover, United States of America
Background: Systemic inflammation may adversely affect the lipid profile
in AS and PsA patients (pts)1. Treatment with some TNF and JAK inhibitors have reported increased total cholesterol (TC) and triglycerides (TG)
despite reduction in inflammation2-3. Secukinumab (SEC), a fully human
monoclonal antibody that directly inhibits IL-17A, has demonstrated a sustained efficacy and consistent safety profile in pts with AS and PsA4
Objectives: To evaluate the long-term effect of SEC on key lipid parameters in AS and PsA pts from pooled phase 3 clinical trials, through 208
weeks (wks)
Methods: This post hoc analysis included pooled data from MEASURE 1-4
(SEC 150 mg) in AS (N = 892) and FUTURE 2-5 studies (SEC 150/300
mg) in PsA (N = 2049), from pts treated with SEC or placebo (PBO).
Serum TC, TG, LDL- and HDL-cholesterol and TC/HDL-C levels were
assessed at baseline (BL), Wks 16, 104 and 208 in overall population and
in sub-groups by prior anti-TNF therapy, concomitant methotrexate (MTX)
and BL statin usage. Shift of common terminology criteria for adverse
events (CTCAE) grade from BL through Wk 208 were also analysed
Results: BL characteristics were comparable across SEC and PBO
groups. Lipid levels were stable in SEC treated AS and PsA pts through
Wk 208 (Table) with mean change (mmol/L) from BL in AS: TC = ±0.1,
TG = 0.1-0.2, LDL-C = ±0.1, HDL-C = ±0.04 and TC/HDL-C = ±0.2 and
PsA: TC = ±0.2, TG = 0.001-0.2, LDL-C = ±0.2, HDL-C = ±0.06 and
TC/HDL-C = ±0.2. Stable lipid values were also seen across key subgroups by prior anti-TNF therapy, concomitant MTX and BL statin usage,
which remained stable through Wk 208. No Change in CTCAE lipid
grades was observed in >90% of SEC-treated pts through Wk 208
Conclusion: SEC did not adversely affect the lipid profile and TC/HDL-C
ratio in pts with AS and PsA, over 4 years. The lipid profile remained
stable with SEC treatment and was sustained irrespective of prior antiTNF status, concomitant MTX and BL statin usage
REFERENCES:
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of: Novartis, Jianyuan Wang Employee of: Novartis


Lipid levels in AS and PsA pts through Wk 208

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<th>Parameters</th>
<th>Wk 150 mg (N=504)</th>
<th>SEC 300 mg (N=461)</th>
<th>SEC 150 mg (N=907)</th>
<th>PBO (N=288)</th>
<th>PBO (N=681)</th>
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<tr>
<td>TC (&lt;5.2)*</td>
<td>4.92 (802)</td>
<td>4.90 (802)</td>
<td>4.99 (409)</td>
<td>5.07 (905)</td>
<td>5.12 (675)</td>
</tr>
<tr>
<td>LDL-C (&gt;1.5)*</td>
<td>3.09 (208)</td>
<td>3.08 (208)</td>
<td>3.11 (460)</td>
<td>3.18 (899)</td>
<td>3.17 (630)</td>
</tr>
<tr>
<td>HDL-C (&gt;1.5)*</td>
<td>1.44 (74)</td>
<td>1.43 (74)</td>
<td>1.43 (460)</td>
<td>1.44 (899)</td>
<td>1.47 (630)</td>
</tr>
<tr>
<td>LDL-C/HDL-C</td>
<td>2.08 (199)</td>
<td>2.07 (199)</td>
<td>2.02 (460)</td>
<td>2.09 (899)</td>
<td>2.25 (630)</td>
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| n, number of pts with data at both BL and at that time point; N, total number of pts

FRIO0402 **SECUKINUMAB FOR AXIAL SPONDYLOARTHRITIS: DRUG SURVIVAL IN REAL-WORLD SETTING AND RESPONSE FACTORS**

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BACKGROUND: IL-17 inhibition has been proved effective in patients with ankylosing spondylitis (AS) in clinical trials and it has been added to the most recent national and international treatment guidelines. However, real-world data of its use is still scarce.

OBJECTIVES: This study aims to analyze drug survival of secukinumab for axial spondyloarthritis (AxSpA) in a real-world setting and identify response factors.

METHODS: Multicentric observational, retrospective, longitudinal study conducted in 4 tertiary hospitals of the Madrid region. Patients over 18 y.o. with clinical diagnosis of AxSpA and having received at least one dose of secukinumab between January 2016 and October 2018 were included. Medical records were reviewed to collect demographic and clinical data related to AxSpA, its features and treatment. Statistical analysis was performed including bivariate analyses (considering withdrawal of drug during study period or not) and survival analysis with Kaplan-Meier and Cox regression. Reasons for discontinuing therapy are described. To detect influential variables, demographic characteristics, HLA-B27 positivity, radiographic features, previous biologic therapies, comorbidities and extra-articular involvement were analyzed.

RESULTS: Out of 143 patients included, 89 (62%) maintained secukinumab therapy at the end of the observation period (Dec 31, 2018), with an average drug survival time of 17 ± 8.2 months. 54 patients (38%) withdrawn therapy, due to primary ineffectiveness (26%), secondary ineffectiveness (14), adverse events (7) and other reasons (7). Median time to withdrawal was 6 months (0-21). No significant differences were found between groups, but a tendency to higher number of female patients in the group with higher drug survival time (41%, p = 0.07), non-radiographic AxSpA (35% vs 27%, p = 0.053) and lower HLA-B27 positivity (50% vs 65%, p = 0.052) was noted in the group withdrawing therapy. Previous exposure to biologic therapy did not differ (75% vs 71%, p = 0.37). Number of bDMARDs before Secukinumab therapy was also similar in both groups; the proportion of patients with previous exposure to 2 or more bDMARDs were 17% vs 22% (p = 0.373). Neither differences were found in all other variables studied (demographic, hip arthropathy, syndesmophytes, extra-articular involvement –uveitis, psoriasis, inflammatory bowel disease– or in comorbidities (tobacco exposure, hypertension, diabetes mellitus, dyslipidemia, ischemic heart disease, malignancy).

Conclusion: This study assessing drug survival of secukinumab in real-world setting showed a trend to lower drug survival in comparison to clinical trial data. No differences were found in the treatment withdrawal group. Population in which secukinumab is prescribed in real-world setting differs from clinical trials, with higher previous exposure to bDMARDs and higher comorbidity.

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FRIO0403 **HIGH BASELINE PATIENTS COMPARED WITH EVALUATOR’S GLOBAL ASSESSMENT IS ASSOCIATED WITH LOWER RETENTION AND REMISSION RATES OF FIRST TNF INHIBITOR IN AXSPA PATIENTS – DATA FROM THE EUROSPA COLLABORATION**

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BACKGROUND: Discordance between baseline patient’s and evaluator’s global assessment of disease activity is common.1 However, the impact of such discordance on retention and remission rates of TNF inhibitor (TNFi) therapy in axial spondyloarthritis (axSpA) patients remains unexplored.

OBJECTIVES: To assess the impact of baseline discordance, defined as “patient’s minus evaluator’s global assessment of disease activity” (ΔPEG), on retention and remission rates of first TNFi in female and male axSpA patients across Europe.

METHODS: AxSpA patients from 10 European registries participating in the European Spondyloarthritis Research Network Collaboration (EuroSpa) were included. Retention rates after 6/12/24 months (55% retention rate for both male and female patients) were assessed with Kaplan-Meier analyses, with comparison between baseline ΔPEG quartiles with log rank test, stratified by gender. Proportions of patients in BASDAI remission (≤42) and ASDAS inactive disease (<1.3) after 6/12/24 months were derived for different ΔPEG quartiles compared with Chi-square test, stratified by gender.

RESULTS: A total of 9013 axSpA patients were included. Mean(SD) age for women(n=3639)/men(n=5374) were 42.7(12.0)/41.7(12.0) years, disease duration 5.1(7.4)/9.8(7.7) years, median(25-75 percentiles) baseline ΔPEG

Science Abstracts

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TNFi retention rates as well as proportions of patients achieving BASDAI<4 was achieved by 49% and ASDAS<1.3 by 9% of the patients. Results: Data from axSpA patients treated with secukinumab in routine care from 12 countries in the European Spondyloarthritides Research Collaboration (EuroSpA) were pooled. Time from treatment initiation to data cut was >= 6 months. Group comparisons were performed with independent t-test, Mann-Whitney U-test, ANOVA, Kruskal-Wallis and Chi-square test, as appropriate. Kaplan-Meier analyses with log rank test were performed for comparison of secukinumab drug survival. Results: A total of 1556 axSpA patients were included. Overall, 6-month BASDAI<4 was achieved by 49% and ASDAS<1.3 by 9% of the patients. bDMARD naïve compared with non-naïve secukinumab starters had shorter disease duration, higher baseline disease activity, a higher proportion were men and a higher proportion achieved crude and LUNDEX adjusted 6-month BASDAI<4 but not ASDAS<1.3 (table).
Drug retention was higher for bDMARD naïve compared with non-naïve patients (figure 1a). Baseline characteristics and disease activity (data not shown) as well as drug retention differed in-between the European registries (figure 1b).

Figure 1a. Pooled 6-month secukinumab retention rates for axSpA patients in EuroSpA, as well as compared between the bDMARD naïve and non-naïve patients (log rank test; p<0.001).

Figure 1b. Pooled 6-month secukinumab retention rate as well as compared across 11 registries in EuroSpA (log rank test; p=0.001). ICEBIO was excluded from the Kaplan-Meier plot (<10 patients).

Conclusion: This study of >1500 patients in 12 European countries provides real-world data on the effectiveness of secukinumab in patients with axSpA, adding evidence to existing RCTs. A majority of the patients was previous bDMARD users and had long disease duration. BASDAI <4 was achieved by 49% of the patients and ASDAS <1.3 by 9% at 6 months. Overall retention rate was 83% at 6 months, with significant differences across the registries and higher retention rates for bDMARD naïve compared with non-naïve axSpA patients.

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Disclosure of Interests: Brigitte Michelsen Grant/research support from: Unrestricted grant: Novartis, Consultant for: Novartis, UCB, Cecile Heegaard Brahe Grant/research support from: Unrestricted grant: Novartis, Joho Asking Grant/research support from: Karolinska Institutet (JA) has or has had research agreements with the following pharmaceutical companies, mainly in the context of the ATRIS national safety monitoring programme for rheumatology biologicals: Abbvie, BMS, MSD, Eli Lilly, Pfizer, Roche, Samsung Bioepis, and UCB, Consultant for: Karolinska Instutute for rheumatology biologicals: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Mercck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, Speakers bureau: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Mercck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, Merete L. Helland Grant/research support from: BMS, MSD, AbbVie, Roche, Novartis, Biogen, Pfizer, Consultant for: Eli Lilly, Speakers bureau: Orion Pharma, Biogen, Pfizer, CellTrion, Merck, Samsung Bioepis


FRI0405 AQUILA STUDY IN GERMANY – REAL WORLD DATA ON SECUKINUMAB’S EFFECTIVENESS IN PSORIATIC ARTHRITIS PATIENTS – RESULTS FROM AN INTERIM ANALYSIS

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Background: Psoriatic arthritis (PsA) is a chronic, progressive, inflammatory disorder of skin and joints, it impacts both physical and emotional well-being, and increases the risk of comorbidities. Thus, improvement of disease activity as well as emotional well-being is of utmost importance in treatment of PsA patients (pts). In clinical trials, secukinumab, an anti-interleukin (IL)-17A monoclonal antibody, has shown to significantly improve signs and symptoms of PsA.

Objectives: To evaluate real-world interim data on the effectiveness of secukinumab on treatment outcomes and quality of life (QoL) in pts with PsA.

Methods: AQUILA is an ongoing, 52-week (wk) non-interventional study enrolling 2000 pts with active PsA and ankylosing spondylitis. Here, we report interim results of effectiveness in a subgroup of PsA pts treated with secukinumab.

Validated questionnaires were used to measure effectiveness of secukinumab on:

- disease activity
- Physician’s Global Assessment (PhGA, 0=no disease activity, 10=most intense disease activity),
- Psoriasis Area and Severity Index (PASI),
- American College of Rheumatology (ACR) joint count and C-reactive protein (CRP),
- and QoL.
- Psoriatic Arthritis Impact of Disease 12–item score (PsAID–12),
- Medical Outcomes Study (MOS) SLEQ scale and Beck’s Depression Inventory II (BDI–II).

Pts who were already under secukinumab treatment or just about initiating secukinumab therapy, based on medical therapeutic need, were included; in both scenarios, disease activity at start of secukinumab treatment was used as starting point for analysis. Treatment decision was made independently of participating in this study. Pts were observed from...
Results: At BL, 641 PsA pts were included of whom 385 (60.1%) com-
pleted 52 wks so far (i.e. at the time of data cut-off for this interim anal-
ysis; 58.5% (n=375) of the pts were female and 41.5% (n=266) were
male, mean age was 52.6 years. About 66% (n=424) were pre-treated
with biologics. Mean PhGA improved from 5.3 at BL (n=571, 89.1%) to
2.5 at wk 52 (n=341, 53.2%). Mean absolute PASI improved from 8.1 at
BL (n=211, 32.9%) to 1.2 at wk 52 (n=147, 22.9%). More than half of
the documented pts (51 out of 94) achieved a 100% reduction (PASI
100) in skin symptoms at wk 52. The mean number of tender/swollen
joints (ACR) was reduced from 7.6 (n=436, 68.0%) to 3.9 (n=437, 68.2%) to
3.0 (n=241, 37.6%) at wk 52. The percentage of pts with CRP >3mg/L dropped from 43.0% at BL (n=230) to 36.6% at wk
52 (n=112). Mean PsA-ID improved from 5.0 at BL (n=602, 93.9%) to
3.3 at wk 52 (n=343, 53.5%). The percentage of PsA pts with high dis-
 ease activity (score ≥ 5) assessed by PsA-ID decreased from 61.0% at
BL (n=387) to 26.2% at wk 52 (n=90). MOS sleep scales did not change
relevantly over time. With respect to pts with a BDI-II reduction of
at least 3 score points, the mean value improved from 16.4 (mild
depression) at BL to 8.0 (no depression) at wk 52 (n=123, 19.2%).
Conclusion: Secukinumab reduced disease activity and improved QoL
already within this subgroup of PsA pts. Thus, real-world data from the
AQUILA study show that, in clinical routine, secukinumab treatment up to
one year provides a clear benefit for PsA pts in clinical and QoL
parameters.

REFERENCES:

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MSD, Novartis, Pfizer, Roche, and UCB.; Daniel Peterlik Employee of:
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Speakers bureau: Eli Lilly and Company.


FRID0406

AQUILA STUDY IN GERMANY – REAL WORLD DATA ON EFFICACY AND SAFETY OF SECUKINUMAB IN ANKYLOSING SPONDYLITIS PATIENTS – RESULTS FROM AN INTERIM ANALYSIS

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Background: Ankylosing spondylitis (AS) is characterized by chronic
inflammation of the spine and is at high risk to cause inflammation, pain,
and stiffnessextraspinally as well. Thus, important aims in therapy of AS
are pain reduction and maintenance of physical functioning. Secukinumab,
a fully human monoclonal antibody that selectively neutralizes interleukin
(IL)-17A, has already shown significant efficacy in the treatment of AS in
clinical trials.1

Objectives: The aim of this interim analysis is to evaluate the effective-
ness of secukinumab on disease activity, physical functioning and quality
of life in AS patients (pts) in a real world setting.

Methods: AQUILA is an ongoing, multi-center, 52-week (wk) non-interven-
tional study enrolling 2000 pts with active AS and psoriatic arthritis in
Germany. Here, we report interim results of effectiveness in a subgroup
of AS pts treated with secukinumab. Validated questionnaires were used to measure the effectiveness of secu-
kunumab on:

- disease activity
- Physician’s Global Assessment (PhGA: 0=no disease activity, 10=most
  intense disease activity),
- Bath Ankylosing Spondylitis Disease Activity Index (BASDAI),
- C-reactive protein (CRP)
- physical functioning
- global functioning: Assessment of Spondyloarthritis Health Index, (ASAS
  HI), and key aspects of sleep
- Medical outcomes Study Sleep Scale (MOS),
- severity of depression
- Beck’s Depression Inventory Version II (BDI-II).

Pts who were already under secukinumab treatment or just about initiat-
ing secukinumab therapy, based on medical therapeutic need, were
included; in both scenarios, disease activity at start of secukinumab treat-
ment was used as starting point for analysis. Treatment decision was
made independently of participating in this study. Pts of hip joints treated
from BL up to wk 52 according to clinical routine. Real-world effectiveness
of secukinumab was assessed prospectively and analyzed as observed.

Results: This interim analysis describes 311 AS pts who were included at
BL and of whom 178 (57.2%) have completed wk 52 so far (i.e. at the
time of data cut-off for this interim analysis). 63.3% (n=197) of the
pts were male and 36.7% (n=114) female, mean age was 47 years. About
70% (n=221) of the pts were pre-treated with biologics. Physicians
reported a mean PhGA value of 5.9 at BL (n=282; 90.7%) which
improved to 2.6 at wk 52 (n=168; 54.0%). Mean BASDAI value was
reduced from 5.6 at BL (n=301, 96.6%) to 4.0 at wk 52 (n=171, 55.0%).
With regard to inflammation parameters, the percentage of pts with a
CRP of >3mg/L decreased from 54.7% (n=140) to 40.0% (n=58) at wk 52.
Further, mean ASAS-HI value decreased over time from 8.2 at BL (n=274,
88.1%) to 6.3 at wk 52 (n=156, 50.2%). MOS sleep scale did not change
time over time, yet only few BL documentations for these scales were
available (range n=26 to 44). Regarding depression mood of the
pts, while at BL 40.7% (n=101) of the pts suffered from mild to severe
depression (BDI-II score between 14 and 63), 30.3% (n=46) did so in
wk 52. This is reflected by a drop of mean BDI-II value from 13.0 at
BL (n=248, 79.7%) to 10.6 at wk 52 (n=152, 48.9%).

Conclusion: This is a limited subset of AS pts, secukinumab reduced
disease activity and improved quality of life for up to one year as
reported by validated physicians’ as well as pt-reported outcomes.
Overall, this interim analysis gives promising insights into treatment effects
of secukinumab on pts’ physical and mental well-being under real-world
conditions.

REFERENCES:

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FRID0407

TWO-YEAR ULTRASOUND CONTROLLED STUDY OF HYALINE CARTILAGE AND SYNOVIAL LAYER STRUCTURE OF HIP JOINTS IN PATIENTS WITH ANKYLOSING SpondyLitis DURING TREATMENT WITH ADALIMUMAB

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Background: The impairment of hip joints has significant prognostic value
on functional status of patients with Ankylosing spondylitis (AS) [1]. One
of possible yearly marker of hip joints structure damage in patients with
AS may be changing in volume of hyaline cartilage [2]. Objectives.

Objectives: To investigate changes in width of hyaline cartilage and syn-
ovial layer of hip joints in patients with coxitis, associated with AS under
treatment with adalimumab (ADA) during 2 years.

Methods: The 28 patients with AS and clinical, ultrasonic and radi-
ographic signs of coxitis (21 male, 7 female, average age is 35.4 years
old, duration of disease is 12-132 months) were included into study. All
patients were being treated by NSAIDs at least 3 months before they
started to take ADA (40 mg subcutaneously every 2 weeks). Treatment
with ADA was continued during 24 months. Patients were observed at
month 0, 12 and 24 months of treatment including measurements of pain
visual analog scale (VAS) in hip movements, maximal distance between
ankles, pelvic X-ray and sonography of hip joints by 10-18 MHz probe.
BASRI-Hips index was applied for radiographic estimation of structural
damage of hip joints [3]. During sonography width of hip joint capsule
and hyaline cartilage were measured. The Mann-Whitney-U test was used
for comparison of changes in clinical and sonographic data between two
groups of patients.
Results: It was determined that painVAS at hip movements was decreased (23.1 [12.3; 32.3] mm at month 12 and 19.7 [11.8; 32.9] mm at month 24 vs 73.7 [59.5; 82.6] mm at month 0, p<0.05) and maximal distance between ankles was increased (112.5 [94.7; 122.2] mm at month 12 and 116.2 [91.2; 125.0] mm at month 24 vs 78.7 [63.4; 86.8] mm at month 0, p<0.05) in observed patients under treatment with ADA. It was also found that ultrasound measured width of hip joint capsule was decreased from 11.8 [10.3; 12.7] mm at month 0 to 8.7 [8.1; 9.4] mm at month 12 (p<0.05) and 7.5 [6.6; 8.5] mm at month 24 (p<0.05). The ultrasound measured width of hyaline cartilage in observed patients was increased from 0.8 [0.6; 1.1] mm at month 0 to 1.0 [0.8; 1.2] mm at month 12 (p<0.01) and 1.2 [1.0; 1.7] mm at month 24 (p<0.05) under treatment with ADA. The BASRI-Hips index had not changed in observed patients at the end of 24-months period. The differences in changes of hip cartilage width between patients with joint capsule width at month 24 less than 9 mm and more than 9 mm was determined (p<0.05): +0.6 [0.3; 0.8] mm vs +0.1 [-0.1; 0.2] mm.

Conclusion: Treatment with ADA leads to decrease of clinical and sonographic signs of coxitis in patients with AS and improves of hyaline cartilage structure. The increase of width of hip hyaline cartilage was observed in patients with absence of ultrasound signs of hip joints synovial inflammation in patients with AS. MRI-controlled studies are needed to confirm ability of THF inhibitors to restore cartilage volume in patients with coxitis, associated with AS.

REFERENCES:
[3] MacKay K, Brophy S, Mack C, et al. The development and validation of a non-biological background medication or switch to open-label biologics at 5 yrs at baseline [BL]) from C-axSpA and baseline. AxSpA treated with CZP (400mg at Wks 0/2/4, then 200mg every 2 wks), and could adjust double-blind, PBO-controlled study, pts were randomised 1:1 to PBO or CZP (400mg at Wks 0/2/4, then 200mg every 2 wks), and could adjust double-blind treatment.

Disclosure of Interests: None declared
FEMALE ANKYLOSING SPONDYLITIS PATIENTS HAVE A SUBSTANTIALLY LOWER TNFI TREATMENT RESPONSE THAN MEN

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Background: Accumulating data revealed difference in treatment efficacy in biologicals in women with axial spondyloarthritis (axSpA) (1). Objectives: The aim of this study was to assess gender differences in TNFI inhibitor treatment response up to a five year biological treatment Methods: Radiographic axSpA patients (AS) were recruited from the Amsterdam Spondyloarthritis cohort (the AmSpA cohort) of the VU University center and Reade. This prospective, observational cohort study included consecutive AS patients who were treated with TNFI inhibitors (TNFI) (infliximab, adalimumab, etanercept or golimumab). Data of this cohort was collected between January 2000 until December 2018. Inclusion criteria were: AS diagnosis according to the modified New York criteria and start with a first TNFI. Patients were evaluated at baseline, three months, six months and once yearly up to five years follow-up.

Disease activity was determined with the Ankylosing Spondylitis Disease Activity Score (ASDAS) and the Bath Ankylosing Spondylitis Index (BASDAI). Multivariable GEE analyses were performed to assess the delta difference between baseline and 1 year.

Results: 389 AS patients were included in the AmSpA cohort. Thirty-three of these 389 patients were excluded since they were not TNFI naive or their treatment status was unknown (7.5%), of whom the majority was never treated with TNFI (infliximab, adalimumab, etanercept or golimumab). Data of this cohort was collected between January 2000 until December 2018. Inclusion criteria were: AS diagnosis according to the modified New York criteria and start with a first TNFI. Patients were evaluated at baseline, three months, six months and once yearly up to five years follow-up. Disease activity was determined with the Ankylosing Spondylitis Disease Activity Score (ASDAS) and the Bath Ankylosing Spondylitis Index (BASDAI). Multivariable GEE analyses were performed to assess the delta difference between baseline and 1 year.

Conclusion: In radiological axial SpA, female patients had significantly lower level of TNFI treatment response at six and twelve months on the ASDAS-CRP and had a higher drop-out rate compared to males. This strongly indicates an important gender difference in especially the twelve first months of TNFI treatment.

REFERENCES:


TFR0410 TNFI THERAPY REDUCES SPINAL RADIOGRAPHIC PROGRESSION IN AXIAL SPONDYLOARTHRITIS (PARTIALLY) BY DECREASING DISEASE ACTIVITY

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Background: Recent observational data suggest that TNFI reduce spinal radiographic progression in radiographic axial spondyloarthritis (r-axSpA) mostly by inhibiting disease activity. Yet, resolution on the controversial effect of TNFI on structural progression is yet to be achieved.

Objectives: To investigate whether in r-axSpA TNFI have an indirect (through ASDAS) and/or direct effect on spinal radiographic progression.

Methods: Patients (pts) with axial spondyloarthritis (axSpA), fulfilling the modified New York criteria (mNY) were included in this prospective, observational cohort (ALBERTA FORCAST). Clinical and imaging data were collected at baseline and every 2 years up to 10 years of follow-up. Radiographs of the spine were independently scored by 2 central readers and one adjudicator (if disagreement), with known chronological order but blinded to clinical data, using the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS). The indirect effect of TNFI on mSASSS progression was evaluated by testing the interaction between TNFI and ASDAS at the start of each 2-year interval. If significant (p<0.15), the association between mSASSS at t and mSASSS at the end of the interval (t+1) was assessed in 3 groups of exposure to TNFI: i) treatment in all visits; ii) treatment in some visits; and iii) never treated.

Results: In total, 314 pts were included (74% males, mean symptom duration 17.8 (SD 11.7) years, 83% HLA-B27 positive and 7% previously treated with ≥1 TNFI). The interaction between ASDAS and TNFI at t was significant (p=0.10). A gradient was seen for the effect of ASDAS at t on mSASSS at t+1, which was more than 2 times higher in patients never treated with TNFI (β (95% CI): 0.41 (0.13; 0.68) compared to those always treated (β (95% CI): 0.16 (0.00; 0.31)) (Figure), showing that treatment with TNFI diminishes the effect of ASDAS on mSASSS. In addition to the indirect effect, TNFI also directly associated with less mSASSS progression: Pts receiving TNFI at t had on average 0.87 mSASSS-units less on t+1 compared to those not treated (β (95% CI): -0.80 (-1.37; -0.22)) and this was noted independently of ASDAS. Importantly, this effect remained significant after PS-adjustment (β (95% CI): -0.80 (-1.37; -0.22)).

Conclusion: This data is in line with previous evidence showing that treatment with TNFI limits spinal radiographic progression in pts with r-axSpA by decreasing disease activity. Additionally, a direct effect of TNFI reducing mSASSS progression, and independent of ASDAS inflammation, is also seen suggesting that other mechanisms also contribute to the structural effect of TNFI.
REFERENCES:

Disclosure of Interests: Alexandre Sepriano: None declared, Sofia Ramiro Grant/research support from: MSD, Consultant for: Abbvie, Lilly, MSD, Novartis, Pfizer, Sanofi, Speakers bureau: Abbvie, Lilly, MSD, Novartis, Pfizer, Sanofi, Stephanie Wichuk: None declared, Praveena Chiochwanwichawat: None declared, Terrie MacCoshem: None declared, Joel Paschke: None declared, Désirée van de Heijde Consultant for: Abbvie, Amgen, Astellas, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Dalichi, Eli-Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, Union Chimique Belge, Robert B.M. Landewé: None declared, Walter P. Maksymiwich Grant/research support from: Abbvie, Novartis, Pfizer, Consultant for: Abbvie, Boehringer, Celgene, Galapagos, Lilly, Novartis, Pfizer, UCB

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FR0411 COMPARABLE CLINICAL RESPONSES BUT HIGHER TREATMENT ADHERENCE OF SECUKINUMAB COMPARED TO TNF INHIBITORS IN SPONDYLARTHROPSIS PATIENTS: LONG-TERM PROSPECTIVE OBSERVATIONAL STUDY IN A TERTIARY HOSPITAL OF GREECE

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Background: Data regarding effectiveness and persistence to therapy with anti-IL17 agent secukinumab (SEC) in spondyloarthritis (SpA) patients of real world clinical practice are very limited.

Objectives: To assess characteristics of SpA patients starting therapy with SEC versus tumor necrosis factor inhibitors (TNFi) in routine clinical care and compare clinical responses and treatment retention at 2 years.

Methods: All patients starting a bDMARD in the Rheumatology Department of the University Hospital of Heraklion, Crete, are included in a prospective observational study after their written informed consent. Data concerning disease activity at pre-specified time-points, drugs, comorbidities and any adverse events are recorded. For the present study we analyzed all consecutive patients with axial (AxSpA) or peripheral SpA (pSpA) starting or switching bDMARD therapy, either a TNFi or SEC from 1/2015 till 12/2018. We excluded patients with IBD-related SpA, starting or switching from a bio-originator to a biosimilar TNFi. We compared disease activity scores improvement at 6 months using linear regression analysis and treatment retention using Kaplan-Meier survival curves with log-rank test and Cox regression. Inverse propensity score weighting (IPW) was used to adjust for the potential confounding of gender, age, disease duration, previous bDMARDS and csDMARDS number, diagnosis (AxSpA vs pSpA), presence of peripheral arthritis and co-therapy with csDMARDs.

Results: A total of 239 patients with SpA started/switched bDMARD (SEC:69, TNFi:170). SEC was the >3rd bDMARD in 63% of patients compared to 17% of TNFi (p<0.001). Patients’ characteristics at baseline were comparable except for disease duration (median (IQR): 5 (1.5-11) years in SEC vs. 0.9 (2.4-6) in TNFi, p=0.001). AxSpA was the diagnosis in 78% patients starting SEC and 79% starting TNFi while peripheral arthritis was slightly more common with SEC (81% vs 76% in TNFi). Monotherapy tended to be more common with SEC compared to TNFi (52% vs 42%, p=0.16). Baseline disease activity regarding both axial and peripheral arthritis was comparable in the two groups. Unadjusted 2-year treatment retention was similar in the two groups, both overall (SEC: 63%, TNFi: 56%, p=0.18) and due to failure or adverse events. However, when we selected only patients on 1st or 2nd bDMARD (SEC:26, TNFi:131), 2-year survival of SEC was higher than that of TNFi (95% vs. 95%, p=0.027). Similarly, SEC tended to have higher TNFi in patients with pSpA (p=0.11). After IPW, SEC administration was an independent predictor for higher bDMARD retention overall (HR (95%CI)=0.48 (0.33-0.69), p=0.001) and specifically due to discontinuation for failure (HR=0.58 (0.38-0.88), p=0.011) and for adverse events (HR=0.21 (0.08-0.62), p=0.004).

Mean BASDAI and ASDAS improvements at 6 months were similar in patients with AxSpA receiving SEC or TNFi [Mean (SD) bBASDAI: 1.6 (2.5) vs 1.4 (2.5), respectively (p=0.78) and ASDAS: 0.7 (1.4) vs 1.0 (1.5), p=0.44]. Similarly, in patients with peripheral arthritis, IADAS28 at 6 months was comparable in the two groups (p=0.88). Adjusted linear regression with IPW provided similar results to the unadjusted analyses in both axial and peripheral disease.

Conclusion: In SpA patients of real-world, administration of SEC results in similar clinical responses but higher treatment adherence compared to TNFi, especially if Secukinumab is the 1st or 2nd bDMARD. Larger number of patients and longer follow-up is needed to confirm these data.

Disclosure of Interests: None declared


FR0412 SPINAL AND SACROILIAC JOINTS INFLAMMATION IN PATIENTS WITH RADIOPHAGIC AXIAL SPONDYLOARTHROPSIS TREATED WITH NETAKIMAB – 16-WEEKS RESULTS OF MULTICENTER, RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE III ASTERA STUDY

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Background: Efficacy and safety of netakimab (NTK), a humanized anti-interleukin 17A antibody, have been previously established in two phase 2 clinical trials in patients with radiographic axial spondyloarthritis (r-axSpA)1 and psoriasis2. ASTERA is a randomized, double-blind, placebo (PBO)-controlled phase III trial, aimed to demonstrate efficacy and safety of NTK in subjects with r-axSpA (NCT03447704).

Objectives: To evaluate the effect of NTK on inflammation in spine and sacroiliac joints (SIJ) at Week (Wk) 16 in ongoing ASTERA study in patients with active r-axSpA.

Methods: 228 eligible adults with active r-axSpA were randomized into 2 study arms (1:1) to receive 120 mg of NTK or PBO, administered as SC injections at Wk 0, 1, 2, and then q2wk through Wk 16. After Wk 16 all patients will start to receive NTK up to week 52. Inflammation in spine and SIJ was assessed with magnetic resonance imaging (MRI) at baseline and Wk 16. The following scoring methods were used: the Berlin spine score (derived from Ankylosing Spondylitis Spine MRI Activity (ASpi-MRI-a) Score for spine assessment and the SPARC score for SIJ assessment. All images were evaluated by central reader, blinded to treatment.

Results: Both arms were comparable in the Berlin spine score (4.18 ± 4.58 in NTK arm vs. 4.19 ± 4.32 in PBO arm) and the SPARC score (5.67 ± 8.33 in NTK arm vs. 5.23 ± 7.86 in PBO arm) at baseline (p=0.05). Data analysis at Wk16 revealed that NTK arm achieved significant decline in bone marrow edema in direct comparison with PBO arm: by Wk 16 the mean change from baseline in the Berlin spine score was -2.16 ± 2.87 in NTK arm vs. -0.30 ± 1.55 in PBO arm (p=0.001) and the mean change from baseline in the SPARC score was -3.80 ± 6.68 in NTK arm vs. -1.82 ± 4.12 in PBO arm (p=0.01).

Conclusion: the treatment with NTK at a dose 120 mg leads to improvement in spine and SIJ inflammation in patients with active r-axSpA by Wk16, as compared with PBO.

REFERENCES:
Disclosure of Interests: Alexander Smirnov: None declared, Inna Gaydu- kova Grant/research support from: JSC BIOCAD, Speakers bureau: patient from Pfizer, Novartis, Abbvie, Biocad, Selgene, MSD, Sanofi does not exceed 10 000 euros, V Mazurov Grant/research support from: JSC BIOCAD, Shandor Erdes Grant/research support from: JSC BIOCAD, Speakers bureau: JSC BIOCAD, Tatiana Dubinina: None declared, Olga Nesmeyanova Grant/research support from: JSC BIOCAD, Alena Ilivanova Grant/research support from: JSC BIOCAD, Alena Kudzner: None declared, Nikolay Sorkoa: None declared, Anna Ereemeva Grant/research support from: JSC BIOCAD, JSC Chinese Employee of: JSC BIOCAD, Roman Ivanov Employee of: JSC BIOCAD

The frequencies of ADA and NAb positive were similar between the two groups at different time points. Through week 24, 79.13% of 412 patients in HS016 and 79.91% of 229 patients in adalimumab group developed ADAs, and 17.48% of 412 in HS016 and 18.78% in 229 in adalimumab group developed NABs.

Conclusion: The results of efficacy, PK, safety, immunogenicity from the study conducted in Chinese AS patients support a high similarity between HS016 and the adalimumab.

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Table 1 Response rates (%) at week 12 and week 24.

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Pharmacokinetic values from 188 AS patients in HS016 group and 109 in adalimumab group were analyzed. The geometric means for steady-state maximum plasma concentration (Cmax) and area under the plasma concentration-time curve from time zero to infinity (AUCinf) were similar between HS016 group and adalimumab group. The proportions of treatment-emergent adverse events, serious adverse events and injection site reactions were similar between the two groups (table 2).

Table 2. Adverse events in AS patients with HS016 or adalimumab.

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ASAS, the Assessment in SpondyloArthritis International Society; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index.

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Disclosure of Interests: Feng Huang: None declared, Fei Sun: None declared, Weiguo Wan: None declared, Lijun Wu: None declared, Liang Dong: None declared, Xiao Zhang: None declared, Tae-hwan Kim: None declared, Raj Sengupta: Grant/research support from: AbbVie, Celgene Corporation, Merck Sharp & Dohme, Novartis, Pfizer, and UCB, Lidaslav Senolt: Grant/research support from: AbbVie, Consultant for: AbbVie, Bristol-Myers Squibb, Celgene Corporation, Merck Sharp and Dohme, Novartis, Pfizer, Roche, UCB, Yi Chen: Shareholder of: Novartis, Employee of: Novartis, Brian Porter: Shareholder, Eileen Dong: None declared, Xiao Zhang: None declared, Tae-hwan Kim: None declared, Weiguo Wan: None declared, Lijun Wu: None declared, Liang Dong: None declared.

REFERENCES:


Acknowledgement: The authors wish to thank the patients and study personnel who made this trial possible, and the study investigators: Hongsheng Sun (Department of Rheumatology, Shandong Provincial Hospital), Dan Wang (Wuhan Puai Hospital), Xiaoxia Wang (the Second Hospital of Shantou Medical University), Zhengyue Jiang (the First Hospital of JILIN University), Liq Bi (the China-Japan Union Hospital of JILIN University), Yan-hong Huang (Beijing Jishuitan Hospital), Ju Liu (Jiujiang NO.1 People's Hospital), Xiaomei Li (Anhui Provincial Hospital), Hao Zhang (the Third Hospital of Central South University), Cibo Huang (Beijing Hospital), Longxin Ma (Yancheng City NO.1 People's Hospital), Yonghong Zhang (Luoyang Orthopedic Hospital), Zhijun Li (the First affiliated hospital of Bengbu Medical College), Chenghui Huang (the Second affiliated hospital of Guangzhou Medical University), Lin Chen (Jilin Province People's Hospital), Junsong Li (Daging Oilfield General Hospital), Xiuxi Liu (the First Affiliated Hospital of Shanxi Medical University).

Disclosure of Interests: None declared


Methods: A multicenter, randomized, non-inferiority, double-blinded, ADA controlled clinical trial with 24 weeks of follow-up was conducted in China. Participants with active AS defined as BASDAI ≥ 4 and average back pain score (VAS 0-10) ≥ 4 were eligible for participation. Participants were randomly assigned to receive BAT1406 (40mg q2w) or adalimumab (40mg q2w) at a ratio of 2:1 for 24 weeks. Primary outcome was the proportion of patients achieving ASAS20 response at 12 weeks. Inclusion of the 95% CI of the ASAS20 response difference within a ± 15% margin was required for equivalence. Secondary outcomes included ASAS40, ASAS5/6, BASDAI50 response, patient reported outcomes, safety and immunogenicity. This trial is approved by China Food and Drug Administration (number 2015LS05751).

Results: 554 eligible patients were enrolled from Jan 2017 to Aug 2017 and randomly assigned to receive BAT1406 (n=363) or Adalimumab (n=191) participants, 514 completed the study. Patients (86.5% of whom were male and whose mean age was 31.6 years) had a mean disease duration was 5.82 years. Over 12 weeks, 75.69% of patients in BAT1406 group and 73.68% in ADA group (between group difference 1.6%, 95% CI [-0.9% to 0.1%]) achieved ASAS20 response (per-protocol set; adjusted treatment difference 2.16%, 95% CI [-6.9% to 11.22%]). Outcomes for secondary end points were consistent with the primary efficacy finding. The frequency of adverse events (AEs) was comparable between groups ([BAT1406 318[87.1%] vs ADA 162 (85.3%)), as well as serious AEs, adverse drug reactions and discontinuations due to AEs. Similar positive rate was found in two groups for anti-drug antibodies up to week 24.

Conclusion: The study met the primary endpoint of demonstrating equivalent efficacy of BAT1406 and ADA. BAT1406 was comparable in tolerance, safety and immunogenicity with ADA in active AS patients.

Disclosure of Interests: Jian Wu: None declared, Zhenchun Zhang: None declared, Shuangyan Cao: None declared, Ji eruo Gu: None declared, number of randomised pts (N=109) (N=218) (N=153) (N=363)

Table. Wk 16 data

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
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<tbody>
<tr>
<td></td>
<td>(N=305)</td>
<td>(N=153)</td>
</tr>
<tr>
<td>ASAS20</td>
<td>58.4*</td>
<td>36.6</td>
</tr>
<tr>
<td>ASAS40</td>
<td>43.9*</td>
<td>17.0</td>
</tr>
<tr>
<td>hsCRP2,3</td>
<td>0.39*</td>
<td>1.05</td>
</tr>
<tr>
<td>ASAS20*</td>
<td>47.2*</td>
<td>17.6</td>
</tr>
<tr>
<td>BASDAI2</td>
<td>-2.79</td>
<td>-1.50</td>
</tr>
<tr>
<td>SF-36 PCS2</td>
<td>7.43*</td>
<td>4.60</td>
</tr>
<tr>
<td>ASQoL2</td>
<td>-4.83*</td>
<td>-2.93</td>
</tr>
<tr>
<td>ASAS 25</td>
<td>16.7*</td>
<td>6.5</td>
</tr>
</tbody>
</table>
| *P < 0.0001;  †P < 0.001; ‡P = 0.01; ‡P < 0.05 vs. PBO (P-values are adjusted for overall and un-adjusted for Chinese populations). NRI for binary and MMRM for continuous variables.

1% responders; 2 LS mean change from BL; 3 ratio of post-BL/BL; LS, least squares; N, total number of randomised patients.
Background: The first symptoms of ankylosing spondylitis (AS) patients usually begin prior to 45 years, but can occur later in life.

Objectives: The purpose of this study is to evaluate the efficacy and safety of anti-TNFα treatment in late-onset AS (LoAS) patients in comparison to those with adult onset AS (AoAS).

Methods: We studied AS patients in TURKBio registry between the dates of January 2011 and November 2018. All the patients fulfilled the modified New York criteria for AS and were classified into 2 groups based on their age at symptom onset: AoAS (age>16 but ≤45 years); and LoAS (age>45 years). In both groups, the following data were compared: (1) epidemiological variables; (2) clinical manifestations, including signs and symptoms at diagnosis; (3) laboratory results; (4) disease activity markers and follow-up parameters (BASDAI, ASDAS-CRP and HAQ); (5) radiographical parameters at baseline. The frequency of using drugs and adverse events were compared.

Results: A total of 2551 AS patients (91.1% with AoAS and 8.9% with LoAS) were included in the study. LoAS group had more female patients, older age, shorter disease duration and diagnostic delay, higher disease activity, and symptoms at diagnosis; (3) laboratory results (4) disease activity markers and follow-up parameters (BASDAI, ASDAS-CRP and HAQ); (5) radiographical parameters at baseline. The frequency of using drugs was similar between the groups (Table 1). The frequency of using drugs was higher in the LoAS group than in the AoAS group, as the use of glucocorticoids and sulfasalazine was more common in the LoAS group. The LoAS group had a higher frequency of anti-TNFα treatment, the mean improvement in BASDAI was significantly higher in the LoAS group compared to the AoAS group.

Conclusion: Our data showed that almost 8.9% of the patients with AS had late-onset of symptoms. The results suggested that LoAS patients might have different demographic, clinical features, disease activity parameters at baseline. The frequency of anti-TNFα use and response rate to the treatment was also similar in LoAS to those in AoAS patients. The LoAS patients seem to have more common severe adverse events compared to the AoAS patients possibly related to their older age.

References:

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who were on a stable NSAID dose for ≥2 weeks. In Period 1, all patients received ETN (50 mg/week) plus NSAID for 24 weeks. At week 24, patients who achieved inactive disease qualified for Period 2 and were withdrawn from ETN treatment for 40 weeks. In Period 3, patients who experience a flare during Period 2 will be retreated with ETN for 12 weeks. Efficacy outcomes for Period 1 included the proportions of patients achieving inactive disease and 20% and 40% improvements in ASAS disease activity (ASAS20 and ASAS40), as well as the changes from baseline in the Spondyloarthritis Research Consortium of Canada (SPARCC) scores for the sacroiliac joint (SPARCC-SIJ) and the spine (SPARCC-Spine). Efficacy analyses presented here were performed on the observed cases.

Results: Of 209 treated patients, 112 (54%) were men, 186 (89%) white, 142 (68%) had MRI-evident sacroiliitis, and 162 (76%) were HLA-B27-positive. The mean baseline score for ASDAS-CRP was 3.5, 8.5 for SPARCC-SIJ, and 2.7 for SPARCC-Spine. Twenty-one (10%) patients discontinued the trial. A significant decrease in ASDAS-CRP score was observed at all post-baseline visits (Panel A). At Week 24, 62% (117/190) and 76% (144/190) achieved ASAS20 and ASAS40, respectively, and there was a significant reduction from baseline in SPARCC-SIJ (-5.8; P<0.001) and SPARCC-Spine (-1.5; P=0.002). Seventy-nine (38%) patients experienced TEAEs, and 1 (0.5%) patient experienced a serious TEAE (cellulitis).

Conclusion: Majority of patients with active nr-axSpA and an inadequate response to NSAIDs achieved inactive disease and reduction of inflammation in both the SJ and the spine with 24-week open-label ETN treatment. There were no unexpected safety signals.

REFERENCES:


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Disclosure of Interests: Filip van den Bosch Consultant for: AbbVie, BMS, Galapagos, Janssen, Lilly, Merck, Novartis, Pfizer and UCB, Speakers bureau: AbbVie, BMS, Janssen, Lilly, Merck, Novartis, Pfizer and UCB, James Cheng-Chung Wei Grant/research support from: Abbvie, BMS, Celgene, Janssen, Novartis, Pfizer, and UCB pharma, Consultant for: TSH Taiwan, Speakers bureau: Janssen, Novartis, Pfizer and TSH, Peter Nash Grant/research support from: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Atul Deodhar Grant/research support from: AbbVie, Amgen, Eli Lilly, GSK, Janssen, Novartis, Pfizer, and UCB, Consultant for: AbbVie, Amgen, BMS, Eli Lilly, Janssen, Novartis, Pfizer, and UCB, Francisco J. Blanco Consultant for: AbbVie, Bioiberica, BMS, GSK, Grünenthal, Janssen, Lilly, Pfizer, Regeneron, Roche, Sanofi, TRB Chemedica, and UCB, Jack F. Bukowski Shareholder of: Pfizer, Employee of: Former employee of Pfizer, Ronald Pedersen Shareholder of: Pfizer, Employee of: Pfizer, Bonnie Vlahos Shareholder of: Pfizer, Employee of: Pfizer

Outcomes of Dose Reduction of TNF-Inhibitors in Axial Spondyloarthritis at 24 Months

Liz Van Rossum, Claire Harris, Annie Gilber, Raj Sengupta, Cathal Boyle, Karl Gaffney, Karl Machado, Andrew Keef, East Kent Hospital University Foundation Trust, Canterbury, United Kingdom; 2Northwick Park Hospital, London, United Kingdom; 3AKGfellyert, Brighton, United Kingdom; 4Royal National Orthopaedic Hospital, Bath, United Kingdom; 5Norfolk and Norwich Hospital, Norwich, United Kingdom

Background: Some patients with inflammatory arthritis who respond well to TNF inhibitor (TNFi) treatment continue to do so after dose reduction. In Axial Spondyloarthritis (axSpA) dose optimisation is desirable but the extent of benefit is unclear and predictors of therapeutic response to dose reduction are unknown.

Objectives: To observe responses to dose reduction of TNFi treatment in axSpA patients and to seek preliminary predictors of low-dose therapeutic response.

Methods: AxSpA Patients at 4 UK centres were allowed to reduce their doses of TNFi therapy if they had met UK (NICE) response criteria and remained well for at least 6 months and wished to do so. There was no pre-determined dose-reduction schedule. The proportion of dose reduction was calculated as a percentage, in mg per month, of the original, standard dose. All patients completed BASDAI and BASFI questionnaires at each visit with annual BASMI measurement. CRP levels were measured frequently. Individuals who continued to take reduced-dose treatment throughout the 24-month period were designated “Remainers” (REM) and those who reverted to full-dose treatment were designated “Reverters” (REV). Data were collected at 6 timepoints: 1: immediately before starting TNFi treatment; 2: at the point of dose reduction; 3: at the point of reversion to full-dose treatment (REV only); 4: 6 months after dose reduction; 5: 12 months after dose reduction; 6: 24 months after dose reduction.

Results: 58 patients (86%/male) who had reduced their dose of TNFI treatment were observed for 24 months. 47 (81%) were REM and 11 (19%) were REV. Mean disease duration prior to biologic therapy was 22.6 years for remainers and 18.6 years for reverters. Mean dose reduction was 38% and 41%, respectively. These 47 REM (95%/male) were of mean age 53.6 (range 36 to 71) years, compared with the 11 REV (63.6%/male) whose mean age was 51.9 (range 39 to 71) years. Mean BASDAI, BASFI and BASMI scores and CRP levels at the designated time points are shown in table 1.

Mean BASDAI scores reduced from 1.9 to 1.4 (28%) from dose reduction to 24 months whereas REV mean BASDAI scores increased from 1.8 to 2.4 (34%) from dose reduction to dose reversion. REM mean BASFI scores reduced from 2.5 to 1.4 (43%) from dose reduction to 24 months whereas REV mean BASFI scores increased from 2.8 to 3.3 (19%) from dose reduction to dose reversion. REM mean CRP scores decreased from 4.1 to 0.7mg/dl (83%) from dose reduction to 24 months and REV mean CRP scores also decreased from 4.7 to 3.5mg/dl (25%) from dose reduction to dose reversion.

Conclusion: Amongst these selected patients with axSpA 85% continued to respond to TNFI treatment in spite of 38% dose reduction. Reverters were more likely to be female and to have relatively low CRP levels at the initiation of TNFI treatment; reversion was preceded by modest rises in BASDAI, BASFI and BASMI but by continued fall in CRP levels.

Disclosure of Interests: Liz Van Rossen Grant/research support from: UCB, Abbie, Consultant for: Novartis, Speakers bureau: Abbie, UCB, Novartis, Claire Harris Consultant for: Abbie, Speakers bureau: Abbie, Abbie, Annie Gilber Consultant for: Boehringer, Raj Sengupta Grant/research support from: Abbvie, Celgene Corporation, Merck Sharp & Dohme, Novartis, Pfizer, and UCB, Speakers bureau: Abbvie, Celgene Corporation, Merck Sharp & Dohme, Novartis, Pfizer, and UCB, Cathal Boyle: None declared, Karl Gaffney Grant/research support from: Abbie, Pfizer, Consultant for: Abbie, Lilly, Novartis, UCB, Speakers bureau: Abbie, Biogen, Gilead, Lilly, Novartis, UCB, Pedro Machado Consultant for: AbbVie, BMS, Celgene, Janssen, MSD, Novartis, Pfizer, Roche and UCB, Speakers bureau: Abbvie, BMS, Celgene, Janssen, MSD, Novartis, Pfizer, Roche and UCB, Andrew Keef: None declared


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<th>T/P</th>
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<td>47</td>
<td>3.9</td>
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<td>11</td>
<td>6.7</td>
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</table>

Ixekizumab Significantly Improves Self-Reported Overall Health in Patients with Active Ankylosing Spondylitis/Radiographic Axial Spondyloarthritis: SF-36 Results of Two Phase 3 Trials

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Background: Using the Short Form-36 (SF-36) questionnaire, previous studies have determined that anklyosing spondylitis/radiographic axial spondyloarthritis (AS/axSpA) significantly impacts patients’ health-related quality of life (HRQoL). Ixekizumab (IXE), a humanized anti-interleukin-21A monoclonal antibody, improves disease signs and symptoms in patients with AS/axSpA. 1,2,3 Week 16 SF-36 results from two clinical trials with IXE are presented here (NCT02696785 and NCT02696798).

Objectives: To evaluate the efficacy of IXE versus placebo (PBO) in improving HRQoL assessed by the SF-36 questionnaire in patients with active AS/axSpA who were either naïve to biologic therapy or have failed or been intolerant of one or two TNF inhibitors (TNFI).

Methods: COAST-V and -W are randomized, double-blind, placebo-controlled clinical trials. Enrolled patients were adults with active AS/axSpA classified by ASAS criteria who fulfilled mHbY of sacroiliitis (central reading), with Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and back pain ≥4. In COAST-V, patients naïve to biologic agents were randomized 1:1:1:1 to receive 80 mg IXE every 4 weeks (Q4W), 80 mg IXE every 2 weeks (Q2W), adalimumab 40 mg Q2W (ADA), or PBO. In COAST-W, patients who had failed on or were intolerant of one or two TNFI were randomized 1:1:1 to 80 mg IXE Q4W, 80 mg IXE Q2W, or PBO. In both studies, patients in the IXE arms were randomized to receive either 80 mg or 160 mg IXE as the starting dose. Comparisons of change from baseline to Week 16 in norm-based SF-36 scores between active groups and PBO were performed using mixed model for repeated measures.
Results: Biologic naïve and TNFi-experienced patients treated with IXE reported significantly greater improvement than PBO patients in SF-36 Physical Component Summary and the physical functioning, bodily pain, general health, and vitality domains. No changes between treatments were reported in Mental Component Summary scores. The greatest numerical improvements with IXE were observed in the bodily pain and patient global pain domain. Similar improvements were reported in the IXE Q4W, IXE Q2W, and ADO groups.

Conclusion: IXE improved self-reported HRQoL, as measured by the SF-36 questionnaire, at Week 16 in patients with active AS/r-axSpA who were naïve or experienced with biologic treatments.

REFERENCES:

Conclusion: IXE significantly improved pain, inflammation, and fatigue in patients with r-axSpA.

REFERENCES:


Table 1. Statistical Analysis of Bioequivalence-Pharmacokinetic Analysis Set

<table>
<thead>
<tr>
<th></th>
<th>Statistic</th>
<th>Ismeans 95% CIs</th>
<th>GLSM</th>
<th>95% CIs</th>
<th>HS016 compare with adalimumab 90% CIs</th>
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<tbody>
<tr>
<td>AUC0-t(N=68)</td>
<td>2418702.15 (2227341.01, 2626504.01)</td>
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<td></td>
</tr>
<tr>
<td>AUCmax (ng/mL)</td>
<td>42136 (3951.58, 4049.36)</td>
<td></td>
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<td></td>
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<tr>
<td>Cmax (ng/mL)</td>
<td>8.23 (8.19, 8.31)</td>
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</table>

Of the 136 subjects, 128 had adverse events (AEs) with 63 (92.6%) and 65 (95.6%) AEs occurring in the HS016 and China-licensed adalimumab, respectively. Among these AEs, 172 from 50 subjects (73.5%) in HS016 group and 148 from 55 subject (80.9%) in China-licensed adalimumab were treatment emergent adverse event. The proportion of confirmed anti-drug antibody responses in the 2 study arms were, 25.0% (17 cases) and 22.1% (15 cases) at day 14, 50.0% (34 cases) and 42.6% (29 cases) at day 42, for the HS016 and China-licensed adalimumab arms, respectively. Neutralizing antibodies were all negative at day 14 for both groups, except 2 cases (3.7%) and 1 case (1.6%) at day 42, for the HS016 and China-licensed adalimumab arms, respectively.

Conclusion: It is concluded that HS016 have shown a similar PK to China-licensed adalimumab in healthy male subjects, and no meaningful differences in safety of immunogenicity were observed.

Disclosure of Interests: None declared.


Psoriatic arthritis

FR0423

NAIL ULTRASONOGRAPHY FINDINGS IN GRAYSCALE AND POWER DOPPLER TO DIFFERENTIATE PSORIATIC ARTHRITIS, PSORIASIS AND CONTROL INDIVIDUALS

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Background: The early diagnosis of psoriatic arthritis (PsA) on patients with psoriasis (PsO) is challenging, but may prevent functional impairment. Patients with nail psoriasis have an odds ratio of nearly 3.0 of developing psoriatic arthritis. Ultrasoundography is a replicable, radiation-free method that could be used to identify nail changes before clinical manifestations.

Objectives: To verify if nail changes identified via ultrasoundography can differentiate between PsA and PsO patients as well as between PsA/PsO patients and a control group.
Methods: Single-center, cross-sectional study. PsA patients were consecutively enrolled, PsO and controls were matched by age and gender with the PsA group. PsO patients must have had the diagnosis of psoriasis of any subtype. PsA patients had to fulfill the CASPAR criteria. Exclusion criteria, for all groups included: other joint inflammatory disease; dermatological or systemic disease that could modify the nail structure. Ultrasound examination was performed using a MyLab 50 system (Esaote Biomedeca, Genova, Italy), equipped with a linear probe of 18 MHz in greyscale (GS) and 8.0 MHz in power doppler (PD). The exams were performed in a room with temperature between 22°C and 26°C, after a 10 minutes rest period. Patients were seated, with hands and fingers in a neutral position over the table. The nails were scanned on a longitudinal plane. The 2nd and 3rd fingernails of both hands were examined. Through GS, the following characteristics were assessed: 1) the trilaminar appearance of the nail plate (NP), that was classified according to Wortsman characterization of changes on psoriatic nails (I – IV), 2) the nail plate thickness (NPT), 3) the nail bed thickness (NBT), and 4) the nail matrix thickness (NMT). The signal of PD in the nail matrix and in the nail bed were evaluated together and classified according to Guitierrez et al.’s score (1-3). Comparisons between independent means were analyzed using ANOVA or Kruskal-Wallis test. The association between categorical variables was calculated by chi-squared test or Fisher’s exact test.

Results: In the trilaminar structure (TS) evaluation, 137(99.3%) of the nails from control group had no change in the TS; for PsO group, 32 of the analyzed nails presented TS alterations, as follows: 9 type I, 5 type II, 7 type III and 11 type IV. For PsA group, there were also 32 of the analyzed nails that presented TS changes; 4 type I, 15 type II, 9 type III and 4 type IV. The mean NPTs SD (mm) was higher on both PsA and PsO groups when compared to the control group: 0.73 ±0.14 and 0.72 ±0.15 vs.0.67±0.10 (p=0.001), respectively. NBT and NMT means did not differ among groups. There was also no statistical difference between groups regarding the degree of nail PD, as well as no difference in the grayscale and PD evaluated parameters between PsA/PsO nails both with or without clinical involvement.

Conclusion: Alterations of the trilaminar structure of the NP and the NPT showed differentiation between psoriatic nails and the control group, but no differentiation between PsO and PsA nails. PD, NMT and NBT means also had no differences between groups. Studies with larger sample sizes are necessary to clarify the utility of these parameters in the evaluation of psoriatic patients.

REFERENCES:

FR10424 DIFFERENCES AND SIMILARITIES ACCORDING TO GENDER IN PATIENTS WITH PSORIATIC ARTHRITIS INITIATING BIOLOGICAL THERAPY

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Background: The evolution of the disease is heterogeneous among patients with psoriatic arthritis (PsA). Specifically, the influence of gender on the disease outcomes (and the need of a more intensive treatment) has been pointed. However, data regarding this are scarce.

Objectives: to analyse the disease profile in male and female patients with PsA starting biological treatment.

Methods: Data from an observational prospective cohort including all patients with PsA initiating biological therapy from 2002-2018 in a university hospital was conducted. Demographic information, laboratory tests, disease presentation (axial presentation, including oligoarticular affection, and poviarticular presentation), disease activity indexes (ASDAS and DAPSA for axial and peripheral-only presentations, respectively) and concomitant treatment were collected before starting biological drug. Patients were stratified by gender to compare the characteristics of the populations. Chi-squared for categorical and t-student tests for continuous variables were used to analyse the differences between groups.

Results: Out of 109 included patients, 55 (51%) were males and 54 (49%) females. Baseline gender-stratified characteristics are shown in Table 1. Including the whole population of the study, mean age at diagnosis was 57 ± 14.6 years, mean PsA duration was 17.7 ± 9.2 years, and mean Body Mass Index (BMI) was 27.2 ± 4.9. Axial or oligoarticular presentation was shown in 57 patients (52%), whereas 52 patients (48%) had poviarticular manifestations. Mean baseline ASDAS was 3.2 ± 1.0 and mean baseline DAPSA was 25.4 ± 13.6. Biological therapies initiated included etanercept in 42% of the cases, infliximab in 25%, adalimumab in 19%, golimumab in 7% and secukinumab in 6%. No significant differences were observed between genders for most of the characteristics including age at starting biological, disease duration, BMI, smoking habit, positive HLA B27 and rheumatoid factor, baseline activity, baseline ESR, baseline CRP, baseline sulsalazine (SSZ), baseline prednisone (PRD), baseline patient global assessment and biological drug use. However, there were substantial differences between gender in some other characteristics. While males had more frequently a predominant axial disease (p<0.01), females more frequently presented a poviarticular disease (p=0.02) and received methotrexate more frequently (p<0.02). These differences in methotrexate use might be explained by the predominance of peripheral presentation in female patients.

Conclusion: In clinical practice, biological therapy (TNFi and IL-17i) is prescribed in a similar frequency in male and female patients with PsA. Nevertheless, the predominant articular manifestation behind the prescription of the biological therapy is different among genders: while men have predominant axial disease, women have predominant peripheral manifestations. These differences in clinical presentation in both genders may contribute to differences in therapeutic management, such as increased use of methotrexate in women with PsA who initiate biological therapy.

Table 1. Gender-stratified characteristics at the visit starting the biological therapy. Results are shown as mean (standard deviation) or absolute number (percentage).

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Male n=55 (51 %)</th>
<th>Female n=54 (49 %)</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>55.8 (12.2)</td>
<td>58.3 (16.7)</td>
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<tr>
<td>Disease duration (years)</td>
<td>17.3 (7.3)</td>
<td>16.1 (16.9)</td>
<td>0.6</td>
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<tr>
<td>BASDA</td>
<td>3.1 (2.0)</td>
<td>3.3 (2.4)</td>
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<tr>
<td>BASDA</td>
<td>23.3 (11.8)</td>
<td>29.4 (15.5)</td>
<td>0.01</td>
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<tr>
<td>ESR</td>
<td>198.2 (18.9)</td>
<td>196.3 (17.5)</td>
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<td>ESR</td>
<td>11.9 (16.9)</td>
<td>9.7 (10.3)</td>
<td>0.1</td>
</tr>
<tr>
<td>Baseline PGA</td>
<td>43.1 (20.8)</td>
<td>50.4 (26.8)</td>
<td>0.4</td>
</tr>
<tr>
<td>Baseline MTX</td>
<td>27 (49.1 %)</td>
<td>38 (70.6 %)</td>
<td>0.02</td>
</tr>
<tr>
<td>Baseline SSK</td>
<td>19 (18.2 %)</td>
<td>8 (14.8 %)</td>
<td>0.6</td>
</tr>
<tr>
<td>Baseline PRD</td>
<td>14 (25.5 %)</td>
<td>20 (37.1 %)</td>
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<tr>
<td>Enfusimub</td>
<td>15 (27.9 %)</td>
<td>12 (22.2 %)</td>
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<tr>
<td>Etanercept</td>
<td>6 (11.6 %)</td>
<td>15 (27.9 %)</td>
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<tr>
<td>Golimumab</td>
<td>24 (43.6 %)</td>
<td>22 (40.7 %)</td>
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<td>Secukinumab</td>
<td>6 (11.6 %)</td>
<td>2 (3.7 %)</td>
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Disclosure of Interests: None declared.

LITERATURE REVIEW OF PATIENT PERSPECTIVES ON THE MANAGEMENT AND TREATMENT OF PSORIATIC ARTHRITIS

Annelies Boonen1, Neil Betteridge2, Andreas Pinter3, Colleen McHorney4, Catherine Reed5, Maastricht University, Maastricht, Netherlands; 2Ned Betteridge Associates, London, London, United Kingdom; 3University Hospital Frankfurt, Frankfurt, Germany; 4Eli Lilly, Windlesham, United Kingdom; 5Evidera, London, United Kingdom; 6Evidera, Bethesda, United States of America

Background: A patient-centred approach to the management and drug treatment of psoriatic arthritis (PsA) has been advocated by a multidisciplinary group of experts to improve skin and joint symptoms and health-related quality of life (HRQoL).

Objectives: To examine perspectives of patients with PsA on: (1) disease management and treatment goals, (2) disease management and treatment satisfaction, and (3) treatment adherence, including reasons for discontinuation. Areas of interest were those related to medication, symptom resolution, everyday living and overall HRQoL.

Methods: A targeted literature review was conducted to identify peer-reviewed literature on patient experience with PsA management and drug treatment. English-language articles published between 1 January 2010–6 October 2018 reporting qualitative or quantitative evidence from cross-sectional or longitudinal observational studies were identified from searches conducted using MEDLINE (via PubMed) and Embase. Selection criteria included adult patients with PsA (self-reported or clinician-diagnosed); drug-treatment studies could consider only regulatory-approved treatments for PsA and other studies had to provide evidence of patient perspectives on disease management and treatment goals, experiences and/or satisfaction. Studies involving paediatric/adolescent populations were excluded, as were results for PsA not distinguishable from other diseases.

Results: The literature search identified 266 titles, of which 48 duplicates were removed. The remaining 218 abstracts were screened: 58 full-text articles were assessed for eligibility and 16 articles were selected for full-text review. Of these 16 articles, 9 were primarily related to patient perspective on disease management, 6 to patient satisfaction and 1 to treatment adherence; some articles covered more than one of these objectives. None of the articles studied whether explicit consideration of treatment goals from the patient perspective would influence management or outcome of care. Symptom resolution, reduced fatigue, improved sexual relations, improved HRQoL and ability to participate in daily activities were consistently identified by patients as important aspects for disease management and daily living with PsA. Articles on patient satisfaction focused largely on general satisfaction with medication rather than satisfaction specifically with holistic PsA management. Notwithstanding, symptom resolution was clearly linked to greater patient satisfaction with medication. Patient dissatisfaction with PsA treatment was influenced by their attitude towards treatment, concerns about PsA medication, the physician-patient relationship and lack of patient involvement in decision-making. Treatment adherence has not been widely explored but mainly relates to perceptions about, and experiences with, medications, including efficacy and adverse events.

Conclusion: This literature review identified a lack of research on patient perspectives of PsA management and treatment goals. It also highlighted the lack of patient involvement in determining management and/or setting personal goals, which may ultimately affect satisfaction. There remains a lack of clarity on PsA symptoms and other disease- or patient-related parameters that impact patient satisfaction/dissatisfaction and patient-centred reasons for treatment discontinuation. The findings of this review will be used to develop a PsA patient survey to further explore patient perspectives to improve care in PsA.

REFERENCES:

Disclose of Interests: Annelies Boonen: None declared, Neil Betteridge Consultant for: Amgen, Eli Lilly, Grunenthal, GSK, Heart Valve Voice, Janssen, Roche, Sanofi Genzyme and Sanofi Regeneron, Speakers bureau: Amgen, Eli Lilly, Grunenthal, GSK, Heart Valve Voice, Janssen, Roche, Sanofi Genzyme and Sanofi Regeneron, Andreas Pinter Consultant for: AbbVie, Amirrall Hermal, Amgen, Biogen Idec, Boehringer Ingelheim, Celgene, GSK, Eli Lilly and Company, Galdema, Hexal, Janssen, LEO Pharma, Medac, Merck Serono, Mitsubishi, MSD, Novartis, Pfizer, Tığıncal Pharma, Regeneron, Roche, Sandoz Biopharmaceuticals, Schering-Plough and UCB Pharma, Speakers bureau: AbbVie, Amirrall Hermal, Amgen, Biogen Idec, Boehringer Ingelheim, Celgene, GSK, Eli Lilly and Company, Galdema, Hexal, Janssen, LEO Pharma, Medac, Merck Serono, Mitsubishi, MSD, Novartis, Pfizer, Tığıncal Pharma, Regeneron, Roche, Sandoz Biopharmaceuticals, Schering-Plough and UCB Pharma, Julie Hill Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Savita Anand Consultant for: Contracted by Eli Lilly and Company to conduct the literature review, Colleen McHorney Consultant for: Contracted by Eli Lilly and Company to conduct the literature review, Catherine Reed Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company


IXEKIZUMAB MAKES REMISSION AND LOW DISEASE ACTIVITY POSSIBLE IN PATIENTS WITH PSORIATIC ARTHRITIS: TWO-YEAR RESULTS IN TNF INADEQUATE RESPONDERS OR BIOLOGIC-NAIVE PATIENTS

Laura C. Coste1, Alexis Ogdie2, Prashanth Sunkureddy3, Lisa Kerr4, Matthew Hulford5, Philip Hettwell6, 7University of Oxford, Oxford, United Kingdom; 2Penn Medicine, Philadelphia, United States of America; 3Clear Lake Rheumatology, League City, United States of America; 4Eli Lilly and Company, Indianapolis, United States of America; 5Univ of Leeds, School of Medicine, Leeds, United Kingdom

Background: Psoriatic arthritis (PsA) is a heterogeneous inflammatory disease that can involve peripheral and axial joints, skin, and entheses. A number of validated composite indices have been developed, not only to measure overall disease activity for PsA, but also to provide thresholds for treat-to-target goals. These include MDA (Minimal Disease Activity), DAPSA (Disease Activity in PsA), and PASDAS (PsA Disease Activity Score). We have previously demonstrated that higher proportions of PsA patients treated with ixekizumab (IXE), a monoclonal antibody that selectively targets interleukin-17A, achieved therapeutic thresholds defined by MDA, DAPSA, and PASDAS versus placebo (PBO) up to Week 24.

Objectives: To explore the extent to which IXE can help biologic-naive or tumor necrosis factor inhibitor (TNFi) inadequate responder patients achieve treat-to-target goals, as defined by composite indices incorporating multiple disease domains, through 108 weeks of treatment.

Methods: Data were analyzed from all patients initially randomized to 80 mg IXE every 4 weeks after a 160-mg starting dose in 2 double-blind, PBO-controlled phase III trials investigating the efficacy and safety of IXE. For SPIRIT-P1 (NCT01695239), patients (N=107) were bDMARD naïve. For SPIRIT-P2 (NCT02349295), patients (N=122) had an inadequate response or were intolerant to TNFis. The following composite measures and definitions were used: MDA and Very Low Disease Activity (VLDIA) (see Figure); DAPSA Low Disease Activity (LDA) (<14 and >4) and remission (<4); PASDAS LDA/VLDA (<3.2≤c≤1.9); and GRACE (GRAppa Composite score) LDA (≤2.3), Modified nonresponder imputation (mNRI; missing data treated as nonresponse for patients discontinued due to lack of efficacy or adverse events; multiple imputation for all other missing data) was used for all analyses.

Results: Therapeutic threshold results at Week 108 are summarized in the Figure. Whether measured using MDA, DAPSA, PASDAS, or GRACE, the proportions of IXE-treated patients achieving designated therapeutic thresholds were sustained through 2 years of treatment. Efficacy was similar between SPIRIT-P1 and SPIRIT-P2.

Conclusion: High proportions of IXE-treated patients, whether biologic naïve or TNFi inadequate responders, achieved treat-to-target goals, as defined by composite indices incorporating multiple disease domains, through 2 years of treatment.

REFERENCES:
Disclosure of Interests: Laura C Coates Grant/research support from: AbbVie, Celgene, Lilly, Novartis and Pfizer, Consultant for: AbbVie, Amgen, BMS, Celgene, Galapagos, Gilead Sciences Inc., Janssen, Lilly, Novartis, Pfizer, Prothena Corp and UCB, Alexandre Oudjane Grant/research support from: (To my university) Novartis, Pfizer, Grant/research support from: Novartis, Pfizer, Grant/research support from: Novartis, Pfizer, Consultant for: AbbVie, Bristol-Myers Squibb, Celgene, Corrona, Eli Lilly and Company, Novartis, Pfizer, and Takeda, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Corrona, Eli Lilly, Novartis, Pfizer Inc., Takeda, Consultant for: Abbvie, Amgen, BMS, Celgene, Corrona, Lilly, Novartis, Pfizer, Takeda, Consultant for: Abbvie, Amgen, BMS, Celgene, Corrona, Eli Lilly and Company, Matthew Huthford Shareholder of: Eli Lilly and Company, Maria Jose Moreno: None declared, Ana HARO: None declared, Meritxell Fernandez Matilla: None declared, Nagore Fernandez-Llanio: None declared, Glisy Peluso: None declared, Elisia Gremese: None declared, Catholic University of the Sacred Heart, Institute of Rheumatology, Rome, Italy, Fondazione Policlinico Universitario A. Gemelli IRCCS, Department of Psychology, Rome, Italy, Fondazione Policlinico Universitario A. Gemelli IRCCS, Department of Rheumatology, Rome, Italy

Background: Depression is one of the most common comorbidities in patients with Psoriatic Arthritis (PsA) but risk factors for mood disorders in these patients are still largely unrecognized. Pre-inflammatory cytokines involved in the pathogenesis of PsA have been also associated with depressive symptoms in patients without systemic autoimmune diseases.

Objectives: The aim of this study is to determine risk factors for depressive symptoms and compare serum cytokines concentrations in subjects with and without depressive symptoms in a court of PsA patients.

Methods: Eighty consecutive patients with PsA were screened for depressive symptoms with depression subscale of the Hospital Anxiety and Depression Scale (HADS-D). A validated cut-off of 8 was used to define patients with significant depressive mood. Patients with and without depressive symptoms were compared for the prevalence of general risk factors for depression, comorbidity, psoriatic disease age of onset, duration, activity and domains affected, treatment and serum levels of IL-6, TNF-α and IL-17A.

Results: Mean disease duration of skin disease and articular disease was 18.8 ± 15.3 years and 9.0 ± 11.1 years, respectively. All patients had a history of peripheral arthritis, 41.3% had dactylitis, 38.8% had enthesitis, 21.3% had spondylitis 82.5% had a psoriatic skin disease and 51.2% had psoriatic nail disease. According to DAPSA index, 20.0% were in remission, 50.0% in Low Disease Activity, 20.0% in Moderate Disease Activity and 10.0% in High Disease Activity. Thirty-five (43.8%) were in Minimal Disease Activity. Thirty-three patients (41.3%) had depressive symptoms according to HADS. Patients with and without depressive symptoms did not differ in terms of age, gender, comorbidity, general risk factors of depression, psoriatic disease age of onset, duration, domains affected, DAPSA activity, MDA achievement, PASI, HAQ, VAS pain, the intensity of treatment, serum TNF-α, IL-17A and IL-23. Serum levels of IL-6 were higher in patients with depressive symptoms. A cut-off of 2.27 pg/ml of serum IL-6 had the best ability to predict a HADS-D score using the higher Youden Index of the ROC curve (AUC = 0.682; p = 0.006). Multivariate logistic regression analysis revealed that serum IL-6 > 2.27 pg/ml was a predictor of depressive symptoms even when adjusted for DAPSA, HAQ and PASI (OR = 3.06; CI 1.14-8.20; p = 0.026).

Conclusion: Higher serum IL-6 is associated with depressive symptoms independently from articular and cutaneous disease activity and degree of disability. This association suggest a direct role of systemic inflammation in the modulation of mood in PsA patients.

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Background: Psoriatic disease (PsD) refers to a systemic condition, probably driven by chronic and complex inflammatory mechanisms. PsD patients experience a fickle mixture of cutaneous (nail dystrophy, psoriatic lesions, seborrheic and musculoskeletal (MSK: arthritis, enthesitis, dactylitis, spondylitis)) inflammatory features, variously associated with other co-morbidities (ocular or bowel inflammatory disease, increased cardiovascular risk and metabolic syndrome). Current evidence is limited in respect of the management of early, treatment-naïve PsD.

Objectives: To assess the literature with a focus on pharmacological interventions in early, treatment-naïve PsD.

Methods: Seven research questions were formulated according to the PICO approach: are interventions effective in obtaining control of overall PsD activity? Are interventions effective on peripheral arthritis? Are interventions effective on dactylitis? On enthesis? On skin and nails? Criteria for including records were: adult human participants; participants with cutaneous features of PsD; participants with MSK features of PsD; double blind, single blind and non-blinded RCTs, well-designed prospective studies/surveys. The search protocol was registered on PROSPERO [1], the search was performed between June 2018 and January 2019.

Results: Resources available were widely explored (4 databases, 5 trial registers, 5 conference archives; see figure). The search retrieved 156,348 references (publication range 1946–2019) of which 308 (0.2%) qualified for full-text-assessment (FTA, figure); 7 (0.004%) fulfilled the selection criteria and only 4 underwent data extraction.

Meta-analysis was impossible due to data heterogeneity (disease classification criteria, outcome measures and intervention durations). Although no clinical study adopted comprehensive composite indexes as primary outcome measures, 40% of FTA references described more than one component of PsD (i.e.: cutaneous and MSK) at least within the baseline characteristics. A substantial proportion of FTA references did describe, among participants recruited, many who were early untreated PsD at baseline. Unfortunately, separate analyses were not possible due to unavailability of the original dataset. A subset (10%) of the FTA references did describe, among participants recruited, many who were early untreated PsD at baseline. Unfortunately, separate analyses were not possible due to unavailability of the original dataset. A substantial proportion of FTA references did describe, among participants recruited, many who were early untreated PsD at baseline. Unfortunately, separate analyses were not possible due to unavailability of the original dataset. A substantial proportion of FTA references did describe, among participants recruited, many who were early untreated PsD at baseline. Unfortunately, separate analyses were not possible due to unavailability of the original dataset.

Conclusion: Few studies addressed early, treatment naïve PsD. The underrepresentation of such data may be related to trial-enrolment criteria. More studies are needed to investigate this identified unmet need.

REFERENCES:

EFFECT OF PHOSPHODIESTERASE 4 INHIBITION WITH APREMILAST ON BODY WEIGHT AND VASCULAR FUNCTION IN PSORIATIC ARTHRITIS – INITIAL RESULTS FROM THE IMMUNE METABOLIC ASSOCIATIONS IN PSORIATIC ARTHRITIS (IMAPA) STUDY

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Background: Psoriatic arthritis (PsA) is associated with obesity and increased cardiometabolic risk. Weight loss is associated with improved disease activity and has been noted with the phosphodiesterase 4 (PDE4) inhibitor apremilast.

Objectives: To investigate the effects of PDE4 inhibition with apremilast on body weight, vascular function and disease activity in psoriatic disease.

Methods: The Immune Metabolic Associations in Psoriatic Arthritis (IMAPA) study is a prospective, open label study of adults receiving apremilast 30mg BD as part of routine care for psoriasis and/or PsA. Cardiometabolic, anthropometric, and disease activity assessments were performed at baseline, months 1, 3, and 6. A subgroup underwent endothelial function assessment by Endo-PAT at baseline and month 3. Repeated measures mixed models were used to compare changes in body weight, waist circumference, systolic & diastolic BP, reactive hyperaemia index (RHI), and disease activity markers with apremilast.

Results: 53 participants were recruited; mean age (SD) 52 (13) years, 72% female. 10% (5/53) lost ≥5% body weight. Statistically significant improvements in 66/68 joint count, DAS28-ESR, PtGA, PGA, pain-VAS, LEI, and ESR were seen at month 6. There was no statistically significant change in RHI, SBP, or DBP (table 1). Weight change showed no statistically significant correlation with change in joint or skin disease activity markers.

Conclusion: Apremilast was associated with modest weight loss and reduced disease activity over 6 months. There did not appear to be any significant alteration in endothelial function, however this was assessed in relatively small numbers and many patients had baseline results within normal range. Improvements in disease activity with apremilast appear largely independent of weight change in this cohort.

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Background: Evaluating psoriatic arthritis (PsA)-related enthesis is diagnostically and therapeutically essential, but may be very complex due to the wide range of signs and symptoms that partly overlap or coexist with the clinical features of fibromyalgia (FM) [1,2].

Objectives: The primary aim was to compute the prevalence of clinical and ultrasonographic signs of enthesitis in patients with PsA, FM or both. The secondary aim was to assess the impact of FM on disease activity and clinical scores.

Methods: This single-centre, observational cross-sectional study involved 103 consenting patients: 39 with PsA (CASPAR criteria), 23 with FM (2016 criteria), and 41 with both. Standard PsA and FM clinical, laboratory and, and clinical data were recorded. Disease activity in PsA and PsA-FM patients was assessed using BASDAI and ASDAS. The entheses were assessed using LEI and MASES score. All of the patients under- went B-mode (grey scale) ultrasonography, the US findings were scored using the GUESS.

Results: The mean age of the patients was 53.6 years, SD ± 9.47. Females accounted for 64.1% of the PsA patients (disease duration 9.13 years, SD ± 6.9), 95.6% of FM patients (disease duration 5.09 years, SD ± 3.6), and 92.3% of the patients with PsA-FM (disease duration 7.9 years, SD ± 5.5). There were no-between group differences in the patients’ BMI. None of the FM subjects reported any personal or family history of psoriasis. The mean BASDAI was 3.6 ± 3.1 in the PsA group, and 1.2 ± 4.45 in the PsA-FM group. The median BASDAI was significantly higher in PsA-FM than in PsA patients (p=0.001), with no statistically significant difference between FM and PsA-FM groups (6 [IQR 2] vs 7 [IQR 3]; p=0.737). The median LEI was significantly higher in FM or PsA-FM patients (p<0.001), with no statistically significant difference between these two groups (6 [IQR 2] vs 7 [IQR 3]; p=0.658). The median GUESS was significantly higher in PsA vs FM group (9 [IQR 7.5] vs 3 [IQR 2]; p<0.001), and in PsA-FM vs FM group (8 [IQR 4.5] vs 3 [IQR 2]; p<0.001). No statistically significant difference was found between PsA and PsA-FM group (9 [IQR 7.5] vs 8 [IQR 4.5]; p=0.12). No statistically significant Spearman correlation coefficient (rho) was found between GUESS and BASDAI/LEI in any of the groups. There was a correlation between GUESS scores and disease duration in PsA (rho=-0.37; p=0.019, 95% CI 0.10-0.61) or PsA-FM (rho=0.38; p=0.016, 95% CI 0.19-0.61), but not in the FM group, and GUESS scores correlated with BMI (rho=0.2; p=0.05, 95% CI 0.00-0.37) and dyslipidemia (rho=0.34; p=0.006, 95% CI 0.11-0.58) in all groups.

Conclusion: The use of a clinical examination and ultrasonic scores alone may overestimate active enthesitis in FM patients. As US was more frequently positive in patients with PsA and PsA-FM than in those with FM, it may be useful in differentiating pain due to enthesitis from enthesial pain due to FM.

10). SEC was used by 18% (n=19), and MTX by 42% (n=43, 25% sc, 13% oral, 4% unknown), respectively. Eighty percent had a combination therapy of MTX and SEC. Twenty-seven percent used GC and/or other biologics/conventional disease modifying antirheumatic drugs (DMARDs). Mean glucocorticoid cumulative dose (GCCD) was 12 ± 22.0 g. Patients with SEC showed a significantly longer disease duration (median: 24 years vs. 13 years) compared to MTX, but showed no other differences in baseline-characteristics or risk factors. T-Scores of both femora were significantly lower in the MTX versus the SEC group. We could not find significant differences between these groups with regard to physical activity, back pain, movement restriction, fracture rates or GCCD. Twenty-five percent of the MTX users and 27% of the patients in the SEC group additionally had GC while; in contrast to no patient in the combination group.

Conclusion: The prevalence of osteoporosis in patients with PSO or PSEA was found to be as high as in the normal population. However, there was a high frequency of peripheral fragility, but not vertebral fractures. Patients with PSO or PSEA patients treated with SEC had a longer disease duration and lower hip BMD, but showed no differences in back pain, physical activity or movement restrictions compared to MTX users.

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THE RELATIONSHIP BETWEEN SYMPTOMS OF AUTONOMIC DYSFUNCTION AND CARDIOVASCULAR DISEASE IN PATIENTS WITH PLAQUE PSORIASIS

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Background: The incidence of cardiovascular disease (CVD), diabetes mellitus, metabolic syndrome and subclinical atherosclerosis is markedly increased in patients with psoriatic arthritis (PsA). The autonomic nervous system is the visceral nervous system of the body consisting of two parts; sympathetic and parasympathetic. Patients with PsA have predominantly parasympathetic involvement autonomic nervous system.

Objectives: The aim of this study was to evaluate the symptoms of autonomic dysfunction and their relationship with cardiovascular involvement and other clinic parameters in patients with PsA.

Methods: The study included patients diagnosed with PsA according to the CASPAP criteria. For evaluation of cardiovascular involvement, body mass index (BMI), abdominal obesity, hypertension (HT), diabetes mellitus (DM), hyperlipidemia (HL), metabolic syndrome, fasting glucose levels, lipid levels, systolic and diastolic blood pressures (SBP-DBP) were assessed. DAPSA (Disease Activity in Psoriatic Arthritis), BASDAI (Bath Ankylosing Spondylitis Disease Activity Index), Leeds enthesis index, Psoriasis Area Severity Index (PASI), Psoriatic Arthritis Quality of Life (PsAQoL) and Health Assessment Questionnaire (HAQ) were used to assess patients clinical situations. The Composite Autonomic Symptom Score (COMPASS-31) (range:0-100) consisting of 6 subdivisions including orthostatic, vasomotor, secretomotor, gastrointestinal (GIS), bladder and pupilomotor was used for the symptomatics of autonomic dysfunction. The Mann-Whitney U-test, student’s t-test and Spearman’s correlation coefficient were used for statistical analysis. P<0.05 was considered statistically significant.

Results: A total of 64 subjects (43 female, 21 male) with a mean of age 49 years (SD:12.3) and disease duration of 59 months (SD:71.3) were recruited into the study. The patients had HT (23.4%), DM (17.2%), abdominal obesity (62.5%), metabolic syndrome (45.3%) and dyslipidemia (42.2%). The mean total COMPASS-31 score was 19.7 (SD:8.3). There was no significant difference in COMPASS-31 scores in patients with or without HT, DM, dyslipidemia. Bladder scores were significantly higher in patients with abdominal obesity and metabolic syndrome (p<0.05). GIS and pupilomotor scores were significantly higher in patients with enthesis (p<0.05). Significant correlations were found between: LDL and bladder (r=0.392), cumulative doses and GIS (r=0.300), pupilomotor (r=0.365) scores; DAPSA and total COMPASS-31 (r=0.310), secretomotor (r=0.359) scores; BASDAI and total COMPASS-31 (r=0.483), GIS (r=0.327), secretomotor (r=0.309), pupilomotor (r=0.302) scores; fatigue and total COMPASS-31 (r=0.503), GIS (r=0.577), pupilomotor (r=0.302) scores; HAQ and total COMPASS-31 (r=0.476), orthostatic (r=0.388), bladder (r=0.371) scores; PsAQoL and total COMPASS-31 (r=0.601), orthostatic (r=0.549), secretomotor (r=0.414), pupillo (r=0.380) scores.

Conclusion: The total score of COMPASS-31 and its subdivisions were high in PsA patients as compared with literature data on healthy subjects. The symptoms of autonomic dysfunction were increased in PsA patients. Disease activity, functional impairment, fatigue, LDL and quality of life are associated with autonomic dysfunction. Autonomic symptoms improve with disease control.

REFERENCES:

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THE INFLUENCE OF BASELINE DEMOGRAPHICS AND DISEASE CHARACTERISTICS ON Efficacy of AN ORAL, SELECTIVE TYK2 INHIBITOR, BMS-986165, IN PATIENTS WITH PLAQUE Psoriasis in a Phase 2 TRIAL

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Background: BMS-986165 is an oral, selective inhibitor of tyrosine kinase activity of Tyk2 (pseudokinase), an enzyme that acts as a transcription (STAT)-dependent cytokine signalling pathways involved in the pathophysiology of psoriasis (PsO). In a 12-week, Phase 2 trial of BMS-986165 in patients with moderate to severe plaque PsO, including those with baseline (BL) musculoskeletal symptoms, Psoriasis Area and Severity Index (PASI) 75 responses (primary endpoint) were highest at doses ≥3 mg twice daily (BID; 67–75%) vs placebo (7%; P<0.001), with a favourable safety profile.

Objectives: To evaluate the influence of BL demographics (weight, body mass index, age) and disease characteristics (age of onset, presence of musculoskeletal symptoms, disease duration, previous biologic use, PASI score, static Physician Global Assessment [sPGA] score, Dermatology Life Quality Index [DLQI] score) on Week 12 efficacy for the 3 most effective doses of BMS-986165 (3 mg BID, 6 mg BID, and 12 mg once daily [QD]) in the trial.

Methods: Adults with moderate to severe plaque PsO (body surface area [BSA] ≥10%; PASI score ≥12, sPGA score ≥3) were randomised equally to 1 of 5 oral doses of BMS-986165 (3 mg every other day, 3 mg QD, 4 mg BID, 6 mg BID, 12 mg QD) or placebo for 12 weeks.

Results: A total of 267 patients were treated; subgroup analyses based on BL characteristics are reported for patients treated with the most effective doses of BMS-986165 (≥3 mg BID; n=134). BMS- 986165 showed no meaningful differences in efficacy among almost all of the 3 subgroups, including age of onset, presence of muscu- loskeletal symptoms, and disease duration (Table), with some varia- bility across subgroups. Small patient numbers may underlie observed fluctuations in results. Similar consistency in responses was seen regardless of BL age (18–45 years, n=66; ≥45 years, n=68), weight
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ACHIEVING THE TREATMENT TARGETS OF REMISSION OR LOW DISEASE ACTIVITY (LDA) IN PSORIATIC ARTHRITIS (PsA) IS ASSOCIATED WITH SIGNIFICANTLY IMPROVED QUALITY OF LIFE, FUNCTION AND PAIN

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Background: The link between reaching a state of remission or LDA and patient-reported outcomes in PsA has been little explored in an observational setting.

Objectives: This analysis investigates the potential effect of reaching remission or LDA according to cDAPSA and achievement of VLDA/MDA on patient-reported outcomes such as HRQoL, functioning and pain in an observational cohort of PsA patients.

Methods: PsABoI (NCT026027278) is an ongoing real-world observational study in 8 European countries where PsA patients receive 1st-, 2nd- or 3rd-line biologics (starting either ustekinumab [UST] or a TNFi). Of 563 UST- or TNFi-treated patients enrolled Dec 2015 – Aug 2017, 303 had data available from their 6-month follow-up. Disease states were defined using cDAPSA ≤4 for remission and ≥13 for LDA (data available for 250 patients) and VLDA 7/7 and MDA 5/7 criteria (data available for 206 and 260 patients, respectively). HRQoL was assessed by the generic instrument EQ5D and the PsA specific tool PsAID-12. Physical functioning was measured by the HAQ-DI and pain with a Pain VAS (0–100).

Results: For the 303 patients, mean age was 49.7 (standard deviation [SD] 12.8) years, mean disease duration was 7.2 (SD, 8.2) years, and 50.5% were women. Figure 1 shows data at 6 months for cDAPSA remission, cDAPSA LDA, VLDA, and MDA in UST- and TNFi-treated patients. Start of treatment with either UST or TNFi did not significantly influence the rates of these outcomes at 6 months. cDAPSA remission/LDA and VLDA/MDA achievement (yes vs no) was associated with better general and disease-specific HRQoL assessments, (EQ5D VAS, PsAID-12) physical function (HAQ-DI) and Pain (VAS) shown by non-overlapping confidence intervals in Figure 2.

Conclusion: In real-life, treatment with either UST or a TNFi leads to considerable and comparable numbers of patients reaching LDA or remission. Reaching such LDA is associated with clinically important improvements exceeding minimal clinically important differences for QoL, functioning and pain experience. Our data therefore strongly support a treat-to-target strategy in routine care for PsA.

REFERENCES:


Disclosure of Interests: Laure Gossec Grant/research support from: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis-Sandoz, Pfizer, Sanofi, and UCB, Consultant for: AbbVie, Biogen, BMS, Celgene, Janssen, Lilly, MSD, Nordic Pharma, Novartis-Sandoz, Pfizer, Roche, Sanofi, and UCB, Consultant for: L. Gossec has received honoraria from Celgene as investigator for this study, Paul Bergmans Shareholder of: Johnson & Johnson, Employee of: Janssen, Kurt de Vlam Consultant for: Pfizer Inc, Consultant for: Johnson & Johnson, Elisa Gremese Consultant for: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Sanofi, UCB, Roche, and Pfizer, Speakers bureau: BMS, Speakers bureau: Pfizer, Speakers bureau: Pfizer, Speakers bureau: BMS, Speakers bureau: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Sanofi, UCB, Roche, and Pfizer, Beatriz Joven-Ibáñez Speakers bureau: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Sanofi, UCB, Roche, and Pfizer, Speakers bureau: Pfizer, Umut Kalyoncu, Adeline Ruyssen-Witrand, Ying Ying Leung, Rossana Scrivo, Laure Gossec, Clemence Gorlier, Maarten de Wit, Laura C. Coates, Umut Kalyoncu, Adeline Ruyssen-Witrand, Ying Ying Leung, Rossana Scrivo, Juan D. Cañete, Penelope Palominos, Sandra Tälli, Andra Balanescu, Uta Kiltz, Sibel Aydin, Inna Gaydukova, Emmanuelle Denis, Ana-Maria Orba, Ennio Lubrano, Josef S. Smolen, ReFlaP study group, PARIS, France

Patient-Defined Flares in Psoriatic Arthritis: What Do They Mean? An Analysis of Change Between 2 Visits in 222 Patients

Laure Gossec, Clemence Gorlier, Maarten de Wit, Laura C. Coates, Umur Kalyoncu, Adeline Ruyssen-Witrand, Ying Ying Leung, Rossana Scrivo, Juan D. Cañete, Penelope Palominos, Sandra Tälli, Andra Balanescu, Uta Kiltz, Sibel Aydin, Inna Gaydukova, Emmanuelle Denis, Ana-Maria Orba, Ennio Lubrano, Josef S. Smolen. ReFlaP study group. PARIS, France

Background: In psoriatic arthritis (PsA), disease fluctuations lead to periods of flares which impact patients’ lives and treatment retention, these flares have been little studied.

Disclosure of Interests: This study was sponsored by Janssen

Acknowledgement: This study was sponsored by Janssen

Results: For the 303 patients, mean age was 49.7 (standard deviation [SD] 12.8) years, mean disease duration was 7.2 (SD, 8.2) years, and 50.5% were women. Figure 1 shows data at 6 months for cDAPSA remission, cDAPSA LDA, VLDA, and MDA in UST- and TNFi-treated patients. Start of treatment with either UST or TNFi did not significantly influence the rates of these outcomes at 6 months. cDAPSA remission/LDA and VLDA/MDA achievement (yes vs no) was associated with better general and disease-specific HRQoL assessments, (EQ5D VAS, PsAID-12) physical function (HAQ-DI) and Pain (VAS) shown by non-overlapping confidence intervals in Figure 2.

Conclusion: In real-life, treatment with either UST or a TNFi leads to considerable and comparable numbers of patients reaching LDA or remission. Reaching such LDA is associated with clinically important improvements exceeding minimal clinically important differences for QoL, functioning and pain experience. Our data therefore strongly support a treat-to-target strategy in routine care for PsA.
Objectives: To explore the frequency of flares in patients with PsA, and to assess the validity of patient-defined flares against PsA disease activity.

Methods: ReFlap (NCT03119805, ref) was a longitudinal study in 14 countries of consecutive adult patients with definite PsA, aged more than 2 years of disease duration. Patients were seen twice in the context of usual care, around 4 months apart. The proportion of flares was computed at the second visit according to a patient-reported question: “At this time, are you having a flare of your psoriatic arthritis, if this means the symptoms are worse than usual?” and a symmetrical physician question. These definitions were compared with a change in disease activity defined as transition to a more active disease category based on the Disease Activity in Psoriatic Arthritis (DAPSA) categories. Agreement was calculated using prevalence-adjusted kappas. Validity of patient-reported flares was assessed by comparing patients who flared with patients who did not flare at the second visit using clinical and patient-reported variables. Finally, for patients flaring, effect sizes corresponding to a patient transition to flare state were calculated by standardized response means (SRMs) for continuous outcomes, with p values based on McNemar test or rank signed test. There was no imputation of missing data.

Results: Overall, 222 patients were analysed: 127 (58.8%) were male, mean age was 53 ± 12.3 years, mean disease duration was 10.8 ± 8.3 years of disease duration. Patients were seen twice in the context of usual care, around 4 months apart. The proportion of flares was computed at the second visit according to a patient-reported question: “At this time, are you having a flare of your psoriatic arthritis, if this means the symptoms are worse than usual?” and a symmetrical physician question. These definitions were compared with a change in disease activity defined as transition to a more active disease category based on the Disease Activity in Psoriatic Arthritis (DAPSA) categories. Agreement was calculated using prevalence-adjusted kappas. Validity of patient-reported flares was assessed by comparing patients who flared with patients who did not flare at the second visit using clinical and patient-reported variables. Finally, for patients flaring, effect sizes corresponding to a patient transition to flare state were calculated by standardized response means (SRMs) for continuous outcomes, with p values based on McNemar test or rank signed test. There was no imputation of missing data.

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Employee of: AbbVie, Patrick Zueger Shareholder of: AbbVie, Employee of: AbbVie, Jacqueline O’Brien Employee of: Corrona, Heather J. Litman: None declared, Hua Feng Employee of: Corrona, Robert McLean: None declared

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FRI0440

PERCEIVED INFLUENCE OF HEALTH STATUS ON SEXUAL ACTIVITY IN PATIENTS WITH PSORIATIC ARTHRITIS IS ASSOCIATED WITH MUSCULOSKELETAL MANIFESTATIONS BUT NOT WITH PSORIASIS SKIN MANIFESTATIONS

Glenn Haugeberg1, Brigitte Michelsen1, Arthur Kavanaugh2, 3

Background: Psoriatic arthritis (PsA) is a heterogeneous disease involving multiple domains including the musculoskeletal system and the skin. The disease may have a significant impact on various aspects of quality of life including sexuality.

Objectives: To explore the prevalence of self-reported problems with sexual activity in patients with PsA, and any associations with demographic and disease related variables as well as treatment.

Methods: PsA patients were consecutively recruited from a Norwegian rheumatology outpatient clinic. Data collection included information on demographics, measures of PsA disease activity (both skin and musculoskeletal manifestations), patient reported outcome measures and treatment. The perceived effect of health status on sexual activity was assessed using question 15 in the Health Related Quality of Life (HRQoL) instrument 15D. The question reads: My state of health: 1. Has no adverse effect on my sexual activity. 2. Has a slight effect on my sexual activity. 3. Has a considerable effect on my sexual activity. 4. Makes sexual activity almost impossible. 5. Makes sexual activity impossible. For analytical purposes the answers were dichotomized into “no/little negative effect (answers 1 and 2)” and “large negative effect (answers 3-5). For group comparisons we used Chi-square test for categorical variables and student t-test for continuous variables. Adjusted logistic regression models were also applied.

Results: Among the 135 PsA patients assessed mean (SD) age was 52.1 (10.2) years and 51.1% were men. The majority of patients (111 patients, 82.2%) reported their state of health to have no/little effect on sexual activity, this also when adjusting for age and sex.

Conclusion: Approximately 20% of the PsA patients reported their health status to have a large negative effect on their sexual activity. Only disease duration and measures reflecting musculoskeletal disease were found to have a negative effect on sexual activity among PsA patients; skin psoriasis did not have an impact.

Disclosure of Interests: Daha D. Gladman1, Philip Heilemann2, Atul Deodhar3, Alice B. Gottlieb4, Dafna D. Gladman1, Henning Boehncke5, Xie L. Xu6, Stephen Xu7, Elizabeth C. Hsia6,7, 8.

Background: Psoriatic Arthritis Disease Activity Score (PASDAS), GRAppa Composite score (GRADE) index, modified Composite Psoriatic Disease Activity Index (mCPDAI), and Disease Activity Index for Psoriatic Arthritis (DAPSA) are composite indices recently developed to assess disease activity in psoriatic arthritis (PsA).

Objectives: The effect of guselkumab (GUS) on these indices was evaluated in a phase 2 study in patients with active psoriatic arthritis.

Methods: Patients with ≥3 tender and ≥3 swollen joints, C-reactive protein ≥3 mg/L, and ≥3% body surface area (BSA) of plaque psoriasis despite treatment were randomized 2:1 to receive GUS 100 mg subcutaneously (N=100) or placebo (PBO, N=49) at Weeks 0, 4, and every 8 weeks thereafter through Week44. At Week16, patients with <5% improvement in both swollen and tender joint counts were eligible for early escape (EE) to open-label ustekinumab. All remaining PBO patients crossed-over to receive GUS 100 mg at Weeks 24, 28, 36, and 44 (PBO→GUS). The PsA composite indices through Week24 were analyzed using last-observation-carried-forward for missing data and data post EE. After Week24, observed data were used. Missing baseline data were excluded in the analyses.

Results: Baseline PASDAS, GRACE, mCPDAI, and DAPSA showed moderate to high disease activity (mean (SD): 6.53 (1.079), 6.08 (1.208), 7.6 (2.15), and 46.65 (20.391), respectively), and were generally comparable between PBO and GUS. At Week24, GUS significantly decreased PASDAS, GRACE, mCPDAI, and DAPSA scores (mean (SD) change from baseline: -2.50 (1.59), -2.73 (1.76), -3.8 (2.72),
-23.08 (20.21), respectively) vs PBO (mean (SD) change from baseline: -0.49 (1.33), -0.35 (1.39), -0.8 (2.16), -4.97 (20.11), respectively, all p<0.001). Significantly more GUS-treated patients achieved a low or very low disease activity state defined by PASDAS, GRACE, and mCPDAI (35.0%, 29.6%, and 45.9%, respectively) vs PBO (41.1%, 21.1%, and 10.4%, respectively, all p<0.001). In addition, 12% of GUS- vs 0% of PBO-treated patients achieved DAPSA remission (p<0.01). Post Week24, improvements in PASDAS, GRACE, mCPDAI, and DAPSA were also observed in PBO–GUS patients (39.9%, 39.3%, 71.4%, and 50.0% achieved disease activity states of low, very low, or remission at Week 44), and were maintained through Week44 in GUS patients (45.8%, 42.2%, 62.7%, and 51.1% achieved disease activity states of low, very low, or remission, respectively).

Conclusion: GUS demonstrated consistent improvements based on all PsA composite indices evaluated, and efficacy was maintained through Week44.

REFERENCES:


FR0441 EFFECTIVENESS OF YTTRIUM KNEE SYNOVECTOMY IN PSORIATIC OR SERONEGATIVE ARTHRITIS WHO HAVE FAILED CONVENTIONAL THERAPY

Mark Hoey, Victoria Mc Dowell, Adrian Pendleton. Musgrave Park Hospital, Rheumatology, Belfast, United Kingdom

Background: Radiation synovectomy with Yttrium 90Y is indicated for refractory arthritis of various aetiologies e.g. inflammatory joint diseases such as rheumatoid arthritis, seronegative arthritids such as psoriatic arthritis and reactive arthritis, Haemophilic arthritis, Calcium pyrophosphate dihydrate (CPPD) arthritis and pigmented villonodular synovitis (PVNS). 1 Treatment of inflammatory arthritis has improved due to more effective therapy and earlier treatment therefore Yttrium therapy is less commonly used.

Objectives: To assess the response to Yttrium 90Y synovectomy in patients with Psoriatic arthritis or seronegative arthritis with synovitis affecting the knee joint in a cohort of patients who had failed conventional DMARDs, biological DMARDs or intra-articular steroid injections. To identify any possible predictors of good or poor response. To develop a standard operating procedure to improve consistency and also allow service to be potentially expanded.

Methods: Retrospective chart and electronic care record review of all patients receiving Yttrium therapy in Northern Ireland from March 2016 to April 2018. Patient demographics, MRI findings, conventional and biological DMARD use, previous intra-articular steroid use were recorded. Patients were reviewed approximately six months following treatment. The medical notes were reviewed to decide whether there had been a good or poor response to treatment and data analyzed to look for factors that may predict response. The process was evaluated and we developed a standard operating procedure to improve consistency and safety going forward.

Results: 17 patients in total received Yttrium therapy, 9 males. Age range was 18-75 with a mean 41. 10 patients were diagnosed with seronegative arthritis and 7 with psoriatic arthritis. All patients had an MRI of the affected joint(s) which confirmed synovitis in all cases. 9 MRIs showed no significant degenerative changes, 5 showed mild degenerative changes and 3 moderate/severe. All patients had previously received intra-articular steroid injection. 12 patients also were receiving or had failed treatment with a conventional or biological DMARD.

Long disease duration (OR 1.005, p<0.01), but not age, predicted NAFLD. In particular, those with disease duration of 10 years or more were of higher risk (OR 2.79, p<0.001). Cardiovascular risk factors including hypertension, diabetes mellitus, dyslipidaemia, and established cardiovascular diseases were not found to be predictors of NAFLD among PsA. None of the treatment agents including steroid, conventional synthetic or biological disease modifying anti-rheumatic drugs (DMARDs) was found to be risk factor for NAFLD.

Conclusion: NAFLD was common among patients with PsA, though it seldom led to significant hepatic impairment or interruption of treatment of PsA. Patients with longer duration of psoriatic arthritis were at risk of developing fatty liver. Traditional cardiovascular risk factors, established cardiovascular diseases or use of any particular treatment agent were not found to be predicting factor of development of NAFLD in PsA.

REFERENCES:

Disclosure of Interests: None declared
not appear to predict response in this group. There were no adverse events reported.

Conclusion: Yttrium therapy is not widely used with only one unit in Northern Ireland performing the procedure. The use of effective DMARDs and biological therapy has improved management of psoriatic and rheumatoid arthritis. In spite of this some patients still have refractory disease. We have shown in this observational study that in patients with knee synovitis despite treatment with DMARDs, biologics and intra-articular steroids, Yttrium synovectomy showed good efficacy, is a relatively low cost and generally safe treatment option for these patients.

Going forward this study and our standard operating procedure will allow us to develop criteria to help select patients for Yttrium therapy and standardize our treatment.

REFERENCES:

Disclosure of Interests: None declared


FRIS0443 IMPACT OF APREMILAST ON PSAID CORE COMPONENTS IN PATIENTS WITH A LIMITED NUMBER OF ACTIVE JOINTS: RESULTS FROM THE REAL-WORLD, PROSPECTIVE, MULTICENTRE REWARD STUDY

Tim Jansen1, Eric-Jan Kroot2, Arrie van Vliet3, Jan Pander3, Marijn Vis4.

Background: Recent data suggest that patients with moderately active psoriatic arthritis (PsA) and a limited number of active joints have a high likelihood of achieving treatment goals with apremilast treatment.1,2 Real-world evidence on the effect of apremilast on patients’ perception of the impact of their disease is limited.

Objectives: To describe the effects of apremilast on the impact of disease in the real world as measured by the Psoriatic Arthritis Impact of Disease (PsAID) questionnaire in PsA patients with SJC ≤4 at baseline.

Methods: The prospective, multicentre, observational REWARD study (The Netherlands) is investigating apremilast treatment in real-world patients with PsA. Descriptive statistics were assessed for disease measures, including swollen joint count (SJC; 0–66) and tender joint count (TJC; 0–68), PsAID (0–10) and patient perception of pain based on the visual analog scale (VAS; 0–100 mm) among patients with limited number of swollen joints (SJC ≤4) at baseline. We report the effects of apremilast on these disease measures at treatment initiation and at the first 6 months of treatment with a data cutoff of December 2018.

Results: A total of 48 patients from 9 clinics who were receiving apremilast were included in this interim analysis. Among these patients, 31 (65%) had SJC ≤4 and 17 (35%) had SJC >4 at baseline. Of patients with SJC ≤4 at baseline, 18 and 8 had at least 3 and 6 months of follow-up, respectively, at the time of data cutoff. Results are reported for patients with available data at each time point. Baseline characteristics for patients with SJC ≤4 included a mean age of 54 years, mean BMI of 29.1 and mean years since PsA diagnosis of 7.0 years; 58% of patients were female, 90% had prior csDMARD use and 29% had prior biologic use. For patients with SJC ≤4, disease measures were reported as follows: the mean SJC at baseline, 3 and 6 months were 1.1, 0.6 and 0.1 and the mean TJC at baseline, 3 and 6 months were 4.5, 3.6 and 1.5. The mean PsAID scores at baseline, 3 and 6 months were 4.2, 3.4 and 2.6. Individual PsAID domain scores by time points are shown (Figure). Patients with a limited number of swollen joints showed gradual improvements in all domains of the PsAID. Mean Pain VAS scores at baseline, 2 weeks, 6 weeks, 3 months and 6 months were 47, 48, 39, 29 and 26 in these patients.

Conclusion: Results from the real-world, prospective, multicenter, observational REWARD study suggest that PsA patients with a limited number of active swollen joints may benefit from apremilast treatment. Apremilast was associated with improvements in the perceived impact of disease, as observed by reductions in the PsAID and its core components.

REFERENCES:

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**FR10445** IDENTIFICATION OF PSORIATIC ARTHRITIS USING AN ADMINISTRATIVE CLAIMS-BASED ALGORITHM

Hemin Lee1, Julia Ford2, Yinzhu Jin1, J. Adriano, Santiago Ortiz1, Angela Y. Tong1, SeoYoung Kim2,3; Brigham and Women’s Hospital, Division of Pharmacoepidemiology and Pharmacoeconomics, Department of Medicine, Boston, United States of America; Brigham and Women’s Hospital, Division of Rheumatology, Immunology, and Allergy, Boston, United States of America

**Background:** Accurately identifying psoriatic arthritis (PsA) in large electronic healthcare database is critical for epidemiological studies.

**Objectives:** To develop and validate a claims-based algorithm to identify patients with PsA.

**Methods:** We conducted a retrospective chart review of the Partners Healthcare electronic medical record linked to Medicare claims from year 2012 to 2014. 7 claims-based algorithms were developed to identify PsA: 1) ≥2 International Classification of Diseases, Ninth Revision (ICD-9) codes for PsA (696.0) and at least one diagnosis of psoriasis (696.1) by any physician; 2) ≥2 diagnosis of PsA with at least 1 diagnosis by rheumatologist; 3) ≥2 PsA diagnosis with at least 1 diagnosis by rheumatologist and ≥1 diagnosis of rheumatoid arthritis (714.0); 4) ≥2 diagnosis of PsA and at least 1 diagnosis of psoriasis by dermatologist; 5) ≥1 diagnosis of PsA by rheumatologist and ≥1 diagnosis of psoriasis by dermatologist; 6) ≥2 diagnosis of PsA by any physician and ≥1 claims for PsA medication; 7) ≥2 diagnosis of PsA with at least 1 diagnosis by rheumatologist and ≥1 claims for PsA medication. The ICD-9 codes were separated by ≥7 days but <365 days. Medical record by the treating physician was considered as the gold standard, and two independent physicians confirmed the presence of PsA. Positive predictive value (PPV) and 95% confidence intervals (CI) of the algorithms were calculated.

**Results:** The 7 algorithms identified 357, 399, 315, 223, 215, 372, and 276 records, respectively. Approximately 45% of the identified records with adequate data were reviewed. The PPV of the algorithms ranged from 75.2% to 88.6% (Table 1). Mean age of identified PsA patients ranged from 72.6 to 73.5 years old. Presence of psoriasis 1 year prior to index date of PsA ranged from 54.2% to 89.2%. Algorithm 6 which captured ≥2 diagnosis of PsA and ≥1 claims for PsA-related medications identified second highest number of patients (n=372) yet still yielded high PPV of 82.4% (95% CI 76.5, 88.3).

**Conclusion:** All seven claims-based algorithms had a high PPV of 75-89% in identifying PsA. A claims-based algorithm utilizing two or more diagnosis codes of PsA by any physician with a claim for PsA medication can be a useful and efficient tool to identify the PsA population in large claims databases.

**REFERENCES:**


**Table 1. Predictive Values of Proposed Algorithms for Identifying Psoriatic Arthritis**

<table>
<thead>
<tr>
<th>Algorithms</th>
<th>Records Identified</th>
<th>Charts Reviewed (%)</th>
<th>PsA per treating MD</th>
<th>PPV%</th>
<th>95% CI</th>
</tr>
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<tbody>
<tr>
<td>Diagnosis only</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>1. ≥2 diagnosis of PsA and ≥1 diagnosis of psoriasis by any physician</td>
<td>357</td>
<td>71.2</td>
<td>68.0, 82.3</td>
<td></td>
<td></td>
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<tr>
<td>Diagnosis with Specialist Visit</td>
<td></td>
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<tr>
<td>2. ≥2 diagnosis of PsA with at least 1 diagnosis by rheumatologist</td>
<td>399</td>
<td>185</td>
<td>80</td>
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<tr>
<td>3. ≥2 diagnosis of PsA with at least 1 diagnosis by rheumatologist and ≥1 diagnosis of RA</td>
<td>315</td>
<td>147</td>
<td>81.6</td>
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<tr>
<td>4. ≥2 diagnosis of PsA and at least 1 diagnosis of psoriasis by dermatologist</td>
<td>223</td>
<td>95</td>
<td>77.9</td>
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<td></td>
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<tr>
<td>5. ≥1 diagnosis of PsA by rheumatologist and ≥1 diagnosis of psoriasis by dermatologist</td>
<td>215</td>
<td>114</td>
<td>85.1</td>
<td></td>
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<tr>
<td>Diagnosis and Medication Dispensing</td>
<td></td>
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<tr>
<td>6. ≥2 diagnosis of PsA and at least 1 medication dispensing for PsA</td>
<td>372</td>
<td>159</td>
<td>82.4</td>
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<tr>
<td>7. ≥2 diagnosis of PsA with at least 1 diagnosis by rheumatologist and at least 1 medication dispensing for PsA</td>
<td>276</td>
<td>123</td>
<td>88.6</td>
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</table>

*PsA, Psoriatic arthritis; MD, Medical doctor; PPV, Positive predictive value; ICD, International Criteria of Diagnosis; RA, Rheumatoid arthritis

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**FR10446** ATTAINMENT OF MINIMAL DISEASE ACTIVITY (MDA) IN PSORIATIC ARTHRITIS (PSA) PATIENTS (PTS) DEPENDING ON THE TIME OF SYNTHETIC (S) DMARD INITIATION IN CLINICAL PRACTICE: RUSSIAN PSA REGISTRY (RU-PSART) DATA

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**Background:** According to the EULAR recommendations and treat to target strategy sDMARD are the first line of PsA therapy. But there are contradictory data about the efficacy of sDMARDs in PsA pts. Data was collected from 25 rheumatology clinics of the Russian Federation.

**Objectives:** To investigate the cumulative frequency and the time of MDA attainment in early and long-term PsA after starting sDMARDs in clinical practice.

**Methods:** 253 (MF-93/160) PsA pts according to CASPAR criteria were included in the RU-PSART, after signing consent participation forms; median age 65 (Min–Max 20 – Max 82) years. All patients were divided into two groups according to disease duration at time of sDMARDs initiation: early PsA ≤2 yrs. (165pts) and long-term PsA≥2 yrs (88pts). All pts underwent standard clinical examinations of PsA and psoriasis activity. All pts were treated with the following sDMARDs: Oral Methotrexate (MTX) (10/3pts), intramuscular MTX (30pts), Subcutaneous MTX (78pts), Leflunomide (7pts), Sulfasalazine (24pts), Apremilast (10pts), Tolctafilit (1pts). MDA was defined as ≥5 of the following criteria: tender joint count ≤1, swollen joint count ≤1, PASI≤1 or BSA≤3, patient pain global assessment VAS≤15, patient’s global disease activity VAS≤20, HAQ≤0.5, enthesis count ≤1. The cumulative frequency and the time of MDA attainment were calculated in both groups. Kaplan-Meier cumulative analysis, Me [Min-Max], ORs with 95% CI, Breslow, Tarone-Ware, Log Rank tests were performed. All CI-1, p<0.05, were considered to indicate statistical significance.

**Results:** MDA has been achieved by the use of sDMARDs treatment in 39 out of 165 (24%) pts with early PsA and in 4 out of 88 (5%) pts with long-term PsA. Early PsA pts have more chance to achieve MDA in comparison to long-term PsA pts: OR=4.65 [CI 95%: 2.2-16.9]. Comparative analysis has shown that cumulative frequency of MDA achievement after sDMARDs initiation was significantly higher (42% vs 5%) and faster (21 months vs 11 yrs.) in early PsA than in long-term PsA (p≤0.05 for Bre-slow, Tarone-Ware and Log Rank tests) (Fig. 1). The cumulative frequency and the time of MDA achievement were calculated by Kaplan-Meier analysis in both groups.

**Conclusion:** Our study suggests that sDMARDs initiation (mostly MTX-monotherapy) at an early stage of PsA allows to achieve MDA significantly faster and more often than in long-term PsA.


Disclosure of Interests: ELENA GUBAR: None declared, Yulia Korsakova: Speakers bureau: Celgene Corporation, Janssen, Maria Sedunova: None declared, Igor Pristavsky: None declared, Irina Unnova: None declared, Irina Bordareva: None declared, Snezana Kudishina: None declared, Alexander Lila: Speakers bureau: Pfizer, Inc., MSD, Novartis, AbbVie Inc., Celgen Corporation, Biocad, Janssen, UCJ, Inc.

Disclosure of Interests: None declared, Julia Ford: None declared, Adrian J. Santiago Ortiz: None declared, Angela Y. Tong: None declared, SeoYoung Kim: Grant/research support from: Pfizer, Bristol-Myers Squibb, Roche/Genentech and AbbVie.

Background: Early started therapy of psoriatic arthritis with the goal to achieve minimal disease activity can slow the joint damage progression. Data concerning the persistence of psoriatic arthritis (PsA) patients on biologics in real clinical practice are insufficient.

Objectives: to analyze the survival of biological treatment of PsA and detect possible predictors of persistence on biologics.

Methods: PsA patients from Moscow Unified Arthritis Registry (MUAR) treated with biologics were included in study. Unadjusted survival analysis was performed by the Kaplan-Meier method. The search for independent risk predictors of the therapy discontinuation was carried out by the multivariate Cox regression.

Results: We recruited 236 treatment episodes in 141 PsA patients enrolled in MUAR, 61 men (43%); mean age was 50.1 ± 11.5 years. We used the following biologics: etanercept (71 patients), infliximab (51), adalimumab (50), ustekinumab (35), golimumab (11), certolizumab pegol (7). In unadjusted analysis mean treatment survival was longer with etanercept, adalimumab and infliximab. As significant independent predictors of withdrawal risk (potential confounders) low education, mutilating or polyarticular form of PsA, heel pain, shoulder joints swelling and absence of neck pain at the disease onset were detected. After the adjusting data for confounders there was no significant difference in risk of withdrawal between different biologics. Neither the year of onset of the case of treatment nor the number of previous biDMARDs show a significant relation with the risk of drug withdrawal (Picture 1). This data show the difference between the patterns of treatment survival of rheumatoid arthritis and psoriatic arthritis.

Conclusion: our analysis of PsA treatment persistence in real clinical practice detected several factors associated with withdrawal risk. These data can provide specialists with a tool for personalized treatment.

Disclosure of Interests: None declared


**REAL-WORLD EXPERIENCE OF SECUKINUMAB FOR PSORIATIC ARTHRITIS**


Background: Secukinumab, an inhibitor of IL-17, is a new option for the treatment of Psoriatic Arthritis (PsA) which has shown efficacy in clinical trials. However, real-world data of its use is still scarce.

Objectives: This study aims to analyze the experience of using secukinumab for PsA in four tertiary hospitals.

Methods: Multicentric observational, longitudinal, retrospective study conducted in 4 tertiary hospitals of the Madrid region. Patients with clinical diagnosis of PsA and having received at least one dose of secukinumab were included. Medical records were reviewed to collect demographic and clinical data (body mass index, BMI, risk factors cardiovascular disease, cancer, HBV/HCV infection), features of PsA (extra-articular involvement, radiological damage), previous therapies, assessment of the disease and response data at 6 months of secukinumab (joint counts, CRP, DAPSA, reasons for discontinuation, adverse events). Descriptive statistic analysis using mean and standard deviation was performed.

Results: 177 patients, of which 115 female (65%) were included. Mean age was 53 y.o.(SD 15) and average duration of the disease was 9 years (SD 7), 169 patients (95%) had peripheral disease (34% joint erosions), 84 (47%) had axial disease (68 with radiological damage), 148 (84%) had psoriasis, 61 (34%) showed dactylitis and 111 (63%) had enthesis. Average BMI was 28.4 (SD 6), with an obesity rate of 37% (52 pt). Observed comorbidities were hypertension (22 pt, 12%), diabetes mellitus (22 pt, 12%), dyslipidemia (58 pt, 33%), active smoking (55 pt, 31%) and others: 20 patients had HBV infection, 5 had HCV infection and 12 had malignancy.

Regarding previous treatments, 90% had received cDMARDs, particularly methotrexate (77%) and 119 (67%) had been exposed to at least one bDMARD (32% to one, 25% to two, 20% to three and 21% to four or more). 69% were on 150 mg dose and 31% on 300 mg dose. At baseline, average tender joint count was 7 (SD 8), swollen joint count was 4 (SD 4), CRP 7 mg/l and DAPSA 26. At 6 months of secukinumab therapy, tender joint count had decreased to 5 (SD 8), swollen joint count 2 (SD 3), CRP 5 mg/l and DAPSA 17. Thirty-eight (47%) of the patients with the data available (80) had DAPSA ≤14 (low activity) and 9 DAPSA >14 (remission). In naïve to biologic patients, DAPSA varied from 27 in the baseline visit to 16 at 6 months, and in the other group of patients with biologic experience, DAPSA varied from 24 to 17 at 6 months (if they had been exposed to 3 or more biologics, DAPSA from 18 to 10 at 6 months).

Average drug survival time was 20 months (1-34). 79 patients (44.6%) withdrew therapy, due to primary ineffectiveness (40), secondary ineffectiveness (28), adverse events (9) and other reasons (3). Adverse events do not differ from those reported in clinical trials.

Conclusion: Secukinumab in real-world setting had been indicated in a population of PsA with a high percentage of axial involvement (47%), with an important previous exposure to biologics, and with higher comorbidity than that reported in clinical trials. Response data were favorable, 47% of patients achieved remission or low activity by DAPSA, and similar profile of adverse events to the one reported in the clinical trials was observed.

REFERENCES:


Disclosure of Interests: MARIA MARTIN LOPEZ: None declared, Marta Valero: None declared, Valentina Empereire: None declared, Carolina Merino Argumànez: None declared, Javier Bachiller-Corral: None declared, Jose Campos Esteban: None declared, Ana Pérez Gómez: None declared, Beatriz Joven-Ibáñez Speakers bureau: Celgene, Novartis, MSD, Pfizer, Abbvie, and Janssen


**EFFECTIVENESS OF BIOLOGIC DRUGS WITH DIFFERENT MECHANISM OF ACTION IN PSORIATIC ARTHRITIS. AN APPRAISAL FROM THE APULIAN REGISTRY BIOPURE**

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Background: In the last decade, the number of drugs available for patients affected with psoriatic arthritis (PsA) is increased and rheumatologists have multiple choices to manage PsA refractory to conventional disease-modifying anti-rheumatic drugs (cDMARDs). However, the possibility
of identifying disease’s or patient’s related characteristics to drive the optimal choice is still under investigation.

Objectives: We aimed at evaluating the effectiveness and drug survival of the biological drugs (bDMARDs) and apremilast indicated for the treatment of PsA patients with inadequate response to cDMARDs. To this purpose, PsA patients on treatment with bDMARDs or Apremilast recorded into the Apulian BIOPURE registry have been retrospectively analyzed.

Methods: We retrospectively assessed PsA patients, fulfilling CASPAR criteria, starting a biologic drug or apremilast from June 2016 through December 2017. At baseline and at last observation within the time frame of the study, DAPSA, PASI, ASDAS-CRP, the presence of enthesis and dactylitis were collected. Rate of patients achieving DAPSA based remission was assessed at last observation. The persistence on the first treatment was evaluated by Kaplan-Meier survival curves. Estimated hazard ratios (HRs) of discontinuing therapy or achieving remission were assessed by multivariate stepwise backward Cox regression models, adjusting for patient demographics (gender, age) and disease characteristics (disease duration, number of prior bDMARDs, baseline DAPSA, PASI, presence of enthesis and dactylitis, type of current drug).

Results: We recruited 450 PsA patients (268, 60% female) with mean age 53 (±11) years, disease duration 19 (±13) months, 337 (75%) naïve to bDMARDs. At baseline, 404 had peripheral joint involvement and 46 axial disease, DAPSA was 18 (±10), PASI 1.6 (±3), ASDAS-CRP 2.5 (±1), 48/355 (13.5) had dactylitis and 78/231 (33%) showed enthesitis. Table 1 shows the type of drugs. At last observation, the rate of patients who achieved the DAPSA remission was significantly higher in naïve patients (25%) than in those bDMARDs experienced (14%, p=0.02). The rate of drug survival was not significantly different among drugs (Figure 1). Cox-regression multivariate models showed that independent baseline factors negatively associated to drug persistence were prior bDMARD treatment (HR 0.70, 0.50-0.97 (95% CI), p=0.03) and the absence of axial disease (HR 0.56, 0.35-0.91 (95% CI), p=0.02). Negative predictors of DAPSA remission were prior bDMARD treatment (HR 0.40, 0.19-0.83 (95% CI), p=0.01), gender female (HR 0.51, 0.29-0.91 (95% CI), p=0.02), and the absence of dactylitis/(HR 0.36, 0.19-0.68 (95% CI), p=0.002).

Conclusion: A good rate of DAPSA remission is achievable with all the current available drugs in PsA in settings of real life. Predictors of remission and persistence on treatment were being male and naïve to prior bDMARDs. No difference among drugs was detected.

Table 1. Treatments

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Frequency</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adalimumab</td>
<td>85</td>
<td>17.8</td>
</tr>
<tr>
<td>Certolizumab</td>
<td>56</td>
<td>12.4</td>
</tr>
<tr>
<td>Golimumab</td>
<td>61</td>
<td>13.6</td>
</tr>
<tr>
<td>Etanercept</td>
<td>65</td>
<td>14.4</td>
</tr>
<tr>
<td>Secukinumab</td>
<td>104</td>
<td>23.1</td>
</tr>
<tr>
<td>Ustekinumab</td>
<td>43</td>
<td>9.6</td>
</tr>
<tr>
<td>Apremilast</td>
<td>41</td>
<td>9.1</td>
</tr>
<tr>
<td>All</td>
<td>450</td>
<td>100</td>
</tr>
</tbody>
</table>

Figure 1. Kaplan-Meier curves of drug survival of PsA patients on different therapies.

Disclosure of Interests: Nicola Maruotti Speakers bureau: N Maruotti has received speaker honoraria from Pfizer outside this work, Giorgio Carlino Consultant for: G Carlino had received consulting fees from Pfizer, Janssen, AbbVie, MSD, BMS, Leonardosanto Consultant for: L Sante has received consulting fees and/or speaker honoraria from Abbvie, MSD, Novartis UCB outside this work, Laura Quarta: None declared, Romano Bucci Consultant for: R Bucci has received consulting fees and/or speaker honoraria from Pfizer, Sanofi, MSD, BMS, Speakers bureau: R Bucci has received consulting fees and/or speaker honoraria from Pfizer, Sanofi, MSD, BMS, Carmelo Zuccaro Consultant for: C Zuccaro has received consulting fees and/or speaker honoraria from MSD, Abbvie, Novartis, Pfizer, Janssen outside this work, Speakers bureau: R Zuccaro has received consulting fees and/or speaker honoraria from MSD, Novartis, Pfizer, Janssen outside this work, Angelo Semeraro Speakers bureau: A Semeraro has received speaker honoraria from Sanofi, Roche, AbbVie, MSD, BMS, Novartis, Antonio Marsico: None declared, Daniela Mazzotta: None declared, Paola Chiara Francesca Falappone Consultant for: FC Falappone had received consulting fees and/or speaker honoraria from Amgen, Abbott, MSD, BMS, outside this work, Speakers bureau: PC Falappone had received consulting fees and/or speaker honoraria from Amgen, Abbott, MSD, BMS, outside this work, Florencio Ianonne Consultant for: F Ianonne has received consulting fees and/or speaker honoraria from Pfizer, AbbVie, MSD, BMS, Novartis, Lilly, UCB outside this work, Speakers bureau: F Ianonne has received consulting fees and/or speaker honoraria from Pfizer, AbbVie, MSD, BMS, Novartis, Lilly, UCB outside this work.

SECUKINUMAB PROVIDES SUSTAINED IMPROVEMENTS IN THE SIGNS AND SYMPTOMS IN PSEUDORHEUMATOID ARTHRITIS: FUTURE 5 YEAR EFFICACY AND SAFETY RESULTS FROM A PHASE 3 TRIAL

Disclosure of Interests: Philip J Mease Grant/research support from: Abbvie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, SUN and UCB. Consultant for: Abbvie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, SUN and UCB. Philip J Mease: Employee of: Novartis, Grant/research support from: Abbvie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, SUN and UCB.

Effectiveness endpoints SEC 150 mg Group vs SEC 75 mg Group (n=161)1 vs SEC 75 mg Group (n=147)1

<table>
<thead>
<tr>
<th>Efficacy endpoints</th>
<th>SEC 150 mg Group</th>
<th>SEC 75 mg Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACR202</td>
<td>89/131 (67.9)</td>
<td>98/127 (77.2)</td>
</tr>
<tr>
<td>ACR302</td>
<td>69/131 (53.7)</td>
<td>65/127 (51.2)</td>
</tr>
<tr>
<td>ACR502</td>
<td>49/131 (37.4)</td>
<td>43/127 (33.9)</td>
</tr>
<tr>
<td>PASI902</td>
<td>48/72 (66.7)</td>
<td>47/71 (66.2)</td>
</tr>
<tr>
<td>HAQ-DI, mean change from baseline (SD)</td>
<td>-0.4 (0.56)</td>
<td>-0.5 (0.61)</td>
</tr>
<tr>
<td>SF-36 PCS, mean change from baseline (SD)</td>
<td>6.6 (1.33)</td>
<td>5.9 (0.86)</td>
</tr>
</tbody>
</table>

Table 1. Summary of Efficacy Results at Week 260

Disclosure of Interests: Philip J Mease Grant/research support from: Abbvie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, SUN and UCB. Consultant for: Abbvie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, SUN and UCB. Philip J Mease: Employee of: Novartis, Grant/research support from: Abbvie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, SUN and UCB. Philip J Mease: Employment of: Novartis, Grant/research support from: Abbvie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, SUN and UCB.

1 Secukinumab 150 and 75 mg arms include 60 and 121 pts, respectively, who were dose escalated to 150 and/or 300 mg at wk 156 or later
2Pts with psoriasis affecting ≤3% body surface area at baseline (150 mg: N = 89; 75 mg: N = 82)
3Pts (N = 99 [150 mg] and 91 [75 mg]) with enthesitis at baseline
4Pts (N = 83 [150 mg] and 77 [75 mg]) with dactylitis at baseline, number of evaluable pts: n, total number of randomised pts: n, number of responders
TOFACITINIB IN PATIENTS WITH PSORIATIC ARTHRITIS: ANALYSIS OF DERMATOLOGIC ENDPOINTS FROM 2 PHASE 3 STUDIES

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Background: Psoriatic arthritis (PsA) is a chronic, systemic inflammatory disease; the onset of dermatologic symptoms often precedes rheumatic manifestations. Tofacitinib is an oral Janus kinase inhibitor for the treatment of PsA. It has been shown that tofacitinib can improve dermatologic symptoms in patients (pts) with PsA.2,3

Objectives: To investigate the efficacy of tofacitinib in improving additional dermatologic endpoints in adult pts with active PsA.

Methods: This analysis included data from 2 placebo (PBO)-controlled, double-blind, Phase 3 studies in pts with active PsA and an inadequate response (IR) to ≥1 conventional synthetic disease-modifying antirheumatic drug (csDMARD) who were tumour necrosis factor inhibitor (TNFi)-naïve (OPAL Broaden [12 months; NCT01877668]; N=422) or had an IR to ≥1 TNFi (OPAL Beyond [6 months; NCT01882439]; N=394).2,3 Pts must have had active plaque psoriasis at screening only and were required to receive a stable dose of 1 csDMARD. Pts were randomised to tofacitinib 5 mg twice daily (BID), 10 mg BID, adalimumab 40 mg subcutaneous (SC) injection every 2 weeks (OPAL Broaden only) or PBO (advanced to tofacitinib 5 or 10 mg BID at Month [M]3). Percentage (% change from baseline (BL) (Δ) in Psoriasis Area and Severity Index (PASI) total score, % of pts achieving >75% PASI improvement from BL (PASI75) stratified by BL PASI severity (≥0 to <3, ≥3 to <10, ≥10) and Pts’ Global Joint and Skin Assessment-Visual Analogue Scale Psoriasis severity question (PGJS–VAS Psoriasis) were measured at M1, 3, 6, and at M9 and 12 (OPAL Broaden only); % ΔPASI total score and PASI75 were measured only in pts with BL affected body surface area (BSA) ≥3% and PASI >0. Safety endpoints were also analysed.

Results: BL demographics were similar between treatment groups and endpoints were also analysed. Serious adverse events (AEs) were similar across treatment groups up to M6 in OPAL Broaden and M12 in OPAL Beyond (Table). Similar effects across these endpoints. Serious adverse events (AEs) and discontinuations due to AEs were similar across treatment groups up to M6 in OPAL Beyond and M12 in OPAL Broaden.

Conclusion: In pts with PsA (TNFi-naïve or TNFi-IR), tofacitinib improved dermatologic endpoints, and responses were maintained to the end of each study. Tofacitinib may provide a treatment option for pts with active PsA, including the dermatologic symptoms of PsA.

REFERENCES:

Disclosure of Interests: Joseph F. Merola Consultant for: Biogen IDEC, Abbvie, Amgen, Eli Lilly and Company, Novartis, Pfizer, Janssen, UCB, Samumed, Celgene, Sanofi Regeneron, Merck, and GSK, Kim Papp Grant/research support from: AbbVie, Akros, Allergan, Amgen, Anacor, Arcutis, Astellas, Baxalta, Boehringer Ingelheim, Bristol-Myers Squibb, Can-File, Celgene, Coherus, Dermira, Dow Pharma, Eli Lilly, Galdemra, Genentech, Gilead, GlaxoSmithKline, InflaRx GmbH, Janssen, Kyowa Hakko Kirin, Leo, MedImmune, Merck (MSD), Merck Serono, Moberg Pharma, Novartis, Pfizer, PRCL Research, Regeneron, Roche, Sanofi-Aventis/Genzyme, Takeda, UCB, Valeant/Bausch Health; Consultant for: AbbVie, Akros, Amgen, Baxter, Boehringer Ingelheim, Celgene, Coherus, Eli Lilly, Forward Pharma, Galdemra, Janssen, Kyowa Hakko Kirin, Merck (MSD), Merck Serono, Novartis, Pfizer, Regeneron, Sanofi-Aventis/Genzyme, Takeda, UCB, Valeant/Bausch Health; honoraria: AbbVie, Akros, Amgen, Baxter, Boehringer Ingelheim, Celgene, Coherus, Eli Lilly, Janssen, Kyowa Hakko Kirin, Merck (MSD), Merck Serono, Novartis, Pfizer, Regeneron, Sanofi-Aventis/Genzyme, UCB, Valeant/Bausch Health, Speakers bureau: AbbVie, Amgen, Astellas, Baxter, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Dow Pharma, Eli Lilly, Galdemra, Janssen, Merck (MSD) Novartis, Pfizer, Regeneron, Sanofi-Aventis/Genzyme, UCB, Valeant/Bausch Health; advisory boards: AbbVie, Amgen, Astellas, Baxter, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Dow Pharma, Eli Lilly, Galdemra, Janssen, Merck (MSD), Novartis, Pfizer, Regeneron, Sanofi-Aventis/Genzyme, Valeant/Bausch Health; steering committee: AbbVie, Amgen, Boehringer Ingelheim, Celgene, Coherus, Eli Lilly, Janssen, Kyowa Hakko Kirin, Merck (MSD), Novartis, Pfizer, Regeneron, Sanofi-Aventis/Genzyme, Valeant/Bausch Health; scientific officer: AbbVie, Amgen, Boehringer Ingelheim, Celgene, Coherus, Eli Lilly, Janssen, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Novartis, Pfizer Inc Roche, Sanofi, UCB, Conway, Pfizer Inc, Roche, Sanofi, UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Novartis, Pfizer Inc Roche, Sanofi, UCB, Jordi Gratacos-Masmitja Grant/research support from: Pfizer Inc, Consultant for: Pfizer Inc, Speakers bureau: Pfizer Inc, Diamant Thaçi Grant/research support from: AbbVie, Almirall, Anagen, Bio Skin, Biogen-Idec, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Chugai, Dermira, Dignity, Eli Lilly, Forward Pharma, GlaxoSmithKline, Janssen Cilag, Leo Pharma, Novartis, Pfizer, Regeneron, Roche, Sandoz-Hexal, Sanofi, and UCB, Consultant for: AbbVie, Almirall, Bristol-Myers Squibb, Celgene, Dignity, Galapagos, Leo Pharma, Eli Lilly, Novartis, Pfizer, and UCB, honoraria: AbbVie, Almirall, Anagen, Bio Skin, Celgene, Dignity, Eli Lilly, Galdemra, Merck Sharp & Dohme, Novartis, Pfizer, Roche-Posay, Sandoz-Hexal, Sanofi, and UCB, Consultant for: AbbVie, Almirall, Bristol-Myers Squibb, Celgene, Dignity, Eli Lilly, Galapagos, GlaxoSmithKline, Janssen Cilag, Leo Pharma, Morphans, Novartis, Pfizer, Sandoz, Sanofi, and UCB, Daniela Graham Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Consultant for: Pfizer Inc, Employee of: Pfizer Inc, Min-Ann Hsu Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Cunshun Wang Shareholder of: Pfizer Inc, Employee of: Pfizer Inc, Pamela Young Shareholder of: Pfizer Inc, Employee of: Pfizer Inc

Does Discordance Between Baseline Patient’s and Evaluator’s Global Assessment of Disease Activity Impact Retention and Remission Rates of TNF Inhibitors in Patients with Psoriatic Arthritis? Data from the EUROSPA Research Collaboration

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Background: Discordance between baseline patient’s and evaluator’s global assessment of disease activity is common and may reduce the likelihood of remission following tumor necrosis factor inhibitor (TNFi) treatment in patients with psoriatic arthritis (PsA).

Objectives: To explore the impact of discordance, defined as patient minus evaluator’s global assessment (ΔPEG), on retention rates and remission rates (DAS28(3)/CRP) in PsA patients ini-

Results: A total of 5422 PsA patients were included. Mean (SD) age for women (n=2968/men=(n=2487) was 49.3(12.5)/47.4(11.7) years, disease duration 6.6(7.3)/6.7(7.2) years, median (25-75 percentiles) baseline ΔPEG 17(0-38)/10(0-30) mm. Retention rates and DAS28(4)/CRP but not DAS28(3)/CRP remission rates were lower for higher quartiles of baseline ΔPEG (table, figure).

Conclusion: High baseline discordance (ΔPEG) was associated with lower TNFi retention rates and with DAS28(4)/CRP but not DAS28(3)/CRP remission rates after 6, 12 and 24 months’ follow-up in both male and female PsA patients. The choice of remission criteria in the follow-up of PsA patients may affect important treatment decisions, and may be of particular impact in patients with high baseline ΔPEG.

REFERENCES:

Acknowledgement: Novartis Pharma AG and IQVIA for supporting the EuroSpA collaboration.

Disclosure of Interests: Brigitte Michelsen Grant/research support from: AbbVie, Pfizer, Roche, UCB, MSD, Eli Lilly, Novartis, Pfizer, MSD, Eli Lilly, Novartis, Pfizer, MSD, Eli Lilly. Consultant for: Novartis, Pfizer. Michael Nissen Consultant for: AbbVie, Pfizer, Roche, UCB, MSD, Eli Lilly, Novartis, Pfizer, MSD, Eli Lilly, Novartis, Pfizer. Apolipoprotein B, HbA1c, CRP, ESR, ultrasensitive CRP, Apolipoprotein were collected. Other variables were collected from patients with peripheral joint involvement were included. Demographic (sex, age), clinical [duration of the disease, DAS28, current treatment, body mass index (BMI), CVRF, vascular events] and analytical variables (atherogenic index, glomerular filtration (GF-MDRD), fibrinogen, glycosylated hemoglobin (HbA1c), CRP, ESR, ultrasensitive CRP, Apolipoprotein A1, apolipoprotein B) were collected. Other variables were collected from the clinical history retrospectively. Basal vascular risk was estimated through SCORE tool. Extracranial carotid artery was explored with an Esote MyLab70XVG ultrasound with linear probe (7-12mHz) and an

Evolution of Subclinical Atherosclerosis in Patients with Psoriatic Arthropathy

I Montolio-Chiva1, M Robustillo-Villanovia2, A Sendra-García1,2, Marta Aguilar-Zamora1, C Vengara-Dangond6, Ana V Orenes Vera1,1, I Vázquez-Gómez3,4, A Martínez-Ferell5, Ella Valls-Pascual5, O Ybáñez-García5, V Náñez-Monje5,7,1, I Torner-Hernández1,2, Juanjo A. Jurek-Sanchez1,2,1, Universitary Peset Doctor Hospital, Valencia, Spain, 2La Plana Hospital, Villarreal, Spain, 3Foundation for the promotion of sanitary and biomedical research in the Valencian Community (FISABIO), Valencia, Spain, 4NIM Hospital, Madrid, Spain.

Background: Patients with psoriatic arthritis (PsA) have a higher prevalence of classical vascular risk factors (CVRF) and early atherosclerosis determined by chronic inflammation.

Objectives: To study the evolution over time of different vascular damage evaluation measures in patients with PsA and investigate the factors related to these changes.

Methods: Pre-post longitudinal study with analytical components. PsA patients with peripheral joint involvement were included. Demographic (sex, age), clinical [duration of the disease, DAS28, current treatment, body mass index (BMI), CVRF, vascular events] and analytical variables (atherogenic index, glomerular filtration (GF-MDRD), fibrinogen, glycosylated hemoglobin (HbA1c), CRP, ESR, ultrasensitive CRP, Apolipoprotein A1, apolipoprotein B) were collected. Other variables were collected from the clinical history retrospectively. Basal vascular risk was estimated through SCORE tool. Extracranial carotid artery was explored with an Esote MyLab70XVG ultrasound with linear probe (7-12mHz) and an
automatic program that measures intima media thickness (IMT) by radio-
frequency (‘Quality intima media thickness in real-time’), and the presence
of ateroma plaques was evaluated following Mannheim consensus. Pulse
wave velocity (PWV) was measured through Mobil o graph® disposable.
We retrospectively studied 3 years later, IMT: 900 μ and PWV: 100 μ
were considered as pathological values. Statistical analyses were per-
formed using SPSS 22.0 program.

Results: 108 patients were included. Twelve patients excluded due to
high vascular risk [previous event and/or diabetes type II or type I with
target organ injury]. Repeated VOP measurement was only available in
49 patients. 62.5% of patients were women and the mean age was 54.2
(SD 1.3) years. Mean disease duration was 93.1 (SD 12.7) months and
mean DAS28 was 1.7 (SD 0.1). 22.4% of patients received glucocorti-
coids, 47.8% NSAIDs, 83.6% DMARDs and 37.3% biological drugs. Mean
BMI was 26.5 (SD 0.5) kg/m², 38.8%, 28.4% and 43.3% of patients were
smokers, hypertensive (11.9% on ARA2, 3% on IECA, 1.5% on cal-
inus, 13.4% and 20.4% had a pathological IMT or PWV, respectively.
Mean SCORE was 1.06 (SD 0.1). Baseline, 23.9% of patients had atherosomatous plaques,
and 13.4% and 20.4% had a pathological IMT or PWV, respectively.
Three years later, we detected new and/or atherosomatous plaques rises
in 19.4% of patients and PWV and IMT worsening in 10.2% and 1.5%
of patients, respectively. As per logistic regression analysis, high baseline
SCORE (16.9%), high systolic blood pressure (8.6%), GF-MDRD (8.2%),
fibrogen (6.9%) and the presence of diabetes and/or dyslipidemia were the factors
that most contributed to the progression of vascular damage, with independ-
ence of the therapeutic objective used for their treatment.

Conclusion: Progression of vascular damage is mainly related to CVRF
in patients with PsA, therefore it is essential to intervene on CVRF early.

Disclosure of Interests: None declared


USE OF SECUKINUMAB IN PSORIATIC ARTHRITIS AND
ANKYLOSING SPONDYLITIS…REAL WORLD DATA

Ozgul Muftullar, Hilary Mcike, Antirn Area Hospital, Rheumatology, Antirn, United Kingdom

Background: Secukinumab was the IL-17 inhibitor licensed for use in
Psoriatic Arthritis (PsA) and Ankylosing Spondylitis (AS). The aim of this
study was to evaluate the effectiveness and safety of Secukinumab in our
cohort of patients.

Objectives: In order to assess the effectiveness and safety of Secukinu-
hab, a retrospective analysis of patients treated with this drug in the
Netherlands Health and Social Care Trust was undertaken.

Methods: Retrospective data was collected from the Local Biologic data-
base. All patients who were on Secukinumab were selected. They were
divided into two arms, Psoriatic Arthritis and Ankylosing Spondylitis. From
this baseline, it was divided into five groups and patient cohort data was
collected. Patients were seen routinely at three monthly intervals and outcomes were collected up to a 12 month period.
From patient notes drug response and adverse effects were recorded.

Results: 41 patients with psoriatic arthritis were treated with
Secukinumab over the 12-month period studied. Twenty-six patients were
female and fifteen were male, with ages ranging from 26 to 70. Only 12
of the patients were on concomitant methotrexate, all met the NICE start
criteria with required DAS 76 scores. Seven of the patients were biologic
naive (17%) at commencement of drug.

Of all the patients who responded, most had some response by 3
months, and all had further response by six months. Sixteen patients (39%)
discontinued treatment due to no response, one
due to increasing shortness of breath, wheeze and rash, and one patient
developed colitis.

Other side effects were noted, which did not cause the drug to be dis-
continued. Five patients had rash and urticaria, three reported headaches.
Infections were fairly common, five patients had chest infections, four
had sinusitis and three had urinary tract infections. Four patients reported
thrust, one oral thrush and three vaginal.
A total of 18 patients with Ankylosing Spondylitis were commenced on
Secukinumab 11 males and 7 females. A third (6/16) were biologic
naive. Ages ranged from 27 to 65.
In the first three months of commencement there was a reduction in
BADSAl scores of all patients. This remained at six months. Inflammatory
markers CRP and ESR were also reduced.

Seven patients discontinued Secukinumab after six months due to side
effects or lack or perceived response by the patient (seen in 1 patient).

Two patients had a loss of efficacy. The remaining four patients noted
cutaneous skin infections, sinus symptoms or headaches as noted in the
PsA arm of the audit.

Conclusion: Patients in the Northern Trust starting Secukinumab generally
have severe disease and most have had prior treatment with biologics.
There was a high incidence of non responders in this group, however in
those patients who responded there was a good response rate at 3
months, and these patients were still on treatment at 12 months. Side
effects were as expected, with infections being the most commonly
reported side effects.

REFERENCES:

secukinumab for psoriatic arthritis and axial spondyloarthritis. Rheumatol-

Acknowledgement: Department of Rheumatology Antirn Area Hospital

Disclosure of Interests: None declared

Conclusion: This study showed that the burden of disease in axial PsA has a significantly different between genders. Female patients with PsA who have axial involvement have higher disease activity, physical disability, functional limitation and higher depression and anxiety risk than male patients. Therefore, we suggest that new strategies should be developed for more effective treatment of axial PsA in female patients.

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Table: Summary of results

<table>
<thead>
<tr>
<th>Variable</th>
<th>SEC</th>
<th>PBO N=231</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACR20&lt;sup&gt;1&lt;/sup&gt;</td>
<td>16  66.7%</td>
<td>52  81.2%</td>
</tr>
<tr>
<td>ACR50&lt;sup&gt;1&lt;/sup&gt;</td>
<td>16  43.1%</td>
<td>52  54.1%</td>
</tr>
<tr>
<td>PASI 75&lt;sup&gt;1&lt;/sup&gt;</td>
<td>150 52.0%</td>
<td>52  62.3%</td>
</tr>
<tr>
<td>HAQ-DI</td>
<td>52  0.6%</td>
<td>52  0.6%</td>
</tr>
<tr>
<td>SF-36 PCS</td>
<td>52  8.0%</td>
<td>52  8.0%</td>
</tr>
<tr>
<td>Resolution of dactylitis, %&lt;sup&gt;2&lt;/sup&gt;</td>
<td>52  3.6%</td>
<td>52  3.6%</td>
</tr>
<tr>
<td>Resolution of enthesitis, %&lt;sup&gt;2&lt;/sup&gt;</td>
<td>52  3.6%</td>
<td>52  3.6%</td>
</tr>
</tbody>
</table>

<sup>1</sup> P<0.001; <sup>2</sup> P<0.001; <sup>3</sup> P<0.05 vs. PBO; NRI data for binary and MMRM data for continuous variables presented at Wk 16. 3 Mean change from baseline (n); 4 Data from pts with enthesitis/dactylitis at BL: N=98/58 [300 mg]; 67 [150 mg]; 84 [150 mg no LD] and 118 [PBO]; N=97/49 [300 mg]; 72 [150 mg]; 85 [150 mg no LD] and 102 [PBO]. Table shows number of pts with enthesitis/dactylitis at BL: N=98/97 (300 mg); 67/72 (150 mg); 84/102 [150 mg no LD] and 118/102 [PBO]. Total number of pts with enthesitis/dactylitis at BL: N=98/97 (300 mg); 67/72 (150 mg); 84/102 [150 mg no LD] and 118/102 [PBO]. N, number of pts with nail PsO in each group; n, number of evaluable pts at Wk 52.

Disclosure of Interests: Peter Nash Grant/research support from: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Novartis, Pfizer Inc, Roche, Sandofi, UCB; Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Novartis, Pfizer Inc, Roche, Sandofi, UCB, Pfizer, UCB; Grant/research support from:AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, SUN and UCB; Consultant for: AbbVie, Amgen, BMS, Galapagos, Gilead Sciences Inc., Janssen, Lilly, Novartis, Pfizer, SUN and UCB, Speakers bureau: AbbVie,

REFERENCES:

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OBJECTIVE MEASURES OF PSORIASIS SEVERITY AND THE RISK FOR PsA: RESULTS FROM THE INCIDENT HEALTH OUTCOMES AND PSORIASIS EVENTS PROSPECTIVE COHORT STUDY

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Background: Psoriasis severity is a presumed risk factor for development of psoriatic arthritis (PsA) but most studies have examined this question retrospectively. Additionally, it remains unclear whether obesity and body surface area of psoriasis (BSA) are independent risk factors for PsA.

Objectives: We examined the association of psoriasis severity, obesity and other potential risk factors for the development of PsA in patients with psoriasis.

Methods: Between 2008-2011, patients with at least one code for psoriasis aged 25-60 years in The Health Improvement Network were randomly selected and questionnaires were sent to their general practitioners. The mean age was 46 and 53% were female. BSA was provided for 8,881 patients of which 52% had mild psoriasis, 36% moderate psoriasis, and 12% severe psoriasis. Mean follow up time was 4.2 years (SD 2.1); the incidence of PsA based on categories commonly used for epidemiological studies. Data through 2015 were used in the current analysis. After excluding patients with PsA at baseline, the incidence of PsA among patients with psoriasis was calculated. Cox proportional hazard ratios were used to examine the risk of developing PsA among patients with mild (<3%), moderate (3-10%) and severe (>10%) psoriasis. We also examined other covariates including obesity, depression, recent infections, smoking, and comorbidities in univariable models. Factors significant at the univariable level were included in multivariable models. We additionally tested an interaction between BSA and obesity.

Results: Among 10,474 questionnaires sent, 9,987 (95%) were returned and, of those, 9,069 (91%) had confirmed psoriasis. The mean age was 46 and 53% were female. BSA was provided for 8,881 patients of which 52% had mild psoriasis, 36% moderate psoriasis, and 12% severe psoriasis. Mean follow up time was 4.2 years (SD 2.1): the incidence of PsA was 5.4 cases per 1,000 person years. In univariable models, age and sex were not associated with PsA but obesity, BMA (continuous), BSA (continuous and category) and depression were significantly associated with development of PsA. The final multivariable model included BSA category (ref mild, moderate: HR 1.44, 95%CI: 1.02-2.03, severe HR 1.99, 1.28-3.11), history of depression (1.69, 1.22-2.34), obesity (1.64, 1.19, 2.25), age (HR 0.99, 0.98-1.00) and female sex (HR 0.72, 0.52-0.99). There was not a statistically significant interaction between BSA and obesity although patients that were obese and had >10% BSA had the highest risk (HR 3.90, 2.22-6.85).

Conclusion: In this large prospective cohort study, we found that body surface area is a strong predictor of developing psoriasis over the next 4-7 years and obesity is an additive risk factor.

REFERENCES:

Acknowledgement: Funded by NIH/NAMS K23 AR063764.

Disclosure of Interests: Alexis Ogdie Grant/research support from: (To my university) Novartis, Pfizer, Grant/research support from: Novartis, Pfizer, Grant/research support from: Novartis, Pfizer, Consultant for: Abbvie, Bristol-Myers Squibb, Celgene, Corrona, Eli Lilly and Company, Novartis, Pfizer, and Takeda, Consultant for: Abbvie, Amgen, Bristol-Myers Squibb, Celgene, Corrona, Eli Lilly, Novartis, Pfizer, Inc, Takeda, Consultant for: Abbvie, Amgen, UCB Pharma, Consultant for: Abbvie, Amgen, UCB, Pfizer, Alexi Ogdie Shareholder of: Novartis, Employee of: Novartis, Luminita Quebe-Fehling Shareholder of: Novartis, Employee of: Novartis, Corine Galliez Shareholder of: Novartis, BMS, Employee of: Novartis


PREVALENCE OF DISEASE DOMAIN PRESENTATIONS AMONG PATIENTS WITH PSORIATIC ARTHRITIS: RESULTS FROM THE CORRONA PSORIATIC ARTHRITIS/SPONDYLOARTHRITIS (PSA/SPA) REGISTRY

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Background: Psoriatic arthritis (PsA) is a heterogeneous, chronic inflammatory disease of the skin and musculoskeletal system. Six key domains of PsA have been identified to help guide treatment: peripheral arthritis, axial disease, enthesitis, dactylitis, and psoriatic skin and nail disease. The most common mutu-

Objective: To describe the prevalence of disease domain presentations among patients with PsA in the Corrona PsA/SpA Registry.

Methods: This study included adult patients with PsA enrolled in the Corrona PsA/SpA Registry between March 2013 and August 2018. PsA cases were evaluated for the presence of 6 disease domains at enrollment: enthesitis (Spondyloarthritis Research Consortium of Canada enthesitis count > 0), dactylitis (dactylitis count > 0), peripheral arthritis (PA); tender and/or swollen joint count > 0), nail psoriasis (global nail psoriasis visual analog scale > 0), axial disease (physician-reported presence of spinal involvement, based on clinical judgment and/or radiographs or MRI showing sacroiliitis), and skin disease (BSA > 0%). The most common mutually exclusive disease presentations were summarized among all patients.
with PsA and those who initiated biologics using frequency counts and percentages.

**Results:** Of 2617 patients with PsA enrolled in the Corrona PsA/SpA Registry, 1698 patients (64.9%) had multidomain disease presentations, 617 (23.6%) had single-domain presentations, and 302 (11.5%) had no presentations. Overall, 1814 (69.3%) patients presented with skin disease, 1523 (68.2%) with PA, 1042 (39.8%) with nail psoriasis, 539 (20.6%) with enthesitis, 319 (12.2%) with axial disease, and 235 (9.0%) with dactylitis at enrollment. Among all patients with PsA, the most common disease presentations were skin disease (2.7%), PA + skin disease (11.7%), and PA + nail psoriasis + skin disease (10.3%) (Figure 1). A total of 354 patients initiated biologics at enrollment. Of these, 289 patients (81.6%) had multidomain disease presentations, 45 (12.7%) had single-domain presentations, and 20 (5.6%) had no presentations; 273 patients (77.1%) presented with PA, 267 (75.4%) with skin disease, 159 (44.9%) with nail psoriasis, 115 (32.5%) with enthesitis, 70 (19.8%) with dactylitis, and 64 (18.1%) with axial disease at enrollment. The most common disease presentations were PA + nail psoriasis + skin disease (11.6%), PA + skin disease (11.3%), and enthesitis + PA + nail psoriasis + skin disease (8.8%), and enthesitis + PA + skin disease (5.9%) (Figure 2).

**Conclusion:** The majority of patients with PsA presented with multiple disease domains. Biologic initiators generally had a higher prevalence of all disease features. These results may increase the physician awareness of the heterogeneity of disease presentations among patients with PsA, which can be important for the development of an effective management plan.

**REFERENCES:**


**Acknowledgement:** This study was sponsored by Corrona, LLC. Corrona is supported through contracted subscriptions with multiple pharmaceutical companies. The abstract was a collaborative effort between Corrona and Novartis, with financial support provided by Novartis.

**Disclosure of Interests:** Alexis Ogdie Grant/research support from: (To my university) Novartis, Pfizer, Grant/research support from: Novartis, Pfizer, Grant/research support from: Novartis, Pfizer, Grant/research support from: Novartis, Pfizer, Consultant for: AbbVie, Bristol-Myers Squibb, Celgene, Corrona, Eli Lilly and Company, Novartis, Pfizer, and Takeda, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Corrona, Eli Lilly, Novartis, Pfizer Inc, Takeda, Consultant for: AbbVie, Amgen, BMS, Celgene, Corrona, Lilly, Novartis, Pfizer, Takeda, Peter Hur Employee of: Peter Hur is an employee of Novartis Pharmaceuticals Corporation, East Hanover, New Jersey, USA, Mei Liu Employee of: M. Liu is an employee of Corrona, LLC, Sabrina Rebello Employee of: Corrona, LLC, Robert McLean: None declared, Blessing Dube Employee of: B. Dube is an employee of Corrona, LLC, Meghan Glynn Employee of: M. Glynn is an employee of Corrona, LLC, Philip J Mease Grant/research support from: AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, SUN and UCB, Consultant for: AbbVie, Amgen, BMS, Galapagos, Gilead Sciences, Inc., Janssen, Lilly, Novartis, Pfizer, SUN and UCB, Speakers bureau: AbbVie, Amgen, BMS, Celgene, Genentech, Janssen, Lilly, Novartis, Pfizer and UCB

companies. The abstract was a collaborative effort between Corrona and Novartis, with financial support provided by Novartis.

Table 1. Demographics, Treatment Profiles, Disease Activity, Quality of Life, and Work Productivity

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Multidomain (n = 1688)</th>
<th>Single Domain Psa (n = 617)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>53.5 (13.0, 78.8)</td>
<td>54.1 (13.0, 88.7)</td>
<td>0.24</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>1009 (60.0)</td>
<td>554 (88.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td>n = 1055</td>
<td>n = 508</td>
<td>0.04</td>
</tr>
<tr>
<td>White</td>
<td>548 (53.3)</td>
<td>372 (73.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Black</td>
<td>96 (9.3)</td>
<td>40 (7.9)</td>
<td>0.07</td>
</tr>
<tr>
<td>Other</td>
<td>39 (3.7)</td>
<td>23 (4.5)</td>
<td></td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>30.7 (24.0, 40.0)</td>
<td>31.4 (27.0, 40.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of disease, years</td>
<td>11.6 (3.8, 32.0)</td>
<td>11.6 (3.5, 29.0)</td>
<td>0.36</td>
</tr>
<tr>
<td>Duration of disease, months</td>
<td>139 (9.0, 442)</td>
<td>129 (9.0, 442)</td>
<td>0.72</td>
</tr>
<tr>
<td>Women's health index, n (%)</td>
<td>48.2 (16.2, 88.0)</td>
<td>48.2 (16.2, 88.0)</td>
<td>0.98</td>
</tr>
</tbody>
</table>

Table 2. Multidomain vs Single-Domain Impact on Outcomes—Multivariable Regression Coefficients

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Multidomain (95% CI)</th>
<th>Single Domain Psa (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
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<tr>
<td>Physician global assessment</td>
<td>12.3 (10.3, 14.3)</td>
<td>12.0 (10.0, 14.0)</td>
<td>&lt;0.001</td>
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<td>Physician global assessment of psoriasis</td>
<td>14.3 (12.3, 16.4)</td>
<td>14.0 (12.0, 16.0)</td>
<td>&lt;0.001</td>
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<tr>
<td>Patient pain</td>
<td>14.0 (12.0, 16.0)</td>
<td>14.0 (12.0, 16.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Patient-reported fatigue</td>
<td>19.6 (17.6, 21.6)</td>
<td>19.6 (17.6, 21.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Patient global assessment</td>
<td>9.6 (9.3, 9.9)</td>
<td>9.6 (9.3, 9.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HAQ-DI</td>
<td>0.26 (0.20, 0.32)</td>
<td>0.26 (0.20, 0.32)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>EQ-5D</td>
<td>0.07 (0.05, 0.09)</td>
<td>0.07 (0.05, 0.09)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>% Work time missed</td>
<td>2.71 (2.57, 2.84)</td>
<td>2.71 (2.57, 2.84)</td>
<td>0.013</td>
</tr>
<tr>
<td>% Impairment while working</td>
<td>8.63 (8.52, 8.73)</td>
<td>8.63 (8.52, 8.73)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>% Overall work impairment</td>
<td>11.6 (11.5, 11.7)</td>
<td>11.6 (11.5, 11.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>% Activity impairment</td>
<td>13.4 (13.3, 13.6)</td>
<td>13.4 (13.3, 13.6)</td>
<td>&lt;0.001</td>
</tr>
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</table>

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FR0461 GENETIC ANALYSIS OF THE NF-KB PATHWAY CAN BE USEFUL TO DISTINGUISH PATIENTS AT RISK OF PSORIATIC ARTHRITIS WITHIN THE SPECTRUM OF PSORIATIC DISEASE

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Background: Psoriasis and psoriatic arthritis (PsA) are the main manifestations of what is now known as psoriatic disease. Both entities share common genetic pathways, but they also differ. The NF-KB pathway has been implicated in the genesis of psoriatic disease, but the differential contribution of this genetic pathway to the risk of psoriasis and PsA is not fully understood.

Objectives: Our aim was to study the association of common polymorphisms at genes of the NF-KB pathway in patients with psoriasis and psoriatic arthritis.

Methods: The study involved a total of 690 psoriatic disease patients (187 of them with PsA) and 550 controls. We genotyped three common polymorphisms in NFKB1 (rs3217713 indel), NFKB1 (rs7152376), and NFKBIZ in 690 psoriatic disease patients (397 of them with PsA) and 550 controls.

Results: The rare NFKB1 rs7152376 C was significantly more frequent in the PsA group vs. controls (0.42 vs. 0.36; p=0.04, OR=1.29, 95% CI=1.01-1.63). Compared to PsA patients, PsA controls showed a significantly higher frequency of the rs7152376 C (0.42 vs. 0.31; p=0.001). In reference to the genotypes, carriers of rs7152376 C (CC+CT) were significantly more frequent in PsA as compared to controls (0.66 vs. 0.58; p=0.06). However, the frequency of these carriers was significantly higher in PsA vs. skin psoriasis (p=0.004). Thus, our data showed significant association between the rare NFKB1 rs7152376 C allele and PsA, and a trend toward the opposite effect for skin psoriasis. Neither NFKB1 rs230526 nor NFKBIZ rs3217713 indel were associated with the risk of developing psoriasis or PsA.

Conclusion: We found a significant association between NFKB1 variants and PsA. Our study shows that alterations in the same genetic pathway may have differential effects on different manifestations of psoriatic disease. Additional studies from larger cohorts and different populations are necessary to validate these results.

References:

Disclosure of Interests: None declared


FR0462 UNDERSTANDING MEDIATORS OF PAIN REDUCTION IN PSORIATIC ARTHRITIS PATIENTS TREATED WITH TOFACITINIB: ROLE OF INFLAMMATION


Background: Pain is a priority for patients (pts) with psoriatic arthritis (PsA) and physicians. Tofacitinib is an oral Janus kinase inhibitor for the treatment of PsA. As pain is a multidimensional phenomenon, there is growing interest in understanding mechanisms of pain relief during treatment with tofacitinib.

Objectives: To examine the potential role of inflammation in the effect of tofacitinib on pain in pts with PsA, using mediation modelling.

Methods: Data were from the Phase 3 OPAL Broaden (NCT01877668) and OPAL Beyond (NCT01882439) studies of pts with active PsA treated with tofacitinib on pain in pts with PsA, using mediation modelling.

Disclosure of Interests: None declared

with tofacitinib 5 mg twice daily (BID) or placebo; pts were tumour necrosis factor inhibitor (TNFi)-naïve or had previous inadequate response (IR) to ≥1 TNFi. All pts continued on a stable dose of a single conventional synthetic DMARD. Analyses used pooled and individual trial data (mean scores from Months 1, 2 and 3). Mediation modelling seeks to explain mechanisms underlying an observed relationship between independent and dependent variables via other explanatory variables (mediators). In this model, pain (100 mm visual analogue scale) was the designated dependent variable, treatment (tofacitinib 5 mg BID vs placebo) the independent variable and inflammation, measured by swollen joint count (SJC) and C-reactive protein (CRP), was a mediator. The primary model designated treatment effect on pain mediated via CRP/SJC as an indirect effect and treatment effect not attributable to CRP/SJC as a direct effect. Models were re-specified based on final results; model invariance by population (TNFi-naïve vs TNFi-IR pts) was assessed.

Results: In the pooled analysis (N=469), 25.9% (p<0.01) of the tofacitinib treatment effect on pain was mediated by CRP/SJC (indirect effect), of which changes via CRP and SJC were 17.8% (p<0.01) and 8.1% (p<0.05), respectively. The treatment effect on pain not attributable to CRP/SJC (direct effect) was 74.1% (p<0.0001). In TNFi-naïve and TNFi-IR pts, indirect effects via SJC were not statistically significant. In the re-specified model with CRP as sole mediator, the indirect effect was 21.3% (p<0.01) and 36.1% (p<0.05) and 16.7% (p<0.05) for TNFi-naïve and TNFi-IR pts, respectively (Figures B, C); the 19.4% difference between TNFi-naïve vs TNFi-IR pts was not statistically significant.

Conclusion: While inflammation, as assessed by CRP/SJC, was a significant mediator of the overall treatment effect on pain in tofacitinib-treated pts with PsA, the majority of the treatment effect was not attributable to CRP/SJC changes. When mediators were assessed individually, only CRP was a significant mediator in the pooled analysis. In the re-specified model, CRP-mediated effects differed in TNFi-naïve vs TNFi-IR pts, but this was not statistically significant. These results suggest that CRP/SJC-associated inflammation only partially explains pain in PsA; other potential mediators need to be identified to better understand the treatment effect of tofacitinib on pain.

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**Table 1. Impact of manifestations on PROs: Adjusted* regression coefficient and p-values**

<table>
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<tr>
<th>Outcome measure (N patients with data available)</th>
<th>Manifestation</th>
<th>Coef.</th>
<th>P value</th>
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<td>EQ-5D VAS (N=784)</td>
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*Adjusted for age, gender, number of joints affected, time since diagnosis.

**REFERENCES:**


**Figure 1. Risk estimates of resolution of enthesitis**
Figure 2. Standardized mean difference of different enthesis score

Figure 3. Risk estimates of resolution of dactylitis

Figure 4. Standardized mean difference of different dactylitis score
PREDICTION OF INCIDENT FRAGILITY FRACTURES THROUGH RADIOFREQUENCY ECHOCOGRAPHIC MULTI SPECTROMETRY (REMS)

**Giovanni Adami**1, Giovanni Arioli2, Gerolamo Bianchi2, Maria Luisa Brandi4, Carla Caffarelli5, Sergio CASCiaro6, Loredana Cavalli4, Luisella Cianferotti6, Davide Gatti11.

**Background:** Radiofrequency Echographic Multi Spectrometry (REMS) is an innovative non-ionizing technique used for diagnosing osteoporosis at lumbar spine and femoral neck sites. In accordance with the results of a multicentre clinical study, REMS T-score values were highly correlated with Dual-energy X-ray absorptiometry (DXA) T-scores [1].

**Objectives:** To determine the predictive value in terms of fragility fracture risk reduction of the REMS T-score compared to DXA T-score in a representative female population.

**Methods:** We enrolled 1370 women (30-90 y, BMI ≤ 35 kg/m²) from 2013 to 2017. We performed in all patients both DXA and REMS lumbar scans. All analyses were performed under the strictest adherence to the corresponding guidelines. All patients underwent a follow-up lasting up to 5 years to assess the incidence of fragility fractures. Patients were stratified in two groups: patients who suffered a fragility fracture during the follow-up period (Group X) and those who did not (Group Y). Through an iterative process, the two groups were then age-matched with an enrolment proportion of 1:2. The finally obtained groups were identified as Group A (with incident fractures) and Group B (without fractures). The performance of REMS T-score in discriminating between Group A and Group B was quantitatively assessed and compared with DXA.

**Results:** Fragility fractures incidence was 14.0% (192 out of 1370 patients, mean follow-up 3.6 ± 0.8 years). Group A included 180 patients (mean age 67.2 ± 7.2 years) and Group B included 360 patients (mean age 67.3 ± 3.5 y). Group A and Group B did not show significant differences with respect to height (p=0.41), weight (p=0.68) and BMI (p=0.32). As expected we found significant differences in REMS T-score (-2.68 ± 1.28 in Group A vs -2.03 ± 1.23 in Group B, p<0.001) and DXA T-score (-2.52 ± 1.20 in Group A vs -2.08 ± 1.17 in Group B, p<0.001). REMS T-score ≤ -2.5 identified Group A patients with sensitivity = 65% and specificity = 58% (OR=2.6). DXA T-score identified Group A patients with sensitivity = 57% and specificity = 57% (OR=1.7).

**Conclusion:** REMS T-score resulted an effective predictor for the risk of incident fragility fractures in a representative population-based sample of female subjects. Reported OR values showed also that REMS had a better performance than DXA in the considered population, showing higher values for both sensitivity and specificity in the identification of fragile patients.

**REFERENCES:**


**Disclosure of Interests:** Giovanni Adami: None declared, Giovanni Arioli: None declared, Gerolamo Bianchi: None declared, Maria Luisa Brandi: None declared, Carla Caffarelli: None declared, Sergio Casciaro Shareholder of: Sergio Casciaro owns stocks of Echolight Spa., Loredana Cavalli: None declared, Luisella Cianferotti Speakers bureau: Abiogen Pharma, Bruno Farmaceutici, Shire, Francesco Conversano Shareholder of: Francesco Conversano owns stock of Echolight Spa, Maurizio Muratore: None declared, Daniele Perrone: None declared, Antonella Grimaldi: None declared, Maurizio Muratore: None declared, Daniele Perrone: None declared, Paola Pisani: None declared, Eugenio Quarta: None declared, Davide Gatti: None declared, Carla Caffarelli: None declared, Francesco Conversano: None declared, Andrea Giusti: None declared, Stefano Gonnelli: None declared, Antonella Grimaldi: None declared, Maurizio Muratore: None declared, Daniele Perrone: None declared, Stefano Gonnelli: None declared, Antonella Grimaldi: None declared, Maurizio Muratore: None declared, Daniele Perrone: None declared, Paola Pisani: None declared, Eugenio Quarta: None declared, Davide Gatti: None declared.

**FRI0466**

RISK FACTORS ASSOCIATED WITH THE DEVELOPMENT OF FRACTURES IN GLUCOCORTICOID TREATED PATIENTS. THE ROLE OF HYPOGONADISM

**Helena Florez1**, José Hernández-Rodríguez2, Afra Muxu2, Josep Lluís Carrasco2, Sergio Prieto-González2, Silvia Ruiz-Gaspá1, María C. Cid1, Ana Monegal2, Núria Guaralbés1, Pilar Peris1, Hospital Clinic, University of Barcelona, Metabolic Bone Diseases Unit, Department of Rheumatology, Barcelona, Spain; Hospital Clinic, University of Barcelona, Department of Nuclear Medicine, Barcelona, Spain; University of Barcelona, Biostatistics, Department of Basic Clinical Practice, Barcelona, Spain

**Background:** Glucocorticoid-induced osteoporosis (GIOP) is a common form of secondary osteoporosis (OP). Fractures in GIOP frequently occur with higher bone mineral density (BMD) than expected and typically at treatment initiation, complicating the identification of patients at risk of fracture.

**Objectives:** Identify risk factors associated with fragility fracture development in GC-treated patients.

**Disclosure of Interests:** None declared
Methods: 127 patients (aged 62±18 years, 63% women, 46% postmenopausal) on GC treatment (prednisone ≥5mg/day, >3 months) were included. Clinical data collected included: risk factors for OP and fractures, dose and GC-treatment duration, previous fractures and disease activity, anthropometric data, bone metabolism parameters (including gonadal axis study), BMD analysis (DXA: OP: T-score ≥-2.5, TBS (degraded microarchitecture [DMA]<1.230), dorsolumbar X-ray (assessing vertebral fractures [VF]) and FRAX risk (GC-adjusted).1

Results: Most patients received GC treatment for vasculitis or polyarthritis rheumatica during 47±69 months (mean daily dose: 14.5mg). 17% had VF, 28% had fragility fracture (VF + non-VF), 29% OP and 71% DMA. Patients with VF received more GC-boluses (57.1% vs. 29.5%, p=0.003), were older (68±13 vs. 60±19 years, p=0.02), postmenopausal (100% vs. 67%, p=0.015) and/or men with testosterone <250ng/dL (67% vs. 11%, p=0.017) and had higher TBS values (1.100 vs. 1.220, p=0.001) and higher FRAX risk (17 vs. 9, p=0.003); patients with fragility fractures showed higher accumulated GC-doses (6.1±13 vs. 6±18g, p=0.046). On multivariate analysis, hypogonadism (OR 14.3; IC95% 2.2-100, p=0.01) and having received GC-boluses (OR 3.40; IC95% 1.1-11.8, p=0.01) were the principal factors associated with VF. Hypogonadism (OR 7.1; IC95% 1.5-38.7, p=0.01) and having a FRAX >20 (OR 6.97; IC95% 1.3-51.7, p=0.02) were factors related to the presence of fragility fractures. Men with testosterone <250ng/dL had higher BMI (29.4 vs. 26.3, p=0.005) and disease activity (ESR 23 vs. 12, p=0.005) and lower TBS (1.050 vs. 1.210, p=0.001); age, daily and cumulated GC doses were similar to subjects with normal testosterone levels.

Conclusion: Hypogonadism is a major risk factor for developing fractures in GC-treated men and women, whereas receiving GC-boluses is related to VF, indicating the importance of evaluating the gonadal axis in these patients.

REFERENCES:

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EFFECTS OF DIFFERENT VITAMIN D SUPPLEMENTATION SCHEMES IN POSTMENOPAUSAL WOMEN

Stefano Benard, Addolorata Corrado, Angiola Mele, Cinzia Rotondo, Antonello Trotta, Natalia Mansuetto, Francesco Paolo Cantatore. Rheumatology Clinic, Department of Medical and Surgical University, University of Foggia, Foggia, Italy

Background: Vitamin D exerts different extra-skeletal effects, including a positive effect on muscle function. Circulating levels of the 25 hydroxy-activated Vitamin D (25(OH)D) reflect the body Vitamin D reserve; to reach the optimal serum 25(OH)D threshold, Vitamin D supplementation is often requested. The commonest Vitamin D supplementation is represented by cholecalciferol (D3), but the hydroxylated Vitamin D metabolite 25(OH)D represents a therapeutic alternative.

Objectives: The aim of the study was to evaluate the efficacy of the calcifediol supplementation compared to various cholecalciferol administration schedules in increasing the 25(OH)D vitamin D serum levels and the effects on muscular function in post-menopausal women.

Methods: 60 post-menopausal women aged ≤ 65 years with low serum 25(OH)D levels (8-24 ng/mL) were included in the study. Recruited patients were randomly assigned to receive oral Vitamin D 1000 UI/day according to different regimens. 1) cholecalciferol (D3) 300.000 UI; single oral dose; 2) monthly cholecalciferol 100.000 UI for three consecutive months; 3) weekly cholecalciferol 7000 UI; 4) weekly HyD 7000 UI. At baseline and every three months, for 12 months, the following parameters were evaluated: serum levels of 25(OH)D; PTH, calcium, phosphates; at baseline and every 15 days muscular function was evaluated using the Timed Up and Go (TUG) and the Sit to Stand test.

Results: Weekly administration of HyD induced a significantly faster and greater increase of 25(OH)D levels, compared to the other treatment groups (at 12 months: +384% vs +145%, + 220%, + 246% in groups 1, 2, 3, respectively); the increase appeared after 1 month from baseline. D3 300.000 UI single dose induces a slower increase of 25(OH)D compared with weekly administration and weekly supplementation. An increase of muscular strength was observed after 12 months in all supplementation groups, starting from 1 month from baseline, with a greater effect in subjects treated with weekly HyD compared to D3 treated subjects (TUG 6 sec- ond vs 7.3, 7.7, 7.9 in groups 1, 2, 3, respectively, Sit to Stand 16.2 vs 15.4, 15.3, 15.7 in groups 1, 2, 3 respectively). Overall, the effects on 25(OH)D levels and on muscular function were greater in subject treated with weekly D3 compared to subject treated with monthly or single dose D3. No differences in PTH, calcium and phosphate serum levels were found between supplementation groups.

Conclusion: Supplementation with calcifediol is more effective and faster compared to cholecalciferol in increasing 25(OH)D serum levels; further, weekly cholecalciferol is more effective and faster compared to single dose or monthly administration. Increase in circulating levels of 25(OH)D is associated to an improvement of muscular strength.

REFERENCES:

Disclosure of Interests: Stefano Benard: None declared, Addolorata Corrado: None declared, Angiola Mele: None declared, Cinzia Rotondo: None declared, Antonello Trotta: None declared, Natalia Mansuetto: None declared, Francesco Paolo Cantatore Speakers bureau: PFIZER, ROCHE
EFFECT OF DISCONTINUATION OF DENOSUMAB IN SUBJECTS WITH RHEUMATOID ARTHRITIS TREATED WITH GLUCOCORTICOIDS

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Disclosure of Interests: Nancy Lane5, Piet Geusens6, Peter Butler2, Li Chen 2, Daria B. Crittenden2, Robin Dorm2, Stanley Cohen2, Kenneth Saag1, Michele Mcdermott2, Jonathan Adachi3, Willem Lems4, Will Meelems4

Background: Denosumab, a monoclonal antibody against RANKL, is approved for the treatment of glucocorticoid (GC) induced osteoporosis (GIO). In postmenopausal women with osteoporosis, denosumab discontinuation leads to a transient increase in bone turnover above baseline, peaking at 12 months from the last dose, and a corresponding decline in bone mineral density (BMD). To better understand the effects of denosumab discontinuation in GC-treated patients, we analyzed a subgroup receiving GCs at baseline from a phase 2 study of denosumab in subjects with rheumatoid arthritis (RA), followed for 12 months after discontinuing denosumab discontinuation.

Objectives: To evaluate changes in bone turnover and BMD in subjects with RA on GCs treated with denosumab, after discontinuing denosumab for 12 months.

Methods: This double-blind, placebo-controlled study enrolled subjects with RA who were randomized to receive denosumab 60 mg, denosumab 180 mg, or placebo subcutaneously for 12 months, and followed for progression of structural damage. Subjects were followed for an additional 12 months after denosumab discontinuation. Outcome measures in this subgroup analysis of subjects treated with GCs at study baseline included percent change from baseline in serum C-terminal telopeptide of type I collagen (CTX) and lumbar spine (LS) and total hip (TH) BMD on- and off-treatment. Baseline mean (SD) prednisone equivalent dose (mg/day) was 6.1 (2.4), 5.2 (2.1), and 6.1 (3.2) in the placebo, denosumab 60 mg, and denosumab 180 mg groups, respectively. Data on CTX are reported as median and interquartile range. Percent changes in LS and TH BMD at each time point were assessed based on a repeated-measures model adjusting for treatment, baseline use of steroids, previous use of biologics, and baseline BMD value.

Results: Among 218 subjects in the phase 2 study, 82 (26 placebo, 27 denosumab 60 mg, 29 denosumab 180 mg) were included in this analysis. After 12 months of denosumab treatment, CTX decreased from baseline in both groups (Figure); in the off-treatment period, CTX returned to baseline by 18 months and was overall similar to placebo at 24 months. BMD increased at the LS and TH at 12 months with denosumab treatment (Figure) and returned to baseline levels after 12 months of discontinuation.

Conclusion: Like all non-bisphosphonate medications for osteoporosis, denosumab is reversible with discontinuation. In this small subgroup of GC-treated subjects with RA, BMD gains achieved with denosumab were lost upon discontinuation, consistent with observations in postmenopausal women receiving denosumab for osteoporosis. In this analysis of short-term denosumab use in subjects with RA receiving GCs, bone turnover was reduced with denosumab and gradually returned to baseline upon discontinuation, without a clear increase to above-baseline levels in the off-treatment period.


FRI0471 | BONE QUALITY ASSESSMENT IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Background: Type 2 diabetes mellitus (T2DM) is a risk factor for osteoporotic fractures although bone mineral density is normal or even increased. Thus, diabetes may be associated with a reduction of bone strength that is not reflected in the measurement of bone mineral density (BMD)

Objectives: The aim of this study was to compare BMD with a non-invasive assessment of trabecular microarchitecture, (Trabecular bone score) TBS, in patients with T2DM

Methods: In a prospective cross-sectional study, trabecular microarchitectural analysis was examined in patients with T2DM and non diabetic control subjects. The exclusion criteria were diseases (hyperthyroidism, Cushing’s syndrome, primary hyperparathyroidism, renal failure, malabsorption), rheumatic diseases and/or medications that might affect bone and mineral metabolism, post menopausal women. Lumbar spine BMD was measured by dual-emission x-ray absorptiometry (DXA), and TBS was calculated by examining pixel variations within the DXA images using TBS Insight

Results: 205 patients (108 male, 97 female), aged 25 to 60 years with T2DM and 205 non diabetic control subjects ((105 male, 100 female) Mean TBS was lower in T2DM (1.256±0.103 vs. 1.291±0.101, p=0.001). Mean BMD was higher in T2DM Z score (0.516±1.346 vs. -0.815±1.53, p= 0.016).

Conclusion: In T2DM,TBS is lower than control subjects. Abnormal trabecular microarchitecture may help explain the paradox of increased fractures at a higher BMD in T2DM

REFERENCES
Disclosure of Interests: None declared

Figure 1. Survival curve in new bone fracture onset of teriparatide and teriparatide acetate.

FR0473

ASSESSING THE CLINICAL RELEVANCE OF BONE DENSITOMETRY SCREENING IN PATIENTS UNDER 40 YEARS OF AGE: INDICATIONS AND RESULTS

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Background: Guidelines for the diagnosis and treatment of osteoporosis in patients under the age of 40 years are lacking. The International Osteoporosis Foundation (IOF) working group has recommended dual-energy X-ray absorption (DXA) screening should only be performed in this age group if patients have an associated chronic disease such as inflammatory bowel disease (IBD) in conjunction with a vertebral fracture or multiple fractures elsewhere. For these patients, a T-score of < -2.5 can be used to diagnosis low BMD but the term osteoporosis may not be appropriate and there is minimal evidence supporting the use of bisphosphonates (BPs).

Objectives: In patients under 40 years of age undergoing DXA screening, to determine (1) the indication and (2) the DXA results (age adjusted Z score and standard T score), in order to conclude whether DXA screening in this group was appropriate and relevant for making meaningful treatment decisions.

Methods: Clinical details for all DXA scans requested for patients less than 40 years of age were obtained from the Mid Cheshire Hospital NHS Trust radiology department for a 6 month period from July to December 2018 inclusive. Descriptive data was produced regarding basic patient demographics, DXA indication and DXA results in the form of Z- and T-scores at the neck of femur (NOF) and spine.

Results: In total, 35 patients under the age of 40 years underwent DXA screening in the defined time period. The mean age of patients was 30.5 years (s.d. 6.0) and 24 patients (69%) were female. The youngest patients were 19 years. Regarding indications, only two patients (6%) were appropriate for DXA screening according to the IOF suggested guidelines, both of whom had vertebral fractures. Twenty seven patients (77%) had an established diagnosis of a disease known to cause OP but no history of fracture. Regarding results, at the NOF and spine respectively mean Z-scores were -0.88 (s.d. 1.19) and -0.945 (0.93). Only three patients (9%) had Z- or T-score of < -2.5: two patients who had a history of thoracic vertebral fracture, and a patient with high steroid use for IBD but no fracture history.

Conclusion: The majority of patients aged less than 40 years referred for DXA screening are being referred due to associated diagnoses with no history of fracture, not in keeping with IOF recommendations. Of the 33 patients with no history of fracture, only one patient (3%) had a T-score consistent with low BMD. There is little evidence to support bisphosphonate use in this group. We therefore conclude that DXA screening in patients less than 40 years should be reserved for those with a history of fracture.

REFERENCES:


Disclosure of Interests: None declared
Background: Bariatric surgery is increasingly common due to the obesity epidemic. However, there is controversial evidence about the association between bariatric surgery and fracture risk. This may be due to the fundamental differences between patients undergoing bariatric surgery with patients who do not, raising the question: within patients who fracture, are they an increased risk of fracture after surgery? And if so, who is at risk of fracture?

Objectives: 1. To investigate the association between bariatric surgery and risk of three fracture locations using a within person study design comparing a) the year incidence post surgery to the 5 years pre surgery, b) splitting the 5 year post surgery risk into two windows 0-2 and 2.01 – 5 years. 2. To predict who is at risk of fracture following bariatric surgery.

Methods: A self-controlled case series analysis (SCCS) and Stepwise logistic regression (LR) were conducted. Patients undergoing bariatric surgery were identified in the clinical practice research datalink (CPRD) GOLD dataset and linked to hospital episode statistics (HES) data. Prior outcome was any fracture (any skeletal sites except skull and digits). Secondary outcomes were major (hip, spine, forearm and humerus) and peripheral fractures (forearm and lower leg). For the SCCS, Poisson models in those who fractured were fit to calculate Incidence Rate Ratios (IRR) for the aforementioned time windows. Potential predictors were selected with an exit p-value of 0.157 and their predictive performance was reported using a C-statistic.

Results: Of 5,492 patients undergoing bariatric surgery, 252 patients had 272 any fractures, 75 (60) major fractures and 126 (135) peripheral fractures. Average BMI was 43.9. Major fracture risk increased nearly three-fold following surgery: IRR (95% CI) 2.70 (1.31, 5.57). Conversely, the incidence of any and peripheral fractures did not change: IRRs 1.17 (0.86, 1.60) and 0.92 (0.60, 1.42) respectively. Any and major fracture risk increased in the 3rd to 5th year post-surgery: IRRs of 1.73 (1.08, 2.77), 4.98 (1.94, 12.78) respectively. 7 variables were identified which may predict major fracture with a high c-statistics of 0.77 (0.71, 0.88).

Conclusion: Few patients had fractures (252/5492). The incidence of major osteoporotic fracture is increased after bariatric surgery by nearly 3 fold. To then increase to 5 fold in the 2-5 year window. Multiple factors were identified for patients at risk of major fracture post-operatively. External validation is needed. Further research is needed on post-bariatric surgery care to minimise fracture risk.

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ISCHEMIA MODIFIED ALBUMIN IN OSTEOPOROSIS

Background: Osteoporosis is a common bone metabolism disease, characterized by low bone mass and pathological fractures. This disease is caused by loss of balance in bone resorption and formation. It is thought that this imbalance is associated with increasing in reactive oxygen species (ROS) and/or insufficiency of antioxidant defense (1). ROS adversely affect the formation and life cycle of osteoclasts, osteoblasts and osteocytes (2). Albumin has many functions such as the transport of molecules, the oncotic pressure of plasma and antioxidation. The damage of the ROS to the N-terminal of the albumin reduces the carrying capacity of the albumin and thus the antioxidant capacity. This damage is evaluated by decreasing the cobalt binding capacity of albumin called ischemia modified albumin (IMA), and IMA shows oxidative damage (3).

Objectives: The aim of this study was to determine IMA levels of patient with osteoporosis.

Methods: OP was diagnosed by T score of bone mineral density (BMD), IMA, albumin levels and IMA/Albumin ratio (IMAR) were studied from the sera of patients with osteoporosis (OP) and healthy volunteers (control) (4). Patients who had any chronic disease such as diabetes mellitus, hypertension, and etc. and any acute disease such as infection were excluded from study. Results were shown as mean ± standard deviation or median (IQR) according to the distribution of variables. p<0.05 was considered significant.

Results: The study included 28 female patients in OP group and 26 female volunteer in control groups. The mean age was 65.5 ± 5.4 and 66.4 ± 7.4 for OP and control groups, respectively (p=0.616). Median (IQR) lumbar T scores of BMD of OP group were -3.1 (-3.32; -2.85). The albumin values of OP and control groups were 4.38 ± 0.13 and 4.40 ± 0.11, respectively; and no significant difference was found between the groups (p = 0.441). The IMA and IMAR results of the OP group were 0.65 (0.61; 0.74) and 0.15 (0.14; 0.17), respectively; and 0.46 (0.40, 0.55), and 11 (0.09; 0.13) in the control group, respectively. (Figure 1). Both IMA and IMAR results were significantly lower in the OP group than in the control group (high ABSU) (p <0.001; for all).

Conclusions: The cobalt binding capacity of albumin decreased in patients with osteoporosis. To the best of our knowledge, this study is the first determining IMA levels in osteoporosis. It is known that the cobalt binding capacity of albumin decreased after oxidative damage. It is shown that IMA is increased in some diseases associated with oxidative stress. Similarly, it was showed that thiol-disulfide balance was shifted to disulfide side in postmenopausal osteoporosis and it was an indicator of oxidative stress (1, 2). In the light of these results, oxidative stress is thought to play role in the pathophysiology of osteoporosis. As a result, antioxidant replacement such as N-acetyl cysteine, lipoic acid, vitamin C, etc. may be recommended to the patients with osteoporosis.

REFERENCES:

Disclosure of Interests: None declared

STUDY OF CORTICAL AND TRABECULAR COMPARTMENTS THROUGH 3D-SHAPER IN LUNG TRANSPLANTED PATIENTS

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Background: Osteoporosis in lung transplant (LT) patients is a frequent complication. Glucocorticoid treatment (GC) is a prominent risk factor (RF) that alters both bone mass and architecture. Studying the volumetric BMD using 3D-SHAPER software would help the study of architecture.

Objectives: To study the change in cortical surface density, volumetric trabecular density and integral volumetric density measured by 3D-SHAPER before and after LT as well as changes in bone mineral density (BMD) measured by densitometry (DXA).

Methods: LT patients assessed in Rheumatology are included. The demographic characteristics, diagnosis of lung disease and RF of low bone mass prior to LT are collected. Patients were grouped into 3 groups according to the type of disease, these being: Chronic Obstructive Pulmonary Disease (COPD), Interstitial Lung Diseases (ILD) and OTHER pathologies. Bone mass was evaluated by DXA (GE-LUNAR) before and after 6 months after LT and 3D-SHAPER software (v2.7, Galgo Medical) was applied in all DXAs.

Results: 49 LT patients were included (46.9% women), with an average age of 56.9 ± 8.7 years. In the ILD group, a higher proportion of patients with a low calcium intake (p = 0.027) and with high doses of GC (p = 0.001) was observed. COPD group presented the highest proportion of smokers (p = 0.027). Prevalence of osteoporosis prior to LT was 24.5%, higher in COPD (p=0.007). Values of BMD and 3D-SHAPER as well as the percentage of post-transplant variation are shown in Table 1. Of the 47 patients, 19 (39.8%) started osteoactive treatment before LT, with a higher percentage of patients treated in the COPD group (p = 0.007). Of 42 patients, we have DXA at 6 months post-transplant, with a prevalence of osteoporosis of 23.8%. 27/42 patients underwent post-transplant osteoactive treatment, with an average treatment time until DXA was 19.2 ± 26.1 months, with no differences between groups.

Conclusion:

- Prevalence of low bone mass is high both before and after the transplant.
- Prevalence of some osteoporosis RFs was different between the lung disease groups.
- COPD group presented a worse bone mass before LT. Subsequently, they experienced a significant improvement in BMD and volumetric measurements with respect to the other two groups, which showed losses of these parameters. COPD was the group most treated for osteoporosis and with a lower proportion of patients with GC at high doses.
- Trabecular BMDv was the most altered measure of 3D-SHAPER, with greater decrease in patients with GC at high doses and lower in those with osteoactive treatment.

Disclosure of Interests: None declared

PRE-TRANSPLANT TOTAL COPD ILD OTHERS
(n=47) (n=11) (n=30) (n=8)

BMD pre-transplant (mean) g/cm² (T-score)
| Lumbar Spine | 1.074 (-1.02) | 0.907 (2.16) | 1.131 (0.55) | 1.051 (1.18) |
| Femoral Neck | 0.886 (-1.28) | 0.798 (-1.18) | 0.895 (1.04) | 0.846 (1.35) |
| Total Hip | 0.907 (-1.15) | 0.812 (2.07) | 0.950 (0.79) | 0.878 (1.27) |

3D-SHAPER (mean) 155.6 (-1.19) 143.9 (-1.90) 163.3 (0.67) 147.2 (1.26)

| BMDs Cortical: g/cm²(T-score) | 146.1 (-1.69) | 115.4 (-2.65) | 155.3 (-1.64) | 153.6 (1.97) |
| BMDv Trabecular: g/cm²(T-score) | 296.0 | 258.4 | 309.4 | 106 |
| BMDv Integral: g/cm² | | | 297.5 | |

BMD post-transplant (mean)

| % change BMD (mean:DE) | -1.26 ± 10.3 | 9.38 ± 11.6** | -3.22 ± 7.3 | -7.03 ± 7.7** |
| Lumbar Spine | 4.34 ± 7.3 | -6.74 ± 6.5 | -5.43 ± 6.9 | -5.57 ± 9.3 |
| Femoral Neck | -3.22 ± 11.8 | -1.14 ± 3.5* | -4.07 ± 6.2 | -6.58 ± 5.6†† |
| Total Hip | 6.0 | | | |

% change 3D-SHAPER (mean:DE)

| % change BMD | 1.59 ± 5.9 | 0.14 ± 4.9 | -2.53 ± 6.5 | -0.59 ± 4.9 |
| BMDs Cortical | 11.6 | 1.87 ± 4.3* | -4.67 ± 6.5 | 5.11 |
| BMDv Trabecular | 3.11 | | | |
| BMDv Integral | 6.3 | | | |

* p<0.05, ** p<0.01 respect previous, *p<0.05, **p<0.01 COPD vs. ILD; †p<0.05, ††p<0.01 COPD vs. OTHERS; # only in women.
**FRI0478**

**SPINAL MOBILITY AND BONE MINERAL DENSITY IN SPONDYLOARTHROSIS**

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**Background:** Osteoporosis is the most frequent comorbidity in axial spondyloarthritis (axSpA). The change in spinal mobility (traditional measures) in patients with axSpA has been associated with low bone mineral density (BMD) although the data are variable (DIM, lateral flexion, BASMI).

**Objectives:** The aim of our study is to understand the relationship between spinal mobility, BMD and fragility fractures.

**Methods:** Analytical, observational, longitudinal, and retrospective study of a cohort of patients with axSpA (ASAS criteria). Perimenaopausal or menopausal women, diseases and/or osteoporosis treatments, biological drugs, immunosuppressive drugs (at least one year before), and treatment with drugs that interfere in the bone metabolism were excluded; bisphosphonates, ranelate of strontium, selective modulators of the estrogen receptor, calcitonin, hormone therapy, denosumab and teriparatide, among others.

**Results:** 74 patients were studied, 67 were classified as axSpA and 7 as peripheral SpA. Bivariate analysis showed that the group of patients with osteoporosis (14,86%) had a worse DIM (p = 0,001), fragus to wall distance (p = 0,001) and lateral flexion (p = 0,045) than patients who did not have osteoporosis. The multiple regression analysis indicated that lumbar spine T-score was independently associated with BASMI index (B 0,895, p=0,028), and with lower levels of 25 OH vitamin D (B 0,895, p=0,028).

**Conclusion:** UCOAOSMI is a validated metrological index with three-dimensional measurements of human spinal mobility that shows higher levels of objectivity and precision than traditional measures. Subsequent studies will compare mobility parameters (UCOAOSMI) and BMD of patients with axSpA. Clarifying the relationship between spinal mobility, BMD and fragility fractures would help us to better understand the course of the disease in axSpA.

**REFERENCES:**


**Disclosure of Interests:** Laura Bautista: None declared, Asunción Salmoral: None declared, Inmaculada Gómez Gracia: None declared, Ladhesa Pineda Lourdes: None declared, Pérez Sánchez Laura: None declared, Gómez García Ignacio: None declared, Inmaculada Concepción Aranda-Valera: None declared, María del Carmen Abalos-Aguilera: None declared, Gamido Castro Juan Luis: None declared, Font Ugalde Pilar: None declared, María del Carmen Castro Villegas: Paid investigator for: MSD, Abbvie, Pfizer, Janssen, Lilly, Roche, Alejandro Escudero Conteras: None declared, Eduardo Collantes Estevez: None declared

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**FRI0480**

**CHANGES IN CIRCULATING SCLTA-4 FOLLOWING ZOLEDRONIC ACID INFUSION**

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**Background:** Acute phase response (APR) is a transient, flu-like reaction to first exposure to intravenous nitrogen-containing bisphosphonate (NBP). APR is characterised by a strong inflammatory response, associated with increases in circulating levels of IL-6 and TNF-, that is thought to be due to activation and increased proliferation of γδ T cells related to the molecular mechanism of action of NBP. Cytoytic T-Lymphocyte Antigen-4 (CTLA-4), in both its soluble (s) and membrane-bound forms, is involved in the downregulation of T cell proliferation, cell cycle progression and cytokine production. High levels of serum sCTLA-4 have been reported in several autoimmune diseases, and its role as both inhibitor and enhancer of the immune response has been proposed.

**Objectives:** To evaluate the potential relationship between sCTLA-4 and the development of APR in patients treated with zoledronic acid (ZOL).

**Conclusion:** The trend for increasing low trauma distal forearm fractures in women age 40-59 yrs may reflect the decreased use of hormone replacement therapy, which would likely have particularly impacted this age group. The decrease in fractures in men age ≥ 80 yrs may reflect greater recognition, in recent years, of osteoporosis in older men and initiation of treatment. Whether changes in practice patterns are actually contributing to these observed trends warrants further review.

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**FRI0479**

**TRENDS IN LOW TRAUMA DISTAL FOREARM FRACTURE INCIDENCE IN WOMEN AND MEN OVER 1995-2015 IN OLMSTED COUNTY, MINNESOTA, USA**

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**Background:** It is unclear how recent practice changes of decreased use of hormone replacement therapy and drug holidays from bisphosphonate therapy have impacted incidence of fragility fractures. Fragility (low trauma) fractures at the distal forearm in women may be more likely to be impacted by these changes as compared with men.

**Objectives:** We examined the trends in distal forearm fracture incidence over 1995-2015, in both women and men, from Olmsted County, Minnesota, USA.

**Methods:** Using the Rochester Epidemiology Project, a unique medical records linkage system that allows access to all (inpatient and outpatient) community medical records for Olmsted County residents, we identified all incident distal forearm fractures among residents age ≥18 years between 1995-2015. Available medical records were reviewed by trained nurse abstractors to validate distal forearm fractures identified and to determine their antecedent cause (pathological process [e.g., malignancy], severe trauma [e.g., motor vehicle accidents, sports/other recreational activities] and low trauma [by convention, equivalent to a fall from standing height or less]). Overall incidence rates were summarized separately for women and men, as well as by 5 year strata for different age groups (ages 18-39, 40-59, 60-79 and ≥ 80 yrs). Rates for women and men were each directly age-adjusted to the population distribution of US whites in 2010.

**Results:** Between 1995-2015, we identified 2727 distal forearm fractures in women (70%, median age 62 yrs; 1915 due to low trauma) and 1193 distal forearm fractures in men (30%, median age 48 yrs; 450 due to low trauma), 92.3% of which were in whites. The overall age-adjusted annual incidence of first distal forearm fracture over 1995-2015 was 233 per 100,000 person-years (p-y) for women and 113 per 100,000 p-y for men. When considering only fractures due to low trauma, the overall age-adjusted annual incidence of first distal forearm fracture over 1995-2015 was 169 per 100,000 p-y for women and 49 per 100,000 p-y for men. Rates of low trauma distal forearm fracture appear to be stable in younger (18-39 yrs) women, but since 2005, seem to be increasing in women age 40-59 yrs (Table). In contrast, rates in older women appear to be decreasing or are stable since 2005. In men, the rates of low trauma distal forearm fracture appear to have relatively unchanged over the past 20 years, except in men age ≥ 80 yrs where the rates have generally been lower since 2005 (Table).

**Conclusion:** The trend for increasing low trauma distal forearm fractures in women age 40-59 yrs may reflect the decreased use of hormone replacement therapy, which would likely have particularly impacted this age group. The decrease in fractures in men age ≥ 80 yrs may reflect greater recognition, in recent years, of osteoporosis in older men and initiation of treatment. Whether changes in practice patterns are actually contributing to these observed trends warrants further review.

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**Disclosure of Interests:** None declared

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Methods: Included in the study were patients treated with a single intra-
venous ZOL infusion 5 mg. Exclusion criteria were previous treatment with 
ZOL, treatments interfering with CTLA-4, and estimated glomerular fil-
tration rate <35 ml/min. APR was defined as a rise in axillary tempera-
ture of 1°C or more at any time during the first 48 hours and an increase in 
musculoskeletal pain by more than 10 mm in a visual analogue scale 
(VAS, from 0 to 100 mm). Clinical and laboratory parameters were 
assessed at baseline, before ZOL, and at 24, 48 and 72 hours after the 
infusion.

Results: Ten female patients (mean age 73-10 years) were included (2 
avertbral fractures and the remaining had osteoporosis), 5 of whom 
experienced APR (APR+) associated with the expected increases in 
s serum CRP and IL-6. Baseline levels of sCTLA-4 did not differ between 
APR+ and APR- patients and decreased significantly in all from 32.9 ng/ 
ml to 24-9 ng/ml (p=0.007) at 24 hr, 16-8 ng/ml (p=0.004) at 48 hr and 
7-6 ng/ml (p=0.001) at 72 hr. Absolute value of sCTLA-4 and mean% 
change of sCTLA-4 after ZOL were not statistically different between 
APR+ and APR- patients. At 72 hr, sCTLA-4 decreased by 77% (-23%) 
in APR+ and by 81% (-20%) in APR- (p=0.786). There were no statisti-
cally significant correlations between serum sCTLA-4 levels with any cli-
nical or biochemical parameter of APR.

Conclusion: Our study is in accordance with our hypothesis, sCTLA-4 was not related to the 
ocurrence of the APR after ZOL. The significance of the substantial 
decrease of circulating levels of sCTLA-4 after ZOL in all studied patients 
warrants further investigation.

Disclosure of Interests: Géraldo Bianchi Consultant for: Alfa-Sigma, 
Amgen, BMS, Celgene, Medac, UCB. Speakers bureau: Abbie, Abiogen, 
Alfa-Sigma, Amgen, BMS, Celgene, Daniele Saverino: None declared, 
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last 3 years, Consultant for: Amgen, Axosure, Gador, Radius Health, 
UCB, Speakers bureau: Amgen, UCB.


FRIO481 MEDIATORS OF BONE METABOLISM (DKK1, OPG 
SCLEROSTIN AND RANKL) IN A COHORT OF PATIENTS 
WITH ELDERLY-ONSET ARTHRITIS

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Mato Soria1, Susana Holgado Perez2, Maria Aparicio Espinar1, Angélica Prier-
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Background: Patients with elderly-onset arthritis have greater comorbidity 
than young patients, with a higher incidence of osteoporosis (OP), prob-
ably mediated by increased bone resorption. However, there are few data 
on bone metabolism mediators in this population.

Objectives: To analyze bone remodeling mediators (DKK1, sclerostin, 
osteoprotegerin [OPG], and RANKL) in patients with elderly-onset arthritis 
and its relationship with bone mineral density.

Methods: Longitudinal observational study that included patients with elde-
ry-onset arthritis (> 65 years) without diagnosis of OP or on antioste-
oporotic treatment. Phospho-calcium metabolism, quantification of bone 
remodeling mediators (ELISA, R&D systems) and bone densitometry, 
determined in all patients at diagnosis and at 12 months. The results 
were compared with a control group of the same age and sex 
(n=14). The statistical study was performed using SPSS.

Results: We included 73 patients (37F: 36M), with a mean age of 75±7 
years. Most were diagnosed with rheumatoid arthritis (RA) (n=43), fol-
lowed by polyarthritis rheumatica (n=16) and others (n=14). Fifteen 
patients were rheumatoid factor (RF) positive and 23 were ACA positive. 
Five patients had erosions at the diagnosis. 88.64% of patients with RA 
noticed an increase in musculoskeletal pain by more than 10 mm in a visual 
analogue scale (VAS, from 0 to 100 mm). Clinical and laboratory parameters were 
assessed at baseline, before ZOL, and at 24, 48 and 72 hours after the 
infusion.

At diagnosis, patients with elderly-onset arthritis had higher levels of 
DKK1 and CTX than the control group, with no statistically significant dif-
fences in sclerostin, OPG, and RANKL values (table 1). In addition, 
DKK1 values were negatively correlated with sclerostin (r=-0.286, 
p=0.016) and OPG (r=-0.276, p=0.020), 31.9% had densitometric OP. We 
found no significant differences in bone remodeling mediators between 
patients with/monthly basophil OCP.

At 12 months, DAS28- VSG was <2.6 in 38.1%. The mean corticosteroid 
dose was 5.5 mg/day with a cumulative dose of 1630±426 mg. 45.8% 
received antiresorptive treatment (28 patients’ bisphosphonates and 5 
denosumab). The prevalence of OP at 12 months was 31.3% and 4 
patients had new fractures during (4 vertebra and 1 femur fractures). We 
observed a marked decrease in the values of DKK1 (-18.89%, p<0.001) 
and sclerostin (-46.76%, p<0.001) and an increase in OPG (11.97%, 
p=0.018).

We didn’t found relationship between bone metabolism mediators and 
cumulative corticosteroid dose. There were no differences in terms of 
diagnosis (RA or PRM), ACPA positivity, activity scores or treatment with 
bisphosphonates.

Conclusion: Patients with elderly-onset arthritis have higher DKK1 values 
than the control group, and this correlate negatively with sclerostin and 
OPG. The marked decrease in Dkk-1 and sclerostin at 12 months, and 
the increase in OPG, suggests a role for these mediators in the bone 
metabolism of this population. It is important to note the high prevalence 
of OP in this group of patients.

Table 1. We excluded patients treated with denosumab. 1 p<0.005 with respect to the 
control group. 2 p<0.05 with respect to baseline

Disclosure of Interests: None declared


FRIO482 RISK FACTORS FOR FRAILITY FrACtURE IN 
PATIENTS WHO SMOKE: AN OBSERVATIONAL STUDY

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Background: Smoking is a risk factor for osteoporosis and increases the 
likelihood of a fragility fracture. It is included in the FRAX™ tool, which 
is used as an aid for bone mineral density (BMD) referral and as a risk 
stratification for the propensity of developing a fragility fracture. The addi-
tive effect of other risk factors including demographics increasing the risk 
of fracture has not been explored in a large cohort.

Objectives: To investigate the additive predictors of fracture in patients 
who have smoking as their only risk for fracture, referred for BMD 
estimation.

Methods: Patients who were referred for bone mineral density (BMD) esti-
mation in a scanner in the North West of England between June 2004 
and October 2015 were included in the analysis. Patients with only 
smoking as a FRAX™ risk factor were then analysed. All patients have 
their other risk factors for fracture and demographics recorded at time of 
scan. All patients with other FRAX™ indications for scanning were 
excluded including Rheumatoid Arthritis, Excess Alcohol, Steroids, family 
history of fracture and Secondary Osteoporosis. Patients in the smoking 
group were divided into those that had experienced a fracture and those 
that had not before comparing with Chi-squared test for categorical varia-
tbles and T-test for continuous variables. Univariate and multivariate logis-
tic models were then fitted to examine predictors of fracture in this group.

Results: 35,759 patients were referred for scanning during the period. 
4096 (11.45%) were referred with smoking as their only indication for 
scanning. Mean age at scan was 64.43 (SD 12.38) and 3244 (79%) of 
the report were females. 1663 (40.6%) had a fracture. Fractures were 
more prevalent in males with 383 (44.9%) compared to 1280 (39.46%) 
in females (p<0.05).

Univariate predictors shown in the Table 1 below.
In the multivariate model, the only variables associated with increased fracture risk was increasing age at scan decreased BMD total left and increased percentage body fat. All other factors did not significantly increase fracture risk in this cohort.

Conclusion: Our study suggests that many risk factors are associated with fragility fractures in those with smoking as their only risk factor; the best predictor was age at scan, BMD and gender. The percentage body fat association with increased fracture risk is quite surprising and would need further study. Percentage body fat is not currently included in the FRAX™ tool.


FRD0483 INTEREST OF A SYSTEMATIC SCREENING OF OSTEOPOROSIS IN HEART TRANSPLANT PATIENTS

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Background: Osteoporosis is common among patients with end-stage heart disease. A rapid decrease of bone mineral density (BMD) is usually observed after heart transplantation. Bone loss is probably linked to gluconocorticoids and calcineurin inhibitors use and vitamin D deficiency. The prevalence of osteoporosis seems to be favored by a low BMI, which is common during CD in relation to the associated malabsorption. Thus, screening for osteoporosis should be advocated early in the course of CD.

Objectives: The aim of this study was to evaluate the interest of a systemic screening of osteoporosis in heart transplant patients.

Methods: We performed a prospective monocentric study including patients, who had heart transplantation in our hospital, from December 2016 to January 2019. The following parameters were systematically assessed: history of cardiac disease, immunosuppressive therapies, glucocorticoids, previous history of low trauma fracture, known risk factors of osteoporosis, treatment received for bone disease management (calcium, vitamin D and bisphosphonates). Blood tests with creatinine clearance, calcium and vitamin D levels, were assessed. Bone densitometry and spine radiographs (to search asymptomatic vertebral fractures) were assessed in all patients. Osteoporosis was defined respectively for patients ≥50 years and <50 years as a T-score ≤−2.5 SD and Z-score ≤−2 SD either at lumbar spine (L2-L4), femoral neck or hip.

Results: A total of 42 patients were included (76.7% male), mean age was 58.1±10.6 years, mean duration after transplantation was 2.6±3.1 years. Past or active smoking statuses were observed in 26 patients (mean 23.9 pack-years). Calcium, vitamin D and bisphosphonates were administered in 13 (30.9%), 10 (23.8%) and one patients, respectively. All patients received prednisone (mean dose: 10.75±4.9 mg per day). Mean lumbar spine BMD was 1.03±0.25 g/cm2 and left femoral neck BMD 0.85±0.15 g/cm2. Osteoporosis was observed in 18 (45%) patients. Only one hip fracture was known before heart transplantation. Incidental low trauma fractures after transplantation were diagnosed in 14 patients (33.3%). 11 patients with vertebral fractures (mean 2 vertebral fractures per patient) including 4 patients with asymptomatic vertebral fractures. Others low trauma fractures were hip fracture, proximal humerus and fibula for one patient each. Mean duration between transplantation and the first low trauma fracture was 7.5±3.7 months. Low level of calcemia was found in 20 patients (47.6%) and low level of vitamin D (≤30ng/ml) in 32 patients (76.2%) associated with secondary hyperparathyroidism in 21 patients (51.2%), mean creatinine clearance was 51.7±19.9 ml/min. After evaluation, specific treatment of osteoporosis was started for 33 patients (78.6%): zoledronic acid (n=20), denosumab (n=8), alendronate (n=4) and teriparatide (n=1).

Conclusion: Systematic screening of osteoporosis seems to be useful in heart transplant patients. Osteoporosis was observed in half of these patients with a high frequency of low trauma fracture after heart transplantation, particularly in the first year.

Disclosure of Interests: None declared


FRD0485 RESULTS OF BONE MINERAL DENSITY DURING CELIAC DISEASE: ABOUT 83 CASES

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Farhat Hached Hospital, Rheumatology, Sousse, Tunisia

Background: The prevalence of osteopenia during celiac disease (CD) can range from 38% to 72%. In fact, it is a pathology that causes bone loss and is associated with a higher fracture risk compared to the general population.

Objectives: The aim of this work is to determine the frequency and factors associated with the decline in bone mineral density in adult subjects with CD.

Methods: This is a retrospective study, over a period of 4 years (from January 2016 to December 2019) and including patients followed up for MC who had a measurement of bone mineral density (BMD) by DXA. Clinical, anthropometric and densitometric data (BMD at the femoral and vertebral site) were recorded.

The WHO criteria for the definition of osteoporosis and osteopenia have been used.

Results: 83 patients were collected among them 12 were men (sex ratio = 0.16). The average age was 38.2 years old. The average body mass index (BMI) was 21.64 kg/m² [13.05-31.9 kg/m²]. Undernutrition (BMI <19 kg/m²) was found in 21 cases. It was associated with hyperthyroidism in 5 cases, autoimmune hepatitis in 1 case and primary amenorrhoea in 2 cases. 2 patients had a history of fragility fracture, and 5 patients had a history of fragility fracture in a first-degree relative.

Osteodensitometry showed low bone mass in 36 cases: osteoporosis in 23 patients (27.7%) and osteopenia in 13 cases. Osteoporosis was found in 21 patients: 1 man and 20 women. Mean femoral BMD was 0.887 g/cm³ and vertebral BMD was 0.999 g/cm³. The mean T-score at the femoral site and the vertebral site were -1.28 SD and -1.26 SD, respectively. No correlation was found between age and BMD and bone status. Comparing patients with a BMI <19 kg/m² to those with a BMI ≥ 19 kg/m², BMD at the vertebral site was significantly lower in malnourished subjects (p = 0.01), a significant correlation was found between BMI and vertebral BMD (p=0.000).

Conclusion: The decline in BMD was observed in third of our patients. It seems to be favored by a low BMI, which is common during CD in relation to the associated malabsorption. Thus, screening for osteoporosis should be advocated early in the course of CD.

Disclosure of Interests: None declared

including the TUG test. TUG performance was considered low if it took, 15 seconds or longer. A vertebral fracture assessment (VFA) image was obtained which was subsequently scored for the presence of significant vertebral deformities. VF grade 1 were excluded.

Results: Eighty-four patients were included. The mean age of our patients was 62.29±8.27 years with an average body mass index (BMI) of 31.45±6.21 kg/m² [18.18-44.38]. According to the WHO classification 42 patients (50%) had osteoporosis. Among 84 women, 47 had a low TUG performance, subjects with low TUG performance had an older age (57.94 vs 65.71 years) (p<0.001), and had a significantly lower BMD at femoral neck (0.825 g/cm² vs 0.752 g/cm²) (p<0.001). There was no significant difference between the two groups regarding duration of meno-

Discussion of Interests: None declared


FR0486

NO IMPACT OF ANTI-RANK LIGAND AND PTH ANALOGUES ON CARDIOVASCULAR RISK IN IDIOPATHIC AND POSTMENOPAUSAL OSTEOPOROSIS: A SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS

Laurence Ferreger, Yannick Degboe, Michel Laroche, Arnaud Constantin, Adeline Ruysse-Witrand, Hospital Center University Toulouse – Cassealard

Background: Emerging evidence suggests a possible association between osteoporosis and cardiovascular disease.¹,² The mutual effects of drugs used in these two diseases are now a point of interest. Two meta-analy-

Methods: A systematic literature review was conducted in December 2017 in the PubMed, Embase, Cochrane databases, and updated on PubMed in December 2018, by selecting trials including a treatment (anti-

References:

REFERENCES:


Disclosure of Interests: None declared


FR0487

UTILITY OF TRABECULAR BONE SCORE(TBS) FOR FRACTURE RISK ASSESSMENT IN GLUCOCORTICOID-INDUCED OSTEOPOROSIS

Helena Florez¹, José Hernández-Rodríguez², África Mux¹, Josep Lluis Carrasco³, Sergio Prieto-González⁴, Silvia Ruiz-Gaspá³, María C. Cid⁴, Ana Monegua⁵, Núria Guasch-Taberner⁶, Pilar Perti⁴. Hospital Clinic, University of Barcelona, Metabolic Bone Diseases Unit. Department of Rheumatology, Barcelona, Spain; ²Hospital Clinic, University of Barcelona, Institut d’Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Vasculitis Research Unit, Department of Autoimmune Diseases, Barcelona, Spain; ³Hospital Clinic, University of Barcelona, Department of Nuclear Medicine, Barcelona, Spain; ⁴Hospital Clinic, University of Barcelona, Biostatistics, Department of Basic Clinical Practice, Barcelona, Spain

Background: Glucocorticoid-induced osteoporosis (GIOP) is the one of the most common forms of secondary osteoporosis (OP). Fractures in GIOP frequently occur with higher than expected bone mineral density (BMD) values. The Trabecular Bone Score (TBS) is a gray-level textural index derived from DXA images that provides information about bone microarchi-

Methods: 127 patients on chronic GC treatment (≥ 5mg/day) were included (mean age 62±18 years, 63% women) in this cross-sectional study. The medical history and anthropometric data were collected, as well as measurements of bone metabolism parameters, bone densitometry (DXA) at lumbar spine and femur (considering OP when T-score ≤-2.5), TBS (considering degraded microarchitecture [DMA] with values <1.230) and dorsolumbar X-ray to assess vertebral fractures (VF), BMD and TBS

Disclosure of Interests: None declared


FR0486

NO IMPACT OF ANTI-RANK LIGAND AND PTH ANALOGUES ON CARDIOVASCULAR RISK IN IDIOPATHIC AND POSTMENOPAUSAL OSTEOPOROSIS: A SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS

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Disclosure of Interests: None declared


FR0487

UTILITY OF TRABECULAR BONE SCORE(TBS) FOR FRACTURE RISK ASSESSMENT IN GLUCOCORTICOID-INDUCED OSTEOPOROSIS

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Methods: 127 patients on chronic GC treatment (≥ 5mg/day) were included (mean age 62±18 years, 63% women) in this cross-sectional study. The medical history and anthropometric data were collected, as well as measurements of bone metabolism parameters, bone densitometry (DXA) at lumbar spine and femur (considering OP when T-score ≤-2.5), TBS (considering degraded microarchitecture [DMA] with values <1.230) and dorsolumbar X-ray to assess vertebral fractures (VF), BMD and TBS

Disclosure of Interests: None declared

sensitivity, specificity and positive and negative predictive values (PPV, NPV) were evaluated to determine the diagnostic accuracy of the two methods.

Results: Most of the patients were receiving GC treatment for vasculitis or polyarthritis rheumatica over a mean period of 47.7±69 months at a mean daily dose of 14.5mg. 17% had VF, 28% any type of fragile fracture (VF + no-VF), 29% OP and 71% DMA. In patients with VF, low TBS (DMA) was more common than densitometric OP (76%, p<0.03 vs. 36%, p<0.05). Similar results were observed when analysing patients with any fragile fracture (69%, p=0.02 vs. 36%, p<0.05). The diagnostic accuracy of TBS was greater than BMD on evaluating VF, with a sensitivity, specificity, PPV and NPV of 0.76, 0.53, 0.25 and 0.92 for TBS and 0.38, 0.72, 0.22, and 0.85 for BMD, respectively. Specificity increased to 0.89 for VF and 0.99 for any fragile fracture on combining both assessments (OP+DMA).

Conclusion: TBS has greater discriminative power than BMD measurement and could be useful as a complementary tool for fracture risk assessment in OIFP.

Disclosure of Interests: Helena Florez: None declared, José Hernández-Rodríguez : None declared, Africa Muxí: None declared, Josep Lluís Carrasco: None declared, Sergio Prieto-González: None declared, Silvia Ruiz-García: Consultant for: Novartis. Mónica C. Carnicer: Consultant for: Kiniksa Pharmaceuticals, Consultant for: Roche, GSK, Janssen, Abbvie, Speakers bureau: Boehringer-Ingelheim, Vifor, Ana Monegal Speakers bureau: Eli Lilly, Amgen, Núria Guardafins Consultant for: Advisory Boards from: Amgen, Alexion and UCB, Speakers bureau: Fees and lectures from Eli Lilly, Pilar Peris Speakers bureau: Personal Fees and Non-financial support (attendance to congresses) from Amgen and Eli Lilly

FRIO488 ROLE OF DUAL-PHOTON X-RAY ABSORPTIOMETRY (DXA) IN PREDICTION OF FRACATURE AND MORTALITY

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Background: The presence of a fragile fracture leads to a high risk for a subsequent fracture and mortality. Although bone mineral density (BMD) does not reflect the real fracture risk in many conditions, it is a well-established predictor of fracture risk and for many years, dual-photon X-ray absorptiometry (DXA) has been the reference standard for measuring BMD.

Objectives: To evaluate the predictive significance of femur BMD and T-score obtained by DXA in the outcomes fracture and mortality of elderly patients with a previous fragility hip fracture.

Methods: Longitudinal retrospective study of patients referred to the Rheumatology department’s Fracture Liaison Service (FLS) from March 2015 until March 2017 aged ≥65 years old. Demographic and clinical data were collected including DXA results. Statistical analysis was performed with STATA. Hazard ratios (HR) were calculated through cox regression, adjusted to age and degree of dependence.

Results: From a total of 522 patients, 214 performed DXA (77.6% with STATA. Hazard ratios (HR) were calculated through cox regression, were collected including DXA results. Statistical analysis was performed with STATA. Hazard ratios (HR) were calculated through cox regression, adjusted to age and degree of dependence.

Results: From a total of 522 patients, 214 performed DXA (77.6% with STATA. Hazard ratios (HR) were calculated through cox regression, adjusted to age and degree of dependence.

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RESULTS:


FRIO489 THE ASSOCIATION BETWEEN CT-MEASURED BONE ATTENUATION AND PREVALENT VERTEBRAL FRACTURES IN THE THORACIC SPINE DIFFERS ACCORDING TO VERTEBRAL FRACTURE LOCATIONS

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Background: Subjects with prevalent vertebral fractures (VF) have lower bone mineral density (BMD) in the lumbar spine and hip than subjects without prevalent VF. However, VFs are not equally distributed across the thoracic spine. They occur preferentially at T7-T8 and T11-T12, which are the highest loaded vertebral regions during daily activities. (1).

Objectives: We evaluated the association of BMD with prevalent VFs at non-preferential locations (nprVFs: T4-T6 and T9-T10) and at preferential locations (pVFs: T7-T8 and T11-T12).

METHODS: Baseline CT images of T4-T12 in smokers with and without COPD were analysed for the presence of VFs according to Genant. Bone attenuation (BA), expressed in Hounsfield units (HU), was measured in all non-fractured vertebrae. Linear regression was used to compare mean BA and logistic regression was used to estimate the association between BA and prevalent VFs. All analyses were adjusted for age and sex.

Results: Prevalent VFs were most frequently located at T7-T8 (in >6% of vertebrae) and T11-T12 (in >4% of vertebrae).

At subject level and compared to subjects without prevalent VFs, mean BA of all non-fractured vertebrae was significantly lower in subjects with any prevalent VFs (-21%, p<0.0001). There was a significant progressive trend (p<0.0001) in decrease in mean BA of all non-fractured vertebrae between subjects with only prVFs (-15%), with only nprVFs (-25%, p<0.05 vs prVFs) and with both nprVFs and prVFs combined (-32%, p<0.0001 vs prVFs) (all p<0.0001 compared to subjects without VF). At each individual non-fractured vertebral level, each BA decrease of 5% was associated with a 2.0-2.5 increased odds of any prevalent VF, a 1.5-1.9 increased odds of only prVF, a 2.2-3.4 increased odds of only nprVF and a 3.8-4.6 increased odds of prVF and prVFs combined.

Conclusion: In addition to BA, other factors such as vertebral load during daily activities may determine the location of a VF. The location of a VF may be a potential in vivo marker of the load/strength ratio of bone.

REFERENCES:

GOAL-DIRECTED TREATMENT OF OSTEOPOROSIS IN PATIENTS WITH RHEUMATOID ARTHRITIS USING DENOSUMAB FOR THREE YEARS

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Background: Osteoporosis (OP) is frequently concomitant with rheumatoid arthritis (RA). Effective treatment has to be performed in OP in RA (RAOP). Denosumab (DMB) is one of the promising drugs for the treatment of RAOP. We reported results of 12-month DMB treatment for RAOP. Denosumab (DMB) is one of the promising drugs for the treatment of RAOP. Longer duration or earlier initiation of DMB treatment for RAOP is not possible in LS-BMD and in TH-BMD when 3-year DMB treatment was used as treatment for RAOP. This study suggested that achievement of treatment goal within 3 to 5 years of starting therapy was achieved treatment goal in 19.2% at 1 year, 28.8% at 2 years and 44.4% at 3 years (Fig1A). The achiever had significant lower baseline T-score of TH-BMD (-2.6 vs. -3.3: p<0.01) than the non-achiever did. The achiever had significant lower baseline T-score of TH-BMD (-2.6 vs. -3.3: p<0.01) than the non-achiever did. The aim of this retrospective study is to evaluate whether 3-year DMB treatment can achieve treatment goal of OP reported recently from TBCR-BONE.

Methods: This study used 78 female RAOP patients who completed 3-year DMB treatment for RAOP. 36 patients in whom baseline T-score of LS-BMD were -2.5 or less were included in LS-BMD analysis. 52 patients in whom baseline T-score of TH-BMD were -2.5 or less were included in TH-BMD analysis in the same way. As was in clinical setting in Japan, 60mg DMB was administered every 6 months with vitamin D3 agent. Patients’ characteristics, time course of T-score and baseline characteristics related to achievement of treatment goal (T-score>2.5) were investigated.

Results: Baseline characteristics of 78 patients: Mean age was 71 years. RA duration was 17 years. Prednisolone user was 32%, LS-BMD analysis (n=35) T-score was significantly increased (-3.5 at baseline, -3.0 at 1 year, -2.9 at 2 years, -2.6 at 3 years). The rates of patients who achieved treatment goal were 30.6% at 1 year, 38.9% at 2 years and 44.4% at 3 years (Fig1A). The achiever had significant lower baseline fracture risk by FRAX (20.1% vs. 33.9%; p=0.013), significant lower baseline mHAQ (0.45 vs. 1.05; p=0.03) and significant lower baseline T-score of LS-BMD (3.0 vs. -3.9; p=0.01) than the non-achiever did. TH-BMD analysis (n=52) T-score was significantly increased (3.2 at baseline, -3.0 at 1 year, -2.9 at 2 years, -2.9 at 3 years). The rates of patients who achieved treatment goal were 19.2% at 1 year, 28.8% at 2 years and 25.0% at 3 years (Fig1B). The achiever had significant lower baseline bone turnover marker (PINP and TRACP-5b) and significant lower baseline T-score of TH-BMD (-2.6 vs. -3.3; p<0.01) than the non-achiever did. Cut-off values at baseline for achievement of treatment goal calculated using receiver operating characteristic analysis was -3.4 in LS-BMD and -2.7 in THBMD.

Conclusion: This study suggested that achievement of treatment goal in RAOP is possible in LS-BMD and in TH-BMD when 3-year DMB treatment was used as treatment for RAOP. Longer duration or earlier initiation of DMB treatment is necessary to achieve the goal. Although response in LS-BMD was related to fracture risk and physical function, response in TH-BMD was related to bone turnover. We will report 5-year results in the future.

REFERENCES:

Disclosure of Interests: Yuji Hirano: None declared, Yasuhide Kanayama: None declared, KyoSuKe Hattori: None declared, Daisuke Kihira: None declared, Naoki Ishiguro Grant/research support from: AbbVie, Asahi Kasei, Astellas, Chugai, Daiichi-Sankyo, Eisai, Kaken, Mitsubishi Tanabe, Otsuka, Pfizer, Takeda, and Zimmer Biomet. Consultant for: Ono, Speakers bureau: Astellas, Bristol-Myers Squibb, Daiichi-Sankyo, Eli Lilly, Pfizer, and Taisho Toyama, Toshihisa Kojima research support from: Chugai Pharmaceutical (Investigator Initiated Study), Novartis, Nippon Kayaku, Eli Lilly, Eisai, Speakers bureau: Chugai Pharmaceutical, Takeda Pharmaceutical, Pfizer, Eli Lilly Japan, Bristol Myers Squibb, Ono Pharmaceutical, Daiichi Sankyo, Astellas, UCB, Janssen Pharmaceutical, Tanabe Mitsubishi.

MANAGEMENT OF SECONDARY OSTEOPOROSIS FRACTURES IN FRACTURE LIAISON SERVICE OF REIMS HOSPITAL IN FRANCE: STUDY AT 25 MONTHS OF FOLLOW-UP

HITTINGER Ambre1, Jean-Hugues Salmon2, Jean Paul Eschard2, Isabelle Charlal-Lambrecht1, 1Reims University Hospital, Rheumatology, Reims, France; 2Reims University Hospital, Rheumatology, Reims, France

Background: Osteoporosis is a major public health issue, progressing with the aging of the population and responsible for nearly 400,000 fractures/year in France. Fracture Liaison Services (FLS) are systems of detection and secondary prevention of osteoporotic fractures. These systems are recognized as effective by international scientific societies.

Objectives: The aim of this study was to evaluate the efficiency of Reims Hospital FLS protocol after 25 months of implementation.

Methods: We performed an ambispective monocentric observational study at the Reims Hospital between April 2016 and May 2018. We included patients over 50 years who were hospitalized in the orthopedic department for osteoporotic fractures. These patients were evaluated clinically, biologically and radiographically during a one-day hospitalization in the rheumatology unit. Therapeutic compliance and fracture recurrence were assessed in consultation at 3-month and 1-year telephone interviews.

Results: Sixty-four/242 patients (26.4%) identified in orthopedic service were included. The average age was 72 years old with a sex ratio of 1:1.0. The most common fracture was the proximal end of the femur for 25 patients (35%). Fifty-five patients (85.9%) had an indication for osteoporosis treatment, the most prescribed was zoledronic acid for 45 patients (81.9%). Twenty-four/55 patients (43.6%) started their treatment and 22/24 (91.7%) were still treated at one year. One patient (1.63%) died within the follow-up period. Twelve/55 patients (21.8%) presented a new fall and 7/55 patients (12.7%) experienced a new fracture.

Comparative analysis of observant versus non-observant population groups at 1 year showed that non-observant patients had significantly more recurrent falls (93.54% versus 68.18%, p = 0.024) and received treatment of zoledronic acid (93.56% versus 63.64%, p = 0.010).

Further analysis showed that our low rate of initiation treatment was due to difficulties in implementing bisphosphonates, mainly because of the dental care needed. However, we observed a high rate of treatment adhesion at 1 year, once the treatment is started. During this study, we identified 2 areas of improvement: therapeutic education to improve patient adherence and fall risk factors to decrease recurrent fall rate.

Conclusion: There is a real benefit to the establishment of this FLS with a high rate of therapeutic compliance at 1 year follow-up. However there are opportunities for improvements in treatment initiation through patient therapeutic education.

REFERENCES:
CALCULATING FRAX SCORE IN CLINICAL PRACTICE: PITFALLS AND PROBLEMS

Navneet Kaur1, Barbara Mendez2, Avneet Vig3, Beverly Johnson1, Tony Francis4, 1Albert Einstein College of Medicine/Jacobi Medical Center, Rheumatology, Bronx, United States of America; 2Cleveland Clinic Martin Health, Rheumatology, Port St. Lucie, United States of America; 3Christiana Hospital, Nuclear Medicine, Newark, United States of America

Background: Osteoporosis related fractures cause significant morbidity and mortality. FRAX score uses clinical risk factors and country-specific data in addition to Bone Mineral Density (BMD) to assess patients with high 10-year risk of hip (>3%) or major osteoporotic (>20%) fracture. We noticed discrepancies between radiologist reported and physician calculated FRAX scores at our hospital. We hypothesized that providers are calculating FRAX score differently as BMD in the FRAX calculator is an optional input variable.

Objectives: This study was initiated to see the differences in results when FRAX score is calculated using T-score, BMD and no BMD and how this difference can influence treatment.

Methods: Retrospective chart review of 1200 DEXA reports from 2013 to 2015 was done. Patients between ages of 40-90 years with T-score ranging from ≤ -1 to >2.5 at femoral neck were included in the study. Patients already on osteoporosis therapy and/or with T-score when FRAX score is calculated using T-score, BMD and no BMD value and radiology reported scores by radiologist in the chart was also reviewed. Subsequently, FRAX scores obtained using T-score, no BMD value and radiology reported scores were compared against FRAX score calculated using femoral neck BMD (gold standard)

Results:

Table 1. shows demographic information for 237 patients who met inclusion criteria.

Demographics

<table>
<thead>
<tr>
<th>Race</th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Hispanic</td>
<td>131</td>
<td>(54.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>71</td>
<td>(29.9%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caucasian</td>
<td>15</td>
<td>(6.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asian</td>
<td>20</td>
<td>(8.5%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average Age</td>
<td>67±10.5 years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>226</td>
<td>(95.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>11</td>
<td>(4.7%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average Height</td>
<td>159.3 ± 7.6 cm</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average Weight</td>
<td>71 ± 13 kg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>27.9 ± 4.9</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous fracture</td>
<td>13</td>
<td>(5.4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current smoking</td>
<td>14</td>
<td>(5.9%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steroid use</td>
<td>48</td>
<td>(20.3%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>RA</td>
<td>26</td>
<td>(11%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Secondary osteoporosis</td>
<td>8</td>
<td>(3.4%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alcohol use</td>
<td>3.1%</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

When FRAX score calculated using BMD was compared with FRAX score calculated without BMD, number of patients with high 10-year fracture probability decreased from 49 to 11 patients, which was a statistically significant decrease of 77.6% (p<0.001). When data was stratified according to age, there was significant overestimation of risk in patients >65 years (p<0.0001) when FRAX was calculated without BMD.

Conclusion: FRAX score calculation without BMD leads to both statistically and clinically significant overdiagnosis especially in elderly.

Interchanging T score and BMD to calculate FRAX score leads to same treatment decision.

Further education of providers regarding FRAX score is needed.

Disclosure of Interests: Navneet Kaur: None declared, Barbara Mendez: None declared, Avneet Vig: None declared, Beverly Johnson: Employee for: I am a consultant for the rheumatology education group, Employee of: I have been paid indirectly by pharma as a consultant for the rheumatology education group, Tony Francis: None declared


REFERENCES:
[1] https://www.sheffield.ac.uk/FRAX/tool.jsp

FRIO493 CLINICAL EFFICACY OF DENOSUMAB IN PATIENTS WITH OSTEOPOROSIS BETWEEN RHEUMATOID ARTHRITIS AND PRIMARY OSTEOPOROSIS; 24 MONTHS OF FOLLOW-UP

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Background: Denosumab (DMB) is a fully human monoclonal antibody to the receptor activator of nuclear factor-kappaB ligand (RANKL) that blocks its binding RANK, inhibiting the development and activity of osteoclasts, decreasing bone resorption, increasing bone density and reducing fracture risk. Also DMB is a useful therapeutic agent for both rheumatoid arthritis (RA-OP) and primary osteoporosis (P-OP). However there is still few comparative study of clinical efficacy of DMB between RA-OP and P-OP.

Objectives: To compare the clinical efficacy of DMB in patients with osteoporosis between rheumatoid arthritis and primary osteoporosis for 24 months.

Methods: RA patients diagnosed according to the 2010 ACR/EULAR criteria, RA-OP and P-OP patients met at least one of the following criteria were eligible: a bone mineral density T score of -2.5 or less at the lumbar spine or total hip and either one or more moderate or severe vertebral fractures or two or more mild vertebral fractures. All patients were initiated DMB from between October, 2013 and August, 2016. The final study cohort of 61 RA-OP and 50 P-OP patients received continuous DMB therapy more than 24 months. The DMB dose was 60mg at once every 6 months. In all cases native or activated vitamin D has been used. We reviewed the results for 24 months about the increase and decrease of bone mineral density(BMD) of lumbar spine(LS) and total hip (TH) by DEXA and bone turnover markers, intact n-terminal propeptide type I procollagen(PINP) and tartrate-resistant acid phosphatase form 5b (TRACP-5b).

Results: In the patients of RA-OP (n=61) and P-OP (n=50), the number of female was each 56(92%) and 45(90%) cases (p=0.741). The mean age was 72.7 ± 7.5 and 76.8 ± 7.8 years old (p=0.006); disease duration of RA-OP patients was 12.6 ± 12.9 years; the body mass index was 20.4 ± 2.7 and 20.3 ± 3.0 (p=0.687) and the FRAX was 27.2 ± 15.7 and 24.6 ± 11.1 (p=0.745). Clinical findings related to RA-OP at baseline were as follows; CRP 0.8 ± 1.1; DAS-CRP 3.28 ± 1.36; HAQ 1.16 ± 1.04 in RA-OP patients and in the patients of RA-OP and P-OP, bone turnover markers and bone mineral density at baseline were as follows; PINP 57.7 ± 32.2 and 64.0 ± 32.7 μg/l (p=0.151); TRACP-5b 563

Disclosure of Interests: Navneet Kaur: None declared, Barbara Mendez: None declared, Avneet Vig: None declared, Beverly Johnson: Employee of ownership of Johnson and Johnson stock over 10,000 USD, Consultant for: I am a consultant for the rheumatology education group, Employee of: I have been paid indirectly by pharma as a consultant for the rheumatology education group, Tony Francis: None declared

CORRELATION OF METACARPAL BONE MASS MEASURED EITHER BY DUAL X-RAY DENSITOMETRY OR DIGITAL X-RAY RADIOGRAMMETRY WITH SEVERITY OUTCOMES IN PATIENTS WITH EARLY ARTHRITIS

Irene Llorente, Saturnino González, Eugenio Escolano, Ana María Ortiz, Alberto García-Vadillo, Isidoro González-Álvaro, Santos Castañeda. University Hospital La Princesa, Rheumatology Department, Madrid, Spain; University Hospital La Princesa, Radiology department, Madrid, Spain

Background: Rheumatoid arthritis (RA) is a systemic autoimmune disorder that predominantly affects small joints of the hands and feet. X-ray digital radiogrammetry (DXR) is a validated technique for the evaluation of bone mineral density (BMD) in the diaphysis of metacarpals (MC) that has demonstrated that low bone mass at this location correlates with worse radiographic progression (1). However, this technique is not available in our environment. Dual X-ray densitometry (DXA) is a simple, accessible, and widely validated technique for the study of osteoporosis. Our group has previously validated the reproducibility of MCP measurements by DXA (2).

Objectives: To study the relationship between baseline MC BMD measured by DXA or DXR and disease severity in patients with early arthritis at 2 years follow-up.

Methods: 202 patients belonging to PEARL (Princess Early Arthritis registral longitudinal) study were included. Demographic, laboratory, radiographic and therapeutic data were recorded by protocol. Most patients (87%) were women, 59% fulfilled 2010 ACR criteria and 41% were classified as undifferentiated arthritis. More than 60% were seropositive (60% RF; 58% anti-CCP). Median disease duration at first visit was 4.6 months, median DAS28 4.2 and HAQ 0.875. The BMD of 2nd to 4th MC was measured by DXR at the standardized software by Sectra (Linköping, Sweden) applied on graphs of hands submitted in digital format (GE® DX Definium 8000). Baseline non-dominant hand DXA was performed using a densitometer Hologic® QDR4500. To arrive to 4th MC BMD, we created 3 regions of interest (ROI) similar to that generated in the DXR measurements; briefly, the ROIs cover the mid-third of each MC diaphysis, avoiding overlapping of ROIs. The statistical study was performed with Stata 12 for Windows, including linear correlation between MC-BMD and various variables of disease severity such as disease activity (DAS28), disability (HAQ) or cumulative DMARD treatment after 2 years of follow-up were included in order to determine whether there was an association with MC-BMD.

Results: The MCP-BMD measured by DXA and DXR at baseline showed a good correlation (r = 0.87, p < 0.001). As expected, being female (β coefficient -0.0381, p = 0.0001) and age > 65 years (β coefficient -0.076, p = 0.0001) were associated with lower BMD, whereas high body mass index (β coefficient 0.002 x kg/m², p = 0.004) was associated with higher BMD.

Conclusion: Despite of the good correlation between DXR and DXA, our data obtained either with DXA or DXR do not confirm the association of low MC-BMD measured with DXR and more aggressive disease in patients with early arthritis.

REFERENCES:

A. Lorenzo: None declared, Nieves Martin: None declared, Carlos Rodriguez-Lozano: None declared


Table

<table>
<thead>
<tr>
<th>Age, mean (SD)</th>
<th>73.4 (10)</th>
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<tr>
<td>BMI, mean</td>
<td>27.4</td>
</tr>
<tr>
<td>Fracture type, N (%)</td>
<td></td>
</tr>
<tr>
<td>Forearm</td>
<td>71 (18)</td>
</tr>
<tr>
<td>Hip</td>
<td>130 (44)</td>
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<tr>
<td>Humerus</td>
<td>77 (20)</td>
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<tr>
<td>Vertebral</td>
<td>52 (13)</td>
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<td>Others</td>
<td>49 (13)</td>
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<tr>
<td>Previous fracture</td>
<td>51 (13)</td>
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<tr>
<td>Hip fracture of parents</td>
<td>36 (9)</td>
</tr>
<tr>
<td>Smoking</td>
<td>81 (21)</td>
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<td>Corticoids</td>
<td>24 (6)</td>
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<tr>
<td>Rheumatoid arthritis</td>
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<td>Secondary osteoporosis</td>
<td>17 (4)</td>
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<tr>
<td>Alcohol</td>
<td>68 (18)</td>
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<tr>
<td>Density (%)</td>
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<td>Normal</td>
<td>30</td>
</tr>
<tr>
<td>Osteopenia</td>
<td>43</td>
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<tr>
<td>Osteoporosis</td>
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<tr>
<td>FRAX, mean (SD)</td>
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</tr>
<tr>
<td>Major fracture</td>
<td>8.4 (5)</td>
</tr>
<tr>
<td>Hip fracture</td>
<td>4.3 (4)</td>
</tr>
<tr>
<td>Treatment prescribed, (%)</td>
<td></td>
</tr>
<tr>
<td>Bishothonate or equivalent</td>
<td>58</td>
</tr>
<tr>
<td>Referral to primary care</td>
<td>64</td>
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<tr>
<td>Persistence at 12 months</td>
<td>53</td>
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</table>

FRIO497 OSTEOPOROSIS IN PRIMARY CARE – ARE WE MISSING A TRICK?
Sultana Parvin1, Mannaj Barhey2, Talib Abubacker3, Muhammad Khurram Nisar4
1Luton and Dunstable University Hospital, Rheumatology, Luton, United Kingdom; 2Woodland Avenue Practice, Primary care, Luton, United Kingdom; 3Bed House Medical Centre, Primary care, Luton, United Kingdom

Background: Globally various incentive schemes have been employed in primary care to improve early diagnosis and management of several rheumatic conditions. In the UK, the Primary Care Quality and Outcomes Framework (QOF) rewards general practices for the provision of ‘quality care’ and helps to fund further improvements in the delivery of clinical care. Currently, there is one quality indicator in place for secondary prevention of osteoporosis. In order to help establish an integrated care pathway encompassing the whole patient journey between primary and secondary care, we undertook a detailed survey of two GP practices.

Objectives: The aims of the exercise were to identify the utility of quality indicator and any gaps in the model of care for the high-risk osteoporosis patients.

Methods: An independent service evaluation tool was employed to interrogate the IT system used in the GP surgeries. All patients over the age of 65 were extracted from the database and FRAX analysis was undertaken. Those with medium to high FRAX score (i.e. ten-year risk of >20% for major osteoporotic fracture and/or >5% for hip fracture) were captured to explore whether they were offered further evaluation and bone-sparing therapy as necessary.

Results: Of 18,248 patients registered in the multi-cultural urban practices, 6796 were >65 years old. 793 had pre-defined moderate-high FRAX score. 300 (37%) had a confirmed diagnosis of osteoporosis. Median age was 78 (range 65-103 years). 249 (83%) were women. 88.5% were White and remaining of other ethnicities.

Conclusion: This study highlights the inadequacy of quality indicators in the overall management of osteoporosis burden in primary care. It relies heavily on active identification process for high-risk individuals and correct coding of fragility fracture. However the vast majority of patients with moderate-high risk, based on case finding strategy advised by international bodies e.g. FRAX, remain hidden. Less than 10% of patients with confirmed osteoporosis fulfil the quality outcome in this survey. The QOF hence fails to reflect the nature of disease burden in the primary care thereby risking the management strategies skewed towards too small a cohort and missing the big picture. It is clear that quality indicators for osteoporosis need to be aligned to risk stratification model. This will allow better identification of at-risk individuals and improved care pathway for patients requiring bone active therapies.

Disclosure of Interests: Sultana Parvin: None declared, Mannaj Barhey: None declared, Talib Abubacker: None declared, Muhammad Khurram Nisar Grant/research support from: Muhammad Khurram Nisar undertakes clinical trials and received support (including attendance at conferences, speaker fees and honoraria) from Roche, Chugai, MSD, Abbvie, Pfizer, BMS, Novartis, Celgene, Mallinckrodt, UCB and Lilly, Consultant for: Muhammad Khurram Nisar undertakes clinical trials and received support (including attendance at conferences, speaker fees and honoraria) from Roche, Chugai, MSD, Abbvie, Pfizer, BMS, Novartis, Celgene, Mallinckrodt, UCB and Lilly, Speakers bureau: Muhammad Khurram Nisar undertakes clinical trials and received support (including attendance at conferences, speaker fees and honoraria) from Roche, Chugai, MSD, Abbvie, Pfizer, BMS, Novartis, Celgene, Mallinckrodt, UCB and Lilly


FRIO497 TRABECULAR BONE SCORE AND MALNUTRITION IN A COHORT OF SYSTEMIC SCLEROSIS PATIENTS
Sabrina Pezzi1, Massimo Patane1, Veronica Tomatis1, Andrea Casabella1, Carmen Pizzoniti1, Carlotta Schiorene1, Luca Carmisciano1, Alessio Signori1, Maurizio Cutillo1, 1IRCCS San Martino Polyclinic Hospital, Genoa, Italy, Research Laboratory and Academic Division of Clinical Rheumatology, Department of Internal Medicine, University of Genova, genoa, italy; 2IRCCS San Martino Polyclinic Hospital, Genoa, italy, 3Biostatistics Unit, Department of Health Sciences, University of Genova, Genoa, italy, genoa, italy

Background: Systemic sclerosis (SSc) is a connective tissue disease characterized by initial microvascular damage, immune system activation and progressive fibrosis of the skin and internal organs. Gastrointestinal (GI) involvement induce malnutrition due to gastrointestinal symptoms, GI dismotility and malabsorption that are related to fibrosis of bowel wall and bacterial overgrowth(1). Therefore the disease is associated with secondary osteoporosis with a few studies evaluating the bone microarchitecture(2).

Objectives: To evaluate a relationship between malnutrition and bone microarchitecture detected by trabecular bone score (TBS) in SSc patients.

Methods: 38 patients(6 male and 32 female) fulfilling ACR 2013 criteria for SSc underwent DXA to detect quantitative lumbar spine bone mineral density and TBS. DXA also assess body composition with a software that provides the physical quantitative parameters, including free fat mass index (FFMI), that identifies the patient with malnutrition/values <15 kg/m2 in women and 17 kg/m2 in men, according to the ESPEN criteria (2). Bone mass index was calculated for all SSc patients and every patient completed a diary reporting GI symptoms possibly related to intestinal disbiosis. Fastig blood samples were obtained in order to analyse some biochemical parameters of malnutrition (total proteins(g/L), albumin(g/L), serum total cholesterol(mg/dl) and blood lymphocyte count (N/mm3). Continue variables were summarized as mean and standard deviation(SD) or median and inter quartile range (IQR), discrete variables were summarized with count and percentage. Correlation was tested with Pearson or Spearman method. T-test was used to compare TBS between dichotomic groups Uni and multivariate linear regression models were used as well the Multiple R-squared variation was applied. The multivariate linear regression was performed with a stepwise approach to select the best model using highest AIC criteria.

Results: The mean age of patients was 64±13.3 years with mean disease duration 19.2±7.6 years. 36.8% of patients was found malnourished. The univariate analysis showed that only higher age of patients correlated to lower TBS(p<0.001). The R-squared of multivariate linear regression showed that about 45% of the TBS variations(TBSv) can be explained by the variation of the following variables(age, disease duration, lymphocyte count). Age explains about 25% of the TBSv. Older patients had lower TBS, with approximately 0.05 points of TBS loss every decade(= 0.05). The presence of symptoms possibly related to intestinal disbiosis, added to the model, might explains about 12% more of TBSv. Patients with symptom related to bacterial overgrowth had lower TBS respect to patients without(0.08), regardless of other variables(p=0.002). Disease duration, added to the model, further explains about 4% more of TBSv and suggest a trend between highest disease duration (regardless of other variables) and higher TBS(p = 0.103). Lymphocyte count added to
FRIO498  

HIGH SERUM URIC ACID LEVEL IS ASSOCIATED WITH LOWER INCIDENCE OF OSTEOPOROSIS IN POSTMENOPAUSAL WOMEN: DATA FROM THE KOREAN NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY

Eun-Jung Park1, Yeoung Hee Eun2, In-Young Kim2, Hyemin Jeong3, Jiseok Kim3.
1Institute of Rheumatology, Clinical rheumatology VI, Belgrade, Serbia; 2Institute of Rheumatology, Clinical rheumatology III, Belgrade, Serbia; 3Institute of Pharmaceutical Industry Associations (EFPIA). Arch Osteoporos.

Disclosure of Interests: None declared

References:


Results:

Participants was 63.2 years and mean of SUA was 4.4 mg/dL. The effect of SUA on osteoporosis in postmenopausal women was not statistically significant according to univariable logistic regression (OR 0.977, 95% CI 0.855-1.116, p = 0.729). However, SUA was negatively associated with incidence of osteoporosis in postmenopausal women with statistical significance after adjusting for age, obesity, amount of drink, smoking, intake of calcium, rheumatoid arthritis, thyroid diseases, and loss of activity (OR 0.867, 95% CI 0.752-0.999, p = 0.048).

Conclusion: Our data demonstrated that high SUA is associated with lower incidence of osteoporosis in postmenopausal women. This result suggests a protective role of SUA in metabolic bone diseases.

References:


Disclosure of Interests: None declared
INCIDENCE OF CLINICAL FRACTURES IN ADULTS WITH KIDNEY TRANSPLANT

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Background: Chronic kidney disease is associated with an increased risk of fractures. However, the existing evidence investigating the incidence of fractures after kidney transplant is scarce.

Objectives: To evaluate the incidence of clinical fractures in patients with kidney transplant and analyze the possible factors that may influence its occurrence.

Methods: A retrospective observational study of patients who underwent kidney transplant between 2005 and 2015 in a tertiary hospital was conducted. A minimum follow-up period of 6 months after transplant was required. Sociodemographic and anthropometric data, clinical risk factors for bone fractures, drugs use (steroids, immunosuppressive drugs, vitamin D analogues, calcium and vitamin D supplements and calcimetics), as well as biochemical and densitometric data to assess bone metabolism were retrieved from medical records. The occurrence of new clinical fractures after the transplant and throughout the follow-up period was recorded. The statistical analysis included univariable analysis using chi-square and Fisher’s exact tests for the qualitative variables and T-Student and Mann-Whitney U for the quantitative variables. Subsequently, logistic regression multivariable analysis was carried out to investigate which factors were associated with fractures occurrence.

Results: A total of 163 patients were included, 63 (38%) females, with a mean age of 51 ± 14.6 years. The etiology of kidney disease was polycystic kidney disease (24.2%), glomerulonephritis (23.6%), diabetes mellitus (5.5%), vasculopathy (5.5%), connective tissue disorders (2.4%) and miscellany (38.7%). The daily average dose of steroids one year after transplant was 5.8 ± 4.4 mg. Bone densitometry was performed before transplant in 27 patients (19.6%), ten of whom (37%) presented osteopenia and 7 (26%) osteoporosis. The ten-year probability of bone fracture risk (FRAX) before transplant was 2.6 ± 2.6. Mean follow-up after transplant was 8.7 ± 3.5 years. During this period, 23 (13.9%) patients suffered a clinical fracture, with an average time of appearance after transplant of 5.5 ± 3.3 years. These were located in hip (6 - 26.1%), vertebrae (2 - 8.7%), extremities (9 - 39.1%) and hands and feet (6 - 26%). One year after transplant, 65.6% had vitamin D deficiency (<30 ng/dl serum calcium levels) and 12.2% had levels compatible with osteomalacic range (<10ng/dl).

The data of the descriptive study stratified by the fracture occurrence are shown in Table 1. Compared with the subgroup patients without (Fx -), the patients with (Fx +) post-transplant fractures showed to be more frequently female (60.9% vs 34.5%, p=0.01), older (50.1 ± 14.6 vs 56.3 ± 14.1, p=0.03), had more pre-transplant major clinical FRAX (2.4 ± 1.9 vs 4 ± 4.7, p=0.03), and higher levels of PTH (98.2 ± 75.7 vs 140.1 ± 86.9, p=0.02) and serum alkaline phosphatase [ALP] (90.2 ± 37 vs 117.6 ± 60.4, p=0.02) after one year of transplant. Also, a trend to present a higher prevalence of pre-transplant clinical fractures was observed in the second group (5.6% vs 17.4%, p=0.06). No difference in the use of immunosuppressants were detected. The multivari- able analysis showed a significant association between post-transplant fractures and female gender (OR of 3.8, p=0.01) and higher levels of ALP (OR of 1.01, p=0.03).

Conclusion: In patients with kidney transplant, an incidence of clinical fracture of 13.9% is observed after a mean follow-up of 8.7 years. The female population seems especially susceptible to present fractures. The persistence of a possible pre-transplant autonomous secondary hyperparathyroidism one year after kidney transplant seems to influence the risk of fractures.

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EVALUATION OF BONE QUALITY BY TRABECULAR BONE SCORE (TBS) IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Systemic lupus erythematosus (SLE) patients shown an increased risk of low bone mass as a result of multifactorial events: osteopenia, persistent inflammation, low vitamin D levels (photosen- sitivity) and glucocorticoid treatment. Trabecular Bone Score (TBS), is an index extracted from the dual-energy X-ray absorptiometry (DXA) that provides an indirect measurement of bone axial microarchitecture and allows to get information about bone quality in several rheumatic diseases (1-4).

Objectives: The aims of this study were to examine the prevalence and risk factors for low bone mineral density (BMD) (osteoporosis or osteopenia) in female patients affected by SLE and to compare with matched healthy subjects (CNT). Methods: 40 female patients (mean age 47±14 years) affected by SLE and 40 age- matched CNT (mean age 49±8 years) were enrolled. Bone Mineral Density (BMD, g/cm²) of the lumbar spine (L1-L4) was analyzed using a DXA scan (GE, Lunar Prodigy) Lumbar spine TBS was derived for each spine DXA examination using the TBS index (TBS Insight Medimaps).

Results: The mean BMD±SD was 0.85±0.22 g/cm² at the lumbar spine and 0.64 ± 0.32 g/cm² at the hip in SLE patients. The prevalence of osteopenia was 39.0%, and 16.4% of osteoporosis in SLE patients. Most of SLE patients (70%) presented a bone loss that was significantly lower when compared with control group (p<0.001). Likewise, lumbar spine TBS
score was found significantly lower in SLE patients compared with CNT (0.868±0.227 vs 1.482±0.113; p<0.001, respectively). An history of high-dose oral glucocorticoids (> 10 mg/day) was associated with the preservation of BMD at the lumbar spine but not in spinal trabecular bone as obtained by TBX analysis.

Conclusion: SLE is associated with significant trabecular bone loss, which could not be caused by glucocorticoid therapy. This study confirms the role of TBS as new and safe diagnostic tool for the quantification of the bone quality in chronic and systemic inflammatory rheumatic diseases, such as SLE.

REFERENCES:

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FR0502

CORRELATION OF THE DAILY DIETARY INTAKE OF CALCIUM WITH THE LEVEL OF BONE MINERAL DENSITY IN PATIENTS WITH HUMAN IMMUNODEFICIENCY VIRUS INFECTION

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Background: There are few studies in which the relationship between daily calcium intake and bone mineral density (BMD) in patients with human immunodeficiency virus (HIV) infection has been evaluated, as well as its correlation with other factors of risk for the development of fragility fractures in this population.

Objectives: To determine the correlation of daily calcium intake with the most predictive risk factors for fragility fracture in patients with HIV infection, as well as BMD values in a cohort of patients followed in a Tertiary Madrid hospital.

Methods: Cross-sectional evaluation of a prospective study carried out in a specialized unit in HIV/AIDS of a tertiary Madrid hospital. We included asymptomatic consecutive patients with HIV infection, older than 50 years, followed regularly between January 2014 and December 2016.

Results: A total of 128 patients were included (35 women, 27%), with a mean age of 57 years (range: 50-83) and body mass index of 23.8 kg/m² (range: 15.6-33.5). The mean time of HIV infection was 256 months (range: 202-306) and of antiretroviral therapy (ART) 219.7 months (range: 156-247). The average calcium intake obtained by dietary calculation (without supplementation) was 563.8 g/day (462-2772). Among the risk factors for fragility fracture (included in the FRAX): 44 (34%) reported smoking, 11 (9%) family history of fracture, 54 (42%) previous history of osteoporosis/osteopenia. Although a lower calcium intake was found in patients with vertebral fractures, this was not significant (486 (236) vs 583 (317), p = 0.09).

Conclusion: Although recent meta-analyses show that calcium intake in non-HIV population is not related to the development of fragility fractures, in our cohort (with the limitations of a cross-sectional study) a probable association of daily calcium intake with a low BMD is evidenced. These findings should be confirmed in the longitudinal analysis of the data of the cohort.

REFERENCES:

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FR0503

USING BONE MINERAL DENSITY VERSUS THE RATIO OF BODY MASS INDEX TO BONE MINERAL DENSITY TO PREDICT FRACTURE RISK IN HYPERTHYROIDISM

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Background: Euthyroidism is important in the development of a normal skeletal system, with thyroid hormones acting as important regulators of bone homeostasis in adults. Hyperthyroidism, whether current or previous, increases the risk of developing osteoporotic fractures by stimulating osteoclastic bone resorption and hence bone remodelling, which overall results in decreased bone mineral density (BMD). Generally, BMD is used as a predictor of fracture risk; however there has been recent research that suggests using the ratio of BMD to Body Mass Index (BMI) is a better marker of predicting fracture risk in obese patients than BMI alone.

Objectives: Our research set out to find whether BMI alone or the ratio of BMI to BMD is a better predictor of fracture risk in patients with current or previous hyperthyroidism.

Methods: Data were used from a cohort of patients with current or previous hyperthyroidism, referred for DXA scan to a District General Hospital between June 2004 and October 2010. The following were recorded: age, sex, whether a fracture was sustained, whether they had had steroid therapy at any point, BMI, BMD at L1-L4, BMD at femoral neck (left and right) and BMI at hip (left and right). Logistic regression models were fitted using fracture as the dependent variable. The independent variables for the first set of logistic regression models were BMI and for the second set BMI:BMD ratio at the same levels. Data were adjusted for sex and age and scan. The fit of logistic models were compared using area under the ROC curves (AUC).

Results: 720 patients were used in the study, of whom 643 (89.3%) were female. Mean age was 63.6 years (SD 11.6) with age range of 28.4 to 89.6 years. 120 (16.7%) were recorded to have had steroid therapy at any point. BMI, BMD at L1-L4, BMD at femoral neck (left and right) and BMI at hip (left and right). Logistic regression models were fitted using fracture as the dependent variable. The independent variables for the first set of logistic regression models were BMI at each level and for the second set BMI:BMD ratio at the same levels. Data were adjusted for sex and age at scan. The fit of logistic models were compared using area under the ROC curves (AUC).

Conclusion: This study identifies that the BMI:BMD ratio does not provide a better indication of fracture risk than BMI alone in our cohort of patients with current or previous hyperthyroidism. We have previously shown that the same is true for patients with rheumatoid arthritis. A limitation of this study is not stratifying by presence of other diseases or steroid use.
Further work will be done to study the role of the ratio in predicting fracture risk in patients with other conditions.

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**Carligil, synovium and bone**

**FR00504**

**TOCILIZUMAB CONTROLS BONE TURNOVER IN EARLY POLYMIALGIA RHEUMATICA**


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**Background:** Tocilizumab has been proved to be an alternative to corticosteroids in treating polymyalgia rheumatica. Considering the action on interleukin-6 on bone turnover an effect of tocilizumab is supposed. Few data are available about bone turnover in rheumatoid arthritis patients treated with tocilizumab but no data are available in polymyalgia rheumatica patients.

**Objectives:** This study explores changes in the bone homeostasis by testing the N-terminal collagen type I extension propeptide (PINP) marker for osteo-formation and the carboxy-terminal region of collagen type I (CTX-I) marker for osteo-resorption in patients taking tocilizumab for poly-myalgia rheumatica (PMR).

**Methods:** Twenty patients were included in the prospective open-label TENOR study (Clinicaltrials.gov NCT01713842) and received three monthly tocilizumab infusions, followed by corticosteroids starting at week (W)12. PINP and CTX-I were tested at inclusion (W0), after tocilizumab but before steroid initiation (W12), at the end of the protocol (W24) and were compared to healthy controls. Information regarding disease activity, inflammatory parameters and interleukin-6 levels were collected during the follow-up of the patients.

**Results:** Polymyalgia rheumatica patients were characterized by higher levels of CTX-I relative to healthy controls matched in age and sex at baseline. PINP levels increased at W12 (p=0.008, versus W0) following tocilizumab introduction and CTX-I levels decreased at W24 and after steroid initiation (p=0.001, versus W0) (figure 1). Such modifications explain the altered correlation observed between PINP and CTX-I at W0 (r=0.255 at W0 versus r=0.641 in healthy controls) and its correction after treatment (r=0.760 at W12 and r=0.767 at W24). Finally, greater changes in PINP were observed in patients whose circulating IL-6 levels decreased after tocilizumab therapy.

**Conclusion:** Control of bone turnover, in part through the inhibition of the IL-6 axis, is observed during tocilizumab and subsequent steroid treatment of polymyalgia rheumatica.

**FR00505**

**CORRELATIONS BETWEEN CARTILAGE MOLECULAR COMPOSITION DETERMINED BY RAMAN SPECTROSCOPY AND MANKIN SCORE: IMPACT OF INTER AND INTRA-VARIABILITY**

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**Background:** Osteoarthritis (OA) is an incurable disease and methods for its early diagnosis are still an unmet clinical need. Raman spectroscopy (RS) presents potential as a diagnosis technique based on the detection of peaks that can be assigned to cartilage components and molecular rearrangements during disease progression. 5Mankin score (MS) is the main validated method to evaluate severity of cartilage degradation considering structure, cell distribution, Saffrin- O staining and tidemark integrity.

**Objectives:** To evaluate the correlations between OA cartilage RS assigned peaks and MS, considering the inter- and intra-variability of different observers.

**Methods:** RS analysis (Subscore-I, structure: 0-6; -II, cellularity: 0-3; and -III, safranin-O staining: 0-4; Total Score: 0-13) of human OA cartilage explants from 22 donors (age range: 32-92), obtained from lesion (n=22) and/or adjacent tissues (n=14), was performed by 3 blinded observers (O1, 2 and 3). Moreover, one of the observers performed the scoring in triplicate, with at least one month between observations. Inter- and intra-observer variability was determined by kappa and intraclass correlation (ICC) coefficients. Raman spectra were obtained with a FT-Raman Bruker RFS100 (λ=1064nm) and main peaks assigned (6 ratios related to proteoglycans, collagen, lipid index or calcium phosphate). Spearman’s non-parametric correlation coefficient rho was used to compare MS and RS assigned peaks.

**Results:** Inte-observers variability indicated good (ICC>0.74) or moderate agreement (ICC<0.5) for all scores in lesions, whilst only a good agreement (ICC>0.70) was found for subscore-I, in adjacent tissues, and no agreement for the remaining parameters (subscores -II, -III, and total scoring). However, when performing analysis using kappa coefficients, a simultaneous agreement between the 3 observers was not observed. Intra-observer variability revealed good concordance (ICC>0.6) for all subscores and total scoring in cartilage for both sites, except for subscore -III, in adjacent tissues. In this case, ICC results were confirmed by kappa coefficients. Spearman’s correlation coefficient between cartilage main peaks assigned by RS and MS indicated significant differences between observers(Fig.1). Correlations were found for a greater number of MS subscores in O1 (6) regarding O2 (4) or O3 (3) which could be related to the observers’ experience (being O1>O2>O3). These correlations were mostly found in lesions (5, 3 and 1 for O1, 2 and 3, respectively) in comparison to adjacent tissues (2, 1 and 2 for O1, 2 and 3, respectively).

**Conclusion:** Evenhough inter-observation correlations for MS were in the moderate-good range, when analyzing kappa coefficients (categorial variables) these were not maintained. In addion, inter- and intra-observer variability results for adjacent tissues revealed possible limitations when characterizing early to mild OA. In view of MS-RS correlations, a reader dependency is underlined, indicating MS subjectivity and further limitations in the validation of RS using MS.

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**FR0506 ROLE OF MITOCHONDRIA FROM PATIENTS WITH OA IN CELLULAR SENESCENCE**

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**Background:** Chondrosenescence, chondropathy and autophagy contribute to cell death and tissue damage in OA. The mitochondria are related with these three processes implicated in the cartilage degeneration. Mitochondrial dysfunction is well documented in OA and has the capacity to promote abnormalities in chondrocyte viability contributing to cartilage degeneration. Cybrids are optimal cellular models to study the mitochondrial function, since they carry different mitochondrial variants with the same nuclear background, therefore, excluding the variations because of nuclear genome.

**Objectives:** The aim of this work is to study the role of human OA mitochondria in the cellular senescence, apoptosis and autophagy. **Methods:** Cybrids were developed using 143B.TK Rho-0 cell line (nuclear donor) and platelets (mitochondrial donors) from healthy (N) and knee OA donors. Senescence level was measured by real-time PCR method. The percentage of mitochondrial depolarization was evaluated incubating cells with DiC1(5) in presence of FCCP 1μM using Flow Cytometer. The percentage of apoptotic cells was measured by Flow Cytometry using Annexin-V. Autophagy was evaluated through the developed of Microtubule-associated protein 1A/1B-light chain 3 (LC3) WB. Appropriate statistical analyses were performed with GraphPad Prism v6. **Results:** The gene expression corresponding to senescence marker proteins (p53/30) showed higher levels in OA cybrids than in N (4.35±1.63; 1.21±0.42 respectively, p<0.0005). Similarly, OA cybrids showed higher increment depolarized mitochondria under negative stimuli in comparison with basal condition than N (2.57±1.20; p<0.0005; 1.76±0.99; p<0.05 respectively). The analysis of apoptotic levels, when the cells were submitted for a positive stimuli with staurosporine (2 μM) and an inflammatory environment with IL-1β (10 ng/ml), OA cybrids reflected a statistically significant increase in positive cells for Anexine-V in comparison with N cybrids in both conditions (staurosporine 15.65±3.39; 6.41±0.88 respectively, p<0.05; IL-1β 0.92±0.10; 1.47±0.24 respectively, p<0.05). Autophagy was analyzed studying LC3 a marker for autophagosome formation and the results showed that LC3 activation was reduced in OA cybrids (1.19±0.24; 1.41±0.21 respectively, p=0.05).

**Conclusion:** Mitochondria from OA patients is involved in cellular senescence, apoptosis and autophagy (three relevant processes involved in OA).

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organization. Therefore, it may provide additional, important information compared to conventional section-based histology. Moreover, analyzing patients with medial compartment knee OA, we found that the medial OA menisci had higher histopathological scores than both reference medial menisci, as well as the lateral meniscus from the same knee.

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Study the effect of human umbilical cord mesenchymal stem cells derived exosomes(hUCMSC-exos) on bone destruction in Collagen Induced arthritis (CIA) rats.

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Background: Rheumatoid arthritis (RA) is a highly disabling autoimmune disease, characterized by destruction of the cartilage and bone, which is difficult to reverse. Mesenchymal stem cells-derived exosomes (Mesenchymal stem cells-derived Exos) is a kind of extracellular vesicles, produced by MSCs in resting or stress state, which can simulate the tissue repair effect of its maternal cells and may be a new breakthrough point in the treatment of RA bone destruction.

Objectives: Study the effect of human umbilical cord mesenchymal stem cells derived exosomes(hUCMSC-exos) on bone destruction in Collagen induced arthritis CIA rats.

Methods: 1. After isolated by differential centrifugation, hUCMSCs was cultured in which was identified by morphology and surface markers. 2. Grouping: The CIA rats were randomly divided into CIA group, MTX group, hUCMSCs group, hUCMSC-exos low concentration group, hUCMSC-exos medium concentration group, hUCMSC-exos high concentration group, and a healthy control group. 3. Efficacy evaluation: the efficacy of hUCMSC-exos on CIA rats was evaluated by measuring joint swelling, arthritis index, micro-ct scanning and pathological score. The expression levels of RANKL and OPG in the serum of rats in each group were detected by ELISA. The levels of the above factors in the synovial fluid of rats in each group were detected by RT-PCR, and the mRNA levels were detected by quantitative RT-PCR for superoxide dismutase (SOD), interleukin-15 (IL-15), matrix metalloproteinase-1 (MMP-1) and vascular endothelial growth factor (VEGF).

Results: All the ratios LA:ALA of caused a remarkable reduction in MMP-1(P<0.001). Marginal reduction in VEGF was noted with 1:1, 4:1 and 8:1 ratios (P<0.05). IL-15 was noted with 1:1, 2:1 and 4:1 while a marked up-regulation was noted for 8:1 and 16:1 (P<0.01). Lastly, a significant MMP-1 reduction was caused by all the ratios of DGLA:DPA, except 4:1. The selected ratios were efficient against VEGF (P<0.001). A consistent high SOD was revealed by all the ratios excluding 4:1. The selected ratios were efficient against VEGF (P<0.001).

Conclusion: Consequence of synovial inflammation in typical and atypical forms results in cartilage-loss, osteophytes and pain. RA ratios when used in equivalent, was found highly effective against IL-15, MMP-1 and VEGF, whereas inflammation increases with increase in their proportions. Low SOD indicated lower oxidative-stress while it was up-regulated in response to high stress. FAs work in two distinct ways, membrane incorporation and metabolic modulation. Unsaturated fatty acid increases membrane fluidity and thus improves cell signaling. Analysis of treated and untreated cells showed incorporation of FAs in cell membrane, which improves membrane fluidity and status of signal transduction.

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FRID512
RETRO-INVERSO TAT-BECLIN-1 INDUCES SYNOVIAL FIBROBIS AND DOES NOT PROTECT CARTILAGE FROM DEGENERATION IN A MOUSE MODEL OF OA

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Background: Beclin-1 is a component of the autophagy pathway necessary for formation of autophagosomes, contributing to autophagy-mediated cellular homeostasis. Enhancing autophagy through inhibition of mTOR activity, either via genetic deletion in chondrocytes or intra-articular injection of rapamycin, attenuates progression of surgically-induced models of osteoarthritis (OA). Retro-inverso TAT-Beclin-1 is a cell-permeable peptide which competes for binding to the endogenous Beclin-1 inhibitor GAFR-1, thus promoting autophagy. It is unknown whether activation of Beclin-1 is sufficient to protect joints from osteoarthritis progression.

Objectives: For this study, we sought to determine if retro-inverso TAT-Beclin-1 could attenuate OA progression in a surgically-induced mouse model.

Methods: Eight-week old C57BL/6 mice underwent destabilization of the medial meniscus (DMM) surgery to induce OA, or sham surgery as a control. Mice were injected intra-articularly with retro-inverso TAT-Beclin-1 (2 mg/kg in 5 μl) twice weekly for 2 or 9 weeks. Mice were sacrificed at 10-weeks post-surgery. Knee joints were stained with Safranin-O/Fast green to evaluate cartilage degeneration and Masson’s trichrome to determine degree of synovitis using OARSI scoring for mice. Sections were stained for α-SMA (myofibroblast) and CD45 (hematopoietic-origin cell) to evaluate changes in markers of fibrosis and inflammation, respectively.

Results: As opposed to the effects of mTOR deletion in cartilage or rapamycin treatment in joints, injection of retro-inverso TAT-Beclin-1 for 2 into knee joints of mice with DMM-induced OA had no effect on the degree of articular cartilage degeneration in the tibia or femur as compared to PBS-injected controls. However, in both sham and DMM mice, retro-inverso TAT-Beclin-1 for 2 or 9 weeks of treatment induced a pronounced thickening of the synovium with increased cell numbers and collagen deposition compared to PBS-treated mice. The increased number of synovial cells in 9-week treated mice did not show substantial expression of α-SMA- or CD45+ cells, suggesting the increased number of cells and matrix in the synovium was independent of myofibroblast differentiation or inflammatory influx.

Conclusion: Contrary to our expected results, retro-inverso TAT-Beclin-1 did not attenuate cartilage degeneration. Rather, it promoted substantial synovial thickening that likely involved cell proliferation and collagen deposition. This severe fibroblastic phenotype appears independent of myofibroblast differentiation or inflammation, normally associated with typical fibroblastic responses. To evaluate the potential for dose responses with retro-inverso TAT-Beclin-1 in synovial joints, we are currently modifying our dosing strategy in an effort to determine possible disease-modifying effects of this novel Beclin-1 activator.

Disclosure of Interests: None declared.


FRID513
HISTONE-ACETYLTRANSFERASES CBP AND P300 REGULATE AUTOPHAGY AND PROTEASOMAL DEGRADATION IN SYNOVIAL FIBROBLASTS

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Background: Proteosomal degradation and autophagy are the major catabolic pathways that maintain the homeostasis of cells and are associated with cell survival. The histone acetyltransferases CARM response element binding protein binding protein (CBP) and p300 are close homologues and widely accepted as redundant proteins.

Objectives: To analyse individual functions of CBP and p300 in catabolic pathways in rheumatoid arthritis (RA) synovial fibroblasts (SF).

Methods: SF were isolated from knee, shoulder and hand joints of RA patients undergoing joint replacement surgery. The expression of CBP and p300 was silenced by transfection of antisense LNA gapmeRs (12.5 nM). 24h after transfection cells were stimulated with TNF-α (10 ng/ml, 24h). Transcriptions were determined by RNA-seq (Illumina NovaSeq 6000, n=6). Pathway enrichment analysis of RNA-seq data (fold change >1.5, FDR <0.05) was performed using DAVID bioinformatic resources. Autophagy was assessed by Western blotting using LC3B conversion and p62 as autophagy substrate (n=4) in presence and absence of bafilomycin A1 (100 nM, 4h), a lysosomal inhibitor. Cell death was analysed using the CytoTox-Glo cytotoxicity assay.

Results: The top pathway identified after silencing of p300 in SF in presence (p=1.33x10^-10) and absence of TNF-α (p=1.76x10^-10) was ‘proteasome’, with an enrichment of genes contributing to ‘proteasome assembly’ and ‘proteasome regulation’. The expression of several genes encoding proteasome subunits was increased after p300 silencing but unaffected by silencing of CBP. Genes contributing to the biological processes ‘autophagy’ (p=0.05) and ‘regulation of autophagy’ (p=0.05) were enriched after silencing of CBP and p300, whereas ‘autophagy assembly’ was only affected by CBP silencing. In RNA-seq data, the expression of MAP1LC3B, encoding the autophagy marker LC3B, and the autophagy substrate p62, was increased by p300 silencing but slightly decreased by CBP silencing. In line with the RNA expression, silencing of CBP reduced the conversion of LC3B and the protein expression of p62 in presence and absence of TNF-α. Results were similar in presence of bafilomycin A1, indicating a decrease in autophagy seen in synovial fibroblast cultures. In contrast, the conversion of LC3B and p62 expression were increased after silencing of p300 in unstimulated SF, indicating increased autophagy. This effect was lost for LC3B after treatment with TNF-α, and LC3B conversion was even delayed in presence of bafilomycin A1. This indicates a blockage of autophagy after silencing of p300 in TNF-α-stimulated SF. In line with this, silencing of p300 in SF (n=6, p<0.05) increased cell death only in presence of TNF-α. Viability of SF was not affected by silencing of CBP.

Conclusion: Here we identified p300 as a major regulator of the proteasome in SF and provide first evidence for individual functions of CBP and p300 in regulating autophagy in SF.

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FRID514
NEW DIAGNOSTIC BIOMARKER OF BONE TISSUE METABOLISM DISORDERS IN RHEUMATOID ARTHRITIS

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Background: Bone mineral density and proteins/peptides determination in blood and urine as markers of bone resorption and formation are currently used to diagnose osteoporosis (OP) and metabolic bone diseases. However, these methods have some disadvantages for bone turnover evaluation. Recent evidence suggests that in RA changes in the secretion of hormones of white adipose tissue can be revealed [1,2,3,4]. One of them is Adiponectin possessing anti-inflammatory, anti-diabetic and anti-atherogenic properties. Changes in Adiponectin levels may reflect influence of immune inflammation on bone turnover.

Objectives: To study the clinical and diagnostic value of serum Adiponecin determination in RA patients complicated by OP.

Methods: We examined 86 women with documented diagnosis of RA and mean disease duration of 6.5±0.88 years. We used EULAR/ARA 2010 criteria to diagnose the patients. Female patients with II degree of disease activity (DAS28), Steinbrocker stage II (erosive), rheumatoid factor- and anti-cyclic-citrullinated peptide antibody-positive were prevalent. We excluded patients who had surgery or developed an infection within the last 8 weeks, pregnant and breast-feeding women, patients with heart, liver or kidney disease, immune deficiency, leukopenia or chronic infection. A control group of 45 healthy females aged of 25 and 59 years were included in the study. There were no reported findings of
joint pain and RA symptoms in the group. The groups were adjusted for age (p<0.05) and showed no statistically significant differences.

We measured serum Adiponectin levels (µg/ml) using Human Adiponectin ELISA commercial test systems (BioVendor, Czech Republic, cat # R01902020100). We used spectrophotometer with wavelength of 450 nm to detect the test results ([MultiSkan- immunoenzyme analyzer, Finland]). We plotted a curve using computer software. We diagnosed OP using dual-energy X-ray absorptiometry with LUNAR DPX PRO (GE, USA).

Results: Serum adiponectin levels in the control group were 12.5±2.9 µg/ml. Adiponectin levels in healthy subjects measured as M ± 25% ranged between 0.44 and 24.56 µg/ml. Patients with OP and RA had significantly higher levels of serum Adiponectin (p<0.001). Mean serum Adiponectin levels in RA patients who had normal bone density and had no OP were 35.21±0.6 µg/ml. Mean serum Adiponectin levels in OA patients with low bone mineral density were 52.4±2.69 µg/ml. Adiponectin levels of 44 µg/ml and higher were associated with osteoporosis. Adiponectin levels of 43.9 µg/ml and lower were associated with normal bone density.

Conclusion: Thus, we revealed that Adiponectin levels depend on osteoporosis presence in RA patients. We suppose that Adiponectin determination may be useful laboratory marker for OP diagnosis. The test may be used to reduce the risk of low-energy fractures and to improve the quality of life in RA.

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HSP90AA1, A CHAPERONE-MEDIATED AUTOPHAGY, IS A CHROMOSOME-ASSOCIATED WITH DEFECTIVE AUTOPHAGY IN OSTEOARTHRITIS

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Background: In osteoarthritis (OA), defects in cellular homeostasis, such as autophagy, are evident and precede joint damage (1). We have shown that there is a defect in autophagy in OA human chondrocytes and cartilage (2). Indeed, pharmacological activation of autophagy protects against joint damage (3). Our working hypothesis is that joint damage in OA could be due to a failure of autophagy that can be detected in the blood and tissue of patients.

Objectives: The objective of this study is to identify biomarkers associated with autophagy defects that could facilitate the development of personalized therapeutic strategies to prevent OA progression.

Methods: A comparative analysis of 35 autophagy genes was performed in blood from a Prospective OA Cohort of A Coruña (PROCOAC) of Non-OA and knee OA patients. Non-OA patients (Age: 61.4± 1.16 years; BMI: 25.25 ± 0.52; Females, n=18) and Knee OA patients (Age: 65.50 ± 1.05 years; BMI: 29.55 ± 0.67; Females, n=18, OA grade II-IV) were profiled using PrimePCR autophagy human panel array (Bio-Rad). Confirmatory studies of the candidate genes were performed in blood from Non-OA patients (Age: 60.13 ± 1.12 years; BMI: 24.85 ± 0.59; Females; n=30) and Knee-OA patients (Age: 68.4 ± 1.11 years; BMI: 29.65 ± 0.55; Females; n=30, OA grade III-IV) by Taqman Technology. A quantitative proteomic analysis of defective autophagy genes regulated upon deletion of Atg5 in human OA chondrocytes was performed by iTRAQ analysis. Moreover, the candidate gene was evaluated as a potential biomarker in human cartilage from Normal (n=19) and Knee-OA (n=20) patients in both spontaneous aging (6, 12, 18, and 30 months old, n=3) and surgically-induced OA (10 weeks after surgery, n=4) in mice by immunohistochemistry. Remarkably, the consequences of candidate gene silencing on autophagy, FOXO signaling, inflammation, senescence and cell death by apoptosis was investigated by gene expression and flow cytometry.

Results: 15 autophagy-related genes were downregulated in blood from knee OA patients compared to non-OA patients (p<0.05). Importantly, key autophagy-related genes, including ATG16L2, ATG12, ATG4B and MAP1LC3B, involved in relevant process including initiating autophagy, phagophore extension and autophagosome formation, were significant downregulated in knee OA patients (p<0.05). Interestingly, HSP90AA1 and HSPA8, chaperone-mediated autophagy genes involved in stress response and protein folding, were significant downregulated (p<0.001). In addition, several regulators of autophagy and apoptosis, such as Bnip3, Bcl-2 and Bcl2L1 were downregulated (p<0.01). Confirmatory studies for MAP1LC3B and HSP90AA1 showed a significant downregulation (p<0.001) in blood from knee OA patients. Remarkably, total proteome screening of human OA chondrocytes with defective autophagy, showed a significant reduction of HSP90AA1 (p<0.05). Remarkably, HSP90AA1 expression was reduced in OA cartilage (p < 0.01) and in spontaneous aging and surgically-induced OA in mice (p < 0.05). Interestingly, HSP90AA1 silencing increased LC3 and FOXO1 expression (p > 0.01), might be as a protective response, and increased Nfkb and p16 expression (p < 0.05) at 48 hours. In addition, genetic deletion of HSP90AA1 increased cell death by apoptosis (p < 0.05). These data indicate that HSP90 might be a potential biomarker associated with defective autophagy in OA.

Conclusion: We identified biomarkers of defective autophagy as a mechanism of central homeostasis, which gives us a general vision of the disease mechanisms linked to OA clinical reality.

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Disclosure of Interests: Irene Lorenzo: None declared.


CHONDROGENIC EFFECT OF KARTOGENIN ON AN IMMORTALIZED CELL LINE DERIVED FROM MESENCHYMAL STROMAL CELLS ISOLATED FROM HUMAN BONE MARROW

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Background: Mesenchymal stromal cells (MSCs) currently tested in regenerative medicine approaches for osteoarthritis (OA) present limitations in obtaining stable hyaline-like cartilage phenotype. Kartogenin (KGN) has been recently described to promote both reparative and protective effects hampering the hypertrophic effects of chondrogenesis.1

Objectives: The aim of this study is to evaluate the chondrogenic effect of kartogenin on an immortalized cell line (3a6), using a conventional cell pellet model and gold-standard chondroinductor transforming growth factor 3 (TGF-β3), as positive reference.

Methods: 3a6 cells, originally obtained from a 61-year old Asian woman bone marrow, was cultured under pellet culture system with basal (DMEM, low glucose) or commercial chondrogenic medium, supplemented with 10 ng/ml TGF-β3 or 100nM KGN for 3, 7, 14 and 21 days. Total RNA was isolated and real-time quantitative reverse transcription-polymerase chain reaction (RT-qPCR) was performed, using custom-made primers for run-related transcription factor 1 (RUNX1), proteoglycan 4 (PRG4), cartilage intermediate layer protein (CILP), collagen type-II (COL2A1), X (COL10A1) and -I (COL1A1), using RPL13A as housekeeping. Proteoglycans and zonal markers protein synthesis was evaluated by safranin-O (SO) staining and lubrican/PRG4 and CILP immunohistochemical analysis (both 1:50), respectively. The experiment was performed in triplicate and differences judged using one-way ANOVA with Bonferroni’s corrections, considering p<0.05 significantly different.
Results: The molecular analysis of KGN- and TGF-β3-chondrogenic induced 3α6 pellets is depicted in figure 1A. For zonal markers expression, both conditions showed a significant downregulation in PRG4 with time, concomitant with an upregulation of CILP, for TGF-β3 but not for KGN-induced cells. However, PRG4 and CILP were found on the protein level (Figure 1B) for both conditions. The studied zonal markers were found heterogeneously distributed for KGN-induced pellets (Figure 1C). This difference is also supported by proteoglycans SO staining, with an earlier formation of a more mature tissue for KGN- than TGF-β3-induced pellets. No expression was found for the main hyaline-like cartilage collagen (COL1A1). RUNX1 was practically unaltered in both conditions. For hypertrophic markers, RUNX2 was upregulated at 14 days in TGF-β3-, whilst in KGN-induced cells its expression seems to be delayed, although no significant differences were found. In both conditions, COL10A1 was very low, until 21 days. COL1A1 presented a significant upregulation at 14 days for TGF-β3- whilst in KGN-induced cells expression was non-significant.

Conclusion: This is the first study to report the chondrogenic effect of kartogenin on 3α6 immortalized human bone marrow MSCs line. On the molecular level, no significant differences were found between KGN- and TGF-β3-chondrogenic induction, although transition into a hypertrophic phenotype seems to be delayed. On the protein level, zonal markers and proteoglycan synthesis were found improved by kartogenin after 14 days.

REFERENCE:

Disclosure of Interests: carolina guanche-varela: None declared, cristiano rodríguez-perere: None declared, elena fernandez-burguera: None declared, tamara hernida gómez: None declared, noa oyanes: None declared, francisco j. blanco consultant for: AbbVie, bionera, bms, gsk, grünenthal, janssen, Lilly, pfizer, regeneron, roche, sanofi, trb chemedica, and ucb, joana magalhães: None declared

Results: Participants had a mean age 47±9 yrs and 6 out 7 (86%) were female. All had KL grade ≥2 with substantial knee pain at baseline. Enough SF (>500 uI) could be obtained from n=7 at baseline, n=4 at midpoint, and n=3 at endpoint of distraction. For the first time in this same group, we show how MSC number initially decline upon KJD (figure 1A-B) as seen previously in our animal study [4]. Also, MSCs present in the SF showed changes in their gene expression profile upon KJD, most clearly observed during the treatment (3 weeks; figure 1C). GFDF5 and Grem1 present with a statistically significant increased expression (p<0.05) during treatment while FAB4 expression was decreased. ACAN, PTHR1, and DDR expression had the tendency to increase over time. ADAMTS4, Sox9 and PTHLH expression showed a trend to decrease over time.

Conclusion: This explorative study provides the first-time data on changes in SF MSC number and their gene expression profiles upon knee joint distraction. As such, first clues are provided for the involvement of MSCs in the regenerative process induced by joint distraction for knee joint distraction. As such, first clues are provided for the involvement of MSCs in the regenerative process induced by joint distraction for end-stage knee OA. The fall in SF MSC number during distraction suggests adhesion to the arthritic surfaces in the KJD environment as found in our previous work in canine KJD [4]. Further studies are necessary to unravel the processes involved.

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Background: Ankylosing spondylitis (AS) is associated with enthesis inflammation and new bone formation. Resident populations of lymphocytes have been identified at the enthesis that on stimulation with IL-23 produce pro-inflammatory cytokines including IL-17A and IL-22 (1) which drive inflammation and may also influence osteogenesis. Surprisingly, enthesis resident mesenchymal stem cells (MSCs) have not been phenotypically or functionally characterised.

Objectives: To determine if human enthesis including entheseal soft tissue and peri-entheseal bone harbours a population of MSCs. Furthermore, to investigate the effect of spondyloarthritides associated pro-inflammatory cytokines on MSC osteogenesis.

Methods: Samples from healthy the spinoous process and interspinous ligament (male = 5, female = 10, median age = 19) were divided into entheseal soft tissue (EST) and peri-entheseal bone (PEB) and enzymatically digested (1). MSCs content was assessed using a CFU-F assay. Flow cytometry was used to examine expression of MSCs specific markers in plastic adherent cultures. Following osteogenic, chondrogenic and adipogenic inductions, osteogenesis was qualitatively by alkaline phosphatase and alizarin red staining and quantitatively by measurement of calcium accumulation. Chondrogenesis and adipogenesis were assessed using glycosaminoglycan assay and oil red o staining respectively. Osteogenic cultures were also supplemented with IL-17A (50ng/ml), IL-22 (10ng/ml) or TNF-α (1ng/ml).

Results: As a proportion of total cellularity EST developed approximately 5 fold more colonies than matched PEB (p<0.001). Cultured cells were overwhelmingly positive for expression of MSC markers CD73, CD90, CD105 (PEB median 98.66% range: 95.17-98.96%, EST median 98.42% range: 98.12-98.89%) however some CD34 expression was noted particularly in EST cultures (PEB median 0.34% range: 0-2.91%, EST median 1.1% range: 0-2.53%) and osteogenesis was qualitatively by alkaline phosphatase and alizarin red staining and quantitatively by measurement of calcium accumulation. Chondrogenesis and adipogenesis were assessed using glycosaminoglycan assay and oil red o staining respectively. Osteogenic cultures were also supplemented with IL-17A (50ng/ml), IL-22 (10ng/ml) or TNF-α (1ng/ml).

Conclusion: Both the EST and PEB contain cells that meet the ISCT criteria defining MSCs. However, MSCs from these sources are functionally distinct in terms of their differentiation potential and response to inflammatory cytokines. The cytokines tested had a negative influence on osteogenesis in the conditions tested.

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MITOCHONDRIAL BACKGROUND IMPACT ON THE JOINT DEGENERATION PROCESS DURING AGING AND FORCED EXERCISE: A CONPLASTIC MOUSE MODEL

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Background: Several studies indicated that osteoarthritis has a strong genetic component with a prevalent role of mitochondria and mtDNA variation. Conplastic mice (BL/6 NZB) strain was developed with the NZB/OlaHsd nuclear genome and the NZB/OlaHsd mtDNA to compare with the original C57BL/6J nuclear genome (BL/6). The results were found in various OA animal models and patients. Despite the severity of OA, the initial triggers of this disease are mostly unknown. Recent studies suggest that, metabolism is important for maintaining cartilage function, and aberrant metabolic activities in chondrocytes have been shown in various OA animal models and patients. In the present study, we aimed to investigate the influence of the mtDNA variation in the joint deterioration using mice with the same nuclear genome but different mtDNA variants (named conplastic mice) during aging and forced exercise.

Methods: Conplastic mice (BL/6NZB) strain was developed with the C57BL/6J/OlaHsd nuclear genome and the NZB/OlaHsd mtDNA to compare with the original C57BL/6J/OlaHsd strain (BL/6). Knee joints from BL/6NZB mice as well as from BL/6NZB mice were processed and cut into coronal sections. The mice were sacrificed at 25, 75 and 90 weeks of age and knee joints were collected for histological analysis. All sections were stained with Hematoxylin-Eosine and Safranin O-fast green and graded using a Rankin scoring system. Another group of mice from both BL/6 and BL/6NZB strains were subjected to exercise by running in a treadmill 400m/day three times a week. After 75 and 90 weeks of age, mice were sacrificed and knee joints were processed for histological analysis. Cartilage expression of markers of autophagy like LC3 and metalloproteases like MMP-13 were also analysed by immunohistochemistry in both strains. The results are given as mean ± SEM and statistical analysis was performed using non parametric unpaired t-test (Graph Pad Prism v 6.0).

Results: In response to aging, conplastic mice BL/6NZB presented reduced cartilage Rankin score at 25 (p=0.0079), 75 (p=0.0087) and 90 (p=0.064) weeks when compared with mice of the original strain BL/6 at the same age. Specifically, we showed a reduced score in both femoral condyle (FC) and tibial plateau (TP) of BL/6NZB mice that reached the statistical significance at 25 (FC: p=0.0317; TP: p=0.0079), 75 (FC: p=0.0411; TP: p=0.0238) and borderline the statistical significance at 90 (FC: p=0.0649; TP: p=0.0628) weeks of age. These results were accompanied with more expression of LC3 in cartilage from BL/6NZB mice at 75 weeks when compared with cartilage from BL/6 at the same age (p=0.0152). We also reported a significant decrease of LC3 expression in cartilage from mice at 75 weeks when compared with mice at 25 weeks in both strains confirming the decrease of autophagy with aging. Difference in MMP13 cartilage expression between the two mice strains were also found. In the mice subjected to exercise, BL/6NZB presented an increased cartilage score in the medial compartment (p=0.0286) and lateral compartment (p=0.057) of the joint at 90 weeks when compared with BL/6NZB mice at the same age.

Conclusion: This study demonstrated that aging and forced exercise in conplastic mice BL/6NZB are associated with a reduced joint deterioration compared with the original strain BL/6. Moreover, we showed that mtDNA variants can improve the aging process at joint level through the modulation of autophagy. These results support the hypothesis that mtDNA background has a role in the process of joint damage, suggesting that mtDNA has potential as novel therapeutic target in OA associated to aging.

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Disclosure of Interests: Morena Scotece: None declared, Ignacio Rego-Perez: None declared, Ana Victoria Lechuga Vieco: None declared, Purificación Figueira-Fernández: None declared, Jose Antonio Enriquez: None declared, Francisco J. Blanco Consultant for: AbbVie, Bioiberica, BMS, GSK, Grünenthal, Janssen, Lilly, Pfizer, Regeneron, Roche, Sanofi, TRB Chemedia, and UCB


TLR-1/2 SIGNALING IMPAIRS MITOCHONDRIAL OXIDATIVE PHOSPHORYLATION IN CHONDROCYTES VIA THE INDUCTION OF NITRIC OXIDE

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Background: Osteoarthritis (OA) is a degenerative disease that causes progressive loss of joint function, representing a severe health problem plaguing this ageing world. Cartilage matrix degradation and cartilaginous matrix production are closely associated with OA clinical symptoms. Recent studies suggest that, metabolism is important for maintaining cartilage function, and aberrant metabolic activities in chondrocytes have been shown in various OA animal models and patients. Despite the severity of OA, the initial triggers of this disease are mostly unknown. Small molecules generated during physiological catabolic reactions often function as damage-associated molecular patterns (DAMP) to activate innate immunity through receptors such as Toll-like receptors (TLR), resulting in enhanced expression of matrix metalloproteinases (MMP) and cartilage factors. Here we studied the effect of various TLR signaling on chondrocyte protein production and mitochondrial oxidative phosphorylation (OXPHOS).

Methods: Chondrocytes were obtained from the femoral condyles of C57BL/6JOlaHsd nuclear genome and the NZB/OlaHsd mtDNA to compare with the original C57BL/6J nuclear genome (BL/6). The results were found in various OA animal models and patients. This project is designed to investigate the roles of TLR signaling in the development of OA and the involved molecular mechanisms.

Results: TLR-1/2 and TLR-2/6 stimulation drastically impaired the cartilage matrix production, as they imposed the lowest pellet growth, lowest expression of matrix proteins COL2 and AGC1, but highest expression of matrix degrading enzymes MMP3, ADAMTSS, and the catabolic factor NO. Remarkably, this phenomenon is associated with drastically diminished OXPHOS activity, as shown by the reduction of both basal and maximal respiratory capacity. Moreover, blockade of NO production reversed the adverse effect imposed by TLR-1/2 stimulation, namely restored their OXPHOS activities and COL2 and AGC1 production in a dose-dependent manner.

Conclusion: Among the whole spectrum of TLR signaling, stimulation of TLR-1/2 and -2/6 impose the strongest inhibition on chondrocyte pellet growth by suppressing matrix protein synthesis and facilitating matrix degradation. TLR-1/2 stimulation causes the reduction of OXPHOS capacity, which is mediated by the induction of NO. Thus, TLR-1/2 stimulation, via inducing NO production, impairs the mitochondrial respiration in chondrocytes and thus possibly promotes the development of OA.

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HUMAN MONOCLONAL ACPAS INDUCE MOBILITY OF PRIMED SYNOVIAL FIBROBLAST IN A PAD-DEPENDENT PATHWAY
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Background: Anti-citrullinated protein antibodies (ACPA) play an important role in rheumatoid arthritis (RA) pathogenesis. They recognize a wide number of citrullinated targets and show limited cross-reactivity to acetylated ones.1

Objectives: We aimed to investigate the effect of monoclonal ACPAs with different binding patterns on RA synovial tissue derived fibroblasts (SF). Methods: Synovial fibroblasts were isolated from synovial tissue of RA patients by enzymatic digestion. ACPA and control monoclonal antibodies (mAbs) were derived from single B cells isolated from RA patients. Two monoclonal ACPA (1325:01B09 and 1325:05C06) showed cross-reactivity to acetylated-targets while four of them (1325:04C03, 1325:07E07, 14CFCT2D09, 14CFCT2H12) did not(1). mAbs were tested in synovial fibroblast migration (Tirucaly live time image analysis) and osteostet formation (TRAP) assays. The role of mAbs cross-reactivity was tested in fibroblast migration assays using inhibitors of peptidylarginine deiminases (Cl-amidine), histone acetyltransferase (anacardic acid) and histone deace-tylase (trichostatin A). Binding patterns of monoclonal ACPAs were tested in synovial biopsies obtained from both healthy donors and RA patients.

Results: One acetylation cross-reactive ACPA (1325:01B09) and two with no cross reactivity (14CFCT2D09 14CFCT2H12) significantly enhanced fibroblast migration (mean±SD fold increase of 1.9±0.4, 1.7±0.4 and 1.8±0.6, respectively) compared to control mAbs 1362:01E02 (p<0.05), while having no effect on osteostet formation. In contrast, one acetylation non-cross-reactive ACPA (1325:04C03) promoted osteostetogenesis (mean±SD fold increase of 1.6±0.05) compared to control mAbs 1362:01E02 (p<0.05), while having no effect on fibroblast migration. Cl-amidine completely abolished the effect of 1325:01B09, while neither anacardic acid nor trichostatin A had any effect. Moreover, the fibroblast-promoting ACPA (1325:01B09) but not the osteostetic ACPA1325:04C03 co-localize with CD55-positive SF in the inflamed rheumatoid synovium. No detectable signals were found in healthy synovium.

Conclusion: Monoclonal ACPAs have distinct cellular effects on synovial fibroblasts and osteostets that are not related to cross reactivity towards acetylated targets.

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VISAFTIN-MEDIATED OSTEODESTRUCTIVE EFFECTS ARE REDUCED

DURING ADIPOGENIC DIFFERENTIATION OF MSC ON MINERALIZED BONE FRAGMENTS
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Background: Osteoporosis (OP), as an age-related disease, is characterized by bone loss, increased fracture risk and poor regeneration. During aging and OP bone marrow adiposity is increased due to a shift of osteogenic towards adipogenic differentiation of bone marrow mesenchy-mal stem cells (MSC). The differentiation of MSC into adipocytes or osteoblasts is an important determinant of bone structural integrity. It is known, that fatty tissue not simply functions as energy storage but is metabolically highly active. Therefore, adipocyte-derived factors such as adipokines might influence MSC differentiation.

Objectives: The role of interactions between adipocyte-derived factors and MSC in the pathogenesis of OP is not fully elucidated. Thus, we ana-lyzed the presence of the adipokine visfatin in bone tissue and its effects on MSC differentiation in standard culture vs. spongioza.

Methods: The spongioza of femoral heads of patients with osteoarthritis (OA) after hip replacement surgery, or after osteoporotic femoral neck fracture were used for RNA- and MSC-isolation. Adipogenic MSC differen-tiation was performed with/without visfatin and its inhibitor Apo866 as well as SB203580 p38-MAPK inhibitor. For the transfer and differentiation of MSC on cancellous bone, bone fragments were purified and sterilized. Gene expression was measured by Realtime PCR. Protein production was evaluated by ELISA.

Results: Elevated visfatin-level were observed in OP compared to non-osteoporotic OA bone. Visfatin-induced secretion of proinflammatory factors was lower during adipogenesis on cancellous bone then in standard cell culture (e.g. 14d IL6, x-fold: standard culture 151±110, spong. 40±30, n=7). Significantly elevated MMP13 mRNA as well as protein expression production could be stimulated during adipogenesis on spongiosa as well as in standard cell-culture. However visfatin-mediated MMP13 expression was markedly reduced in the presence of cancellous bone (e.g. 21d, x-fold: standard culture 81±89, spong. 13±21, n=7). Inhibition of visfatin by Apo866 decreased the visfatin-induced cytokine release but not for the p38-MAPK inhibitor, p38-MAPK inhibitor did not influence cytokine release but reduced MMP13 expression in a time dependent manner.

Conclusion: Visfatin level was elevated in osteoporotic vs OA bone. Therefore, visfatin-mediated increase of MMPs and proinflammatory cyto-kines during adipogenic differentiation might influence bone turnover at the adipose tissue/bone interface. Our results support the idea that the extracellular matrix attenuates visfatin-mediated detrimental effects during adipogenesis. The observed visfatin-mediated effects most likely depend on different signaling pathways.

Disclosure of Interests: Lali Tsiklauri: None declared, Janina Werner: None declared, Klaus Frommer: None declared, Stefan Rehart: None declared, Sabine Wensisch: None declared, Ulf Müller-Ladner Grant/ research support from: supported by an unrestricted educational grant from Celgene GmbH, Elena Neumann: None declared.


IL37 AMELIORATES EXPERIMENTAL MURINE OSTEOARTHRITIS

Arjan van Caam1, Ellen van Gellen, Joyce Aarts, Elly Vitters, Esmee Balsma Davidson, Peter van der Kraan. Radboud university medical center, Experimental Rheumatology, Nijmegen, Netherlands

Background: Osteoarthritis (OA) is the world’s most common degenerative joint disorder and leads to pain and disability. Currently, no disease-modi-fying drugs are available, resulting in a large unmet clinical need. Recently, we have shown that the anti-inflammatory cytokine IL37 lowers pro-inflammatory cytokine production, MMP3 activity and sulfated glyco-saminoglycan loss from ex vivo cultured chondrocytes and human cartilage explants. In this study, we further explored the ability of IL37 to amelio-rate OA pathology by studying its effects both in vitro on synovial fibro-blasts and in vivo in collagenase-induced OA.

Objectives: To establish if IL37 can ameliorate experimental OA pathology

Methods: Primary synovial fibroblasts were obtained from synovial biop-sies of 10 patients undergoing total joint replacement surgery. IL37 was overexpressed in these cells using an adenovirus and subsequently cells were challenged with IL1β or OA-synovium conditioned medium. Collage-nase-induced OA (GIOA) was induced by injecting 10 weeks old female C57BL6J with a single intra-articular injection of 3 units of collagenase type VIII. Four days after collagenase injection, Ad-IL37 or Ad-Luc (+ control) was intra-articular injected in the right knee joint of mice. Two weeks later this injection was repeated. Mice were sacrificed on day 7, 28 and 42 after collagenase-injection. Synovial thickening, cartilage damage and osteophyte formation were measured histologically. IL37, MMP3 and VDIPEN expression were investigated by immunohistochemistry.
Results: In primary synovial fibroblasts, IL37 overexpression significantly reduced IL11r- and OAS-CM-induced expression of MMP1, MMP3, IL1B and IL6 by more than 50%. In naïve knee joints, IL37 overexpression did not induce synovial thickening, cartilage damage or osteophyte formation and no overt immune response was detected after 28 days. Strikingly, in CIOA, at day 7, IL37 overexpression significantly reduced synovial thickening and the presence of the metalloproteinase-generated aggrecan-degradation neopeptide VDIPEN in cartilage. At day 28 of CIOA, cartilage degradation was significantly reduced by IL37 treatment at the lateral and medial femur by respectively 46% and 41%, and osteophyte size at the medial femur was reduced by 70%. At day 42 of CIOA, IL37 overexpression could no longer be detected. Osteophyte size formation at the medial femur was still significantly reduced by 46% at this time point, but only a trend (p = 0.06) towards reduced cartilage damage was observed on both femur and tibia.

Conclusion: Our results show that IL37 inhibits the production of catabolic mediators in synovial fibroblasts, similar to our previously obtained results in cartilage. Furthermore, IL37 clearly lowered synovial thickening and ameliorated cartilage damage and osteophyte formation in murine experimental OA. These results indicate that IL37 acts on multiple tissues and OA-related processes, which supports IL37 as a potential therapeutic agent for OA.

Disclosure of Interests: None declared

Disclosure of Interests: None declared
**Isorhamnetin inhibited the production of NO and PGE2, and the expression of iNOS and COX-2. The production of COMP and CTX-II were also inhibited in MIA-induced OA rats.**

**Conclusion:** Isorhamnetin may modulate the inflammatory progression of OA in MIA-induced OA rats. The prevention of cartilage damage was found in OA after adequate isorhamnetin treatment. Isorhamnetin may serve as a potential agent for the management of OA.

**REFERENCES:**


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**Disclosure of Interests:** None declared


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**FR10532**

**SONIC HEDGEHOG PROMOTES PROLIFERATION, MIGRATION AND INVASION OF FIBROBLAST-LIKE SYNOVIOCYTES IN RHEUMATOID ARTHRITIS VIA P38-MAPK SIGNALING**

Shangling Zhu, Yiming Shi, Yuanmei Ye, Xiaoxue Feng, Jianlin Huang. The Sixth Affiliated Hospital, Sun Yat-sen University, Guangzhou, China

**Background:** Abnormal activation of Sonic hedgehog (Shh) signaling has been found in synovium from patients with rheumatoid arthritis and inhibition of Shh signaling pathway suppresses the proliferation and migration of fibroblast-like synoviocytes in rheumatoid arthritis (RA-FLS). However, the mechanism how Shh signaling promotes tumor-like behavior of RA-FLS is not well elucidated.

**Objectives:** In this study, we aimed to investigate the effect of Shh on p38 MAPK kinase signaling and hypothesized that Shh promotes proliferation, migration and invasion of RA-FLS via p38-MAPK signaling.

**Methods:** Cultured RA-FLSs were treated with Smoothened agonist (SAG) or IL-1beta combined with Smoothened antagonist (Cyclopamine). The levels of phosphorylation of p38, its upstream kinases including TGFbeta activated kinase 1 (TAK1), MKK3, MKK6 and downstream target MAPKAPK2 (MK2) were determined by western blot. The functional state of p38 was determined using in vitro kinase assay. Cell proliferation was evaluated by Cell Counting Kit-8 assay. Cell migration and invasion were performed by Transwell assay. The expression of matrix metalloproteinase proteins (MMPs), IL-6 and IL-8 was examined by real-time PCR.

**Results:** SAG rapidly increased phosphorylation of p38, TAK1, MKK3, MKK6 and MK2 in RA-FLS and combination of SAG and p38 inhibitor significantly decreased the phosphorylation of these kinases (P<0.01). Inhibition of Shh significantly decreased the levels of phosphorylation of p38, TAK1, MKK3, MKK6 and MK2 in IL-1beta stimulated RA-FLS (P<0.05). In vitro kinase assay showed that stimulation of SAG significantly increased the kinase activity, and the kinase activity was inhibited by p38 inhibitor. Furthermore, SAG increased cell proliferation, migration, invasion and production of MMP1, MMP3, MMP13, IL-6 and IL-8. However, these enhanced activities of RA-FLS were inhibited in the presence of p38 inhibitor.

**Conclusion:** The study indicates that Shh is associated with activation of p38 MAPK signaling in RA-FLS and Shh may promote the tumor-like behavior of RA-FLS via p38 signaling.

**Acknowledgement:** This work was supported by grants from the National Natural Science Foundation of China (81571584, 81701609).

**Disclosure of Interests:** None declared


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**Paediatric rheumatology**

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**FR10534**

**ORAL GLUCOCORTICOIDS AND NEWLY TREATED DIABETES MELLITUS, HYPERTENSION, AND THROMBOSIS IN CHILDREN WITH CHRONIC DISEASES**

Daniel Hopton1, Fenglong Xie2, Long Chen2, Melissa L. Mann2, Jeffrey Curtis3, Brian Strom1, Timothy Beukelman2. Rutgers University, New Brunswick, NJ, United States of America; 2University of Alabama at Birmingham, Birmingham, AL, United States of America

**Background:** Systemic glucocorticoid use is associated with a well-known spectrum of toxicities. Nonetheless, the risks of cardiometabolic complications in children are poorly understood.

**Disclosure of Interests:** None declared


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**Disclosure of Interests:** None declared


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**FR10535**

**ETHNICITY AND NEONATAL LUPUS RISK IN A LARGE MULTI-ETHNIC COHORT**

Talia Diaz1, Daniela Dominguez1, Lawrence Ng1, Franklin Silverio1, Andrea Knight1, Earl Silverman1, Linda Hiraki2, 3, *The Hospital for Sick Children, Rheumatology, Toronto, Canada; 4Child Health Evaluative Sciences, The Hospital for Sick Children, Toronto, Canada*

**Background:** Neonatal Lupus (NL) is an acquired autoimmune disorder of newborns secondary to the transplacental passage of maternal anti-Ro and/or anti-La. Approximately 2% of children exposed to these antibodies develop NL. Prior studies have suggested that babies of non-European ancestry have a higher proportion of cardiac NL when compared to babies of European ancestry. This finding has not been consistently replicated.

**Objectives:** To examine the association between ethnicity and clinical manifestations of NL in our multi-ethnic population.

**Methods:** We conducted a cohort study of our large, multi-ethnic NL clinic population. The Neonatal Lupus clinic at the Hospital for Sick Children, Toronto, Canada was established in 1986. Children born to anti-Ro and/or anti-La antibody positive mothers are referred to the NL clinic. Antenatal testing is completed due to maternal rheumatologic diagnosis, a prior child born with NL and/or a history of symptoms that prompted physician testing for these antibodies. Beginning in 2011, families routinely reported ethnicity (Canadian census categories). We divided our NL patient cohort in European and non-European groups; the non-European group includes patients of African, Latin American, Eastern Asian, South Asian and Mixed non-European ancestry (i.e. combination of two or more of non-European ethnicities). We included children assessed in the NL clinic ≤ 1 year of age between January 2011 to April 2018. There were 59 children censored for this analysis (7 missing ethnicity and 52 Mixed European-Non European ancestry). We analyzed prospectively collected data from our NL database, on specific NL manifestations: cardiac (heart block, myocarditis, endocardial fibroelastosis), dermatologic (typical rash of NL), hematologic (cytopneas), hepatic (transaminits) and neurologic (macer- rophyelitis). The frequency of NL clinical manifestations was compared among ethnicity groups (Fishers’ exact test). We tested the association between ethnicity and NL clinical manifestations in logistic models.

**Results:** Our study included 301 children, 149 (50%) female and 162 (55%) with NL (Table 1). The median follow-up period was 12.2 months (IQR 8.9, 28.8 months). Ethnicity data was available for 294 (98%) of the children. The non-European group (40%) was comprised of East Asian (14%), South Asian (13%), African (10%), Latin American (2%) and Mixed Non-European ancestry (17%). We did not observe a difference between European and Non-European babies in the proportion with NL, nor any difference in the frequency of specific NL manifestations (p-values > 0.3).

**Conclusion:** In our multi-ethnic NL cohort of children born to mothers with positive anti-Ro and/or anti-La antibodies, there was no association between ethnicity and NL, nor specific NL manifestations. Future analyses will examine the effect of maternal ethnicity and rheumatic disease status on the risk of NL and specific NL manifestations.

**REFERENCES:**


Table 1. Neonatal Lupus Clinical Manifestations in European and non-European children.

<table>
<thead>
<tr>
<th>Manifestation</th>
<th>European</th>
<th>Non-European</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>45 (45%)</td>
<td>72 (50%)</td>
<td>0.51</td>
</tr>
<tr>
<td>NL</td>
<td>48 (48)</td>
<td>80 (56)</td>
<td>0.29</td>
</tr>
<tr>
<td>Cardiac</td>
<td>10 (21)</td>
<td>11 (14)</td>
<td>0.32</td>
</tr>
<tr>
<td>Dermatologic</td>
<td>11 (23)</td>
<td>19 (24)</td>
<td>1.00</td>
</tr>
<tr>
<td>Hematologic</td>
<td>18 (38)</td>
<td>33 (41)</td>
<td>0.71</td>
</tr>
<tr>
<td>Hepatic</td>
<td>26 (54)</td>
<td>42 (53)</td>
<td>1.00</td>
</tr>
<tr>
<td>Neurologic</td>
<td>6 (13)</td>
<td>4 (5)</td>
<td>0.17</td>
</tr>
</tbody>
</table>

**Disclosure of Interests:** None declared

Objectives: We sought to quantify rates of newly treated diabetes mellitus, hypertension, and venous thromboembolism (VTE) associated with oral glucocorticoid exposure in children. We hypothesized that oral glucocorticoids were associated with each complication in a dose-dependent manner, most strongly with current or recent glucocorticoid exposure.

Methods: Using Medicaid claims data (2000-2010), we identified children ages 1-18 diagnosed with immune-mediated diseases (inflammatory bowel disease, juvenile idiopathic arthritis, or psoriasis) or a non-immune comparator condition (attention-deficit/hyperactivity disorder) based on diagnostic codes ± pharmacy claims. We studied time-varying oral glucocorticoid exposures using pharmacy claims after a ≥6-month glucocorticoid-free baseline period, categorizing dose as low (<0.25 mg/kg/day), medium (0.25-0.99 mg/kg/day), or high (≥1 mg/kg/day) based on prescribed prednisone-equivalent dosage and age/sex-imputed weights. Primary outcomes were incident treatment of diabetes (type 1 or 2), hypertension, and VTE. We used Cox regression and weighted cumulative exposure models to estimate adjusted hazard ratios (aHRs) and number needed to harm (NNH) for varying patterns of glucocorticoid exposure.

Results: We followed 932,517 children (21.3% glucocorticoid-exposed) for 1.6 million person-years. Glucocorticoid usage varied by disease (Table). After adjusting for age, sex, race/ethnicity, calendar year, inclusion diagnosis, comorbidities, other medications, and healthcare usage, we found strong dose- and time-dependent relationships between glucocorticoid exposure and rates of newly treated diabetes, hypertension, and VTE (Figure 1). These effects increased with longer durations of exposure and declined within 6 months after stopping (Figure 2). Sustained low-dose exposures (e.g., 0.1 mg/kg/day) appeared relatively safe (aHR<1.2), but risks increased even with brief high-dose exposures (2 mg/kg/day x7 days) (aHR 1.7-2.2). Risk differences were highest for hypertension (number needed to harm (NNH): 2 mg/kg/day x7 days, 6,206-17,894; 2 mg/kg/day x30 days, 233-671) and lowest for VTE (NNH: 2 mg/kg/day x7 days, 54,886-612,350; 2 mg/kg/day x30 days, 1,977-22,045). Absolute risks were higher for children with immune-mediated diseases (e.g., diabetes, 2 mg/kg/day x30 days, NNH: 424-691) than for those with ADHD (NNH: 959).

Table. Distribution of dose and duration of oral glucocorticoids by disease cohort.

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Aspect</th>
<th>25th</th>
<th>50th</th>
<th>75th</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADHD</td>
<td>Duration</td>
<td>7</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>ADHD</td>
<td>Dose</td>
<td>0.41</td>
<td>0.74</td>
<td>1.24</td>
</tr>
<tr>
<td>IBD</td>
<td>Duration</td>
<td>5</td>
<td>27</td>
<td>47</td>
</tr>
<tr>
<td>IBD</td>
<td>Dose</td>
<td>0.29</td>
<td>0.59</td>
<td>0.92</td>
</tr>
<tr>
<td>JIA</td>
<td>Duration</td>
<td>5</td>
<td>5</td>
<td>30</td>
</tr>
<tr>
<td>JIA</td>
<td>Dose</td>
<td>0.16</td>
<td>0.33</td>
<td>0.88</td>
</tr>
<tr>
<td>PSO</td>
<td>Duration</td>
<td>5</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>PSO</td>
<td>Dose</td>
<td>0.3</td>
<td>0.63</td>
<td>1.14</td>
</tr>
</tbody>
</table>

Units: duration, days; dose, mg/kg/day.

Diabetes mellitus (aHR 95% CI)
- Dose >1600 mg/day: 1.60 (1.45, 1.77)
- Dose 1-1600 mg/day: 1.83 (1.63, 2.04)
- Current low dose: 2.89 (1.79, 4.67)
- Current medium dose: 4.73 (3.55, 6.99)
- Current high dose: 5.93 (3.94, 8.91)

Hypertension (aHR 95% CI)
- Dose >1600 mg/day: 1.58 (1.44, 1.72)
- Dose 1-1600 mg/day: 1.87 (1.63, 2.07)
- Current low dose: 2.74 (1.93, 3.90)
- Current medium dose: 7.59 (5.59, 11.18)
- Current high dose: 19.13 (13.43, 23.73)

Venous thromboembolism (aHR 95% CI)
- Dose >1600 mg/day: 1.10 (0.80, 1.53)
- Dose 1-1600 mg/day: 2.20 (1.51, 3.21)
- Current low dose: 6.09 (3.43, 10.79)
- Current medium dose: 7.71 (4.82, 12.98)
- Current high dose: 10.16 (6.94, 20.22)

Conclusion: In children with various chronic conditions, current oral glucocorticoid use is strongly associated with newly treated diabetes, hypertension, and VTE in a dose- and duration-dependent fashion. Hypertension is a more common glucocorticoid-related complication than diabetes or VTE, but in absolute terms, all of these complications are uncommon in children.

REFERENCES:

Disclosure of Interests: Daniel Horton Grant/research support from: Bristol-Myers Squibb, for unrelated research, Fenglong Xie: None declared, Lang Chen: None declared, Melissa L. Manning: None declared, Jeffrey Curtis: None declared, Brian Strom: None declared, Timothy Beukelman Consultant for: Novartis, UCB

Figure 1. Associations of glucocorticoid timing and dose with newly treated outcomes based on Cox regression models.

Figure 2. Associations of glucocorticoid timing and dose with newly treated outcomes based on weighted cumulative exposure models.

REFERENCES:

Disclosure of Interests: Daniel Horton Grant/research support from: Bristol-Myers Squibb, for unrelated research, Fenglong Xie: None declared, Lang Chen: None declared, Melissa L. Manning: None declared, Jeffrey Curtis: None declared, Brian Strom: None declared, Timothy Beukelman Consultant for: Novartis, UCB
OBJECTIVES: Our study aimed to compare the accuracy of serum bioarkers for the diagnosis of MAS complicating s-JIA and to investigate the clinical significance of serum neopterin levels as an indicator of disease activity and diagnosis of MAS complicating s-JIA.

Methods: Serum cytokine levels (neopterin, IL-18, and CXCL9) and soluble tumor necrosis factor receptor type I (sTNFR-I) and II were determined by enzyme-linked immunosorbent assay in 78 patients with s-JIA, including 21 with MAS. The accuracy of these levels for the diagnosis of MAS was compared. Next, serum neopterin levels, in total 125 patients with s-JIA, including 30 with MAS, 15 with Epstein-Barr virus-induced hemophagocytic lymphohistiocytosis (EBV-HLH), and 15 with Kawasaki disease (KD), as well as 28 healthy controls (HCs) were analysed. Results were compared with the clinical features of MAS.

Results: Receiver operating characteristic curve analysis revealed area under the curve values and cut off values of neopterin, IL-18, CXCL9, sTNFR-I/II ratio and ferritin were 0.94/55/4/3/2, 0.52/95/84/5/2, 0.93/5/4/3/2, and 0.88/7/8/6/5, respectively. Serum neopterin levels were significantly elevated in patients with MAS and EBV-HLH compared with those in patients with acute-phase s-JIA and KD. Serum neopterin levels profoundly and rapidly increased as MAS developed and were effectively used and discontinued in 72% of patients. No patients on anti-TNF inhibitors were the most frequently used (47 patients), with the highest efficacy rate (>90% complete response), while Etanercept was less effective and discontinued in 72% of patients. No patients on anti-IL1 drugs were the best maintenance treatment in patients with FMF.

Conclusion: Serum neopterin levels may be used as a promising indicator of disease activity in s-JIA and for evaluating it. It may also be a useful marker to diagnose the transition to MAS from active phase s-JIA.

REFERENCES:

Disclosure of Interests: None declared

FRI0536 FAMILIAL MEDITERRANEAN FEVER (FMF): A SINGLE CENTER EXPERIENCE FROM TURKEY

Ayge Tanjatir, Şerife Gül Karadag, Hatife Emine Sommez, Mustafa Çağan, Nuray Akbay Ayaz. University of Health Science, Karuni Sultan Süleyman Research and Training Hospital, Pediatric Rheumatology, Istanbul, Turkey

Background: Familial Mediterranean fever (FMF) is the most common monogenic autoinflammatory disease mainly affecting ethnic groups living at Mediterranean region. Since the discovery of the Mediterranean Fever (MEVF) gene, molecular genetic testing has been used as a diagnostic adjunct especially in atypical cases (1, 2). Although substantial progress has been achieved about the etiopathogenesis of FMF during the past 20 years, the diagnosis is still based on clinical criteria.

Objectives: To define the demographic, clinical and laboratory characteristics of children with FMF and then to compare the identification capacity of 3 validated FMF diagnostic criteria (Tel-Hashomer, Livneh and Pediatric) at our cohort (3-5).

Methods: The medical records of 1685 children diagnosed and followed up as FMF were reviewed retrospectively. All patients were evaluated for three diagnostic criteria.

Results: A total of 1685 children (839 girls, 846 boys) were involved in the study. Family history of FMF was positive in 46.1%. The mean ± standard deviation of current age, age at symptom onset, onset at disease was 13±5.4, 5±4±15, 7±8±4±1 years, respectively. Median (min-max) follow-up period was 3 (0.5-18) years. Among 1685 patients, 82.8% had fever, 78.2% had abdominal pain, 36.1% had arthritis, 22.6% had chest pain and 16.6% had erysipelas-like erythema. Three patients had biopsy proven amyloidosis. Concomitant disease was present in 140 (8.3%) patients. Most of them (40.7%) were diagnosed with juvenile idiopathic arthriti and FMF. Henoch-Schönlein vasculitis was observed in 35 (25%) patients. Median (min-max) PRAS score was 7 (3-13). Forty-four patients (2.6%) were unresponsive to adequate doses of colchicine. Among them, 16 (36.4%) were treated with anakinra and 28 (63.6%) received canakinumab. Children homozygous for M694V were found to have more severe course of disease and higher PRAS scores (p<0.001). Furthermore, 34 (77.3%) of colchicine resistant patients carried at least one M694V variant. When we applied the diagnostic criteria to our cohort, 99.5% met the Livneh criteria, 91.6% fulfilled the pediatric criteria and 82.9% satisfied the Tel-Hashomer criteria.

Conclusion: This is the largest pediatric cohort studied and presented since now. We believe that the large numbers of our cohort is convincing at the point of discussing phenotype-genotype relations. We confirmed that carrying M694V mutation is associated with increased disease severity. On the other hand, we compared two adult and one pediatric validated diagnostic criteria at a largest group of children with FMF.

REFERENCES:

Disclosure of Interests: None declared

FR0537 LONG-TERM OUTCOMES AND TREATMENT EFFICACY IN PATIENTS WITH TNF RECEPTOR-ASSOCIATED AUTOINFLAMMATORY SYNDROME (TRAPS): A SERIES OF 290 CASES FROM THE EUROFEVER/EUROTARPS INTERNATIONAL REGISTRY

Riccardo Papa1, Thiruosa Lane2, Taryn Youngstein2, Tanner Reiz3, Charalampia Papadopoulos1, Nicolaio Ruperto1, Paul Brogan1, Philip N. Hawkins2, Patricia W2, Marco Gattorno1, Helen J. Lachmann2, Patricio Ruperto1, Maria Giannini3, Clinica Pediatra e Reumatologia, Genova, Italy; 1Division of Medicine, Royal Free Campus, University College London, National Amyloidosis Centre, LONDON, United Kingdom; 2UCL Great Ormond Street Institute of Child Health, Department of Infection, Inflammation and Rheumatology, LONDON, United Kingdom

Background: Tumour necrosis factor (TNF) receptor-associated periodic syndrome (TRAPS) is one of the best known monogenic auto-inflammatory syndrome resulting from an autosomal dominant variation in the TNF super family receptor 1A (TNFRSF1A) gene.

Objectives: To define best treatment approach in patients with TRAPS and effect on long-term outcomes.

Methods: We reviewed all data on patients with TNFRSF1A variants enrolled in the Eurofever/EUROTARPS international registry.

Results: Data on 290 patients were available. Patients with R92Q, P46L or intronic variants (49%) displayed milder disease than 147 patients with mutations affecting other coding regions, with less frequent abdominal pain and skin rashes (P<0.01), higher efficacy rate of colchicine as maintenance treatment, and none developed AA amyloidosis. Almost 90% of patients with exon mutations required maintenance therapy. Anti-interleukin (IL) 1(1) drugs were the most frequently used (47 patients), with the highest efficacy rate (>90% complete response), while Etanercept was less effectively used and discontinued in 72% of patients. No patients on anti-IL1 drugs treatment developed polyarthritis and 10 patients with amyloidosis have been successfully treated with anti IL-1 agents with preservation of native renal function in 7 and excellent long-term transplanta function in 2. Nine women had a history of failure to conceive and seven had successful pregnancies without fertility treatment following complete disease control with anti-IL1 drugs. Long term safety profiles for anti IL-1 agents were excellent even in the presence of comorbidity.

Conclusion: Anti-IL1 drugs are the best maintenance treatment in TRAPS with potential to reverse the most serious disease complications of AA amyloidosis and infertility. The diagnosis of TRAPS should be considered very carefully in patients carrying R92Q, P46L or intronic TNFRSF1A variants.

REFERENCES:
MAY SOME OF THE MEFV GENE VARIANTS CAUSE PFAPA SYNDROME LIKE SYMPTOMS?

YILDIZ Mehmet, Amra Adrovic, Ipek Ulkeroy, Neslihan Gucuyener, Oya Koker, Sezgin Sahin, Kenan Barut, Ozgur Kasapcopur. Cerrahpasa Medical School, Istanbul University Cerrahpasa, Department of Pediatric Rheumatology, Istanbul, Turkey

Background: PFAPA syndrome is characterized by periodic fever, aphthous stomatitis, pharyngitis and cervical adenitis. As diagnosis usually depends on clinical diagnostic criteria, sometimes it can be difficult to distinguish this clinical entity from the other periodic fever syndromes, especially in regions endemic for FMF.

Objectives: The objective of the study is to evaluate the PFAPA patients’ MEFV gene variation frequencies (if it was performed) and relations between detected variants and clinical manifestations in pediatric PFAPA patients.

Methods: Nine hundred and thirty-seven patients that were recorded to our database as PFAPA syndrome were evaluated. Patients were reached by phone and asked about characteristics of their fever episodes, presence of acute phase reactant elevation, pharyngitis, aphthous stomatitis/aphthous tonsillitis, cervical lymphadenopathy, arthralgia, arthritis, abdominal pain, headache, nausea or vomiting, chest pain, diarrhea, skin changes, myalgia and conjunctivitis in the course of fever attack, if they had tonsillectomy, if they were attack-free after tonsillectomy and if they had clinical response to steroid or colchicine.

Results: There were 937 PFAPA patients in our database. MEFV gene analysis was performed in 407 (43%) of PFAPA patients and 305 of them had at least one mutation. Most common MEFV mutations of patients were: R202Q heterozygotes (25.9%), M694V heterozygotes (24.2%), E148Q heterozygotes (13.4%), P369S heterozygotes (9.8%), and V726A heterozygotes (8.6%), respectively. 54.5% of detected mutations were located in exon 2, 40.3% of them were located in exon 10 and 5.3% of them were located in exon 3 of the MEFV gene. Patients were divided into five groups according to their mutations’ localization and groups were compared according to clinical features. There were significant differences between groups according to presence of pharyngitis, arthralgia, abdominal pain, myalgia and tonsillectomy history (Table 1).

Conclusion: In this study, we reported increased frequency of MEFV mutations in a large PFAPA patients cohort. Frequency differences of clinical features between groups suggest that some of the MEFV gene mutations may modify phenotype of PFAPA syndrome. Furthermore, underlying MEFV gene mutations possibly lead to PFAPA like clinical presentation in FMF patients. Another remarkable finding of this study is the relatively high P369S mutation rates in patients with PFAPA syndrome.

REFERENCES:

Disclosure of Interests: None declared


Table 1. Comparison of patients according to their mutations’ location and clinical features.

<table>
<thead>
<tr>
<th>Exon 2</th>
<th>Exon 3</th>
<th>Exon 10</th>
<th>No Mutation</th>
<th>MEFV study performed</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharyngitis</td>
<td>Yes</td>
<td>21</td>
<td>9(40.9)</td>
<td>45</td>
<td>28 (87.5)</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td>87.5</td>
<td>13</td>
<td>(80.4)</td>
<td>4</td>
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WNT6 MUTATION CAUSES AN EARLY ONSET GRANULOMATOUS INTESTINAL DISEASE WITH RECURRENT HEMOHOGYCIC LYMPHOMIHOSTIOSITIC SYNDROME (HLH)

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Background: Use of NGS in patients with unclassifiable disease lies a possible approach to the identification of novel disease causing genes.

Objectives: We report a patient with an early onset inflammatory bowel disease with granulomatous lesions and recurrent HLH episodes carrying a missense mutation in the WNT6 gene.

Methods: A trio based Whole Exome Sequencing (WES) approach was used. Cytokine levels were measured by multiplex assay and by specific ELISAs.

Results: Ten years old Caucasian boy affected by early onset pan-collitis from 9 months of age. Since the disease onset the patient is on glucocorticoid treatment with amino acidic enteral nutrition and oligo antigenic diet. Because of recurrent disease relapses at any attempt of glucocorticoid withdrawal, azathioprine and cyclosporine treatments were also added. At 2 years of age he received total colectomy with ileostomy.
Because of insufficient disease control, treatment with a TNF-inhibitor (infliximab) was started with apparent improvement of intestinal symptoms. However, persistent granulomatous inflammatory disease of the distal portion of the ileo-caecal anastomosis persisted. Moreover, the patient presented recurrent HLH episodes that required high dose of glucocorticoid and cyclosporine-A treatment. Except one HLH episode related to a varicella zoster infection, the other HLH events were most likely triggered by his underlying inflammatory condition. During the HLH episodes levels of IL-18 were moderately elevated (10.880 pg/ml), the IFN-gamma induced chemokine CXCL9 was markedly high (21.871 pg/ml) and remained markedly elevated also during clinical and laboratory HLH remission (3.121 pg/ml and 9.929 pg/ml respectively). Considering the early disease onset, primary immunodeficiency and early intestinal bowel disease onset were genetically ruled out as well as chronic granulomatous diseases through extensive NGS panels. WES revealed carriage of a private (MAF: 1/125568, TOPMED), predicted pathogenic (CADD: 31), homozygous variant of WNT6 (c.793G>C; p.(Asp265His); NM_006522.3). The patient is now partially controlled on low dose of oral glucocorticoid (0.1 mg/kg), cyclosporine-A (5mg/kg) and antimicrobial treatment.

Conclusion: WNT signalling has been primarily described as a regulatory pathway in ontogeny and homeostatic processes. Schaele at al. demonstrated that WNT6 is expressed in: 1) granulomas lesions in human lung of Mycobacterium tuberculosis-infected mice. Moreover, they found that the transcription factor c-Myc is significantly induced in murine macrophages by WNT6. This identifies WNT6 as a novel factor driving macrophage polarization toward an M2-like phenotype, suggesting a role for WNT6 in macrophage differentiation. Our case suggests defective function of WNT6 might be involved in the development of a granulomatous disease, WNT6 role in macrophage differentiation and polarization might also be important in the activation of the IFN-gamma pathway and in recurrent HLH episodes.

REFERENCES:

Disclosure of Interests: Claudia Bracaglia: None declared, Daniela Knafelz: None declared, Flammatta Bracci: None declared, Antonella Insalaco: None declared, Giulia Manucci: None declared, Maruanda Pardeo: None declared, Antonia Pascarella: None declared, Marcello Niceta: None declared, Francesca Pantaleoni: None declared, Andrea Ciolfi: None declared, Bronislava Papadatou: None declared, Marco Tartaglia: None declared, Antonella Pascarella: None declared, Fabrizio De Benedetti Grant/research support from: Abbvie, SOBI, Novimmune, Roche, Novartis, Sanofi, Pfizer


FRI0540

A NOVEL AUTOINFLAMMATORY DISEASE CHARACTERIZED BY NEONATAL-ONSET CYTOPENIA WITH AUTOINFLAMMATION, RASH, AND HEMOPHAGOCYTOSIS (NOCARH) DUE TO ABERRANT CDC42 FUNCTION

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Background: Despite continuous advances in the identification of novel causative genes, several patients with a clinical autoinflammatory pheno-type remain unclassifiable

Objectives: to describe a novel hematological and autoinflammatory disorder in three unrelated patients caused by a de novo missense mutation of CDC42

Methods: Whole exome sequencing was used to identify the novel variant. The functional impact of the novel CDC42 function on hematopoiesis and inflammation was assessed through patient peripheral blood and bone marrow analyses, protein behavior and immune and non-immune cell functioning through in vitro biochemical and functional assays and in vivo C elegans modeling.

Results: Patients shared the same de novo missense mutation of CDC42 (NM_001791, Chr1:22417990, c.556C>T, p.R186C). Disease features included neonatal-onset cytopenia with dyshematopoiesis, autoinflammation, rash, and hemophagocytosis (collectively termed NOCARH syndrome) (Table). An altered hematopoietic compartment (prevalence of early differentiation elements and substantially decreased clonogenic progenitors) was demonstrated. Complementary assays documented the unique consequences of this mutation on CDC42 localization and function, and its disruptive effect on cell behavior and developmental processes, possibly linked to actin dysregulation. Increased secretion of IL-1β, and particularly of IL-18, was observed via ex vivo spontaneous release from unstimulated bone marrow mononuclear cells and by high levels in bone marrow supernatants and plasma. IFNγ was also increased and correlated to WNT6 levels which were strictly related to ferritin levels. Treatment with anakinra and emapalumab, a monoclonal antibody to IFNγ, was identified as critical in the survival of one patient, who underwent successful hematopoietic stem cell transplantation.

Conclusion: The p.R186C amino acid substitution in CDC42 underlies a novel, unique syndrome where CDC42 functional dysregulation has pleiotropic effects, causing hematopoietic disturbance, hyperinflammation, and immune impairment. Early recognition and control of HLH, through neutralization of IFNγ, followed by hematopoietic stem cell transplantation, appear to be crucial to survival.

Disclosure of Interests: Michael T. Lam: None declared, Simonata Coppola: None declared, Oliver H. Krumbach: None declared, Giusi Prencipe: None declared, Antonella Insalaco: None declared, Cristina Citak: None declared, Immacolata Brigida: None declared, Serena Scala: None declared, Marcella Nicola: None declared, Andrea Ciolfi: None declared, Alexandre Carisey: None declared, Mohammad Akbarzadeh: None declared, Andrea Finocchi: None declared, Franco Locatelli: None declared, Alessandro Aiuti: None declared, Reza Ahmadian: None declared, Jordan S. Orange: None declared, Fabrizio De Benedetti Grant/research support from: Abbvie, SOBI, Novimmune, Roche, Novartis, Sanofi, Pfizer

HIGHLY ELEVATED FERRITIN LEVELS ARE ASSOCIATED WITH HAEMOPHAGOCYTIC LYMPHOPHILOPATHY - MACROPHAGE ACTIVATION SYNDROME WHEN CONSIDERED AS A SUGGESTING TREATABLE DIAGNOSIS? A RETROSPECTIVE SERVICE EVALUATION OF DIAGNOSIS IN PATIENTS WITH FERRITIN >10,000 MICROGRAM/L

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BACKGROUND: Haemophagocytic lymphohistiocytosis (HLH)/macrophage activation syndrome (MAS) is a hyperinflammatory syndrome potentially leading to critical illness. Early recognition reduces mortality but diagnosis requires a high index of suspicion. Highly elevated ferritin levels (HEF) >10,000 µg/L are highly specific for HLH/MAS [1] and should prompt consideration of hyperinflammation. Diagnostic guidelines for HLH, requiring the presence of ≥5/8 criteria [2], and classification criteria for MAS complicating systemic juvenile idiopathic arthritides (sJIA) have been published [3].

OBJECTIVES: To assess recognition of HLH/MAS in a paediatric population with HEF.

METHODS: This retrospective study was conducted at 11 centres under local service evaluation permissions. Biochemistry databases identified patients ≤16 years with serum ferritin >10,000 µg/L during a 3-year period. Each case was assessed against the 2004 HLH criteria and, for patients with sJIA, the 2016 MAS criteria. Due to limited access to some of the laboratory tests, previously-published modified HLH criteria using a threshold of ≥45 (excluding tissue haemophagocytosis, decreased natural killer cell function, increased soluble interleukin-2 receptor) were also applied to all patients [4].

RESULTS: 153 patients (55.6% male) were identified. Patient diagnoses included: infections (29.4%), rheumatological (17.0%) and malignancies (17.0%). A diagnosis of HLH/MAS was made by the treating clinical team in 39.9% and considered in a further 16.3%. Using all available data, 30/153 (19.6%) met ≥5/8 criteria and 93.3% of these patients were diagnosed with HLH/MAS by the treating team. 56 (36.6%) met ≥45 criteria and 33 (59.9%) of these were diagnosed with HLH/MAS by clinicians. HLH/MAS was not documented as being considered in the differential in 23.2%. Of 23 patients with sJIA, 62.6% met MAS classification criteria and 89.5% of these were diagnosed with MAS by the treating clinicians. Overall mortality was 32.7% (50/153) and was 27.9% (17/61) in patients diagnosed with HLH/MAS during their admission.

CONCLUSION: Although HEF is highly specific for HLH/MAS, the diagnosis was only made or considered in just over half of paediatric patients with this laboratory result. Increased awareness of this potentially-lethal condition is likely to lead to earlier treatment and reduced mortality.

REFERENCES:

Disclosure of Interests: Ethan Sen: None declared, Beverley Almeida: None declared, Louise Moran: None declared, Charlene Foley: None declared, Nagla Abdelrahman: None declared, Rosie Close: None declared, Ema-Louise Long: None declared, Joshua Bennett: None declared, Jason Palman: None declared, Catriona Anderson: None declared, Kirsty McLellan: None declared, Samundeeswari Deepak: None declared, Kathy Gallagher: None declared, Peter Bale: None declared, Kamran Mahmood: None declared, Clare Pain: None declared, Flora McFerlane: None declared, Athimalaipet Ramanan Consultant for: AbbVie, UCB, Sobi, Eli Lilly, Speakers bureau: Speaker fees/honoraria from Abbvie, Sobi, Eli Lilly and UCB, Speakers bureau: AbbVie, UCB, Sobi, Eli Lilly, Rachel Tattersall: None declared.


CLINICAL PRESENTATION, GENETIC ANALYSIS AND IFN-Score in Patients with Undefined Interferonopathies

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Background: In the last years, an expanding group of complex genetic disorders characterized by disturbance of the homeostatic control of IFN-mediated immune responses, have been identified, so called type I interferonopathies. An increased expression of type I IFN regulated genes, IFN signature (IS), is described in these conditions. IS represent a useful tool in clinical practice to classify patients with suspected interferonopathies.

OBJECTIVES: To evaluate the correlation between clinical presentation, genetic analysis and IFN-score in 10 patients with undefined interferonopathies.

METHODS: Patients with suspected interferonopathy based on the presence of typical clinical manifestations (neuropsychiatric, mucocutaneous symptoms), laboratory parameters (complement deficiency, low platelet count, presence of autoimmunity), instrumental abnormalities (cerebral calcification), were screened for the IFN-score. Defined IFN-mediated diseases were excluded. Patients presenting with a high IFN-score value (above a fixed cut-off of 10) underwent genetic screening by running a panel of 24 genes known to be involved in interferonopathies.

RESULTS: 10 patients with suspected interferonopathy followed in a single pediatric rheumatology center were included. 7/10 presented with recurrent episodes of fever (table). Patient 2, 3 and 7 displayed neurological manifestation resembling inflammatory bowel diseases were described while patients 5, 7 and 10 suffered from recurrent abdominal pain, diarrhoea and patient 10 from hypertransaminasemia. Half of the patients complained arthromyalgia; arthritis developed in patient 2. Cutaneous involvement presented in 3 patients (1,3,6) respectively with a widespread panniculitis of trunk and limbs, aspecific vasculitis and Schönlein Henoch purpura. Other cutaneous manifestation were urticarial rash (pt 2) and an erythematous, desquamative confluent eczema (pt 4). Autoimmun-ity was confirmed in 2/10 patients. Two patients (4, 6) had an immunological defect with recurrent infections. The genetic analysis resulted negative in patients 1 and 7 and is still ongoing in patients 5, 6 and 8. Patients 2,3,4,9 and 10 carried one mutation in at least one IFN correlated gene not confirming the diagnosis. All patients presented an increased IS ranging from 14,2 to 172,5.

CONCLUSION: An elevated IFN-score represent a useful instrument in the clinical practice to classify patients with suspected interferonopathy. It may represent an important tool to select those patients to be genetically screened with a defined panel of interferonopathies correlated genes. In those patients in which the genetic analysis result negative, the presence of IFN signature might suggest a type I interferonopathy.
of a positive IFN-score, confirming an activation of this inflammatory path- way, may guide the clinicians in the management of these patients and may support therapeutic decisions.

Disclosure of Interests: S. Federici: None declared, Gian Marco Mor- enti: None declared, Chiara Passarella: None declared, Claudia Bracaglia: None declared, Camelia Gerarda Luana Raffaele: None declared, Fabrizio De Benedetti Grant/research support from: Abbvie, SOBI, Novimmune, Roche, Novartis, Sanofi, Pfizer, Antonella Insalaco: None declared


FRID543 EFFICACY AND SAFETY OF INTRAVENOUS GOLIMUMAB IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS: RESULTS FROM A PHASE 3 OPEN-LABEL STUDY

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Background: Canakinumab is approved for the treatment of systemic juvenile idiopathic arthritis (sJIA) and also has demonstrated efficacy in the treatment of polyarticular juvenile idiopathic arthritis despite methotrexate therapy through 28 weeks of treatment. Methods: A multicenter, Phase 3, single arm, open-label trial was con- ducted using intravenous golimumab at a dose of 80mg/m2 given at weeks 0 & 4, then every 8 weeks thereafter, in pediatric patients ages 2-17 years old with active polyarticular juvenile idiopathic arthritis despite methotrexate therapy. Patients received commercial MTX weekly at same BSA-based dose as at time of study entry. All the results below are based on full analysis set which includes all patients who received at least 1 dose of study agent. Results: 180 patients were screened (130 enrolled, 127 treated) with the first patient screened on 22Dec2014; last patient first treated 26Dec2017, & last patient’s Wk28 visit was 09Jul2018. Proportion of JIA ACR 30,50,70, & 90 responders at Wk28 was 83.5%,79.5%,70.1%, & 46.3%, respectively. 29.1% of patients met criteria for inactive disease at Wk28. Median change from baseline for JADAS 10, 27, & 71 was -14.20, -16.60, & -20.32, respectively at Wk28. JADAS 10, 27, & 71 minimal disease activity was met by 15% of patients at Wk28. Proportion of patients experiencing at least 1 treatment-emergent AE through Wk28 was 77.2%. MedDRA system organ class with highest inci- dence of AEs was Infections & infestations (57.5%); most commonly reported AE upper respiratory tract infection (17.3%); then nasopharyngitis (15.5%). Six patients experienced serious AEs through Wk28: Herpes zos- ter disseminated, Infective exacerbation of bronchiectasis, Sepsi, Var- cella, Mycosis fungoides, & Suicidal ideation. These events resulted in permanent discontinuation of intravenous golimumab, except for Varicella. Conclusion: Intravenous golimumab delivered at a dose of 80mg/m2 at weeks 0 & 4 then every 8 weeks thereafter and appears to be effective in these patients with a safety profile similar to other TNF inhibitor therapies.

Disclosure of Interests: Niccolò Ruperto Grant/research support from: The Gaslini Hospital, where NR works as full-time public employee, has received contributions (> 10,000 USD each) from the following industries in the last 3 years: BMS, Eli-Lilly, GlaxoSmithKline, F Hoffmann-La Roche, Janssen, Novartis, Pfizer, Sanofi. This funding has been re-invested for the research activities of the hospital in a fully independent manner, without any commitment with third parties. Consultant for: Received honoraria for consultations or speaker bureaus (< 10,000 USD each) from the following pharmaceutical companies in the last 3 years: Abylixx, Abb-Vie, AstraZeneca-MedImmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sinergie, Sobi and Takeda. Speakers bureau: Received honoraria for consultations or speaker bureaus (< 10,000 USD each) from the following pharmaceutical companies in the past 3 years: Abylixx, Abb-Vie, AstraZeneca-MedImmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sinergie, Sobi and Takeda. Alberto Spindler: None declared. César Francisco Pacheco Tena Grant/research support from: Janssen Research & Development, LLC, Ingrid Louw Consultant for: Advisory committee: Roche, Novartis, Pfizer, Gabriel Vega Cornejo Grant/ research support from: I currently have no conflicts of interest, I am only setting protocols for the pharmaceutical industry with Parexel, Sanofi and Bristol-Myers Squibb., Daniel Kingsbury Grant/research support from: Clini- cal trial support from Bristol-Myers Squibb, Michael Clark Chair/Shareholder of Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Karen Bensley Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Xiaoming Li Shareholder of: Johnson & Johnson, Employee of: Janssen Research & Development, LLC, Hermine Brunner Grant/research support from: Bristol-Myers Squibb, Pfizer, Consultant for: Pfizer, Bristol-Myers Squibb, Janssen, Novartis, Lilly, Roche, GlaxoSmithKline, Sanofi, Speakers bureau: Novartis, Roche


FRID544 EFFICACY AND SAFETY OF CANAKINUMAB IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS—EXPERIENCE USING DATA OF THE BIKER REGISTRY

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Background: Canakinumab is approved for the treatment of systemic juvenile idiopathic arthritis (sJIA) older than 2 years. Objectives: The aim of the German Biokinetics Registry (BiKeR) is the surveil- lance of JIA patients exposed to biologics. Methods: Baseline demographics and disease activity parameters were documented. Efficacy was determined using the JADAS and the proposed criteria for inactive disease on medication. Safety assessments were based on reports of adverse events (AE). All reports have been coded according to MedDRA. Results: 48 sJIA patients with 82.5 patient-years (PY) of exposure to Canakinumab were recorded in the German BiKeR registry. The total observation time (from date of first dose until last follow-up, censored, if another biologic was started) was calculated with 109.9 PY. The cohort treated with Canakinumab had experienced long disease dura- tion of 2.9±3.8 years (mean ± SD), 21 (44%) were pre-treated with methotrexate, 10 (21%) with Etanercept, 3 (6%) with Adalimumab, 18 (38%) with Anakinra and 19 (40%) with Tocilizumab. Concomitantly, 9 (18.8%) received methotrexate, 22 (45.8%) NSAIDs and 23 (48%) sys- temic corticosteroids. At last follow-up upon treatment, 48.4%/44%/42%/38% of patients reached PsA.CRD30/50/70/90 improvement. 8 patients (16.7%) had inactive disease according to the Wallace criteria. The median (IQR1-IQR3) JADAS10 score decreased from 12.6 (6.2-15.8) at baseline to 5.0 (0.0-2.8). During ongoing treatment, approximately 82% of patients achieved a JADAS defined minimal disease activity; while 64% reached a JADAS defined remission at last follow-up. 125 adverse events (AE) were recorded (114 events/100PY [95% CI 96- 136]). Of these, 22 qualified as serious adverse events (SAE) (20/100PY [13-30]). 100 AEs were observed during exposure or up to 90 days follow- up after the last exposure to Canakinumab (121/100PY [99-147]). 19 qualified as SAE (23/100PY [15-36]). Adverse Events of Special Interest were serious and medically important infection (n=4), cytopenia (n=4), macrophage activation syndrome (n=3). There was no opportunistic infection, intestinal perforation, anaphylaxis or other hypersensitivity, thrombolic event, evolving autoimmune disease, car- diac or cerebral event, bleeding, malignancy, or death. A total of 38 patients (79%) discontinued treatment, 8 (17%) due to lack or efficacy, 16 (33%) due to remission and 2 (4%) because of intolerance. Conclusion: The current analysis adds to the established safety profile of Canakinumab and demonstrates that safety was comparable and consis- tent with the overall AE profile of Canakinumab in paediatric patients. MAS occurred in 3 sJIA patients and might be a JIA-associated fea- ture. Infections were the most frequent AE, but only two serious infec- tions were reported. No new safety signals specific to the paediatric population were identified for Canakinumab; the risk profile of Canakinumab remains positive for the approved paediatric indication sJIA.

REFERENCES:
HEMODYNAMIC MEASUREMENTS AND ARTERIAL TRAJECTORIES OF DISEASE ACTIVITY OVER THE FIRST THREE YEARS FOLLOWING JUVENILE IDIOPATHIC ARTHRITIS DIAGNOSIS

Stephanie Sloop-Worall, Kimme Hygg, Lucy Wedderburn, Wendy Thomson, Nophar Gelman. The University of Manchester, Centre for Health Informatics, Manchester, United Kingdom; The University of Manchester, Arthritis Research UK Centre for Epidemiology, Manchester, United Kingdom; Central Manchester University Hospitals NHS Foundation Trust, Manchester Academic Health Science Centre, NIHR Manchester Musculoskeletal Biomedical Research Centre, Manchester, United Kingdom; Great Ormond Street Hospital NHS Foundation Trust, Paediatric Rheumatology, London, United Kingdom; NIHR Great Ormond Street Hospital Biomedical Research Centre, London, United Kingdom; The University of Manchester, Arthritis Research UK Centre for Genetics and Genomics, Manchester, United Kingdom; The University of Manchester, The Manchester Molecular Pathology Innovation Centre, Manchester, United Kingdom

Background: The advent of biological therapies and early aggressive treatment strategies have drastically changed prognoses for children and young people (CYP) with juvenile idiopathic arthritis (JIA). Clinical trials and observational research have demonstrated improvements in disease for the majority, but not all, CYP over time. It is not currently known what the patterns of disease activity are in CYP with JIA and how these cluster over time.

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Results: 63 JIA subjects and 50 healthy controls were included, mean age 11.5 ± 2.8 vs 10.7 ± 3.2 years (p = 0.17) and 70% vs 54% females, respectively. Both groups were also similar (p > 0.05) for nutritional state, sedentary lifestyle, smoking habits and family history of cardiovascular risk. Table 1 show lipid profile of both groups. Subtypes of JIA were: RF positive polyarthritis (29%), RF negative polyarthritis (29%), oligoarthritis (19%), enthesitis-related arthritis (14%) and systemic arthritis (9%). Mean time of disease evolution was 4 ± 3 years. There were no significant differences between groups in the main hemodynamic parameters (table 2). When comparing inactive vs active disease and active disease vs controls there were no differences either, we found a discrete trend to less carotid distensibility and higher cfPWV in patients with active disease compared to controls [0.63 ± 0.17 mm vs 0.66 ± 0.15 mm (p = 0.94) and 6.12 ± 2.86 m/s vs 5.42 ± 0.75 m/s (p = 0.33), respectively]. 59% of subjects with JIA were inactive according to the ILAR classification (9%). Mean time of disease evolution was 4 ± 3 años. There were no differences either, we found a discrete trend to less carotid distensibility and higher cfPWV in patients with 0-4 years than in patients with >4 years of evolution (p = 0.01).

**TABLE 1. LIPOID PROFILE**

<table>
<thead>
<tr>
<th>LIPID</th>
<th>JIA</th>
<th>CONTROLS</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triglycerides</td>
<td>94 ± 56</td>
<td>85 ± 36</td>
<td>0.22</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>141 ± 22</td>
<td>152 ± 26</td>
<td>0.06</td>
</tr>
<tr>
<td>HDL cholesterol</td>
<td>45 ± 12</td>
<td>47 ± 10</td>
<td>0.36</td>
</tr>
<tr>
<td>LDL cholesterol</td>
<td>77 ± 21</td>
<td>87 ± 22</td>
<td>0.01</td>
</tr>
<tr>
<td>VLDL</td>
<td>18 ± 11</td>
<td>17 ± 7</td>
<td>0.52</td>
</tr>
</tbody>
</table>

†Mann-Whitney U test.

Finally, cfPWV was higher in patients with 0-4 years than in patients with >4 years of evolution (p = 0.01).

**TABLE 2. HEMODINAMIC MEASUREMENTS**

<table>
<thead>
<tr>
<th>MEASUREMENT</th>
<th>JIA</th>
<th>CONTROLS</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>cIMT (mm)</td>
<td>0.42 ± 0.16</td>
<td>0.40 ± 0.70</td>
<td>0.11</td>
</tr>
<tr>
<td>Carotid distensibility</td>
<td>0.64 ± 0.16</td>
<td>0.66 ± 0.15</td>
<td>0.78</td>
</tr>
<tr>
<td>cfPWV (m/s)</td>
<td>5.77 ± 2.86</td>
<td>5.42 ± 0.75</td>
<td>0.66</td>
</tr>
<tr>
<td>AIx (%)</td>
<td>69 ± 15</td>
<td>69 ± 12</td>
<td>0.64</td>
</tr>
</tbody>
</table>

†Mann-Whitney U test.

Conclusion: We found a tendency to increased cardiovascular risk when the disease has more than 4 years of evolution, specially in patients with persistent active disease. Traditional and non-traditional cardiovascular risk factors add up in this population. We need longterm follow-up studies.

REFERENCES:

Disclosure of Interests: Jorge E. Rubio Silveira Grant/research support from: Grants from Roche and Abbvie for some national meetings, C. Araceli Arellano Valdez Grant/research support from: Grants from Roche for multiple national and international meetings., Speakers bureau: different conferences about Tocilizumab in meetings., Carlos Ramos Becerra: None declared, Myriam Mendez Nuñez: None declared, David Cardona Müller: None declared, Oscar Mares Flores: None declared, Priscilla Vega Garcia: None declared, Fernando Grover Páez: None declared, Alberto Taciuco Parra: None declared, Markus Hufnagel: None declared, Wolfgang Emminger: None declared, Ariane Klein: None declared

Objectives: To explore latent patterns of clinical juvenile arthritis disease activity scores (cJADAS) following a diagnosis of JIA.

Methods: CYP with JIA were selected if enrolled in the Childhood Arthritis Prospective Study (CAPS), a UK multicentre inception cohort, before January 2015. cJADAS10 scores were calculated based on components (active joint count up to 10, physician global, patient/parent global) collected at diagnosis, six months, one year and then annually to three years. CYP were excluded if no cJADAS10 scores were available within this time frame. Group-based trajectory models were constructed to model latent groups of cJADAS10 scores. Linear, quadratic and cubic polynomials were tested, with one to six trajectories tested within each polynomial group. An optimal model within each polynomial group was selected using Bayesian Information Criteria. The final model was then selected from this shortlist based on model parsimony and clinical plausibility.

Results: Of 1183 CYP selected, the majority were female (65%) and of white ethnicity (90%) with oligoarticular JIA the most common JIA category (45%). The optimal model identified five cJADAS10 quadratic trajectories (Figure 1): Low-low (59%, initial cJADAS10 median: 6.1), moderate-low (16%, initial cJADAS10 median: 11.5) and three groups with high disease activity at initial presentation (initial median cJADAS10: 17.7 to 19.1). A high-low group experienced the greatest improvement (15%, median improvement 17.2 (IQR 13.7 to 20.1)), and a high-moderate group lesser improvement (8%, median improvement 7.3 (IQR 0.8 to 9.0)). A final high-low-high group experienced improvement to one year followed by disease relapse (5%).

Conclusion: Disease activity in CYP with JIA does not improve in a uniform manner following initial presentation to paediatric rheumatology. Five latent trajectory groups have been identified, with three of these displaying different patterns following initial high disease activity at diagnosis. Identifying distinguishing characteristics for each group may aid the stratification of different treatment strategies to facilitate personalised medicine in JIA.

Figure 1. Latent trajectories of cJADAS10 scores in young people with JIA over the first three years following diagnosis

Acknowledgement: On behalf of CAPS and CLUSTER

Disclosure of Interests: Stephanie Shoop-Worrall Grant/research support

Disclosure of Interests: : Jessica Tibaldi: None declared, Yasser El Miedany: None declared, Priyankar Pal: None declared, Soamarat Vilaiyuk: None declared, Raju Khubchandani: None declared, Claudia Braccaglia: None declared, Tapan K Sabui: None declared, Sujata Sawhney: None declared, Ricardo Russo: None declared, Flávio R. Szajnbok: None declared, Floriano Cinzas: None declared, Francesca Minoia: None declared, Motsesom A. Alsuwiti: None declared, Ekaterina Alexeeva: None declared, Mikhail Kostik: None declared, Maria Cristina Maggio: None declared, Nicolo Ruperto: None declared, Alessandro Consolaro: None declared, Angelo Ravelli: None declared, G. Gaslini: None declared, G. Gaslini: None declared, G. Gaslini: None declared, G. Gaslini: None declared, G. Gaslini: None declared, G. Gaslini: None declared.

References: The sJADAS was found to be a valid instrument for the assessment of disease activity in sJIA. This composite score is feasible and easily applicable in standard clinical practice, which should result in its widespread acceptance and use. The strong responsiveness to clinical change over time indicates that the sJADAS is suitable to assess therapeutic response in sJIA clinical trials.

Disclosure of Interests: : Jessica Tibaldi: None declared, Yasser El Miedany: None declared, Priyankar Pal: None declared, Soamarat Vilaiyuk: None declared, Raju Khubchandani: None declared, Claudia Braccaglia: None declared, Tapan K Sabui: None declared, Sujata Sawhney: None declared, Ricardo Russo: None declared, Flávio R. Szajnbok: None declared, Floriano Cinzas: None declared, Francesca Minoia: None declared, Motsesom A. Alsuwiti: None declared, Ekaterina Alexeeva: None declared, Mikhail Kostik: None declared, Maria Cristina Maggio: None declared, Nicolo Ruperto: None declared, Alessandro Consolaro: None declared, Angelo Ravelli: None declared, G. Gaslini: None declared, G. Gaslini: None declared, G. Gaslini: None declared, G. Gaslini: None declared, G. Gaslini: None declared.

References: The sJADAS was found to be a valid instrument for the assessment of disease activity in sJIA. This composite score is feasible and easily applicable in standard clinical practice, which should result in its widespread acceptance and use. The strong responsiveness to clinical change over time indicates that the sJADAS is suitable to assess therapeutic response in sJIA clinical trials.
EFFICACY AND SAFETY OF TOCILIZUMAB IN SYSTEMIC AND POLYARTICULAR YOUNG IDIOPATHIC ARTHRITIS – DATA OF THE BIKER REGISTRY

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Background: Since 2011 Tocilizumab is approved for systemic juvenile idiopathic arthritis (JIA) and since 2013 for polyarticular JIA

Objectives: To describe efficacy and safety of Tocilizumab in clinical practice in polyarticular (pJIA) and systemic JIA (sJIA) patients using the German Biologics registry (BíkerR).

Methods: Baseline demographics and disease activity parameters have been documented. Efficacy was determined using the JADAS10 prospectively. Safety assessments were based on adverse events reports (AE) processed according to MedDRA

Results: Until October 1, 2018, 345 JIA patients treated with Tocilizumab were registered, representing 635 patient-years (PY) of observation. The cohort treated with Tocilizumab had experienced disease duration of 5.5 +/-4.3 years (mean+/-SD) for sJIA and 5.9+/-4.1 years for pJIA. sJIA/pJIA patients received pretreatment with MTX 72%/95%, Enanercept 30%/85%, Canakinumab 2%/0%. Concomitantly, sJIA/pJIA patients received NSAIDs 64%/57%, systemic steroids 72%/35%, MTX 55%/54%, other DMARDs 4%/8%. At last follow-up, 63%/80%/51%/43% of sJIA and 56%/49%/40%/30% of sJIA patients reached JADAS30/50/70/90 criteria. After 2 years of treatment JADAS remission was reached by 50%/43% and JADAS minimal disease activity by 67%/67%.

586 AE were reported during exposure plus 90 days of observation. The rate was significantly higher in sJIA (104/100PY [95% CI 92-119]) than in pJIA patients (79 [79-90]; RR 1.3; p=0.003). 75 qualified as serious AE (SAE) with a higher rate in sJIA (22[16-29]) vs. 8 [5-12]; RR 2.6; p=0.001). The most frequent AE in the sJIA/pJIA cohort were grouped in the MedDRA SOC infections and infestations (n=92/76). Compared to pJIA, rates were significantly higher in sJIA patients for blood and lymphatic (RR 2.4; p=0.019), immune system (RR 2.6; p=0.04), infections & infestations (RR 1.7; p=0.001) and nervous system disorder (RR 2.6; p=0.012) and lower for general and administration site (RR 0.4; p=0.023). 169 patients (49%) discontinued treatment, 17% due to remission, 22% due to lack of efficacy and 9% because of intolerance.

Conclusion: The analysis adds to the established safety profile of tocilizumab in paediatric patients with systemic & polyJIA. Differences were notable between pJIA and sJIA cohorts, the latter with higher rates of total number of adverse events, serious AE, infections and cytopenias, probably due to higher doses or shorter application intervals. No new safety signals specific to the paediatric population were identified in this large cohort of JIA patients.

REFERENCES:

SARILUMAB, A HUMAN MONOCLONAL ANTIBODY TO THE INTERLEUKIN-6 (IL-6) RECEPTOR, IN POLYARTICULAR-COURSE YOUNG IDIOPATHIC ARTHRITIS (PCJIA): A 12-WEEK MULTINATIONAL OPEN-LABEL DOSE-FINDING STUDY

Fabrizio De Benedetti1, Immaculada Calvo Padare2, Nadina E. Rubio Pérez2, Alexey Maschari3, Pierre Quartier4, Zbigniew Zubér5, Marina Stanislavv6, Raul Bantía7, Daniel Clemente Garuño8, Gabriel Vega Corujo9, Nancy Liu10, Christine Xu11, Angeliki Giannoulou12, Bolariye Akirade12, Lydie Baret-Cormel13, on behalf of DRI13925 investigators. 1Spedale Pediatrico Bambino Gesù, Rome, Italy, 2Instituto de Investigación Sanitaria La Fe, Valencia, Spain, 3University Hospital Dr. José Eleuterio González, Monterrey, Mexico, 4Centre of Pediatric Hematology, Oncology and Immunology, Moscow, Russian Federation, 5Necker Hospital, Paris, France, 6Andrzej Frycz Modrzewski Krakow University, Krakow, Poland, 7IVA Nasonova Research Rheumatology Institute, Moscow, Russian Federation, 8Bioreuma, Concepción, Chile, 9Hospital Infantil Universitario Niño Jesús, Madrid, Spain, 10CREA de Guadalajara, Jalisco, Mexico, 11Sanofi, Bridgewater, NJ, United States of America, 12Regeneron, Tarrytown, NY, United States of America, 13Sanofi, Paris, France

Background: Sarilumab blocks IL-6 from binding to membrane and soluble IL-6 receptor-a. Sarilumab is approved for adults with rheumatoid arthritis (RA) and is being investigated in a Phase 2 trial (NCT02776735)
in 2–17-year-old patients (pts) with pcJIA, comprising rheumatoid-factor (RF)-positive and RF-negative polyarticular and extended oligoarticular JIA.

Objectives: Evaluation of pharmacokinetics (PK), pharmacodynamics (PD), safety, and efficacy of 3 subcutaneous (SC) sarilumab doses in pcJIA.

Methods: A 12-week dose-finding study was performed to identify an appropriate sarilumab dose for use in the pcJIA population. Pts were divided by body weight into 2 groups: A (30–60 kg) and B (10–30 kg), and received sequential ascending doses of sarilumab, Dose 1 (Group A/B): 2.0/2.5 mg/kg qw; Dose 2 (Group A/B): 3/4 mg/kg qw; and Dose 3 (Group A/B): 2.0/2.5 mg/kg qw. Pts were targeted to achieve similar exposure to adult RA doses (150 mg qw2, 200 mg qw2, and 150 mg qw).

Primary outcome was PK; secondary outcomes were safety, PD, and efficacy of sarilumab.

Results: 42 pts enrolled (20/22 in Groups A/B); mean age was 13.0±5.2 years. At baseline, mean pcJIA duration, number of active joints, and JADAS27-CRP were 4.6±1.7 years, 17.2±11.0, and 22.2±19.1, in Groups A/B, respectively. As in adult pts, sarilumab exhibited nonlinear PK with target-mediated drug disposition (TMDD). Following repeated SC administrations, exposure increased in a greater than dose-proportional manner and accumulated 1.9–4.5 fold over 12 weeks. Sarilumab exposure was similar in both weight groups for each dose (Figure), and comparable to corresponding adult doses. Treatment (AE) rates were: for A in Groups 1, 2, and 3, respectively: JADAS27-CRP mean % changes from baseline in Doses 1, 2, and 3 were -74.6%, -87.9%, and -87.9%, respectively.

Conclusion: Sarilumab exhibited nonlinear PK with TMDD. Doses tested in pcJIA yielded similar exposure in both weight groups and were comparable to equivalent doses in adults with RA. All dose regimens proved effective for decreasing disease activity. Safety profile was consistent with class effects; higher incidences of neutropenia were observed with Dose 1 (Group A/B): 2.0/2.5 mg/kg qw; Dose 2 (Group A/B): 3/4 mg/kg qw; and Dose 3 (Group A/B): 2.0/2.5 mg/kg qw. Pts were targeted to achieve similar exposure to adult RA doses (150 mg qw2, 200 mg qw2, and 150 mg qw). Primary outcome was PK; secondary outcomes were safety, PD, and efficacy of sarilumab.
BACKGROUND: Research on Juvenile Idiopathic Arthritis (JIA) should have the primary goal to ultimately improve the lives of the affected patients and help health professionals provide the best care for them. Therefore, these end users of research evidence – patients, carers (parents/caregivers) and clinicians – should be included in the process of identifying research priorities. Importantly, patients and carers can use their unique experiential knowledge from living with the disease to give vital input to researchers in designing a study. Combining this input with the goal of research priorities setting in different regions are needed in order to provide more relevant data on issues that matter most.

METHODS: The method for research priority setting developed by the James Lind Alliance (JLA) is used [3]. This method consists of several steps with the end goal of creating a top 10 list of research priorities agreed on by all parties. First, a steering group with equal representation of patients, parents and clinicians was assembled. We are now in the process of collecting research questions through an online survey. Focus groups are being held to ensure the inclusion of younger patients. Questions will be clustered and checked against the evidence. Next, the process of interim priority setting will follow, in which a shortlist of up to 30 questions will be assembled. During a final workshop in which all parties are equally represented, the top 10 research priorities will be established.

RESULTS: A total of 321 PFAPA, 118 FMF and 45 JIA patients with mean age of 7.23±2.9, 14.7±3.09, 13.5±4.8 years, respectively, were included in the study. A 45% (146/322) of PFAPA, 50% (59/118) of FMF and 58% (23/45) of JIA patients were female. We found quite high sensitivity (90%) of newly proposed PFAPA criteria: 289 out of 321 (90%) patients followed up as PFAPA syndrome fulfilled newly proposed PFAPA criteria, as well. When applied to patients diagnosed with FMF and JIA, 46 out of 118 (39%) FMF and 10 out of 45 (22%) JIA patients also fulfilled newly proposed PFAPA criteria. Specificity of recently proposed PFAPA criteria was found to be 61% and 77%, among FMF and JIA patients, respectively. Positive predictive value was 86% and 97%, negative predictive value was 69% and 50% for FMF and JIA patients, respectively.

CONCLUSION: Recently proposed PFAPA criteria have satisfactory high sensitivity. Specificity of recently proposed criteria is still under expectation in regions endemic for FMF. Multicentric studies with higher patients’ number in different regions are needed in order to provide more relevant data on performance of newly proposed PFAPA criteria.

REFERENCES:

Disclosure of Interests: None declared
CANAKINUMAB AS A FIRST-LINE AND SECOND-LINE BIOLOGIC FOR TREATMENT OF SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS IN CHILDREN UNDER 4 YEARS OF AGE

Ekaterina Alneyeva1, Tatiana Dvoryakovskyakaya1,2, Ksenia Isaeva1, Rina Denisova1, Margarita Soloshenko1, Anna Fetisova1, Anna Mamutova1, Maria Rudnitskaya1, Dariya Vankova1, Ivan Krulin1, Kristina Chibisova1, Alina Alshevskaya3, Andrey Moskalev3, Ekaterina Alexeeva1,2, Tatyana Dvoryakovskaya1,2, Ksenia Isaeva1

Background: Development of biologics and their launching into clinical practice has yielded significant progress in pediatric rheumatology. Nevertheless, treatment of severe disorders, and systemic JIA in particular, still remains a challenge. JIA often has the early-onset form. If its course is aggressive and persistent, patients exhibit poor response to treatment with first-line biologics. Effectiveness of the second-line and subsequent biologics, as well as the optimal sequence of prescribing drugs belonging to different classes to children younger than 4 years, remains an open question.

Objectives: To compare the efficacy of canakinumab (CAN) in children with sJIA younger than 4 years (in biologic-naïve patients and when prescribed as a second-line biologic).

Methods: The study was conducted as a subanalysis of the prospective cohort study to evaluate the efficacy of biologics in children with sJIA. Comparative analysis involved 17 patients who had initiated CAN treatment at the National Medical Research Center of Children’s Health (Moscow, Russia) when aged < 4 years (9 biologic-naïve patients (the naïve group) and 8 patients switched from tocilizumab therapy (the switched group)). Treatment efficacy was evaluated according to the dynamics of clinical and laboratory signs using the ACRPedri criteria. The Wallace criteria were used to evaluate whether or not remission had been achieved. Treatment safety was evaluated according to the data presented in the Adverse Event Reports.

Results: At baseline, patients had comparable duration and severity of the disease. The biologic proved efficacious already after 4 weeks of treatment. Five (55.6%) patients in the naïve group and 4 (50%) patients in the switched group achieved ACR90 (p=0.999) within one year of treatment. A state of inactive disease according to the Wallace criteria was achieved in one patient in each group, (12.5% and 11.1%, respectively (p=0.999). JADAS-71 decreased significantly from 12.8 (IQR 10.4-16.2) to 4.4 (IQR 2.6-8.0) in the naïve group (p=0.012) and from 11.6 (IQR 8.138) to 2.35 (IQR 1-3.03) in the switched group (p=0.017).

Conclusion: CAN was found to be highly efficacious and have a good safety profile in children younger than 4 years regardless of prior biologic treatment.

DISCLOSURE OF INTERESTS: None declared

DNASE1L3 VARIANT IN HYPOCOMPLEMENTEMIC URTICARIAL VASCULITIS SYNDROME IDENTIFIES A DIFFERENT CLINICAL PHENOTYPE

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Background: Hypocomplementemic urticarial vasculitis syndrome (HUVS) is a rare disease characterized by persistent urticarial lesions and hypocomplementemia associated with systemic features involving musculoskeletal, pulmonary, renal and gastrointestinal systems. Systemic lupus erythematosus (SLE) develops in >50% of patients with HUVS, although the pathogenesis is unknown.

Objectives: We describe 6 paediatric patients with HUVS, three of whom carry a homozygous variant of DNASE1L3 and present a peculiar clinical phenotype.

Methods: A Targeted Resequencing using a panel including genes known to already be mainly associated to Interferonopathies Lupus-like (DNASE1, DNASE2, DNASE1L3, TREX1) on the Illumina NextSeq® platform was performed. All variants identified were confirmed by Sanger sequencing and, when possible, family members were tested to study the segregation of identified variants. We applied in silico studies only to variants with an allele frequency ≤1%.

Results: All patients described are Caucasian and 3 of them are female. Two patients presented at onset with extended cutaneous manifestation, joint and abdominal involvement with cholecytitis. They did not develop renal or pulmonary involvement. In contrast, the other four patients presented a more severe disease. All of them developed renal involvement (from microhaematuria up to nephrotic syndrome) with renal biopsy showing mesangial glomerulonephritis in three patients and pauci-immune glomerulonephritis (ANCA negative) in one. Moreover, two of them developed also pulmonary vasculitis (Table 1). A homozygous DNASE1L3 variant (c.290_291delCA) was identified in three of these patients. All of them were treated with glucocorticoid and dapsone at onset. Cyclophosphamide, mycophenolate mofetil and azathioprine were used in patients with renal involvement. None of them developed SLE.

Table 1. Patients’ clinical characteristics

<table>
<thead>
<tr>
<th>Pt 1</th>
<th>Pt 2</th>
<th>Pt 3</th>
<th>Pt 4</th>
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<tr>
<td>Age at onset</td>
<td>9 y/6 m</td>
<td>12 y</td>
<td>3 y 10 m</td>
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<tr>
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<td>Renal</td>
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</tbody>
</table>

Conclusion: HUVS is very rare disease in childhood. Approximately 50% of HUVS patients develop SLE. Genetic susceptibility to SLE is recognized and DNASE1L3-related SLE have been reported. Özçakar et al. have described 5 children from two families with HUVS who carry the same variant on DNASE1L3 that we report here (1). Our patients confirm that variant in DNASE1L3 can cause HUVS and support the hypothesis that this variant is responsible of a more severe phenotype with major organ involvement (renal and pulmonary). Patients with HUVS need to be flagged very strictly for the risk to develop SLE. Presence of variant in DNASE1L3 can identify patients with more severe disease and high risk to develop major organ involvement. These patients need more aggressive and possibly life-long immunosuppressive treatment.

REFERENCES:

DISCLOSURE OF INTERESTS: Marco Ranalli: None declared, Chiara Passarelli: None declared, Virginia Messia: None declared, Manuela Pardeo: None declared, Emanuela Sacco: None declared, Antonella Insalaco: None declared.
Influence of anti-Tumor Necrosis Factor (TNF) drug immunogenicity on the treatment effectiveness in juvenile idiopathic arthritis (JIA) using serum calprotectin as a disease activity marker. Multicenter study. ITACA study

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Background: There is a lack of evidence about the loss of efficacy of anti-TNF agents in JIA and its possible relation to the immunogenicity generated. In the last years there has been interest in the role of serum calprotectin in children diseases, including JIA.

Objectives: To assess the immunogenicity and bioavailability of anti-TNF drugs, their relationship with disease activity and the clinical utility of serum calprotectin in monitoring JIA patients.

Methods: This is a 12-month prospective, multicenter, non-interventional, observational study. Patients from 2 to 18 years diagnosed with non-systemic JIA according to ILAR criteria and receiving treatment with IFX, ADA or ETN were included. The patients were evaluated using the CHAQ and the juvenile arthritis disease activity score (JADAS 71) and determination of anti-TNF drug, anti-drug antibody and calprotectin serum levels were performed.

Results: 222 patients were included. At month 12, 181 (81.5%) continued receiving treatment, and 205 (94.5%) had positive serum levels of anti-TNF drug (96.2% of ETN, 93.5% of ADA and 66.7% of IFX) at baseline and at 12 months serum levels were positive in 161 (95.3%) patients (97.5% ETN, 93.2% ADA and 100% IFX). In total, 16 (7.3%) patients presented anti-drug A (1 of 106 anti-ETN, 13 of 109 anti-ADA, 2 of 3 anti-IFX) at baseline and 4 patients (2.4%) (0 of 81 anti-ETN, 4 of 88 anti-ADA, 0 of 1 anti-IFX) at 12 months. Regarding the relationship between anti-TNF levels or anti-drug Abs, disease activity, and functional disability overall, statistically significant differences were not observed between the groups. Patients with high levels of serum calprotectin at the baseline visit (16 of 216) showed higher JADAS-71 score [1.23 (2.06 SD) vs. 2.01 (3.44 SD) and CHAQ [0.11 SD (0.28 SD)] vs. 0.17 (0.40 SD)] compared with normal calprotectin group, although no statistically significant differences were observed (p = 0.066 and p = 0.288) between the groups with a normal and high level of serum calprotectin and the number of patients was small.

Conclusion: The low prevalence of anti-drug Abs observed was in consonance with the high proportion of patients with a positive serum level of anti-TNF drug. These data suggest an appropriate management of the long-term treatment of Spanish JIA patients, who showed a maintained inactive disease/low disease activity state and a very low functional disability state as a consequence of a low immunogenicity and good bioavailability of anti-TNF drugs.

Table 2: JADAS-71 score according to immunogenicity and bioavailability of anti-TNF drugs

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<thead>
<tr>
<th>Serum anti-TNF (Negative)</th>
<th>Serum anti-TNF (Positive)</th>
<th>Anti-drug antibodies (Negative)</th>
<th>Anti-drug antibodies (Positive)</th>
<th>Total</th>
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<td>Baseline</td>
<td></td>
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<tr>
<td>N</td>
<td>22</td>
<td>197</td>
<td>200</td>
<td>19</td>
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<tr>
<td>Mean (SD)</td>
<td>1.52 (2.66)</td>
<td>1.35 (2.29)</td>
<td>1.36 (2.28)</td>
<td>1.99</td>
</tr>
<tr>
<td>p value</td>
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<td>Month 12</td>
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<tr>
<td>N</td>
<td>20</td>
<td>178</td>
<td>182</td>
<td>16</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>2.19 (2.61)</td>
<td>0.94 (1.90)</td>
<td>0.98 (1.97)</td>
<td>2.06</td>
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<td>p value</td>
<td>0.009</td>
<td>0.039</td>
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Disclosure of Interests: Immaculada Calvo Grant/research support from: received research grants from Pfizer, Roche, Novartis, Clementia, Sanofi, MSD, BMS and GSK, Consultant for: Advisory boards: Novartis, AbbVie, Speakers bureau: AbbVie, Roche, Novartis, SOBI, Consuelo Modesto: None declared, Maria Montoro Shareholder of: Maria Montoro is employee of and shareholder in Pfizer, Employee of: Maria Montoro is employee of and shareholder in Pfizer, Begoña Laiz: None declared, Estibaliz Iglesias: None declared, Estefanía Quesada-Massachs: None declared, B Lopez-Montesinos: None declared, R Bou: None declared, M.I. Gonzalez-Fernández: None declared, J Fonnes: None declared, A Rodriguez: None declared, J.J. Sanchez: None declared, J Calzada: None declared, Tamara Rodriguez: None declared, Mireia Lopez-Corbeto: None declared, Susana Gómez Employee of: I am a current employee of Pfizer; Jordi Anton Grant/research support from: JA has received grant/research support, consulting fees and/or honoraria from AbbVie, Alexion, BMS, ChemoCentryx, Gebro, GSK, Novartis, Pfizer, Roche, Sanofi and Sobi.

GENETIC SCREENING IN PATIENTS WITH UNDIFFERENTIATED PERIODIC FEVER SYNDROME

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Background: Autoinflammatory diseases (AID) are a group of hereditary diseases characterised by inflammation periods accompanied with clinical findings such as fever, skin rash, lymphadenopathy, abdominal pain, musculoskeletal symptoms, and with sign of inflammation in the blood. Each disease has own typical clinical findings and they are associated with mutations in specific genes such as in MEFV gene in familial Mediterranean fever (FMF), MVK gene in hyperimmunglobulin D syndrome (HIDS), TNFRSF1A gene in tumor necrosis factor-alpha receptor associated periodic fever syndrome (TRAPS) and NLRP3 gene in cryopyrin associated periodic fever syndrome (CAPS) (1,2). Also in some patients with periodic fever syndrome (PFS), clinical signs of these diseases can be seen but no mutation can be detected in the related genes (3,4). There are also patients exhibit the incomplete phenotype of a disease or overlap signs of more than one AID. The diagnosis of these undifferentiated patients have difficult and may not be possible by a single target gene analysis (5). Screening of the periodic fever syndrome (PFS) panel including various AID genes may be beneficial to define the atypical cases. Molecular genetics has an important role for lead to diagnosis in these patients.

Objectives: The aim of this study was to investigate the genotypic diagnosis in patients with non-characteristic PFS findings for any AID.

Methods: This is a prospective study and conducted between June 2016 and December 2016. Next-generation sequencing (NGS) analysis was performed by using “Fever and Autoinflammatory Syndrome panel: Panel by Sophia Genetics” including 8 genes (MEVF, MVK, NLRP3, NLRP12, TNFRSF1A, TNFRSF11A, LTIP2 and PSTPIP1) in 30 patients with undifferentiated PFS. Clinical features and genetic results were evaluated together and final diagnoses were determined.

Results: Thirty patients included in the study did not have typical clinical features for any of the eight monogenic diseases in the PFS panel. In the result of the genetic screening; disease-causing mutation was found in MEFV gene in 12 patient, in NLRP3 gene in four patient, in NLRP12 gene in two patient and in MVK gene in one patient. Also, genetic variants of uncertain significance (VUS) in different genes were shown in five patient. No mutation was detected in remaining six patient. The final diagnosis was made by both phenotypic and genotypic data. 12 patients were diagnosed with FMF, four were FCAS, two were FCAS2, one was TRAPS and one was HIDS. Patients with negative genetic screening or had mutation as VUS, were followed as undifferentiated PFS.

Conclusion: Autoinflammatory diseases may not always be appear with typical clinical findings of related diseases. In such patients, target gene sequencing and detection of underlying disease can be challenging. Our study has shown that the NGS analysis may help to determined the diagnosis in patients with non-characteristic PFS findings for any AID.

REFERENCES:

Disclosure of Interests: None declared

NOVEL G-CSF RECEPTOR MUTATION CAUSING NEUTROPAENIA AND AUTO-IMMUNE DISEASE

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Background: Novel G-CSF receptor mutation causing neutropaenia and auto-immune disease:

We present 2 brothers, born to consanguineous (second cousin) parents, with persistent, moderate neutropaenia secondary to a previously undiagnosed mutation in the CSF3R gene.

Objectives: Both brothers had associated autoimmune phenomena – one with poly-arthicular arthritis and the other with kerato-conjunctivitis.

Methods: Patient A is a 13-year old boy who was referred with a history of recurrent knee swelling. His father described that, from an early age, whenever he had a viral illness he developed marked swelling of his knee which settled spontaneously over a few days. In between episodes he remained completely well and fully active. Growth was normal and there was no history of recurrent or unusual infections. U&S & MRI confirmed the presence of large effusions in the knees during these episodes.

On examination A had clinical evidence of synovitis in his right knee which settled spontaneously over 3 weeks. However a few months later his arthritis subsequently extended to involve his other knee, both hips, elbow and shoulder. He was treated with Etanercept with good clinical response.

Patient H is the younger brother of A. He was diagnosed with severe eczema at age 3 which needed treatment with topical steroids & tacrolimus, along with oral montelukast, to control. He subsequently developed vernal kerato-conjunctivitis which required high-dose cyclosporine & steroid eye-drops to control.

Initial Investigations: Both A and H had been noted from an early age to have neutropaenia. This was initially noted during admission for a viral illness but repeat samples over several years showed persistent neutropaenia (Patient A 0.27 – 0.94, patient H 0.9 - 1.1). Patient A also had markedly raised ESR (range 27 – 120mm/hr) noted during episodes of arthritus. All other investigations were reported as normal.

Results: Whole exome sequencing of patient A revealed a novel homozygous single nucleotide variant c.909C>A affecting exon 8 of the CSF3R gene on Chr. 1. This was confirmed by Sanger sequencing, and the same homozygous mutation was found in patient H.

Patient H was noted to have neutropaenia. This was initially noted during admission for a viral illness but repeat samples over several years showed persistent neutropaenia (Patient A 0.27 – 0.94, patient H 0.9 - 1.1). Patient A also had markedly raised ESR (range 27 – 120mm/hr) noted during episodes of arthritus. All other investigations were reported as normal.

Conclusion: G-CSF is a crucial cytokine that induces proliferation, differentiation, & survival of myeloid progenitors. This variant has not, to our knowledge, been previously described. It is compatible with low level neutrophil production, as in our patients, which may be boosted by GM-CSF, but not G-CSF.

Other recessive loss-of-function mutations in CSF3R have been found in patients with severe congenital neutropaenia. These patients are, unsurprisingly, refractory to rhG-CSF treatment.

It is not clear how this mutation is linked to autoimmunity in these 2 boys. Theoretically both G-CSF, which is likely to be circulating in high concentrations, and GM-CSF, which may be increased to stimulate neutrophil production, have been shown to have pro-inflammatory effects, and indeed are potential targets for future treatment modalities in autoimmune diseases.

Disclosure of Interests: None declared


PREVALENCE OF SUBCLINICAL SACRITISITIS IN YOUNG PATIENTS WITH INFLAMMATORY BOWEL DISEASE REVEALED BY ENTERO-MRI

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Background: Sacritisis is one of the extraintestinal manifestations associated with inflammatory bowel disease (IBD), and may be underdiagnosed especially in the pediatric age. MR-enterography (Enteror-MRI) is currently the gold standard imaging technique for the detection of sacritisis.
the imaging gold standard to assess intestinal disease activity and to detect complications in patients with IBD. Only few studies have been conducted on adult patients with IBD in order to define the role of this technique in assessing sacroiliitis, while no data are available on pediatric patients.

Objectives: To study the prevalence of inflammatory sacroiliitis on MRI performed for intestinal investigation in an IBD pediatric population.

Methods: This is a retrospective study conducted on patients suffering from IBD followed in our gastroenterology department between 2010 and 2018 whose enterocol-RM (1.5 or 3 Tesla, Philips depending from year of scanning) were blindly and independently scored by two readers experienced in pediatric musculoskeletal imaging. Each sacroiliac joint was divided into 4 quadrants. Signs of sacroiliitis were identified according to the ASAS criteria, with a particular attention to the presence of bone marrow edema (using T2 weighted sequences with fat suppression), diffusion restriction in DWI sequences (Diffusion Weighted Imaging) or DWIBS (Diffusion Weighted Imaging with Background Suppression) and post-contrastographic uptake in dynamic acquisitions. Demographics, IBD characteristics, clinical, radiological, and laboratory data were recorded and a dedicated Excel database was constructed. Results were elaborated using descriptive statistics.

Results: A total of 34 patients (10 F, 24 M, age at scanning range 5-20 yrs, median 15) were included in the study, for a total of 59 enterocol-MRI evaluated (some patients were subjected to more than one scan). Two out of 34 patients were affected by Ulcerative Colitis, 32 by Crohn disease. Joint examination resulted negative in all patients, and none complained of articular symptoms including back pain. In 5 IBD patients (4 CD, 1 UC) a monolateral slight degree of sacroiliitis (grade 1) was radiologically identified. They were all males, without clinical laboratory-radiologic inflammatory signs of intestinal activity, with the exception of a patient who presented signs of intestinal and sacroiliac inflammation at his first enterocol-MRI, while 18 months later, at his MRI control under pharmacological treatment, signs of sacroiliitis were still present in the absence of intestinal signs of inflammation.

Conclusion: Asymptomatic sacroiliac involvement therefore can be underdiagnosed in these patients. Enterocol-MRI with specific sequences could be a good tool to detect early signs of sacroiliac inflammation.

REFERENCES:

Disclosure of Interests: None declared

FRIO559 VALIDATION OF NORDIC JUVENILE IDIOPATHIC ARTHRITIS CLINICAL PREDICTION MODELS IN A CANADIAN COHORT

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Background: Validation of clinical prediction tools for juvenile idiopathic arthritis (JIA) in populations different than those in which they were first developed is essential to understand their applicability across healthcare settings.

Objectives: To determine if clinical prediction tools to predict 1) non-achievement of remission off medication and 2) functional disability, developed in the Nordic cohort can be directly applied to JIA patients in the Canadian Research in Arthritis in Canadian Children emphasizing Outcomes (ReACCh-Out) cohort; and to assess performance of the prediction tools if model parameters are fine-tuned to the Canadian cohort.

Methods: Since the Nordic models were developed to predict outcomes 8 years after disease onset but the follow-up of the ReACCh-Out cohort was shorter, we chose to cross-validate the tools in a subpopulation of 513 subjects at the 3 years follow-up (3.75 years after onset). Attainment of remission off medications was determined by a panel of 3 pediatric rheumatologists as previously described and functional disability was defined as a Childhood Health Assessment Questionnaire Disability Index (CHAQ)=0. Missing data was handled with multiple imputation by chained equations and prediction ability was assessed with c-index and Receiver Operator Characteristic (ROC) curves. The Nordic models were first evaluated exactly as published on the entire Canadian cohort. Then we fine-tuned the model coefficients using repeated runs of cross-validation in the Canadian cohort. This way, fine-tuned models were tested in patients not included in the fine-tuning process while also minimizing the standard error of prediction.

Results: In total, 408 of 506 evaluable patients (81%) were not on remission and 137 of 361 evaluable patients (38%) had functional disability at the 3-year visit. The Nordic model for predicting non-achievement of remission had a c-index of 0.68 (95%CI 0.62-0.74) when directly applied, and a c-index of 0.74 (0.70-0.78) when it was fine-tuned for the Canadian population. The latter values are comparable to those reported in the Nordic cohort (median AUC 0.78, IQR 0.72-0.82). Table 1 shows fine-tuned coefficient values along-side the original values. The Nordic model for predicting functional disability had a c-index of 0.57 (0.50-0.63) when directly applied, and fine-tuning failed to improve its performance, a c-index of 0.53 (0.43-0.63). Figure 1 shows ROC curves for fine-tuned models in the multiple splits.

Conclusion: After fine-tuning of coefficients, the Nordic model for prediction of non-achievement of remission had similar prediction ability in Canadian patients with JIA. We could not confirm the validity of the Nordic model for prediction of functional disability in Canadian patients.

REFERENCES:

Table 1. Prediction models for non-remission off medications 3.75 years after JIA onset

<table>
<thead>
<tr>
<th>Variable</th>
<th>Original Nordic</th>
<th>Fine-tuned Canada</th>
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<tr>
<td>Constant</td>
<td>1.58 (SE 0.44)</td>
<td>0.26</td>
</tr>
<tr>
<td>Cumulative active joint count</td>
<td>0.04 (SE 0.05)</td>
<td>0.13</td>
</tr>
<tr>
<td>ESR in mm/L</td>
<td>0.03 (SE 0.02)</td>
<td>-0.01</td>
</tr>
<tr>
<td>CRP &gt; 10 mg/L</td>
<td>-0.07 (SE 0.09)</td>
<td>0.12</td>
</tr>
<tr>
<td>Morning stiffness &gt; 15 min</td>
<td>1.16 (SE 0.45)</td>
<td>0.36</td>
</tr>
<tr>
<td>Physician global assessment</td>
<td>0.16 (SE 0.46)</td>
<td>0.15</td>
</tr>
<tr>
<td>ANA positive</td>
<td>1.25 (SE 0.50)</td>
<td>-0.02</td>
</tr>
<tr>
<td>HLA-B27 positive</td>
<td>1.37 (SE 0.54)</td>
<td>0.84</td>
</tr>
<tr>
<td>Ankle joint arthritis</td>
<td>1.10 (SE 0.49)</td>
<td>0.67</td>
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SE= Standard Error

Figure 1. ROC curves for the multiple fine-tuning splits

Disclosure of Interests: None declared
**FRIO560**

**EFFICACY AND SAFETY OF ANAKINRA IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS – DATA OF THE BIKER REGISTRY**

Ariane Klein, Veronika Ntam Atemkeng, Frank Dressler, Ivan fooldevari, Rolf Michael Küster, Tori Hospach, Gerd Ganser, Kirsten Minden, Dirk Foeßl, Frank Weller-Heinemann, Jasmin Kuenmerle-Deschner, Boris Huegel, Christoph Rietschel, Eggert Lillenthal, Gerd Homelf, BIKER-Registry, BIKER-Registry, Sankt Augustin, Germany

**Background:** Anakinra (ANA) is recommended for treatment of systemic juvenile idiopathic arthritis (sJIA) and has recently received EMA approval. Objectives: To describe safety and effectiveness of ANA in clinical practice in sJIA patients documented in the German Biologics registry (BiKeR).

**Methods:** Demographic and clinical parameters of the patients were recorded at BiKeR enrollment, ANA effectiveness was evaluated by half-yearly evaluation of disease activity using JADAS-10. Safety assessments were based on MedDRA-coded adverse events (AE) reports.

**Results:** Until December 1, 2018, 50 sJIA patients treated with ANA were registered, representing 113.4 patient-years (PY) of observation, with 10 patients (20%) receiving ANA for at least 4 years. The cohort treated with ANA had experienced a prior disease duration of 3.5±3.8 years (mean±SD). Most sJIA patients treated with ANA received pretreatment: 35 patients (70%) were pretreated with at least one other biologic, mostly etanercept (n=28), followed by tocilizumab (6) and canakinumab (1). Further pretreatments included methotrexate (MTX, n=35), ciclosporine A (n=13), azathioprine (n=8) and other DMARDs at lower frequency, 39 patients had received corticosteroids. Concomitant treatment consisted of NSAIDs (n=20), systemic steroids (n=35), MTX (n=29) and other DMARDs (n=8). At month 3, JADAS minimal disease activity (MDA)/JADAS remission and inactive disease according to Wallace [1] were observed in 42%/37% and 47%, respectively. After one year of treatment, the rates were 62%/45% and 56%, respectively (Figure 1).

**Conclusion:** The current analysis adds to the established safety profile of Anakinra and demonstrates that in ANA treated patients with sJIA the rate of SAEs was comparable and consistent with the overall AE profile of ANA in pediatric patients. Hospitalisation was the usual reason for classification as serious AE. New safety signals specific to the paediatric population were identified in this large cohort of JIA patients.

**Disclosure of Interests:** Ariane Klein: None declared, Veronika Ntam Atemkeng: None declared, Frank Dressler Paid instructor for: Abbvie, Pfizer, Novartis, Ivan Foeßlvari Consultant for: Chugui, Novartis, Rolf Michael Küster: None declared, Tori Hospach Speakers bureau: Chugui, Roche, Novartis, Gerd Ganser: None declared, Kirsten Minden Consultant for: Abbvie, Dirk Foeßl Grant/research support from: not specified, Consultant for: not specified, Speakers bureau: not specified, Frank Weller-Heinemann: None declared, Jasmin Kuenmerle-Deschner Grant/research support from: Jasmin Kuenmerle-Deschner is an employee of University of Tuebingen, Germany, and received consultants/speakers fees from Novartis and SOBI pharmaceuticals and grant support from SOBI and Novartis., Consultant for: Jasmin Kuenmerle-Deschner is an employee of University of Tuebingen, Germany, and received consultants/speakers fees from Novartis and SOBI pharmaceuticals and grant support from SOBI and Novartis., Speakers bureau: Jasmin Kuenmerle-Deschner is an employee of University of Tuebingen, Germany, and received consultants/ speakers fees from Novartis and SOBI pharmaceuticals and grant support from SOBI and Novartis., Boris Huegel: None declared, Christoph Rietschel: None declared, Eggert Lillenthal: None declared, Gerd Homelf: None declared DOi: 10.1136/annrheumdis-2019-eular.2808

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**FRIO561**

**COMPARISON OF INITIAL PRESENTATIONS BETWEEN JUVENILE IDIOPATHIC ARTHRITIS CHILDREN WITH SYSTEMIC ONSET WITH NON-BIOLOGIC MONOCYCLIC AND PERSISTENT COURSES**

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**Background:** Juvenile idiopathic arthritis with systemic onset (soJIA) may have mononcylic, polycyclic or relapsed course [1]. There were not known soJIA course predictors.

**Objectives:** The aim of our study was to evaluate initial clinical or laboratory features of the patients with soJIA who had mononcylic course without biologics.

**Methods:** In the present study were included data about 130 soJIA patients. After selection we identified a subgroup of the soJIA patients (n=22) who successfully achieved remission without any biologic medication and were stable in the remission off-medication at least two years. The second group consisted of the patients with chronic persistent course (n=83). The remained 25 patients were excluded due to missing data or who did not meet the selection criteria. We evaluated routine clinical (fever, rash, hepatosplenomegaly, serositis, lymphadenopathy, MAS, joint involvement) and laboratory (WBC, PLT, Hb, ferritin, ALS, AST, LDH, GGT, ALP, albumin, Na, triglycerides, ESR, CRP, prothrombin, fibrinogen) soJIA features in the onset of the disease.

**Results:** Patient with mononcylic course have no any differences except the ferritin level: 275 (133; 698) ng/ml vs 950 (150; 3240) ng/ml, (p=0.04), time to achievement remission 17.7 (8.2; 38.0) months vs 60.2 (36.0; 90.0) months (p=0.00002) and rare elbow involvement 4.6% vs 30.9% (p=0.01). The parameters, associated with possible mononcylic course are in the table.

**Conclusion:** Patients with soJIA initially have quite similar clinical presentations independently the further clinical course. The prediction of possible course of soJIA is a difficult problem. Patients with soJIA with monocyclic course were younger and had less impressive laboratory activity. Further investigations required.

**REFERENCE:**


**Disclosure of Interests:** None declared DOi: 10.1136/annrheumdis-2019-eular.7991

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**FRIO562**

**CONCENTRATION OF SURVIVIN IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA) – DIAGNOSTIC AND PROGNOSTIC VALUE**

Joanna Lipinska1, Joanna Swiadowska-Jaros1, Krystyna Wyka2, Elżbieta Smolewska1, Medical University of Lodz, Department of Pediatric Cardiology and Rheumatology, Łódź, Poland, 1Medical University of Lodz, Department of Pediatrics, Oncology, Hematology and Diabetology, Łodź, Poland

**Background:** Survivin is an anti-apoptotic protein that has been suggested as a predictive marker of severe course of adult rheumatoid arthritis and could be used for preclinical recognition of rheumatoid process.

**Objectives:** The goal of the study was to evaluate the diagnostic and prognostic value of survivin in Juvenile Idiopathic Arthritis (JIA).

**Disclosures of Interests:** None declared
Methods: Sixty three children with newly diagnosed JIA (46 girls and 17 boys) aged 1.5-17 years and 32 healthy children as a control group appropriately matched in terms of sex and age, hospitalized in the Department of Pediatric Cardiology and Rheumatology, Medical University of Lodz due to functional disorders of the cardiovascular system were included into the study. Concentration of survivin was assessed by an ELISA test in blood and 18 matched synovial fluid samples collected from JIA patients and in sera of children from control group.

Results: Children with JIA were divided according to the subtype of the JIA. In 68.2% of patients oligoarthritis was diagnosed. The disease activity was established on the basis of JADAS-27 criteria, distinguishing three levels of rheumatoid process activity: low, medium and high. The largest group comprised children of low activity (56%). The concentration of survivin was significantly higher in JIA compared to the controls (p=0.00041). Higher concentration of survivin correlated positively with the presence of anti-CCP antibodies (p=0.004) and with higher disease activity (p=0.0014). The higher survivin concentration was found more often in polyarticular and systemic JIA onset. In all synovial fluid samples the concentration of survivin was higher than in matched blood (p=0.0002).

Conclusion: On the basis of the conducted study, it could be concluded that the higher concentration of survivin is being associated to more severe course of the JIA. Determination of survivin may be helpful in the diagnosis of JIA and may be used to identify a group of children with early arthritis and JIA with bad prognosis who should be treated more aggressively early from the disease onset.

REFERENCES:

Disclosure of Interests: None declared

FRIO563 A NATIONAL SURVEY ACROSS GENERAL PÆDIATRICIANS REGARDING IMMUNIZATION PRACTICES IN CHILDREN WITH RHEUMATIC DISEASES

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Background: Robust scientific evidence on the safety and efficacy of certain vaccines in patients with rheumatic diseases is available; therefore guidelines regarding immunizations in this vulnerable group of children are published via a variety of official health organizations/societies including the Greek Rheumatology Society. Nonetheless, the uptake of specific immunizations is suboptimal. In Greece, vaccinations are mainly delivered by primary care paediatricians.

Objectives: The purpose of this study was to describe the knowledge, attitude and current practice of General Paediatricians working in primary care regarding vaccination in children with rheumatic diseases on immunosuppressive medication across Greece and to identify barriers and facilitators that could be used to promote uptake.

Methods: This was a cross-sectional survey, conducted with an anonymous questionnaire of 25 items distributed to Paediatricians via an online platform. Data collected included demographics, questions on knowledge, perceptions and opinions as well as advice given to families. Additionally, questions addressed three specific categories: live-vaccines, non-live vaccines and annual influenza vaccine. This study was approved by the “P. & A. Kyriakou” Children’s Hospital Research and Ethics Committee.

Results: Out of 400 questionnaires sent out, 256 were returned. Mean age was 48 years age (±8.2) mean duration of working as a Paediatrician was 15 years (±6.7). 25% of the respondents worked in rural areas and the remaining in urban areas. 67% worked in the private sector. The majority (78%) of doctors felt that vaccination in children with rheumatic diseases is of pivotal importance. 50% gave specific advice on immunisations at initial diagnosis and 25% checked vaccination status at regular intervals. Responders were using a variety of guidelines in order to reach a clinical decision; still 45% were unaware of the existing national guidelines. 50% were hesitant to adhere to the national vaccination scheme without expert input. Reasons were: not convinced from current literature that the vaccine is safe (32%), afraid to cause disease flare (43%), unable to deal with parental concerns/refusal (54%). 12% of responders felt that the rheumatic disease may have been triggered by a vaccine. The majority (95%) were pro annual influenza vaccination, while a minority (15%) was against live vaccines administration even if the patient was not on immunosuppressive treatment. 75% of doctors were keener to administer booster doses rather than primary doses. While 75% of respondents would postpone vaccinations in all cases if disease was active.

Conclusion: Variation in opinion and clinical practice exists. Overall, although Greek Paediatricians are well informed regarding efficacy and side effects of immunizations, there are steps to be made from principle to practice. Further research will allow the development of clear guidelines to aid in the management of increasing numbers of children with rheumatic diseases.

Disclosure of Interests: None declared

FRIO564 PSTPIP1- ASSOCIATED MYELOID-RELATED PROTEINEMIA INFLAMMATORY SYNDROME/PAMI SYNDROME: CASE REPORT AND REVIEW OF THE LITERATURE

Manel Meibri, Katerina Theodoropoulou, Michael Hofer, Lausanne, Pediatric Rheumatology, Lausanne, Switzerland

Background: PAMI syndrome is a recently described condition, previously known as Hyperzincemia/Hypercalprotectinemia (Hz/Hc) syndrome. It is a very rare auto-inflammatory disorder characterized by a chronic systemic inflammation, cutaneous and osteo-articular manifestations, hepatosplenomegaly, anemia and neutropenia. Increased blood levels of MRP 8/14 (S100A8/A9 or calprotectin) and zinc distinguish this condition. Specific pathogenic mutations in PSTPIP1 gene (p.E250K and p.E257K) were identified as the genetic cause of this condition.

Objectives: Case presentation and review of literature

Case Presentation: We report a case of 13 months age female referred to our unit for recurrent episodes of osteoarthritis. Physical examination showed hepatosplenomegaly. Blood work revealed a systemic inflammation, a microcytic anemia and neutropenia. A complete workup for metabolic disorders, oncologic processes and uncommon infections was negative. Because of history of recurrent osteoarthritis, a whole-body MRI was performed and confirmed a multifocal osteomyelitis. Whole exome sequencing identified the missense p.E250K in the PSTPIP1 gene.

Methods: A literature search on PAMI syndrome was performed until the 15 October 2018. Pubmed was screened using a combination of the following terms: Hyperzinncemia, Hypercalprotectinemia, E250K mutation, PSTPIP1 mutation, PAPA with E250K mutation.

Results: We identified 20 cases of PAMI syndrome in the literature. PAMI syndrome is an early onset inflammatory disease with a median age of 2.4 years. Clinical manifestations include osteo-articular manifestations (80%), skin lesions (45%), hepatosplenicomegaly (68%), lymphadenopathy (42%), growth failure (58%) and hemorrhagic diathesis with recurrent epistaxis and/or haematoma tendency in 5 patients. All cases had relevant abnormalities in hematologic parameters: mild to severe neutropenia and anemia (100%). Thrombocytopenia (42%). Systemic inflammation was confirmed in 94% using the monitoring of CRP, ESR or SAA. Zinc and MRP 8/14 blood concentrations were markedly elevated in all tested patients. Genetic analyses of PSTPIP1 gene revealed the two specific identified mutations (p.E250K and p.E257K) in all patients. Response to the treatment was variable with no consistently effective therapy. Most common therapeutic options were AINS, Corticosteroids (n=9), Anakinra (n=9), Anti-TNF (n=6) and Cyclosporine A (n=4).

Conclusion: PAMI syndrome is a rare auto inflammatory condition which should be considered in patients with undefined systemic inflammation and neutropenia, even without skin or osteo-articular manifestations. Zinc and serum MRP 14/8 measurement may be helpful tools for the diagnostic orientation in these cases.

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A MULTINATIONAL STUDY OF THROMBOTIC MICROANGIOPATHY IN MACROPHAGE ACTIVATION SYNDROME: A DREADFUL CONDITION WHICH IS LIKELY UNDER-RECOGNIZED

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FRI0566 STUDY ON SERUM DNAASE1 ACTIVITY IN PEDIATRIC ONSET SYSTEMIC LUPUS ERYTHEMATOSUS FROM A TERTIARY CARE CENTRE IN NORTH WEST INDIA

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Background: DNAase is an apoptotic endonuclease responsible for degradation of chromatin released by inappropriately cleared dead cells. DNAase1 activity in systemic lupus erythematosus (SLE) patients is lower than that in inactive disease in studies conducted in adult SLE patients from developed country. There is a paucity of data on DNAase1 activity in paediatric SLE from India.

Objectives: To measure the serum level of DNAase1 in pediatric-onset SLE patients and to correlate the disease activity groups based on Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) score and compared the serum DNAase1 level between the two groups.

Methods: A cross-sectional observational study was conducted over a period of 1 year. Thirty-three consecutive children with pediatric-onset SLE were enrolled and divided into active and inactive disease activity groups based on Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) score and compared the serum DNAase1 level between the two groups.

Results: Out of 33 children enrolled, 13 (39.3%) had active disease (SLEDAI score ≥ 3) and 20 (60.6%) had inactive disease activity. Mean age at diagnosis was 8.5 years and 10.2 years in active and inactive disease activity groups respectively. There is female preponderance (66.7%) in the enrolled patients. Anti nuclear antibody (ANA) was positive in 90.9% of patients. The most common pattern of ANA was diffuse pattern (48.4%). There is female preponderance (66.7%) in the enrolled patients. Anti nuclear antibody (ANA) was positive in 90.9% of patients. The most common pattern of ANA was diffuse pattern (48.4%). There is female preponderance (66.7%) in the enrolled patients. Anti nuclear antibody (ANA) was positive in 90.9% of patients. The most common pattern of ANA was diffuse pattern (48.4%). There is female preponderance (66.7%) in the enrolled patients. Anti nuclear antibody (ANA) was positive in 90.9% of patients. The most common pattern of ANA was diffuse pattern (48.4%).
inactive group. Antiphospholipid antibody was present in 3 (23.1%) in active disease activity group and 5 (25%) in inactive disease activity group. The mean serum concentrations of DNAase1 were 15.394 ng/ml in active disease group and 15.205 ng/ml in inactive disease group. There was no statistically significant difference in the serum DNAase1 concentrations between the two groups (p=0.943). There was also no significant difference in the mean serum concentration of DNAase1 in patients with or without nephritis (p= 0.080).

Conclusion: The present study could not establish any correlation between serum DNAase1 levels and disease activity in pediatric-onset SLE. There was no association between serum DNAase1 levels and organ involvement such as nephritis in the enrolled patients

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Disclosure of Interests: None declared

FRI0568
ABATACEPT THERAPY EXPERIENCE IN THE CASE SERIES OF PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS ASSOCIATED WITH OVERLAP SYNDROME AND/OR SJÖGREN’S SYNDROME
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Background: The choice of Biologics in patients with juvenile idiopathic arthritis (JIA) who have overlap syndrome with juvenile onset of systemic lupus erythematosus (JSLLE), juvenile dermatomyositis (JDM), juvenile systemic sclerosis (JSSc) and juvenile Sjögren’s syndrome (JSS) is difficult. TNF inhibitors are limited in this kind of disorders and abatacept (ABA) seems to be the favorable option for children, but there are not enough studies in pediatric overlap syndrome and JSS.

Objectives: The evaluation of the abatacept therapy in case series of patients with JIA associated with overlap syndrome and/or JSS.

Methods: Patients who fulfilled the criteria for JIA and the criteria of above mentioned rheumatic disorders and received abatacept therapy according to JIA indication in real clinical practice of our rheumatological clinic.

Results: 11 patients included in the retrospective study (6 girls, 3 boys). The average age of patients was 15.1 years (from 7 to 18 years). Mean duration of disease was 5.4 years. 9 patients were RF positive, 4 patients had ACCP. All of the patients had antinuclear antibody (from 1:320 to 1:2560), 3 patients had positive anti-Ro antibody. Sjögren’s syndrome was the most common concomitant autoimmune disorder (n = 1), JIA with psoriatic arthritis or other spondyloarthropathy (n = 2), JSSc (n = 2), JSLLE (n = 1). 7 patients were treated by a low dose of prednisolone (median 5.7 mg/day). All patients received methotrexate in dose 10-15 mg/m2/week. ABA was indicated as first line of biology therapy in 10 patients, in one patient after adalimumab withdrawal due to severe flare. Mean duration of abatacept treatment was 23.7 month (from 6 to 78). The most of the patients (82%) had excellent stable effect of ABA treatment, but two patients needed to be switched to rituximab due to secondary inefficacy. We observed wonderful result of treatment with full remission of arthritis, calcinosis regression and resolving of Sjögren’s syndrome in the boy with overlap syndrome treated by ABA for 78 months. The serconversion from initial levels of RF 32.9 IU/ml (>2N), anti-Ro antibody 1:840, anti-Ro antibody 200 U/ml (>9N) to negative results was registered. The ABA was good tolerated in all patients. In one case it was canceled due to pregnancy.

Conclusion: ABA is efficacy and safety option in patients with pediatric overlap syndrome and JSS. ABA is good alternative to anti-B cell therapy and preferable choice among Biologics in such category of patients.

Disclosure of Interests: None declared

FRI0568
THE USE OF NEXT GENERATION SEQUENCING PANEL IN UNDIFFERENTIATED AUTOINFLAMMATORY DISEASES IDENTIFY A SEPARATE SUBSET OF COLCHICINE-RESPONSER RECURRENT FEVERS DISTINCT FROM PFAPA SYNDROME
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Background: The number of monogenic innate immune system disorders classified as systemic autoinflammatory diseases (SAID) has increased during the recent years. However, more than 70% of patients with clinical manifestations of SAID not achieved a molecular diagnosis, thus getting into the so-called undifferentiated or undefined SAID (uSAID).

Objectives: The aim of the present study is to characterize a subgroup of patients with recurrent fever episodes distinct to PFAPA that turned out to be negative to a large 41-gene NGS panel.

Methods: We designed an NGS panel including 41 genes clustered in seven subpanels.

Results: Fifty patients were enrolled in the study. 34 patients (72%) displayed recurrent fever and sixteen presented a chronic inflammatory disease course. A total of 100 gene variants were found (mean 2 per patient; range 0-6). Mutations with a sure or possible diagnostic impact were detected in five patients (10%). Differently from PFAPA syndrome (table), genetically negative patients with recurrent fever episodes presented episodes that lasted on average of six days (P<0.0001), Abdominal pain and limb pain were the most common symptoms. The classic PFAPA triad (pharyngotonsillitis, aphthosis and cervical lymphadenopathy) was less frequently reported (P<0.0001) while skin rash and arthritis were more frequent (P<0.0001). Eighteen patients were exclusively treated with steroid on demand with a high response rate (94%). In 18 patients, colchicine treatment was used with an overall complete or partial response of 78%.

Conclusion: Even with a low molecular diagnostics rate, an NGS-based approach is able to provide a final diagnosis in a proportion of uSAID patients. It also allows the identification of a subgroup of genetically negative patients with recurrent fever responding to steroid on demand and colchicine.

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Disclosure of Interests: Riccardo Papa: None declared, Marta Rusmini: None declared, Stefano Volpi: None declared, Roberta Caorsi: None declared, Paolo Picco: None declared, Alice Grossi: None declared, Francesco Caroli: None declared, Francesca Bovis: None declared, Valeria Musson: None declared, Laura Obici: None declared, Cinzia Castrana: None declared, Angelo Raveli Grant/research support from: Angelini, Abb-Vie, Bristol-Myers Squibb, Johnson & Johnson, Novartis, Pfizer, Reckitt Benkiser, and Roche, Speakers bureau: Angelini, Abb-Vie, Bristol-Myers Squibb, Johnson & Johnson, Novartis, Pfizer, Reckitt Benkiser, and Roche, Mauriella E van Gijn: None declared, Isabella Ceccherini: None declared, Marco Gattorno Grant/research support from: MG has received unrestricted grants from Sobi and Novartis.

References:


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WHAT DOES IT MEAN TO BECOME PREGNANT WITH JUVENILE IDIOPATHIC ARTHRITIS? A MONOCENOTIC EXPERIENCE IN A TERTIARY CENTRE OF MILAN

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Background: During the last seventeen years, biological and non-biological therapies have been used in our center in an open prospective study for the treatment of refractory JIA not only in paediatric age but also in young adults. The availability of more effective drugs for JIA has dramatically increased the number of patients willing to become pregnant. Data regarding the effect of JIA on pregnancy outcome are scant.

Objectives: The study aims to evaluate the capability of JIA patients to become pregnant, the effects of drugs on pregnancy outcome and the impact of gestation on the disease course.

Methods: JIA patients regularly followed up in our Transition Clinic of the Division of Rheumatology, Gaetano Pini Institute of Milan, were enrolled in the study at the presence of pregnancy test. During the whole pregnancy patients underwent monthly clinical examination and obstetric ultrasound. Data regarding disease activity and pregnancy course (fetal morphometric parameters, fetal heart rate, fetal growth, Doppler velocimetry) were collected.

Gestational age, birth weight and APGAR score were also recorded.

Results: 29 pregnancies in 23 women affected by refractory JIA became pregnant during a 17 years follow up. All patients had a long lasting polyarticular disease (median duration of 23 years) not responsive to DMARDs and became pregnant during biologic therapy. Patients were treated with Etanercept (11 patients), Golimumab (4 patients), Rituximab (3 patients), Adalimumab and Certolizumab (2 patients respectively) as monotherapy, and in most of the cases after multiple switches. One woman was treated with Etanercept during the first pregnancy and Adalimumab during her second pregnancy. Three patients decided for an elective termination and 3 experienced an early miscarriage; among 23 pregnancies resulting in live born infants, only 3 had premature births and 1 cleft palate. A pregnancy was complicated by gestosis, two by placental detachment. All the babies were followed up during the 17 years of observation and did not experience any major late complication. Eight patients were subjected to intra-articular infiltrations during pregnancy to switch off the disease. 18 patients resumed therapy shortly after childbirth and only 7 patients decided to breastfeed.

Conclusion: Despite a large amount of studies demonstrating the safety of anti-TNF during pregnancy, data regarding the effects of biologics on pregnancy outcome in JIA are still lacking. The very low number of patients treated with traditional DMARDs achieving low disease activity underline the pivotal role of new biologic drugs in the management of aggressive long standing JIA, to improve the quality of life of these patients, including family planning. In our experience, no greater number of unexpected complications or side effects were observed in JIA patients during pregnancy compared to the other autoimmune diseases. Discontinuation of therapy has increased the risk of flare, requiring local therapy, confirming that EULAR recommendations for the use of biologics during pregnancy can be applied also in JIA.

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MEASUREMENT PERFORMANCE OF REDUCED VERSIONS OF MUSCLE STRENGTH TOOLS IN JUVENILE DERMATOMYOSITIS

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Objectives: To investigate whether reduced versions of the MMT8 and CMAS are equally reliable as the original tools.

Methods: The following 4 reduced instruments were devised: 1) MMT4 (score 0-40); 2) MMT6 (score 0-60), composed of the same items of MMT4 plus biceps brachii and quadriceps; 3) head lift time of CMAS (0-120 seconds or 0-5 points); 4) sum of CMAS head lift time in points and the 6 sit-ups maneuvers of CMAS (score 0-11).

Results: All reduced instruments revealed strong correlations (r > 0.7) with muscle activity VAS and total DAS, moderate correlations (r = 0.4-0.7) with physician’s global VAS, muscle DAS, skin activity VAS, pain VAS, parent’s overall wellbeing VAS, and CK. Correlations with skin DAS and fatigue VAS were low (r < 0.4). Cronbach’s alpha was excellent (0.92-0.95) for all reduced tools for which this property could be assessed. SRM was good-to-moderate (0.60-0.91) for all reduced instruments in patients judged as improved by the physician. All reduced tools discriminated strongly between patients classified in different disease activity states by the physician (p < 0.0001), and between patients whose parents were satisfied or not satisfied with their children’s disease status (p < 0.0001). Overall, the metrologic performance of the reduced instruments was comparable to that of MMT8 and CMAS.

Conclusion: We found that reduced versions of the MMT8 and CMAS have good psychometric properties and perform similarly to the original tools in a population of patients followed in standard clinical care. Our results suggest that these simplified and shortened instruments could serve as surrogate for the complete measures in routine practice, particularly in a busy clinical setting.

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FR00573

COGNITIVE IMPAIRMENT IN CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS: EARLY DETECTION WITH MR SPECTROSCOPY AND ITS ASSOCIATION WITH MOG ANTIBODIES

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Background: Systemic lupus erythematosus (SLE) is a chronic inflammatory disease characterized by the presence of various autoantibodies. Unnoticed and progressive cognitive impairment may develop in the course of disease even without overt neuropsychiatric (NP) features. Some authors attributed this mild impairment to the immune-mediated myelinopathy. Evidence exists that myelin oligodendrocyte glycoprotein (MOG) might act as a mediator of interactions between myelin and the immune system.

Objectives: To detect the role of MOG-Ab in neurologic manifestations of childhood-onset SLE (cSLE) and to better delineate the actual grade of cognitive dysfunction in non-NPSLE children.

Methods: MOG-Ab levels were studied in all healthy subjects (n=28) and in all patients with (NPSLE =9) and without (non-NPSLE=36) overt neuropsychiatric manifestations. All of the non-NPSLE group and healthy group underwent brain MR and MRS examination. However, only 20 subjects in each group met the MRS imaging standards for evaluation. In the non-NPSLE group, 29 cSLE patients were further evaluated by neurocognitive tests. Sixteen children with non-NPSLE were assessed by both MRS and neurocognitive tests.

Results: The mean age of the SLE patients at study time was 16.22±3.22 years. MOG-Ab was detected positive neither in cSLE nor in healthy group.

In children with non-NPSLE, verbal IQ ranged from 40 to 108 (mean: 79.06±17.66), performance IQ ranged from 42 to 111 (mean: 92.03±16.28), and full-scale IQ ranged from 40 to 106 (mean: 84.31±16.39). There were 15 patients (51%) in non-NPSLE group with a full-scale IQ under 85. There was no significant difference between the non-NPSLE group and healthy group in all patients with (NPSLE =9) and without (non-NPSLE=36) overt neurologic manifestations. All of the non-NPSLE group and healthy group underwent brain MR and MRS examination. However, only 20 subjects in each group met the MRS imaging standards for evaluation. In the non-NPSLE group, 29 cSLE patients were further evaluated by neurocognitive tests. Sixteen children with non-NPSLE were assessed by both MRS and neurocognitive tests.

Conclusion: More than a half of our patients in non-NPSLE group were found to have a full-scale IQ under 85. Cognitive impairment may develop insidiously in cSLE children even without any overt symptom or sign. There was no association of MOG-Ab with cSLE, whether neuropsychiatric manifestations present or not. A causal relationship between immune-mediated myelinopathy and neuropsychiatric involvement/cognitive impairment could not be suggested, since there has been no patient with positive MOG-Ab and there has been no difference in choline, creatine/creatinine levels in cSLE patients and healthy subjects. Decrease in the NAA/Creatine level of the left frontal white matter in MRS, which is a finding of neuronal loss, may be used as a first sign of cognitive impairment in patients with cSLE.

FR0574  CLINICAL RESPONSE TO HIGH-DOSE INTRAVENOUS METHYLПREDNISOLONE IN CHILDHOOD AUTOIMMUNE UVEITIS: A RETROSPECTIVE ANALYSIS

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Background: Intracocular inflammation accounts for up to 10-15% of total blindness cases [1]. The incidence of uveitis in children ranges among 4.9/100,000, and a significant number of patients develop chronic courses and irreparable complications [2]. An impressive 74% of children with juvenile idiopathic arthritis (JIA)-associated uveitis are legally blind at diagnosis [3]. This underscores the importance of timely diagnosis and effective anti-inflammatory treatment.

Objectives: To evaluate the clinical response to high-dose intravenous methylprednisolone (IVMP) in children and adolescents with autoimmune uveitis.

Methods: A retrospective chart review was conducted in two tertiary referral centers in Germany (TU Dresden and University of Würzburg) to investigate treatment responses to IVMP (10-30mg/kg/day on three successive days with a total of one to five IVMP at monthly intervals) in children and adolescents (<16 years) with autoimmune uveitis diagnosed between 2003 and 2016. Clinical features of uveitis, disease activity, outcomes, and concomitant anti-inflammatory treatment were documented at treatment initiation, after 3 and 6 months.

Results: Fifty-six patients (93 affected eyes) with a median age of 7.4 (range: 2.5-16.7) years were included. In 29% of patients uveitis was associated with JIA. Uveitis was predominately located in the anterior segment (43%), bilateral (66%) and recurrent (43%). Complications occurred in 77% of patients and included visual loss, synechiae, cataract, and/or retinal lesions. Patients with active uveitis received between 1 and 5 IVMP. Visual acuity improved significantly (0.52±0.33 to 0.69±0.30 at 3 months (p=0.001), 0.78±0.31 to 0.6 ± 0.31 (p=0.001)) independent of the number of IVMP. Furthermore, anterior chamber cells (45% to 18%, p=0.01), synechiae (47% to 32%, p=0.005), keratic precipitates (27% to 18%, p=0.01), papillary edema (30% to 13%, p=0.001) and/or macular edema (15% to 4%, p=0.01) improved 3 months after IVMP. Over all, children treated with 3 or more IVMP (n=27) (as compared to 1 IVMP (n=18)) experienced fewer relapses (Median 1 [0-6] vs 3 [0-13], p=0.186), developed fewer cataracts (7% vs 39%, p=0.02) and less frequently required treatment with biologics (19% vs 39%, p=0.174).

Conclusion: High-dose IVMP induces rapid improvement in children with autoimmune uveitis. Data suggest improved outcomes in children treated with three or more courses of IVMP when compared to one course (without reaching statistical significance). Prospective randomized trials in larger cohorts are required to confirm results.

REFERENCES:

Disclosure of Interests: None declared

FR0575  PREVALENCE OF OVERWEIGHT AND OBESITY IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Children with juvenile idiopathic arthritis (JIA) may have an increased risk for overweight and obesity, which could be an additional risk factor for inflammatory arthritides. The aim of the study was to determine the prevalence of overweight and obesity in children and adolescents with JIA, and to assess the association between overweight and disease parameters in this population.

Objectives: The aims of this study were to determine the prevalence of overweight and obesity in children and adolescents with JIA, and to assess the relationship between overweight and disease parameters in this population.

Methods: We assessed the weight (kg) and height (cm) according to the standard deviation score (SDS) in a cross-sectional study of JIA children. The diagnosis of JIA was based on the International League of Association of Rheumatology (ILAR) criteria. Overweight and obesity were defined by the Body Mass Index (BMI) (weight/height^2) matched on age and sex and in reference to the French curves. Children were classified as obese if their BMI was ≥ 95th percentile, overweight if their BMI was between the 85th and 94th percentile, and healthy weight if their BMI was between the 5th and 84th percentiles. Functional disability was determined by the Childhood Health Assessment Questionnaire (CHAQ).

Results: Fifty-five patients (38 boys and 17 girls) with JIA were enrolled in this study. The median age was 8.5 ± 4.12 years (range 6–14). Thirty-one patients (53%) had persistent oligoarticular JIA, 15 (27%) had polyarticular JIA, 5 patients (9%) had systemic JIA, and 4 (7%) had enthesitis-related arthritis. The median disease duration was 3.2 ± 2.8 years. Twelve patients had active disease at the time of the study with a mean CHAQ 27 of 6.9 ± 2.7. The mean CHAQ was 1.4 ± 0.5. Nine-teen children (52.7%) had received corticosteroids during an average period of 1.7 years [0.6-3] with a mean of 10mg/day of prednisone or equivalent. The mean BMI was 14.56 ± 2.1 kg/m^2. Twenty-two patients (40%) were overweight, 15 (27%) were obese and 18 (33%) have normal weight. Patients with normal weight, overweight and obese represented respectively 60%, 20% and 20% of systemic forms, 53%, 27% and 20% of polyarticular form, 39%, 32% and 29% of persistent oligoarticular forms, and 50%, 25% and 25% of enthesitis-related arthritis forms. Obesity was more frequent in older patients (p=0.021) with significant functional impairment (p=0.001) and with active disease (p=0.001). Only systemic JIA was more likely to be associated with overweight (p=0.031) and obesity (p=0.024). There was no relationship with other subtypes of JIA (p=0.428) or with corticosteroid treatment (p=0.636).

Conclusion: In our study, more than 60% of patients were overweight. Severely functional limitation, systemic JIA, and active disease were the most correlated parameters with obesity. Better management of the activity and functional status of the disease may reduce overweight in children with JIA.

Disclosure of Interests: None declared
Greece, between September 2015 and June 2018 and 42 healthy controls.

Results: Patients with FMF presented similar systolic Blood Pressure (sBP), central Systolic Pressure (cSP) and cf-PWV values to controls, but significantly higher Aix75 values (patients vs. controls, 19.76% and 9.36%), (p<0.05). Only one FMF patient had cf-PWV > 95th percentile. Statistical analysis in FMF patients showed that Aix75 adjusted for age and sex associated with complete response compared to partial response to treatment (B=-17.78 95% CI:31.17-(-4.40), P<0.05) and the presence of M694V.M680I genotype (B=-16.75 95% CI: -33.81-0.30, P<0.05). Cf-PWV presented an inverse relationship with colchicine treatment duration (B=-0.003, 95% CI: (-0.006)-0.00, P<0.05). Cf-PWV values adjusted for age and sBP associated with attacks frequency for <2 months vs. >2 months, B=0.48 95% CI: 0.01-0.96, P<0.05). Addition of colchicine treatment duration to the model, attenuated the association between cf-PWV and attack frequency, supporting the protective role of colchicine.

Conclusion: The normal values of cf-PWV in FMF patients may reflect the compliance to colchicine treatment, that seems to have a protective role against vessel inflammation. However, the increased values of Aix75 need further investigation.

REFERENCES:

Disclosure of Interests: None declared

FRIO577 ANTI-PHOSPHOLIPID SYNDROME SECONDARY TO PEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS. EXPERIENCE IN A THIRD-LEVEL HOSPITAL IN MEXICO CITY

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Background: Antiphospholipid syndrome (APS) is a multisystemic autoimmune disease that is characterized by thromboembolic events, pregnancy morbidity and other manifestations in the presence of elevated titers of antiphospholipid antibodies.(1)

APS can be either primary, occurring as an isolated clinical entity, or secondary to other diseases including infections, malignancy or autoimmunity, the latter associated in particular with systemic lupus erythematosus (SLE). (2)

Patients with SLE can produce a great variety of autoantibodies, including the so called antiphospholipid antibodies (aPLs), such as lupus anticoagulant (LA); anti-cardiolipin antibodies (aCL) or anti-beta2Glycoprotein-1 antibodies (anti-beta2GPI). (2) These aPLs have been described in 20-40% of SLE patients.

Objectives: To report frequency of patients with antiphospholipid syndrome secondary to pediatric systemic lupus erythematosus (pSLE) at National Institute of Pediatrics in Mexico City from 2005-2016. We then identified patients with positive antiphospholipid antibodies (aPLs) and/or clinical manifestation of antiphospholipid syndrome (APS).

Methods: Retrospective study that included all pediatric systemic lupus erythematosus (pSLE) patients diagnosed at National Institute of Pediatrics in Mexico City from 2005 to 2016. We then identified patients with positive antiphospholipid antibodies (aPLs) and/or clinical manifestation of antiphospholipid syndrome (APS). Demographic, clinical and laboratory features were extracted from their clinical records. Study approved by the local Ethics Committee.

Results: Over the 12-year study period, we collected 295 patients with a diagnosis of pediatric systemic lupus erythematosus (pSLE). Eighty patients (27.11%) had at least a positive antiphospholipid antibody (aPL) or a clinical manifestation of antiphospholipid syndrome (APS). Figure 1 shows our study population. Of these 80 patients, 75 (93.75%) had a positive aPL at moment of pSLE. With respect to the remaining 5 cases, 3 of them developed a positive aPL during follow-up, while the remaining 2 cases presented a clinical feature of APS simultaneously to pSLE diagnosis and their serology persisted negative during follow-up.

Twenty (25%) patients had a clinical manifestation associated to APS. Concerning these patients, 11 (55%) patients presented clinical features of APS at time of pSLE diagnosis, 6 (30%) patients developed it during follow-up and the remaining 3 (15%) patients had previous history of a clinical manifestation associated to APS prior to pSLE diagnosis. Nevertheless, 2 of these 20 patients never reported positive antiphospholipid antibodies.

Antiphospholipid antibodies (aPLs) were positive in 27% of cases with psLE. And more than 90% of cases had positive aPLs at moment of pSLE diagnosis, which is why we strongly agree with international recommendations of performing aPLs screening simultaneously to pSLE diagnosis.

REFERENCES:

Disclosure of Interests: None declared
LACC1 MUTATION IN THREE SIBLINGS WITH POLYARTHRITIS WITHOUT SYSTEMIC MANIFESTATIONS

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Background: Juvenile idiopathic arthritis (JIA) is a complex group of disorders characterized by wide phenotypic diversity and genetic heterogeneity. It has multifactorial etiology varying among different subtypes. There are emerging reports on new gene loci being identified especially in familes with many affected members (1,2).

Objectives: To report 3 siblings with polyarthritides who were detected to have mutation in Laccase domain containing 1 (LACC1) gene.

Methods: We reviewed case records of 3 siblings with infantile onset polyarthritides and performed whole exome sequencing on their DNA samples for LACC1, MMP2 and WHISP genes.

Results: A non-consanguineous family from north-western part of India reported with 3 daughters having polyarticular joint disease. The chronology of symptoms was similar in all 3 children. Joint symptoms started in later half of infancy with swelling of knee and ankle. This disease was progressive and over the following 2 years there was involvement of spine, sacroiliac joints and in 3 patients (20%) in the “Standard therapy group”. However, the difference is not statistically significant (p = 0.598).

Conclusion: Our study shows that corticosteroid therapy is associated with a faster resolution of Sydenham’s Chorea’s symptoms compared to treatments considered of first line, such as: no therapy, valproate or pimozide.

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PREDNISONE VERSUS STANDARD THERAPY IN SYDENHAM’S CHOREA: RESULTS FROM A RETROSPECTIVE STUDY

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Background: Sydenham’s chorea is a major and delayed manifestation of acute rheumatic fever [1] and is considered to be a prototype of an autoimmune disorder triggered by an infectious agent. Aside from conventional symptomatic treatment (carbamazepine, valproate, neuroleptics), the use of steroids has also been advocated, mainly in severe, drug-resistant cases, or if clinically disabling effects develop with first line therapies. However the evidence of corticosteroids efficacy is weak.

Objectives: To describe the efficacy of corticosteroids therapy versus standard therapy in children affected by Sydenham’s Chorea in a cohort of Italian patients with acute rheumatic fever (ARF).

Methods: A retrospective observational study was conducted. The hospital records for all children diagnosed as having ARF between January 2007 and December 2017 in the Pediatric Rheumatology Division of the Meyer Children Hospital (Florence) and IRCCS Burlo Garofolo (Trieste) were reviewed. The diagnosis of ARF was made by pediatric rheumatologists and all the children discharged with a ICD 9 code consistent with ARF were included. For the purpose of the study only patients with Sydenham’s Chorea were enrolled. Files were analyzed for demographic data, clinical and laboratory findings on admission and during the hospital stay and patients with incomplete information were excluded. Time and resolution of choreic symptoms were evaluated in consideration of presence or absence of corticosteroid therapy.

Results: Thirty patients were enrolled; 23 out of 30 (76%) had generalized chorea, 15 (50%) were treated with prednisone (2 mg/kg/day in a single administration per day for 14 days before tapering), 11 (36.6%) were not treated with medications and 4 (13.3%) received pimozide or sodium valproate. We considered together patients who did not receive any specific therapy for chorea and patients who received only symptomatic anti-chorea drugs (pimozide in 3 cases and sodium valproate in 1 case). Therefore we obtained two groups of 15 participants each: “Prednisonone group” and “Standard therapy group”. The time required for clinical improvement in the two groups appeared statistically different (P = 0.002). In “Prednisonone group” the median time for improvement was 4.0 days (interquartile range: 3) whereas in “Standard therapy group” it was 16.0 days (interquartile range: 16). Furthermore, the “Prednisonone group” had a median remission time of 30.0 days (interquartile range: 34) whereas “Standard therapy group” presented a median remission time of 135.0 days (interquartile range: 309 (P < 0.001). At least one episode of relapse occurred in 1 (6.7%) out of 15 patients in the “Prednisonone group” and in 3 patients (20%) in the “Standard therapy group”. However, the difference is not statistically significant (p = 0.25).

Conclusion: Our study shows that corticosteroid therapy is associated with a faster resolution of Sydenham’s Chorea’s symptoms compared to treatments considered of first line, such as: no therapy, valproate or pimozide.

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ULTRASONOGRAPHY SCORE CORRELATES WITH DISEASE ACTIVITY IN JUVENILE IDIOPATHIC ARTHRITIS – ENTHESIS RELATED ARTHRITIS – A CROSS SECTIONAL OBSERVATIONAL STUDY FROM INDIA

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Background: Enthesis is a distinct clinical hallmark of spondyloarthritis in children and adults. Ultrasonography (US) is a powerful tool to detect enthesitis. There are only a few studies on US detected enthesitis in Juvenile Idiopathic Arthritis - Enthesitis Related Arthritis (JIA-EAR) from India.

Objectives: To assess the presence of clinical and US detected enthesitis in JIA- ERA and to correlate with disease activity.

Methods: 51 consecutive JIA-ERA patients fulfilling the ILAR classification criteria were evaluated clinically and sonographically from October 2016 to September 2017 in a tertiary care centre from Northern India. Enthesitis was clinically assessed using the MASES (Mastricht Ankylosing Spondylitis Enthesis Score). Additionally peripheral enthesal sites of lower limb (insertion of plantar fascia at calcaneal tuberosity, insertion of Achilles at superior pole of calcaneus, quadriceps tendon at superior pole of patella and patellar tendons proximally at inferior pole of patella and distally at anterior tibial tuberosity) were clinically and sonographically assessed for enthesitis. The clinical assessment included JADAS 27 and BASDAI for disease activity and BASFI for function. Ultrasound was performed with a multi-frequency linear-array transducer (8-13MHz) using B-mode settings of dynamic range (40-50dB); GS- frequency (11-13 MHz); GS gain (60 dB). Power Doppler (PD) mode settings used: pulsed repetition frequency (400-800 Hz); PD-gain (highest possible gain with minimum background noise). US parameters (hypo echogenicity, increased thickness of entheses, intratendinous calcification, enthesophyte and erosion(s)) were assessed according to OMERACT 2014 definitions of ultrasonography
findings of enthesitis (1). Each parameter at every site was scored as 1 if present and 0 if absent. Grading of Power Doppler signals was done as per definition by Kiris et al (2); Grade 0-no signal, Grade 1- separate dot signals or short linear signals, Grade 2- vascularity involving less than half of the enthesis, Grade 3-vascularity involving more than half of the enthesis. US enthesis score was calculated by adding 1 point for each positive finding and the grade of PD. PD score was calculated by adding the grade of PD. Presence of clinical and US detected enthesitis was correlated with parameters of disease activity by Spearman’s correlation coefficient.

**Results:** The mean age of patients was 14.3± 3.2 years with mean duration of disease 34.6±4.9 months. Male: Female ratio was 7.5:1. Clinical enthesitis was seen in 36 of the 51 patients (70.5%) while US detected enthesitis in all (p<0.001). The mean JADAS score, BASDAI and BASFI were 17.1±10.2, 4.1 ±2.4 and 37.2±27.2 respectively, indicating active disease. The US enthesis score correlated positively with JADAS (r = 0.3, P<0.03), BASDAI (r = 0.39, P=0.005) and BASFI (r = 0.38, P=0.006). PD score correlated positively with BASFI (r = 0.33, P= 0.02), but did not correlate with JADAS (r = 0.22, P=0.1), BASDAI (r= 0.24, P= 0.08).

**Conclusion:** Ultrasound is more sensitive in detecting enthesitis in JIA-ERA than clinical assessment. The US enthesis score correlated positively with disease activity which has implications for treatment.

**REFERENCES:**


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**FRIO581**

**COMPARISON OF CLINICAL CHARACTERISTIC IN ADULTS AND CHILDREN WITH GOUT**

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**Background:** The incidence of gout in China is increasing in adults as well as children. The clinical manifestations of juvenile gout are not well described due to the limited number of cases in the past. Delineating the features of adult and juvenile gout may help pediatric providers recognize gout more effectively.

**Objectives:** We aim to describe and compare the clinical characteristic of adults and children with gout.

**Methods:** A total of 51 juvenile gout patients (age ≤ 18 years) and 337 adult gout patients in our hospital from Jan 2016 to Dec 2018 were enrolled in the study. Clinical parameters and laboratory data of the 2 groups were analyzed.

**Results:** The average age of onset in children with gout was 15.0±1.9 years and the youngest patient was 8 years old. Compared to the adult group, juvenile gout patients displayed lower BMI (23.0±3.8 vs. 25.6±3.5 kg/m², P<0.001) but higher serum uric acid levels (9.98±2.65 vs. 8.09 ±2.47 mg/dL, P<0.001). Interestingly, systemic inflammation was less prominent in children compared to adult as illustrated by lower C-reactive protein levels (7.1±13.5 vs. 23.7±40.7 mg/L, P<0.004) and lower erythrocyte sedimentation rate (12.7±12.9 vs. 33.1±34.2 mm/h, P<0.001). Renal function impairment was rare in children compared to adults (serum creatinine 98.73±11.04 vs 120.38±34.58 μmol/L, P<0.001). In terms joint manifestations, juvenile gout was associated with greater finger joint involvement (23.53% vs. 8.82%, P<0.001) and less knee involvement (11.76% vs. 41.84%, P<0.001) compared to adults. Ankle involvement was slightly more common in the pediatric group (49.02% vs. 30.56% in adults, P=0.009) while MTP was similarly affected (50.98% vs. 32.94%, P=0.012). In addition, tophi was found in four cases (7.8%) in the juvenile group compared to 113 cases in adults (33.5%), suggesting that although less common, advanced features of gout can also occur in children.

**Conclusion:** Juvenile gout is associated with higher serum uric acid levels and greater involvement of finger joints. Correlations with BMI and systemic inflammation were less prominent compared to gout in adults. These findings will help clinicians better recognize gout in children.

**REFERENCES:**


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**Other orphan diseases**

**FRIO582**

**NON-INFEKTIOUS UVEITIS AS A MANIFESTATION OF THE IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME IN PATIENTS INFECTED BY HIV**

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**Background:** Immune reconstitution inflammatory syndrome (IRIS) is a paradoxical clinical worsening of an already known condition or the new onset of an inflammatory manifestation that is presumably related with the immune reconstitution after starting highly active anti-retroviral therapy (HAART) in patients infected by the human immunodeficiency virus (HIV).

**Objectives:** The aim of this study is to describe the clinical characteristics, presentation and response to immunosuppressive treatment in patients with uveitis secondary to ocular IRIS in our cohort of patients infected by HIV.

**Methods:** Retrospective review of clinical charts of patients diagnosed with HIV and non-infectious uveitis. Data collected included: demographics, anatomic classification of the uveitis, phenotypic diagnosis of the uveitis, other systemic immune-mediated disorders (IMD), time from HIV diagnosis to uveitis, CD4 count, viral load, treatment and complications of treatment and time of follow-up.

**Results:** Nine-teen patients (17 males) were included in the study. The mean age at the time of HIV diagnosis was 35.4±9.6 years. The time lag between HIV diagnosis and the onset of uveitis was 9±8.9 years. Mean CD4 count was 649±292 cells/ml, while the viral load was undetectable in 13 out of 17 cases. In 2 patients, there were a worsening of a previous IMD and in 6 patients another IMD was diagnosed prior to or concurring with the uveitis diagnosis (3 cases of reactive arthritis). The most common anatomic classification of the uveitis was anterior (13 cases). The use of immunosuppressive therapies to control either the uveitis or the additional IMD was necessary in 6 patients (including biologics in 4 cases) during the follow-up. Only one patient had a complication of the immunosuppressive treatment. The mean follow-up was 43.8 months (range: 0.6 -115.7).

**Conclusion:** Non-infectious uveitis could be the first manifestation of immune-mediated systemic disease in patients with well-controlled HIV infection. Immunosuppression appeared to be a safe therapeutic option in our cohort of patients.

**REFERENCES:**


**Disclosure of Interests:** Ester Carreño Speakers bureau: Abbvie and Allergan, Andrea Maria Alvear Torres: None declared, Neltia Muñoz; None declared, Francisco Javier de la Hera Fernandez: None declared, SHEILA
NEUROMYELITIS OPTICA OVERLAPS FREQUENTLY WITH SYSTEMIC RHEUMATIC DISEASES IN AFRICAN-AMERICANS: EXPERIENCE AT A LARGE US ACADEMIC MEDICAL CENTER

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Background: Neuromyelitis optica (NMO) and neuromyelitis optica spectrum disorders (NMOSD) are immune-mediated demyelinating disorders of the central nervous system, primarily characterized by optic neuritis and longitudinal extensive transverse myelitis. Antibodies to aquaporin-4 (AQP4-IgG) are highly specific markers of NMOSD. The coexistence of NMOSD with systemic rheumatologic autoimmune disease has been well documented, especially systemic lupus erythematosus (SLE) and Sjögren syndrome (SS) [1]. Several recent studies have demonstrated that NMOSD may disproportionately affect black patients [2,3].

Objectives: Our objective was to characterize African-Americans diagnosed with NMO at our academic medical center, and identify any associate systemic rheumatologic autoimmune diseases.

Methods: We conducted a retrospective chart review of adult African-American patients diagnosed with NMO at a single academic medical center between 2011 and 2017. The charts reviewed were identified using ICD codes for NMO, transverse myelitis and optic neuritis. The diagnosis of NMO was then confirmed as per the 2015 International Consensus Diagnostic Criteria. The diagnosis of SLE and SS were also confirmed based on existing diagnostic criteria.

Results: Of the 60 charts reviewed, 25 patients (41.7%) met criteria for NMO, and of those, 21 patients (84%) were African-American. Of the 21 African-American NMO patients, 89.5% (n=19) were AQP4-IgG positive, 95.2% were women, and 38.1% had an associated systemic rheumatologic autoimmune disease. In 60% of the NMO patients with SLE, the diagnosis of NMO preceded the SLE diagnosis. Conversely, in 100% of the NMO patients with SS, the diagnosis of NMO either followed, or was made simultaneous to, the SS diagnosis. Notably, 80% of the NMO patients with SS had concurrent neuropsychiatric manifestations, and 78.6% of the African-American patients in whom ANA testing was performed (n=19), with anti-SSA (64.3%, n=14) and anti-SSB (50%, n=11) the next most prevalent autoantibodies. Mean age of NMO onset was 46.7 years (SD 13.6). Transverse myelitis was the most common presenting manifestation (71.4%), followed by optic neuritis (61.9%).

Conclusion: Our population had a higher mean age of onset (46.7 vs 33 years) compared with other cohorts of seropositive NMO African-Americans [2]. Additionally, African-Americans with NMO at our institution had a higher female:male distribution than has been documented[3]. Not surprisingly, SLE was the most common associated systemic rheumatic disease in our cohort, however the frequency of SLE and ANA positivity in our NMO cohort was higher than has been reported (23.8% and 78.6%, respectively) [4]. Additional larger studies are needed to further explore how NMOSD in African-Americans may differ from other populations.

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Disclosure of Interests: Michael Belsky: None declared, Hassan Amer: None declared, Sunita Dia: None declared, Christopher Collins: Grant/research support from: Exagen, Consultant for: Exagen, AbbVie, Speakers bureau: Exagen, AbbVie, Novartis, Konstantinos Loupasakis: None declared.

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EFFICACY AND SAFETY OF RITUXIMAB FOR INDUCTION OF REMISSION AND MAINTENANCE OF IGG4-RELATED DISEASE: EXPERIENCE FROM AN ITALIAN NATIONAL REFERRAL CENTRE

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Background: IgG4-related disease (IgG4-RD) is a systemic fibro-inflammatory disease. Treatment is based on corticosteroids (CS) but up to 50% of patients may relapse. Rituximab (RTX) has emerged as an effective treatment option[1].

Objectives: To assess the free relapse rate (FRR) in patients receiving or not maintenance RTX therapy. Secondary outcomes: time to relapse, incidence of adverse events and differences in FRR between Group 2a and 2b patients.

Patient # | Age (years) | Sex | N° of Organs involved | IgG4-RD (% of patients) | PGA | ESR (mm/h) | CRP (mg/L) | lgG4 (mg/L) | Concomitant DMARD therapies | Previous DMARD therapies | Outcomes after RTX induction | Relapses (time to relapse) | N° of RTX infusions | RTX Adverse Events | Follow-up (months)
--- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | ---
**Group 1**
1 | 29 | F | 3(Pm, Ns, Ph) | 12 | 90 | 38 | 25 | 1001 | No | CTX | PR | No | 1 | No | 32
2 | 47 | M | 2(Ly, Sg) | 6 | 50 | 8 | 1,2 | 4420 | No | MTX | DR | No | 1 | No | 30
3 | 70 | F | 1(Ao) | 6 | 70 | 26 | 3,7 | 850 | MTX | No | DR | Yes(7) | 2 | No | 26
4 | 52 | M | 2(Bd, Pa) | 6 | 60 | 19 | 1,3 | 3360 | No | No | DR | Yes(7) | 2 | No | 26
5 | 52 | M | 4(Pm, Sis, Or, Pa) | 15 | 90 | 7 | 21 | 1700 | No | MTX | DR | Yes(12) | 2 | No | 18
6 | 52 | M | 3(Ly, Sg, Lu) | 12 | 70 | 8 | 1,9 | 7904 | MTX | No | CR | Yes(11) | 2 | No | 18
7 | 80 | F | 3(Pa, Ly, Bd) | 6 | 90 | 22 | 6 | 3630 | No | MTX | DR | Yes(9) | 2 | No | 18

**Group 2**
1 | 53 | M | 5(Ly, Sis, Lg, Pa, Sj) | 12 | 80 | 7 | 0,1 | 5713 | No | AZA | CR | 0 | 3 | No | 18
2 | 49 | F | 4(Ly, Lg, Or, Ph) | 15 | 90 | 22 | 0,3 | 13800 | No | No | CR | 0 | 4 | No | 20
3 | 16 | F | 3(Or, Ls, Ly) | 9 | 60 | 6 | 0,2 | 630 | No | No | DR | 0 | 7 | No | 48
4 | 28 | F | 4(Ly, Ph, Or, Ns, Sj) | 15 | 90 | 65 | 5,7 | 2990 | No | CTX | CR | 0 | 3 | Yes | 18
5 | 73 | F | 3(Or, Ly, Ma) | 12 | 70 | 17 | 1,2 | 21800 | MTX | AZA | CR | 0 | 5 | Yes(Rash) | 30
6 | 51 | F | 3(Lg, Or, Lu) | 12 | 70 | 16 | 6,9 | 2530 | No | No | DR | 0 | 4 | No | 18
7 | 76 | M | 1(Bd) | 6 | 70 | 31 | 36 | 470 | No | No | DR | 0 | 3 | No | 21

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EFFICACY OF CANAKINUMAB AS FIRST-LINE THERAPY OF ADULT-ONSET STILL’S DISEASE

Giulio Cavalli, Alessandro Tomelleri, Giacomo De Luca, Lorenzo Dagna.

Methods: Data of IgG4-RD patients treated with RTX and followed-up for >18 months were reviewed. Patients were treated with two 1 g RTX doses 15 days apart (standard dose SD) and then divided into: patients receiving RTX in case of relapse (Group 1) and patients receiving maintenance AXT treatment 6 monthly (Group 2). Patients in Group 2 received a first maintenance treatment RTX SD and were then further divided into patients receiving RTX SD (Group 2a) or single 1 g RTX dose (Group 2b).

Results: 14 IgG4-RD patients were included. Median number of organs involved was 3 (IQR = 1–5). Baseline median physician global assessment (PGA) was 70 (50–90), IgG4-RD responder index (IGG4-RD RI) 12 (6–12), Median eosinophil count, CRP, ESR, and serum IgG4 level were 100 cells/μL (50–1,800), 19 mm/h (6–64), 3.7 mg/L (0.1–36) and 3.17 mg/L (470–21,800) respectively. Indications for RTX were: relapse in 10/14 (71%), partial response in 3/14 (21%) and first-line treatment in 1/7 (14%) patient. CR5 were stopped in 5 patients and reduced by month 3 in remaining patients (p < 0.001). Median eosinophil count, CRP and ESR levels did not change significantly. 8 (57.1%), 5 (35.7%) and 1 patient (7%) were on disease remission (DR), complete remission (CR), and partial remission (PR), respectively. Median number of RTX courses was 2 (2–3) in Group 1, 3 (3–7) in Group 2a, and 4 (3–5) in Group 2b. Organ involvement, PGA, IgG4-RD RI, ESR, CRP, and serum IgG4 levels were not significantly different between the 2 Groups at baseline. FRR at 18 months in Group 1 was significantly lower than that in Group 2 (29% vs 100%, p = 0.006). 5 (71%) patients in Group 1 relapsed on average 9 (7–12) months after RTX induction. 2 (14%) patients had hypersensitivity reactions during RTX induction. 6 (43%) patients, 3 in Group 1 and 3 in Group 2, experienced low-grade infections.

Conclusion: RTX is a safe and effective treatment in IgG4-RD. Both SD and single 1 g RTX dose seem effective in maintenance.

REFERENCES:

Disclosure of Interests: Giulio Cavalli: None declared, Alessandro Tomelleri: None declared, Giacomo De Luca Speakers bureau: Pfizer, Sobi, Corrado Campochia Consultant for: Dr. Corrado Campochia received consultation honoraria from Pfizer., Elena Baldissera Consultant for: Consultation honoraria from Novartis and Rottapharm, Speakers bureau: Pfizer, Sobi, Novartis.


FR0586 THE EFFECT OF TOCILIZUMAB IN THE PREVENTION OF FAMILIAL MEDITERRANEAN FEVER ATTACKS

Seda Cokel, Erine Tekgoz, Muhammet Cinar, Sedat Yilmaz. University of Health Sciences, Gulhane Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Ankara, Turkey

Background: Familial Mediterranean Fever (FMF) is the most frequent hereditary autoinflammatory disease in the worldwide. Colchicine is the mainstay of the treatment that is used for both preventing the attacks and developing amyloidosis. In case of colchicine resistance, which constitutes almost 5% of all patients, there are some alternatives such as anti-TNF agents, IL-6 and IL-1 antagonists. These agents have also been used in patients with established amyloidosis secondary to FMF. Tocilizumab (TCZ), an IL-6 receptor antagonist, although is effective in the treatment of amyloidosis, little known about its effectiveness in the preventing of febrile attacks.

Objectives: In this study, we aimed to find out whether TCZ therapy decrease the frequency of recurrent attacks of FMF or not.

Methods: This retrospective cross-sectional study designed in a tertiary rheumatology clinic between the years 2009 and 2019. A total of 15 patients were given intravenous TCZ at a dose of 8mg/kg/month, to improve amyloidosis associated with FMF. Data of demographic and clinical characteristics of patients were obtained retrospectively from patient files.

Results: Three female and 12 male patients received TCZ for amyloidosis treatment. The mean age of patients was 42.07±14.37 years and disease duration was 25.73±10.86 years. All of the patients had biopsy results providing amyloidosis. According to international severity scoring system for FMF, all of the patients had severe disease. Demographic and clinical data were shown in Table 1. The frequency of attacks was evaluated during TCZ treatment, and it was reported that 1 patient had no response, 6 patients had decreased attack frequency and 8 patients had no attacks. Serious adverse effects were seen in none of the patients.
MEFV: Mediterranea Fever, TCZ: Tocilizumab

Conclusion: Tocilizumab is found to be effective on improvement of amyloidosis. In the current analysis, we found that TCZ also decreases the frequency of recurrent attacks in patients with FMF. Besides, TCZ is well tolerated among the patients. Further and prospective studies with larger sample are needed to support these results.

REFERENCES:

Disclosure of Interests: None declared

FRI0588 THE SCALE OF ACTIVITY IN IDIOPATHIC LOBULAR PANNICULITIS
Olya Egorova, Boris Belov, Svetlana Glukhova. V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation

Background: Idiopathic lobular panniculitis (ILP) refers to chronic systemic connective tissue lesions (M 35.6). The disease develops with typical clinical symptoms and is characterized by alternating periods of stable condition (remission) and active manifestations (exacerbations). Assessment of the activity and identification of the disadvantageous predictors is the main task in monitoring patients with ILP; however, the “gold standard” has not been developed yet. Objectives: to create a rating scale for the inflammatory process activity in ILP on the basis of clinical and laboratory parameters

Methods: We examined 67 patients (9 men and 58 women) with the ILP diagnosis verified in the V.A. Nasonova Research Institute of Rheumatology in 2007-2017. The age of patients ranged from 20 to 76 years, the average duration of the disease was 78.91±48.50 months. At the time of treatment at the institute only 16 patients (23.88%) were diagnosed with ILP. All the patients underwent comprehensive clinical examination and laboratory and instrumental examination of biochemical and immunological parameters, radiography or computed tomography (CT) of the chest organs, as well as pathomorphological examination of skin and subcutaneous fat biopsies from the node area.

Results: Analysis of clinical manifestations allowed to identify four forms of ILP: nodular (30 patients), plaque (10), infiltrative (15) and mesenteric (12), which had specific clinical and laboratory features. Based on the obtained data we developed a scale of the ILP activity (SA), which includes a description of the state of the 7 organ systems. The maximum score for individual systems is from 1 to 3 points depending on the number of estimated parameters. The total maximum possible score is 42 points. The score includes all types of damage since the onset of the disease (caused directly by ILP or developed as a result of therapy), while taking into account only signs that persist for 6 months. Score <5 shows inactive disease, 5-10 - low disease activity, 11-20 - moderate activity and >20 - high activity of the disease. Thus, low disease activity is characterized by the predominance in the clinical picture of limited moderately painful indurations in the absence of any significant changes in laboratory tests. At the moderate disease activity, changes in various localization with a predominance of proliferative disorders (common painful compaction of the 1st and/or 3rd stage, moderate area of damage to the trunk and limbs, sublebile temperature, cognitive impairment, mesenteric disorders, etc.) are revealed against the background of less pronounced laboratory tests. ILP with high activity is characterized by the presence of fever and other common signs of the disease, the predominance of the 2nd stage with a pronounced VAS pain intensity of the indentation, the common nature of the defeat of the pancreas, involvement of the lungs, heart and gastrointestinal tract in the pathological process.

Conclusion: In fact, SA is an analysis of the organ damage, assessment of the symptoms severity, and it takes into account the development of exacerbations with the involvement of new organs in the process of the disease. The proposed ILP SA is of practical importance. Further
research and possibly search for new parameters of the ILP activity are needed.

Disclosure of Interests: None declared

FR0589
IS THERE AN OVERLAP OF ANTINEUTROPHIL CYTOPLASMATIC ANTIBODY-ASSOCIATED VASCULITIDES WITH IGG4-RELATED DISEASE OR NOT?

Abdulkareem Ertugrul, Erdinç Can Bölek, Gözde Kübra Yardımcı, Sule Apras Bilgen, Omer Karadag, Hacettepe University Vascularitis Centre, Ankara, Turkey

Background: Pseudotumor orbita, pachymeningitis, periaortitis could be seen in both ANCA-associated vasculitis and IgG4-RD. Sometimes it may be difficult to differentiate these two entities. The co-occurrence/concurrence of Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides (AAV) and IgG4-related disease (IgG4-RD) was recently published by a collaborative EUVAS group [1].

Objectives: Firstly, we aimed to investigate ANCA positivity of our IGG4-RD cohort. Secondly, a literature review of co-occurrence/concurrence of AAV and IgG4-RD was done.

Methods: Data of totally 62 patients with IgG4-RD in Hacettepe Vascularitis Center Database was used. Patients were diagnosed with IgG4-RD according to comprehensive diagnostic criteria [2]. Dataset of patients including demographic data, clinical characteristics, and imaging and laboratory findings of IgG4-RD was re-evaluated in terms of AAV and ANCA test.

At next step, we performed a systematic literature review of the PUBMED database covering the time period until April 2018. Relevant publications were searched using the MeSH terms “IgG4-related disease” and “Eosinophilic Granulomatosis with Polyangiitis”, “IgG4-related disease and Anti-Neutrophil Cytoplasmic Antibody-Associated Vasculitis” and “IgG4-related disease and Granulomatosis with Polyangiitis”.

Results: Totally 29 (46.7%) of our patients had ANCA results. Out of 29 patients 15 (51.7%) were considered as probable, 10 (34.5%) as definite and 4 as possible (13.8%) for IgG4-RD. Three (10.3%) of these patients had ANCA positivity. All of these ANCA titers were in low degree positivity (MPO-ANCA 1/100, MPO-ANCA 1/32 and PR3 ANCA 1/100). These three patients didn’t have any findings of vasculitis and didn’t have granuloma in their biopsy. When we evaluate these three patients with regards to meeting the Ig G4 -RD criteria, 1 was definite, 1 was probable and 1 was possible. In literature review, we found 17 cases that having both features of IgG4-RD and AAV (Table). These cases were re-evaluated according to the ‘Comprehensive Diagnostic Criteria for IgG4-RD’. Diagnoses of IgG4-RD were definite in 11 cases (64.7%), probable in 2 cases (11.8%) and possible in 4 cases (23.5%). ANCA were positive in 15 of 17 patients (88%). ANCA were directed against proteinase 3 (PR3-ANCA) in 6 patients and were directed against myeloperoxidase (MPO-ANCA) in 5 patients. Other four cases had both MPO-ANCA and PR3-ANCA. All PR3-ANCA positive cases have high titers of ANCA, whereas only one MPO-ANCA positive case has low titers of ANCA.

Conclusion: None of our IgG4-RD patients have any overlap with ANCA-associated vasculitis. Only in 3 patients (10.3%), ANCA positivity was detected without any histopathologic evidence. Just two patients of literature review, seemed to be full compatible with both diseases. Even though ANCA-associated vasculitis and IgG4-RD share clinical features, we think this might be as co-occurrence instead of a histopathologic link.

REFERENCES:

Disclosure of Interests: None declared

FR0590
UVEITIS SECONDARY TO CHECKPOINT INHIBITORS

JAVIER GARCIA, Eugenio Perez-Blazquez. HOSPITAL 12 DE OCTUBRE, MADRID, Spain

Background: The introduction of immunotherapy (immune checkpoint inhibitors, ICI) has led to a revolution in oncological treatments. The inhibitors of CTLA4 (ipilimumab), of PD1 (pembrolizumab, nivolumab) and of the ligand of PD1 (atezolizumab, avelumab, durvalumab) regulate T activation and its effector function, being effective for the treatment of various types of cancer1. However, this effect leads to a series of immune-mediated adverse events, among which uveitis of autoimmune mechanism have been described in about 1% of treatments2.

Objectives: Methods: descriptive study of retrospective review of the cases of a tertiary hospital with about 1000 treatments between the beginning of 2014 and the end of 2018.

Results: A series of 4 cases of uveitis of autoimmune origin associated with ICI is presented (see table). The series described has characteristics similar to the information previously reported in the literature2, with an incidence of around 0.4%, according to the previously described, with frequencies of ocular toxicity around 1%, being the uveitis is the most frequent form of presentation. The time of presentation of uveitis since the beginning of treatment has been in all cases in the first 6 months. The frequencies of ocular toxicity around 1%, being the uveitis is the most frequent form of presentation. The time of presentation of uveitis since the beginning of treatment has been in all cases in the first 6 months. The frequencies of ocular toxicity around 1%, being the uveitis is the most frequent form of presentation. The time of presentation of uveitis since the beginning of treatment has been in all cases in the first 6 months. The frequencies of ocular toxicity around 1%, being the uveitis is the most frequent form of presentation. The time of presentation of uveitis since the beginning of treatment has been in all cases in the first 6 months. The frequencies of ocular toxicity around 1%, being the uveitis is the most frequent form of presentation. The time of presentation of uveitis since the beginning of treatment has been in all cases in the first 6 months. The frequencies of ocular toxicity around 1%, being the uveitis is the most frequent form of presentation. The time of presentation of uveitis since the beginning of treatment has been in all cases in the first 6 months. The frequencies of ocular toxicity around 1%, being the uveitis is the most frequent form of presentation. The time of presentation of uveitis since the beginning of treatment has been in all cases in the first 6 months. The frequencies of ocular toxicity around 1%, being the uveitis is the most frequent form of presentation. The time of presentation of uveitis since the beginning of treatment has been in all cases in the first 6 months. The frequencies of ocular toxicity around 1%, being the uveitis is the most frequent form of presentation. The time of presentation of uveitis since the beginning of treatment has been in all cases in the first 6 months.

References:
[1] JAVIER GARCIA, Eugenio Perez-Blazquez. HOSPITAL 12 DE OCTUBRE, MADRID, Spain

Disclosure of Interests: None declared
Conclusion: Uveitis is an infrequent, although potentially serious, immune-mediated side effect of ICI. Early recognition, discarding other causes of uveitis, particularly the masquerade syndrome, and early intervention are key to a good prognosis. The collaboration between the oncology teams and the ocular inflammation units must be close to establish the correct diagnosis and treatment, as well as to decide individually on the reintroduction or not of the oncological treatment. The implementation of registries on the adverse effects of these drugs can help to dimension the problem more accurately.

REFERENCES:

Disclosure of Interests: None declared

FR0591 RHEUMATIC IMMUNE-RELATED ADVERSE EVENTS ASSOCIATED WITH TREATMENT WITH IMMUNE CHECKPOINT INHIBITORS: A CASE SERIES FROM TWO REFERRAL CENTRES
Sebastian C. Rodriguez-García1, David Lobo2, Raul Castellanos-Moreira1, Ana Milena Milán Arciniegas2, Roberto Gumucio1, Ana Laiz2, Virginia Ruiz-Exiqued1, Berta Magallares1, Cesar Díaz-Torné2, Patricia Moya1, Ivan Castellví1, Hector Corominas3, Jose A. Gómez-Puerta1. 1Hospital Clínic de Barcelona, 2Hospital de la Santa Creu i Sant Pau, 3Hospital Clinic de Barcelona, Barcelona, Spain; 1Hospital de la Santa Creu i Sant Pau, Rheumatology, Barcelona, Spain

Background: Immune checkpoint inhibitors (ICI) against CTLA-4 or PD-1/PD-L1 improve the survival of patients with advanced malignancies including melanoma, lung cancer among other tumours. Because of its mechanism of action, ICI are prone to produce different immune-related adverse events (irAEs), including musculo-skeletal manifestations.

Objectives: Our aim was to describe the experience with rheumatic irAEs in two tertiary centres.

Methods: All adult patients referred to the Rheumatology department from 2015 to 2018 because of the onset of musculo-skeletal symptoms following treatment with an ICI were included. Data collected comprised demographic features as well as ICI indication and type, history of rheumatic disease, disease manifestations at irAE onset, laboratory tests, ultrasound findings and treatment. Diagnostic and treatment approach was done according clinical judgment and in a daily clinical practice setting.

Results: 20 patients were included, 50% female, with a mean age of 61.5 years (range 32-83). The indication for ICI was melanoma in 10 cases, lung cancer in 5, urothelial neoplasia in 2 and squamous skin, breast and head and neck cancer in 1 case each. Pembrolizumab was the most used ICI accounting for 9 cases (1 combined with epacadostat), 8 patients were treated with Nivolumab (4 combined with Ipilimumab), 2 wit Atezolizumb (1 combined with Ibatuzumab) and 1 Ipilimumab in monotherapy.

A history of previous rheumatic disease was reported in 8 patients (1 seropositive RA, 1 Spondyloarthritis, 1 SLE, 1 gout, 1 chondrocalcinosis, 1 fibromyalgia, 1 De Quervain tendinitis, 1 hand osteoarthritis) and 1 had psoriasis.

The most frequent irAE presentation was arthritis with 8 cases (40%), arthralgia in 4 cases (20%), 1 case of myalgia, 2 presented PMR-like symptoms, 1 tenosynovitis and 2 paraesthesia (1 with associated dysesthesia).

After assessment, 7 patients were diagnosed as undifferentiated arthritis, 1 leucocytoclastic vasculitis, 1 small-vessel vasculitis, 2 psoriatic-like arthritis, 1 tenosynovitis, 2 PMR and 6 were classified as having non-inflammatory symptoms.

Antibody status was analyzed in 16 patients. Anticytotoxic peptide antibodies, rheumatoid factor and HLA B27 were negative in all cases (except for 1 patient with seropositive RA), ANAs were positive in 4 (including 1 patient with previous SLE) but without any specificities (i.e. ENAs) and ANCA were negative in one case with small-vessel vasculitis. Ultrasound assessment was performed in 6 patients, 3 presented synovial hypertrophy with positive power Doppler (1 with tenosynovitis associated), 1 peritendinous fluid collection, 1 elbow joint effusion and 1 bilateral supraspinatus calcified tendinopathy.

Most patients were treated with glucocorticoids 12 (60%) and NSAID 6 (30%) and only 3 patients had to discontinue ICI treatment due to irAEs.

Conclusion: Our results were in line with previous studies showing that musculo-skeletal irAEs associated to ICI may present as a flare of a previous known rheumatic disease or as a de novo symptom. Most patients presented with asymmetric mono or oligoarthritis having a good response to GC and NSAID without the need of adding DMARD or withdrawal of ICI therapy.

Disclosure of Interests: Sebastian C Rodriguez-García: None declared, DAVID Lobo: None declared, Raul Castellanos-Moreira: None declared, Ana Milena Milán Arciniegas: None declared, Roberto Gumucio: None declared, Ana Laiz Consultant for: Lilly, Novartis, AbbVive, MSD, UCB and Janssen, Speakers bureau: Lilly, Novartis, Aboixive, MSD, Syntel, Lilly, MSD, Berta Magallares: None declared, Cesar Díaz-Torné: None declared, Patricia Moya: None declared, Ivan Castellví: None declared, Hector Corominas: None declared, Jose A. Gómez-Puerta Consultant for: Pfizer, Roche, Speakers bureau: Abbvie, BMS, Janssen, MSD, Pfizer, Roche

FR0592 CLINICAL CHARACTERISTICS OF OLDER AGE-ONSET BEHÇET SYNDROME PATIENTS
Gül Guzelant Ozkoo1, Yılmaz Ozyazgan2, Cem Mat1, Vedat Hamuryudan1, Hasan Yazıcı1, Emre Seyahi1, 1Istanbul University-Cerrahpasa, Medical Faculty of Cerrahpasa, Dermatology, Istanbul, Turkey; 2Istanbul University-Cerrahpasa, Medical Faculty of Cerrahpasa, Ophthalmology, Istanbul, Turkey; 3Istanbul University-Cerrahpasa, Medical Faculty of Cerrahpasa, Dermatology, Istanbul, Turkey

Background: The usual onset of Behçet syndrome (BS) is in the 3. decade. Older age-onset defined as fulfilling the ISG criteria after 40 years of age is rare. One study from our center had reported the severity of eye disease was not different between early onset (≤ 24 years) and late onset (> ≥ 25 years) group. (1). While there is ambiguity in the definition of older onset, a few case series (2,3) coming mostly from ophthalmology or dermatology settings describe a similar or less severe clinical picture among late onset patients (pts) compared to early onset.

Objectives: To evaluate clinical characteristics of older onset pts and to compare them with classic onset pts.
Methods: The charts of 3335 BS pts who were registered between 2000 and 2010 were reviewed retrospectively. Pts who fulfilled ISG criteria for BS after 40 years of age were defined as older onset, while those who fulfilled the criteria before 30 as classic onset. For each older onset chart, 2 consecutively registered early onset charts were selected. Only clinical manifestations at presentation were recorded. A clinical activity index (1) was modified and calculated.

Results: There were only 134(70 M/64 F) pts with older onset BS, which gave a prevalence of 4% in the whole cohort. Age of onset was 40-44 years of age in 54 pts, 45-49 years in 47 and 50+ in the remaining 32. As controls 268(163 M/105 F) classic onset pts were selected. Demographic and clinical characteristics among older and classic onset pts are described for males and females separately, in Table. The frequency of skin manifestations, arthritis and eye disease as well as the mean clinical activity scores were significantly higher among male classic onset pts compared to older onset male pts. Interestingly, the frequency of those with positive pathergy test, vascular involvement and severe eye involvement did not seem to be different among older and classic onset male pts. On the other hand, clinical characteristics and total activity scores were similar between older and classic onset groups among females (Table). The main limitation is that the information was based solely on patient's charts and outcome information was not available.

Conclusion: Compared to classic onset pts, males tend to be less frequent in older cohort. At presentation, older onset male pts had significantly less frequent skin, joint, eye disease, and significantly lower total activity scores compared with classic onset pts. There was no difference between the classic and older onset group, among females.

| Table. Clinical characteristics of older age-onset and classical-onset BS pts (Males/ Females) |
|---|---|---|---|---|---|
| Age at ISG criteria fulfilling, yrs | Oral ulcer, n (%) | Genital ulcer, n (%) | Papulo-pustular lesions, n (%) | Nodular lesions, n (%) | Arthritis, n (%) |
| Olders (n=163) | 47.0 ± 6.0 | 24.2 ± 4.5 | 46.6 ± 5.7 | 23.1 ± 4.4 |
| Classical (n=64) | 64 (100) | 60 (96) | 137 (84) | 5.60 ± 3.15 | 13 (21) | 6 (96) | 0.307 |
| P | 0.050 | 0.845 | 0.0001 | 0.006 |
| Olders (n=163) | 61 (99) | 63 (100) | 138 (86) | 51 (80) | 39 (61) | 29 (45) | 41 (64) | 0.710 |
| Classical (n=64) | 105 (100) | 105 (100) | 138 (100) | 90 (96) | 71 (68) | 60 (87) | 42 (65) | 0.142 |

**References:**


Disclosure of Interests: None declared.
Table 1. Comparing of clinical features between patients with HLH complicated with rheumatic diseases or tumor

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>Patients with rheumatic diseases (n=7)</th>
<th>Patients with tumor (n=5)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean)</td>
<td>17.66 yrs (38.7)</td>
<td>29.59 (47.8)</td>
</tr>
<tr>
<td>Male/Female</td>
<td>15/3</td>
<td>3/2</td>
</tr>
<tr>
<td>Fever</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Cytopenia (&lt;2 blood cell)</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Abnormal liver function tests</td>
<td>71.4%</td>
<td>100%</td>
</tr>
<tr>
<td>Hypofibrinogenemia</td>
<td>28.6%</td>
<td>100%</td>
</tr>
<tr>
<td>Hypertrophic cardiomypathy</td>
<td>10.0%</td>
<td>80%</td>
</tr>
<tr>
<td>Hypertriglyceridemia</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Increased lactate</td>
<td>83.3%</td>
<td>80%</td>
</tr>
<tr>
<td>Tumor</td>
<td>57.1%</td>
<td>100%</td>
</tr>
<tr>
<td>Splenomegaly/Heptomegaly</td>
<td>85.7%</td>
<td>75% (3/4)</td>
</tr>
<tr>
<td>Fulfill the 2004 HLH criteria 100%</td>
<td>100%</td>
<td></td>
</tr>
<tr>
<td>Treatment Ciclosporin</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>42.9%</td>
<td>0</td>
</tr>
<tr>
<td>Etoposide (VP-16)</td>
<td>14.3%</td>
<td>40%</td>
</tr>
<tr>
<td>Prognosis</td>
<td>71.4%</td>
<td>40%</td>
</tr>
<tr>
<td>Control during inpatient period</td>
<td>28.6%</td>
<td>60%</td>
</tr>
<tr>
<td>Dead or give up</td>
<td>28.6%</td>
<td>60%</td>
</tr>
</tbody>
</table>

Conclusion: Clinical features of HLH patients complicated with tumor or rheumatic diseases were comparable in many aspects. Yet patients with tumor have more hypofibrinogenemia and lung involvement, and tend to be treated with VP-16 and Chemical therapy, and have much worse prognosis.

References:


Table 1

<table>
<thead>
<tr>
<th>Cancer Cases</th>
<th>SIR 95% Confidence Interval</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female &lt;20-years</td>
<td>5/1.45</td>
<td>3.44</td>
</tr>
<tr>
<td>Female ≥50-years</td>
<td>1/23.9</td>
<td>0.42</td>
</tr>
<tr>
<td>Male &lt;20-years</td>
<td>28/43.08</td>
<td>0.65</td>
</tr>
<tr>
<td>Male ≥50-years</td>
<td>10/23.9</td>
<td>0.42</td>
</tr>
</tbody>
</table>

Disclosure of Interests: Enime Bilgin: None declared, Deniz Can Güven: None declared, Serdar Ceylan: None declared, Ozge Aybi: None declared, Riza Can Kardas: None declared, Bora Fritliatar: None declared, Tolga Yildirim: None declared, Seza Ozen Consultant for: Seza Ozen is receiving consultancy fees from Novartis, Speakers bureau: Roche, Omer Dizdar: None declared, Kadir Mutlu Hayran: None declared, Umut Kalyoncu Grant/research support from: MSD, Roche, UCB, Novartis, Pfizer Consultant for: MSD, Abbvie, Roche, UCB, Novartis, Pfizer and Abdi Ibrahim, Speakers bureau: MSD, Abbvie, Roche, UCB, Novartis, Pfizer and Abdi Ibrahim


Table 1

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Number of Patients</th>
<th>Observed Cancer Cases</th>
<th>Expected Cancer Cases</th>
<th>SIR 95% Confidence Interval</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20 years</td>
<td>5</td>
<td>3.44</td>
<td>2.76-7.05</td>
<td>0.003</td>
<td></td>
</tr>
<tr>
<td>≥50 years</td>
<td>10</td>
<td>0.42</td>
<td>0.21-0.75</td>
<td>0.002</td>
<td></td>
</tr>
</tbody>
</table>

Disclosure of Interests: Aydan Koken Aysal, Onay Gencel, Gercek Can, Berin Zergin, Sinem Burcu Kocael: None declared, Aliaha Canlik, Sedatcin Ustlu, Ali Karikas, Mehri Birlik, Servet Akar, Fatos Oneri: None declared, Dokuz Eylul University School of Medicine, Rheumatology, Izmir, Turkey: Izmir Kapi Celebi University Faculty of Medicine, Rheumatology, Izmir, Turkey: Dokuz Eylul University Faculty of Medicine, Rheumatology, Izmir, Turkey: Dokuz Eylul University Faculty of Medicine, Internal Medicine, Izmir, Turkey: None declared.

Background: IgG4-related disease is a recently recognised inflammatory disease of unknown etiology, often seen in men over the age of 50 and may affect many organs and systems with elevated serum IgG4 levels and typical histopathological features.


Table 1

<table>
<thead>
<tr>
<th>Gender</th>
<th>Age Group</th>
<th>Number of Patients</th>
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<th>Number of Patients</th>
<th>Observed Cancer Cases</th>
<th>Expected Cancer Cases</th>
<th>SIR 95% Confidence Interval</th>
<th>P value</th>
</tr>
</thead>
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<tr>
<td>&lt;20 years</td>
<td>5</td>
<td>3.44</td>
<td>2.76-7.05</td>
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<tr>
<td>≥50 years</td>
<td>10</td>
<td>0.42</td>
<td>0.21-0.75</td>
<td>0.002</td>
<td></td>
</tr>
</tbody>
</table>
The most commonly (68.5%) used imaging method for diagnosis was computed tomography (CT). All the patients used initial glucocorticoid treatment. 4 patients (7.5%) received only glucocorticoid, others were under- went the following treatments combined with glucocorticoid: azathioprine (AZA) (60.4%), methotrexate (MTX) (11.3%), rituximab (RTX) + AZA (9.4%), MTX + AZA (5.7%), RTX (3.8%) and infliximab (1.9%).

In the follow-up, a significant decrease in acute phase reactants was found in 62% of the patients at their last visits. While 27.3% of the patients had complete remission, 36.4% had partial remission, 20.5% had stable course, 13.6% had progression in the disease and 2.3% had recurrence. In 16 patients (64.3%) out of 28 patients who were in partial or complete remission, remission was achieved by using glucocorticoid and AZA combination treatment.

Conclusion: In conclusion, we have described a considerably large series of patients with IgG4-related disease from Turkey. The results of the study suggested that AZA and glucocorticoid combination treatment was commonly used in Turkish patients with IgG4-related disease and it might be a good treatment option to achieve remission.

REFERENCES:

Disclosure of Interests: Aydan Köken Avşar: None declared, Önyar Gerçik: None declared, Nerçen Can: None declared, Berrin Zengin: None declared, Sadettin Uslu: None declared, Ali Karakas: None declared, Merih Bilirik: None declared, Servet Akar Grant/research support from: MSD, Abbvie, Roche, UCB, Novartis, Pfizer, Agen, Consultant for: MSD, Abbvie, Roche, UCB, Novartis, Pfizer, Agen, Speakers bureau: Pfizer, Falcao Onen: None declared.
AA AMYLOIDOSIS IN RECIPIENTS OF CADAVERIC DERIVED PITUITARY GROWTH HORMONE – POTENTIAL EFFECT OF AN AMYLOID ENHANCING FACTOR

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Background: The development of Creutzfeldt–Jakob disease (CJD) in individuals treated with human cadaveric pituitary-derived growth hormone (c-hGH) was reported in 1985 resulting in its immediate withdrawal(1). Amyloid-β protein (Aβ) deposits have been found at autopsy in individuals previously exposed to c-hGH and misfolded Aβ peptide was recently identified in archived vials of human c-hGH; this induced Aβ pathology in an experimental model(2). The suggestion that contaminants in c-hGH could seed protein misfolding is reminiscent of the concept of amyloid enhancing factor (AEF), in which administration of tiny amounts of amyloidotic material is associated with acceleration of experimentally induced murine AA amyloidosis(3). In humans AA amyloid is a rare complication of chronic inflammation in which the amyloid fibrils are derived from Serum Amyloid A protein (SAA), a circulating component of the acute phase response.

Objectives: To seek evidence of prior exposure to c-hGH in patients with AA amyloidosis.

Methods: A database of 782 patients with AA amyloidosis seen between 1990 & 2017 was searched using: pituitary, craniopharyngioma & growth hormone. Only patients exposed to c-hGH were included. 20 patients eventually required long-term FUP were 100% and 78% respectively. Additionally, juvenile arthritis disease activity score (JADAS)-10 ≤ 1 scores were reported for ANA or CAN, CAN, ETN and TCZ as 52%, 48%-91%, 20% and 36% at short-term FUP. The mean changes in JADAS-71 scores at short-term FUP for ANA and TCZ were 10% and 11% respectively while the corresponding scores at long-term FUP were 13% and 14% (p<0.001).

All interventions were generally well tolerated by SJIA patients; infections, injection site reactions and macrophage activation syndrome were reported for all biologics. Other complications included gastrointestinal disorders, pharyngitis, skin disorders, increase in liver enzymes etc.

Conclusion: The current interventions especially ANA, CAN, ETN and TCZ were found to be effective and generally well tolerated in SJIA. However, the lack of head-to-head studies limits a rigorous comparison.

REFERENCES:

FR06000 FIRST SINGLE-CENTERED COHORT OF CHINESE PATIENTS WITH PEDIATRIC SAPHO

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Background: The SAPHO syndrome (Synovitis, Acne, Pustulosis, Hyperostosis and Osteitis) is an disease entity with chronic inflammatory osteoarticular symptoms and typical dermatological lesions. Pediatric SAPHO is regarded as equivalent of Chronic Recurrent Multifocal Osteomyelitis (CRM0) or Chronic Non-bacterial Osteomyelitis (CNO). There have already been several pediatric SAPHO cohorts about Caucasian populations. No Chinese cohorts have been reported.

Objectives: The aim of this study was to evaluate clinical features and treatment for all pediatric SAPHO patients admitted to Peking Union Medical College Hospital from April 2014 to August 2018 [1].

Methods: We conducted a single-centered non-intervention retrospective study of 24 pediatric SAPHO patients who were diagnosed with Khan’s modified criteria in PUMCH from April 2014 to August 2018 [1]. The demographic (sex, age, onset age, follow-up years), clinical (bone and skin symptoms), laboratory (ESR, CRP, HLA-B27, ANA, IL-6, IL-8, TNF-α), imaging (CT, MRI, bone scintigraphy), histologic (lymphocytic, granulocytic) and treatment (medications and effect) data were collected.

Results: Detailed information of 15 male and 9 female was available. The mean ± SD age at onset of bone and skin symptoms was 11.7 ± 3.8 and 14.4 ± 2.7 years, respectively. The duration of follow-up was 19.2 ± 15.2 months. 17 (71%) patients had skin manifestations (46% Severe Acne, all male; 21% Palmpoplantar Pustulosis, all female; 4% psoriasis), Involvement of bone lesions varied (42% anterior chest wall, 29% mandible, 50% peripheral bones, 21% spinal bones), ESR, CRP, IL-6, IL-8, IL-10 was elevated in 88%, 96%, 50%, 71%, 70% patients, respectively. 11 did bone biopsy (6 dominantly lymphocytic, 3 granulocytic, 2 both). CT, MRI and bone scintigraphy were performed in 79%, 96% patients, respectively. A total of 6 patients have been treated with NSAIDs, 10 with bisphosphonate, 10 with TNF-α antagonist, 1 with Glucocorticoids, with a variable response. 70% patients showed complete remission after bisphosphonate or TNF-α antagonist therapy.
Conclusion: High serum IgG4 was very common in liver diseases without IgG4 related diseases especially in HBV hepatitis. Differential diagnoses should be made in patients with hepatitis accompanied with high serum IgG4.

REFERENCES:
[1] No.

Disclosure of Interests: None declared

Table 2. Effect of different treating choices for 24 pediatric SAPHO patients

<table>
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<th>Medications</th>
<th>Remission</th>
<th>Partial response</th>
<th>No response</th>
<th>Total</th>
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</thead>
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<tr>
<td>NSAIDs</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>6/24</td>
</tr>
<tr>
<td>Bisphosphonates</td>
<td>7</td>
<td>2</td>
<td>1</td>
<td>10/24</td>
</tr>
<tr>
<td>TNF-α antagonist</td>
<td>7</td>
<td>3</td>
<td>0</td>
<td>10/24</td>
</tr>
<tr>
<td>Glucocorticoids</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1/24</td>
</tr>
</tbody>
</table>

Conclusion: This is the first Chinese cohort of pediatric SAPHO patients. Their bone lesions could be divided into 4 types, anterior chest wall, mandible, peripheral bones and spinal bones. We also provide evidence that bisphosphonate and TNF-α antagonist are useful for pediatric SAPHO treatment.

REFERENCES:

Disclosure of Interests: None declared

FRI0602 SERUM IMMUNOGLOBULIN G4 LEVEL IN INHEPATITIS B WAS HIGHER THAN AUTOIMMUNE LIVER DISEASE IN A CHINESE POPULATION

Zetao Liao, Yanli Zhang. Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China

Background: High serum level of Immunoglobulin G4 (IgG4) was detected in autoimmune hepatitis (AIH), but little was known in other types of hepatitis such as hepatitis B, primary biliary cholangitis (PBC) and primary sclerosing cholangitis (PSC).

Objectives: The aim of this study is to evaluate the level of serum IgG4 in hepatitis B and autoimmune liver disease.

Methods: Hepatitis B and autoimmune liver disease patients were enrolled between January 1st and August 30th 2018. Diagnosis of Hepatitis B, AIH, PBC and PSC was basing on corresponding classification criteria, and established IgG4 related diseases were excluded. The levels of serum IgG4 were determined by nephelometric assay. The cut-off value of serum IgG4 was 2.01 g/L. Serum IgG4 among different liver diseases were compared.

Results: 161 HBV hepatitis and 112 autoimmune liver diseases (52 AIH, 57 PBC, 3 PSC) were enrolled in this study. The HBV hepatitis patients were younger than patients with autoimmune liver disease (44.79±12.56 vs 52.52 ± 11.16 years old). In total, 61 patients (22.34%) had elevated serum IgG4 level. IgG4 level in HBV hepatitis was significantly higher than in AIH, PBC, respectively (1.64±1.80 vs 1.11±1.16, 1.64±1.80 vs 0.96±0.87 g/L, p<0.05).

Conclusion: High serum IgG4 was very common in liver diseases without IgG4 related diseases especially in HBV hepatitis. Differential diagnosis should be made in patients with hepatitis accompanied with high serum IgG4.

REFERENCES:
[1] No.

Disclosure of Interests: None declared
Sarcoidosis in a Tertiary Hospital Systemic Sarcoidosis. Study of 381 Patients

Neurological 4(7)

Increased levels of ACE were associated with clinical remission of the S remitted. In 54% of the patients the S had a chronic course and in 14%) or biological treatment (1 patient with Adalimumab and another with Infliximab). In 94% of the patients have been treated with oral glucocorticoids, 52% and biological agents (table 2).

Disclosure of Interests: None declared


FR10603 SARCOIDOSIS IN A TERTIARY HOSPITAL Isabel Madroñal García, Clara Aguilera Cros, Maria Dolores Arcila Duran, Lara Mendez, Maritza Gomez Vargas, Alberto Ruiz Roman, Ricardo Juan Gil Velez, Jose Antonio Rodriguez Portal, Noemí Patricia Garrido Puñal, Esteban Rubio Romero. Hospital Universitario Virgen del Rocio, Reumatología, Sevilla, Spain

Background: Sarcoidosis (S) is a systemic granulomatous disease of unknown etiology. The most frequent affection is pulmonary, ocular and cutaneous, although sarcoidosis can damage other organs, such as the musculoskeletal system.

Objectives: To describe the clinical characteristics and the radiological pattern, in a cohort with predominant pulmonary S, as well as to establish the relationship between the angiotensin converting enzyme (ACE) levels and the S course (chronification or remission).

Methods: This is a retrospective descriptive study of patients treated in our hospital, since 2008 to 2018, with diagnosis of S. The data was obtained through the review of medical records. The delay in the diagnosis of S was defined as the difference in months between the initial diagnostic suspicion and the final diagnosis of S. We use Chi-square tests to study the association between ACE levels and the course of the disease.

Results: Fifty-five patients (31 women) were included, with a mean age of 52 ± 12 years. The first diagnosis was: 85% S, 10% lymphoma and 4% tuberculosis. The median of months for the definitive diagnosis of S was 5.5 months. Extrapulmonary clinical manifestations in table 1. The ACE is increased in 38 patients (70%). Simple x-ray and high resolution tomography of chest were done in all patients. Pulmonary stage 2 was the most frequent (51%), followed by stage 3 (16%), stage 0 (14%) and stage 4 (9%). In 90% of the patients, histological confirmation was obtained by transbronchial (47%), cutaneous (11%) or lymph node biopsy (29%). 94% of the patients have been treated with oral glucocorticoids, 52% associate immunosuppressive therapy (Methotrexate 27% and Azathioprine 14%) or biological treatment (1 patient with Adalimumab and another with Infliximab). In 54% of the patients the S had a chronic course and in 43% S remitted. Increased levels of ACE were associated with clinical remission of the disease and normal levels with chronically (p: 0.013).

Extrathoracic Clinical Manifestations

Conclusion: The results of our study resembles, in general, what has been published in the literature. In our study, elevated ACE is associated with remission of the disease, contrary to the published, in which increased levels of ACE in symptomatic patients may reflect disease activity.

Disclosure of Interests: None declared


FR10604 SYSTEMIC SARCOIDOSIS. STUDY OF 381 PATIENTS FROM A TERTIARY UNIVERSITY HOSPITAL IN THE NORTH OF SPAIN José Luis Martín-Vartaras1, Lara Sánchez Bilbao1, Iñigo González-Mazón1, Raul Fernandez Ramón1, D. Prieto-Peña1, David Martínez-Lopez1, Eva Pería Saiz-Pardo1, Belén Alenaz-Mateo1, Monica Caldentén-Goecke1, Rosalía Demetrio-Pablo1, Vanesa Calvo-Rio1, Miguel A. González-Gay1, Ricardo Blanco1. 1H.U.M. Valdecilla, Rheumatology, Santander, Spain; 2H.U.M. Valdecilla, Ophthalmology, Santander, Spain; 3H.U.M. Valdecilla, Paediatrics, Santander, Spain

Background: Sarcoidosis is a systemic granulomatous disease characterized by the presence of non-necrotizing granulomas in different parenchyma.

Objectives: To describe demographic, clinical and analytical features in a cohort of patients with Sarcoidosis diagnosis from northern Spain during the last twenty years.

Methods: Descriptive study of 381 patients diagnosed with sarcoidosis during the period 01/01/1999 to 01/01/2019. Biopsy and/or clinical and compatible imaging tests were required for the diagnosis of sarcoidosis. Demographic parameters, clinical manifestations, complementary tests and treatment were registered. Results are expressed as mean±SD or as median and interquartile range (IQR) as appropriate.

Results: 381 patients (192 female/191 male, ratio 1:1), with a mean age of 45.5±15.4 years at disease onset, and with 94.8% of Spanish nationality. 33% were smokers at diagnosis and 6.3% had tuberculosis (Table 1). The sarcoidosis incidence rate in our population was 3.3 cases/100000 p/year, similar to other national series. Most frequent clinical manifestations were as follow: pulmonary symptoms (72.3%), general symptoms (37.3%), skin involvement (31%), joint manifestations (27.9%), ophthalmological manifestations (13.0%), digestive disorders (9.3%), neurological symptoms (6.5%), nephrological (4.7%) and cardiological involvement (1.6%) (Table 1). In addition, 11.5% of the patients had a Löfgren syndrome, 0.5% a Heerford syndrome and up to 11.5% had mediastinal adenopathy as an incidental finding in simple chest radiography. A simple chest radiograph was performed in all patients. 83.7% presented abnormal patterns: stage I (41.4%), stage II (32%), stage III (7.6%) and stage IV (3.8%). In addition, 29.9% and 10.5% of patients presented pathological scintigraphy and PET respectively. Biopsy was performed in 81.9%, with a mediastinal approach in 43.3% (Table 2).

After a median follow-up of 11.0 [6.0-17.0] years, we observed that up to 32% of patients never received treatment. In the remaining 68%, the main treatment was oral glucocorticoids with a mean dose of 43.4±19.1 mg/day. Other treatments used were conventional immunosuppressants and biological agents (Table 2).

Disclosure of Interests: None declared


Table 1. Albumin and LDH, and associations to oncological response and rheumatic irAE development

<table>
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<th>Oncological non-responders</th>
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<td>LDH (units/L)</td>
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<td>237</td>
<td>0.16</td>
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No rheumatic irAE  Rheumatic irAE  p-value

<table>
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<tr>
<th></th>
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<tr>
<td>Albumin (g/L)</td>
<td>34.0</td>
<td>34.9</td>
<td>0.41</td>
</tr>
<tr>
<td>LDH (units/L)</td>
<td>254</td>
<td>238</td>
<td>0.57</td>
</tr>
</tbody>
</table>

Table 1. Albumin and LDH, and associations to oncological response and rheumatic irAE development

H/I%

Skin 15(27)
Neurological 4(7)
Cardiac 8(14)
Renal 2(4)
Ocular 7(13)
Monoaarthritis 3(5)
Polarthritis 6(11)
Bilateral swelling in ankles 8(14)
Asplenia 5(9)
Hepatosplenomegaly 8(14)

No rheumatic irAE  Rheumatic irAE  p-value

<table>
<thead>
<tr>
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<th>Rheumatic irAE</th>
<th>p-value</th>
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<tr>
<td>Albumin (g/L)</td>
<td>34.0</td>
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Hepatosplenomegaly 8(14)

Table 1. Albumin and LDH, and associations to oncological response and rheumatic irAE development

H/I%
Conclusions: Results obtained were similar to other national and international series, with the exception of non-predominance of female sex and the highest percentage of ocular involvement in our study. Currently, biological treatment (especially anti-TNF-alpha) is used more frequently.

References:

Disclosure of Interests: José Luis Martín-Varillas: None declared, Lara Sánchez Bilbao: None declared, Iñigo González-Mazo: None declared, Raúl Fernández Ramón: None declared, D. Prieto-Pería: None declared, David Martínez-Lopez: None declared, Eva Peña Sainz-Pardo: None declared, Belén Atienza-Mateo: None declared, Monica Calderón-Goercke: None declared, David Martinez-Lopez: None declared, Eva Peña Sainz-Pardo: None declared, A. García-Sánchez Bilbao: None declared, Iñigo González-Mazón: None declared.


FRIO065

EFFECTIVENESS AND SAFETY OF OFF-LABEL USE OF TOCILIZUMAB IN AUTOIMMUNE DISEASES: A MULTICENTER STUDY IN INTERNAL MEDICINE DEPARTMENTS

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Objectives: To describe off-label use, efficacy and tolerance of TCZ use in Internal Medicine Departments.

Methods: This is a retrospective, descriptive and multicenter study from 9 departments of Internal Medicine. Data were reported using a standardized case report file in January 2019.

Results: Fifty one patients were included (19 men, 32 women). Mean age was 55.6 ± 17 years (range 23 - 80). TCZ was used in:
- 12 connective tissue diseases (23.5%): relapsing polychondritis (n=6), systemic sclerosis (n=3), anti-synthetase syndrome (n=1), and unclassified connective tissue disease (n=3).
- 10 vasculitis (19%): Takayasu arteritis (n=7), Cogan disease (n=1), panarteritis nodosa (n=1), unclassified vasculitis (n=2).
- 10 ophthalmologic conditions (19%): non infectious posterior uveitis (n=8), sympathetic ophthalmitis (n=1), Basowd orbitopathy (n=1).
- 8 adult-onset Still’s diseases (16%).
- 5 cases of polyarticular rheumatism (10%).
- 3 miscellaneous diseases (6%): idiopathic AA amyloidosis, multicentric non HHV8 Castelmann disease, Erdheim Chester disease (1 case each).

Mean disease duration was 7.5 ± 6.4 years. In 44 cases (86%) TCZ was administered for refractory disease to corticosteroids and immunosuppressive drugs. Previous therapies included corticosteroids (83%), methotrexate (66%), TNF inhibitor drug (44%), azathioprine (20.8%), mycophenolate (12%), cyclophosphamide (8%), rituximab (10%), hydroxychloroquine (6%), anakinra in 2 patients and interferon, dapsone, etoposide, leflunomide, abatacept, salazopyrin or intra-venous immunoglobulin in 1 patient each.

TCZ was initiated as first-line therapy (15.5%), second-line therapy (17.5%), third-line therapy (31%), fourth-line therapy (19%), fifth-line therapy (14%), sixth-line therapy (12%) or as seventh line therapy in one case. TCZ was associated with methotrexate in 3 cases (6%). Treatment route was intravenous (96%).

At the end of the follow up, 41 patients (80%) were still using TCZ, with a mean follow up period of 22 ± 3 months (range 1-90). In these patients, daily corticosteroid use significantly decrease from 16.5 ± 18 mg to 5.7 ± 13.7 mg (p<0.005, using paired T test). Considering the 28 patients using TCZ since more than 6 months, short term efficacy was 93% (2 cases of loss of efficacy).

TCZ was interrupted in 10 patients (19%), because of treatment failure (n=2), loss of efficacy (n=2) or side effect (n=6). Side effects were infection (2 pneumonias, zonaria, sinus infection), puritus (n=1), urticaria (n=1), dyslipidemia (n=1), high blood pressure (n=2), infusion-related reaction (n=1), bullous dermatitis (n=1), acute renal failure (n=1), angioedema (n=1), mouth ulcers (n=1).

Conclusion: TCZ is used in various autoimmune diseases. TCZ allowed a significant corticosteroids reduction and short term efficacy was 93% in patients using TCZ for more than 6 months. Nevertheless TCZ was interrupted in 19% of the patients. TCZ use will probably be more common in the future to treat refractory autoimmune diseases.

Disclosure of Interests: None declared

variables were collected. Statistical analysis was performed with SPSS.25.

Results: We included 116 patients from which 55% were women, with a mean age at diagnosis of T1D 18.7 (± 12.2) SD years. Average age at autoimmune disease diagnosis was 39.8 (± 12.2) SD years. Average time of evolution between onset of T1D and autoimmune comorbidity was 10.1 (± 10.6) SD years, except one patient with autoimmune thyroiditis 10 years before T1D. Autoimmune manifestations were showed by 19/116 patients (16.4%); with the following diagnoses: autoimmune hypothyroidism: 10 patients (8.6%); autoimmune polyglandular syndrome: 3 patients (2.6%), RA in 2 patients (1.8%). As well, 1 patient with celiac disease, 1 with cutaneous lupus erythematosus (CLE), 1 with psoriasis and another one with IgG4-related orbital inflammatory disease, (0.9% respectively). Three patients developed ocular manifestations (2 rheumatoid polyarthritis and 1 with limited joint mobility or cheiroarthropathy). 4/19 patients (21%) showed cutaneous lesions (2 with vitiligo, 1 CLE and 1 with psoriasis). Hematological alterations type pemphigus amiliar in one patient. No visceral involvement was found. Antibodies were detected to be organ-specific: 7/17 antibodies to thyroid peroxidase (TPO) (+) and 3/17 antibodies to thyroglobulin (+) and one with anti-gludain IgA (+). ANA (+) was detected in four patients (two fine granular pattern, one nucleolar and one homogeneous) with negative specificities and 1 patient RF (+). No Anti-CCP antibodies were detected.

Conclusion: 1) 16% of patients with T1D presented autoimmune comorbidity at 10 years after the onset of endocrinopathy, 2) Autoimmune hypothyroidism was the most prevalent autoimmune manifestation (8.6%), followed by autoimmune polyglandular syndrome and RA, similar to other studies. 3) We highlight the unusual finding of IgG4-related orbital inflammation as comorbidity of T1D. 4) The cutaneous lesions (21%) were the most common clinical manifestation in patients with T1D and autoimmun- ity. We emphasize the absence of visceral involvement.

REFERENCES:

[3] -Kiani AK et col, 2015, Genetic link of type 1 diabetes susceptibility loci followed by autoimmune polyglandular syndrome and RA, similar to other studies.

Disclosure of Interests: None declared


FRID067

IDENTIFICATION OF UNMET NEEDS RELATED TO RARE AND COMPLEX CONNECTIVE TISSUE AND MUSCULOSKELETAL DISEASES (RCTDS) ACROSS EU: THE EXPERIENCE OF THE ERN RECONNET

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Background: The European Reference Network on Rare and Complex Connective Tissue and Musculoskeletal Diseases (ERN ReCONNET) is a virtual Network that aims to improve and standardize the quality of care offered to rCTDs patients in Europe, empower patients, share knowledge and expertise, enhance research, support efficient use of resources. ERN ReCONNET covers 10 rCTDs: APS, UCTD, Idiopathic Inflammatory myopathies, IgG4, MCTD, Systemic sclerosis, Relapsing Polychondritis, SLE, SJogren and EDS.

Objectives: Identification of unmet needs in diagnosis, monitoring and management of rCTDs after literature review of existing clinical practice guidelines (CPGs).

Methods: After the review of existing CPGs, the most relevant unmet needs, both for clinicians and patients, were identified by discussion among the members of the network.

Results: A considerable number of unmet needs were identified. In particular, the lack of shared classification criteria, of evidence-based CPGs, validated tools for the assessment of treatment response and disease activity/damage are the major unmet needs especially for the rarest rCTDs. Transversal topics for all rCTDs that need to be addressed are the scarcity of EU/international randomised controlled trials, the identification of patient-reported outcomes and non-adherence to treatment, quality of life indicators, the need to develop composite disease activity scores for all rCTDs and specific (inter)national web-based registries. Patients highlighted the need of a more holistic approach to rCTDs, demanding more attention to pain, fatigue and psychological aspects related to the diseases and the promotion of an early diagnosis.

Conclusion: The identification of rCTDs unmet needs provided a very useful picture on future actions to be undertaken in order to provide a better care to patients. Many activities are ongoing towards these goals in ERN ReCONNET. These will be possible as a result of a EU collaboration among rCTDs stakeholders, the main added value of ERN ReCONNET.

Acknowledgement: Thanks to all ERN ReCONNET Steering Committee, to the EUCORP EuroCare, providers, eFGs and Team for huge support.

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ventricular arrhythmias and 1 was found to have incidental abnormal myocardial uptake on PET imaging. 8 of the 9 patients had abnormal myocardial uptake on PET imaging. All but 1 patient had been initially treated with oral steroids (1 refused) and 7 of the 9 patients had also been given oral DMARDs; methotrexate (n=6), azathioprine (n=2), hydroxychloroquine (n=2) and mycophenolate mofetil (n=1). Biologics used were adalimumab (n=5), infliximab (n=3) and rituximab (n=1). The most common indication for biologics was progression of disease despite optimal doses of standard therapy, followed by intolerance or contraindication to standard therapy. 75% of the patients were noted to have marked clinical improvement with the addition of a biologic. 4 out of 9 patients had decreased myocardial uptake on PET following treatment with a biologic. One patient had no change on PET and 4 have not had repeat imaging done yet. None of the patients had worsening of left ventricular systolic function with the addition of a TNF alpha antagonist. There were no reported major infections or significant adverse events that were attributable to the use of biologics.

Conclusion: Based on our small cohort, biologics (mainly TNF alpha antagonists) appear to be safe and efficacious as salvage therapy for cardiac sarcoidosis. However, there is a need for prospective studies to further validate these findings as well as to identify the subset of patients that would benefit from early initiation of these therapies.

REFERENCES:

Disclosure of Interests: None declared

FRIO610
CRYOPYRIN-ASSOCIATED PERIODIC SYNDROME: A SERIES OF CASES IN A ADULT PATIENTS’ COHORT WITH AUTOINFLAMMATORY SYNDROME IN A THIRD LEVEL HOSPITAL

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Background: The Cryopyrin-associated Periodic Syndrome (CAPS) or cryopyrinopathies are part of the spectrum of autoinflammatory diseases. The term cryopyrinopathy encompasses three clinical entities such as: CINCA/NOMID (chronic infantile neurologic, cutaneous and articular/neonatal onset multisystem inflammatory disease), Muckle-Wells disease and FCAS (familial cold-associated periodic syndrome). There are three different diseases that would be part of the same clinical spectrum, ranging from CINCA/NOMID (more serious) to FCAS (the less severe). It is more frequent in pediatric age although they can also be observed in adulthood. They are characterized by mutations in the NLRP3 gene and have an autosomal dominant inheritance pattern.

Objectives: To describe the clinical characteristics and genetic variants of a cohort of patients in adulthood diagnosed with cryopyrinopathy and with follow-up in a 3rd level hospital.

Methods: Retrospective descriptive study in adults patients with diagnosis of cryopyrinopathy since 2013 (year of introduction of genetic tests in the hospital laboratory) until now. The data was obtained from the review of medical records. All patients with mutations in NLRP3 gene and clinically compatible with this diagnosis were reviewed.

Results: Of a total of 44 patients in adulthood diagnosed with periodic fever syndromes (FMF, TRAPS, cryopyrinopathies, HIDS) and compatible genetic mutations, 7 patients (15.9%) were diagnosed with cryopyrinopathies, presenting 6 of them (13, 6%) mutations in NLRP3 gene. 1 patient was diagnosed with Muckle Wells based on clinical criteria without genetic test. 6 patients (13.6%) were women. 4 patients (9.1%) presented mutations in heterozygosis in exon 3 of NLRP3 gene (p.(V100M). 1 patient presented heterozygous mutation in exon 3 of NLRP3 gene (p.R260W) and another patient presented a mutation in heterozygosis in exon 3 of the NLRP3 gene (p.S726C). The mean age at diagnosis was 38 years (IQR 13-71 years). The total of patients diagnosed with cryopyrinopathy showed elevation of acute phase reactants. 6 patients (13.6%) presented fever, joint symptoms (arthritis and/or arthralgia) and myalgias. 4 patients (9.09%) showed cutaneous involvement in the form of urticarial rash. 4 patients (9.09%) showed neurosensory deafness since childhood. 3 patients (6.8%) presented ocular involvement in form of conjunctivitis and/or uveitis. In 3 cases (6.8%), anti-IL1 (anakinra) or anti-TNF were used.

Conclusion: Cryopyrinopathies are autoinflammatory diseases that occur mainly in the pediatric age, but there are also cases in adulthood. We must consider its diagnosis in those cases with periodic fever, arthralgia or arthritis, sensorineural deafness, APR elevation and urticarial rash. The genetic diagnosis will help us to confirm the diagnosis and avoid a delay in it. Disclosure of Interests: None declared

Table 1. Baseline Characteristics
<table>
<thead>
<tr>
<th>Age (years +/- SD)</th>
<th>Female</th>
<th>Diagnosed autoimmune or inflammatory condition</th>
<th>Recurrent pericarditis (&gt;1 episode)</th>
<th>Time since initial episode (months +/- SD)</th>
<th>Prior NSAID use</th>
<th>Prior Colchicine use</th>
<th>Prior CS use</th>
<th>Pericardial effusion on ECHO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anakinra plus conventional therapy</td>
<td>60.3+/-17.3</td>
<td>66.7 (8)</td>
<td>83.3 (10)</td>
<td>33.3 (4)</td>
<td>49.4+/-78.9</td>
<td>25.0 (3)</td>
<td>25.0 (3)</td>
<td>50.0 (6)</td>
</tr>
<tr>
<td>% (n=12)</td>
<td>50 (11)</td>
<td>40.9 (9)</td>
<td>27.3 (6)</td>
<td>18.2 (4)</td>
<td>18.2 (4)</td>
<td>18.2 (4)</td>
<td>45.4 (12)</td>
<td>63.6 (14)</td>
</tr>
<tr>
<td>Conventional therapy only</td>
<td>56.8+/-17.8</td>
<td>49.1+/-11.7</td>
<td>25 (3)</td>
<td>25 (3)</td>
<td>50.0 (6)</td>
<td>18.2 (4)</td>
<td>45.5 (10)</td>
<td></td>
</tr>
<tr>
<td>% (n=32)</td>
<td>0.590</td>
<td>0.441</td>
<td>0.638</td>
<td>0.210</td>
<td>0.051</td>
<td>0.638</td>
<td>0.093</td>
<td>0.653</td>
</tr>
<tr>
<td>p-value</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>
Conclusion: In hospitalised patients with new-onset or recurrent pericarditis (secondary or idiopathic) refractory or intolerant to CT, Anakinra is associated with improved symptom relief and decreased recurrence risk. Extended continuation of Anakinra after symptom relief does not reduce post-treatment relapse risk.

Disclosure of Interests: : None declared


FRIO612 IMMUNE-RELATED ADVERSE EVENTS ASSOCIATED WITH IMMUNOTHERAPY. LONG-TERM FOLLOW-UP OF 102 PATIENTS FROM A REFERRAL SINGLE CENTER

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Background: Immune checkpoint blockade therapy (ICBT) has shown remarkable benefit in different cancer types. Blockade of intrinsic down-regulators of immunity increases the activity of the immune system, which can lead to different immune-related adverse events (irAEs). Our aim was to assess the immune-related adverse events in patients who received anti-cytotoxic T-lymphocyte antigen 4 (CTLA-4), anti-programmed cell death 1 (PD-1) or anti-programmed cell death ligand 1 (PD-L1).

Objectives: Our aim was to assess the incidence, treatment and evolution of irAEs due to ICBT.

Methods: We set up an observational study of patients treated with Nivolumab and Pembrolizumab (anti-PD1), Atezolizumab (anti-PD-L1) and Ipilimumab (antiCTLA-4) for solid organ tumors. All these patients were followed in a single reference University Hospital from March-2015 up to December-2018. The main outcome was to determine the incidence of irAEs.

Results: We studied 102 patients (63/39) with a mean age of 60.6 ±9.7 with lung (n=63), melanoma (21), kidney (11), gastric (3), bladder (1), and colon cancer (n=3). Only 7 patients had a previous diagnosis of an immunemediated disease: psoriasis (n=2), psoriatic arthritis (1), systemic lupus erythematosus (1), spondyloarthritis (1), rheumatoid arthritis (1) and skin lupus (1). ICBT was performed as follows: nivolumab (52), pembrolizumab (35), atezolizumab (10) and ipilimumab (5).

After a median of 5 [2.5-10.5] months since the ICBT onset, we observed 87 (85.3%) patients with different irAEs, summarized in TABLE. ICBT discontinuation was required in 39 patients. 36 patients received specific treatment (prednisone, antihistamine, levothyroxine and thiamazol), obtaining a good response in 31 cases (79.5%). ICBT was reintroduced in 28 patients (71.8%) after resolution of the adverse event, with an appropriate tolerance in all cases.

Gastrointestinal irAEs were the most frequent (n=39, 41.1%), with severe manifestations in 4.9% of the patients. Among these 39 patients, only 11 of them required specific treatment, with oral prednisone in all cases. The diagnosis of gastrointestinal irAEs was based on the clinical manifestations and the laboratory tests. The cutaneous most frequent irAE was rash (n=7, 6.8%), followed by vitiligo (n=2, 1.9%). 15 patients developed a rheumatological irAE (14 arthralgias/arthritis and 1 aortitis).

Patients who developed any type of irAE had a better answer to ICBT (70.1%) than those who did not (20%).

Conclusion: In our study, the majority of autoimmune side effects due to ICBT were gastrointestinal, thyroiditis and rheumatological. The develop of any irAE could be an indicator of good response to ICBT.

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Background: Recently the term 'interstitial pneumonia with autoimmune features' (IPAF) has been proposed to identify patients with interstitial lung disease and autoimmune characteristics, not fulfilling the criteria for specific connective tissue diseases (CTD). Until now, only few data are available about the clinical and serological features of IPAF patients, their survival and the possible evolution in a CTD.

Objectives: Aim of the study was to investigate the therapeutic choices in IPAF patients, their efficacy and safety.

Methods: Fifty-two patients (mean age at diagnosis 65.5±11.0 years, female/male ratio 29/23) were consecutively enrolled and prospectively followed for 45±31.6 months.

Data about therapies, disease onset, serological, clinical and therapeutic features, pulmonary function tests and high-resolution computed tomography were periodically repeated. A worsening of lung function was defined as a reduction of 10% compared to baseline of forced vital capacity (FVC) and diffusion lung capacity of CO (DLCO).

Results: An immunosuppressive therapy was prescribed in 15 patients (namely cyclophosphamide in 4, mycophenolate mofetil in 6 and azathioprine in 6, respectively), while 6 patients were treated with anti-fibrotic therapies (pantoprozol or nintedanib). Thirty-three patients took corticosteroids, associated to other drugs in 18 patients, and alone in 15. Finally, no therapies were prescribed in 16 patients. At the end of follow-up FVC remained stable in 35% of patients, worsened in 50% and increased in 15%; DLCO remained stable in 25.8% of patients, worsened in 58.1% and increased in 16.1%.

Mean survival was 94±8.5 months, and no differences were recorded according to the kind of therapy, while survival was significantly associated to the lung function at baseline (FVC and DLCO were confirmed to be significantly associated to death at multivariate analysis).

The treatment was generally well tolerated. In 7/15 patients treated with immunosuppressive therapy was recorded at least an adverse event, responsible for the treatment discontinuation only in 3 patients.

Conclusion: The therapeutic strategy in IPAF patients reflects the ethiopathogenicity of the disease. Waiting for specific trials in this population, therapeutic strategies in IPAF patients need to be carefully tailored for each patient according to both clinical and laboratory features, pulmonary function tests and high-resolution computed tomography.

REFERENCES:

EVALUATION OF COMPLIANCE AND RELATED FACTORS IN COLCHICINE TREATMENT IN FAMILIAL MEDITERRANEAN FEVER PATIENTS

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Background: Familial Mediterranean Fever (FMF) is an autoinflammatory disease requiring long-term treatment. Increasing the compatibility with colchicine treatment in patients with FMF is the first step for preventing amyloidosis. Patients' beliefs about medicines and treatment may affect treatment adherence and treatment success.

Objectives: The aim of this study was to determine adherence to colchicine treatment and related factors in FMF patients. In addition, patients' beliefs about colchicine, which are one of the important factors affecting the treatment adherence of patients, were evaluated.

Methods: Total of 179 patients with FMF was included in this study. The demographic and clinical features and MEFV gene mutations were recorded. The treatment adherence of the patients was assessed using a Compliance Questionnaire on Rheumatology (CQR). The Beliefs About Medicines Questionnaire (BMO-T) was used to assess patient's beliefs about colchicine. The relationship between compliance of treatment and clinical characteristics of patients were assessed.

Results: One hundred thirteen (63.1%) of the patients were male. The mean age of patients was 34.5 ± 12.7 years and mean delay in diagnosis was 6.7 ± 3.4 years. The mean dose of colchicine was 1.37 ± 0.43 mg/day and, the percentage of patients using colchicine regularly was 66.5%. Adherence to treatment was higher in patients with concomitant diseases than those without comorbidities (p = 0.028). In addition, treatment compliance was higher in married patients compared to single patients (p = 0.013). The colchicine dose used in compatible patients was higher than in non-compatible patients (p = 0.003) (Table 1). We also found that as the BMO-T Specific Necessity scores increased, compliance with treatment increased. On the other hand, as the BMO-T General Overuse and General Harm scores increased, non-compliance with treatment increased (Table 2).

Conclusion: In patients with FMF, it is important to evaluate the compliance with the treatment due to the importance of colchicine to prevent amyloidosis that may occur in patients without treatment. As this study shows it is also important to determine patients' beliefs about medicine in terms of their influence on patients' compliance with treatment.

Disclosure of Interests: None declared


ANAKINRA TREATMENT IN RECURRENT PERICARDITS: SINGLE CENTER EXPERIENCE

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Background: Recurrent pericarditis (RP) is a well-known condition characterized by recurrent episodes of pericardial inflammation. Alternative treatments have been reported for recurrent pericarditis related to FMF as well as patients with idiopathic recurrent pericarditis (IRP) (1). Alternative treatments have been reported for cases with colchicine resistant RP.

Objectives: The aim is to present our data regarding anakinra treatment in recurrent pericarditis either related to FMF or idiopathic, who are resistant to colchicine.

Methods: Patients who had received anakinra with a diagnosis of recurrent pericarditis either idiopathic or secondary to FMF followed in our autoinflammatory disease center between 2014-2018 were evaluated retrospectively. Treatment decisions were based on patients' files, demographic and clinical features, response to other treatment approaches such as NSAI, colchicine, were evaluated. All patients have been genetically screened for monogenic autoinflammatory diseases (MEVF, NOD2, NLRP3, NOD2). Patients who had at least 3 attacks were administered anakinra 100 mg/day. Therapeutic efficacy, as well as side effect profile of anakinra is also assessed.

Results: There were 5 patients (3 male and 2 female) with the diagnosis of RP. 1 was related to FMF and 4 were idiopathic. The mean age of

Table 1. Demographic features and treatment response during anakinra therapy

<table>
<thead>
<tr>
<th>Patient ID</th>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Duration of pericarditis</th>
<th>Prior medications</th>
<th>Number of recurrences before anakinra</th>
<th>Anakinra treatment duration (mo)</th>
<th>Time to corticosteroid discontinuation (mo)</th>
<th>Number of recurrences after daily dose of anakinra</th>
</tr>
</thead>
<tbody>
<tr>
<td>1*</td>
<td>23</td>
<td>M</td>
<td>RPF</td>
<td>129</td>
<td>Colchicine, NSAIDs</td>
<td>6</td>
<td>1</td>
<td>9</td>
<td>0 (0-1)</td>
</tr>
<tr>
<td>2</td>
<td>32</td>
<td>F</td>
<td>IRP</td>
<td>128</td>
<td>Colchicine, NSAIDs</td>
<td>7</td>
<td>4</td>
<td>NA</td>
<td>0 (0-1)</td>
</tr>
<tr>
<td>3*</td>
<td>40</td>
<td>F</td>
<td>RPF</td>
<td>21</td>
<td>Colchicine</td>
<td>6</td>
<td>8</td>
<td>1</td>
<td>0 (0-1)</td>
</tr>
<tr>
<td>3</td>
<td>20</td>
<td>M</td>
<td>IRP</td>
<td>11</td>
<td>Colchicine</td>
<td>3</td>
<td>8</td>
<td>2</td>
<td>0 (0-1)</td>
</tr>
<tr>
<td>5</td>
<td>25</td>
<td>M</td>
<td>FMF</td>
<td>30</td>
<td>Colchicine</td>
<td>5</td>
<td>15</td>
<td>1</td>
<td>0 (0-1)</td>
</tr>
</tbody>
</table>

F: Female, M: Male, CS: Corticosteroid, HCQ: Hydroxychloroquine, NA: Not applicable

*Oxidative stress was unsuccessful in these patients

Table 2. Beliefs about Medicines Questionnaire Scale Scores in Adherent and Nonadherent Patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Discontinuous</th>
<th>CQR Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMQ-T-Specific Concerns</td>
<td>≥80% n=29</td>
<td>&lt; 80% n=150</td>
</tr>
<tr>
<td>BMQ-T-Specific Necessity</td>
<td>4.8 (4.1-5.0)</td>
<td>3.8 (3.5-4.25)</td>
</tr>
<tr>
<td>BMQ-T-General Overuse</td>
<td>2.8 (2.2-3.8)</td>
<td>2.8 (2.4-3.6)</td>
</tr>
<tr>
<td>BMQ-T-General Harm</td>
<td>2.25 (1.75-3.25)</td>
<td>2.75 (2.25-3.25)</td>
</tr>
<tr>
<td>BMQ-T-General Necessity</td>
<td>1.75 (1.38-2.63)</td>
<td>2.38 (2.0-3.0)</td>
</tr>
</tbody>
</table>

Z: Mann-Whitney test. Data represented as median (25th-75th percentile). CQR, Compliance Questionnaire on Rheumatology.
the group was 28±8 (range 20–40). All patients diagnosed with IRP were negative for autoinflammatory genetic screening, while a MEFV variant (K695R het.) was detected in the FMF patient. Median duration of follow-up was 30 months (range 11–129). In table 1, demographic and clinical features are given. The median number of recurrence was 6 before anakinra treatment. No episode of pericarditis was observed in any of the patients after the initiation of anakinra. The response to anakinra persisted even after the dose was reduced to 100 mg/alternate day in 3 patients, and 2, recurrence of pericarditis was observed and anakinra was escalated to initial dose. It was possible to discontinue corticosteroid treatment in all patients. Currently all patients continue anakinra treatment. No side effect including injection site reaction, has been observed by now.

Conclusion: Anakinra seems to be a safe and effective treatment approach for colchicine resistant recurrent pericarditis. However recurrence may occur during dose tapering.

REFERENCES:

Disclosure of Interests: None declared

FR0617 APPLICATION OF AUTO-INFLAMMATORY DISEASE DAMAGE INDEX (ADDI) TO PATIENTS WITH FMF AND RELATED FACTORS WITH DAMAGE

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Background: Familial Mediterranean Fever (FMF) is the most frequent auto-inflammatory disease caused by MEFV gene mutations. Available reports investigated only specific components of damage such as amyloidosis. All possible organ targets of damage have not been entirely evaluated before. Such as Disease severity index which is emerged especially for FMF do not cover entire damage domains related to FMF. Recently, a new scoring system (Auto-inflammatory disease damage index) was developed and validated for autoinflammatory diseases. Objectives: We aimed to investigate damage accrual caused by FMF and associated features with damage. Methods: All patients recruited from FMF in Central Anatolia (FICA) cohort, however in 2, recurrence and duplication disabled cross-sectional, multicenter accessible web-based cohort. This study is comprising 970 adult patients (mean age 35.3 ±12.1 years, 61.5% female). Demographic data, FMF disease characteristics, co-morbid conditions, disease complications were meticulously questioned and laboratory features and genotype data (if available) were recruited from patient files. FMF caused damage was assessed by auto-inflammatory disease damage index (ADDI) which is recently validated. Association between damage and demographic, disease and treatment characteristics were analyzed.

Results: Proportions of FMF manifestations were fever 83.1%, peritonitis 91.5%, pleuritis 47.9%, arthritis 43.3% and skin rash 26.2%. Dominant attack types were fever in 6.2%, serositis in 65.7%, musculoskeletal in 16.8% and all types of attacks were common in rest of patients. MEFV mutations were available in 814 subjects and 75.9% of these subjects were harboring M694V mutation (42.5% homozygous for M694V). Among all 63.1% patients were well responded to colchicine and 10.8% were non-responders. Median ADDI score was 1 (min 0-max 11). Most common FMF related damages were observed in musculoskeletal, reproductive and kidney domains. Chronic musculoskeletal pain was present in 49%, joint deformity in 2.9%, infertility in 8.6%, amenorrhea in 3.9%, proctitis in 6.9%, amyloidosis in 5.9% and renal failure in 3.7% of the patients. 411 (54.2%) of patients had no damage accrual. M694V homozygous mutation, male gender and colchicine nonresponse were found to be the independent predictors of damage. Conclusion: M694V homozygous mutation, colchicine non-response and male gender were predictors of damage and effective therapeutic interventions must be undertaken to prevent from damage in these patients.

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INPATIENT BURDEN AND COMORBIDITIES OF SARCOIDOSIS: NATIONWIDE INPATIENT SAMPLE 2013–2014

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Background: Little is known about the inpatient burden and healthcare utilization among patients with sarcoidosis. Previous studies have focused on trends of hospitalization rate of patients with sarcoidosis over time [1] but none has investigated their inpatient prevalence, mortality and expenditures.

Objectives: The current study was conducted with the aims to shed more light on those characteristics as well as to investigate the comorbidities of sarcoidosis using the data from a large national database.

Methods: Patients with sarcoidosis were identified within the Nationwide Inpatient Sample (NIS) database of the years 2013 and 2014 using the ICD-9 diagnostic code. NIS is the largest publicly available inpatient database in the US. Data for more than seven million individual hospitalization across all-payers in the United States (US) is recorded annually in the NIS database. This is itself a 20% stratified sample of over 4,000 non-federal acute care hospitals from more than 40 states of the US and is representative of 95% of hospital discharges nationwide. Data on patient and hospital characteristics, comorbidities, total hospital costs and total hospitalization charges was collected. A propensity-matched cohort of patients with sarcoidosis from the same database was created and used as comparators for the analysis of comorbidities. Inpatient prevalence of sarcoidosis was calculated using all admissions in the NIS database as denominator. Odds ratios (OR) comparing the prevalence of comorbidities between cases with sarcoidosis and propensity-matched controls without sarcoidosis were calculated.

Results: A cohort 78,055 patients with sarcoidosis was identified from the database, corresponding to an inpatient prevalence of 2.21 cases per 1,000 admissions. The most common reasons for admission among patients with sarcoidosis in this cohort were as follows: pneumonia (34.3%), respiratory failure (26.1%), cardiomyopathy (10.9%), coronary artery disease (9.2%), acute kidney injury (8.5%) and atrial fibrillation (5.5%). Analysis of comorbidities found that patients with sarcoidosis had significantly higher odds of atrial fibrillation, conduction abnormalities, aortic valvulopathy, congestive heart failure and cardiomyopathy compared to propensity-matched patients without sarcoidosis (Table 1).

After adjusting for confounders, patients with sarcoidosis displayed a mean additional $27,205 (p<0.01) for total hospitalization charges (the amount of money that each hospital billed for providing its service on each case) when compared to hospitalization of patients without sarcoidosis.

Conclusion: The inpatient prevalence of sarcoidosis was relatively high compared to its overall incidence. Hospitalization of patients with sarcoidosis was associated with a significantly higher total hospitalization charges (the amount of money that each hospital billed for providing its service on each case) when compared to hospitalization of patients without sarcoidosis.

Disclosure of Interests: None declared

Table 1. Odds ratio comparing comorbidities between patients with sarcoidosis and patients without sarcoidosis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Adjusted odds ratio</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atrial fibrillation</td>
<td>1.41</td>
<td>1.13-1.76</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Conduction abnormalities</td>
<td>2.04</td>
<td>1.45-2.89</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>1.10</td>
<td>0.84-1.29</td>
<td>0.26</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>1.23</td>
<td>1.04-1.45</td>
<td>0.02</td>
</tr>
<tr>
<td>Cardiomyopathy</td>
<td>1.25</td>
<td>1.08-1.44</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Aortic valvulopathy</td>
<td>1.78</td>
<td>1.30-2.44</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Figure 1. The proportion of FMF patients with SpA related disorders (A) and their impact on FMF patients’ survival (B)
ASSOCIATIONS BETWEEN ORGAN INVOLVEMENTS AND GENDER, ALLERGY, AND MALIGNANCY IN 166 PATIENTS WITH IGG4-RELATED DISEASE

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Disclosure of Interests: Hajime Yoshifuji: None declared, Mirei Shirakashi: None declared, Yuzo Kodama: None declared, Tsutomu Chiba: None declared, Motohisa Yamamoto: None declared, Hiroki Takahashi: None declared, Kazushige Uchida: None declared, Kazuki Okazaki: None declared, Tetsuya Ito: None declared, Shigeyuki Kawa: None declared, Kazunori Yamada: None declared, Mitsuhiro Kawano: None declared, Tsuneyo Mimori: None declared, Hiroshi Goto: None declared, Yasuharu Sato: None declared, Tadashi Yoshino: None declared, Kyo University, Kyoto, Japan; 2Kobe University, Kobe, Japan; 3Kansai Electric Power Hospital, Osaka, Japan; 4Sapporo Medical University, Sapporo, Japan; 5Kansai Medical University, Hirakata, Japan; 6Shinshu University, Matsumoto, Japan; 7Matsumoto Dental University, Shinjoj, Japan; 8Kanazawa University, Kanazawa, Japan; 9Hiroshima University, Hiroshima, Japan; 10University of Occupational and Environmental Health, Fukuoka, Japan; 11Kyushu University, Fukuoka, Japan; 12Tokyo Metropolitan Komagome Hospital, Tokyo, Japan; 13University of Toyama, Toyama, Japan; 14University of Tsukuba, Tsukuba, Japan; 15Tokyo Medical University, Tokyo, Japan; 16Okayama University, Okayama, Japan

Background: Symptomatic differences between male and female patients with IgG4-related disease (IgG4-D) have been reported [1]. Associations between IgG4-D and allergy and malignancy have also been reported, although they are controversial.

Objectives: We previously analyzed the treatment course of IgG4-D using a multi-center cohort [2]. In the present study, we investigated the associations between organ symptoms and gender, allergic diseases, and malignancies.

Methods: Data of 166 patients with a definitive diagnosis of IgG4-D were retrospectively analyzed.

Results: The cohort consisted of 108 men (65%) and 58 women (35%). Most frequently, the submandibular gland (52%), pancreas (46%), lachrymal gland (43%), and thyroid gland (43%) included the thyroid gland (43%), and lymph node (38%) were affected. Furthermore, we assessed the frequencies of female sex, allergy, and malignancy in patients with each affected organ (Table 1). The organs with high frequencies of women included the lachrymal gland (50%), lungs (44%), and submandibular gland (43%). Those with low frequencies of women included the thyroid gland (0%), retroperitoneum (17%), and para-aorta (19%). In addition, allergic diseases were found in 60 patients (36%) (Fig. 1A). The organs with high frequencies of allergy included the thyroid gland (50%), submandibular gland (47%), and lachrymal gland (40%). Those with low frequencies of allergy were the para-aorta (38%), prostate gland (30%), and retroperitoneum (31%). Malignancies were found in 23 (14%) patients (Fig. 1B). Organs with high frequencies of malignancy included the para-aorta (38%), prostate gland (30%), and retroperitoneum (21%). In comparison, those with low frequencies of malignancy included the thyroid gland (0%), lungs (8%), and kidney (8%).

Conclusion: Craniofacial organ involvement was associated with female sex and presence of allergic diseases, suggesting that allergy may contribute to onset of IgG4-D in some patients. Abdominal organ involvement was associated with male sex and presence of malignancies, suggesting that malignancy may in part contribute to IgG4-D.

Table 1. Frequencies of female sex, allergy, and malignancy in patients with indicated affected organ.

<table>
<thead>
<tr>
<th>Organ</th>
<th>Women (%)</th>
<th>*1</th>
<th>Allergy (%)</th>
<th>*2</th>
<th>Malignancy (%)</th>
<th>*3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eyelid orbit</td>
<td>23</td>
<td>L</td>
<td>38</td>
<td>H</td>
<td>15</td>
<td>H</td>
</tr>
<tr>
<td>Lachrymal gl.</td>
<td>50</td>
<td>H</td>
<td>40</td>
<td>H</td>
<td>11</td>
<td>L</td>
</tr>
<tr>
<td>Parotid gl.</td>
<td>36</td>
<td>H</td>
<td>36</td>
<td>L</td>
<td>18</td>
<td>H</td>
</tr>
<tr>
<td>Submandibular gl.</td>
<td>43</td>
<td>H</td>
<td>47</td>
<td>H</td>
<td>13</td>
<td>L</td>
</tr>
<tr>
<td>Thyroid gl.</td>
<td>0</td>
<td>L</td>
<td>50</td>
<td>H</td>
<td>0</td>
<td>L</td>
</tr>
<tr>
<td>Lung</td>
<td>44</td>
<td>H</td>
<td>32</td>
<td>L</td>
<td>8</td>
<td>L</td>
</tr>
<tr>
<td>Pancreas</td>
<td>31</td>
<td>L</td>
<td>32</td>
<td>L</td>
<td>18</td>
<td>H</td>
</tr>
<tr>
<td>Bile duct</td>
<td>23</td>
<td>L</td>
<td>33</td>
<td>L</td>
<td>15</td>
<td>H</td>
</tr>
<tr>
<td>Kidney</td>
<td>40</td>
<td>H</td>
<td>36</td>
<td>-</td>
<td>8</td>
<td>L</td>
</tr>
<tr>
<td>Retroperitoneum</td>
<td>17</td>
<td>L</td>
<td>31</td>
<td>L</td>
<td>21</td>
<td>H</td>
</tr>
<tr>
<td>Para-aorta</td>
<td>19</td>
<td>L</td>
<td>13</td>
<td>L</td>
<td>38</td>
<td>H</td>
</tr>
<tr>
<td>Prostate gl.</td>
<td>0</td>
<td>L</td>
<td>30</td>
<td>L</td>
<td>30</td>
<td>H</td>
</tr>
<tr>
<td>Lymph node</td>
<td>41</td>
<td>H</td>
<td>38</td>
<td>H</td>
<td>13</td>
<td>L</td>
</tr>
<tr>
<td>Total</td>
<td>35</td>
<td></td>
<td>36</td>
<td></td>
<td>14</td>
<td></td>
</tr>
</tbody>
</table>

*1, *2 Malignancy (H, L, or 0) are marked if the frequency is higher, lower, or no change respectively, when compared to the total frequencies of female sex (35%), allergy (36%), and malignancy (14%).

Disclosure of Interests: Hajime Yoshifuji: None declared, Mirei Shirakashi: None declared, Yuzo Kodama: None declared, Tsutomu Chiba: None declared, Motohisa Yamamoto: None declared, Hiroki Takahashi: None declared, Kazushige Uchida: None declared, Kazuki Okazaki: None declared, Tetsuya Ito: None declared, Shigeyuki Kawa: None declared, Kazunori Yamada: None declared, Mitsuhiro Kawano: None declared, Shintaro Hirata: Yoshiya Tanaka: Masatomi Moriyama: Seiji Nakamura: Terumi Kanisawa: Shoko Matsu: Hiroki Tsubo: Takayuki Sumida: Motoko Shibata: Hiroshi Goto: Yasuharu Sato: Tadashi Yoshino: Tsuneyo Mimori: Kyoto University, Kyoto, Japan; Kobe University, Kobe, Japan; Kansai Electric Power Hospital, Osaka, Japan; Sapporo Medical University, Sapporo, Japan; Kansai Medical University, Hirakata, Japan; Shinshu University, Matsumoto, Japan; Matsumoto Dental University, Shinjoj, Japan; Kanazawa University, Kanazawa, Japan; Hiroshima University, Hiroshima, Japan; University of Occupational and Environmental Health, Fukuoka, Japan; Kyushu University, Fukuoka, Japan; Tokyo Metropolitan Komagome Hospital, Tokyo, Japan; University of Toyama, Toyama, Japan; University of Tsukuba, Tsukuba, Japan; Tokyo Medical University, Tokyo, Japan; Okayama University, Okayama, Japan

REFERENCE:
Diagnostics and imaging procedures

**FRI0622** JOINT TENDERNESS AND ULTRASOUND INFLAMMATION IN EARLY RHEUMATOID ARTHRITIS PATIENTS INCLUDED IN THE ARCTIC TRIAL

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**Background:** A tender joint count is part of most disease activity scores and remission criteria in rheumatoid arthritis (RA). A recent study found that tender joint count might not reflect inflammatory activity, assessed by ultrasound, in established RA (1).

**Objectives:** To explore if tender non-swollen joints is associated with sub-clinical inflammation, assessed by ultrasound, in DMARD-naïve early RA patients.

**Methods:** DMARD-naïve RA patients with <2 years symptom duration from first swollen joint and indication for DMARD treatment were included in the ARCTIC trial (2). For the current analyses we used data from the baseline examination, including a tender joint count assessed by Ritchie Articular Index and a 44-swollen joint count. The Ritchie Articular Index treat certain joints as a single unit (as the MCP-joints), and scoring of tenderness in joints and joint groups is graded 0-3. All patients underwent an ultrasound examination of 34 joints, with a semi-quantitative 0-3 score for power Doppler in each joint. An ultrasound atlas was available for reference (3). We predefined the wrist and the MCP 1-5 joints as joint areas of interest since they are commonly involved in RA and were assessed both clinically and by ultrasound. We selected only joints that were clinically non-swollen, and assessed the association between joint tenderness and ultrasound power Doppler signal by mixed logistic regression models with patient-specific intercept to adjust for within-patient dependencies. The analyses were repeated using generalized estimating equations for robustness. The frequency and odds ratio (OR) of ultrasound power Doppler activity (yes/no) in tender non-swollen wrists compared to non-tender non-swollen wrists were calculated. Similar analyses were performed for the MCP joints.

**Results:** A total of 222 patients with complete baseline data were included. 63% were female, median [SD] age 53.6 [41.2, 62.3], symptom duration 5.8 [2.9, 10.4] months, swollen joint count 9 [4, 15], joint tenderness 7 [4, 13] and power Doppler score 7 [3, 14]. Of 444 wrists, 268 were not swollen. The frequency of power Doppler signal >0 in tender non-swollen wrists was 50% (18/36), compared to 23% (53/232) in non-tender non-swollen wrists. The frequency and odds ratio (OR) of ultrasound power Doppler activity (yes/no) in tender non-swollen wrists compared to non-tender non-swollen wrists was calculated. Similar analyses were performed for the MCP joints. Similar results were found for the non-swollen MCP-joints (Table).

**Table:** The frequency and odds ratio (OR) of ultrasound power Doppler (PD) activity in Ritchie positive versus Ritchie negative non-swollen wrists and MCP joints

<table>
<thead>
<tr>
<th>PD-signal positive if Ritchie positive</th>
<th>PD-signal positive if Ritchie negative</th>
<th>OR (CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-swollen wrist, n=268</td>
<td>18/36 (50%)</td>
<td>53/232 (23%)</td>
<td>4.32 (1.47</td>
</tr>
<tr>
<td>Non-swollen MCP joints, n=165</td>
<td>15/35 (43%)</td>
<td>28/130 (22%)</td>
<td>4.84 (1.31</td>
</tr>
</tbody>
</table>

**Conclusion:** Ultrasound power Doppler activity was more frequent in non-swollen wrists and non-swollen MCP joints if the joints had been scored as tender or painful by Ritchie Articular Index. Our findings indicate that in early RA patients, tenderness might reflect inflammation which is not detectable clinically.

**REFERENCES:**

Disclosure of Interests: Nina sundsland: None declared, Anna Birgitle Aga Consultant for: AbbVie, Pfizer, and Pfizier, Paid instructor for: UCB, Hilde Bemer Hammer Grant/research support from: AbbVie, Pfizer and Roche, Paid instructor for: AbbVie, Pfizer, UCB, Novartis, Roche, Speakers bureau: AbbVie, Pfizer, UCB, Novartis, Roche, Tii Iihii Consultant for: Grünenthal, Novartis, Speakers bureau: Grünenthal, Novartis, Tore K. Kvin Grant/research support from: AbbVie, BMS, MSD, Pfizer, Roche and UCB., Consultant for: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celine, Gelttron, Ely Lilly, Hospira, Merck-Serono, MSD, Novartis, Oktal, Orion Pharma, Pfizer, Roche, Sandzod, Sanofi, Mylan and UCB, Speakers bureau: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celine, Gelttron, Ely Lilly, Hospira, Merck-Serono, MSD, Novartis, Oktal, Orion Pharma, Pfizer, Roche, Sandzod, Sanofi and UCB, Esper Haavardsholm Grant/ research support from: Pfizer, UCB, Roche, MSD, and AbbVie, Consultant for: Pfizer, Paid instructor for: Pfizer, Speakers bureau: Pfizer, UCB, Roche, and AbbVie, Siri Lillegreven: None declared


**FRI0623** MRI-DETECTED DIGITAL FLEXOR TENOSONVITIS IN BILATERAL PROXIMAL INTERPHALANGEAL JOINTS CONTRIBUTE TO JOINT TENDERNESS IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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**Background:** Independent predictive value of ultrasonography-detected digit flexor tenosynovitis has been reported for rheumatoid arthritis (RA) development in patients with early arthritis, and it also was reported as an independent risk factor of flare in remission RA. However, proximal interphalangeal joints (PIPJs) were scarcely evaluated by MRI, nor recommended by RAMRIS so far.

**Objectives:** To explore the characteristics of MRI-detected inflammation in bilateral PIPJs in early RA patients and its clinical significance.

**Methods:** Early RA patients who fulfilled 2010 ACR/EULAR classification criteria with disease duration ≤1 year and DAS28-CRP ≥2.6 were recruited. New methodology of 3.0T whole-body MRI with contrast-enhanced imaging was used to scan bilateral hands simultaneously. MRI tenosynovitis, synovitis and ostesitis were scored referring to the 2016 updated RAMRIS. Clinical data were collected.

**Results:** 1) Among 75 patients recruited, the median age was 49 years old (IQR: 38-59) with 71% female. The median disease duration was 7 months (IQR: 3-12) and the mean DAS28-CRP was 5.1 (IQR: 4.2-6.1). Forty-four patients (59%) were treatment-naive who had never taken any DMARDs or glucocorticoids before recruitment. Both joint tenderness and swelling were present the most frequently in PIPJ2 and PIPJ3 (48% 61% and 43% 56%, respectively, Figure 1A,2). MRI tenosynovitis, synovitis and ostesitis were detected in 84%, 100% and 83% of the patients; and respectively in 21% 44%, 43% 56% and 5% 11% of various PIPJs. There were 12% 30%, 28% 40%, and 2% 8% of PIPJs without tender or swollen showing MRI tenosynovitis, synovitis and ostesitis respectively. When non-dominant hands were used as self-control, the frequency of digit flexor tenosynovitis in dominant interphalangeal joint (IPJ) of thumb, PIPJ2 and PIPJ4 was 16% 18% higher than the non-dominant counterparts, indicating a potential impact of overuse on dominant tenosynovitis. 3) Tenosynovitis affects pericarticular digit flexor tendon compartment and 65% 87% of tenosynovitis in PIPJs occurred together with synovitis in joint cavity and/or ostesitis in subchondral bone. Among tender IPJ of thumb, 50% of them showed MRI synovitis together with digit flexor tenosynovitis, which was significantly more than those who showed MRI synovitis alone (21, Chi-square test, p<0.017). Similar trend was found in tender PIPJ2 (45% vs. 26%, p<0.01). Generalized Estimating Equations with multivariate logistic regression showed not only MRI synovitis but also digit flexor tenosynovitis in bilateral PIPJs independently had more than twice probability of joint tenderness (both p<0.01, Figure 1B).

**REFERENCES:**
Conclusion: This preliminary study showed MRI-detected digit flexor tenosynovitis in bilateralPIPJs contributed to joint tenderness in early RA patients independently of synovitis which should not be ignored in clinical practice.

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Disclosure of Interests: None declared


FR10625 ASSESSING SYNOVITIS IN PATIENTS WITH RHEUMATOID ARTHRITIS BY ULTRASOUND – AN AGREEMENT STUDY EXPLORING THE MOST ACTIVE SIDE

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Background: Though ultrasound examination of all RA patients - if offered a very tight clinical control – may not be necessary for obtaining clinical remission (1,2), there are still patients where ultrasound may have a role in monitoring disease activity. Scoring synovitis unilaterally will by far reduce the examination time, however, no consensus exists on how to choose the side to be examined and if one side per se is always the most inflamed side.

Objectives: To assess ultrasound (US) inflammation and sensitivity to change in hands, aiming to identify if the right hand, the dominant hand, or the hand with more clinically swollen joints (SwJ) is per se the most inflamed and more sensitive to change, and hence the preferred side for unilateral scoring of synovitis by US in rheumatoid arthritis (RA) patients.

Methods: This is an agreement study exploring the impact on US scoring methods in a longitudinal study of early RA (ARCTIC trial, n=230) and established RA (ULRABIT trial, n=212) patients initiating conventional and biological Disease Modifying Anti-Rheumatic Drugs, respectively. Tender and swollen joint count for 28 joints (TJC28 and SJC28) and C-reactive protein (CRP mg/L) were obtained. Using the hands as model, bilateral MCP 1-5,PIP 2-3 and wrists were evaluated by US using a 0–3 scoring system for grey-scale (GS) and power Doppler (PD) ultrasound using EULAR/OMERACT combined score (0-27). Targeted synovitis was defined to correspond to a 95% Confidence Interval around the observed paired mean difference: -2.99 to +2.99.

Conclusion: The U9 score gave the best correlation with disease activity parameters. It is simple and applicable and gives a high degree of flexibility to the sonographer according to the clinical picture.

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Results: 437 RA patients were included in the current analysis; 71% women, 79% anti-CCP pos, 71% RF pos, median(IQR) age 54(42-62) years, CRP 7(3-16), SJJC28 5.3(2-6) and TJC28 6.2(28). The median (IQR) PD sum score was 3(0-7) for right hand and 2(0-5) for left hand, GS sum score was 5(2-9) for both hands, and GLOESS was 5(2-10) for right hand and 5(2-9) for left hand. The average ultrasound measured inflammation at baseline and 3 months follow-up are shown in the table. The hands with more vs fewer SwJ had more inflammation at baseline for all sum scores, all p<0.0011) and had a greater change for all sum scores at 3 months follow-up (all p<0.0005). No such differences were found between the dominant vs non-dominant or the right vs left hands at any time points – see table.

Conclusion: Based on this study, assessment of the dominant hand is not superior to the non-dominant hand in inflammatory activity evaluated by US. The hand with clinically more SwJ at baseline is likely to have more active inflammation according to GS, Doppler and GLOESS sum scores and exhibit a greater change, and is potentially the best choice for unilateral US scoring systems.

REFERENCES:

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DIFFICULTIES WITH MAKING A FIST IN PATIENTS WITH CLINICALLY SUSPECT ARTHRAGLIA: AN EARLY PHENOMENON PREDICTIVE FOR RA THAT IS RELATED TO MRI-DETECTED TENOSYNOVITIS

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Background: Difficulties with making a fist in patients presenting with recent-onset arthralgia of small joints, in whom there is no clinically detectable arthritis, is often considered a risk factor for the development of inflammatory arthritis. The fact that rheumatologists consider difficulties with making a fist a feature of imminent Rheumatoid Arthritis (RA) is also reflected by this sign being incorporated in the EULAR definition of arthritis suspicious for progression to RA. However, to date there is little comprehension of its predictive value and underlying cause in patients with recent-onset arthralgia.

Objectives: This study was performed to 1) determine if difficulties making a fist is indeed predictive for the development of clinical arthritis, and 2) evaluate if this sign is associated with subclinical joint inflammation, detected by magnetic resonance imaging (MRI).

Methods: 566 patients presenting with recent-onset (<1 year) arthralgia of small joints that were consecutively included in the Clinically Suspect Arthralgia (CSA) cohort were studied. At baseline the ability to completely close the fist (all fingertips touching the palm) was assessed at physical examination. Additionally, contrast-enhanced 1.5T MRI of wrist, 2nd-5th metacarpophalangeal (MCP) and 1st-5th metatarsophalangeal (MTP) joints was performed. MRI findings were scored for synovitis, bone marrow edema (BME) and tenosynovitis in line with the RAMRIS. MRI-detected subclinical inflammation was considered present if it was more than observed in symptom-free controls from the general population in the same age-category (n=193). Patients were followed on the development of clinically detectable inflammatory arthritis identified at joint examination (median follow-up 19 months); none of the patients received DMARDs before the development of clinical arthritis. χ2 tests, logistic and Cox proportional hazards regression were used as appropriate.

Results: At first presentation 12% of CSA-patients had difficulties making a fist, which only 13% of both hands, Having difficulties making a fist was predictive for development of clinical arthritis in univariable analysis (HR 2.47 (95% CI 1.46-4.19)) and in multivariable analysis (HR 2.16 (1.25-3.74) corrected for age, CRP, ACPA and MRI-detected subclinical inflammation). Patients with difficulties making a fist had significantly more often MCP tenosynovitis (flexor tenosynovitis and extensor periteninitis combined) than patients who did not experience these problems (42% versus 16%, p<0.001). The main difference was seen in MCP flexor tenosynovitis (39% versus 10%, p<0.001). MCP flexor tenosynovitis was significantly associated with difficulties making a fist in univariable (OR 5.6 (95% CI 3.2-9.9)), and multivariable regression (OR 5.7 (3.2-10.2)) corrected for extensor periteninitis, synovitis and BME in MCP joints). Extensor periteninitis, synovitis and BME in MCP joints were not associated with difficulties making a fist (multivariable OR 0.7 (0.2-2.1), 0.99 (0.5-2.1) and 1.6 (0.7-4.1), respectively).

Conclusion: Difficulties making a fist in patients with CSA is predictive for future inflammatory arthritis development. This sign is presumably caused by MCP flexor tenosynovitis in a significant proportion of patients.

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DOES ADDING AN US EXAMINATION OF SHOULDERS, TO A ROUTINE DAS28 SCORE, IMPROVE THE ACCURACY OF DISEASE ACTIVITY SCORES AND DISEASE STATUS? RESULTS OF A SINGLE CENTRE PILOT STUDY

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Background: The DAS28 forms the mainstay of current RA and other chronic inflammatory arthritis (CIA) (i.e. peripheral spondyloarthritides [SpA]) management in clinical practice. DAS28 has certain limitations. Some joints especially the shoulders are difficult to evaluate correctly using this method. The shoulder is deep and highly affected by rotator cuff tendon lesions either due to degenerative or inflammatory arthritis This structural damage can produce pain and swelling. A swollen shoulder joint can be difficult to palpate by physical examination. Using a clinical approach can be inaccurate to ascertain whether shoulder involvement is actually due to true RA-derived inflammatory activity or other degenerative or structural causes.

Objectives: To investigate the added value of adding a US assessment of shoulders to DAS28 scores and on disease activity status, in patients with CIA (RA or peripheral SpA) in either disease remission or low disease states who had shoulder pain.

Methods: Patients were recruited prospectively over a 3-month period. Each patient had a standard DAS28 performed followed by a formal physical shoulder examination, of both shoulders, including testing active and passive range of movements. A complete US examination of both shoulders was carried out by a rheumatologist experienced in this technique. All patients were examined using the same real-time US machine (Esaote MyLab Twice) using a linear probe, 3-13 MHz frequency and a linear probe, 5-13 MHz frequency. All patients were examined by a rheumatologist experienced in this technique. All patients were examined using the same real-time US machine (Esaote MyLab Twice) using a linear probe, 3-13 MHz frequency and a linear probe, 5-13 MHz frequency.

Results: Thirty-eight patients [82% females; mean (± SD) age 60.3 (11.96) years] were included. In 33 out of 38 (87%) [C195%: 76-98%] patients the original DAS28 was greater than the US-modified DAS28. This percentage was significantly greater than 50% (p < 0.001). The mean ± SD reduction of DAS28 in those patients who showed DAS28 decrease was 0.73 ± 0.39 units. Twenty-five patients (65.8%) maintained the same disease activity status with original DAS28 and US-modified
DAS28. The remaining 13 (34.2%) patients changed their status: 11 (28.9%) patients moved from low activity to remission while 2 (5.3%) patients moved from low activity to moderate activity. Figure 1 and 2 demonstrate some of the ultrasound findings observed in our patient group.

Figure 1: Biceps tenosynovitis in a. transverse and b. longitudinal views.

![Figure 1](image)

Figure 2: Subacromial-subdeltoid (SASD) bursitis in a. transverse and b. longitudinal views.

Conclusion: This study showed that patients improved their disease activity scores and status after an US assessment of their shoulders. A low percentage increased their disease status after shoulder US which can provide valuable additional information in clinical practice. Rheumatology (Oxford) 2007; 46: 975-9.

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Disclosure of Interests: Konstantinos Triantafyllias: None declared, Caroline Heller: None declared, Michele De Blasi: None declared, Peter Galle: None declared, Andreas Schwarting: None declared, ACRUA Rheumatology Center, Bad Kreuznach, Germany; Internal Medicine I, University Medical Center of the Johannes Gutenberg University, Rheumatology and Clinical Immunology, Mainz, Germany; Internal Medicine I, University Medical Center of the Johannes Gutenberg University, Gastroenterology, Mainz, Germany; Internal Medicine I, University Medical Center of the Johannes Gutenberg University, Rheumatology and Clinical Immunology, Mainz, Germany

Background: Valid assessment of disease activity leads to improvement of long-term outcomes in patients with rheumatoid arthritis (RA) (1). Clinical disease activity assessment tools such as the Disease Activity Score 28 (DAS28) are partially subjective and do not always depict the real inflammatory burden. Ultrasound (US) and Hand-MRI are important diagnostic modalities which can nevertheless be time consuming (US, MRI), expensive (MRI) or usually performed unilaterally (MRI). Thus, further diagnostic tools are needed. Optical spectral transmission (OST) is a new modality able to assess the blood-specific absorption of light transmitted through a tissue promising quantification of inflammation in the finger and wrist joints of RA patients (commercial device: HandScan - Hemics, The Netherlands)(2).

Objectives: To examine the diagnostic value of OST in detecting inflammation in patients with RA and to evaluate for the first time its relationship with disease activity markers and various anthropometric and epidemiologic patient characteristics.

Methods: OST-Measurements were performed in 168 RA-patients and 114 healthy controls. The difference between OST in the two groups was statistically examined and subsequently controlled for the effect of possible confounding factors. Moreover, association of OST with clinical, ultrasound and serological RA activity markers was evaluated. Finally, relationship of OST with radiographic joint pathology and various anthropometric and epidemiologic parameters (BMI, hand-size, gender, age) was examined.

Results: OST was significantly higher in the patients group in comparison to the control group, even after adjustment for the effects of various confounding factors (p<0.001). OST correlated in both groups significantly with gender, hand-size and Body Mass Index (all: p<0.001). In the patients group, OST correlated significantly with all examined disease activity markers (DAS28, ESR, counts of tender/swollen joints, VAS; all, p<0.001) and with age (p=0.001). OST showed significant correlations with a power Doppler ultrasound-Score (p=0.001) and with a combined power Doppler/grey scale ultrasound-Score (p<0.001). Finally, receiver operating characteristic showed the best OST performance at the level of metacarpophalangeal joints level (AUC=0.75; 95%CI=0.686-0.821).

Conclusion: OST correlated with serological and clinical disease activity markers as well as with different anthropometric and epidemiological parameters of RA-patients. OST could therefore prove to be a good non-interventional complementary tool to assess RA activity next to well established diagnostic methods such as the US or MRI.

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Disclosure of Interests: Konstantinos Triantafyllias: None declared, Caroline Heller: None declared, Michele De Blasi: None declared, Peter Galle: None declared, Andreas Schwarting Grant/research support from: GSK, Pfizer, AbbVie, Novartis, Roche, Speakers bureau: GSK, Novartis DOI: 10.1136/annrheumdis-2019-eular.5573
APPLICATION OF AN ADVANCED NOISE REDUCTION ALGORITHM FOR IMAGING OF HANDS IN RHEUMATIC DISEASES – EVALUATION OF IMAGE QUALITY COMPARED TO STANDARD DOSE IMAGES

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Background: X-ray is the fundamental imaging technique in diagnosis and follow up of rheumatic diseases. As patients often require sequential X-rays, dose reduction is of great importance. New advanced noise reduction algorithms allow for a dose reduction of up to 50%.

Objectives: The aim of this study was to evaluate, whether the application of an advanced noise reduction algorithms is feasible in the context of imaging of rheumatic diseases.

Methods: A total of 268 patients were enrolled prospectively into three tiers: 80%, 64% and 50% dose reduction groups. All patients received imaging of one hand (laterality randomly assigned) with low-dose technique and of the contralateral side with standard protocol. All images were evaluated by two blinded independent readers who scored (on a scale of 1 to 5) the visualisation of bony cortex, trabeculae and joint spaces of fingers and wrist separately as well as soft tissue and overall contrast. Score values were analysed using T-tests for paired samples.

Results: Overall image quality (expressed by mean sum scores out of 40) of the 50% low-dose images was 31.52 (SD 1.94) vs. 31.66 (SD 1.82) for standard images (p=0.001). Bony contours as well as trabeculae was equally well visualized in both image sets. An image example is given in Fig. 1 (Left hand: 50%-dose image; right hand: standard-dose image). Soft tissue visualization was slightly lower for low-dose compared to standard images (mean score of 3.81 vs. 3.89; p=0.001).

Conclusion: Overall image quality of low dose images was not inferior to standard dose images. Therefore, application of low-dose technology based on advanced noise estimation algorithms in the context of imaging of rheumatic diseases is feasible.

Disclosure of Interests: Katharina Ziegeler: None declared, Stefan Siepmann: None declared, Alexander Beck: None declared, Alexander Lembcke: None declared, Bernd Hamm Grant/research support from: Siemens, GE, Bayer, Samsung, Canon, Guerbet, Kay Geert A. Hermann Speakers bureau: AbbVie, MSD, Pfizer, UCB, Samsung


DIAGNOSTIC UTILITY OF FLUORESCENCE OPTICAL IMAGING IN INDIVIDUALS WITH SUSPECTED ARTHRITIS – A PROBABILISTIC APPROACH

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Background: In the arsenal of available techniques used for arthritis pre-diction and diagnosis1, fluorescence optical imaging (FOI) has been proven useful in detecting clinically manifest and silent synovitis of the hands and wrists of patients with various rheumatic diseases, particularly rheumatoid arthritis (RA)2.

Objectives: To assess the diagnostic utility of FOI in individuals with joint symptoms referred for further rheumatologic investigation, using a probabilistic approach.

Methods: Those with increased suspicion of inflammatory arthritis were referred to the rheumatology unit and clinic of Karolinska University Hospital. On acquiring informed consent and medical history, the standard clinical examination coupled with ultrasound findings of fingers, wrists and feet were assessed. Laboratory results included ESR, CRP, RF, and ACPA tests. Using the above information, a diagnostic probability assessment was completed by the responsible rheumatologist, where the probability of a) any inflammatory joint disease and b) rheumatoid/RA was given on a 5-point scale – ranging from unlikely (0-20%) to very likely (80-100%) probability. Subsequently, an FOI examination was performed. After reviewing the image reports in consensus, post-FOI diagnostic probabilities were again scored, using the same scale. If no score change in probability resulted, the rheumatologist was asked to mark whether FOI was still helpful in the diagnostic decision-making. Proportions of individuals with maximal and minimal diagnostic certainty pre- and post-test were compared using Fisher exact tests, and one-sample binomial tests for assessing the helpfulness of FOI in the absence of pre- and post-test probability score changes.

Results: Of 24 individuals screened, 21 without prior rheumatic diagnosis were included (66.7% female, 11 RF (+), 10 ACPA (+), with age average and symptom duration (SD) of 55.6 (±18.1) years and 13.9 (±15.3) months respectively). The final diagnoses were: early RA (n=17), other inflammatory joint disease (n=3), and non-inflammatory joint disease (n=1). Regarding diagnosis of any inflammatory arthritis, where the proportion of patients for whom diagnostic certainty was maximal – namely, combining <20% (lowest probability) or >80% (highest probability) of diagnostic likelihood – there was an increase from 52.4% (n=11/21) maximal certainty before FOI to 80.1% (17/21) maximal certainty after FOI (p=0.035). Regarding early RA, the maximal diagnostic certainty increased from 57.1% (12/21) to 71.4% (15/21) (p=0.002), respectively. In the event that diagnostic certainty scores didn’t change pre- vs. post-test (15/21 cases, any inflammatory joint disease; 13/21 cases, early RA), the diagnosing rheumatologist indicated that FOI was still helpful in setting a final diagnosis for most cases (86.7% (13/15) p=0.007; 84.6% (11/13), p=0.022, respectively).

Conclusion: FOI significantly increased the diagnostic certainty and confidence of rheumatologists in establishing the presence and absence of inflammation in individuals suspected of inflammatory arthritis. The changes from pre- to post-test quantify the diagnostic utility of FOI in probabilistic terms.

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Disclosure of Interests: Yogan Kisten: None declared, Adrian Levitsky: None declared, Hamed Rezaei: None declared, Aase Hensvold: None declared, Erik Af Klint: None declared, Ronald van Vollenhoven Grant/research support from: AbbVie, BMS, GSK, Pfizer, UCB, Consultant for: AbbVie, AstraZeneca, Biogen, Biotest, BMS, Celgene, Gilead, GSK, Janssen, Lilly, Novartis, Pfizer, UCB, Speakers bureau: AbbVie, Lilly, Pfizer, UCB, Anca Catrina Grant/research support from: Yes, but not for the presented study.

**FR10631 MUSCLE STIFFNESS AND WEAKNESS IN RHEUMATOID ARTHRITIS – A SHEAR WAVE ELASTOGRAPHY STUDY**

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**Background:** Myopathy is a recognised but less investigated symptom of rheumatoid arthritis (RA) compared to other extra-articular manifestations. To date, the documentation of myopathic features in RA is poorly detailed. No studies have yet utilised a non-invasive quantitative method to define and investigate these features. Shear wave elastography (SWE), a novel ultrasound technology, can measure muscle stiffness to provide insight into the biomechanical properties of skeletal muscle.

**Objectives:** 1- To investigate muscle stiffness (using SWE) and strength in three cohorts of RA patients compared to healthy controls.

2- To study the association between muscle strength and stiffness in RA.

**Methods:** Shear wave velocity (SWE), as a measure of muscle stiffness, was evaluated in the quadriceps, hamstrings and biceps brachii in 80 RA patients from three disease activity groups newly diagnosed treatment naïve RA [n=29; mean age 56.8 ± 10.6 years], persistent active RA for at least 1 year [n=18; 60.9 ± 15.9 years] and remission RA for at least 1 year [n=33; 65.9 ± 11.6 years]. The participants performed various muscle tests (handgrip strength, expanded timed get up and walk test (ETGUG), chair stand and isokinetic knee extension/flexion) to assess their strength and physical performance. One-way ANOVA was used to compare SWE and muscle assessment results, and Pearson’s correlation was used to evaluate the correlation between muscle stiffness and strength.

**Results:** Mean SWV was not significantly different amongst the RA groups or compared to the healthy controls (p>0.05). For example, the rectus femoris SWV was 1.68±0.15 m/s for healthy controls, 1.68±0.18 m/s for new RA, 1.70±0.16 m/s for active RA and 1.68±0.14 m/s for remission RA (p=0.96). The muscle assessment results are presented in table 1 and compared to healthy controls in figure 1. Overall, the active and new RA groups showed significant muscle weakness compared to healthy controls. The remission RA group did not show a significant difference except in the isokinetic knee strength (-21%; p=0.027). The correlations between SWE and the muscle assessment results were weak and insignificant (r<0.30; p>0.05).

**Conclusion:** Muscle stiffness, as determined using SWE, does not appear to be altered or associated with muscle weakness in RA patients. The remission RA group showed significantly better strength and physical performance compared to new untreated or persistently active RA groups. Future research should investigate the significant muscle weakness in RA in addition to developing prevention and therapeutic strategies.

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**Table 1. Muscle assessment results for all participants.**

<table>
<thead>
<tr>
<th>Test</th>
<th>Healthy controls (a)</th>
<th>New RA (b)</th>
<th>Active RA (c)</th>
<th>Remission RA (d)</th>
<th>p-value</th>
<th>Post hoc</th>
</tr>
</thead>
<tbody>
<tr>
<td>ETGUG, Total time (sec)</td>
<td>16.6 (4.3)</td>
<td>20.7</td>
<td>21.5</td>
<td>18.2 (4.5)</td>
<td>0.002</td>
<td>a,b,c</td>
</tr>
<tr>
<td>Number of chair stands in 30 sec</td>
<td>17.0 (5.8)</td>
<td>12.3</td>
<td>9.5 (8.3)</td>
<td>14.0 (5.4)</td>
<td>&lt;0.001</td>
<td>a,b,c</td>
</tr>
<tr>
<td>Handgrip strength (kg)</td>
<td>31.5 (13.7)</td>
<td>17.3</td>
<td>17.3</td>
<td>26.6 (10.9)</td>
<td>&lt;0.001</td>
<td>a,b,c</td>
</tr>
<tr>
<td>Knee extension (Nm/kg)</td>
<td>1.29 (0.42)</td>
<td>1.06</td>
<td>0.93</td>
<td>1.20 (0.40)</td>
<td>0.026</td>
<td>a,c</td>
</tr>
<tr>
<td>Knee flexion torque (Nm/kg)</td>
<td>0.75 (0.27)</td>
<td>0.53</td>
<td>0.60</td>
<td>0.59 (0.25)</td>
<td>0.006</td>
<td>a,b,d</td>
</tr>
<tr>
<td>Knee extension power (W/kg)</td>
<td>0.75 (0.29)</td>
<td>0.58</td>
<td>0.52</td>
<td>0.68 (0.28)</td>
<td>0.029</td>
<td>a,c</td>
</tr>
<tr>
<td>Knee flexion power (W/kg)</td>
<td>0.47 (0.18)</td>
<td>0.32</td>
<td>0.34</td>
<td>0.34 (0.18)</td>
<td>0.005</td>
<td>a,b,d</td>
</tr>
</tbody>
</table>

*The signs > or < indicate that the group(s) are significantly higher or lower at 0.05 significance level compared to others.*

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**FR10632 ASSOCIATION BETWEEN ULTRASOUND DIAGNOSIS AND ANALYTICAL AND SEROLOGICAL DATA IN PATIENTS WITH SUSPECTED PRIMARY SJÖGREN SYNDROME**

Laura Barrio Nogal, Cristina Bóhórquez, Lucia Ruiz, Adrián Abbasi, Ana Pérez Gómez, Alisa Movasat, Ana Sánchez Atreo, Fernando Albarrán, Eduardo Cuende, Paula Pretel, Valentina Emperiale, Melchor Álvarez de Mon. Hospital Universitario Príncipe de Asturias, Madrid, Spain

**Background:** Pathophysiology of primary Sjögren syndrome (SSp) is characterized by oligoclonal B-cell proliferation and ectopic lymphoid tissue formation. The association between ultrasound glandular parenchyma heterogeneity and hyperproduction of autoantibodies, which in turn represents characteristic B-cell hyperactivity of SSp, is described.

**Objectives:** To study the association between major salivary gland ultrasonography (MSGUS) and their respective pathological grades with the analytical and serological data, and activity indexes obtained in patients with suspected SSp.

**Methods:** 72 patients were recruited consecutively with clinical and/or analytical suspicion of SSp from the Rheumatology outpatient consultations at the Príncipe de Asturias Hospital (2015-2018). Demographic, serological and validated activity indexes, ESSPRI and ESDAI, were collected. All of them underwent a MSGUS and their results were classified in three grades according to the-Conenc et al system: normal (grade 0 and 1), mild (grade 2) and moderate-severe (grades 3 and 4). The final SSp diagnosis was made using both 2002 AECG and 2016 ACR/EULAR classification criteria. Data were analyzed using the software STATA. Association between MSGUS and qualitative variables was described according to the number of cases and the percentage by grades of MSGUS; the significance of the associations was tested with the Chi square test. For the quantitative variables, the association was described with median and interquartile range (IQR) by grades of MSGUS and the significance of the association was verified with the non-parametric test of Kruskal-Wallis.

**Results:** From patients with pathological MSGUS: 51% had antiRo52, 51%, antiRo60 and anti-La positive; 62% hypergammaglobulinemia, 40% positive rheumatoid factor (RF), 6% and 13% C3 and C4 hypocomplementemia, respectively. Mean values were obtained: ESR 36, CRP 1.6, RF 12, ESSPRI 5.6 and ESDAI 2. Statistically significant differences (p<0.05) were only found in antiRo52 and hypergammaglobulinemia variables in patients with normal MSGUS exam compared to those with...
POSSIBLE ADVANTAGES OF 18F-FDG PET/CT-MR IN STANDARD REFERENCE VALUES OF METACARPAL activity was evaluated using Pouchot criteria and had a regular follow-up at the Rheumatology Unit. Disease analyzed. All AOSD patients were diagnosed according to Yamaguchi PET/MR and 9 PET/CT performed at Padova University Hospital were

**REFERENCES:**


<table>
<thead>
<tr>
<th>TABLE 1. ASSOCIATION BETWEEN MSGUS GRADES AND THE ANALYZED VARIABLES</th>
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<tbody>
<tr>
<td>MSGUS</td>
</tr>
<tr>
<td>-------</td>
</tr>
<tr>
<td>AntiRo 52%</td>
</tr>
<tr>
<td>AntiRo 60%</td>
</tr>
<tr>
<td>AntiLa%</td>
</tr>
<tr>
<td>Hypergammaglobulinemia</td>
</tr>
<tr>
<td>Rheumatoid factor%</td>
</tr>
<tr>
<td>Hypocomplementemia</td>
</tr>
<tr>
<td>C3%</td>
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<tr>
<td>C4%</td>
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<tr>
<td>ESR mean</td>
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<tr>
<td>CRP mean</td>
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**REFERENCES:**


**FO0634** STANDARD REFERENCE VALUES OF METACARPAL HEAD CARATILAGE THICKNESSMEASUREMENT BY ULTRASOUND IN HEALTHY SUBJECTS

Eduardo Cicinella1, Emilio Filippucci, Andrea Di Matteo2, Jana Humakova, Marco Di Carlo1, Karel Pavelka3, Walter Grassl1, Polytechnic University of Marche, Rheumatology Clinic, “Carlo Urbani” Hospital, Jesi, Italy; 2Charles University, Institute of Rheumatology, Department of Rheumatology, First Faculty of Medicine, Prague, Czech Republic.

Background: The hyaline cartilage of metacarpal head (MH) is frequently involved in patients with chronic arthritis. Moreover, in a recent study a high correlation has been found between the anatomical and sonographic (US) measurements of hyaline cartilage2. However, only very few data are available on the prevalence of pathological findings and the standard reference values in healthy subjects (H).

Objectives: To determine the prevalence of the US abnormalities at metacarpal head (MH) in H, and to measure MH cartilage thickness (CT) in order to provide standard reference values. Methods: US examinations were performed on 944 metacarpophalangeal (MCP) joints of 118 consecutive H using a MyLab Two (Esaote Biomedica, Genoa, Italy), equipped with a high frequency probe (up to 22 MHz). H were recruited among the staff of Rheumatology Department of the “Carlo Urbani” Hospital (Jesi, Ancona, Italy), students in medicine and patients’ healthy relatives. Exclusion criteria were: hand pain (VAS score >1/10) or stiffness in the previous month or hard tissue enlargement of MCP, proximal and distal interphalangeal joints.

The MH hyaline cartilage from II to V digits of both hands was scanned with the MCP joints in maximum flexion in longitudinal and transverse dor- sal views, paying attention on maintaining an angle of 90° between the direction of the US beam and the cartilage surface2. CT was scored both semi-quantitatively (using a five-grade scoring system5) and quantita- tively (using the mean value of longitudinal and transverse measurements of the CT). Moreover, the presence of osteophytes and bone erosions was recorded.

The association between CT and demographic data was analyzed.

Results: The semi-quantitative score: Cartilage damage was found in 21 out of 118 H (17.8%) and in 59 out of 944 MHs (6.3%); grade 1 and grade 2 in 43 (4.6%) and in 16 (1.7%), respectively. No grades 3 and 4 were detected. Osteophytes and bone erosions were respectively found in 12 (10.1%) and in 8 (6.7%) out of 118 H and in 24 (2.5%) and in 12 (1.3%) out of 944 MHs. A slight correlation between semi-quantitative score and the presence of osteophytes was found (r=0.16, p=0.01). No association between bone erosion and cartilage thinning was found.
Quantitative assessment: A significantly thicker cartilage was found in males [0.71±0.10 mm (mean±SD)] than in females [0.68±0.12 mm, (mean ±SD)] (p<0.01). No significant difference was found between left and right side for each digit (p>0.05).

CT value of the II MH was significantly greater than the one of the other fingers (p<0.01). No difference was found between the CT values of III, IV and V MH (p>0.05).

There was a significant association between the CT value and gender (r=0.39; p<0.01), age (r=-0.33; p=0.01), height (r=-0.28; p<0.01) and grade of the semiquantitative scoring system (r=-0.19, p<0.01). No correlation was found between the CT value and weight (p=0.20).

Conclusion: This study confirms the presence and provides data on the prevalence of US abnormalities at MH level in healthy individuals. Moreover, overall values for US CT of MH were reported.

REFERENCES:

Disclosure of Interests: P Az Collado: None declared, Silvia Magni-Manzon; Consultant for: Abbvie, Speakers bureau: Abbvie, MARTINA STEINER: None declared, Tracy Ting: None declared, Patricia Vega Fernandez: None declared, Clara Malaltia: None declared, Ana Rodriguez: None declared, George Bruyn: None declared, Helen Keen: None declared, Lene Terslev Speakers bureau: Speakers fee from : Roche, Novartis, Pfizer, MSD, BMS, Celgene

sensitive to joint space alterations (T1: SE 40%, SP 94%; SWI: SE 80%, SP 100%).

Conclusion: While T1 weighted MRI provides sufficient diagnostic accuracy for the detection of erosions, the CT-like images derived from SWI allow for a more accurate depiction of structural lesion of the SI-join. SWI provides additional information identifying sclerosis. However, it is not suited to replace T1-weighted imaging because fatty metaplasia of the bone marrow or inside an erosion cavity cannot be detected.

REFERENCES:

Disclosure of Interests: Torsten Diekhoff Paid instructor for: MSD, AbbVie, Novartis, Canon, but less than 10,000€. Kay-Geert Hermann Paid instructor for: MSD, AbbVie, Novartis, but less than 10,000€. Fabian Proft Grant/research support from: Novartis, Consultant for: yes but less than 10,000. Paid instructor for: yes but less than 10,000, Speakers bureau: yes but less than 10,000, Mikhail Protopopov: None declared, Torsten Diekhoff Paid instructor for: MSD, AbbVie, Bristol-Myers Squibb, Roche, Consultant for: Pfizer, MSD, AbbVie, Bristol-Myers Squibb, UCB, Roche, Novartis, Gilead, Samsung, Sandoz and Lilly, Steven Tanner: None declared, Andrew Grainger: None declared, Paul Emery Grant/research support from: Pfizer, MSD, AbbVie, Bristol-Myers Squibb, Roche, Consultant for: Pfizer, MSD, AbbVie, Bristol-Myers Squibb, UCB, Roche, Novartis, Gilead, Samsung, Sandoz and Lilly, Steven Tanner: None declared, Andrew Grainger: None declared, Andrea Ladas: None declared, Philip O’Connor: None declared, Al Lyn Tan: None declared

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Figure 1. T2 measurements in myositis patients compared with healthy controls in the hamstrings

Figure 2. T2 measurements compared to semi-quantitative scores in myositis patients and healthy controls


MUSCLES IN MYOSITIS PATIENTS WITH NORMAL MRI APPEARANCE HAVE HIGHER QUANTITATIVE T2 COMPARED TO THOSE IN HEALTHY CONTROLS

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Background: Myositis is an autoimmune disease which can cause a decrease in quality of life and increased mortality. Clinical presentation includes muscle weakness, myositisositis, raised muscle enzymes and myalgia. Currently, diagnosis is reliant on subjective clinical examinations, blood tests, conventional MRI and invasive muscle biopsies. Quantitative T2 imaging offers a non-invasive measurement of muscle oedema which could help improve the understanding of muscle pathology and potentially inform diagnosis (1).

Objectives: To evaluate whether quantitative T2 MRI of muscles is sensitive enough to be able to detect differences in myositis patients compared to healthy controls, and how it compares with current radiologist scoring methods.

Methods: 19 active myositis patients (12 female, mean age 55 ± 18) diagnosed according to the Bohan and Peter myositis criteria (Mean CK 1511 ± 11291) and 19 age and gender matched healthy controls had an MRI scan of their dominant thigh. Imaging was performed using a fat-suppressed turbo-spin echo (TSE) sequence with 16 echo times, evenly spaced from 9.9ms to 153.4ms. Quantitative T2 measurements were obtained from regions of interest (ROI) drawn manually within the individual muscles that make up the quadriceps and hamstrings with no distinction made between affected and unaffected muscles. A mono-exponential fit was used to obtain an estimate of the T2 from each ROI. Two radiologists semi-quantitatively scored by consensus the muscles on a 4-point visual scale as either no oedema (0), mild oedema (1), moderate oedema (2) or severe oedema (3). In addition to MRI, all participants had knee extension and flexion measured as power and torque on an isokinetic dynamometer. Differences were assessed using independent T-tests.

Results: Quantitative T2 values were significantly higher (P<0.001) in myositis patients compared to healthy controls with mean measurements in the hamstrings (figure 1) of 47ms in patients and 40ms in healthy controls, and in the quadriceps 52ms in patients and 41ms in healthy controls, whilst muscle strength and power were significantly reduced (P<0.001). Interestingly, 8 myositis patients scored as having no oedema in the muscles by the radiologists (score = 0) still had significantly higher T2 values than 8 age and gender matched healthy controls (P=0.003 in hamstrings and P=0.001 in quadriceps) with mean T2 measurements in the hamstrings (figure 2) of 43ms in patients with no oedema and 37ms in healthy controls and in the quadriceps 43ms in patients with no oedema and 40ms in healthy controls. These results were consistent across both muscle groups and the individual muscles.

Conclusion: Quantitative T2 measurements can detect muscle differences between myositis patients and healthy control groups. They are also sensitive to differences between the muscles of myositis patients which are assessed to have no oedema by radiologist scoring, and healthy controls. This suggests that subtle systemic changes in muscle in myositis patients, which go undetected in semi-quantitative scoring, can be detected using quantitative T2 measurements. This shows the potential for T2 measurements to be a diagnostic measure in the diagnosis and management of myositis.

Acknowledgement: The research is supported by the NIHR infrastructure at Leeds.

Disclosure of Interests: Matt Farrow: None declared, John Biglands: None declared, Paul Emery Grant/research support from: Pfizer, MSD, AbbVie, Bristol-Myers Squibb, Roche, Consultant for: Pfizer, MSD, AbbVie, Bristol-Myers Squibb, UCB, Roche, Novartis, Gilead, Samsung, Sandoz and Lilly, Steven Tanner: None declared, Andrew Grainger: None declared, Andrea Ladas: None declared, Philip O’Connor: None declared, Al Lyn Tan: None declared

REFERENCES:

Significantly higher T2 in myositis patients compared to healthy controls in hamstrings

: Significantly higher T2 in myositis patients scored 0 (no oedema) compared to healthy controls in hamstrings

Figure 1. T2 measurements in myositis patients compared with healthy controls in the hamstrings

Figure 2. T2 measurements compared to semi-quantitative scores in myositis patients and healthy controls

LUMBAR SPINE BONE MASS DENSITY AS A PREDICTOR OF FRACTURES IN PATIENTS WITH COELIAC DISEASE: AN OBSERVATIONAL STUDY

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Background: Previous studies have indicated that Lumbar spine Bone Mineral Density (BMD) could be used as an indicator to predict fractures in patients with coeliac disease (1). Patients with coeliac disease are at a higher risk of developing fragility fractures as a result of the underlying metabolic pathology. Despite previously highlighting the lumbar spine BMD usefulness in predicting fractures, score systems, like the FRAX score still has not acknowledged it. Additionally, recent data suggested that using a ratio of BMD mass index (BMI) to BMD could increase the predictive models for fracture.

Objectives: Through a large observational study, we set out to determine the various predictors of fractures in patients with coeliac disease. Age, gender and lumbar BMD were some of the factors that were considered in relation to fractures. This data was scrutinised to assess specifically the lumbar BMD’s ability to predict fractures with and without using the BMI ratio.

Methods: A sample of 788 patients with coeliac disease referred for bone density estimation to a scanner in the North west of England from 2004-2010 was used to assess various predictors of fractures. Data were initially analysed using simple statistical analyses (chi-squared for categorical variables and t-test for continuous variables) to compare patients who had sustained a fracture to those that had not sustained a fracture. The data was then subject to further analysis initially using univariate and then multivariate logistic regression models. Variables analysed included Lumbar spine L1-L4 BMD, BMI/BMD ratio, gender, age at scan, family history of fractures, alcohol, smoking and rheumatoid arthritis. In order to further assess the Lumbar spine BMD’s vs BMI/BMD in predicting fractures, the data was further adjusted for age and gender and models compared using areas under the receiver operating characteristic (ROC) curve.

Results: Out of the 788 patients referred in the analysis period, 159 (20.2%) sustained a fracture. The mean age at the time of the fracture was 55.4 (SD 14.4). A total of 576 (73.1%) were female and of those 127 (22%) had sustained a fracture. Female gender was significantly associated with fracture (p=0.003). Patients with fractures were older 59.2 years (SD 14) compared to 54 years (SD 14) (p=0.001). Using the multivariate model, it was evident that even after being adjusted for gender and age, the lumbar spine BMD was a good predictor of fractures (OR 0.98 95%CI 0.92-0.93). This performed better than the ratio of BMI/BMD. AUC 0.64 vs AUC 0.62.

Conclusion: The FRAX tool should consider using lumbar spine BMD as an indicator of fragility fractures in patients with coeliac disease. We have shown using both univariate and multivariate analyses that many factors are associated with fragility fractures, but the lumbar spine BMD was the best predictor. This study took the data another step further and adjusted the data for gender and age and added the ratio of BMI to BMD, but still reached a similar conclusion. Lumbar spine BMD should be taken into consideration with more care in this group of patients.

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Disclosure of Interests: Mariam Gaddah: None declared, Manwan Bukhari: Speakers bureau: Bristol-Myers Squib, UCB celltech, Roche/Chugai, Pfizer, Abbvie, Merck, Menarini, Sanofi-aventis, Eli-Lilly, Janssen and Novartis.

COMPARING DISEASE ACTIVITY IN THE WRIST BY REPEAT SYNOVIAL BIOPSY, RAMRIS MAGNETIC RESONANCE SCORE AND EULAR-OMERACT ULTRASOUND SCORE: A 6-MONTH PROSPECTIVE TRIAL IN EARLY AND LONGSTANDING RHEUMATOID ARTHRITIS

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Background: Standardized scoring systems for Rheumatoid Arthritis (RA) joint disease activity are validated in different imaging modalities and objectives: To determine the effect of retinal outer nuclear layer thinning on the progression of hydroxychloroquine retinopathy. Methods: We used a Heidelberg Spectralis(R) Spectral Domain Ocular Coherence Tomography (SD OCT) scanner to record the volume of the ONL in 194 eyes of 100 patients who have been on Hydroxychloroquine for 5 years or more. Volume data was analysed using the Statistical Package for Social Sciences (SPSS), we used logistic regression method to determine the probability of developing maculopathy based on the degree of reduction of the ONL volume. We correlated the loss of ONL to changes in visual fields.

Results: Mean age: 62.2 years, 20% males and 80% females. Diagnosis: 68% rheumatoid arthritis, 14% Sjogren’s syndrome, 16% Systemic Lupus and 2% others. Mean duration of use was 6.3 years. Logistic regression results show strong negative correlation between the ONL volume and probability of toxicity, a reduction of 0.5 mm3 of the ONL volume carries a 51% chance of developing maculopathy (P<0.001), the Hosmer-Lemeshow test indicates a high significance with a high P value of 0.61. Onset and progression of visual field defects strongly correlate to loss of ONL volume of 50% or more (P<0.000) and age above 35 years (P<0.0001).

Conclusion: Outer nuclear layer volume reduction provides an accurate and objective way of predicting the development of hydroxychloroquine retinopathy, this method also helps building a cooperative relationship between ophthalmologists and rheumatologists to establish an effective screening service.

REFERENCES:

Disclosure of Interests: Hani Hasan Grant/research support from: Bayer, Heidelberg Engineering, Speakers bureau: Bayer, Khin Yein: None declared, Tareg Mudawi: None declared, Elizabeth Price: None declared, Guy Smith: None declared.
include Larsen score for radiographs, RAMRIS for magnetic resonance imaging (MRI) and EULAR-OMERACT score for ultrasound (US). However, pairwise correlations between all three imaging modalities and their correlations with synovial histopathological assessment have not been performed.

Objectives: To investigate the relationship between histological synovitis and radiological synovitis, assessed by conventional X-ray, US and MR imaging at baseline and after 6 months. Imaging was conducted on the same hand as biopsied. MRI was performed at baseline for all, and also at 6 month for the ERA group, and scored with the RAMRIS system. Wrist X-ray was scored by Larsen score at baseline and after 6 month. Hand US examination at baseline, 3 and 6 months was scored by the EULAR-OMERACT US system. Synovial biopsy inflammation at baseline and 6 months was determined by the Larsen score, scores for CD20, CD3, CD138, CD68 staining, and classification of synovial pathotypes.

Results: In the ERA group at baseline, Krenn score was strongly correlated with both EULAR-OMERACT US combined score (r=0.77, p<0.001) and RAMRIS MRI synovitis score (r=0.85, p<0.001), while uncorrelated at 6 months (r=0.18, p=0.38 and r=0.14, p=0.65). In the LRA group at baseline, these scores correlated strongly (r=0.83, p<0.001) to moderately (r=0.61, p=0.002), and persisted at 6 months for US score (r=0.81, p<0.001). Larsen score was not correlated with Krenn score at any point in any group. For all RA patients, change in Krenn score between baseline and 6-month biopsy, was correlated with both change in EULAR-OMERACT US combined score (r=0.65, p<0.001) and change RAMRIS MRI synovitis score (r=0.50, p=0.03), but not to change in Larsen score. Patients with the lymphoid pathotype had higher US combined score, MRI synovitis score (r=0.50, p=0.03), but not to change in Larsen score. MRI synovitis score and Krenn-score at baseline compared to other pathotypes (all p<0.05).

Conclusion: The MRI RAMRIS synovitis score and EULAR-OMERACT US scoring system are sensitive measures of histological synovitis in LRA and ERA. After 6 months, this correlation persists in the established RA group despite effective treatment, but not in the ERA group. This suggests that ERA and LRA may have different responses to treatment and that ERA could potentially be used to estimate disease extent. We suggest the ‘slope’ sign be included in axillary artery ultrasound scan protocols for all patients with suspected GCA and also for monitoring disease activity in LVGCA.

REFERENCES:

Disclosure of Interests: Kate Smith: None declared, Abdullah Khan: None declared, Bhaskar Dasgupta Consultant for: Roche, GS, Sanofi, BMS, Abbvie, Speakers bureau: Roche

FRI0642 THE ‘SLOPE SIGN’: A FEATURE OF LARGE VESSEL VASCULITIS?
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Background: Ultrasonography in large vessel vasculitis (LVV) has become popular as a non-invasive, radiation-free, point of care examination that allows assessment of entire temporal and axillary vessels. EULAR recommends ultrasound as first line imaging of giant cell arteritis (GCA) and LVV (1) and poly/ polymyalgia rheumatica (PMR). Cranial and large vessels GCA (LV GCA) are considered the two subtypes of the disease. Ultrasonography in cranial GCA is well established, with the non-compressible halo of temporal arteries considered the key diagnostic finding. In LV GCA, increased intra-medial thickness (cut off >1.0 mm), is the preferred method of diagnosis. There are other causes of thickening of arterial wall, such as atherosclerosis. Atherosclerotic US changes in US are localized and discrete, however, at times it may be challenging to differentiate vasculitic from atherosclerotic changes.

Objectives: We describe the ‘slope sign’ as a unique additional finding in US scan of axillary arteries in LV GCA. Ultrasound scan of the axillary arteries in patients with LVGCA, is a secondary confirmation alongside the abnormal IMT, of LV disease. Biologics therapy has reduced the utility of inflammatory markers in GCA and highlighted need for imaging in disease assessment (2). The ‘slope sign’ may not only differentiate increased IMT of LVV from atheroma but also the area under the ‘slope’ could potentially be used to estimate disease extent. We suggest the ‘slope’ sign be included in axillary artery ultrasound scan protocols for all patients with suspected GCA and also for monitoring disease activity in LVGCA.

Disclosure of Interests: None declared

FRI0641 USE OF MAGNETIC RESONANCE IMAGING FOR ASSESSMENT OF PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES – A SUBANALYSIS OF THE PROMETHEUS STUDY
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Background: Prometheus study was a prospective, randomized, assessor-blind multicenter trial, conducted to evaluate the efficacy and safety of the combination therapy with methotrexate and glucocorticoids (GC) compared to GC treatment only in patients with polymyositis (PM) and dermatomyositis (DM). Muscle MRI has been used to assess disease activity and response to treatment.

Objectives: To assess MRI findings we developed new semi-quantitative scoring method and used it for activity assessment and evaluation of treatment effect after 3 months of therapy.

Methods: In a novel semi-quantitative assessment of edema, we used scoring 0, 1, 2, and 3 according to intensity of signal in each of the 16 thigh muscles. Muscle damage was evaluated in 3 basic thigh muscle compartments and pelvic muscles using Goutallier grading (0 – 5) based on extent of fatty replacement. Both sides were assessed, an average was made for each muscle, and values were summed up in the total score. Images were scored by 2 independent evaluators and the mean was used. Manual muscle test (MMT) and creatine kinase (CK) were measured and patient’s global assessment (PGA), physician’s GA (PGA) and muscle disease activity (MDA) were recorded on visual analogue scales.

Results: Seventeen patients had MRI images taken before the baseline visit. 8 had also the second MRI after 3 months of therapy. There was a significant reduction of total MRI edema score (MRI ES) after 3 months in patients with PM and DM (from the mean 17.4 points, SD 13.7 to 8.0 points, SD 12.3; p=0.025). No significant progression of fatty atrophy was observed (from 16.0 points, SD 8.8, to 19.4, SD 4.6; p=0.3). At baseline, a significant correlation between MRI ES and MMT was noted (r=0.27). There was also a borderline association of MRI ES with muscle strength evaluated by MMT (r=0.3). In a subset of 8 patients with longitudinally performed two MRI evaluations we found a good correlation between

Table: Mean maximum and normal IMT and length of ‘slope’ in LV GCA patients

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<th>Maximum (Proximal) IMT</th>
<th>Normal (Distal) IMT</th>
<th>Slope Length</th>
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<tr>
<td>Mean (SEM) mm</td>
<td>1.23 (0.04)</td>
<td>0.52 (0.03)</td>
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Conclusion: Presence of the ‘slope sign’ in the ultrasound scan of the axillary arteries in patients with LVGCA, is a secondary confirmation alongside the abnormal IMT, of LV disease. Biologics therapy has reduced the utility of inflammatory markers in GCA and highlighted need for imaging in disease assessment (2). The ‘slope sign’ may not only differentiate increased IMT of LVV from atheroma but also the area under the ‘slope’ could potentially be used to estimate disease extent. We suggest the ‘slope’ sign be included in axillary artery ultrasound scan protocols for all patients with suspected GCA and also for monitoring disease activity in LVGCA.
Conclusion: We proposed a new semi-quantitative scoring system for assessment of MRI images in patients with PM and DM. This system was applied to record degree of muscle edema and fatty replacement in a subpopulation of patients treated in the Prometheus study. A significant reduction of MRI ES and no relevant progression of muscle atrophy and fatty replacement after 3 months of therapy was demonstrated. Initial MRI edema score correlated with some clinical and laboratory parameters (PGA, CK) but was not predictive to a degree of improvement during treatment. The results are limited by a small sample size, particularly in the subset with longitudinal MRI.

Acknowledgement: Supported by the project (Ministry of Health, Czech Republic) for conceptual development of research organization 00023728 (Institute of Rheumatology).

Disclosure of Interests: Kateřina Kubinová: None declared, Jiří Vencovský Consultant for: Samsung, Speakers bureau: AbbVie, Novartis, Pfizer, Sanofi, Eli Lilly, Biogen, UCB, MSD, Werfen, Roche


FRI0643 SPINE AND SACROILIAC JOINTS LESIONS ON MRI IN PATIENTS WITH EARLY AXIAL SPA: CORRELATION WITH CLINICAL AND DISEASE ACTIVITY INDICES IN 24-MONTHS FOLLOW UP (ITALIAN ARM OF SPACE STUDY)

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1Rheumatology Unit, University Hospital of Padova, Department of Medicine–DIMED, Padova, Italy; 2University Hospital of Padova, Radiology Unit, Padova, Italy

Background: Recently several studies have focused on the use of magnetic resonance imaging (MRI) that might facilitate early diagnosis and monitor the disease activity of axial spondyloarthritis (axSpA) features over time and relate to radiographic damage; identify the predictive factors for a more exhaustive manner the role of imaging in the monitoring of activity disease and radiological progression.

Disclosure of Interests: None declared


FRI0644 ANALYSIS OF CARDIOVASCULAR RISK AND CAROTID INTIMA-MEDIA THICKNESS IN PATIENTS WITH PSORIASIS

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Background: Psoriasis (Ps) is associated with atherosclerosis and an increased risk of cardiovascular disease (CVD). Currently, a new automated ultrasound software, based on radio frequency, called QIMT (quantitative intima media thickness) technology, proved to be a useful method for assessing subclinical atherosclerosis with the measurement of the intima-media thickness (IMT) in carotid arteries.1-2

Objectives: To analyze the ultrasound results of the QIMT and Framingham score for psoriasis patients submitted to two types of treatments: methotrexate (MTX) and tumor necrosis factor inhibitor (TNF-α).

Methods: Fifty patients with psoriasis in plaques, were divided into two groups, using MTX and using TNF-α (infliximab and adalimumab). We
evaluated the measurement of abdominal circumference, blood pressure, body mass index (BMI) and presence of metabolic syndrome (SM). In addition, we evaluated cardiovascular risk with the Framingham score and IMT of the two common carotid arteries using automatic software (QIMT) and laboratory tests, including fasting glycemia and total cholesterol, fractions and triglycerides. Data were analyzed using the t-student, chi-square test and the Mann-Whitney test. For the evaluation of the CVR, univariate and multivariate logistic regression analyses were performed. The level of significance (α) adopted was 5%, being considered statistically significant values of p <0.05.

Results: Total of 50 patients in the study, 25 were on MTX (group 1) and 25 were on ad-TNFα (group 2). Mean age was 54.8 ± 12.5 with a slight male predominance (58%). Total cholesterol, HDL, LDL and triglycerides were lower in the group 1 (76%, 30% and 42% of patients, respectively). Overall, 84% of the patients had high waist circumference and 82% had a BMI above the ideal. There was a statistically significant difference (p <0.05) between the groups for metabolic syndrome results (68% vs. 32%); 44% of the patients in group 1 presented Framingham score intermediate to high and 28% of group 2, in relation to the QIMT. 56% of group 1 and 72% of group 2 showed higher than expected (p= 0.05). For the correlation between QIMT and Framingham Score, the Pearson (r) linear correlation coefficient found was 0.617 (p <0.001), indicating a moderate to strong positive association. The cross-sectional analysis does not provide information on causality and the protective or non-protective effect of the aforementioned therapies in relation to cardiovascular risk was not evaluated.

Conclusion: The results show that patients with Ps have high rates of metabolic syndrome and subclinical atherosclerosis. There was a positive association correlating the Framingham score values with the QIMT measurement, providing evidence for the use of ultrasound in clinical practice.

REFERENCES:

Disclosure of Interests: None declared

**FR00645** EVALUATION OF MARKETED KITS FOR MEASUREMENT OF ABP 501, THE FIRST APPROVED ADALIMUMAB BIOSIMILAR, DRUG CONCENTRATION AND ANTI-DUPLICATE ANTIBODY LEVELS IN PATIENT SERUM

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Background: Adalimumab and its biosimilars are anti-tumour necrosis factor (TNF)-monoclonal antibodies that are approved in Europe as treatment for various autoimmune-related indications, including Crohn’s disease and ulcerative colitis. Despite the clinical success of adalimumab, some patients show a diminished response after prolonged treatment. It is known that serum adalimumab trough levels are correlated with clinical response and the development of anti-adalimumab antibodies (AAA) may negatively impact trough levels. Currently, therapeutic drug monitoring (TDM) is used to measure adalimumab concentration and/or AAA allowing individualized optimization of treatment regimens. This then facilitates better clinical outcomes by avoiding delay in treatment decisions. Therefore, having a single assay that provides reliable TDM for both adalimumab and adalimumab biosimilars is important for physicians and patients. ABP 501, the first adalimumab biosimilar, is approved for the same indications as adalimumab (except those protected by regulatory exclusivity).

Objectives: The aim of this study was to evaluate the Promonitor® TDM kits for measurement of drug levels and AAA in serum samples from a selected representative subset of subjects, treated with ABP 501 or adalimumab reference product (RP) in the phase 3 study (NCT01970475).

Methods: A total of 30 subjects (15 ADA-positive; 15 ADA-negative) served as a representative subset in this evaluation. AAA positive control antibody and serum samples from subjects treated with either ABP 501 or adalimumab RP in the Phase 3 study were used to assess the suitability of the TDM (Promonitor®) kits for AAA (Promonitor® ANTI-ADL) and quantitative drug detection (Promonitor® ADL).

Results: The Promonitor®-ANTI-ADL TDM kit was able to detect a low level (10 ng/ml) of AAA positive control antibodies for ABP 501. In subjects whose serum was evaluated (18 treated with ABP 501 adalimumab biosimilar and 10 treated with adalimumab RP), the TDM kit produced 100% concordant positive or negative AAA results when compared to the assay that had been used in the phase 3 study. The quantitative drug assessment in subjects whose serum was evaluated (11 treated with ABP 501 and 9 treated with adalimumab RP) using the Promonitor® ADL TDM kit displayed a high degree of correlation (average Pearson’s r = 0.987) compared with results obtained in the phase 3 study.

Conclusion: This evaluation indicates that the Promonitor® kits are suitable for use in routine detection of AAA and in quantitating serum levels of the ABP 501 adalimumab biosimilar in patients.

Disclosure of Interests: Monica Rueda, Employee of: Amgen

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Disclosure of Interests: None declared

**FR00646** EFFECT OF LONG-TERM MEDIUM-DOSE STEROID TREATMENT ON 18F-FDG PET/CT FINDINGS TO ASSESS VASCULAR AND MUSCULOSKELETAL INVOLVEMENT IN PATIENTS WITH POLYMYALGIA REUMATICA

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Background: Fluorine-18-fluorodeoxyglucose (18F-FDG) PET/CT has been proposed as a promising tool for both musculoskeletal and vascular involvement in patients with polymyalgia rheumatica (PMR). Glucocorticoids (GC) may decrease the intensity of 18F-FDG uptake. Therefore, performance of PET/CT before steroid therapy is recommended. However, in many patients with PMR, large vessel vasculitis (LVV) is precisely suspected because of steroid resistance after a long-term treatment with GC 1.

Objectives: Our aim was to assess the influence of long-term medium-dose treatment on 18F-FDG uptake to discern if 18F-FDG PET/CT could be useful to evaluate musculoskeletal and vascular involvement in patients under treatment with GC.

Methods: Single-center study of 75 patients with PMR diagnosis based on 2012 EULAR/ACR criteria. All patients underwent a PET/CT scan due to LVV suspicion based on the presence of atypical symptoms and/or persistent symptoms despite steroid therapy. We considered two groups: a) Steroid-naïve PMR patients. b) Steroid-resistant PMR patients. Both musculoskeletal and vascular 18F-FDG uptake was assessed. The statistical analysis was performed with SPSS. Student’s t test or Mann-Whitney U test was used to compare continuous variables, and Chi-squared test or Fisher’s exact test for categorical variables as appropriate.

Results: We evaluated 75 patients, 27 men and 48 women (mean age ± SD: 68.2 ± 10.7 years). PET/CT was performed in 14 steroid-naïve PMR patients (18.7%) and 61 steroid-resistant PMR patients (81.3%). Patients under steroid treatment had received a median dose of Prednisone of 10.0 [5.0-15.0] mg/day during 9.0 [2.0-22.0] months. Vascular 18F-FDG uptake was more frequently detected in steroid-naïve patients. In regard to musculoskeletal 18F-FDG uptake, no statistically significant differences were seen between both groups (TABLE).
COST-EFFECTIVENESS OF RHEUMATOLOGY

REFERENCE:

Disclosure of Interests: None declared

FR00647
COST-EFFECTIVENESS OF RHEUMATOLOGY ULTRASOUND: RETROSPECTIVE AUDIT OF THE AINTREE ULTRASOUND CLINIC
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Background: Ultrasound is useful to guide escalation of synthetic disease-modifying antirheumatic drugs (sDMARDs) and optimization of biological (bDMARDs) in inflammatory arthritis. However, there is limited published evidence of the cost effectiveness of the use of ultrasound in selecting patients for treatment tapering or escalation avoidance [1].

Objectives: To evaluate the usefulness of a Rheumatology-led Ultrasound Clinic.

Methods: Retrospective descriptive analysis of patients evaluated in the Aintree Ultrasound Clinic between January and September 2018. Our Ultrasound Clinic runs once a week and the scans are performed by expert rheumatologists (2 EFSUMB level 3, 1 advance EULAR level). Patients can be referred by specialist nurses or by other rheumatologists. Synovitis is assessed following EULAR/OMERACT guidelines.

Results: 113 patients were analysed and 10 patients were excluded (7 did not attend and 3 excluded due to not enough information available). The mean time from referral to ultrasound was 48.17 days (SD 20.21). Forty seven patients (42%) were referred by a doctor and 65 patients (58%) by a specialist nurse. Rheumatoid arthritis was the most frequent diagnosis with 74 patients (66%), other inflammatory arthritis in 23 patients (23%) and other non inflammatory conditions in 16 patients (14%). The indication for scan was to exclude subclinical inflammation in 91 patients (81%), to exclude inflammatory arthritis in 15 patients (13%) with not clear referral question in 7 patients (6%). The ultrasound was positive for inflammation (defined as >= power doppler OMERACT grade 2 in at least 1 joint)) in 37 patients (33%) all of whom had their treatment changed: sDMARD escalation (n=10), initiation bDMARD (n=4), change of bDMARD (n=2) and steroid therapy (intraarticular or intramuscular injection) the same day of the scan (n=28). Fifty eight patients were on sDMARD treatment: 14 patients had a change in treatment based on the scan (4 patients started biologic drugs, 10 patients had sDMARD escalation). There was no change of treatment in 44 patients, 7 of whom were being considered for bDMARDs before scan. Three of the 29 patients on bDMARD had a change of treatment based on the scan (2 changed to other biologic, in 1 patient another sDMARD was added). Steroidos were administrated the same day of the scan to 28 patients (intraarticular injection 10; intramuscular injection 18).

Conclusion: Ultrasound altered our management in most patients (n=108, 96%). Avoiding escalation to biologics in 7 patients who met clinical criteria saved an estimate of £35,000. We conclude that point of care ultrasound in patients with inflammatory arthritis is cost effective, not only in saving unnecessary escalation to high cost drugs but by prompt treatment of those with active disease.

REFERENCES:

Disclosure of Interests: None declared

FR10404
USEFULNESS OF THE ULTRASOUND IN THE DECISION-MAKING PROCESS ABOUT THE USE OF BIOLOGICALS IN PATIENTS WITH RHEUMATOID ARTHRITIS – EXPERIENCE OF REAL LIFE IN A MIDDLE INCOME COUNTRY
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Background: Rheumatoid arthritis (RA) is an inflammatory autoimmune disease with a prevalence of 0.5 to 1% and the advances in pharmacological treatments offered to manage the disease have achieved many goals; however, the appearance of biologics has made the treatment of RA very costly, which has a great impact in the developing countries where accessibility to these therapies is lower. On the other hand, we now know that patients who are in clinical remission of disease activity by clinimetry in a significant percentage of cases may have the so-called subclinical activity that is found using ultrasound (US).

Objectives: To evaluate the usefulness of ultrasound within the component of evaluation of patients with moderate-severe activity of the disease before they are taken to a medical board making decision process about the initiation or switching of biologics.

Methods: Once a rheumatologist has identified a patient RA with clinical indication for biological therapy, patient is sent, among other things, to a medical board to take a collegiate decision about beginning or switching of biologics. Between 24 and 72 hours before the medical board decision, the patient undergoes an US (normally 12 joints are measured plus those clinically committed at that time), in order to determine if it presents disease activity by US which is considered negative for activity if the patient has synovitis ≤ 1 or has Power Doppler ≤ 1 in a single joint.

Results: During 12 months, 988 patients had clinical indication for using biologic based on moderate or high disease activity; they were evaluated by a multidisciplinary team to define the appropriateness of a therapy; mean DAS28 of patients was 4.81 ± 1.37. Once the patients were evaluated by US, the medical board of decisions did not in all cases decide to initiate or change a biological treatment; the choices made by the team were: 30% initiated or re-initiated biological therapy, in 29% of cases the team decided to wait and continuing observing the patient, 22% were switched to other biologic therapies, 12% did not have indication to start biological therapy because no activity by US and in 5% the medication dose was adjusted. Thus, in a total of 41% of the patients, biological therapy was not started or changed, which is important from the point of view not only clinical but also of the health payers.

REFERENCE:
Conclusion: Basically, this study shows that in patients with clinical indication of biological therapy by RA activity, a previous evaluation and a ultrasound are necessary in order to have a more accurate approach in making decisions; ultrasound is a practical, real-life, cost-low test to define activity in RA patients. Also we avoid high costs therapies for the management of rheumatoid arthritis, therefore we contribute not only to the health outcomes of patients but the health economic aspects in the management of RA.

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FRI0649 PREVALENCE OF ANCA AND ANA IN PATIENTS WITH PULMONARY TUBERCULOSIS

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Background: Tuberculosis is known to have diverse clinical presentations, some of which may mimic systemic autoimmune diseases like ANCA associated vasculitis and systemic lupus erythematosus (SLE) 1. Considering the paucity of specific biomarkers in rheumatologic practices, caution needs to be applied while interpreting ANA and ANCA results, especially in TB endemic areas. Previous studies on prevalence of autoantibodies in tuberculosis have shown contrasting results 2-4. Objectives: To study the prevalence of ANCA subtypes and ANA in patients with bacteriologically confirmed pulmonary tuberculosis.

Methods: Patients with bacteriologically confirmed pulmonary tuberculosis were screened for recruitment. Anti-PR3, anti-MPO, anti-lactoferrin and anti-elastase ANCA subtypes were tested using enzyme-linked immunosorbent assay (ELISA). ANA was done by Indirect immunofluorescence (IIF) using Hep 2 cell lines. Patients who were positive for ANA were tested for presence for various extractable nuclear antigens using line immunoassay.

Results: Eighty nine patients were recruited in the study. Median age was 28 (range 20 – 46) years. The bacteriological confirmation was done via sputum examination in 81 (79 smear and 2 Gene Xpert) patients and bronchoalveolar lavage (BAL) fluid in 8 patients (5 smear and Gene Xpert). Out of 89, 62 patients were treatment naïve for pulmonary TB. The clinical features were fever (70%), Cough (99%), expectoration – (6.7%) patients had positive ANA (IIF). Line immunoassay in these patients detected anti-Schistosoma mansoni ANCA (5.5%) and ANA in 10.1%, ANA-IgM in 22.2%, and ANA-IgG in 11.1% patients respectively.

Conclusion: The NC findings were: morphological alterations (tortuous, bushy and/or ramified capillary) in 100% patients with pAPS, in 77% sAPS patients and in 88% aPL carriers; microhaemorragies in 56% pAPS patients, in 49% sAPS patients and 24% aPL carriers; enlarged hairpins in 23%, 41% and 18% subjects with pAPS, sAPS and aPL carriers respectively. In 6.3% sAPS patients, an early scleroderma pattern was detected. A NC semi-quantitative score 1 was found in 58.9% pAPS patients, in 57.4% sAPS patients and in 70.5% aPL carriers. Among those cases with abnormal NC findings, we found that a higher NC score (>2) was significantly more frequent in pAPS (21.7%) and sAPS (22.2%) patients respect to aPL carrier cases (8.3%) (p<0.005).

Disclosure of Interests: None declared

REFERENCES:

Disclosure of Interests: massimiliano vasile: None declared, Katzia Stefanantoni Consultant for: Only 1 scientific advice for Italfarmaco in 2016, Fulvia Cacciarelli: None declared, Elena Marafioti: None declared, Fabrizio conti: None declared, Valeria Riccieri: None declared, Guido Valesini: None declared.


FRI0650 A NAILFOLD CAPILLAROSCOPY STUDY IN A COHORT OF PATIENTS WITH ANTI-PHOSPHOLIPID ANTIBODIES

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Background: Nailfold capillaroscopy (NC) is a simple and non-invasive diagnostic technique, able to investigate microvascular features. In subjects with anti-phospholipid autoantibodies (aPL) many different endothelial abnormalities have been described.

Objective: We aimed to investigate the role of NC in aPL positive (aPL +) subjects, highlighting the main microvascular alterations, detected by NC.

Methods: We enrolled 39 patients with primary anti-phospholipid syndrome (pAPS) (32 females, mean age 43 years, mean disease duration 7.8 years), 47 patients with secondary anti-phospholipid syndrome (sAPS) due to Systemic Lupus Erythematous (36 females, mean age 44 years, mean disease duration 15.5 years) and 17 aPL+ subjects without any autoimmune disease, defined as aPL carriers (16 females, mean age 42 years). All subjects underwent clinical and laboratory evaluations as well as NC with both characterization of morphological parameters and attribution of a semiquantitative score.

Results: The main NC findings were: morphological alterations (tortuous, bushy and/or ramified capillary) in 100% patients with pAPS, in 77% sAPS patients and in 88% aPL carriers; microhaemorragies in 56% pAPS patients, in 49% sAPS patients and 24% aPL carriers; enlarged hairpins in 23%, 41% and 18% subjects with pAPS, sAPS and aPL carriers respectively. In 6.3% sAPS patients, an early scleroderma pattern was detected.

Conclusion: Our findings show that some NC aspecific abnormalities are more frequently found in aPL positive subjects, mainly in pAPS and sAPS ones. Although not specific, such NC features seem to be associated with the presence of vascular risk factors. Thus NC could be regarded as a useful tool in order to evaluate microcirculation in aPL positive cases.

REFERENCES:
Background: Granulomatosis with polyangiitis (GPA) mainly involves the upper and lower respiratory tracts and kidneys and induces necrotising vasculitis and granuloma. Nasal biopsy has been recommended in GPA-suspected patients to not only completely rule out chronic rhinosinusitis, but also clearly discriminate its aetiology.

Objectives: We investigated whether the classification of GPA could be made without nasal biopsy in immunosuppressant drug-naïve 45 patients with chronic rhinosinusitis who had previously been classified as GPA.

Methods: We retrospectively reviewed the medical records of 45 patients with GPA. Twenty-six patients exhibited chronic rhinosinusitis, among which 16 patients underwent nasal biopsy (10 with granuloma and 6 without granuloma). We applied the 2007 European Medicines Agency algorithm for the classification of GPA, the 2012 Chapel Hill Consensus Conference Nomenclature of Vasculitis and the 2017 American College of Rheumatology/European League Against Rheumatism provisional classification criteria for GPA to them for reclassifying GPA. (Figure1)

Results: The mean age was 58.4 years and 17 patients were men. There were no differences in clinical and laboratory results between those with and without granuloma. Among 6 patients without granuloma on nasal biopsy, 3 patients with only ANCAs and chronic rhinosinusitis could be classified as GPA due to PR3-ANCA (or C-ANCA) positivity. Among 9 patients without nasal biopsy on granuloma, 3 patients with only chronic rhinosinusitis could be classified as GPA due to GPA-specific lung lesions. (Table 1) When we excluded an item of granuloma in 10 GPA patients with granuloma on nasal biopsy, 4 patients without ANCAs could be classified as GPA due to GPA-specific lung lesions and cartilaginous involvement. (Table 2)

Conclusion: Nasal biopsy is necessary and useful for classifying GPA. However, nasal biopsy could be replaced with PR3-ANCA (or C-ANCA) positivity, GPA-specific lung lesions and cartilaginous involvement in GPA suspected patients with chronic rhinosinusitis.

REFERENCES:

Acknowledgement: None
Disclosure of Interests: None declared
Implying and Validating the Predictive Accuracy of MRI Detected Subclinical Inflammation for Rheumatoid Arthritis Development in Clinically Suspect Arthralgia

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Background: Presence of MRI-detected subclinical joint inflammation in clinically suspect arthralgia (CSA) is predictive for progression to Rheumatoid Arthritis. Despite high negative predictive values (84%), its positive predictive value (PPV) is moderate (31%).

Objectives: We studied if, in addition to the presence of inflammation, incorporating information on severity, number and combinations of MRI-inflammatory locations improves the predictive accuracy.

Methods: In the discovery cohort, 225 CSA-patients were followed on clinical arthritis development. Contrast-enhanced 1.5T MRIs were made of unilateral MCP(2-5), wrist and MTP(1-5)-joints at baseline and scored for synovitis, tenosynovitis and bone marrow edema. Severity, number and combination of locations (joint/tendon/bone) with subclinical inflammation were determined, with symptom-free controls of similar age category as reference. Cox regression was used for predictor selection. Predictive values were determined, with symptom-free controls of similar age category as reference.

Results: In both cohorts 15% developed arthritis <1-year. The number of locations HR 3.75 (1.49-9.48) and presence of MCP-extensor peritendinitis HR 2.54 (1.11-5.82); 1-2 locations HR 2.07 (1.05-4.05); ≥3 locations HR 3.81 (1.96-7.42) were independently predictive. Seventy and combinations of inflammatory lesions were not. Based on these variables, five risk categories were defined: no subclinical inflammation, 1-2≥3 locations, without MCP-extensor peritendinitis. PPVs ranged 5% (lowest category; NPV 98%) - 67% (highest category). Similar findings were obtained in the validation cohort; PPVs ranged 4% (lowest category; NPV 96%) - 63% (highest category).

Conclusion: Incorporation of the number of locations with subclinical inflammation and MCP-extensor peritendinitis in MRI-evaluation improved risk stratification, yielding PPVs up to 63-67%. This promotes optimal use of MRI-data in an evidence-based way.

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DECREASING INCIDENCE OF CARDIOVASCULAR DISEASE IN PATIENTS WITH INCIDENT RHEUMATOID ARTHRITIS IN RECENT YEARS

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Background: There is a recognized excess burden of cardiovascular disease (CVD) in patients with rheumatoid arthritis (RA) as compared to the general population. Several studies suggested reduced CVD mortality in RA in recent decades [1-3]. Longitudinal studies on trends in occurrence of CVD events in RA patients over time, and studies comparing trends in CVD events in RA vs general population are lacking.


Methods: The study population comprised Olmsted County, Minnesota residents with incident RA (age ≥18 years, 1987 ACR criteria met in 1980-2009) and non-RA subjects from the same underlying population with similar age, sex and calendar year of index. All subjects were followed until death, migration, or 12/31/2016. Follow-up was truncated for comparability. Incident CVD events included myocardial infarction (MI), stroke (ischemic or hemorrhagic), coronary heart disease (CHD) death and first occurrence of any of these. Patients with CVD events prior to RA incidence/index date were excluded. Cox proportional hazards models were used to compare incident CVD events by decade, adjusting for age and sex. Cumulative incidence of CVD events adjusted for other causes was also computed.

Results: The study included 906 patients with RA (mean age 55.9 years; 69% female). There were 201, 299 and 406 patients with incident RA in 1980-89, 1990-99 and 2000-09, respectively. During median follow-up of 10.6, 10.4 and 10.2 years per decade, CVD events occurred in 31, 38,
and 31 patients. Patients with incident RA in 2000–09 had markedly lower cumulative incidence of any CVD events than patients diagnosed in 1990s and 1980s (Figure). Hazard ratios (HR) for any CVD events demonstrated significant reduction in CVD events among patients with incident RA in 2000s compared with incident RA in 1990s (HR: 0.52, 95% confidence interval (CI): 0.32–0.86) and a reduction approaching significance compared with incident RA in 1990s (HR: 0.65; 95% CI: 0.40–1.05). Patients with incident RA in 2000s were compared with 405 patients without RA in 2000s who experienced 30 CVD events during follow-up. Patients with incident RA in 2000s had no excess in CVD events over subjects without RA (HR: 0.88, 95% CI: 0.53–1.46). Results were similar for MI, stroke and CHD deaths when examined separately.

Conclusion: Our findings show a dramatic reduction in incidence of major CVD events in RA in recent decades. The gap in CVD occurrence between RA patients and the general population may be closing. These findings may reflect increased awareness, improved primary CVD prevention and more optimal RA disease management in recent years. More studies are needed to understand the reasons and implications of these trends.

REFERENCES:

Disclosure of Interests: Elena Myasoedova Grant/research support from: Pfizer, John Davis Grant/research support from: Pfizer, Veronique Roger: None declared, Sara Achenbach: None declared, Cynthia S. Crowson: None declared, Sara Achenbach: None declared, Cynthia S. Crowson: None declared

FR0655 THE IMPACT OF PREGNANCY ON STRUCTURAL PROGRESSION IN PREMENOPAUSAL WOMEN WITH RHEUMATOID ARTHRITIS

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Background: Disease activity often improves during pregnancy and worsens at the postpartum period [1]. The long-term effect of pregnancy on radiographic joint damage progression among premenopausal women with RA has been rarely studied.

Objectives: The aim of this study was to analyse the impact of pregnancy on radiographic progression in premenopausal women with RA.

Methods: This is an observational cohort study of RA patients included in the Swiss Clinical Quality Management in Rheumatoid Arthritis (SCQM-RA). Patients enrolled are followed-up yearly and have radiographic assessments at regular intervals. Information about female reproductive factors, such as pregnancies, breastfeeding and hormonal treatment were retrospectively retrieved using a questionnaire. For this analysis we included premenopausal women with at least two radiographic assessment and full information on reproductive factors. The primary outcome was the rate of radiographic progression (Ratingen erosion score). We analysed the radiographic progression between premenopausal women with at least one pregnancy and those with no pregnancies. Baseline time was the first radiographic assessment. We used a multilevel regression model for longitudinal data, adjusted for potential confounders, such as baseline age, disease duration, DAS-28 and treatment.

Results: Among 1966 women who were interviewed, 430 premenopausal women with sequential radiographic assessments during follow-up were analysed. Half of premenopausal women had at least one pregnancy. Women with at least one pregnancy were older than nulliparous (median of 41 vs 36 years, p=0.001) and had longer disease duration (median of 3.4 vs 2.6 years, p=0.04) (Figure 1). During follow-up, the rate of radiographic progression was lower in women with pregnancies than in nulliparous women [0.9% (95% CI: 0.0 to 1.9) vs 2.1% (95% CI: 0.9 to 3.1) over 10 years, respectively, p<0.04, Figure 1]. In a sub-analysis, the rate of radiographic progression appeared to be lower during the 13-year period after first pregnancy than after this period [0.2% (95% CI: -0.8 to 1.3) vs 2.6% (95% CI: 1.3 to 3.9) over 13 years, respectively, p=0.003]. We found no difference in the rate of radiographic progression between women with a single pregnancy and multiparous women.

Conclusion: In premenopausal women with RA, joint damage progressed more rapidly in nulliparous women than in women with at least one pregnancy. However, we cannot make any definite causal inference, since it is well possible that women renouncing getting pregnant might be patients with more severe disease. Radiographic progression appeared to increase the longer the time since pregnancy.

REFERENCES:

Table 1. Baseline characteristics of premenopausal women of SCQM cohort

<table>
<thead>
<tr>
<th>General and disease characteristics</th>
<th>Women with pregnancies n=213</th>
<th>Nulliparous women n=217</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, median(IQR)</td>
<td>41 (36-45) *</td>
<td>36 (29-43)</td>
</tr>
<tr>
<td>Ever smoking, n (%)</td>
<td>96 (26)</td>
<td>66 (30)</td>
</tr>
<tr>
<td>Alcohol consumption, n (%)</td>
<td>129 (61)</td>
<td>112 (52)</td>
</tr>
<tr>
<td>Disease duration, years, median</td>
<td>3.4 (0.6-8.0) *</td>
<td>2.6 (0.4-7.4)</td>
</tr>
<tr>
<td>(IQR)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sero-positive (ACPA or RF positive)</td>
<td>175 (82)</td>
<td>180 (83)</td>
</tr>
<tr>
<td>n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DAS 28, median(IQR)</td>
<td>3.6 (2.6-4.9)</td>
<td>3.6 (2.4-4.8)</td>
</tr>
<tr>
<td>HAQ-DI, median (IQR)</td>
<td>0.6 (0.3-1.3)</td>
<td>0.6 (0.3-1.3)</td>
</tr>
<tr>
<td>Erosion score,% , median (IQR)</td>
<td>1.0 (0.3-4.9) *</td>
<td>1.4 (0.1-5.0) *</td>
</tr>
<tr>
<td>DMARD treatment, n (%)</td>
<td>181 (85)</td>
<td>186 (86)</td>
</tr>
<tr>
<td>n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biologic treatment, n (%)</td>
<td>70 (33)</td>
<td>72 (33)</td>
</tr>
</tbody>
</table>

p-value <0.05. DAS28: 28 joint Disease Activity Score ESR, HAQ-DI: Health Assessment Questionnaire – Disability Index; DMARD: disease-modifying antirheumatic drugs.

Disclosure of Interests: Deshire Alpizar-Rodriguez: None declared, Frauke Förger: None declared, Axel Finkoth: Grant/research support from: Bristol-Myers Squibb, Pfizer Inc, Consultant for: AbbVie, A2Bio, Bristol-Myers Squibb, MSD, Roche, Pfizer Inc, and UCB

FR0656 ENVIRONMENTAL AND ATMOSPHERIC FACTORS IN SYSTEMIC LUPUS ERYTHEMATOSUS: A REGRESSION ANALYSIS

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Background: Understanding the role of environmental exposures in the development of SLE and their association with SLE activity may help identify modifiable risk factors and potential etiological mechanisms.

Objectives: We hypothesized that changes in fine particulate matter (PM2.5) concentration, ozone concentration, temperature, resultant wind, relative humidity, and barometric pressure are predictive of organ specific flares in lupus.

Methods: 1628 patients who fulfilled 4 of the 11 ACR or SLICC classification criteria for SLE were included in the analysis. The data ranged from 1999 to 2017. Maximum distance between visits was 110 days with 1-month time aggregation units. Disease activity was expressed as Physician Global Estimate (PGA), taken at
every patient visit. A flare was defined as a PGA score increase of 1 point or more compared to the previous visit. Environmental and atmospheric data was obtained from the EPA, including PM2.5 and ozone concentration, temperature, residual surface area, air pressure, and barometric pressure. The average values of each factor for 10 days prior to patient visit was calculated. Univariate and multivariate models were built in order to study the association of these variables with lupus disease activity. The models were adjusted for age, sex, income, racial distribution, and rural vs. urban patient residence. Multivariate logistic regression was used to identify significant determinants associated with lupus flares. Regression was performed for each organ flare outcome. Regression inference was based on generalized estimating equations (GEE) to account for the time repeated outcomes. Standard regression techniques on model building and evaluation were followed, including but not limited to performing both univariate and multivariate regressions, coefficient significance, collinearity, confounding, variable interactions and reductions in model AIC.

Results: Rash, serositis, hematologic, and joint flares were statistically significantly associated (p<0.05) with an increase in temperature in univariate and multivariate analysis. Renal flares were negatively associated with increases in temperature (p<0.05) in univariate and multivariate analysis. PM2.5 concentration was significantly associated (p<0.001) with rash, joint, serositis, neurologic, pulmonary, and hematologic flares in univariate and multivariate analysis. Ozone concentration, residual wind, and relative humidity were significantly associated with lupus flares in univariate analysis only, while barometric pressure had no associations.

Conclusion: There is a strong association between changes in PM2.5 concentration and temperature 10 days prior to patient visit and organ specific lupus activity at the visit. These data could add an important aspect to lupus trials, the outcomes of which may be affected by so far unrecognized environmental factors, and ultimately it could allow predictive modelling of lupus flares which would revolutionize the approach to treatment.


#### FRIO657

**METABOLIC SYNDROME PRECEDES THE ONSET OF HIP AND KNEE PAIN AND THE RISK IS NOT MODIFIED BY DIET OR CHANGES IN BMI**

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**Objectives:** To examine longitudinal data from a large prospective population-based cohort to assess the association between metabolic syndrome components and the subsequent development of either knee or hip pain over 10 years of follow-up. Methods: Known risk factors data were obtained at enrolment to the EPIC-Norfolk cohort between 1993 and 1997. Data were available on anthropometric variables, smoking status and lipid metabolites. Knee and hip pain were self-reported at 18 months, 3 and 10 years when respondents reported significant pain in either knee or hip on most days in the preceding month. Metabolic syndrome components were defined in line with the Alberti formula. Logistic regression was used to investigate metabolic syndrome components: waist circumference (men >102 cm, women >88 cm), low HDL (men <1.0 mmol/L, women <1.3 mmol/L), high triglycerides (>1.7 mmol/L) and their association to incident pain and any effect-modification of dietary patterns and changes in BMI over time. Results: Amongst 20,517 respondents (age at enrolment 59.7 years (SD 9.2), 62% were female), there were 3,886 who reported knee pain and 2,619 who reported hip pain at 18 months. By the end of follow-up there were 2,619 who had developed incident knee pain and 1,752 who had developed incident hip pain. In a logistic model adjusted for age and sex, significant associations were seen for incident pain for ever-smoking (knee: odds ratio 1.22, 95% CI 1.11, 1.33 p<0.001), (hip: odds ratio 1.21, 95% CI 1.08, 1.35 p<0.001) and obesity (knee: OR = 1.70 95% CI 1.51, 1.91 p<0.001), (hip: OR = 1.68 95% CI 1.47, 1.92 p<0.001). Adjustment for obesity, components of the metabolic syndrome associated with pain included waist circumference (knee: OR = 1.17 95% CI 1.03, 1.33 p<0.019), (hip: OR = 1.37 95% CI 1.17, 1.59 p<0.001) and for triglycerides, low HDL (OR = 1.15 95% CI 1.05, 1.27 p<0.003) and high triglycerides (OR = 1.10 95% CI 1.00, 1.21 p=0.043). These associations were not modified by dietary patterns nor changes in weight over the follow-up interval. Conclusion: There is a strong association between metabolic syndrome and a predictor for the future onset of hip and knee pain over an interval of 10 years and the risk is not modified by diet or subsequent weight change. These data suggest that preventative strategies need to be targeted early in the disease course, and should include a range of measures including smoking cessation and those that prevent the onset of metabolic syndrome.


#### FRIO658

**INCIDENCE AND PREVALENCE OF VACCINE PREVENTABLE INFECTIONS IN ADULT PATIENTS WITH AUTOIMMUNE INFLAMMATORY RHEUMATIC DISEASES (AIIRD): A SYSTEMATIC LITERATURE REVIEW InformING THE 2019 UPDATE OF THE EUULAR RECOMMENDATIONS FOR VACCINATION IN ADULT PATIENTS WITH AIIRD**

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**Background:** Despite the well-established fact of a high burden of infections among patients with autoimmune inflammatory rheumatic diseases (AIIRD), little evidence is available regarding the real incidence and prevalence of vaccine preventable infections (VPI) in this population. **Objectives:** To update the evidence on the incidence and prevalence rates of VPI in patients with AIIRD and compare the data to the general population when available. Methods: A systematic literature review was performed using Medline, Embase, and Cochrane library, from October 2009 to August 2018. Search terms were defined for AIIRD and VPI. Observational studies including cohort studies for incidence rates and cross-sectional studies for prevalence rates were included, as well as systematic reviews of cohort studies and meta-analyses. The primary outcome was the incidence or prevalence of VPI in the adult AIIRD population. Meta-analysis was performed when appropriate. Results: The search identified 2876 records, out of which 63 met the inclusion criteria. Data on the following VPI rates was retrieved and analyzed: influenza (incidence: n=4), pneumococcal disease (incidence: n=7), hepatitis B virus (HBV) (incidence and prevalence: n=10), herpes zoster (HZ) (incidence: n=29), human papilloma virus (HPV) (incidence and prevalence: n=13). For influenza, limited data pointed to an increased incidence (409.33 vs 306.12 cases per 100,000 patient-years in patients with rheumatoid arthritis (RA) vs controls, respectively) and influenza-related complications in patients with AIIRD. Data on pneumococcal disease, available mainly for patients with systemic lupus erythematosus (SLE), showed a substantially increased risk in all age groups compared to controls (incidence rate ratio (IRR) 4.7, 95% confidence interval (CI) 3.7-6.0). For HZ, an increased risk was observed across all patients with AIIRD in comparison to the general population: pooled incidence rate 2.4, 95% CI 2.05-2.76, with the highest incidence rates observed in inflammatory myositis (pooled IR 35.98, 95% CI 32.33-39.64), followed by SLE (pooled IR 18.87, 95% CI 8.7-29.64), and RA (pooled IR 11.64, 95% CI 9.37-13.91). Studies on HPV mainly investigated the SLE population in the Latin America and Asia: HPV pooled prevalence 26%, 95% CI 17%-36% and pooled prevalence ratio 1.58, 95% CI 0.74-3.36 in comparison with the general population. In RA, limited data showed a similar prevalence of HPV in patients and controls: pooled prevalence ratio 0.72, 95% CI 0.46-1.12. For hepatitis B virus, pooled prevalence of hepatitis B surface antigen in patients with AIIRD was similar to the general population. 3%, 95% CI 1%-5%.
Conclusion: Current evidence shows an increased risk of vaccine-preventable infections in patients with AIIRD, emphasizing that prevention of infections is essential in these patients.

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Remission Persistence in Rheumatoid Arthritis, Psoriatic Arthritis and Axial Spondyloarthritis Under Biologic Treatment

Background: Patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and axial spondyloarthritis (axSpA) under biologic treatment are increasingly achieving prolonged remission and tapering treatment is becoming standard practice. However, the optimal timing to start tapering remains unclear and predictors of loss of remission (LOR) are missing. Guidelines disagree on whether to wait for 6 or 12 months of sustained remission before tapering.

Objectives: To determine whether longer sustained remission (6 versus 12 months) influences subsequent LOR rates and to identify predictors of LOR.

Methods: We used the Rheumatic Diseases Portuguese Register (Reuma.pt), to identify RA, PsA and axSpA patients on stable biologic treatment in a single center and retrospectively analyze those who achieved sustained remission for at least 6 and 12 months. Survival analysis was used to characterize stability of remission and identify predictors of LOR. The Cox proportional hazards regression was stratified by diagnosis and adjusted for age, gender, smoking, baseline disease activity, type of biologic, previous switches and starting year of biologic treatment.

Results: 195 patients (100 RA, 51 PsA and 44 axSpA) of 1078 patients (785 RA, 116 PsA, 177 axSpA) registered in Reuma.pt at a single center and treated with biologics between 1999 and 2018, had at least one remission period with a minimal duration of 6 months. This corresponded to 310 individual remission periods longer than 6 months, 232 of which (74.8%) were longer than 12 months. Median remission time (since the start of remission period) was 78.6 weeks overall vs. 99.0 weeks for patients with a minimum 12 months remission (difference in median survival: 20.4 weeks). PsA patients showed significantly longer remission periods (p=0.0001), followed by axSpA and RA. We identified active smoking (HR 1.96, p=0.008 for the total population; HR 1.53, p=0.20; HR 7.42, p=0.01, HR 0.74, p=0.79 for RA, PsA and axSpA, respectively), and infliximab use (HR 2.23, p=0.005 for the total population; HR 4.07, p=0.001, HR 3.20, p=0.16, HR 0.62, p=0.62 for RA, PsA and axSpA, respectively; subcutaneous TNF inhibitors (TNFi) used as index category) to be significantly associated with LOR. A sensitivity analysis excluding infliximab patients further suggested female gender (HR 3.21, p<0.001) and duration of disease until first biologic (HR 1.05, p=0.031) as important co-variates.

Figure 1 – time to loss of remission considering a single flare (a) vs. persistent flare (b), all patients (minimum 150 days in remission). Number of failure events indicated in parenthesis.

Figure 2 – time to loss of remission considering a single flare (a) vs. persistent flare (b), only patients with minimum 320 days in remission. Number of failure events indicated in parenthesis.
Results: Before coronary angiography fasting blood samples were collected and plasma levels of interleukin-6 (IL-6), C-reactive protein (CRP) and serum amyloid A (SAA) were measured by immunonephelometry. IL-6 and SAA polymorphisms were genotyped.

Results: During a median observation time of 9.9 years 949 deaths (30.3%) occurred, of these 597 (19.2%) died from cardiovascular events. Plasma levels of IL-6, CRP and SAA were associated with unstable CAD as well as established risk factors including type 2 diabetes, smoking, lower eGFR, lower triglycerides and lower HDL-C. In addition, IL-6 correlated with age, use of lipid lowering therapy and hypertension, SAA correlated with female gender and hypertension, and CRP correlated with female gender, lipid-lowering therapy and BMI. After adjustment for established cardiovascular risk markers and the other two inflammatory markers, SAA was found an independent risk factor for cardiovascular mortality after a short-term follow-up (1 year) with a HR of 1.41 (1.03-1.93, p=0.030), whereas IL-6 was identified as an independent risk factor for long-term follow-up (3, 5-9.9 years) with HRs of 1.21 (1.02-1.43, p=0.006), 1.22 (1.06-1.40, p=0.006) and 1.18 (1.07-1.31, p=0.001), respectively. Although 6 SNPs in the SAA gene were significantly associated with SAA plasma concentrations (none of the IL-6 SNPs associated with IL-6 levels), the genetic risk score was not associated with mortality.

Conclusion: In our large, long-term LURIC cohort study we demonstrate for the first time prospectively that plasma levels of IL-6 and SAA are not only associated with cardiovascular risk factors and the prevalence of CAD but also independently predicted cardiovascular mortality. These findings underline the importance of low-grade systemic inflammation for the cardiovascular risk and the prognostic relevance of inflammatory biomarkers, independently predicting cardiovascular mortality. Although it was not within the focus of this study, our findings might suggest that even low-grade inflammation is unfavourable in chronic rheumatic disease.

Disclosure of Interests: None declared.


LONG- AND SHORT-TERM ASSOCIATION OF LOW- GRADE SYSTEMIC INFLAMMATION WITH CARDIOVASCULAR MORTALITY

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Background: Evidence suggests a critical role for inflammation in the pathogenesis of coronary artery/heart disease (CAD/CHD), implicating inflammatory molecules as central mediators of chronic inflammatory processes within the vascular wall. In this regard, patients with chronic inflammatory disease such as RA and SLE are at increased risk, which was attributed to the high levels of inflammatory mediators. However, less is known about the association of low-grade systemic inflammation with the cardiovascular risk.

Objectives: The aim of the present study was therefore to evaluate biomarkers representing low-grade systemic inflammation and their association with mortality in a large cohort of patients.

Methods: The Ludwigshafen Risk and Cardiovascular Health (LURIC) study included 3316 consecutive patients undergoing coronary angiography between June 1997 and May 2001 with a median follow-up of 9.9 years. Before coronary angiography fasting blood samples were collected and plasma levels of interleukin-6 (IL-6), C-reactive protein (CRP) and serum amyloid A (SAA) were measured by immunonephelometry. IL-6 and SAA polymorphisms were genotyped.

Results: During a median observation time of 9.9 years 949 deaths (30.3%) occurred, of these 597 (19.2%) died from cardiovascular events. Plasma levels of IL-6, CRP and SAA were associated with unstable CAD as well as established risk factors including type 2 diabetes, smoking, lower eGFR, lower triglycerides and lower HDL-C. In addition, IL-6 correlated with age, use of lipid lowering therapy and hypertension, SAA correlated with female gender and hypertension, and CRP correlated with female gender, lipid-lowering therapy and BMI. After adjustment for established cardiovascular risk markers and the other two inflammatory markers, SAA was found an independent risk factor for cardiovascular mortality after a short-term follow-up (1 year) with a HR of 1.41 (1.03-1.93, p=0.030), whereas IL-6 was identified as an independent risk factor for long-term follow-up (3, 5-9.9 years) with HRs of 1.21 (1.02-1.43, p=0.006), 1.22 (1.06-1.40, p=0.006) and 1.18 (1.07-1.31, p=0.001), respectively. Although 6 SNPs in the SAA gene were significantly associated with SAA plasma concentrations (none of the IL-6 SNPs associated with IL-6 levels), the genetic risk score was not associated with mortality.

Conclusion: In our large, long-term LURIC cohort study we demonstrate for the first time prospectively that plasma levels of IL-6 and SAA are not only associated with cardiovascular risk factors and the prevalence of CAD but also independently predicted cardiovascular mortality. These findings underline the importance of low-grade systemic inflammation for the cardiovascular risk and the prognostic relevance of inflammatory biomarkers, independently predicting cardiovascular mortality. Although it was not within the focus of this study, our findings might suggest that even low-grade inflammation is unfavourable in chronic rheumatic disease.

Disclosure of Interests: None declared.


ASSOCIATIONS OF CURRENT AND CHILDHOOD SOCIOECONOMIC STATUS WITH PATIENT-REPORTED HEALTH OUTCOMES AMONG PATIENTS WITH KNEE OR HIP OSTEOARTHRITIS IN A FAMILY PRACTICE SETTING IN MEXICO CITY

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Background: The life-course approach is a useful framework to understanding socioeconomic inequalities in the prevalence and outcomes of chronic disease, and in particular in osteoarthritis (OA). Previous studies have measured Socioeconomic Status (SES) in 2 points of the life-course (childhood and current) and found consistent relationships between them and both prevalence and presence of worse outcomes, but this relationship has been little explored in the Latin-American region where exposure to low SES throughout the life-course is higher than in developed countries.

Objectives: Our aim was to investigate the association of current and childhood SES with functional status, quality of life and disability among patients with knee or hip OA.

Methods: We recruited 146 patients with a mean age of 69.4 yr. 80% were female; 92%, 30% and 45% suffered from knee, hip and other joint OA, respectively. 60% had incomes in the upper 2 quintiles of the general Mexican population. We found current income to be the best predictor of WOMAC (Spearmans r=0.354, p=0.01), AMICAL (r=0.362, p=0.01) and HAQ-DI scores (r=0.335, p=0.01), and education to be correlated with all three scores as well. Occupation type was significantly associated with AMICAL and HAQ-DI but not WOMAC scores. Paternal and maternal education, and maternal occupation type, were significantly associated only with AMICAL scores.

Disclosure of Interests: None declared.

Conclusion: Among patients with knee or hip OA in our setting, current SES is a significant predictor of functional status, quality of life and disability, while childhood SES – best modeled by maternal education – is a significant predictor of quality of life. More research is needed to elucidate the relationship of SES throughout the life course with outcomes among patients with OA.

REFERENCES:

Disclosure of Interests: None declared

FR0662 ACTIVATION AND LEUKOCYTE ADHESION IS ASSOCIATED WITH VASCULAR DAMAGE IN PATIENTS WITH RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS

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Background: Patients with inflammatory rheumatic diseases, such as rheumatoid arthritis (RA) or psoriatic arthritis (PsA), have a higher cardiovascular risk than the general population. There are data in other pathologies about the role of leukocyte adhesion on endothelial damage.

Objectives: To evaluate the relationship between leukocyte adhesion and subclinical vascular damage in patients with RA and PsA.

Methods: Observational, cross-sectional exploratory study. Patients with RA and PsA who had at least one previous vascular study were recruited in a tertiary hospital during a period of 3 months. All of them donated a sample of fresh blood. Neutrophils were isolated and perfused on a monolayer of healthy endothelial cells of the umbilical cord vein to evaluate its degree of activation, determining the leukocyte adhesion parameter. The expression of different adhesion molecules was analyzed by flow cytometry. We also gathered demographic (sex, age, BMI), clinical (disease duration, classical CV risk factors) and analytical (CRP, ESR) variables. The previous vascular studies consisted of an exploration of the extracranial carotid tree with an Essato MyLab70XVG ultrasound scanner with a linear probe (7-12MHz) and an automated program for measuring the carotid intima-media thickness (CIMT) using (“Quality intima media thickness” or “real-time, QIMT”), the presence of atheroma plaques as per the Mannheim consensus and the measurement of pulse wave velocity (v’P) using the Mobi or graph device. We consider as pathologic the vascular study with the presence of abnormal plaque and/or IMT (>900µ) and/or v’P (>10ms). The statistical analysis was performed with the SPSS Statistics 22.0 program.

Results: We included 27 patients, 18 women and 9 men, with a mean age of 58.07 (SD 11.64). Eight patients were diagnosed with RA and 19 with PsA, with mean disease duration of 14 years (SD 7.14). Of these 27 patients, 15 were on biologics, 11 were treated only with DMARDs and one patient was naive for any immunomodulatory treatment. In addition, 14 (51.9%) were taking NSAIIDs and 7 (25.9%) glucocorticoids. Regarding cardiovascular risk factors, 51.9% were exposed to tobacco, 25.9% suffered hypertension, 37% were dyslipidemic, 11% were diabetic and 11% were obese, with an average of 1.41 classic cardiovascular risk factors (SD 1.36) per patient. The previous vascular study had been considered pathological in 44.4% of the patients.

A tendency to greater leukocyte adhesion was observed in these patients with pathological IMT values (>0.059) and in those patients who presented atheromatous plaque (p = 0.66). No significant associations were found in relation to the rest of the adhesion parameters analyzed, nor could subanalyses be performed due to the small sample size.

Conclusion: Our preliminary data suggest that an increase in leukocyte adhesion on the endothelium is involved in the mechanisms of subclinical atherosclerosis in patients with RA and PsA. Studies with a larger sample size will allow us to confirm these findings, as well as the factors implicated in their development.

Disclosure of Interests: None declared

FR0663 TREATMENT WITH BIOLOGIC DRUGS OF PREGNANT WOMEN WITH AUTOIMMUNE DISEASE, EXPERIENCE OF A REFERENCE CENTER IN HIGH RISK PREGNANCY WITH AUTOIMMUNE DISEASES

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Background: Autoimmune diseases predominantly affect women of child-bearing age. These women must be without clinical activity before conception, which is usually achieved thanks to immunosuppressive drugs. Also, information on new drugs does not include their possible effects on pregnancy because pregnant women are usually excluded from clinical trials.

Objectives: The aim of the study is to evaluate the safety of biological drugs (BD) in pregnant patients with different autoimmune diseases (AD).

Methods: Patients were prospectively followed in a reference Spanish center for high-risk pregnancies and AD. Follow-up was performed by a multidisciplinary team with at least one obstetrician and one expert clinician in autoimmune diseases. Females exposed to BD during the periconceptional period or during pregnancy were included in the study. Obstetric and neonatal outcomes were assessed.

Results: Between 2015 and 2018 we identified 37 exposed pregnancies in 35 women affected by different AD. At the start of pregnancy, 18 patients were taking infliximab, 11 adalimumab, 3 natalizumab, 2 rituximab, 1 etanercept y 1 tocilizumab.

BD that required BD were Crohn’s disease (20 patients, 54.1%), ulcerative colitis (7, 18.9%), rheumatoid arthritis (4, 10.8%), ankylosing spondylitis (3, 8.1%) and multiple sclerosis (3, 8.1%). Regarding pregnancies, 5 (13.5%) had left the BD just before the pregnancy. Of these, 1 remained stable and 4 (80%) had a flare during pregnancy requiring restart of BD. Of the 32 pregnancies who took the BD during pregnancy, 8 (25%) abandoned the treatment after knowing the pregnancy, meaning that 2 of them flared; 10 (31.5%) continued with the treatment until the end of the second trimester (week 25-26) and 14 (43.7%) continued during the third trimester, 4 of them kept the drug during the entire gestation due to disease activity.

In our study there was a positive correlation between periconceptional abandonment of the BD and the risk of presenting a flare (p=0.003), especially in the first and second trimesters (p=0.004). However, no relationship was found between BD and infections in the newborn (p=0.05), nor between each of the BD with the risk of infections. Preconceptional treatment reduced the risk of flare (OR 0.545, 95%CI) and the risk of maternal complications (OR 0.5, 95%CI). Indeed, the presence of a flare during pregnancy increased the risk of maternal complications (OR 2.0, 95%CI).

Pregnancies under BD were compared to healthy controls adjusted by age finding no differences in the perinatal delivery rate (p=0.05), in the induction rate of delivery (p=0.05) nor in the cesarean section rate (p=0.05).

Conclusion: In our series, the use of preconceptional BD and/or during pregnancy is not associated with an increase of maternal or fetal complications. However, fewer flares were observed. This may imply that BD can be a good tool for the treatment of women of childbearing age since control of the disease resulted in better maternal-fetal outcomes. However, more studies are needed to determine the usefulness and safety of these treatments during pregnancy.

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DISEASE ACTIVITY IS THE MAJOR DISCRIMINATOR WHEN DEFINING REFRACTORY RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is characterised by the presence of a progressively destructive joint inflammation. Even in times of modern therapeutics, a subgroup of patients continues to be refractory to numerous consecutive therapeutic interventions with regards to control of inflammation and joint damage. To date, there exists no definition for refractory RA.

Objectives: To explore different modifications of a definition for refractory RA.

Methods: Here we defined the base case of refractory RA as patients who had experienced ≥3 treatment courses (with at least one biological failure) over a minimum of 18 months since first treatment initiation (to avoid counting treatment courses that were given for a too short period), and the lack of reaching the treatment goal of low disease activity or remission (defined by a Clinical Disease Activity Index, CDAI, >10). We then modified our working definition based on these four variables (disease duration: 12/18/24 months; disease activity: moderate/high; number of treatment courses: ≥3;≥4; different biologic agents: ≥1/≥2).

Results: From our clinic’s ongoing longitudinal data set we identified 68 refractory patients out of 688 RA outpatients. There was virtually no difference based on modifying disease duration, so we kept our working definition of a minimum disease duration of at least 18 months (n=464; 12 months: n=466; 24 months: n=453). Changing the disease activity component of the definition had a great impact on the identified refractory RA population, by requiring high instead of moderate disease activity (MDA: CDAI >10, n=129 vs. HDA: CDAI >22, n=31). In both, the MDA and the HDA group of patients, we could observe ≥60% of patients, who already experienced at least three treatment courses (MDA, n=82/129; HDA, n=21/31). Above a half in each group qualified as refractory according to the criterion of an addition fourth failed treatment course (MDA, n=64/129; HDA, n=15/31). When further stratifying patients based on the number of failed different biologic DMARDs, we could observe that regardless of the level of disease activity and number of failed treatment courses, most patients experienced at least one or even a second biologic agent (table).

Conclusion: The level of disease activity is the major discriminator when defining a population of refractory RA. The duration of treatment does not significantly impact the identification of refractory RA. The number of failed treatment courses and insufficient responses to biologic DMARDs further helps characterizing patients with refractory RA. Considerations of the impact of these different characteristics of refractory disease may well inform future criteria for refractory RA.

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Disclosure of Interests: None declared

THE ROLE OF CLINICAL JOINT INFLAMMATION AND ACUTE PHASE RESPONSE ON STRUCTURAL PROGRESSION OF PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Psoriatic arthritis (PsA) belongs to the group of the spondyloarthropathies. It is associated with psoriasis and typically seronegative for autoantibodies. PsA disease activity can be measured using the Disease Activity in Psoriatic Arthritis (DAPSA) score which is based on both clinical (e.g., swollen joint count, SJC) and systemic (e.g., C-reactive protein, CRP) markers of inflammation. [1] However, the impact of clinical and systemic inflammation on structural progression is unclear.

Objectives: To determine the contribution of clinical and systemic inflammation on structural progression of patients with PsA.

Methods: In a secondary data analysis, we analyzed patient data from the IMPACT 2 trial of infliximab (INF) vs. placebo (PLC) in patients with established PsA (disease duration in years: INF: 7.5±7.8, PLC: 8.4±7.2). Concomitant methotrexate treatment was allowed but not mandatory in both treatment arms. [2] We obtained modified Sharp-van-der-Heyde scores from X-rays performed at baseline and after one year to compute radiographic progression. We further extracted levels of SJC and CRP and calculated time-averaged SJC (tsSJC) and CRP (tsCRP) values to reflect the clinical and systemic inflammation, respectively. In a multivariable logistic regression model, we assessed the impact of tsSJC, tsCRP, and their interaction, on structural progression. Next, we divided patients into different subgroups depending on their tsSJC and tsCRP levels into active (+) or inactive (-). We tested whether radiographic progression was different in tsSJC+ vs. tsSJC– and tsCRP+ vs. tsCRP– using the Mann-Whitney U test.

Results: 200 patients were enrolled in the IMPACT 2 trial (100 INF, 100 PLC). 151 patients were included in the analyses (76 PLC, 75 INF). Due to drop out or missing data, the remaining 49 patients were not considered for further analyses. Patients in the INF arm showed no radiographic progression (−1.16±3.96), while patients in the PLC arm showed little progression (0.74±2.98). We therefore focused on the 76 PLC and 75 INF patients. Despite the small overall progression, tsSJC, tsCRP, and their interaction were associated with radiographic progression (OR for tsSJC: 1.24, CI 95%: 1.04–1.47, p=0.016; OR for tsCRP: 6.08, CI 95%: 1.12–33.03, p=0.036; interaction term: p=0.097). Radiographic progression was higher in tsSJC+ patients compared to tsSJC– patients (1.05±2.31 and 0.56±2.30, respectively; p=0.16), as well as numerically higher without statistical significance in tsCRP+ vs. tsCRP– patients (1.14±3.23 and 0.05±2.37, respectively; p=0.532). Also, despite the limited power of subgroup analyses, there was evidence that SJC activity plays a role in CRP patients (p=0.076), whereas CRP activity seems to be of less importance in SJC– patients (p=0.643).

Conclusion: In patients with PsA, both clinical and systemic inflammation have impact on structural progression; in patients without systemic inflammation, clinical joint activity may still be considered as a risk factor for progression.

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Disclosure of Interests: Manuel Becede: None declared, Josef S. Smolen Grant/research support from: AbbVie, Eli Lilly, Janssen, MSD, Pfizer Inc, Roche, Consultant for: AbbVie, Amgen, AstraZeneca, Astro, Celgene, Celltrion, Eli Lilly, GlaxoSmithKline, ILTOO, Janssen, Medimmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Samsung, Sanofi, UCB, Daniel Aletaha Grant/research support from: AbbVie, Bristol-Myers Squibb, and MSD, Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medac, Merck, MSD, Pfizer Inc, Roche, and UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medac, Merck, MSD, Pfizer Inc, Roche, and UCB. DOI: 10.1136/annrheumdis-2019-eular.5746
Disclosure of Interests: Carina Borst: None declared, Fariedeh Alasti: None declared, Daniel Aletaha Grant/research support from: AbbVie, Bristol-Myers Squibb, and MSD, Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medac, Merck, MSD, Pfizer Inc, Roche, and UCB, Speaker Bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medac, Merck, MSD, Pfizer Inc, Roche, and UCB

References:


Disclosure of Interests: None declared
RESULTS:
At 18/01/2019, information on 80 098 drug prescriptions in 13 614 patients was collected in the TARDIS-RA registry. Of these 80 098 drug prescriptions, 30 434 (38.0%) were csDMARDs and glucocorticoids, and 49 664 (62.0%) were bDMARD or tsDMARD prescriptions. This last category consisted of 30 380 (61.2%) tumour necrosis factor inhibitor (TNFi) bDMARDs, 17 104 (34.5%) non-TNFi bDMARDs and 2 170 (4.3%) tsDMARDs. Only 642 (2.3%) TNFi biosimilar prescriptions were registered. Fig 1 shows the yearly evolution of bDMARD and tsDMARD prescription in Belgium from 2015 to 2018. At first registered interaction with the rheumatologist, the 13 614 patients had a median (IQR) age of 59 (50-68) years with a median (IQR) disease duration of 9 (4-16) years; 9 666 (73.4%) were female. The clinical characteristics showed a median (IQR) DAS28CRP of 3.6 (2.1-4.8) and a median (IQR) HAQ of 1.1 (0.6-1.8). Of patients at first time registration, 36.7% could be validated as being bionaive and 62.5% as bioexperienced.

Conclusion: Approximately 70 000 individuals in Belgium are estimated to have a RA diagnosis. Depending on numbers of other western European countries, 20%-25% of them would be expected to receive ts/bDMARDs. This suggests that almost the entire Belgian RA population on biologic treatment is covered by TARDIS. The registration of initiation, prolongation and discontinuation of every ts/bDMARD since 2015 combined with the simultaneous collection of demographic and clinical data, will make the TARDIS-RA registry a useful and powerful tool for the long-term drug analyses in Belgian patients with RA.

Disclosure of Interests: Diederik De Cock: None declared, Patrick Dunetz Speakers bureau: Bristol-Myers Squibb, Eli Lilly, Sanofi, Celtrion, Dirk Elewaart: None declared, Bernard Lauwerys: None declared, Rene Westhovens Grant/research support from: Bristol-Myers Squibb, Consultant for: Celtrion, Galapagos-Gilead, Patrick Verschueren Grant/research support from: Unrestricted Pfizer Grant for Early RA research.

REFERENCES:

Disclosure of Interests: David Eldeney: None declared, Moe Zandy: None declared, Oshrat Taye-Shiftman: None declared, Sherief Marzouk: None declared, Jiandong Su: None declared, Zahi Touma Grant/research support from: GSK Canada, Consultant for: UBC, Pfizer, Janssen, Inc

HOW DO GOUT-RELATED COMORBIDITIES AND LIFESTYLE FACTORS CLUSTER IN A LARGE HEALTH SURVEY OF THE GENERAL POPULATION? – RESULTS FROM THE MALMÖ PREVENTIVE PROJECT COHORT IN SOUTHERN SWEDEN

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Background: Several factors (comorbidities and lifestyle) have been shown to be associated or predict hyperuricemia or gout. Since these factors often are closely associated with each other, they may represent a few pathophysiological pathways rather than being individually important predictors. Identifying clusters of such factors may thus lead to a better understanding of the pathways involved in increased risk of gout. Two studies have previously indicated four to five phenotype clusters in prevalent cohorts of gout patients of European ancestry1,2. However, identification of clusters of gout-associated factors in the general population is lacking.

Objectives: To identify clusters of gout-related baseline comorbidities and lifestyle factors among participants in a population-based health survey.

Methods: The Malmö Preventive Project is a screening program for cardiovascular risk factors, alcohol abuse and breast cancer in Malmö, Sweden. Overall, 33,346 individuals (67% male, mean age 45.7 years at inclusion) participated. The study population was screened between 1974 and 1992. A subset of 22,057 individuals (screening period: 1975-1992) was eligible for the cluster analysis. Agglomerative hierarchical cluster analysis was performed to group similar variables and subgroup individuals with similar characteristics, using principal component and Ward’s minimum variance methods in Rv3.5.2, respectively. Variables selected to cluster were obesity (BMI>30 kg/m²), renal dysfunction (eGFR<60 mL/min/1.73m²), diabetes mellitus (DM), hypertension, prevalent cardiovascular disease (CVD), dyslipidemia (abnormal cholesterol or triglyceride values), pulmonary dysfunction (PD, FEV₁/FVC on spirometry<0.7), smoking and use of diuretics.

Results: Overall, 66% of the participants in the cluster analysis were males, mean age was 47 years and mean body mass index 24. Clustering of comorbidities and lifestyle factors indicated three pathways i.e. 1) mainly cardiovascular risk factors and disease, 2) variables associated with insulin resistance and 3) variables associated with PD (Fig A).

Fig Results of cluster analysis illustrating (A) variable and (B) observation clustering

Five different clusters (C1 to C5) were identified based on clustering of observations (Fig1; B), C1 (n=16,063), mean age=46 years, characterized low rate of hypertension (14%) and PD (15%); none had obesity, kidney dysfunction, DM, CVD or dyslipidemia. C2 (n=750; mean age 51 years) had the highest proportions with gout (7.1%) and kidney dysfunction (100%), with no record of DM, CVD or use of diuretics. C3 (n=528; mean age=48 years) had the highest rates of CVD (100%) PD (22%), smoking (74%) and alcohol risk behaviour (41%). C4 (n=3673; mean age=47 years) had the highest percentage of males (75%), the highest BMI (25.91) and the greatest proportions with obesity (34%) and dyslipidemia (74%), regular smoking (65%) and alcohol risk behaviour (36%). C5 (n=1043; mean age=48 years) had by far the highest occurrence of DM (51%), frequent use of diuretics (52%), hypertension (54%) and the highest percentage of abnormal liver enzyme values (16%).

Conclusion: Definition of clusters of comorbidities and lifestyle factors closely associated with gout, identified five separate “pathways” in this large health survey of the general population. “Pathways” relates to lifestyle, metabolism and specific comorbidity patterns. Further analyses will be performed to elucidate how these clusters predicted diagnosed gout in this population.

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SURVEY OF POTENTIAL TOXIC EXPOSURE IN PATIENTS WITH SYSTEMIC SCLEROSIS IN RESCLE REGISTRY. A PRELIMINARY STUDY

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Background: Systemic sclerosis (SSc) is a systemic autoimmune disease with extremely heterogeneous clinical features and unknown etiology, although numerous studies suggest a relationship with environmental and occupational factors. So far there is little information on whether toxic substances can play a relevant role in its phenotypic expression (1).

Objectives: To analyze in a cohort of patients with SSc the proportion of patients exposed to toxic and their correlation with epidemiologic, clinical and serological data.

Methods: A survey was conducted aimed at the knowledge of the working life of patients from six centers belonging to the Spanish Scleroderma Registry (RESCLE), categorizing them in six groups: no potential exposure to toxic substances, potential exposure to silica, to hydrocarbons, to organic solvents, to mixed toxics (silica and/or hydrocarbons and/or organic solvents) and to another toxics. In all patients 87 epidemiological, clinical and analytical variables included in the registry were analyzed, carrying out a comparative study between groups.

Results: 225 SSc patients were selected. Of these, 81 patients (36%) had worked in professions with potential risk of toxic exposure, 64 women out of the 227 included (28%) and 17 men out of the 28 included (60%). The toxic agent most frequently involved was silica in 28 patients (35.8%), followed by hydrocarbons in 21 (25.9%), mixture of toxic...
INCIDENCE OF GIANT CELL ARTERITIS IN 6 DISTRICTS OF PARIS, FRANCE (2015–2017)

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Background: Little is known about the current incidence of giant cell arteritis (GCA) in France.

Objectives: We conducted a prospective, population-based survey over 3 years to estimate the incidence of GCA in inhabitants of Paris, France.

Methods: From January 2015 to December 2017, new GCA diagnoses in 6 districts of northeastern Paris (257,888 inhabitants ≥ 50 years old) were prospectively identified by 1) biannual postal mails to 1,134 general practitioners and other specialists practicing in the study area; 2) quarterly e-mail surveys among 28 hospital departments located in or close to the study area; and 3) new records in the National Health Insurance System database with code M31 (other necrotizing vasculopathies) in the International Classification of Diseases, 10th revision. Clinical data of notified cases were retrieved from medical records. Retained cases lived in the study area at the time of diagnosis, fulfilled the 1990 American College of Rheumatology classification criteria and/or were ≥ 50 years old, with imaging or histology evidence of large-vessel inflammation and increased levels of inflammatory biomarkers. Clinical presentations with no cranial symptoms were classified as large-vessel GCA and otherwise as cranial GCA.

Annual incidence rates were calculated by dividing the number of incident cases by the size of the study population and the study period (in years); 95% confidence intervals (CIs) were calculated by using the Poisson distribution. Completeness of case ascertainment was assessed by a three-source capture-recapture analysis.

Results: Among 61 retained cases (69% females; mean age: 77 [SD: 9.0] years), 57 (93%) were cranial GCA and 4 (7%) large-vessel GCA. GCA diagnoses were supported by temporal artery biopsy findings, imaging of the aorta and its main branches, temporal artery ultrasonography and/or aortic tissue histology in 35 (57%), 18 (30%), 7 (11%), and 1 (2%) cases, respectively. GCA incidence rate (per 100,000 inhabitants/C21 years), 57 (93%) were cranial GCA and 4 (7%) large-vessel GCA. GCA diagnoses were supported by temporal artery biopsy findings, imaging of the aorta and its main branches, temporal artery ultrasonography and/or aortic tissue histology in 35 (57%), 18 (30%), 7 (11%), and 1 (2%) cases, respectively. GCA incidence rate (per 100,000 inhabitants ≥ 50 years old) was estimated at 7.9 cases (95% CI: 6.0–10.1). Completeness of case ascertainment was estimated at 66% (95% CI: 52–90%).

Conclusion: Our annual incidence estimate of GCA is close to the sole published estimate for another French population established 4 decades ago [1] and adds further support to the lower incidence of GCA in non-Scandinavian versus Scandinavian populations. Large-vessel GCA cases seem a rare form of GCA as compared with cranial GCA.

REFERENCES:

Disclosure of Interests: None declared
The association between joint erosions plus autoantibody positivity at initiation of methotrexate or biologic therapy for rheumatoid arthritis and disease activity and disability over one year

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Background: Joint erosions and autoantibody positivity (rheumatoid factor [RF], anti-cyclic citrullinated peptide antibody [anti-CCP]) predict poor outcomes in patients with rheumatoid arthritis (RA). There are limited data on the combination of these factors and clinical and patient reported outcomes over time.

Objectives: To compare the disease activity and disability over 1 year of those with poor prognostic factors at treatment initiation (methotrexate [MTX] or biologics) to those without.

Methods: Patients were recruited to 1 of 2 UK-based multi-centre prospective cohort studies: MTX-starters: Rheumatoid Arthritis Medication Study (RAMS); biologic-starters: Biologics in Rheumatoid Arthritis Genetics and Genomics Study Syndicate (BRAGGSS). Anti-CCP (Axis-Shield Anti-CCP test; U/ml; anti-CCP titre >5 U/ml = anti-CCP+) RF (Beckman Coulter AU4000, RF latex assay; U/ml; RF titre >14 U/ml = RF+) status were determined from baseline (BL) blood samples at the co-ordinating centre; erosions (yes/no) were recorded from medical notes. Missing data resulting from anti-CCP assay failure were imputed using multiple imputation. Patients who were anti-CCP+ and/or RF+ and had erosions were classified as having poor prognosis (PP); all other patients were classified as not having poor prognosis (NPP). Patients completed the Health Assessment Questionnaire (HAQ) and the Disease Activity Score (DAS28) was calculated at BL, 6 months and 12 months. The DAS28 and HAQ scores of the prognostic groups were compared at each assessment using linear regression, adjusted for age, gender and disease duration.

Results: In total, 1179 (PP = 182 [15.4%]) MTX-starters and 1152 (PP = 467 [40.5%]) biologic-starters were included (BL characteristics in Table). For MTX-starters, PP and NPP patients had similar DAS28, whereas for biologic-starters, PP patients had lower DAS28 compared to NPP patients after baseline (adjusted mean difference [95% CI]: MTX-starters BL = 0.1 [-0.1, 0.3]; 6 months = -0.1 [-0.2, 0.0]; 12 months = -0.1 [-0.4, 0.2]; biologic-starters BL = -0.1 [-0.2, 0.0]; 6 months = -0.2 [-0.4, 0.0]; 12 months = -0.4 [-0.6, 0.1]). HAQ scores were similar between PP and NPP patients in both cohorts (adjusted mean difference [95% CI]: MTX-starters BL = 0.08 [-0.04, 0.20]; 6 months = -0.02 [-0.11, 0.15]; 12 months = -0.03 [-0.17, 0.10]; biologic-starters BL = 0.00 [-0.09, 0.08]; 6 months = 0.00 [-0.12, 0.13]; 12 months = 0.01 [-0.14, 0.16]).

Conclusion: PP and NPP MTX-starters had similar outcomes. For biologic-starters, PP patients had lower disease activity after baseline; knowledge of these prognostic factors may have prompted more intensive assessment of PP patients after starting treatment. Patients in both cohorts (adjusted mean difference [95% CI]: MTX-starters BL = 0.1 [-0.1, 0.3]; 6 months = -0.1 [-0.2, 0.0]; 12 months = -0.1 [-0.4, 0.2]; biologic-starters BL = -0.1 [-0.2, 0.0]; 6 months = -0.2 [-0.4, 0.0]; 12 months = -0.4 [-0.6, 0.1]). HAQ scores were similar between PP and NPP patients in both cohorts (adjusted mean difference [95% CI]: MTX-starters BL = 0.08 [-0.04, 0.20]; 6 months = -0.02 [-0.11, 0.15]; 12 months = -0.03 [-0.17, 0.10]; biologic-starters BL = 0.00 [-0.09, 0.08]; 6 months = 0.00 [-0.12, 0.13]; 12 months = 0.01 [-0.14, 0.16]).

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Disclosure of Interests: Jørgen Guldberg-Møller Paid instructor for: Abbvie, Eli Lilly, BK Ultrasound., René Cordtz: None declared, Lars Erik Kristensen: None declared, Lene Dreyer Consultant for: Pfizer, Abbvie, Eli Lilly, BMS, Celgene, Novartis, Pfizer. Consultant for Abbvie, ABBvie, Amgen, Biogen, BMS, Celgene, Eli Lilly, Janssen Pharmaceuticals, and Novartis, Consultant for: Consultant for Abbvie, Amgen, Biogen, BMS, Celgene, Eli Lilly, Janssen Pharmaceuticals, MSD, Novartis, Pfizer, Roche, Sanofi, and UCB Pharma., Speakers bureau: Pfizer, AbbVie, Amgen, UCB, BMS, Biogen, MSD, Novartis, Eli Lilly and Company, and Janssen Pharmaceuticals, Lars Dreyer Consultant for: MSD, UCB and Janssen Pharmaceuticals, Speakers bureau: MSD, UCB and Janssen Pharmaceuticals, Speakers bureau: UCB, MSD, Eli Lilly and Janssen Pharmaceuticals.

rates according to treatment. Comparisons of survival rates between treat-ments were performed using log-rank tests. A p level of <0.05 was con-sidered significant. Statistical analyses were performed using SPSS 24.0

Results: A total of 109 patients (155 eyes; 79.8% female; mean age 53.9 ±12.5 (63 to 81) years) were included. The frequency of the associ-ation between PUK and an autoimmune systemic disease, was 86.3% (94). The leading etiology was RA (52.3%; n=57); VAA (30.3%; n=33), being GPA the foremost recognized in this group (84.8%; 28/33). Other were SLE, PSS, JIA, and ReA.

When PUK started, RA was already diagnosed in 87.7% (50/57); 18.2 (633) of AAV. Mean disease evolution in RA was 15 ± 8.2 years; AAV had 3.9 ± 5.6 years (p<0.05). 29% (n=17) of RA untreated; only 4 (12.2%) AAV were immunosuppressed by the time PUK settled.

Systemic autoimmune activity, was found in 31.5% (18/57) of RA and 90.9 (30/33) of AAV. Antrilagia was foremost referred by RA (94.4%;17/18); ear–nose–throat symptoms were in AAV (86.6%; 20/30). In the latter, some degree of renal dysfunction was found in 33.3% (10/30).

PUK characteristics in RA and AAV. Moderate (34.2%) and mild (383%) PUK were more frequently seen in RA; whereas moderate (36.3%) and severe (33.3%) in AAV (p<0.016). RA associated PUK commonly involved the inferior corneal quadrant (54.3%), as AAV the superior one (73.8%; p < 0.001). Corneal perforation was more frequent in RA than AAV (54.5% vs 22.7%; p=0.481); although the risk of perforation associated to RA didn’t show statistical significance [OR 1.14 [IC 95% 0.8 - 1.63]]. Necrot-izing scleritis was more commonly seen in AAV (RA n=1 vs AAV n=10). The more frequent initiated treatment in RA was oral prednisone combined with oral DMARDs (31.6%; 18/57). More aggressive therapy (MPS, CYC or Rituximab) was designated in 22.8% (n=13). On the other hand.

78.7% (26/33) of AAV were managed with the MPS-pred scheme merged with CYC (38.4%; n=12) or Methotrexate (42.4%; n=14).

Conclusion: RA and AAV are the more frequent autoimmune diseases that can manifest with PUK. In RA, the lack of arthritis could be mis-taken as quiescent, and wrongly undertreated, allowing it to progress to a vasculitic stage. It may impact their life quality if complicated with cor-neal perforation. In AAV the PUK can be the initial symptom of the dis-ease and is associated with a more severe ocular presentation. Routine ophthalmologic examinations might help the rheumatologist to assess RA and AAV activity and treatment.

REFERENCES:

Disclosure of Interests: None declared

FRID0676

PREVALENCE AND UVEITIS CHARACTERISTICS OF A COHORT OF PATIENTS WITH SPONDILIOARTROPATHY

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Background: Uveitis can be a clinical manifestation of different systemic processes, known is the association of anterior uveits with patients with spondiloarthritis (SpA)

Objectives: To describe the prevalence, characteristics and course of ocular inflammatory pathology from a cohort of patients with SpA

Methods: Retrospective descriptive study made in a cohort of 451 SpA patients according to the ASAS classification criteria in a tertiary university hospital from Barcelona. Were selected patients who presented or had presented uveitis (defined according to the SUN1 classification crite-ria) Demographic, clinical, radiological and serological data of the joint disease and characteristics of the ocular affection were collected, as well as the treatment of both

Results: Of the 451 patients reviewed. 43 (9.53%) patients with a history of uveitis were included in the study. From the cohort, the average age at diagnosis of SpA was 37 (± 27) years and 38 (88.4%) had positive HLAB27. The most prevalent subtypes of SpA were Ankylosing Spondylitis (AS): 27 (60.8%) and Psoriatic Arthritis (APSO): 8 (18.6%). The char-ac teristics of the sample are summarized in Table 1.

The average age at the first uveitis outbreak was 45 ± 23 years. The anterior location was more prevalent (n: 39, 90.7%), unilateral (n: 35, 81.4%) and acute onset (n: 42, 97.6%)

Two of patients with anterior uveitis had other associated complications, one had macular edema and other retinal vasculitis. The treatment of uveitis was topical corticosteroids in 39 (90.6%) patients, 2 (4.6%) treatment with oral sulfasalazine. Despite the treatment, 22 (51.2%) patients presented a recurrent course. Table 2 shows the ocular clinical features

Table 1. Clinical characteristics of SpA cohort.

<table>
<thead>
<tr>
<th>PreRx</th>
<th>APSo</th>
<th>EII</th>
<th>HLAB27</th>
<th>Treatment SpA</th>
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Table 2. Clinical characteristics of uveits from SUN criteria.

<table>
<thead>
<tr>
<th>Uveits</th>
<th>Type</th>
<th>Anterior</th>
<th>Intermedia</th>
<th>Posterior</th>
<th>Panuveitis</th>
<th>Unilateral</th>
<th>Bilateral</th>
<th>Sudden</th>
<th>Insidious</th>
<th>Duration</th>
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Age 1° outbreak, years ± DE

45 ± 23

Type

39 (90.7)

Anterior

2 (4.6)

Intermedia

0

Posterior

2 (4.6)

Panuveitis

42 (97.6)

Unilateral

35 (81.4)

Bilateral

8 (18.6)

Sudden

1 (2.3)

Insidious

38 (88.3)

Duration

5 (11.6)

Leukocytosis

13 (30.2)

Persistent (>3 meses) n (%) 22(51.2)

Course

8 (18.6)

Acute " n (%) Recurrent " n (%) 22(51.2)

Chronic " n (%) Treatment Uveitis

39 (90.6)

Corticosteroids topics, n (%) 0

FAME (sulfasalazine), n (%) 2 (4.6)

Conclusion: In our cohort of SpA, prevalence of uveitis was 10%, predomi-nantly in HLA B27 patients and axial involvement, of which 62.8% met criteria for AD and 18.6% APSO with different degrees of axial involvement, including under systemic treatment (FAMEs/Biological). The most prevalent presentation was anterior, unilateral, acute and recurrent uveitis. Being the most used treatment topical corticosteroids.

REFERENCES:

Disclosure of Interests: Sycille Jeria: None declared, Patricia Moya: None declared, Ana Laiz Consultant for: Lilly, Novartis, AbbVie, MSD, UCBC and Janssen, Speakers bureau: Lilly, Novartis, Abbovie, MSD, UCBC and Janssen, Jose Vela: None declared, Jesus Diaz: None declared, Hye- Sang Park: None declared, Berta Magallares: None declared, Ivan Casteliv Consultant for: I received fees less than 5000USD as a consultant for Kern and Actelion, Paid instructor for: I received fees less than 5000USD as a consultant for Kern and Actelion,
IMPACT OF COMORBIDITY ON THE USE OF BIOLOGICAL AND TARGETED THERAPY IN RHEUMATIC DISEASES IN THE CLINICAL PRACTICE

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Background: Comorbid conditions often accompany rheumatic diseases and can influence the prescription of immunosuppressive therapy. Comorbidity seems to be a factor that is still underestimated in actual practice.

Objectives: To study the influence of comorbidity on the prescription of biological and targeted therapies in patients with rheumatic diseases (RD) in clinical practice.

Methods: We perform a retrospective analysis of comorbidity and prescription of biological and targeted immunosuppressors in a group of inpatients with systemic autoimmune RD in rheumatology department. From January 2018 to January 2019, 218 patients with inflammatory RD hospitalized - 146 (67.5%) women, mean age 50.6±14.6 years. Diagnoses: rheumatoid arthritis - 83 patients, spondyloarthritides - 80, systemic lupus erythematosus - 19, systemic scleroderma - 16, ANCA-associated vasculitides - 10, other conditions - 10 patients. Biologics were used in 117 (53.7%) of patients (anti-TNFs – 64 patients, rituximab – 18, tocilizumab – 16, abatacept – 8, secukinumab – 4, uestekinumab – 4, tofacitinib – 3 patients). We examined patients for comorbidities through careful examination of the history, medical records, and general therapeutic laboratory and instrumental screening. The Charlson comorbidity index calculated for every patient.

Results: 174 (79.8%) patients had at least 1 comorbid condition. The most frequent comorbidities were type 2 diabetes (19.5% patients), chronic kidney disease (12.6%), cerebrovascular accident (11.5%), ischaemic heart disease and chronic heart failure (11%), chronic liver disease (7.5%). Mean Charlson index was 2.1±2.05 in total group; it was significantly lower in patients who were treated with biological and targeted therapy (1.84±1.8) than in patients who did not received this therapy (2.76±2.1), p=0.01. Biologics were prescribed in 81.8% of patients without comorbidities, in comparison with 55.3% of patients with Charlson comorbidity index 1 or 2, and 36.3% of patients with Charlson index 3 or more.

Conclusion: Comorbidity has a direct impact on the use of biological and targeted therapy in patients with rheumatic diseases in real clinical practice, limiting the ability to control the activity of the disease. It is necessary to develop a general therapeutic strategy for treating comorbid conditions in patients with rheumatic diseases.

REFERENCES:

Disclosure of Interests: Dmitry Karateev Speakers bureau: Pfizer, Novartis, Janssen, Abbvie, Biocad, MSD, BMS, Hava Hamhoeva: None declared, Helen Luchihina Speakers bureau: Pfizer, Abbvie, Biocad, Aminat Tangieva: None declared

PREVALENCE, PATIENT CHARACTERISTICS, AND TREATMENT OF GOUT AND ASYMPTOMATIC HYPERURICEMIA IN JAPAN: CROSS-SECTIONAL STUDY OF A HEALTH INSURANCE CLAIMS DATABASE

Ruriko Koto1, Akhiro Nakajima2, Hideki Horuchi2, Hisashi Yamanaka3, 1Teijin Pharma Limited, Medical Science Department, Tokyo, Japan; 2Teijin Pharma Limited, Pharmaceutical Development Administration Department, Tokyo, Japan; 3Tokyo Women’s Medical University, Institute of Rheumatology, Tokyo, Japan

Background: The prevalence of gout is increasing worldwide [1,2], but evidence suggests that current treatment practices do not effectively reduce serum uric acid (sUA) levels in many gout patients [3]. In Japan, urate lowering therapy (ULT) is provided to patients diagnosed with asymptomatic hyperuricemia as well as to those with gout. However, the actual treatment situation for asymptomatic hyperuricemia has not been well-documented.

Objectives: To assess the prevalence and characteristics of gout and asymptomatic hyperuricemia and the current treatment practices for these conditions in Japan.

Methods: This retrospective cross-sectional study assessed disease prevalence, patient characteristics, prescriptions, proportion of patients achieving target sUA, and incidence of gouty arthritis among 2,531,383 individuals in a database, using data from Japanese health insurance claims and medical check-ups from April 2016 to March 2017.

Results: Gout was diagnosed in 1.1% (men 1.9%, women <0.1%) of the study population and asymptomatic hyperuricemia in 2.6% (men 4.1%, women 0.4%). Hyperuricemia (sUA >7.0 mg/dL) was identified in 13.4% (men 19.6%, women 1.0%) of cases in which sUA level was measured at check-up. ULT adherence was satisfactory (median medication possession ratio [MPR] of 69.0% for febuxostat and 78.1% for allopurinol in gout, and 79.5% and 88.5%, respectively, in asymptomatic hyperuricemia), but most patients were receiving low-dose ULT. The sUA target (≤6.0 mg/dL) was achieved by less than half of patients treated with either febuxostat or allopurinol (Table). In gout patients, the incidence proportion of gouty arthritis was 47.8% and the incidence rate was 0.74 flares/person-year.

Conclusion: The prevalence of gout in our study population was low. Japanese physicians often treat gout and asymptomatic hyperuricemia with low-dose ULT, and many patients fail to reach their target sUA, suggesting gout management is suboptimal in Japan.

REFERENCES:

Table

<table>
<thead>
<tr>
<th>sUA target (mg/dL)</th>
<th>Febuxostat</th>
<th>Allopurinol</th>
<th>Febuxostat</th>
<th>Allopurinol</th>
</tr>
</thead>
<tbody>
<tr>
<td>(≤6.0 mg/dL)</td>
<td>8215</td>
<td>6521</td>
<td>16312</td>
<td>14220</td>
</tr>
<tr>
<td>Mean prescribed dose</td>
<td>18.9 mg</td>
<td>145.6 mg</td>
<td>16.5 mg</td>
<td>131.3 mg</td>
</tr>
<tr>
<td>Median MPR</td>
<td>69.0%</td>
<td>78.1%</td>
<td>79.5%</td>
<td>88.5%</td>
</tr>
<tr>
<td>Proportion of patients achieving target sUA (%)</td>
<td>44.7%</td>
<td>33.8%</td>
<td>47.8%</td>
<td>35.9%</td>
</tr>
</tbody>
</table>

biological therapies has not been investigated in detail, and little is known about the predictive value of sociodemographic and lifestyle factors.

Objectives: To investigate the predictive value of a panel of potential predictors of death in a cohort of patients with RA followed for up to 12 years during the era of biological treatments.

Methods: Outpatients with RA were recruited consecutively between July 2006 and July 2007 and followed in routine care with prospective registrations in the DANBIO registry until death or August 20th, 2018, whichever occurred first. Baseline variables considered to be potential predictors were: disease activity, disease duration, IgM-rheumatoid factor (IgM-RF), radiographic status (erosive disease yes/no) and medical therapy as well as patient-reported marital status, educational level, comorbidity conditions, smoking, exercise, body mass index (BMI) and health assessment questionnaire (HAQ). Vital status and date of death were extracted from the Danish National Register. A Cox proportional hazards model was used to estimate the hazard ratio for death for each of the potential predictors.

Table: Age-adjusted Cox proportional hazards model with death as outcome.

Results: 3693 patients were recruited at baseline, 75% women, 77% IgM-rheumatoid factor positive, 65% with erosive disease, median (IQR) age 62 years (52-71), disease duration 7 years (3-15), DAS28 3.0 (2.2-3.9), HAQ 0.63 (0.25-1.25). 20% received a biological disease modifying anti-rheumatic drug (DMARD), 71% received a synthetic DMARD and 9% received no DMARD. The median (IQR) duration of follow-up was 11 years (9-11); 1041 patients (28%) died during follow-up. 640 patients received no DMARD. The median (IQR) duration of follow-up was 11 years (9-11); 1041 patients (28%) died during follow-up. 640 patients received no DMARD. The median (IQR) duration of follow-up was 11 years (9-11).

Conclusions: In a large cohort of RA patients followed for a decade in the era of biological treatments, we identified strong clinical (high HAQ, comorbidity), treatment related (glucocorticoid last month), sociodemographic and lifestyle related (male sex, living alone, smoking, physical inactivity, low BMI) risk factors for death. In the effort to prevent a poor long term outcome in patients with RA, this study provides new insight into potentially modifiable baseline variables.

REFERENCES:


3. Central Statistics Office Ireland
Background: Body composition, physical activity and physical performance with knee cartilage thickness and subchondral bone area in young adults were unknown.

Objectives: To describe associations of body composition, physical activity and physical performance with knee cartilage thickness and subchondral bone area in young adults.

Methods: Body composition, physical activity and physical performance were measured 4-5 years prior to knee magnetic resonance imaging (MRI). Cartilage thickness and subchondral bone area of patella and lateral/medial femoral compartment were measured quantitatively from MRI. Total knee cartilage thickness was calculated as the weighted-average according to bone area of each compartment; total knee bone area was calculated as the sum of each compartment. Associations were assessed using linear regression analysis. Age, gender, height (if fat mass or lean mass was predictor) and BMI (if physical activity or physical performance measures were predictors) were examined as potential confounders and were included in the regressions. Mediator was identified using mediation analysis (Stata’s medeff command).

Results: Participants were aged 31-40 years, 48% were female (n = 186). Greater lean mass, but not fat mass, was positively associated with total knee cartilage thickness (β = 0.50 μm/kg, 95% confidence interval (CI): 0.86 to 12.13) and subchondral bone area (β = 13.66 mm²/kg, 95% CI: 5.73 to 21.59). Physical performance measures were positively associated with knee cartilage thickness (long jump: β = 2.36 μm/cm, 95% CI 0.68 to 4.04; hand grip strength: 7.65 mmHg, 1.53 to 13.77; physical work capacity: 1.04 μWatt, 0.27 to 1.81) and subchondral bone area (long jump: β = 4.25 mm²/cm, 95% CI 1.01 to 7.50; hand grip strength: 19.89 mmHg/cm, 8.23 to 31.55; leg strength: 3.32 mmHg/cm, 1.25 to 5.40; physical work capacity: 3.00 μWatt, 1.54 to 4.45). Mediation analysis suggested these associations were mediated by lean mass (effect mediated: 29-95%). Questionnaire based activity measures (including walking, moderate activity, vigorous activity and total activity) were not associated with total knee cartilage thickness or subchondral bone area.

Conclusion: Greater lean mass and better physical performance measures were associated with greater knee cartilage thickness and subchondral bone area in young adults, and the associations of physical performance were largely mediated by lean mass. These findings suggest lean mass may play an important role in maintaining knee joint health in young adults.
DEFINING THE GUT MICROBIOME IN PATIENTS WITH ANCA-ASSOCIATED VASCULITIS

catherine najem1,2, Jung-Jin Lee2, Ceylan Tanes2, Antoine Sreih2, Rennie Rhee2, Abdallah Gearsa2, LI Hongzhe2, Kyle Bittinger2, James Lewis2, Peter Merkel2, 1Temple University Hospital, Rheumatology, Philadelphia, United States of America; 2University of Pennsylvania, Philadelphia, United States of America

**Background:** Although a link between gut microbiome and autoimmune diseases has been suggested, there is a gap in the understanding of the gut microbiome in ANCA-associated vasculitis (AAV).

**Objectives:** This study evaluated the gut microbiome in AAV (granulomatosis with polyangiitis (GPA), microscopic polyangiitis, and eosinophilic granulomatosis with polyangiitis) compared to healthy controls.

**Methods:** Using cross-sectional and longitudinal designs, the gut microbiome was compared among patients with i) newly-diagnosed AAV (active and remission); ii) chronic AAV (active and remission), and iii) healthy controls. Fecal samples were collected using standardized methods and sequenced the bacterial 16S rRNA gene (V1-V2 region). Disease severity was analyzed by sequencing the bacterial 16S rRNA gene (V1-V2 region).

**Results:** 63 fecal samples were studied: 29 active AAV (15 new diagnosis/14 chronic), 20 in remission, and 14 healthy controls. Compared to healthy controls, patients with active AAV had a different microbial composition (p<0.01) (Figure 1A). The relative abundance of the taxa Dialister and Prevotella were different between active and remission AAV. The relative abundance of the genera Faecalibacterium and Sutterella were different between active and remission AAV. Taxa with mean abundance >1% were compared using Wilcoxon rank sum test, correcting for multiple comparisons. Disease severity was assessed with the Birmingham Vasculitis Activity Score for Wegener’s Granulomatosis (BVAS/WG). Effects of medications were studied using mixed effects models.

**Conclusion:** Active AAV is associated with an altered gut microbial composition. Patients in clinical remission have microbial composition similar to healthy controls. Immunosuppressive agents, glucocorticoids, and antibiotics use. Immunosuppressive agents was similar to controls (p=0.54), whereas the gut microbiome of patients with GPA on immunosuppressive agents was similar to controls (p=0.04), whereas the gut microbiome of patients with GPA not on these therapies was significantly different from controls; similar results were found with glucocorticoids and antibiotics use.

**Disclosure of Interests:** None declared


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NOVEL MAPPING FUNCTION ILLUSTRATES NONLINEARITY BETWEEN TRIAL ACR RESPONSE, DAS28 CHANGE AND EULAR RESPONSE CRITERIA

Nuria Navarro Coy1, Kimme Hyrich2, Sue Pavill2, Robert West4, Maya Buch1,5, 1Leeds Institute of Rheumatic and Musculoskeletal Medicine (LIRMM), Leeds, United Kingdom; 2Institute of Inflammation and Repair, Manchester, United Kingdom; 3School of Dentistry, Leeds, United Kingdom; 4Leeds Institute of Health Sciences, Leeds, United Kingdom; 5NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals Trust, Leeds, United Kingdom

**Background:** The American College of Rheumatology (ACR) definition of improvement is a standardised, widely used outcome measure for clinical trials in rheumatoid arthritis. In routine clinical practice (and registries),
improvement is assessed by the DAS28 (Disease Activity Score 28), particularly in the UK, where it is the basis of current NICE guidance.

**Objectives:** To develop a mapping function that charts ACR20/50/70 and ACRn to ∆DAS28 and EULAR response, and determine the relationship between response measures.

**Methods:** Individual patient-level data from the 428 participants randomized to the ATTRACT trial were used. The proportion of participants with ACRn (ACR10-ACR90) response and the change in DAS28 (∆DAS28) at 30 weeks from baseline were calculated and analysed in participants with complete data. The cut points in ∆DAS28 that provided the equivalent proportion of participants achieving ACR10 to ACR90 at 30 weeks overall and per individual arm were searched for through tabulation. Regression models were conducted and misclassification rates calculated to test the accuracy of the mapping function. The minimum and maximum ACRn achieved per EULAR response category were also determined to establish the correlation of these two response criteria. A version 3.4.3 (2017-11-30) was used for all statistical analyses.

**Results:** 53%/27%/12% of all trial participants achieved ACR-ESR 20/50/70 responses, respectively. The mapping function shows that at 30 weeks a 20% improvement in ACR is equivalent to a lower improvement in the DAS28, at 55.8% for ESR and 59.3% for CRP. Similar results were obtained when analysing the individual arms (Table 1 & Figure 1). Baseline DAS28 for all analysed groups was > 6.0. Moderate or good EULAR responses correspond to 80% and 90% improvement in ACR, respectively, whereas the no response EULAR category showed a maximum improvement in ACR-ESR/CRP of 30%-50%, respectively (Figure 2).

**Conclusion:** This novel mapping function enables the comparison of trials through tabulation. Regression models were conducted and misclassification rates calculated to test the accuracy of the mapping function. The minimum and maximum ACRn achieved per EULAR response category were also determined to establish the correlation of these two response criteria. A version 3.4.3 (2017-11-30) was used for all statistical analyses.

**Disclosure of Interests:** Nina Navarro Coy: None declared, Kimnne Hyrich Grant/research support from: Grants to institution: BMS, Pfizer, UCB, Sue Pavitt: None declared, Robert West: None declared, Maya Buch Grant/ research support from: Pfizer LTD, UCB, Consultant for: Abb Vie, Eli Lilly.

**DOI:** 10.1136/annrheumdis-2019-eular.4642

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**REFERENCES:**


**Table 1** Mapping between the ACR criteria and change in DAS28

<table>
<thead>
<tr>
<th>ACR-ESR criteria</th>
<th>IFX arm* (n=86)</th>
<th>Placebo arm (n=88)</th>
<th>Full cohort (n=428)</th>
</tr>
</thead>
<tbody>
<tr>
<td>20% improvement</td>
<td>(Accuracy (%))</td>
<td>(Accuracy (%))</td>
<td>(Accuracy (%))</td>
</tr>
<tr>
<td>27.3 (80)</td>
<td>24 (85)</td>
<td>29.5 (81)</td>
<td></td>
</tr>
<tr>
<td>50% improvement</td>
<td>45 (85)</td>
<td>39 (94)</td>
<td>44 (84)</td>
</tr>
<tr>
<td>70% improvement</td>
<td>55.8 (91)</td>
<td>44 (91)</td>
<td>57.9 (86)</td>
</tr>
<tr>
<td>ACR-CRP criteria</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20% improvement</td>
<td>(Accuracy (%))</td>
<td>(Accuracy (%))</td>
<td>(Accuracy (%))</td>
</tr>
<tr>
<td>27.8 (83)</td>
<td>27 (90)</td>
<td>30 (82)</td>
<td></td>
</tr>
<tr>
<td>50% improvement</td>
<td>46.2 (84)</td>
<td>44 (92)</td>
<td>47.5 (84)</td>
</tr>
<tr>
<td>70% improvement</td>
<td>59.3 (93)</td>
<td>50.8 (92)</td>
<td>50.8 (84)</td>
</tr>
</tbody>
</table>

**Figure 1** Mapping between ACRn (ACR10-ACR90) and DAS28 improvement at 30 weeks.

**Figure 2** Correlation of the EULAR and ACR response criteria at 30 weeks.

**Disclosure of Interests:** Nina Navarro Coy: None declared, Kimnne Hyrich Grant/research support from: Grants to institution: BMS, Pfizer, UCB, Sue Pavitt: None declared, Robert West: None declared, Maya Buch Grant/ research support from: Pfizer LTD, UCB, Consultant for: Abb Vie, Eli Lilly.

**DOI:** 10.1136/annrheumdis-2019-eular.4642

**REFERENCES:**

RELATIONSHIP BETWEEN VITAMIN D NEUROMYELITIS SPECTRUM DISORDERS

Muir 2011
RCT Medicine, Almería, Spain
Monica Solana-Tramunt4, M Guerra-Balic4. Maria Betina Nishishinya1, 6 to 12 months. ranged from 121 to 5615. Patients mean age oscillated between 58-88 years improves muscle mass, strength and performance in older patients.

Background: Sarcopenia is the loss of skeletal muscle mass, strength and function that occurs as a consequence of aging. This condition result in physical disability, which limits the capacity to walk, increases the risk of falls and osteoporotic fractures. Several studies suggested an inverse relation between 25OHD serum levels, muscular strength and physical performance in the eldest.

Objectives: To evaluate if vitamin D supplementation in patients > 50 years improves muscle mass, strength and performance in older patients.

Methods: We performed a systematic review through Medline, Cochrane Library, and EMBASE. Inclusion criteria: 1) patients > 50 years old, 2) objective measurements 4) systematic reviews (SR) 5) randomized clinical trials (RCT) 6) Papers written in English or Spanish.

Results: Five studies were included (4 SR and 1 RCT), n patients ranged from 121 to 5615. Patients mean age oscillated between 58-88 years. receiving variable vitamin D dose. Follow-up period fluctuated from 6 to 12 months.

Conclusion: Vitamin D supplementation in patients > 65 years with inadequate 25OHD serum levels, improve muscular strength.

REFERENCES:

Disclosure of Interests: None declared

FRIO686

RELATIONSHIP BETWEEN VITAMIN D SUPPLEMENTATION AND MUSCULAR STRENGTH IN ELDERLY POPULATION. A SYSTEMATIC REVIEW

Maria Belina Nishishinya1, Claudia Alejandra Pereda Testa2, Adela Cristina Cis5, Monica Solana-Tramunt1, M Guerra-Balic4. 3Hospital HLA Mediterraneo, Almería, Spain; 4Hospital HLA Mediterraneo, Almería, Spain; 5Hospital HLA Mediterraneo, Almería, Spain; 6Instituto Traumatológico Quirón, Barcelona, Spain; 7Hospital HLA Mediterraneo, Almería, Spain; 8Hospital HLA Mediterraneo, Almería, Spain; 9Ramón Llull University.

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REFERENCES:

Disclosure of Interests: None declared
**FR0688**

**PREICTORS OF EROSION AND JOINT SPACE NARROWING PROGRESSION IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS**

*Emil Rydel*1,2, Kristina Forslind*1,4, Jan-Åke Nilsson*1,2, Lennart T.H. Jacobsson*1,3, Carl Turesson*1,2, *Rheumatology, Department of Clinical Sciences, Malmö, Lund University, Malmö, Sweden; 2Department of Rheumatology, Skåne University Hospital, Malmö, Sweden; 3Rheumatology, Department of Clinical Sciences, Helsingborg, Lund University, Helsingborg, Sweden; 4Research and Education, Helsingborg Hospital, Helsingborg, Sweden; *Rheumatology and Inflammation Research, Sahlgrenska Academy at Gothenburg University, Göteborg, Sweden

**Background:** Joint damage in rheumatoid arthritis (RA) includes erosions and joint space narrowing (JSN). Predictors of these processes, and the underlying mechanisms, require further study.

**Objectives:** To investigate the relation between patient characteristics at RA diagnosis and progression of erosions and JSN, over 5 years.

**Methods:** Consecutive early RA patients (symptom duration <12 months), recruited 1995-2005 from a defined area, managed according to usual care with no pre-specified treatment protocol, were followed through 5 years. Radiographs of hands and feet were scored in chronological order by a trained reader according to the modified Sharp-van der Heijde score (SHS), including separate erosion- and JSN scores. The relations between baseline variables and progression of erosion- and JSN scores over 5 years (log transformed), were assessed using linear regression.

**Results:** 233 early RA patients where included. Radiographs at baseline and 5 years were available for 162 patients. Results on predictors of rapid radiographic progression of the total SHS have been reported previously2. The median (interquartile) progression of erosion and JSN scores were 4 (0-8) and 8 (1-16), respectively. RF and anti-CCP predicted progression of erosions and JSN over 5 years, with stronger associations for erosions (Table 1). Baseline erosion- and JSN scores each predicted progression of JSN, while baseline JSN did not predict progression of erosions. In crude analyses, higher disease activity, CRP and ESR were associated with disease activity and GH.

**Table 1. Baseline predictors of progression of erosion and JSN scores (log transformed) from baseline to 5 years in linear regression**

<table>
<thead>
<tr>
<th>Baseline characteristics</th>
<th>Erosion score</th>
<th>JSN score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Crude</td>
<td>Adjusted for</td>
</tr>
<tr>
<td></td>
<td>B p</td>
<td>B p</td>
</tr>
<tr>
<td>Age (per SD)</td>
<td>0.02 0.39</td>
<td>0.02 0.45</td>
</tr>
<tr>
<td>Overweight or obese vs. normal BMI†</td>
<td>-0.05 0.34</td>
<td>-0.03 0.62</td>
</tr>
<tr>
<td>Ever vs. never smokers</td>
<td>0.04 0.12</td>
<td>0.04 0.12</td>
</tr>
<tr>
<td>RF positivity</td>
<td>0.03 0.004</td>
<td>0.03 0.004</td>
</tr>
<tr>
<td>Anti CCP positivity</td>
<td>0.02 0.003</td>
<td>0.02 0.003</td>
</tr>
<tr>
<td>COMP &gt;12 U/L</td>
<td>0.01 0.12</td>
<td>0.01 0.12</td>
</tr>
<tr>
<td>Erosion score (per SD)</td>
<td>0.04 0.12</td>
<td>0.04 0.12</td>
</tr>
<tr>
<td>JSN score (per SD)</td>
<td>0.04 0.12</td>
<td>0.04 0.12</td>
</tr>
<tr>
<td>High vs. moderate ESR</td>
<td>0.12 0.09</td>
<td>0.12 0.09</td>
</tr>
<tr>
<td>ESR (per SD)</td>
<td>0.01 0.001</td>
<td>0.01 0.001</td>
</tr>
<tr>
<td>CRP &gt;9 mg/l (median)</td>
<td>0.06 0.01</td>
<td>0.06 0.01</td>
</tr>
</tbody>
</table>

**NA, not applicable; vs, versus; †** Overweight or obese >25 kg/m2; normal 18.5 – 24.99 kg/m2.

Conclusion: RF, anti-CCP and markers of inflammation and disease activity predicted progression of erosions and JSN, in particular erosions. Development of erosions may predate cartilage damage leading to JSN. Smoking and high baseline levels of COMP predicted progression of erosions, but not JSN. Overweight and obesity may be associated with mechanisms that protect from JSN.

**REFERENCES:**


**FR0689**

**EFFECT OF AIR POLLUTION EXPOSURE ON DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS**

Tommaso Schioppo1, Isabella Scotti1, Simonia Iodicic1, Mirjam Hoxta1, Orazio De Lucia1, Antonella Murgio1, Valentina Bollati1, Francesca Ingegnoli1, 2, 3, 4, *LAMST Pini-CITO*, Division of Clinical Rheumatology, Milano, Italy; 5University of Milan, Department of Clinical Sciences and Community Health, Milano, Italy

**Background:** Environmental exposure (e.g. tobacco smoking, pollution) has been accepted to contribute in autoimmune diseases. Air pollution has been described to be a risk factor for developing rheumatoid arthritis (RA). Currently, RA disease remission is considered an achievable target in a significant proportion of patients. Nevertheless, diseases flares, that significantly contributes to damage progression and disability, remains unpredictable. Thus, factors able to potentially interfere on disease activity should be considered and assessed.

**Objectives:** The aim of our study is to evaluate the influence of particulate matter (PM) on disease activity and general health (GH) in patients with RA.

**Methods:** Consecutive patients with RA (ACR/EULAR Criteria 2010) resident in Lombardy (Italy) were enrolled. In each patient Disease Activity Score on 28 joints (DAS28), Simple Disease Activity Index (SDAI) and patients’ GH were assessed. Daily PM concentrations, estimated by Regional Environmental Protection Agency at municipality resolution, were used to assign short-term exposure from day of visit back to 14 days. Continuous variables are expressed as mean±SD. Categorical variables are presented as absolute numbers and frequencies. Multivariable linear regression models were performed to identify the day of PM10 and PM2.5 independently associated with DAS28, GH and SDAI indices, adjusting for the variables significant at the univariate analysis. GH was log transformed to achieve normality of residuals. β coefficients were reported for 10 μg/m3 increments of PM concentrations. All statistical analyses were performed using SAS 9.4.

**Results:** 258 patients (age at visit 57.4±13.5 years, disease duration 16.2±12.1, female 80.2%, rheumatoid factor and/anti-citrullinated peptide antibodies positivity 60.5%, smokers 15.5%, radiographic damage 41.5%) were enrolled in the study. Multivariable linear regression models were adjusted for radiographic damage, disease duration and age. Increases of PM2.5 and PM10 exposure (9 day before the visit) were significantly associated with worsening of DAS28, SDAI and GH (table below). PM concentrations in days other than 9 days before were significantly associated with disease activity and GH.

<table>
<thead>
<tr>
<th>PM Exposure</th>
<th>β ± SE</th>
<th>95% CI</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PM10 Day 9</td>
<td>0.02</td>
<td>0.05</td>
<td>0.17</td>
</tr>
<tr>
<td>PM10 Day 9</td>
<td>0.11</td>
<td>0.06</td>
<td>0.23</td>
</tr>
<tr>
<td>SDAI</td>
<td>0.09</td>
<td>0.02</td>
<td>0.15</td>
</tr>
<tr>
<td>PM10 Day 9</td>
<td>0.96</td>
<td>0.24</td>
<td>0.00</td>
</tr>
<tr>
<td>GH PM10 Day 9</td>
<td>0.11</td>
<td>0.04</td>
<td>0.03</td>
</tr>
<tr>
<td>PM10 Day 9</td>
<td>0.14</td>
<td>0.05</td>
<td>0.06</td>
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</tbody>
</table>

Conclusion: In our cohort, PM10 and PM2.5 exposure seems to influence RA disease activity with a lag period that can last until 9 days before the visit. Nevertheless, the association between day-to-day PM changes and disease activity do not confirm causation. Further studied are required to evaluate the influence of air pollution on RA activity.

WOMEN WITH RHEUMATOID ARTHRITIS HAVE HIGHER LIFETIME PROFESSIONAL AND NON-PROFESSIONAL EXPOSURE TO SILICA DUST COMPARED TO FRENCH GENERAL POPULATION

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Background: Occupational exposure to silica dust is associated with increased risk of developing ACPA positive Rheumatoid arthritis (RA). Little is known about non-occupational exposure, as there are no available tools to assess it in clinical practice.

The Dust Exposure Life-Course Questionnaire (DELCQ), developed within the SILICOSIS project, a European Research Council Advanced Grant, provides clinical research with a tool derived from social sciences. The DELCQ allows to quantify both occupational and non-occupational (e.g. body care; hobbies such as DIY, woodworking, stone cutting, etc.) exposure to silica and some other inorganic particles during the whole lifetime.

In the DELCQ, the identification of sources of exposure is grounded on an extensive list of products and activities summed up by the International Agency on Research on Cancer and on a wide overview of the literature addressing silica exposure and silica-related (or suspected-to-be-related) diseases.

Objectives: To explore occupational and non-occupational silica exposure in a series of consecutive RA patients and the association of quantified silica dust exposure with major disease features (ACPA positivity) or outcomes (erosive disease).

Methods: The DELCQ was administered to 97 consecutive RA patients (77F, 20M, mean age 59.1±13.3 yrs., 75 ACPA positives, 66 with erosive disease) attending the rheumatology department of Avicenne Hospital (Bobigny, FRANCE). The DELCQ scores of patients were compared to those of 388 controls, matched for sex, age and smoking status, from a 2739-subject national cohort, representative of the general French population (ELIPSSilice). Within RA subjects, the association of the scores with ACPA positivity and with erosive disease was assessed after adjustment for tobacco use.

Results: RA patients had higher median scores of occupational (10 [0, 17] vs. 0 [0, 4]) exposure vs. controls (p<0.0001). Median occupational exposure was higher in both men and women compared to controls matched by age, sex and tobacco use (23.5 [18, 34.5] vs. 2.5 [0, 12] for men and 7 [3, 14] vs. 0 [0, 5] for women, p<0.0001 for both). Non-occupational median exposure was significantly higher only in women with RA (15 [9, 21] vs. 12 [5, 21], p< 0.05). Male vs. female RA patients had higher median occupational scores of exposure (p<0.001), while non-occupational exposure was not significantly different. After adjusting for smoking (smokers>5 pack/y vs. nonsmokers or smokers <5 pack/y), neither professional of non-professional scores were associated with erosive disease, despite a strong negative interaction with tobacco use.

Conclusion: Women with RA have higher professional and non-professional lifetime exposure to silica dust compared to age, and sex-matched subjects from the French general population. In this series, constituted mainly of non-smoking women, exposure to silica may be a relevant environmental factor for the development of RA. Higher occupational exposure in RA is confirmed in men with RA. Neither occupational nor non-occupational exposure was associated with ACPA positivity or erosive disease, likely due to the high prevalence these features in the patient series.

Disclosure of Interests: Johanna Sigaux Speakers bureau: celgene, Catherine Cavaill: None declared, Odile Macchi: None declared, Salima Challal: None declared, Sarah El Rharras: None declared, Mylene Petit: None declared, marie-Christophe Boissier Grant/research support from: Pfizer MSD, Speakers bureau: Pfizer Lilly Biogen, Paul-André Rosental: None declared, Luca Semerano Grant/research support from: pfizer, Speakers bureau: pfizer, roche, msd, bms DOI: 10.1136/annrheumdis-2019-eular.5272
DISCREPANCY BETWEEN THE EFFICACY OF BIOLOGICAL DMARDS BASED ON RANDOMIZED CONTROLLED TRIALS AND THE EFFICACY OF BIOLOGICAL DMARDS IN PATIENTS WITH RHEUMATOID ARTHRITIS: A STUDY USING THE IORRA COHORT

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Background: Randomized controlled trials (RCTs), which are currently considered to provide the highest level of evidence, include patients with high disease activity and exclude those with comorbidities often seen in the real world. With the increasing recognition of the importance of real-world evidence, attention is being paid to discrepancies between RCT-based evidence and the patient population in routine clinical practice; however, few reports assessing these gaps in the context of rheumatoid arthritis (RA) are available.

Objectives: We investigated the discrepancy between the efficacy of biological DMARDs (bDMARDs) in RCTs and the effectiveness of bDMARDs in routine clinical practice in patients with RA based on the IORRA cohort.

Methods: The effectiveness of bDMARDs (etanercept [ETN; n=33], golimumab [GLM; n=29], certolizumab [CZP; n=17], abatacept [ABT; n=19]) and tocilizumab [TCZ; n=24]) in RA patients who newly initiated bDMARD therapy in our hospital in 2016 was compared with the efficacy reported in phase 2 or 3 trials (8 total RCTs: ETN: 1; GLM: 2; CZP: 2; ABT: 1; TCZ: 2) during the RCT’s observational periods. Effectiveness was evaluated by percentages of patients achieving ACR20, ACR50, and ACR70 and clinical remission based on DAS28 remission criteria using the IORRA cohort database. We also compared treatment responses between IORRA eligible and non-eligible patients in the MATSURI study, a phase 2 trial that evaluated TCZ-sc efficacy and safety and had relatively lenient inclusion criteria, since some RA patients in the IORRA cohort belonged to both the eligible and non-eligible groups.

Results: In 7 RCTs (excluding the MATSURI study), very few patients fulfilled the IORRA inclusion criteria (Table). The ACR achievement rates were higher among patients in RCTs, while remission rates were higher among IORRA patients (Table). The average DAS28 at baseline in the RCTs’ group was significantly higher than that in the IORRA group (Table). In the MATSURI study, 13 of 24 patients who newly initiated TCZ-sc met the inclusion criteria in the IORRA. Although the percentages of patients achieving ACR20, ACR50, and ACR70 and clinical remission among eligible patients were similar to those of patients in the MATSURI study, those of non-eligible patients were lower than those of MATSURI patients (Table). This indicates better effectiveness in eligible patients than in non-eligible patients.

Conclusion: Although RA patients in RCTs experienced a better ACR achievement rate than those in routine practice, clinical remission was difficult to achieve. This might be due to the difference in disease activity at the time of bDMARD introduction, suggesting that it is necessary to interpret the efficacy of RCTs based on differences in patient background.

REFERENCES:

Table

Disclosure of Interests: None declared.
RESILIENCE TRAITS IN A LARGE COHORT OF PATIENTS WITH ANKYLOSING Spondylitis (AS), RHEUMATOID ARTHRITIS (RA) AND FIBROMYALGIA (FM)


FRI0693 RESEARCHER GROUPS IDENTITY AND RESILIENCE IN PATIENTS WITH ANKYLOSING Spondylitis (AS), RHEUMATOID ARTHRITIS (RA) AND FIBROMYALGIA (FM)

Background: The study of resilient traits (RT) including self-compassion, self-forgiveness, forgiveness of others, and gratitude has garnered attention for its potential to inform health and healthcare research. Little is known about how RT differ in different patient groups. The purpose of the current study is to compare RT among patients with AS, RA and FM.

Objectives: To examine patient group differences in levels and mental and physical health correlates of self-compassion, self-forgiveness, forgiveness of others, and gratitude.

Methods: We conducted an online survey with patients attending the Gastein Healing Galleries in Bad Gastein, Austria. In this health facility, approximately 12,000 patients suffering from different diseases are treated annually. Of those, 6,465 patients were invited by email to participate anonymously. Socio-demographics and health-related variables including depression, pain, and current health status were measured in all respondents. Also measures of self-compassion, self-forgiveness, forgiveness of others, and gratitude were administered in a subset of participants.

Results: In total 2,017 patients responded (31%) of which a subset of 562 patients with AS (44%), FM (38%), and RA (18%) completed measures of RT. Sex ratio (male/female) was 52%/48%, mean age 57 (SD=11) and level of education was: Elementary School 28%, Junior High School 22%, High School 20%, College 13%, and University 17%. Across patient groups, no differences emerged in levels of self-forgiveness, forgiveness of others, or gratitude (p>0.30), although FM patients reported lower levels of self-compassion compared to patients with AS and RA (p<0.05). Self-compassion, self-forgiveness, forgiveness of others, and gratitude were related to depression in all three patient groups, but gratitude was the only RT that was related to depression, pain, and health across all three patient groups.

Conclusion: We found that only self-compassion varied across patient groups, with FM patients reporting lower levels. All RT were consistently related to depression across the three patient groups, but gratitude was also related consistently across groups to both pain and health. RT may well vary according to patient diagnoses with some traits offering more support and resilience-building to the patient than other traits. An important key for treatment support and management may be to identify which traits are most useful to encourage the development of resilience and health in specific patient groups.

REFERENCES:

Disclosure of Interests: None declared


FRI0694 SELF-REPORTED SLEEPING PROBLEMS AND FATIGUE IN LARGE COHORT OF PATIENTS WITH ANKYLOSING SPONDYLITIS (AS), RHEUMATOID ARTHRITIS (RA) AND FIBROMYALGIA (FM)

Background: Sleep problems and fatigue are very common in rheumatic diseases and painful conditions. There is mounting evidence that sleep problems and fatigue have reciprocal influences on musculoskeletal pain, mood, and overall well-being of patients with rheumatic disorders. In addition, sleeping problems are a risk factor for developing chronic widespread pain.

Objectives: To assess and compare self-reported sleep problems and fatigue in a large cohort of patients with AS, RA and FM.

Methods: We conducted an online survey with patients regularly attending the Gastein Healing Galleries in Bad Gastein, Austria. In this health facility approx. 12,000 patients with a variety of disease are being treated annually. Of those, 6,465 patients were invited by email to participate in the survey anonymously. Sociodemographics and disease-related variables including depression, pain, and current health status were measured in all respondents. Also measures of self-compassion, self-forgiveness, forgiveness of others, and gratitude were administered in a subset of participants. In total 2,017 patients responded (31%) of which a subset of 562 patients with AS (44%), FM (38%), and RA (18%) completed measures of RT. Sex ratio (male/female) was 52%/48%, mean age 57 (SD=11) and level of education was: Elementary School 28%, Junior High School 22%, High School 20%, College 13%, and University 17%

Results: In total 2,017 patients responded (31%) of which a subset of 562 patients with AS (44%), FM (38%), and RA (18%) completed measures of RT. Sex ratio (male/female) was 52%/48%, mean age 57 (SD=11) and level of education was: Elementary School 28%, Junior High School 22%, High School 20%, College 13%, and University 17 %. Across patient groups, no differences emerged in levels of self-forgiveness, forgiveness of others, or gratitude (p>0.30), although FM patients reported lower levels of self-compassion compared to patients with AS and RA (p<0.05). Self-compassion, self-forgiveness, forgiveness of others, and gratitude were related to depression in all three patient groups, but gratitude was the only RT that was related to depression, pain, and health across all three patient groups.

Conclusion: We found that only self-compassion varied across patient groups, with FM patients reporting lower levels. All RT were consistently related to depression across the three patient groups, but gratitude was also related consistently across groups to both pain and health. RT may well vary according to patient diagnoses with some traits offering more support and resilience-building to the patient than other traits. An important key for treatment support and management may be to identify which traits are most useful to encourage the development of resilience and health in specific patient groups.

REFERENCES:

Disclosure of Interests: None declared


FRI0695 NEURAL MANUAL MOBILIZATION VS ROBOTIC ASSISTED MOBILIZATION TO REDUCE PAIN HYPERSENSITIVITY IN HANDOSTEOARTHRITIS: A RANDOMISED CONTROLLED PILOT TRIAL

Background: Recent studies suggest that osteoarthritis (OA) is a mixed pain state and that in some patients' central nervous system factors can play an important role.
Objectives: In this study, we showed some preliminary data on the effectiveness of a manual mobilization vs robotic assisted mobilization, on reduce pain sensitivity in subjects with dominant hand OA.

Methods: A pilot randomized controlled trial was conducted. 50 patients (50 to 90 years old) with a diagnosis of dominant hand OA were randomized into two groups of 25 participants. The experimental group received an intervention of neurodynamic mobilization of median, radial and ulnar nerves plus exercise, the control group received a robotic assisted passive mobilization treatment (Grohes Workstation, Grohes et al., Brescia, Italy) plus exercise. Both groups received 12 treatment sessions over 4 weeks. Pressure pain thresholds (PPTs) were assessed bilaterally over the Radial, Median and Ulnar nerves, first Carpometacarpal (CMC) joint, Hamate bone and in the C5-C6 sympathetic joint. Intensity of pain (Visual analogue scale, VAS), QuickDASH scale, grip and pinch strength were also measured bilaterally. Patients were assessed at beginning, at the end of therapy and after a period of 1 and 3 months.

Results: In comparison with pre-treatment values, the experimental treatment increased the PPTs in the first CMC joint, radial and median nerves (P < 0.05) and this effect was maintained until the 2nd Follow up session in the dominant hand. No significant changes in PPT at the hamate bone and ulnar nerve during treatment were found. No significant interaction for pain intensity (VAS) of hand while executing a grip strength, over the last 24 hours and over the last week also was found. Similarly, grip and pinch of the dominant hand did not increase after treatment.

Conclusion: Neurodynamic mobilization by sliding technique decreases pain in the hand joints in patients with hand OA, suggesting alternative therapies to surgery or to the use of analgesic. This research suggests that these patients can benefit from this approach.

REFERENCES:

Disclosure of Interests: None declared.
products and the development of RA was observed: HR for the fully adjusted model=1.12 (95% CI: 0.78-1.59) (Table 1). Also when evaluating milk and cheese consumption separately, no association with the risk of RA was observed: HR for the highest milk consumption=1.10 (95% CI: 0.82-1.44) and highest cheese consumption HR=1.20 (95% CI: 0.81-1.79), compared with low consumption (fully adjusted models, table 1). Conclusion: In this large population-based cohort study, consumption of dairy products was not associated with risk to develop RA.

Methods: In this randomised controlled single-blinded study patients with a history of lateral upper arm pain with MRI confirmation of rotator cuff pathology or positive testing on a cluster of clinical rotator cuff tests were included. Patients with a recent history of shoulder surgery or a shoulder fracture were excluded. Participants were randomly assigned to complete either 6 weeks (short group) or 12 weeks (long group) of the exercise programme. Both groups performed the same specific set of loaded exercises daily at home and attended 6 clinic-based group exercise sessions2. Participants were assessed at 6 weeks, 3 and 6 months. Shoulder function was assessed using the Constant-Murley (CM) score. Disability was assessed using the QuickDash and the Shoulder Pain and Disability Index (SPADI). Pain was assessed using a visual analogue scale. Group comparisons were made using univariate generalised linear models.

Results: 85 patients were included in this study as per Table 1.

Within each group shoulder function, self-reported disability and pain improved significantly at 3 months (p < .05). Comparisons at 3 months showed the long group had significantly lower pain scores (p = .02). At 3 months there was no significant difference between the two groups in the CM score (p = .415), SPADI score (p = .053) and QuickDash score (p = .245). However, at 6 months, the long group had significantly greater changes in both the CM score (p = .007) and the SPADI score (p = .002).

Conclusion: In the management of patients with rotator cuff related shoulder pain the findings of this study indicate that a 12 week exercise programme results in better outcomes for pain at 3 months and self-disability and shoulder function at 6 months.

REFERENCES:

Disclosure of Interests: None declared

HPR Interventions (educational, physical, social and psychological)

FRI0698-HPR A RANDOMISED CONTROLLED CLINICAL TRIAL COMPARING THE EFFECTIVENESS OF 6 AND 12 WEEKS OF A SHOULDER SPECIFIC EXERCISE PROGRAMME FOR PATIENTS WITH ROTATOR CUFF RELATED SHOULDER PAIN

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Background: Research has shown loaded exercise to be beneficial for patients with rotator cuff related shoulder pain in terms of improving shoulder function, self-reported disability and pain 2. The optimal duration for which these patients should complete a loaded exercise programme to achieve beneficial effects remains unclear.

Objectives: The purpose of this study is to determine if 6 weeks of a supervised shoulder specific exercise programme is as effective as 12 weeks of the same programme, for improving shoulder function, self-reported disability and pain, in patients with rotator cuff related shoulder pain.

Methods: A randomised controlled single-blinded study patients with a history of lateral upper arm pain with MRI confirmation of rotator cuff pathology or positive testing on a cluster of clinical rotator cuff tests were included. Patients with a recent history of shoulder surgery or a shoulder fracture were excluded. Participants were randomly assigned to complete either 6 weeks (short group) or 12 weeks (long group) of the exercise programme. Both groups performed the same specific set of loaded exercises daily at home and attended 6 clinic-based group exercise sessions2. Participants were assessed at 6 weeks, 3 and 6 months. Shoulder function was assessed using the Constant-Murley (CM) score. Disability was assessed using the QuickDash and the Shoulder Pain and Disability Index (SPADI). Pain was assessed using a visual analogue scale. Group comparisons were made using univariate generalised linear models.

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Conclusion: In the management of patients with rotator cuff related shoulder pain the findings of this study indicate that a 12 week exercise programme results in better outcomes for pain at 3 months and self-disability and shoulder function at 6 months.

REFERENCES:

Disclosure of Interests: None declared

FRI0698-HPR DEVELOPMENT OF DELPHI-BASED RECOMMENDATIONS FOR THE MANAGEMENT OF CARDIOVASCULAR COMORBIDITIES IN PATIENTS WITH PSORIATIC ARTHRITIS AND MODERATE-TO-SEVERE PSORIASIS: STUDY PROTOCOL

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Background: Psoriasis (PsO) and Psoriatic Arthritis, (PsA) particularly moderate to severe disease (MS-PSO), are inflammatory systemic
conditions that are associated with a high risk of cardiovascular (CV) complications further beyond the increased prevalence of classical risk factors in this population. Consequently, the early identification of patients with MS-Pso and PsA who may benefit from primary CV prevention is essential. However, medical providers do not routinely screen or counsel their patients for CV risk factors or comorbidities. In addition, paucity of robust clinical data complicates the implementation of management protocols for primary CV prevention in MS-Pso and PsA.

Objectives: To generate expert-based recommendations on the management of CV comorbidities in patients with MS-Pso and PsA through the application of the Delphi technique.

Methods: The development of Delphi-based recommendations included four steps: (1) systematic literature review to explore current information and clinical recommendations on management of CV comorbidities in patients with PsOs and PsA; (2) two subsequent meetings with project coordinators (n = 3) and scientific advisors (n = 7) from different medical specialties (rheumatology, dermatology, endocrinology, internal medicine, pneumology, rehabilitation, psychiatry, and primary care) to examine the results of the review and decide which statements should be included in the final version of the questionnaire; (3) a two-round Delphi questionnaire aimed at specialists in rheumatology and dermatology to assess the degree of consensus on the different points raised; (4) finally, a face-to-face meeting with the project coordinators and scientific advisors to discuss and ratify the results of the Delphi process.

Results: As a result of the literature review and the assessment and approval of scientific advisors, the final version of the Delphi survey contains 52 statements grouped into 35 questions. The questionnaire is divided into 3 topic sections: (1) identification, diagnosis and referral of MS-Pso and/or PsA patients with CV comorbidities (n = 12 statements); (2) management and treatment of CV comorbidities associated with MS-Pso and/or PsA (n = 36); (3) influence of MS-Pso and/or PsA treatments on CV comorbidities and vice versa (n = 4).

Conclusion: This Delphi-based study may fill an important gap in the evidence by providing relevant information on the management of CV comorbidities in patients with MS-Pso and/or PsA.

Disclosure of Interests: None declared. Jose Lopez Esteban Consultant for: I have received fees as an advisory board member for Pfizer, Novartis, Leo Pharma, Lilly, Celgene, Abbvie and Janssen ciad, Eva De Higes Martinez: None declared, Maria Jesus Lopez Navas: None declared, Carlos Guajaro Herraz Consultant for: I have received payments as an advisor for Amgen, Esteve, Ferrer, MSD. Pfizer, Rubió and Sanofi., Speakers bureau: I have received payments as a speaker for Amgen, Pfizer, Novartis, Leo Pharma, Lilly, Celgene, Abbvie and Janssen ciad.

Systematic review: Objective: To evaluate the quality of the current evidence from SRs on the effects of non-pharmacological interventions for the management of FM.

Methods: A systematic search of seven databases (1990-2018) was completed to identify SRs reporting the effects of non-pharmacological interventions on the primary outcomes of pain, function and quality of life (QoL). Data was extracted according to the PICO framework in addition to intervention prescription where appropriate. Methodological quality was assessed using the Assessing the Methodological Quality of Systematic Reviews (AMSTAR-2) instrument (Shea et al 2017). Reviews were classified into 6 categories (1) land-based exercise; (2) water-based exercise; (3) mind-body; (4) electrotherapy; (5) manual therapy and (6) complementary and alternative medicine (CAM). Quality of the included SRs were variable with many interventions scoring low to critically low. High quality evidence was found to support the use of land-based exercise and mind-body therapies for the improvement of pain, function and QoL (Table). In particular aerobic exercise with or without strength training and mind-body therapies demonstrated the best outcome.

Conclusion: With the exception of land-based exercise and mind-body exercise, the quality of evidence for the non-pharmacological management of FM is mostly poor, with more than half of the included reviews scoring low or critically low on the AMSTAR-2 instrument. Improved reporting of outcome data and stricter methodological quality will allow stronger recommendations in the future.

REFERENCES:

Disclosure of Interests: None declared

After the demographic characteristics and disease related data of the individuals were recorded; for the functional status, the Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Metrology Index (BASM1) were used. Six-minute walk test (6MWT) was used for the assessment of aerobic capacity. Group I was attended 40 min aerobic exercises sessions (5-min warm up, 30-min treadmill, 5-min cool down), plus supervised spinal mobility exercises and Group II was attended only supervised spinal mobility exercises per day, 3 times a week, for 12 weeks. Data were analysed Wilcoxon and Mann Whitney U Test.

Results: After training aerobic exercise group, BASMI (p = 0.021), BASDAI (p = 0.002) and 6MWT (p = 0.036) results were statistically significant, while the difference was not significant in BASFI (p = 0.66). It was observed that there was no significant difference in the after training period in the supervised exercises group. BASDAI, in group aerobic exercise group had improved more significantly when compared to supervised exercises group.

Conclusion: As a result of the study, it was noted that when aerobic exercise training applied together with the supervised exercises in ankylosing spondylitis patients, effectiveness on mainly disease activity, spinal mobility and aerobic capacity was increased. Key words: Ankylosing spondylitis, aerobic exercise training, supervised exercise.

REFERENCES:

Disclosure of Interests: None declared

FR0704-HPR
THE EFFECTS OF CLINICAL PILATES TRAINING IN PATIENTS WITH FIBROMYALGIA: A RANDOMIZED CONTROLLED TRIAL
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Background: Fibromyalgia (FM) is a chronic condition characterized by widespread pain, sleep disorders, fatigue and reduced quality of life. Exercise is commonly recommended in the approach of people with FM. Researches support some forms of exercises reduce fibromyalgia symptoms and improve quality of life. Pilates recently has become popular form of exercise which focused core strengthening, posture and coordination of breathing with movement. Studies showed that clinical pilates can be used to provide improvements in patients with FM. However there is no study which compared clinical pilates-based supervised exercises and group exercises on FM patients in literature.

Objectives: The first aim of the study was to investigate the effects of clinical pilates training, secondly to compare the effects of supervised exercises and group exercises training on disease activity, functional status, anxiety, quality of life and biopsychosocial status in individuals with FM.

Methods: 42 voluntary women diagnosed with FM according to 2010 American College of Rheumatology Criteria in the age range of 35-65, who applied to Pamukkale University Department of Internal Medicine, Department of Rheumatology were included in the study. Individuals were randomly divided into two groups, as there would be supervised exercises (Group I, n = 16, mean age 55.38±8,03) and group exercises (Group II, n=26, mean age 47.80±5,87). All participants attended 60 min exercises sessions (10-min warm up, 40-min clinical pilates exercises, 10-min cool down) per day, 2 times a week, for 6 weeks. The training was applied by same physiotherapist who received clinical pilates certificate by an experienced Pilates instructor and physiotherapist. After the demographic characteristics and disease related data of the individuals were recorded; disease activity were assessed with the Fibromyalgia Impact Questionnaire (FIQ), functional status with Health Assessment Questionnaire (HAQ), anxiety with Beck Anxiety Inventory (BAI), quality of life with Short Form 36 (SF-36) scale and biopsychosocial status with the Cognitive Exercise Therapy Approach Scale (BETY). All outcomes were assessed just before and 6 weeks after training. The data were statistically evaluated by the Wilcoxon test and Mann-Whitney Test.

Results: There were no significant differences in baseline demographics between the Group I and Group II (p>0,05). After 6 weeks, for both groups a statistically significant improvement in FIQ, SF-36 (physical and mental component) and BETY also Group II showed a statistically significant improvement in HAQ and BAI (p<0,05). When both group were compared, a significant difference was observed in FIQ (p<0,05) in Group II, whereas no statistical differences were found in other outcomes (p>0,05).

Conclusion: This study showed that clinical pilates training which were applied 6 weeks, resulted in improvement on disease activity, functional status, anxiety, quality of life and biopsychosocial status in individuals with FM. Besides group exercises training provides social interaction so we suggest clinical pilates as an effective and safe method for people with FM.

REFERENCES:

Disclosure of Interests: None declared
functioning and social adjustment, two important components of health-related quality of life. Increased attention to effective management of pain in pediatric scleroderma will likely lead to improved functioning and quality of life.

REFERENCES:

**FRI0706-HPR** COMPARISON OF IMPACT OF VERUM AND PLACEBO THUMB BASE ORTHOSES ON SKIN SURFACE TEMPERATURE AND PRESSURE: A PROOF OF CONCEPT STUDY

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Background: Basal thumb osteoarthritis (OA) can cause significant pain and cause a decline in hand function (Litwic et al 2013). Guidelines for treatment of symptomatic basal thumb OA supports a conservative approach, including splinting to support the carpometacarpal joint (CMCj) and reduce the painful movements of the thumb joint during functional tasks (Zhang et al 2000). Lack of legitimate placebo thumb splint has been a barrier to research to distinguish the specific mechanism of the perceived therapeutic effect of wearing thumb splints. Despite this, splinting of the basal thumb joint remains a common intervention for pain. This research contributed to a national CRN portfolio adopted study examining the clinical effectiveness and efficacy of basal thumb splints for people with basal thumb OA.

Objectives: In the present study, the efficacy of two novel placebo splint designs are examined in comparison to widely used verum thumb splint and no splint for the effect at skin surface interface whilst performing a functional task

Methods: This proof of concept study used a single blind, cross-over design that assessed the effect of wearing different splint conditions on the skin surface interface during a functional hand task. 17 healthy participants (male n=8; female n=9) who met the inclusion criteria were recruited to take part in the study. Skin surface temperature ('°C) and pressure exerted at the skin surface interface was recorded during performance of a standardised hand function task, the nine-hole peg test (9HPT) for four splint conditions i) verum splint (Promedics NC79562), ii) placebo lycra splint (P1); iii) placebo lycra splint ‘lite’ (P2) and iv) no splint. Data were recorded and analysed by one rater using Matlab and SPSS software. Results: It was observed from the mean rank that the verum splint condition caused the greatest pressures compared to all other splint conditions. Post hoc analysis revealed there was no difference in pressure exerted over the CMCj between the no splint condition and P1 (Z=1.577, p=0.115) and P2 (Z= -0.365, p=0.715). The verum splint caused a significant increase in pressure over the CMCj in comparison to all other test conditions (Z= -3.516, p<0.0005). ANOVA showed a significant effect of splint design on temp (F(3,16)=22.96, p=0.005). Post hoc analysis revealed that the verum splint produced a significantly higher skin surface temperature (32.67°C ±1.10°C) than P1 (31.75°C ±1.10°C, p<0.0005), P2 (31.85°C ±1.11°C, p<0.001) and no splint (31.06°C ±1.24°C, p<0.0005) conditions. No differences in skin temperature were shown between placebo designs (p=1.00).

Conclusion: This study is the first to characterise the effect of different thumb splint designs on the skin surface temperature and the mechanical loading force local to the CMCj. This study further informs the specific effect of thumb splints at the joint interface. Identifying that new placebo splint designs do not provide additional support to the thumb joint is a novel supplement to research surrounding thumb splinting intervention and can support the use of these devices as placebo splint conditions in future trials.
Disclosure of Interests: Melissa Domaile: None declared, Paul Whybrow: None declared, Elizabeth Carver-Richardson: None declared, Emma Dures Grant/research support from: Has previously received an independent learning grant from Pfizer, however the work has been completed and the grant has been closed, Rosemary Greenwood: None declared, Pamela Richards: None declared, Joanna Robson: None declared, Robert Stellinga: None declared, Fiona Cramp: None declared

FRIO708-HPR PROGNOSTIC FACTORS ASSOCIATED WITH AN EARLY RESPONSE TO PHYSIOTHERAPY TREATMENT IN PATIENTS WITH CHRONIC NONSPECIFIC NECK PAIN: AN EXPLORATORY PROGNOSTIC MODEL
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Background: Chronic nonspecific neck pain (CNP) is a common health problem worldwide. Previous studies identified sociodemographic and clinical factors associated with successful outcomes in patients at discharge of physiotherapy treatment. However, the prognostic factors associated with an early response to physiotherapy treatment in patients with CNP are unclear. This knowledge may allow to identify a profile of patients with higher odds of improvement at the beginning of treatment, supporting clinical decision-making considering benefits versus non-benefits at short-term.

Objectives: This study aimed to identify prognostic factors associated with an early successful response to Physiotherapy treatment in patients with CNP. The successful response was defined as a reduction on disability of ≥30% after 3-weeks of physiotherapy treatment.

Methods: A prospective cohort study was conducted on 52 patients with CNP lasting ≥3 months, undergoing a physiotherapy treatment programme of mobilisation and exercise (coordination, strength, endurance). Patients were assessed at baseline, and then 3-weeks later. Participants were categorised as having a successful outcome if they scored a difference in their disability above the Minimal Clinical Important Difference (MCID) of the Neck Disability Index (NDI). Logistic regression analysis (backward stepwise conditional method) was used to identify the associations between baseline prognostic factors and outcome. Socio-demographic and clinical characteristics of CNP were included as potential prognostic factors.

Results: A total of 51 participants completed the intervention. At 3-weeks post-treatment, 75% (38/51) of the participants achieved a successful response to physiotherapy treatment. In the final multivariate model (Omnibus Tests p<0.001), an early successful response to Physiotherapy treatment was significantly associated with the disability score (OR 1.16 – CI 95% 1.02-1.32), and pain intensity (OR 1.81 – CI 95% 1.03-3.20) at the baseline. This model improves the classification ability from 74.5 to 81.7%.

Conclusion: This study confirms that patients with medium to high levels of disability and high levels of pain at the baseline, treated with a physiotherapy programme of mobilisation and exercise, are more likely to have increased odds of achieving an early response to treatment in the presence of both variables (+LR=1.71 95% CI: 0.84-3.50) or one variable (+LR=1.45 95% CI: 0.69-3.04).

FRIO709-HPR EFFECTS OF LAND- AND WATER-BASED EXERCISE INTERVENTIONS ON PAIN IN PEOPLE WITH FIBROMYALGIA: A PRELIMINARY REPORT FROM THE AL-ANDALUS RANDOMISED CONTROLLED TRIAL
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Background: Non-pharmacological approaches are the mainstay of treatment in fibromyalgia. The current recommendations of the European League Against Rheumatism (EULAR) for the management of fibromyalgia highlight that exercise is the only therapy with a ‘strong’ evidence [1]. Exercise has been typically implemented on either land- or water-based settings. However, it is unclear whether to perform exercise in different settings has different effects on pain; this knowledge might help to maximise the beneficial effects that exercise has in fibromyalgia [2].

Objectives: To compare the effects of two exercise interventions (land- and water-based training) on pain in people with fibromyalgia.

Methods: From 272 initially randomized, a total of 151 participants (50.6 ±7.6 years old, 98% women) completed all the assessments and attended to at least 70% of the programme; 48, 42 and 61 participants pertained to the land-based exercise, water-based exercise, and usual care (control) groups, respectively. The intervention groups trained 3 non-consecutive days/week (45-60 minutes per session) for 24 weeks. Each session included aerobic exercises, muscular strengthening and stretching for all the major muscle groups. Pain was measured by the 0-100 mm visual analogue scale (VAS) from the Fibromyalgia Impact Questionnaire (FIQ), Catastrophizing and self-efficacy pain-related cognitions were assessed by the Pain Catastrophizing Scale (PCS total score) and pain management subscale (PSE) of the Chronic Pain Self-efficacy Scale (CPSS), respectively. We calculated an algometer score based on the sum of pain thresholds (kg/cm2) of the 18 tender pints according to the 1990 American College of Rheumatology fibromyalgia diagnostic criteria.

The groups were comparable in sociodemographic and clinical characteristics; they only differ on age, which was included as a covariate along with baseline levels of pain.

Results: Adjusting for Bonferroni, most of the between-group comparisons of pain changes over time were not significant. As exceptions, in comparison to the control group, participants in the land-based exercise group lowered catastrophizing and improved algometer score at the post-tests; mean difference (95% interval confidence) [MD(95% CI)] = -4.0 (-7.5 to -0.5) and 6.2 (2.0 to 10.5), respectively. These differences became non-significant at the re-test.

Conclusion: These preliminary results suggest that a 24-week land-based exercise intervention had beneficial effects by reducing pain catastrophizing and increasing algometer score in people with fibromyalgia. However, these benefits were unsustained after the detraining period. In comparison to the control group, a water-based exercise intervention did not show any effect on pain. Although our finding suggest that a land-based exercise intervention may have short-term beneficial effects on pain, these findings must be considered as preliminary until more robust analyses are performed.

REFERENCES:

Acknowledgement: This study was supported by the Spanish Ministry of Economy and Competitiveness (I+D+i DEP2010-15639; I+D+i DEP2013-40908-R; BES-2014-067612) and the Spanish Ministry of Education (FP14/02518; FP15/00002)

Disclosure of Interests: None declared
EFFECTIVENESS OF EXERCISE IN THE MANAGEMENT OF FATIGUE AND SLEEP QUALITY IN FIBROMYALGIA: A SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Non-pharmacological interventions are the mainstay of treatment for fibromyalgia, however, current evidence-based guidelines report that the only therapy supported by ‘strong for’ evidence is exercise intervention for pain in fibromyalgia [1]. While increased fatigue and poor sleep quality are among the most burdensome symptoms in fibromyalgia, there remains limited evidence for the effectiveness of exercise in the management of these symptoms [2,3].

Objectives: To determine the effectiveness of exercise in the management of fatigue and sleep quality in fibromyalgia.

Methods: A systematic search was conducted using PubMed and Web of Science in October 2018 (Prospero Registration No. CRD42018118605). Eligible studies were randomised controlled trials (RCT) including adults with fibromyalgia (population), who received exercise (intervention) compared to usual care (comparator). Outcomes of interest were fatigue and/or sleep quality. No restrictions were applied for language nor for publications date. Random effects meta-analyses were conducted. The Cochrane Collaboration’s tool was used for assessing risk of bias in the included studies. The quality of evidence was evaluated using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) framework.

Results: Twenty RCTs were included, 17 included measures of fatigue (n=1003) and 12 measures of sleep quality (n=731). In comparison to usual care, exercise had beneficial effects on fatigue (Figure 1, P<0.001) but not on sleep quality (Figure 2, P=0.06). The most beneficial interventions for fatigue and improving sleep quality were those in which fatigue was the primary outcome and those based on body-mind interventions, respectively (both, P<0.001). A moderate risk of bias was present in most of the included studies.

Conclusion: According to the GRADE framework, this review provides low-to-moderate quality evidence that exercise is moderately effective for improving fatigue, and moderate evidence of no-meaningless effects of exercise to improve sleep quality. Further high quality RCTs are required to determine the effectiveness of exercise on fatigue, and in particular, sleep quality in fibromyalgia.

REFERENCES:

Acknowledgement: This study was funded by the Health and Social Care Public Health Agency, Northern Ireland (STL/5268/16) and the Spanish Ministry of Economy and Competitiveness (BES-2014-067612).

Disclosure of Interests: None declared

Figure 1. Pooled effects of randomised controlled trials analysing the effectiveness of physical exercise on reducing fatigue in people with fibromyalgia.

Figure 2. Pooled effects of randomised controlled trials analysing the effectiveness of physical exercise on enhancing sleep quality in people with fibromyalgia.

Analyses were conducted using a random effects model. CI, Confidence Interval; df, degrees of freedom; Std, Standardised; SD, Standard Deviation; IV, Inverse Variance; Co-, Co-intervention (Photo, phototherapy; edu, education); C, Cardiorespiratory exercise; F, flexibility exercise; S, Strength training; TC, Tai Chi; QG, Quigong; Y, Yoga; L- and W-B, land- and water-based exercise, respectively.

Acknowledgement: This study was funded by the Health and Social Care Public Health Agency, Northern Ireland (STL/5268/16) and the Spanish Ministry of Economy and Competitiveness (BES-2014-067612).

Disclosure of Interests: None declared

PATIENT PERSPECTIVES ON HOW TO IMPROVE MEDICATION EDUCATION

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Background: EULAR recommends that people with inflammatory arthritis should have access to and be offered patient education throughout the course of their disease (1). The content and delivery of patient education should be individually tailored (2). Patients should be educated on their medication and know its purpose, mode of action, possible side effects and monitoring guidelines (3). Improving patients’ ability to make informed choices and to use medication effectively and safely should result in significant benefits for the health service and improve patient well-being (4). Our institute’s yearly Consumer Quality Index (CQI) revealed that our current medication education needs improvement.

Objectives: To improve medication education from the patient perspective.

Methods: A representative cross-sectional sample of 100 rheumatoid arthritis patients was invited to complete a specially designed questionnaire based on the Satisfaction with Information about Medicines Scale (SIMS) questionnaire (5). All caregivers at our Rheumatology unit (rheumatologists, trainees, rheumatology nurses) participated in single-blinded structured observational sessions of their regular patient consultation with the patient’s consent. Data was collected on the type and content of medication information that was given during the consultation. Local ethical approval was obtained and patient confidentiality was assured.

Results: At present 40 (40%) patients returned the questionnaire. Overall, patients are satisfied with the medication education provided (average overall satisfaction score of 7.4 (0–10). However patients experienced insufficient education on the following topics:
- whether the medication has influence on sex life
- the risk of having side effects
- how to act when side effects occur
- possible interaction with concomitant medication
- whether the medication can cause drowsiness

Between December 2018 and January 2019 caregivers at our unit (4 rheumatologists, 2 trainees, 1 nurse) participated in multiple single-blinded observational sessions. In 100% of observed consultations medication information was provided. However, most caregivers did not address the topic of side effects during their consultation. Furthermore, in all cases caregivers failed to document in the electronic patient file which information was provided.

Conclusion: Rheumatoid arthritis patients express overall satisfaction with medication education but experience an unmet need for information on possible medication effects on their sex life, medication side effects and interaction with concomitant medication. Further analysis of the questionnaires will be performed and a plan of improvement will be implemented to meet the patients need for more and better education on medication. Patient medication education will be implemented in a continuous cycle of improvement.
Efficacy of Graded Activity with and without Comparison of Biopsychosocial Status of Patients with Ankylosing Spondylitis with and Without Anti-TNF Treatment

**Background:** It is known that anti-TNF therapy is given to patients with persistently high disease activity despite conventional treatments according to the ASAS recommendations (1). Although biopsychosocial symptoms were well known, biopsychosocial assessments are insufficient in the literature.

**Objectives:** The aim of this study was to compare the biopsychosocial status between patients with AS who were decided to be treated with anti-TNF treatment and patients with AS who did not receive any anti-TNF treatment. Also, it was aimed to investigate the effectiveness of 3 months anti-TNF treatment on biopsychosocial status.

**Methods:** 74 AS patients who are decided to receive anti-TNF treatment and 38 AS patients, who didn’t, were included in the study. Socio-demographic informations of patients were collected. The mean age of the patients (n = 112) was 41.9±19.8 years. Health Assessment Questionnaire (HAQ) was used to assess functional status and daily living activities. The Hospital Anxiety and Depression Scale (HADS) was used to assess anxiety and depression levels. Biopsychosocial status of the patients was evaluated by the BETY-Biopsychosocial Questionnaire (BETY-BQ). The same evaluations were repeated after 3 months in 36 patients using anti-TNF.

**Results:** A statistically significant difference was observed in BETY-BQ, HADS anxiety and HAQ scores, when the groups were compared. There was no statistically significant difference in HADS depression scores (Table 1). The difference after 3 months of anti-TNF treatment was significant in all parameters (Table 2).

**Conclusion:** It was observed that the patients who were decided to be received anti-TNF treatment had worse functionality, anxiety, and biopsychosocial status than the patients who did not receive anti-TNF treatment. Anti-TNF treatment was found to be effective in three months period in terms of these biopsychosocial symptoms that the patients had.

**REFERENCES:**
Disclosure of Interests: None declared

FR0714-HPR
A PILOT NURSE-LED TELEPHONE TRIAGE LINE OF PATIENTS WITH RHEUMATOLOGIC RARE DISEASES IN A TERTIARY CENTER

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Background: The general rheumatology outpatient clinics are facing an increasing workload. The patients already in evidence with rare or complex inflammatory diseases, such as inflammatory myopathies, systemic lupus erythematosus, mixed connective tissue diseases, systemic sclerosis, Sjogren’s syndrome, relapsing polychondritis, systemic vasculitides and other collagen-vascular diseases are being scheduled for outpatient or hospital assessment at the current visit. However the patients may need earlier appointments, given the possibility of flares or other issues.

Objectives: To assess the role of a nurse-led telephonic triage line in patients with rare rheumatologic diseases.

Methods: The nurses accepting to be enrolled in the programme answered the phone for the patients already in the department’s and their follow-up with rare or complex inflammatory rheumatic diseases. A 2-hours training programme with attending physicians was completed. Respecting confidentiality agreement regulations, the calls were registered with the name, diagnosis and phone number on a standard form. The calls reasons were recorded: appointments scheduling, medical issues or others. The alarming symptoms and signs requiring doctor advice or earlier appointments were checked on a short form: aggravating dyspnea, dysphagia, weakness or Raynaud’s phenomenon, ulcerations, etc. Other issues, such as lumbar pain, joint pain, nausea, heartburn, etc requiring counselling, were registered as well.

Results: Over 2 months, 280 calls from patients with rare rheumatologic diseases were received, out of which 171 (61%) were for scheduling or changing appointments. The rest were for medical advice regarding minor ailments, medication side effects, regular blood tests or other investigations performed after the last visit, issues regarding travelling etc. The triage nurses referred the patients to Emergency in 2 cases (0.7%), to the General Practitioner in 28 cases (10%) or planned an early appointment. However the patients may need earlier appointments, given the possibility of flares or other issues.

Conclusion: When designing PA programs for people with RA, the AR PA guidelines for people who have inflammatory arthritis [3] should be followed. However, it should be noted that engagement and participation in PA interventions is increased when the intervention is of low impact PA and starts at a low-moderate intensity. Individualising the activity to the person and applying behaviour change techniques have also been found to improve participation.

REFERENCES:

Disclosure of Interests: None declared

FR0715-HPR
FACTORS WHICH IMPACT COMPLETION AND NON-COMPLETION OF PHYSICAL ACTIVITY INTERVENTIONS FOR PEOPLE WITH RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW

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Background: Rheumatoid arthritis (RA) is a systemic inflammatory condition which results in pain, fatigue, joint stiffness and an increased risk of cardiovascular issues. Physical activity (PA) has been proven to help reduce the severity of these symptoms and the risk of cardiovascular disease [1]. However, recent literature has shown that people with rheumatoid arthritis do not meet PA guidelines [2]. The systematic review aims to determine the factors which affect the completion rates of adults with RA in PA interventions.

Objectives: 1) Review the effect of the frequency, intensity, time and type of exercise (FITT principle) on participation rates. 2) Review the reasons for dropping out of an intervention and consider how this can be avoided in planning future interventions. 3) Examine the effect of behaviour change techniques used on completion rates.

Methods: A systematic review of the literature was carried out in February 2018. Inclusion criteria were: detailed intervention information, completion rates reported, published between 1998-2018 and published in English. Included papers were assessed using the Cochrane risk of bias tool by two assessors. The relevant data was then extracted, compared and conclusions were drawn.

Results: Nine studies with varying levels of quality were included in this review. Reasons for not completing an intervention could be divided into modifiable and non-modifiable factors; modifiable factors include the FITT principle, the behaviour change component and controlling for adverse outcomes. Non-modifiable factors included the environment, illness/flare-up and accidents. The results found that when people with RA had an individualised PA program that started at a low-moderate intensity they had higher participation rates than those who followed a generalised program, with no behaviour change component. Altering the intervention in response to patient’s pain levels improved completion rates of the intervention.

Conclusion: When designing PA programs for people with RA, the AR PA guidelines for people who have inflammatory arthritis [3] should be followed. However, it should be noted that engagement and participation in PA interventions is increased when the intervention is of low impact PA and starts at a low-moderate intensity. Individualising the activity to the person and applying behaviour change techniques have also been found to improve participation.

REFERENCES:

Disclosure of Interests: None declared

FR0716-HPR
FACTORS WHICH IMPACT COMPLETION AND NON-COMPLETION OF PHYSICAL ACTIVITY INTERVENTIONS FOR PEOPLE WITH RHEUMATOID ARTHRITIS: A SYSTEMATIC REVIEW

Niamh Reynolds, Louise Larkin, University of Limerick, Limerick, Ireland

Background: Rheumatoid arthritis (RA) is a systemic inflammatory condition which results in pain, fatigue, joint stiffness and an increased risk of cardiovascular issues. Physical activity (PA) has been proven to help reduce the severity of these symptoms and the risk of cardiovascular disease [1]. However, recent literature has shown that people with rheumatoid arthritis do not meet PA guidelines [2]. The systematic review aims to determine the factors which affect the completion rates of adults with RA in PA interventions.

Objectives: 1) Review the effect of the frequency, intensity, time and type of exercise (FITT principle) on participation rates. 2) Review the
A COMPARISON OF THE EFFECTIVENESS OF CORE STABILIZATION EXERCISE AND COMBINED EXERCISE ON PAIN, FATIGUE, SLEEP PROBLEM AND HEALTH STATUS IN WOMEN WITH FIBROMYALGIA

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Background: Fibromyalgia (FM) is a syndrome characterized mainly by chronic widespread pain, fatigue, sleep disorders and decrease in health status. Exercise, one of the non-pharmacological approach, has favorable effects on clinic findings in FM, but studies investigating which types of the exercise are more effective in FM are limited.

Objectives: This study aimed to compare the effectiveness of core stabilization exercise (CSE) and combined exercise (CE) on pain, fatigue, sleep problem and health status in women with FM.

Methods: A total of 34 women with FM were included, allocated into the CSE (n:18, age: 43.05±9.23 years, body mass index (BMI): 27.25±5.23 kg/m²) and the CE (n:16, age: 38.43±9.55 years, BMI: 25.62±3.68 kg/m ²) groups. Both the CSE and the CE programs were carried out 2 days a week for 6 weeks under the supervision of a physiotherapist. Pain, fatigue and sleep problems with Visual Analog Scale and health status with Fibromyalgia Impact Questionnaire were evaluated at baseline and after 6-weeks program.

Results: Physical characteristics of the groups were similar (pBMI=0.313). After the program, it was found that pain (p=0.001; p=0.014), fatigue (p=0.002; p=0.011), and sleep problem (p=0.007; p=0.039) decreased, health status (p=0.001; p=0.001) improved in both the CE and the CSE groups, respectively. Moreover, sleep problem decreased in the CE group in comparison to the CSE group (p=0.038); but pain (p=0.003), fatigue (p=0.178), and health status (p=0.098) did not differ between groups.

Disclosure of Interests: None declared

FR0718-HPR THE EFFECT OF THE BIOPSYPHOCOSOCIAL EXERCISE PROGRAM ON PAIN COPING SKILL AND FATIGUE IN RHEUMATIC DISEASES

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Background: Although the trend towards biopsychosocial approaches is increasing today, studies on psychosocial effects of exercise are limited in the literature. There is a need for framed exercise programs to assess the clinical effectiveness of biopsychosocial approaches. The reason why biopsychosocial programs are important may be due to multidimensional features of symptoms such as pain, fatigue.

Objectives: The purpose of this study is to investigate the effectiveness of the biopsychosocial exercise program on pain coping skill and fatigue in rheumatic patients.

Methods: Ninety-one patients with the rheumatic disease were included in this study. The patients were divided into two groups based on a prospective cohort (BETY group, n = 56; and control group, n = 35). BETY is a biopsychosocial exercise approach (1). It was performed in a period of one hour, 3 times a week for 12 weeks and included clinical pilates exercises, dance therapy-authentic movement and pain management information. The control group did not take any exercise treatment. The BETY-Biopsychosocial Questionnaire (BETY-BQ) was used to evaluate the pain coping skill and fatigue as well as assessing whole biopsychosocial status of individuals (2). The answers were given to the 5th question (I don’t know how to control my pain), and the 11th question (I feel tired) of the BETY-BQ were recorded as a 5-point Likert at ranging from ‘yes, always’ to ‘no, never’. Also, the total score of BETY-BQ was recorded. Demographic data were given as mean ± standard deviation (X ± SD), and answers given to the questionnaire were expressed in frequency tables.

Results: The mean ages of BETY group and control group were 49.63 ± 11 and 39.74 ± 10 years and body mass indexes were 26.93 ± 3 kg/m² and 26.54 ± 4 kg/m², respectively. The frequency of answers to the 5th and 11th question and the total score of the BETY-BQ on the first assessment (pre-treatment) and the second assessment (post-treatment) were shown in Table 1.

FR0718-HPR Table 1. Comparison of assessment results

<table>
<thead>
<tr>
<th></th>
<th>BETY group</th>
<th>Control Group</th>
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<tbody>
<tr>
<td></td>
<td>Pre-treatment</td>
<td>Post-treatment</td>
</tr>
<tr>
<td>BETY-BQ (0-120)</td>
<td>54.60±27</td>
<td>38.55±25</td>
</tr>
<tr>
<td>5th question</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes always (%)</td>
<td>24.1</td>
<td>7.4</td>
</tr>
<tr>
<td>Yes often (%)</td>
<td>7.4</td>
<td>3.7</td>
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<td>Yes sometimes (%)</td>
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<td>Yes rarely (%)</td>
<td>25.9</td>
<td>20.4</td>
</tr>
<tr>
<td>No never (%)</td>
<td>16.7</td>
<td>46.3</td>
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</table>
Conclusion: It was concluded that BETY as a biopsychosocial exercise approach is effective in reducing fatigue and improving the pain coping skill as well as the biopsychosocial status of rheumatoid patients. BETY should be kept in mind for further studies in terms of biopsychosocial aspects of pain coping, fatigue, etc.

REFERENCES:


Disclosure of Interests: None declared

FR10720-HPR DEVELOPMENT AND VALIDATION OF A SELF-ADMINISTERED QUESTIONNAIRE MEASURING ESSENTIAL KNOWLEDGE FOR PATIENTS WITH RHEUMATOID ARTHRITIS: THE RHEUMATOID ARTHRITIS ASSESSMENT KNOWLEDGE QUESTIONNAIRE (RAKE)

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Background: Improving knowledge and skills is required for patients with rheumatoid arthritis (RA) to enhance self-management. Measuring knowledge is also part of the educative approach. However, the available Knowledge questionnaires (KQs) (ref 3) needed to be updated according to recent recommendations for RA management and the patients’ needs (ref 3).

Objectives: To develop and validate a new KQ in RA.

Methods: 4 steps. Step1. Selection of knowledge considered essential for patients with RA through Delphi rounds by a working group of rheumatologists, health professionals (HPs) and patients leading to a list of consensus items (ref3). Step2. Two rheumatologists and a rheumatology nurse constructed the first version of the KQ, each question of the KQ referring to a selected item on the list. The formulation was then amended by the working group. A new version was elaborated during a face-to-face meeting of 3 HPs and one patient. Step 3. The KQ was submitted to ten patients for cognitive debriefing, comments were analysed and a the final version was elaborated. Step 4. Multicentric validation in 11 rheumatology departments: acceptability was measured by the rates of missing data per item, reproducibility and sensitivity to change were assessed respectively by test/retest at a 2 weeks interval (Lin’s concordance correlation coefficient) and by testing the KQ before and after patient education sessions. The sample size estimation and statistical analyses were conducted according to COSMIN recommendations, especially concerning thresholds of metrological indexes.

Results: Step1 obtained 45 knowledge items, 32 considered essential and 13 considered useful, selected respectively by more than 2/3 and more than 50% of participants to the Delphi rounds, leading to the RAKE: a 45-items questionnaire, with a 32-items short form. The RAKE contains 6 knowledge domains: disease knowledge (10 items), pharmacological treatment (14), non-pharmacological treatment (7), comorbidities (1), self-care for pain and fatigue (5), adaptive skills to psychosocial and professional issues and health care system (8). The validation included 130 patients, 108 (83.4%) women, mean age 56.4±12.10 years, median disease duration 9 years [4; 23]. The missing data rate per item was <0.05. The RAKE’s internal validity (Kuder-Richardson) was 0.90. Reproducibility (in 72 patients) was 0.86 [0.80; 0.92]. Sensitivity to change was measured in 54 patients. A statistically significant difference in total knowledge score was observed between the two assessment times: 30.1±7.4 vs. 37.7±5.7 (p<0.001), representing an effect size >1.1 [0.7; 1.6]. The RAKE’s
external validity was confirmed by correlation with the RAID score of 0.16 (p=0.08).

**Conclusion:** This study enabled the development and the validation of the RAKE, a Knowledge questionnaire for patients with RA, with a good acceptability, reproducibility and sensitivity to change. This KQ will be helpful to assess the process of knowledge acquisition in patient education approaches.

**REFERENCES:**

**Disclosure of Interests:** Malory RODERE: None declared, Bruno Pereira: None declared, Martin SOUBRIER: None declared, Sonia Tropé: None declared, Francoise Fayet: None declared, Jean David COHEN: None declared, LAURENT GRANGE Consultant for: Laurent Grange has declared, Muriel PIPERNO: None declared, Beatrice Pallot Prades: None declared, João Apóstolo2, P José Antonio. Da Silva 1, Maria Do Céu Barbieri-Figueiredo3.

**FRI0721-HPR**

**EFFECTIVENESS OF NON-PHARMACOLOGICAL AND NON-SURGICAL INTERVENTIONS ON THE IMPACT OF RHEUMATOID ARTHRITIS: AN OVERVIEW OF REVIEWS**

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**Background:** Impact of disease persists in many patients with rheumatoid arthritis (RA) even after inflammatory remission is achieved, requiring the need for adjunctive interventions targeting the uncontrolled domains of disease impact. Several systematic reviews have addressed nonpharmacologic interventions, but there is still uncertainty due to scarce or conflicting results or significant methodological flaws.

**Objectives:** To determine the effectiveness of non-pharmacological and non-surgical interventions upon the impact of RA.

**Methods:** A comprehensive search strategy for 13 databases and grey literature was developed. This review included quantitative systematic reviews that examined the effectiveness of non-pharmacological and non-surgical interventions of any form, duration, frequency and intensity, alone or in combination with other interventions designed to reduce the impact of disease in adult patients with RA. The outcomes were pain, functional disability, fatigue, emotional well-being, sleep, coping, physical well-being and global impact of disease. Critical appraisal and data extraction were performed independently by two reviewers and summarized using a narrative synthesis approach.

**Results:** Eight systematic reviews were included (Figure 1), with a total of 91 RCT’s and nine observational studies (6740 participants). Four systematic reviews examined the effects of multicomponent or single exercise/physical activity interventions, two examined the effects of hydrotherapy/balneotherapy, two evaluated the effects of psychosocial interventions and one assessed the effects of custom orthoses for the foot and ankle. Multicomponent or single exercise/physical activity interventions, psychosocial interventions and custom orthoses appeared to be effective in improving pain and functional disability. Fatigue also improved with the implementation of multicomponent or single exercise/physical activity interventions and custom orthoses. Only exercise/physical activity interventions appeared to be the effective in improving the global impact of disease. None of the included systematic reviews reported on emotional well-being, sleep, coping or physical well-being as an outcome measure. Other types of interventions were not sufficiently studied and their effectiveness is not yet established.

**Conclusion:** Only multicomponent or single exercise/physical activity interventions, psychosocial interventions and custom orthoses seems to be capable of reducing the impact of rheumatoid arthritis. Future evidence should be created and synthesized in the fields identified as knowledge gaps, namely emotional well-being, sleep, coping and physical well-being. Further investigation should be encouraged on the effects of interventions that have not been assessed at all or sufficiently to established their effectiveness, so that robust decisions and recommendations can be made.

**Disclosure of Interests:** None declared

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**FRI0722-HPR**

**THE INVESTIGATION OF THE RELATIONSHIP BETWEEN PSYCHOSOCIAL AND FUNCTIONAL STATUS OF CHILDREN WITH JIA**

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**Background:** JIA is the most common rheumatic disease in children and may result in significant morbidity with joint deformity, growth disorder, and persistence of active arthritis to adulthood (1). According to the model of biopsychosocial pain, emotions affect the degree of functional impairment (2).

**Objectives:** The aim of this study is to investigate the relationship between the psychosocial and functional status of children with juvenile idiopathic arthritis (JIA).

**Methods:** 382 children with JIA were included in the study. Individuals were assessed with the Juvenile Arthritis Biopsychosocial Questionnaire (JAB-Q) (3) and Children Health Assessment Questionaire (CHAQ) applied for functional status (4).

**Results:** The mean age of the subjects included in the study (n = 386) was 12.48 ± 3.81 years. The median value of the JAB-Q functional status was 2 (min: 0 max: 34), psychosocial status was 10 (min: 0 max: 38). And the median value of the CHAQ was 0.25 (min: 0 max: 3). Correlation coefficients and statistical significance were calculated by using Pearson’s test. There was a low positive correlation between BETY-BQ functional status and BETY-BQ psychosocial status (r = 0.347, p <0.001), a low positive correlation between CHAQ and BETY-BQ psychosocial status (r = 0.395, p <0.001). There was a good positive correlation between BETY-BQ functional status and CHAQ (r = 0.679, p <0.001) (Table 1).

**Conclusion:** Only multicomponent or single exercise/physical activity interventions, psychosocial interventions and custom orthoses seems to be capable of reducing the impact of rheumatoid arthritis. Future evidence should be created and synthesized in the fields identified as knowledge gaps, namely emotional well-being, sleep, coping and physical well-being. Further investigation should be encouraged on the effects of interventions that have not been assessed at all or sufficiently to established their effectiveness, so that robust decisions and recommendations can be made.

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Conclusion: The psychosocial status of children is not affected by functional status. Psychosocial status may be affected by different variables. It was concluded that children should be encouraged to participate in social activities independently their functional problems. Further studies are needed to examine the other variables’ effects on psychosocial status in children with JIA.

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Disclosure of Interests: None declared

A MIXED METHOD STUDY TO EXPLORE THE FEASIBILITY AND PATIENT SATISFACTION OF TWO DIFFERENT EXERCISE PROGRAMS IN SYSTEMIC SCLEROSIS ASSOCIATED MICROSTOMIA

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Background: Systemic sclerosis (SSc) is a severe autoimmune disease and fibrotic cutaneous involvement of hands and face is a typical characteristic. Oral involvement with reduced oral aperture is frequent and associated with impaired food intake, oral hygiene and secondary dental problems. Several studies have shown that stretching (placing the thumbs in opposite corners of the mouth hand, pulling outward) and oral augmentation (tongue depressors between the back molars) exercises can increase oral aperture but is often hampered by low adherence rates.

Objectives: The aim of this descriptive explorative mixed method study was to explore feasibility, patient satisfaction and effectiveness of two exercise programs, Therabite and orofacial exercises, in systemic sclerosis associated microstomia.

Methods: We included adult patients suffering from systemic sclerosis (fulfilling the ACR/EULAR 2013 criteria) and microstomia (maximal oral aperture <40mm). We discerned two groups: Group A exercised with a passive jaw motion device (Therabite®), and Group B performed mouth-stretching exercises. Patients were expected to exercise for 10 minutes, 3 times/day for 3 months. Patients were contacted 4 times by telephone to address encountered problems and completed an exercise diary to document the adherence rate. Patients were evaluated at baseline, 3 months (period without intervention), 6 months (after 3 months of intervention) and at 9 months (post-intervention visit). At time point 6 months, semi-structured one to one interviews were conducted. Interviews were recorded, transcribed verbatim and systematically analyzed using Qualitative Analysis Guide of Leuven.

Results: We included 6 women and 3 men, with a median age of 60 years (range 40-75) and a median disease duration of 8 years (range 3-22). At time point 6 months, all patients in group A (n=4) and 4 patients in group B (n=5) improved with a median of 9mm (range 2-10) and 7mm (range 4-11), respectively. One patient had a decrease of 2mm. The compliance, measured as the ratio of executed exercises relative to the planned number of exercises ranged between 63.7% and 98.9% in group A and between 48.5% and 97.4% in group B. Details are shown in Table 1. In the follow-up period, we documented maintenance of the observed increase in oral aperture in those patients that continued exercising daily. In all others, maximal oral aperture declined again. All 9 patients attended the interview. Three main themes emerged from the data: drivers, challenges and perceived improvement. Patients highlighted several drivers to perform the exercises at home, such as the motivation to improve current disability caused by microstomia. Furthermore, they equally highlighted several challenges regarding feasibility, such as the struggle to exercise multiple times a day. Most of the patients were hoping that they could keep their improvement. They were willing to continue practicing if necessary, but with a lower frequency.

Conclusion: This study suggests that both types of intervention can improve maximal oral aperture. The adherence to therapy was higher than expected but none of the patients considered it feasible to continue practicing 3 times/day in the long-term resulting in a decline of improvement post-intervention. This is the first study to report the feasibility of the exercises for the patients and can be very useful for health professionals giving guidance. Future studies are needed in order to define exercise programs that are feasible and can be sustained in the long term.

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THE EFFECTIVENESS OF TAI CHI CHUAN IN OSTEOARTHRITIS OF THE KNEE: A SYSTEMATIC REVIEW

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Background: Osteoarthritis (OA) is the most prevalent joint disease in the elderly. The signs and symptoms are degeneration of joint surface, stiffness, swelling, and decrease in physical function. Knee OA is the most common joint disease and more prevalent among older adults. Tai Chi Chuan is a safe exercise modality of Chinese origin, which may be a potentially in reducing symptoms.

Objectives: The aim of systematic review was to identify the effects of Tai Chi Chuan in the elderly with knee osteoarthritis.

Methods: This systematic review was registered in Prospero (CRD42018096699). MEDLINE, EMBASE, PEDro, Cochrane, Scopus, Scielo, Lilacs and Web of Science, were screened between May 2008 to May 2018 in English, Spanish, Portuguese and Mandarin language. Randomized controlled trials (RCTs) comparing Tai Chi to control conditions were included. All authors independently assessed risk of bias using the risk of bias tool recommended by Jadad index. Outcome measures included were pain, stiffness, muscular strength, functionality and quality of life.

Results: In the search we found 161 studies, MEDLINE (29), Pedro (58), Web of Science (17), Embase (29), Cochrane (6), Scopus (18), Manual search (4). Eight articles were included and seven showed the effectiveness of Tai Chi Chuan, being higher to the interventions of the control groups, consisting of self-care educational activities, or strengthen- ing and endurance exercises of knee flexors and extensors. Only one study, that patients received a lower limb resistance training program, presented better results in pain, stiffness and physical function scores. Tai Chi Chuan was not associated with adverse events.

Conclusion: Tai Chi Chuan was effective in improving pain, stiffness and physical function of sleep quality, in addition to increased speed and step length during gait, and strength gain of knee extensor muscles in elderly patients with knee OA. This systematic review found moderate...
Evidence for short-term improvement of pain, physical function and stiffness in patients with knee AO. More high quality RCTs are urgently needed to confirm these results.

References:

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Disclosure of Interests: Joëlle van den Hoek: None declared, Martin van der Esch: None declared, Marthe van der Leeden: None declared, Willem Lems: Speakers bureau: Amgen Inc., Merck, Eli Lilly and Pfizer, George Metsios: None declared, George D Kilas: Speakers bureau: GDK has received honoraria for lectures, participation in advisory boards and/or hospitality by Roche, AbbVie, Mundipharma, Pfizer, Roche, Sanofi and UCB, Consultant for: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi and UCB, Consultant for: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi and UCB, Consultant for: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi and UCB, Consultant for: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi and UCB.


FRIO725-HPR | A TAILOR-MADE EXERCISE PROGRAM DESIGNED FOR IMPROVING CARDIORESPIRATORY FITNESS IN PATIENTS WITH RHEUMATOID ARTHRITIS AND INCREASED CARDIOVASCULAR RISK

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Background: Rheumatoid arthritis (RA) is associated with low levels of cardiorespiratory fitness (CRF), especially in patients with RA and cardiovascular (CV) risk. The optimization of management of CV risk in patients with RA is an important aim in the treatment, including also exercise, particularly in patients with RA with a high CV risk, defined as a 10-year CV risk of 20% or higher. However, exercise to improve CRF in these patients is challenging since professionals should take multiple factors into account, such as comorbnd conditions related to CV risk. It is unknown which intensity of exercise improves CRF and is safe for patients with RA and CV risk.

Objectives: To design a tailor-made exercise therapy program to improve CRF for patients with RA and CV risk >20%.

Methods: To design a tailor-made exercise therapy program, patients and experts’ opinions were collected, and a systematic literature search on exercise programs in RA and CV risk factors was performed. The ACSM guidelines were also used to gain insight into frequency, intensity, type and progression of the exercises. In addition, a cardiology rehabilitation team and an arthritis rehabilitation team were consulted during the development of the program. The designed program was partly based on cardiac rehabilitation protocols and especially the way the training load was progressively increased, and the tolerability was assessed at every training.

Results: The exercise program, based on the individual maximum HR, is tolerable and safe and might increase cardiorespiratory fitness in patients with RA


FRIO726-HPR | DOES ART THERAPY MAKE A DIFFERENCE IN THE MANAGEMENT OF CHILDREN AND YOUNG PEOPLE WITH RHEUMATIC DISEASES: A MULTI-SITE SERVICE REVIEW TO EXPLORE THE IMPACT OF ART THERAPY IN TWO TERTIARY PAEDIATRIC RHEUMATOLOGY SERVICES IN SCOTLAND

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Background: Art therapy interventions in various medical settings are known to contribute to the mental health and wellbeing of patients. In paediatric rheumatology, there is a well documented unmet need for psychological support for children and families coping with chronic disease and its treatment. The role that art therapy could have in this provision is unknown and there is no evidence-based research to help understand its potential contribution. The Teapot Trust is a Scottish charity working with paediatric rheumatology services offering art therapy to children and young people with rheumatic diseases.

Objectives: This project aimed to evaluate the service provided by art therapists in two tertiary paediatric rheumatology units in Scotland. The objective was to better understand which patients were referred for art therapy; why they were referred; levels of engagement and acceptability of therapy and benefit resulting in improved outcome.

Methods: A retrospective review was conducted of referrals received in the period 2012-2018 to art therapy from paediatric rheumatology services. A mixed method approach was used for gathering quantitative, secondary and qualitative data. Quantitative data was collected by collating numerical and demographic information from referral forms; art therapist service databases; and patient medical records. Secondary and qualitative data has been gathered from pre-existing service information; the use of outcome measurement tools; end of therapy evaluations; end of therapy reports and patient feedback forms.

Results: The demographics of children seen were as expected in a paediatric rheumatology service with the majority being females with juvenile idiopathic. To guarantee safety, the training load was progressively increased, and the tolerability was assessed at every training. Exercises consisted of aerobic and muscle strength exercises. The first four weeks patients trained 30 minutes (which were spread over three exercises) on 65% of the HR max which was gradually increased until 75% of the HR max in the sixth week. From the fifth week three exercises to improve muscle strength were added to the program. From the seventh week interval training started, with a peak of 85% of the HR max and a rest of 65% of the HR max. The program also included motivational interviewing because one of the main reasons for a high CV risk is the inactivity during daily life. All patients were motivated to perform 30 minutes of moderate exercises every day at home.

Conclusion: A tailor-made exercise program to improve cardiorespiratory fitness in patients with RA and CV risk is developed, based on the opinion and expertise of patients and health professionals and supported by a literature review and guidelines. A progressively increase in intensity of the exercise program, based on the individual maximum HR, is tolerable and safe and might increase cardiorespiratory fitness in patients with RA and CV risk.

References:

Disclosure of Interests: Joëlle van den Hoek: None declared, Martin van der Esch: None declared, Marthe van der Leeden: None declared, Willem Lems Speakers bureau: Amgen Inc., Merck, Eli Lilly and Pfizer, George Metsios: None declared, George D Kilas: Speakers bureau: GDK, Has received honoraria for lectures, participation in advisory boards and/or hospitality by Roche, AbbVie, Mundipharma, Pfizer, Roche, Sanofi and UCB, Consultant for: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi and UCB, Consultant for: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi and UCB, Consultant for: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi and UCB.

Conclusion: This retrospective multi-site service review demonstrated that art therapy was well used by clinicians as an appropriate psychological support for children and young people with rheumatic diseases. Engagement with the service was good and feedback positive. The review highlighted the challenge of objectively assessing outcomes, with the need to use validated and standardised assessment tools to collect this systematically. A standardised service evaluation framework will be developed to facilitate future service reviews and is hoped that this represents a first step in developing evidence-based research to investigate the impact and benefit of art therapy in supporting children and young people in paediatric rheumatology.

Disclosure of Interests: None declared


HPR Patients’ perspectives, functioning and health (descriptive: qualitative or quantitative)

FR107268-HPR

INVESTIGATION OF PHYSICAL ACTIVITY LEVELS OF PATIENTS WITH BEHÇET’S DISEASE

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Background: Behcet’s disease (BD), which is followed by a chronic course, is characterised by recurrent mucocutaneous lesions, oral aphthae, genital ulcers, and eye lesions. BD affects skin and mucosal lesions, joint involvement and eye involvement which can cause visual loss. It disrupts the physical and mental health of the individual as well as the disability of the physical functions and can affect the quality of life negatively (1, 2). There is strong evidence for the benefits of Physical activity (PA) on improvements in disease activity, activities and participation; however, people with rheumatic and musculoskeletal diseases (RMDs) are in general less active compared with healthy controls (3-5).

Objectives: The aim of the study was to evaluate PA in patients with BD and also to compare status of PA with healthy controls.

Methods: 67 patients (female=49, male=18) with BD and 66 healthy peers (female=43, male=23) were enrolled in the study. The subjects were recruited in a rheumatology clinic. They were diagnosed with BD by a rheumatologist based on the clinical diagnostic criteria. PA was evaluated with International Physical Activity Questionnaire-Short Form (IPAQ-SF) in all participants. Metabolic Equivalent (MET) values were calculated due to IPAQ-SF. In addition, the pain and fatigue status of patients with BD was asked.

Results: The mean age of the patients was 42.95±10.60 years. The mean disease duration was 14.14±5.13 years. The means of physical activity MET scores were 699.74±508.09 and 2006.75±1162.16 in patients with BD and healthy peers, respectively. It was found that the means of PA MET scores in BD was significantly decreased compared with healthy peers (p<0.001). While 53.7% of patients with BD had low levels of PA and 46.3% had moderate levels of PA, 9.1% of healthy subjects had low level of PA, 47% of them had moderate levels of PA and 43.9% high levels of PA (p<0.001). 86.6% of patients with BD reported pain, 73.1% of them also reported fatigue.

Conclusion: This is the first study to evaluate PA in patients with BD. The level of PA was significantly lower in patients with BD compared to their healthy peers. Decreased PA may be associated with pain and fatigue frequently seen in patients with BD. In future studies, it is recommended to investigate the factors affecting PA in patients with BD.

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References:


Disclosure of Interests: None declared


HPR PATIENTS’ PERSPECTIVES, FUNCTIONING AND HEALTH (DESCRIPTIVE: QUALITATIVE OR QUANTITATIVE)

FR10727-HPR

PREDICTORS OF FUNCTIONAL CAPACITY AT 24 MONTHS FOLLOW-UP IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in childhood and it causes short and long-term disability. Periodic assessment of functional capacity is important to determine the presence or absence of physical disability.

Objectives: To identify predictive factors of absence of functional disability after 24 months follow-up in a cohort of children with JIA treated at a tertiary referral hospital.

Methods: Longitudinal, retrospective, analytical, and observational study. Patients who met the following criteria were included in the study between 2013 and 2016:1 to 16 years old, diagnosis of JIA according to the International League of Associations for Rheumatology (ILAR); recently initiated (3 months) care at our clinic, complete C-HAQ (Childhood Health Assessment Questionnaire) records throughout the follow-up period. Patients were treated according to current guidelines for pharmacological and physical therapy. Functional capacity was assessed according to the C-HAQ every 3 months. For the analysis, the C-HAQ scores were divided into 3 categories: 0 - 0.49 (absence of disability), 0.5 - 1.5 (mild to moderate disability), and 1.51 - 3 (severe disability). Univariate comparisons were made to determine the relationship between different variables with the dependent variable ‘absence of functional disability at 24 months of follow-up’. Independent variables included: disease activity, functional capacity, and treatment-related outcome measures. Those with p values <0.05 were included in a multiple logistic regression analysis. The model was adjusted for basal functional capacity and inflammatory activity at 6 months. Items with a p value <0.05 were considered significant. Adjusted odds ratios (adjOR) and 95% confidence intervals (95% CI) are reported as a measure of association. The precision of the model was analyzed through the Area under the Curve (AUC).
Results: Of a total of 148 patients, 122 met the inclusion criteria. Median age: 7.4 years (IQR 1.1-16.9), 69 female (56.6%). Most patients had Polyarticular (44 patients, 36.1%) or oligoarticular (33 patients, 27%) JIA. At the beginning of the study, 36 patients (29.5%) did not show functional disability; 70 (57.4%) exhibited mild/moderate disability and 16 (13.1%) severe disability. At 24 months, 73 patients (59.8%) had no disability; 37 (30.3%) moderate/mild disability and 12 (9.8%) severe disability. In the multiple logistic regression model, performing regular physical therapy (PT) (adjOR 6.83 [95% CI 2.26 - 20.61], p = 0.001), starting PT within 12 months after diagnosis (adjOR 5.45 [95% CI 1.83 to 16.18], p = 0.002), baseline pain Visual Analogue Scale (pVAS, 0-10) less than 3 (adjOR 4.55 [95% CI 1.58 to 13.12], p = 0.005) and adherence to pharmacological treatment (adjOR 15.23 [95% CI 1.86 to 124.8], p = 0.011) were independent factors for not presenting functional disability at 24 months. The area under the model curve was 0.92 (95% CI 0.88 to 0.97).

Conclusion: The findings of this study reinforce the need of early and regular PT and medical treatment in children with JIA, in order to maintain or improve functional capacity over time. These results are not only statistically significant but clinically relevant since they reflect impact in functional skills in this population. Further studies are needed to confirm these outcomes in larger cohorts with longer follow-up.

REFERENCES:

Disclosure of Interests: None declared

FR0728-HPR | PERCEPTIONS OF PHYSICAL ACTIVITY IN INDIVIDUALS WITH RA – A QUALITATIVE THEMATIC SYNTHESIS
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Background: The effects of physical activity (PA) in rheumatoid arthritis (RA) are well documented and PA is besides pharmacological interventions considered a cornerstone in the treatment. Despite this, many individuals with RA do not reach recommended levels of PA. To highlight aspects involved in supporting a positive PA behavior it is important to understand the patients’ perceptions of the phenomenon. Several qualitative studies have been conducted throughout the years, describing perceptions on physical activity in RA.

Objectives: The aim of this study is to review and synthesize the qualitative literature on physical activity in rheumatoid arthritis.

Methods: A purposive search in electronic databases (MEDLINE, CINAHL, and PEDro) using combinations of terms such as “qualitative methods, qualitative study, interviews, physical activity, exercise and rheumatoid arthritis”, from inception to July 2018 was carried out. Title/abstract and full-text screening were conducted independently by 2 researchers. Further, back-tracking of reference list of retrieved articles was made, and contacts were taken with known experts in the field. Studies were eligible if they qualitatively explored perceptions of different aspects of PA in individuals with RA. Eligible articles were appraised using the McMaster Critical review form. All relevant data were extracted from eligible articles and analyzed inductively using thematic analysis.

Results: 11 primary studies met the inclusion criteria. Studies were conducted in Denmark, Ireland, New Zealand, Sweden, United Kingdom and the United States of America. The sample included 170 individuals with rheumatoid arthritis (129 women, 41 men, aged 21-83). Across the studies, preliminary themes were found: worries and fear (increasing symptoms, worries the disease, safety), awareness of PA (knowledge, information, discussion), social support (competence, guidance, demands, joy), effects on health (retain independence, decrease symptoms, coping with the disease), body awareness (adaptation, pacing, listen to the body, self-efficacy) and determination (motivation, focus, goals, priorities, responsibility). A preliminary synthesis was performed and the continuous interrelation between the themes and the disease itself was described.

Conclusion: It is important that the promotion of PA in individuals with RA is in line with individual challenges and resources, in order to enhance adoption and maintenance of PA behavior. In RA, the disease seems to pervade all aspects related to the individuals’ perception of physical activity. Strategies to enhance this behavior should therefore include minimizing negative perceived consequences of physical activity by raising both cognitive and physical awareness. Another strategy could be focusing on finding proper social support either within health care or preferably outside of health care but with a sense of affinity. Finally, strengthening the individual’s ability to use self-regulation strategies to overcome barriers should be emphasized.

REFERENCES:

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FR0729-HPR | LIVING EVERY-DAY LIFE IN THE SHADOW OF PAIN OR LIVE EVERY-DAY LIFE WITH THE PAIN IN THE SHADOW – A CONSTANT BALANCING
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Background: Approximately 10% of the population report chronic widespread pain (CWP), the condition is more common in women than in men. Long-term pain is a public health problem. For most women, the pain interferes with many aspects of every-day life and implies large consequences. Thus, knowledge about how to facilitate life for these women is important.

Objectives: To explore women’s experiences of how CWP influence their daily life.

Methods: The study has a latent qualitative content analysis design. Individual interviews were conducted in 19 women 45-67 of age, who had reported CWP in a survey 2016. CWP was defined according to the 1990 ACR criteria for fibromyalgia. Pain that had lasted for more than three months, during the last 12 months, was considered chronic. A latent qualitative content analysis was used to analyze the main questions “Can you describe your experiences of living with CWP?” and “How do the CWP influence your life today?” The interviews were recorded, transcribed verbatim and coded into eight subcategories and three categories; represent the manifest content, and a latent theme exploring the interpreted content of women’s experiences of how CWP influence their every-day life.

Results: The interviewed women expressed a life with CWP as “Living every-day life in the shadow of pain” or “Living every-day life with the pain in the shadow” including three categories; the experience of alienation, limitations and plasticity.

1) The experiences of alienation appeared in the subcategories; suspicion and loneliness. Suspicion meant a feeling of not being seriously by healthcare and authorities and loneliness meant not being able to participate in social contexts. 2) The experiences of limitations in daily life includes the subcategories; barriers, stress, and dependence of other people. Barriers meant that fatigue limits the activities in every-day life, stress that constitutes limitations in life and dependence of other people’ support. 3) The experiences of plasticity referred to the subcategories resignation, adjustment and resistance. Resignation meant refraining from activities that could affect the pain, such as gardening, walking and dancing. Adjustment were manifested by making the best of the situation, and resistance meant to resist letting the pain set the terms, to give the pain a fight.

Conclusion: Women with CWP have to deal with their physical, mental, social and spiritual environment in every-day life. They express a constant balancing in their life between mastering the pain in order to continue living as normal, and allowing the pain to set the terms, i.e. living every-day life in the shadow of pain or live every-day life with the pain in the shadow. Healthcare professionals may consider supporting the patients in finding their individual counterweight to manage life in order to reach better treatment outcome.
Background: Pts with systemic lupus erythematosus (SLE) have an increased risk for cardiovascular diseases (CVD) that cannot be explained by traditional risk factors only. Its relevant to search novel cardiovascular risk markers in those pts.

Objectives: We aimed to evaluate carotid atherosclerosis presence in females with SLE and its relationship with traditional and nontraditional cardiovascular risk factors.

Methods: 52 females with low-activity SLE (the median age – 48.2 [41.8; 52.9] years, the median duration of SLE 89.4 [68.9; 101.5] month) without verificated coronary artery disease were enrolled. Control group included 30 pts without SLE compared by risk factors profile. The cardiovascular risk was calculated using SCORE. The total cholesterol (TC), lipoproteins, triglycerides (TG) were measured in the blood. Carotid ultrasound, endothelial-dependent flow mediated vasodilatation (EDVD) by D. Celemajer method were performed. In all pts was calculated body mass index (BMI) and measured blood pressure (BP). All pts received steroid therapy.

Results: High levels of TC, LDL and TG were in 55.8%, 61.5% and 25% of pts with SLE (the median levels 5.9 [5.2; 6.4] mmol/l, 4.1 [3.7; 4.8] mmol/l and 1.8 [1.3; 2.4] mmol/l respectively). The obesity and hypertension were estimated in 51.9% and 63.5% respectively (median BMI – 31.6 [28.4; 33.2] kg/m^2, median systolic BP – 154.2 [138.4; 162.3] mm Hg, median diastolic BP – 90.2 [82.4; 93.7] mm Hg). EDVD was impaired in 32.6% pts with SLE and 16.7% control pts (p<0.05). Carotid atherosclerosis was established in 41 (78.8%) pts with SLE and 48 (54%) control group pts (p<0.05). The majority of pts with SLE have stable carotid atherosclerotic plaques - 32 (61.5%), unstable plaques - 6 (11.5%) pts, in control group – 10 (33.3%) and 2 (6.7%) pts respectively. In the same time the median cardiovascular level matched by SCORE was 2.1 [1.5; 2.9]% in females with SLE, in control group - 1.8 [1.3; 2.5]% (p<0.05). The presence of carotid atherosclerotic plaques in females with low-activity SLE was associated with endothelial dysfunction (OR=2.5, p<0.002), obesity (OR=1.5, p<0.004), duration of steroid therapy (OR=2.8, p<0.0005).

Conclusion: Females with low-activity SLE and moderate cardiovascular risk level are characterized by high frequency of carotid atherosclerosis. The carotid ultrasound may be useful additional tool for the evaluating of cardiovascular risk in these patients.

Disclosure of Interests: None declared

SAT0001
FOSL-2 IS A REPRESSOR OF FOXP3 EXPRESSION DURING TREG DEVELOPMENT AND CONTROLS AUTOIMMUNITY

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Background: Fos like 2 (Fosl-2) is a transcription factor belonging to the AP-1 transcription complex. We have recently described a Fosl-2 transgenic (tg) mouse model which develops a multi-organ inflammatory and autoimmune phenotype. In these mice, we have characterized a decrease in regulatory T cells (Tregs), which preceded the activation of T cells and the development of inflammation.

Objectives: To analyze how Fosl-2 reduces the Treg population and triggers autoimmunity in Fosl-2 tg mice.

Methods: We used previously generated Fosl-2 tg overexpressing and Fosl-2 T cell specific knock out (Fosl-2 ko) mice. For mixed bone marrow transfer experiments, lethally irradiated recipients received a one to one mix of Fosl-2 tg (CD45.2) and wt (CD45.1) bone marrow to create Fosl-2 tg-wt chimera. We addressed the contribution of Tregs to the inflammatory phenotype by co-transferring Fosl-2 tg CD4 T cells and wt Tregs to Rag2-/- recipient mice. Tregs and T cell populations were analyzed by flow cytometry and inflammation was addressed by CD45 staining on paraffin-embedded sections. RNA-sequencing was used to compare wt, Fosl-2 tg and Fosl-2 ko CD4 T cells 24 hours after stimulation with anti-CD3 (2 μg/ml) and anti-CD28 (2 μg/ml).

Results: We first addressed whether Fosl-2 affected Tregs in a cell intrinsic way using mixed bone marrow experiments. In these animals, the CD45.2 Fosl-2 tg CD4 T cells showed a much lower proportion of Tregs compared to the CD45.1 wt population, both in the spleen (0.73%±0.15 vs. 31.6%±3.6, P=0.002) and thymus (1.3%±0.04 vs 3.23%±0.78, P=0.001). This demonstrates that Fosl-2 overexpression represses Treg development in a cell intrinsic way.

In T cell transfer experiments, Rag2-/- mice receiving 10^6 Fosl-2 tg CD4 cells developed lung inflammation 5 weeks after transfer, confirming that T cells are inducers of inflammation in Fosl-2 tg mice. Moreover, co-transfer of either 3*10^6 or 10^7 wt T cells resulted in a dose dependent reduction of inflammation. These data indicated that the decrease in the Treg population in Fosl-2 tg mice is responsible for the induction of inflammation.

We then analysed Fosl-2 transcriptional targets in T cells by RNA-seq. Using a fold change > 1.5 and False Discovery Rate (FDR) of 0.05, we identified 191 differentially expressed genes in both Fosl-2 tg and Fosl-2 ko cells compared to wt. Interestingly, one of the top target genes of Fosl-2 was Foxp3. This unbiased approach thus revealed that Foxp3 expression is repressed by Fosl-2, with a 6.5 fold reduction in Fosl-2 tg cells and a 2.5 fold increase in Fosl-2 ko cells. This effect was confirmed on the protein level with a reduction in Foxp3 induction in Fosl-2 tg cells treated with TGFβ. The repression of Treg development observed in Fosl-2 tg mice could thus be explained by a direct transcriptional control of Foxp3 expression. Additionally, we found that Fosl-2 repressed a set of genes known to be important for Tregs and other T helper cells. This included Nr4a2, a transcription factor involved in Treg development, IRF8 and Eomes, two genes involved in the polarization of Th1 and Th17 cells, or Ccl1 a chemokine important for Treg homeostasis.

Conclusion: Fosl-2 is involved in the control of Foxp3 expression in T cells. Through this, overexpression of Fosl-2 represses Treg development and induces a Treg dependent autoimmune phenotype in mice. This mechanism could thus be involved in the pathogenesis of autoimmune diseases and might represent a therapeutic target to modulate the Treg population.

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References

Background: We previously showed PIM1, among other STAT3-target genes, to be strikingly upregulated in circulating CD4+ T cells of treatment-naïve ‘early’ rheumatoid arthritis (eRA) patients. PIM1 has a recognized role in T cell development, has been implicated in the pathogenesis of autoimmune disorders, and is the target of specific inhibitors in clinical development in oncology; for example PIM1 was recently identified as a promising target in triple-negative breast tumours.

Objectives: We sought to understand the relevance of dysregulated PIM1 gene transcription for T-cell pathobiology during disease initiation and to determine the effects of its inhibition on T cell function. We hypothesised that, amongst a readily-identifiable, high PIM1 expressing subgroup of eRA patients, PIM1 overexpression in CD4+ T cells is a targetable early event in pathogenesis that lies downstream of STAT3-mediated IL-6 signalling.

Methods: Peripheral blood was obtained from consenting treatment-naïve arthritis patients or healthy donors and highly pure CD4+ T cells were isolated. PIM1 knock-down (SMARTpool siRNA, Dharmaco) or protein inhibition (small molecule inhibitors; PIM1-selective TCS-PIM-1, Tocris and panPIM AZD1218) was undertaken. Flow cytometric analysis was then used to assess activation and proliferation following CD3/CD28-mediated stimulation.

Results: In eRA, ex vivo CD4+ T cells exhibited an activated, hyper-proliferative phenotype compared to those isolated from healthy donors. Significantly higher PIM1 mRNA expression in CD4+ CD4+ T cells was seen using PrimeFlow (flow cytometry) compared to that of other inflammatory arthritides. Both PIM1 knock-down, PIM1-specific and panPIM inhibition decreased the activation and proliferation of stimulated eRA (Figure 1A) and healthy donor CD4+ T cells. Moreover, in eRA, PIM1 and panPIM inhibition increased FoxP3 expression (Figure 1B) and increased the proportion of regulatory T cells (Figure 1C).

Conclusion: Taken together, these data implicate PIM1 as prominent among genes whose induction may ‘pre-programme’ CD4+ T cells to function aberrantly in disease. Conceivably, targeting PIM1 may prove an attractive approach to regulating aberrant CD4+ T cell effector function in an identifiable sub-population of early RA patients that exhibit high CD4+ T cell PIM1 expression in their peripheral blood.

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DETECTION OF HIGHLY EXPANDED T CELL CLONES IN THE PERIPHERAL BLOOD OF AT RISK INDIVIDUALS FOR RHEUMATOID ARTHRITIS BEFORE THE CLINICAL ONSET OF THE DISEASE

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Background: Rheumatoid arthritis (RA) is an autoimmune disease with unknown etiopathogenesis. Systemic autoimmunity precedes clinical disease onset, and current evidence suggests that the immune onset of RA takes place out of the joints several years before clinical manifestations. Expanded T cell clones can be found in the synovial tissue of established RA patients. The mechanisms by which systemic immune abnormalities progress to joint-specific autoimmunity are not yet understood.

Objectives: To examine if expanded T cell clone signatures can be detected in the peripheral blood before the development of clinical RA.

Methods: Next-generation sequencing of the T Cell Receptor β (TCRβ) CDR3 repertoire was performed on genomic DNA isolated from blood samples of individuals genetically at risk for RA, namely first-degree relatives of RA patients (RA-FDR) at different pre-clinical phases of disease development (SCREEN-RA cohort), and of matched RA patients used as a control group (SCQM cohort). All individuals were matched for age and sex, and categorized into four groups (n=20/group): Group 1: healthy asymptomatic RA-FDR without autoantibodies or symptoms associated with possible RA. Group 2: Asymptomatic RA-FDR with evidence of systemic autoimmunity associated with RA defined by high levels of anti-citrullinated peptide antibodies (ACPA; 3x> ULN). Group 3: RA-FDR having presented undifferentiated arthritis (n=8) or having developed classifiable RA after inclusion (n=12). Group 4: patients with established RA of less than 3 years duration. T cell clones were identified by their unique TCRβ CDR3 sequence. Clones with a frequency over 0.5% were considered to be highly expanded clones (HEC). Both absolute number and frequency of productive T cell clones was compared between the 4 groups using mixed effect regression models to account for matching.

Results: As expected, the large majority of clones in the peripheral blood were detected at very low frequency (<0.1%) in all groups (Figure 1A). Interestingly, expanded clones (>0.1% of total TCR analysed) tended to occur more frequently in later preclinical phases and established disease. A significant difference among groups was observed for highly expanded clones (HEC) (p=0.001). Specifically, the absolute number of HEC was significantly higher in RA patients (group 4; mean 4.65, p=0.003) and tended to be higher in symptomatic RA-FDR (group 3; mean 3.4, p=0.07) compared to “healthy” RA-FDR (group 1; mean 1.55, Figure 1B). A trend towards a higher frequency of the top 50 expanded clones was also observed in symptomatic RA-FDR (group 3; mean 0.17%) compared to “healthy” RA-FDR (group 1; mean 0.11%). At risk individuals defined by the presence of high ACPA levels (group 2) did not differ from “healthy” RA-FDR in terms of absolute number and frequency of clones.

Conclusion: For the first time, highly expanded T cell clones were detected in the peripheral blood of at risk individuals before the clinical onset of RA, in particular in the later pre-clinical phases of RA development. Tracking these dominant T cell clones in longitudinal analyses and elucidating their role might help to better understand the earliest pathogenic events in RA.

REFERENCE

(n=8) were analysed by flow cytometry. Intrasubject differences were assessed by paired parametric t tests and comparison with PBMC from HV (n=6) by unpaired parametric t test. Parametric data are reported as mean differences (MD) [95%CI]. P values < 0.05 were considered significant.

Results: Among memory prone T cells (CD3+CD4+CD45RO+) in SFMC, the percentage of Tim-3+ cells was increased compared with similar gated PBMC from patients (MD 17.4%, [10.7;24.1], p<0.005) and HV (MD 12.9%, [4.1;21.8], p=0.007). In the joint, more of these Tim-3+ cells co-expressed PD-1 compared with similar gated PBMC (MD 42.8%, [27.8;57.9], p<0.005) (Figure 1). On average, sTim-3 plasma levels were higher in eRA compared with HV (MD 4.6 ng/ml, [3.3;5.9], p<0.005) (Figure 2). In eRA, baseline sTim-3 levels correlated with DAS28CRP (rho=0.28, p=0.048), eRA patients with TSS progression within 24 months of treatment decreased more in plasma sTim-3 during 3 months of treatment compared with patients without TSS progression (median [progression] -1.4 ng/ml, median [no progression] -0.5 ng/ml (U=649.5), p=0.048). The decrease in plasma sTim-3 was not influenced by treatment (median [MTX+ADA] -1.2 ng/ml (U=1015), p=0.4). In SF, sTim-3 levels were increased compared with plasma (MD 37.4 ng/ml, [26.3;48.4], p<0.0001).

Conclusion: Tim-3 expression is upregulated in memory prone T cells in RA joints and the majority co-express PD-1. Levels of sTim-3 are increased in SF. In eRA, baseline sTim-3 plasma levels are elevated and correlate with DAS28CRP. Decrease of sTim-3 during treatment associates with future radiographic progression. We suggest, that Tim-3 expression in memory T cells increased compared with patients without TSS progression (median [progression] -1.4 ng/ml, median [no progression] -0.5 ng/ml (U=649.5), p=0.048). The decrease in plasma sTim-3 was not influenced by treatment (median [MTX+ADA] -1.2 ng/ml (U=1015), p=0.4). In SF, sTim-3 levels were increased compared with plasma (MD 37.4 ng/ml, [26.3;48.4], p<0.0001).

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REFERENCE
IL-23 DRIVES PATHOGENIC TH17 CELLS THROUGH EPIGENETIC REGULATION BY STAT3 IN SLE PATIENTS

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Background: Systemic lupus erythematosus (SLE) is a systemic autoimmune disease characterized by loss of self-tolerance and by broad immune dysregulation, which result in overproduction of autoantibody and immune complexes, leading to the development and progression of SLE. Mechanism underlying their pathogenicity remains widely elusive in human.

Methods: Human naive CD4+ T cells were cultured by Th17 polarizing condition (TGF-β, IL-6, and IL-1β) for 5 days in vitro. To examine the role of specific cytokine, we measured the expression of IL-23 in the response to Th17 cells. We added various cytokines including IL-23 at the late time point (72h), Expression of characteristic markers of pathogenic Th17 cell and STATs phosphorylation (p-STATs) were analyzed by flow cytometry and qPCR. The effect of baricitinib which is Jak1/2 inhibitor on maturation of Th17 cell was investigated. Histone modifications were assessed by chromatin immuno-precipitation (ChIP)-PCR. To define the signals mediated by cytokine required for expansion of Th17 cell in SLE, Th17 phenotype and pSTATs were analyzed from blood samples of lupus patients by multi-color flow cytometry.

Results: In vitro, re-stimulation of Th17 cells with IL-23 markedly induced the characteristic markers of pathogenic Th17 cells such as RORγt and IL-17. IL-23-orientated cytokine response drives p-STAT3, not p-STAT4 for development of mature Th17 cells. IL-23-induced p-STAT3 was inhibited by baricitinib. In addition, proliferation of Th17 cells was suppressed by baricitinib in concentration-dependent manner. The loci of RORγt at STAT binding sites were marked by bivalent histone modifications. After IL-23 stimulation, STAT3 exclusively bound on RORγt gene loci supplemented by activating H3K4me3 and repressing H3K27me3 modifications. In memory Th17 cells, high proportion of IL-23R expression and STAT3/4 activation were identified from SLE patients compared with healthy individuals. Moreover, p-STAT3 was hypersensitively activated by IL-23 stimulation in memory Th17 cell only from lupus patients but not from healthy controls.

Conclusion: This study proves that IL-23 serves as a pivotal factor that drives expansion of pathogenic Th17 cells. IL-23-mediated STAT3 alter histone modification, resulting in inflammatory function of pathogenic Th17 cell that are characteristic in patients with SLE. These findings could be one of the underlying mechanisms of pathogenesis of SLE and helpsful evidence toward novel therapeutic targets for SLE.

REFERENCE

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THE EFFECT OF FCGR3A POLYMORPHISM ON THE INITIAL DEPTH OF B-CELL DEPLETION BY RITUXIMAB, FUNCTIONAL NK-CELL MEDIATED KILLING AND CLINICAL RESPONSE IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Antibody-dependent cellular-mediated cytotoxicity (ADCC) is an important effector mechanism that contributes to the depletion of therapeutic antibody-opsonised cells in vivo. Rituximab (RTX) is an anti-CD20 antibody with a native IgG1 Fc, which crosslinks Fc receptors (FcγRs) expressed on immune effector cells. NK cells, which express FcγRIIIa, are believed to play an important role with less-well-characterised contribution from monocytess/macrophages and neutrophils. A genetic variant in FCGR3A (158V) with an increased affinity for IgG1 has been reported to correlate with clinical response to RTX in RA[1]. Data in SLE are limited as the FCGR locus is characterised by structural variation making genotyping challenging.

Objectives: To assess the effect of FCGR3A-F158V polymorphism on (i) the initial depth of B-cell depletion by RTX; (ii) its functional effect on NK cell-mediated killing (iii) clinical response and (iv) 10-year RTX retention for the treatment of SLE.

Methods: A prospective longitudinal study was conducted in RTX-treated SLE patients in Leeds. B-cells were measured at baseline and 6 weeks using highly sensitive flow cytometry. Complete depletion was defined as total B-cell count<0.001 x 10^9/L. A major clinical response (MCR) was defined as improvement of all active BILAG-2004 domains to grade C/better and no A/B flare at 6 months. We measured qualitative polymorphism for FCGR3A using a multiplex ligation-dependent probe amplification as previously described[2]. Median expression of FcγRIIIa on NK cells in the presence of RTX-coated Raji cells (B-lineage cell line) were assessed using flow cytometry.

Results: 85 SLE patients with at least 2 x BILAG B were studied [Female: 82(96%); mean age (SD): 40(14) years; 60(71%) on concomitant DMARDS; ANA positive: 100%]. In cycle 1 RTX, 64/85(75%) achieved BILAG response [major=36%; partial=39%]. Both complete depletion and MCR were associated with carriage of the FCGR3A allele (158FV or 158VF), OR 2.73 (95% CI 1.13-6.58) and 3.06 (95% CI 1.19-7.58) vs 158FF, respectively. Patients who had complete B-cell depletion post-RTX had higher level of FcγRIIIa on NK cells vs incomplete depletion; p=0.006. Comparing patients with FCGR3A-158V allele carriage vs FF genotype, there was a trend to higher expression of CD3-CD56-CD16+ in the former p=0.073. Moreover, degranulation as defined by ratio between%CD107a+NK cell in Raji cells vs incomplete depletion; p=0.006. Comparing patients with FCGR3A-158V allele carriage vs FF genotype, there was a trend to higher expression of CD3-CD56-CD16+ in the former p=0.073. Moreover, degranulation as defined by ratio between%CD107a+NK cell in the presence of Raji cells + RTX and%CD107a+NK cell in Raji cells only, was higher in the V allele carriers vs FF genotype; p=0.024. Over 10-year follow-up, 27/85 (31.8%) had stopped RTX [primary inefficacy=7; secondary inefficacy=8; HACA=10; death=2]. FCGR3A-158FF genotype was associated with increased risk of RTX discontinuation; OR 2.36 (95% CI 1.08-5.18) after adjusting for age and DMARDS.

Conclusion: An ADCC-enhancing FcγRIIIa variant was associated with initial complete B-cell depletion and MCR in RTX-treated SLE patients. This was supported by functional data on NK cell-mediated cytotoxicity and 10 year outcomes. These results elucidate one mechanism of resistance to rituximab in SLE and may guide development of more effective B-cell targeted strategies. With further validation, this polymorphism may be used to stratify SLE patients for therapy.

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SA0010
FUNCTIONAL BIOMARKER DEVELOPMENT FOR CELL- BASED THERAPY IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid Arthritis (RA) is an autoimmune disease in which faulty treatment prevents joint damage. Autoantibodies such as rheumatoid factors (RF) and anti-citrullinated peptide antibodies (APCA) define a subset of RA patients at the highest risk for damage. Reduction of RA disease activity is associated with improvement in function(s) of regulatory T cells (Treg) and attenuated responses of pro-inflammatory T effector cells (Teff). Human Mesenchymal Stem Cells (hMSC) isolated from bone marrow and culture-expanded have strong immunomodulatory properties; we hypothesize that therapeutic use of hMSC may skew the immune system to resemble its pre-RA state. Lack of available biologic correlates measured early-on that indicate response to treatment limits efficacy assessment of cell-based therapy. Use of clinical response criterion requires large numbers of patients and may be impractical in early stage clinical trials. This work was performed in anticipation of conducting a Phase I safety trial of cell-based therapy in early RA.

Objectives: We set out to develop functional assay(s) as biomarkers of response that would indicate early-on that hMSC were or were not modulating immune function in a manner that could potentially predict potency and efficacy in RA patients.

Methods: Sero-positive female patients with active early RA (RAPID 3 avg 5.7/10 (high severity)) and healthy donor age and sex-matched controls were enrolled. Second passage bone marrow hMSCs were obtained from healthy donors < 30 y.o. (Case Comprehensive Cancer Center Hematopoietic Biorepository and Cellular Therapy Core), Peripheral blood CD4+ T cells were stimulated by cross-linking CD2/CD3/CD28 for 5 days. CD4+ T-cell proliferation rates were measured, and suppression indices defined a subset of RA patients at the highest risk for damage. Autoantibodies such as rheumatoid factors (RF) and anti-citrullinated peptide antibodies (APCA) define a subset of RA patients at the highest risk for damage. Reduction of RA disease activity is associated with improvement in function(s) of regulatory T cells (Treg) and attenuated responses of pro-inflammatory T effector cells (Teff). Human Mesenchymal Stem Cells (hMSC) isolated from bone marrow and culture-expanded have strong immunomodulatory properties; we hypothesize that therapeutic use of hMSC may skew the immune system to resemble its pre-RA state. Lack of available biologic correlates measured early-on that indicate response to treatment limits efficacy assessment of cell-based therapy. Use of clinical response criterion requires large numbers of patients and may be impractical in early stage clinical trials. This work was performed in anticipation of conducting a Phase I safety trial of cell-based therapy in early RA.

Objectives: We set out to develop functional assay(s) as biomarkers of response that would indicate early-on that hMSC were or were not modulating immune function in a manner that could potentially predict potency and efficacy in RA patients. Serial serum from healthy donors and RA patients were studied in vitro to determine if hMSC-conditioned medium could modulate cell activity. hMSC were cultured with and without hMSC-conditioned medium. Results: hMSC-related suppression 32.2 ±7.8 (mean +/- SE) percent in RA CD4+ T-cells compared to 45.7± 8.9 percent for healthy donors CD4+ T cells. We demonstrated that soluble products from hMSC can inhibit proliferative responses of CD4+ T cells from patients with active RA though the studies were not powered to detect differences between RA and healthy donors. With limited number of early RA patients, correlation between level of MSC-related suppression and antibody status were not possible. That being said, the data trend appears promising.

Conclusion: Our ex vivo experiments demonstrated that hMSCs may be suppressive in RA as well as in healthy donors. To our knowledge, this study is the first demonstration of the potential for using ex vivo suppression assays to predict response to cell-based therapy in early RA. Such assays might be performed to predict the efficacy of selected hMSCs to treat RA.

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SAT0011
TRANSCRIPTOMICS UNVEILS UNIQUE BIOLOGICAL PROFILE OF TERTIARY LYMPHOID STRUCTURES GERMINAL CENTERS

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Background: The development of the B cell repertoire is regulated by the process of affinity maturation occurring within the inner part of the B cell follicles [germinal centers (GCs)] within secondary lymphoid organs (SLOs). In autoimmunity, this process might occur within aberrant aggregates of lymphocytes in target organs, such as the ectopic lymphoid structures (ELS) found in the salivary glands of patients with Sjogren’s Syndrome (SS) (1). The phenotypical and functional features supporting ELS which may sustain the development of autoimmune diseases have not been identified. Moreover, functional proof that ELS contribute to the development of autoimmunity independently from SLOs has not been provided.

Objectives: To characterise the transcriptome profile of human ELS isolated from SS salivary glands in comparison with SLOs.

Methods: Frozen minor salivary gland biopsies were obtained from SS patients and selected for presence of GCs+ ELS. Human tonsils were obtained by volunteers undergoing tonsillectomy for clinical need and used as SLO control. In order to detect GCs, all samples were stained for CD21, bcl6, CD20 and CD3. Sequential sections, were stained by Cressyl Violet and GCs (CD21+ infiltrates) from both salivary glands and tonsil were selectively microdissected (Laser Capture Microdissection). Salivary gland small infiltrates and large CD21- infiltrates were microdissected too. RNA was isolated and transcribed. RNA sequencing studies were performed using ClonTech SMARTseq v4 kit. Changes and differences in the expression of specific genes of interest were confirmed with targeted PCR studies.

Results: Transcriptomics analyses revealed that GCs from ELS and SLO exhibit markedly different gene expression profiles. Of note, sequencing unveiled that GCs from ELS are characterized by an aberrant cell-proliferation profile with downregulation of BCL6 and AID, the enzymes responsible for B cell affinity maturation (both p<0.0001). Also in ELS, progressive upregulation of CD21 transcript mirrored increases in infiltrate size and organization (being lowest in small infiltrates and progressively higher in large CD21+ infiltrates, p=0.002). Similar data were obtained for AID, whose expression was significantly higher in large CD21+ infiltrates compared to small infiltrates (p=0.0006). A cytokine signature was identified in ELS GCs based on the expression of TNF, INFγ, BAFF, APRIL, CXCL12, CXCL13, FAS, and FASL, all of which were upregulated compared to GCs from tonsils.

Conclusion: Our studies reveal that GCs forming in ELS exhibit marked transcriptional differences from classic GCs observed in SLOs. Main features characterizing ELS include lower levels of Bcl6 and AID, aberrant apoptosis, and a pathogenic inflammatory cytokine signature. Despite similarities in the anatomical organization and appearance of GCs in ELS and SLO, critical transcriptional differences emerge, which are likely functionally implicated in impaired regulation of the B cell cycle and survival of autoreactive B cell clones, ultimately leading to the development of autoimmune disease.

REFERENCE

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DISTRIBUTION OF CIRCULATING PR3-SPECIFIC B CELLS IN PATIENTS WITH ACTIVE ANCA-ASSOCIATED VASCULITIS

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OBJECTIVES: To determine CD4+CD25+Foxp3+T regulatory (Treg) cell levels in peripheral blood (PB) of patients with autoimmune diseases (AID) and age- and sex-matched healthy controls, and to explore the correlation between the levels of peripheral Treg cells and clinical parameters in AID.

Methods: A total of 1561 AID patients, and 196 age- and sex-matched healthy controls were enrolled. The absolute numbers of CD4+CD25+Foxp3+Treg and other T subsets [total T, CD4+T, CD8+T, T helper 1 (Th1), T helper 2 (Th2), and T helper 17 (Th17) cells] in PB were measured by Flow Cytometer (FCM). Erythrocyte sedimentation rate (ESR) was analyzed by the Westergren method. Serum concentrations of C-reactive protein (CRP) were measured by monoclonal immunoassay.

Results: The absolute numbers of Treg cells in PB of patients with AID [22.90 (18.31, 36.47); p<0.05], which was also seen in rheumatoid arthritis (RA), Sjogren’s syndrome (SS), systemic lupus erythematosus (SLE), systemic vasculitis (SV), idiopathic inflammatory myopathy (IIM) and other diseases. The levels of CD4+T, Th1/Treg, and Th2/Treg in PB of AID patients were higher than those of healthy controls. (2) The absolute numbers of most T cell subsets in PB of most AIDs were lower than those of healthy controls, but the Treg cells were greatly decreased, significantly. The ratio of Treg to other T lymphocyte subsets were higher than those of healthy controls. (3) The levels of inflammatory indicators were inversely associated with numbers of Tregs, total T, CD4+T, CD8+T, Th1 and Th17/Treg cells.

Conclusion: The absolute numbers or function of CD4+CD25+Foxp3+Treg cells were decreased, so it cannot effectively maintain immune tolerance or inhibit inflammatory response, which may be one of the important mechanisms of disease. Treatment promoting CD4+CD25+Foxp3+Treg cell function may become a new strategy for AID therapy.

References:

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DECREASED CIRCULATING CD19+CD24+CD38hi REGULATORY B CELLS IN ACPA POSITIVE RHEUMATOID ARTHRITIS: EFFECT OF IL-6 RECEPTOR BLOCKADE

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Background: CD19+CD24+CD38hi B cells have a regulatory capacity and their frequency is altered in the peripheral blood of patients with various autoimmune conditions, including RA.

Objectives: To determine the frequency of circulating CD19+CD24+CD38hi regulatory B cells (cBreg) in ACPA vs ACPA- patients with RA, and its possible modification by IL-6R blockers.

Methods: Peripheral blood was drawn from ACPA+ (n = 37) or ACPA- (n = 19) RA patients treated with conventional synthetic DMARDs (csDMARDs), and from ACPA+ (n=31) or ACPA- (n=12) RA patients treated with tocilizumab; in addition one age and gender-matched healthy control was studied alongside with each patient (n= 99). After isolation by Ficol–Hypaque gradient, PBMCs were stained with antibodies to CD3, CD4, CD19, CD24, and CD38, and examined by flow cytometry.

Results: A decreased frequency of cBreg cells was observed in ACPA+ but not ACPA- RA patients treated with csDMARDs. Interestingly, the frequency of Breg cells showed a significant negative correlation with ACPA titers (r = -0.44, p = 0.021). In contrast, no correlation was found between the frequency of cBreg cells and either RF titres or disease activity as determined by the DAS28 score. However, not only in ACPA+ but also in ACPA- patients receiving tocilizumab, the percentage of cBreg cells was not different from that observed in HC. Four ACPA+ patients treated with csDMARDs who initiated tocilizumab, demonstrated a significant elevation of their cBreg frequency at 12 months.

Conclusion: A decreased frequency of cBreg cells is apparent in ACPA+ but not ACPA- RA patients receiving csDMARDs, that is related with ACPA titres but not with RF titres or disease activity. In contrast, in ACPA+ patients treated with tocilizumab, the frequency of CD19+CD24+CD38hi B cells is comparable to that observed in HC, suggesting that IL-6R blockade is able to modify the altered Breg cell balance.

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SAT0015 TREATMENT WITH ABACETAPDT BUT NOT WITH TNF BLOCKERS, IS ASSOCIATED WITH A REDUCTION OF CONSTITUTIVELY ELEVATED CIRCULATING FOLLICULAR HELPER T CELLS IN RHEUMATOID ARTHRITIS

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Background: Circulating CD4 T cells that express CXCR5 together with PD-1 and/or ICOS are considered as counterparts of bona fide Th cells and function as B cell helpers. In addition, circulating CD4+CXCR5+PD-1+ICOS+ T cells can be subdivided into three subpopulations: CXCR5+CXCR3+CCR6- (Th1-Th), CXCR5+CXCR3+CCR6+ (Th1-Th) and CXCR5-CXCR3-CCR6- (Th2-Th). Only Th1-Th and Th2-Th but not Th1-Th cells seem to provide B cell help. Altered frequencies of circulating Th cells (cTh) and of cTh cell subpopulations have been associated with autoimmune conditions. We previously described that patients with RA treated with conventional synthetic DMARDs (csDMARDs), demonstrate constitutively altered frequencies of cTh and cTh cell subpopulations that are observed not only in patients with an active disease but also in patients who are in remission.

Objectives: To determine if treatment with biological agents (TNF blockers or abactecept) is able to modify the constitutively altered cTh and cTh subpopulation numbers, observed in RA patients receiving csDMARDs.

Methods: Peripheral blood was drawn from RA patients receiving csDMARDs (n=22), TNF blockers (n=21: 10 infliximab, 6 etanercept, 3 certolizumab, 2 adalimumab), or abactecept (n=17). For each patient, an age and gender-matched healthy control was also studied (n=60). cTh and plasmablast frequencies were determined by flow cytometry of freshly isolated PBMCs.

Results: As described, RA patients receiving csDMARDs demonstrated, whether they had an active or inactive disease, an increased frequency of CD4+CXCR5+PD-1+ and CD4+CXCR3+PD-1+ICOS+ cells, together with an increased frequency of circulating plasmablasts. In addition, the frequency of Th1-Th cells was significantly decreased and the frequency of Th1-Th1 and Th1-Th2 cells were significantly increased as compared with HC; subsequently, the ratio (Th1-Th17+Th1-Th2)/Th1-Th1 was increased in RA: that is, RA patients demonstrated a higher proportion of Th cell subsets bearing a phenotype associated with B cell helping capacity. Interestingly, these alterations were also observed in RA patients treated with TNF blockers, whether they had an active or inactive disease. In contrast, in patients receiving abactept, the frequencies of cTh, cTh cell subpopulations and plasmablasts, were not different from those observed in HC.

Conclusion: Patients with RA receiving csDMARDs or TNF blockers demonstrated a constitutively increased frequency of cTh cells and an overrepresentation of cTh subsets bearing a B cell helper phenotype, suggesting that altered germinal center dynamics play a role in RA pathogenesis. Remarkably, in RA patients treated with abactept these frequencies and ratio were not altered, indicating that costimulation blockage is able to revert the increased generation of Th cells in RA; conversely, TNF neutralization does not seem to affect the generation or recirculation of cTh.

REFERENCE

Disclosure of Interests: Paula Fortea-Gordo: None declared, Laura Nuño: None declared, Alejandro Villalva: None declared, Maria-Jose Santos-Bornez: None declared, Diana Peleleado: None declared, Irene Monjo: None declared, Alejandro Balsa Grant/research support from: Abbvie, Pfizer, Novartis, BMS, Nordic, Sanofi, Consultant for: Abbvie, Pfizer, Novartis, BMS, Nordic, Sanofi, Sandoz, Lilly, Paid instructor for: Pfizer, Speakers bureau: Pfizer, Novartis, UCB, Nordic, Sanofi, Sandoz, Lilly, Maria-Eugenia Miranda-Carus Grant/research support from: Roche Pharma, BMS


SAT0016 RHEUMATOID ARTHRITIS PATIENTS DISPLAY B-CELL DYSREGULATION ALREADY IN THE NAÏVE REPERTOIRE

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Background: Seropositive rheumatoid arthritis (RA) is associated with autoreactivity to citrullinated proteins and rheumatoid factor activity. The adaptive immune system and B cells are postulated to be central in RA pathogenesis, yet possible B-cell dysregulations have not been extensively studied. Here, we use exploratory mass cytometry and next generation sequencing to study overall B cell repertoire shifts in RA patients compared to healthy individuals.

Objectives: We hypothesized that there are an underlying B cells repertoire distortion in RA that may be an important key to understanding the autoimmune pathogenesis.

Methods: B cells enriched from PBMCs from nine ACPA pos., seven ACPA neg. RA patients, and six matched healthy controls were phenotyped with mass cytometry (CyTOF) using a 35-marker panel. Single cell data from all samples were pooled clustered via flowSOM in R to identify distinct cell populations, and visualized with ISNE. Cell numbers in each superpopulation were calculated to identify over-representation in patient groups or controls. ANOVA was performed to account for confounding factors.

Results: A decrease in naive B cell subset numbers was apparent in RA patients compared to healthy controls, with a trend towards a shift in the B cell repertoire in RA patients. RA patients showed an increase in the frequencies of plasma cells and a decrease in the frequency of naive B cells. RA patients also showed an increase in the frequency of CD27- B cells, which are likely to represent memory B cells.

Conclusion: These findings suggest that B-cell dysregulation occurs early in the course of RA, and may be an important contributor to the autoimmune pathogenesis.
Factors such as age, sex, and cell preparation date and differential expression of markers between groups was calculated via t-test. In parallel, PBMC B cell receptor (BCR) repertoires were investigated in 13 ACPA pos. RA patients and six age-matched healthy donors using the Illumina MiSeq platform and PCR multiplex amplification libraries with a molecular barcode strategy to generate full variable region coverage. Sequences were filtered using pRESTO, annotated by IMGT and Change-O, finally generating 587,000 unique V-regions. Total serum IgM levels were screened by sandwich ELISA in 157 population controls, 153 AC帕 pos., and 50 AC帕 neg. RA patients. Variable gene frequency was analyzed by Chi-square with Yates correction and serum IgM levels with Kruskal-Wallis test.

Results: Several B-cell phenotypes were found to be significantly different in AC帕 pos. RA compared to controls including an increase in HLA-DR across subsets, CD11c in IgM memory and CD22 expression in clusters of mature naïve IgM positive B cells. Moreover, we could see lower circulating cell counts in AC帕 pos. RA compared to healthy controls (p = 0.01) and trends for elevation in an CXCR5/CCR6 high transitional B cell cluster (p = 0.06), with parallel lower number of transitional B cells with lower CCR6 expression (p = 0.06). Notably, AC帕 neg. RA generally had an intermediate phenotype between healthy controls and AC帕 pos. RA.

Several significant shifts in the RA BCR repertoire could be observed, including an expected higher frequency of VH N-linked glycosylation in highly mutated B cells (p = 0.0001). Yet, the most striking difference was a significantly higher frequency of VH with low somatic hypermutation (SHM) levels in RA-derived B cells (<5 mutations, p = 0.0001, 14.7% vs 8.7). This was seen in all sequences, both IgM and class-switched, but was especially prominent in IgG1 rearrangements (9.6% vs 18.8% low mutation, p = 0.0001 OR = 2.2 CI: 2.0-2.35). In line with an IgM and low mutation profile in RA, we also observed that both AC帕 pos. (p = 0.0001) and AC帕 neg. (p = 0.001) RA patients have a significant increase in total IgM levels compared to controls (1.4 ± 0.7 vs 1.3 ± 0.7; 1.0 ± 0.6 mg/ml, respectively).

Conclusion: Previous studies have shown that anti-citrulline autoreactivity in RA is primarily originates from memory B cells and characterized by high somatic mutations and N-glycosylation sites. However, here the largest B-cell distortions in AC帕 positive RA are observed in the naïve B cell population that have not undergone germinal center responses. These differences result in extreme baseline shifts and elevated natural autoreactivity as an underlying mechanism in RA pathogenesis.

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REFERENCE

BACKGROUND: Relapsing polychondritis (RP) is an rare inflammatory disease of unknown causes, characterized by recurrent inflammation in cartilaginous tissues of the whole body [1]. The histologic features of the disease include loss of basophilic staining of the cartilage matrix, perichondrial inflammation, cartilage destruction with replacement by fibrous tissue, and perivascular cellular infiltration with plasma cells and lymphocytes. Additional clinical features of the disease include ocular inflammation, vasculitis, audiodesribular dysfunction, myocarditis, cardiac valvular insufficiency, and nonerosive inflammatory arthritis. Many studies have shown that the imbalance of helper T cell 17(TTh17) and regulatory T cell (Treg) is involved in the pathogenesis of autoimmune diseases such as SLE and RA. But little is known about the roles of peripheral immune cell subsets peripheral in RP patients. Up to now, just few studies focus on this issue.

OBJECTIVES: We aimed to analyse the distribution and phenotype of CD4+ T cell subsets in the peripheral blood of patients with RP.

METHODS: The proportion and absolute counts of circulating immune cells were assessed in 14 patients diagnosed as RP and 14 healthy controls. CD4+ T cell subsets were also analysed in 9 untreated RP patients and 9 healthy volunteers by flow cytometry. All statistical analyses were performed with SPSS v. 22.0. Continuous variables were reported as median. For all study variables, comparison among controls and RP subsets was based on the non-parametric Wilcoxon Mann-Whitney exact test. For all analyses, we used two-sided tests, with p-values <0.05 denoting statistical significance.

RESULTS: Proportion and absolute counts of Treg cells were significantly reduced in RP patients in comparison with controls (proportion, 3.61% vs. 5.24%, p<0.001; absolute counts, 27.36/μl vs. 46.56/μl, p<0.001). But there were no significant difference between the percentage and number of Th17, Th1 or Th2 cells in patients with RP and healthy controls. Thus, the ratio of Th17/Treg increased in RP patients (0.25 vs. 0.14, p<0.001), as did the ratio of Th2/Treg (0.28 vs. 0.22, p=0.001) and Th1/Treg (2.75 vs. 1.92, p=0.019)(Figure 1). Similarly, the proportion and absolute counts of Treg cells in untreated RP patients were significantly lower than that in healthy controls (proportion, 3.76% vs. 5.66%, p=0.008; absolute counts, 32.24/μl vs. 50.76/μl, p=0.001).And the ratio of Th17/Treg also increased in untreated RP patients (0.25 vs. 0.15, p=0.003), as did the ratio of Th1/Treg (2.35 vs. 1.88, p=0.014)(Figure 2).

CONCLUSION: Our data suggested that the immune-inflammation in RP patients may be related to the decrease of Treg cells and the imbalance of Th17 or Th1 or Th2 and Treg cells.Reduction of peripheral Treg cells may exacerbate the disease progression by not being inhibited Th cells.

REFERENCE


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**SAT0020** **BLOOD RNA SEQUENCING REVEALS IMMUNOLOGICAL PROCESSES ASSOCIATED WITH THE RESPONSE TO ABATACEPT IN RHEUMATOID ARTHRITIS**

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**Background:** Abatacept (CTLA4-Ig) is an approved biological therapy for the treatment of rheumatoid arthritis (RA). Similar to other biological agents, most patients (60%) respond significantly to this therapy. To date, however, the biological mechanisms underlying the lack of efficacy for this drug are unknown.

**Objectives:** The objectives of the present study were to characterize the biological processes underlying the lack of efficacy of abatacept and to evaluate the blood transcriptome as a valid source for drug response prediction.

**Methods:** A total of n=57 patients diagnosed with RA were recruited for this study from 16 rheumatology departments in Spain. All patients were >18 years old and, had >6 months of disease evolution. The primary clinical response to abatacept was defined at week 12 using the EULAR criteria. Good and moderate responders were aggregated into a single response group, and compared to the no response group of patients. Blood RNA was collected from all patients at baseline. From a subgroup of patients (n=31), blood RNA was also obtained at weeks 12, 24 and 48 of treatment with abatacept. Gene expression levels were determined using paired-end RNA-seq (Illumina). Differential gene expression, association to biological processes, longitudinal association analysis and building of the multigeneric predictor were performed using the R software and the specialized Bioconductor libraries. The the prediction accuracy was evaluated using the ROC AUC.

**Results:** From the 57 patients treated with abatacept, n=10 (17.5%) were good EULAR responders, n=24 (42%) moderate EULAR responders and n=23 (40.5%) non-responders at week 12 of therapy. Biological process analysis identified two significantly distinct biological profiles between responders and non-responders. In responders, we found an association to pathways associated with the effector phase of T cells (e.g. interleukin-15 and Th17 signaling). n=5 non-responders showed instead a strong association to biological processes associated with antigen presentation and activation of T cells (P < 0.005). Using the baseline gene expression profiles, we built a multigeneric predictor of response to abatacept with an AUC > 75%. In the longitudinal cohort, patients were stratified as based on achieving an inactive state (i.e. DAS28 < 3.2). Using this endpoint measure, the longitudinal analysis of the 4 time points corroborated the association of response with antigen presentation (P < 0.01).

**Conclusion:** The analysis of blood RNA profiles of RA patients has enabled the identification of specific biological processes associated with the lack of response to abatacept. Also, we demonstrate that blood expression profiles can be predictive of the response to the drug at week 12 of therapy.

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**SAT0021** **ELEVATED NUMBERS OF C-TYPE LECTIN CD161 POSITIVE PR3-SPECIFIC T-CELLS IN GPA**

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**Background:** Various alterations of the peripheral T-cell compartment have been reported in granulomatosis with polyangiitis (GPA) such as elevated populations of CD4+CD8+ double-positive and CD4+CD161+ and CD28- single-positive effector memory T-cells (TEM) within the total CD3+ T-cell population. Analysis of antigen-specific T-cell subpopulations shows, that PR3-specific T-cells display Th2-type, Th17 and Th22 cytokine profiles in GPA (2). Moreover, concomitant cellular CMV- and Epstein Barr virus (EBV)-infection has been found to be associated with the expansion of CD28- TEM in GPA (1,2). Notably, C-type lectin CD161+ (CD28-CD161+ double-positive) T-cells displaying a polyfunctional memory profile directed against several common viruses have been reported. Furthermore, CD161+ T-cells are involved in the pathogenesis of early stage autoimmune hepatitis (3). CD161 expression on proteinase 3 (PR3)-specific T-cells in comparison to other antigen-specific T-cells has not been described in GPA as yet.

**Objectives:** To determine the amount of C-type lectin CD161 on antigen-specific CD8+ single-positive and CD4+CD8+ double positive T-cells in patients with GPA.

**Methods:** In this study, we analyzed the expression of CD161 and CD28 on circulating antigen-specific CD8+ single-positive and CD4+CD8+ double positive T-cells in HLA-A2 positive patients with GPA (n=21) and healthy controls (n=21) using flow cytometry. Antigen-specific T cells were detected using peptide/MHC class I dextramers containing major peptide epitopes for PR3, Epstein Barr virus (EBV) BMLF1, and Cytomegalovirus (CMV) pp65 (aa 196-177, aa 280-288, and aa 495-504, respectively).

**Results:** Patients with GPA showed a higher frequency of circulating CD8+ single-positive and CD4+CD8+ double positive T-cells displaying a polyfunctional memory profile directed against increased expressions of CD161 compared to HC. Compared to EBV- or CMV-specific T-cells, there was an increased expression of CD161 on PR3-specific T-cells in GPA. In contrast to HC and EBV- or CMV-specific T-cells, the percentage of CD28+ T-cells was expanded within the PR3-specific CD8+ T-cell subset in GPA.

**Conclusion:** These findings suggest a potential role of CD161 as an additional TCR-independent co-stimulatory receptor on PR3-specific T-cells in GPA. The role of these cells in the pathophysiology and as a potential therapeutic target remains to be further investigated.

**REFERENCES**


**Disclosure of Interests:** Sebastian Klapa: None declared, Anja Kerstein: None declared, Andreas Koch: None declared, Silke Pitann: None declared, Relana Nieberding: None declared, Gabriela Riemekasten Consultant for: Chugai, F. Hoffmann-La Roche, Speakers bureau: Chugai, F. Hoffmann-La Roche, Antje Müller: None declared, Peter Lampecht: None declared

THE SUBPOPULATION FEATURES OF DENDRITIC CELLS AS A POTENTIAL BIOMARKER OF EARLY RHEUMATOID ARTHRITIS

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Background: Dendritic cells (DCs) are professional antigen-presenting cells (APCs), which play important role in immune responses. DCs are a heterogeneous population and can be divided into groups: myeloid (mDCs) and plasmacytoid (pDCs). Furthermore, DCs are important in rheumatoid arthritis (RA) pathogenesis through antigen presentation and activation autoreactive T-lymphocytes. As established the different subpopulation DCs can promote different immune reactions. That’s why, it may be possible to consider them as a potential target for the development of new target of the immunopathological disorders therapy.

Objectives: To investigate the subpopulations of peripheral blood DCs (myeloid and plasmacytoid) in patients with early RA as a predictor of responsibility to disease-modifying antirheumatic drugs (DMARDs) treatment.

Methods: Forty nine patients with early RA (duration of the disease up to 12 months) were included in the study. All patients fulfilled ACR/ EULAR criteria (2010) and received methotrexate, leflunomide, sulfasalazine. The study included 16 RA patients with osteoarthritis (OA) used as a control group. Analysis of the content of the B-lymphocytes, myeloid and plasmacytoid DCs, labeled by antibodies against surface markers, was carried out by flow cytometry. B-lymphocytes, subtypes of peripheral blood DCs were characterized by the following phenotypes: myeloid DCs (CD3-CD14-CD19-HLA-DR + CD11c + CD123+), plasmacytoid DCs (CD3-CD14-CD19-HLA-DR + CD11c+CD123+), B-lymphocytes (CD19+). Analysis were performed before treatment and after 3 and 6 months.

Results: Patients with early RA are characterized by significant evaluation of the population of plasmacytoid DCs in comparison of patients with moderate stages of rheumatoid arthritis and osteoarthritis (3.8 vs 2.1 vs 1, p=0.0042). Furthermore, the difference was found in the number of cells with the phenotype B-lymphocytes: 7.95 * 10^6/l vs. 3.6* 10^6/l, respectively (p = 0.014). No significant differences were observed in the number of myeloid DCs. After 6 month of observation we detected reducing amount of plasmacytoid DCs (3.8 before treatment and 2.1 in 6 month, p=0.0042) and B-cells that correlated with activity of disease.

Conclusion: The obtained data indicated that plasmacytoid DCs are predominant in patients with inflammatory arthritis especially in early RA and correlate with activity of disease that can use as a predictor of good response on DMARDs treatment.

Disclosure of Interests: None declared


THE DIFFERENTIAL PRODUCTION OF REACTIVE OXYGEN SPECIES IN T CELL SUBSETS IN PERIPHERAL BLOOD OF RHEUMATOID ARTHRITIS PATIENTS

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Background: T cells play a regulatory role in rheumatoid arthritis (RA) through inducing the homeostasis maintenance and self-tolerance (1). Specifically, the production and the oxidation mechanism of reactive oxygen species (ROS) were out of balance.

Objectives: The aim of the study was to compare ROS productions in T cell subset, which are helper T (Th) cell, cytotoxic T (TC) cell, T helper 17 (TH17) cell and regulatory T (Treg) cell in peripheral blood mononuclear cells (PBMC) of RA patients with RA activity.

Methods: Blood samples were collected from 30 RA patients and 10 healthy adult volunteers under IRB approval. RA activity was divided according to clinical parameter DAS28 (2). PBMC cells were obtained from the whole blood using lymphocyte separation medium density gradient centrifugation. For separation between the live and dead cell populations, PBMC was stained with Live/Dead stain dye. After PBS washing, cells were incubated with antibodies for CD3, CD4, CD8, and CD25. Following fixation and permeabilization, and further stained with antibodies for FoxP3 and IL-17A. For ROS staining, CellRox and MitoSox were used.

Results: The frequency of TH cell was increased and that of TC cell was decreased in the peripheral blood of RA patients. TH17 and Treg cell population were significantly increased more than about 2-3 folds in active and inactive RA than healthy control. When the whole of cellular ROS production was measured, only Treg cell population was significantly increased in RA than control. Although ROS level was steadily increased with RA activity, there was a slight decline in severe RA compared to moderate and low RA. This difference is lager in mitochondrial specific ROS than total cellular ROS. The mitochondrial complex inhibitor reduced Treg cell frequency in PBMC from RA patients.

Conclusion: Treg is the most sensitive to ROS production among T cell subsets in RA. These findings provide a novel approach to regulate Treg function in RA through mitochondrial metabolism related ROS production.

Disclosure of Interests: None declared


TRANSCRIPTOMIC PROFILING OF THE MICROENVIRONMENT DRIVEN RE-SHAPING OF PATHOGENIC CIRCULATORY AND SYNOVIAL HLA-DR+ CD4 T SUBSETS IN ACTIVE JUVENILE IDIOPATHIC ARTHRITIC PATIENTS

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Background: We have previously identified two pathogenic circulatory CD4 subsets in both Teff (CPLs), and Treg (iaTreg) compartments of JIA patients that are HLA-DR+, antigen experienced, pro-inflammatory, correlated positively with disease activity and possessing strong synovial TCR sequence coverage. Despite being two functionally discordant T cell subsets (Teff/iaTreg), their immune-phenotype and association with clinical data suggests that these subsets may originate from a common precursor.

Objectives: We seek to understand how the microenvironment could potentially influence and drive these subsets (CPLs/iaTregs) towards their pathophysiological state. In an attempt to elucidate the common pathological gene drivers, we decided to perform next-generation RNA sequencing on sorted CPLs/iaTregs and conventional Teff/iaTreg counterparts in both circulation and synovium.

Methods: CPLs were sorted as CD3+CD4+CD14- HLA-DR+ CD25-CD127 Teff gate, and iaTregs were sorted as CD3+CD4+CD14- HLA-DR+ CD25+CD127+ Treg gate with FACS Aria II from n=16 active JIA PBMCs, n=8 paired JIA SFMCs, and n=8 healthy paediatric PBMCs. As a comparative control, similar HLA-DR+ counterparts were respectively sorted from the same patients. Sorted cells were lysed and extracted for RNA, and cDNA conversion/amplification were then carried out using SMART-seq v4. Libraries are prepared and multiplexed using Nextera XT DNA library preparation kit, and ran on the Illumina HiSeq High output platform.

Results: Comparative differential gene expression (DEG) analysis within the circulatory compartment indicate transcriptomic convergence between CPLs/iaTreg and divergence away from conventional Teff/iaTreg pools. Circulatory CPLs/iaTregs exhibit (a) common pathway dysregulation in T cell signalling (IFN-g, PD1, CD28 costimulation), (b) restriction in TCR oligo-clonality and (c) common transcription factor drivers (SP1L and E2F1) within the gene regulatory network, suggesting a common driving source acting on these two disparate compartments.

To understand how this convergence originate, we compared CPLs/iaTreg and conventional Teff/iaTreg subsets from (a) healthy circulatory PBMCs, (b) JIA circulatory PBMCs and (c) paired JIA synovium. There was a gradual increase in transcriptomic convergence between Teff/iaTreg, Treg/iaTreg and CPLs/iaTreg across the spacial/disease continuum, that is paralleled by an antigenic convergence in shared TCR clonotypes in CPLs/iaTreg.
The effect of dimethyl fumarate on immune pathways associated with epigenetic regulation, RUNX1 signalling, Rho and GTPase signalling were upregulated.

Conclusion: Our results show that Dimethyl Fumarate exerts a significant inhibition on SLE plasmablast differentiation and antibody production. The transcriptional analysis allowed to dissect B cell transcriptional programmes activated in the context of autoimmune B cell differentiation in SLE. The transcriptional perturbations induced by DMF highlighted some of the gene expression pathways necessary for plasmablast differentiation and survival. In addition, these data provide new insight into DMF pharmacodynamics and may support the repositioning of DMF in the treatment of SLE.

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SAT0025
THE EFFECT OF DIMETHYL FUMARATE ON PLASMABLAST DIFFERENTIATION TRANSCRIPTIONAL PROGRAMMES IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Dimethyl fumarate (DMF), is an immunomodulatory drug approved for the treatment of Multiple Sclerosis (MS) and Psoriasis. The exact mechanism of action of DMF is not entirely known. Anti-inflammatory and immunomodulatory effects have been observed, including the upregulation of NRF-2, the inhibition of TIGAR and the block of the E2 ubiquitin-conjugating enzyme UBE3L. Further evidence from MS patients suggest a modulation on B cell activation. Although beneficial effects of DMF have been observed in animal models of lupus nephritis and limited cases human cutaneous lupus, the effect of DMF on B cell maturation transcriptional programmes in systemic Lupus Erythematosus (SLE) has not been fully investigated.

Objectives: To examine the effect of DMF on SLE plasmablast differentiation and identify the transcriptional changes in cultured SLE B cells after DMF administration.

Methods: B cells were isolated from the peripheral blood of SLE patients (n=15) by negative magnetic sorting. B cell differentiation toward plasma blasts was induced in-vitro by stimulation with TLR-7 agonist Resiquimod, CD40L, IL-2, IL-10 and IL-15 for 5 days in the presence of DMF 25 uM and azathioprine and methotrexate (n=8) or with anti-IL-6 receptor antibody tocilizumab (n=7). The blood samples were taken at baseline and week 24 after treatment. The peripheral immune cell subset was defined based on comprehensive 8-color flow cytometric analysis for human immune system termed “the Human Immunology Project” by NIH and FOCSIT1, and the correlation with clinical characteristics and responsiveness to the therapies were evaluated.

Results: The proportion of CD3+CD4+CXCR3+CCR6+CD38+HLA-DR+ activated Th17 cells and CD3+CD4+CXCR5+ICOS+CD38+ activated Tfh cells in patients with TAK and that of activated Th17 cells and CD19+CD20-CD27+CD7+ double negative effector B cells in patients with GCA were significantly higher compared with HD. At baseline, the frequency of activated Th17 cells showed positive correlation and that of CD4+CD45RA-CD25+CD127+ Th regulatory (Treg) cells showed negative correlation and that of Tfh cell activation was correlated with disease activity of LVV. Although Tfh cell activation was not changed by the conventional immunosuppressive agents. By contrast, tocilizumab reduced Th17 cells and increased Treg cells, indicating that IL-6 blockade may correct the impaired balance of Th17 and Treg cells in patients with LVV.

Disclosure of Interests: Shingo Nakayama, Yusuke Miyazaki, Hiroko Yoshinari, Aki Kabawe, Ippei Miyagawa, Satoshi Kudo, Shunji Fujiko, Shigewa Iwata: None declared, Kazuhiro Nakano, Yoshiya Tanaka, University of Occupational and Environmental Health, Japan, School of Medicine, First Department of Internal Medicine, Kitakyushu, Japan.

Background: The pathogenesis of large vessel vasculitis (LVV) such as Takayasu arteritis (TAK) and giant cell arteritis (GCA) consists of the immune abnormalities including the interaction between vascular dendritic cells, macrophages and T cells. It is reported that genetic polymorphisms in the immune-modulating cytokine genes such as IL-6 and IL-12B are associated with LVV. However, little is known about pathological immune cell subsets targeted by immunosuppressants and/or molecular-target therapy such as IL-6 blockade.

Objectives: The aim of this study was to assess the relationship between the phenotype of peripheral immune cells with clinical manifestations and responsiveness to the treatment in patients with LVV.

Methods: Peripheral blood mononuclear cells were obtained from 22 patients with active LVV (TAK 7, GCA 15) and 19 healthy donors (HD). All patients were treated with high dose glucocorticoid (GC). The study included the patients treated with immunosuppressive agents such as azathioprine and methotrexate (n=8) or with anti-IL-6 receptor antibody tocilizumab (n=7). The blood samples were taken at baseline and week 24 after treatment. The peripheral immune cell subset was defined based on comprehensive 8-color flow cytometric analysis for human immune system termed “the Human Immunology Project” by NIH and FOCSIT1, and the correlation with clinical characteristics and responsiveness to the therapies were evaluated.

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Disclosure: Consistently, IgG and IgM secretion were significantly reduced (p<0.001). DMF treatment induced significant transcriptional changes in both PBs and Naïve B cells, with 269 and 652 genes modulated in PBs and Naïve B cells, respectively (Paj <0.05). Pathway analysis highlighted the downregulation of a number of pathways: detoxification of reactive oxygen species, transcriptional regulation of cell cycle inhibitor and P21, mitophagy and P53/Parkin Mediated mitophagy, interleukin-12 signaling, TP53 and p53 regulation, PERK mediated endoplasmic unfolded protein response, and NF-kB mediated cell survival. Conversely, pathways related to epigenetic regulation, RUNX1 signaling, Rho and GTPase signaling were upregulated.

Conclusion: Overall the data indicate immune-phenotypic convergence between CPLs/Tregs, that is strengthen across disease/spatial states. These findings underscore a potential mechanistic role of the inflammatory microenvironment in shaping two different dichotomous populations, relevant to disease pathogenies and progression.

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Circulating CD3+CD31+CXCR4+ T cells in rheumatoid arthritis patients: correlation with retinal microvascular damage and potential effect of abatacept therapy

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Background: T-cells play a role in pathogenesis of rheumatoid arthritis (RA) and in its cardiovascular (CV) comorbidities [1]. CD3+CD31+CXCR4+ T-cells may be involved in damaged endothelium repair [2]. The percentage of these cells in the peripheral blood was reported to be lower in RA than in healthy controls, as an effect of disease activity rather than of traditional CV risk factors [3]. Abatacept (ABA), a T-cell co-stimulator, is approved for the treatment of RA. In addition to its effect on disease activity, it may have a CV protective action [4].

Objectives: To evaluate CD3+CD31+CXCR4+ T-cells in a cohort of RA patients in correlation with disease activity, CV parameters, and the potential effect of ABA therapy.

Methods: Thirty-one RA patients (median[10th-90th percentile] age=60[40-70] years, baseline C-reactive protein (CRP)=DAS28=43[5.4], body mass index (BMI)=2[17.3-28.6] kg/m², rheumatoid factor (RF) positive:55%, anti-citrullinated peptide autoantibodies (ACPA) positive:77%) were enrolled. Thirteen patients were evaluated before and after 6 months of ABA therapy. Among them, in 5 patients without known CV risk factors (history of arterial hypertension, diabetes, hypercholesterolemia, previous CV events and smoking), a morphological evaluation of retinal arteriules was performed by adaptive optics, a validated technique quantifying microvascular damage [5]. The response to treatment was evaluated with the EULAR response criteria. Phenotypic analysis of peripheral blood T lymphocytes was made by flow-cytometry.

Results: At baseline, no correlation was found between relative CD3+CD31+CXCR4+ T-cell number and age, BMI, CRP DAS28, RF and ACPA titers. However, a negative correlation was observed with retinal wall thickness (Figure 1). After ABA therapy (n=13), no significant differences were found between good-moderate responders (n=10) and non-responders (n=3), but the two groups seemed to show an opposite trend (T0 vs T6: from 23.8[4.5] to 11.9[3.7] and from 20.4[3.2] to 27.4[7.8] mm). The percentage of these cells in the peripheral blood of patients with active RA was detected in the Treg lymphocytes in relation to the control group to total T-reg lymphocytes) in the peripheral blood of patients with active RA was detected in the Treg lymphocytes in relation to the control group (5123.3[4027.8-6145.5] vs 4852.3[3554.9-5788.2] mm²/p=0.04).

Conclusion: In a subgroup of patients without known CV risk factors, CD3+CD31+CXCR4+ T-cell number was inversely related to the possible presence of subclinical CV involvement, as evaluated by retinal microvascular damage. This improved after ABA therapy. These findings may suggest a possible value of CD3+CD31+CXCR4+ T-cell number in the evaluation of microvascular damage, and a possible beneficial effect of ABA on the microcirculation in RA patients.

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to a healthy control group (7.6% versus 5.85%, p = 0.129). After a 12-week treatment with alfalcacidol in patients with RA, an increase in the percentage of activated Treg cells (HAL-DR positive to total T-reg lymphocytes) was observed in relation to the values detected at the beginning of the study, up to the level recorded in the group of healthy controls 6.13% vs. 4.76%, p = 0.219.

Conclusion: It is believed that functional blockade of Treg cells plays the most important role in RA immunopathogenesis, most likely due to inhibition of their function by proinflammatory cytokines or due to an increase in the number of activated effector T cells, or perhaps to the fact that some completely differentiated T reg cells can be very unstable. Our data show that B cells reactive with a citrullinated peptide derived from P.gingivalis (Pg) to express a PAD enzyme that can citrullinate both bacterial and human proteins, it has been hypothesised that the ACPA response may be triggered in the gum mucosa in response to Pg.

Objectives: The main purpose of this study was to investigate if citrulline-reactive B cells reside in inflamed gingival tissue, and to examine ACPA cross-reactivity between citrullinated bacterial and human epitopes on a monoclonal level.

Methods: Using a single-cell antibody cloning approach, 55 recombinant monoclonal antibodies (mAbs) were generated from gingival tissue (GT) CD19+ B cells (n=1 ACPA+ RA/PD patient). Citrulline reactivity was determined using the anti-CCP2 kit (EuroDiagnostics AB), and in-house peptide ELISAs (including a citrullinated peptide derived from Pg PAD (CP3)) and citrullinated peptides derived from human α-ename, fibrinogen, vonwillebrand, fillagrin and histone H3. Reactivity against CP3 and CP2 was also investigated in: 19 mAbs from bronchoalveolar lavage (BAL) CD19+ B cells (n=2 ACPA+ RA patients); 29 mAbs from bone marrow (BM) plasma cells (n=4 ACPA+ RA patients); 142 mAbs from synovial fluid (SF) plasma cells (n=5 ACPA+ RA patients); and 36 mAbs from peripheral blood memory/plasma cells (n=4 ACPA+ RA patients). Predicted germline variants were produced for two of the mAbs.

Results: Among 55 GT mAbs, 14 unique clones (25%) were reactive to the bacterial CP3 peptide. We also detected CP3-reactive mAbs from BAL (n=9/19), BM (n=3/29), SF (n=1/142) and peripheral blood (n=1/36). Interestingly, 11 out of 28 (39%) CP3-reactive clones also bound citrullinated peptides derived from human proteins. Notably, three of these clones were positive in the clinical anti-CCP2 test, and when converted back to the predicted germline sequence, these clones became CCP2 negative, while maintaining reactivity against the bacterial CP3 peptide.

Conclusion: Our data show that B cells reactive with a citrullinated peptide derived from Pg PAD are present in gingival tissue, lungs, bone marrow, and the inflamed joint of ACPA+ RA patients. Moreover, the finding that a number of these clones are cross-reactive with citrullinated peptides derived from human proteins as well as the gold standard CCP2 test suggests mechanisms of molecular mimicry in the generation of ACPA. Importantly, the germline versions of these ACPA were CP3-reactive but not autoreactive, supporting the hypothesis of a bacterial origin for this ACPA response.

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VITAMIN B3 (NAM) SUPPRESSES T CELL ACTIVATION IN AN PRODUCTION OF PRO-INFLAMMATORY CYTOKINES IN VITRO IN A DOSE DEPENDENT MANNER INDICATING THERAPEUTIC POTENTIAL FOR THE TREATMENT OF JIA

Ivana Zvyagin1,2, Lotte Nijhuis1, in vitro inhibits proliferation and activation of Teff cells numbers and functioning, this data demonstrates that VitB3 treatment also CD4+ and CD8+ T-cells was inhibited with VitB3 treatment in a dose ERK phosphorylation was decreased. Furthermore, proliferation of both surface activation markers were downregulated after VitB3 incubation, and significantly decreased the production of the pro-inflammatory cytokines IL-2 Results: Methods: T-cells were isolated from the blood of healthy controls and JIA patients, as well as from the synovial fluid from JIA patients. Cells were stimulated with and cultured in the presence of increasing concentrations of VitB3 (0-9mM) for 1-4 days. Proliferation and expression of activation makers in primary T cells were determined using flow cytometry. Cytokine production was determined by qPCR, Luminex and confocal microscopy, and their mRNA levels were analyzed by semi-qPCR. Cytokines, transcription factors and cell markers related to pathogenic profile of Th cells were analyzed by semi-qPCR, ELISA and flow cytometry. To study the signalling pathways, pull-down assays (Rap1), western-blot (CREB) and ELISA (cAMP) were performed. Expression of different chemokines were analyzed by flow cytometry whereas cell migration assays were performed using transwell membranes.

Results: In vitro VitB3 treatment of JIA patient CD4+ Teff-cells significantly decreased the production of the pro-inflammatory cytokines IL-2 and IFNγ measured both on mRNA and protein level. Correspondingly, surface activation markers were downregulated after VitB3 incubation, and ERK phosphorylation was decreased. Furthermore, proliferation of both CD4+ and CD8+ T-cells was inhibited with VitB3 treatment in a dose dependent manner. Murine reporter cells showed similar results. Experimental outcomes were verified using another SIRT1 inhibitor; EX-527. Conclusion: In addition to the previously demonstrated increase of Treg numbers and function, this data demonstrates that VitB3 treatment also inhibits proliferation and activation of Th cells in vitro. VitB3 treatment could therefore modulate the immunological balance by both increasing tolerance and suppressing immune activation. We envision that VitB3 treatment as an adjuvant therapy has the potential to benefit JIA patients and potentially patients with other autoimmune diseases. To assess the clinical relevance of these findings, we are currently in the preparation of a phase III clinical trial.


VITAMIN B3 (NAM) SUPPRESSES T CELL ACTIVATION IN AN PRODUCTION OF PRO-INFLAMMATORY CYTOKINES IN VITRO IN A DOSE DEPENDENT MANNER INDICATING THERAPEUTIC POTENTIAL FOR THE TREATMENT OF JIA

Ivana Zvyagin1,2, Lotte Nijhuis1, in vitro inhibits proliferation and activation of Teff cells numbers and functioning, this data demonstrates that VitB3 treatment also CD4+ and CD8+ T-cells was inhibited with VitB3 treatment in a dose ERK phosphorylation was decreased. Furthermore, proliferation of both surface activation markers were downregulated after VitB3 incubation, and significantly decreased the production of the pro-inflammatory cytokines IL-2 Results: Methods: T-cells were isolated from the blood of healthy controls and JIA patients, as well as from the synovial fluid from JIA patients. Cells were stimulated with and cultured in the presence of increasing concentrations of VitB3 (0-9mM) for 1-4 days. Proliferation and expression of activation makers in primary T cells were determined using flow cytometry. Cytokine production was determined by qPCR, Luminex and confocal microscopy, and their mRNA levels were analyzed by semi-qPCR. Cytokines, transcription factors and cell markers related to pathogenic profile of Th cells were analyzed by semi-qPCR, ELISA and flow cytometry. To study the signalling pathways, pull-down assays (Rap1), western-blot (CREB) and ELISA (cAMP) were performed. Expression of different chemokines were analyzed by flow cytometry whereas cell migration assays were performed using transwell membranes.

Results: In vitro VitB3 treatment of JIA patient CD4+ Teff-cells significantly decreased the production of the pro-inflammatory cytokines IL-2 and IFNγ measured both on mRNA and protein level. Correspondingly, surface activation markers were downregulated after VitB3 incubation, and ERK phosphorylation was decreased. Furthermore, proliferation of both CD4+ and CD8+ T-cells was inhibited with VitB3 treatment in a dose dependent manner. Murine reporter cells showed similar results. Experimental outcomes were verified using another SIRT1 inhibitor; EX-527. Conclusion: In addition to the previously demonstrated increase of Treg numbers and function, this data demonstrates that VitB3 treatment also inhibits proliferation and activation of Th cells in vitro. VitB3 treatment could therefore modulate the immunological balance by both increasing tolerance and suppressing immune activation. We envision that VitB3 treatment as an adjuvant therapy has the potential to benefit JIA patients and potentially patients with other autoimmune diseases. To assess the clinical relevance of these findings, we are currently in the preparation of a phase III clinical trial.


SCIENTIFIC ABSTRACTS - SUNDAY, 16 JUNE 2019

ARTHRITIS PATIENTS: VIP RECEPTORS IN HEALTHY DONORS AND EARLY PATTERN EXPRESSION AND CELLULAR LOCATION OF CYTOKINES IN VITRO IN A DOSE DEPENDENT MANER INDICATING THERAPEUTIC POTENTIAL FOR THE TREATMENT OF JIA

Lotte Nijhuis1,2, Álvaro2, José Miguel Rodríguez Frade3, Mario Mellado3, María Del Ekaterina Komech1,2, Anastasia Koltakova3, Alena Novikova1, Elena Loginova3, Tatiana Korotaeva3, Tatiana Korotaeva3, Ivan Zvyagin1,2, Lotte Nijhuis1, in vitro inhibits proliferation and activation of Teff cells numbers and functioning, this data demonstrates that VitB3 treatment also CD4+ and CD8+ T-cells was inhibited with VitB3 treatment in a dose ERK phosphorylation was decreased. Furthermore, proliferation of both surface activation markers were downregulated after VitB3 incubation, and significantly decreased the production of the pro-inflammatory cytokines IL-2 Results: Methods: T-cells were isolated from the blood of healthy controls and JIA patients, as well as from the synovial fluid from JIA patients. Cells were stimulated with and cultured in the presence of increasing concentrations of VitB3 (0-9mM) for 1-4 days. Proliferation and expression of activation markers in primary T cells were determined using flow cytometry. Cytokine production was determined by qPCR, Luminex and confocal microscopy, and their mRNA levels were analyzed by semi-qPCR. Cytokines, transcription factors and cell markers related to pathogenic profile of Th cells were analyzed by semi-qPCR, ELISA and flow cytometry. To study the signalling pathways, pull-down assays (Rap1), western-blot (CREB) and ELISA (cAMP) were performed. Expression of different chemokines were analyzed by flow cytometry whereas cell migration assays were performed using transwell membranes.

Results: In vitro VitB3 treatment of JIA patient CD4+ Teff-cells significantly decreased the production of the pro-inflammatory cytokines IL-2 and IFNγ measured both on mRNA and protein level. Correspondingly, surface activation markers were downregulated after VitB3 incubation, and ERK phosphorylation was decreased. Furthermore, proliferation of both CD4+ and CD8+ T-cells was inhibited with VitB3 treatment in a dose dependent manner. Murine reporter cells showed similar results. Experimental outcomes were verified using another SIRT1 inhibitor; EX-527. Conclusion: In addition to the previously demonstrated increase of Treg numbers and function, this data demonstrates that VitB3 treatment also inhibits proliferation and activation of Th cells in vitro. VitB3 treatment could therefore modulate the immunological balance by both increasing tolerance and suppressing immune activation. We envision that VitB3 treatment as an adjuvant therapy has the potential to benefit JIA patients and potentially patients with other autoimmune diseases. To assess the clinical relevance of these findings, we are currently in the preparation of a phase III clinical trial.


SAT0031 Activation of Th lymphocytes alters the pattern expression and cellular location of VIP receptors in healthy donors and early arthritis patients

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Background: CD4+ T helper cells are decisive in the struggle against pathogens and in the maintenance of immune homeostasis. Their activation and differentiation can take many forms and generate immune memory in which the extracellular environment plays a critical role in both homeostatic and pathological states. VIP is one of the best-studied neuropeptides with anti-inflammatory and immunomodulatory actions in normal and pathological conditions [1,2]. There are evidences that VIP...
Methods: We collected paired PB and SF samples from HLA-B*27+ (n=5) and HLA-B*27- (n=7) patients. All patients fulfilled the CASPAR criteria. TCR beta profiling for total P/SFM C samples and T cell subsets was performed using high throughput sequencing of 5’-RACE double-barcoded TCR beta cDNA libraries following by repertoire reconstruction with molecular barcode-based error correction [5].

Results: Clonal diversity in SF was largely restricted compared to PB, with significant enrichment of mostly expanded SF clonotypes compared to PB, suggesting antigen-driven migration and expansion of the T cells into inflamed site. Major clonal expansions of SF were private for each patient, yet SF shared significantly more clonotypes than PB independently from HLA-B*27 status. Most important, in CD8+ subsets from PB and SF we identified the previously described AS-associated T-cell clonotypes. These clonotypes were detected in SF of all HL A-B*27+ patients but not in samples from HLA-B*27- patients, suggesting the HLA-B*27 restriction of the TCR beta motif. The clonotypes were enriched in SF compared to PB, representing up to 1.6% of CD8+ SF T cells. All HLA-B*27+ patients had several variants of the TCR beta clonotypes in SF, suggesting the selection of the TCRs during disease development.

Conclusion: Our results further support the supposed role of the CD8+ T cells in SpAs and suggest that similarity of clinical phenotype between AS and HLA-B*27+ PsA patients could be associated with autoimmune response to similar antigens, represented by HLA-B*27 molecule.

REFERENCES

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Disclosure of Interests: Ekaterina Kornech: None declared, Anastasia Koltakov: None declared, Alena Novikova: None declared, Elena Loginova Speakers bureau: Novartis, Celgene Corporation, Biocad, Janssen, AbbVie Inc, Tatiana Korotaeva Speakers bureau: Novartis, Celgene Corporation, AbbVie Inc, Biocad, Janssen, Pfizer, UCB, Lilly, Ivan Zvyagin: None declared

IMPACT OF RHEUMATOID ARTHRITIS IN LIVER DAMAGE, INVOLVEMENT OF ANTI-CITRULLINATED PROTEIN ANTIBODIES

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Background: Liver damage in rheumatoid arthritis (RA) is most common in the form of asymptomatic abnormal liver biopsies. It is difficult to differentiate between hepatic manifestations of the primary disease and potential hepatotoxicity of the therapies. Inflammation, oxidative stress, apoptosis and loss of lipid droplets are involved in the hepatic fibrogenesis.

Objectives: 1) To analyze the impact of RA in the liver function and 2) To evaluate the direct effect of anti-citrullinated protein antibodies (ACPs) in the liver fibrosis.

Methods: 150 RA patients and 100 healthy donors (HD) were included. Aspartate aminotransferase (AST), alanine aminotransferase (ALT), phosphatase alkaline (ALP), albumin and levels of autoantibodies and inflammatory markers were evaluated in serum. In vitro studies: Hep G2 cells were treated with IgG-ACPAs isolated from RA patients. Molecules involved in lipid metabolism, insulin resistance, oxidative stress and inflammation were analyzed by RT-PCR and Western blot. Activation of intracellular pathways involved in fibrogenesis was analyzed. Lipid accumulation was evaluated by fluorescence microscopy. Mouse model: 20 CB57BL/6 mice were used; 5 mice were used non-diseased group, and 15 were used in CIA modelling. Liver samples were collected. Genes involved in insulin signal, lipid accumulation, macrophage infiltration and polarization and inflammation were evaluated. Activation of intracellular pathways related to fibrogenesis were analyzed. Immunohistochemistry was used to evaluate the percentage of fibrotic cells.

Results: Within the normal range of hepatic enzymes, the percentage of RA patients with levels of AST, ALT and ALP above the mean was significantly higher compared to HD. In contrast, percentage of RA patients displaying levels of albumin below the mean was significantly elevated compared to HD. Differences remained significant after adjusting for potential confounders (treatment). Moreover, high levels of AST and ALT were associated with ACPAs and inflammatory markers. IgG-ACPAs induced the expression of inflammatory and oxidative stress markers and decreased genes involved in insulin signal and lipid accumulation in Hep G2 cells. In addition, lipid content decreased after IgG-ACPAs treatment. The phosphorylation of intracellular pathways involved in fibrogenesis was modulated by IgG-ACPAs. The induction of arthritis in mice elevated inflammatory cytokines and markers of macrophages presence and polarization state M1 and reduced genes related to lipid droplets in the liver. Phosphorylation of ERK and mTOR was increased in the liver of CIA mice. Additionally, the percentage of cells positive for α-smooth muscle antibody was increased in the liver of CIA mice.

Conclusion: 1) RA patients displayed a subclinical alteration of the hepatic enzymes levels associated with levels of autoantibodies ACPAs, which may suggest that RA is associated with an abnormal liver function induced by autoantibodies. 2) ACPAs may induce alterations in hepatic cells, increasing inflammation and oxidative stress, reducing lipid accumulation and activating intracellular pathways, processes closely involved in fibrogenesis. 3) In a CIA mice, arthritis induced inflammation, infiltration of macrophages, reduction of genes involved in lipid accumulation and activation of intracellular pathways involved in fibrogenesis.

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Disclosure of Interests: None declared


INCREASED CARDIOMETABOLIC RISK FACTORS ARE RELATED TO THE ABNORMAL ADIPOCYTOKINE PROFILE AND AUTOIMMUNITY IN RHEUMATOID ARTHRITIS, MODULATION BY TNFALPHA AND IL6 INHIBITORS

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Background: Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by excess morbidity and mortality from cardiovascular disease. In addition, metabolic alterations have been observed in these patients, which significantly contributes to the cardiovascular risk burden. Thus, the identification of therapies able to mitigate the cardiometabolic alterations in RA is essential. In addition, numerous studies suggest that cardiometabolic risks are mediated through adipocytokines. However, this relationship is not completely defined in RA.

Objectives: 1) To evaluate the relationship among cardiometabolic risk factors and the levels of adipocytokines and autoantibodies in RA patients. 2) To analyze the effects anti-TNFα and anti-IL6 therapies on the cardiometabolic alterations.

Methods: 1- A cross-sectional study including 100 RA patients and 50 age-matched healthy donors was carried out. Different parameters related to the cardiometabolic risk were analyzed, including: lipid profile, atherogenic index, ratio ApoB/ApoA, insulin resistance (IR), obesity, hypertension, and the SCORE. Levels of adipocytokines (TNFα, IL6, IL1β, visfatin, adiponectin, leptin and resistin) were evaluated in serum. Carotid intima media thickness (CIMT) was evaluated as atherosclerosis marker. 2- A prospective study in 15 RA patients before and after 3 months of anti-TNFα therapy and 15 RA patients before and after 3 months of treatment with tocilizumab (TCZ) was performed. All the parameters evaluated in the cross-sectional cohort were tested in this prospective study.

Results: RA patients had elevated levels of leptin/adiponectin ratio, visfatin, resistin and inflammatory markers in serum. Our cohort of RA patients displayed increased rates of cardiometabolic risk factors, such as insulin resistance, hypertension, SCORE, pathologic CIMT, atherogenic index and ratio apoB/apoA. The alteration in the levels of adipocytokines were closely related to the autoimmunity, disease activity and clinical inflammatory markers. Of note, visfatin and C3 complement levels were determinant for IR, high levels of SCORE, increased parameters of CVD risk defined by apoB/apoA ratio and pathologic CIMT.

Both biological therapies reduced clinical inflammatory markers and disease activity after 3 months of treatment. Anti-TNFα therapy modulated the cytokine profile, reducing serum levels of IL6, IL-1β, resistin and visfatin, decreasing IR.

Conclusion: 1) Altered adipocytokine profile is closely related to increased cardiometabolic risk factors associated with RA, where autoimmunity and systemic inflammation play a key role. 2) Anti-TNFα and anti-IL6 therapies, administered for 3 months, could have beneficial effects in the reduction of cardiometabolic risk factors in RA.

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SEMAPHORINS: FROM ANGIOGENESIS TO INFLAMMATION IN RHEUMATOID ARTHRITIS

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Background: Sympatral neoangiogenesis is an early and crucial event to promote the development of the hyperplastic proliferative pathologic synovium in rheumatoid arthritis (RA). A recent microarray analysis of Endothelial cells (ECs) issued from patients with RA and matched controls has revealed a differential expression of semaphorin family in RA ECs, which is known to contribute to angiogenesis and autoimmunity/inflammation.

Objectives: Our aim was to study the potential implication of semaphorins in RA pathogenesis.

Methods: mRNA levels of class 3 and 4 Semaphorins (SEMA) SEMA3A, SEMA3E, SEMA4A and SEMA4E, as well as their receptors Plexin-D1 (PLXND1) and Neurothin-1 (NRPI), were measured by real-time quantitative PCR in RA (n = 15) and control (n = 15) ECs. Protein expression of these 4 semaphorins and their receptors was evaluated in ECs of 10 RA patients and controls by western blot, and in the synovial tissue of 10 RA patients and 5 controls by immunohistochemistry and immunofluorescence. Serum concentrations of these 4 semaphorins were measured by sandwich ELISA in a cohort of 130 patients with RA (85% women, mean age: 58 ± 12 years and mean disease duration: 11 ± 30 years) and 30 age- and sex-matched (20%) women) matched controls.

Results: SEMA3A and SEMA4E and their receptors PLXND1 and NRP1 mRNA (Real time quantitative PCR) and protein (western blot analyses) levels were found to be markedly increased in RA ECs compared to control ECs. The expression of SEMA3A, SEMA3E, SEMA4A, PLXND1 and NRP1 was strikingly increased in the synovial tissue of patients with RA. Confluent microscopy with double labeling for CD31 confirmed the prominent endothelial expression of these class 3 and 4 semaphorins and their receptors. SEMA3A serum levels were significantly lower in RA compared to controls (13.93±5.69 vs. 18.29±6.69 ng/mL, P=0.023, r=0.21, P=0.013, r=0.39, P=0.006, r=0.23, respectively). In addition SEMA3A and SEME4D correlated with CRP levels (r=-0.36, P<0.001, r=-0.23, respectively). In addition SEMA3A and SEME4D also correlated with the Disease Activity Score (DAS)-28, (r=0.27, P=0.006 and r=0.23, respectively). SEMA3A, SEMA4A and SEMA4D also correlated with the Global OMERACT-EULAR Synovitis Score, reflecting the intensity of synovial vascualarization measured by power Doppler ultrasonography (r=-0.22, P=0.023, r=0.21, P=0.030 and r=-0.242, P=0.013, respectively). In addition serum levels of the angiogenic markers Tie-2, angiopoietin, Interleukin-6 and soluble Vascular Cell Adhesion Molecule.

Conclusion: Gene expression profiling of ECs identified semaphorins as potential biomarkers and therapeutic candidates in RA. Class 3 and 4 semaphorins are overexpressed in RA ECs, synovial vessels and the serum of patients with RA. They also correlated with validated markers of inflammation and angiogenesis. Thus, semaphorins might be novel and appealing EC-derived inflammatory and proangiogenic targets in RA.

SAT0038

PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR-GAMMA COACTIVATOR-1B FACILITATES PSEUDOPOD FORMATION OF FIBROBLAST-LIKE SYNOVIOCYTES IN RHEUMATOID ARTHRITIS VIA ACTIVATING RHO GTPASES

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Background: Fibroblast-like synoviocytes (FLS) play critical roles on joint inflammation and destruction of cartilage and bone in rheumatoid arthritis (RA) due to their aggressive behavior including increased migration. The Rho family of small GTPases are the master regulators of actin cytoskeleton remodeling which leads to pseudopodia formation and migration. Peroxisome proliferator-activated receptor-gamma coactivator-1 (PGC-1) is a transcriptional regulator which plays important roles on regulating multiple signaling pathways. Our previous study revealed that elevated PGC-1 in RA-FLS promoted their migration and invasion. However, the underlying mechanism remains elusive.

Objectives: To investigate the role of PGC-1 in regulating pseudopodia formation of FLS in RA-FLS and its possible mechanisms.

Methods: Synovial tissues were obtained from six patients with active RA and FLS were isolated and cultured in vitro. RA-FLS were transfected with a lentivirus vector for PGC-1 and/or over-expression, and the effects were investigated. The change of cytoskeleton was stained with fluorescein phallolidin to visualize polymerized actin in lentivirus-transfected RA-FLS.

Results: In preliminary experiments, we found that partial ZAP-70 deficiency (in ZAP-70 heterozygous (ZAP-70 +/-) knockout mice, then stimulated in vitro for 72 hours with anti-CD3/anti-CD28-coated beads. After stimulation, cells were lysed and the homogenates were subjected to Western-blotting using antibodies against activated Caspases-3, -8, and -9, respectively, and other apoptotic markers (cytochrome C, and some important regulator molecules (Cbl-2, Bim and Cbl).

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by qPCR. Their activity was measured using a Rac1, RhoA or Cdc42 Pulldown & G-Lisa Activation Assay Kit.

Results: 1) PGC-1α knockdown inhibited lamellipodia and filopodia formations of RA-FLS compared with Lv-sh-GFP transfection group (cells with lamellipodia: 34% ± 4% vs. 49% ± 4%, P=0.041), while PGC-1α over-expression promoted lamellipodia and filopodia formations of RA-FLS compared with Lv-GFP transfection group (cells with lamellipodia: 50% ± 4% vs. 34% ± 6%, P=0.040; cells with filopodia: 67% ± 7% vs. 52% ± 6%, P=0.045, Figure 1A). 2) PGC-1α knockdown or over-expression did not affect the mRNA expression of Rac1, RhoA or Cdc42 (all P>0.05, Figure 1B). However, PGC-1α knockdown suppressed the activity of Rac1, RhoA and Cdc42 (Pulldown assays: 65%-78% reduction; G-LISA assays: 28%-53% reduction, all P<0.05), while PGC-1α over-expression significantly increased their activity (Pulldown assays: 1.55-1.72 folds; G-LISA assays: 1.43-1.68 folds, all P<0.05, Figure 1C, D).

Conclusion: Our findings revealed that elevated PGC-1α in RA-FLS promotes pseudopodia formation by activating Rho family proteins which imply a novel target on regulating RA-FLS migration.

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GENOTYPE OF THE RHEUMATOID ARTHRITIS SEVERITY LOCUS, RS26232, IS ASSOCIATED WITH INVASIVENESS OF RASFs IN VITRO

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Background: The single nucleotide variant rs26232 has been associated with both the susceptibility to, and severity of, rheumatoid arthritis (RA). There is an allele dose response between rs26232 and radiological damage, with the minor T allele being protective against disease severity. Rs26232 is situated in the first intron of C5orf30, which is a negative regulator of tissue damage and inflammation in RA.

Objectives: The objective of this study is to elucidate the mechanism by which rs26232 may mediate disease severity. We also aimed to determine the genotype-phenotype association of rs26232 in rheumatoid arthritis synovial fibroblasts (RASF).

Methods: RASF were derived from knee biopsies of RA patients taken at arthroscopy (n=33). RASFs were used between passages 3-8. Matrigel-coated Boyden transwell chambers were used to measure invasion. Wound healing (scratch assays) were used to measure migration, whereas proliferation was measured via crystal violet staining of fixed RASF. Intracellular cytokine staining and cell surface markers were measured via flow cytometry. Secreted cytokines were measured in the supernatant of RASF using ELISA. Rs26232 genotype was determined by PCR genotyping assay with allelic discrimination analysis. Anticitrullinated protein antibody (ACPA) status was measured for each participant. Quantitative real-time PCR was used to measure gene expression. Mann-Whitney U test was used to compare two independent groups, Kruskal-Wallis test was used to compare groups of greater than two.

Results: 49% (n=16) of our RASF cohort where homozygous for the major allele CC, 42% (n=14) were heterozygous CT, 9% (n=3) were TT. Rs26232 is associated with invasion of RASFs with the CC genotype being more invasive than the CT genotype (p=0.021). RASFs with the CC genotype had increased ICAM1 and VEGF cell surface expression compared to CT genotype (p<0.001, p=0.05 respectively). MCP1/CCL2 was decreased in CC compared to CT (p=0.013). No association was found between rs26232 genotype and migration, proliferation, or expression of MMP3, TIMP3, IP10 or MIP1a.

Conclusion: Our findings revealed that elevated PGC-1α in RA-FLS promotes pseudopodia formation by activating Rho family proteins which imply a novel target on regulating RA-FLS migration.
seropositive eRA patients. Whereas cTph are related with disease activity, cTfh cells seem to be constitutively elevated.

REFERENCE

Disclosure of Interests: Paula Forteza-Gordo: None declared, Laura Nuño: None declared, Alejandro Villalva: None declared, Diana Peiteado: None declared, Irene Monjo: None declared, Amaya Puig-Kröger: None declared, Alejandro Balsa Grant/research support from: Abbvie, Pfizer, Novartis, BMS, Nordic, Sanofi, Consultant for: Abbvie, Pfizer, Novartis, BMS, Nordic, Sanofi, Sandoz, Lilly, Paid instructor for: Pfizer, Speakers bureau: Pfizer, Novartis, UCB, Nordic, Sanofi, Sandoz, Lilly, Maria-Eugenia Miranda-Carus Grant/research support from: Roche Pharma, BMS


SAT0044
HIGH THERAPEUTIC EFFICACY OF ORAL RAS INHIBITORS IN COLLAGEN INDUCED ARTHRITIS: INHIBITION OF RELEVANT MAP-KINASES AND THE CONSEQUENT INDUCTION OF AUTOACTIVE PATHOGENIC T CELLS AND AUTOANTIBODIES

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Background: The Ras family of GTPases plays an important role in signaling nodes downstream to T cell antigen receptor (TCR) and CD28, potentially lowering the threshold for TCR activation by autoantigens [1]. Somatic mutation in NRAS or KRAS may cause a rare autoimmune disorder coupled with abnormal expansion of lymphocytes. T cells from Rheumatoid Arthritis (RA) patients show excessive activation of Ras/MEK/ERK pathway. The small molecule Farnesylthiosalicylic acid (FTS) interferes with the interaction between Ras/GTPases and their prenyl-binding chaperones to inhibit proper plasma membrane localization and effective downstream signaling. Previous studies in the Lewis rat adjuvant induced arthritis show that FTS attenuates arthritis development and that the inhibition of pathogenic Th17-type cells is a central mechanism of action of this compound [2].

Objectives: To further study the therapeutic efficacy and molecular mechanisms that mediate the immunomodulatory effects of FTS in DBA/1 mouse collagen type-II induced arthritis (CIA) the pre-clinical model.

Methods: Arthritis was induced in 8-10 week old male DBA/1 mice by immunization with collagen type-II (CII) and complete Freund’s adjuvant.

Objectives: 

- Inhibition of relevant MAP-Kinases and the consequent induction of autoactive pathogenic T cells and autoantibodies
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RESULTS: We found that the clinical scores of mice in the FTS and MTX arms was significantly reduced (by ~80%), area under curve) compared to the control arm. Accordingly, FTS therapy significantly reduced joint pathology scores for inflammation, pannus formation, bone resorption, and cartilage damage. FTS also significantly inhibited the production of pathogenic anti-CII autoantibodies, anti-citrullinated peptide antibodies, and notably the de-sialylation of these autoantibodies as compared to control mice (Figure 1). The analysis of the effect of FTS on the T cell response to CII immunization, revealed strong attenuation of IL-22, IL-17, IL-9, GM-CSF, TNF, and IFN-gamma producing pro-inflammatory CD4+ Th cells. Importantly, we found that in vitro FTS treatment during TCR-stimulation (anti-CD3/CD28 mAbs) significantly inhibited the ensuing phosphorylation of multiple critical MAP kinases such as Erk, Akt, p38, and mTOR.

CONCLUSION: We determined in the preclinical CIA model that FTS, a first-in-class oral Ras-GTPase inhibitor, is a potent immune modulator, via the inhibition of TCR/CD28/Ras-dependent activation of critical MAPKs, consequently attenuating the generation of pro-inflammatory autoreactive T cells.

REFERENCES

A NOVEL SMALL MOLECULE, MBS2133, MODULATES OSTEOCLAST PRE-CURSOR METABOLISM TO INHIBIT OSTEOCLAST DIFFERENTIATION: AN ALTERNATIVE THERAPY FOR OSTEOCLYTIC PATHOLOGY IN RA

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease associated with substantial local and systemic bone loss. Despite the availability of several treatment options many patients do not reach low disease activity. Furthermore, current therapeutics generally target inflammation rather than erosive pathology. Thus, there remains a need for new therapies that can target both aspects of the disease. Prior studies have shown that biphynicarboxylic acid small molecule derivatives not only inhibit murine osteoclastogenesis but also attenuate inflammation and bone destruction in murine models of RA.1,2

Objectives: To evaluate a novel small molecule derivative, MBS2133, on human osteoclastogenesis, osteoanastheniaogenesis and cellular function, and to investigate the in vitro mechanism of action.

Methods: Osteoblasts were derived from human mesenchymal stem cells. Cells were differentiated in the presence or absence of MBS2133 and mineralization assessed by Alizarin Red staining. Human CD14+ blood monocytes were differentiated into osteoclasts (OCs) with M-CSF and RANK-L, in the presence or absence of MBS2133, and/or metabolites. Mature OCs were stained with tartrate-resistant acid phosphatase (TRAP) and quantified by light microscopy. Osteolytic activity was assessed on mineral-coated surfaces. Western blot analysis was used to assess down-stream signalling pathways. Changes in the metabolic profile of pre-osteoclasts following 4h exposure to MBS2133 was carried out by liquid chromatography mass spectrometry.

Results: MBS2133 had no effect on the differentiation and function of primary human osteoblasts. In comparison, exposure of RANK-L stimulated CD14+ monocytes to MBS2133 significantly reduced OC differentiation and osteolytic activity of mature OCs. Notably, exposure of pre-OCs to MBS2133 for 2h at initiation of osteoclastogenesis, was sufficient to significantly reduce subsequent OC differentiation. Evaluation of treated pre-osteoclasts revealed that RANKL-mediated phosphorylation of p38 was reduced. Metabolic analysis of pre-osteoclasts revealed that MBS2133 induced a substantial reduction in a range of metabolites associated with glycolysis, oxidative phosphorylation and fatty acid oxidation pathway. Notably, L-carnitine, which facilitates the transportation of fatty acids to the mitochondrial matrix and enables processing and entry into tricarboxylic acid cycle for further energy production, was significantly reduced. In vitro supplementation of L-carnitine inhibited the ability of the compound to switch off OC differentiation and osteolytic activity.

Conclusion: The results of this study demonstrate that MBS2133 specifically modulates the metabolism of myeloid cells, which has a substantial impact on their ability to differentiate into mature osteoclasts. These findings highlight the importance of modulating the glycolysis/oxidative phosphorylation axis in osteoclastogenesis and suggest that targeting the metabolic state of pre-osteoclasts could offer a new therapeutic approach to treat bone resorption in rheumatic diseases.

REFERENCES

Disclosure of Interests: Shatakshi Sood: None declared, Lisa Patel Shareholder of: Shareholder of Istiteto Ltd, Employee of: Employee of Istiteto, Martyn Foster Shareholder of: AstraZeneca, Consultant for: Istiteto, Levicet, Employee of: AstraZeneca, Louise Jopling Shareholder of: Johnson and Johnson (employee), Employee of: Employee of Iansens (Pharma-ceutical arm of Johnson & Johnson) since May 2008 to present day, Rob van’t Hof Shareholder of: OsteoRx Ltd, Iain Greig Shareholder of: Shareholder in OsteoRx Ltd, a spin-out company from the University of Aberdeen, which retains a financial interest in MBS2133, Sam Williams Shareholder of: Shareholders of Istiteto Ltd, Employee of: Employees of Istiteto, Iain McInnes Grant/research support from: AstraZeneca, Celgene, Compugen, Novartis, Roche, UCB Pharma, Consultant for: AbbVie, Celgene, Galvani, Lily, Novartis, Pfizer. UCB Pharma, Carl Goodyear Grant/ research support from: AstraZeneca, BMS, Celgene, Iansens, MedAnnex, Pfizer and UCSB, Speakers bureau: Abbvie

ARE THERE OF SOCIAL SUPPORT AND LOW DECISION LATITUDE AT WORK LINKED TO RISK OF RHEUMATOID ARTHRITIS, AND IF SO, HOW DO THEY RELATE TO OTHER RISK FACTORS? RESULTS FROM THE SWEDISH EIRA STUDY

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Background: The role of psycho-social factors in the development of rheumatoid arthritis (RA) is debated. Objective: We investigated whether psychosocial stress measured as low sense of social support, and low decision latitude at work, were linked to risk of RA, and whether they related to known lifestyle risk factors for RA.

Methods: The Swedish population-based EIRA study included incident RA cases (N=3724) and controls (N=5937), matched for age, sex and residential area. Responders filled in questionnaires regarding self-reported social support, decision latitude at work and life-style factors.

Results: There were 898 cases with low social support and 285 cases with low decision latitude at work (latter only available in first part of study). Low social support was not associated with RA risk in unadjusted analyses (OR=1.05, 95%CI=0.95-1.15). Low decision latitude at work did associate with a higher RA risk in the unadjusted analyses (OR=1.52, 95% CI=1.20-1.94), but this association was no longer significant after further adjustment for smoking, obesity and university degree (adjusted OR=1.24, 95% CI=0.93-1.63). Associations between those lifestyle risk factors and RA were confirmed (no university degree, OR=1.50; smoking OR=1.71; obesity OR=1.15).

Next, we evaluated whether low social support or low decision latitude at work differed by previously established risk factors. Cases with RA reporting low sense of social support were more often men (OR=1.60, 95% CI=1.40-1.83), current smokers (OR=1.46, 95% CI=1.26-1.70), obese (OR=1.29, 95% CI=1.09-1.54), physically inactive (OR=2.78, 95% CI=1.86-3.90) and without a university degree (OR=2.04, 95% CI=1.77-2.36), with similar pattern among the controls. For working-conditions, cases reporting low decision latitude at work were also more often current smokers (OR=2.05, 95% CI=1.33-3.16) and with no university degree (OR=6.23, 95% CI=5.13-13.22), but less often male (OR = 0.40, 95% CI=0.26-0.60).

Again, the pattern was similar among controls. RF/ACPA-positivity did not associate with low social support or low decision latitude. Conclusion: Neither low social support nor low decision latitude at work were associated with an increased risk of RA after adjustment for other known lifestyle risk factors for RA. An initial crude association between
low decision latitude at work and risk for RA was explained by differences in smoking and educational level. However, both low social support and low decision latitude at work associate strongly with known, and here validated, risk factors for RA (smoking, obesity, no university degree) with similar pattern among both cases and controls.

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SAT0047 PRIMARY LYMPHOID TISSUE FROM RHEUMATOID ARTHRITIS PATIENTS HARBOUR CITRULLINE SPECIFIC PLASMA CELLS

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Background: Anti-citrullinated protein antibodies (ACPA) are specific markers with pathological effects in rheumatoid arthritis (RA). ACPA-specific B-cells have been identified in synovial joint fluid and peripheral blood. An increased concentration of ACPA is found in synovial fluid and lung tissue compared to blood suggest local production, partly confirmed by detection of ACPA synovial plasma blasts, but primary lymphoid tissue have not previously been examined.

Objectives: In this study we investigated the plasma cell repertoire in the bone marrow and occurrence of autoantibody producing plasma cells.

Methods: For this study we developed a method to collected and process bone marrow samples from proximal femur in RA patients undergoing hip joint replacement. Bone marrow samples were processed and monoclonal cells were obtained by Ficoll separation. CD138+ plasma cells were single cell sorted by flow cytometry. Paired heavy and light chains were PCR amplified, sequenced, and analyzed by V-Quest and IgBLAST database to annotate variable gene usage. To enrich for ACPA, sequences were selected based on high somatic hypermutation numbers and Fab N-glycosylation sites. Selected sequences were cloned and expressed as Igκ in Expi293 cells. Monoclonal antibody reactivity to citrullinated and arginine form of vimentin, enolase, fibrinogen, histone, tenascin C peptides; carboxymethylated and malondialdehyde-acetaldehyde bovine serum albumin, and tetanus toxoid antigens were examined by ELISA. Included patients were clinical examined and obtaining peripheral blood samples.

Results: After method development and quality analysis we were able to include five bone marrow samples in this study. The five included RA patients, median age 74 (range 66-82) years, had in median 20 (range 4-44) years of destructive disease, all were RF positive, four were females and anti-CCP2-positive, and all except one were treated with anti-rheumatic drugs.

Overall, from the processed bone marrow, 465 paired heavy-light IgG plasma cell sequences were obtained, in total 368 (range 20-194) from ACPA positive patients and 97 from the ACPA negative patient. We observed statistically significant changes in heavy chain variable gene usage with lower usage of VH-1 and higher VH-3 frequency in sequences from ACPA positive RA patients compared to sequences from the ACPA negative RA patient. We also found statistically significant increase in VH N-glycosylation in sequences from the ACPA positive RA patients (22.6% ACPA positive vs 12.4% ACPA negative; p=0.03) but no difference in mutation numbers. From obtained sequences, 34 interesting clones were selected for monoclonal antibody-expression. Among the 34 clones we found two citrulline specific reactive clones (reactivity towards CCP2, citrullinated vimentin and fibrinogen peptides) and one malondialdehyde-acetaldehyde (MAA) reactive clone, originating from three different ACPA positive patients with the most longstanding disease. None of these clones had reactivity towards control antigens such as arginine versions of peptides.

Conclusion: Plasma cells producing ACPA are present in primary lymphoid tissue from RA patients. Further studies of difference in characteristics, Igκ gene usage and N-glycosylation, between ACPA-positive and ACPA-negative patients are needed.

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SAT0048 ANTI-FRACTALKINE MONOCLONAL ANTIBODY AMELIORATE JOINT DESTRUCTION AND SYNOVITIS THROUGH SUPPRESSION OF OSTEOCLAST PRECURSOR MIGRATION AND INDUCTION OF SYNOVIAL CELL DEATH IN COLLAGEN-INDUCED ARTHRITIS MODEL

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Background: In the Phase 1/2 clinical study, E6011, a novel humanized anti-fractalkine (FKN) mAb demonstrated a promising efficacy in active RA patients who were inadequately controlled by MTX and/or TNF-α inhibitors (NCT 02196558). In RA joint tissue, increased expression of fractalkine (FKN) and abundant infiltration of CX3CR1-positive cells were observed. FKN is expressed on endothelial cells and fibroblast-like synovocytes in synovium and also expressed on osteoclasts. CX3CR1 is expressed on monocytes/macrophages and osteoclast precursors (OCPs). Therefore, FKN-CX3CR1 interaction could play pivotal roles in migration, differentiation and activation of those cells. However, the precise mechanism(s) of FKN-CX3CR1 axis in RA, especially on joint destruction resolution to be elucidated.

Objectives: To elucidate the roles of FKN-CX3CR1 axis in cartilage destruction, bone damage and proliferated synovial cells by using anti-FKN mAb.

Methods: For the induction of CIA, mice were immunized with bovine type II collagen. Anti-FKN mAb was injected twice a week. The clinical arthritis score was monitored, and joint destruction was evaluated by soft x-ray and histology. The mRNA expression levels were assessed by quantitative RT-PCR. Blood parameters were measured using ELISA. In vivo, effect of immobilized FKN on RANK ligand (RANKL)-induced osteoclast differentiation was examined. In vivo, bone marrow-derived OCPs were fluorescente-labeled and transferred to CIA mice to evaluate the migration of OCPs into synovium. Inhibitory effect of anti-FKN mAb, etanercept or tofacitinib against OCP migration was assessed. To examine the effect of anti-FKN mAb against proliferated synovial cells, propidium iodide (PI) was injected to anti-FKN mAb-treated CIA mice to evaluate the synovial cell death.

Results: Anti-FKN mAb significantly reduced the arthritis and soft x-ray scores in both prophylactic and therapeutic treatment. Anti-FKN mAb histologically improved synovitis, cartilage destruction and bone damage, with marked reduction of osteoclast numbers. Plasma levels of CCMP and MMP-3 were also decreased. Interestingly, anti-FKN mAb significantly suppressed Trf and Il6 mRNA expression in the affected joints. In vitro, RANKL-induced osteoclast differentiation was enhanced by immobilized FKN, and anti-FKN mAb suppressed FKN-dependent osteoclast formation. In vivo, anti-mFKN mAb strongly inhibited the migration of OCPs into the proliferated synovial cells of mice with CIA, whereas etanercept or tofacitinib had no significantly effect. Importantly, synovial cell death was abundantly found in proliferated synovial cells of mice with CIA after the anti-mFKN mAb treatment.

Conclusion: Anti-FKN mAb remarkably ameliorated the joint destruction with the marked reduction of osteoclasts by the inhibition of both OCP survival and OCP migration in inflamed joint tissues. In addition, anti-mFKN mAb immediately induced synovial cell death in the proliferated synovial cells, suggesting the direct inhibitory effect in the synovium. These results strongly indicate that inhibition of FKN-CX3CR1 axis by a humanized anti-FKN mAb, E6011, is an attractive and affected joints-selective therapeutic strategy for the treatment of both inflammatory synovitis, cartilage destruction and bone damage in RA patients.

REFERENCES


References:


Baricitinib improves joint mobility after injury in a rodent forced-ambulation model

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Background: Movement-evoked pain and impaired joint mobility are common comorbidities in inflammatory diseases such as Rheumatoid Arthritis (RA) and Osteoarthritis. The Janus kinase (JAK) pathway has been implicated in both inflammation and chronic pain. Clinical data suggests that baricitinib, a selective JAK 1/2 inhibitor, can robustly and rapidly alleviate pain in RA. Utilizing a rodent forced-ambulation model, we have previously shown attenuation of gait deficits with analgesics such as opioids, nonsteroidal anti-inflammatory drugs (NSAIDs), and an anti-NGF (Nerve Growth Factor) antibody. However, in this same model a fusion protein blocker of TNFα (tumor necrosis factor alpha) signaling failed to demonstrate efficacy though inflammation was decreased. The present work investigated the potential of baricitinib, recently approved for treatment of RA, to reduce inflamman-induced joint pain and gait impairment in this model of joint inflammation mediated pain.

Objectives: To determine if JAK 1/2 pathway inhibition is effective in treating inflamman-induced joint pain and gait impairment.

Methods: Unilateral joint injury was induced in female Sprague Dawley rats (Harlan, Indianapolis, IN, USA) by unilateral intra-articular injection of 20 μg Complete Freund’s Adjuvant (CFA). Using the GaitScan (CleverSys Inc., Reston, VA) treadmill system, a composite gait score comprising of range of motion, normalized stance distance, stance/swing ratio, and paw size was evaluated over 3 days post-injection. 2 Rats were treated on Day 0 with vehicle, positive control (40 mg/kg Tramadol), or clinically relevant doses of baricitinib (10 mg/kg p.o., 2-hrs prior to each test, q.d.). Dorsal root ganglion (DRG) were harvested post-gait evaluation and Total STAT3 (Cell Signaling, #4904) and phospho-STAT3 (Y705) (Cell Signaling, #9131) protein levels were examined via immunoblotting. The p-values were derived from repeated measures ANOVAs.

Results: In rat DRG homogenates, baricitinib significantly decreased phospho-STAT3 (Y705) protein levels in a dose-dependent manner (p<0.01) with a significant effect after a 3 mg/kg dose and a maximal response after a 10 mg/kg in both the ipsilateral (right) and contralateral (left) sides. Total STAT3 protein levels remained unchanged. Similarly, treatment with baricitinib significantly improved composite gait score at the 10 mg/kg dose (p<0.05) by Day 3.

Conclusion: These data indicate that treatment with baricitinib attenuates CFA-induced joint deficits, a surrogate measure of joint pain. This effect correlated with the pharmacodynamic inhibition of JAK-STAT signaling in DRGs. These data support a role for JAK-STAT signaling in pain signaling and provide an opportunity to investigate the potential mechanism of action of baricitinib in joint pain.

REFERENCES


Photodynamic therapy targeting activated fibroblasts induces synovial cell death in experimental arthritis

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Background: Activated synovial fibroblasts (SF) contribute to rheumatoid arthritis (RA) by producing a multitude of cytokines, chemokines and proteases thus aggravating disease. Activated SF can be distinguished from quiescent fibroblasts by their expression of fibroblast activation protein (FAP). Selective depletion of FAP+ SF in inflamed joints could decrease their contribution to the arthritis process and thus constitute a viable treatment option. Further focussing of the treatment to only those areas affected by the disease can be accomplished by applying targeted photodynamic therapy (PDT). In iPDT a light sensitive molecule, a photosensitizer (PS), is conjugated to a targeting moiety. Upon activation by light this construct produces reactive oxygen species, killing the targeted cells.

Objectives: To this end we developed and tested a therapy that selectively depletes activated SF by targeting FAP on these cells with an
antibody, 28H1, to which the PS, IRDye700DX, for iPDT is attached. Here we investigated the feasibility of using FAP-iPDT to induce cell death in murine articular synovium ex vivo.

**Methods:** After conjugation of the IDRy700DX to 28H1 (28H1-700DX), binding and specificity of the conjugate was determined. Subsequently, iPDT efficiency in vitro was established using a 3T3 fibroblast cell line stably transfected with FAP. Biodistribution using an [111In] In-DTPA-28H1 conjugate with and without IRDye700DX was performed in healthy C57BL/6J mice as well as in CD74+BL6 mice with antigen induced arthritis (AIA). Finally, the potential of FAP-iPDT to induce targeted cell death in the synovial lining was determined by treating knee joints from mice with AIA ex vivo.

**Results:** Conjugation of IDRy700DX to the antibody did not negatively influence the immunoreactive fraction or binding capacity of the conjugate (94.7% for 28H1-700DX). 28H1-700DX was able to efficiently induce FAP-specific cell death in vitro. At 17.6 J/cm² radiant exposure, 89.24% (94.7% for 28H1-700DX). 28H1-700DX was able to efficiently induce Conjugation of IRDye700DX to the antibody did not negatively stably transfected with FAP. Biodistribution using an [111In] In-DTPA-28H1 conjugate with and without IRDye700DX was performed in healthy C57BL/6J mice as well as in CD74+BL6 mice with antigen induced arthritis (AIA). Finally, the potential of FAP-iPDT to induce targeted cell death in the synovial lining was determined by treating knee joints from mice with AIA ex vivo.

**Conclusions:** Here we demonstrated the feasibility of conjugating a PS to an antibody targeting FAP on activated SF without negatively impacting the binding capacity thereof. Furthermore we showed that this construct can then be used to deliver cell specific cytotoxicity through iPDT both in vitro and ex vivo in a mouse model of arthritis. This approach may have therapeutic potential in the treatment of RA.

**Disclosure of Interests:** None declared.

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**SAT0053**

**GLYCOSYLATION IN MAMMALS PROTECTS CITTULLINATED CHEMOKINES FROM PARTIAL DEGRADATION**

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**Background:** Citrullination is a posttranslational modification of specific proteins by peptidylarginine deiminase (PAD) activities. Nowadays citrullination is recognized as a hallmark of rheumatoid arthritis and other autoimmune diseases. In our recent study we have shown a presence of citrullinated chemokines epithelial-derived monocyte chemotactic protein-1 (MCP-1/CCL2), macrophage inflammatory protein-1α (MIP-1α/CCL3) and neutrophil-activating peptide 78 (ENA-78/CXCL5) in biological fluids collected from quick degradation. Chemokines MCP-1/CCL2, MIP-1α/CCL3 and ENA-78/CXCL5 cannot be efficiently used as the standards in modified ELISA assays as chemokines MCP-1/CCL2, MIP-1α/CCL3 and ENA-78/CXCL5 underwent quick partial degradation upon their in vitro citrullination by PAD2 and cannot be detected with either Western blotting or mass-spectrometry. At the same time mammalian cellularly produced specifically glycosylated MCP-1/CCL2, MIP-1α/CCL3 and ENA-78/CXCL5 can be efficiently citrullinated and successfully used as the standards in modified ELISA assays as well as in bioassays.

**Conclusion:** Glycosylation that is lacking in bacterially-produced proteins but occurs in mammalian cells stabilizes citrullinated chemokines thus protecting them from quickly ongoing partial degradation.

**Disclosure of Interests:** None declared

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**SAT0054**

**INVESTIGATING MECHANISMS OF AUTOANTIBODY INDUCED PAIN, BONE LOSS AND ARTHRITIS DEVELOPMENT**

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**Background:** In rheumatoid arthritis (RA), autoantibodies against citrullinated proteins (ACPAs) have been reported to be associated with bone loss, pain and tenosynovitis prior to disease onset.

**Objectives:** We aimed to investigate if transfer of human ACPAs into mice could reproduce these clinical observations.

**Methods:** Monoclonal ACA (1325:04C03 and 1325:01B09) and control (1362:01E02) antibodies (mAbs) were generated from synovial plasma or serum of B cells from RA patients. In combination of monoclonal ACPAs or control antibody were injected in BALB/c female mice (12-16 Weeks) with or without a consequent intra-articular injection of LPS after 8 days. Pain-like behavior was monitored by measuring mechanical hypersensitivity using von Frey filaments every 3 days and estimation by up-down Dixon method. Bone mineral density was measured by micro-CT. Using specially designed mobilization casts, dedicated mouse MRI imaging were scanned and evaluated for any signs of soft tissue joint inflammation. Blinded to ACPA and controls, the MRI images were scored for the presence of synovial thickening, effusion and tendon inflammatory changes by 3 readers in consensus.

**Results:** ACPAs (1325:04C03 and 1325:01B09) induced significantly more pronounced pain-like behavior (lasting for at least 4 weeks) and reduction of the trabecular bone thickness in the hind limbs, whereas no such effect was seen with the control mAbs generated in the same way as the monoclonal ACPAs. While no macroscopic sign of joint inflammation could be detected, preliminary MRI data shows that sub-clinical joint inflammation (such as tenosynovitis) in mice injected with ACPAs but not those injected with control mAb. Intra-articular LPS injection resulted in significantly increased prolonged mechanical hypersensitivity in mice initially receiving sub-optimal doses of monoclonal ACA as compared to those receiving control mAb. This was associated with higher levels of sub-clinical arthritis diseases and demonstrated citrullination of ENA-78/CXCL5 as an efficient macrophage chemoattractant in a contrast with non-citrullinated ENA-78/CXCL5. In our current work we found that citrullinated in vitro bacterially produced chemokines cannot be efficiently used as the standard in modified ELISA assays (ELISA) assays designed to detect citrullinated chemokines.

**Objectives:** In our work we aimed generate a procedure for preparation of stable citrullinated chemokines suitable for research applications and to validate a hypothesis that posttranslational modifications occurring in mammalian cells can stabilize chemokines can also protect citrullinated chemokines from quick degradation.

**Methods:** MCP-1/CCL2 and MIP-1α/CCL3 were cloned from total RNA isolated from synovial fibroblasts obtained from RA patient. Both bacterially-produced and mammalian cells-produced recombinant human chemokines were citrullinated by commercial rabbit PAD2. Success in citrullination was confirmed with Western blotting and mass-spectrometry. Citrullinated chemokine concentrations were measured by modified sandwich ELISA assays.

**Results:** Both commercially available and self-made bacterially produced chemokines MCP-1/CCL2, MIP-1α/CCL3 and ENA-78/CXCL5 undergo quick partial degradation upon their in vitro citrullination by PAD2 and cannot be detected with either Western blotting or mass-spectrometry. At the same time mammalian cellularly produced specifically glycosylated MCP-1/CCL2, MIP-1α/CCL3 and ENA-78/CXCL5 can be efficiently citrullinated and successfully used as the standards in modified ELISA assays as well as in bioassays.

**Conclusion:** Glycosylation that is lacking in bacterially-produced proteins but occurs in mammalian cells stabilizes citrullinated chemokines thus protecting them from quickly ongoing partial degradation.

**Disclosure of Interests:** All human subject samples were collected after approval by the Institutional Review Board of the Academic Medical Center/University of Amsterdam, Amsterdam, The Netherlands (Protocol MEC 07/079 #10.17.0708) and provision of informed consent by the patients.

**REFERENCE**

‘Defense response’ (p=8.11×10^{-22}) and ‘cytokine activity’ (p=1.27×10^{-23}) were the most significantly enriched gene ontology terms for genes regulated in TNF stimulated hand SF. These processes were less prominently enriched in stimulated knee (1.58×10^{-15} and 8.64×10^{-16}) and shoulder SF (2.02×10^{-11} and 3.20×10^{-11}), where ‘cell cycle’ (p=2.29×10^{-20} in knee and p=2.18×10^{-20} in shoulder), and ‘DNA packaging complex’ (p=4.63×10^{-29} in knee and p=8.91×10^{-20} in shoulder) were the most significantly enriched gene ontology terms. These processes were not significantly enriched in stimulated hand SF.

**Conclusion:** SF from different joints in RA react differently to TNF stimulation. In particular hand SF reacted different to TNF stimulation than shoulder and knee SF, which appeared more similar. These qualitative and quantitative differences of the inflammatory response might translate into joint-specific pathotypes of synovitis with distinct therapeutic responses and disease outcomes.
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SAT0056

TASS315, A NOVEL BRUTON’S TYROSINE KINASE INHIBITOR, DEMONSTRATES POTENT EFFICACY AGAINST BONE DESTRUCTION IN AN ANIMAL MODEL FOR RHEUMATOID ARTHRITIS

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Background: Bone erosions and cartilage damages are a pathological hallmark of rheumatoid arthritis (RA) and are associated with poor functional outcome. Aberrant activations of osteoclasts induced by receptor activator of nuclear factor-kappa B ligand (RANKL), are involved in the bone erosions of RA. It has also been recently shown that under chronic inflammatory conditions such as RA, inflammatory cytokines in joints induce pathological osteoclast differentiation and cause excessive bone resorption independent of RANKL-RANK signaling. The Bruton’s tyrosine kinase (BTK) signaling pathway plays a pivotal role in inflammatory response and bone resorption. Thus, targeting BTK may be efficacious against not only inflammation but also bone erosion by regulating activation of effector cells such as B cells, macrophages and osteoclasts in RA. We have already shown the inhibitory effects of TASS315 on RANKL-dependent osteoclast activation. However, it remained uncertain whether TASS315 inhibits osteoclast activation induced by inflammatory cytokines.

Objectives: In this study, we evaluated the effects of TASS315 on osteoclast activation induced by inflammatory cytokines (in vitro) and the infiltration of tartrate-resistant acid phosphatase (TRAP)-positive osteoclasts in the joint of a mouse CIA model.

Methods: In vitro biochemical assay was performed using available kinase assay panels. The BioMAP® Diversity PLUS panels were used to determine the profile of TASS315 in primary human cell systems. The effects of TASS315 on osteoclasts were assessed by examining osteoclast-mediated bone resorption. TASS315 was orally administrated once a day in an established mouse CIA model. TRAP-positive osteoclasts were counted manually. Bone mineral density (BMD) and bone erosion were assessed using micro-CT analysis. The mechanical properties of the tibia were evaluated by a compression test of proximal metaphysis using a material testing machine.

Results: TASS315 selectively inhibited the enzyme activity of BTK and had less off target inhibition against other kinases. In BioMAP® systems, TASS315 decreased the production of IgG and the expression of cytokines (TNF-α, IL-6, IL-17A). TASS315 also inhibited osteoclast-mediated bone resorption induced by inflammatory cytokines. On the other hand, anti-RANKL antibody did not inhibit bone resorption induced by inflammatory cytokines. Furthermore, in the mouse CIA model, TASS315 significantly ameliorated paw swelling and pathological changes. TASS315 significantly decreased the infiltration of TRAP-positive osteoclasts in the joint and also showed improved BMD and bone erosion by time-dependent micro-CT analysis. In vehicle-treated mice, the mechanical strength of tibia was decreased compared with normal mice. TASS315 treated mice recovered the decreased parameters of the mechanical strength compared with vehicle-treated mice. These results show that TASS315 improves bone erosion in murine model for RA through direct inhibition of osteoclast activation induced by inflammatory cytokines as well as RANKL.

Conclusion: Our study demonstrates that TASS315 would be an attractive RA therapeutic drug that could improve bone destruction as well as inflammation.

REFERENCE


Disclosure of Interests: None declared


SAT0057

CREASED MICRONORNA-155 IS ASSOCIATED WITH A SPECIFIC DEFECT OF ANTI-INFLAMMATORY M2 MACROPHAGES POLARIZATION BOTH IN HUMAN RHEUMATOID ARTHRITIS AND IN COLLAGEN-INDUCED-ARTHRITIS MICE

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Background: Monocytes/macrophages are key players in the pathogenesis of Rheumatoid arthritis (RA). Monocytes can differentiate into pro-inflammatory macrophages (M1-like) or into anti-inflammatory, macrophages (M2-like). We previously found a defect of monocytes polarization into M2-like macrophages, in RA patients and not in healthy donors (HD) or in patients with other inflammatory diseases (such as connective tissue diseases or spondyloarthritides), and a propensity for preferential maturation towards M1-like pro-inflammatory macrophages that could contribute to synovial inflammation.

M1-155 expression has been shown elevated in RA synovial macrophages and in blood monocytes. M1-155 inhibits mRNA of 2 important proteins involved in programming of M2 macrophages (SOG and C/EBP-β).

Objectives: We assessed if miR-155 could play a role in the defect of monocytes polarization into M2-like macrophages both in human RA and in a mouse model of collagen-induced-arthritis (CIA) mice.

Methods: Monocytes were isolated from PBMCs for HD and RA by negative selection. Purified monocytes were transfected using AMAXA technologies with mir-155 mimic (for HD) or anti-miR155 (for RA) or controls mits. Then monocytes were incubated in the presence of human serum (SAB) (M2-like) for 6 days. Expressions of total macrophages markers (CD11b and CD71), M2-like macrophages markers (CD163, CD206 and Arg-1), M1-like macrophage marker (iNOS) were evaluated by flow cytometry, ELISA or immunofluorescence.

A. Monocytes from healthy donors
B. Monocytes from RA patients
C. Monocytes from CIA or control mice

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The defect of monocytes capacity of differentiation into M2-like phenotype was also found in in CIA mice as compared to controls, with a decreased expression of CD206, IL-10 secretion and Arginase-1 expression (Fig. 1C). MR155 was also involved in this defect in mice: its expression level was the same in M1-like macrophages between controls and CIA mice, whereas it was increased in M2-like CIA macrophages compared to controls mice (Fig. 1C).

Conclusion: MR155 plays a key role in the specific defect of anti-inflammatory M2 macrophages polarization found both in human rheumatoid arthritis and in CIA mice. MR155 could represent a new therapeutic target in RA that can be tested in the mouse model of CIA.

Disclosure of Interests: Audrey Paolotti: None declared, franneley reynaud: None declared, julien rohmer: None declared, juliette pascaud: get in RA that can be tested in the mouse model of CIA.

Scientific Abstracts

TREATMENT ACTIVE RHEUMATOID ARTHRITIS AND THE EFFECT OF THE TYPES AND PREVALENCE OF ENDOSTEAL DNA DAMAGE IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA)

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Background: Increased endogenous DNA damage poses a serious threat to cell health, since it may lead to mutagenesis, genomic instability and cellular apoptosis. DNA damage accumulation in immune cells occurs in patients with chronic inflammatory diseases, however; little is known on the types and prevalence of endogenous DNA damage in patients with Rheumatoid arthritis (RA).

Objectives: To study DNA damage response and repair network in patients with active RA and to test the hypothesis that anti-rheumatic treatment influences this network.

Methods: Peripheral blood mononuclear cells were isolated from 15 patients with active RA and 65 apparently healthy controls; 8 patients were re-examined after 12-week treatment. Endogenous DNA damage was determined using alkaline comet assay. Specific markers for single-strand DNA breaks (SSBs; RPA32) and double-strand DNA breaks (DSBs; γH2AX, 53BP1) were measured using western-blot. Formation of DNA damage was assessed by oxidative stress and abasic DNA sites measurements. Chromatin organization and the two subpathways of the fundamental nucleotide excision repair mechanism, namely, transcription-coupled repair (TCR) and global genome repair (GGR), were assessed along the N-ras gene.

Results: A 3-fold increase of endogenous DNA damage levels (Olive Tail Moment reflecting both SSBs and DSBs) was evident in active RA [mean±SD: 12.8±7.5 versus 4.5±2.4, p<0.001], as well as induction of RPA32, γH2AX and 53BP1, higher oxidative stress levels and increased abasic sites, compared to controls. While TCR capacity was preserved, GGR capacity was deficient in all active RA patients. Moreover, a more condensed chromatin structure was found in active RA compared to controls. Following treatment, chromatin structure loosened, GGR capacity was restored, oxidative stress and abasic sites decreased and levels of endogenous DNA damage reached control values in all patients.

Conclusion: Deregulated chromatin organization, deficient DNA repair capacity and augmented formation of DNA damage contribute to the accumulation of endogenous DNA damage in patients with active RA and are reversible after treatment. Additional studies to better understand the negative impact of DNA endogenous damage accumulation may create new therapeutic opportunities for patients with RA.

Disclosure of Interests: None declared


Apolipoprotein B derived peptides inhibit production of pro-inflammatory cytokines in PBMC of rheumatoid arthritis (RA) patients and improve arthritis in animal model of RA

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Background: Alpha-enolase (ENO1) is a multifunctional glycolytic enzyme. The cell-surface expression of ENO1 is increased in monocytes isolated from peripheral blood mononuclear cells (PBMCs) of RA patients. In previous experiments, we reported apolipoprotein-B (apoB) to be a novel ligand of cell surface expressed ENO1 and to enhance chronic inflammation in RA (1).

Objectives: This study was performed to evaluate agonistic or antagonistic function of peptide sequences within apoB, which modulated severity of arthritis in K/BxN serum transfer arthritis mouse model.

Methods: Peptides binding to ENO1 were evaluated by peptide microarray. Peptides were designed to have twelve amino acids overlap. Levels of pro-inflammatory cytokines produced by PBMCs were measured after treatment with peptides in RA patients and healthy controls (HCs). To evaluate the agonistic function of peptides, RA PBMCs pre-treated with peptides were stimulated with apoB and pro-inflammatory cytokines were measured in culture supernatant. Peptides PBMCs stimulated with apoB. These three peptides were named IP (inhibitory peptide)1, IP2 and IP3. IPs were injected after induction of the arthritis in K/BxN serum transfer mice in vivo. Ankle thickness and arthritis score to determine whether peptides could reduce arthritis severity.

Results: Among eighty five peptides from apoB, five peptides exhibited strong binding to ENO1. Two peptides increased production of pro-inflammatory cytokines, IL-1β, IL-6 and TNF-α, but three peptides did not change levels of pro-inflammatory cytokines in RA and HCs. How- ever the three peptides reduced production of pro-inflammatory cytokines in RA PBMCs stimulated with apoB. These three peptides were named IP (inhibitory peptide)1, IP2 and IP3. IPs were injected after induction of the arthritis in K/BxN serum transfer mice in vivo. Ankle thickness and arthritis scores were substantially reduced in IPs treated group than control group, and synovial inflammation, bone erosion and cartilage damage of arthritis were less severe in the IPs-treated groups. Especially, IP2 showed the most significant effect.

Conclusion: The apoB derived peptides interacting with ENO1 could have novel therapeutic effect in RA.

Disclosure of Interests: None declared


Apolipoprotein B derived peptides inhibit production of pro-inflammatory cytokines in PBMC of rheumatoid arthritis (RA) patients and improve arthritis in animal model of RA

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Background: Alpha-enolase (ENO1) is a multifunctional glycolytic enzyme. The cell-surface expression of ENO1 is increased in monocytes isolated from peripheral blood mononuclear cells (PBMCs) of RA patients. In previous experiments, we reported apolipoprotein-B (apoB) to be a novel ligand of cell surface expressed ENO1 and to enhance chronic inflammation in RA (1).

Objectives: This study was performed to evaluate agonistic or antagonistic function of peptide sequences within apoB, which modulated severity of arthritis in K/BxN serum transfer arthritis mouse model.

Methods: Peptides binding to ENO1 were evaluated by peptide microarray. Peptides were designed to have twelve amino acids overlap. Levels of pro-inflammatory cytokines produced by PBMCs were measured after treatment with peptides in RA patients and healthy controls (HCs). To evaluate the agonistic function of peptides, RA PBMCs pre-treated with peptides were stimulated with apoB and pro-inflammatory cytokines were measured in culture supernatant. Peptides PBMCs stimulated with apoB. These three peptides were named IP (inhibitory peptide)1, IP2 and IP3. IPs were injected after induction of the arthritis in K/BxN serum transfer mice in vivo. Ankle thickness and arthritis score to determine whether peptides could reduce arthritis severity.

Results: Among eighty five peptides from apoB, five peptides exhibited strong binding to ENO1. Two peptides increased production of pro-inflammatory cytokines, IL-1β, IL-6 and TNF-α, but three peptides did not change levels of pro-inflammatory cytokines in RA and HCs. However the three peptides reduced production of pro-inflammatory cytokines in RA PBMCs stimulated with apoB. These three peptides were named IP (inhibitory peptide)1, IP2 and IP3. IPs were injected after induction of the arthritis in K/BxN serum transfer mice in vivo. Ankle thickness and arthritis scores were substantially reduced in IPs treated group than control group, and synovial inflammation, bone erosion and cartilage damage of arthritis were less severe in the IPs-treated groups. Especially, IP2 showed the most significant effect.

Conclusion: The apoB derived peptides interacting with ENO1 could have novel therapeutic effect in RA.

Disclosure of Interests: None declared

SAT0060

CHOLESTEROL SEQUESTERING IN MACROPHAGES CONTRIBUTES TO THE LIPID PARADOX IN CHRONIC ARTHRITIS

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Background: Patients with active rheumatoid arthritis (RA) have increased cardiovascular mortality, paradoxically associated with reduced circulating lipid levels (1-3). Several disease-modifying antirheumatic drugs (DMARDs), such as the JAK inhibitor tofacitinib, ameliorate disease activity along with an increase in serum lipids (4, 5). We previously demonstrated in vitro that tofacitinib favored cholesterol efflux from macrophages through an ABCA1-dependent mechanism (6). Furthermore, tofacitinib-treated chronic arthritic rabbits showed increased circulating lipids and decreased lipid accumulation within the synovium (6).

Objectives: Our aim was to explore in vivo whether inflammation impedes cholesterol efflux from macrophages, and whether tofacitinib restores macrophage cholesterol release during chronic arthritis. For that purpose, we assessed the ability of intraperitoneally-injected 3H-cholesterol labelled macrophages to efflux cholesterol to circulating lipoproteins in collagen-induced arthritis (CIA) mice treated with tofacitinib or placebo, as compared to healthy controls.

Methods: DBA/1J mice were randomly assigned to healthy controls (Control, n = 9), CIA (CIA, n = 6) and CIA mice receiving 50 mg/kg/day tofacitinib, orally, for three consecutive days, starting on day 39 after CIA induction and coinciding with disease peak (CIA+TOFA, n = 6). The day after, 3H-cholesterol labeled RAW264.7 macrophages were intraperitoneally injected into mice and tracer appearance was monitored in plasma lipoprotein fractions, synovium, liver, bile and feces.

Results: The CIA group showed higher C-Reactive protein levels (CRP, µg/ml; Control: 10.50±5.9; CIA: 13.86±1.05, p≤0.03 vs. Control) and lower circulating 3H-cholesterol levels (% of injected disintegrations per minute (dpm)/ml; Control: 1.29±0.11, CIA: 0.92±0.11, p≤0.04 vs. Control). Both serum CRP and 3H-cholesterol –particularly the HDL fraction– were restored to baseline after the treatment with the JAK inhibitor (CIA+TOFA: 10.97±0.67 µg/ml and 1.37±0.20 % of injected dpm/ml, respectively, p≤0.05 vs. CIA). Concomitantly, we observed an upward trend in 3H-cholesterol accumulation within the synovium of CIA animals as compared to controls, which tended to normalize with the treatment.

Conclusion: Systemic inflammation induces cholesterol sequestering within macrophages in vivo by acting on cholesterol efflux transporters (6). Tofacitinib favors cholesterol release to plasma lipoproteins, hence increasing circulating cholesterol. This is not only due to a decrease in inflammation –as the effect is likely shared with some other shared, DMARDs may have, but also to a direct mechanism on ABCA1 transporters that favors cholesterol efflux. To our knowledge, this is the first report suggesting that cholesterol dynamics in the macrophage may contribute to the overall circulating cholesterol levels, especially considering that this phenomenon may occur in other cell types, such as adipocytes.

REFERENCES

Disclosure of Interests: None declared

SAT0061

IMPORTANT ROLE OF CD11C+ CELLS IN INFLAMMATORY ARTHRITIS

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Background: Dendritic cells (DCs) are important antigen presenting cells (APCs) and therefore they play an important role in bridging the innate and the adaptive immune response. DCs can be divided in different sub-sets with specific functions. As powerful APCs, DCs are thought to play an important role in the induction of autoimmune diseases such as rheumatoid arthritis. However, the active role of DCs in joint inflammation is not known yet.

Objectives: Investigation of the role of DCs cells in joint inflammation and destruction.

Methods: We analyzed histological sections of K/BxN serum transfer arthritis as well as hTNFtg arthritis for the presence of CD11c+ cells by immunohistochemistry. We used CD11c-diphtheria toxin receptor (DTR) transgenic mice. K/BxN serum transfer arthritis was induced, and mice were given either DT or PBS or in wt and BARF3 deficient mice. In addition CD11c DTR mice were crossed into hTNFtg animals and also received either DT or PBS. The severity of arthritis was determined clinically and histologically.

Results: Both CD8+CD11c+ and CD11b+CD11c+ can be found in synovial tissue in TNF driven arthritis. Upon depletion of CD11c+ cells clinical signs of K/BxN serum transfer arthritis were significantly reduced. Histological analysis found reduced synovial inflammation after the depletion of CD11c+ cells in K/BxN arthritis. In addition, local bone destruction and the number of osteoclasts was also significantly reduced. In addition to K/BxN arthritis, we found that also in TNF-driven arthritis depletion of CD11c+ cells led to a striking reduction of synovial inflammation and a complete depletion of osteoclasts.

Conclusion: These data show that in addition to initiating an adaptive immune response, CD11c+ dendritic cells, are also involved in innate effector mechanisms of inflammatory arthritis. Especially CD11b+CD11c+ and monocyte derived inflammatory seem to play a role in inflammatory arthritis, suggesting that they could be an important therapeutic target.

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SAT0062

STRATIFIED MEDICINE FOR RHEUMATOID ARTHRITIS: PREDICTING RESPONSE TO BIOLOGIC THERAPY USING IMMUNE CELL SIGNATURES

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Background: Treatment selection of biologic therapy for patients with rheumatoid arthritis (RA) is currently a trial and error process, with approximately 40% failing to respond well to the first biologic. The lack of biomarkers to predict treatment response leads to further pain, joint damage, patient anxiety and is cost ineffective for those who are non-responders.

Objectives: We aim to identify immune signatures from a pre-treatment blood test to inform the choice of treatment strategies for stratified medicine.

Methods: RA patients with active disease (DAS28 > 5.1) who failed to respond to conventional DMARDs and were due to commence biologic treatment were included in the BRAGGSS cohort. Peripheral blood mono-nuclear cells (PBMCs) taken before the initiation of biologic treatment were available for 300 patients (good (60%), moderate (25%), and non-

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responders (15%) to various biologics (anti-TNFs (68%), Rituximab (16%), Tocilizumab (13%), Abatacept (3%)). PBMCs were left unstimulated (anti-CD3/CD28 beads or 10 ng/mL LPS) and stained with three flow cytometry panels including specific surface, intracellular and intranuclear markers to deeply characterise the function of several subsets of monocytes, NK cells, T cells and B cells (e.g. disease-associated cell populations such as PD-1+CXCR5 peripheral T helpers (Rao DA Nature 2017), CD27+HLA-DR+ effector CD4+ T cells (Fonseka CY Sc Transl Med 2018) and cytotoxic PD-1+CXCR5 CD8+ T cell subsets. Total CD11c+ autoimmune-associated B cells, CD14+IL-18+ pro-inflammatory monocytes (Zhang F BioRxiv 2018)). Hypothesis-free clustering algorithms were also used for data analysis to identify unreported cell populations. Statistical association testing was performed using mixed effects ordinal (EULAR responder status and linear (DAS28 or its components)) regression models.

**Results:** Preliminary interim analysis identified associations between pan-biologic non-response and spontaneous expression of pro-inflammatory cytokines (Th1, Th17 lineage) by CD4+ T cells (p < 0.003). Good response to all biologic drugs was independently associated with the number of CD56dimCD16+ NK cells (p < 0.001). Good response to anti-TNFs was associated with TNFα, IFNγ and perforin producing CD4+ T cells after in vitro stimulation with anti-CD3/CD28 (p < 0.02).

**Conclusion:** Ongoing work involves the replication of these results. The identification of immune cell types associated with response to a particular class of biologic drugs (e.g. anti-TNFs, but not other classes) might inform the choice of first line biologic drugs based on individual patients' immune profiles (stratification to treatment response categories or cytokines generally associated with non-response to all biologics could represent new therapeutic targets, at least in some patient groups).

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**SAT0083** ASSOCIATION OF SMOKING WITH TRIPLE CONCORDANT SEROPositivity IN RA PATIENTS, AND WITH RHEUMAtoid FACTOR IN THE REMAINING PATIENTS

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**Background:** The contribution of cigarette smoking to the risk of rheumatoid arthritis (RA) is large for seropositive than for seronegative patients. Current pathogenic models explain this difference via the production of anti-citrullinated protein antibodies (ACPA) induced by protein citrullination of monocytes, NK cells, T cells and B cells (e.g. disease-associated cell populations. Although their relevance to CV disease is uncertain. Recently, the expression of angiotensin-converting enzyme (ACE) expression has been significantly larger than with two antibodies (OR = 1.54, p = 1.4 x 10^{-6}), whereas the association with the presence of two antibodies was not larger than with one autoantibody (OR = 1.11, p = 0.3). In the patients remaining after exclusion of the triple seropositive, the smokers were exclusively associated with the RF (OR = 1.28, p = 0.003) and OR = 1.30, p = 0.004 in the double and single positive patients, respectively. This association was independent of the reference, either the triple seronegative (OR = 1.29, p = 0.001) or all the RF patients (OR = 1.32, p = 0.002).

**Conclusion:** Smoking increases RA susceptibility by promoting pathways leading to the concurrent presence of the three RA autoantibodies and, in its defect, to the production of RF. These actions are not covered by current pathogenic models and suggest that smoking accelerates epitope spreading.

**REFERENCE**


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**SAT0064** EXPANSION OF CD16+ MONOCYTE SUBSETS AND ACE EXPRESSION ARE ASSOCIATED WITH ARTERIAL THICKENING AND VASCULAR FUNCTION IN VERY EARLY RHEUMATOID ARTHRITIS

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**Background:** monocytes are largely recognized as drivers of the atherosclerosis development, the leading determinant of cardiovascular (CV) morbidity in rheumatoid arthritis (RA). Far from being a unique population, functionally and phenotypically subpopulations can be distinguished, although their relevance to CV disease is uncertain. Recently, the expression of angiotensin-converting enzyme (ACE) expression has been significantly larger than with two antibodies (OR = 1.54, p = 1.4 x 10^{-6}), whereas the association with the presence of two antibodies was not larger than with one autoantibody (OR = 1.11, p = 0.3). In the patients remaining after exclusion of the triple seropositive, the smokers were exclusively associated with the RF (OR = 1.28, p = 0.003) and OR = 1.30, p = 0.004 in the double and single positive patients, respectively. This association was independent of the reference, either the triple seronegative (OR = 1.29, p = 0.001) or all the RF patients (OR = 1.32, p = 0.002).
described, with some heterogeneity being observed across monocyte sub-sets. However, although previously linked to blood pressure control, the significance of ACE expression on monocytes remains obscure.

**Objectives:** To evaluate whether monocyte subsets and ACE expression are associated with surrogates of CV subclinical disease in very early RA patients.

**Methods:** Patients were recruited upon early referral to the rheumatology department. All patients were untreated at the time of sampling. The frequency of classical (CD14+CD16-) and non-classical (CD14/CD16+) monocyte subpopulations and ACE expression were assessed by flow cytometry in peripheral blood. Plaque occurrence, CIMT and stiffness parameters were analyzed by Doppler ultrasound in internal carotid, middle cerebral and basilar arteries.

**Results:** 53 patients were recruited, 47 fulfilling 2010 ACR/EULAR classification criteria for RA (36 women, 26 FRI+ and 26 ACFA+) and 6 fulfilling criteria for Clinically Suspected Arthralgia (CSA) (6 women, 3 FRI+ and 2 ACFA+). Non-classical and intermediate monocytes were positively associated with CIMT (r=0.413, p=0.005 and r=0.353, p=0.018, respectively), as well as with pulsatility (r=0.332, p=0.026 and r=0.323, p=0.030) and resistivitiy indices (r=0.286, p=0.050 and r=0.277, p=0.045) at the left internal carotid artery. Expansion of CD16+ monocytes was not associated with disease activity, measured as DAS28 or SDAI (all p>0.050), but frequency of intermediate monocytes paralleled duration of the symptoms (r=0.324, p=0.020). ACE expression was higher in CD16+ monocyte subsets than in their classical counterparts. ACE expression was not associated with blood pressure, individual traditional CV risk factors, body mass index nor with mSCORE (all p>0.050). ACE expression on intermediate and classical monocytes was correlated with CIMT (r=0.382, p=0.010 and r=0.349, p=0.019, respectively). Moreover, ACE expression in all monocyte subsets was strongly associated with resistivity and pulsatility indices at the inter- nal carotid artery (all p<0.010).

**Conclusion:** The expansion of CD16+ monocyte subsets and the ACE expression are associated with arterial wall thickening and vascular functionality in treatment-naive RA patients, hence suggesting a very early role for monocyte traits in this scenario. None declared


**SAT0065**

**WNT5A INCREASES RHEUMATOID SYNOVIOCYTE MIGRATION THROUGH RYK RECEPTOR AND RHO-ROCK PATHWAY**

Antonio González, Carmen Conde.

**Background:** Fibroblast-like synoviocytes (FLS) are pivotal in inflammation and joint damage of rheumatoid arthritis (RA). These cells acquire an aggressive phenotype of rheumatoid synoviocytes. To analyse the molecular mechanisms involved in the activation of AKT and GSK3 against native chicken CII were significantly higher in T-bet -/- mice. However, IgG2a antibody production was significantly lower in T-bet -/- mice compared to B6 wild-type mice and the incidence of arthritis was around 1.5-fold higher. 2) The levels of total IgG2, IgG3 antibodies against native chicken CII were significantly higher in T-bet -/- mice. However, IgG2a antibody production was significantly lower in T-bet -/- mice compared to B6 mice. 3) The number of CD4+ T (CD3+CD4+), CD8+ T (CD3+CD8+) and CD19+ B (CD19+) cells, as well as macrophages (CD11c+CD11b+Gr1-), neutrophils (CD11c+CD11b+Gr1+), NK cells (CD3+CD56+) in the lymph node was not different but the number of NKT (CD3+CD1+IL-2+) cells was significantly decreased in T-bet -/- mice.

**Results:** 1) CIA developed in the T-bet -/- mice was more severe than that of B6 wild-type mice and the incidence of arthritis was around 1.5-fold higher. 2) The levels of total IgG2, IgG3 antibodies against native chicken CII were significantly higher in T-bet -/- mice. However, IgG2a antibody production was significantly lower in T-bet -/- mice compared to B6 mice. 3) The number of CD4+ T (CD3+CD4+), CD8+ T (CD3+CD8+) and CD19+ B (CD19+) cells, as well as macrophages (CD11c+CD11b+Gr1-), neutrophils (CD11c+CD11b+Gr1+), NK cells (CD3+CD56+) in the lymph node was not different but the number of NKT (CD3+CD1+IL-2+) cells was significantly decreased in T-bet -/- mice. 4) T-bet knockout (T-bet -/-) mice (C57BL/6, B6 background) were generated as previously described (3). T-bet -/- mice were immunized with CIA and CFA, and the incidence and severity of CIA was assessed. 2) Anti-CII antibodies in the sera from T-bet -/- mice on day 60 after the first immunization were measured. 3) Lymph node cells from B6 or B- bet -/- mice immunized with CIA were analyzed by flow cytometry using antibodies specific for CD3, CD4, CD8, CD11b, CD11c, CD19, Gr1 and NK1.1. 4) The lymph node cells described above were cultured in the CIA containing medium, then the cytokine production was assayed by ELISA.

**References**

Disclosure of Interests: None declared.

REFERENCES

SA10067
SECRETORY ANTIBODIES TO CITRULLINATED PEPTIDES IN PLASMA AND SALIVA FROM RHEUMATOID ARTHRITIS PATIENTS AND THEIR UNAFFECTED FAMILY MEMBERS
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Background: Mucosal involvement in early phases of rheumatoid arthritis (RA) pathophysiology has emerged as an attractive hypothesis, supported by several findings. Elevated levels of antibodies against citrullinated peptides/proteins (ACPAs) can be found during a long pre-symptomatic period, preceding manifest arthritis. Secretory antibodies are produced at mucosal surfaces, but can also be detected in the circulation. Secretory ACPA in plasma has been demonstrated in patients with RA (1). First-degree relatives (FDRs) of patients with RA can be regarded as potential pre-RA patients or at-risk individuals. In a previous study, a higher prevalence of ACPA was found in FDRs than in healthy controls (2), with IgA-ACPA being more common than IgG-ACPA. We hypothesized that formation of secretory ACPA is an early step in RA development, preceding the occurrence of regular non-secretory ACPA, and consequently secretory ACPA would be prevalent in a large proportion of FDRs.

Objectives: To evaluate secretory ACPA in plasma and saliva from patients with RA and FDRs.

Methods: We analyzed secretory antibodies to 2nd generation cyclic citrullinated peptides (anti-CCP) in plasma from 194 patients with RA and 191 FDRs unaffected by RA and saliva samples from 25 RA patients, 21 first-degree relatives and 11 controls. In plasma, cutoff for secretory ACPA was set at the 99th percentile of healthy blood donors. In saliva, a positive test was defined as a difference between optical density values for IgA anti-CCP and IgA anti-cyclic arginine peptide (delta OD value) >2 SD above the mean delta OD value of the controls. Mann-Whitney U test was used for continuous variables and Pearson Chi-square for categorical variables.

Results: Secretory ACPA occurred in 37 (19.1%) of RA patients but only in 2 (1%) of FDRs (table 1). Salivary IgA ACPA was found in 3/25 (12%) of patients with RA, but not in any of the 21 FDRs. 27% of FDRs were positive for regular non-secretory IgA ACPA in plasma, and out of them, only 2 individuals (5%) were positive for secretory ACPA in plasma. Among FDRs negative for regular ACPAs, no one was positive for secretory ACPA. Secretory ACPA had the highest PPV for identifying patients, while IgG ACPA had the highest negative predictive value (table 2).

Conclusion: Secretory ACPA in plasma and saliva was rare in FDRs. Circulating secretory ACPA had the highest PPV of the RA-related antibodies tested to identify RA in these families. This implies that mucosal production of ACPA is not common in an at-risk population, but may be important in the transition from increased risk to actual RA disease.

SA10068
CIRCADIAN RHYTHMS OF IMMUNE SYSTEM IN HEALTHY INDIVIDUALS AND PATIENTS WITH RHEUMATOID ARTHRITIS
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Background: Chronobiological aspects play an important role in rheumatoid arthritis (RA), with major symptoms such as joint pain and stiffness follow a day-night-cycle that peak in the early morning. The circadian behavior of symptoms has been attributed to the rhythmic expression of cytokines and hormones1,2. Animal models of autoimmune inflammation demonstrated that immune cells, which belong to the vast producers of such cytokines, circulate in a circadian manner and that the circadian rhythm of circulating immune cell is different in health and disease3. Moreover, coordinating timing of glucocorticoid therapy (chronotherapy) results in a greater reduction of morning stiffness and pain compared with the same glucocorticoid dose taken in the morning4.

Objectives: Here, we aim to analyse the circadian rhythms of circulating immune cell populations in the periphery of healthy individuals and RA patients in order to optimize treatment strategies.

Methods: We performed a 24-hours study involving 14 eligible RA patients and 12 healthy individuals to monitor the dynamic occurrence of diverse immune cells in the periphery. A week prior to study day, the biological rhythms were synchronized by scheduled activities and food intakes. On the study day, blood was drawn every 2 hours throughout 24 hours using peripheral venous catheter. The participants were provided with regular meal, allowed to eat snacks ad libitum and carry passive activities. Blood samples were subsequently analyzed by flow cytometry using TruCount Beads to count absolute cell numbers. RNA from CD14+ monocytes was analyzed by real-time PCR to monitor the circadian clock genes expression.

Results: We investigated major immune populations and found chronobiological differences in NK T cells, NK cells, CD8 T cells, CD4 T cells and regulatory T cells (Tregs) of healthy individuals and patients with RA. In RA Tregs showed a lag phase of 5 hours, while CD8 and CD4 T cells showed a mild reduction of the amplitude. NK T cells and NK cells did not circulate in a circadian manner in healthy individuals, but they exhibited circadian pattern in RA. In addition, the qPCR data also indicated a disrupted circadian rhythm on RNA level. Among ten clock genes that were examined, REVERBx, PER1, and PER2 showed altered expression in RA patients. The expression of REVERBx was suppressed by 50% and the rhythm of PER1 was diminished in RA patient.
Furthermore, the rhythm of PER3 was present exclusively in RA patients, but not in healthy participants.

Conclusion: Taken together, we conclude that the circadian rhythms of immune cells in RA patients are different from that in healthy individuals. The alteration can be observed on both cellular and RNA level. We postulate that the alterations in circadian rhythms may contribute to disease manifestations and may have impact for optimizing diagnosis and therapy in RA. Further analysis is required to expand the data set. It is also of interest to investigate the functionality of circadian clock genes in immune cells.

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Disclosure of Interests: None declared


SAT0069 PROTECTIVE EFFECT OF PROTOCATECHUIC ACID RICH FRACTION OF TRIANTHEMA PORTULACASTRUM AGAINST COLLAGEN INDUCED RHEUMATOID ARTHRITIS VIA GUT MICROBIOTA MODULATION

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Background: Rheumatoid arthritis, a chronic inflammatory joint disease affects people all over the world. Triantehma portulacastum (TP) has been traditionally utilized for the treatment of rheumatism. Abeer Abdelal1, Rasha Ghazali2, Rehab Elzem3, Fatema Dwedaw4, Reham Shams-Eldeen5, Noah Kandeer6. 1Department of Internal Medicine, Rheumatology Unit, Faculty of Medicine, Alexandria University, Alexandria, Egypt; 2Department of Medical Biochemistry, Faculty of Medicine, Alexandria University, Alexandria, Egypt; 3Department of Physical Medicine, Rheumatology and Rehabilitation, Faculty of Medicine, Alexandria University, Alexandria, Egypt; 4Department of Chemical Pathology, Medical Research Institute, Alexandria University, Alexandria, Egypt

Methods: Hydroethanolic extract of TP was fractionated with three different solvents (ethyl acetate, chloroform and n-butanol) and quantitatively analyzed with HFLC-DAD method which revealed n-butanol fraction of TP (BFTP) is rich in protocatechueic acid along with other phenolic compounds. Animals were randomly divided into five groups. Four groups were injected with bovine type-II collagen (BTC-II; 100 μg) in Freund’s complete adjuvant (0.1 ml) intradermally. On day 21, animals were again treated with BTC-II along with booster incomplete Freund’s adjuvant injection. After 24 hrs, animal groups were administered intraperitoneally with their respective drug treatment, i.e., vehicle, BFTP (100, 200 and 400 mg/kg b.w) and methotrexate (3 mg/kg b.w), respectively once in a day for next 21 days. At the end of experiment serum level of pro-inflammatory cytokines was determined, and gut microbiota was analyzed by using illumina HiSeq.

Results: Results revealed BFTP preadministered group exhibited significantly reduced level of paw swelling and arthritis score as compared to vehicle group. Immunohistological studies of mice ankle soft tissue also supported the protective effect of BFTP. Additionally, BFTP repair altered gut microbial communities by reducing relative loads of inflammatory microbes such as Mucispirillum, Helicobacter and Lachnospiraceae.

Conclusion: The results conclude that BFTP possess beneficial anti-inflammatory response in arthritic model and can be used as a potential anti-arthritis agent for the management of arthritis.

Disclosure of Interests: None declared


Rheumatoid arthritis – prognosis, predictors and outcome

SAT0070 PROTEOMIC SPECTRUM PROFILE IN INFLAMMATORY AND DEGENERATIVE ARTHRITIS

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Background: The identification and quantification of protein biomarkers present in tissues and body fluids is a new area of interest in the clinical management of rheumatic diseases. Proteomics may identify novel biomarker(s) which assist in understanding the pathogenesis of rheumatic disorders with diagnostic and prognostic implications. In addition, proteomic techniques in RA may be helpful to identify newer autoantibodies and inflammatory acute phase proteins.

The integration of potential biomarkers resulting from rheumatoid proteomics analyses in differential diagnosis of rheumatologic disorders is not yet fully established and so several studies are needed to confirm the efficacy of these approaches.

Objectives: The purpose of this study was to use Matrix Assisted Laser Desorption Ionization – Time of Flight – Mass Spectrometry (MALDI-TOF-MS) to identify differentially expressed disease-related and condition-specific peptide in serum of patients with Rheumatoid arthritis (RA) and osteoarthritis (OA).

Methods: Hundred participants were divided into three groups as following: RA group (35 patients with Rheumatoid arthritis representing patients with inflammatory arthritis); OA group (35 patients with Osteoarthritis representing patients with non-inflammatory arthritis); healthy control group (30 healthy volunteers). All participants were subjected to full history taking; clinical examination; and clinical Assessment of disease activity in RA patients using Disease activity score 28 (DAS-28); routine laboratory investigations; Acute phase reactants; serological tests; plain x-ray of affected joints, as well as serum proteomic profile using Magnetic beads (MB) separation and (MALDI–TOF–MS). Using the spectral data from the three groups, three different classification models for the three groups were generated using OA, SNR and QC algorithms. The OA model showed the best sensitivity and specificity in the three trials (RA versus control, OA versus control, and RA versus OA).

Results: In comparing RA versus control group; the results revealed 101 peaks that discriminated the RA from the control group; 53 were significant (PWKW p<0.05) and 48 nonsignificant. Three peaks (14;25;62) were significant and peak 75 and 23 were nonsignificant. Finally the RA group was discriminated from the OA group, the trial showed 113 peaks 73 were significant (PWKW p<0.05) and 40 nonsignificant. Five peaks were integrated (75:7767.82 40:2953.29 41:2991.59 48:4054.75 68:6434.51), and all integrated peaks were significant. The integrated peaks showed that all peaks were downregulated except peak 40 was upregulated.

Conclusion: Data obtained from proteomic analysis allow differentiation between RA, OA, and healthy subjects. Because of its simplicity and accuracy, (MALDI–TOF–MS) is a promising method for identifying differentially expressed inflammatory versus degenerative disease-related peptide.

REFERENCE

Disclosure of Interests: None declared

**SAT0071**

**ANALYSIS OF CHRONOLOGICAL CHANGES IN JAPANESE VERSION OF HEALTH ASSESSMENT QUESTIONNAIRE SCORE AND FACTORS ASSOCIATED WITH J-HAQ REMISSION AT 5 YEARS AFTER DISEASE ONSET IN PATIENTS WITH RHEUMATOID ARTHRITIS USING THE IORRA COHORT**

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**Background:** Recent advances in rheumatoid arthritis (RA) treatment including the introduction of biologics have greatly affected treatment strategies for RA, achieving remission as a realistic treatment target. However, few reports have been concerned chronological changes in long-term physical dysfunction among large numbers of RA patients in daily practice.

**Objectives:** To evaluate chronological changes in Japanese version of Health Assessment Questionnaire score (J-HAQ) score and J-HAQ remission rates at 5 years after RA onset using the Institute of Rheumatology, Rheumatoid Arthritis (IORRA) cohort.

**Methods:** RA patients who developed RA between 2000 and 2010 and who first visited our hospital during the year of RA onset were divided into two groups: 1) former onset group (RA onset between 2000 and 2005) and 2) recent onset group (RA onset between 2006 and 2010). J-HAQ scores and J-HAQ remission rates at baseline and at 5 years after onset were investigated for each group, and factors associated with J-HAQ remission after 5 years were assessed by logistic regression analysis. Methotrexate (MTX), corticosteroid (steroid) and biologic DMARDs user (bDMARDs) was defined as the patients if they were used each medication during the observation period.

**Results:** The former onset group and recent onset group included 357 and 291 RA patients, respectively. For the former onset group, the average J-HAQ score/J-HAQ remission rate at baseline and 5 years after the onset was 0.659/54.6% and 0.430/71.4%, respectively. The recent onset group showed significant improvements relative to the former onset group in J-HAQ score/J-HAQ remission rates at baseline and 5 years of 0.705/52.2% and 0.316/78.4%, respectively (p < 0.001). Significant factors associated with achieving J-HAQ remission at 5 years after RA onset were: patients in the recent onset group (p < 0.001), male (p < 0.001), lower J-HAQ score (p < 0.001) at baseline, and non-steroid user (p < 0.001).

**Conclusion:** In daily practice, J-HAQ scores for RA patients remarkably improved with recent advances in RA treatment strategies. To achieve J-HAQ remission at 5 years of RA onset, beginning treatment in the early disease stage is needed to prevent deterioration of J-HAQ and treatments that avoid steroid use appear to be important.

**Acknowledgement:** We thank all patients who participated in the IORRA survey and all of the members of the Institute of Rheumatology, Tokyo Women’s Medical University, for the successful management of the IORRA cohort.


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**SAT0072**

**EVALUATION OF RHEUMATOID ARTHRITIS TREATMENTS AND JOINT OUTCOMES IN RHEUMATOID ARTHRITIS-ASSOCIATED INTERSTITIAL LUNG DISEASE**

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**Background:** RA-associated interstitial lung disease (RA-ILD) is an extra-articular manifestation of RA and is one of the leading causes of death in patients with RA.1 Previous studies have indicated that clinical factors such as age, sex, smoking and autoantibody positivity are strongly associated with RA-ILD.2 There is also evidence of active RA being related to increased risk for clinically apparent ILD.3 However, there are limited data on how pts with RA-ILD are managed for their joint conditions and joint outcomes.

**Objectives:** To evaluate RA treatment patterns in pts with subclinical and clinical RA-ILD compared with pts with RA without ILD, and to assess joint disease activity at baseline and change in disease activity by treatment in all cohorts.

**Methods:** Data from adult pts with RA enrolled in a longitudinal sequential RA registry were analysed. Pts in the registry were evaluated annually by a rheumatologist for disease activity and treatment, and semi-annually on multiple clinical patient-reported outcomes (PROs) and resource utilisation parameters. Pts with chest computed tomography (CT) scans performed during treatment were considered for ILD and with blood samples were included in this analysis. Pts with chest CT scans that were indeterminate for ILD were excluded from the study. Pts were then divided into two mutually exclusive groups: non-ILD RA pts and RA-ILD pts. RA-ILD pts were further divided into subclinical and clinically evident ILD. Date of chest CT scan was considered the index date. The two cohorts were compared using descriptive statistics to summarise baseline differences in demographics, disease activity measures, serostatus and treatments. Kruskal–Wallis test for continuous variables and chi-square test for categorical variables were performed, with two-sided significance level of 0.05. Multivariable linear regression was used to evaluate change from baseline to 12 months in joint disease activity for pts with available data at baseline and follow-up.
Results: 75 pts with chest CT scans were included in the analysis. Of these, 38.7% (n=29) were non-ILD RA and 61.3% (n=46) had some manifestation of RA-ILD. Of the RA-ILD cohort, 63.0% (n=29) and 37.0% (n=17) were classified as subclinical and clinically evident RA-ILD, respectively. At the time of chest CT scan, RA-ILD (vs non-ILD RA) pts were older with longer disease duration, a greater proportion were male and had higher anti-citrullinated protein antibody and RF titres (Table 1). In terms of RA treatments, a significantly greater proportion of RA-ILD (vs non-ILD RA) pts were on corticosteroids (CS; 47.8% vs 29.7%) and a significantly greater proportion of clinically evident RA-ILD (vs non-ILD RA) were on non-TNF inhibitor (TNFi) biologics. RA-ILD (vs non-ILD RA) pts had numerically higher joint disease activity and modified HAQ score at baseline (Table 1). However, the change in joint disease activity and PROs in RA-ILD pts was numerically greater vs non-ILD RA pts. In a multivariable analysis, RA-ILD status did not impact change in joint disease activity, but baseline joint disease activity was significantly associated with reduction in joint disease activity at 12 months (Table 2).

Conclusion: RA-ILD pts compared with non-ILD RA pts in clinical practice are more likely to be managed with CS therapy and non-TNFi bDMARDs. The improvement in joint disease activity was similar between RA-ILD and non-ILD RA pts. The analysis was limited by small sample size; further studies with larger pt numbers are required to confirm the findings.

Table 2. Multivariable analysis of change in disease activity (CDAI)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Estimate</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>0.8</td>
<td>(-12.5, 15.0)</td>
</tr>
<tr>
<td>No ILD (vs ILD)</td>
<td>-3.9</td>
<td>(-12.8, 5.1)</td>
</tr>
<tr>
<td>RA duration, years</td>
<td>0.1</td>
<td>(-0.5, 0.3)</td>
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<tr>
<td>Baseline CDAI score</td>
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<td>(0.0, 0.8)</td>
</tr>
<tr>
<td>No CS (vs CS)</td>
<td>-3.6</td>
<td>(-13.3, 6.3)</td>
</tr>
</tbody>
</table>

RA-ILD vs non-ILD C: noncorticosteroids; IL: interstitial lung disease

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SAT0074

DAS-28 DISEASE ACTIVITY DEFINES THE TNFRI/2 CO-EXPRESSION PROFILE IN RHEUMATOID ARTHRITIS PATIENTS

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Background: TNF-\alpha acting as main proinflammatory cytokine in rheumatoid arthritis (RA) immune processes. However, TNF-\alpha activity and functions may be regulate not only by soluble receptors (which act as decays) but also by number, density, and co-expression of its membrane-bound receptors type 1 and 2 (TNFR1 and TNFR2).

Objectives: To analyze the TNFR1/2 co-expression profile in RA patient with different disease activity in comparison to healthy donors (HD).

Methods: PBMC were analyzed from 46 HD and 84 patients with RA using flow cytometry. Patients were divided according to the DAS-28 index into groups with high (n=22, 34.4%), moderate (n=30, 46.9%) and low (n=12, 18.6%) disease activity. Co-expression of TNFR1/2 was evaluated as percentage of cell with different receptors. Number of receptors of each type per cell was counted using QuantItone PE beads (BD, USA). The following populations were analyzed: total monocyte pool; common pool of B lymphocytes; common pool of T lymphocytes; cytotoxic T cells (CD8\textsuperscript{+}), T helper cells (CD4\textsuperscript{+}), activated (CD25\textsuperscript{+}) and naive T cells (CD4CD25\textsuperscript{+})

Methods: Early RA (ERA) and LS-RA patients with conventional DMARDs insufficient response were enrolled in this observational, investigative, monocentric, non-randomized, no profit study, and treated with CTLA4-Ig in combination with methotrexate. Each enrolled RA patients underwent peripheral blood sampling and CD4+ cells isolation using magnetic micro-beads at baseline and after 6-12 months follow-up.

Flow cytometric analysis (FACS) for CD4 positive cells phenotype was performed to assess T-regulatory cells (Treg) as CD4+/CD25+/CD127- and CD4+/CD25+/Foxp3+, respectively. STAT3/STAT5 gene expression on CD4+ cells was performed by RT-PCR for each enrolled patient at every time-point follow-up. Low disease activity (LDA) and disease remission (DAS) achievement were assessed at 6 and 12 months follow-up (FU), respectively.

Results: A total of 35 patients were enrolled in the study (16 ERA and 19 LS-RA, respectively). At baseline, ERA and LS-RA did not differ based on clinical parameters. Eight (22.9%) withdrew from the study because of treatment failure (n=6), severe infection (n=1) and death (n=1). LDA or DAS remission within twelve months follow-up were achieved in 28/34 (82.4%) and 16/34 (47.1%) patients, respectively, without any significant difference among ERA and LS-RA. There were no significant differences in the demographic and clinical characteristics of RA patients at study based on LDA or DAS remission status achievement within 12 months FU, even stratifying patients based on disease duration. FACS analysis showed CD4+/CD25+/CD127- and CD4+/CD25+/Foxp3+ cells decrease during CTLA4-Ig treatment (p<0.01 and p<0.02, respectively after 12 months FU), despite disease duration and severity (R=0.549, p=0.02, respectively). Moreover, baseline STAT3/STAT5 ratio in PB patients directly correlates with Treg cells percentages (CD4+/CD25+/CD127- cells %): R=0.518, p=0.03; CD4+/CD25+/Foxp3+ cells %: R=0.349, p<0.02, respectively. Finally, baseline STAT3/STAT5 expression ratio on CD4+ cells > 0.93 (obtained by ROC analysis: AUC=0.754 +/- 0.100; Sensitivity 70.0%, Specificity: 80.0%) arose as baseline predictor factor of LDA achievement in RA patients treated with CTLA4-Ig [OR(95%CI): 12.0 (1.98-72.89)].

Conclusion: STAT3/STAT5 expression ratio in T cells at baseline identify RA patients better responding to CTLA4-Ig, which decreases Treg cells.

Disclosure of Interests: Stefano Alivernini Speakers bureau: BMS, Barbara Tolusso: None declared, Anna Laura Fedele: None declared, Clara Di Mario: None declared, Luca Petraca: None declared, Maria Rita Gigante: None declared, Gianfranco Ferraccoli Speakers bureau: BMS, Roche, Elisa Gremente Consultant for: AbbVie, BM2, Celgene, Janssen, Lilly, MSD, Novartis, Sanofi, UCS, Roche, and Pfizer, Speakers bureau: BMS, Speakers bureau: Roche, Speakers bureau: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Sanofi, UCS, Roche, and Pfizer

BACKGROUND: Patients with rheumatoid arthritis (RA) have a higher risk of cardiovascular diseases (CVD) and stroke. More knowledge about associated factors is needed since it could have implications on different treatment strategies.

Objectives: To study factors associated to CVD and stroke development in patients with established RA.

Methods: A questionnaire was sent twice to patients with established RA in the BARFOT cohort, in 2010 (n=1525) and in 2017 (n=1046) with a response rate of 73% and 68% respectively. 950 patients responded to the first questionnaire and 898 patients to the second. In a multivariate regression analysis, age, OR (66.7 vs 62.8%); mean DAS28-CRP (4.4 vs 4.7); mean HAQ (1.0 vs 1.1) were associated to CVD. Patients that developed stroke at both questionnaires. In a multivariate regression analysis age, OR (95% CI) 1.071 (1.015-1.129), male gender 7.459 (2.664-20.883) and reporting treatment with conventional DMARD 0.510 (0.259-1.004) were associated to stroke at the second questionnaire. There were no associations between reported use of NSAIDs and development of CVD or stroke in this study.

Conclusion: Knowledge about factors associated to cardiovascular disease is important when treating patients with RA. Long-term treatment with corticosteroids seems to increase the risk to develop CVD. Treatment with DMARDs, especially conventional DMARDs, seems to decrease the risk to develop stroke. There were no association between developing CVD or stroke and NSAIDs in this study.

Disclosure of Interests: None declared


SAT0076 EARLY REMISSION IS ESSENTIAL TO PREDICT LONGTERM REMISSION: CLINICAL RESULTS OF THE BELGIAN CAP48 RA COHORT

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Background: Early therapeutic intervention is crucial for patients with early rheumatoid arthritis (ERA). The goal of remission is achievable in a proportion of ERA patients.

Objectives: To evaluate the rate of patients in remission at 6 months and to correlate the 3 year remission rate. To identify baseline characteristics differences between patients achieving remission or not, and to report the best remission composite criteria to be used in daily care.

Methods: The Belgian CAP48 cohort supported by the French speaking radiotelevision (RTBF) is a unique prospective observational study of patients less than 50 years old with a recent diagnosis of ERA. All patients are native to DMARD therapy and were recruited in different rheumatologic centers in Brussels and Wallonia. At baseline and every 6 months, demographic, specific clinical evaluation, questionnaires and laboratory were completed and treatment was adapted according each physician decision.

Results: 207 RA patients from 16 centers were analysed (162 F, 45 M, mean age 36.0 years, 27.8% with baseline erosion, 62.3% with ACPA, 59.9% with FR, mean HAQ 1.9, mean DAS28-CP 4.54, mean SDAI 59.9% with FR, mean HAQ 1.9, mean DAS28-CP 4.54, mean SDAI 59.9% with FR, mean HAQ 1.9, mean DAS28-CP 4.54, mean SDAI 59.9% with FR, mean HAQ 1.9, mean DAS28-CP 4.54, mean SDAI 59.9% with FR, mean HAQ 1.9, mean DAS28-CP 4.54, mean SDAI 59.9% with FR, mean HAQ 1.9, mean DAS28-CP 4.54, mean SDAI 59.9% with FR, mean HAQ 1.9, mean DAS28-CP 4.54, mean SDAI 59.9% with FR, mean HAQ 1.9, mean DAS28-CP 4.54, mean SDAI 59.9% with FR, mean HAQ 1.9, mean DAS28-CP 4.54, mean SDAI 59.9% with FR, mean HAQ 1.9, mean DAS28-CP 4.54, mean SDAI 59.9% with FR, mean HAQ 1.9, mean DAS28-CP 4.54, mean SDAI 59.9% with FR, mean HAQ 1.9, mean DAS28-CP 4.54, mean SDAI 59.9% with FR, mean HAQ 1.9, mean DAS28-CP 4.54, mean SDAI 59.9% with FR, mean HAQ 1.9, mean DAS28-CP 4.54, mean SDAI 59.9% with FR, mean HAQ 1.9, mean DAS28-CP 4.54, mean SDAI 59.9% with FR, mean HAQ 1.9, mean DAS28-CP 4.54, mean SDAI 59.9% with FR, mean HAQ 1.9, mean DAS28-CP 4.54, mean SDAI 59.9% with FR, mean HAQ 1.9, mean DAS28-CP 4.54, mean SDAI 59.9% with FR, mean HAQ 1.9, mean DAS28-CP 4.54, mean SDAI 59.9% with FR, mean HAQ 1.9, mean DAS28-CP 4.54, mean SDAI 59.9% with FR, mean HAQ 1.9, mean DAS28-CP 4.54, mean SDAI 59.9% with FR, mean HAQ 1.9, mean DAS28-CP 4.54, mean SDAI was older and more often not treated with any DMARD, 30% vs. 18%, p=0.069. There were no other significant differences between the groups. In a multivariate regression analysis age, OR (95% CI) 1.081 (1.047-1.117) and reporting treatment with conventional DMARD 0.510 (0.259-1.004) were associated to stroke at the second questionnaire. There were no associations between reported use of NSAIDs and development of CVD or stroke in this study.

Conclusion: Knowledge about factors associated to cardiovascular disease is important when treating patients with RA. Long-term treatment with corticosteroids seems to increase the risk to develop CVD. Treatment with DMARDs, especially conventional DMARDs, seems to decrease the risk to develop stroke. There were no association between developing CVD or stroke and NSAIDs in this study.

Disclosure of Interests: None declared

The time for diagnosis and treatment initiation is statistically shorter in “long term remission” group compared to the “no remission group” (mean of 1.4 months vs 3.4 months; p=0.042).

Additionally, global remission (DAS28-CRP<2.6, HAQ<0.5 and no X-ray progression) was observed in 41.5% of the long term remission group. The majority of these patients (79%) are treated with Methotrexate.

**Conclusion:** Early and long term remission is an achievable goal in our observational CAP 48 study cohort. Early diagnosis is critical in standard of care. At 6 months, DAS28-CRP and SDAI were the best remission criteria to predict long term remission.

Acknowledgement: We are grateful to all participating investigators and clinical staffs which have made crucial contributions to the development of this Project.

**Disclosure of Interests:** Tatiana Sokolova: None declared, Aleksandra Avramovska: None declared, Pascales Sidiras: None declared, Sandra Kleinberg: None declared, Stephanie Dierckx: None declared, Laurent Meric de Bellefon: None declared, Serge Schreiber: None declared, Cila Ribbens: None declared, Michel Malaise: None declared, Maria Stoennou Grant/research support from: Abbvie, Roche, Wyeth, Silvana Di Romana: None declared, Valérie Badot: None declared, Patrick Durez Speakers bureau: Bristol-Myers Squibb, Eli Lilly, Sanofi, Celltrion

**DISCLAIMER:** The time for diagnosis and treatment initiation is statistically shorter in “long term remission” group compared to the “no remission group” (mean of 1.4 months vs 3.4 months; p=0.042).

**Results:** Baseline characteristics and follow-up duration of each ACPA/erosions group are shown in table 1. Baseline DAS and HAQ were slightly higher in erosions+ patients. Follow-up duration was similar between the 4 groups. We found statistically significant differences in DAS and HAQ change over time between the 4 groups, both after maximum follow-up durations of 6 months and of 1 year (table 1), but differences were small and not clinically relevant.

Patients who were erosions-/ACPA- were less likely to switch treatment [HR (95% CI) 0.79 (0.69; 0.90)] compared to a reference group of erosions-/ACPA+ patients. Patients who were erosions+/ACPA- [HR (95% CI) 0.92 (0.79; 1.08)] or erosions+/ACPA+ [HR (95% CI) 1.01 (0.92; 1.10)] were not statistically significantly different from the reference group in their likelihood to switch treatment. No effect modification was found by country, medication or symptom duration.

**Conclusion:** In this analysis of worldwide real life data, we found statistically significant, but no clinically relevant differences in treatment response to initial DMARD therapies as measured by DAS and HAQ in ACPA-/erosions-, ACPA+/erosions-, ACPA+/erosions+ and ACPA-/erosions+ RA patients. However, ACPA-/erosions- patients were less likely to switch treatment. Thus, in newly diagnosed RA patients who are treated according to modern treatment strategies, the (combined presence of) ACPA and erosions was no risk factor for worse disease activity or physical functioning, although ACPA-/erosions- patients had fewer treatment changes.

**Disclosure of Interests:** Sytske Anne Bengstra Grant/research support from: Bristol-Myers Squibb provided funding for the completion of this Project.

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**SAT0077 IMPACT OF THE COMBINED PRESENCE OF EROSIONS AND ACPA ON 6 AND 12 MONTHS CLINICAL OUTCOMES OF RHEUMATOID ARTHRITIS: RESULTS FROM THE METEOR REGISTRY**

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**Background:** Despite efforts to predict treatment response, treatment of rheumatoid arthritis (RA) patients remains mostly a case of trial and error. Presence of erosions and ACPA are often considered poor prognostic factors based on their association with radiographic damage progression, but with the introduction of treat-to-target ever fewer patients develop significant radiographic damage. Therefore research into prognostic factors should focus on clinical outcomes.

**Objectives:** To investigate in newly diagnosed RA patients if presence of erosions and/or ACPA are associated with functional ability, disease activity and treatment survival during the first year of treatment in daily practice.

**Methods:** Newly diagnosed patients with a clinical diagnosis of RA, ≥3 months follow-up and available data on ACPA, erosions and medication were identified in the international, observational METEOR registry (n=4,623). Timing and frequency of follow-up visits were according to daily practice. We focused at results after a maximum follow-up duration of 6 months or of 1 year from baseline. Associations between the presence of erosions and/or ACPA (4 groups) with the change of DAS and HAQ over time were assessed using linear mixed models.

**Results:** Baseline characteristics and change of DAS and HAQ over time were assessed using linear mixed models. Presence of erosions and/or ACPA were associated with functional ability, disease activity and treatment survival during the first year of treatment in daily practice.

**Conclusion:** Early and long term remission is an achievable goal in our observational CAP 48 study cohort. Early diagnosis is critical in standard of care. At 6 months, DAS28-CRP and SDAI were the best remission criteria to predict long term remission.

**Disclosure of Interests:** Sytske Anne Bengstra Grant/research support from: Bristol-Myers Squibb provided funding for the completion of this Project.
MAJOR CHANGES IN THERAPY PRODUCE SIGNIFICANT CLINICAL IMPROVEMENT ACROSS A BROAD RANGE OF CLINICAL DISEASE ACTIVITY IN US VETERANS WITH RHEUMATOID ARTHRITIS

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Background: Our recent work showed that 41% of patients with moderate/severe rheumatoid arthritis (RA) by Disease Activity Score for 28 joint count (DAS28) did not have changes in RA therapy as recommended by current guidelines (1). Reasons identified for the decision not to escalate therapy was provider’s opinion that RA disease was adequately controlled despite moderate/severe disease activity by DAS28, and that changes in therapy may not produce significant improvements in disease activity (1).

Objectives: 1) Compare short-term differences in ACR20 response between patients with and without a major therapeutic change (MTC) over a range of disease activity; 2) Determine whether ACR20 responses vary by disease activity measures (DAMs) used to assess disease activity (i.e., DAS28, Clinical Disease Activity Index [CDAI], Routine Assessment of Patient Index Data 3 [RAPID3]);

Methods: Each clinic visit for US Veterans enrolled in the VA Rheumatoid Arthritis (VARA) registry was evaluated if the visit had: 1) a complete set of DAMs (DAS28, CDAI, RAPID3) recorded; 2) two other visits with all DAMs between the preceding 18 months separated by at least 60 days and one visit with all DAMs between 60 and 180 days following the visit date; 3) clinical data available for 18 months prior to visit date; and 4) ≥6 tender and ≥6 swollen joints at visit date. Each patient was assessed for MTC within 1 week before and 30 days after visit date. MTC was defined as any of the following: 1) initiation of new biologic or nonbiologic disease-modifying antirheumatic drug (DMARD) or prednisone (as new agent or after 90-day gap during baseline); 2) escalation of DMARD dose by ≥25%; or 3) increase in monthly average prednisone dose by ≥25%; and/or 4) injection of 2 or more joints with corticosteroids.

Clinical improvement was defined as an ACR20 response comparing each eligible visit DAM to the DAM at the first follow-up visit DAM observed between 60 and 180 days of the eligible visit DAM. ACR20 response was compared between eligible visits with and without a MTC and stratified by quartiles of disease activity by each DAM. The Generalized Estimating Equations (GEE) model was fitted using the exchangeable working covariance structure to account for clustering of visits within patients. Models for each DAM were adjusted for age, disease duration, race, seropositive status, comorbidities, disease stability, and recent medication changes in the observations period prior to the visit date.

Results: There were 383 patients (92% were male, mean age was 62.9 years, mean disease duration was 12.5 years, 83% tested positive for rheumatoid factor, and 79% positive for anti-cyclic citrullinated peptide antibodies) who contributed 1,193 eligible visits. Visits with a MTC had a higher rate of ACR20 response in comparison to visits without a MTC at all levels of disease activity. A MTC at a visit with the highest disease activity (quartile 4) consistently had the largest proportion of follow-up visits with an ACR20 response. The overall effect for MTC was statistically significant across all 3 DAMs. Across quartiles, the MTC group consistently had a higher proportion of follow-up visits with ACR20 response compared to the group without a MTC. Risk Ratios from the adjusted analysis are presented in the table.

Conclusion: All patients with active RA have a significant potential to benefit with a MTC. This potential for improvement was seen across all degrees of disease activity and with all three DAMs.

REFERENCE


SAT0079 PREDICTING PATIENTS WITH HIGH PAIN & PSYCHOLOGICAL SYMPTOMS (P&PSS) IN EARLY RHEUMATOID ARTHRITIS USING LATENT CLASS ANALYSIS. RESULTS FROM THE TACERA, A LONGITUDINAL COHORT

Lewis Carpenter, Katie Bechman, Andrew Cope, Elena Nikiphorou, James Galloway, Sam Norton, On behalf of all the researchers of the Towards A Cure for Early Rheumatoid Arthritis (TACERA) working group. King’s College London, London, United Kingdom

Background: Despite advances in the treatment of rheumatoid arthritis (RA), pain and psychological symptoms remain a burden for many patients. The precise relationship between inflammation and patient reported symptoms, such as pain, fatigue and mental health in the disease is unclear. However, evidence suggests that over time there may be discordance between inflammation markers and levels of P&PSS. Therefore, to better understand the relationship between inflammation and patient reported symptoms, such that some patients with low inflammation will experience persistent symptoms. It is hypothesised that three distinct patient sub-groups exist; low inflammation/low symptoms, low inflammation/high symptoms, and high inflammation/high symptoms.

Objectives: To identify sub-groups of patients with respect to inflammatory markers and levels of P&PSS over time.

Methods: Demographic, clinical and laboratory data were recorded at baseline (pre-treatment), 6, 12, and 18-months from 239 early RA patients recruited to the Towards A Cure for Early Rheumatoid Arthritis (TACERA) cohort. Individual components of the DAS28 (tender joints, swollen joints, ESR, CRP and patient global) were used to identify sub-groups using longitudinal latent class analysis (LCA). Logistic regression models identified variables associated with class membership at 6, 12 and 18-months follow-up.

Results: LCA indicated two rather than the hypothesised three sub-groups; low inflammation/low symptoms and low inflammation/high symptoms. This was likely because ESR and CRP were well controlled by 6-months and maintained by 18-months for the majority of individuals. There were 86 (36%) 59 (35%) and 41 (39%) classified as having high symptoms at 6, 12 and 18-months. 78% of patients initially in the low symptom group remained in the low symptom group between 6 and 18-

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ACR20 response with or without major therapeutic change (MTC)

<table>
<thead>
<tr>
<th>DAMs</th>
<th>quartiles (Q)</th>
<th>With MTC</th>
<th>Without MTC</th>
<th>Risk Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAS28 Overall effect</td>
<td>34% (25%, 39%)</td>
<td>22% (15%, 28%)</td>
<td>1.52 (1.33, 1.80)</td>
<td></td>
</tr>
<tr>
<td>Q1: 6.5-8.7</td>
<td>25% (17%, 35%)</td>
<td>15% (10%, 22%)</td>
<td>1.60 (0.98, 2.44)</td>
<td></td>
</tr>
<tr>
<td>Q2: 4.5-6.5</td>
<td>30% (21%, 39%)</td>
<td>16% (10%, 23%)</td>
<td>1.80 (0.98, 3.28)</td>
<td></td>
</tr>
<tr>
<td>Q3: 2.5-4.5</td>
<td>36% (23%, 49%)</td>
<td>21% (15%, 29%)</td>
<td>1.93 (0.98, 3.81)</td>
<td></td>
</tr>
<tr>
<td>Q4: 0-2.5</td>
<td>41% (33%, 50%)</td>
<td>32% (23%, 42%)</td>
<td>1.95 (1.12, 3.36)</td>
<td></td>
</tr>
<tr>
<td>CDAI Overall effect</td>
<td>36% (21%, 41%)</td>
<td>21% (15%, 29%)</td>
<td>1.91 (1.10, 2.25)</td>
<td></td>
</tr>
<tr>
<td>Q1: 6.5-8.7</td>
<td>31% (22%, 41%)</td>
<td>15% (10%, 23%)</td>
<td>2.01 (1.33, 3.03)</td>
<td></td>
</tr>
<tr>
<td>Q2: 4.5-6.5</td>
<td>27% (20%, 35%)</td>
<td>16% (10%, 23%)</td>
<td>1.93 (0.98, 3.81)</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>

Data presented with 95% confidence intervals.
months. Rheumatoid Factor (RF) positivity and higher baseline fatigue were associated with high symptoms at 6months; decreasing ESR from 6 to 12-months was associated high symptoms at 12months, and having high symptoms at 12-months, along with reduced Swollen Joint Count (SJC), CRP and MCSI from month 12 to 18 was associated with high symptoms at 18-months.

Conclusion: Tight treatment control resulted in controlled Inflammation by 6-months, resulting in just two main patient sub-groups; those with low and high PAPS. Over one-third of patients experienced high pain and psychological symptoms. Membership of the high symptom group was associated with RF positivity but was mainly driven by prior symptom experience. Whilst inflammatory control remains a primary target, other treatments targeting pain, fatigue and mental health must be considered to reduce the burden of disease.

Disclosure of Interests: Lewis Carpenter: None declared, Katie Bechman: None declared, Andrew Cope: None declared, Elena Nikiphorou: None declared, James Galloway Consultant for: Pfizer Inc, Sam Norton: None declared


SAT0080 COMPARISON OF INFLAMMATORY CYTOKINES LEVELS IN RHEUMATOID ARTHRITIS WITH CAROTID PLAQUE; CASE-CONTROL STUDY

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Hospital Universitario Dr. José Eleuterio González, Rheumatology, Monterrey, Mexico

Background: There is a 50% increase in cardiovascular mortality in RA compared to controls. Chronic inflammation causes endothelial dysfunction and accelerated atherosclerosis. Key molecular pathways in this process are dependent on cytokines like TNF-α, IL-1, IL-6, among others, which are shared with RA. Increased disease activity could contribute to atherosclerosis. Carotid ultrasound (US) has recently been recommended as a screening tool for early detection of subclinical atherosclerosis.

Objectives: To compare different cytokines between Mexican-mestizo RA-subjects with/without carotid plaque (CP).

Methods: An observational cross-sectional trial was designed. Inclusion criteria: age between 40-75 years old, fulfillment of the 2010 ACR/EULAR classification criteria, and detection of a CP during a carotid US. Subjects with a prior diagnosis of cardiovascular disease or a poor US window were excluded. RA subjects were matched to controls (RA patients without CP) by age and cardiovascular (CV) comorbidities. Every subject had a carotid US performed; reviewed by two board-certified radiologists. Cytokines measured were IL-1, IL-6, TNF-α, VCAM-1, ICAM-1 and MMP-9, using an ELISA reader (GloMax E9022). Descriptive analysis was done with frequencies (%), median (q25-q75), and comparisons between groups with Chi square test and Mann U Whitney’s test.

Results: 71 subjects were included, 95.8% were females, with a median age of 58 years (54.65). Levels of cytokines in Table 2. Comparisons between groups are in Table 2. Groups were well balanced, with no differences in CV comorbidities (p>0.05). No significant differences among cytokine levels regarding CP were found. Subjects in remission (n=12, 33%) had a lower prevalence of CP (p=0.05, OR: 0.3; 95% CI; 0.1-0.9) and a lower median IL-1 level than those with higher disease activity (p=0.05). No significant differences were found among any of the compared cytokines.

Table 2. Clinical characteristics.

<table>
<thead>
<tr>
<th>Variable</th>
<th>CP (n=37)</th>
<th>No CP (n=34)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years median (q25-q75)</td>
<td>59.2 (54.8-66.1)</td>
<td>57.7 (53.6-61.2)</td>
<td>NS</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>35 (94.6)</td>
<td>33 (97.1)</td>
<td>NS</td>
</tr>
<tr>
<td>Dyslipidemia, n (%)</td>
<td>7 (18.9)</td>
<td>6 (17.6)</td>
<td>NS</td>
</tr>
<tr>
<td>T2DM, n (%)</td>
<td>10 (27)</td>
<td>7 (20.6)</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>12 (32.4)</td>
<td>10 (29.4)</td>
<td>NS</td>
</tr>
<tr>
<td>BMI, median (q25-q75)</td>
<td>29 (26.5-31.1)</td>
<td>27.9 (24.6-33.2)</td>
<td></td>
</tr>
<tr>
<td>Disease duration, months ± SD</td>
<td>12.4 ± 9.9</td>
<td>10.6 ± 9.9</td>
<td>NS</td>
</tr>
<tr>
<td>DAS28 CRP, median (q25-q75)</td>
<td>2.9 (2.5-3.9)</td>
<td>2.8 (2.3-3.1)</td>
<td>NS</td>
</tr>
<tr>
<td>MTX n, (%)</td>
<td>17 (45.9)</td>
<td>22 (64.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Prednisone, n (%)</td>
<td>27 (73)</td>
<td>24 (70.6)</td>
<td>NS</td>
</tr>
<tr>
<td>IL-1 pg/ml, median (q25-q75)</td>
<td>8.7 (6.7-10.1)</td>
<td>7.9 (6.1-9.3)</td>
<td>NS</td>
</tr>
<tr>
<td>TNF-α pg/ml, median (q25-q75)</td>
<td>76 (61-101)</td>
<td>76 (61-96)</td>
<td>NS</td>
</tr>
<tr>
<td>IL-6 pg/ml, median (q25-q75)</td>
<td>4.4 (4.1-4.9)</td>
<td>4.4 (3.9-4.8)</td>
<td>NS</td>
</tr>
<tr>
<td>ICAM ng/ml, median (q25-q75)</td>
<td>91 (61-118.5)</td>
<td>83.5 (61-217.2)</td>
<td>NS</td>
</tr>
<tr>
<td>VCAM ng/ml, median (q25-q75)</td>
<td>58.1 (42.1-64.8)</td>
<td>54.3 (35.1-65.9)</td>
<td>NS</td>
</tr>
<tr>
<td>MMP9 pg/ml, median (q25-q75)</td>
<td>811 (711-938.5)</td>
<td>801 (704.7-931)</td>
<td>NS</td>
</tr>
<tr>
<td>Remission (DAS 28-CRP&lt;2.6), n (%)</td>
<td>12 (33.3)</td>
<td>20 (58.8)</td>
<td>0.032</td>
</tr>
</tbody>
</table>

Conclusion: In our cohort subjects in remission had a lower prevalence of CP (OR= 0.3, 0.1-0.9). No difference was found between cytokines regarding CP. Subjects with active disease had a higher level of IL-1 than subjects in remission. To our best knowledge, this is the first study to evaluate levels of cytokines in Mexican RA-subjects.

REFERENCES


Disclosure of Interests: None declared


SAT0081 BOTH OVERFAT AND MYOPENIA ARE ASSOCIATED WITH PHYSICAL DYSFUNCTION IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Comprehensive disease control has been recommended by EULAR guidelines for rheumatoid arthritis (RA) which includes simultaneous achievement of stringent control of the signs and symptoms of inflammation, the absence of radiographic progression and normal physical function. Identifying those patients at high risk of disability at a sufficiently early stage of their disease course presents a major challenge. The associations of body mass index (BMI) and body composition (BC) with physical activity function in RA patients still obscure.

Objectives: To investigate the characteristics of BC and BMI in RA patients and their association with physical activity function.

Methods: Consecutive RA patients were recruited and clinical data including disease activity, function and radiographic assessment were collected. BC was assessed by bioelectric impedance analysis. Overfat was defined by body fat percentage (BF%) as ≥25% for men and ≥35% for women. Myopenia was defined by appendicular skeletal muscle mass index (ASMli) ≤7.0kg/m² in men and ≤5.7kg/m² in women. Subjects were categorized by BMI as underweight (BMI<18.5 kg/m²), normal weight (18.5 kg/m² ≤BMI<24 kg/m²), overweight (24 kg/m² ≤BMI<30 kg/m²) and obese (BMI≥30 kg/m²) according to Chinese criteria. Physical dysfunction was defined by HAQ-DI>0.5.

Results: There were 516 RA patients (mean age 49.8±12.9 years old with 83% women) recruited, and 37% with physical dysfunction. Compared with those with normal physical function, RA patients with physical dysfunction
were older with longer disease duration, and had higher disease activity indicators including timing of morning stiffness, 28TJC, 28SJC, PIGA, PGa, PanVAS, ESR, CRP, DAS28-CRP, SDI and CDAI, as well as higher radiographic assessment including mTSS, JSN subcore and JE subcore (all \(P<0.05\)). As for BMI and BC, RA patients with physical dysfunction had higher BF% (mean 31.05\% vs. 29.02\%, \(P=0.007\)) and prevalence of overweight (44\% vs. 27\%, \(P<0.001\)), lower ASMI (mean 5.73 vs. 6.11, \(P<0.001\)) and higher prevalence of myopenia (55\% vs. 38\%, \(P<0.001\)) than those with normal physical function, while no difference in BMI between two groups. After adjustment confounding factors, multivariable logistic regression analysis showed overweight (OR=2.990, 95\%CI: 1.695-5.274) and myopenia (OR=1.960, 95\%CI: 1.191-3.225) were positively associated with physical dysfunction respectively. Further compared with patients with normal fat, patients with overweight had significantly higher rates of dysfunction of all eight physical activities including dressing, rising, eating, walking, hygiene, reaching, gripping and activities respectively (all \(P<0.01\)), with the highest rate 57.5\% in eating dysfunction and the lowest rate 38.6\% in dressing dysfunction. Comparisons between patients with and without myopenia showed similar results with the highest rate 52.4\% in eating dysfunction and the lowest rate 37.7\% in rising dysfunction in those with myopenia.

Conclusion: Overfat and myopenia are present in near half RA patients with physical dysfunction which are associated with dysfunction of all eight physical activities especially eating.

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Disclosure of Interests: None declared


ASOCIATIONS OF BASELINE CLINICAL AND SLEEP INTERVENTION WITH AUDIBILITY IN RHEUMATOID ARTHRITIS IN AN ACPA POSITIVE COHORT

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Background: Subjects who are in the preclinical rheumatoid arthritis (RA) state can be identified through serum elevation of circulating RA-related autoantibodies, including rheumatoid factor (RF) and antibodies to citrullinated protein antigens (ACPA), prior to the clinical appearance of inflammatory arthritis (IA) and RA. Studying Preclinical RA may identify factors and pathways to disease development, and help to identify therapeutic targets for prevention. Furthermore, trials in ACPA+ subjects have been completed or are underway with the primary goal to prevent future IA/RA. However, relatively few individuals have been studied through the evolution of the Preclinical ACPA+ state to Classified RA. As such there are still many gaps in the understanding of the clinical and immunologic evolution from Preclinical to Classified RA.

Objectives: The study objective is to identify the clinical, environmental and immunologic factors/paths that are associated with incident IA/RA development in individuals with ACPA elevations.

Methods: We created a cohort of 86 ACPA+ subjects who at their baseline study visit did not have a historical or examination (66/68 count) evidence of IA/RA. ACPA+ was defined as a serum elevation of anti-CCP3 (IgG, Innova) on \(>2\) occasions above the established cut-off \(>20\) units). These subjects were recruited over 18 months through community health fair screening. ACPA testing of first-degree relatives of patients with RA, and rheumatology clinics. Clinical, environmental and biomarker factors, including RF IgA and IgM [Inova] and high-sensitivity C-reactive protein [hsCRP], were assessed at the baseline visit. Herein we present interim analyses of baseline visits on the whole ACPA+ cohort and longitudinal follow-up on a subset of subjects, with a specific focus on factors that are associated with baseline symptoms and rates of self-reported joint pain, morning stiffness or fatigue. hsCRP positivity (\(>3\) mg/L) was associated with increased rates of self-reported fatigue of \(>0\) on VAS (20\% vs. 41\%, \(p=0.04\)). Ever smoking was associated with increased rates of self-reported morning joint stiffness (18\% vs 50\%, \(p<0.01\)). In addition, in analyses of longitudinal follow-up data available to date, 10/86 subjects (12\%) developed IA classified as RA (2010) a median of 293 days after baseline BMI and BC, RA individuals with incident RA exhibited a higher BMI compared to those who did not (27 vs. 32, \(p=0.03\)). In addition, positivity for hsCRP and RF, and higher median anti-CCP3 levels, were present in those who developed incident IA/RA although not statistically significant.

Conclusion: Within this new cohort of prospectively followed ACPA+ individuals, smoking and an elevated hsCRP are associated with clinical symptoms of stiffness and fatigue, respectively. The relationship of stiffness and smoking suggests this factor is related to early joint symptoms, and the association of high BMI with incident RA may indicate this is a modifiable risk factor for RA (de Hair 2013). This prospective study will continue, with further study of the factors/pathways that may influence well-being in ACPA+ individuals as well as may influence predictive of or causally linked to the future IA/RA.


PREVALENCIA DE FRAILTY Y SU ASOCIADA FACTORES EN PACIENTES CON RHEUMATOID ARTHRITIS: A CROSS-SECTIONAL ANALYSIS

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Background: The concept of frailty is a recent issue in the rheumatologic field, but, by now, the prevalence of frailty among individuals with rheumatoid arthritis (RA) has not been extensively examined and few studies on frailty in RA adults have been completed. Moreover, the relationship between frailty and sociodemographic or disease characteristics in RA are unknown.

Objectives: The aims of the present research were to assess the prevalence of frailty and its potential associated factors in adult patients with RA.

Methods: Consecutive RA patients and healthy controls were recruited according the Survey of Health, Ageing and Retirement in Europe Frailty Instrument (SHARE-FI) (1), and classified as frail, pre-frail or non-frail. Patients underwent to a clinical assessment in order to establish disease activity (Simple Disease Activity Index [SDAI]), function (Health Assessment Questionnaires Disability Index [HAQ-DI]), comorbidities (modified Rheumatic Disease Comorbidity Index [mRDCCI])(2), and radiographic damage (Simple Erosion Narrowing Score [SENS]). Chi-square, analysis of variance (ANOVA), and multinomial logistic regression analyses were used to test the prognostic value of frailty for the outcomes of interest.

Results: 210 consecutive RA patients were included (72 male, 138 female) and the mean age was 60.4 years. The study group was composed by 100 healthy controls (63 females and 47 males). The mean age of RA patients was \(59.1\) years. According to SHARE-FI criteria, 35 RA patients (16.6\%) were categorized as frail, 68 (32.4\%) as pre-frail, and 107 (51\%) as non-frail; while 8 control subjects were categorized as frail, (8\%), 17 as pre-frail (17\%), and 75 as non-frail (75\%) (chi-squared 12.6; \(p=0.0016\)). The results from logistic regression analysis revealed that age (odd ratio [OR] = 1.12, 95\% confidence interval [CI] = 1.07-1.17; \(p<0.0001\)), comorbidities (OR = 1.51, 95\% CI = 1.01-2.27; \(p= 0.0446\)), and high disease activity (OR = 1.10, 95\% CI = 1.04-1.16; \(p=0.0006\)) were independently associated with frailty in IA/RA patients (Fig. 1).

Conclusion: Frailty or pre-frailty are common in RA. The SHARE-FI may be a specific tool for the screening of frailty in RA and may summarize...
the results of a comprehensive RA assessment providing a marker of deficits accumulation. Future studies will need to examine longitudinal relationships between frailty and health outcomes in RA.

The correlations (Spearman’s rho) between Survey of Health, Ageing and Retirement in Europe Frailty Instrument (SHARE-FI) and age (A), modified Rheumatic Disease Comorbidity Index (mRDCI) (B), and Simplified Disease Activity Index (SDAI) (C).

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Disclosure of Interests: Marco Di Carlo: None declared, sonia farah: None declared, eleonora Di Donato: None declared, marina carotti: Speakers bureau: Abbvie pfizer novartis roche bms sanofi, Fausto Salaffi: Grant/research support from: Abbvie, Roche, Novartis, BMS, Pfizer, Sanofi, Speakers bureau: Abbvie, Roche, Novartis, Pfizer, Sanofi, BMS


SAT0084 IDENTIFICATION OF POOR PROGNOSTIC JOINT LOCATIONS IN AN EARLY, RAPIDLY PROGRESSING RA COHORT: A POST HOC ANALYSIS OF THE AGREE STUDY

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Background: Early RA patients (pts) often present with different areas of joint involvement, but limited data exist to identify which specific joint locations may be indicative of greater disease severity.

Objectives: This analysis investigated the baseline (BL) prevalence of swelling and erosions in individual joint locations and their possible association with disease characteristics and prognostic factors in a unique cohort of early erosive RA patients using the AGREE study population.

Methods: In this post-hoc analysis of the Phase III AGREE study where methotrexate (MTX) naïve RF and/or ACPA seropositive pts with early (≤2 years [yrs]) erosive RA were treated with abatacept (ABA) plus MTX (n=256) or MTX (n=253), prevalence of BL swollen joint status (present, absent) was analysed for 6 large and 14 small joint locations: respectively wrists, elbows, shoulders, jaw, knees, ankles and MCP1-5, PIP2-5 and MTP1-5. Similarly, prevalence of BL erosive joint status was analysed for wrist; MCP1-5, PIP2-5 and MTP1-5. The association between BL disease characteristics and BL swelling or erosions was investigated for the individual joints.

Results: In this cohort of early, seropositive erosive RA (n=509), BL swelling was most frequently observed in the wrist (91.90%) and MCP2 joint (90.1%), whereas BL erosion was most frequently observed in the MTP5 joint (43.5%) (Table 1). BL swelling in the knee, jaw, wrist and elbow was highly associated (p<0.001) with higher tender and swollen joint counts, higher DAS28 (CRP) and higher SDAI and CDAI. As expected, patients with BL presence of erosions had a higher total Genant-modified Sharp score (TSS) whatever the joint location. Overall, men seem more prone for erosions, and this is seen in all joint locations, except for the wrist. Moreover, in this already highly seropositive cohort, patients with BL erosions were more ACPA, but not RF, positive for all evaluated joints of the feet. BL swelling does not seem to be associated with erosive status, neither in the individual joint nor in the TSS, except for the MCP2 joint (erosion positivity was 21% and 4% and TSS was 7.4 [9.5] and 4.7 [5.6] in swollen and non-swollen MCP2 joints respectively).

Conclusion: In this cohort of early, seropositive erosive RA, swelling in the knee, jaw, wrist and elbow seems to be associated with the poorest prognosis, whereas BL MCP2 swelling seems to be associated with joint damage. While the data require further validation, a difference in joint location presentation may identify patients for an intensive treatment or a personalized treatment approach.

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Disclosure of Interests: Patrick Durez Speakers bureau: Bristol-Myers Squibb, Eli Lilly, Sanofi, Celtiion, Rene Westhoovers Grant/research support: from: Bristol-Myers Squibb, Consultant for: Celtrion, Galapagos-Gilead, Yedid Elbez Employee of: Employee of Excetaya which received funding from: Bristol-Myers Squibb as core research organization. Sofie Robert Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Harris A Ahmad Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb

SAT0085
A MATRIX RISK MODEL FOR PREDICTING 5-YEAR RADIOGRAPHIC PROGRESSION IN A COHORT OF EARLY RHEUMATOID ARTHRITIS TREATED ACCORDING TO T2T STRATEGY
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Background: In the treatment strategy of early rheumatoid arthritis (ERA) it is of pivotal importance to detect those patients who are at risk of radiographic progression (RP) in order to avoid decline in both functional capacity and quality of life.
Objectives: To identify baseline predictive factors for 5-year RP in an observational cohort of ERA treated according to treat-to-target (T2T) strategy, and to create a matrix risk model including the strongest predictors.
Methods: A total of 212 ERA patients with less than 12 months of disease duration (mean age 52.8±13.9 years, 75% female, 74.5% seropositive) and with available radiographs at 5 years of follow-up (FU), were enrolled in the study. ERA patients fulfilled the 2010 ACR criteria for RA and were followed according to the T2T strategy. At baseline, and every three months, the ACR/EULAR core data set variables were recorded. At baseline and every year, hand and foot radiographs were examined according to modified Total Sharp score (mTSS). At each visit, clinical improvement and remission were evaluated according to EULAR criteria. The achievement of Comprehensive Disease Control (CDC) (28-joint Disease Activity Score using C reactive protein <2.6, Health Assessment Questionnaire <0.5) was assessed every year of FU.
Results: Fifty-six ERA patients (26.4%) had erosions on hand and foot radiographs performed at baseline. At 5 years of FU additional 56 subjects (26.4%) developed RP. ERA patients showing RP were in higher percentage ACPA positive (78.6%) and erosive at baseline (41.1%) compared to subjects not manifesting RP (65.4%) ACPA positive, p=0.07; 21.2% erosive at baseline, p=0.004, respectively. Moreover, radiographic progressors had a VERA disease (disease duration less than three months) with lower frequency (21.4%) compared to non progressors (34.6%, p=0.07). CDC was achieved at twelve months of FU more frequently by non progressors (52.6%) compared to non progressors (34.6%, p=0.07). CDC is the advisable treatment goal, the radiological damage is not fully prevented in case of ACPA positivity.

Disclosure of Interests: Anna Laura Fedele: None declared, Dario Bruno: None declared, Barbara Tolusso: None declared, Luca Pellico: None declared, Gianfranco Ferraccioli: Speakers bureau: BMS, Roche, Eliisa Gremsene Consultant for: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Sanofi, UCB, Roche, and Pfizer, Speakers bureau: BMS, Speakers bureau: AbbVie, BMS, Celgene, Janssen, MSD, Novartis, Sanofi, UCB, Roche, and Pfizer

SAT0086
EVALUATION OF MEDICATION PERSISTENCE IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH NON-TNF INFLAMMATION-MODIFYING ANTI-RHEUMATIC DRUGS
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Background: Persistence to prescribed biologic (b)DMARDs, such as TNF inhibitors (TNFi), in patients (pts) with RA has been suboptimal, with rates ranging from 30–80%. There are limited data on the persistence of non-TNFi bDMARDs and targeted synthetic DMARDs, such as tofacitinib (TOF).
Objectives: To compare medication persistence in pts with RA treated with different non-TNFi DMARD treatment options including abatacept (ABA), TOF and tocilizumab (TOC), and to evaluate characteristics (e.g. demographics, comorbidities, baseline treatments) of these pts.
Methods: Pts (≥18 years) from the Truven MarketScan® administrative claims database with RA (≥2 claims for RA identified with International Classification of Diseases [ICD]-9 or ICD-10) being treated with a non-TNFi DMARD from Jan 2006 to Sep 2017 were included. The date of the first claim of a drug of interest on or after diagnosis of RA was considered the index date. Pts were required to have at least 6 months of continuous enrolment prior to the index date (baseline). Pts with claims of other bDMARDs at the index date were excluded from the study. Persistence was defined as the number of days from the index date to the first switch or discontinuation of the index date DMARD, or end of the study period, or end of enrolment, whichever came first. Pts were stratified by prior TNFi use (TNFi-naïve or TNFi-experienced) and by prior corticosteroid (CS) use. Pairwise comparison of persistence between the non-TNFi DMARDs was performed, with ABA as the reference using Kruskal–Wallis test. A p value of <0.05 was considered statistically significant.
Results: A total of 30,556 pts satisfied the inclusion and exclusion criteria, of which 20,410, 5048 and 5098 were initially treated with ABA, TOF and TOC, respectively. Overall, the ages of therapy initiation for the ABA and TOF cohorts were similar, while the TOC cohort was slightly younger. The majority (80%) of the study population was female. The proportion of pts with prior CS use was lower in the ABA cohort vs the other cohorts. Overall, the comorbidity index between treatment cohorts was similar; however, there were some differences in types of comorbidities at baseline (Table 1). The ABA cohort tended to have a lower proportion of pts with chronic obstructive pulmonary disease/emphysema, pulmonary nodules, dyslipidaemia and osteoarthritis, while the proportions of pts with heart failure, ischemic heart disease and lupus were higher relative to other cohorts (Table 1). Overall, mean (SD) time on therapy for pts in the ABA cohort was longer compared with pts in the TOF (338 [418] vs 257 [288] days) and the TOC cohorts (338 [418] vs 294 [345] days). Similar differences were observed when further stratified by pts’ prior use of TNFi and CS (Table 2).
Conclusion: Based on the analysis of a large US claims database, pts with RA who were prescribed abatacept had higher persistence with therapy compared with other non-TNFi DMARDs such as TOF and TOC, regardless of prior use of TNFi and CS. Further analysis of medication persistence adjusting for pt characteristics is warranted.

Table 1. Baseline characteristics by cohort

<table>
<thead>
<tr>
<th>ABA</th>
<th>TOF</th>
<th>TOC</th>
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</thead>
<tbody>
<tr>
<td>n=262,410</td>
<td>337,168</td>
<td>181</td>
</tr>
<tr>
<td>TNF-naive</td>
<td>292,069</td>
<td>252,915,950</td>
</tr>
<tr>
<td>TNF-experienced</td>
<td>317,147</td>
<td>312,200,950</td>
</tr>
<tr>
<td>GS-naive</td>
<td>302,433</td>
<td>263,118,950</td>
</tr>
<tr>
<td>GS-experienced</td>
<td>312,167</td>
<td>294,131,950</td>
</tr>
</tbody>
</table>

Values are expressed as mean (SD) median, in days reported

Table 2. Persistence by cohorts: overall and stratified by prior TNF and CS use

<table>
<thead>
<tr>
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| Values are expressed as mean (SD) median, in days reported

SAT0087 REAL-LIFE GOLIMUMAB PERSISTENCE IN PATIENTS WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASES: FINAL RESULTS OF THE GO-PRACTICE STUDY


Results: 770 patients selected from January 2015 to March 2016 at 134 sites, of which 754 included in the analysis. Mean age was 46 years and 61% were female. Most had AS (63%), followed by RA (23%) and PsA (14%). Mean duration of rheumatic disease was 7.6 years and 37% had previously received biologics. The proportion of patients who received 1, 2, 3 and 4 biologics were 18%, 11%, 6% and 2%, respectively. Most patients were prescribed 50mg GLM monthly (97%). Concomitant treatments included disease-modifying anti-rheumatic drugs (38%), corticosteroids (19%) and NSAIDs/analgesics (71%). Persistence of GLM at 2 years was 52.4% (56.5%, 45.1% and 52.6% for RA, PsA and AS respectively), and in the AS group was higher for biologics naïve than biologics pretreated patients (59.2% vs. 42.7%, P<0.01).

Conclusion: GLM persistence in real-life is satisfactory at 2 years and accompanied by clinical improvements in RA, PsA and AS patients.

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COMPARISON OF THE INITIAL DIAGNOSTIC FINDINGS AND ONSET FACTORS OF RHEUMATOID ARTHRITIS (RA) IN ELDERLY ONSET RA AND ADULT ONSET RA BY MULTICENTER COHORT – ARE THERE ANY DIFFERENCES OF ONSET FACTORS? –

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Background: In recent years, it has been reported that elderly onset RA (EORA) is a pathology different from that adult RA (AORA) 1). It has been reported that RA is due to genetic background, and many other factors. However it is not clear whether EORA and AORA share onset factors.

Objectives: We compared the initial diagnostic finding of EORA and AORA patients who were diagnosed by RA specialist at their own hospi- tal. We also compared the presence or absence of the onset factors between EORA and AORA.

Methods: 1185 patients at 18 facilities who were initially diagnosed with RA were included. EORA (n=398) was defined by disease onset at over 60 years and AORA (n=732) was defined by disease onset from16 to 59 years. We compared blood examination, clinical findings, presence of bone erosion, gender, age, and background factors pre-onset (family his- tory, history of smoking/operation, presence of periodontal disease/gyneco- logical diseases/digestive system diseases) between EORA and AORA.

Clinical findings were analyzed with Mann-Whitney U-test and frequency of pre-onset history were analyzed by 2 × 2 Chi square test.

Results: The average age of EORA and AORA were 72 years and 54 years old. The ratio of female was 75% in EORA, but 84% in AORA, a significant difference (P<0.01). The average values of CRP (ug/ml) were 2.0 in EORA, but it is 1.3 in AORA, significantly lower (P<0.001). Also ESR (mm/1h and MMP-3 (ng/ml) of EORA were 46 and 83, whereas those of AORA were 36 and 29 significant as CRP. On the other hand, TJC, SJC, PaGA and PhGA were not significantly different.

We also compared the prevalence of onset factors between EORA and AORA. There was no clinical significant difference in smoking history and gynecological conditions. The presence rate of stress and family history in AORA were 71% and 38%, whereas that in EORA was 54% and 26%, significantly lower (P<0.001). On the other hand, the presence rate of history of gastrointestinal disease, periodontal disease and operation history in AORA were 43%, 36% and 40%, but those in EORA were 49%, 46% and 52%, significantly higher(P<0.01).

As in previous reports2), the ratio of men and those who have inflammatory values in EORA were significantly higher, but there was no difference in SJC, PaGA, and PhGA. This study verified in Japanese EORA as the other reports. There were differences in the presence rate of onset factors between the two groups, whereas EORA had many external factors such as surgical history, whereas AORA had genetic factors and stress in their backgrounds. Regarding the presence of bone erosion, it was caused by the period from the appearance of the symptoms until the diagnosis and was unrelated to age at onset.

Conclusion: This study suggests that the onset of EORA is more likely to be attributed to external factors than genetic factors.

REFERENCES


SAFETY AND EFFICACY OF LY3373641, A BRUTON'S TYROSINE KINASE INHIBITOR IN PATIENTS WITH RHEUMATOID ARTHRITIS: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED, 2-PART PHASE 2 STUDY

Mark C. Genovese1, Alberto Spindler2, Akira Sagawa3, Won Park4, Anna Dudnek5, Jeanne Liao6, Rahul Shinh7, Melanie Chan7, William Barkhuizen8, Ajay Nirula7.

LY3373641 is an irreversible covalent inhibitor of Bruton’s tyrosine kinase (BTK), a key signaling molecule in the B-cell-receptor and Fc-receptor pathways and mediator of B-cell– and myeloid-cell-dependent inflammatory arthritis.1,2 RA-JUVENATE was a multicentered, randomized, double-blind, placebo-controlled, 2-part Phase 2 trial with long-term extension (LTE) in adult patients (pts) with rheumatoid arthritis (RA).

Objectives: The objective of this analysis is to present the primary results from Part B of the study.

Methods: In Part A, 36 pts with at least mildly active RA were randomized 1:1:1:1 to receive oral LY3337641 5, 10, or 30 mg or placebo (PBO) once daily (QD) for 4 weeks (wks) with the primary objective of safety and tolerability. There were no safety signals to preclude moving to Part B; pts in Part A were not eligible to participate in Part B. In Part B, 250 pts with active moderate to severe RA were randomized 1:1:1:1:1 to receive oral LY3337641 5 (N=63), 10 (N=62), or 30 mg (N=63) or PBO (N=62) QD for 12 wks. The primary endpoint of Part B was the proportion of pts achieving ≥20% improvement in American College of Rheumatology criteria (ACR20) at Wk 12. A logistic regression model was used to compare each LY3337641 dose to PBO for primary and secondary endpoints. Nonresponder imputation was used to impute missing data. After an interim analysis showed a low likelihood of demonstrating efficacy at the conclusion of the trial, the sponsor discontinued Part B of the study, including the LTE. Efficacy results (except analysis of low disease activity and remission) included pts who completed through Wk 12 at the time of study discontinuation; safety was results included all pts who received ≥1 dose of study drug. Results: Of the 250 pts (mean age 51.0 years; 86.4% female; mean disease duration 11.2 years) randomized in Part B, 189 (75.6%) completed 12 weeks and 180 entered the LTE (72.0%); 61 discontinued study treatment in Part B. The most common reasons for discontinuation were drug-related (27 [10.8%]), withdrawal by subject (8 [3.2%]), adverse event (8 [3.2%]), and lack of efficacy (4 [1.6%]). There was no statistically significant difference in the ACR20 response between any treatment group of LY3373641 and PBO at Wk 12 (p=0.05 for all comparisons; Table); a high placebo rate was noted, but no underlying reason was identified in post hoc analyses. There were 5 serious adverse events; 2 in PBO pts (joint dislocation and cholecystitis acute) and 3 in 30-mg pts (foot fracture, multiple injuries, and venous thrombo- sis). There was 1 death (30-mg pt, multiple injuries after a 4-story fall down elevator shaft). There were no safety findings that precluded continuation of the study.

Conclusion: Although there were no safety findings that precluded continuation of the study, the study sponsor determined that the observed benefit-risk profile of LY3373641 in the study did not warrant its continuation.
GUT MICROBIOTA COMPOSITION IS CONTINGENT INCREASED FREQUENCY AND DEFECTIVE
DISEASE PHASES IN RHEUMATOID ARTHRITIS


Methods:

Table. Efficacy and safety outcomes at Week 12

| Treatment | Change from baseline, observed (mean, SD) | Significant differences
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>-1.8 (1.1)</td>
<td></td>
</tr>
<tr>
<td>ACPA+</td>
<td>-1.1 (1.2)</td>
<td></td>
</tr>
<tr>
<td>ACPA+5</td>
<td>-1.0 (1.1)</td>
<td></td>
</tr>
<tr>
<td>ACPA+10</td>
<td>-0.7 (1.1)</td>
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</tr>
</tbody>
</table>

Results: Microbiota composition analysis showed that RA patients had a decrease in the gut microbial species richness compared to HC (p<0.01). In particular, the principal coordinate analysis (PCoA) visualization of UniFrac distances and analysis of group similarities (ANOSIM) showed that faecal microbiota composition differs between RA and HC (p<0.01) confirmed by the LEfSe analysis showing that RA microbiota is enriched of Bacteroidetes and Proteobacteria, whereas HC were enriched of Verrucomicrobida and Firmicutes. Considering the RA cohort, no significant differences in microbiota composition were found stratifying patients based on autoantibody profile, disease duration and BMI category. However, considering the disease phase, RA patients with active disease (DAS<3.7) showed significant differences in α-diversity compared to RA patients in LDA score in sustained clinical remission (p<0.01) with a relative abundance of Haemophilus parainfluenzae in high disease activity patients (p=0.01). A slightly higher α-diversity in RA patients with the higher adherence to Mediterranean diet (p=0.10).

Conclusion: Despite limited sample size, this study strengthens the concept of significant microbiota differences in RA, contingent with disease phases, compared to HC. The evaluation of microbiota composition in the patients follow-up according to response to therapies is ongoing.

REFERENCES


SAT0090 GUT MICROBIOTA COMPOSITION IS CONTINGENT WITH DISEASE PHASES IN RHEUMATOID ARTHRITIS

Elisa Grenesca1, Stefano Alivernini2, Barbara Tolusso3, Brunella Posteraro4, Maurizio Sanguinetti5.

Background: Increasing evidences suggest that alterations in the gut microbiota may contribute to the pathogenesis and influence the clinical outcome of Rheumatoid arthritis (RA).

Objectives: To characterize the gut microbiota composition in RA patients in different disease phases contingent to therapeutic regimens.

Methods: Forty-four RA patients (7 naïve to treatment, 13 MTX-IR and 24 in sustained clinical and ultrasound remission under conventional and biMARD combination therapy, respectively) (age 55±11.4 years, 79.5% female and 59.1% positive for ACPA and/or RF) and 20 age/sex matched healthy controls (HC) were enrolled in the study. At study entry, RA specific data set were collected and dietary habits were recorded using the 14-items Mediterranean Diet Adherence Screener (MedDAS) questionnaire. DNA was extracted from stool samples of each patient amplified and 16S rRNA gene V3–V4 region was sequenced using an Illumina MiSeq10 platform. For downstream sequence analysis, a combination of software packages QIIME (v1.9.1) and VSEARCH (v1.1) was used and a biological observation matrix (BIOM) at different taxonomic levels (from phylum to genus) was produced. The BIOM was analysed using the Web-based program Microbiome Analyst. Statistical analyses were performed using the R phyloseq software package. Differences in the relative abundance of individual bacterial taxa between a priori defined groups were assessed by LEfSe analysis.

Results: Microbiota composition analysis showed that RA patients had a decrease in the gut microbial species richness compared to HC (p<0.01). In particular, the principal coordinate analysis (PCoA) visualization of UniFrac distances and analysis of group similarities (ANOSIM) showed that faecal microbiota composition differs between RA and HC (p<0.01) confirmed by the LEfSe analysis showing that RA microbiota is enriched of Bacteroidetes and Proteobacteria, whereas HC were enriched of Verrucomicrobida and Firmicutes. Considering the RA cohort, no significant differences in microbiota composition were found stratifying patients based on autoantibody profile, disease duration and BMI category. However, considering the disease phase, RA patients with active disease (DAS<3.7) showed significant differences in α-diversity compared to RA patients in LDA score in sustained clinical remission (p<0.01) with a relative abundance of Haemophilus parainfluenzae in high disease activity patients (p=0.01). A slightly higher α-diversity in RA patients with the higher adherence to Mediterranean diet (p=0.10).

Conclusion: Despite limited sample size, this study strengthens the concept of significant microbiota differences in RA, contingent with disease phases, compared to HC. The evaluation of microbiota composition in the patients follow-up according to response to therapies is ongoing.

REFERENCES


Table 1. Demographic and clinical characteristics of the study subjects

Fig1. Flow cytometry analysis of CD4+CD25+Foxp3+ Treg cells in healthy controls (HC), stable remission RA patients and active RA patients.

Fig2. Function analysis of CD4+CD25+Foxp3+ Treg cells in RA and healthy controls.

Fig3. Correlation analysis of CD4+CD25+Foxp3+ Treg cells with clinical data.
Low serum level of vitamin D at time of diagnosis is associated with higher one-year remission rate in patients with newly diagnosed RA, treated aggressively during follow-up: post-hoc analyses of the CIMESTRA trial

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Background: Vitamin D is often low in Rheumatoid Arthritis (RA), and immunomodulatory properties of vitamin D might be associated with disease course in RA (1).

Objectives: To evaluate association between baseline vitamin D metabolites and one-year remission, in newly diagnosed, treatment-naïve RA patients, aggressively treated during follow-up.

Methods: The CIMESTRA-cohort comprises 160 newly diagnosed RA patients, treated aiming at remission with methotrexate and intraarticular steroid, further randomized 1:1 to cyclosporine or placebo-cyclosporine (2). A total of 158 patients had vitamin D metabolites measured at time of diagnosis. Dietary vitamin D supplementation was recommended in accordance with the national guidelines. Serum vitamin D_total (sum of 25OHD2 and 25OHD3) and 1,25(OH)2D at time of diagnoses were measured by LC-MS/MS or RIA. D_total were dichotomized at 50 nmol/l, and 1,25(OH)2D categorized in tertiles. Primary outcome was remission (DAS28-CRP < 2.6) after one year. Associations were calculated using logistic regression, presented as Odds Ratios with 95% Confidence Intervals (95%CI). Adjustment of analyses included sex, age, symptom duration prior to diagnosis, DAS28-CRP and season of diagnosis.

Results: In univariate analyses, neither D_total nor 1,25(OH)2D at time of diagnosis predicted remission at year one. In adjusted analysis, D_total < 50 mmol/l at time of diagnosis showed better odds for achieving one-year remission, compared to sufficient D_total. OR 2.56, 95%CI (1.11; 5.90) p = 0.03. 1,25(OH)2D was not associated to remission.

Conclusion: Low D_total at time of diagnosis is associated to increased odds for achieving remission at year one in early, treatment naïve RA patients, treated aggressively during follow-up.

REFERENCES

Acknowledgement: Søren Møller, biostatistician at OFEN, Odense, for statistical support.

Disclosures of Interests: Mette Herly Grant/research support from: Pfizer Denmark, unrestricted grant, used for salary. The Danish Rheumatism Association, patient association, 6 months salary as part of PhD study, Speakers bureau: The Danish Rheumatism Association. Torkell Ellingsen: None declared.

Disclosure of Interests: Mette Herly Grant/research support from: Pfizer Denmark, unrestricted grant, used for salary. The Danish Rheumatism Association, patient association, 6 months salary as part of PhD study, Speakers bureau: The Danish Rheumatism Association. Torkell Ellingsen: None declared.
number of color pixels to all the pixels in a selected range of interest (ROI). The study was approved by the proper ethics committee. Statistical analysis: differences between groups were analyzed using U Mann-Whitney test (continuous variables). Correlations between quantitative variables were assessed with the Spearman correlation coefficient. Statistical significance was set at p<0.05.

Results: DAS28: mean 6.0 (SD=0.9); median 6.1 (IQR: 5.5 - 6.6); SDAI: mean 61.1 (SD=36.3); median 51.3 (36.8 - 76.4). No correlation was found between CFI and age, platelet count, CRP, RF, ACPA, DAS28 and SDAI as well as with the disease duration. But there was a strong positive correlation between CFI and PDUS results, r = 0.71; p < 0.05. As expected, DAS28 and SDAI strongly correlated with inflammatory markers (ESR, CRP). The results showed, that CFI between 2.6% ia an equivalent of PDUS grade 1, CFI 8-50% of PDUS grade 2 and CFI > 50% of PDUS grade 3.

Conclusion: although PDUS is a method to assess synovial inflammation, through the determination of the synovial vascularization, its results, regardless of the scoring system employed, do not correlate with the systemic inflammation indicators, such as ESR and CRP or with the disease activity – which needs further explanation. The approximate equivalence of CFI and of PDUS scoring system is as follows: CFI > 50% - PDUS grade 3, CFI 8-50% - PDUS grade 2, CFI 0-8% - PDUS grade 1, which confirms previously published research.

Disclosure of Interests: None declared


SAT0094

UNITED STATES RHEUMATOLOGY PRACTICE-BASED REAL-WORLD EVIDENCE OF METHOTREXATE UTILIZATION AND RESPONSE TO THERAPY IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH INTRAVENOUS GOLIMUMAB

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Background: AWARE (Comparative and Pragmatic Study of Golimumab IV Versus Infliximab in Rheumatoid Arthritis) is an ongoing Phase 4 comparative study designed to provide a real-world assessment of intravenous golimumab (GLM) and intravenous infliximab (IFX) in patients (pts) with rheumatoid arthritis (RA). The primary objective of AWARE is to assess the incidence of infusion reactions, the concomitant use of methotrexate (MTX) is also reported. The FDA approved label for GLM states that it is indicated for the treatment of patients with moderately to severely active RA in combination with MTX; however prospectively obtained real world evidence based data on the rate of GLM use without MTX has not been reported.

Objectives: Here we compare patient demographics, disease characteristics, response to therapy and discontinuation of GLM treated patients with and without concomitant MTX from an interim analysis (IA) of the AWARE study.

Methods: AWARE is a prospective, noninterventional, observational, multicenter 3-year study conducted in the US. RA pts (1,200 adults) were enrolled at the time of initiating treatment with GLM or IFX. All treatment decisions including MTX utilization are made at the discretion of the treating rheumatologist. Imputations of CDAI data were not performed at this IA. Data shown are mean ± standard deviation.

Results: 678 GLM pts were enrolled; of these 487 (71.8%) were GLM Plus-MTX and 191 (28.2%) were GLM No-MTX. Demographics are shown in the table. Response to therapy was assessed with CDAIs and shown in the figure below. Overall, 92.6% of GLM Plus-MTX and 91.5% of GLM No-MTX pts had a baseline (BL) categorical CDAI disease activity of moderate or high, and 7.4% of GLM Plus-MTX and 8.5% of GLM No-MTX pts had a BL categorical CDAI disease activity of low or remission. Discontinuation from the study during the period of this IA was similar between the GLM Plus-MTX (173/487; 35.5%) and GLM No-MTX (64/191; 33.5%). 7.9% of GLM No-MTX pts reported leflunomide use.

Conclusion: At BL 28.2% of pts on GLM did not report concomitant MTX use. The demographics of the GLM Plus-MTX pts did not differ remarkably from GLM No-MTX pts. The reported early response to treatment, assessed by CDAI score after 3 months and 6 months was similar in the GLM Plus-MTX and GLM No-MTX groups. These preliminary IA data suggest that in a real-world rheumatology practice setting, use of GLM with or without concomitant MTX led to similar CDAI scores at 3 and 6 months in RA pts with predominantly moderate to high BL CDAI disease category.


SA0095

MEDIATION NECESSITY AND CONCERN BELIEFS ARE DISTINCT, INTERACTIVE PREDICTORS OF TREATMENT ADHERENCE IN RHEUMATOID ARTHRITIS

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1Harbor UCLA Medical Center, West Carson, United States of America; 2Sun Valley Research & Development, LLC, Palo Alto, United States of America

Background: Medication adherence is instrumental for the successful management of rheumatoid arthritis (RA) to a goal of remission. Awareness of medication necessity and concerns regarding its use influence adherence and respectively foster or undermine the achievement of treatment goals.

Objectives: We explored the unique and interactive roles of patient beliefs about the necessity of RA medications and concerns about them in predicting adherence to prescribed treatments.


Methods: We evaluated 316 patients with established RA from a single center. Beliefs about the necessity of RA medications and concerns regarding their use were evaluated with the Beliefs about Medicines Questionnaire-Specific (BMQ) Necessity and Concerns scales (range 5-25). Self-reported rheumatoid arthritis treatment adherence was assessed using the Simplified Medication Adherence Questionnaire (SMAQ, range 0-6). Multivariable linear regression evaluated the effects of necessity, concerns and their interactions with adherence. A latent profile analysis (LPA) subsequently classified patients in groups according to patterns of necessity and concerns; adherence scores were then compared across latent groups using ANCOVA.

Results: Full adherence (SMAQ score 6/6) was reported by 101 (32%) patients. Necessity and concerns had independent and opposing contributions to adherence (β=0.21 and β=0.28 respectively, p<0.001 and figure 1a) even after adjustments for age, gender and disease duration. An interaction between necessity and concerns with adherence was also observed (p<0.009), post-hoc simple-slope tests showed that necessity predicted adherence with increasing concerns. Johnson-Neyman technique revealed that while concerns were significantly associated with adherence across the entire range of necessity scores, necessity was significantly related to adherence only at BMQ Concerns scores >13. LPA revealed four latent patient groups: Low necessity/Low concerns (indifferent, n=33), Low necessity/High concerns (skeptical, n=70), High necessity/High concerns (ambivalent, n=92) and High necessity/Low concerns (accepting, n=121). Adherence varied across groups even after adjusting for between group differences (p<0.002, Figure 1b); adherence was highest in the accepting group and lowest in the skeptical group.

Conclusion: The relationship between necessity and concern beliefs regarding RA medications significantly influences adherence behavior and may further direct physicians to effectively target their education efforts. A message aimed at reducing concerns might be more effective in the ambivalent subgroup, whereas emphasizing medication necessity may be more fruitful in the skeptical group.

Figure 1. Interaction between Necessity and concerns on medication adherence in RA

Disclosure of Interests: George Karpouzas Grant/research support from: Pfizer, Consultant for: Sanofi-Genezyme-Regeneron, Janssen, Roche-Genentech, Pfizer, Speakers bureau: BMS, Sanofi-Genezyme-Regeneron, Janssen, Roche-Genentech, Elizabeth Hernandez: None declared, Vibeke Strand Consultant for: AbbVie, Amgen, Bayer, BMS, Boehringer Ingelheim, Celgene, Celltrion, CORRONA, Crescendo, EMD Serono, Genentech/Roche, GSK, Horizon, Inmexid, Janssen, Kezar, Lilly, Merck, Novartis, Pfizer, Regeneron, Samsung, Sandzox, Sanofi, Servier, UCB, Sarah Ormseth: None declared


SAT0096 CORRELATION OF GROWTH FACTORS WITH RHEUMATOID ARTHRITIS CLINICAL COURSE INDICATORS

Elena Komarova, Boris Rebrov, Anna Blagodarenko, Natalia Bludova, Galina Bekrka, Lugsanik State Medical University, Lugansk, Ukraine

Background: The evaluation of early destruction markers in rheumatoid arthritis (RA) is of significant clinical importance for improving the patient’s life quality. One of the immunological markers of RA early diagnosis and of severe disease is antibodies to cyclic citrullinated peptide (ACCP). Instrumental methods for early diagnosis of RA include the ultrasound of joints and bone-cartilage erosions (US), vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF) and surrounding synovial vascularization. These parameters of blood and cartilage erosions, the growth of pannus mass and contribution to the development of bone and cartilage erosions.

Objectives: to establish the correlation of growth factor indicators with markers of the destructive course of rheumatoid arthritis.

Methods: 194 patients with a diagnosis of RA were examined, among the examined patients women prevailed - 86.6%, the age was 47.7 ± 10.22 years. Positive by the presence of ACCP (>20 U/ml) was 77%, and negative - 23.2%. The ELISA in the serum was determined by the concentration of CRP and TNF-α (Vector-Test, Russia), antibodies to cyclic citrullinated peptide (ACCP) (Euroimmun, Germany), VEGF and FGF (BCM Diagnostic, Canada). Ultrasound of the joints was performed by the device “ESAOTE MyLAB40” (Netherlands, 2011) with a linear sensor of 7.5 L 70 (frequency 7.5 MHz), semi-quantitative evaluation of indicators was used: effusion into the joint space (JS), synovial thickness, vascularization of the synovial membrane (SM), the presence of pannus and bone-cartilage erosion.

Results: Direct correlations with CRP and ACCP levels (p = 0.02; p = 0.01, respectively), TNFα and DAS28 (<0.001) were established during analysis of the correlation between VEGF and RA clinical course indicators. Analysis of the correlation of VEGF and ultrasound indices of the joints in the examined patients RA established strong direct links with the JS effusion parameters and the SM vascularization assessment (p <0.001, in all cases), and a direct interaction of weak force with the indicator of pannus (p = 0.04) was found. Regression analysis revealed the dependence of the variability of the SM vascularization assessment on the level of VEGF in the blood showed a sufficient value of the coefficient of determination (0.57), and the data of the normalized index DW = 2.59 reliably indicate the absence of autocorrelation (0.06). Direct correlations with R6 stage (p <0.001) and the rate of CRP (p = 0.02) were established during analysis of correlation links of FGF with the RA clinical course. Analysis of the correlation of FGF and ultrasound indices of the joints in the examined RA patients established strong direct correlations with the indicators of the thickness of SM, pannus, and bone-cartilage erosion (p <0.001, in all cases), the direct correlation of weak force (p = 0.04) was with the SM vascularization assessment index. Regression analysis of the dependence of the variability of the SM thickness indicator on the FGF blood level showed a sufficient value of the multiple correlation R² = 0.47. Also showed a regression analysis of the dependence of the variability of pannus and bone and cartilage erosion indices on the FGF blood level (R² = 0.51; R² = 0.46, respectively), which evidences the regression line approximation to the observed data.

Conclusion: According to the correlations of VEGF, FGF levels with CRP, ACCP, assessment of synovial vascularization and bone-cartilage erosions - the high levels of VEGF, FGF in the blood can be used as markers of severe destructive course of RA and of the high rate of disease progression, which requires the early aggressive basic therapy of RA with the use of genetically engineered biologic drugs prescription.

Disclosure of Interests: None declared


SAT0097 ASSOCIATION BETWEEN PHYSICAL ACTIVITY AND SUBSEQUENT CHANGES IN DISEASE ACTIVITY IN PEOPLE LIVING WITH RHEUMATOID ARTHRITIS

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Background: Various studies have found that rheumatoid arthritis (RA) patients perform less physical activity than the general population, likely due to joint pain and impaired physical function. However, recent studies suggest that physical activity may have a beneficial effect on inflammatory and could therefore contribute to reducing RA disease activity. A greater understanding of the relationship between physical activity levels and RA disease activity would be valuable for physical activity counseling of RA patients.

Objectives: The aim of this study was to evaluate the association between baseline physical activity levels and subsequent changes in measures of disease activity in patients with RA using self-reported data.

Methods: We conducted a longitudinal study using 2015-2017 data from a postal survey administered to an RA cohort derived from a population-based cohort for BC originally assembled using physician billing data and a previously validated algorithm. Subjects were grouped into three levels (Low, Medium and High) of physical activity (PA) at the baseline year (2015) according to the specifications of the International Physical Activity Questionnaire. We examined whether physical activity at baseline was associated with a change over time in RA disease activity outcomes.
from 2015 to 2017. We fitted linear mixed models for Rheumatoid Arthritis Disease Activity Index (RADA), Fatigue visual analog scale (VAS), and Pain VAS scores separately with/without adjusting for age, sex, sociodemographic factors, body mass index, RA duration, physical function (Modified Health Assessment Questionnaire [mHAQ]), smoking, depression and other comorbidities at baseline. Models include the outcome at three years (2015-2017) as the dependent variables, an indicator variable representing the year of measurement (2015-17), PA level at baseline, their interactions, and baseline characteristics as covariates. Models include random effects for subjects to account for correlations among within-subject repeated measures. Missing values were imputed using multiple imputation methods. The analyses were conducted using R 3.5.

**Results:** Of the 169 patients who responded to the 2015 survey, 29.6%, 42.0%, and 28.4% had low, medium, and high levels of PA in 2015, respectively. There were no significant differences in RADA (p=0.67), Fatigue (p=0.78), and Pain (p=0.98) at baseline (Figure 1). The low PA group experienced significant worsening of disease activity outcomes over time, including yearly increases of 0.31 in RADA (p=0.007), 0.41 in Fatigue (p=0.007), and 0.43 in Pain (p=0.007). Those in the medium and high PA groups at baseline experienced either a decrease or no change in their disease activity outcomes over time. The interaction terms for PA level and year show that the low PA group had significantly different time trends for RADA, Fatigue, and Pain compared to the medium and high PA groups (all p values <0.05). The results remain robust after adjusting for age, sex, and other covariates.

**Conclusion:** Across RADA, Fatigue VAS, and Pain VAS scores, RA patients with a low PA level demonstrated a significant increase in disease activity over the span of three years. The trends for both the high and medium PA groups differ significantly from that of the low PA group, showing small, overall decreases in disease activity over time. These results add to the accumulating evidence that physical activity may reduce disease activity and is an essential aspect of RA management.

**Disclosure of Interests:** Kiera Lee-Pii: None declared, Hui Xie: None declared, Yufei Zheng: None declared, Linda Li: None declared, Diane Lacaille Grant/research support from: Bristol-Myers Squibb and Eli Lilly Canada

**Background:** RA patients who are ACPA-positive (ACPA+) are known to have worse prognosis. Less is known regarding predictors of treatment outcomes in ACPA-negative (ACPA-) patients.

**Objectives:** We investigated whether autoantibodies captured on a custom array were associated with response to therapy in ACPA RA patients.

**Methods:** RA patients were recruited to either the Biologics in RA Genomics and Genomics Study Syndicate (BRAGGSS, starting adalimumab, established disease) or the RA Medication Study (RAMS, starting methotrexate, early disease). Serum samples were collected at pre-treatment and 3/6 months in BRAGGSS/RAMS, respectively. Treatment groups were pooled for analysis. ACPA was measured using a commercially available ELISA (Axis-Shield Diagnostics Ltd, Dundee, UK). Pre-treatment RA and healthy blood donor control (HC) serum samples were incubated on a bead-based assay (Luminex FlexMap 3D) containing 376 human protein antigens associated with autoimmune disease (39 in citrullinated [cit] form) to detect autoantibodies. Median fluorescence intensity (MFI) values were calculated for each autoantibody for RA and HC, then normalised and log2-transformed. The 95th percentile for each autoantibody in HC was used to determine whether an RA sample was positive/negative for that autoantibody. Proteins with <10% frequency in RA patients were excluded from analysis. Linear regression was used to determine autoantibodies differing in MFI between RA and HC; p-values were adjusted using the Benjamini-Hochberg correction. Significant autoantibodies (adjusted p<0.05) were tested for associations with treatment outcomes in RA patients only using: (i) linear regression for improvement in DAS28; (ii) logistic regression for good/poor vs all EULAR response. All regression was adjusted for age, gender, disease duration and baseline disease activity.

**Results:** 168 patients with RA were included in analysis (mean age 59.6 years, mean disease duration 14.3 years, 126 (75%) female patients, 90 (53.6%) ACPA+ patients). 34 autoantibodies were differentially expressed in RA patients, only one of which (TNP2, a superfamily member 13, TNFSF13) was lower than in HC, 93/34 autoantibodies were in cit-form. In multivariate models of all differently expressed autoantibodies, heterogeneous nuclear ribonucleoprotein A1 (HNRNPA1) was significantly associated with EULAR response (coefficient (coef) 0.7, 95% CI 0.1-1.3), and cit-vimentin (VIM) was significantly associated with poor EULAR response (ORadj 4.2, 95% CI 1.1-18.3) and reduced odds of good EULAR response (ORadj 0.2, 95% CI 0.1-0.8). ACPA remained the best predictor of treatment response. In a subanalysis of the 78 ACPA—patients, cit-cleavage and polyadenylation specificity factor subunit 6 (CPSF6) was significantly associated with worse DAS28 (coef -1.8), 95% CI (-3.6) (-0.1). cit-Dnaj homolog subfamily B member 1 (DNAJB1) was significantly associated with DAS28 improvement (coef 2.2, 95% CI 0.6-3.8). No autoantibody was associated with EULAR response.

**Conclusion:** A subset of ACPA-patients have ACPA fine specificities not seen by a commercial assay. Larger ACPA profiling may provide additional information on treatment response. This requires validation with larger sample sizes and replication in an independent cohort.

**REFERENCE**

**Disclosure of Interests:** Stephanie Ling: None declared, Nisha Nair: None declared, Darren Plant: None declared, Hans-Dieter Zucht: Employee of: Hans-Dieter Zucht is an employee of Protagen AG, Petra Budde: Employee of: Petra Budde is an employee of Protagen AG, Peter Schulz-Knape: Shareholder of: Peter Schulz-Knape is a shareholder of Protagen AG, Consultant for: Peter Schulz-Knape is a consultant to Protagen AG, Employee of: Peter Schulz-Knape is an employee of Protagen AG, MATURA Consortium: None declared, Anne Barton: None declared.

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SAT0099 THE RELATIONSHIP OF RHEUMATOLOGY ATTITUDES INDEX WITH OUTCOME MEASURES OF RHEUMATOID ARTHRITIS IN AN ASIAN PATIENT POPULATION

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Background: The Rheumatology Attitudes Index (RAI) is a questionnaire comprising of fifteen questions that assesses a patient’s beliefs and perception of helplessness and the ability to control rheumatoid arthritis (RA). However, the relationship between RAI and patient demographics, disease activity and functional status is inadequately explored.

Objectives: We analysed the association of RAI with educational level, Physician’s Global Assessment of Activity (DGA), Patient’s Global Assessment of Activity (PGA), Disease Activity Score (DAS 28), and Health Assessment Questionnaire (HAQ). We also investigated if RAI is sensitive to change over a six-month period in comparison with DGA, PGA, DAS28 and HAQ.

Methods: All patients from Tan Tock Seng Hospital, a tertiary hospital in Singapore, who fulfilled the 1987 ACR criteria for RA, and completed the self-administered RAI questionnaire twice over six months were included. We analysed the DAS28, DGA, PGA and HAQ. Repeated measure ANOVA was used to analyse the association between RAI and educational level. Spearman correlation was used to study the association between RAI and the parameters DAS 28, HAQ, DGA and PGA, both cross-sectionally and longitudinally. We used SPSS version 19.0 (IBM Corp, Armonk, NY). P-value <0.05 was considered statistically significant.

Results: There were 501 patients suitable for study. The mean age of disease onset was 43 years and mean disease duration was 15 years. The majority were Chinese (83.4%), married (68.5%) and most (79.4%) received fewer than 10 years of education. About half (50.7%) of the participants suffered from hypertension, 13.6% diabetes mellitus, 61.5% hyperlipidaemia, 20.8% renal disease, 21.6% liver disease and 16.6% thyroid disorder. Patients with <10 years education have higher RAI scores (p<0.001) compared to those with ≥10 years of education. Cross-sectionally, weak positive correlation was found between RAI and DAS 28 (r = 0.225, p<0.001), DGA (r = 0.107, p=0.017) and PGA (r = 0.283, p<0.001). On the other hand, there was moderate positive correlation between RAI and HAQ (r=0.440, p<0.001). Weak positive correlation was found between the change in RAI compared to changes in DAS 28 (r = 0.114, p=0.011), HAQ (r = 0.249, p<0.001), DGA (r = 0.163, p<0.001) and PGA (r = 0.155, p<0.001).

Conclusion: Higher RAI scores denoting greater perceived helplessness were associated with higher RA activity. HAQ, PGA and DGA, RAI was responsive to change over a six-month period compared with these four parameters. High RAI score was also associated with lower educational level. Higher RAI scores reflects higher disease activity and worse functional status in a cross-sectional cohort and for the same patient level. Higher RAI scores reflects higher disease activity and worse functional status cross-sectionally and longitudinally. We used SPSS version 19.0 (IBM Corp, Armonk, NY). P-value <0.05 was considered statistically significant.

REFERENCE


SAT1000 IN THE ABSENCE OF GUIDELINES, HOW ARE RHEUMATOLOGISTS MANAGING ANTI-CCP POSITIVE PATIENTS WITHOUT CLINICAL SYNOVITIS?

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Background: The emphasis on early referral and treatment of rheumatoid arthritis (RA) means rheumatologists are now seeing patients earlier in the natural history of RA. Despite clear guidelines for the management of early arthritis, there are no guidelines on how to manage anti-CCP positive (CCP+) patients with symptoms but no clinical synovitis who are at-risk of developing RA. Given the frequent use of ultrasound (US) in early arthritis clinics, we hypothesised that imaging is being used by rheumatologists to guide the management of these at-risk patients.

Objectives: To survey national practice to identify, in the absence of any guidelines, how CCP+ patients without clinical synovitis are being managed by rheumatologists in the UK and specifically to investigate how imaging is being used to guide management in the ‘pre-arthritis’ phase of RA.

Methods: Anonymous questionnaires were completed by rheumatologists working in 39 different UK hospitals. 44/47 (94%) rheumatologists reported they are referred CCP+ patients who have musculoskeletal (MSK) symptoms but no clinical synovitis in their routine clinical practice. Of these, 32/44 (73%) were referred <5 patients per year. In CCP+ patients with ‘inflammatory symptoms’ but no clinical synovitis, 36/44 (82%) would request an US scan to help guide management and 2/44 (5%) would request an MRI scan. All respondents would follow these patients regularly and 5/44 (11%) would consider a clinical trial. In CCP+ patients with ‘non-inflammatory’ symptoms and no clinical synovitis, 18/44 (41%) would request an US scan, 13/44 (30%) would observe in clinic and 12/44 (27%) would discharge back to primary care. When specifically asked about use of high-resolution imaging in CCP+ patients without clinical synovitis, 40/44 (91%) reported they used imaging, with most (37/40, 93%) using US. In patients where power Doppler (PD) signal is present on US in at least one joint, most (55%) would start disease-modifying anti-rheumatic drug (DMARD) treatment (figure 1) and 16% would treat according to RA guidelines. In patients with US tenosynovitis but no US synovitis, most (73%) would treat with either corticosteroids alone (48%) or a DMARD (48%). In contrast, in patients with no US synovitis or US tenosynovitis, 23/37 (62%) would observe without therapy while 12/37 (32%) would discharge the patient (figure 1).

Conclusion: UK rheumatologists are routinely referred CCP+ patients in the pre-arthritis phase of RA and often treat these patients with synthetic DMARDs, guided by US findings. Whether this pragmatic approach is an appropriate one needs to be tested in clinical trials with RA prevention as the ultimate ambition. Guidance on management of these patients would clearly be helpful.

Disclosure of Interests: Kulveer Markajo Grant/research support from: Abbvie, UCB, Christopher Briggs: None declared, Paul Emery Grant/ research support from: Pfizer, MSD, AbbVie, Bristol-Myers Squibb, Roche, Consultant for: Pfizer, MSD, AbbVie, Bristol-Myers Squibb, UCB, Roche, Novartis, Gilead,Samsung, Sandoz and Lilly DOI: 10.1136/annrheumdis-2019-eular.6913

Figure 1: The management of anti-CCP positive patients without clinical synovitis according to ultrasound findings as reported in a survey of consultant rheumatologists in the UK. RA, rheumatoid arthritis; Mtx, methotrexate; HCq, hydroxychloroquine.
SAT0101  INTRAHOSPITAL MORTALITY IN PATIENTS WITH RHEUMATOID ARTHRITIS: OBSERVATIONAL STUDY AT THE NATIONAL LEVEL OVER A 17-YEAR PERIOD (TREND-AR STUDY)

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Background: There have been important changes in the management of RA in the last 20 years, such as T2T strategy or new biologic agents. The potential impact of these therapeutic strategies on important outcomes such as inhospital mortality due to different causes is not known.

Objectives: To analyze the incidence and tendency of mortality by different causes (global, cardiovascular, infectious, neoplasm, and others) in patients with RA, in Spain, during the period 1999-2015.

Methods: Retrospective cohort study based on the exploitation of the database that collects a minimum basic set of data (MBDS) of all patients with RA during the 17 years of the study period, corresponding to a total of 18,641 hospital exitus (5.5% of the incomes). 63.4% were women. To analyze cases of inhospital death and the main diagnosis of these cases. The causes of death in the hospital, global, by sex and in periods 1999-2001, 2003-2006, 2007-2010 and 2011-2015 are described. The results are expressed in absolute numbers and in proportion to the total number of deaths.

Results: There was a total of 338,343 hospital admissions in patients with RA during the 17 years of the study period, corresponding to a total of 176,097 patients (117,985 women and 58,112 men). There was a total of 18,641 hospital exits (5.5% of the incomes). 63.4% were women. The mean age was 74.6 (SD 10.1) (in females of 77.2 (SD 10.2) and in males 71.9 (SD 9.9) p <.001). The mean of Charlson index was 3.2 (SD 2.4). The mean age increased linearly from 73.5 (1999-2002) to 78.23 (2011-2015). The following table shows the causes of death grouped by sex and period:

<table>
<thead>
<tr>
<th>% of deaths (both sexes)</th>
<th>1999-2001</th>
<th>2003-2006</th>
<th>2007-2010</th>
<th>2011-2015</th>
<th>Total (both sexes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular (non-infectious)</td>
<td>22.81%</td>
<td>24.36%</td>
<td>24.14%</td>
<td>24.14%</td>
<td>24.03%</td>
</tr>
<tr>
<td>Infectious</td>
<td>10.51%</td>
<td>10.51%</td>
<td>20.28%</td>
<td>21.82%</td>
<td>20.18%</td>
</tr>
<tr>
<td>Respiratory (non-infectious)</td>
<td>10.27%</td>
<td>10.90%</td>
<td>19.84%</td>
<td>19.84%</td>
<td>19.92%</td>
</tr>
<tr>
<td>Neurological</td>
<td>11.54%</td>
<td>11.87%</td>
<td>12.59%</td>
<td>13.49%</td>
<td>13.20%</td>
</tr>
<tr>
<td>Gastrointestinal (non-infectious)</td>
<td>9.38%</td>
<td>9.41%</td>
<td>3.09%</td>
<td>9.32%</td>
<td>8.99%</td>
</tr>
<tr>
<td>Gout</td>
<td>7.35%</td>
<td>6.77%</td>
<td>4.84%</td>
<td>7.37%</td>
<td>7.19%</td>
</tr>
<tr>
<td>Renal failure</td>
<td>4.46%</td>
<td>4.45%</td>
<td>4.09%</td>
<td>4.44%</td>
<td>4.31%</td>
</tr>
<tr>
<td>Nephrolithiasis (non-infectious)</td>
<td>3.46%</td>
<td>2.79%</td>
<td>2.82%</td>
<td>3.22%</td>
<td>3.04%</td>
</tr>
<tr>
<td>Extravascular</td>
<td>2.62%</td>
<td>2.33%</td>
<td>2.43%</td>
<td>2.62%</td>
<td>2.53%</td>
</tr>
<tr>
<td>Hemorraghic (non-neoplastic)</td>
<td>2.30%</td>
<td>2.30%</td>
<td>1.97%</td>
<td>2.03%</td>
<td>2.22%</td>
</tr>
<tr>
<td>Neurological (non-infectious)</td>
<td>1.49%</td>
<td>1.09%</td>
<td>1.14%</td>
<td>1.02%</td>
<td>1.06%</td>
</tr>
<tr>
<td>Other</td>
<td>1.22%</td>
<td>1.22%</td>
<td>1.40%</td>
<td>1.08%</td>
<td>1.23%</td>
</tr>
<tr>
<td>Sids</td>
<td>0.64%</td>
<td>0.63%</td>
<td>0.62%</td>
<td>0.63%</td>
<td>0.63%</td>
</tr>
</tbody>
</table>

Conclusion: The main causes of inhospital mortality in patients with RA in Spain were cardiovascular (24%), infections (20%), respiratory-non-infectious (15%) and neoplasms (12%). The average age of death increased 5 years in the study period. The deaths from infections, respiratory and neoplasms have increased, while those of digestive origin and AR extrarticular have decreased.

Disclosure of Interests: None declared

SAT0102  ASSOCIATION BETWEEN BASELINE HAEOMOBLOGIN LEVELS AND RADIOGRAPHIC JOINT DAMAGE PROGRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH BARICITINIB OR STANDARD OF CARE

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Background: In patients with active rheumatoid arthritis (RA), haemoglobin (Hb) levels have been inversely associated with radiographic progression of structural joint damage.1-3 In two randomized 52-week (wk) studies, baricitinib (BARI), a selective JAK1/JAK2 inhibitor, reduced radiographic progression in patients with moderate to severe active RA who had received no/minimal prior methotrexate (MTX; RA-BEGIN)4 or had inadequate response to MTX (RA-BEAM).5

Objectives: To assess the association between baseline Hb levels and structural damage progression and to study the effect of BARI 4-mg once daily on structural damage progression at 52 wks based on baseline Hb levels.

Methods: Data from the modified intention-to-treat (mITT) populations of RA-BEGIN (MTX=210, BARI 4-mg=159, BARI 4-mg + MTX =215 patients) and RA- BEAM (placebo [PBO]=488, adalimumab [ADA]=328, BARI 4-mg=487 patients) were included for analysis. Structural damage progression was defined as change from baseline (CFB) greater than the smallest detectable change (SDC) in the modified total Sharp score (mTSS) at wk 52. In RA-BEGIN SDC was 1.4 and in RA-BEAM SDC was 1.5. Missing mTSS data at wk 52 were imputed using linear extrapolation based on baseline data and the most recent radiographic data prior to the missed radiograph. Observed proportions of patients with CFB in mTSS >SDC at wk 52 were calculated for low (males <13.0g/dL, females <12.0g/dL) or normal baseline Hb for each treatment arm from both studies. Multivariate logistic regression (MLR) was used to study the association of baseline Hb with structural joint damage at 52 wks. The MLR included treatment, baseline Hb (g/dL), baseline hsCRP (Normal £3mg/L; Elevated >3mg/L), baseline CDAI, baseline HAQ-DI, BMI, smoking status; structural progression at 52 wks was more pronounced in patients with moderate to severe active RA who had received no/minimal prior methotrexate (MTX; RA-BEGIN)4 or had inadequate response to MTX (RA- BEAM).5

Conclusion: In patients with RA, lower baseline Hb levels were associated with increased structural damage progression. Treatment with BARI 4-mg reduced structural progression, irrespective of patient baseline Hb status; structural progression at 52 wks was more pronounced in patients with low baseline Hb receiving MTX alone (RA-BEGIN) or PBO and background MTX (RA- BEAM).

REFERENCE
Objectives: To explore if achieving T2T biological remission and individual patient treatment goals overlap in RA patients with initially low, moderate, or high disease activity (LDA, MDA, or HDA). Disease activity was measured with the Clinical Disease Activity Index (CDAI) and the Disease Activity Score (DAS28). Individual patient goals were assessed with the Goal Attainment Scale (GAS) at baseline and after three to five months. The number and proportion of patients who reach the T2T target, but not their individual goals and vice versa were calculated.

Results: We enrolled 162 patients in the study (131 [80.9%] women, median age 59.0, IQR= 49-71). 101 patients (62%) had a follow up visit with no missing data after three months. Of these, 48 (47.6%) patients had low disease activity (LDA), 43 (42.6%) had MDA, and 10 (9.9%) had HDA at baseline. Median age 59.0, IQR= 49-71). 101 patients (62%) had a follow up visit with no missing data after three months. Of these, 48 (47.6%) patients had low disease activity (LDA), 43 (42.6%) had MDA, and 10 (9.9%) had HDA at baseline.

Conclusion: Our results indicate that most patients achieving T2T attain their individual treatment goals but a respectable part of T2T outcomes might be more important for patients to set individual treatment goals which are related to their specific life context. For this reason, Ferreira at al [2] recently proposed a dual T2T strategy including both biological remission and individual patient goals and vice versa.
had to be supplemented by the individual patient reported treatment goals.

REFERENCES

Table 1. Comparison of achieved T2T and individual patient goals

<table>
<thead>
<tr>
<th>T2T achieved, n (%)</th>
<th>Yes</th>
<th>No</th>
<th>Overall</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient goal(s) achieved, n</td>
<td>44 (66.3)</td>
<td>22 (33.7)</td>
<td>66 (100)</td>
</tr>
<tr>
<td>(%)</td>
<td>(43.6)</td>
<td>(21.8)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>18</td>
<td>17</td>
<td>35 (54.7)</td>
</tr>
<tr>
<td></td>
<td>(17.6)</td>
<td>(16.9)</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>62</td>
<td>39</td>
<td>101</td>
</tr>
<tr>
<td></td>
<td>(61.4)</td>
<td>(38.6)</td>
<td>(100.0)</td>
</tr>
</tbody>
</table>

Acknowledgement: We want to thank all patients who participated in this study. Further thanks to the students Marie Louise Brand, Saskia Langthaller, Hanna Møes and Jim Schmeckebieker for assisting in patient recruitment.


SAT0105 HAND DISABILITY IN RHEUMATOID ARTHRITIS: AN ENGINEERED GLOVE FOR THE COMPUTERISED QUANTIFICATION OF THE DAMAGE
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Background: Tenderness, swelling and loss of motility of the joints are the main determinants of the disability function (DF) of Rheumatoid Arthritis (RA) patients (RApts). The evaluation of DF is performed by Patient Reported Outcomes (PROs), like Health Assessment Questionnaire (HAQ). The lack of objective evaluation of DF is one of the most important “unmet needs” in RA. The Hand Test System (HTS, ETT) is an engineered glove, nowadays applied for neuroscience studies to evaluate hands motility with interesting perspectives of use in other clinical research fields.

Objectives: To quantify the DF of RApts by the analysis of speed and right execution of fingers opposition movement in both hands, evaluated by HTS. To verify the correspondence with the HAQ.

Methods: In this pilot study 14 consecutives RApts (3 males, 11 females, age 61 ± 11.5 years, mean duration of disease 11.21 ± 5.07 years, classified according to 2010 ACR/EULAR criteria, and 13 healthy controls (HC – 7 males, 6 females, age 50 ± 15 years) were enrolled from the RA clinic. After consent, all participants undergone HTS test that recognized the touches between the finger tips during the opposition movements of the hands in standard sequences of movements, after dressed the glove. A multiple finger evaluation (MFE) and a single finger evaluation (SFE) were performed using a dedicated software that provided the physician the following quantitative parameters: Touch Duration (TD), Inter Tapping Interval (ITI) and Movement Rate (MR). Average time for hand 2 minutes. RApts compiled the HAQ and a tender and swollen joint count of the hands was performed. Continuous variables were summarized as mean and standard deviation (SD) or median and interquartile range (IQR), discrete variables were summarized with count and percentage. Variables with skewed distribution was converted to natural logarithm. T-test was used to compare log glove parameters between groups. Pearson's r and p value were used to report the correlation between log-converted glove parameters and HAQ score.

Results: In MFE, glove parameters TD and ITI were significantly higher in RApts (TD 257.34 ± 123.93 ms, ITI 377.8 ± 211.35 ms) than HC (TD 172.25 ± 59.36 ms, ITI 177.98 ± 78.53 ms) (p = 0.004 and p < 0.001) and MR was significantly lower in RApts (1.51 ± 0.47 Hz) compared to HC (2.87 ± 0.9 Hz) (p <0.001). TD of RApts had a significant correlation with the total score of the HAQ (Pearson r = 0.79, p = 0.001). In SFE non-active fingers (NAF, not swollen and not tender) of RApts seemed to perform slightly better than a clinically active finger (AF) but significantly worse than average HC finger (ANOVA, p < 0.001).

Conclusion: HTS is a new easy and totally safe tool that seems to quantify in an objective manner the hand DF in RApts. The significant correlation found with HAQ underlines the value and versatility of self-assessment tools in clinical practice. Further studies are ongoing with larger number of RApts to validate its application to monitor the improvement or the worsening of RA in order to optimize pharmacological treatments. The study is now extended in other Rheumatic and Musculoskeletal Diseases.

REFERENCE

SAT0106 NOVEL SUBCLASS OF INTRAVASCULAR NON-CLASSICAL SYNOVIAL MONOCYTES ARE CRITICAL FOR RHEUMATOID ARTHRITIS
Anna Montgomery, Deborah Winter, Harris Perlman, Northwestern University, Medicine/Rheumatology, Chicago, United States of America

Background: There are at least three populations of circulating monocytes: classical, intermediate and non-classical. We demonstrated that circulating non-classical monocytes are required for the effector phase of arthritis and spontaneous models of arthritis in mice. While the vast majority of studies on monocytes have focused those in circulation, very little is known about the monocytes in the synovium.

Objectives: The aim of this study was to examine the heterogeneity of tissue monocytes with those circulation and determine their involvement in inflammation.

Methods: Female 8-10-week-old NRR1A1–/–, C57Bl/10 TCR14Dmaly.J2D4, and C57Bl/6 mice were used in all studies. C3XR1-Cre mice were utilized for cell tracking studies and joint shielded bone marrow chimeras via administration of tamoxifen (tam). Intravascular monocytes were identified using fluorescent anti CD45 antibody before perfusion. STIA was induced via I.V. KBxN sera. Monocyte populations were quantified by flow cytometry and FACS sorted for RNA-sequencing (RNA seq). Nonclassical tissue mono- cytes were identified CD45+CD11b+Ly6G TIM4 CD64 Ly6C– and subdivided into intravascular (CD45-labeled, CD43+), trans-vascular (CD45-labeled CD43–) and extravascular (no CD45-labeled). Human synovium was obtained from ultrasound guided synovial biopsies and CD45+ cells were FAC-Sorted for single cell RNA seq.

Results: NRR1A1–/– mice exhibit a 95% reduction in circulating Ly6C– monocytes but retain Ly6C+ cells in the joint and develop STIA. The transcriptional profiling of bulk populations of Ly6C+ cells in the synovium are distinct from those circulating in the blood. We then identified three populations of Ly6C+ monocytes in the joint; extra-vascular, trans-vascular cells, and intra-vascular cells using 18 color flow cytometry. Lineage tracing studies reveal that the origin of extra-vascular and trans-vascular synovial monocytes are from the embryo while the intravascular monocytes are derived post-natally. The intravascular monocytes are depleted with clodronate loaded liposomes while the extravascular and trans-vacular remain unaffected. Moreover, the intravascular monocytes rapidly expand during the first hour of STIA, increasing by 30x in population size. RA patients also display similar populations of non-classical monocytes using single cell RNA seq.

Conclusion: We have identified and described three previously uncharacterized populations of non-classical monocytes cells in the joint, an intravascular adherent, a trans-vascular population and an extra-vascular
BIOMARKERS OF CLINICAL RELAPSE AND RADIOLOGICAL PROGRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS IN REMISSION: OBSERVATIONAL STUDY OF 5 YEARS OF FOLLOW-UP

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Background: Patients with Rheumatoid Arthritis (RA) in remission will present flares during the evolution of the disease. Definitive biomarkers have not been identified to predict flares and radiographic progression (RP) in this kind of patients

Objectives: To search biomarkers of clinical relapse and RP in patients with RA in clinical remission

Methods: RA patients in clinical remission (DAS28-ESR<2.6 for >6 months) were selected. Clinical, epidemiological and serological data were analyzed. MRI of dominant hand, ultrasound assessment of knees and hands and serum levels of inflammation and angiogenesis biomarkers were evaluated at 0 and 48 weeks. Synovial biopsy was performed in patients with subclinical synovitis. Patients were follow-up for 5 years. Radiological data were collected. Clinical relapse was defined as the loss of remission status involving a therapeutic intervention. RP was defined as the change of baseline therapy for RA. Only 10% of RA patients lost clinical remission (DAS28-ESR) after 5 years of follow-up. BMI, baseline bone edema, PD signal at 12 months and first-year rate of CXCL16 and VSG levels were predictors of joint flares. BMI, baseline bone edema, PD signal at 48 weeks, Synovial mast cells were associated with structural progression. Macrophages and T cells in ST were higher in patients suffering structural progression. Only 10% of RA patients had RP along the study. Sinovial mast cells were associated with disease flares. Macrophages and T cells in ST were higher in patients with RP in an exploratory analysis.

REFERENCE

Disclosure of Interests: None declared

CHARACTERISTICS OF MULTIRESISTENT PATIENTS TO BIOLOGICAL TREATMENTS IN RHEUMATOID ARTHRITIS, AND ASSOCIATED FACTORS: AN OBSERVATIONAL AND RETROSPECTIVE STUDY IN 385 PATIENTS

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Background: Despite a wide range of biological treatments (bDMARDs) in the management of rheumatoid arthritis (RA), some patients fail in different lines of treatment. Currently, there is no consensus definition of multiresistance to bDMARDs in RA.

Objectives: The aim of our study was to describe the characteristics of “multiresistant” patients and to establish associated factors with multiresistance to bDMARDs in RA.

Methods: In this observational and retrospective study were identified patients who had failed for administration of a bDMARD at Rouen University Hospital (France) between January 2007 and July 2017 (sources: diagnostic coding using International Classification of Diseases 10th revision and traceability of intra-hospital pharmacy). In the absence of a consensus definition, multiresistance to bDMARD was defined in this study by failure, primary and/or secondary, to at least 2 bDMARDs. The clinical and paraclinical characteristics of these patients at the initiation of the first bDMARD were collected using data from their standardized monitoring, then compared to those of patients who received a single bDMARD effective for 10 years or more, constituting the “responder” group.

Results: We identified 794 patients; 385 constituted our active RA file under bDMARD, 192 patients excluded for different reasons (6 patients not fulfilling the ACR/EULAR 2010 criteria, 18 followed in another department, 45 for missing data at bDMARD’s initiation, 50 not found in computerized file, 73 for whom the expected bDMARD was never started) and 217 lost to follow-up. Among our active RA file under bDMARD (385 patients), 53 were “multiresistant” (at least 2 bDMARDs failed), and 50 patients received a single and effective bDMARD for 10 years or more, after excluding some patients for missing data (Figure 1). The mean age of “multiresistant” patients at initiation of bDMARD was 50.3 years (±13.2 years), and the sex ratio was 2.8 women/1 man. They presented erosive RA (77.4%), rheumatoid factor and anti-citrullinated peptide antibodies positive (73.6%), highly active (median number of tender and swollen joints 8/28, median visual analog scale disease activity 70/100, median C-Reactive protein (CRP) 21 mg/L, mean Disease Activity Score 28 CRP mean 5.36±1.28), and with high functional impact (Health Questionnaire Median Assessment: 1,500/3). The age of disease onset was significantly later in “multiresistant” patients than in “responder” patients (43±14.2 years versus 37.9±10.7 years, p = 0.042). No demographic, anamnestic, clinical and paraclinical characteristics differed significantly between “multiresistant” and “responder” patients.

Conclusion: It is an original work, counting in the literature as a single similar study [1], with nevertheless significant methodological differences. There is no consensus definition of multiresistance to bDMARD in RA, and its mechanisms remain misunderstood. Identifying predictive factors would make it possible to early identify patients with a refractory profile, in order to adapt the therapeutic strategy. Multidrug resistance in RA remains one of the challenges in the management of this pathology.

REFERENCE
SMOKING CESSATION IN PATIENTS WITH RA IS ASSOCIATED WITH REDUCED CVD EVENT RATES AND IMPROVED LIPID PROFILES AND PREDICTS LOWER RA DISEASE ACTIVITY


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Background: Smoking is a major risk factor for development of both cardiovascular disease (CVD) and rheumatoid arthritis (RA) and causes an attenuated response to antirheumatic treatment.

Objectives: The aim of this study was to compare disease activity and CVD risk factors across smoking status in RA patients. Further to evaluate the impact of smoking cessation on risk of future CVD events in these patients.

Methods: RA disease characteristics, CVD risk factors and relevant medication were recorded in patients from 10 countries (Norway, UK, Netherlands, USA, Sweden, Greece, South Africa, Spain, Canada and Mexico). Information on CVD events were collected after a median follow-up of 3.54 years (inter-quartile range 2.51 – 6.06). Adjusted analysis of variance, logistic regression and COX proportional hazards analyses with time to event as response variable were applied to compare RA disease activity (measured by DAS28), CVD risk factors and CVD event rates across current, former and never smokers.

Results: Among the 3311 included RA patients (1012 former, 887 current and 1412 never smokers), 235 experienced a CVD event(s) during follow-up. At enrollment into the study current smokers were more likely to have moderate/high disease activity compared to former and never smokers (p<0.001 for both) (Figure 1). There was a gradient of worsening CVD risk factor profiles (lipoproteins and blood pressure) from never smokers, via former smokers, to current smokers. Furthermore, after 3.54 years of follow up former and never smokers had significantly lower CVD event rates compared to current smokers (hazard ratio (95% confidence interval): 0.70 (0.51, 0.95), p=0.02 and 0.48, (0.34, 0.69), p<0.001, respectively) (figure 2). The CVD event rates for former and never smokers were comparably.

Conclusion: We show for the first time that smoking cessation in RA patients was associated with lower disease activity, improved lipid profiles and was a predictor of reduced rates of CVD events.

Disclosure of Interests: None declared

Figure 1. Disease activity across smoking status

Figure 2. Risk of future CVD event across smoking status in RA patients

COX proportional hazards regression model adjusted for age, sex, statin and antithrombotic use. HR; hazard ratio, 95% CI: 95% confidence interval.

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**SAT0110**

HIGH SERUM LONG-CHAIN OMEGA-3 FATTY ACIDS ARE ASSOCIATED WITH 6-MONTH LOWER DISEASE ACTIVITY IN EARLY RA: RESULTS FROM THE ESPOIR COHORT

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**Background:** Dietary long-chain polyunsaturated fatty acids (PUFAs) of the n3 and n6 families are involved in immune homeostasis and can contribute to modulate inflammatory processes. Dietary intake of n3PUFA (by either supplementation or fish consumption) has been inversely associated with RA incidence in different populations. Some evidence suggests that, in subject at high risk of developing rheumatoid arthritis (RA), high erythrocyte membrane content in long-chain n3PUFA is associated with lower ACPA prevalence and progression to RA. While long-chain n6PUFA are considered mainly proinflammatory, some, like gamma-linolic acid (GLA), are endowed with anti-inflammatory activity, and the erythrocyte content in n6 linoleic acid was inversely associated with the development of RA in a nested-case control study. No study hitherto evaluated the longitudinal association between individual PUFA profile and disease activity in early RA.

**Objectives:** To characterize serum profiles of PUFA and to determine their association with baseline variables and with 6-month disease activity in a cohort of patients with early RA.

**Methods:** Serum PUFAs were quantified by gas chromatography-mass spectrometry (GCMS) in 594 patients with early RA at the time of recruitment in the French Etude et Suivi des POlyarthrites Indifférenciées Récentes (ESPOIR) cohort. Principal component analysis on 19 serum fatty acids with 14 to 22 carbon atoms allowed to determine 3 orthogonal patterns of baseline serum PUFA. Pattern 1 included high proportions of short-chain fatty acids, pattern 2 was high in n3 long-chain PUFA (EPA et DHA), pattern 3 was rich in n6 long-chain fatty acids (among which, GLA had the highest concentration). Patients were stratified in tertiles according to how much they fitted into each pattern, with tertile 1 meaning lowest and tertile 3 highest fitting into the pattern. The association of PUFA patterns with baseline variables was tested in univariate analysis. The association with 6-month disease activity (with high disease activity defined as DAS28≥5.1) was tested in multivariable analysis after adjustment on baseline CRP, corticosteroid and/or NSAIDs use, socioecon-omic status, ACPA and RF positivity, traditional and biologic DMARDS treatment between 0 and 6 months after inclusion.

**Results:** In baseline univariate analysis, pattern 1 was associated with high BMI, active smoking and with non-Caucasian origin. Profile 2 was associated with higher socioeconomic status and inversely associated with DAS28 and CRP. Profile 3 was associated with ACPA positivity and higher baseline CRP. In multivariable analysis, fitting into pattern 2 and 3 was associated with lower odds of having active disease after 6 months (OR for tertile 3 vs. tertile 1: 0.49 [95% CI 0.25 to 0.97, p=0.05] for pattern 2 and 0.51 [0.28 to 0.95] for pattern 3, respectively).

**Conclusion:** In a cohort of early RA patients, we could identify a high serum long-chain n3PUFA profile associated with low disease activity between 0 and 6 months of follow-up in the cohort. This is consistent with a presumed immunomodulatory action of n3PUFA. Despite the base- line association with disease severity features, like ACPA positivity and high CRP, a high serum long-chain n6PUFA profile is also associated with 6-month lower disease activity, possibly due to the presence of high concentrations of GLA in this profile.

**SAT0111**

RED CELL DISTRIBUTION WIDTH IS A MARKER OF EARLY RESPONSE TO METHOTREXATE IN RHEUMATOID ARTHRITIS

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**Background:** Red blood cell distribution width (RDW) has recently emerged as a possible surrogate biomarker of inflammation. Its potential role as prognostic biomarker has not been evaluated yet in Rheumatoid Arthritis (RA).

**Objectives:** The following study aims to evaluate the potential prognostic role of RDW in the prediction of early response to methotrexate (MTX).

**Methods:** We performed a retrospective analysis of clinical records of patients affected by RA, according to ACR/Eular classification Criteria. The baseline RDW was recorded and correlated with disease activity scores and inflammatory markers. The response to treatment was evaluated at the 3-months follow-up visit according to Eular response criteria.

**Results:** We selected 88 patients (58 females, 65.9%), with a median age of 62 [52-69] years. 61 patients were positive for Rheumatoid Factor (RF) and/or anticitrullinated antibodies – anti-CCP (69.3%). The median DAS28 for Erythrocyte sedimentation rate (DAS28ESR) at the diagnosis was 4.16 [3.33-5.00] while the median RDW was 14.0 [13.1-14.9]%. The baseline RDW was directly associated to CRP (r=0.250; p=0.02), but not with ESR (p=0.02) or DAS28ESR (p=0.40). All the patients received methotrexate (MTX) at a median dose of 10 [5-10] mg/week, 79 (89.8%) also received prednisone (median dose 5 [5-10] mg/day) and 20 hydroxychloroquine in addition to MTX. A significant trend towards a larger RDW was reported from patients with a good Eular response at three months (13.5 [13.0-14.4]%) to those with a moderate response (14.0 [13.2-14.7]%) and finally to those with a poor response (14.6 [13.6-16.0%]; p=0.004). At logistic regression, RDW (p=0.02), but not CRP or ESR (p=0.70 and p=0.37 respectively), was a predictor of a good Eular response. Moreover, in a further logistic regression model, baseline RDW (p=0.03) and baseline DAS28ESR (p=0.0009) were the only predictors of a good Eular response at three months, while age, gender, MTX and prednisone dosage and seropositivity did not fit the model.

After the treatment RDW significantly increases (14.7 [14.0-15.7%]) and the variation of RDW from baseline is inversely related to the variation of DAS28ESR (r=0.263; p=0.02). The increase of RDW is significantly higher in patients with a good Eular response, with a trend towards a smaller increase in case of moderate and poor response (0.95 [0.35-1.35%] vs. 0.65 [0.1-1.9%] vs. 0.2 [0.62-0.77%]; p=0.015).
Conclusion: RDW is a promising predictor of early response to MTX in RA; in this context, it performs better than classical inflammatory markers. Moreover, RDW significantly increases after MTX initiation, proportionately to response to treatment, suggesting a potential role for RDW as a marker of MTX effectiveness.

Disclosure of Interests: None declared


SAT0112

NO DIFFERENCE IN TREATMENT CONTINUATION OF DIFFERENT BIOLOGICS IN ELDERLY PATIENTS > 70 YEARS COMPARED TO YOUNGER PATIENTS ≤ 65 YEARS

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Background: Due to demographic changes an increasing number of persons reach an age above 70 years. Therefore, the adequate therapy of elderly patients with rheumatoid arthritis (RA) is an increasingly important topic.

Objectives: To compare treatment continuation of several biologic DMARDs in patients ≤ 65 with elderly patients > 70 years, stratified by onset of disease (young onset (<65 years) and late onset (>65 years)) and by seropositivity.

Methods: The German register RABBIT is a prospective longitudinally followed cohort of RA patients enrolled with a new start of a DMARD after at least one csDMARD failure. For the current analysis patients who were enrolled with a biologic DMARD between 01/2007 and 04/2018 were included. Kaplan Meier methods were applied to analyse treatment continuation.

Results: Among the 9,819 RA patients included in the analysis, 7,972 were ≤ 65 years old and 1,847 were older than 70 years (among them 180 patients above 80 years). Among the patients ≤ 65 years, 28% received a csDMARD and 72% a bDMARD, while among the patients above 70 years, 35% received a csDMARD and 65% a biological. Elderly patients with a young disease onset (YORA) were more frequently women and more frequently seropositive, on average had a higher number of prior treatment failures, a worse physical function and were more likely to have joint erosions than elderly patients with late onset (LORA) (Table 1). On all bDMARD treatments investigated, elderly RA patients showed the same treatment continuation as seen in younger patients. While neither the age of the patients nor the age at disease onset changed the continuation of biologics, patients being seronegative had a significantly lower continuation with rituximab and abatacept treatment, irrespective of age (Figure 1).

Conclusion: These results suggest that bDMARD treatment may be used for elderly patients with the same effectiveness as in younger patients.

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SAT0113

LIMITING FACTORS OF REACHING ACR/EULAR BOOLEAN REMISSION IN EARLY RA PATIENTS TREATED ACCORDING TO CURRENT GUIDELINES

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Background: Abrogation of inflammation is important to prevent irreversible joint damage and maximize health-related quality of life in early RA patients. The ACR/EULAR Boolean remission criteria have the most stringent remission definition. (1) It has been reported that patient global assessment (PGA) is the variable most commonly scored above the cut-off in patients who almost fulfill the ACR/EULAR Boolean remission criteria. (2)

Objectives: To assess which components of the ACR/EULAR Boolean criteria that most often limit attainment of remission in modernly treated
early RA, and quantify the extent of subclinical inflammation in these patients.

Methods: DMARD-naive early RA patients included in the treat-to-target ARCTIC trial were followed by a strict tight control regime aiming for DAS remission and no swollen joints, with an additional target of ultrasound remission in half of the patients.(3) Examination of all patients included 44SJJC, Ritchie articular index (RAI), laboratory tests, patient reported outcomes included physical function (PROMIS), ultrasound (US) of 32 joints and magnetic resonance imaging (MRI) of the dominant hand and wrist (scored according to RAMRIS). Patients with complete clinical data at the 2-year follow-up visit were included in the current analyses. We assessed the proportion of patients fulfilling ACR/EULAR Boolean remission (based on 44 joints) and the proportion of patients fulfilling three out of four remission criteria, and in such cases, which were the limiting factors. We compared physical function and imaging inflammation (assessed by US power Doppler score, US grey scale score, MRI synovitis and bone marrow edema) in patients reaching complete ACR/ EULAR Boolean remission to patients not reaching ACR/EULAR Boolean remission due to the most often limiting factors. We compared physical function and imaging inflammation (assessed by US power Doppler score, US grey scale score, MRI synovitis and bone marrow edema) in patients reaching complete ACR/EULAR Boolean remission to patients not reaching ACR/EULAR Boolean remission due to the most often limiting factors. Chi2 test and Wilcoxon rank sum test were used for the comparisons.

Results: Of the 203 patients included, 62% were females, mean (SD) age was 52 (13) years, and 81% were ACPA positive. ACR/EULAR Boolean remission was achieved by 112 of 203 patients after 24 months (55%), while 49 (24%) fulfilled three of the four remission criteria. Among these 49 patients, the major limiting factor for not reaching remission was PGA (n=29, 59%), with tender joints as the second most common limiting factor (n=11, 22%) (Figure). In patients not achieving remission due to PGA, the median [IQR] PGA value was 3.1 [2, 4.4]. Subclinical inflammation measured by ultrasound and MRI was not significantly different in patients from achieving ACR/EULAR Boolean remission compared to patients not achieving remission due to PGA and/or tender joints (Table), but the latter reported more subjective symptoms such as fatigue and impaired physical function.

Conclusion: PGA and tender joints are the variables most often limiting patients from achieving ACR/EULAR Boolean remission, also in a treat-to-target setting with high remission rates. The level of subclinical inflammation is not elevated in these patients compared to patients in ACR/ EULAR Boolean remission. Further research is still needed to assess which clinical remission criterion is best suited to guide treatment.

References:
FLARING OF RHEUMATOID ARTHRITIS DUE TO TAPERING OF DMARDS: HOW DOES IT AFFECT PATIENTS' WELL-BEING? A STUDY ON PATIENT REPORTED OUTCOMES

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Background: Previous studies have shown that it is possible to taper DMARDs in RA patients with an inactive disease, but this is accompanied with a high chance of disease flares. Current recommendations advise to taper DMARDs from a clinical viewpoint. However, data on the feasibility of tapering DMARDs from a patient’s perspective are sparse.

Objectives: To determine the impact of flare after DMARD-tapering on patients quantifying the changes in patient relevant domains e.g. functional ability, fatigue, quality of life, and worker productivity, and to explore the duration of the effect.

Methods: Data were used from all 113 patients that flared after tapering DMARDs in the TARA study, a multicenter randomised controlled trial in which patients in sustained remission (DAS28<2.6 & SJC<10) tapered either their csDMARDs or TNF-inhibitor per protocol. For the current analysis, we compared the following secondary outcomes before and after flare over time: DAS44, functional ability (HAQ-DI), fatigue (BRAF-MDQ), quality of life (EQ-SD and SF36), anxiety and depression (HADS), morning stiffness, VAS general health, and worker productivity. Follow-up started three months before flare, at the moment of flare, and every 3 months thereafter. These were compared to baseline values, calculated by taking the average of 12, 9 and 6 months before flare. We used Linear Mixed Models (LMMs) with a random intercept and an autoregressive covariance matrix to determine an overall effect of flare. We adjusted for multiple testing with a Bonferroni correction. For determining the duration of the effect of a flare, we tested if the separate time points differed from the baseline with the same model. For the worker productivity we used descriptive statistics.

Results: In total, 113 patients experienced a flare. Patients who had a flare had a less stable course of the outcomes over time, compared with patients without flare (Figure 1A-G). When comparing all time points to baseline, statistical significant differences were found for DAS44 (p<0.0001), VAS general health (p<0.0001), morning stiffness (p<0.0001), HAQ-DI (p<0.0002), EQ-SD (p<0.0001), BRAF-MDQ (p<0.04), and the SF36 physical component scale (p<0.0004) (Figure 1A-H). The duration of these effects was more than 12 months for the DAS44, morning stiffness, and VAS general health. For the HAQ-DI, EQ5D, BRAF-MDQ, and SF36 PCS the duration of the effect of a flare was 6 months (Figure 1H). The effect sizes, expressed as differences with baseline, are indicated in Figure 1H and were rather small for most outcomes. The number of patients with paid work and unemployment were not affected by flare. The amount of sick leave increased from 1 to 1.3 days per month after flare had a less stable course of the outcomes over time, compared with patients in sustained remission. The amount of sick leave increased from 1 to 1.3 days per month after flare. These were compared to baseline values, calculated by taking the average of 12, 9 and 6 months before flare. We used Linear Mixed Models (LMMs) with a random intercept and an autoregressive covariance matrix to determine an overall effect of flare. We adjusted for multiple testing with a Bonferroni correction. For determining the duration of the effect of a flare, we tested if the separate time points differed from the baseline with the same model. For the worker productivity we used descriptive statistics.

Conclusion: Having a flare does affect patient reported outcomes. It affects DAS44, VAS general health, morning stiffness, functional ability, quality of life, and fatigue. This effect lasted for more than 6 months. Although we only found minor differences with baseline on group level, on the individual patient level this can still be of great importance.

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SAT0116 DYNAMIC PREDICTION OF FLARES IN RHEUMATOID ARTHRITIS USING JOINT MODELLING AND MACHINE LEARNING: SIMULATION OF CLINICAL IMPACT WHEN USED AS DECISION AID IN A DISEASE ACTIVITY GUIDED DOSE REDUCTION STRATEGY

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Background: Most rheumatoid arthritis (RA) patients on a biological DMARD achieve and maintain remission or low disease activity. Then, tapering the drug is safe and cost-effective, but with increased risk of short-lived flares and joint damage progression. We developed so-called dynamic prediction models, using joint-modelling (JM) and machine learning (ML) respectively to predict an individual patient’s risk of flaring. These models can make short-term (e.g. 3 month) predictions repeatedly at every clinic visit, based on routine care data, i.e. the longitudinal course of the patients’ disease activity and medication, demographic and disease characteristics.

Objectives: To externally validate the JM and ML model and evaluate the clinical impact on flare occurrence and bDMARD use, when using predictions as decision aid for tapering bDMARDs in a protocolised disease activity guided tapering strategy.

Methods: For external validation, an RCT comparing protocolised dose reduction (stepwise increase injection interval, until flare or discontinuation, n=121) with usual care (n=59) was used.1 Both models were applied to the trial data and AUC-ROC and calibration were assessed. To simulate our dose-reduction strategy, first, we defined optimal cut-offs for predictions using Youden’s index as well as a cut-off at higher/lower predicted risks. Thereafter we applied them to the dose reduction arm of the trial. Assumptions were that 1) no further tapering was performed when the cut-off was reached without any flares occurring over time in the simulation and 2) when in the trial a flare occurred for which the bDMARD dose was increased to a value higher than when tapering was stopped in simulation, this flare occurred and the higher dose was used in simulation as well.

Results: AUC-ROC’s in external validation were, as expected, somewhat lower than in the development cohort: 0.76 (95%CI 0.61—0.88) and 0.67 (0.52—0.77) versus 0.78 (0.70—0.85) for JMML and ML respectively, and still satisfactory. Calibration was better for ML, resulting in different cut-offs for the models. Results show that about 40% and 50% of flares can be prevented respectively and that the majority (66% and 76%) of the dose reduction can be maintained using the optimal cut-offs in our prediction aided dose reduction strategy over 18 months. Table 1 shows the proportion of full dose used, mean number of flares per patient, and percentage of patients experiencing a flare for several cut-offs as well as in the disease activity guided dose reduction strategy (in bold). As context values are also shown for usual care (trial control arm; in italic).

Conclusion: Both models proved to be externally valid. Using them to aid decisions on biological dose reduction has the potential to reduce the occurrence of flares significantly while largely retaining the reduction in dose as obtained by a disease activity guided dose reduction strategy.

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Background: Currently, with increased awareness of early diagnosis and intervention and the identified association of early remission with a better clinical outcome in patients with rheumatoid arthritis (RA), shorter time to remission appears to be a more attractive goal. There are several studies reported the prevalence of early remission, no study so far has demonstrated the issue in Chinese population. Moreover, further investigative studies need to be performed due to limited and conflicting predictors of early remission in previous studies.

Objectives: To assess rates of early remission and investigate the concordance across different remission definitions, and to identify predictors of early remission in Chinese patients with RA.

Methods: For this study, clinical records were retrospectively reviewed for RA patients at rheumatologic clinic in Peking University First Hospital from 2009 to 2018. Disease activity and remission were determined according to DAS28-ESR, CDAI, SDAI, and Boolean criteria. Early remission was defined as time to remission < 6 months. A secondary definition evaluated early remission as ≤ 3 months. Logistic-regression analyses were performed to identify determinants of early remission.

Results: 869 consecutive patients contributing 8,640 clinic visits were studied. Early remission rates were respectively 42.0% (DAS28-ESR), 25.0% (CDAI), 29.4% (SDAI), and 26.1% (Boolean). Notably, patients achieving remission within 6 months more frequently attained sustained remission by contrast to those not achieving early remission (68.7±7.5% vs. 31.2±33.1%, P<0.0001). Further logistic-regression analyses revealed male (OR=1.421-1.74, p<0.05), early RA (OR=1.64-2.22, p<0.05), as well as initial hydroxychloroquine treatment (OR=1.41-1.81, p<0.05) were independently associated higher probability of early remission, as demonstrated by nearly all definitions, while a higher baseline disease activity (DAS28-ESR, CDAI, and SDAI) lowered the possibility of early remission in corresponding remission indices. However, the significant associations of treatment-naive, serological features with early remission were not confirmed.

Conclusion: Early remission was strongly associated with sustained remission, however infrequently achievable in real-life practice. Male, early RA, a low baseline disease activity, and initial hydroxychloroquine treatment were stable independent predictors of early remission.
Background: Combination therapy with DMARDs for treating RA is standard of care. However, certain rates of adverse events (AEs) are unavoidable. The stigmas are how to predict the risk and how to define drug withdrawal sequence based on data mining from the SSDM.

Methods: SSDM is an interactive mobile disease management tool, including two application systems (Apps) for both the doctors and the patients. The patients can input medical records (including medication and laboratory test results) and perform self-evaluation (DAS28, HAQ) via App. The data synchronizes to mobiles of authorized rheumatologists through cloud and advises could be delivered. In previous studies, we demonstrated that patients could master SSDM after training. In order to develop a prediction model and the master algorithm, abnormal white blood cell counts (WBC) and alanine aminotransferase (ALT) elevation were targeted. Data was collected, extracted, validated, and Bayesian networking, data mining, modeling were performed. WBC under 4k/ml is defined as leukopenia (LP), over 10k/ml as infection predisposing (IP), and ALT > 40 U/L as ALT elevation.

Figure 1: Bayesian network and data processing: Patients master (black in boxes) and the rate of LP, IP and ALT elevation in 31 regiments.

Figure 2: Bayesian network and data processing: Patients master (black in boxes) and the rate of LP, IP and ALT elevation in 31 regiments.

Disclosure of Interests: None declared

Rheumatoid arthritis – biological DMARDs

COMPARATIVE EFFECTIVENESS OF TOFACITINIB AND TNF INHIBITORS SINCE 2014, IMPACT OF COMBINATION WITH METHOTREXATE

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Background: Tofacitinib (TOFA), a targeted synthetic DMARD, has been approved for the treatment of rheumatoid arthritis (RA) in Canada since April 2014. This oral agent preferentially inhibits signalling by cytokine receptors associated with JAK1 and JAK3 subunits. It is also indicated for the treatment of PsA and UC since October 2018. Clinical experience with this molecule has been increasing, and questions relating to its efficacy and long-term safety are of interest. Data collection through RHumatologie de Québec (CORQ), a Quebec based clinical database and registry, allows comparison of newer options with more traditional agents such as tumor necrosis factor inhibitors (TNFi).

Objectives: The current analysis compares TOFA to TNFi used with and without methotrexate (MTX) among patients with RA.

Methods: Data collected since January 1, 2014 (when TOFA became available in Canada) at the Institut de Recherche en Rhumatologie de Montréal (IRRIM) and the Centre de l’Ostéoporose et de Rhumatologie de Québec (CORQ) was extracted from Rhumatologie de Québec (CORQ) on January 7, 2019. Patients initiated on TOFA or a TNFi (adalimumab, certolizumab, etanercept, golimumab, infliximab) without or with MTX were selected. Data include baseline characteristics (socio-demographic variables, concomitant and past medication, comorbidities and the Charlson comorbidity index (CCI)), variables measured over time (lab results, patient and physician-reported outcomes, and disease activity measures) and persistence data (treatment duration, reason for cessation). The groups were compared to identify potential confounder, and persistence data were analyzed using Kaplan-Meier and Cox methods.

Results: A total of 480 patients were prescribed TOFA (n=162) or a TNFi (n=318) since January 1, 2014. Of those, 57% (n=92) and 70% (n=224) were treated with MTX in the TOFA and TNFi group respectively and mean disease duration was 12.1 (standard deviation=11.0) and 7.2 (8.1) years. TOFA and TNFi represent the first treatment following csDMARD-IR for 33% (TOFA) and 62% (TNFi). In the TOFA group, 84% were women, 15% were smokers and the mean age at treatment initiation was 57.7 (11.5) years. In the TNFi group, 77% were women, 12% were smokers and the mean age at treatment initiation was 54.2 (13.7) years. At treatment initiation, patient global, pain and fatigue assessments, made on a visual analogue scale ranging from 1 to 10, were 5.6 (2.5), 5.9 (2.7) and 5.7 (2.9) in the TOFA group and 5.0 (2.9), 5.5 (3.0) and 5.1 (3.1) in the TNFi group. Baseline disease activity was assessed as moderate or high/severe in 85.9% and 76.7% of TOFA (7 patients (DAS28/4-ESR criteria). Among the 56 (35%) TOFA and 146 (46%) TNFi patients ceasing therapy, reasons for cessation were “inefficacy” (TOFA: 64% vs TNFi: 56%) and “adverse events” (TOFA: 16% vs TNFi: 11%). Patients remaining on TOFA and TNFi therapy at last follow-up had an average treatment duration of 1.7 (1.1) and 2.7 (1.5) years and no difference in retention was observed between TOFA and TNFi treated patients (log-rank p=0.41). Patients treated with a TNFi in combination with MTX had better treatment retention than those treated without MTX (log-rank p=0.04) while patients treated with TOFA+MTX had similar retention (log-rank p=0.96). These results remain unchanged when adjusted for gender, age at treatment initiation, disease duration, and comorbidities.

Conclusion: In our real-world data registry, treatment with TNFi and TOFA yielded similar retention over time. Subjects treated with TNFi and MTX remained on treatment longer than those treated without MTX while subjects treated with tofacitinib with or without MTX had similar retention.

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adalimumab were more pronounced among patients with higher baseline serum IL-6 levels.

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SAT0122 COMPARISON OF REAL-WORLD PERSISTENCE OF SUBCUTANEOUSLY ADMINISTERED BIOMATIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUG (DMARD) THERAPY AMONG PATIENTS WITH RHEUMATOID ARTHRITIS (RA) SWITCHING FROM ANOTHER BIOLOGIC


Background: The EULAR and ACR clinical guidelines recommend switching to a different disease-modifying antirheumatic drug (DMARD) when biologic treatment failed. Experience treatment failure or toxicity. Lack of efficacy and adverse events are among the most commonly reported reasons for switching biologic therapies. Limited information is available regarding biologic drug persistence among subcutaneously administered (SC) biologic agents in the real-world setting, as well as for comparative information on biologic persistence for SC biologics among patients with rheumatoid arthritis (RA) who are naive to biologic treatment.

Objectives: To compare persistence of SC biologic DMARDs (i.e., bDMARDs) in patients with RA as subsequent-line therapy following a failure of first line bDMARDs.

Methods: US administrative claims data were used to create a longitudinal cohort of adult patients with RA initiating SC biologic between 1/1/2012 and 6/30/2017 (initiation date = index). Patients were required to have failed 1st bDMARD to enter study (but could later switch therapy) and to have 6 and at least 3 months of continuous enrollment pre- and post-index (date of prescription for bDMARD). Those with other autoimmune conditions were excluded from the study. Outcomes were biologic persistence, defined as number of days between initiation date and last supplied day of last fill. Parametric survival models with exponential distribution with robust variance estimator were used to compare outcomes for tocilizumab versus other biologics, adjusting for differences in baseline characteristics, accounting for correlation among different bDMARD episodes.

Results: There were 10,301 patients with 12,704 bDMARD episodes: abatacept (n=2,998), adalimumab (n=3,599), certolizumab (n=982), etanercept (n=2,760), golimumab (n=745), or tocilizumab (n=1,630). Mean age was 51.0-53.3. Mean [SD] Elixhauser comorbidity scores were significantly higher (p<0.001) for tocilizumab (2.8 [2.3]) compared to abatacept (2.5 [2.2]), adalimumab (2.5 [2.1]), certolizumab (2.4 [2.0]), etanercept (2.4 [2.0]), or golimumab (2.4 [2.2]). Adjusted median days (95% CI) of persistence were: abatacept 320 (305, 335); adalimumab 280 (268, 293); certolizumab 282 (261, 284); etanercept 289 (274, 304); golimumab 304 (274, 333); and tocilizumab 333 (311, 356). Tocilizumab had significantly higher persistence compared to adalimumab, certolizumab, and etanercept (Figure 1). Of patients who were observed for 12 months, 45% of patients initiated tocilizumab bi-weekly and 55% initiated weekly. Of the 347 patients initiating bi-weekly tocilizumab, 33% switched to weekly over 12-month follow up; the mean time to switch was 177 days. After 12 months of follow-up, approximately 68% of patients finished on weekly dosing and 32% on biweekly dosing.

Conclusion: Among patients with RA who previously used ≥1 other biologic, tocilizumab-treated patients had similar or statistically significantly better biologic persistence compared with other biologics.

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SAT0123 RISK FOR TUBERCULOSIS DURING TREATMENT WITH BIOLOGIC THERAPY: IS IT TIME FOR REVIEWING SCREENING PROTOCOL? – RESULTS FROM BRAZILIAN REGISTRY OF BIOLOGICAL THERAPIES IN RHEUMATIC DISEASES (BIOBADABRASIL)


Background: As Brazil is accountable for 33% of the tuberculosis (TB) burden in Americas, with an annual incidence of 3.35/100,000 in 2017[1], the occurrence of tuberculosis infection in patients with rheumatic diseases in use of biological therapy is a recurrent concern.

Objectives: To assess incident TB among patients with rheumatic disease in use of biological therapy in a country with high incidence of TB.

Methods: BiobadaBrasil is a multicentric prospective cohort study involving patients with rheumatic diseases who started the first biologic or a synthetic disease modifying anti-rheumatic drug (DMARD)[6]. This analysis includes patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS) recruited from Jan 2009 to Aug 2018 and followed-up for one or multiple courses of treatment until censoring or incident TB. The primary outcome was the incidence of tuberculosis (in any organ site). The history of exposure to tuberculosis, chest Rx, screening and treatment for latent tuberculosis infection (LBTI), and use of prophylactic isoniazid were evaluated before each course of treatment. Multivariate Cox proportional hazards models (with DMARDs included as time-varying covariates) were used to estimate hazard ratios (HR) and 95% confidence intervals (CI); analyses were performed with the Survival package of R.

Results: Sample: 2858 patients (female =70.2%; RA = 72%, AS=20%, and PsA = 8%). A total of 31 (1.1%) patients developed tuberculosis during treatment. One patient on abatacept and one on tocilizumab developed TB while all the others were on TNF-inhibitors[29]. The median (interquartile range) exposure to the current DMARD course was 11.1 (5.9-20) months. TB patients did not significantly differ from others regarding disease duration, sex or age. Almost half (n=14,45%) of TB patients did not present evidence of previous exposure or any screening positive test for TB; 9 (29%) TB patients had received adequate LTBI treatment (isoniazid) recently or in the past. Furthermore, 8(26%) had incomplete/ inconsistent screening. The overall incidence of TB was 1.9/1000 patients/year, and was not significantly different among the diseases (1.63 for RA, 2.06, for AS, and 3.79/1000/year for PsA). In univariate analysis, exposure to anti-TNF monoclonal antibodies (HR 3.1, 95%CI 1.18-8.15, p=0.02) and presence of any marker of previous contact with TB (positive history of TB, known contact with TB, positive TST, or abnormal chest X-ray: HR 4.2 (2.1-8.5, p<0.001) were positively associated with the risk of TB. Including simultaneously these variables in the Cox model, they were independent risk factor for TB (p<0.05).

Conclusion: Monoclonal anti-TNF antibodies and previous exposure/diagnosis of TB are independent risk factors for developing TB in Brazil. TB
cases occurred both early and lately during treatment courses, suggesting LTBI screening failures, treatment non-adherence or re-exposure. Current application and content of the protocol for screening and treatment of LTBI needs to be reviewed.

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PATIENTS. EFFECTS OF BIOLOGICAL DRUGS.

Objectives: 1- To characterize the serum molecular profile associated to the increased cardiovascular risk in Rheumatoid Arthritis (RA) patients. 2- To evaluate the in vivo and in vitro effects of biological drugs on the reestablishment of this altered molecular profile.

Methods: Serum samples of 280 RA patients and 100 healthy donors (HD) were studied. miRNomes were identified using next-generation sequencing miRNA assay (HTG EdgeSeq technology). The inflammatory profile, Nefosis-derived products, and circulating biomolecules related to oxidative stress were quantified using commercial kits. The Cardiovascular Risk SCORE for RA patients was calculated following EULAR recommendations. Current circulating miRNAs were evaluated as early atherosclerosis marker. The in vivo effects of biologic drugs such as Infliximab (IFX), Tocilizumab (TCZ) and Rituximab (RTX) were evaluated before and after 6 months of therapy in 45, 20 and 25 RA patients, respectively. Serum from RA patients with high and low CV risk scores - either before and after IFX, TCZ and RTX therapies-, were further added to HUVECs, monocytes, and neutrophils purified from HD, and activity profiles were evaluated.

Results: The mRNA whole transcriptome assay identified 104 circulating miRNAs altered in RA patients. Functional classification (IPA) established those miRNAs with altered expression, reducing the CV risk in RA patients. Mechanistic in vitro studies showed that levels of a number of those altered biomolecules and circulating microRNAs were predictors of a high Cardiovascular Risk SCORE and the presence of a pathologic CIMT in RA patients.

The in vivo treatments with IFX, TCZ and RTX for six months reduced disease activity and induced the re-establishment of normal levels in those altered biomolecules in RA patients. Mechanistic in vitro studies showed increased pro-inflammatory profiles of leukocytes subsets and HUVECs after treatment with serum from high CV risk score-RA patients. These profiles were reversed by incubation with serum from those patients after biologic drugs treatment.

Conclusion: 1. Specific mediators of inflammation, oxidative damage and Nefosis, along with the microRNAs modulating their expression, coordinately contribute to the higher CV risk score present in RA patients. 2. Biologic drugs such as IFX, TCZ and RTX, restore the normal levels of these altered biomolecules, reducing the CV risk in RA patients.

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SA10125

LONG-TERM SAFETY WITH SARILUMAB PLUS CONVENTIONAL SYNTHETIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS AND SARILUMAB MONOTHERAPY IN RHEUMATOID ARTHRITIS: AN INTEGRATED ANALYSIS WITH 9,000 PATIENT-YEARS OF FOLLOW-UP

Roy Fleischmann1, Yong Lin2, Gregory St John3, des loneliness and her independence, and in combination with csDMARDs in Phase 3 trials.

Objectives: We assessed long-term safety from the sarilumab clinical development program in adult patients with RA who received subcutaneous (SC) sarilumab in eight clinical trials and their open-label extensions: MOBILITY (NCT01061736), TARGET (NCT01197597), ASCERTAIN (NCT01768752), EASY (NCT02057250), COMPARE (NCT01764997), ACT11575 (NCT01217814), COMPARE (NCT02325290), ONE (NCT02121210), and the open-label extension EXTEND (NCT01146652).

Methods: Data (cut-off Jan 15, 2018) were pooled from patients on sarilumab+csDMARD (N=2867) or sarilumab monotherapy (N=471). Patients had received sarilumab 200 mg or 150 mg q2w SC, except for 151 patients from MOBILITY Part A who received 100 mg qw, 150 mg qw, or 100 mg q2w. Treatment-emergent (TE) adverse events (AEs), AEs of special interest (AESIs), and discontinuations were assessed.
Results: Demographics were similar between combination and monotherapy pools (mean age 52 years; 81–83% female), and 38.7% and 8.5% of patients had received prior bDMARDs. Cumulative drug exposure was 7,985.5 and 796.7 patient-years (PY), with maximum duration 7.3 and 3.5 years. Exposure-adjusted rates of TEAEs, serious AEAs, and TEAEs leading to discontinuations were similar (Table). Infections were the most common AEIs. Rates of serious infection were 3.7 and 1.0/100 PY for combination and monotherapy, respectively, and were not associated with decreased absolute neutrophil counts (ANCs). Incidences of ALT > 3× upper limit of normal and ANC <1.0 giga/L were 10.3% and 12.7% for combination, respectively, and 5.5% and 14.9% for monotherapy. Rates of confirmed GI perforation for combination and monotherapy were 0.1 and 0/100 PY. Analyzing data by 6-month intervals showed no increase in rate over time for serious infections, malignancy, major adverse cardiac events, or ANC <1.0 giga/L.

Conclusion: The long-term safety profile of sarilumab, either as monotherapy (observed for >3.5 years) or as csDMARD (observed for >7 years), remains stable and consistent with the anticipated profile of an IL-6R blocker.

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SAT0126

A PHASE 2 STUDY OF E6011, AN ANTI-FRACTALKINE MONOCLONAL ANTIBODY, IN PATIENTS WITH RHEUMATOID ARTHRITIS INADEQUATELY RESPONDING TO BIOLOGICS

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Background: Fractalkine (CX3CL1, designated as FKN hereafter) is the sole member of the CX3C-chemokine which leads to both actions, chemotaxis and cell adhesion for leukocytes expressing the cognate receptor, CX3CR1, during their migration. We have conducted clinical trials of E6011, a novel humanized anti-FKN monoclonal antibody, for patients with rheumatoid arthritis (RA) in Japan1. This is the first report of a Phase 2, multicenter, randomized, double-blind, placebo-controlled, parallel-group comparison study of E6011 in RA patients inadequately responding to biologics (NCT02960490).

Objectives: To evaluate efficacy and safety of E6011 compared with placebo.

Methods: During the 24-week double-blind period, patients with moderately to severely active RA of inadequate response to biologics were randomly assigned to E6011 400 mg or placebo groups at a 1:1 ratio. Patients who continued the study beyond Week 12 were further allocated to E6011 200 mg or 400 mg at a 1:1 ratio within the initially assigned group. Patients received either E6011 400 mg or placebo at Weeks 0, 1, 2, and every 2 weeks subsequently until Week 10 and then E6011 200 mg or 400 mg every 2 weeks between Weeks 12 and 22 in a double- blind manner. This abstract reports the results from the first 12-week placebo controlled period.

Results: A total of 64 subjects (33 in the placebo group and 31 in the E6011 400 mg group) received study drug. Of the 64 subjects, 55 completed and 9 discontinued study treatment prematurely during the 12-week placebo controlled double-blind period. The ACR20 response rate at Week 12 (non-responder imputation), the primary endpoint, was 27.3% (9/ 33 subjects) in the placebo group and 22.6% (7/31 subjects) in the E6011 group. ACR50 and ACR70 response rate at Week 12 were 3.0%, 0% in the placebo group and 9.7%, 3.2% in the E6011 group, respectively. Numerically greater improvement from baseline was found for some parameters of the ACR components in the E6011 group, however, no statistically significant differences were found in any of the ACR compo- nents between the placebo and E6011 groups. From the exploratory PK exposure analysis, there was a tendency that the effect of E6011 became clearer in the subjects who achieved higher serum trough E6011 concentration. Adverse events that occurred in at least 2 subjects in the E6011 group were stomatitis, injection site erythema, nasopharyngitis, and blood creatine phosphokinase increased. As a result, E6011 was well tolerated with no notable safety concerns at doses of 400 mg when administered subcutaneously for 12 weeks.

Conclusion: E6011 400 mg was well tolerated but did not show clear efficacy at Week 12 compared with placebo in RA patients with inadequately responding to biologics. Further investigation to seek an optimal clinical dose and evaluation period of E6011 are warranted.

REFERENCE


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LONG-TERM OUTCOME OF CHILDREN BORN TO MOTHERS WITH CHRONIC ARTHRITIS WHO WERE EXPOSED IN UTERO TO TNFi WITH THOSE OF UNEXPOSED CHILDREN BORN TO PATIENTS WITH THE SAME AGE AT CONCEPTION AND DISEASE.

Methods: An ad-hoc created questionnaire was used to collect data on birth and growth parameters, breastfeeding, weaning, developmental milestones, vaccinations and illnesses.

Results: 122 live births in 97 women with chronic arthritis (65 RA and 32 SpA) were observed: 59 pregnancies were exposed to TNfi at the time of conception and 63 pregnancies were TNFi-naive. In 57/59 (97%) pregnancies, TNFi was discontinued at positive pregnancy index. In 2/59 (3%) pregnancies TNFi was maintained throughout pregnancy due to active disease at conception. TNFi was restarted in 16/57 pregnancies (28%) (10 ETA, 5 CTZ, 1 ADA) during the 2nd-3rd trimester due to moderate/severe flare (median exposure 22 weeks). In second group, TNFi (1 ETA, 1 CTZ) was introduced in 2/63 (3%) pregnancies during the 2nd trimester due to a severe flare. In 16/63 (25%) pregnancies were managed with an increase of prednisone (max 10mg/day). To investigate the long-term follow-up of children exposed in utero to TNFi, 61 children exposed to TNFi at conception or during 2nd-3rd trimester (median age 29 months) and 61 unexposed children (median age 49 months) were compared. No significant differences in growth parameters and developmental milestones were observed. No excess nor particular pattern of congenital defects/malformations were observed. In both groups, vaccinations were performed according to the national schedule (no live vaccines in the first year of life) without relevant complications (Figure 1).

Conclusion: TNFi may be required in patients that experienced flare during pregnancy and they are effective in controlling maternal disease and ensures a good pregnancy outcome without complications for the health and growth of exposed children.


The disease of bDMARDs,1,2 However, there are limited data indicating which factors, if any, are prognostic of flares after tapering. Moreover, association between underlying inflammation and disease flare following tapering remains unclear. Objective: To investigate association between residual disease activity at double-blind (db) bi identified by MRI and occurrence of flares in SCA RA pts randomized to an adalimumab (ADA) dose tapering regimen controlled by ADA withdrawal (w/d).

Methods: Pts in SCR (DAS28[ESR] or CRP ) >2.6 for at least 6 mos and at screening (DAS28[ESR] <2.6) on ADA 40 mg eow were enrolled in this phase 4, randomized, db, parallel group study. Following 4-wksol open-label lead-in (OL-LI) during which SCR was confirmed, pts were randomized to tapering and w/d arms for 36 wks. Pts experiencing flare (defined as either DAS28[ESR] >2.6 and DAS28 [ESR] increase >0.6 from bl or DAS28[ESR] increase >1.2 from bl, irrespective of absolute DAS28[ESR]) received rescue OL ADA 40 mg eow for up to 16 wks. The primary endpoint was the association between bl hand and wrist synovitis and bone marrow edema (BME) RAMRIS scores and their composite with flare occurrence. Secondary endpoints were association between pt and disease characteristics and occurrence of flare, time to and occurrence/severity of flares, maintenance of remission, and time to and regain of clinical remission following flare. Logistic regression, descriptive statistics (counts and proportions with 95% CI) and Kaplan-Meier estimates are provided. Last observation carried forward was used for missing data. Treatment-emergent adverse events were monitored.

Results: Of 146 pts who entered the OL-LI period, 122 were in SCR at wks 0 and 4 and were randomized to taper (n=102) or w/d (n=20) arm. Pts were female (75%) with ~13 yrs of active disease, received ADA for >3 yrs (75% >2 yrs in SCR). Bl disease activity measures were: DAS28[ESR] >1.7; composite synovitis and BME RAMRIS score: 4.0, and >85% pts were in CDAI and/or SDAI remission. In the taper and w/d arms, 37% (36%) and 9% (45%) pts experienced flare, respectively. Time to flare was 18.0/13.3 wks (Q1 for taper/w/d withdrawal arm). At wks 12/24/36, flare rates were 13.1/24.7/34.9% in the taper arm and 10.0/35.0/40.0% in the w/d arm. Neither of the bl RAMRIS scores nor their composite was associated with flare occurrence in the taper arm (Table). Only bl HAO-DI was associated with flare occurrence. Through 16 wks of OL rescue with ADA 40 mg eow, 38% and 50% of pts in the taper and w/d arms, respectively, regained clinical remission; approximately 85% in both arms were in clinical remission by DAS28[ESR] <2.6 at week 40. No new serious risks or safety signals were identified.

Conclusion: A relatively low flare rate was observed among this established RA population in longstanding SCR who tapered or withdrew ADA. Baseline HAO-DI, but not MRI inflammation, was found to be associated with flare occurrence, which may be reflective of the very low bl MRI inflammation scores in this sustained remission cohort. A relatively low flare rate was observed among this established RA population in longstanding SCR who tapered or withdrew ADA. Baseline HAO-DI, but not MRI inflammation, was found to be associated with flare occurrence, which may be reflective of the very low bl MRI inflammation scores in this sustained remission cohort. A relatively low flare rate was observed among this established RA population in longstanding SCR who tapered or withdrew ADA. Baseline HAO-DI, but not MRI inflammation, was found to be associated with flare occurrence, which may be reflective of the very low bl MRI inflammation scores in this sustained remission cohort.
ANTI-CITRULLINATED PEPTIDE ANTI-BODIES TITERS DECREASE AFTER RITUXIMAB BUT NOT AFTER ABATACEPT OR TNF BLOCKERS TREATMENT: A REAL-LIFE ANALYSIS

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Background: There is an increasing body of evidence suggesting a direct pathophysiological role of ACPA in Rheumatoid Arthritis (RA). Therefore, on the top of clinical, biological and imaging remission, one target could be immunological remission, defined as the normalization of the ACPA titers after therapy. In this sense, data related to the capacity of different biologics to normalize ACPA are contradictory.

Objectives: To evaluate the changes in ACPA titers before and after treatment with different biologics.

Methods: RA patients treated with biologics were identified via the hospital’s pharmacy and/or the Electronic Medical Record of the patients; thereafter, for each patient, ACPA titers before/after treatment were retrieved from the department of biology. To be included, patients had to be diagnosed with RA, to have received a biologic (either abatacept IV or SC, TNF-inhibitors(TNFi) (Infliximab iv and Etanercept SC), or Rituximab IV) and to have at least two dosages of ACPA (at least one before and one after biologic treatment). ACPA titers were compared before and after treatment in each of the treatment groups. A mixed model analysis including an interaction between the drug and time was performed. A mixed model analysis including an interaction between the drug and time was performed. A mixed model analysis including an interaction between the drug and time was performed. A mixed model analysis including an interaction between the drug and time was performed.

Results: Among the 328 selected RA patients 92 patients (female: 84%, mean age: 62 years) had enough biological data to be included for the analysis: 36 patients had received rituximab, 21 abatacept, 35 TNFi. Mean (Standard deviation) ACPA levels in the whole group before treatment was 904.8 (1164.6) UI/L. ACPA titers (summarized in figure 1) decreased significantly after Rituximab (from 1287 (1322) to 301(387) UI/L; p<0.005) but not after Abatacept (from 857(1166) to 1352(1241) UI/L) or TNF blockers (from 593(881) to 1116(1241) UI/L). ACPA titers (summarized in figure 1) decreased significantly after Rituximab (from 1287 (1322) to 301(387) UI/L; p<0.005) but not after Abatacept (from 857(1166) to 1352(1241) UI/L) or TNF blockers (from 593(881) to 1116(1241) UI/L). Modelling of ACPA titers over follow-up (mixed models) revealed a significant interaction between drug and time, suggesting a drug effect of such variation (Figure).

Conclusion: In this real-life study, ACPA titers decrease slightly only after Rituximab therapy. These data suggest that there is potentially a huge unmet need in RA if the target is to achieve an immunological remission.

Disclosure of Interests: Stephane Hilliquin: None declared, Loriane Guttermann: None declared, Claire Goulvestre: None declared, Jerome Avouac: None declared, maxime dougados Grant/research support from: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma, Consultant for: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma, Anna Moltó: None declared.


SA10131 SAFETY AND EFFECTIVENESS OF DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS (bDMARDs) IN OLDER ADULTS WITH RHEUMATOID ARTHRITIS: A RETROSPECTIVE COHORT STUDY

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2University of Alberta, Division of Rheumatology, Department of Medicine, Canada

Background: Rheumatoid arthritis is common among older adults and biological disease-modifying antirheumatic drugs (bDMARDs) are effective in treating this population. However, older patients reportedly experience more adverse events (AEs) with effectiveness being either equivalent or worse than younger patients.

Objectives: Our primary objective was to compare the AEs associated with the use of bDMARDs and their relative effectiveness in three age groups: Group 1 (75+), Group 2 (65-74 years) and Group 2 (55-64 years) patients. We explored if sex, disease activity, baseline functional impairment, and the type of bDMARDs used differed across the three age groups as a secondary objective.

Methods: A retrospective cohort study of adults 55+ with RA seen between Jan 1, 2007 and July 31, 2009 was performed utilizing the RAPPORT (Rheumatoid Arthritis Pharmacovigilance Program and Outcomes Research in Therapeutics) database housed in Edmonton, Alberta, Canada. Baseline characteristics (age, sex, DAS28 score, HAQ score, types of bDMARDs used), drug effectiveness (based on DAS28 score) and associated AEs were compared across the three age groups. Descriptive statistics (Mean, SD, percentages) were used. An intention to treat analysis with chi-square testing for categorical variables and t testing for continuous ones were used to test for the significance of differences found.

Results: A total of 333 patients met our entry criteria (69.4% female, 30.6% male) with 52, 125 and 156 from groups 1, 2 and 3 respectively. Group 1 patients had a significantly higher mean HAQ score (2.16) compared to the younger groups (P<0.005) and a mean DAS28 (5.52) score significantly higher than the 55-64 group (P<0.05). Group 1 patients were more likely to experience AEs (p<0.05), which were more likely to be infectious (p<0.05), life threatening/severe (p<0.05), cause discontinuation of treatment (p<0.05) and multiple (p<0.05) compared to the younger groups. We also interestingly found the remission rate to be significantly higher in Group 1 patients compared to Group 2 (p<0.05). Etanercept was the most commonly used drug among all age groups. Rituximab and abatacept were much less frequently used. Rate of AEs and therapy effectiveness did not differ significantly by sex across the three age groups.

Conclusion: Older adults aged 75+ treated with bDMARDs for RA are at a significantly higher risk of AEs, which should be included in the treatment discussion. The higher remission rate in those 75+ compared to those 65-74, which has not been reported previously, warrants further study.

REFERENCES
SAT0132
LONG-TERM SAFETY, IMMUNOGENICITY AND EFFICACY IN RANDOMIZED, DOUBLE-BLIND, AND OPEN-LABEL EXTENSION STUDIES COMPARING FKB327, AN ADALIMUMAB BIOSIMILAR, WITH THE ADALIMUMAB REFERENCE PRODUCT IN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS

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Background: FKB327 is a biosimilar of adalimumab reference product (RP). Studies with adalimumab biosimilars have shown no increase in safety signals or immunogenicity versus RPs studied at 52 weeks. Objectives: To study the long-term safety, immunogenicity and efficacy of FKB327 compared with Adalimumab RP in a randomized double blind (DB) phase 3 study in patients (pts) with active rheumatoid arthritis (RA) inadequately controlled with methotrexate (MTX) and in a subsequent randomized, open-label extension (OLE) study with treatment switching assessed long-term safety, efficacy, PK, and immunogenicity.

Methods: Pts aged ≥18 years with moderate-to-severe, active RA (2010 ACR/EULAR criteria) for ≥3 months and receiving a stable dose of MTX were randomized 1:1 to FKB327 or RP (40 mg subcutaneously [SQ]) every other week with MTX. In the OLE study, pts who completed the DB study with clinical response and no serious adverse events (AEs) were rerandomized in a 2:1 ratio to FKB327 or RP. All pts received FKB327 through week 76 (Period 2). The primary end point was safety; the secondary end point was efficacy. Pooled data for up to 2 years were analyzed to assess long-term safety, Incidence rates of treatment-emergent AEs were adjusted by overall exposure to enable safety comparison of FKB327 and RP.

Results: Of 728 pts in the DB study, 645 were enrolled in the OLE; of those, 572 and 515 pts completed periods 1 and 2, respectively. Safety results from the pooled data were comparable between treatment sequences. Mean serum drug concentrations appeared to be in steady-state in all treatment sequences in Period 1 and comparable among sequences in Period 2. The proportion of pts with positive antidrug antibody (ADA) status in Period 1 was comparable between treatment sequences, and the majority of patients with positive ADA status had neutralizing activity. The mean proportion of patients achieving an ACR20 response remained stable between studies and was similar for all treatment sequences.

Conclusion: The safety, immunogenicity, and efficacy of FKB327 were maintained over long-term treatment and after switching between the biosimilar and RP.

SAT0133
TREATMENT PATTERNS, PERSISTENCE, AND DURABILITY IN RHEUMATOID ARTHRITIS PATIENTS WITH INADEQUATE RESPONSE TO BIOLOGIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS (BDMARDS)


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Background: EULAR and ACR recommend bDMARDS, as monotherapy or in combination with methotrexate, in patients whose rheumatoid arthritis (RA) remains active despite methotrexate use.1 Treatment options for bDMARD inadequate response (IR) patients vary. Understanding the real-world treatment patterns and treatment duration in bDMARD IR patients may help identify the most suitable next treatment.

Objectives: We studied treatment patterns, treatment persistence, and treatment durability in bDMARD IR patients who switched to another treatment regimen.

Methods: In US health plan claims data, this study selected adult RA bDMARD patients: those with ≥2 RA diagnoses ≥30 days apart, who newly initiated a bDMARD (1/1/2012 - 3/31/2017; baseline) and then switched to another bDMARD or JAKi (index date, ID). All patients had continuous ≥1-year enrollment before and after ID. Patient characteristics were evaluated at baseline; treatment patterns, persistence, and durability (duration) were evaluated during pre- and post-index periods. Kaplan-Meier curves were used to evaluate treatment persistence.

Results: Among 105,039 patients who were initiated on bDMARDS, 19,085 (18%) demonstrated IR; among those, 4,656 met all the selection criteria: median age 54 years, 22% male, 17% from Northeast, 26% Midwest, 42% South, 15% West. At baseline, 26% used tumor necrosis factor inhibitors (TNFi) monotherapy and 64% used TNFi in combination with conventional synthetic disease-modifying antirheumatic drugs (csDMARD). Baseline median treatment duration was 8.3 months overall, including 5.6 months for monotherapy and 9.4 months for combination therapy. Upon switch, 46% of patients used monotherapy (28% TNFi, 11% other bDMARD, 7% janus kinase inhibitors [JAKi]), and 54% used bDMARD in combination with csDMARD (37% TNFi + csDMARD, 12% other bDMARD

Table. Summary of Efficacy & Safety End Points at Week 30 (Period 2); Full Analysis Set

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<tr>
<td>ACR20 response rate</td>
<td>n</td>
<td></td>
<td></td>
<td></td>
<td>185</td>
<td>98</td>
<td>92</td>
<td>189</td>
</tr>
<tr>
<td>Responders, n (%)</td>
<td>154</td>
<td>82</td>
<td>79</td>
<td>158</td>
<td>83.2</td>
<td>83.7</td>
<td>79.6</td>
<td>83.6</td>
</tr>
<tr>
<td>95% CI</td>
<td>77.1</td>
<td>74.8</td>
<td>77.0</td>
<td>77.5</td>
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<td></td>
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<tr>
<td>ACR50 response rate</td>
<td>n</td>
<td></td>
<td></td>
<td></td>
<td>185</td>
<td>98</td>
<td>92</td>
<td>189</td>
</tr>
<tr>
<td>Responders (%)</td>
<td>112</td>
<td>57.6</td>
<td>50</td>
<td>113</td>
<td>60.5</td>
<td>58.2</td>
<td>53.4</td>
<td>59.8</td>
</tr>
<tr>
<td>95% CI</td>
<td>53.7</td>
<td>47.8</td>
<td>45.6</td>
<td>52.4</td>
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<tr>
<td>DAS28-CRP response rate</td>
<td>n</td>
<td></td>
<td></td>
<td></td>
<td>183</td>
<td>99</td>
<td>92</td>
<td>189</td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>3.04</td>
<td>3.28</td>
<td>3.20</td>
<td>3.13</td>
<td>1.237</td>
<td>1.385</td>
<td>1.247</td>
<td>1.239</td>
</tr>
<tr>
<td>Range</td>
<td>1.27</td>
<td>1.27</td>
<td>1.363</td>
<td>1.2</td>
<td>7.1</td>
<td>7.1</td>
<td>6.3</td>
<td>7.4</td>
</tr>
</tbody>
</table>

ADA indicates American College of Rheumatology; ADA, antidrug antibody; CI, confidence interval; DAS28, Disease Activity Score-28 with C-reactive protein; F, FKB327; H, adalimumab; SD, standard deviation.
+ csDMARD, 4% JAKI + csDMARD). Median treatment duration was longer for combination therapy than monotherapy (13.1 vs. 5.8 months, p<0.001). TNFi showed a trend towards shortest treatment duration and lowest 12-month treatment persistence among monotherapies and combination therapies. (Table) JAKI showed best treatment persistence among monotherapies (Figure 1; p-value=0.0004) and combination therapies (Figures 2; p-value<0.0001).

Conclusion: In biologic DMARD IR patients, the first bDMARD treatment lasted, on average, for 8.3 months before switch. Post-switch, TNFi showed a trend towards the shortest durability and JAKI showed the longest durability. The data suggest substantial unmet need in bDMARD patients. A well-tolerated effective therapy, with potent clinical efficacy and improved treatment durability may benefit this patient population.

REFERENCE

Disclosure of Interests: Robin K Dore Grant/research support from: Gilead Sciences, AbbVie, Amgen, Lilly, Pfizer, Regeneron, Sanofi, Consultant for: AbbVie, Amgen, Lilly, Speakers bureau: AbbVie, Amgen, Lilly, Sanofi, Regeneron, Pfizer, UCB, Jenya Antonova Shareholder of: Gilead Sciences, Employee of: Eli Lilly and Company, Mediimmune, Genterich, Gilead Sciences, Chakkarin Burudpakdee Grant/research support from: Gilead Sciences, Xin Wang Grant/research support from: Gilead Sciences, Consultant for: Gilead Sciences, Burak Ozbay Shareholder of: Gilead Sciences, Employee of: Abbott Laboratories, Abbvie, Mark C. Genovese Grant/research support from: Sanofi/Genzyme, Genentech/Roche, RPPharm, Consultant for: Sanofi/Genzyme, GENENTECH/Roche, RPPharm


SAT0134 COMPARING REAL-WORLD RETENTION RATES IN A MATCHED COHORT OF RHEUMATOID ARTHRITIS PATIENTS WHO EITHER REMAINED ON THE ETANERCEPT ORIGINATOR OR SWITCHED TO A BIOSIMILAR

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Background: In Germany, the first etanercept biosimilar was licensed in 2016. In contrast to other European countries there is no uniform recommendation for the prescription of biosimilars.

Objectives: To compare treatment survival between patients who were switched from the etanercept originator to the etanercept biosimilar SB4 and patients who stayed on the originator treatment.

Methods: We used data of rheumatoid arthritis patients observed in the prospective, longitudinal RABBIT (Rheumatoid Arthritis: Observation of biologic therapy) cohort until November 2018 who were treated with the etanercept originator (oETA) for at least six months. Patients who thereafter were switched to the biosimilar SB4 (bsETA) were matched (1:n) to patients who stayed on the original treatment using prescription time distribution matching [1] to control for survival bias. Matching criteria were sex, time of switch or corresponding duration of originator treatment in non-switchers and age as well as DAS28 at the time of switching or corresponding time point in non-switchers. The retention rates over one year were analyzed using Kaplan-Meier curves.

Results: Overall, 1,751 patients fulfilled the inclusion criteria of whom 113 were switched to bsETA. Of these, 102 switchers could be matched to 598 patients who remained on oETA. In both groups, 78% of the patients were female, mean age was about 59 years, DAS28 was 3.2 and physical function as well as numbers of prior biologics were similar. Patients who remained on oETA were more often rheumatoid factor positive (71% vs. 63%), had more erosions (56% vs. 47%) and had more frequently three or more comorbidities (34% vs. 28%) than those who were switched to bsETA. The most common reason for switching was costs (79%). After one year, 35% of the patients in both groups had stopped the respective treatment (oETA: n=210, bsETA: n=36). The main reasons for withdrawal were loss of efficacy (oETA: 57%, bsETA: 26%) and adverse events (oETA: 20%, bsETA: 42%). In both groups about the same portion of the adverse events that led to treatment discontinuation were serious events (24% vs. 27%). Kaplan-Meier curves showed similar retention rates over 12 months for bsETA and oETA (figure). Nine bsETA patients were switched back to oETA.

Conclusion: Retention rates of etanercept treated RA patients who were either switched to the biosimilar SB4 or who stayed on the originator are comparable. Only few patients switched back to the originator.

REFERENCE

Figure. Treatment continuation in etanercept patients who were either switched to the biosimilar SB4 or stayed on the originator.

Acknowledgement: Disclosure: RABBIT is supported by a joint, unconditional grant from AbbVie, Bristol-Myers Squibb, Celtrion, Hexal, Lilly, MSD Sharp & Dohme, Pfizer, Roche, Samsung Bioepis, Sanofi-Aventis und UCB.

Disclosure of Interests: Lisa Baganz: None declared, Anja Strangfeld Speakers bureau: Speakers fees from Bristol-Myers Squibb, MSD, Pfizer, Roche, Peter Herzer Speakers bureau: Pfizer, Andreas Krause Consultant for: Pfizer, Speakers bureau: Pfizer, Hans-Peter Tony Consultant for: Eli Lilly and Company, Speakers bureau: Eli Lilly and Company, Angela Zink Speakers bureau: Speakers fees from AbbVie, Janssen, Pfizer, Roche, Sanofi

SA81035 MAINTAINING REMISSION IN PATIENTS WITH ESTABLISHED RHEUMATOID ARTHRITIS WHILE TAPERING ETANERCEPT: AN INSIGHT IN THE TAPERING TRIAL

Delphine Bertrand1, Julie Mannaerts1, Valérie Badot1, Stephanie Bond1,2, Laurel Young1, Katherine Poulsen1, Helen L. Barrett3, Andrew L. Taylor4, Claire Barrett1.

Background: EULAR 2016 recommendations for the management of Rheumatoid Arthritis (RA) suggest to consider tapering of biological Disease-Modifying Antirheumatic Drugs (bDMARDs) in patients in sustained remission. More insight on the effect of tapering strategies is needed in daily practice.

Objectives: To investigate maintaining disease control after spacing dosages of etanercept 50mg from weekly to every other week (EOW) in a pragmatic randomized controlled trial (RCT).

Methods: Patients with RA who were in remission according to the disease activity score 28 (DAS28) remission criteria for at least 6 months and treated with etanercept 50mg weekly for at least a year were included in the one-year non-blinded multicentre TapERA (Tapering Etanercept in RA) RCT (EudraCTnumber 2012-004631-22). Patients were 1:1 randomly assigned to continue etanercept 50mg weekly or to taper to 50mg EOW. Patients who lost remission (DAS28 C-Reactive Protein (CRP) > 2.6) received nonsteroidal anti-inflammatory drugs and if needed were re-escalated to etanercept weekly. If remission was still not reached, treatment had to be adapted, at the discretion of the treating rheumatologist. The outcomes were proportion of patients in DAS28 remission at 6 and 12 months, proportion in sustained remission and proportion regaining remission after reintroducing weekly etanercept (intention to treat analysis). Missing components of DAS28 were imputed using expectation maximization.

Results: In total, 69 patients (69.6% female) with a mean ± standard deviation (SD) age of 55.7 ± 11.3 years and a mean ± SD disease duration of 14.7 ± 8.0 years were included. The weekly and EOW group consisted of 35 and 34 patients respectively. At the month 6 visit 77.1% of patients in the weekly and 76.5% of the EOW group were in remission (p=0.547) and 68.6% and 58.8% respectively maintained remission on every visit (p=0.400) (Table 1).

Three (8.6%) patients of the weekly and 11 (32.4%) of the EOW group required a treatment adaptation, which was statistically significantly different (p=0.014) and there was no difference between the weekly and EOW group in the mean ± SD DAS28 CRP at the first time of losing remission in patients flaring, namely 3.1 ± 0.6 and 3.1 ± 0.5 respectively (p=0.957).

Eleven patients were re-escalated to a weekly treatment after a mean ± SD duration of 4.5 ± 3.1 months. Of these, 54.5% (6/11) regained remission after a mean ± SD duration of 4.7 ± 1.7 months. Of the 5 patients not regaining remission, 1 switched to a weekly regimen on the last trial visit, 1 required switching to another bDMARD and 3 patients had no additional treatment changes (mean ± SD DAS28 CRP at month 12: 3.4 ± 0.2). Two patients of the EOW group restarted weekly etanercept while still being in remission.

Table 1: Proportion of patients of the weekly and EOW group in remission and LDA

<table>
<thead>
<tr>
<th>Weekday group (n=35)</th>
<th>EOW group (n=34)</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Remission at M6 (n%)</td>
<td>27 (77.1)</td>
<td>36 (105.5)</td>
</tr>
<tr>
<td>LDA at M6 (n)</td>
<td>7 (20.6)</td>
<td>10 (29.4)</td>
</tr>
<tr>
<td>Sustained Remission at M6 (n)</td>
<td>21 (60.6)</td>
<td>20 (58.8)</td>
</tr>
<tr>
<td>Sustained LDA at M6 (n)</td>
<td>21 (60.6)</td>
<td>21 (61.5)</td>
</tr>
<tr>
<td>Remission at M12 (n)</td>
<td>30 (85.7)</td>
<td>24 (70.6)</td>
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<tr>
<td>LDA at M12 (n)</td>
<td>13 (39.4)</td>
<td>19 (56.5)</td>
</tr>
<tr>
<td>Sustained Remission at M12 (n)</td>
<td>13 (44.1)</td>
<td>14 (41.2)</td>
</tr>
<tr>
<td>Sustained LDA at M12 (n)</td>
<td>13 (44.1)</td>
<td>14 (41.2)</td>
</tr>
<tr>
<td>Patients with treatment disruption due to inefficacy loss (n)</td>
<td>3 (8.6)</td>
<td>11 (32.4)</td>
</tr>
</tbody>
</table>

Conclusion: Approximately half of the EOW group was in sustained remission after 1 year and two thirds remained on their reasigned treatment. Further, one in two patients in sustained remission after reintroducing etanercept weekly. Therefore tapering of etanercept in EOW seems a feasible strategy in patients with RA in sustained remission, potentially leading to a beneficial cost-saving and safety profile.

Disclosure of Interests: Delphine Bertrand: None declared, Julie Mannaerts: None declared, Valérie Badot: None declared, Stephanie Bond: None declared, Laurel Young: None declared, Katherine Poulsen: None declared, Helen L. Barrett: None declared, Andrew L. Taylor: None declared, Claire Barrett: None declared, Kathleen Poulsen: None declared, Helen L. Taylor: None declared, Claire Barrett: None declared, University of Queensland, Brisbane, Australia; 2James Cook University, Townsville, Australia; 3Mater Health Services, South Brisbane, Australia; 4Royal Perth Hospital, Perth, Australia

SA81036 CONSISTENCY WITH INTERNATIONAL GUIDELINES REGARDING MOTHERS WITH RHEUMATOLOGIC DISEASES EXPOSED TO TUMOUR NECROSIS FACTOR INHIBITORS (TNFI) DURING THE ANTE- AND POSTNATAL PERIODS AND CHANGE OVER TIME

Stephanie Bond1,2, Laurel Young1, Katherine Poulsen1, Helen L. Barrett3, Andrew L. Taylor4, Claire Barrett1.

Background: Many women with rheumatologic diseases require ongoing treatment with TNFI during pregnancy to maintain remission or low disease activity. Until recently, there has been a paucity of published evidence regarding the safe use of these medications during the ante- and postnatal periods to guide clinical practice.

Objectives: To observe compliance with current guidelines for TNFI therapy in Australian women with rheumatologic diseases during the ante- and postnatal periods and change over time.

Methods: All Australian women with rheumatologic diseases, exposed to biologics (bDMARDs) and targeted synthetic disease modifying antirheumatic drugs (tsDMARDs) during the preconception, antenatal and/or post-partum periods were eligible to participate in the Pregnancy Exposed to Biological (PEB) study. Commencing in 2015, recruitment was via invitation from patient’s treating rheumatologists, community groups, and social media. Following self-referral to the study, retrospective data was collected, including rheumatologic condition and management recommendations made by health professionals.

Results: Preliminary data is available for 37 infants born to 29 mothers from Feb 2009-Dec 2018. Of these, 32 women received TNFI. We assessed 3 outcomes – TNFI continuation during pregnancy, TNFI continuation during lactation and vaccination practice in infants exposed to TNFI. Women exposed to non-TNFI bDMARDs and tsDMARDs were excluded from this abstract, as these are not recommended for use during the perinatal period (2).

Specialist Society Guidelines from the British Society of Rheumatology and the British Health Professional in Rheumatology were published in 2016 regarding the safety of TNFI during pregnancy (2). Prior to guideline publication, 67% (n=16/24) of the women in PEB ceased their TNFI pre-conception. Of those in PEB who became pregnant subsequent to guideline publication, only 25% (n=2/8) ceased TNFI pre-conception. Overall, 40.6% (n=13/32) women received a TNFI during the antenatal period consistent with guidelines, which improved from 33.3% (n=8/24) pre-publication, to 62.5% (n=5/8) post publication. 84.4% (n=27/32) women exposed to TNFI breastfed their infants. Prior to availability of evidence regarding the safety of TNFI during lactation, 79.2% (n=19/24) of infants were breastfed. After publication, 100% (n=8/8) infants exposed to TNFI were breastfed.

In total, 96.9% (n=31/32) of the infants exposed to TNFI in PEB were vaccinated. Rotavirus vaccine should have been delayed in 43.8% (n=14/ 32) infants, but was not. 9.4% (n=3/32) infants had live vaccines deferred until only 3 months; 3.1% (n=1/32) infants had live vaccines unnecessarily delayed. Only 3.1% (n=1/32) infants had live vaccines appropriately delayed until 7 months. Compliance with vaccination recommendations increased from 43.5% (n=10/24) pre-publication to 62.5% (n=5/8) post publication of guidelines.

Conclusion: Preliminary data from PEB suggests that there has been a shift in practice following the publication of Specialist Society Guidelines, with increasing numbers of women continuing TNFI therapy during pregnancy and the postpartum period, in keeping with current evidence. Compliance with vaccination recommendations could be improved to be more consistent with published international guidelines.

Disclosure of Interests: Stephanie Bond: None declared, Laurel Young: None declared, Katherine Poulsen: None declared, Helen L. Barrett: None declared, Andrew L. Taylor: None declared, Claire Barrett: None declared, University of Queensland, Brisbane, Australia; 2James Cook University, Townsville, Australia; 3Mater Health Services, South Brisbane, Australia; 4Royal Perth Hospital, Perth, Australia


Saturday, 15 June 2019 1137
SAT0137  PATIENTS (PTS) SWITCHED TO SARILUMAB FROM ADALIMUMAB ACHIEVE CLINICALLY IMPORTANT IMPROVEMENTS IN RA DISEASE ACTIVITY: RESULTS FROM MONARCH TRIAL OPEN-LABEL EXTENSION (OLE)

Gerd Rüdiger Burmester1, Howard Amital2, Andrea Rubbert-Roth3, Hubert van Hoogstraten4, Leon M. Gervitz5, Karthinathan Thangavelu6, Gregory St John7, Mark C. Genovese7.

1Charité University Medicine, Berlin, Germany; 2Sheba Medical Center, Ramat Gan, Israel; 3Kantonsspital St. Gallen, St. Gallen, Switzerland; 4Sanofi Genzyme, Bridgewater, NJ, United States of America; 5Sanofi Genzyme, Boston, MA, United States of America; 6Regeneron Pharmaceuticals, Inc., Tarrytown, NY, United States of America; 7Stanford University Medical Center, Palo Alto, CA, United States of America

Background: In MONARCH (NCT02332590), sarilumab monotherapy (200 mg subcutaneously [SC] every 2 weeks [q2w]) demonstrated superior benefit to adalimumab monotherapy (40 mg SC q2w) in DAS28-ESR, ACR20/50/70 response, HAQ-DI, and CDAI in pts with RA and inadequate response/intolerance to methotrexate.

Objectives: To assess long-term safety/efficacy in RA pts continuing sarilumab or switching from adalimumab to sarilumab monotherapy in the ongoing OLE of MONARCH.

Methods: Pts completing MONARCH were eligible for the OLE, in which they received sarilumab 200 mg SC q2w. Efficacy and safety data were reported up to OLE Wk 48 and March 2017, respectively. Responder rates were based on the intent-to-treat population. Continuous efficacy endpoints were based on the observed population.

Results: Of 369 pts enrolled in MONARCH, 320 (87%) entered OLE (switch: n=155; continuation: n=165). By safety data cut-off, pt attrition was similar in switch (24; 15.5%) and continuation groups (22; 13.3%), as were treatment-emergent adverse events (AEs) (switch: 76.1%, 267.4/100 PY; continuation: 70.9%, 230.2/100 PY) and infections (switch: 41.9%; continuation: 35.8%). For DAS28-ESR and CDAI endpoints, >40% of switch pts achieved a minimally important difference (MID) improvement from OLE baseline by OLE Wk 12, increasing to >50% by OLE Wk 48. Additionally, >40% of switch pts achieved a MID in DAS28-CRP and a minimally clinically important difference (MCID) in HAO-DI from baseline to OLE Wk 12, increasing to >50% by OLE Wk 48. Additionally, >40% of switch pts achieved a MID in DAS28-CRP and a minimally clinically important difference (MCID) in HAQ-DI from baseline to OLE Wk 48. Of pts achieving CDAI ≤10 from baseline to OLE Wk 24 of the OLE, 70.7% (switch group) and 83.5% (continuation group) achieved sustained response at OLE Wks 36 and 48. In the randomized controlled phase, response rates were higher in sarilumab-treated than adalimumab-treated pts, hence fewer pts in the continuation group achieved additional MID during OLE (data not shown). AEIs of special interest are reported (Table). Two deaths occurred in the switch group (malignancy; cerebrovascular accident) versus one in the continuation group (subarachnoid hemorrhage). No GI-related AEIs (ulcers/perforations/diverticulitis) were observed.

Conclusion: Pts switched from adalimumab to sarilumab experienced clinically meaningful improvements in signs and symptoms of RA. Safety observations in OLE were generally consistent with those in MONARCH.

Acknowledgement: Study funding and editorial support (Helen Johns, Adelphi) were provided by Sanofi Genzyme and Regeneron.
Abatacept (ABA) is a biologic DMARD (bDMARD) used to treat rheumatoid arthritis (RA) since 2006. There are limited data on clinical efficacy of ABA, and on predictors for ABA treatment response.

**Methods:** In an observational cohort study, based on data from a large national quality register database, patients with RA diagnosis who initiated treatment of RA between bionaïve patients and patients with previous bDMARD experience. Male sex also predicted LUNDEX corrected HAQ response, more likely to have significant HAQ disability, measured by HAQ, were less likely to remain on treatment and achieve EULAR good response to abatacept. Patients with extensive disability, measured by HAQ, were less likely to remain on treatment and achieve a EULAR Good Response, but more likely to have significant HAQ improvement.

**REFERENCE**


**Table 1. Significant predictors of Lundex EULAR good response. Bivariate and adjusted analysis. Odds ratios (95% CI).**

**Predictors**

<table>
<thead>
<tr>
<th></th>
<th>Bivariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td>6 months</td>
<td>12 months</td>
<td></td>
</tr>
</tbody>
</table>

**Disclosures:**

- **Disclosure of Interests:**
  - Gerd Rüdiger Burmester: Consultant for: Roche, Sanofi-Genzyme, Speakers bureau: Roche, Sanofi-Genzyme, Howard Ami-
  - 1Lund University, Clinical Sciences Malmö, Malmö, Sweden
  - Giovanni Cagnotto: Consultant for: Novartis, less than 3000 Euro.
  - Minna Willim: None declared.
  - Lennart Jacobsson: Consultant for: Eli-Lilly, Janssen, Novartis, Pfizer, Speakers bureau: Abbvie., Michele Compagno: None declared, Saeds Saevarsdottor Employee of: Part-time employee at deCODE Genetics/Amgen Inc, working on genetic research unrelated to this project., Carl Turesson: None declared.

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**SATO138**

**PREDICTORS OF CLINICAL EFFICACY OF ABATACEPT IN RHEUMATOID ARTHRITIS: DATA FROM A LARGE OBSERVATIONAL STUDY**

**Giovanni Cagnotto,**1,2 Minna Willim,3 Lennart Jacobsson,4 Michele Compagno,2,5 Saeds Saevarsdottor,6 Carl Turesson

**Background:** Abatacept (ABA) is a biologic DMARD (bDMARD) used to treat rheumatoid arthritis (RA) since 2006. There are limited data on clinical efficacy of ABA, and on predictors for ABA treatment response.

**Objectives:**

- To compare the effectiveness of ABA in the treatment of RA between bionaïve patients and patients with previous bDMARDs.
- To investigate predictors of clinical response to ABA.

**Methods:**

- In an observational cohort study, based on data from a large national quality register database, patients with RA diagnosis who initiated treatment with ABA between April 2006 and November 2017 were included.
- LUNDEX corrected response was defined as the fractions remaining on the drug and achieving the outcome among all who initiated treatment (1). Clinical response at 6 and 12 months was evaluated by means of LUNDEX corrected EULAR (L-EULAR) Good Response and LUNDEX corrected HAQ response (change of ≥0.3 from baseline) (L-HAQ). Predictors for clinical response were investigated using logistic regression, with significance based backwards selection of variables for the final multivariate model. The study was supported by an unrestricted grant from Bristol Myers-Squibb.

**Results:**

- 2716 RA patients were included in the study. More patients in the bionaïve population achieved L-EULAR Good Response and L-HAQ response at 6 and 12 months than bDMARDs experienced patients (Fig. 1a and 1b).
- Male sex, no previous bDMARD exposure and a low HAQ score were independent predictors of L-EULAR Good Response at 6 and 12 months (Table 1). Lack of previous bDMARD exposure also predicted L-HAQ response at 6 and 12 months. There was a positive associations between baseline HAQ and L-HAQ response at 6 months (multivariate adjusted odds ratio 1.73; 95% CI 1.46-2.05).

**Conclusion:** In patients with RA, response rates for treatment with abatacept were substantially higher in bionaïve patients than in those with previous bDMARD experience. Male sex also predicted LUNDEX corrected EULAR good response to abatacept. Patients with extensive disability, measured by HAQ, were less likely to remain on treatment and achieve a EULAR Good Response, but more likely to have significant HAQ improvement.
SAT0139  A MULTICENTRE, RANDOMISED, DOUBLE-BLIND, PARALLEL ACTIVE-CONTROLLED CLINICAL TRIAL COMPARING PHARMACOKINETICS, PHARMACODYNAMICS, SAFETY AND EXPLORATORY EFFICACY BETWEEN HLX01 AND EUROPE-SOURCED RITUXIMAB AS A NEW INDICATION IN CHINESE MODERATE TO SEVERE PATIENTS WITH RHEUMATOID ARTHRITIS

Xiaofeng Zhang1, Yongyu Wang2, Zhenyu Jiang2, Zhouch Zhang2, Lan He2, Xiao Zhang2, Xin Li3, Xumei Liu3, Jian Xu4, Cibo Huang1, Rui Liu1, Xiaoxia Zuo1, Baogeng Zhao3, Wenting Gu1, Katherine Chai3, Xinjun Guo3, Xin Zhang3, Eugene Liu10, Alvin Liu11, Weidong Jiang3, Scott Liu3, Pei Hu11, Xiao Chen12.

Background: Biologic products, such as rituximab and adalimumab, have revolutionized the treatment for chronic inflammatory disorders, providing an option to patients who were non-responsive to conventional systemic therapies. In China, rituximab is only approved for the treatment of certain haematologic malignancies. At present, there are several approved biosimilars in Europe but none in China. HLX01, a China-manufactured proposed rituximab biosimilar, was first developed for patients with non-Hodgkin’s lymphoma later as a new drug for the treatment for autoimmune diseases. Currently, HLX01’s biosimilar NDA for the treatment of non-Hodgkin’s lymphoma is being reviewed by authorities in China.

Results: Evaluation of clinical PK, safety and exploratory efficacy in RA patients to support the development of HLX01 for the treatment of autoimmune diseases.

Methods: We conducted a multi-centre, randomised, double-blind, parallel active-controlled clinical trial to compare the PK, PD safety and exploratory efficacy (ACR20 and DAS28-CRP) between HLX01 and EU-RTX in patients with moderately to severely active RA. All patients had an inadequate response to treatment with disease-modifying antirheumatic drugs (DMARDs). The PK equivalence was achieved if 90% confidence intervals (CIs) for the test-to-reference ratios of area under the curve from time zero to infinity (AUC(0-inf)) and maximum observed concentration (Cmax) fall within the pre-defined 80-125% equivalence margin.

Conclusion: We report successful demonstration of similarity in PK, safety and efficacy between first China-manufactured biosimilar of rituximab, HLX01, and Europe-sourced rituximab in patients with moderate to severely active rheumatoid arthritis. These results support the Phase 3 confirmatory clinical trial for the development of HLX01 for the treatment of rheumatoid arthritis.


Background: Tofacitinib (TOFA), a targeted synthetic DMBD, has been approved for the treatment of rheumatoid arthritis (RA) in Canada since April 2014. This oral agent preferentially inhibits signalling by cytokine receptors associated with JAK1 and JAK3 subunits. It is now indicated for the treatment of psoriatic arthritis (PsA) and ulcerative colitis (UC) since October 2018. Clinical experience with this molecule has been increasing both in RA and other rheumatic conditions and long-term safety are of interest. Data collection through RHUMADATA, a Quebec based clinical database and registry, allows comparison of various advanced treatment options including TOFA and non-TNFi biologic agents (i.e., agents with other modes of action - OMA) such as fusion proteins (abatacept), and IL-6 (sarilumab, tocilizumab) and CD20 inhibitors (rituximab).

Objectives: This analysis compares TOFA and OMA used with and without methotrexate (MTX).

Methods: Data collected since January 1, 2014 (since TOFA became available in Canada) at the Institut de Recherche en Rhumatologie de Montréal (IRRMM) and the Centre de l’Ostéoporese et de Rhumatologie de Québec (CORQ) was extracted from the Rhumadata® on January 7, 2019.
2019. The selected patients had initiated therapy with either TOFA or OMA (either without or in combination with MTX). The collected data include baseline characteristics (socio-demographic variables, concomitant and past medication, comorbidities and the Charlson comorbidity index (CCI)), variables measured over time (laboratory test results, patient and physician-reported outcomes), and disease activity measures such as CDAI and DAS28(4)-ESR and persistence data (treatment duration, reason for cessation). The groups were compared to identify potential confounders, and persistence data were analyzed using Kaplan-Meier and proportional hazard methods.

Results: A total of 483 patients were initiated on TOFA (n=162) or an OMA (n=321) since January 1, 2014. Of those, 57% (n=92) and 59% (n=191) were treated with MTX in the TOFA and OMA group respectively. These represent the first treatment following csDMARD inadequate response for 33% (TOFA) and 29% (OMA) of these patients. These patients had a mean disease duration of 12.1 (standard deviation=11.0) and 11.1 (10.3) years. In the TOFA group, 84% were women, 15% were smokers, and the mean age at treatment initiation was 57.7 (11.5). In the OMA group, 75% were women, 18% were smokers, and the mean age at treatment initiation was 57.3 (12.0) years. Patient global, pain and fatigue assessments, made on a visual analogue scale ranging from 1 to 10, were 5.6 (2.5), 5.9 (2.7) and 5.7 (2.9) in the TOFA group and 5.7 (2.5), 6.1 (2.7) and 6.0 (2.8) in the OMA group. Disease activity was assessed as moderate or high/severe in 85.9% and 88.3% of patients (DAS28(4)-ESR criteria). Among the 56 (35%) TOFA and 149 (46%) OMA patients ceasing therapy, reasons for cessation were “inefficacy” (TOFA: 64% vs OMA: 59%) and “adverse events” (TOFA: 16% vs TNFi: 17%). Patients remaining on TOFA and OMA therapy at last follow-up had an average treatment duration of 1.7 (1.1) and 2.6 (1.4) years. No difference in retention was observed between TOFA and OMA treated patients (log-rank p=0.6138). Patients treated with an OMA/MTX had with an OMA/MTX had similar retention (log-rank p=0.2640) as did patients treated with TOFA/MTX (log-rank p=0.9553). These results remain unchanged when we adjust for age at treatment initiation, gender, disease duration, and comorbidities (CCI) using Cox models.

Conclusion: OMA and TOFA have similar retention as do subjects treated with OMA or TOFA with or without MTX.

**DISCLOSURE OF INTERESTS**

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**Disclosure of Interests:** Rebecca Davies: None declared, Lianne Kearsley-Fleet: None declared, Mark Lunt: None declared, Kath Watson: None declared, Kimme Hyrich Grant/research support from: Grants to institution: BMS, Pfizer, UCB.


**SAT0141**

**FREQUENCY AND REASONS FOR SWITCHING BACK TO BIOLOGIC ORIGINATOR FOLLOWING INITIAL SWITCH TO BIOLOGIC BIOSIMILAR**

Rebecca Davies, Lianne Kearsley-Fleet, Mark Lunt, Kath Watson, Kimme Hyrich, BSRBR-RA Contributors Group. University of Manchester, ARUK Centre for Epidemiology, Manchester, United Kingdom

**Background:** Since February 2015, a number of biosimilar drugs have been introduced for treatment of rheumatoid arthritis (RA) in the UK. Biologics are required to have no clinically meaningful differences in efficacy or safety from the originator product. There are clear cost-saving implications when switching patients to a biosimilar product as it is the longer-term implications of switching have yet to be studied.

**Objectives:** To describe the frequency of switching back to biologic-originator (BIO-O) in patients who initially switch from BIO-O to biologic biosimilar (BIO-B), focusing on etanercept (ETA) and infliximab (INF).

**Methods:** The study population comprised RA subjects recruited to BSRBR-RA from 30/11/2018 who had switched from BIO-O to BIO-B (INF and ETA) and had completed at least one further study follow-up following switch. Baseline characteristics at point of switch and the proportion of patients who were recorded as switching back to BIO-O or discontinuing BIO completely following switch with reasons are described.

**Results:** Nine hundred and sixty six patients were included (760 switching from ETA-O; 206 switching from INF-O). After a median follow-up of 22.5 months post-switch, the majority of patients remained on BIO-B (ETA-B = 95% (81%), INF-B =166 (81%)). Seven percent of patients switched back to originator, with a majority following reports of ineffectiveness or feeling generally unwell (Table). Eleven percent stopped BIO completely, with a majority stopping for serious adverse events such as malignancy or infection. Similar results were seen for both ETA and INF. Six ETA and 3 INF reported injection or infusion related reactions following switch (0.9% overall) leading to switch back (4 ETA) or biologic discontinuation (2 ETA/3 INF).

**Conclusion:** Data from this study show that the majority of patients who switched from BIO-O to BIO-B remain on the biosimilar over the short term. A small proportion of patients have switched back to the originator drug with the majority doing so for reports of ineffectiveness rather than safety concerns. Hypersensitivity reactions, such as infusion reactions were rare reasons to stop either drug completely or switch back to originator.

**Table 1**

<table>
<thead>
<tr>
<th>Patients Switching from O to B</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>BIO-O before switch years</td>
<td>760 (79)</td>
</tr>
<tr>
<td>Infliximab</td>
<td>206 (21)</td>
</tr>
<tr>
<td>% Female</td>
<td>66 (58-72)</td>
</tr>
<tr>
<td>Disease duration, years</td>
<td>75</td>
</tr>
<tr>
<td>DAS28 score</td>
<td>20 (13-28)</td>
</tr>
<tr>
<td>Time on BIO-O before switch</td>
<td>3.2 (2.2-4.2)</td>
</tr>
<tr>
<td>All values are median (IQR) or n(%).</td>
<td></td>
</tr>
</tbody>
</table>

**SAT0142**

DIFFERENCES IN PATIENT CHARACTERISTICS AND PATTERNS OF TREATMENT BY DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS (DMARD) IN BDMARD NAIVE VERSUS EXPERIENCED PATIENTS

Robin K. Dore1, Leslie Harold2, Taylor Blakeley, Ketichi Emezuamun2, Derya Anttimezora, Joel Kremer1,2. 1Private Practice, Tustin, United States of America; 2University of Massachusetts Medical School, Worcester, United States of America; 3Corona, LLC, Waltham, United States of America; 4Gleed Sciences, San Francisco, United States of America; 5Abbany Medical College, Albany, United States of America

**Background:** For RA patients (pts), EULAR and ACR recommend various DMARDs. Available treatments have short durability and low persistency.

For RA patients (pts), EULAR and ACR recommend various DMARDs. Available treatments have short durability and low persistency. For RA patients (pts), EULAR and ACR recommend various DMARDs. Available treatments have short durability and low persistency.
biologic naive vs experienced may help clinicians tailor treatment decisions to pts needs.

**Objectives:** This study aimed to compare DMARD initiation events in biologic naive vs experienced pts.

**Methods:** In the Corrona registry (as of 2/28/2018), we selected DMARD initiation events (with at least one 6-month follow up) and stratified them on whether the initiator was biologic naive or experienced. We compared pts baseline characteristics (demographic, clinical, treatment) between strata. We used Kaplan-Meier curves to describe time to discontinuation and log rank test to assess differences in persistence.

**Results:** For 48,246 RA pts, 10,347 DMARD initiations (index date, baseline; on 11/2012 or thereafter) in 6,858 adults were identified. Within initiations, 38% (n=3,931) occurred in bDMARD naive pts. Females comprised 76% (naive) vs 80% (experienced). Despite comparable age and retirement status (Table), the bDMARD experienced initiators had RA for longer (mean: 12.6 vs 5.4), were more likely to be disabled (19.6% vs 11.0%), had marginally higher CDAI scores (mean: 19.1 ± 17.8), more likely to discontinue index treatment due to elevated CDAI (15.5% vs 10.9%), and had a shorter treatment duration (mean: 13.8 vs 15.1 months) than bDMARD naïve initiators. Persistency was higher in the bDMARD naive than in experienced initiators (Figure)

**Conclusion:** The marked difference in RA duration and pts disability status, despite comparable age, confirms prior reports that bDMARD experienced pts do not respond as well to therapy as bDMARD naïve pts. The increased CDAI scores and shortened durability of response suggests that there is still a need for new efficacious and well-tolerated RA therapy.

**Table. Patient and treatment characteristics**

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All initiations</th>
<th>bDMARD naïve</th>
<th>bDMARD experienced</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Demographics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td>Male (n=74,969) 69.9</td>
<td>71.8</td>
<td>68.1</td>
<td>0.0031</td>
</tr>
<tr>
<td>Age (median, IQR)</td>
<td>59.2 (49, 69.1)</td>
<td>60.8 (49.8, 69.3)</td>
<td>58.9 (49.6, 69.1)</td>
<td>0.8</td>
</tr>
<tr>
<td>Tobacco</td>
<td>1989 (16.3)</td>
<td>23.0</td>
<td>15.9</td>
<td>0.0031</td>
</tr>
<tr>
<td>Method</td>
<td>3015 (29.1)</td>
<td>32.3</td>
<td>28.6</td>
<td>0.0031</td>
</tr>
<tr>
<td>CDAI (mean, SD)</td>
<td>6.3 (5.9, 10.4)</td>
<td>7.0 (6.7, 10.7)</td>
<td>5.6 (5.3, 9.9)</td>
<td>0.0031</td>
</tr>
<tr>
<td>CDAI (median) (IQR)</td>
<td>6.0 (4.0, 9.0)</td>
<td>6.5 (4.5, 10.0)</td>
<td>5.0 (3.0, 8.0)</td>
<td>0.0031</td>
</tr>
<tr>
<td>Therapy initiation (n, %)</td>
<td>2566 (25.6)</td>
<td>29.8</td>
<td>21.4</td>
<td>0.0031</td>
</tr>
<tr>
<td>Combination Therapy</td>
<td>6661 (67.2)</td>
<td>70.5</td>
<td>63.9</td>
<td>0.0031</td>
</tr>
<tr>
<td>Mean treatment duration (months)</td>
<td>14.3</td>
<td>13.4</td>
<td>15.1</td>
<td>13.9</td>
</tr>
<tr>
<td>Reasons for discontinuation of index therapy (n, %)</td>
<td>4916</td>
<td>164</td>
<td>202</td>
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<tr>
<td>One or more reasons</td>
<td>925 (18.5)</td>
<td>37.6</td>
<td>15.9</td>
<td>549 (11.9)</td>
</tr>
<tr>
<td>Safety</td>
<td>1146 (23.7)</td>
<td>34.5</td>
<td>18.3</td>
<td>25.6 (9.9)</td>
</tr>
<tr>
<td>Effectiveness</td>
<td>1202 (24.5)</td>
<td>29.3</td>
<td>16.3</td>
<td>22.8 (10.5)</td>
</tr>
<tr>
<td>Persistent</td>
<td>104 (2.1)</td>
<td>19.2</td>
<td>10.3</td>
<td>15.5 (10.9)</td>
</tr>
<tr>
<td>Infection</td>
<td>14  (0.3)</td>
<td>2.6</td>
<td>0.5</td>
<td>0.31 (0.04)</td>
</tr>
<tr>
<td>Safety: serious side effect, minor side effect, facial rash, side effects of tocilizumab, treatment, and infection.</td>
<td>0.32</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Effectiveness: inadequate initial response, failure to maintain initial response, and use of safety</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>a. Patients are counted as discontinuing due to high disease activity (SDAI &lt; 40) on discontinuation reason is reported and (C)DIS@2 means time of assessment.</td>
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</table>

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**Disclosure of Interests:** Robin K Dore Grant/research support from: Gilead Sciences, AbbVie, Amgen, Lilly, Pfizer, Regeneron, Sanofi, Consultant for: AbbVie, Amgen, Lilly, Speakers bureau: AbbVie, Amgen, Lilly, Sanofi, Regeneron, Pfizer, UCB, Leslie Harrod Grant/research support from: Pfizer, Consultant for: AbbVie, BMS, Genentech, Taylor Blachley Employee of: Corrona, LLC, Kelechi Emeranu Employee of: Corrona, LLC, Jerya Antinova Shareholder of: Gilead Sciences, Employee of: Eli Lilly and Company, Medimmune, Genentech, Gilead Sciences, Joel Kremer Grant/research support from: AbbVie, Genentech, Lilly, Novartis, Pfizer, Consultant for: AbbVie, Amgen, BMS, Genentech, Lilly, Regeneron, Sanofi, Pfizer

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**SAT0143 SAFETY AND EFFECTIVENESS OF BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS IN ELDERLY PATIENTS WITH RHEUMATOID ARTHRITIS**

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**Background:** Elderly population with rheumatoid arthritis (RA) is increasing. However, these patients are frequently excluded from clinical trials and data on effectiveness and safety of biologic Disease-Modifying Anti-Rheumatic Drug (bDMARD) is scarce.

**Objectives:** To assess the persistence of 1st bDMARD and the effectiveness and safety of bDMARD among elderly (≥65 years).

**Methods:** Prospective multicenter cohort-study of RA patients starting a 1st bDMARD registered at Reuma.pt. Demographic and disease characteristics, comorbidities, medications, disease activity at baseline and follow up (3, 6 and 12 months) and adverse events (AE) were compared between elderly and adult (<65 years) patients. Treatment persistence was estimated using Kaplan-Meier analysis. Effectiveness was measured as EULAR crude response rates, LUNDEX corrected, and adjusted for baseline characteristics.

**Results:** 2400 patients were included, of which 486 aged ≥65 years (table 1). Crude median persistence in bDMARD was 19.7 months (95% CI 14-25) in adults and 14.5 (95%CI 3-26) in elderly patients (log rank test, p=0.46) (figure 1). EULAR response (crude and LUNDEX corrected) was similar in the two groups at 3 and 6 months (figure 2). After adjustment for baseline characteristics, response rate was inferior in elderly at 12 months (p=0.01). There were 697 AE reported. Except for infections, more common in elderly patients (p=0.03), the rates of severe AE, opportunistic infection, allergic reactions, cancer or hospitalizations were similar in the two groups, as well as the time to 1st AE occurrence (figure 2).

**Conclusion:** Our findings showed that persistence of 1st bDMARD was similar in adults and elderly RA patients. Though elderly had more severe disease and comorbidities at baseline, bDMARD treatment was equally effective and safe in the short term. However, it is necessary to consider the greater risk of infection in elderly when prescribing a biologic.

**Table 1:** Baseline characteristics. N: number; IQR: interquartile range; SD: standard deviation; RF: Rheumatoid factor; CCP: Cyclic Citrullinated Peptide; BMI: Body Mass Index; DAS: disease activity score, CDAI: clinical disease activity Index, SDAD – simple disease activity index, HAQ-DI: health assessment questionnaire disability index. When p value<0.05 no value is presented.

**Table 2:** Result of the characteristics, N: number; IQR: interquartile range; SD: standard deviation; RF: Rheumatoid factor; CCP: Cyclic Citrullinated Peptide; BMI: Body Mass Index; DAS: disease activity score, CDAI: clinical disease activity Index, SDAD – simple disease activity index, HAQ-DI: health assessment questionnaire disability index. When p value<0.05 no value is presented.
SAT0144 UNDERSTANDING THE LONG-TERM OUTCOME OF RITUXIMAB – IMPLICATIONS FOR MANAGEMENT
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Background: In patients with rheumatoid arthritis (RA), rituximab (RTX) is often prescribed after loss of response to TNF inhibitors; however, little is known about the long-term outcome of patients receiving treatment with RTX. Previous work [1,2] has shown that aiming for “complete B-cell depletion with clinical response” (CD-R) leads to an optimal management of the disease but unfortunately not all patients maintain this status. Whether CD-R can be regained with RTX retreatment remains unclear.

Objectives: To assess the outcome of RA patients treated with consecutive cycles of RTX, focusing on those who achieved complete B-cell depletion with clinical response.

Methods: A prospective 12 year observational study was conducted in RA patients who were treated with RTX in Leeds. Consecutive cycles of RTX consisting of 2 infusions of 1000mg were administered either on clinical relapse or a 6-monthly basis. B-cells were measured using highly sensitivity flow cytometry at 0 and 2 weeks post-RTX. Complete depletion (CD) was defined by total B-cell count <0.0001x10⁹/L at week 2. Clinical response was defined by EULAR response criteria and CD-R was seen as the optimal outcome.

Results: 755 patients participated in the study of which 723 had complete data (see fig.1). The mean (range) number of RTX cycles administered was 3.8 (1-14). 76% (549/723) of patients reached CD-R at some stage during therapy while 24% (174/723) never did. The latter patients had a shorter period of RTX treatment vs CD-R with an OR of 7.98 after adjusting for age, gender, prior therapy with TNF-I and concomitant DMARDs (95% CI 5.86-10.86); p<0.001 (see fig.2). 84% of those who were retreated with RTX recovered CD-R (77% of them did it in the following cycle). Half of the patients that reached CD-R maintained it in prospective cycles but 47% lost it subsequently. A third of the patients that lost either clinical response or B-cell depletion were switched to other medication without receiving further cycles. Overall, at the end of the study, 55% of all patients treated with RTX (400/723) remained in CD-R.

Conclusion: Most patients treated with RTX will achieve CD-R, but approximately half of them will lose this optimal status at some point. In patients who achieve CD-R but subsequently lose it, retreatment with RTX appears to be an effective strategy since 80% of them will regain it and will maintain long-term treatment with therapy

REFERENCES

SAT0145 ON TAPERING THERAPY FOR RA PATIENTS IN CLINICAL REMISSION; FLARE ON CS-DMARDS IS PREDICTED BY CLINICAL PARAMETERS AND ULTRASOUND, WHEREAS T-CELL ABNORMALITIES ARE PREDICTIVE FOR B-DMARD TAPERING
Hanna Gul, Frederique Ponchel, Paul Emery. Leeds Institute of Rheumatic and Musculoskeletal Medicine, Rheumatology, Leeds, United Kingdom

Background: Tapering of disease-modifying therapy (DMARDs) is recommended by EULAR/ACR for rheumatoid arthritis (RA) patients who achieve sustained remission on stable therapy(1,2). However, there is no guidance on how to manage this in clinical practice.

Objectives: We aimed to assess flare over 12 months in RA patients in sustained remission who were offered structured tapering of either conventional synthetic (cs) or biologic (b) DMARDs.

Methods: A prospective 12 year observational study was conducted in RA patients who were treated with RTX in Leeds. Consecutive cycles of RTX consisting of 2 infusions of 1000mg were administered either on clinical relapse or a 6-monthly basis. B-cells were measured using highly sensitivity flow cytometry at 0 and 2 weeks post-RTX. Complete depletion (CD) was defined by total B-cell count <0.0001x10⁹/L at week 2. Clinical response was defined by EULAR response criteria and CD-R was seen as the optimal outcome.

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Conclusion: Most patients treated with RTX will achieve CD-R, but approximately half of them will lose this optimal status at some point. In patients who achieve CD-R but subsequently lose it, retreatment with RTX appears to be an effective strategy since 80% of them will regain it and will maintain long-term treatment with therapy

REFERENCES
inflammation related cells, IRC) data were collected. Flare over a period of 12 months was assessed using several definitions in order to evaluate their relevance for clinical outcomes. Associations with baseline characteristics were assessed using univariate statistics (Mann-Whitney-U and Chi-square). No correction for multiple testing was attempted.

Results: 98 patients (cs-DMARDs n=66, b-DMARDs n=32) accepted tapering and achieved at least 12 months follow-up. In the cs-DMARD group 55% were female; the median age was 64 years and median remission duration 25 months. For b-DMARDs 63% were female; the median age was 61 years and median remission duration 28 months. There was great heterogeneity in terms of flare rate according to the definitions used (Figure 2). Flare on tapering b-DMARDs was more commonly observed (29-70%) compared to cs-DMARDs (24-52%). Demographics were not associated with flare by any definition (except longer disease duration for cs-DMARD patients who lost Boolean remission status). Clinical (notably seropositivity) and US measures were associated with flare for cs-DMARDs. Reduced Treg and higher IRC' at baseline were associated with flare in patients tapering b-DMARDs.

Conclusion: Flare rate varied with the definition used and was more great heterogeneity in terms of flare rate according to the definitions used (Figure 2). Flare on tapering b-DMARDs was more commonly observed (29-70%) compared to cs-DMARDs (24-52%). Demographics were not associated with flare by any definition (except longer disease duration for cs-DMARD patients who lost Boolean remission status). Clinical (notably seropositivity) and US measures were associated with flare for cs-DMARDs. Reduced Treg and higher IRC' at baseline were associated with flare in patients tapering b-DMARDs. These results will help formulate further tapering strategies.

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EFFECTS OF BIOLOGICAL DISEASE-MODIFYING ANTI-RHEUMATIC DRUG TREATMENT ON PHYSICAL ACTIVITY, MUSCLE POWER, AGILITY AND INHIBITION OF FALL IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: It has been demonstrated that biological DMARDs treatment rapidly improved sign and symptom in patients with rheumatoid arthritis (RA). Those were evaluated using composite measures or biomarkers in daily clinical practice or clinical studies. Although rapid improvement of composite measures or biomarkers is important in the treatment of RA, primary important goal of treatment is improvement of long term health-related quality of life (HR-QOL) [1]. HR-QOL is based on physical function such as muscle power and agility.

Objectives: This study investigated the efficacy of bDMARDs on physical function and fall risk in patients with RA.

Methods: Periodic evaluation of physical function by the staffs in rehabilitation center in our institute has been performed in addition to routine rheumatology evaluation (SDAI, biomarkers, mHAQ) in RA patient initiated their first bDMARDs treatment from Oct. 2015 to Feb. 2018. 47 cases was registered in total. Evaluation of physical function included evaluation of muscle power (grasping power [GP] and knee extension power [KEP]), agility (Time up and go test [TUG] and 10m walking time [10mW]) and questionnaire using mHAQ, portable fall risk index [2] and the 25-question geriatric locomotive function scale (locomo25) [3] at baseline (initiation of bDMARDs), 1month, 3months, 6months and 12months. Disease activity of RA (SDAI, CRP, MMP-3) was evaluated at same time point. Although 26 cases have passed one year from initiation of bDMARDs treatment, 9 cases dropped out from evaluation of physical function due to stopping of bDMARDs treatment or patient’s hope not to e evaluated on physical function or major joint surgery performed in patient which was influence physical function. Results of early 17 cases who completed evaluation at 12 months were investigated in this study.

Results: Baseline patients characteristics was as follow (n=17): mean age 59.1 years old, RA duration 13.7 years. Mean SDAI 19.6, mean CRP 1.9mg/dl. Used bDMARDs were tocilizumab in 5 cases, golimumab in 4 cases, etanercept in 3 cases, abatacept in 3 case, certolizumab in 1 case and infliximab-biosimilar in one case. Date is presents as mean values at baseline-1-3-6-12 months below. SDAI and CRP were significantly improved on and after one months except KEP at 3 months (GP [kg]: 12.3-14.1-15.9-16.9; KEP [kg]: 2.6-3.1-3.1-3.4-3.5). TUG at 10mW significantly improved on and after one months except TUC at 3months and 10mW at 3 months (TUG [s]: 9.3-8.0-8.2-7.3-7.4; 10mW[s]: 8.3-7.7-7.5-6.9-6.8). MHAQ significantly improved on and from 6 months (0.46-0.33-0.19-0.20-0.12). Locomo25 significantly improved on and from 1 month (31.7-30.6-28.5). Portable fall risk index significantly improved at only 12 months (8.8-8.6-7.8-7.6-6.8).

Conclusion: Signs and symptoms of RA were rapidly improved after the initiation of bDMARDs treatment and improvement of physical function was also rapidly improved. The changes from baseline and one month were more drastic in composite measure or biomarker of inflammation than that in muscle power and agility in respect with p-values. Inhibition of fall were achieved 12 months after bDMARDs initiation. These results suggested that physiotherapy might play an important role in RA patients treated with bDMARDs to gain more rapid improvement of physical function.

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Disclosure of Interests: None declared.


SAT0148 IMMUNOGLOBULIN A LEVELS IN ADDITION TO RHEUMATOID FACTOR PREDICTS REMISSION ACHIEVEMENT WITH ABATACET IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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Background: Biological disease modifying antirheumatic drugs (bDMARDs) now play an important role of clinical practice for patients with rheumatoid arthritis (RA). Abatacept (ABT) has a biologic agent that has an unique mechanism of action suppressing T lymphocyte activation. Although many prediction studies about therapeutic responses to bDMARDs for RA have been conducted to date [1], few studies has focused on ABT.

Objectives: The aim of this study was to identify predictive clinical biomarkers for remission achievement with ABT in RA patients.

Methods: We retrospectively reviewed consecutive patients with RA who started ABT from 2010 through 2018 in Keio University Hospital. We defined early ABT use as the initiation of ABT within two years from diagnosis without radiographic progression in hand X rays, and stratified the patients into the early ABT users and the late ABT users. Baseline characteristics were compared between patients who achieved CDAI remission achievement at 6 months and those who did not in both groups.

Results: One hundred and seven RA patients who were treated with ABT with baseline information available were enrolled in the study. Among them, 15 patients were classified into the early ABT users and 92 were the late ABT users, and the remission rates at 6 months were 40% and 24%, respectively. In the early ABT users, patients who achieved CDAI remission at 6 months showed significantly higher IgA levels than those who did not achieve remission (390 mg/dL vs 279 mg/dL, P=0.04, respectively). The difference in IgA disappeared in the late ABT users (332 mg/dL vs 313 mg/dL, P=0.60, respectively). Principal compont analysis revealed that in the early ABT users, patients who...
achieved remission and those who did not could not be clearly separated by the levels of IgA, IgG, rheumatoid factor, and albumin (Figure), whereas those baseline characteristics were mostly overlapped in the late ABT users (cut-off value for predicting remission with sensitivity and specificity in the early ABT users: IgA 342 mg/dL with 83% and 100%, IgG 1880 mg/dL with 50% and 100%, rheumatoid factor 152 IU/mL with 50% and 100%, albumin 3.7 g/dL with 88% and 67%, respectively). The area under the curves of receiver operating characteristic curves to predict remission were 0.833 of IgA and 0.778 of rheumatoid factor to predict response of ABT.

Conclusion: We identified serum IgA titer was the novel predictive factor for response of ABT.


Efficacy of Tocilizumab for Suppressing Radiographic Progression of Cervical Lesions in Patients with Rheumatoid Arthritis: Comparison with Methotrexate; Three Years of Follow-Up - A Multicenter Registry Study -

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Background: Cervical lesions are known to occur at high frequency as a complication of rheumatoid arthritis (RA). Treatment with biological agents are more clinically effective than the DMARDs that were in use previously, in particular, with their efficacy in suppressing joint destruction having been emphasized. We reported the efficacy of infliximab, anti-tumor necrosis factor antibodies for suppressing the radiographic progression of RA cervical lesions at ACR2009, EULAR2010, 11, 12, 13, 14, 16 and 18. However there is still few studies of efficacy of against RA cervical lesions of Tocilizumab (TCZ), anti-interleukin 6 receptor antibody.

Objectives: To evaluate the efficacy of TCZ for suppressing the radiographic progression of RA cervical lesions comparison with MTX for 3 years.

Methods: We used TCZ or MTX for treating Japanese patients with active RA who fulfilled the ACR criteria in 1987. The final study cohort of each 50 and 75 patients received continuous TCZ and MTX treatment for at least 3 years. For evaluation of cervical lesions, the atlanto-dental interval (ADI), the space available for the spinal cord (SAC), and the Ranawat value were measured by plain lateral radiographs in the flexion position, at initiation and Year 1,2 and 3.

Results: In the patients receiving TCZ (n=50) and MTX (n=75), the number of female were each 38(76%) and 52(69%) cases(p<0.046); the mean age was 58.7 ± 13.0 and 63.6 ± 11.0 years old (p=0.046); disease duration was 7.7 ± 7.8 and 8.0 ± 9.5 years (p = 0.027) and the mean dose of MTX was 9.2 ± 3.6 and 8.2 ± 2.9 mg/w (p=0.146). Clinical findings related to RA were as follows: CRP 4.2±3.4 and 1.7±2.3 mg/dl(p<0.001); ESR 55.0±24.0 and 31.9 ± 21.8 mm/h(p<0.001); MMP3 401 ± 311 and 223 ± 350ng/ml(p<0.001); the number of RF-positive 40 (80%) and 60(80%) cases(p<0.001); 2) During the follow up: joint pain (p < 0.0001), high HAQ (p < 0.001), high CRP (p<0.001), high ESR (p<0.001), high MMP3 (p<0.001), high RF (p<0.001), high anti-CCP (p<0.001) were increased. The number who was able to suppress progression of RA cervical lesions more than MTX treatment.

Conclusion: this study suggested that TCZ treatment can be used to suppress the progression of RA cervical lesions more than MTX treatment.

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SAT0151

TIME TO INITIATION OF BIOLOGIC DISEASE-MODIFYING ANTIRHEUMATIC DRUGS IN THE FRENCH COHORT ESPOIR

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Background: Access to biologic Disease-Modifying Anti-Rheumatic Drugs (DMARDs) of early rheumatoid arthritis (RA) patients is highly variable across countries and may depend on patient characteristics, disease expression, physicians behaviors as well as care organization in the patient region of living.

Objectives: 1) To assess the time to initiation of bDMARDs in the French cohort ESPOIR, and 2) To assess the factors associated with the timing of bDMARD initiation.

Methods: In this national multicenter cohort, 813 adult patients with suspected or confirmed early RA were included between December 2002 and March 2005, and followed up during 10 years. In the present analysis, we considered only patients who were fulfilling the ACR-EULAR 2010 criteria for RA at baseline. The primary outcome was the time to initiation of a biologic DMARD, in months, since diagnosis. It was assessed by Cox model based survival analysis with time dependent covariates; the threshold used for p-value was 0.05. Predictors colinearity was then assessed by adjusted tests. All statistical analysis were done with R version 3.5.1.

Results: Among the 658 patients fulfilling the ACR-EULAR 2010 criteria for RA (77% women, 52% smokers at baseline, mean-aged 48 at diagnosis, with positive RF in 46.6%, positive ACPA in 43% and polyarticular presentation at baseline in 54.5%), 178 patients (31%, CI 95%=27%-34.7%) initiated a biologic DMARD during the 10-year follow-up (Figure 1). Variables associated with an earlier bDMARD initiation included: 1) at baseline: younger age (p = 0.0016), younger age of first joint pain (0.0014), younger age of first joint swelling (0.0014), 2) during the follow up: joint pain (p < 0.0001), high HAQ (p < 0.0016).

SAT0150

EFFICACY OF TOCILIZUMAB FOR SUPPRESSING RADILOGRAPHIC PROGRESSION OF CERVICAL LESIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS COMPARISON WITH METHOTREXATE; THREE YEARS OF FOLLOW-UP - A MULTICENTER REGISTRY STUDY -
PREVALENCE AND SUCCESS OF 1,25(OH)₂D AND IL-6 BLOCKADE SYNERGISTICALLY

Figure 1: Biotherapy cohort in the ESPORI cohort

Table 1. Results of the multivariate analysis

<table>
<thead>
<tr>
<th>Covariates</th>
<th>Hazard-ratio (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of 1st joint pain</td>
<td>0.97 (0.96; 0.98)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>DAS28</td>
<td>2.04 (1.84; 2.26)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Structural damage on X-rays</td>
<td>2.90 (1.64; 3.22)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Positive ACBA</td>
<td>2.01 (1.40; 2.89)</td>
<td>0.000176</td>
</tr>
</tbody>
</table>

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Disclosure of Interests: Jatin Misty: None declared, Catherine Smith: None declared, Malama Sumbwanyame: None declared, Margaret Sibley: None declared. Patrick KIELY Paid instructor for: Amgen, Gilead, BMS, Speakers bureau: Abbvie, BMS, UCB, Lilly, Pfizer

SAI0153
1,25(OH)₂D AND IL-6 BLOCKADE SYNERGISTICALLY REGULATES RHEUMATOID ARTHRITIS VIA SUPPRESSION OF TH17 AND OSTEOCLASTOGENESIS
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Background: Immune cells express vitamin (vit) D receptor and vit D is known as a potent immune-modulator.

Objectives: To assess the prevalence and success of subcutaneous bDMARDs in routine care, per disease indication and bDMARD class, and the cost saving implications.

Methods: Dose interval information was collected prospectively in patients on subcutaneous bDMARDs with RA, PsA and AS attending for routine review at St George’s University Hospitals NHS Foundation Trust from October – November 2018. Department practice is that bDMARD dose reduction is discussed (but not mandated) with patients in sustained remission on a ‘try and see’ basis, without TDM.

Results: Data on 88 patients (female 46) were collected, RA 39, PsA 36, AS 13, mean age 50 years (range 24-78), TNFi n=75, other bDMARDs n=13. The dose interval was per licence in 79.5%, less frequent in 18% and more frequent in 2.5%. In those taking a bDMARD less frequently than per licence, the dose interval was increased by a mean 2.15 x licenced interval (range 1.14 – 6 x); in RA 1.88x, PsA 2.12x and AS 2.64x. Dose reduction had been attempted in 32%, but failed due to loss of efficacy in 43% of these (13.6% of entire cohort), including 50% with RA, 46% PsA and 20% AS. In those attempting a dose reduction, there was no difference in the% sustaining this for Etanercept 57% (8/14) and Adalimumab 50% (5/10) but lower for all TNFi (54%, 13/24) treated patients compared to other bDMARDs (75%, 3/4).

Dose reduction had not been attempted at any stage in 66% (RA 72%, PsA 61%, AS 62%). Cost savings from 16 patients with sustained dose reduction over 3 years in this cohort were £97,653, extrapolated to 18% of the entire population (~1500) on subcutaneous bDMARDs at our Trust makes £1.65 million saving over 3 years.

Conclusion: ‘Try and see’ dose reduction of subcutaneous bDMARDs has been attempted in one third of patients in routine care, with more success in AS where 80% sustained a lower dose at a mean 2.64 x licenced interval, compared to 50% of RA and 54% PsA patients at 1.88 and 2.12 x licenced interval respectively. Guidelines, possibly based on TDM, are needed to optimise current practice which falls short of the success of dose reduction in clinical trials (3). Even with a ‘try and see’ approach failing in 43% of attempts, the cost savings are very substantial to the healthcare economy.
seems to suppress Th17 and osteoclasts differentiation in RA patients in synergy with tocilizumab.

REFERENCE


Disclosure of Interests: None declared

SA10154
STABILIZATION OF RHEUMATOID ARTHRITIS ASSOCIATED INTERSTITIAL LUNG DISEASEBY RITUXIMAB: A SINGLE CENTER EXPERIENCE WITH LONG-TERM FOLLOW-UP

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Background: Interstitial lung disease (ILD) is the most significant pulmonary manifestation of Rheumatoid Arthritis (RA) [1], contributing to decreased quality of life, progressive chronic disability and high utilization of healthcare resources. Treatment is challenging with mixed results from different biologics while Riluximab (RTX) has the most encouraging data based on retrospective observational studies. [2]

Objectives: To evaluate the efficacy and safety of RTX in patients with RA-ILD in the context of daily practice.

Methods: Observational retrospective study (2009-2019) of patients with a diagnosis of RA-ILD from a cohort of RTX-treated RA patients in the University Hospital of Heraklion. ILD was diagnosed by HRCT and monitored by means of pulmonary function tests (PFTs), HRCT and 6-minute walking test (6MWT, clinically important difference >50 m). RTX was used at standard dose (1 gr x2/6 months). ILD progression was defined by any of: decrease of pre-RTX forced vital capacity (FVC) >10%, or diffusion capacity of carbon monoxide (DLCO) >15% predicted score, or death from progressive ILD. Improvement was defined by any of: increase of pre-RTX FVC >10% or DLCO >15% predicted. All other patients were classified as having stable disease. RA activity was assessed by DAS28 (ESR).

Table: Baseline End of follow-up

<table>
<thead>
<tr>
<th>ESR (n)</th>
<th>Baseline</th>
<th>Follow-up</th>
</tr>
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<tbody>
<tr>
<td>Stable</td>
<td>10/12(83.9%)</td>
<td>9/12(75%)</td>
</tr>
<tr>
<td>Improvement</td>
<td>2/1(20%)</td>
<td>2/1(20%)</td>
</tr>
<tr>
<td>Worsening</td>
<td>0/2(0%)</td>
<td>0/3(0%)</td>
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<table>
<thead>
<tr>
<th>FVC, n (%)</th>
<th>Baseline</th>
<th>Follow-up</th>
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<tr>
<td>Stable</td>
<td>10/17(59%)</td>
<td>10/17(59%)</td>
</tr>
<tr>
<td>Improvement</td>
<td>1/12(8.3%)</td>
<td>1/12(8.3%)</td>
</tr>
<tr>
<td>Worsening</td>
<td>1/12(8.3%)</td>
<td>1/12(8.3%)</td>
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<table>
<thead>
<tr>
<th>DLCO, n (%)</th>
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<td>10/17(59%)</td>
<td>10/17(59%)</td>
</tr>
<tr>
<td>Improvement</td>
<td>1/12(8.3%)</td>
<td>1/12(8.3%)</td>
</tr>
<tr>
<td>Worsening</td>
<td>1/12(8.3%)</td>
<td>1/12(8.3%)</td>
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</table>

<table>
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<tr>
<th>HRCT, n (%)</th>
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<td>Stable</td>
<td>11/35(31.4%)</td>
<td>11/35(31.4%)</td>
</tr>
<tr>
<td>Improvement</td>
<td>1/27(3.7%)</td>
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<tr>
<td>Worsening</td>
<td>2/27(11.1%)</td>
<td>2/27(11.1%)</td>
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<table>
<thead>
<tr>
<th>DAS28 (ESR) (median IQR)</th>
<th>Baseline</th>
<th>Follow-up</th>
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</thead>
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<tr>
<td>Stable</td>
<td>3.0(2.9-4.9)</td>
<td>2.1(2.9-5.5)</td>
</tr>
<tr>
<td>Improvement</td>
<td>1.0(1.0-1.2)</td>
<td>1.0(1.0-1.2)</td>
</tr>
<tr>
<td>Worsening</td>
<td>2.0(1.0-2.7)</td>
<td>2.0(1.0-2.7)</td>
</tr>
</tbody>
</table>

Results: Of 247 RA patients treated with RTX, 16 (11 women, 5 men) had RA-ILD (prevalence 6.5%). 12/16 (75%) had radiographic pattern of UIP and 4/16 (25%) had NSIP. 9/16 (56%) were positive for ACPA and/or RF. The median (IQR) age at RTX initiation was 66 (54-77) years, ILD duration prior to RTX was 5.2 (1-15) years. Number of prior biologics was 1 ± 4 and 11/16 (69%) had been treated with concomitant DMARDs. 1/16 (6.25%) had previously received Cyclophosphamide. Concomitant COPD was present in 3/16 (19%) of the patients. Follow-up while on RTX was 37 (6-136) months. The overall dose of RTX was 13 (2-40) q. Following RTX treatment, new-onset ILD was diagnosed in 3/247 patients (incidence=1.2%). During follow-up, data for ILD were available for 13/16 patients. Post-RTX, 10/13(76%) showed stabilization, 1/13 (7.7%) had improvement, while 2/13(15.3%) had progression of RA-ILD. 1/16(6.25%) switched to Cyclophosphamide. During follow-up period, 6 admissions were recorded due to infections (4 for community-acquired pneumonia and 2 for hospital-acquired pneumonia) and 1/16(6.25%) patient died after progression of ILD.

Conclusion: In this cohort of RA-ILD, the majority of patients treated with RTX showed stabilization of lung disease, while RA improved significantly, over a prolonged follow-up period. RTX appears to be an acceptable and safe therapeutic choice for patients with RA-ILD. Nevertheless, randomized studies are warranted to prove any clinical effectiveness of RTX in RA-ILD.

REFERENCES


Disclosure of Interests: None declared

SA10155
THE PRESENCE OF ANTI-NUCLEAR ANTIBODIES BEFORE ANTI-TNF THERAPY IS A RISK FACTOR FOR THE APPEARANCE OF ANTI-DRUG ANTIBODIES IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: TNF inhibitors (TNFi) revolutionized the treatment of rheumatoid arthritis (RA), but have often developed anti-drug antibodies (ADrA) and also induced other autoimmune pathology. [1, 2].

Objectives: To determine whether the presence of anti-nuclear antibodies (ANA) predict the development of ADrA and clinical efficacy in RA patients treated with TNFi, infliximab (IFX) or adalimumab (ADA).

Methods: A total of 92 RA patients, 38 cases treated with IFX and 54 cases with ADA, were prospectively enrolled. Observation period of IFX-treated group was 3 years, and that of ADA-treated group was 1 year. ANA were measured by indirect fluorescent assay using a Computer-aided microscope system with HEp20-10 cells. The concentrations of anti-IFX antibodies (HACA) and anti-ADA antibodies (AAA) were measured by radioimmunoassay at Sanquin Diagnostic Services, Netherlands. Clinical response to therapy was judged by EULAR response criteria based on Disease Activity Score (DAS) 28-CRP.

Results: Thirteen (34.2%) of 38 patients in IFX group and 18 (33.3%) of 54 patients in ADA group became positive for HACA and AAA, respectively, during the treatment. All of the ADA-positive patients were ANA-positive before the therapy. In contrast, none became ADA-positive after treatment in 15 RA patients negative for ANA before therapy (6 cases in IFX group and 9 cases in ADA group), and the positive rate for ADrA was significantly different between ANA-positive and negative patients (p=0.0018). In addition, the positive rate for HACA was significantly higher in patients positive for ANA titers of ≥640 (p=0.034), but that for AAA was not related to ANA titers. Next, ANA became positive in 4 of 6 ANA-negative patients and AAA titers increased in 21 of 32 ANA-positive patients after IFX treatment. HACA positive rate was significantly higher in patients with ANA titers of ≥640 after IFX treatment (p=0.0045). AAA titers of patients in ADA group were mostly unchanged after treatment, and were not related to the appearance of AAA.

Disclosure of Interests: None declared
Continuation rate of TNFi (IFX and ADA) treatment was significantly lower in ADRa-positive patients than in those negative (p = 0.0066 and p = 0.0127, respectively). In IFX group, patients with ANA titers of ≥160 before treatment and those with ANA titers of ≥320 after treatment positive showed worse EULAR treatment response (p = 0.037 and p = 0.033, respectively). In ADA group, 7 of 9 ANA-negative patients before treatment showed moderate or good EULAR response, but positive ANA both before and after treatment was not connected with to the clinical response.

Conclusion: The presence of ANA before IFX or ADA is a risk factor for the appearance of ADRa, while ADRa did not appear in any patient negative for ANA before treatment. ANA of high titers before and after IFX treatment predicted existence of ADRa and possibly leading to the treatment failure.

REFERENCES

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METHOTREXATE DISCONTINUATION AND DOSE DECREASES AFTER THERAPY WITH TOCILIZUMAB: RESULTS FROM THE CORRONA RHEUMA TOID ARTHRITIS REGISTRY

Dimitrios A. Pappas1,2, Taylor Blachley2, Steve Zlotnick3, Jennie H. Best3, Kelechi Emereunru5, Joel Kremer4,5. 1Columbia University, New York, United States of America; 2Corrona, LLC, Southborough, United States of America; 3Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, United States of America; 4Albany Medical College and The Center for Rheumatology, Albany, United States of America

Background: Methotrexate (MTX) is frequently prescribed with biologic disease-modifying antirheumatic drugs. Evidence has shown that tocilizumab (TCZ) monotherapy is effective in the treatment of patients with rheumatoid arthritis (RA). Similar outcomes have been shown in patients responding to TCZ combination therapy who discontinued MTX or remained on combination therapy.

Objectives: To examine MTX discontinuation and dose decreases in patients with RA initiating TCZ and to describe disease activity outcomes in a real-world setting.

Methods: TCZ-naive patients enrolled in the Corrona RA Registry who initiated TCZ and had a 6-month follow-up visit without discontinuation of TCZ were included. Patients were grouped by MTX dose at the time of TCZ initiation (≤ 10 mg, > 10 to ≤ 15 mg, > 15 to ≤ 20 mg, > 20 mg). The primary outcome was the proportion of patients with changes in MTX use at 6 months. Changes in disease activity (Clinical Disease Activity Index [CDAI]) and patient-reported outcomes (PROs) over the follow-up period were described.

Results: Of 444 eligible patients, 82.7% were female, and 83.7% were white, with a mean (SD) disease duration of 11.6 (9.3) years and a baseline CDAI score of 24.0 (15.4). The mean (SD) MTX dose at baseline was 17.7 (5.8) mg. Overall, a total of 139 patients (31.3%) discontinued or decreased MTX at 6 months (overall mean [SD] dose change, −3.0 [7.5] mg); across baseline MTX dose groups, the proportion of patients who discontinued or decreased MTX at 6 months ranged from 28.2% to 38.2%. Improvements in CDAI scores and PROs were observed at 6 months for all baseline MTX dose groups and in patients who discontinued, decreased, maintained, or increased MTX doses at 6 months (Table 1). Similar patterns and results were observed at 12 months (not shown).

Conclusion: A considerable proportion of patients initiating TCZ were able to discontinue or decrease the dose of MTX after TCZ initiation. Patients who were able to discontinue or decrease MTX experienced similar improvements in disease activity and functionality. Discontinuing or decreasing MTX may be an effective treatment strategy for patients initiating TCZ combination therapy.

REFERENCES

Acknowledgement: This study was sponsored by Corrona, LLC, and the analysis was funded by Genentech, Inc. Access to study data was limited to Corrona, and Corrona statisticians completed all of the analyses; all authors contributed to the interpretation of the results. Corrona has been supported through contracted subscriptions in the last 2 years by AbbVie, Amgen, Boehringer Ingelheim, Crescendo, Eli Lilly and Company, Genentech, Gilead, GSX, Janssen, Merck, Momenta Pharmaceuticals, Novartis, Pfizer Inc, Regeneron, Roche, Sun, UCB and Valeant.


REAL-WORLD EVALUATION OF PERSISTENCE WITH EARLY-LINE ABATACEPT VERSUS TUMOR NECROSIS FACTOR-INHIBITORS FOR RHEUMATOID ARTHRITIS COMPLICATED BY POOR PROGNOSTIC FACTORS

Damian Del Puello1, Ilina Yermilov2, Sarah Gibbs2, Michael Broder2, 1Bristol-Myers Squibb, Lawrenceville, NJ, United States of America; 2Partnership for Health Analytic Research, LLC, Beverly Hills, CA, United States of America

Background: Abatacept reduces signs and symptoms, inhibits the progression of structural damage, and improves physical function in adult patients with moderately to severely active rheumatoid arthritis (RA). Real-world data on its use as an early-line biologic agent are limited.

Objectives: To assess 12-month treatment persistence in early-line abatacept versus tumor necrosis factor inhibitor (TNFi) treated patients with RA complicated by poor prognostic factors.

Methods: We performed a multicenter retrospective medical record review of adult RA patients with poor prognostic factors treated at 5 United States clinics located in the West, Midwest, and Southeast. Patients were treated with abatacept or TNFi as the first biologic treatment at the clinic (defined as early line). Poor prognostic factors included positive anti-cyclic citrullinated peptide antibodies, positive rheumatoid factor antibodies, increased C-reactive protein levels, elevated erythrocyte sedimentation rate levels, or presence of joint erosions. TNFis included adalimumab, etanercept, infliximab (and their biosimilars), certolizumab pegol, or golimumab. Data were collected from biologic treatment initiation (between 8/9/11 and 11/4/16), for ≥1 year. Patients with Crohn’s disease, ankylosing spondylitis, psoriatic arthritis, or anul fistula were excluded. Demographic, disease, and treatment information (start, stop, reason for discontinuation) was abstracted. Treatment persistence (continuation of index treatment with gap ≤60 days) at 12 months and time to discontinuation were reported. Multivariate logistic and Cox regressions were used to compare 12-month persistence and overall discontinuation rate between abatacept and TNFi, controlling for demographic and clinical characteristics (age, sex, Charlson comorbidity index, RA duration), baseline utilization, and clinic.

Results: Data on 209 patients (88 abatacept, 121 TNFi) were collected. Abatacept patients were older than TNFi patients (64.36 vs. 57.23 years, p = 0.001). There were no significant differences in either gender (79.55% vs. 72.73% female, p = 0.257) or duration of treatment at the clinic (5.79 vs. 5.10 years, p = 0.226) in the abatacept and TNFi cohorts. Median time to discontinuation was 1,672 days for abatacept vs. 612 days for TNFi (p = 0.002). At 12 months, 86.36% of abatacept patients were persistent
vs. 65.29% of TNFi patients (p<0.001). In the Cox model, rate of discontinuation was 77% higher in TNFi patients (Hazard Ratio 1.767, 95% Confidence Interval (CI) 1.133-2.806, p=0.0158). In the logistic regression, the odds of TNFi patients being persistent at 12 months was 52% lower than abatacept patients, although this statistic was not statistically significant (Odds Ratio 0.485, 95% CI 0.208-1.33, p=0.0947). Reasons for discontinuation of index treatment differed between cohorts, including discontinuation due to disease progression (27.76% vs. 53.85%), insurance coverage (15.44% vs. 12.82%), and adverse events of medication (27.8% vs. 11.54%) in abatacept and TNFi patients, respectively (p<0.001).

Conclusion: In a real-world setting, RA patients with poor prognostic factors are significantly less likely to discontinue abatacept compared with TNFi patients. This difference may be explained by the lower proportion of patients discontinuing abatacept due to disease progression or adverse events related to medication.

Disclosure of Interests: Damamrie Paul Shareholder of: Bristol-Myers Squibb, Employee of: Damamrie Paul is an employee of Bristol-Myers Squibb, Jirina Yermilov Employee of: I am an employee of the Partnership for Health Analytic Research (PHAR) LLC, which was paid by BMS to conduct the research described in this abstract, Sarah Gibbs Employee of: I am an employee of the Partnership for Health Analytic Research (PHAR) LLC, which was paid by BMS to conduct the research described in this abstract. DOI: 10.1136/annrheumdis-2019-eular.331

Table. Cox-regression analysis. HR for discontinuation of golimumab

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<tr>
<th>Hazard Ratio</th>
<th>95% Confidence Interval</th>
<th>p</th>
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<tr>
<td>Candler (men vs women)</td>
<td>1.83</td>
<td>(1.17-2.95)</td>
</tr>
<tr>
<td>Age at golimumab initiation</td>
<td>1.09</td>
<td>(0.96-1.03)</td>
</tr>
<tr>
<td>Smoking habit (smoker vs non-smoker)</td>
<td>1.32</td>
<td>(0.94-1.85)</td>
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<tr>
<td>Smoking habit (past smoker vs non-smoker)</td>
<td>1.12</td>
<td>(0.89-1.47)</td>
</tr>
<tr>
<td>Overweight (vs normal)</td>
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<td>(0.87-1.92)</td>
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<tr>
<td>Obesity (vs normal)</td>
<td>1.17</td>
<td>(0.77-1.77)</td>
</tr>
<tr>
<td>Second vs first biological drug</td>
<td>2.41</td>
<td>(1.69-3.43)</td>
</tr>
<tr>
<td>Third vs first biological drug</td>
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<td>RA vs PsA</td>
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<td>Other DMARD</td>
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<td>(1.23-3.63)</td>
</tr>
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</table>

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Disclosure of Interests: Manuel Pombo: None declared, Carlos Sánchez-Piedra: None declared, Eduardo Cuende: None declared, Raquel Martín-Domenech: None declared, Javier del Pino: None declared, Cristina Campos-Fernández: None declared, Javier Manero: None declared, Blanca García-Magallon: None declared, Fernando Sánchez-Alonso: None declared, Federico Diaz-Gonzalez: None declared, María J. Arteaga: None declared, Luis Cea-Calvo: None declared, J. Juan. Gómez-Reino: None declared, Hospital Clínico Universitario de Santiago, Santiago de Compostela, Spain; Spanish Society of Rheumatology (SER), Madrid, Spain; Rheumatology (SER), Madrid, Spain; Hospital Principe de Asturias, Madrid, Spain; Hospital Clínico Universitario de Salamanca, Salamanca, Spain; Hospital Universitario de Gran Canaria Doctor Negrín, Las Palmas, Spain; Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain; Merck Sharp and Dohme, Madrid, Spain.

Background: Survival, or persistence in treatment with a biological drug can be considered an indirect measure of efficacy, safety and tolerability.

Objectives: We assessed the probability of persistence (survival) of treatment with golimumab in patients with rheumatic diseases and the factors associated to persistence with up to 6 years of follow-up.

Methods: BIOBADASER is the Spanish registry of biological drugs of the Spanish Society of Rheumatology and the Spanish Medicines Agency. A data-base analysis was done in December 2018 on all the patients aged 18 years or more who had initiated golimumab for one of the approved indications (rheumatoid arthritis [RA], axial spondyloarthritis [SpA] or psoriatic arthritis [PsA]). The probability of persistence was calculated with a Kaplan-Meier test. Factors related to persistence were analyzed with a Cox-regression model.

Results: 581 patients were included (165 [29.4%] RA, 249 [42.9%] axial SpA and 167 [28.7%] PsA), mean age 51 [12] years, 53% women. Median duration of disease at the onset of golimumab was 8.0 (3.0-14.7) years. Golimumab was prescribed as first biological drug in 37.9% of the patients, as second in 32.1% and as third or further in 30.0%. Concomitant medications at golimumab initiation included steroids (28.2%), methotrexate (MTX) (35.5%), sulphasalazine (7.2%) and leflunomide (13.9%). The probability of persistence of treatment with golimumab since treatment initiation included steroids (28.2%), MTX (35.5%), sulphasalazine (7.2%) and leflunomide (13.9%).

The probability of persistence of treatment with golimumab since treatment initiation was 74.3% at year 1 (95% CI 70.3 – 77.8), 63.5% at year 2 (59.0 – 67.8), 60.5% at year 3 (55.9 – 65.8), 54.5% (49.1 – 59.7) at year 4 and 5, and 52.1% (44.9 – 57.7) at year 6. Persistence was higher when golimumab was used as first biological agent (p-log rank <0.001) and for the treatment of axial SpA or PsA compared to RA (p-log rank <0.001). As first biological drug the probability of persistence was 82.8% (year 1) and 66.5% at year 4. At year 5, survival rates (all lines of therapy) were 59.7, 63.4% and 37.3% for axial SpA, PsA and RA respectively. Cox-regression analysis (table) showed that the probability of persistence in treatment with golimumab therapy was higher in first vs second or third biological line patients (Hazard Ratio [HR] for discontinuation: 1.78 for second and 2.41 for third or further line versus first line), in SpA and PsA patients (HR discontinuation of RA patients: 1.94 versus PsA), and lower in women (HR: 1.62), in those needing steroids (HR: 1.47) or DMARDs different to MTX (HR: 2.17). Patients treated with MTX had higher but non-significant persistence rate (HR discontinuation 0.79, table).

Conclusion: The probability of persistence (survival) on therapy with golimumab was high up to 6 years of follow-up and was higher in patients treated with golimumab vs PsA and SpA, and lower in those needing steroids, DMARDs different to MTX and in women.

Table. Cox-regression analysis. HR for discontinuation of golimumab
PREFERENCES OF EUROPEAN RHEUMATOLOGISTS ON THE DISCONTINUATION OF BIOLOGICAL DISEASE- MODIFYING ANTIRHEUMATIC DRUGS IN PATIENTS WITH RHEUMATOID ARTHRITIS

Lukas Schlager, Michaela Loiskandl, Daniel Aletaha, Helga Radner. Medical University of Vienna, Department of Rheumatology, Vienna, Austria

Background: The introduction of biologic disease-modifying antirheumatic drugs (bDMARDs) revolutionized the treatment of rheumatoid arthritis (RA) and made remission (REM) or low disease activity (LDA) a realistic goal for most patients. It was shown that the discontinuation of bDMARDs in patients in REM or LDA is feasible (1,2) and that the physician’s opinion plays an important part in the decision to discontinue (3). However, there is no reliable way of identifying patients who would benefit from bDMARD discontinuation after reaching REM or LDA.

Methods: A systematic literature review was conducted with the aim of identifying predictors of successful bDMARD discontinuation in RA patients. Rheumatologists were asked to state whether they find the presented parameter important to support their decision to discontinue bDMARD therapy or not. They also had the opportunity to state parameters they consider important.

Results: 313 rheumatologists from 29 different European countries responded. Most of the participants have been practicing for 10 to 20 years and see 10 to 25 RA patients per week. The majority of the parameters were considered important by the participants, with 19 out of the 34 presented parameters being considered important by $\geq 70\%$. The most commonly considered parameters were (percentage of participants who considered the parameter important): Time in REM or LDA (99%), disease activity score – 28 joints (90%), smoking status (35%), gender (13%), interleukin-6 (9%), rheumatoid factor (41%), and shared epitope (8%). An overview of responses is given in figure 1 and figure 2. The most frequently mentioned parameter in the comments was the patient’s opinion on discontinuation (n=28).

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Figure 1. Opinion on presented parameters

Figure 2. Opinion on presented parameters
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[3] Strand V, Miller P, Williams SA, Saunders K, Grant S, Kremer J. Discontinu-
ity of Biologic Therapy in Rheumatoid Arthritis: Analysis from the Cor-

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SAT0161

SUSTAINED MODERATE DISEASE ACTIVITY (SMDA) IN RHEUMATOID ARTHRITIS PATIENTS ON BIOLOGIC THERAPIES IS ASSOCIATED WITH 5 YEARS FUNCTIONAL LIMITATION AND SERIOUS ADVERSE EVENT DEVELOPMENT: EVIDENCE TO SUPPORT TREAT-TO-TARGET APPROACH FOR PATIENTS IN SMDA AND ESPECIALLY THOSE IN HIGH SMDA

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Background: Registry data have shown that treatment with biologic disease modifying antirheumatic drugs (bDMARDs) induces remission or low disease activity in up to 50% of Rheumatoid Arthritis (RA) patients, yet 30-50% of patients remain in moderate disease activity (MDA) with limited data on their long-term prognosis 1.

Objectives: To assess the long-term outcome of RA patients with sustained MDA on bDMARDs, in clinical practice.

Methods: We analyzed data from the Hellenic Registry of Biologic Therapies. Disease activity, function, treatments of patients starting a bDMARD are recorded prospectively every 3-6 months. Herein, we included patients with at least 5 years of follow-up, irrespective of treatment switches. If DAS28-ESR was at the same disease activity range for at least 50% of the follow-up time, patients were assigned to one of 3 main groups: sustained remission or low disease activity (sRLDA) with DAS≤3.2, sustained moderate disease activity (sMDA) with 3.2<DAS≤5.1 and sustained high disease activity (sHDA) with DAS>5.1. Patients in sMDA were further divided into subgroups low and high sMDA (50% of follow-up has DAS lower or greater than 4.2 respectively). Function at 5 years based on Health Assessment Questionnaire (HAQ) was the primary outcome, while cumulative serious adverse events (SAEs) and bDMARDs switches were also analyzed.

Results: Out of 527 patients with available data, 90 (17%), 295 (56%) and 142 (27%) were assigned to sRLDA, sMDA and sHDA groups respectively. At baseline, sMDA patients were older, more often women, had received more csDMARDs and had higher DAS, HAQ and EuroQol status compared to sRLDA group. During follow-up, sMDA patients had more bDMARDs switches as compared to sRLDA (mean t sd: 1.82 ±1.03 vs 1.26 ±0.53, p<0.0001). Notably, patients in sMDA had significant improvement in HAQ at 5 years compared to baseline (p<0.0001), yet they presented significantly higher HAQ compared to sRLDA group (mean t sd: 0.55 ±0.47 vs 0.30 ±0.31, p<0.0001). Trajectories of longitudinal HAQ for groups sRLDA, sMDA and sHDA, were clearly differentiated during treatment course (Figure 1). Clusters sRLDA, sMDA and sHDA also displayed differential 5 years outcomes (p<0.0001) regarding SAEs (Figure 1). Interestingly, within sMDA patients, the low sMDA patient subgroup had better long-term outcome (p<0.05) concerning both HAQ at 5 years and cumulative SAEs as compared to patients in high sMDA subgroup.

Conclusion: In clinical practice 56% of RA patients on bDMARDs have sustained MDA in spite of bDMARDs switches, presenting 5 years worse functional status and more SAEs compared to patients in sRLDA. These data support the treat-to-target approach for patients in sMDA and especially those with high sMDA.

REFERENCE


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SAT0162

A POOLED ANALYSIS OF 1-YEAR CLINICAL OUTCOMES AMONG 6-MONTH RESPONDERS AND NON-RESPONDERS FROM THREE RANDOMISED CONTROLLED STUDIES OF TNF INHIBITOR BIOSIMILARS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: SB4, SB2, and SB5 are biosimilars of etanercept, infliximab, and adalimumab. Phase III randomised, double-blind studies were conducted to compare efficacy and safety between biosimilars and reference products.

Objectives: Assess and compare 1-year outcomes among 6-month responders and non-responders.

Methods: Patients who had 6-month data from each phase III study were pooled and categorised, based on their disease status at 6 months (week 24 for etanercept and adalimumab and week 30 for infliximab) and 1 year (week 52 for etanercept and adalimumab and week 54 for infliximab).

Responders included patients who achieved an ACR20 response or low disease activity (including remission) by DAS28, SDAI, and CDAI at 6 months. Those who did not or dropped out were considered non-responders.

Primary outcome was the proportion of responders who maintained responses from 6 months to 1 year or non-responders at 6 months who achieved responses at 1 year.

Results: Data from 1461 patients were included in the analysis. For all treatments combined, 81.1% of ACR20 responders, 69.6%, 77.8%, and 77.0% of responders with DAS28, SDAI, and CDAI low disease activity (LDA) at 6 months maintained their responses at 1 year, and 33.9%, 18.8%, 26.7%, and 24.9% of 6-month non-responders achieved responses at 1 year, respectively. The proportions of patients maintaining or achieving an ACR20 response or DAS28, SDAI, and CDAI LDA at 1 year were similar across different treatment groups (Table 1).
Conclusion: A pooled analysis of TNF inhibitor biosimilars and reference products showed that about 20-30% of responders lost their response, while about 20-30% gained it. Thus, the overall stability of disease fluctuation in our 1-year phase III studies is a consequence of a similar success and failure rate. The validity of the data can be seen by the similarities in these outcomes between different types of TNF-inhibitors and similarity between biosimilars and respective reference products.

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Background: Rheumatoid arthritis (RA) patients (pts) have a 1.5 to 2-fold increased risk for cardiovascular (CV) events and CV mortality [1]. Traditional risk factors as well as underlying disease, including therapy with glucocorticoids (GC) contribute to the increased CV risk. Typical risk factors include age, male sex, hypertension, adiposity, and diabetes mellitus [2].

Objectives: The exploratory post-hoc analysis of the non-interventional study (NIS) ICHIBAN (NCT 01194401, final dataset) investigated the CV risk of RA pts during intravenous tocilizumab (TCZ) treatment over 2 years. Materials: Data of 3164 pts (total) who received at least one dose of TCZ were available. Analysis focuses on the CV events myocardial infarction (MI), coronary heart disease (CHD), and stroke. The incidence of respectively treatment-emergent adverse events (TEAEs) (according to MedDRA preferred term) and/or AESs of special interest (AESIs, recorded by the investigator) was evaluated. The following risk factors (at baseline (BL)) were analysed: sex, age, smoking status, RA duration, DAS28, CDAI, seropositivity, CRP, comorbidities, previous therapies, concomitant therapies, and combinations thereof.

Results: At BL, pts were more frequently female (74.8%), on average 55.5 years old, had a mean BMI of 26.9 kg/m2, and mean RA duration of 9.7 years. 72% of pts suffered from comorbidities (37% hypertension, 17% osteoporosis, 10% diabetes mellitus). The majority (66.4%) was pre-treated with TNF inhibitors, while 30.0% received csDMARDs only. Co-medication was csDMARDs in 50.7% of pts and GC in 60.6%. Overall, 46.6% of pts experienced at least 1 TEAE. The rate of pts who experienced a CV event was 0.8% for MI, 0.4% for CHD, and 0.6% for stroke (Table 1).

Table 1 Treatment-emergent adverse events (TEAEs) during TCZ treatment

<table>
<thead>
<tr>
<th>Event</th>
<th>Rate of pts (%)</th>
<th>Rate of AEs per 100 patient years</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI</td>
<td>0.4</td>
<td>4.6 (1474)</td>
</tr>
<tr>
<td>CHD</td>
<td>0.6</td>
<td>14.9 (472)</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.5</td>
<td>6.9</td>
</tr>
</tbody>
</table>

For patients with typical risk factors a higher rate of CV events was observed: male pts, pts of higher age, pts who were anti-CCP negative, and pts who suffered from diabetes mellitus, coronary heart disease (only for CHD), asthma, and renal insufficiency (see Table 2 for details; exploratory p-values are given).

Interestingly, no differences were observed between subgroups of smoking status, RA duration, DAS28, CDAI, CRP, previous therapies, concomitant therapies, and combinations thereof (data not shown).

Conclusion: In the NIS ICHIBAN, with its long-lasting patient population, the rate of CV events during TCZ treatment was comparable to former
investigations [1, 3, 4]. In pts with the typical risk characteristics at BL, i. e. male sex, higher age, diabetes mellitus, and CHD, higher rates of CV events were observed. In addition, increased rates were also found in anti-CCP negative pts and in pts with asthma or renal insufficiency

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SAT0164

COMPARISON OF THE RETENTION RATE OF EACH BIOLOGICAL DISEASE-MODIFYING ANTI-RHEUMATIC DRUG GROUP ACCORDING TO THE STATUS AND CONCENTRATION OF ANTI-CYCLIC CITRULLINATED PEPTIDE ANTIBODY AND RHEUMATOID FACTOR: DOUBLE CENTER CLINICAL STUDY

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Background: Although biological disease-modifying antirheumatic drugs (bDMARDs) have markedly improved the clinical course for patients with rheumatoid arthritis (RA), there are no reliable predictors of treatment response in individual patients. The drug retention rate in observational studies can be considered as a composite measure and index of drug effectiveness1).

Objectives: The aim of this study was to investigate potential predictors for bDMARDs by clarifying and comparing the retention ratio of bDMARDs according to the status and concentration of anti-cyclic citrullinated peptide antibody (anti-CCP), rheumatoid factor (RF), and anti-nuclear antibody (ANA).

Methods: We included consecutive RA patients from Mitsui Memorial Hospital and Kawakita General Hospital (both in Tokyo) who received bDMARD treatment between April 2018 and August 2018. We obtained data on the administered bDMARDs and the reason for discontinuation for each patient, and collected patient information, including the status of RF and ANA, at the initiation of each bDMARD, as well as the baseline status and concentration of anti-CCP. We categorized infliximab, etanercept, adalimumab, golimumab, and certolizumab pegol as TNF inhibitors (TNFi), and compared the TNFi group with the tocilizumab (TCZ) group and abatacept (ABT) group in terms of patient characteristics and retention rate. Statistical analysis of the group comparison was performed using one way ANOVA and Kruskal-Wallis tests, and categorical data were assessed by Fisher’s exact test. The retention ratio was compared using the Kaplan-Meier generalized Wilcoxon test.

Results: This study included 214 patients (male 34, female 180, mean age 66.8) and 305 bDMARD cases were analyzed. The TNFi group included 160 cases, and the TCZ group and ABT group comprised 66 and 79 cases, respectively. Overall, the ABT group had the highest retention rate compared with the TNFi and TCZ groups, and the persistency rate of the ABT group at 60 months was 66.1%. Reasons for discontinuation of bDMARDs were insufficient efficacy (63.0%) and adverse events (29.4%). There was no significant difference regarding to the retention rate between anti-CCP negative and positive patients or between RF-negative and positive patients in each bDMARD group. After stratifying all patients according to anti-CCP status and concentration, among the three bDMARD groups, the ABT group (n=70) had the highest retention rate (p<0.05) in the anti-CCP-positive category, whereas the TCZ group (n=12) had the highest retention rate (p=0.27) in the anti-CCP-negative category. The persistency rates of the ABT group in the ≥ 100 U/ml category at 60 months was 73.4%. Moreover, the ABT group (n=59) had the highest retention rate (p<0.05) in the RF-positive category, whereas the TCZ group (n=20) had the highest retention rate in the RF-negative category (p=0.15). The persistency rate of the ABT group in the RF-positive category at 60 months was 68.3%. There were no significant differences in the retention rate among the three bDMARD groups in the ANA-negative or positive categories.

Conclusion: The status and concentration of anti-CCP, and the status of RF were found to be useful predictors for bDMARD efficacy in patients with RA.

REFERENCE

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SAT0165

PERSPECTIVES OF WOMEN WITH CHRONIC RHEUMATIC DISEASES ON THEIR JOURNEY TO MOTHERHOOD: COMPARISON OF SURVEYS FROM ASIA-PACIFIC AND EUROPE

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Background: The onset and diagnosis of chronic rheumatic disease (CRD) in women often overlap with their peak reproductive years. A previous survey1 reported fears and misconceptions amongst women with CRD in Germany, France, UK, Italy and Spain (EUS) on their journey to motherhood.

Objectives: To explore the perspectives of women with CRD in Asia-Pacific (APAC) regarding disease management and pregnancy, and the support they receive compared with patients in Europe.

Methods: Women of childbearing age (18-45 years) with self-reported moderate to severe CRD (rheumatoid arthritis [RA], psoriatic arthritis [PsA], axial spondyloarthritis [axSpA]) from Australia (AUS), Japan (JPN) and Hong Kong (HKG) completed a 20-min online survey (Sep–Nov 2018), similar to the previous EUS survey. Participants had been pregnant in the past 2–5 years.

Results: 210 APAC participants had CRD (RA: n=122, PsA: n=48, axSpA/AS: n=40); 306 EUS participants had CRD. Most APAC participants had moderate CRD (77%; severe: 23%). In their most recent pregnancy, 40% of the women were actively trying to get pregnant, 40% were neutral and 20% were either not thinking about a pregnancy or were actively trying to avoid it. Prior to pregnancy, women consulted rheumatologists (62%) or primary care physicians (26%) or OB/ONs (20%; multiple responses were possible). Pregnancy planning was first discussed with a healthcare professional (HCP) at diagnosis (33%), at treatment initiation.
Golimumab as First, Second or at Least Third Biologic Agent in Patients with Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA) or Ankylosing Spondylitis (AS): Post Hoc Analysis of a Non-interventional Study in Germany

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Background: Golimumab (GLM) has demonstrated efficacy in RA, PsA, and AS in several randomized clinical trials with biologic-naïve patients. Data from real world practice comparing biologic naïve and experienced patients are lacking.

Objectives: The aim of this post hoc analysis is to assess effectiveness of GLM used as first, second, or at least third biologic agent in RA, PsA and AS in a real-life setting.

Methods: Post hoc analysis of the non-interventional, prospective, 24-month GO-NICE study with RA, PsA and AS patients (pts.) starting GLM 50mg SC once monthly in a real practice setting in Germany, details were shown earlier (1,2). Endpoint measures DAS28-ESR, PsARC, and BASDAI are shown as observed.

Results: In 1458 pts. with RA, PsA or AS GLM was administered as first (n=305, 286, 292, resp.), second (n=104, 136, 130, resp.), or at least third biologic agent (n=64, 79, 58, resp.). Biologic agents in previous treatments included Adalimumab (348), Etanercept (287), Infliximab (139), Tocilizumab (27), Rituximab (15), Certolizumab (14), or Abatacept (n=12, 43.0, 30.8, 34.2, 34.2% with PsA, and 53.8, 49.2, 41.4% with AS completed the study until month 24. RA pts: (n=473) RF was positive in 78.9%, 70.2%, and 59.4%, AC/P + in 76.2%, 78.4%, 59.0%, and disease duration was 9.7, 10.1, 14.3 years, in pts. with GLM use as 1st, 2nd, at least 3rd line respectively. DAS28 score at BL was 5.0, 4.9, 5.1 in first, second, and at least third line use of GLM, respectively and dropped significantly in all groups (table). After 3 months of treatment 27.5%, 19.5%, 14.5% of pts. were in remission (<2.6), after 24 months 45.3%, 50.0% or 33.3%, respectively. PsA pts: (n=501) Disease duration was 12.4, 13.7, 13.8 yrs in pts. with GLM use as 1st, 2nd, at least 3rd line respectively. PsARC response was achieved in 74.9%, 51.0% and 50.0% in first, second, and at least third line use of GLM, respectively. AS pts: (n=483) HLAB27-positive in 81.2%, 80.8%, and 74.1%, in pts. with GLM use as 1st, 2nd, at least 3rd line respectively. At BL 162 pts. had extra-articular manifestations, most commonly iritis, enthesitis, IBD, and dactylitis (in 31.2%, 35.9%, and 43%, pts. respectively. Pts. with at least 2 previous bDMARDs had higher BASDAI at BL than pts. with GLM use in 1st or 2nd line: 5.7 vs. 5.0, and 4.9. After 24 months of treatment the mean BASDAI scores decreased significantly (>0.001 vs. BL) to 2.1, 2.9, 2.9 in 1st, 2nd, and at least 3rd line use of GLM, respectively. Overall safety findings were comparable to those reported in controlled trials and no new safety signals were detected.

Conclusion: In this non-interventional study of pts. with RA, PsA and AS, golimumab therapy was effective, with better outcomes achieved in biologic-naïve pts. Significant improvement of DAS and BASDAI was also achieved with GLM use in second line. Third line use of GLM results in less benefit.
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SAT0167
INCREASED HIGH MOLECULAR WEIGHT ADIPONECTIN AND LEAN MASS DURING TOCILIZUMAB TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS. A 12 MONTH MULTICENTER STUDY

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Background: Patients with rheumatoid arthritis (RA) have an increased risk of cardiovascular (CV) diseases. TNFa blockade in RA patients has been associated with weight gain, increase in fat mass and variations in serum adipokines. Adiponectin (Adp), a protein produced by adipocytes, plays a beneficial role in insulin sensitivity and CV disease prevention, especially its high molecular weight (HMW) isoform.

Objectives: To analyse the changes in serum adipokines and especially Adp (total and HMW) and body composition during TCZ therapy in RA patients.

Methods: Multicenter open-label study. All patients enrolled had active RA (2010 ACR/EULAR criteria and DAS28 <3.2) with previous inadequate response to a csDMARDs and/or bDMARDs. They all were TCZ naïve (2010 ACR/EULAR criteria and DAS28 <3.2) with previous inadequate response to a csDMARDs and/or bDMARDs. They all were TCZ naïve

Results: A total of 2531 patients were included: 1154 RA (45.59%), 680 PsA (26.87%), and 697 AS (27.54%). Age groups: there were 64 young patients (25.52%), 2166 adults (85.57%), 243 elderly adults (9.6%), and 58 very elderly adults (2.29%). Comorbidities increased with age, while smoking rates decreased. Methylxate use was similar in all age groups (33.99% in the total sample), but corticosteroid treatment increased with age (young 27.7%, adults 47%, elderly adults 64.36% and the very elderly 70.21%). 77.87% received anti-TNF treatment, and 22.13% other biological treatment. Methotrexate use was similar in all age groups.

Conclusion: These variations in Adp during TCZ treatment may have a positive impact on the CV risk of RA patients and may contribute to the protective role of TCZ against the CV burden in RA.

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SAT0168
IMPACT OF AGE ON THE APPEARANCE OF ADVERSE EVENTSAT THE BEGINNING OF BIOLOGICAL TREATMENT: DATA FROM THE BIOBADASER 3.0 REGISTRY

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Background: Current medical advances are allowing patients with chronic arthritis to live to advanced ages. Although the risks of biological therapies in elderly patients have been previously evaluated, data are scarce since they are mainly derived from clinical trials, in which elderly populations are often underrepresented or event excluded (patients up to 75 years old). In addition, comparisons between such studies are difficult due to the absence of a consensus in defining the groups’ age.

Objectives: To evaluate the impact of age on the appearance of adverse events (AE) in patients with rheumatic diseases (rheumatoid arthritis -RA-, ankylosing spondylitis -AS- and psoriatic arthritis -PsA) at the start of biologic treatment.

Methods: Multicenter prospective study in a real-world setting. Information was obtained from BIOBADASER, a national safety registry of patients with rheumatic diseases treated with biologics or targeted synthetic disease modifying anti-rheumatic drugs. For this analysis, all patients included in this registry since 2000 and diagnosed with RA, AS or PsA were included, and classified into four categories according to age at initiation of biologic treatment: young (< 25 years-old), adults (25-64 years-old), elderly (65-75 years-old) and very elderly (> 75 years-old). Data collected included: 1) patient’s data 2) data on treatment and 3) data on AE. Proportions, means and standard deviations were used to describe the population. Poisson regression model was carried out to explore factors associated with the appearance of AEs. Crude and adjusted incidence rate ratios (IRR) were calculated.

Results: A total of 2531 patients were included: 1154 RA (45.59%), 680 PsA (26.87%), and 697 AS (27.54%). Age groups: there were 64 young patients (25.52%), 2166 adults (85.57%), 243 elderly adults (9.6%), and 58 very elderly adults (2.29%). Comorbidities increased with age, while smoking rates decreased. Methylxate use was similar in all age groups (33.99% in the total sample), but corticosteroid treatment increased with age (young 27.7%, adults 47%, elderly adults 64.36% and the very elderly 70.21%). 77.87% received anti-TNF treatment, and 22.13% other biological drugs. Poisson regression model showed an increased probability of suffering a first adverse event with increasing age regardless of the...
A NOVEL FORMULATION OF CT-P13 FOR SUBCUTANEOUS ADMINISTRATION: WEEK RESULTS FROM A PART 2 OF PHASE III RANDOMIZED CONTROLLED TRIAL IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: CT-P13 subcutaneous (SC) formulation showed comparable efficacy and safety with CT-P13 intravenous (IV) formulation in rheumatoid arthritis (RA)1 and Crohn’s disease2 preliminary studies (Part 1).

Objectives: The purpose of this study was to demonstrate non-inferiority (NI) of efficacy and compare safety profiles of CT-P13 SC to CT-P13 IV in RA patients over 30 weeks of Part 2.

Methods: In this randomized, controlled, double blinded, phase III study, RA patients received CT-P13 IV 3 mg/kg at Weeks 0 and 2 and were randomized at Week 6 to receive CT-P13 SC 120 mg every 2 weeks or CT-P13 IV 3 mg/kg every 8 weeks. From Week 30, all patients received CT-P13 SC 120 mg every 2 weeks. The primary efficacy endpoint, change of DAS28 (C-reactive protein [CRP]) from baseline to Week 22, would be non-inferior to the IV arm with a margin of 0.22.

Results: 121 RA patients were randomized to receive CT-P13 SC 120 mg (n=61) or CT-P13 IV 3 mg/kg (n=60). Demographics and baseline characteristics were well balanced between the groups. The primary efficacy endpoint was non-inferior (95% CI 0.88, 1.26). No differences were observed in the safety endpoints.

Conclusion: The CT-P13 SC 120 mg formulation was non-inferior to the IV arm in terms of efficacy and had a comparable safety profile.
Conclusion: The study demonstrated NI of efficacy for CT-P13 SC to the CT-P13 IV. Also, CT-P13 SC showed similar efficacy and safety profiles to CT-P13 IV up to Week 30. CT-P13 SC could provide a favorable benefit to patients with an alternative convenient way of administration.

REFERENCES


SAT0171

A RETROSPECTIVE ANALYSIS OF LONG TERM SAFETY UP TO FIVE YEARS OF INFILXIMAB BIOSIMILAR CT-P13 IN PATIENTS WITH RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS

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Background: Long term safety and efficacy of anti-TNF inhibitors in rheumatic diseases is an important aspect of patient treatment. CT-P13 is the first infliximab biosimilar approved by EMA and FDA and has demonstrated comparable efficacy and safety with reference infliximab in rheumatoid arthritis (RA)1,2 and ankylosing spondylitis (AS)3,4. However, long term data of infliximab biosimilar to date has been limited to two years.5,6

Objectives: To demonstrate drug survival and long term safety and efficacy of CT-P13 up to 5 years in patients with RA or AS, including patients who switched from reference infliximab to CT-P13 (switched patient). Primary endpoints were safety and drug survival up to 5 years analyzed by Kaplan-Meier curve.

Results: We identified 1579 patients (515 RA and 337 AS) who were switched from reference infliximab to CT-P13 (switched patient). We observed no new safety signals. The frequency of serious adverse events (SAEs) was similar between groups and the occurrence of SAEs of respiratory tract infection was 3.90% in patients with RA and 4.15% in patients with AS. The most common reason for discontinuation for both RA and AS was not related to infliximab biosimilar-CT-P13.

Disclosure of Interests: Tae-Hwan Kim1, Shin-Seek Lee2, Won Park2, Yeong Wook Song3, Chang-Hee Suh4, SooYoung Kim5, Youngnam Lee3, Daehyun Yoo1, None declared.

REFERENCES

SLE, Sjögren’s and APS – clinical aspects (other than treatment)
Conclusion: Higher renal gallium uptake predicts higher active inflammation in LN. Changes of gallium uptake ratio were correlated with histopathological parameters and daily urine protein. Renal gallium scan appears to be a valuable non-invasive tool in assessing activities of LN.

REFERENCES

Background: In the last few decades many studies have investigated the role of major salivary glands ultrasound (SGUS) in the diagnostic work-up of patients with suspected primary Sjögren’s syndrome (pSS). Recent development of ultra-high-resolution ultrasound systems (UHFUS), with frequencies as high as 70 MHz and capability resolution as fine as 30 μm, has permit new diagnostic applications to a variety of superficial targets including labial salivary glands (LSGs). To date, however, no information are available regarding the use of UHFUS for the study of LSGs in humans.

Objectives: To evaluate the feasibility and the diagnostic accuracy of UHFUS of LSGs in patients with suspected SS and to assess the correlations between LSG histopathology, UHFUS and SGUS.

Methods: Consecutive patients with clinically suspected pSS were included in this study. All patients underwent a complete diagnostic work-up including conventional SGUS and LSG biopsy. The same expert pathologist calculated for all the samples the focus score (FS), number of foci and evaluated the presence of ectopic germinal centers (GCs). UHFUS of LSG was performed by specialized radiologists scanning first the central compartment of the inferior lip, and then both peripheral compartments. The following parameters were evaluated: distribution of the glands, parenchymal inhomogeneity (score 0-3, from normal to evident), fibrosis and eco color-Doppler vascular pattern and grade of vascular intensity.

Results: We included 32 patients with suspected pSS. At the end of the work-up, pSS diagnosis was confirmed in 12/32 (37.5%) cases. No differences between pSS patients and no-SS sicca controls were observed in UHFUS findings related to LSG distribution and eco color-Doppler vascular parameters. By contrast, pSS patients presented statistically significant differences in peripheral UHFUS inhomogeneity (p<0.006), and a higher degree of fibrosis (p<0.01). Considering a score ≥2 in parenchymal inhomogeneity as suggestive for pSS, UHFUS appeared less specific than conventional SGUS (UHFUS Sp=70% vs SGUS Sp=95%) but more sensitive (UHFUS Se=83.3% vs SGUS Se = 58.3%). In addition, when we investigated the relationship between UHFUS, SGUS and LSG histopathology we found that the correlation coefficients between UHFUS inhomogeneity and LSG FS (UHFUS r=0.706** vs SGUS r=0.393*), number of foci (UHFUS r=0.712** vs SGUS r=0.445*), and number of ectopic GCs (UHFUS r=0.525** vs SGUS r=0.141), were significantly higher than those observed with conventional SGUS.

Conclusion: The application of UHFUS to the study of LSG in pSS appeared feasible and sensitive. Because of the anatomical details obtained with this technique and its stronger correlation with LSG histopathology, UHFUS might offer unique advantages over the existing major salivary gland imaging modalities in pSS assessment.

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Objectives: This case report is presented to emphasize that the deterio-
ration of certain clinical and laboratory findings of an SLE patient should
alert the physician for development of MAS.

Methods: We reported a monogenic lupus patient with MAS clinic with
acute pancreatitis, who had c1qA gene mutation.

Results: A 9-year-old male was first referred with photosensitivity and
erythematous crusted lesions on his extremities and face while he was 2
years old. ANA was positive (1/1000 dilution) and skin biopsy from
lesions was compatible with subacute lupus. Steroid, methotrexate and
hydroxychloroquine were administrated. Patient’s male identity and atypical
age for lupus was further evaluated with “whole exome sequencing” method.
Complement c1qA gene mutation was detected. Monthly fresh
frozen plasma and IVIG treatments were added, which able to control
the disease to some extent.

He had acute gastroenteritis and fever, leading to activation of skin and
oral mucosa lesions with on bilateral parotitis in his last visit (Figure-A).
His body temperature was 39.9°C. USG confirmed the parotitis. Regard-
ing infectious gastroenteritis, IVIG and plasma with broad-spectrum antibi-
ocitics were administrated. Despite treatment, high fever persisted. He had
hypotension, irritability, and hepatosplenomegaly with abdominal tenderness
on physical examination. Abdomen CT was compatible with acute pan-
creatitis (Figure-B), and he had high amylase and lipase levels. Despite
IV hydration with intense therapy, developing pancytopenia, hypoalbumine-
ria, increase in hepatic enzymes, decrease in fibrinogen and ESR with
erased CRP and ferritin levels were alerts for MAS. Bone marrow aspi-
ration demonstrated hemophagocytosis (Figure-C). Pulse high dose IV
methyl prednisolone treatment was started. Clinical and laboratory find-
ings, particularly ferritin level, improved in the third day of treatment. Ste-
roids were gradually reduced while cyclosporine was added. He is under
remission with low dose steroid, cyclosporine-A and regular plasma infu-
sions per 3 weeks.

Figure A. Bullous and crusted lesions on face and around oral mucosa. B. Shortening of
the pancreas tail in CT. C. Hemophagocytic cells in the bone marrow.

Conclusion: MAS is rarely seen in course of monogenic J-SLE, but may
be serious. It is the first juvenile monogenic lupus case with MAS in the
English literature, to best of our knowledge. It is important to distinguish
this mortality clinical condition from the flare of disease and appropriate
management should be started as soon as possible.

REFERENCE

Disclosure of Interests: Serkan Turkuca: None declared, Tugce Tunca
Kucukali: None declared, Asena Baserdem: None declared, Erbil Unsal
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Speakers bureau: Novartis, AbbVie, Roche, Koçak Pharma

SAT0178
THE EFFICACY AND SAFETY OF ANTI-PNEUMOCOCCAL VACCINATION IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Systemic lupus erythematosus (SLE) is a complex, multi-factorial chronic systemic autoimmune disease, characterized by a clinically relapsing and remitting course, affecting women more commonly than men. It has an estimated prevalence of 20 to 150 cases per 100,000 persons. The immune system dysregulation in SLE patients is associated with a higher risk of infections, including pneumococcal pneumonia. Anti-pneumococcal vaccines represent a valuable and effective preventative tool to mitigate and counteract pneumococcal pneumonia. However, the efficacy and safety of anti-pneumococcal immunization in SLE patients is both controversial and not completely agreed upon. Indeed, several epidemiological studies investigating the anti-pneumococcal vaccine safety and efficacy in patients suffering from SLE have reported short-term immunogenicity with elevated anti-pneumococcal antibody titres but inconsistent long-term findings, with some studies finding poor responses, mainly for long-term immune protection.

Objectives: We conducted a systematic review and meta-analysis to better understand the efficacy and safety of pneumococcal vaccination administered to SLE patients.

Methods: A comprehensive literature search in accordance with the ‘Preferred Reporting Items for Systematic Reviews and Meta-Analysis’ (PRISMA) guidelines was performed. We mined also the gray literature and searched also for unpublished studies, presented at congresses either as oral communications or posters. We were able to identify 18 studies. All studies were designed as longitudinal investigations, in particular, of high quality, being randomized, double-blind trials. Four studies had control groups.

Results: Total sample size included 601 participants. Vaccine immunogenicity in terms of subjects with protective antibody titers ranged from 36% to 97.6%. According to our systematic review and meta-analysis, high erythrocyte sedimentation rate (ESR), older age, earlier SLE onset, high disease activity, and immunosuppressive therapy were found to be statistically significant predictors of poor immunogenicity, although belimumab was found to have no significant impact. With regard to safety, no serious adverse events were found, with up to one third of cases reporting mild/low-grade complaints.

Conclusion: Due to the high risk of pneumococcal infection in SLE patients and the safety and, at least partial, effectiveness, according to our systematic review and meta-analysis, in such patients, preventive strategies mainly by immunization, are required in all age groups and, in those needing immunosuppressive therapy, immunization should be given prior the initiation of the treatment.

Disclosure of Interests: Mohammad Adawi: None declared, Nicola Luigi Bragazzi: None declared, Dennis McGenagle Consultant for: Lilly, Novartis UCB, Speakers bureau: Lilly, Novartis UCB, Naïm Mahroum: None declared, Giovanni Damiani: None declared, Charlie Bridgewood: None declared, Howard Amital Grant/research support from: Pfizer, AbbVie, Janssen, Grant/research support from: Pfizer, AbbVie, Janssen, Consultant for: Pfizer, Merck Sharp & Dohme, Consultant for: Pfizer, Merck Sharp & Dohme, Speakers bureau: Pfizer, Merck Sharp & Dohme, Janssen, Sanofi, Bristol-Myers Squibb, Abbvie, Neopharm, Speakers bureau: Pfizer, Merck Sharp & Dohme, Janssen, Sanofi, Bristol-Myers Squibb, Abbvie, Neopharm, Abdulla Watad: None declared


SAT0179
CHANGE IN IMMUNOLOGICAL PARAMETERS DURING FOLLOW-UP OF PATIENTS WITH PRIMARY SJÖGREN’S SYNDROME: DATA FROM THE FRENCH ASSESS COHORT

Paulina Szafors1, Cédric Lukas1, Jacques-Eric Gottenberg2, Xavier Mariette3, Bernard Combe3, Jacques Morel1. 1164 Saturday, 15 June 2019

Background: Primary Sjögren’s Syndrome (pSS) is associated with a biological panel of B cell activity markers such as hypergammaglobulinemia, rheumatoid factor (RF), decreased C3/C4 complement, cryoglobulinemia, and an increase in IgM-microglobulin, used to calculate the biological domain of The EULAR Sjögren’s Syndrome Disease Activity Index (ESS-DAI). In 80% of patients, anti-nuclear autoantibodies, especially anti-Ro/SSA and anti-La/SSB, are also observed. The change in these biological tests during follow-up of pSS patients has been poorly investigated.

Objectives: The objectives of our study were to assess the change in immunological parameters during the follow-up of pSS and to analyse the association with the clinical evolution.

Methods: We analysed data from the French prospective multicenter ASSESS cohort, including 395 patients with pSS. Clinical and biological data were collected at the baseline, then annually. Patients were included if at least two biological assessments and concomitant CineESSDAI activity scores were available, based on standardized clinical evaluations of the patients. Anova, Wilcoxon and Chi-square tests were used to analyse the relationship between the clinical evolution and immunological profile.

Results: 362 of 395 patients had required data to allow their inclusion. The mean number of visits was 5.5. In 81.7% of patients, the biological status did not change throughout the 5-year follow-up (Table 1). The clinical evolution was not related to the immunological changes observed between the previous two visits (p>0.30). There was no significant difference between the number of abnormal immunological markers and the CineESSDAI activity score (p=0.437) at the same visit. Disease activity according to the CineESSDAI score remained stable in 257 patients (out of 351 with available data) during follow-up: 175 patients (49.8%) were in remission and 82 (23.3%) had an active disease. The number of abnormal biological markers at baseline was associated with subsequent clinical evolution: detection of ≥5 B cell activity markers at baseline was a bad prognostic marker, (present in 12.4% of patients having persistent disease activity, versus 3.6% among patients with clinical favourable outcome) (p=0.04).

Conclusion: The biological profile of pSS patients is usually stable over time, especially if the initial assessment is negative, but a higher immunological activity profile might be a bad prognostic factor. Changes in biological parameters do not predict the subsequent clinical course. In conclusion, it is not relevant to systematically repeat the complete immunological screening in pSS patients.

Table 1: Immunological variations during the follow-up of patients from the ASSESS cohort

<table>
<thead>
<tr>
<th>Immunological markers</th>
<th>Number of patients with positive marker at baseline, n (%)</th>
<th>Change during follow-up, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rheumatoid factor</td>
<td>37/63 (58.7)</td>
<td>12 (19.0)</td>
</tr>
<tr>
<td>Cryoglobulinemia</td>
<td>16/233 (7.0%)</td>
<td>24 (7.4)</td>
</tr>
<tr>
<td>Hypogammaglobulinemia</td>
<td>106/287 (32.3)</td>
<td>9 (3.0)</td>
</tr>
<tr>
<td>Hypogammaglobulinemia</td>
<td>75/57 (6.0%)</td>
<td>3 (0.5)</td>
</tr>
<tr>
<td>Anti-SSA</td>
<td>12/25 (49.0)</td>
<td>3 (9.0)</td>
</tr>
<tr>
<td>Anti-SSB</td>
<td>11/201 (5.0%)</td>
<td>10 (4.9)</td>
</tr>
<tr>
<td>C3 Complement 0.05g/L</td>
<td>12/197 (6.4%)</td>
<td>7 (3.6)</td>
</tr>
<tr>
<td>C4 Complement 0.05g/L</td>
<td>12/198 (6.4%)</td>
<td>7 (3.5)</td>
</tr>
<tr>
<td>ANA ≥1/50U/L</td>
<td>151/203 (74.4)</td>
<td>27 (13.3)</td>
</tr>
<tr>
<td>Anti-SSA positivity</td>
<td>516/389 (52.6)</td>
<td>18 (5.3)</td>
</tr>
<tr>
<td>Anti-SSB positivity</td>
<td>49/179 (27.3%)</td>
<td>7 (3.9)</td>
</tr>
<tr>
<td>Monoclonal gammopathy</td>
<td>17/254 (6.3%)</td>
<td>45 (17.7)</td>
</tr>
</tbody>
</table>

Disclosure of Interests: Paulina Szafors: None declared, Cédric Lukas: None declared, Jacques-Eric Gottenberg Grant/research support from: Bristol-Myers Squibb, Consultant for: Bristol-Myers Squibb, Lilly, Pfizer, Sanofi-Genzyme, UCB Pharma, Consultant for: Bristol-Myers Squibb, Lilly, UCB, Sanofi-Genzyme, Pfizer, Xavier Mariette Consultant/research support from: Servier, Consultant for: AstraZeneca, Bristol-Myers Squibb, GlaxoSmithKline, Janssen, Pfizer, UCB Pharma, Bernard Combe Consultant: Abbvie, Bristol-Myers Squibb, Gilead, Janssen, Eli Lilly, MSD, Novartis, Pfizer, Roche-Chugui, Sanofi, UCB, Jacques Morel: None declared

SAT0180  EVALUATION OF FRAILTY IN SJÖGREN’S SYNDROME: CREATION OF A FRAILTY INDEX

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Background: Frailty is a condition characterized by the reduction of the individual’s homeostatic reserves, leading to an increased vulnerability to stressors and an increased risk of unfavourable events. The aging of the population and the consequent need to implement new paradigms of care and assistance, have given this tool a growing interest in many medical disciplines. In rheumatology, however, the interest is still limited. The Frailty Index (FI), developed on an arithmetical model of deficit accumulation, is an accurate tool for assessing frailty, providing an estimate of the biological aging.

Objectives: Creation of a FI to be used in clinical practice in patients with Sjögren’s syndrome (SS) and evaluation of the correlations with patient’s age, duration of illness, activity and disease damage at baseline and in the following 5 years.

Methods: The FI is composed by a checklist of non-predefined variables (deficits) constituted by symptoms, signs, diseases, disabilities, and laboratory findings. The deficits must meet these criteria: age-related; associated with negative outcomes; multidimensional (referring to different domains of the health status); present in at least 1%, but not more than 80% of the sample. To each variable is assigned the value of 0 (no deficit) or 1 (deficit). The FI is the ratio between deficits present by the individual and the total number of deficits considered, thus providing a measure of frailty ranging between 0 (no frailty) and 1 (maximum of frailty). A FI was developed for patients with SS consisting of 43 items (17 comorbidities, 14 signs and symptoms, 5 disabilities and 7 laboratory findings). Statistical analysis was performed with Spearman’s test for correlation assessment, the Mann Whitney test for comparing non-parametric variables and the Pearson test for correlation.

Results: FI was administered to a first small group of 30 female consecutive patients recruited as outpatients at the clinic dedicated to SS. The average age was 57.2 yrs, mean age at diagnosis 52.7 yrs and average disease duration 4.7 yrs. At the time of completing the FI, the average disease activity (ESSDAI) was 3.4, the mean value of the damage (SjDDI) 1.6 and the average score of FI equal to 0.21. A statistically significant correlation between FI and age has been reported (p = 0.017). No significant correlations between frailty and duration, activity and disease damage have been highlighted at the moment.

Conclusion: For the first time a FI was developed for patients with SS consisting of 43 items. The data shows a relationship between age and FI. The correlation is statistically significant, similarly to what is reported in the literature for other conditions. This confirms that FI is indeed an objective marker of aging and even though the sample population is young (average age = 57.2 years), FI maintains its main properties. This tool can be used to assess the health status of patients, making it possible to identify those at greater risk of trajectories or unfavourable outcomes. It is currently being administered the FI to patients with SS whose clinical course will be evaluated in the next 5 years (complications, mortality, hospitalization, institutionalization and disability).

REFERENCES

Disclosure of Interests: None declared

SAT0181 CONTRACEPTIVE COUNSELING AND USE AMONG WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS AT RISK FOR UNPLANNED PREGNANCY

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Background: Systemic Lupus Erythematosus (SLE) is an autoimmune disease that primarily affects women of reproductive age. Disease activity and medication use can complicate pregnancies in SLE, due to the disease itself and/or exposure to teratogenic medications. Therefore, these patients should be counseled and are candidates for highly effective contraceptive methods.

Objectives: To examine contraceptive counseling and use among SLE patients attending our Rheumatology Department.

Methods: Cross-sectional study in which women aged 15-50 followed in our Rheumatology Centre with SLE diagnosis completed a researcher-administered survey. Premenopausal women who were sexually active were considered at risk of pregnancy. We compared self-reported rates of contraceptive counseling and use, stratified by treatment with teratogenic medications, and by history of thrombosis or antiphospholipid antibodies (aPL). The statistical analysis was performed using SPSS 23.0, and p<0.05 was taken to indicate statistical significance.

Results: 95 women were interviewed, of these, 60 were considered to be at risk for unplanned pregnancy. Their mean age was 36 years (range 17-48), and median disease duration 9.9 years (range 0.25-37.0). 85% were aware of the complications associated with pregnancy in their medical condition and 73.3% had received contraceptive counseling. Fifty-six patients (93.3%) reported consistent contraceptive use. Younger patients were more likely to have received contraceptive counseling (55.0 [17-46] years versus 42.5 [20-48] years, p=0.021). Counseling was more frequently reported by patients with higher educational level (p=0.026). Those who were counseled were using more effective contraceptives and in logistic regression contraceptive counseling was a predictor of highly effective contraceptive use (OR=13.1, p=0.001).

Women using teratogenic medications or with a history of thrombosis were no more likely to have received contraceptive counseling or to use more effective contraceptive methods. Those with positive aPL were using more effective contraceptives (p=0.024). In our model, having a high school degree and positive lupus anticogulant predicted contraceptive counseling (OR=12.6, p=0.041; OR=3.1, p=0.02, respectively).

Conclusion: This study highlights the importance of contraceptive counseling in SLE patients at risk for unplanned pregnancy. A multidisciplinary team including rheumatologists, gynecologists and family physicians is needed to improve the education and provision of adequate contraceptive counseling to these women.

REFERENCES

Disclosure of Interests: None declared

SAT0182 DYSLIPIDEMIA, HYPERTENSION, LUPUS NEPHRITIS AND HIGHER PREDIOSOMAL USAGE CONTRIBUTES TO EVOLUTION OF CAROTID INTIMA-MEDIA THICKNESS IN MILD SYSTEMIC LUPUS ERYTHEMATOSUS: A 7-YEAR FOLLOW-UP STUDY

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Background: In SLE accelerated progression of carotid plaque and contribution of inflammatory factors for premature vascular changes have been reported. Effect of classical risk factors on progression of carotid intima-
media thickness (cIMT) in patients with SLE in comparison with population controls is not clear.

**Objectives:** To examine in SLE and population controls (1) prevalence of risk factors over time; (2) evolution of cIMT; (3) risk factors promoting cIMT evolution.

**Methods:** The study sample originated from the SLEVIC cohort (SLE vascular impact cohort study) which included consecutive patients with SLE and age and sex matched population controls. Seven years after inclusion all participants were asked to take part in the follow-up investigation. The standardized data collection and carotid ultrasound were performed at two assessments, 7 years apart. Effect of risk factors on cIMT over-time was examined with linear mixed models adjusted for age, sex and traditional CV risk factors.

**Results:** A total of 77 patients with SLE (68% of original cohort), 87% females, at inclusion mean age 47 years, disease duration 11.4 years, SLEDAI 3.0, SLICC/ACR 1.1, and 74 controls (61% of original cohort), 89% females, mean age 51 years, completed 7-years follow-up. At inclusion, patients with SLE were younger and had lower levels of LDL than controls but were more likely to have hypertension and higher levels of triglycerides (TG). Between the assessments both groups were measured with an increase in blood pressure, levels of total cholesterol (TC), LDL, but at follow-up the patients still had lower TC, LDL and HDL levels and higher TG than controls. At both assessments, patients used more frequent antihypertensive and aspirin than controls, p<0.001. The mean cIMT increased statistically significant in patients and controls, average increase during progression of 0.009 mm/year in patients and 0.011 mm/year in controls, p<0.001 for change in both groups, with no inter-group difference, p=0.867 age- and sex-adjusted.

In multivariate analysis, the patients showed a statistically significant association between mean cIMT over-time and higher systolic blood pressure, lower levels of HDL, higher TC/HDL- and LDL/HDL-ratio, higher triglycerides, dyslipidemia and detection with (any) carotid plaque at inclusion. In the control group, lower levels of HDL, history of dyslipidemia and finding with bilateral plaque at inclusion were associated with cIMT over-time. At follow-up, hypertension and blood lipid measures in patients (with exception for TG) and HDL in controls were still significantly associated with cIMT over-time. Of all, the strongest association was shown for HDL in both patients and controls. Effect of other cardiometabolic risk factors at inclusion and cumulative risks were not significantly after adjustment for age and sex.

In the patients, history of nephritis at inclusion and follow-up, and a higher average dose of prednisone used since diagnosis, but not other treatments, were associated with cIMT over-time.

**Conclusion:** We observed similar progression of cIMT over 7 years in patients with long-standing mild well-controlled SLE disease and population controls. Our findings suggest importance of recognition of dyslipidemia and hypertension, and support recommendation to limit use of corticosteroids in patients with SLE as a part of CV risk management. The factors protecting or promoting atherosclerotic progression should be further explored.

**Disclosure of Interests:** Sofia Ajeanana: None declared, Thomas Gustafs- son: None declared, Tomas Jogestrand: None declared, Ingrid Hafström: None declared, Johan Frostegård Shareholder of: Minor shareholder and inventor in startup-company Althera Biotechnologies, but they do not produce drugs yet and rheumatology is not in their focus.

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**LUPUS NEPHRITIS: A RETROSPECTIVE LONGITUDINAL STUDY LOOKING FOR CHRONIC RENAL DISEASE ASSOCIATED FACTORS, FROM THREE SOUTH-EUROPEAN COHORTS OF PATIENTS IN FOLLOW-UP SINCE 2000**

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**Background:** Renal involvement in systemic lupus erythematosus (SLE) is the most frequent severe manifestation and carries a bad prognosis.

**Objectives:** To analyze the outcome of lupus nephritis (LN) in terms of chronic kidney disease development (CKD).

**Methods:** Design: multicentre retrospective observational study. Patients: SLE patients (ACR97) with biopsy proven LN attending to three South European Rheumatology departments. Variables: demographics, SLE related variables, including global activity (SLEDAI-2K), renal flares, therapies, ACR response criteria and CKD. Statistical analysis: descriptive bivariate and multivariate analysis exploring factors associated to CKD.

**Results:** Seventy-six patients with biopsy-proven LN were included, 90.7% female; mean age: 33 years; mean disease: duration 14 years; mean follow-up time (since LN diagnosis): 8,5 years. LN class III, IV and V were present in 22%, 75% and 3% of the cases, respectively. At LN diagnosis 68 (89%) patients had a severe renal flare. Forty-one (56.1%) and 49 (64.4%) had HTA and nephrotic syndrome, respectively. The mean 24h proteinuria levels at LN diagnosis was 4.6g. Mean SLEDAI-2K at the time of flare was 20.3, with 69 (65.7%) patients having an extrarenal flare.

The treatments used to induce remission were: glucocorticoids (100%); pulses M-prednisolone in 49 (64%) and oral prednisone (mean starting dose): 43 mg/day (±20.6); intravenous cyclophosphamide in 42 (55%) patients; mycophenolate mofetil (MMF) in 21 (27%) patients; calcineurin inhibitors in 5 (11%) patients; rituximab in 4 (5.2%) patients; and oral cyclophosphamide in 4 (5.2%) patients. Forty-eight (63%) patients were receiving hydroxychloroquine. MMF was the immunosuppressant (IS) more frequently used (52%) as maintenance therapy.

At 3, 6 and 12th months, the mean proteinuria was 2.93/24h, 1.53g/24h, 1.1g/24h, respectively (p<0.001). Fifty-five (77.5%) of patients achieved complete response and 61 (84.7%) presented complete or partial response. Median time to renal remission: 12.5 months (6,17.5). In 32 patients (42%) it was possible to discontinue IS. Sixteen (21.9%) patients developed CKD, 4 (5.3%) needing dialysis and 1 (0.76%) renal transplantation. Serious infection was recorded in 23 (34.8%) patients. Five (6.6%) patients died (2 cardiovascular cause).

In the bivariate study, the following variables were significantly associated with CKD: male sex, hypertension, ACEI drugs, severe infection after LN, temporal dysalisis, non ACR renal response, non use of hydroxychloroquine, time to achieve 10mg/day of prednisone, previous creatinine to LN, maximum creatinine at LN, hyperlipidemia at 3 months of LN, active urinary sediment at 12 months, creatinine at 6 and 12 months, proteinuria at 6 and 12 months.

In the logistic regression model, using genetic algorithms, we found that proteinuria at 6 months was significantly associated with CKD (OR:2.95; 95%CI 1.9:9.29, p= 0.03). Hypertension and male sex were marginally associated (p=0.06, both).

**Conclusion:** A considerable percentage of LN patients developed renal chronic failure (21.9%). A high percentage of ACR response was achieved using medium dose (40mg) of glucocorticoids for induction. A significant reduction of proteinuria was achieved at 3 months, but proteinuria at 6 months was the only factor finally associated with CKD.

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**SAT1018 ASSOCIATION OF SERUM AND URINE LEVELS OF TWEAK, MCP-1 AND NGAL WITH DISEASE ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Background:** TWEAK, MCP-1 and NGAL, mediators in pathogenesis of systemic lupus erythematosus (SLE), are proinflammatory cytokines/chemokines that are thought as potential biomarkers reflecting disease activity (1).

**Objectives:** In this study, we aimed to investigate the association of serum (s) and urine (u) levels of TWEAK, MCP-1 and NGAL with disease activity in both renal and non-renal SLE.

**Methods:** Thirty active patients with SLE (15 renal and 15 non-renal) were recruited. Thirty-one inactive patients with SLE (16 renal and 15
non-renal), 14 patients with ANCA-associated vasculitis (AAV) all of whom had active renal involvement and 20 healthy volunteers were selected as control groups. Serum and urine levels of TWEAK, MCP-1 and NGAL were tested using ELISA.

**Results:** Sixty-one SLE patients, 51 (83.6%) of whom were female, with a median disease duration of 83 (23.5-135) months and a median age of 35 (27-47.5) were included in the study. Serum and urine levels of TWEAK and NGAL were significantly higher in the active SLE group compared with the inactive SLE (n=31) group (tTWEAK: p=0.005; uTWEAK: p=0.026; sNGAL: p<0.001; uNGAL: p=0.002); whilst no significant differences regarding serum and urine MCP-1 levels were observed (p=0.189 and p=0.106), tTWEAK (p=0.237), sMCP-1 (p=0.141), uMCP-1 (p=0.208), sNGAL (p=0.419) and uNGAL (p=0.443) levels did not differ between patients with active LN and non-renal active SLE; yet levels of sTWEAK were higher in patients with active LN (p=0.006). There were no differences between active LN and renal active AAV. Levels of all biomarkers were correlated with SLEDAI (tTWEAK: p=0.001; uTWEAK: p=0.006; sMCP-1: p=0.049; uMCP-1: p=0.014; sNGAL: p=0.001; uNGAL: p=0.002).

**Conclusion:** sTWEAK, uTWEAK, sNGAL and uNGAL are significant biomarkers showing disease activity in SLE. However, our results implicate that these biomarkers may not be specific for SLE, and can be elevated in patients with active renal involvement of AAV. sTWEAK may be of use for discriminating active nephritis from non-renal active disease in SLE. Further studies are awaited to confirm these results (This study was funded by Istanbul University with the project number TTU-2017-24738 and Turkish Society for Rheumatology).

**REFERENCE**


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**THE EFFECTS OF DISEASE ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS ON COGNITIVE FUNCTION**

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**Background:** Cognitive dysfunction (CD) affects up to 90% of systemic lupus erythematosus (SLE) patients and significantly impacts patient quality of life. The cause is multifaceted with many factors common across chronic diseases. It is thus difficult to ascertain the direct impact active disease in SLE has upon immediate cognitive function.

**Objectives:** The aim of this study was to investigate the effects of active disease in SLE on CD. We compared cognitive measures in SLE patients with stable disease activity (SLE-S) to those with active disease (SLE-F).

**Methods:** 34 SLE-S and 24 SLE-F were recruited, all meeting 1997 ACR criteria. Active disease was defined as BILAG A or B with a change in SLE-S and 24 SLE-F were recruited, all meeting 1997 ACR criteria. SLEDAI-2K £ criteria. Active disease was defined as BILAG A or B with a change in

**Results:** There were no differences between the SLE-S and SLE-F groups or between v1 and v2 on demographic and clinical measures except disease activity. The SLE-F group scored higher than the SLE-S group on the MADRS depression scale (p=0.003) but no other significant differences in psychiatric symptoms were observed. There were no significant differences on the CANTAB® for either comparison (table 1). The fMRI showed a SLE-S vs SLE-F difference in n-back related response in the medial prefrontal cortex (p=0.012; figure 1). No v1 vs v2 differences were found, nor for either comparison for the FERT.

**Table 1. Baseline characteristics, SLE-S vs SLE-F**

<table>
<thead>
<tr>
<th>Variable</th>
<th>SLE-F (n=24)</th>
<th>SLE-S (n=34)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>36 (12)</td>
<td>39 (11)</td>
<td>0.330</td>
</tr>
<tr>
<td>Male (%)</td>
<td>16 (67)</td>
<td>19 (56)</td>
<td>0.538</td>
</tr>
<tr>
<td>Oral corticosteroids (mg/d)</td>
<td>15 (63)</td>
<td>12 (35)</td>
<td>0.061</td>
</tr>
<tr>
<td>Current immunosuppressant use (%)</td>
<td>18 (75)</td>
<td>19 (58)</td>
<td>0.281</td>
</tr>
<tr>
<td>Current antimalarial use (%)</td>
<td>18 (75)</td>
<td>19 (58)</td>
<td>0.432</td>
</tr>
<tr>
<td>Biologic medication</td>
<td>4 (17)</td>
<td>3 (9)</td>
<td>0.003</td>
</tr>
<tr>
<td>MADRS</td>
<td>8 (4, 12)</td>
<td>4 (1, 8)</td>
<td>0.003</td>
</tr>
<tr>
<td>Depression &amp; anxiety</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current</td>
<td>Base value</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cognitive dysfunction (CD)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** In a cohort well matched on confounding factors these results suggest that active disease does not impair cognitive function. However, the differences in the medial frontal cluster during the working memory task may indicate the use of compensatory mechanisms to maintain cognitive function as has been found elsewhere. Alternatively, as this is a default mode network region, often implicated in self-reflective processes it may be that CD is more directly associated with differences in mood. As such when treating SLE patients with self-reported CD it is important to consider factors other than disease activity.

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SAT0186  Ω MORTALITY IN CHILDREN WITH JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS IN AN ARGENTINE PEDIATRIC CENTRE.

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Background: Juvenile systemic lupus erythematosus (JSLE) is a complex multisystemic autoimmune disease, often causing irreversible damage, reduced quality of life and life expectancy. Data on causes of death and time trends in infant lupus mortality are limited.

Objectives: The aim of this study was to determine mortality in a pediatric cohort.

Methods: This retrospective study included patients with childhood onset lupus (fulfilling ACR 1997) who were diagnosed at the Paediatric centre in Santa Fe Argentine, Alassia Children Hospital from 1991 to 2018 and had 15 years of age at presentation.

Results: This study included 54 JSLE children (FM:12.5:1) with a mean age of onset lupus 12 years (range 4-15 years). During a mean follow-up in our centre of 3 years (range 12m–10 years), 12 patients (24%) was died; 5 during the follow-up in our centre and 7 in adult centre, 4 lost to follow-up.

The average age of death was 16 years (range 10-29 years) and the average since diagnose time was 17 months (range 3m-15 years).

The principal system involved was renal (100%), 10 patients with diffuse proliferative lupus nephritis (WHO class IV), 2 membranous lupus nephritis (WHO class V), 5 patients (41.6%) with hematomal disorders (2 pancytopenia, 2 leukopenia, 1 Macroage Activation Syndrome). 3 patients had thrombosis. 5 patients (41.6%) with neurological involvement (4 psychosis, 1 depression). One patient with liver dysfunction. There one death related to renal biopsy.

The principal cause of mortality was active disease and infection. Menin- gococcal meningitis, Klebsiella peritonitis, Pneumococcal cellulitis of the neck, peritonitis and 1 patient with disseminated tuberculosis.

Conclusion: Over all, similar trends were observed for RA and pSS cohorts despite minor changes in pSS therapy. Work participation has improved significantly over two decades in pSS. A greater perception of pSS without systemic manifestations may have caused a shift towards less severely affected patient cohorts today.

REFERENCE


Acknowledgement: The database is funded by unconditional grants from the German Collaborative Arthritis Centres and from a consortium of 9 pharmaceutical companies to the German Academy for Continuing Medical Education in Rheumatology.

Disclosure of Interests: Johanna Calhoff: None declared, Katja Thiele: None declared, Thomas Dörner: Grant/research support from: Eli Lilly, Janssen, Roche, UCB Pharma, Consultant for: Eli Lilly, Janssen, Roche, UCB Pharma, Speakers bureau: Eli Lilly, Janssen, Angela Zink: Speakers bureau: Speakers fees from AbbVie, Janssen, Pfizer, Roche, Sanofi, Jörg Henes: None declared, Jutta Richter: Grant/research support from: GlaxoSmithKline and UCB Pharma for performing the LuLa-study., Katinka Albrecht: None declared


SAT0187  TRENDS IN EMPLOYMENT AND HOSPITALIZATION IN PATIENTS WITH SJÖGREN’S SYNDROME 1993–2016: RESULTS FROM THE GERMAN NATIONAL DATABASE

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Background: During the last 20 years, employment rates increased substantially in the German population and also in patients with arthritis [1]. Whether patients with primary Sjögren’s syndrome (pSS) also show this trend is less clear in the absence of new treatment options.

Objectives: To assess trends in treatment and outcomes in patients pSS, focusing on employment, hospitalization and medical treatment in the past two decades.

Methods: From 1996 to 2016, ~300 patients with pSS were documented annually in the National Database of the German Collaborative Arthritis Centres. Data on treatment, physician assessment of disease activity, patient-reported outcomes, hospitalization and employment were collected and compared to patients with rheumatoid arthritis (RA), matched 1:1 for age, sex and disease duration for each calendar year.

Results: Patients with pSS (>90% female, age ~44 years at disease onset, disease duration ~10 years) were more frequently assessed to be in low disease activity in 2016 (93%) than in 1996 (62%, p<0.01). Treatment with antimalarials increased (31% to 50%, p<0.01) and less patients were on glucocorticoids (50% to 34%, p<0.01); Less than 5% were treated with biologics in 2016. The percentage of employed patients (>65 years) increased by 21 percentage points (43% to 64%, p<0.001), exceeding the increase observed for RA patients (+15 percentage points).

In 2016, significantly less patients compared to 1996 were on early retirement (22% and 10%, p<0.01), hospitalized/year (13 and 7%, p<0.08) or on temporary sick leave (27% compared to 39%, p<0.09). This trend is comparable to RA patients.

Conclusion: Overall, similar trends were observed for RA and pSS cohorts despite minor changes in pSS therapy. Work participation has improved significantly over two decades in pSS. A greater perception of pSS without systemic manifestations may have caused a shift towards less severely affected patient cohorts today.

REFERENCE


SAT0188  WHOLE BLOOD VERSUS SERUM HYDROXYCHLOROQUINE LEVELS FOR DRUG MONITORING OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: PRELIMINARY RESULTS OF A PHARMACOLOGICAL STUDY

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Background: In order to assess the pharmacokinetic/pharmacodynamic relationship of hydroxychloroquine (HQC) in patients with systemic lupus erythematosus (SLE), HQC levels have been measured in whole blood as well as in serum but both methods have never been compared. In addition, cut offs for non-adherence (classically 200ng/mL but also 100 ng/mL) have been established only in whole blood.

Results: Patients with pSS (>90% female, age ~44 years at disease onset, disease duration ~10 years) were more frequently assessed to be in low disease activity in 2016 (93%) than in 1996 (62%, p<0.01). Treatment with antimalarials increased (31% to 50%, p<0.01) and less patients were on glucocorticoids (50% to 34%, p<0.01); Less than 5% were treated with biologics in 2016. The percentage of employed patients (>65 years) increased by 21 percentage points (43% to 64%, p<0.001), exceeding the increase observed for RA patients (+15 percentage points).

In 2016, significantly less patients compared to 1996 were on early retirement (22% and 10%, p<0.01), hospitalized/year (13 and 7%, p<0.08) or on temporary sick leave (27% compared to 39%, p<0.09). This trend is comparable to RA patients.

Conclusion: Overall, similar trends were observed for RA and pSS cohorts despite minor changes in pSS therapy. Work participation has improved significantly over two decades in pSS. A greater perception of pSS without systemic manifestations may have caused a shift towards less severely affected patient cohorts today.

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Disclosure of Interests: Johanna Calhoff: None declared, Katja Thiele: None declared, Thomas Dörner: Grant/research support from: Eli Lilly, Janssen, Roche, UCB Pharma, Consultant for: Eli Lilly, Janssen, Roche, UCB Pharma, Speakers bureau: Eli Lilly, Janssen, Angela Zink: Speakers bureau: Speakers fees from AbbVie, Janssen, Pfizer, Roche, Sanofi, Jörg Henes: None declared, Jutta Richter: Grant/research support from: GlaxoSmithKline and UCB Pharma for performing the LuLa-study., Katinka Albrecht: None declared

Objectives: The aims of this study were (1) to compare these two pharmacological approaches, and (2) since it would be very interesting to retrospectively assess severe non-adherence in clinical trials or in large cohort of patients in which only serum samples are usually available, to determine if serum HCQ level cut offs could be established for identification of severe non-adherent patients.

Methods: The HCQ and desethylchloroquine (DCQ) levels were measured in serum and whole blood from 573 SLE patients. The risk factors for active SLE (SLEDAI score >4) were identified using multiple logistic regression. HCQ serum level was also measured in 51 non-adherent patients (whole blood HCQ level <200 ng/mL).

Results: The mean HCQ and DCQ levels were 916 ± 449 and 116 ± 55 ng/mL in whole blood, respectively; and 469 ± 223 and 63 ± 31 ng/mL in serum, respectively. The mean ratio of serum/whole blood level for HCQ and DCQ were 0.53 ± 0.15 and 0.57 ± 0.21, respectively. A strong positive correlation was found between serum and whole blood levels of HCQ (rho=0.837 [95% CI 0.810-0.860], p<0.0001), and DCQ (rho=0.771 [95% CI 0.736-0.802], p<0.0001). In the multivariate analysis, only corticosteroids (p=0.044), immunosuppressant (p=0.027), HCQ whole blood level (p=0.023) and hemoglobin (p=0.009) were identified as an independent risk factor of active SLE but serum HCQ level was not. Given the mean ratio of serum/whole blood level for HCQ was 0.53, we extrapolated that serum HCQ level cut offs of 106 and 53 ng/mL would correspond to the previously used cut-off of 200 and 100 ng/mL of HCQ in whole blood. Using HCQ serum level cut off of 106 ng/mL, 43 of 51 patients (84%) with blood HCQ levels <200 ng/mL would also have been considered as non-adherent. The positive and negative predictive value of HCQ serum level <100 ng/mL to detect non-adherence were 96.6% and 63.6%, respectively. Of these 51 patients, 25 patients (49%) exhibited HCQ whole blood concentration below 100 ng/mL. Using HCQ serum level cut off of 53 ng/mL, 23 of 25 patients (92%) with HCQ whole blood level<100 ng/mL, would also have been considered as non-adherent. The positive and negative predictive value of HCQ serum level <53 ng/mL to detect non-adherence were 82.1% and 90.9%, respectively.

Conclusion: Our data support the use of whole blood rather than serum as the matrix for drug monitoring of HCQ levels in SLE patients. However, when whole blood is not available, our results support the use of HCQ serum level to assess non-adherence with a cut off of 106 ng/mL, corresponding to 200 ng/mL in whole blood.

Disclosure of Interests: None declared.


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A NOVEL DEVICE FOR RAPID MINOR SALIVARY GLAND BIOPSY IN SUSPECTED SJÖGREN’S SYNDROME

Alexandre Dumusc1, Bettina Bannert2, Diana Dan1, Thomas Huegle1.

Objectives: To describe and compare clinical, serological and histological features of patients with primary Sjögren’s syndrome (pSS) associated non-Hodgkin’s lymphomas (NHLs) in 3 cohorts, from Greece (1) and Italy (2).

Methods: 140 consecutive pSS patients with NHLs who fulfilled the 2002 AEG criteria for Sjögren’s were included in the study. Patients were recruited from 3 centers (Udine, Pisa, Athens, cohort named UPA), two from Italy (Udine and Pisa University Hospitals with a total of 63 cases, named cohort UP) and one from Greece (University of Athens with 77 cases, named cohort A). Age at NHL onset, NHL subtype and distribution, SS disease duration until lymphoma development, serum anti-SSA/SSB antibodies and rheumatoid factor, history of salivary gland enlargement, cryoglobulinemia with or without vasculitis and C4 hypocomplementemia before the onset of NHL were recorded and compared.

Results: The Greek cohort (A) had a median age at lymphoma diagnosis 58 years (range: 28-90 years) and the (UP) cohort a median age at diagnosis of lymphoma 55.6 years (range: 25-77 years). The median time from SS to lymphoma diagnosis was 65.8 months (range: 0-456 months) vs 48 months (range: 0-276 months) for (A) and (UP) cohort respectively. The commonest histologic subtypes such as, MALT (mucosa associated lymphoid tissue), diffuse large B cell (DLBCL) and nodal or splenic marginal zone (MZ) lymphomas were observed in similar frequencies between

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LYMPHOMA IN PRIMARY SJÖGREN’S SYNDROME: A RETROSPECTIVE CLINICAL STUDY WITH PATIENTS FROM THE UPA (UDINE, PISA, ATHENS) GROUP

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Background: Lymphoma development in Sjögren’s syndrome has significant impact on morbidity and mortality of the disease.

Objectives: To describe and compare clinical, serological and histological features of patients with primary Sjögren’s syndrome (pSS) associated non-Hodgkin’s lymphomas (NHLs) in 3 cohorts, from Greece (1) and Italy (2).

Methods: 140 consecutive pSS patients with NHLs who fulfilled the 2002 AEG criteria for Sjögren’s were included in the study. Patients were recruited from 3 centers (Udine, Pisa, Athens, cohort named UPA), two from Italy (Udine and Pisa University Hospitals with a total of 63 cases, named cohort UP) and one from Greece (University of Athens with 77 cases, named cohort A). Age at NHL onset, NHL subtype and distribution, SS disease duration until lymphoma development, serum anti-SSA/SSB antibodies and rheumatoid factor, history of salivary gland enlarge-

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the 2 cohorts. The proportion of pSS NHLs patients with MALT lymphomas and >1 involved sites was significantly higher in cohort (A) compared to (UP) cohort [25/51 (49%) vs 5/40 (12.5%), p=0.0003] while extranodal localization of DLBC lymphomas was less frequent in Greek compared to Italian patients [2/12 (16.7%) and 4/10 (40%) respectively]. No significant differences were observed regarding anti-Ro/SSA, anti-La/SSB, rheumatoid factors (RF) or history of parotid gland enlargement. Interestingly, no significant difference was also observed in the frequencies of serum cryoglobulinemia (without vasculitis) and C4 hypocomplementation. Importantly, cryoglobulinemic skin vasculitis was significantly more frequent in cohort (A) than in cohort (UP) [33/77 (42.9%) vs 12/63 (19.0%), p=0.0027] as well as bone marrow involvement by lymphoma [21/77 (27.2%) vs 4/63 (6.3%) respectively, p=0.0015].

Conclusion: The similar lymphoma histologic subtypes, coupled with the differences in the frequency of cryoglobulinemic skin vasculitis and bone marrow involvement by lymphoma between Greek and Italian patients, suggest potential diversities in genetic background, environmental factors, disease progression and pathologic pathways in different cohorts, offering novel perspectives to study the biology of SS associated lymphomagenesis.

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REFERENCES

Disclosure of Interests: None declared

SAT0191 LOW SOCIOECONOMIC STATUS AND HEALTH RELATED QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS
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Background: Socioeconomic factors have been considered as possible confounding factors in the attribution of greater damage accrual in Afro-Caribbean and Hispanic patients with Systemic lupus erythematosus (SLE). Patients with SLE often experience long-term morbidity that can adversely affect their health-related quality of life (HRQoL).

Objective: To analyze the relation between socioeconomic status, damage accrual and HRQoL

Methods: Analytic study in a cohort of SLE patients that were closely monitored in an autoimmunity program in Colombia. We stratified patients with damage (SDI ≥1) and no damage (SDI <1) and according to socioeconomic status as a surrogate value for economic income with dichotomization in low and medium/high income. We performed a non-parametric analysis of related simples of Wilcoxon in each of the dimensions of quality of life in EuroQol 5d.

Results: We analyzed 400 Colombian patients. Baseline median age was 49 years (15 IQR) with median age at diagnosis and disease duration of 37 years (17 IQR) and 9 years (13 IQR) respectively. There were 94% female patients and 17.3% late onset SLE. Most frequent clinical manifestations were hematological (82.8%), mucocutaneous (75.3%) and nephritis (33.8%). Only 4.5% had neurological involvement. The mean SLEDAI were 1.18 and 0.65 at first and second measurement respectively, in the first measurement 97.1% of the patients had a SLEDAI ≤4. The mean SDI was 0.7275 at first measurement and 0.985 at the second measurement. When comparing the intervention in patients with SDI ≥1 there was a significative improvement in the Quotidian Activities, Pain/Discomfort, Anxiety/Depression domains, independent of economic income. In patients with medium-high income there was also a significative improvement in the mobility and personal care domains. In the no-damage groups there was only a positive impact in the Anxiety/Depression domain in a statistically significant manner, and the medium-high income subgroup had improvement in the Pain/Discomfort domain. We didn’t find other statistically differences in the other domains. Low economic income seems to exert a negative influence in the different HRQoL domains with independance regarding treatment strategy, specially in patients with no damage accrual. In patients with higher income and damage accrual the opposite seems to appear, which could be related with a better ability or resources to cope with the consequences of the disease.

Conclusion: In Colombian patients with SLE, socioeconomic status (as a reflection of income) might be related with HRQoL. This relationship could be influenced by damage accrual

REFERENCE

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### Table: Low vs High Income

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**p Value:**
- 0.004
- 0.003
- 0.001
- 0.002
- 0.01
- 0.001

**Final p Value:**
- 0.035
- 0.03
- 0.01
- 0.001

**Statistical Tests:** Wilcoxon test
MYOSITIS IN PATIENTS WITH PRIMARY SJÖGREN’S SYNDROME: DATA FROM A FRENCH NATIONWIDE SURVEY

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Background: Myositis is recognized as a manifestation of primary Sjögren’s syndrome (pSS). Grading muscle involvement using the EULAR Sjögren Syndrome Disease Activity index (ESSDAI) does not require biopsy-proven active myositis or extensive immunological investigations. However, several studies have reported that a high proportion of pSS-associated myositis is either inclusion body myositis (IBM) or an overlap syndrome (n=7). Among the 29 patients without associated condition likely to explain inflammatory muscle involvement were included. They were categorized and sub-classified. The symptom checklist section of the MDHAQ can provide clues that help discriminate between SLE patients with and without FM. The most discriminating symptoms were muscle pain, swelling (of hands, ankles and in other joints), back pain, neck pain, problems with thinking and dry mouth (all p<0.001). Grouping the above 8 symptoms, a cut-off of ≥4 gave a sensitivity of 91% and specificity of 88%, correctly classifying 89% of patients when compared to FM criteria. Overall, patients with FM reported a mean total of 23.6 items on the symptom checklist, compared to 8.09 for patients without FM.

Conclusion: The symptom checklist section of the MDHAQ can provide clues that help discriminate between SLE patients with and without FM. Clinicians can find valuable information in the specific symptoms experienced by the patient, as well as the overall number of symptoms. Grouping the discriminatory symptoms together in the questionnaire may assist clinicians to consider the diagnosis of FM more easily in patients with SLE.

REFERENCES


THE USE OF A SYMPTOM CHECKLIST TO RECOGNISE PATIENTS WITH COMORBID FIBROMyalgia ON A BACKGROUND OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Fibromyalgia (FM) and systemic lupus erythematous (SLE) are both characterised by non-specific symptoms such as pain and fatigue. To make diagnosis even more challenging, fibromyalgia is over-represented in the SLE population.

Objectives: To identify which symptoms can discriminate between patients with comorbid FM and patients without comorbid FM in the SLE population, using a routinely distributed questionnaire.

Methods: Patients with SLE (n=88) completed a Multi-Dimensional Health Assessment Questionnaire (MDHAQ) [1] and the 2011 FM Criteria questionnaire [2]. FM status was determined using the 2016 modification of the 2010/2011 FM criteria [3]. The MDHAQ contains a 60-item symptom checklist section, giving a score of 0-60. Patients with complete data were analysed for specific symptoms that were discriminating for FM using student’s t test with Bonferroni correction.

Results: SLE patients with FM reported a higher prevalence of positive responses for every symptom except for ‘dark or bloody stools’ and ‘burning in sexual organs’. Nineteen symptoms demonstrated a significant difference between those with and without FM. The most discriminating symptoms were muscle pain, swelling (of hands, ankles and in other joints), back pain, neck pain, problems with thinking and dry mouth (all p<0.001). Grouping the above 8 symptoms, a cut-off of ≥4 gave a sensitivity of 91% and specificity of 88%, correctly classifying 89% of patients when compared to FM criteria. Overall, patients with FM reported a mean total of 23.6 items on the symptom checklist, compared to 8.09 for patients without FM.

Conclusion: The symptom checklist section of the MDHAQ can provide clues that help discriminate between SLE patients with and without FM. Clinicians can find valuable information in the specific symptoms experienced by the patient, as well as the overall number of symptoms. Grouping the discriminatory symptoms together in the questionnaire may assist clinicians to consider the diagnosis of FM more easily in patients with SLE.

REFERENCES


EVALUATION OF PSYCHOMETRIC PROPERTIES OF THE PATIENT-REPORTED OUTCOMES MEASUREMENT INFORMATION SYSTEM (PROMIS) PHYSICAL FUNCTION 10-ITEM SHORT FORM IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: While the PROMIS (Patient-Reported Outcomes Measurement Information System) physical function short form 10a (PF10a) is both practical and acceptable for implementation in routine clinical practice, its psychometric properties have not been evaluated in Systemic Lupus Erythematosus (SLE).

Objectives: The objectives of our study were to examine the validity and responsiveness of PF10a in SLE among a racially/ethnically diverse clinic population and develop estimates of the minimally important difference (MID).

Methods: Data were derived from electronic health records for all SLE patients seen in a university-based rheumatology clinic between 2013 and 2018. We evaluated the PF10a’s floor and ceiling effects among different racial/ethnic groups. Construct validity was assessed by examining Spearman’s correlation coefficients between the PF10a and other patient-reported pain (scale 0-10) and pain visual analogue scale (VAS) (scale 0-100), physician-reported (SLE disease activity index (SLEDAI)) and laboratory (erythrocyte sedimentation rate (ESR)) measures. Known-group validity was assessed by evaluating effect size (Cohen’s d) between categories of pain (no pain vs. moderate-severe pain). We used standardized response means to examine the responsiveness of the PF10a to longitudinal changes in pain and SLEDAI. MID was estimated using distribution based and anchor-based methods.

Results: We included 612 patients in cross-sectional analyses of validity and 462 patients in longitudinal analyses of responsiveness. Mean age was 40.5±14.6, 87% were female and 32% Caucasian. The PF10a had ceiling effects above the commonly accepted criteria of 15% among Caucasian (23%), Asian (23%) and Other (17%) race/ethnicities, and no floor effects. Construct validity analyses showed strong correlations (r=0.66, p<0.05) with pain VAS, moderate correlations (r=0.58, p<0.05) with pain, and weak correlations with ESR (r=0.25, p<0.05) and SLEDAI (r=0.16, p<0.05). Construct validity analyses showed large differences among pain groups (Cohen’s d=1.49, p<0.05). The PF10a was responsive to improvements in pain (SRM=0.5) and SLEDAI (SRM=0.49). Distribution-based MIDs were +2 for improvement and -7 for deterioration. Anchor-based MIDs were +2 for improvement, -3 for deterioration with pain as anchor and +5 for improvement, -5 for deterioration with SLEDAI as anchor.

Conclusion: Although the PF10a showed some ceiling effects, it had good validity in this young racially/ethnically diverse sample with SLE. The PF10a was responsive to improvements in pain and disease activity. The anchor-based MIDs appear to be similar to those reported for PF10a in rheumatoid arthritis(1). This information supports the use of the PF10a in SLE and provides important information to facilitate interpretation of scores.

REFERENCE

SAT0196
SYSTEMIC DISEASES ASSOCIATED WITH AUTOIMMUNE LIVER DISEASES
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Background: Autoimmune liver diseases are considered as a group of hepatobiliary injuries mediated by abnormal immunity in subjects with genetic predisposition. It mainly includes autoimmune hepatitis, primary biliary cholangitis, primary sclerosing cholangitis and overlap syndrome. They are oftenly associated with different manifestations of autoimmune systemic diseases such as systemic lupus erythematosus, CREST syndrome ....

Objectives: The aim of this study was to evaluate the prevalence and the characteristics of systemic diseases associated with autoimmune hepatopathies.

Methods: We carried out a retrospective study from January 1996 to December 2018 including all patients with autoimmune liver diseases followed in our department: 64 primary biliary cholangitis (PBC), 22 autoimmune hepatitis (AIH), 23 overlap syndrome (OS), 15 primary sclerosing cholangitis (PSC).

Results: One hundred and twenty four patients were included in our study: 107 women and 17 men with an average age of 55 years (18-87 years). An immunological disorder was found in 58 cases (48%): [20 PBC/12 AIH/12 OS/6 PSC] with a female predominance (Sex ratio (Men/Women) = 0.09). Systemic diseases included respectively: Sjögren’s syndrome in 20 cases, systemic lupus erythematosus in 7 cases, rheumatoid arthritis in 5 cases, CREST syndrome in 11 cases and autoimmune thyroiditis in 2 cases. The discovery of autoimmune disorder was in most cases concomitant to the diagnosis of the autoimmune liver disease (87%). Our study showed biological assessment perturbation in 20 cases with positivity of : anti-centromere antibodies (11 cases), anti-SSA antibodies (5 cases), anti-cardiolipin antibodies (4 cases) and rheumatoid factor (5 cases).

Conclusion: Our study shows a strong prevalence of systemic disease during autoimmune hepatopathies. A systematic screening for clinical and biological immune manifestations are highly recommended in those patients.

INCIDENCE AND OUTCOME OF NON-TYPHOID SALMONELLA BACTEREMIA IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN COMPARISON WITH RHEUMATOID ARTHRITIS AND PRIMARY SJÖGREN’S SYNDROME

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Background: Non-typhoid Salmonella (NTS) infection is an important problem in patients with systemic lupus erythematosus (SLE) [1, 2]. However, less is known about the incidence rate (IR) for NTS bacteremia. Objectives: To evaluate the IR of NTS bacteremia in patients with SLE, in comparison to rheumatoid arthritis (RA) and primary Sjögren’s syndrome (SjS), and by comparison with other Gram-negative bacilli (GNB) bacteremia including Escherichia coli (E. coli) and Pseudomonas aeruginosa (PsA). Furthermore, to access the survival outcome after NTS bacteremia.

Methods: In this single-center retrospective cohort study, we analyzed the registry of catastrophic illnesses database for patients fulfilled the criteria of SLE, RA, and SjS in National Taiwan University Hospital. The patients aged over 20 years, with adequate follow-up during January 1, 2008 to December 31, 2017 were included. Only new episodes of positive blood cultures during the observation period were taken into analysis. Cox proportional hazards regression model was applied for calculating the incidence rate ratio (IRR) of bacteremia between different diseases, and the hazard ratio (HR) of mortality.

Results: This study included 5953 patients. NTS bacteremia happened in 33 cases, among which 27 (81.8%) were group D1 and 4 (12.1%) were group B Salmella. The baseline characteristics, IR of each GNB bacteremia, and the IRR adjusted for age, sex, diabetes mellitus (DM) as well as chronic kidney disease (CKD) are shown in Table 1. Compared to patients with RA, the IRR for NTS bacteremia was highest in SLE. The IRR for E. coli bacteremia in patients with SLE also increased in comparison with RA, although not as high as for NTS bacteremia. When compared to SjS, patients with SLE still had an elevated IRR of 3.52 (95% CI: 1.29–9.63, p=0.014) for NTS bacteremia. In SLE patients, DM increased the IR for NTS bacteremia (IRR: 4.43, 95% CI: 1.71–11.43, p=0.002; adjusted for age and sex).

In the 33 cases with NTS bacteremia [male: 21.2%; age: 49.0 (37.9–64.2) years], the median observation time to event was 11.1 (IQR, 3.0–38.1) months. No recurrent bacteremia was found. There were 14 (42.4%) deaths, and 7 (21.2%) died within 60 days after NTS bacteremia. The median time to all-cause mortality was 54 (IQR, 17–153) days. In survival analysis, an abnormal body mass index (BMI) (BMI, normal >18.5 and ≤24) at the onset of bacteremia had a crude HR of 6.20 (95% CI: 1.64–23.52, p=0.007). The diagnosis of SLE, age, gender, DM, CKD, levels of C-reactive protein and white blood cell count did not significantly increase HR.

Conclusion: Among the GNB bacteremia, patients with SLE were especially susceptible to NTS bacteremia when compared to RA and SjS. DM was a risk factor. The mortality rate after NTS bacteremia was high, and an abnormal BMI may predict it.

REFERENCES

Disclosure of Interests: None declared

SAT0198
PERIPHERAL NERVOUS SYSTEM INVOLVEMENT IN PRIMARY SJÖGREN’S SYNDROME—UNCOMMON OR UNDERESTIMATED PROBLEM?

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Background: Systemic manifestations are common in primary Sjögren’s syndrome (pSS) and play a major role in the prognosis. Neurological complications may affect both the peripheral (PNS) and central nervous system (CNS). The incidence varies from several to several dozen per cent. The course of the disease and the severity of the symptoms may be mild and self-limiting or progressive, leading to permanent neurological deficits. It is worth remembering that the symptoms of nervous system involvement may precede the onset of symptoms of dryness, and diagnosis of pSS may be delayed after a certain duration of neurological symptoms.

Objectives: The aim of the study was to determine the prevalence of PNS involvement among symptomatic and asymptomatic patients with the diagnosis of pSS in our University Clinical Centre.

Methods: We studied a consecutive group of fifty unselected patients aged from 33 to 74 years (mean 55.8 years). All patients fulfilled the criteria for the diagnosis of pSS. Additional connective tissue diseases and diabetes were the exclusion criteria. Disease activity was evaluated according to the EULAR Sjögren’s syndrome disease activity index (ESS-DAI). All patients underwent clinical neurological examination and nerve conduction study (NCS) of nine peripheral nerves. For the classification of polymyopathies the ESTEEME (European Standardized Telerematic Tool to Evaluate Electrodiagnostic Methods) guidelines were used. Clinical examination and nerve conduction study were performed and evaluated by one certified neurologist.

Results: Of our 50 patients, 48 were female with a mean (±SD) age 53.6±10.5 years and mean disease duration 7.9±5.3 years. Two were male with mean age 43.7±25.8 years and mean disease duration 5.7±1.6 years. The mean age at diagnosis was 50.4±14 years. 23 (46%) patients fulfilled the criteria for the diagnosis of neuropathy. The most common PNS manifestation was sensorimotor neuropathy 11/23 (47%), mononeuropathy was present in 6/23 (26%) patients, pure axonal sensory neuropathy was present in 1/23 (4.3%) patient, axonal motor neuropathy in 1/23 (4.3%), SFN in 1/23 (4.3%) and cranial nerve involvement was present in 4/23 (17.4%) (one of the patients both had cranial and sensorimotor neuropathy). Neurological symptoms preceded the diagnosis of pSS in 8 (35%) of 23 PNS+ patients. The frequency of following symptoms and extradural manifestations was significantly higher in PNS+ compared to PNS- patients: salivary gland enlargement (74% vs 44% p<0.05), respiratory tract involvement (65% vs 37% p<0.05) and myelophenopathy (61% vs 19% p<0.05). The mean ESSDAI in patients with and without neurological involvement was 7.6±8.2 and 4.7±4.58 respectively (p=0.245). In this subgroup the use of cyclophosphamide, due to extradural manifestations, was increased (p=0.05).

Conclusion: We found that PNS involvement is a common extradural manifestation of pSS (46% in our group). Sensorimotor neuropathies were most frequent. Involvement of the PNS seems frequent but remains underestimated. NCS is a non-invasive test which might be useful at diagnosis and follow-up. Guidelines for the diagnosis and treatment of peripheral neuropathies in patients with pSS are needed.

Disclosure of Interests: None declared

Scientific Abstracts
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POLYAUTOIMMUNITY IN SYSTEMIC LUPUS ERYTHEMATOSUS. DATA FROM A LARGE SPANISH COHORT: SPANISH SOCIETY OF RHEUMATOLOGY REGISTRY OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (RELESSER).

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Methods: The basis for defining polyautoimmunity was the presence of at least 2 SLE criteria associated with other autoimmune diseases. Main outcome: Polyautoimmunity was defined as patients who fulfilled criteria for SLE and other autoimmune disease: autoimmune thyroiditis, rheumatoid arthritis, systemic sclerosis or inflammatory myopathy and mixed connective tissue disease. Multiple autoimmunity syndrome (MAS) was defined as patients who met SLE criteria and at least two other autoimmune diseases.

Results: From 3679 (91.4%) patients included in the registry, 501 (12.8%) had polyautoimmunity in patients with SLE. A family history of SLE was 12.4% and MAS in 12.7% for antiphospholipid syndrome.

Conclusion: SLE patients associated polyautoimmunity in 14%, MAS in 2%. More studies are needed to better understand the increase of polyautoimmunity in these patients.

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UNUSUAL SYSTEMIC LUPUS ERYTHEMATOSUS/ SJOEGREN'S SYNDROME PHENOTYPE IN A PATIENT WITH A TNFAIP3 GENE MUTATION

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Background: Mono-allelic mutation in tumor necrosis factor alpha induced protein 3 (TNFAIP3) has been found to cause haploinsufficiency of A20 protein, the cause of an early-onset auto inflammatory disease resembling Behcet’s Disease (BD). Single nucleotide polymorphism in TNFAIP3 may also contribute to susceptibility to systemic lupus erythematosus (SLE). Several mutations in TNFAIP3 have been shown to be disease-causing, including a single case with heterozygous mutation in the TNFAIP3 gene for c.811C>T: p.(arg271?) with a BD-like phenotype.

Objectives: To report the case of a child with heterozygous mutation TNFAIP3 (c.811C>T: p.(arg271?) with an unusual SLE/SS (Sjogren syndrome) phenotype, thus expanding the phenotype associated with this mutation; and describe the disease course and treatment.

Methods: Clinical details were retrospectively collated using routine clinical records. The molecular cause of the phenotype was investigated using a targeted gene next generation sequencing (NGS) panel (the vasculitis and inflammation panel, VIP). Confirmation of findings detected by NGS were confirmed using conventional Sanger sequencing in the index case and subsequently in the parents.

Results: A 4yr old Caucasian female presented with a 2-year history of photosensitive malar rash, mouth ulcers, hair loss, arthralgia, livedo reticularis, cervical lymphadenopathy and hepatosplenomegaly. Laboratory tests revealed anemia, raised inflammatory markers and hypocomplementemia; RF, ANA and anti Ro positivity, raised C1q antibodies and low C1Q level. 7 out of 11 classification criteria for SLE were met and treatment with hydroxychloroquine was commenced. Subsequently she developed blepharitis, acute anterior uveitis, chilblains and discoid skin lesions. Azathioprine and oral steroids were added. Due to young age at disease onset, NGS screening was performed and revealed heterozygous mutation in TNFAIP3 c.811C>T: p.(arg271?) Screening of both parents revealed the same mutation in the mother, who is asymptomatic. The child further developed Raynaud’s and underwent renal biopsy for intermittent proteinuria which revealed ISN/RPS Class III and V lupus nephritis. Azathioprine was switched to mycophenolate mofetil. One year later her skin symptoms continue to improve, uveitis is in remission and her renal function is normal. Prednisolone was tapered off.

Figure: chilblain and discoid skin lesions, Raynaud’s and histopathological changes from a renal biopsy consistent with glomerulonephritis.
Cardiovascular Events in Systemic Lupus: The Role of Cardiovascular Risk and SLE-Related Factors

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Background: Patients with SLE may have an increased risk of cardiovascular (CV) events due to the contribution of disease-related factors.

Methods: Two hundred and sixty two consecutive SLE patients (age 42.9 ± 14.5 years, 89% female, disease duration 11.5 ± 8.2 years) have been evaluated, 240 (92%) with articular, 226 (86%) with cutaneous, 167 (64%) with hematological, 61 (23%) with serositis involvement respectively and 86 (33%) with lupus nephritis (LN) and 105 (40%) with neuropsychiatric SLE (NPSLE). The follow-up data were collected and information on traditional CV risk factors (age, sex, diabetes, smoking, arterial hypertension, dyslipidemia), disease-specific parameters (SLEDAI-2K, chronic steroid therapy, current antimalarial and other immunosuppressive therapy) and autoantibody profile (ANA, anti-SSa/Ro, anti-SSb/La, IgA and IgM Rheumatoid factor (RF), complement reduction, anticardiolipin (ACLA), anti-beta2-glycoprotein 1 (anti-B2GPI), lupus anticoagulant (LAC)) were analyzed for each patient. As CV manifestations, acute cardiac and cerebrovascular ischemic events and chronic ischemic heart disease were considered.

Results: Twenty-seven SLE patients (10.3%) experienced CV events during the follow-up period with a significantly higher rate of male sex (24% in males vs 8.6% in females, p=0.001) among the considered demographical parameters. Among those patients, 10 (37%) presented cerebrovascular accidents, 6 (22%) acute cardiac ischemic events, 7 (26%) chronic ischemic heart disease and 4 (15%) both cardiac and cerebrovascular events during the follow up period. In particular, SLE patients who experienced CV events during the follow up were older at disease onset than patients who did not experience CV events during the follow-up (42.2 ± 19.4 vs 29.8 ± 13.1 years, p<0.001). Considering the traditional CV-related risk factors, among the SLE cohort, patients who experienced CV events during the follow up were more likely having concomitant dyslipidemia (p=0.03), diabetes mellitus (p=0.01) and arterial hypertension (p=0.001) compared to SLE patients who did not experience CV events. Considering the disease-related parameters, no significant association between CV events development and ANA, anti-SSa/Ro, anti-SSb/La positivity and complement reduction was found (p=0.05) despite SLE patients who experienced CV events during the follow-up were more likely with concomitant neurological involvement (p=0.002) and ongoing chronic corticosteroid therapy (p=0.03) compared to SLE patients who did not experience CV events.

Finally, considering the anti-phospholipid antibodies (aPL) profile, SLE patients who experienced CV events during the follow-up were more likely positive for anti-B2GPI (p <0.001), ACLA (p=0.0001) and LAC (p <0.0001) compared to SLE patients who did not experience CV events. In addition, multivariate analysis revealed that, aPL positivity arose as an independent risk factor associated with CV events development in SLE patients contingent to the number of aPL positivities (single aPL positivity, OR 4.52 (0.97-21.18); double aPL positivity, OR 23.95 (4.39-130.76); triple aPL positivity, OR 34.01 (7.64-151.40)).

Conclusion: in SLE patients, aPL positivity significantly increases the risk of CV events development regardless to the traditional CV risk factors contingent to the number of aPL positivities.

REFERENCE:

Disclosure of Interests: Anna Maria Paglionicia: None declared, Valentina Varriano: None declared, Luca Petricca: None declared, Clara Di Mario: None declared, Maria Rita Gigante: None declared, Giacomo Tanti: None declared, Barbara Tolusso: None declared, Gianfranco Ferraccioli: Speakers bureau: BMS, Roche, Elisa Gremese Consultant for: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Sanofi, UCB, Roche, and Pfizer, Speakers bureau: BMS, Speakers bureau: Abbvie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Sanofi, UCB, Roche, and Pfizer


Evaluation of Left Atrial Myocardial Deformation as Marker of Subclinical Damage in Patient with Systemic Lupus Erythematosus

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Background: The left ventricle diastolic dysfunction (LVDD) may be the only manifestation of cardiac involvement in patients with systemic lupus erythematosus (SLE), preceding systolic dysfunction. The myocardial deformation of left atrium (LA) through the evaluation of LA global longitudinal strain (LALS) may be useful in assessing diastolic function since the lower the LALS the worse is the diastolic function.

Objectives: The main objective of this study was to evaluate the LA function through myocardial deformation by strain and strain rate derived from speckle tracking echocardiography in patient with SLE without any cardiovascular symptoms and compare with Control Group (CG). To compare LA strain of patients with active, inactive SLE disease and control group and determine the independent factors associated with depressed LALS.

Methods: A cross sectional study was performed. Fifty patient that fulfilled 2012 SLICC classification criteria for SLE were included and they were compared with fifty age- and gender-matched healthy subjects as control group. Myocardial deformation was measured by transthoracic...
Correlation between the serum 1,25(OH)2D3 level and clinical data of patients with primary Sjögren’s syndrome.

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Background: The role of vitamin D in regulating immune function in autoimmune diseases has been extensively studied. While there is less research on vitamin D in Sjögren’s syndrome. This study will explain the relationship between vitamin D and Sjögren’s syndrome.

Objectives: To explore the relationship between the serum 1,25(OH)2D3 level and the changes of disease activity in patients with Primary Sjögren’s Syndrome (PSS) [1], and to explore whether supplementation of VD could be a potential therapy for the treatment of PSS.

Methods: PSS patients (n=60, according to the 2002 International Classification (Diagnostic) Standard for Sjögren’s Syndrome) were enrolled and health individuals were normal controls. Laboratory examinations were analyzed including that serum levels of 1,25-dihydroxycholecalciferol [1,25(OH)2D3], lymphocytes and CD4+ T cell subsets by flow cytometry, urine pH value, ALT, AST, BUN, Cr, IgG, C3, C4, ESR, CRP, serum levels of 1,25(OH)2D3. Physical examination data include Salivary flow rate, secretion of tears, breakup time of tear film (BUT), and labial glands biopsy.

Results: Compared with that in normal controls, the levels of serum VD in patients with PSS was decrease significantly, Z=-7.367, P<0.001(Figure 1). Spearman correlation analysis and comparison with the collected indexes, showed that VD was significantly correlated with secretion of tears (r=-0.455, p<0.002), IgG (R=-0.581, p<0.000), B cell absolute count (R=-0.474, p=0.002), B cell percent (R=-0.391, p=0.005), Th1 absolute count (R=0.318, p=0.003), Th17 absolute count (r=-0.297, p=0.034), Th17
diabetic retinopathy.

REFERENCES

Table 2: Correlation between the serum 1,25(OH)2D3 level and clinical data

<table>
<thead>
<tr>
<th>Correlation</th>
<th>BMI</th>
<th>disease duration</th>
<th>ESSDAI</th>
<th>base salivary flow rate</th>
<th>stimulant salivary flow rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum 1,25(OH)2D3 level</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.56</td>
<td>0.51</td>
<td>0.21</td>
<td>0.43</td>
<td>0.55</td>
<td>0.21</td>
</tr>
</tbody>
</table>

*P<0.005, **P<0.01, ***P<0.001
Results are given as median (P 25,P75), patients with PSS 10.2 0 (9.00,15.11), healthy people 20.71 (15.16,28.41), Z=-7.37 P<0.001

Disclosure of Interests: None declared


SAT0204 LUPUS LOW-DISEASE ACTIVITY STATE VS SLE RESPONDER INDEX IN A “REAL-LIFE” SETTING

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Background: Systemic lupus erythematosus (SLE) is a chronic multi-organ autoimmune disease characterised by a heterogeneous pathogenic background and by protein clinical manifestations. Recent efforts in identifying novel agents for therapeutic interventions have led to disappointing results and designing a reliable way to assess drug efficacy and verify the achievement of remission, has become itself a major challenge. The SLE responder index (SRI) is a composite tool developed and validated in clinical trials to define in patients with active disease an acceptable response to investigational agents. The role of SRI outside clinical trials has not been defined. The lupus low disease activity state (LLDAS) has been originally validated in a cohort-based setting and it focuses on the achievement of fixed conditions rather than variations from baseline. A formal comparison of these tools outside clinical trials has not been performed.

Objectives: To prospectively assess the performance of SRI and LLDAS in a “real world” observational setting.

Methods: One hundred-thirty-one consecutive patients SLE were subdivided into two groups based on the need or not to escalate their immune suppressive treatment. Clinimetrics including Physician Global Assessment scale (PGA), SLE Disease Activity Index 2000 (SLEDAI-2K) and British Isles Lupus Assessment Group index (BILAG) 2004 version were measured at baseline and at six and 12 months, together with laboratory data and treatment changes. LLDAS and SRI were calculated at each time point.

Results: LLDAS achievement correlated with treatment de-escalation over 12 months (p<0.2, p=0.034, OR=4.1 with 95%CI=1.2-14.4), whereas SRI-4 achievement did not. LLDAS responses were more frequent in patients with lower basal SLEDAI-2K (i.e SLEDAI-2K=6; 2y=21.5, p=0.001, RR=8.4 with 95%CI=3.2-25.0), while SRI-4 responses were more prevalent among patients with higher basal SLEDAI-2K and/or severe renal activity at baseline (y=5.9, p=0.025, RR=10.8 with 95%CI=1.1-103.1).

Conclusion: The level of serum VD in PSS patients was significantly lower than that in normal controls, which was negatively correlated to secretion of tears, IgG, the absolute number of B, Th1, and Th17, the percentage of B and Th17, and ratios of Th1/Th2 and Th17/Tregs. Raising serum VD levels by supplementation of VD, may be a potential Therapy for Sjogren’s syndrome.

REFERENCES

Figure 1. Comparison of VD levels(ng/ml) between patients with PSS and healthy people

Lupus Low Disease Activity State vs SLE
A CYKOTINE “SCAR SIGNATURE” CHARACTERIZES PATIENTS WITH FATIGUE IN SYSTEMIC LUPUS ERYTHEMATOSUS AND SJÖGREEN’S SYNDROME

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Background: Fatigue is highly prevalent in systemic lupus erythematosus patients (SLE) and primary Sjögren’s syndrome (pSS) and represents one of its unmet needs.[1] Its pathogenesis is multifactorial, with the activity of the underlying disease exerting a prominent role, along with psychological factors and co-morbid conditions. Previous studies evaluating fatigue and cytokines in patients with SLE and pSS have yielded inconclusive results.

Objectives: We aimed to evaluate patient-reported outcome measures reflecting fatigue and their correlation to serum cytokines in patients with SLE and pSS and healthy volunteers (HV). A panel of circulating cytokines, chemokines and growth factors was compared between groups, correlated to the level of fatigue and within SLE and pSS to global disease activity. The objective was to identify cytokines reflecting the degree of fatigue, which could be exploited as biomarkers and therapeutic targets.

Methods: We performed a cross-sectional study on subjects included in the Swiss SLE Cohort Study (SSCS). All subjects were evaluated clinically and had a serum sample taken. Fatigue was assessed by FAS (Fatigue Assessment Scale) and by the vitality subscale (VT) of the Med-ics Outcomes Study 36-Items Short Form Healthy Survey. Clinical activity in SLE and pSS patients was determined by a 4-point Likert-scale Physician’s Global Assessment (PGA). SLE activity was assessed with the SLE Disease Activity Index score with the Safety of Estrogens in SLE National Assessment modification (SELENA-SLEDAI). Serum cytokines were assessed by multiplex bead array analysis (ProcartaPlex, Thermo-fisher Scientific, USA). P values were adjusted for multiple comparisons.

Results: Fifty-six patients with SLE, 18 with pSS and 18 healthy volunteers (HV) were included between November 2015 and June 2016. There were no significant differences between groups regarding to age, gender and body mass index (BMI), FAS and VT correlated strongly (Spearmann’s rho -0.87, p<0.01). FAS was significantly higher in patients than in healthy individuals (median FAS 23 [16-31], 28[20.5-35], 17 [15-27] in SLE, pSS and HV respectively; p=0.02). Patients with SLE and pSS displayed higher serum levels of interferon (IFN)-gamma (median [IQR] 10.29 [4.94-15.25] pg/mL in SLE, 9.64 [6.25-13.86] pg/mL, undetectable in HV; p<0.01). Interleukin (IL)-10 also was only detected in pSS and SLE. Hepatocyte growth factor (HGF) was more expressed in patients than in controls (p< 0.01). The levels of most other cytokines (IFN-alpha, IL-1 alpha, IL-2, IL-4, IL-6, IL-17, IL-21 and IL-23) were not detectable. Only HGF displayed a significant correlation with FAS (P Pearson 0.29, p< 0.01).

Conclusion: Patients with SLE and pSS display a molecular pattern of chronic inflammatory conditions, with higher serum levels of IFN-gamma, IL-10 and HGF. The latter two are both involved in regeneration and tissue repair (“scar signature”).[2] HGF levels correlated independently with...
the degree of fatigue. More studies are needed to understand the role of this pleiotropic growth factor in self-perceived fatigue in SLE and pSS.

REFERENCES

Disclosure of Interests: None declared

SAT0206 FACTORS ASSOCIATED WITH HYDROXYCHLOROQUINE USE IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH END STAGE RENAL DISEASE
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Background: Hydroxychloroquine (HCQ) use in SLE has been associated with a lower risk of end-organ damage, SLE flares, and thrombosis, with potential mortality benefit among SLE with end stage renal disease (ESRD)1, 2, 3. However, fewer than 30% of SLE continue HCQ after ESRD onset4. It has not been studied what factors are associated with HCQ use after ESRD. Understanding these factors may inform future studies assessing the safety and efficacy of HCQ in SLE-ESRD. However, fewer than 30% of SLE continue HCQ after ESRD. Understanding these factors may inform future studies assessing the safety and efficacy of HCQ in SLE-ESRD.

Methods: We performed a retrospective chart review of SLE patients with ESRD at a single tertiary care center between 2010-2017. All included patients met ACR and/or SLICC criteria for SLE and had at least one visit with rheumatology, nephrology, or primary care, before and after the development of ESRD. SLE-related symptoms, serologic markers of disease activity, and rheumatology visits were identified, both pre- and post-ESRD onset. Transplanted patients were excluded at the time of their first renal transplant.

Results: A total of 69 patients were included, 58 had pre-ESRD data. Of these patients, 33/58 (57%) were taking HCQ prior to ESRD onset. Following the diagnosis of ESRD, 40/58 (53%) were prescribed HCQ within six months after ESRD onset. Of these, 60/69 (%) were taking HCQ prior to ESRD onset. The last documented visit, and one patient initiated HCQ six months after ESRD onset (prescribed by a rheumatologist). At the last documented visit, 35/69 (51%) had an active HCQ prescription.

Patients taking HCQ were younger, more likely to be followed by a rheumatologist, had a higher frequency of documented arthritis, higher frequency of corticosteroid use and immunosuppressive medication use (Table 1). A history of oral ulcers, cytopenias, and elevated levels of dsDNA at any point (either pre or post-ESRD onset) was not significantly associated with HCQ use at the last visit.

Conclusion: HCQ is more likely to be continued among patients with signs of persistently active SLE. HCQ was more likely to be prescribed by a rheumatologist and was associated with the presence of arthritis. Limited systemic evaluation and documentation by the different providers may have resulted in under-reporting of some of the SLE symptoms. However, these findings reflect the “real-world” experience with HCQ use after ESRD in a large tertiary care center.

REFERENCES

Disclosure of Interests: None declared

Table 1. Factors associated with HCQ use at the last visit post-ESRD4

<table>
<thead>
<tr>
<th>HCQ last ESRD visit</th>
<th>N=35</th>
<th>HCQ last ESRD visit</th>
<th>N=34</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at ESRD onset, median (IQR)</td>
<td>33 (26, 46)</td>
<td>46 (29, 53)</td>
<td>0.05</td>
<td></td>
</tr>
<tr>
<td>Time from ESRD onset to the last visit, months, median (IQR)</td>
<td>40 (21, 72)</td>
<td>59 (11, 99)</td>
<td>0.3</td>
<td></td>
</tr>
<tr>
<td>Women, n(%)</td>
<td>29 (83)</td>
<td>28 (82)</td>
<td>0.95</td>
<td></td>
</tr>
<tr>
<td>Arthritis, n(%)</td>
<td>7 (20)</td>
<td>0</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Rash, n(%)</td>
<td>2 (6)</td>
<td>1 (3)</td>
<td>0.61</td>
<td></td>
</tr>
<tr>
<td>Oral ulcers, n(%)</td>
<td>1 (3)</td>
<td>0</td>
<td>0.33</td>
<td></td>
</tr>
<tr>
<td>Alopecia, n(%)</td>
<td>1 (3)</td>
<td>2 (6)</td>
<td>0.52</td>
<td></td>
</tr>
<tr>
<td>Serositis, n(%)</td>
<td>2 (6)</td>
<td>3 (10)</td>
<td>0.59</td>
<td></td>
</tr>
<tr>
<td>Cytopnia, n(%)</td>
<td>27 (78)</td>
<td>26 (79)</td>
<td>0.75</td>
<td></td>
</tr>
<tr>
<td>Low complement, n(%)</td>
<td>16 (50)</td>
<td>19 (58)</td>
<td>0.54</td>
<td></td>
</tr>
<tr>
<td>Elevated dsDNA, n(%)</td>
<td>12 (39)</td>
<td>10 (31)</td>
<td>0.54</td>
<td></td>
</tr>
<tr>
<td>Corticosteroid use, n(%)</td>
<td>31 (89)</td>
<td>23 (72)</td>
<td>0.08</td>
<td></td>
</tr>
<tr>
<td>Immunosuppressive use, n(%)</td>
<td>25 (71)</td>
<td>14 (42)</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>Rheum visit post ESRD at least once, n(%)</td>
<td>29 (85)</td>
<td>20 (59)</td>
<td>0.02</td>
<td></td>
</tr>
</tbody>
</table>

4Symptoms and medications recorded as ‘ever’ after ESRD onset

SAT0207 DEVELOPMENT OF QUESTIONNAIRES TO ASSESS HEALTHCARE UTILIZATION AND ACCESS IN PATIENTS WITH PRIMARY SJÖGREN’S SYNDROME AT THE DIAGNOSIS AND DURING THE DISEASE COURSE
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Background: The geographic variation in healthcare spending, utilization and quality, across and within countries is well documented. Objectives: In this study, we develop and validate a tool to collect comparable information in Europe to establish practice profiles in the disease management and treatment of patients with Primary Sjögren’s Syndrome (pSS). Methods: Two questionnaires, one to newly diagnosed patients and one for patients at their follow-up visits, have been developed and validated through a pilot survey. The questionnaires aim to assess the pSS patients’ experience and satisfaction with the primary care and specialist services received. The questionnaires consist of 30 items and collect patient-reported data on: type and intensity of treatments and services received, costs, patients’ satisfaction, patients’ overall health and socio-demographic characteristics. A narrative-based medicine section is also included to explore patients’ journey to pSS diagnosis. The questionnaires are administered to a sample of pSS patients attending >20 clinical centers within the European Horizon2020 project “Harmonics”. Additionally, a short questionnaire is administered to the specialists of the clinical centers to collect data on their organization.

Results: Preliminary results of pilot survey based on questionnaires administered to 164 pSS patients (157 F; 7 M, mean (SD) age = 60 (12.2) years) from 5 clinical centers have been analyzed. The majority of the respondents had a primary or secondary school (59%). Both the total number of specialists involved in the care other than the rheumatologist and the number of treatments received in the last 12 months before the interview varies among patients and across centers (p<0.001). Although, as expected, the most frequently involved specialists were the ophthalmologist (90%) followed by the gynecologist and the dentist. Additionally, patients with lower education have attended on average less specialists (p<0.001). Findings from the survey to clinicians also show significant geographic variations in the organization of the care to pSS in the participating centres and in the level of integration among different professionals and care settings. On average, 4 professionals (i.e. clinicians and nurses) per centre are involved in care of pSS patients although with significant differences among centre (min=1, max=10) also in the mix of the staff. In 80% of the centres clinicians use written documentation to exchange patients’ information, followed by periodic meetings with colleagues (58%) and phone calls with the family doctor (37%). In 54% of the centres the newly diagnosed patients are provided with information pamphlet and...
patients health education is performed in 35% of the center through periodic individual meetings.

Conclusion: Preliminary results confirm that the questionnaire is a valid tool to assess and compare patterns of care for pSS patients in terms of the use of treatments and services across and within providers. Once available the questionnaires from all the centres, patient-reported data linked with information from clinical records will allow to measure the patients journey more comprehensively along the care pathway and to identify best practices in terms of the level of perceived quality and the way the care is delivered and, moreover, opportunities for increasing value for patients.

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TEN-YEAR OVERALL SURVIVAL AND STANDARIZED MORTALITY RATIO IN THE LONGEST SINGLE CENTER COHORT OF PATIENTS WITH PRIMARY SJOGREN’S ASSOCIATED LYMPHOMAS

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Background: The development of non-Hodgkin’s Lymphoma (NHL) in Sjögren’s syndrome (SS) contributes to an inferior survival compared to SS patients without lymphoma.

Objectives: To record the long-term outcomes of SS patients with and without NHLs with 10-year survival curves and standardized mortality ratio (SMR) for first time in the literature.

Methods: In order to estimate the effect of NHL development in SS outcome, we expanded the follow-up time of the previously published cohort of SS-associated NHL cases and we retrospectively compared them with age- and sex-matched SS patients without NHL from our center. As outcome end-points, overall and event-free survivals (OS and EFS, respectively) were used. An event was defined as disease relapse or progression, histological transformation or death. Ten-year survival plots and SMR compared to General Greek population was calculated. The impact of rituximab in the outcome of SS-associated NHL treated patients was also studied.

Results: From a total of 712 consecutive SS patients who fulfill the 2002 AECG classification criteria for Sjögren’s, 77 were diagnosed with NHL. The prevalence of MALT and DLBCL lymphoma in the total SS cohort was 7.1% and 1.7% respectively. The median follow-up time from SS diagnosis was 16.67 years (range: 4.00-38.91 years) corresponding to a total of 1263.71 person-years for SS-associated NHL patients and 17.92 years (range: 2.00-34.00 years) with a total of 1380 person-years for SS patients without NHL. The median time from SS to lymphoma diagnosis was 5.5 years (range: 0.38 years) and the median follow-up time after lymphoma diagnosis was 8.2 years (range: 0.1-26.2 years) months. During follow-up, 15 patients from the SS-NHL group died, 11 of whom due to lymphoma-related causes, while only 2 patients died in the control group (one due to advanced ovarian cancer and one due to cardiac arrest) (p=0.0013). Patients with SS associated NHL displayed a significantly higher risk of death (HR=5.95, 95%CI: 1.66 - 21.38, log-rank test, p=0.0006) compared to their counterparts without lymphoma. The corresponding age-adjusted SMR of SS with and without NHLs versus the general Greek population was 7.94 (95%CI: 6.82-9.06) and 1.06 (95%CI -0.06-2.18) respectively. In addition, 18 patients with SS-associated NHL (23.38%) experienced lymphoma relapse or progression and 2 (2.6%) lymphoma transformation; The vast majority of recorded events (27 of 29 events) were observed within the first ten years from NHL diagnosis and DLBCL was associated with the worst outcome; The 10-year EFS% and OS% for DLBCL was 22.22% and 48.61% respectively while for MALT were 68.15% and 82.03%, respectively. Interestingly, the introduction of rituximab in the anti-lymphoma chemotherapeutic regimens didn’t offer any long-term survival benefit.

Conclusion: Herein, we present the longest, to our knowledge, follow-up time of patients with SS-associated NHL; The majority of events that determine the morbidity and mortality of SS-NHL patients have already occurred within the first ten years from NHL diagnosis. In individuals with SS, the evolution of NHL was found to have a detrimental effect in patients’ survival. Among them, DLBCL patients experienced the worst outcome.

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A SIMPLIFIED APPROACH FOR SLE PATIENTS TO REPORT DISEASE ACTIVITY USING A REVISITED VERSION OF THE SWEDISH SYSTEMIC LUPUS ACTIVITY QUESTIONNAIRE

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Background: The Systemic Lupus Activity Questionnaire (SLAQ) is a validated questionnaire, which captures patients’ assessments of SLE-related symptoms and disease activity (1). However, it is extensive and in a recent study we found that some questions were difficult to answer, added little information, or had poor correlation with physicians’ assessments (2). Thus, herein we revised the Swedish version of the questionnaire (SWE-SLQAR), building on previous results and we also asked patients for input. Our aim was to get an improved and shorter version, more suitable for clinical work and online registries. The original SLAQ includes 26 items, while SWE-SLQAR includes 20 items.

Objectives: We compared patients’ assessments of SLE disease activity, as reported in the SWE-SLQAR, with physicians’ assessments using SLE activity measure (SLAM) and SLE disease activity index (SLEDAI-2K). In addition, we evaluated the performance of the symptom items of SWE-SLQAR as compared to the corresponding items in SLAM.

Methods: Patients filled out SWE-SLQAR prior to physicians’ assessments. Correlations between SWE-SLQAR-total, subscales, (Symptom score, Patients global) and SLAM-excluding the 7 laboratory items (SLAM-nolab), SLAM and SLEDAI-2K as well as between the corresponding items in SLAM and SLE-DAQ, were evaluated using Spearman’s ρ.

Results: We included 101 patients, 85% women, median age 43 (IQR 22) years, disease duration 14 (IQR 15) years. Patients reported more symptoms than recorded by doctors. Correlations between patients’ and physicians’ assessments were for SLE-nolab: SWE-SLQAR total, ρ=0.674, Symptom score, ρ=0.670, and Patients global, ρ=0.667, as expected the correlations were lower for SLAM: SWE-SLQAR total, ρ=0.472, Symptom score, ρ=0.467, and Patients global, ρ=0.501. No correlations were found between patients’ and physicians’ assessments when using SLEDAI-2K (p>0.09 for all). Of symptom items fatigue (p=0.741), alopecia (p=0.695) and weight loss (p=0.517) showed highest degree of correlation. Notably, symptoms of dyspnea/pleuritic chest pain had no correlation between patients’ and physicians’ assessments (p=0.152, p=0.130).

Conclusion: We conclude that SWE-SLQAR performed equally well as SLAQ (2), demonstrating that it can be used to monitor disease activity. We encourage further use of SWE-SLQAR and recommend its implementation in clinical care, we believe it is especially well suited to support digital and telephone contacts. However further attention is needed to evaluate the discrepancy between physicians’ and patients’ evaluation of thoracic pain/symptoms.

Table. Characteristics of participants

<table>
<thead>
<tr>
<th>SWE-SLQAR total (0-37)</th>
<th>8</th>
<th>3.5-13</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom score (0-19)</td>
<td>9</td>
<td>4-13.5</td>
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<tr>
<td>Patients global (0-10)</td>
<td>4</td>
<td>1-7</td>
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<tr>
<td>SLAM</td>
<td>4</td>
<td>2-8</td>
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<tr>
<td>SLAM nolab</td>
<td>3</td>
<td>1-6</td>
</tr>
<tr>
<td>SLEDAI-2K</td>
<td>2</td>
<td>2-5.5</td>
</tr>
</tbody>
</table>
Background: Sjögren syndrome (SjS) is an autoimmune disorder characterized by inflammation and destruction of exocrine glands. The presence of autoantibodies (AA) against the Ro52/TRIM21, an RNP complex binding to the stem-loop structure of human cytoplasmic RNA, might be relevant in the SjS pathology. It has been suggested that distinguishing between antibody reactivity against Ro60 and Ro52/TRIM21 could be helpful in terms of evaluating clinical course, features and even pre-symptomatic stages of the disease (1).

Objectives: To evaluate the prevalence of anti-Ro52/TRIM21 antibodies in a cohort of patients diagnosed with primary SjS.

Methods: In this cross-sectional study we evaluated 179 patients with primary SjS according to the ACR classification criteria who had been admitted between December 2008 and December 2018 to our outpatient clinic. All patients had ANA titers higher than 1:320 (2) in at least two positive determinations for any pattern. ANA, anti-Ro52, anti-Ro60, anti-La and rheumatoid factor (RF) were tested by immunoblot (Euroimmun, Lübeck, Germany).

Results: In our cohort the median age at diagnosis was 57 years (range: 20–85 years) with a clear dominance of females (n=160, 89%). The most frequent reported ANA patterns were speckled (93%), while only few patients had a homogeneous (6%) pattern. 177/179 were positive for Ro60, and 52/179 for Ro52/TRIM21. Anti-La and rheumatoid factor (RF) were tested by immunoblot (Euroimmun, Lübeck, Germany).

Conclusion: Our results showed that anti-Ro52/TRIM21 but not anti-Ro60 is present in virtually all patients with SjS and had the most prevalent antibody reactivity. This finding needs to be considered in the current classification criteria of SJS (2), which include the presence of anti-Ro60, rather than anti-Ro52/TRIM21. Also, including the anti-Ro52/TRIM21 measurement in larger cohorts and longitudinal studies would also help us in improving the knowledge of its pathogenic role and to define of more focused diagnostic/therapeutic strategies.

REFERENCES


CLINICAL FEATURES OF ANEURYSMAL BEHÇET DISEASE

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Background: Arterial aneurysmatic lesions are one of the unique features of Behçet’s disease (BD). However, it is difficult to determine which BD patients will develop an aneurysm.

Objectives: In this study, we aimed to determine the differences between BD patients with and without an arterial aneurysm.

Methods: Data of the 23 BD patients with an arterial aneurysm was published as an abstract in 2013 (1). We retrospectively reviewed the medical records of 441 patients with BD according to International Study Group (ISG) criteria between January 2013 and June 2018. Totally, we determined 45 BD patients with an arterial aneurysm. Six patients with isolated carotid and/or cranial arterial aneurysms who were followed by other clinics excluded from the analysis. Overall, 39 BD patients with an extracranial and extra carotid aneurysmal involvement studied in the data. Study regarding demographic features, clinical, laboratory and vascular imaging findings were collected.

Results: A total of 39 BD patients (Male: 76.9%) with an arterial aneurysm were analyzed in this study. Mean age, mean age of diagnosis and a median follow-up of patients were 40.9±11.0 years, 29.7±7.7 and 71.8 (2-186) months, respectively. The mean age at the onset of the arterial aneurysm was 36±11.5 years. The median time lag between the onset of BD and detection of an aneurysm was 63.6 (0-482) months. The prevalence of male patients in BD with aneurysms, without aneurysms and only mucocutaneous involvement was 76.9%, 52.3%, and 34.3%, respectively. Comparison of BD patients with and without an aneurysm shown in table 1. Multivariate analysis, having a venous thrombosis was the sole risk factor for the development of arterial aneurysm (OR 10.53, 95% CI 1.53-72.71) (Table). Distribution of aneurysms was shown in the figure. At the first diagnosis, a median number of the aneurysm was 1 (1-4), the median number of an aneurysm was 39 mm (10-80) and median diameter of an aneurysm was 39 mm (10-80) and 16 (41%) patients had more than one aneurysm. Type of the firstly detected aneurysm was as follows; 38.5% sacular, 17.9% fusiform, 15.4% pseudoa neurysm and 26% dissecting aneurysm. Aneurysm type was not known in 17% and only mucocutaneous involvement in 21% of BD patients.

Conclusion: Aneurysm was the diagnostic symptom in 25% of BD patients with an aneurysm. The median time lag between the onset of BD and detection of an aneurysm was almost 5 years. In aneurysm BD, there may exist sex dominance and having venous thrombosis is the most important risk factor. Although pulmonary arteries have an important role in the BD course, the involvement of the aorta and iliac arteries can be seen frequently.

REFERENCES

Table. Clinical features of Behçet disease patients with and without arterial aneurysm

<table>
<thead>
<tr>
<th>Age (mean±SD, year)</th>
<th>40.9±11.0</th>
<th>41±11.8</th>
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<tr>
<td>Age at diagnosis (mean±SD, year)</td>
<td>29.7±7.7</td>
<td>29.2±9.1</td>
<td>0.504</td>
</tr>
<tr>
<td>Fever, %</td>
<td>36.7</td>
<td>48.0</td>
<td>0.235</td>
</tr>
<tr>
<td>Oral ulcers, %</td>
<td>100</td>
<td>99.7</td>
<td>1</td>
</tr>
<tr>
<td>Genital ulcers, %</td>
<td>80.6</td>
<td>74.5</td>
<td>0.425</td>
</tr>
<tr>
<td>Pathergy, %</td>
<td>34.5</td>
<td>44.8</td>
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</tr>
<tr>
<td>Erythema nodosum, %</td>
<td>33.3</td>
<td>43.3</td>
<td>0.20</td>
</tr>
<tr>
<td>Papulopustular lesions, %</td>
<td>47.2</td>
<td>54.9</td>
<td>0.374</td>
</tr>
<tr>
<td>Ocular involvement, %</td>
<td>28.2</td>
<td>51.2</td>
<td>0.006</td>
</tr>
<tr>
<td>Ankylosing spondylitis, %</td>
<td>27.8</td>
<td>28.8</td>
<td>0.9</td>
</tr>
<tr>
<td>Gastrointestinal involvement, %</td>
<td>7.7</td>
<td>4.6</td>
<td>0.423</td>
</tr>
<tr>
<td>Neurologic involvement, %</td>
<td>5.1</td>
<td>18.7</td>
<td>0.033</td>
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<tr>
<td>Fever, %</td>
<td>24.3</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>Mucocutaneous involvement, %</td>
<td>30.1</td>
<td>0.001</td>
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APREMLAST IN REFRACTORY ORAL AND/OR GENITAL ULCERS IN BEHÇET’S DISEASE. MULTICENTER STUDY OF 49 CASES IN CLINICAL PRACTICE


Background: Oral and/or genital aphthous ulcers are the most common symptoms of Behçet’s disease (BD), and are often refractory to conventional treatment. The inhibitor of phosphodiesterase-4 Apramast (APR) has demonstrated efficacy in the treatment of these manifestations.

Objectives: To assess the efficacy and safety of APR in BD patients with oral and/or genital ulcers refractory to conventional treatment.

Methods: National multicenter open-label study on 49 BD patients treated with APR at maintained standard dose of 30 mg twice daily, with the initial 5-day titration schedule in 38 cases. The main outcome was achievement of oral and/or genital ulcers remission.

Results: We included 49 patients (35 women/14 men), mean age of 44.5 ±13.4 years. Before APR, all patients had received several systemic conventional and/or biological drugs: oral corticosteroids (n=45), colchicine (n=48), NSAIDs (n=21), methotrexate (n=27), azathioprine (n=23), cyclosporine (n=9), dapson (n=6), adalimumab (n=12), infliximab (n=8), tocilizumab (n=3), etanercept (n=3), sulfasalazine (n=2), cyclophosphamide (n=2) and/or others (pentoxifylline, thalidomide, mycophenolate mofetil, hydroxychloroquine, golimumab, 1 each). The main clinical symptoms for starting APR were oral (n=18) and genital (n=22) aphthous ulcers or both (n=29). After a mean follow-up of 8.3±6.8 months, most of the patients experienced main clinical improvement and prednisone dose was reduced or discontinued (TABLE). In this period of time, 31 patients developed any side-effect, most of them transitory: nausea (n=12), diarrhea (n=11),
SAT0216  PATIENT PERCEPTIONS OF PHYSICAL ACTIVITY AFTER A DIAGNOSIS OF GIANT CELL ARTERITIS: A SECONDARY ANALYSIS OF MULTINATIONAL QUALITATIVE DATA

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Background: Giant cell arteritis (GCA) is the most common vasculitis in the UK, with an incidence of 220 cases/million in adults over 50 years of age. The physical symptoms as well as the side effects of glucocorticoids may impact patients’ ability to exercise. Maintaining physical activity (PA) has been shown to be beneficial to disease activity in other inflammatory conditions, and is also a specific priority for GCA patients.

Objectives: To explore patient perceptions of physical activity in GCA.

Methods: A cross-sectional study of patients with proven GCA in the UK and three other European countries. Mixed methods approach using a survey and qualitative interviews. A thematic analysis of the qualitative data was performed.

Results: 127 patients completed the survey, and 15 interviews were conducted. Overall, patients reported significant barriers to PA, including fear of exercise and physical symptoms, lack of facilities, and limited time. Education, motivational interviewing, and personalised strategies may be beneficial components of an intervention to support physical activity in patients with GCA.

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ARTERITIS: A QUALITATIVE STUDY

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Background: Giant cell arteritis (GCA) is the most common form of vasculitis. Diagnosis is difficult due to multiple presenting symptoms: headache, jaw and limb claudication, myalgia and visual impairment. Access to care may be delayed because often multiple providers are involved in the diagnosis of GCA and disease management. Treatment with high-dose glucocorticoids (GCs) can relieve symptoms and prevent vision loss, but GC-related adverse events are common; GCA often relapses once GCs are tapered.

Objective: To understand the GCA patient care pathway and unmet needs in GCA through in-depth patient interviews.

Methods: US patients with GCA were recruited through outreach to physicians and The Vasculitis Foundation, which used email newsletters and social media to recruit 50% of participating patients. Extensive individual interviews with patients were conducted by qualitative researchers by phone or in person and explored patients’ perspectives and experiences from the onset of GCA symptoms to diagnosis and disease management. Patients were asked open-ended questions and encouraged to share their stories to provide additional insights into the patient journey and their individual perspectives. The qualitative data collected were analyzed using human-centered design methodology, including patient typologies (personas: optimist, fearful, stoic or despondent), forced temporal journey maps, forced semantic zoom (stakeholder system mapping) and affinity mapping for pattern recognition of unmet needs.

Results: A total of 28 patients were interviewed; 23 (82%) were women and mean age was 69 years (Table). The number of patients in each persona category is shown in the Table. Stoic and optimist personas had medium to high levels of self-advocacy and a positive-engaged attitude about their condition, while fearful and despondent personas had low levels of self-advocacy with disengaged/negative attitudes toward their condition. Patients often ascribed their milder GCA symptoms to causes such as stress and did not consult a physician until they developed moderate to severe symptoms, such as persistent headache, jaw pain or visual disturbances. Patients with existing inflammatory disorders were less likely to share symptoms of GCA unless the symptoms substantially worsened. In most cases, physicians diagnosed GCA based on abnormal erythrocyte sedimentation rate, often followed by a temporal artery biopsy. After diagnosis of GCA, all patients received GS with little information on the chronicity of GCA. Few patients were offered treatment alternatives to GCs. Overall, patients managed their GCA independently, with moderate support from friends or family, and sought to balance relief of GCA symptoms with the adverse effects of GCs. Patients concentrated on tapering and discontinuing GCs, with less concern about relapse. Furthermore, patients who were most uncomfortable with the adverse effects of GCs often waited until their GCA symptoms became debilitating before telling their physician. Almost all patients reported searching for a support group after the diagnosis.

Conclusion: Patients with GCA experience adverse effects from GCs and remain focused on reducing their GC dose. For those with inflammatory comorbidities, diagnosis of GCA is another burden in a debilitating journey that results in a sense of disempowerment and resignation toward their condition and paucity of therapeutic options. Patients with GCA want a clearer understanding of treatment options and access to support groups. Patients’ attitudes and self-advocacy vary depending on their personas; recognizing these personas may help HCPs coordinate patient care. Increased awareness of GCA among patients and HCPs may accelerate the path to diagnosis and treatment, and emerging therapies may help reduce GC burden.

Acknowledgement: This study was funded by Genentech, Inc.


EFFICACY AND SAFETY OF TOCILIZUMAB IN GIANT CELL ARTERITIS INDEPENDENTLY OF THE INITIAL PREDNISONE DOSE


Background: Tocilizumab (TCZ) has been approved for the treatment of Giant Cell Arteritis (GCA). It showed to be effective to induce remission, prevent relapses and decreases the cumulative prednisone dose. However, the glucocorticoids are the mainstay in the acute treatment of GCA.

Objectives: Our aim was to compare the efficacy and safety of the initial dose of prednisone at the onset of TCZ treatment.

Methods: Retrospective, multicenter study on 134 patients with GCA in treatment with TCZ. We compared two subgroups of patients according to the initial dose of prednisone at TCZ onset. Clinical efficacy, analytical improvement and safety was studied.

Results: We studied 134 patients (101 w/33 m) and made a comparative study between 2 groups: a) TCZ and ≤ 15 mg of prednisone; 68 (50.7%) cases, and b) TCZ and > 15 mg of prednisone, 66 (49.3%) patients. It is summarized in Table 1. It was not a statistical significance according to age, sex and evolution time of disease. In the group receiving > 15 mg of prednisone, the patients presented more visual involvement (p<0.001) at TCZ onset. In terms of prolonged remission and relapses no significant difference was seen between both groups. The risk of presenting adverse effects (11.8% vs 36.4%) and severe infections (4.4% vs 19.7%) was related with the prednisone dose, being more frequent in the group with > 15 mg of prednisone (p=0.001 and p=0.006, respectively).

TABLE 1

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>PREDNISONE ≤ 15 mg (n=68)</th>
<th>PREDNISONE &gt; 15 mg (n=66)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolonged remission (%)</td>
<td>62 (91.1)</td>
<td>51 (77.3)</td>
<td>0.003</td>
</tr>
<tr>
<td>Relapses (%)</td>
<td>5 (7.4)</td>
<td>15 (22.7)</td>
<td>0.003</td>
</tr>
<tr>
<td>Visual involvement (%)</td>
<td>3 (4.4)</td>
<td>12 (18.2)</td>
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</tr>
<tr>
<td>Serious infections (%)</td>
<td>3 (4.4)</td>
<td>2 (3.0)</td>
<td>0.907</td>
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</tbody>
</table>

Conclusion: According with our results, we can conclude that TCZ is equally effective in terms of prolonged remission and relapses, with ≤ 15 mg of prednisone at treatment onset. Being the most important data, the higher risk to develop adverse effects, as well as infections with higher doses of prednisone.

TABLE 2

<table>
<thead>
<tr>
<th>TABLE 2</th>
<th>SERIOUS INFECTIONS</th>
<th>(%)</th>
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<tbody>
<tr>
<td>Gastrointestinal</td>
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<tr>
<td>Hernia</td>
<td>1 (1.5)</td>
<td></td>
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<tr>
<td>Fungal Infection</td>
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<tr>
<td>Bacterial Infection</td>
<td>3 (4.5)</td>
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<tr>
<td>Prevalence</td>
<td>11 (16.7)</td>
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<tr>
<td>Prevention</td>
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<tr>
<td>Pneumonia</td>
<td>2 (3.0)</td>
<td></td>
</tr>
<tr>
<td>Recurrent urinary infection and sepsis</td>
<td>2 (3.0)</td>
<td></td>
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<tr>
<td>Urinary tract</td>
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<td>And or sepsis</td>
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REFERENCES


Disclosure of Interests: None declared, Norberto Ortego: None declared, Sabela Fernández: None declared, J. Lorí-Ortego: None declared, Ángel García-Manzaranes: None declared, Norberto Ortego: None declared, Sabela Fernández: None declared, Francisco Ortiz-Sanzú: None declared, Montserrat Corteguera: None declared, J. Luis Hernández: None declared, Miguel A. González-Gay: None declared, Raquel Dos-Santos: None declared, Ángel García-Manzaranes: None declared, Norberto Ortego: None declared, Sabela Fernández: None declared, Francisco Ortiz-Sanzú: None declared, Montserrat Corteguera: None declared, J. Luis Hernández: None declared, Miguel A. González-Gay: None declared.
USE OF TOCILIZUMAB IN AORTITIS. A MULTICENTER STUDY OF 79 PATIENTS


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Background: Aortitis can be idiopathic or associated with other conditions. It is frequently refractory to conventional immunosuppressive therapy. Tocilizumab (TCZ), an anti-IL-6 receptor antibody seems to be effective and safe.

Objectives: Our aim was to assess the efficacy and safety of TCZ at short and long follow-up in a series of patients with Aortitis.

Methods: Retrospective, multicenter study of 79 patients diagnosed of inflammatory aortitis based on imaging techniques (PET/CT, CT angiography and/or MR angiography).

Results: Studied 79 patients (61 w/ 18 m), 59 (74.7%) cases were Aortitis secondary to Giant Cell Arteritis (GCA), while 20 (25.3%) were Aortitis secondary to Polyarteritis Nodosa (PAN). TCZ proved to be effective in both pathways, allowing clinical and analytical improvement, as well as a reduction of corticoid dose, without increasing the risk of relapse. However, the improvement in imaging techniques seems to be slower.

Conclusion: Our results show that idiopathic aortitis occurs in younger patients compared with aortitis secondary to GCA. TCZ proved to be effective in both pathways, allowing clinical and analytical improvement, as well as a reduction of corticoid dose, without increasing the risk of relapse. However, the improvement in imaging techniques seems to be slower.

REFERENCE

Disclosure of Interests: Monica Calderón-Goercke: None declared, J. Loricer: None declared, D. Prieto-Peña: None declared, Vicente Aldasoro: None declared, Santos Castañeda Consultant for: Amgen, BMS, Pfizer, Lilly, MSD, Roche, Sanofi, UCB, Igancio Villa-Blanco: None declared, Alicia Humbria: None declared, Clara Moriano: None declared, Susana Romero-Yuste: None declared, J. Narváez Consultant for: Bristol-Myers Squibb, Catalina Gomez-Arango: None declared, Eva Perez-Pampín: None declared, Rafael Melero: None declared, Marcelino Revenga: None declared, Noelia Alvarez-Rivas: None declared, Francisca Sivera: None declared, Maria Álvarez del Buero: None declared, Luisa Marena Rojas: None declared, Eva Galindez: None declared, Beatriz Arca: None declared, Carlos Vázquez: None declared, Pau Luch: None declared, Eva Salgado-Pérez: None declared, Cristina Luna-Gomez: None declared, Francisco J. Tojos Sanzén de Miera: None declared, Nagore Fernández-Llanio: None declared, Antonio García: None declared, Carmen Larena: None declared, Natalia Palmo-Fontana: None declared, Vanesa Calvo-Rio: None declared, Carmen González-Vela: None declared, Alfonso Corrales: None declared, María Valeria García: None declared, Elena Aurrecoechea: None declared, Raquel Dos-Santos: None declared, José Luis Martín-Varillas: None declared, Susana Romero-Yuste: None declared, J. Luis Hernández: None declared, Miguel A. González-Gay: Grant/research support from: Prof. MA Gonzalez-Gay received grants/research supports from: Abbvie, MSD, Jansen and Roche.

Speakers bureau: Consultation fees/participation in company sponsored speakers’ bureau from: Pfizer, Lilly, Sobi, Celgene, Novartis, Roche and Sanofi, Ricardo Blanco. Grant/research support from: Abbvie, MSD, and Roche, Consultant for: Abbvie, Pfizer, Roche, Bristol-Myers, Jansen, Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Jansen.


OFF-LABEL USE OF BIOLOGICAL THERAPIES IN RELAPSING AND/OR REFRACTORY POLYARTERITIS NODOSA

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Background: Polyarteritis nodosa (PAN) is a rare systemic necrotizing vasculitis of medium- and small-sized arteries, not associated with anti-neutrophil cytoplasmic antibodies (ANCA). Conventional treatments include glucocorticoids (GCs) for non-severe disease and a combination of GCs and immunosuppressive agents for severe disease. Nevertheless, some patients have refractory and/or relapsing disease.

Objectives: We examined the use of off-label biological therapy for relapsing/refractory PAN.

Methods: This retrospective European collaborative study included patients with PAN meeting ACR criteria and/or Chapel Hill Consensus Conference 2012 definitions. Treatment efficacy and safety were recorded. Remission was defined as the absence of vasculitis manifestations (BVAS = 0) with a prednisone dose ≤5 mg/day. Partial response was defined as a BVAS = 0 with a prednisone dose between 6 and 10 mg/day.

Results: Fifty-one patients (24 men, 27 women; median age 51 years) were included. Eighteen (35%) patients received TNF-alpha blockers, 16 (31%) received rituximab (RTX), 9 (18%) tocilizumab (TCZ), and 8 (16%) other biologics (including alemtuzumab in 2 and abatacept in 1). Previous treatments were: GCs in all patients, cyclophosphamide (61%), azathioprine (53%), methotrexate (45%) and mycophenolate mofetil (47%). At inclusion, median BVAS was 5 (range 0-18), including 5 (2-12) in the TNF-alpha blockers group, 5 (2-12) in the RTX group and 4 (0-6) in the TCZ group. After median follow-up of 34.4 months (IQR 21.5-59.5), remissions, partial responses and treatment failure, respectively, were noted in 41%, 6% and 53% for TNF-alpha blockers recipients, 25%, 12% and 63% for RTX recipients, and 57%, 0% and 43% for TCZ recipients. No remission was noted in patients treated with anakinra, alemtuzumab and abatacept. Median BVAS dropped to 3 at 6 months, 0 at 12 months and 0 at last follow-up in the TNF-alpha blockers group, to 3.5, 0 and 2 in the RTX group, respectively, and 0, 0 and 0 in the TCZ group. A GC-sparing effect seemed more important with TNF-alpha blockers and TCZ. Median GCs dose decreased from the baseline 15 mg/day to 10 at 6 months, 5 at 12 months and 5 at last follow-up in the TNF-alpha blockers group, from 15 mg/day to 10 at 6 months, 5 at 12 months and 5 at last follow-up in the RTX group, and from 15 mg/day to 7 at 6 months, 5 at 12 months and 5 at last follow-up in the TCZ group. Four (22%) patients stopped TNF-alpha blockers because of allergic reaction in one and refractory disease in 3. Six (38%) stopped RTX because of refractory disease. Finally, 4 (44%) stopped TCZ because of adverse effects.
events in 2 (testicular abscess and worsening renal failure) and refractory disease in 2.

Conclusion: The results of this study suggest that TNF-alpha blockers and TCZ may achieve higher rates of remission and GC-sparing in relapsing and/or refractory PAN than other biologics. Our data warrant further study to confirm or not these findings.

Disclosure of Interests: | Alice Canzian: None declared, Omer Karadag: None declared, Anne Coris: None declared, Francois Maurier: None declared, Maria Santorelli: None declared, Laura Denis: None declared, Sebastien Sanges: None declared, Claire De Moreuil: None declared, Cecile-Audrey Durel: None declared, Stephane Durupt: None declared, Marie Jachet: None declared, Diane Rouzaud: None declared, Carlo Salvatori: None declared, Franco Schiavoni: None declared, Lorenzo Dagna Consultant for: Prof Lorenzo Dagna reviewed consentul honoraria from Abbvie, Amgen, Biogen, Bristol-Myers Squibb, Celltrion, Novartis, Pfizer, Sanofi-Genzyme, and SOBI. Fabrice Bonnet: None declared, David Jayne: None declared, Silvia Sartorelli: None declared, Laure Denis: None declared, Benjamin Terrier: None declared, Alice Canzian: None declared, Omer Karadag: None declared, Fabienne Kossak: None declared, Marlène Garido: None declared, Guillaume Darrasse-Jèze: None declared, Patrick Piccoli: None declared, David Saadoun: Grant/research support from: Roche, Abbvie, Astra Zeneca, Bayer, Boehringer Ingelheim, Gilead, Glaxo Smith Kline, Janssen, Merck Sharp Dohme, Pfizer, Roche, Servier, and Vifor., Speakers bureau: d'Abbivie, Astra Zenequa, Bayer, Boehringer Ingelheim, Gilead, Glaxo Smith Kline, Janssen, Merck Sharp Dohme, Pfizer, Roche, Servier, and Vifor., David Saadoun Grant/ research support from: Roche, Servier, Consultant for: R. Jussus, Cellgene, Abbvie, Roche


SA0223 COOPERATION OF T FOLLICULAR HELPER CELLS AND B CELLS IN TERTIARY LYMPHOID STRUCTURES IN TAKAYASU ARTERITIS

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Background: Takayasu's arteritis (TA) and giant cell arteritis (GCA), the two most common types of large vessel vasculitis (LVV), are characterized by an inflammatory granulomatous infiltrate mainly located in the media and the adventitia. However, distinct histological features of the immune response are poorly known.

Objectives: To investigate distinct pathological mechanisms of the immune response in patients with GCA and TA.

Methods: We performed comparative immunohistochemistry analysis of aorta of GCA and TA patients. We performed microarray gene analysis of purified CD4+ T cells of TA and GCA patients. Reverse transcriptase PCR, flow cytometry analysis and cell culture were used to investigate T and B cells subpopulations in 54 patients with TA, 52 with GCA and 60 controls.

Results: We found higher proportion of tertiary lymphoid structures composed of CXCR5+ CD4+, PD-1+ and CD20+ cells in inflammatory aortic lesions in TA as compared to GCA. We demonstrated increased proportion of aortic B cells in TA.

We next evaluated differentiation of circulating CD4+ T cells in both diseases. Among circulating T cells, seven genes differentially expressed in CD4+ T cells of TA compared to GCA patients, we identified a specific “T follicular helper” (Thf) signature in TA patients. We also found a specific Tfh signature in TA patients. Flow cytometry analysis confirmed increased circulating Thf, defined as CXCR5+ CD4+ T cells, in TA patients as compared to GCA and healthy donors (HD) [median of 15.4 (10.30-8.1%) versus 5.3 (1.4; 12.2%) and 9.7 (5.6; 12.5%) (-p<0.0001 and -p=0.0001)] in TA, GCA and HD, respectively. Among Tfh subpopulations, Thf-17, CXCR5+ CXCR6+, CXCR3- CD4+ cells, were specifically increased in TA. Functionally, CXCR5+ CD4+ T cells of TA patients helped B cells to differentiate into memory cells, to proliferate and to secrete type G immunoglobulins.

We sequenced the TCR repertoire αβ in CD3+CD4+CXCR5- and CD3+CXCR5+ cells, in aortic and blood samples from 2 patients. In both patients, we identified oligoclonal profile of TCR repertoire only for aortic CXCR5+ cells, suggesting antigenic selection of CXCR5+ CD4+ T cells.

Conclusion: We provide evidence of the presence of tertiary lymphoid structures composed of Tfh and B cells in TA aorta. We identified a specific Tfh signature in circulating CD4+ T cells that distinguishes TA and GCA patients. The key cooperation of Tfh and B cells in TA and the oligoclonal repertoire of CXCR5+ CD4+ T cells strongly suggest the role of antigenic trigger.

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SA0222 FACTORS ASSOCIATED WITH DAMAGE PROGRESSION IN BEHÇET’S SYNDROME UVEITIS

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Background: Uveitis in Behçet’s syndrome (BS) follows a recurrent disease course with inflammatory exacerbations causing damage in the uvea, retina and optic nerve even with treatment. Frequent attacks and posterior involvement are considered as predictors of poor visual outcome.

Objectives: The aim of this study is to delineate the predictors of damage in more detail using a standard screening method among a group of BS patients with long term regular follow-up.

Methods: Patients with uveitis who were registered in our multidisciplinary BS clinic between 1990 and 2018 were screened. Among these, 50 patients who were followed for at least 10 years, who were regularly seen in our clinic at least once in every 4 months, who did not have > Grade 2 damage at baseline, and who represented different levels of damage severity during the last visit (between Grade 0 and 5) were selected. The damage severity was graded according to a validated damage grading instrument (5-worst) specifically developed for BS uveitis (Ozyazgan et al. in preparation). One patient was later excluded because it was realized that he did not fulfill these criteria. A standard form was used for retrieving data on demographics, baseline and final visual acuities, number and localization (anterior/posterior/panuveitis) of attacks during follow-up, presence of retinal inflammation, retinal hemorrhage and hypopyon uveitis. Candidate factors for damage progression were compared between patients who had a progression in damage score and those who did not.

Results: 98 eyes of 49 patients (M:F=35:14, mean age at baseline 27.8 years, mean follow-up duration 20.9±5.5 years, mean number of visits 79±32.4) were evaluated. The mean visual acuity was 0.02±0.08 at baseline and 0.47±0.52 at the final visit. The mean number of attacks was 13.2±9.4. Damage grades at baseline were Grade 0 in 79, Grade 1 in 16 and Grade 2 in 3 eyes. Damage grades at final visit were Grade 0 in 15, Grade 1 in 21, Grade 2 in 32, Grade 3 in 12, Grade 4 in 10 and Grade 5 in 8 eyes. There was damage progression in 81/98 eyes at the final visit. Isolated anterior uveitis attacks were not associated with progression of damage (2.5±2.9 vs 2.8±5.5; p=0.7). Parameters that were significantly more frequent among patients with damage progression were: number of attacks (14.5±10.8 vs 23.3±12.3; p=0.008), number of posterior attacks (0.4±1.2 vs 6.5±4.9; p<0.001), number of panuveitis attacks (0.8±3.1 vs 6.6±5.0; p<0.001), number of attacks with severe vitrous opacity preventing examination of the retina (0 vs 1.4±1.9; p<0.001) and retinal hemorrhages in the arcuate area (0.1±0.2 vs 0.7±1.4; p<0.001), and the number of hypopyon attacks (0.2±1.0 vs 0.9±1.3; p=0.019).

Conclusion: This study confirmed that the anterior uveitis attacks were not associated with progressive damage in BS, whereas posterior and panuveitis attacks, attacks causing severe vitreous opacity, retinal infarcts and hemorrhage in the arcuate area and hypopyon attacks are important predictors of damage. Patients showing these features should be treated more aggressively.

REFERENCE
Disclosure of Interests: Yilmaz Ozuyzan Speakers bureau: ABBVIE, Didar Ucar: None declared, Mustafa Erdogan: None declared, Yesim Ozguler: None declared, Gulen Hatemi Consultant for: Abbvie, Amgen, BMS, Janssen, MSD, Pfizer, UCB, Speakers bureau: Abbvie, Amgen, BMS, Janssen, MSD, Pfizer, UCB, Speakers bureau: Abbvie, Amgen, BMS, Janssen, MSD, Pfizer, UCB, Sebahattin Yurdakul: None declared, Vedat Hamuryudan Consultant for: Abbvie, Amgen, BMS, Janssen, MSD, Pfizer, UCB, Speakers bureau: Abbvie, Amgen, BMS, Janssen, MSD, Pfizer, UCB, Izzet Fresko: None declared, Melike Metlikgolu: None declared, Emine Seyahi: None declared, Serdal Ugurlu: None declared, Hasan Yazici: None declared


SAT0224 PRESENTATION, MANAGEMENT AND OUTCOME OF ANCA ASSOCIATED VASCULITIDES IN ITALY: A 20-YEAR FOLLOW-UP STUDY

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Background: ANCA associated vasculitis (AAV) are systemic diseases with a wide spectrum of clinical presentation and organ involvement.

Objectives: To analyze presentation, management and 5-years-outcomes of AAV patients diagnosed between 2000 and 2018 in the monocentric cohort of Padova Vasculitis Center.

Methods: We retrospectively collected all AAV patients diagnosed between 2000 and 2018 and followed in the Vasculitis Center of Padova University. We focused on demographic and clinical features at baseline, first line immunosuppressive (IS) treatment, 6 months mortality, 5-years-relapse rate and survival rate.

In the analysis, we kept separate eosinophilic granulomatosis with polyangiitis (EGPA) from granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA).

Results: We identified 171 patients (F/M 93/78) with AAV diagnosed since 2000 (61 between 2000-2010 and 110 between 2011-2018, % of increase in diagnosis rate +183%): 82 (48%) were GPA, 28 (16%) MPA and 61 (36%) EGPA. The patients were mostly Caucasian (98%), with a mean age at diagnosis of 58±16.1 years, slightly younger if diagnosed in the second decade (2010-2018) than in first decade (2000-2010) (59.5±16.6 years vs 61±14.7 years, p=0.049). ANCA were tested in 163 patients: 23% ANCA negative, 37% cANCA/PR3, 39% pANCA/MPO and 1% double positive.

GPA/MPA patients were mostly ANCA positive at diagnosis (96/110 patients), in particular we counted 12 (15%) GPA/ANCA negative patients, 55 (68%) GPA-PR3, 13 (16%) GPA-MPO, 1 GPA with double positivity while MPA resulted only ANCA positive, 22 (82%) MPA-MPO and 5 (19%) MPA-PR3. In EGPA group, only 28/54 presented with ANCA positivity, all p-ANCA/MPO specificity.

Disease severity at diagnosis was assessed only in GPA/MPA patients: 12/101 limited disease, 34 early systemic, 29 generalized and 26 severe. In particular, GPA/MPA more frequently presented with systemic symptoms (76%), ENT and lung involvement (respectively 62% and 66%). Renal vasculitis was reported in 65% of patients with a mean eGFR of 50.2±39.6 ml/min. Moreover, we registered 17 alveolar haemorrhages, 4 cardiac involvement and 3 gastrointestinal (GI) disease. EGPA patients, instead, presented more frequently with ENT (85%) and lung involvement (96%) (mostly uncontrolled asthma and pulmonary infiltrates), 31 (54%) EGPA presented nerve involvement (4 with CNS involvement) and 9 (16%) with cardiac involvement. Interestingly, no renal or GI vasculitis was reported. The first line IS treatment administered was: cyclophosphamide (CYC) in 66 (38%), rituximab (RTX) in 14 (8%), azathioprine (AZA) in 27 (16%), methotrexate (MTX) in 25 (14%) and mycophenolate (MMF) in only 5 (3%).

Mortality rate at 6 months in all cohort resulted of 1.2% (2 event), while the 5-years survival calculated with Kaplan Meier method was 94.3% (8 events). All deaths occurred in the GPA/MPA group. A relapse occurred in 36% of patients, with a significant higher frequency in GPA/MPA than in EGPA (46.3% vs 17%, P=0.017).

Conclusion: Our cohort is characterized by significant higher rate of AAV diagnosis in the last decade and this could reflect the increasing incidence and prevalence reported in literature. Interestingly, GPA diagnosis, especially with CANCA/PR3 specificity, was prevalent in our cohort despite some authors reported an higher prevalence of MPA in Mediterranean area. Finally, EGPA confirmed a better outcome at last follow up than GPA and MPA, but we noted that no renal and GI involvement was observed in our EGPA patients.

REFERENCE

Disclosure of Interests: None declared


SAT0225 TARGETED SERUM METABOLIC PROFILE IN PATIENTS WITH TAKAYASU ARTERITIS

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Background: Takayasu arteritis (TAK) is a chronic inflammatory arteritis that mainly affects aorta and, its major branches. Often the course is unpredictable and it remains a challenge to assess disease activity despite the availability of acute phase reactants and imaging modalities. Management heavily relies on physician global assessment. Analysis of serum metabolites using nuclear magnetic resonance spectroscopy is a promising exploratory approach towards identifying new biomarkers in TAK which may cast some light on disease pathogenesis and disease activity.

Objectives: Aim of the study was to evaluate the performance of serum amino acids as determinants of disease activity in TAK.

Methods: Patients with TAK fulfilling ACR 1990 criteria were enrolled and disease activity assessed using ITAS2010 and ITAS-A[2]. Samples were analysed using 1D 1H 800 MHz Nuclear magnetic resonance spectrometer equipped with a Cryoprobe (at 300 K). The spectra were processed and the concentration of amino acids were measured with respect to internal reference metabolite formate assuming its concentration 10 µM in commercial software program CHENOMX (www.chenomx.com) and the resulting normalized values were compared using Tukey’s multiple comparison test and diagnostic potential was evaluated using receiver operating characteristic (ROC) curve analysis.

Results: 45 active TAK patients with ITAS-A ≥4 and 59 inactive TAK patients with median age 27 years [IQR, 22-35 and IQR, 23-37 years respectively] were enrolled. Female to male (F:M) ratio was 3.5:1 and 4.9:1 and median duration of illness 5 [IQR, 2-9] years and 3 [IQR, 1-6] years in active and inactive group respectively. Majority had class V disease. 43 individuals served as health control (HC) with mean age 30±4 years and F:M ratio of 4.3:1. Serum levels of Phenylalanine (Phe), Tyrosine (Tyr), Histidine (His), Valine (Val) and Alanine (Ala) were found to be decreased in TAK patients suggesting augmented utilization in the immune-metabolic pathways mainly to replenish the energy demand and self-repair mechanism under conditions of inflammation and oxidative stress. An analysis of amino acids ratio revealed significantly higher His/Tyr, Ala/Tyr and Val/Tyr ratio in HC when compared to active TAK patients. Ratio were lower in active TAK when compared to inactive TAK patients but only Val/Tyr ratio was significant (AUCRO, 0.64 and p, 0.01). Ratio served as a gradient with lowest value in active disease and gradually increasing and moving towards HC as disease was getting controlled.

Figure 1: Comparison of various amino acid ratio in active and inactive TAK patient with respect to healthy control. Ratio served as a gradient with lowest in active disease and gradually moving towards HC as disease was getting controlled.
Conclusion: The present targeted NMR based metabolomics study demonstrated that the serum metabolic profiles of amino acid may help guide therapy and ratio of Val/Tyr can differentiate active from inactive patients. However, future studies on large patient cohorts are required to establish its clinical utility.

REFERENCES

Disclosure of Interests: None declared

SAT0226
INFILXIMAB FOR THE TREATMENT OF REFRACTORY POLYARTERITIS NODOSA
Shira Ginsberg1, Izlach Rosner1, Gile Sobodin1, Michael Rosenbaum1, Lisa Kaly1, Nizar Jiries1, Nina Boulan1, Abid Awisat1, Haya Hussein1, John Greenwood4, Maya Buch2,3, Jacqueline Andrews3.

Background: Polyarteritis Nodosa (PAN) is a necrotizing vasculitis predominantly affecting medium and small size arteries (1). Cyclophosphamide, a drug with narrow therapeutic range and poor safety profile, constitutes the treatment of choice for PAN vasculitis with major organ involvement. (2)

Objectives: To describe our clinical experience in treating refractory PAN with infliximab (a TNF inhibitor), a drug with good tolerability and better safety profile than cyclophosphamide.

Methods: Twenty-six PAN patients were admitted to our rheumatology unit between 2006 and 2017, of whom 9 patients, with severe and refractory disease, were treated with infliximab after failure of standard treatment. We describe herein the patients’ characteristics, clinical manifestations, severities and response to infliximab treatment and review the current literature.

Results: Complete remission was defined as the absence of features of active disease and withdrawal of prednisone therapy. Significant improvement was defined as clinical improvement and prednisone dose reduction of at least 50% or a 50% reduction in immunmodulatory medications other than prednisone. After 4 months of treatment, 8/9 (89%) patients achieved significant improvement, with two of them achieving complete remission.

Conclusion: We suggest anti TNF agents, and in particular infliximab, are relatively safe and efficacious treatment options in refractory PAN. A randomized controlled trial should be done in order to objectively evaluate infliximab in PAN.

REFERENCES

Disclosure of Interests: None declared

SAT0227
MYOCARDIAL FIBROSIS IS ASSOCIATED WITH ANCA STATUS, ORGAN INVOLVEMENT AND DISEASE SEVERITY IN PATIENTS WITH GRANULOMATOIS WITH POLYANGIITIS
Alessandro Giolio1,2,3, Raluca-Bianca Dumitru1,2,3, Peter Swoboda4, Sven Plein5, John Greenwood6, Maya Buch7, Jacqueline Andrews7.

Objectives: To describe our clinical experience in treating refractory PAN with infliximab (a TNF inhibitor), a drug with good tolerability and better safety profile than cyclophosphamide.

Methods: Twenty-six PAN patients were admitted to our rheumatology unit between 2006 and 2017, of whom 9 patients, with severe and refractory disease, were treated with infliximab after failure of standard treatment. We describe herein the patients’ characteristics, clinical manifestations, severities and response to infliximab treatment and review the current literature.

Results: Complete remission was defined as the absence of features of active disease and withdrawal of prednisone therapy. Significant improvement was defined as clinical improvement and prednisone dose reduction of at least 50% or a 50% reduction in immunmodulatory medications other than prednisone. After 4 months of treatment, 8/9 (89%) patients achieved significant improvement, with two of them achieving complete remission.

Conclusion: We suggest anti TNF agents, and in particular infliximab, are relatively safe and efficacious treatment options in refractory PAN. A randomized controlled trial should be done in order to objectively evaluate infliximab in PAN.

REFERENCES

Disclosure of Interests: None declared

Table 1. CMR measures†

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<td>LV end diastolic volume, mL/m²</td>
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<td>LV mass index, g/m²</td>
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<tr>
<td>LV mass/LV and diastolic volume, g/mL</td>
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<td>LV function</td>
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<tr>
<td>LV ejection fraction,%</td>
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<td>58 (53, 62)</td>
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<td>LV peak systolic strain</td>
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<td>Elevation, deg</td>
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<td>13.8 (11.6, 16.0)</td>
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<td>Myocardial tissue characterization</td>
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<tr>
<td>Native T1 (ms)</td>
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<td>1203 (1185, 1233)</td>
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<tr>
<td>Extracellular volume, μm²/μL</td>
<td>25.0 (23.3, 27.2)</td>
<td>23.6 (20.5, 25.1)</td>
<td>0.009</td>
</tr>
<tr>
<td>LGE, %</td>
<td>6.25 (24)</td>
<td>6.25 (0)</td>
<td>0.010</td>
</tr>
<tr>
<td>LGE scar tissue, μm²/μL</td>
<td>1.25 (0.81, 2.63)</td>
<td>0 (0)</td>
<td>NA</td>
</tr>
</tbody>
</table>

†Continuous data are presented as mean (interquartile range).

Conclusion: Patients with GPA had significant myocardial abnormalities on CMR compared to HV; ANCA status, systemic organ involvement and disease severity were associated with CMR markers of myocardial fibrosis. CMR could be a useful tool for identification and future risk stratification of myocardial involvement of GPA.

Disclosure of Interests: None declared, John Greenwood: None declared, Maya Buch Grant/research support from: Pfizer LTD, UCB, Consultant for: Abbvie, Eli Lilly, EMD Serono, Pfizer Ltd., Sanofi, Jacqueline Andrews: None declared
glucocorticoids. Currently, only limited data on dynamics of peripheral leukocytes and leucocyte subset composition before, during and after treatment is available.

**Objectives:** To gain insight into the dynamics of leucocytes during the entire disease course and to determine whether patients in treatment-free remission resemble healthy controls.

**Methods:** Newly-diagnosed, treatment-naïve GCA (N=42) and PMR (N=31) patients were prospectively followed for up to 7 years. Absolute numbers of leucocyte subpopulation, both myeloid (neutrophils, monocytes) and lymphoid (CD4 and CD8 T-cells, B-cells and NK-cells) were measured at fixed time points. Laboratory inflammation markers (CRP, ESR, platelets and haemoglobin) were assessed as well. Values were compared with age-matched healthy controls (N=51) and infection controls (N=13). A stable treatment-free remission group for at least 6 months was defined.

**Results:** Neutrophil and monocyte numbers were higher in baseline GCA and PMR patients compared to healthy controls, whilst NK-cell numbers were reduced. In baseline GCA patients, CRP correlated positively with monocyte numbers. In baseline PMR patients, B-cell numbers were lowered and B-cell and NK-cell numbers correlated negatively with CRP. During glucocorticoid treatment, fluctuations in numbers of all leucocyte subsets were observed but neutrophil and monocyte numbers remained elevated and NK-cells numbers remained lowered during the entire treatment period (fig. 1). CRP and ESR were reduced by GC treatment and only moderately elevated during relapses. GCA patients in treatment-free remission still had elevated neutrophil and monocyte numbers. In addition, ESR and CRP numbers, were elevated whilst haemoglobin was lowered. PMR patients in treatment-free remission still had elevated monocytes while NK-cell and CD8+ T-cell numbers were decreased. Inflammatory markers and haemoglobin was normal.

**Conclusion:** In baseline GCA and PMR patients a shift towards the myeloid lineage is observed. This myeloid bias persisted in spite of GC treatment and also in treatment-free remission, suggesting a long-term effect of inflammation (an inflammatory imprint) on the peripheral blood compartment. Only GCA patients showed persistently elevated inflammatory markers; whether this reflects ongoing subclinical disease remains to be investigated.
The mean time from onset of GCA to intracranial involvement was 17 months (±38). All patients had neurologic symptoms, 33% (n:3) had a stroke and 22% (n:2) had a transient ischemic attack. IC-GCA was diagnosed by cranial imaging in 8 patients and by autopsy in one. Cranial imaging modalities used included magnetic resonance angiography (n=8), CT angiography (n=2) and cerebral angiography (n=2). Intracranial vasculitis most commonly affected the internal carotid artery 78% (N=7) followed by the vertebral artery 56% (n=5), posterior cerebral artery 56% (n=5), middle cerebral artery 44% (n=4), anterior cerebral artery 33% (n=3) and posterior inferior cerebral artery 11% (n=1). Stenosis was present in 89%, occlusion in 33%, dilatation in 11%, and wall thickening in 11%.

All patients received glucocorticoids. For treatment of intracranial disease, additional agents included: cyclophosphamide (67%), Tocilizumab (22%). Despite treatment, outcomes for patients with IC-GCA were poor. Five of nine patients died during a mean length of follow-up of 2.4 months. Additional agents included: cyclophosphamide (67%), Tocilizumab (22%).

**Conclusion:** Although rare, IC-GCA is associated with significant morbidity and mortality. In our cohort, the incidence of IC-GCA was 1.2 per 100,000 individuals per year. Nine patients died during a mean length of follow-up of 2.4 months. All patients had neurologic symptoms, 33% (n:3) had a stroke and 22% (n:2) had a transient ischemic attack.

**Disclosure of Interests:** None declared


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**SAT0231 AGE AND THE CLINICAL FEATURES OF ADULT IGA VASCULITIS**

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**Background:** IgA vasculitis (IgAV) is a common vasculitis of adult populations, and the disease in adults is still poorly defined.

**Objectives:** The aim of our study was to evaluate the potential influence of age on the presentation of adult IgAV.

**Methods:** We analyzed medical records of adult, histologically proven IgAV cases, diagnosed and followed at our tertiary referral rheumatology center between January 2010 and December 2018. We stratified IgAV cases into four groups, based on the patient's age at presentation (18-39, 40-59, 60-79, ≥80 years). The clinical features were compared between the groups.

**Results:** During the 10-year observation period we identified 265 new IgAV cases (60.0% males, median (IQR) age 64 (45–77) years). Skin, joint, gastrointestinal tract (GIT), GIT and renal involvement developed in 265, 103 (38.9%), 80 (30.2%), and 118 (44.5%) cases, respectively. Younger adults (≤40 years) more frequently reported an infection prior to IgAV, and developed arthritis or GIT involvement. Severe renal involvement was less common under the age of 40 years. The incidence of skin limited IgAV and of necrotic purpura increased with patient age. Follow-up data were available for 189 patients. During a median (IQR) follow-up of 12 (6-24) months, 29 (15.3%) patients relapsed. Relapsing disease was more frequent in younger adults (≤40 years), compared to older ones.

**Table 1. Age and clinical features of adult IgAV**

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>Age interval</th>
<th>Number of cases</th>
<th>Male gender (%)</th>
<th>Prior infection (%)</th>
<th>Generalized purpura (%)</th>
<th>Skin necroses (%)</th>
<th>Skin limited IgAV (%)</th>
<th>Joint involvement (%)</th>
<th>Arthritis (%)</th>
<th>GIT involvement (%)</th>
<th>Severe GIT involv. (%)</th>
<th>Renal involvement (%)</th>
<th>Severe renal involv. (%)</th>
<th>Elevated serum IgA</th>
<th>Renal involvement (n, %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>18-39</td>
<td>49</td>
<td>63.3</td>
<td>57.1</td>
<td>49.0</td>
<td>14.3</td>
<td>16.3</td>
<td>63.3</td>
<td>28.6</td>
<td>42.9</td>
<td>14.3</td>
<td>36.7</td>
<td>2.0</td>
<td>22.6</td>
<td>25.0 (3/12)</td>
</tr>
<tr>
<td></td>
<td>40-59</td>
<td>69</td>
<td>68.1</td>
<td>36.2</td>
<td>52.2</td>
<td>43.5</td>
<td>18.8</td>
<td>49.3</td>
<td>14.5</td>
<td>34.8</td>
<td>7.2</td>
<td>43.5</td>
<td>15.9</td>
<td>45.6</td>
<td>13.2 (7/53)</td>
</tr>
<tr>
<td></td>
<td>60-79</td>
<td>96</td>
<td>62.5</td>
<td>28.1</td>
<td>50.0</td>
<td>55.2</td>
<td>35.4</td>
<td>30.2</td>
<td>14.6</td>
<td>21.9</td>
<td>7.3</td>
<td>50.0</td>
<td>14.8</td>
<td>56.5</td>
<td>13.0 (8/63)</td>
</tr>
<tr>
<td></td>
<td>≥80</td>
<td>79</td>
<td>41.2</td>
<td>21.6</td>
<td>45.1</td>
<td>62.7</td>
<td>41.2</td>
<td>17.6</td>
<td>2.0</td>
<td>27.5</td>
<td>2.0</td>
<td>43.1</td>
<td>11.8</td>
<td>48.6</td>
<td>18.6 (13/73)</td>
</tr>
</tbody>
</table>

Legend: Generalized purpura; purpura extending above the waistline; GIT: gastrointestinal tract; severe GIT involvement: bloody diarrhoea or ileus or bowel perforation; severe renal involvement: nephrotic syndrome with acute renal failure or nephrotic syndrome.

Data on age related variations in the clinical presentation of IgAV are presented in Table 1.

**Conclusion:** We found subtle age related differences in the presentation and during follow up of adult IgAV.

**Disclosure of Interests:** None declared


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**SAT0232 DISTRIBUTION OF MACROPHAGE SUBSETS IN TEMPORAL ARTERY BIOPSY OF PATIENTS WITH GIANT CELL ARTERITIS**

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**Background:** Giant cell arteritis (GCA) is a granulomatous vasculitis characterized by recruitment of T-cells and monocytes to the vessel wall. Upon recruitment, monocytes are activated and differentiate into macrophages. These leishmanial macrophages take on different phenotypes depending on cues from the microenvironment. These macrophages are known to produce pro-inflammatory cytokines, chemokines, matrix-metallo-proteinases (MMPs), and growth factors contributing to amplification of the inflammatory response, vessel wall injury and remodeling. However, current knowledge regarding macrophage subsets in GCA lesions is limited.

**Objectives:** To examine the distribution of macrophage subsets in GCA lesions.

**Methods:** Immunohistochemistry was performed on consecutive sections of paraffin-embedded temporal arteries of biopsy-confirmed GCA patients (n = 11) with antibodies to selected markers of inflammation and tissue remodeling (Table 1). Positive cells were scored in three layers of the vessel wall (adventitia, media-intima, inner-intima) using a semi-quantitative scoring system. Expression by macrophages was confirmed by double staining with the macrophage transcription factor PU.1.

**Table 1. Immunohistochemistry panel. AB019**

<table>
<thead>
<tr>
<th>Pro-inflammatory</th>
<th>Tissue remodeling</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-6</td>
<td>CD206 (MR)</td>
</tr>
<tr>
<td>IL-18</td>
<td>IL-10</td>
</tr>
<tr>
<td>IL-12</td>
<td>FR-β</td>
</tr>
<tr>
<td>IL-23</td>
<td>MMP-12</td>
</tr>
<tr>
<td>CD64</td>
<td>MMP-9</td>
</tr>
<tr>
<td></td>
<td>MMP-2</td>
</tr>
</tbody>
</table>

**Results:** The pro-inflammatory marker CD64 and pro-inflammatory cytokines (IL-12, IL-23 and IL-1β) were strongly expressed by macrophages throughout the vessel wall, most prominently in the adventitia. However, subsets of these CD64+ macrophages also showed concomitant expression of the tissue remodeling markers CD206 and FR-β in specific compartments of the lesions. More specifically, CD206+ macrophages were mainly found along the media borders which co-localized with positive MMP-9 staining. Interestingly, FR-β positivity was also found in the inner-intima of TABs with a high degree of intimal hyperplasia. FR-β expression was significantly higher in the inner-intima region in TABs with...
massive intimal hyperplasia compared to TABs with mild intimal hyperplasia (p = 0.01).

Conclusion: Based on the expression of markers of inflammation and tissue remodeling, different subsets of infiltrating macrophages can be distinguished. Macrophages in vascular lesions of GCA patients display a distinct spatial distribution pattern within the inflamed vessel wall (Figure 1). Adversarial macrophages express highest level of pro-inflammatory cytokines indicating pro-inflammatory functions of these macrophages. Co-localization of CD206 and MMP-9 along media borders indicates a role for CD206+ macrophages in collagen digestion and angiogenesis. Additionally, the association of increased numbers of FR-β+ macrophages with extensive intimal hyperplasia suggests that FR-β+ macrophages promote myofibroblast proliferation.

REFERENCE

Disclosure of Interests: William Febry Jiemy: None declared, Yannick van Sleen: None declared, Annemiek Boots Grant/research support from: grants 2014-2016 and 2015-2017 for: Roche, Consultant for: Roche and Janssen Biotech, Fee for serving as an employee of the UMCG received speaker fees and consulting fees from Roche which were paid to the UMCG


SAI10231 VALIDATION OF A NOVEL DISEASE CLASSIFICATION IN HACETTEPE TAKAYASU ARTERITIS COHORT

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Background: Takayasu Arteritis (TAK) is a rare idiopathic granulomatous large vessel vasculitis and it is a clinically heterogeneous disease. Various classifications and subsets which based on distribution of arterial lesions were defined in the literature in order to exhibit and predict different disease courses.

Objectives: We aimed to validate a new disease subsets developed by Goel et al in our TAK series (1).

Methods: We retrospectively evaluated the medical records of 164 TAK patients followed at Department of Rheumatology and Department of Pediatric Rheumatology in Hacettepe University, Ankara, Turkey between August 2005 and October 2018. The pediatric-onset (< 18 years of age at disease diagnosis) and adult-onset patients fulfilled the Ankara 2008 and the American College of Rheumatology (ACR) 1990 criteria for TAK, respectively. Patients were assigned to three clusters (Cluster 1: Abdominal Predominant, Cluster 2: Aortic Arch Predominant, Cluster 3: Focal Disease) using a decision tree defined in the original study (1). Demographics, clinical and laboratory features, treatment regimens were compared between in three groups.

Results: There were forty-two (25.6%), sixty-three (38.4%) and fifty-nine (36%) patients in Cluster 1, 2 and 3, respectively. Demographic and clinical data was summarized in Table-1. Cluster 1 included approximately half of patients (45.6%) with pediatric-onset TAK (p = 0.048), Baseline acute phase reactants (Enzyme Sedimentation Rate:ESR and C-reactive protein:CRP) and age at disease diagnosis were slightly lower in Cluster 1, however none of them did not reach statistical significance (p = 0.94, p = 0.99 and 0.56, respectively). In contrast, cerebrovascular accident rates were slightly higher in Cluster 2 (p = 0.24). Although anti-TNF biological agents were more frequently used for treatment in Cluster 1 (p =0.004), cyclophosphamide and/or overall biological agents usage was similar in three groups (p =0.15).

Conclusion: Decision tree which defined by Goel et al. was applied to our single center pediatric and adult TAK cohort. In contrast to original validation cohorts, there was no difference among three clusters of our cohort except pediatric-onset disease and anti-TNF usage. Dissimilarities among the cohorts in terms of new classification system may be caused either of patients or ethnic/regional differences.

REFERENCE
b/c. -378a, -423, -3184; p_adj < 10^{-9}), whereas 60 miRNAs were decreased (e.g. miRNA-128, -937, -30c, -328, 26a, p_adj < 0.005), thereby representing the IgAV-associated serum miRNA signature. The mirROR platform identified 426 protein-coding genes as targets of the 54 DE miR- NAs (log2 fold change ≥ 1), p_adj < 0.01. As analyzed by STRING, these miRNA target genes were enriched in distinct molecular networks and biological pathways, including “Phosphoproteins (FDR 7.4∗10^{-4}), “Alternative splicing” (FDR 2.8∗10^{-7}), “Regulation of actin cytoskeleton” (FDR 0.008), “Proteoglycans in cancer” (FDR 0.009) and “Fagomma receptor dependent phagocytosis” (FDR 0.01) (Figure 2). Additionally, miRNA gene targets formed three distinct molecular clusters, specifically “Chemokines and their receptors”, “Ubiquitination process” and “Vesicle, endocytosis, lysosomes and their trafficking” (Figure 2). This suggests that the altered miRNAs in IgAV regulate diverse cellular functions, reflecting or contrib-uting to the key aspects of disease pathogenesis.

Conclusion: Here we report for the first time an IgAV-associated serum miRNA signature. The altered miRNAs clearly discriminate IgAV patients from HC, and might play a key role in the pathogenesis of IgAV. Our study sets the basis for the identification of novel, serum-based disease biomarkers in vasculitis.

Disclosure of Interests: ALCIUZA HOCEVAR: None declared, Kiija Lakota: None declared, Thomas Grentzinger: None declared, Alexis Sara- zin: None declared, Neža Brezovec: None declared, Tadeja Kuret: None declared, Oliver Distler Grant/research support from: Prof. Distler has/had consultancy relationship within the last 3 years with Actelion, AnaMar, Bayer, Boehringer Ingelheim, ChemomAb, espeRare foundation, Genentech/Roche, GSK, Inven- tiva, Italfarmaco, IQvia, Lilly, medac, Medimmune, Mitsubishi Tanabe Pharma, Pharmacystics, Novartis, Pfizer, Sanofi, Serodapharm and UCB in the area of potential treatments of scleroderma and its complications. Consultant for: Prof. Distler has/had consultancy relationship within the last 3 years with Actelion, AnaMar, Bayer, Boehringer Ingel- heim, ChemomAb, espeRare foundation, Genentech/Roche, GSK, Inven- tiva, Italfarmaco, IQvia, Lilly, medac, Medimmune, Mitsubishi Tanabe Pharma, Pharmacystics, Novartis, Pfizer, Sanofi, Serodapharm and UCB in the area of potential treatments of scleroderma and its complications. In addition, he had/has consultancy relationship within the last 3 years with A. Menaprii, Amgen, Abbvie, GSK, Mepha, MSD, Pfizer and UCB in the field of arthritis and related disorders, Sasa Cucnik: None declared, Oliver Voinet: None declared, Sněžna Sodin-Semiř: None declared, Mat- ija Tomšič: None declared, Mojca Frank-Bertončič: None declared


SAT0235 BIOLOGICAL THERAPY IN NEUROBEHÇET. MULTICENTER STUDY OF 29 PATIENTS

José Luis Martín-Vara1, Irico González-Mazón1, Belén Atienza-Mateo1, Monica Calderón-Goerke1, D. Prieto-Peña1, Lara Sánchez Bilbao1, Vanesa Calvo-Rio1, Santos Castañeda1, Esther Vicente1, Olga Martínez González1, Clara Moriano1, Elvira Diez Alvarez4, José Luis Andreu Sánchez2, Concepción Delgado Beltrán3, Marta Loredo Martínez3, J. Naváez3, Ángel Ramos Calvo3, Francisca Sivera4, Enrique Raya4, Ñorberto Ortego5, José Luis Celles-Jubilo5, Ana María Brandy-Garcia6, Alejandro Oliver7, Sabela Fernández8, Ricardo Gómez de la Torre7, Ignacio Torre-Salaberri8, Julio Sánchez9, Ana Urruticoechea-0, Delgado Beltrán6, Marta Loredo Martínez6, J. Narváez7, Angel Ramos Calvo3, Francisca Sivera4, Enrique Raya4, Norberto Ortego5, Jose Luis Celles-Jubilo5, Ana María Brandy-Garcia6, Alejandro Oliver7, Sabela Fernández8, Ricardo Gómez de la Torre7, Ignacio Torre-Salaberri8, Julio Sánchez9, Ana Urruticoechea-0

Background: Behçet’s disease (BD) is a variable vessel vasculitis and typically presents with mucocutaneous involvement. However, any organ can be affected, being the neurological affection (neurobehçet, NB) one of the most serious manifestations. 

Objectives: Our aim was to assess the efficacy and safety of biological therapy as treatment of NB.

Methods: We set up a multicenter observational study of 29 patients with NB on treatment with biological therapy (BT). NB diagnosis was made by neuroimaging, CSF analysis and/or suggestive clinical signs of central and/or peripheral nervous system involvement, excluding infectious causes or more prevalent pathology. Results are expressed as means±SD or as median and interquartile range (IQR) as appropriate.

Results: 29 patients (15♂/14♀) with an average age of 39.6 ± 10.5 years. HLA-B51 was positive in 48.3% of the patients.

We set up a multicenter observational study of 29 patients with NB on treatment with biological therapy (BT).

Figure 1. Heatmap based clustering analysis of serum miRNA expression

Figure 2. STRING Protein networks of gene targets of DE miRNAs
brainlessment (n=1), encephalopathy (n=4), optic neuritis (n=2), dysphasia (n=1), polyneuropathy (n=6), cognitive impairment (n=4), and non-steroidal psychosis (n=1), while the remaining 6 patients (20.7%) presented aseptic meningitis as a non-parenchymal affection (Table). Prior to BT, patients had received the following treatment: Abbbvie, Pfizer, Roche, Bristol-Myers, Janssen, Speakers bureau: Consultation fees/participation in company sponsored speaker’s bureau from Pfizer, Lilly, Sobi, Celsege, Novartis, Roche and Sanofi., Ricardo Blanco Grant/research support from: Abbv, MSD, and Roche, Consultant for: Abbbvie, Pfizer, Roche, Bristol-Myers, Janssen, Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen

**Conclusion:** BT, especially anti-TNF, seems effective and safe for treatment in NB.

**Table.**

<table>
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After a median of 31 [10-60] months since the beginning of the neurologic symptoms, the following BT was initiated: infliximab (IFX)(n=17), adalimumab (ADA)(n=7), tocilizumab (TCZ) (n=2), golimumab (GOL) (n=2) and Etanercept (ETN) (n=1). A first switch to ADA was necessary in 8 patients with IFX due to primary failure. In addition, 2 of them needed a second switch to TCZ, getting a partial response. The BT was discontinued in 5 patients, 2 of them for obtaining clinical remission and the remaining 3 for inefficacy. After a median follow-up of 5.4±4.6 years, complete response was obtained in 15 patients, partial response in 11 and no response in the remaining 3. We observed an anaphylactic reaction and psoriasis induced by IFX, without other serious adverse events (Table).

**Conclusion:** BT, especially anti-TNF, seems effective and safe for treatment in NB.

**Disclosure of Interests:** José Luis Martín-Varillas: None declared, Ilígio González-Mazo: None declared, Belén Alienza-Mateo: None declared, Monica Calderón-Goercke: None declared, D. Prieto-Peña: None declared, Lara Sánchez Bilbao: None declared, Vanesa Calvo-Río: None declared, Santos Castañeda Consultant for: Amgen, BMS, Pfizer, Lilly, MSD, Roche, Sanofi, UCB, Esther Vicente: None declared, Olga Maiz: None declared, Clara Moriano: None declared, Elvira Díez Álvarez: None declared, José Luis Andreu Sánchez: None declared, Concepción Delgado Santos Castañeda Consultant for: Amgen, BMS, Pfizer, Lilly, MSD, Roche, Sanofi, UCB, Esther Vicente: None declared, Olga Maiz: None declared, Clara Moriano: None declared, Elvira Díez Álvarez: None declared, José Luis Andreu Sánchez: None declared, Concepción Delgado Santos Castañeda Consultant for: Amgen, BMS, Pfizer, Lilly, MSD, Roche, Sanofi, UCB, Esther Vicente: None declared, Olga Maiz: None declared, Clara Moriano: None declared, Elvira Díez Álvarez: None declared, José Luis Andreu Sánchez: None declared, Concepción Delgado

Figure 1. Simulations of ANCA-time profile in patients with MPO-ANCA (red line) and PR3-ANCA (purple line), using typical pharmacodynamic parameters. The central curve are the median dynamics of ANCA and the shadow are 90% prediction intervals.

**Background:** Rituximab is approved in patients with anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis (AAV). Antibodies to proteinase 3 (PR3-ANCA) or myeloperoxidase (MPO-ANCA) decrease with therapy (1) and may therefore be used as biomarkers.

**Objectives:** To investigate the relationship between rituximab concentration and ANCA levels in AAV patients.

**Methods:** 92 AAV patients from the RAVE trial (rituximab for ANCA-associated vasculitis) were assessed. Both MPO-ANCA, and PR3-ANCA antibody levels were used as biomarkers. ANCA levels were measured at baseline, at months 1, 2, 4, 6, 9, 18, and every 6 months until the second rituximab cycle if any, using ELISA supplied by Euroimmun. A semi-mechanistic model including a deep compartment which was sensitive to rituximab and a feedback mechanism, and a blood compartment were tested to describe the concentration-ANCA autoantibodies relationship. A population modeling approach using sequential methods was used for model building. Influence of sex, body surface area (BSA), BVAS/WG score, newly diagnosed status, major renal involvement at baseline, and relapse were investigated as covariates on pharmacodynamics parameters.

**Results:** A two compartment model including feedback mechanism from the circulating ANCA well described the concentration autoantibody relationship. The mean (interindividual standard deviation) estimated rituximab IC50, assessing potency, in patients with MPO-ANCA and PR3-ANCA were 21.9 mg/l (28%) and 11.2 mg/l (48.6%), respectively. Moreover, among patients with PR3-ANCA, rituximab IC50 was higher in patients with major renal involvement at baseline (p=2.47 x 10-2) and newly 6 months until the second rituximab cycle if any, using ELISA supplied by Euroimmun. A semi-mechanistic model including a deep compartment which was sensitive to rituximab and a feedback mechanism, and a blood compartment were tested to describe the concentration-ANCA autoantibodies relationship. A population modeling approach using sequential methods was used for model building. Influence of sex, body surface area (BSA), BVAS/WG score, newly diagnosed status, major renal involvement at baseline, and relapse were investigated as covariates on pharmacodynamics parameters.

**Results:** A two compartment model including feedback mechanism from the circulating ANCA well described the concentration autoantibody relationship. The mean (interindividual standard deviation) estimated rituximab IC50, assessing potency, in patients with MPO-ANCA and PR3-ANCA were 21.9 mg/l (28%) and 11.2 mg/l (48.6%), respectively. Moreover, among patients with PR3-ANCA, rituximab IC50 was higher in patients with major renal involvement at baseline (p=2.47 x 10-2) and newly diagnosed status (p=6.42 x 10^{-5}) than in others.
SAT0237 MYOCARDIAL FDG-PET/CT FINDINGS IN CHILDREN WITH TAKAYASU ARTERITIS

Kenichi Nishimura, Seira Hattori, Ayako Murase, Ai Ohnishi, Ryoki Hara, Shuichi Ito. Fukaura 3-9, Yokohama, Japan

Background: Takayasu arteritis (TAK) is a chronic large-vessel vasculitis affecting the aorta and its major branches. In Japan, 18F-fluorodeoxyglucose positron emission tomography with computed tomography (FDG-PET/CT) was approved since April 2018. Recently, usefulness of FDG-PET/CT to diagnose TAK or assess disease activity has been reported. However, the findings in children with TAK except for vascular lesions remain unknown.

Objectives: We aimed to retrospectively analyse the FDG-PET/CT findings in children with TAK except for vascular lesions.

Methods: This is a single-center retrospective observational study. We evaluated 9 children with TAK and compared them with 10 children with other rheumatic disease (systemic juvenile idiopathic arthritis; 5, polyarticular juvenile idiopathic arthritis; 1, juvenile dermatomyositis; 1, Crohn’s disease; 2, Klüver’s disease; 1) (control group). All children underwent FDG-PET/CT before the treatment. We compared the two groups for the age at performed FDG-PET/CT, sex, duration of onset to performed FDG-PET/CT, FDG-PET/CT findings. Binary data were analyzed by Fisher’s exact test.

Results: Median age of the performed FDG-PET/CT was 13.9 (range: 11.1-14.9) years old in TAK children and 5.4 (1.4-12.4) years old in control group. Both groups included 6 females. Median duration of onset to performed FDG-PET/CT was 1 (range: 0-12) months in TAK children and 0 (0-12) months in control group. FDG accumulation in bone marrow was observed in 7 TAK patients (78%) and in 7 (70%) of control group. Moreover, FDG accumulation in spleen was observed in 7 TAK patients (78%) and in 10 (100%) of control group. These findings were common in both groups. The other hand, FDG accumulation in left ventricular myocardium was observed in 8 TAK patients (89%) but in 3 (30%) of control group (p<0.02). Six TAK children received follow-up FDG-PET/CT. Myocardium FDG accumulation was continued in 3 children but resolved in 2. TAK children with persistent accumulation in myocardium had ascending aorta dilation later. A two compartments model including feedback mechanism.

Conclusion: FDG accumulation in left ventricular myocardium would be a characteristic finding in children with TAK, and possibly related to later ascending aorta dilation.

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REFERENCES

Disclosure of Interests: None declared
PREDICTION OF LONG-TERM EVOLUTIONARY PROFILES IN EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS (CHURG–STRAUSS) BASED ON BASELINE AND FOLLOW-UP CHARACTERISTICS

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Background: Eosinophilic granulomatosis with polyangitis (EGPA) (Churg–Strauss) is a small-vessel necrotizing vasculitis characterized by blood and tissue eosinophilia and asthma. Glucocorticoids (GCs) control the disease, but GC-dependence is frequent. Evolving concepts distinguish vasculitis-related symptoms from asthma and/or ENT manifestations. That distinction has become even more important since the development of B-cell and eosinophil-targeted therapies.

Objectives: This study aimed to describe and identify characteristics predicting long-term EGPA outcomes.

Methods: We set up a multicenter European cohort that included 636 EGPA patients. Based on recent consensus, we distinguished 4 EGPA-evolutionary profiles: GC-dependent asthma and/or ENT manifestations (requiring prednisone >7.5 mg/d), GC-dependent asthma and/or ENT manifestations (BODI)

Development and Preliminary Validation of the Behçet’s Syndrome Overall Damage Index (BODI)

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Background: Irreversible organ damage is considered a core outcome by the OMERACT working group. However, no specific tools are currently available to detect and measure damage accrual in Behçet’s syndrome (BS) patients.

Objectives: To develop and preliminarily validate the Behçet’s syndrome Overall Damage Index (BODI).

Methods: A preliminary version of the instrument (p-BODI) was developed by reviewing pre-existing tools (e.g. Vasculitis damage index (VDI)) and through an extensive literature review. p-BODI was then reviewed and implemented by a multi-rounds Delphi process, involving an international and multidisciplinary (5 rheumatologists, 4 internists, 1 ophthalmologist, 1 neurologist) panel of experts in BS management and a patients’ delegate. A group of clinicians (CG), not involved in the BODI development, was asked to independently score a set of clinical vignettes, in order to test the instrument reliability, after a training process consisting of a user manual and a video-tutorial. Then, Cohen’s K and intra-class correlation coefficient (ICC) between assessors and gold standard were calculated. Afterwards, BODI validation was conducted according to the OMERACT Filter 2.0 in a multicenter BS cohort.

Results: Starting from a list of 120 candidate items, the final version of BODI consisted of 4 overarching principles, 30 items and 12 sub-items (each of them scores one point) grouped in 8 domains (figure).

In terms of reliability, the mean K coefficient was 0.84 (95%CI 0.78 to 0.90) and the ICC was 0.88 (95%CI 0.80-0.95). Validation cohort consisted of 228 BS patients (41.9% males), with a median (IQR) age and disease duration of 46.9 (35.5-55.0) and 11.7 (5.8-20.7) years, respectively. Overall, prevalence of any BODI damage (BODI >1) was 56% with a median score of 1.0 (0-2.0). In regard of construct validity, BODI score significantly correlated with VDI (Spearman’s rho 0.693, p<0.001). Besides, BODI score did not correlate with BDCAF (rho 0.016, p=0.807), contrary to VDI (rho 0.141, p<0.034). Such results support the validity of BODI, unlike VDI, in discriminating damage from current disease activity in BS. On multiple regression analysis, factors independently associated to higher BODI damage score were male gender (β coefficient 0.143; p=0.014), longer disease duration (β coefficient 0.221; p<0.001), past major organ involvement (β 0.377; p<0.001) and required use of anti-TNFα inhibitors (β 0.222; p<0.001). Full agreement among the CG was reached in judging BODI as a credible comprehensive, easy to use instrument. Thomas Bonnotte: None declared. Xavier Puéchal: None declared.
HEALED TEMPORAL ARTERITIS. ANALYSIS OF CLINICAL FEATURES

Objectives: We analyzed clinical features of patients with healed TA, but these are non-specific and can also be seen in other conditions that are unlikely to benefit from prolonged steroid treatment. It is not clear if a pathological diagnosis of healed TA helps to support treatment. Unfortunately a biopsy does not always strengthen support for treatment. At the end of the day, the diagnosis of TA remains a clinical one and early involvement of Rheumatology may help avoid unnecessary biopsies and treatment. Ultrasound, MRA, and PET-CT scan may be able to fill the gap when biopsy fails to confirm the diagnosis.

Disclosure of Interests: None declared


SAT0242
SENSITIVITY OF TEMPORAL ARTERY BIOPSY IN giant cell arteritis: systematIc literature review and meta-analySIs of clInical data

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Background: The role of temporal artery biopsy (TAB) as a reference test for the diagnosis of giant cell arteritis (GCA) is currently questioned by the use of non-invasive imaging techniques such as temporal artery ultrasonography (TA-US). Although TAB is highly specific, a subset of patients with a clinical diagnosis of GCA does not show the characteristic histopathological signs. The lack of knowledge of the proportion of GCA cases with positive findings on TAB hampers comparisons of the sensitivity of TAB and imaging tests for diagnosing GCA.

Objectives: We performed a systematic literature review and meta-analysis to estimate the sensitivity of TAB in GCA and to identify factors that may influence the estimate.

Methods: We searched MEDLINE via PubMed, EMBASE and CENTRAL databases for articles reporting TAB in GCA that were published from 1990 to 2017, with no language restriction. Eligibility criteria included studies with >30 GCA cases fulfilling the original or modified 1990 ACR classification criteria for GCA. From eligible publications, two independent researchers extracted the main methodological, geographic, demographic, and clinical characteristics and the number of TAB-positive cases among all cases with interpretable results for TAB. By meta-analysis, we computed the pooled proportion of TAB-positive GCA cases by using a random-effects model with a binomial-normal distribution and assessed heterogeneity by the I² statistic. Subgroup and meta-regression analyses were used to examine the effect of 16 covariates (e.g., geographic, demographic, clinical and study descriptors) on TAB positivity.

Results: Among 3820 screened publications, 32 independent studies (3092 GCA patients in total) were used for the analysis. The pooled proportion of TAB positivity was estimated at 77.3% (95% confidence interval 71.8–81.5%), with high between-study heterogeneity (F=90%). Subgroup analysis suggested a potential influence of year of publication (Table). This result was confirmed by univariate (P=0.0008) and multivariate meta-regression (P=0.0004). No other analyzed covariate significantly influenced the sensitivity of TAB in GCA.

Conclusion: The 77% estimated sensitivity of TAB in GCA indicates that it is not inferior to that of TA-US (1). The decline in TAB-positive GCA cases over time could reflect an increasing propensity of clinicians to accept GCA diagnosis in the absence of proof by TAB. The unexplained high between-study heterogeneity could also reflect differences in TAB sampling, processing or interpretation.

REFERENCES
Effects of tofacitinib suppressed pulmonary vasculitis in a murine model

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Background: We reported allergic granulomatous vasculitis with eosinophil infiltration in an asthma model of C57BL/6 sensitized with ovalbumin (OVA). TGF-beta and IL-6 are thought to play an important role in fibroblast proliferation and is critical to vascular remodeling in vasculitis. Tofacitinib inhibits vascular endothelial cells proliferation and canalization.

Methods: C57BL/6 mice (6-8 weeks) were sensitized with ovalbumin (OVA) and alun. The positive controls (n=9) were exposed to aerosolized OVA daily for 7 days. The other group of mice (tofacitinib treated mice (n=9)) were administered with tofacitinib (100mg/kg intraperitoneal administration) in parallel with daily exposure to aerosolized OVA for 7 days. On 7th day, bronchoalveolar lavage (BALF) was performed and the lungs were excised for pathological analysis. Cytokines in BALF were measured.

Results: The total cell number and the number of Eosinophils in BALF on the 7th day were decreased significantly in the tofacitinib-treated mice compared with those of the control-positive mice. The blood eosinophil counts in the tofacitinib treated mice were lower on the than those in the positive control.

Conclusion: Tofacitinib suppressed pulmonary vascular remodeling in a murine model of allergic vasculitis with eosinophil infiltration. Tofacitinib is a hopeful therapeutic drug for Eosinophilic granulomatosis with polyangiitis.

Conclusion: The spectrum of clinical presentations in Indian patients is different from those reported in previous cohorts. Anti TNF therapy was effective in majority.

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Disclosure of Interests: None declared


SAT0245 CHOROIDAL EVALUATION IN PATIENTS WITH CHILDBIRTH POLYARTERITIS NODOSA (PAN) AND ADENOSINE DEAMINASE-2 DEFICIENCY (DADA-2)
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Background: Polyarteritis nodosa (PAN) is a systemic necrotizing vasculitis affecting small or medium arteries with a negative ANCA serology and no evidence of glomerulonephritis.

Objectives: The aim of this study was to evaluate the choroid with optical coherence tomography (OCT) in children with polyarteritis nodosa (PAN) and adenosine deaminase-2 deficiency (DADA-2).

Methods: The study included all PAN and DADA-2 patients (n=15), examined between June 2017 and September 2018, and an age and gender-matched control group (n=15). After oculomotor evaluation, choroidal images taken with sd-OCT (Heidelberg Spectralis) were evaluated with regard to choroidal thickness (ChT) at five points (750 and 1500 microns from the center of the fovea both in the temporal, nasal quadrant and under the fovea), total subfoveal choroidal area (TCA), luminal area (LA), stromal area (SA) and choroidal vascularity index (CVI).

Results: None of the patients had active ocular complaints or findings. The mean (±SD) age was 8.4 ± 3.69 years. ChT at 3 points, TCA, LA, and SA were found to be higher in patients with PAN and DADA-2. The CVI values were similar in both groups. No correlations were found between the OCT findings, activity score index (PVAS) and the biochemical parameters (Erythrocyte sedimentation rate, leukocyte, C-Reactive Protein).

Conclusion: The results of this study showed that the choroid was thicker in patients with PAN and DADA-2 than in the control group, suggesting that PAN and DADA-2 may affect the choroid. Ophthalmologic evaluation is important in PAN and DADA-2 patients, even in the absence of relevant complaints.

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Disclosure of Interests: Hafize Emin Sonmez: None declared, Abdullah Ağın: None declared, Sibel Kadayıfçilar: None declared, Ayta Batayorğlu: None declared, Özge Deliktaş: None declared, Selcan Demir: None declared, Yelda Bilginer: None declared, Bora Eldem: None declared, Seza Özen Consultant for: Seza Özen is receiving consultancy fees from Novartis, Speakers bureau: Roche


SAT0246 USING BONE MINERAL DENSITY VERSUS THE RATIO OF BODY MASS INDEX TO BONE MINERAL DENSITY TO PREDICT FRACTURE RISK IN POLYMYALGIA RHEUMATICA
Khojesta Talebi, Marwan Bukhari. Royal Lancaster Infirmary, Lancaster, United Kingdom

Background: Polymyalgia Rheumatica (PMR) is the commonest inflammatory rheumatic condition that affects the elderly population and treatment with long-term corticosteroids is common. Whilst steroid treatment is beneficial in managing symptoms, it has many side effects including increasing the risk of osteoporosis and hence fractures. There has been recent research that suggests using the ratio of BMI to Body Mass Index (BMI) is a better marker of predicting fracture risk in obese patients than BMI alone.

Objectives: Our research set out to find out whether BMI alone or the ratio of BMI to BMI is a better predictor of fracture risk in patients with PMR.

Methods: Data were used from a cohort of PMR patients referred for DEXA scan to a District General Hospital between June 2004 and October 2010. The following were recorded: age, sex, whether a fracture was sustained, whether they had had steroid therapy at any point, BMI, BMD at L1-L4, BMI at femoral neck (left and right) and BMI at hip (left and right). Logistic regression models were fitted using fracture as the dependent variable. The independent variables for the first set of logistic regression models were BMI at each level and for the second set BMI: BMD ratio at the same levels. Data were adjusted for sex and age at scan. Logistic models were compared using area under the ROC curves (AUC).

Results: 714 patients were used in the study, of whom 532 (75%) were female. Mean age was 70.5 (SD 8.84) with age range 45.8 to 96.5 years. 703 (98%) were recorded to have had steroid therapy at any point. Mean BMI was 28.2 kg/m² (SD 5.24), 156 (22%) had sustained a fracture. Odds ratios and AUC values for each level were as shown in the table. The fit of the models using the BMI alone was superior to the fit of the models using the ratio as the AUC values were greater for BMI alone.

Table 1 – Odds ratios (age- and sex-adjusted) and AUC values

<table>
<thead>
<tr>
<th>Level</th>
<th>Odds Ratio and CI (BMI)</th>
<th>AUC</th>
<th>Odds Ratio and CI (BMI:BMD)</th>
<th>AUC (BMI:BMD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>L1</td>
<td>0.192 (0.0656, 0.6960)</td>
<td>0.6789</td>
<td>1.04 (1.01, 1.07)</td>
<td>0.6621</td>
</tr>
<tr>
<td>L2</td>
<td>0.139 (0.0529, 0.358)</td>
<td>0.6977</td>
<td>1.05 (1.03, 1.09)</td>
<td>0.6777</td>
</tr>
<tr>
<td>L3</td>
<td>0.192 (0.0795, 0.463)</td>
<td>0.6681</td>
<td>1.06 (1.03, 1.09)</td>
<td>0.6730</td>
</tr>
<tr>
<td>L4</td>
<td>0.243 (0.108, 0.544)</td>
<td>0.5837</td>
<td>1.05 (1.02, 1.08)</td>
<td>0.6731</td>
</tr>
<tr>
<td>L 1 to L4</td>
<td>0.150 (0.0560, 0.400)</td>
<td>0.6837</td>
<td>1.06 (1.03, 1.09)</td>
<td>0.6737</td>
</tr>
<tr>
<td>L FEMORAL NECK</td>
<td>0.103 (0.0219, 0.5392)</td>
<td>0.6727</td>
<td>1.04 (1.01, 1.06)</td>
<td>0.6576</td>
</tr>
<tr>
<td>R FEMORAL NECK</td>
<td>0.0785 (0.0143, 0.430)</td>
<td>0.6837</td>
<td>1.05 (1.02, 1.08)</td>
<td>0.6750</td>
</tr>
<tr>
<td>L TOTAL</td>
<td>0.0980 (0.0233, 0.412)</td>
<td>0.6824</td>
<td>1.06 (1.03, 1.10)</td>
<td>0.6777</td>
</tr>
<tr>
<td>R TOTAL</td>
<td>0.0623 (0.0136, 0.285)</td>
<td>0.6971</td>
<td>1.07 (1.04, 1.11)</td>
<td>0.6821</td>
</tr>
</tbody>
</table>

Conclusion: This study identifies that the BMI:BMD ratio does not provide better indication of fracture risk than BMI alone in our cohort of patients with PMR. We have previously shown that the same is true for patients with rheumatoid arthritis. A limitation of this study is not stratifying by steroid use.

Further work will be done to study the role of the ratio in predicting fracture risk in patients with other conditions.

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DISCLOSURE OF INTERESTS: Khojasteh Talash: None declared, Marwan Bukhari: Speakers bureau: Bristol-Myers Squib, UCB Celltech, Roche/Chugai, Pfizer, Abbvie, Merck, Menarini, Sanofi-aventis, Eli-Lilly, Janssen and Novartis.


FEMALE SEX AND AGE AT DIAGNOSIS ARE ASSOCIATED WITH A DECREASED POSSIBILITY OF DRUG DISCONTINUATION IN GIANT CELL ARTERITIS: DATA FROM A MULTICENTER PROSPECTIVE COHORT OF 177 PATIENTS

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Background: Giant cell arteritis (GCA) usually requires long-term therapy with corticosteroids and/or Disease Modifying Anti-rheumatic Drugs (DMARDs) but the exact factors that are associated with drug discontinuation in these patients have not been well defined.

Objectives: To evaluate the baseline or on-treatment factors that influence drug survival in GCA.

Methods: Data were derived from an ongoing, multicenter, prospective cohort study of patients with GCA. During the 1st phase of the study, data regarding demographic and clinical characteristics at baseline, type of treatment, adverse events of therapy and co-morbidities were retrospectively collected and analyzed. Predictors of drug discontinuation were examined by univariate and multivariate logistic regression analyses.

Results: One hundred and seventy seven patients were included in the study; 70% (n=120) were women with a mean age at diagnosis of 74 ± 8.4 years. Diagnosis was established by temporal artery biopsy in 127 patients (72%), ultrasound of temporal arteries in 37 patients (21%) and large vessel imaging in 10 patients (6%). At diagnosis, the median ESR and CPR were 103 mm/h and 63 mg/L, respectively. All patients were treated initially with prednisone: 41 mg, while 12 (7%) of patients received pulse steroids. At the 1st patient evaluation (median follow-up from diagnosis: 3 years), the median daily steroid dose was 5 mg, while in 34% (n= 62) and 8% (n= 14) of patients a synthetic or biologic DMARD had been added, respectively. During that period, 24% (n=43) of patients had discontinued corticosteroids and 18% (n=32) all treatments by the 1st patient evaluation. By univariate analysis, DMARD use was associated with a higher possibility for corticosteroid discontinuation (OR=2.3, p=0.017) but by multivariate logistic regression analysis only female sex (OR=0.49, p=0.07) and age at diagnosis (OR=0.94, p=0.01) were associated with a decreased risk for corticosteroid discontinuation. Similar results were found for discontinuation of all drugs [female sex (OR=0.4, p=0.05) and age at diagnosis (OR=0.9, p=0.046)].

Conclusion: In this large GCA cohort, only one out of four patients managed to discontinue corticosteroids and 20% all treatments -3 years after diagnosis. Multivariate analysis revealed only female sex and age at diagnosis as independent factors for treatment discontinuation.

Acknowledgement: Supported by grants from the Greek Rheumatology Society and Professional Association of Rheumatologists.

Disclosure of Interests: None declared


SAT0248 CLINICAL OUTCOMES OF PATIENTS WITH GIANT CELL ARTERITIS TREATED WITH TOCILIZUMAB IN REAL-WORLD CLINICAL PRACTICE

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Background: Previously, the GIACTA study demonstrated the superiority of subcutaneous (SC) tocilizumab (TCZ) plus prednisone vs prednisone alone in achieving sustained glucocorticoid (GC)-free remission in patients with giant cell arteritis (GCA). 1

Objectives: To evaluate the effectiveness and safety of SC and intravenous (IV) TCZ in real-world clinical practice.

Methods: We performed a retrospective analysis of GCA patients treated with TCZ at a single center (MGH) between 2010-2018. Annual relapse rate, time to disease relapse, number of relapses, prednisone use, and adverse events (AE) before and after TCZ initiation were assessed. Disease relapse was defined as the re-appearance of clinical manifestations of GCA (e.g., cranial symptoms) that required treatment modification.

Results: A total of 60 GCA patients were included in the analysis. Table 1 depicts the baseline characteristics and the treatments received by this cohort. The median (IQR) disease duration before TCZ use was 0.6 (0.2-1.6) years. Fifty-eight patients (96.7%) received concomitant prednisone (mean [SD] dose: 30 [18.3] mg daily) at the time of TCZ initiation. Patients received TCZ for a median (IQR) period of 7.0 (3.3-14.9) years.

Seven patients (11.7%) successfully tapered off prednisone during TCZ treatment.

Previously, the GiACTA study demonstrated the superiority of TCZ in patients with GCA as indicated by a reduced incidence of relapses and by the ability to discontinue prednisone. The occurrence of AEs and SAEs (many due to GC) did not differ substantially while patients were on or off TCZ. These real-world findings support the previously reported efficacy and safety profile of TCZ in patients with GCA.

REFERENCE


Table 1. Patient baseline characteristics and treatments

<table>
<thead>
<tr>
<th>Total Patients (N = 60)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
</tr>
<tr>
<td>Female sex, n (%)</td>
</tr>
<tr>
<td>Caucasian ethnicity, n (%)</td>
</tr>
<tr>
<td>Clinical manifestations at disease onset</td>
</tr>
<tr>
<td>Headache, n (%)</td>
</tr>
<tr>
<td>Scalp tenderness, n (%)</td>
</tr>
<tr>
<td>Jaw claudication, n (%)</td>
</tr>
<tr>
<td>Amaurosis fugax, n (%)</td>
</tr>
<tr>
<td>Transient blurry vision, n (%)</td>
</tr>
<tr>
<td>Diplopia, n (%)</td>
</tr>
<tr>
<td>PMR symptoms, n (%)</td>
</tr>
<tr>
<td>ESR (mm/h), mean (SD)</td>
</tr>
<tr>
<td>CRP (mg/L), mean (SD)</td>
</tr>
<tr>
<td>Positive TA biopsy, n (%)</td>
</tr>
<tr>
<td>Prednisone dose (mg/day) at disease onset, mean (SD)</td>
</tr>
<tr>
<td>Use of other immunosuppressants before TCZ initiation, n (%)</td>
</tr>
<tr>
<td>Duration of disease before TCZ initiation (years), median (IQR)</td>
</tr>
<tr>
<td>Prednisone dose (mg/day) at TCZ initiation, mean (SD)</td>
</tr>
<tr>
<td>Received TCZ IV, n (%)</td>
</tr>
<tr>
<td>Received TCZ SC, n (%)</td>
</tr>
<tr>
<td>Duration of TCZ treatment (years), mean (SD)</td>
</tr>
<tr>
<td>Duration of TCZ treatment (years), median (IQR)</td>
</tr>
</tbody>
</table>

CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; IV, intravenous; PMR, polymyalgia rheumatica; SC, subcutaneous; TA, temporal artery; TCZ, tocilizumab.
Table 1: Clinical outcomes and adverse events

<table>
<thead>
<tr>
<th></th>
<th>OR TCZ (n = 66)</th>
<th>Or TCZ (n = 45)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up time, median (IQR), years</td>
<td>0.60 (0.25-1.17)</td>
<td>0.59 (0.22-1.59)</td>
</tr>
<tr>
<td>Patients with ≥ 1 relapse, n (%)</td>
<td>43 (71.7)</td>
<td>18 (60.0)</td>
</tr>
<tr>
<td>1 relapse</td>
<td>19 (31.7)</td>
<td>11 (18.3)</td>
</tr>
<tr>
<td>2 relapses</td>
<td>11 (18.3)</td>
<td>3 (5.0)</td>
</tr>
<tr>
<td>3 relapses</td>
<td>1 (1.6)</td>
<td>3 (5.0)</td>
</tr>
<tr>
<td>≥ 4 relapses</td>
<td>9 (15.0)</td>
<td>1 (1.7)</td>
</tr>
<tr>
<td>Time to relapse, median (IQR), years</td>
<td>0.5 (0.3-0.7)</td>
<td>2.1 (0.5-6.2)</td>
</tr>
</tbody>
</table>

Adverse events: D; ChE, Cholinesterase; LA, histamine, LA, histamine; Hb, hemoglobin; LDH, lactate dehydrogenase; PMN, polymorphonuclear leukocytes; TCZ, tocilizumab; WBC, white blood cell count.


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tions in inflammatory bowel disease: a single institution study of non-neo-
LAR/PRINTO/PRES criteria for Henoch-Schonlein purpura, childhood polyar-
Results: 134 cases were reviewed, concerning 80 PMR (mean age 67.9) and 54 “controls” (mean age 68.1). Overall, PET muscle damage was observed in 27 cases (34%) in PMR and 6 cases (11%) in controls (p<0.004). The damage is bi or multi-focal in 16/27 cases. The affected sites are: thighs and ischium-leg (n = 10), spinal (11), pectoral/subscapular (5), deltoid (1), trapezius (1). Fasciitis was found in 4 cases. As expected, PMR patients exhibited higher TEP scores than controls (p<0.001). In PMR patients, PET muscle involvement was associated with higher ESR values (p<0.05), but not with age, CRP or global PMR PET score.

Conclusion: Muscle involvement assessed by 18F-Fluorodeoxyglucose PET-CT is frequent in PMR (1/3), located at usual sites of symptoms of the disease, without association with age, CRP levels or global PET score for PMR. Muscle should be carefully evaluated during PET in cases of PMR; these pictures may be a new diagnosis feature of the disease.

REFERENCES


Disclosure of Interests: None declared


SA20251

SEX- AND AGE-RELATED DIFFERENCES IN CLINICAL MANIFESTATIONS OF BEHÇET’S DISEASE IN A LARGE COHORT OF CHINA PATIENTS

Background: Behçet’s disease (BD) is a systemic vasculitis with multiple symptoms such as recurrent oral and genital ulceration, skin lesions, ocular lesions, and other systemic affections. Studies have been conducted to reveal sex- and age-related differences in clinical characteristics of BD in different countries, but up to now sex and age influence for Chinese BD patients is very limited.

Methods: We retrospectively reviewed the medical records of BD patients followed up in the Departments of Rheumatology, Peking Union Medical College Hospital, Department of Rheumatology, Beijing, China; General Hospital of Tianjin Medical University, Department of Rheumatology, Tianjin, China.

Results: A total of 489 BD patients were included in our database: 286 males (58.49%) and 203 females (41.51%). Sex ratio M/F was 1.41, with a median age of 34 years (interquartile range: 28-44 years). Recurrent oral ulceration was the most common manifestation (90.32%), followed by genital ulceration (71.17%), skin lesions (57.67%), vascular lesions (25.36%), and ocular involvement (24.13%). Gastrointestinal (GI) involvement (15.13%), positive pathergy test (14.11%), and neurological involvement (5.93%) were less frequently observed. The comparative study between males and females revealed that ocular lesions (28.67% vs 17.73%, P=0.005), vascular lesions (31.47% vs 16.75%, P< 0.001) and positive pathergy test (17.83% vs 8.37%, P=0.002) were more common in male, while genital ulceration was more common in female (64.34% vs 80.79%, P<0.001). Regarding age difference, ocular lesions (P<0.017) were more frequently observed in younger patients, while vascular lesions (P=0.002) and GI symptoms (P=0.010) were more frequent in older patients. Gender differences of these manifestations were more prominent in certain age groups among 20-50 years old than other groups.

Conclusion: These analyses support that the clinical features of Chinese BD were different depending on sex and age.

REFERENCES


Scleroderma, myositis and related syndromes

SA20252

AN EVALUATION OF THREE DIFFERENT METHODS TO EVALUATE SKIN IMPAIRMENT IN SYSTEMIC SCLEROSIS PATIENTS

Background: One of the characteristics of systemic sclerosis (SSc) is an increase in dermal thickness (DT) (1-3). Although the standard method to evaluate the extent of skin involvement is the modified Rodnan skin score (mRSS) (3,4), high frequency ultrasounds (US) and the plicometer skin test (Plicometry) (5-8) are now being used in SSc patients.

Methods: The aim of this study was to determine any correlations between mRSS, US and Plicometry during the evaluation of skin impairment in SSc patients.

Results: A significant positive correlation was observed between the three methods used to evaluate DT in the SSc patients (mRSS vs US r=0.64, p<0.0001; mRSS vs Plicometry r=0.97, p<0.0001; US vs Plicometry r=0.55, p<0.0001). Conversely, there was no correlation between these parameters in the CNT group (p>0.05). The intraclass correlation coefficients for mRSS was 0.95, 0.97 for US and 0.96 for Plicometry. Data collection for mRSS took almost 10 minutes, 15 minutes for Plicometry and 20 minutes for US.

Conclusion: This study demonstrates a significant relationship between mRSS, US and Plicometry in the DT evaluation of SSc patients. The SSc patients had statistically significantly higher values than HS when the 3 techniques were used to evaluate the seventeen skin areas.

REFERENCES


Disclosure of Interests: None declared

PROGNOSTIC VALUE OF CARDIAC MAGNETIC VASODILATOR THERAPY IN THE LONG TERM PROGNOSTIC VALUE OF CARDIAC MAGNETIC VASODILATOR THERAPY IN THE LONG TERM

Late Gadolinium Enhancement 3.871 (1.289 – Mass
Right Ventricular End-Diastolic Indexed Right Atrial Area 1.384 (1.059 – Right Ventricular Ejection Indexed Left Atrial Area 1.244 (1.007 –

Background: Cardiac involvement is frequent in patients with systemic sclerosis (SSc). It is often subclinical, but significantly affects the prognosis of the disease. Cardiovascular magnetic resonance (CMR) is the non-invasive gold standard to quantify biventricular functional parameters and to perform a myocardial tissue characterization.

Objectives: To evaluate the prognostic value of CMR for cardiac events in SSc.

Methods: Two hundred and seventy-three SSc patients with a thorough clinical assessment underwent a CMR exam using a 1.5 T GE scanner. We quantified biventricular function parameter by SSFP cine images, oedema by STIR T2 images, and macroscopic fibrosis by late gadolinium enhancement (LGE) technique. Patients were followed-up and cardiac events were recorded as new onset of pulmonary arterial hypertension (PAH), new onset of heart failure (HF), or at least sustained ventricular tachycardia.

Results: Mean follow-up was 23.9 ± 17.0 months. During the follow-up a total of 14 events occurred (3 new onset PAH, 5 new onset HF, 6 ventricular tachycardia). CMR predictors of cardiac events by univariate analysis were left and right ventricular ejection fractions, indexed left and right atrial areas, and LGE (see Table). Myocardial fibrosis by LGE was the only independent predictor at multivariate analysis (hazard ratio 3.175; 95% CI 1.021-9.870, see Figure).

Conclusion: Cardiac magnetic resonance anatomical and functional parameters of both the left and right heart have significant prognostic value in patients with SSc.

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VASODILATOR THERAPY IN THE LONG TERM PREVENTION OF MYOCARDIAL MANIFESTATIONS IN SYSTEMIC SCLEROSIS (SSC): RESULTS FROM DESSCIIPHER INCEPTION COHORT STUDY

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Background: Calcium channel blockers (CCB) and angiotensin-converting enzyme inhibitors (ACEinh) are known to improve in the short term, cardiac perfusion and function in patients with SSc (Paris JU. et al. Rheum Dis Clin North Am 2014). No study has been carried out so far to investigate the long-term effectiveness of these drugs.

Objectives: To address this topic and other aspects of the management of SSc, the DeSSciipher (To decipher the optimal treatment of SSc) project was submitted to and financed by the European Community (FP7-HEALTH n°305495).

Methods: From Dec.1, 2012 to Nov. 30, 2015, 512 SSc patients who, as inclusion criterion, had no significant gut or lung or kidney involvement, were treated for 0.5-4 years (median 2.31) with either (n= 359: group 1) vasodilator therapy (i.e. CCB, or ACE-inh or Angiotensin II receptor blockers [AgIIrb] or a combination of them i.e. CCB plus either ACEinh or AgIIrb) or (n= 153: group 2) no vasodilator therapy. The 296 patients of the 2 groups, who had been assessed at baseline and along the follow-up for conduction blocks (CB), ventricular arrhythmias (VA), pacemaker implantation (PMI), left ventricular ejection fraction (LVEF) < 55% and angioscopic heart failure (CHF), and sudden cardiac death (SCD) during follow-up, were investigated for the cumulative incidence rate (IR) of all these events. The IR of single manifestations were calculated in the patients investigated for each of them. Cox regression analysis was carried out in the 296 patients with a missing value to identify independent predictors of the occurrence of any myocardial manifestation.

Results: During 1164 patient-years follow-up, 6/508 were implanted a PM,10/506 developed a LVEF<55%, 2/492 a CHF,11/325 a VA, 36/305 a CB, none underwent a SCD, any of these manifestations intervening in 59 out of the 296 investigated for all the manifestations. The IR of PM and VA was greater in group 2 patients as compared with group 1 (1.3 vs 0.2x100 pts/year; p=0.02) and (2.7 vs 1.1x100 pts/year; p=0.077). In stepwise Cox regression analysis, male gender (HR 2.44, 95%CI 1.3-4.6; p=0.005), age at enrollment (HR 2.97, 95%CI 1.7-5.2; p=0.007) and vasodilator therapy (HR 0.41, 95%CI 0.2-0.7; p=0.002) were independent positive and respectively, negative predictors of new onset cardiac manifestations.

Conclusion: Long term vasodilator therapy is likely to have a preventative role on the occurrence of myocardial manifestations of SSc.

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declared, Oliver Distler Grant/research support from: Prof. Distler received research funding from Actelion, Bayer, Boehringer Ingelheim and Mitsubishi Tanabe to investigate potential treatments of sclerodermia and its complications. Consultant for: Prof. Distler has/had consultancy relationship with the early years with Actelion, ARAFAR, Bayer, Boehringer Ingelheim, ChemonAb, espeRare foundation, Genentech/Roche, GSK, Inventa, Italfarmaco, iOvia, Lilly, medac, MedImmune, Mitsubishi Tanabe Pharma, Pharmacyclics, Novartis, Pfizer, Sanofi, Sorapharm and UCB in the area of potential treatments of sclerodermia and its complications. In addition, he had/has consultancy relationship within the last 3 years with A. Menarini, Abbie, GSK, Mepha, MSD, Pfizer and UCB in the field of arthritis and related disorders, Britta Maurer Grant/research support from: Grant/research support from: AbbVie, Protagen, Novartis; consultant for: MSD, Pfizer, Roche and Astellas. Elise Siegert Shareholder of: Astra Zeneca, Grant/research support from: Actelion, Consultant for: AEC Partners, Speakers bureau: Actelion, Norsk, Ulrich Walker Grant/research support from: Unrestricted grant from Abbott for the publication of the the CD-PASS II app, Veronica Jaeger Grant/research support from: Has received an unrestricted grant from AbbVie to support the creation of the CD-PASS II app, Marc Frerix: None declared, Ingo Helmut Tanner: None declared, Ulf Müller-Ladner Grant/research support from: Project supported by an unrestricted educational grant from Celgene GmbH, Gabrielle Valentin Grant/research support from: MSD, Pfizer, biogen, Speakers bureau: MSD, amgen, biogen, Lilly, sanofi, phizer.

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### SAT0255

**EVALUATION OF THE CARDIOVASCULAR INVOLVEMENT OF SYSTEMIC SCLEROSIS USING NON-INVASIVE CARDIAC IMAGING TECHNIQUES**

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**Background:** Systemic sclerosis (SSc) is a systemic disease that may affect many organs; among them, cardiac involvement. The prevalence of cardiac involvement in SSc varies depending on the sensitivity of the methods used for its detection. Indirect evidence suggests that subclinical cardiac involvement may eventually occur in the vast majority of patients with SSc. Early detection and monitoring of myocardial involvement are integral to SSC management, as cardiovascular involvement is known to be a poor prognostic indicator when present.

**Objectives:** To describe myocardial perfusion abnormalities and potentially associated coronary arteries lesions using non-invasive imaging techniques in a group of patients with SSc and suggestive symptoms of myocardial involvement (symptomatic) in comparison with a control group of patients with SSc without cardiac symptoms.

**Methods:** A retrospective observational study was performed including a total of 61 patients diagnosed with SSc, 52 symptomatic, with dyspnea and/or chest pain (57.98 ± 12.3 years, 45 women) and 9 asymptomatic controls (50.2±15.21 years, 8 women).

All patients underwent a post-stress (treadmill or pharmacological) myocardial perfusion gated-SPECT, a cold-induced stress SPECT, that were compared to a rest SPECT (to assess ischemia and/or necrosis), as well as a cardiac CT-angiography (to assess significant coronary arteries lesions, considering stenosis of more than 50%)

**Results:** Twenty-one out of the 52 symptomatic patients (50%) showed myocardial perfusion defects in the stress-rest SPECT: 13 (25%) showed ischemia, 10 (19.2%) had myocardial perfusion abnormalities; 13 (25%) fibrosis/necrosis, and 6 (11.5%) ischemia and necrosis. In the cold-induced SPECT, 17 patients (32.7%) showed mycardial perfusion abnormalities: 10 (19.2%) showed ischemia, 13 (25%) fibrosis/necrosis, and 6 (11.5%) ischemia and necrosis. In the other hand, of the 9 asymptomatic patients only 1 (11%) had ischemia and necrosis in the stress-rest SPECT, being only positive for necrosis in the cold-induced SPECT images. In the cardiac CT-angiography, 7/52 patients (13.4%) showed significant coronary lesions, 4 (57.2%) of them with perfusion defects in the SPECT images, and 3 (42.6%) without significant perfusion alterations.

Of the 9 asymptomatic patients, 1 (11%) had significant coronary lesions, being the same patient who presented perfusion defects in myocardial SPECT images.

**Conclusion:** The gated-SPECT is a sensitive tool for detecting myocardial perfusion alterations, normally with no associated significant coronary lesions, suggesting microvascular abnormalities. In this cohort, myocardial perfusion abnormalities were detected in 50% of symptomatic patients, whereas in only 11% of non-symptomatic patients.

**REFERENCES**


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### SAT0256

**EFFICACY AND SAFETY OF ANTIINFECTIVE THERAPY IN DIFFUSE INTERSTITIAL PULMONARY DISEASE ASSOCIATED WITH SYSTEMIC AUTOIMMUNE DISEASES**

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**Objectives:** Assess the efficacy and safety of antiinfective agents (pifierine-done and niteranib) in refractory diffuse interstitial lung disease (DILD) associated with systemic autoimmune diseases (SAD).

**Methods:** Open observational study in patients with active symptomatic DILD-SAD (evidence of clinical and functional impairment) despite treatment with glucocorticoids (GC) and immunosuppressant therapy.

**Results:** We included 13 patients (8 women) with a mean age (± SD) of 55 ± 12 years (range, 7-71). The baseline SAD were: eight systemic sclerosis, one rheumatoid arthritis, one ankylosing spondylitis, one microscopic polyangiitis with pulmonary fibrosis and one interstitial lung disease with autoimmune characteristics (IPAF). Mean time from diagnosis to initiation of antiinfective therapy was 3 ± 8.2 years (IOR 25-75%: 1.6-9.5).

The histopathological patterns found were: seven cases (54%) of usual interstitial pneumonia (UIP), three (23%) nonspecific interstitial pneumonia (NSIP), two cases (15%) combined pattern of pulmonary fibrosis and emphysema (CPFE), and one (8%) non-classifiable pulmonary fibrosis (without histospecific radiological pattern).

In addition to GC, the previous therapy tested for DILD was mycophenolate mofetil (MMF) in 77% of the patients, cyclophosphamide (8 cases, and/or bleomycin) in 46%, and rituximab (RTX) in 54% (the number of RTX cycles administered were 4 ± 3.3 range, 1-9). Despite this, during the year prior to start the antiinfective drugs, all patients presented a worsening in the values of % pFVC (-8.77%) and% pDLCO (-6.71%) in 10 patients (77%) and with rituximab in 3 (23%). In addition to GC at doses between 5 and 20 mg/ day in 10 patients (77%) and with rituximab in 3 (23%). In addition to GC at doses between 5 and 20 mg/ day in 10 patients (77%) and with rituximab in 3 (23%).

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**Scientific Abstracts**
duration of follow-up was 15 months (range 3-59). At the end of the follow-up period, 10 of the 13 patients (77%) were still in treatment. In 2 patients (15%) the therapy failed, requiring lung transplantation in 1 case (after 7 months of therapy), while an autologous hematopoietic stem cell transplantation was conducted in the other patient (after 13 months of anabiotic). In one patient (8%) the treatment was discontinued due to adverse effects.

When quantifying the degree of response in patients who continued treatment, only 9 of the 10 patients were included in the analysis, since 1 had only 3 months of therapy. In these 9 patients there was an improvement of pFVC (mean: ±5.13; SD: 8.38) and pDLOD (±4.42; SD: 5.06). The evolution of the efficacy variables analyzed is shown in the table.

The response in the Pulmonary function testing (PFT) in these 9 patients categorized according to the definitions of the American Thoracic Society was as follows: A) pFVC: stabilization in 5 cases and improvement in 4; B) pDLOD: stabilization in 7 cases and improvement in 3.

The frequency of adverse effects was 31% (413), but only the treatment was withdrawn in 1 patient (8%). Three patients presented digestive discomfort that forced to reduce the dose of the anabiotic. One patient developed a toxic hepatitis due to nintedanib after 4 months of treatment that forced the withdrawal of the drug, replacing it 1 month ago with placebo and the follow-up died.

Conclusion: Our data provides evidence of the safety and tolerability of both pirfenidone and nintedanib in patients with DIDL-SAD refractory to GC and immunosuppressant therapy.

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SAT0257 THE SIGNIFICANCE ON THE TRANSITION THROUGH DIFFERENT PATTERNS OF NAILFOLD MICROVASCULAR DAMAGE ON THE COURSE OF SYSTEMIC SCLEROSIS
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Objective: To investigate the timing of transition through different patterns of nailfold microvascular damage in systemic sclerosis (SSc) patients and to determine the significance of this transition.

Methods: In the period January 2012 to December 2017, 400 SSc patients were followed up by nailfold videocapillaroscopy (NVC) the same operator (SPD) every 6 months. Demographic, clinical and laboratory data were recorded. The capillaroscopic findings were classified as normal, nonspecific or scleroderma pattern (‘early’, ‘active’, or ‘late’). The evolution on the NVC pattern over time was monitored and recorded.

Results: The transition of microangiopathy was seen in 53/400 (13.25%) SSc patients. At the baseline 11/53 (21%) patients had the non-specific changes, the early pattern had 25/53 (47%) patients, and the active pattern had 17/53 (32%) SSc patients. The mean ± SD time of progression from one to another NVC patterns was 27.68 ± 35.11 months. Improvement of the NVC patterns was found in 15/53 (28%) patients and deterioration in the remaining 38 (72%) patients. The mean time of progression from nonspecific to early pattern (in 10 patients) and nonspecific to active pattern (in 1 patient) was 14.5 ± 9.73 vs. 12 months, respectively. Time of changed from early to nonspecific (in 7 patients), early to active (in 17 patients) and early to late pattern (in 1 patient) was 30.65 ± 22.56 vs 22.29 ± 16.61 vs 24 months, respectively. Time of changed from active to early (in 8 patients) and active to late pattern (in 9 patients), was 26.25 ± 11.11 vs 18.00 ± 13.97 months, respectively. Progression of nonspecific to early or active NVC pattern was related with limited form of SSc (91%), diffuse hand swelling (54%), arthralgia/arthritis (45%) and involvement of lungs (48%). Also, progression of early to active NVC pattern was related with limited form of SSc (64%), sclerodactyly (48%) and involvement of lungs (48%). In contrast, progression of active to late NVC pattern was related with diffuse form of SSc (53%), digital ulcerations (35%) and more frequent involvement of lungs (65%). These differences in the frequency of involvement of certain organs were not statistically significant.

Conclusion: These results demonstrate dynamic transition of microvascular damage through different NVC patterns of microangiopathy in about 13% of SSc patients. Patients with rapid progression from the early to active, as well as active to the late NVC patterns (>2 years) should be monitored closely, because they are at risk of further significant damage to the internal organs.

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SAT0258 SEXUAL HEALTH IMPAIRMENT IN WOMEN WITH SYSTEMIC SCLEROSIS
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Background: Systemic sclerosis (SSc) is a chronic autoimmune disease that may affect all aspects of life including sexual function.

Objectives: To assess sexual function, pelvic floor function and sexual quality of life women with SSc compared to age-sex-matched healthy controls (HC). To subanalyze sexual function in sexually active individuals.

Methods: In total 47 women with SSc (mean age: 50.5, disease duration: 5.6 years, lcsSc/idcsSc: 27/20, mRSS: 12.7, ESSG activity index: 2.5), who fulfilled the ACR/EULAR 2013 criteria, and 47 healthy women (mean age: 50.5) filled in 11 well-established and validated questionnaires assessing sexual function, pelvic floor function, quality of life, fatigue, physical activity and depression. Data are presented as mean±SEM.

Results: Compared to HC, patients with SSc had significantly higher prevalence and greater severity of sexual impairment (FSFI, BISF-W), pelvic dysfunction (PISO-12, PFQ07), and worse sexual quality of life (SQol-F) (table 1). There were no significant differences in sexual function between limited and diffuse SSc. Even sexually active SSc patients reported significantly greater sexual health impairment compared to sexually active HC. Sexual health impairment in SSc was associated with dis-
ease activity/duration, health status, physical activity, fatigue and depression (table 2).

Conclusion: Women with SSc reported significantly impaired sexual function, sexual quality of life and pelvic floor function than age-matched HC. Worse scores in SSc were associated with disease activity/duration/health status, physical activity, fatigue, and depression.

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SAT0259

PREDICTIVE FACTORS FOR TREATMENT RELATED MORTALITY AND MAJOR ADVERSE EVENTS AFTER AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR SYSTEMIC SCLEROSIS: RESULTS OF A LONG TERM FOLLOW-UP MULTI-CENTRE STUDY

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Background: Autologous hematopoietic stem cell transplantation (HSCT) has shown superior efficacy to cyclophosphamide pulse therapy in systemic sclerosis (SSc) but its application is hampered by high treatment related mortality (TRM). To date factors, other than smoking, predicting TRM has shown superior efficacy to cyclophosphamide pulse therapy in systemic subtype who were treated because of interstitial lung disease. The aims of this study were to analyse possible differences correlated with major events.

REFERENCES

Disclosure of Interests: Sandra van Bijnen: None declared, Maaike Boonstra: None declared, Cornelia van den Enden: None declared, Julia Sperigros: Grant/research support from: Boehringer Ingelheim, Anne Schouffoer: None declared, Jacob M. van Laar: Grant/research support from: Genentech, Consultant for: F. Hoffmann-La Roche, Thomas Huizinga Consultant for: Merck, UCB, Bristol Myers Squibb, Biostat AG, Pfizer, GSK, Novartis, Roche, Sanofi-Aventis, Abbott, Crescendo Bioscience Inc., Nycoderm, Boehringer, Takeda, Zydus, Epirus, Eli Lilly, Alexandre Voskuyl: None declared, Walter van der Velden: None declared, Frank van den Hoegen: None declared, Jeska de Vries: None declared, Madelon Vork: Grant/research support from: Madelon Vork has received unrestricted research funding from Actelion and Therabel, Consultant for: Madelon Vork was a consultant for Actelion, Boehringer-Ingelheim, Speakers bureau. Actelion, Boehringer-Ingelheim, Roche


SAT0260

MUSCULAR INVOLVEMENT OF THE LOWER LIMBS IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES: A MRI EVALUATION

Simone Barosi1, Barbara Mugellini2, Alessandra Tripoli3, Giacomo Aringhieri2, Chiara Cardelli1, Elisa Cioffi1, Vanna Zampa1, Davide Caramella1, Marta Mosca1, Rossella Neri1, University of Pisa, Rheumatology Unit, Pisa, Italy; 2University of Pisa, radiology Unit, Pisa, Italy; 3University of Pisa, radiology Unit, Pisa, Italy

Background: Since many years, muscular magnetic resonance imaging (MRI) has been used in the diagnosis and follow-up of patients with idiopathic inflammatory myopathies (IIM), but the clinical significance and the pattern of the muscular alterations (edema, fatty infiltration and atrophy) in different subsets of the disease are still not well defined.

Objectives: The aims of this study were to analyse possible differences in the involved muscles between dermatomyositis (DM) and polymyositis (PM); the correlations between the pattern of muscular involvement in different subsets of the disease and disease parameters in a monocentric cohort of patients.

Methods: We retrospectively collected data from 85 patients with poly and dermatomyositis (EULAR/ACR criteria) who performed pelvic and thighs muscle MRI from January 2010 to December 2018: 27 had DM and 58 PM, mean age 58.6±13.4 years, mean disease duration of 45±73 months. The images in 22 muscles for the presence of muscular edema, fatty infiltrates and atrophy were assessed by a dedicated radiologist. Moreover, data about serum creatine kinase (CK) and manual muscle

Table 1: demographic and disease related factors

<table>
<thead>
<tr>
<th>Table 1: demographic and disease related factors</th>
<th>Male/female</th>
<th>49/43</th>
</tr>
</thead>
<tbody>
<tr>
<td>LcSScDecSSc</td>
<td>4/88</td>
<td></td>
</tr>
<tr>
<td>Age at HSCT mean (SD) (year)</td>
<td>6.8 (10.3)</td>
<td></td>
</tr>
<tr>
<td>Disease duration at HSCT mean (SD)/year</td>
<td>2.4 (2.4)</td>
<td></td>
</tr>
<tr>
<td>mRSS mean (SD)</td>
<td>26 (10.1)</td>
<td></td>
</tr>
<tr>
<td>Antibodies: ANA, A TA, Anti-RNP positive</td>
<td>88/92, 34/92, 1/92</td>
<td></td>
</tr>
<tr>
<td>Ever smoker</td>
<td>54/84</td>
<td></td>
</tr>
<tr>
<td>FVC as% pred. mean (SD)</td>
<td>84.9 (22.7)</td>
<td></td>
</tr>
<tr>
<td>DLCO as% pred mean (SD)</td>
<td>55.1 (16.2)</td>
<td></td>
</tr>
<tr>
<td>LVEF &lt;50% (by echo)</td>
<td>3/92</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: In this national cohort study of HSCT in patients with SSc and poor prognosis we observed a median event-free survival of 4.3 years. TRM was 10.8% and major events occurred in 13%. TRM was correlated to male gender. Low LVEF, male gender and older age were correlated with major events.
CHARACTERISTICS ASSOCIATED TO SCLERODERMAL RENAL CRISIS, AND INCIDENCE VARIATION OVER TIME IN THE RESCLE REGISTRY

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Background: Scleroderma Renal Crisis (SRC) is a serious complication of Systemic Sclerosis (SSc). Nowadays, it seems that there is a reduction in its prevalence and mortality1. Objectives: To evaluate the characteristics of patients with SSc in a large cohort of SSc patients. To investigate predictors of SRC, and epidemiologic differences over time. Methods: 1933 patients were collected in ongoing registry of Spanish SSc patients – RESCLE. We did descriptive study and epidemiologic analysis. Results: Out of 1933 SSc, 43 (2.2%) developed SRC. Univariate analysis showed significant differences of SRC vs. non-SRC population: SSc subtypes: diffuse cutaneous SSc (dcSSc), 72% vs. 19%; limited cutaneous SSc (lCSSc), 26% vs. 61%. Demographics: Female gender, 77% vs. 89%; time from SSc onset to SRC diagnosis, 3.0±8.0 vs. 6.6±9.5 years; arterial hypertension (HT), 56% vs. 32% 1st manifestation: Raynaud’s phenomenon (RP), 68% vs. 82%. Clinical manifestations: RP, 88% vs. 96%; digital ulcers, 70% vs. 38%; arthritis, 45% vs. 20%; myositis, 30% vs. 13%; joint contractures, 45% vs. 18%; intestinal involvement, 24% vs. 11%; malabsorption, 24% vs. 7%; interstitial lung disease 58% vs. 41%; pulmonary HT, 56% vs. 29%; periarticular effusion, 28% vs. 7.4%; periarticular stiffness, 24% vs. 8.3%; ischiadic neuropathy, 31% vs. 12%; diastolic dysfunction, 67% vs. 34%. Capillaroscopy: active pattern 77% vs. 33%. Immunological data: anti-Topoisomerase I, 39% vs. 20%; anti-centromere, 15% vs. 49%; anti-ARNAPol III, 45% vs. 11%. Prognosis: Overall mortality, 56% vs. 18%; SSc-related mortality, 83% vs. 49%. Survival at 5, 10, 20, and 30 years was 73% vs. 96%, 56% vs. 92%, 28% vs. 80%, and 28% vs. 67%, respectively. Treatment: ACEI use, 35% vs. 14%, corticoid use, 51% vs. 25%. Multivariate analysis: dcSSc subtype, RR 22.68 (5.81-88.51) p<0.001; intestinal malabsorption, RR 7.35 (2.55-21.18) p<0.001, and active capillaroscopy pattern RR 7.26 (1.61-32.7) p<0.010. Prevalence of SRC in dcCSSc subtype 7.8%, and in lCSSc subtype 0.9%. P over decades: P-80’s, 3.8%; P-90’s, 2.7%; P-00’s: 2.3% and P-10’s: 0.9%, achieving statistical significance in the last decade PRR: 0.33 (0.13-0.85) = 0.014.

Conclusion: In RESCLE cohort, SRC predominated in dcSSc patients, and it was associated to intestinal malabsorption, and an active pattern by capillaroscopy. SRC showed a very poor prognosis. Finally, we evidenced a decreasing prevalence of SRC over time in our cohort.

REFERENCE
malignant conditions in systemic sclerosis

GAZE PATTERN ANALYSIS IN THE ASSESSMENT OF DIGITAL ULCERS IN PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: The assessment of chronic wounds such as digital ulcers (DUs) in systemic sclerosis relies heavily on visual aspects. However, inter-rater variability in the assessment and definition of digital ulcers is low and there are no evidence-based data concerning the visual assessment of digital ulcers.

Objectives: We analysed gaze pattern data in order to evaluate differences in the visual assessment of digital ulcers in systemic sclerosis patients.

Methods: We analysed gaze pattern data from 36 subjects: 9 expert medical professionals (EMP), 8 non-expert medical professionals (NEMP), 9 medical graduates (MG) and 10 lay persons (novices). Assessment was done using a mobile eye-tracking device that tracks eye movements of subjects. Twenty pictures from digital ulcers of SSC patients were presented to each subject, 30 seconds each and characteristics of gaze pattern data were analysed. The analysis comprised the scan path and the dwell times (for areas of interest, AOI), fixation counts and the entry time for each picture and subject. Areas of interest were defined as the wound area, wound margin, wound surroundings and distracting non-relevant parts of the pictures. The visual assessment of the digital ulcers was accompanied by questions for each subject about their assessment of the DUs, the expected healing of the ulcer, the medical treatment of the patient.

Results: Most significant differences were found between novices and medically educated groups (expert medical professionals, non-expert medical professionals, medical graduates - EMP, NEMP, MG). Dwell times in the wound area for novices differed statistically significantly from all medically educated groups (1.76s-3.1s less). Above all, novices had lower dwell times in wound margin and wound surrounding and spent more time in areas with other distracting features of the picture and white space (up to 1.92s longer). Correspondingly, they had less fixation points and longer overall scan paths in wound areas. Similar gaze pattern data were observed for medically educated groups, however NEMP had a statistically significantly lower dwell time in the wound area than EMP. Questionnaire responses were compared to an expert opinion (gold standard) and EMP had significantly more correct answers on prognosis and treatment than MG for wound assessment, but not better than NEMP.

However, treatment and prognosis were best in the EMP group with statistical difference to the NEMP and MG group.

Conclusion: For the first time, we provide evidence-based data on the visual assessment of digital ulcers in SSC. These data will be useful for the development of a structured educational programme for young physicians, rheumatology trainees and medical graduates. A key finding is that the visual assessment of digital ulcers should increasingly emphasize the importance of pathologic changes in the wound margin and surrounding area of the wound. Hence a structured approach should focus on all areas of the wound while discarding distracting visual information. An adequate terminology should be used alongside.

REFERENCE


**Determinants of Renal Resistive Index (RRI) at Renal Artery Doppler Ultrasound in Systemic Sclerosis (SSc): More than General Population Factors**

Cosimo Bruni¹, Edoardo Rosato², Antonietta Gigante², Vanessa Maestripieni¹, Glulia Tesei¹, Marco Chiostrò¹, Gemma Lepe¹, Silvia Belfando Randone¹, Serena Guiducci¹, Sergio Castellani¹, Maria Boddi¹, Marco Matucci-Cerinic¹, ¹Careggi University Hospital, Firenze, Italy; ²Sapienza University of Rome, Roma, Italy

**Background:** RRI can be measured on renal artery Doppler ultrasound, showing the difficulty blood flows encounter distally from where it is measured. RRI can be determined by vascular and interstitial renal features: studies on the general population showed arterial hypertension, arteriosclerosis, low-grade inflammation, diabetes mellitus, hyperuricaemia as possible causes of renal vasculopathy or tubular-interstitial nephropathy, thus determining altered RRI values. Studies on SSc have shown increased RRI values, associated with nailfold-videoendoscopy pattern and history of digital ulcers.

**Objectives:** To identify determinants of RRI in SSc patients.

**Methods:** SSc patients fulfilling the 2013 ACR/EULAR criteria were enrolled from two SSc-care units. Data regarding SSc clinical manifestations, instrumental, and laboratory evaluation for renal, cardiac and cardiovascular involvement were collected. RRI was measured at least once in each patient. Linear regression analysis was carried out to determine predictors for baseline RRI and change in RRI in time (ΔRRI).

**Results:** 380 patients [aged 57 (46-68) years, 12% males] were enrolled in the study. On univariate analysis, both general population determinants (age, arterial hypertension, diabetes mellitus, hyper-lipidaemia, and hyper-uricaemia) and SSc specific features [time from Raynaud’s phenomenon onset, ACA positivity, scleroderma renal crisis history, estimated systolic pulmonary arterial pressure on Echo (sPAP), presence of dyspnea, %DLCO and presence of lower intestinal symptoms] predicted RRI values, with only age and sPAP being significant independent predictors at baseline. Follow-up RRI, available for 230 patients, showed that none of the general population determinants was predictive for ΔRRI.

**Conclusion:** Data show that among general population determinants, age is the only predictive factor for RRI in SSc patients. However, only age and sPAP were predictive for ΔRRI. Therefore, the use of specific age-adjusted cut-offs (table 1) are recommended when assessing SSc patients.

**Disclosure of Interests:** Cosimo Bruni: None declared, Edoardo Rosato: None declared, Antonietta Gigante: None declared, Vanessa Maestripieni: None declared, Glulia Tesei: None declared, Marco Chiostrò: None declared, Gemma Lepe: None declared, Silvia Belfando Randone: None declared, Serena Guiducci: None declared, Sergio Castellani: None declared, Maria Boddi: None declared, Marco Matucci-Cerinic: Grant/research support from: Actelion, MSD, Pfizer, BMS, Chemomab, Sanipedia, Speakers bureau: Actelion, BMS, MSD, Janssen DOI: 10.1136/annrheumdis-2019-eular.3514

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**Digital Ulcer (DU) and Ventricular Arrhythmias Predict the Late Gadolinium Enhancement (LGE) in Cardiac Magnetic Resonance (CMR) in Systemic Sclerosis (SSc): Proposal of Candidate Red Flags for Early Referral**

Cosimo Bruni¹, Luna Gargani², Alessia Pepe³, Antonella Mekoni⁴, Daniele De Marchi⁴, Giancarlo Todiene⁴, Gennaro D’angelo⁵, Alberto Moggi Pignone⁵, Serena Guiducci⁵, Marco Matucci-Cerinic⁵, ¹Careggi University Hospital, Firenze, Italy; ²CNR IFC Istituto di Fisiologia Clinica, Pisa, Italy; ³Fondazione Toscana Gabriele Monasterio, Pisa, Italy

**Background:** In SSc, cardiac involvement either primary or secondary, is frequently subclinical. In myocardial diseases, CMR is considered the non-invasive gold standard to diagnose myocardial tissue involvement and LGE has a significant impact on prognosis.

**Objectives:** To identify the predictors of the presence of LGE in SSc patients.

**Methods:** Patients fulfilling the 2013 ACR/EULAR classification criteria were assessed with CMR (1.5 T GE scanner) when clinically indicated. Data on demographics, clinical SSc features, laboratory and instrumental tests for cardio-pulmonary, microvascular and renal involvements were recorded at the time of CMR evaluation. Binary regression analysis was performed with SPSS version 25.0.

**Results:** 317 SSc patients (284 women, mean age 52±14) were enrolled in the study. LGE-CMR was present in 32.9% and Myocardial edema (ME-CMR) in 6.1% of patients. On univariate regression analysis, %DLCO values, NYHA functional class, history of DU (hDU), TAPSE and couples of ventricular premature beats (VPBc) were predictors of LGE-CMR or ME-CMR. At multivariate analysis, TAPSE (OR 0.832, 95% CI 0.727-0.951, p=0.007), hDU (OR 3.893, 95% CI 1.614-9.387, p=0.002) and VPBc (OR 2.38, 95%CI 0.959-18.738, p=0.057) were independent predictors for LGE-CMR. Presence of pericardial effusion was the only predictor for ME-CMR (OR 3.379, 95% CI 1.018-12.988, p=0.047).

**Conclusion:** DU history, ventricular ectopic beats on 24 hours ECG, TAPSE impairment and pericardial effusion on echocardiography may predict myocardial LGE. More studies are necessary to further verify and validate these “red flags” to refer the patients to CMR.

**Disclosure of Interests:** : Cosimo Bruni: None declared, Luna Gargani: None declared, Alessia Pepe: None declared, Antonella Mekoni: None declared, Daniele De Marchi: None declared, Giancarlo Todiene: None declared, Gennaro D’angelo: None declared, Alberto Moggi Pignone: None declared, Serena Guiducci: None declared, Marco Matucci-Cerinic Grant/research support from: Actelion, MSD, Pfizer, BMS, Chemomab, Sanipedia, Speakers bureau: Actelion, BMS, MSD, Janssen DOI: 10.1136/annrheumdis-2019-eular.5618

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**Serum Anti-Heterogeneous Nuclear Ribonucleoprotein Antibody Characterizes Systemic Sclerosis with Anti-centromere Antibody and Severe Raynaud’s Phenomenon with Digital Ulcers**

Natasa Isailovic¹, ²Angela Cerbelini, Carolina Golinò³, Elena Generali³, Maria De Santis³, Marta Caprioli³, Giacomo Maria Guidelli³, Piercarlo Sarzì-Puttini³, Minou Satoh¹, Carlo Selmi¹, ³Humanitas Clinical and Research Hospital, Rheumatology and Clinical Immunology, Rozzano (MI), Italy; ²Luigi Sacco University Hospital, Rheumatology, Milan, Italy; ³University of Milan, Milan, Italy; ⁴University of Occupational and Environmental Health, Clinical Nursing, School of Health Sciences, Kitakyushu, Japan

**Background:** Systemic Sclerosis (SSc) is characterized by the presence of serum autoantibodies (autoAbs) which may be crucial in the diagnosis, prediction of organ involvement, follow-up, and treatment choices. However, SSc sera can be negative for autoAbs identified using commercially available tests, and several new and rare autoAbs have been identified in the last decade with immunoprecipitation (IP) techniques. We recently reported a new IP pattern corresponding to anti-heterogeneous nuclear ribonucleoprotein (anti-hnRNP) antibodies in a cohort of SSc patients.

**Objectives:** To analyze the IP pattern of anti-hnRNP antibodies in SSc sera and determine their clinical and laboratory correlations.

**Methods:** We investigated sera from 63 consecutive patients with SSc attending our Unit between 2014 and 2018, using protein-IP of 35S-methionine-labeled K562 cell extract followed by SDS-PAGE and autoradiography, and IP-Western Blot for hnRNP-L and C1+C2 following

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**Scientific Abstracts**

**Determination of renal resistive index (RRI) at renal artery doppler ultrasound in systemic sclerosis (SSc): More than general population factors**

Cosimo Bruni¹, Edoardo Rosato², Antonietta Gigante², Vanessa Maestripieni¹, Glulia Tesei¹, Marco Chiostrò¹, Gemma Lepe¹, Silvia Belfando Randone¹, Serena Guiducci¹, Sergio Castellani¹, Maria Boddi¹, Marco Matucci-Cerinic¹. ¹Careggi University Hospital, Firenze, Italy; ²Sapienza University of Rome, Roma, Italy

**Background:** RRI can be measured on renal artery Doppler ultrasound, showing the difficulty blood flows encounter distally from where it is measured. RRI can be determined by vascular and interstitial renal features: studies on the general population showed arterial hypertension, arteriosclerosis, low-grade inflammation, diabetes mellitus, hyperuricaemia as possible causes of renal vasculopathy or tubular-interstitial nephropathy, thus determining altered RRI values. Studies on SSc have shown increased RRI values, associated with nailfold-videoendoscopy pattern and history of digital ulcers.

**Objectives:** To identify determinants of RRI in SSc patients.

**Methods:** SSc patients fulfilling the 2013 ACR/EULAR criteria were enrolled from two SSc-care units. Data regarding SSc clinical manifestations, instrumental, and laboratory evaluation for renal, cardiac and cardiovascular involvement were collected. RRI was measured at least once in each patient. Linear regression analysis was carried out to determine predictors for baseline RRI and change in RRI in time (ΔRRI).

**Results:** 380 patients [aged 57 (46-68) years, 12% males] were enrolled in the study. On univariate analysis, both general population determinants (age, arterial hypertension, diabetes mellitus, hyper-lipidaemia, and hyper-uricaemia) and SSc specific features [time from Raynaud’s phenomenon onset, ACA positivity, scleroderma renal crisis history, estimated systolic pulmonary arterial pressure on Echo (sPAP), presence of dyspnea, %DLCO and presence of lower intestinal symptoms] predicted RRI values, with only age and sPAP being significant independent predictors at baseline. Follow-up RRI, available for 230 patients, showed that none of the general population determinants was predictive for ΔRRI.

**Conclusion:** Data show that among general population determinants, age is the only predictive factor for RRI in SSc patients. However, only age and sPAP were predictive for ΔRRI. Therefore, the use of specific age-adjusted cut-offs (table 1) are recommended when assessing SSc patients.

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CLINICAL FEATURES OF INTERSTITIAL LUNG DISEASE

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Background: Myositis-specific and myositis-associated autoantibodies (MSA and MAA) have been used for more detailed classification and prediction of clinical course of idiopathic inflammatory myopathies (IIM). Interstitial lung disease (ILD) is known to be complicated with approximately 50% of IIM patients, having poor prognosis.

Objective: The aim of this study is to investigate clinical features of ILD in Korean adult patients with IIM according to the autoantibody profile including MSA and MAA.

Methods: We conducted a multicenter cohort study including 108 adult patients (age≥18 years) who have been diagnosed as IIM by ENMC criteria MSA and MAA were screened with Immunoblot assay using Euroimmun antibody line strip (EUROIMMUN, Germany). Clinical information including the time of developing ILD and imaging findings of chest CT was reviewed using medical record.

Results: ILD was found in about half (52.8%, 57 of 108) of enrolled patients and closely associated with the presence of anti-ARS Abs, anti-MDAS and anti-Ro52. Among 43 patients, Anti-ARS Abs were most common (46.5%) and included anti-Jo-1 (23.3%), -OJ (2.3%), -EJ (9.3%), -PL7 (14%), and -PL12 (7%) (Figure 1). To analyze the correlation of autoantibodies with pattern of ILD onset, we stratified the 43 patients into three groups: into ILD-preceding (7/43, 16.3%) and myopathy-preceding group, 50% of patients (6/12) were UIP and a half of patients had pulmonary function which required treatment (DLCO<65%).

Conclusion: In our study, ILDs were accompanied by over half of the cases of IIM and most of them had autoantibodies. There are characteristic clinical features by onset time of ILD, so paying attention to them will help early diagnosis and prognosis prediction of ILDs.

REFERENCE


SOT0268 CLINICAL FEATURES OF INTERSTITIAL LUNG DISEASE ASSOCIATED WITH KOREAN IDIOPATHIC INFLAMMATORY MYOPATHIES ACCORDING TO THE AUTOANTIBODY PROFILE

Disclosure of Interests: Natasa Isailovic: None declared, Angela Ceribelli: None declared, Carolina Gorlino: None declared, Elena Generali: None declared, Giacomo Maria Guidelli: None declared, Piercarlo Sarzi-Puttini: None declared, Minoru Satoh: None declared, Carlo Selmi Grant/research support from: AbbVie, Janssen, MSD, Novartis, Pfizer, Consultant for: AbbVie, Sanofi-Genzyme, UCB, Speakers bureau: AbbVie, Alfa-Sigma, Biogen, Bristol-Myers Squibb, Celgene, Eli-Lilly, Janssen, Merck Sharp and Dohme, Novartis, Pfizer, Roche, Sanofi-Genzyme, UCB

Objective: To develop a comprehensive ICF core set for SSc and to conceive a patient-centered ICF-based questionnaire assessing activities and participation in patients with SSc.

Methods: The development of the ICF comprehensive core set followed 2 steps (2). In the first step, meaningful concepts related to SSc were collected using data source triangulation from patients (N=18), experts (N=10) and literature (N=174 articles). In the second step, concepts were linked to the best-matching ICF categories by 2 independent reviewers according to prespecified linking rules (3). Finally, patient-reported activities and participation categories of the comprehensive ICF core set were translated into understandable questions.

Results: After linking concepts to ICF codes, 151 ICF categories were collected from focus groups, 22 from experts and 82 from literature. After fusion of the sources and removal of duplicates, the comprehensive ICF core set included 165 categories: 1 at the first level, 158 at the second level, 6 at the third level, with 50 categories on body functions, 15 on body structures, 53 on activities and participation and 47 on environment and health.

Conclusion: We developed a comprehensive ICF core set that offers a conceptual framework for SSc patients’ care and health policy. Using a patient-centered approach, we conceived a patient-centered ICF-based questionnaire, the Cochin Scleroderma ICF-65 questionnaire, assessing activities and participation in patients with SSc.

Table 1. microangiopathy pattern and autoantibody positivity in ever smokers and never smokers in all SSc patients and in gender-based sub-cohorts. ATA: anti-topoisomerase I, ACA: anti-centromere, ARA: anti-RNA polymerase III, NVC: nailfold videocapillaroscopy.

<table>
<thead>
<tr>
<th>Microangiopathy</th>
<th>Autoantibodies</th>
<th>Male</th>
<th>Female</th>
<th>Ever smokers</th>
<th>Never smokers</th>
<th>ever smokers</th>
<th>never smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATA positive</td>
<td>11% (15/133)</td>
<td>17%</td>
<td>9%</td>
<td>8/21</td>
<td>3/15</td>
<td>2/12</td>
<td>6/13</td>
</tr>
<tr>
<td>ACA positive</td>
<td>27% (36/133)</td>
<td>34%</td>
<td>24%</td>
<td>10/21</td>
<td>9/15</td>
<td>8/12</td>
<td>8/13</td>
</tr>
<tr>
<td>ARA positive</td>
<td>12% (16/133)</td>
<td>14%</td>
<td>9%</td>
<td>3/21</td>
<td>3/15</td>
<td>2/12</td>
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</tr>
</tbody>
</table>

REFERENCES


RELATIONSHIP BETWEEN ANTI-MDA5 ANTIBODIES AND CANCER: RETROSPECTIVE ANALYSIS OF AN INTERNATIONAL AND MULTIDISCIPLINARY COHORT

Ludovico De Stefano1, Santos Castañeda2, Ellen De Langhe3, Jörg Distler4, Johannes Knitza5, Ilaria Cavazzana6,7, Alain Meyer7, Jorge Rojas-Serrano8, Eugenio Arigoni9, Federica Furini10, Marcello Govoni11, Paola Parrocchini11, Giovanni Zanframundo1, José Antonio P. da Silva12, Elisa Pedrollo13, Florenzo Iannone14, Carlomaurizio Montecucco1, Lorenzo Cavagna1.

Objectives: To describe the relationship between malignancy and anti-MDA5 antibodies in IIMs.

Methods: Patients with anti-MDA5+ IIMs and a history of cancer were included in this study. Data were retrospectively collected. Because of the lack of RP-ILD shared definitions, we defined RP-ILD as an admission to the Intensive Care Unit (ICU) for IIMs related respiratory insufficiency.

Results: In our cohort (n=133, 67% females) we identified 17 patients (13%) with a history of cancer (8 males [47%], 9 females [53%]; median age at IIMs onset 62 years [IQR 53-67], at cancer diagnosis 56 years [IQR 51-66]). All but 1 patient had solid tumours, 5 (29%) had breast cancer. The 13 surviving patients had a median rheumatological follow-up of 47 and 66 (infection after RP-ILD in ICU) months after cancer diagnosis. The 0.1136 annrheumdis-2019-eular.4565

Conclusion: This is the first study addressed to tackle the relationship between cancer and anti-MDA5+ IIMs. Although in some cases no clear relationship could be established, IIMs and cancer can be proved because of the time gap, in others the timing of occurrence of cancer and IIMs was very close, suggesting a link between these manifestations. Finally, we emphasize the importance of an accurate neoplasm screening in anti-MDA5+ RP-ILD, because treatment refractoriness could suggest the paraneoplastic nature of the manifestation.

REFERENCES


Disclosure of Interests: Ludovico De Stefano: None declared. Santos Castañeda Consultant for: Amgen, BMS, Pfizer, Lilly, MSD, Roche. Sanofi, UCB, Ellen De Langhe: None declared, Jörg Distler: None declared. Johannes Knitza: None declared, Ilaria Cavazzana: None declared, alain meyer: None declared, Jorge Rojas-Serrano: None declared. Eugenio Arigoni: None declared, Federica Furini: None declared, Marcello Govoni Paid instructor for: Pfizer, Roche, Speakers bureau: Pfizer, Abbvie, MSD, Roche, Eli-Lilly, Cellgene, Sanofi, Janssen, paola parrocchini: None declared, Giovanni Zanframundo: None declared, José Antonio P. da Silva: None declared, elisa pedrollo: None declared, Florenzo Iannone Consultant for: F Iannone has received consultancy fees and/or speaker honoraria from Pfizer, AbbVie, MSD, BMS, Novartis, Lilly. UCB outside this work. Speakers bureau: F Iannone has received consultancy fees and/or speaker honoraria from Pfizer, AbbVie, MSD, BMS, Novartis, Lilly. UCB outside this work. Carlomaurizio Montecucco Speakers bureau: AbbVie, Bristol-Myers Squibb, Cellgene, Sanofi, Genzyme, Lilly, MSD, Pfizer, UCB, Lorenzo Cavagna: None declared DOI: 10.1136/annrheumdis-2019-eular.4565

RITUXIMAB SIGNIFICANTLY DIMINISHES CD66+ B CELLS IN SYSTEMIC SCLEROSIS

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Background: Rituximab (RTX) is a monoclonal antibody that targets the CD20 surface marker. This results in a reduction of CD20+ immune cell populations, foremost B cells. B cell depletion via RTX was found to be beneficial for patients suffering from systemic sclerosis (SSc), leading to an improvement of skin fibrosis and autoimmunity (1). However, little is known about the influence of RTX on specific B subsets in SSc.

Objective: The purpose of this study was to further characterize the effect of RTX on B cell populations in patients with SSc.

Methods: Peripheral blood samples from 37 patients suffering from SSc (mean age: 54 ± 1.64 SEM, female ratio: 0.78) and 10 age-matched healthy participants were drawn over a sampling period of 2 years. 20 SSc patients in this study group were at the time under RTX treatment and the modified Rodnan Skin score (mRSS) was measured before and after treatment start. The percentage of CD19+ / CD20+ lymphatic cells and CD19+CD20+ B cells co-expressing either CD5, CD24, CD27 or CD86 on their surface was done by surface freshly isolated PBMCs. A quantitative flow cytometric bead-based assay (QuantiBRITE PE kit from Becton Dickinson) was used for the estimation of CD19 antibodies bound per cell. All cytometric measurements were performed using a standardized BD LSIRfortessa platform.

Results: RTX induced a significant decrease in mRSS from 19.7 ± 2.8 to 8.1 ± 1.7 (mean ± SEM; p<0.000). In addition, CD19+CD20+ cells were diminished as a result of the treatment. Thus, the frequency of CD19+CD20+ cells in the non-treatment group was 13% ± 0.3% compared to 0.7% ± 0.2% (p = 0.048). Within the B cell population 33.3% ± 3.6% were positive for CD26, a checkpoint molecule for the activation of T cells during an immune response. RTX treatment significantly decreased this B cell population to 11.2% ± 4.7% (p = 0.039). Quantification of the number of CD19 molecules on the surface of CD19+CD20+ B cells revealed a significantly lower number in SSc patients compared to healthy participants. The mean ± SE of molecules per cell was 6862 ± 625 and 7449 ± 569, respectively (p = 0.001).

Conclusion: RTX treatment in SSc might not only be effective by reducing B cells but also by down regulation of the CD86 B cell surface marker on B cells. This would indicate that B cells under RTX treatment are less capable of activating T cells.

REFERENCES

SAT0273 

PREDICTIVE VALUE OF THE REVISED EUROPEAN SCLERODERMA TRIALS AND RESEARCH GROUP ACTIVITY INDEX (EUSTAR-AI)

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1University of Campania; 2University of Bari; 3University Hospital Zurich, Rheumatology, Zurich, Switzerland

Background: Disease activity as measured by the European Scleroderma Study Group Activity Index (EScSG-AI) (1) has been recently found to predict the development of damage over time in an early systemic sclerosis (SSc) cohort (2). The European Scleroderma Trials and Research Group Task Force for the Development of Revised Activity Criteria for SSc recently succeeded in identifying a preliminarily revised activity index (EUSTAR-AI) that had a greater construct validity than the EScSG-AI i.e. performing better in identifying patients with active disease (3).

Objectives: To assess in patients with SSc the predictive value of the EUSTAR-AI for disease severity accrual.

Methods: SSc patients from the EUSTAR database with a disease duration from the onset of the first non-Raynaud sign/symptom to 5 years were first extracted. Patients were considered for the study if they presented the following features: a) availability of items included in the EUSTAR-AI, in the EScSG-AI and in the Medsger severity scale at baseline and yearly for 2 consecutive years; b) availability of vital status at the last observation; c) availability of other disease features known to predict disease progression (male sex, clinical and serological subset).

To capture the disease activity variations over time, we calculated the EUSTAR-AI and EScSG-AI adjusted mean (area under the curve over time). Disease progression was based on the Medsger severity scale and included accrual of a Δ≥1 summed severity score and of a Δ≥1 severity in each organ systems at the 2 year follow-up visit compared with the initial visit. To explore specific determinants of disease progression, logistic regression analysis was carried out.

Results: A total of 549 patients satisfied the entry criteria. Univariate logistic regression analysis (among sex, age, clinical and serological subset, EScSG-AI and EUSTAR-AI adjusted mean and baseline severity score), EScSG-AI adjusted mean (OR 1.41 95%CI 1.20-1.67), antinuclear antibody positivity (OR 1.72 95%CI 1.20-2.47), diffuse subcutaneous (OR 1.46 95%CI 1.01-2.10) and EUSTAR-AI adjusted mean (OR 1.41 95%CI 1.23-1.61) predicted disease severity accrual. Multivariate analysis revealed that the EUSTAR-AI adjusted mean was the best predictor of disease progression (Table1). Moreover, when logistic regression analysis the EUSTAR-AI adjusted mean also predicted severity accrual of lung (OR 1.32), heart (OR 1.40), skin (OR 1.48) and peripheral vascular disease (OR 1.45).

Conclusion: The adjusted mean EUSTAR-AI has a distinct predictive value for disease progression and development of severe organ involvement in SSc and works better than EScSG-AI.

REFERENCES


SAT0274 

THE EFFECT OF RITUXIMAB ON LUNG FUNCTION AND SKIN SCORE IN SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE. LONG-TERM OBSERVATION

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Background: There is a large clinical experience about the efficiency of rituximab (RTX) for the treatment of systemic sclerosis (SSc). There are several studies showing the decrease in skin induration and interstitial fibrosis in the lungs as the effect of therapy. However, there are not many long-term observations.

Objectives: To describe the efficacy of RTX on lung function and skin score in patients with systemic sclerosis-associated interstitial lung disease, in long-term follow-up.

Methods: This study included 71 patients (pts) with SSc. Data were collected prospectively. The mean follow-up period was 42 mo (12-72). Mean age was 46 years (17-66), female-59 (83%), diffuse cutaneous subset of the disease had 42 (59%), Scl-70 positivity-73% of pts. Duration of the disease was 5,6±4,4 yrs. All pts received concomitant treatment with low dose prednisolone and 45% - with immunosuppressants. The following indicators were evaluated: forced vital capacity,% predicted (FVC), diffusing capacity for carbon monoxide,% predicted (DLCO) and Rodnan skin score (mRss) over a periods of 12-18 months (point 1), 24-30 months (point 2), 36-42 months (point 3), 48-54 months (point 4) and 60-72 months (point 5) after the start of therapy. The results are presented in the form of mean values, delta, median, upper and lower quartile.
PERFORMANCE OF THE ANTISYNTHETASE

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Objectives: We performed an observational retrospective study in one center during the period 06/2008-06/2018. We searched all the myositis immunoblots (Euroimmun assay) requested by the Rheumatologists under suspicion of ASSD or myositis. We assessed: 1) the rate of cases with positive ARS; 2) the rate of cases with both positive ARS and swollen myositis. Results: 140 myositis immunoblots were searched. Twenty-seven cases (19.3%) presented positive ARS: anti-Jo1 (n=13), anti-PL-12 (n=7), anti-PL-7 (n=1), anti-EJ (n=2), and anti-OJ (n=4). Twenty-five of these cases (76.9%) fulfilled Connors’ criteria, and 15 (50.0%) additionally met Solomon’s criteria. Thus, the fulfillment of Connors’ and Solomon’s criteria in patients with a positive ARS was of 92.6% and 55.5%, respectively.

Conclusion: The presence of a cytoplasmic pattern was considerably higher in patients with ASSD than when only a nuclear pattern is presented. However, the presence of a cytoplasmic pattern does not exclude the detection of ARS in the myositis immunoblot and the fulfillment of Solomon’s criteria.

REFERENCES

Disclosure of Interests: None declared


SAT0275

PERFORMANCE OF THE ANTISYNTHETASE SYNDROMES AND THEIR INDIRECT IMMUNOFLUORESCENCE PATTERNS IN THE ANTISYNTHETASE SYNDROME DIAGNOSIS

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Background: The antisynthetase syndromes (ASSD) are characterized by the presence of anti-aminoacyl transfer RNA synthetase (ARS) autoantibodies, which disturb the binding of amino acids to the transfer RNA during the protein synthesis. ARS can be detected by indirect immunofluorescence (IIF), and can be identified by immunoblot assay and ELISA (Enzyme-Linked ImmunoSorbent Assay) and immunoblotting. The main clinical features of the ASSD are myositis, arthritis, interstitial lung disease, Raynaud’s phenomenon, mechanic hands, and fever. Two ASSD diagnosis criteria have been developed; those proposed by Connors, and the stricter criteria proposed by Solomon (1, 2). Objectives: To evaluate the performance of the ARS and their IIF patterns in the ASSD diagnosis.

Methods: We performed an observational retrospective study in one center during the period 06/2008-06/2018. We searched all the myositis immunoblots (Euroimmun assay) requested by the Rheumatologists under suspicion of ASSD or myositis. We assessed: 1) the rate of cases with positive ARS; 2) the rate of cases with both positive ARS and swollen myositis. Results: 140 myositis immunoblots were searched. Twenty-seven cases (19.3%) presented positive ARS: anti-Jo1 (n=13), anti-PL-12 (n=7), anti-PL-7 (n=1), anti-EJ (n=2), and anti-OJ (n=4). Twenty-five of these cases (76.9%) fulfilled Connors’ criteria, and 15 (50.0%) additionally met Solomon’s criteria. Thus, the fulfillment of Connors’ and Solomon’s criteria in patients with a positive ARS was of 92.6% and 55.5%, respectively.

All cases (100%) with positive ARS presented positive immunofluorescence: 19 (70.4%) showed a cytoplasmic pattern (10 of them with an associated nuclear pattern) and 8 cases (29.6%) presented only a nuclear pattern. On the other hand, 99 of the 113 cases (87.6%) with negative ARS presented positive IIF: 29 (25.7%) showed a cytoplasmic pattern (21 of them with an associated nuclear pattern) and 42 cases (37.2%) presented only a nuclear pattern.

Correlating the ARS positivity, IIF pattern and the diagnosis criteria fulfillment:

- 13 of 15 cases (86.6%) with positive ARS and Solomon’s criteria fulfilled a cytoplasmic pattern; and 2 of 15 cases (13.3%) presented only a nuclear pattern.
- 13 of 19 cases (68.4%) with positive ARS and cytoplasmic pattern fulfilled Solomon’s criteria; and 6 only fulfilled those from Connors’.

Conclusion: One-fifth of the immunoblots requested by Rheumatologists presented positive ARS; almost all these cases fulfilled Connors’ criteria, and more than a half fulfilled the stricter Solomon’s criteria. All patients with positive ARS, and a high rate of those without ARS, presented positive IIF. The presence of a cytoplasmic pattern was considerably higher in patients with ARS positivity and in those that met Solomon’s criteria. Thus, our results suggest that in patients evaluated by a Rheumatologist, with clinical suspicion of ASSD or myositis and with ARS positivity, the probability of fulfilling Solomon’s criteria is higher when the IIF presents a cytoplastic pattern than when only a nuclear pattern is observed. Nevertheless, presenting only a nuclear pattern does not exclude the detection of ARS in the myositis immunoblot and the fulfillment of Solomon’s criteria.

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SAT0276

STUDY OF THE EPIDEMIOLOGICAL, CLINICAL AND ANALYTICAL CHARACTERISTICS IN PATIENTS WITH SYSTEMIC SCLEROSIS AND CANCER IN VALL D’HEBRON HOSPITAL

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Background: Scleroderma or systemic sclerosis (SSc) is a systemic, chronic autoimmune disease characterized by a great clinical heterogeneity. In recent years, studies have proven that there is a relationship between SSc and neoplasia. SSc is associated with an increased risk of certain types of cancer, particularly lung, liver, hematological, non-melanoma skin and urothelial cancer. Despite this increase, the relative risk of developing cancer is still low in these patients. In the literature, neoplasms have been described in 3-11% of patients with SSc.

Objectives: Our objective is to analyze the epidemiological, clinical and analytical characteristics previously described as possibly linked to the development of a cancer in patients with systemic sclerosis (SSc) in the Vall d’Hebron Hospital cohort.

Methods: We analyzed 583 patients in the Vall d’Hebron Hospital cohort of SSc. The inclusion criteria were age > 18 years and the diagnosis of SSc limited, diffuse and SSc sine scleroderma. The different variables were analyzed by univariate statistical analysis with SPSS v21.
THE 100 MOST INFLUENTIAL PUBLICATIONS IN STUDY OF QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC SCLEROSIS: A BIBLIOMETRIC STUDY

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Background: In recent years, a large volume of important clinical and scientific papers about systemic sclerosis can be found in the most influential journals. Bibliometric analysis is a statistical method that enables researchers to analyze citation patterns and highlight characteristics of highly cited scholarly work. It has been infrequently utilized in Rheumatology1,2. Prior studies have not addressed the bibliometric literature gap in the field of systemic sclerosis. Objectives: This study aims to identify the 100 most cited papers in systemic sclerosis and to describe their characteristics. Methods: We sought to assess the characteristics of the top 100 most referenced citations in systemic sclerosis. We searched the Scopus and Web of Science databases to identify all articles relating to ‘Scleroderma’, ‘limited’ or ‘diffuse Systemic Sclerosis’ and ‘CREST syndrome’. Articles were arranged in descending order of citations and were scrutinized by two independent reviewers. Selected articles were analyzed with respect to number of citations, publication year, journal characteristics, research type, focus area, authors and countries of authors of publications. Results: Retrieved articles were published mostly in rheumatology journals (n=42) with impact factors ranging between 3.47 and 12.35 in these journals, followed by journals in general medicine, pulmonology, and experimental biomedical research. Journals with the highest number of top-cited articles included Arthritis and Rheumatism (n=25), followed by the New England Journal of Medicine (n=8) and Annals of the Rheumatic Diseases (n=6). Studies conducted in USA, UK, and Italy that were published in high-impact journals had the highest citation count. Temporal analysis indicated that the majority of top-cited articles were published between 1996 and 2014 (n=65). The most productive 5-year time period was between 2000 and 2005 when 23 of the 100 most cited publications were produced. Among retrieved citations, guidelines and recommendations comprised 5% of all articles, narrative reviews 21%, randomized clinical trials 12%, observational studies 35%, non-randomized clinical studies (basic and translational research) 24%, case series 1%, and meta-analyses 2%. Our analysis shows that articles defining the classification criteria of Systemic Sclerosis were among the most cited work followed by those describing the pathophysiology of the disease. Other highly cited areas included cellular and molecular mechanisms of fibrosis (with special emphasis on the role of TGF-β) and Randomized Controlled Trials for Bosentan and Epoprostenol in the treatment of pulmonary hypertension. Regarding individual organ manifestations, Pulmonary and Cardiac complications (pulmonary hypertension, lung disease, myocardial effects) (n=21) were of highest interest, while other articles focusing on Cutaneous (ulcers, skin changes, Raynaud’s phenomenon) (n=16), Renal (renal crises) (n=3) and Gastrointestinal complications (dysmotility) (n=1) were cited to a lesser extent. Interestingly, articles primarily describing hematopoietic stem cell transplants as a viable treatment option did not feature on this list. Conclusion: Our study provides the first bibliometric overview of the most highly cited scientific papers on systemic sclerosis. These findings provide useful insights into trends of published work and may serve as a useful guide to researchers in this field.

REFERENCES


Disclosure of Interests: None declared
To find out the contributing factors to impaired QoL, with the help of a newly developed patient reported questionnaire.

Methods: In this cross-sectional study, all consecutive adult patients with SSc, satisfying 2013 ACR/EULAR classification criteria, attending a tertiary rheumatology clinic in Western India from January 2016 to March 2017 were compared to age and sex-matched controls. A new questionnaire [Indian Systemic Sclerosis QoL questionnaire (Indian SyS-QoL)] was developed to identify the contributing factors to impaired QoL with feedback from 15 SSc patients and 11 rheumatologists. This questionnaire had 10 factors and each was scored by individual patients between 0-3 (0-no impact; 3-severe impact on QoL in previous month). Demographic data, clinical profile and relevant investigations were recorded. Patients filled Medical Outcomes Trust Short Form 36 version 2 (SF-36v2) questionnaire, Indian SyS-QoL questionnaire and Indian Health Assessment Questionnaire – (Indian QAQ).

Results: 94 SSc patients (7 males; 87 females) were compared to 100 age and sex-matched controls. QoL was significantly impaired in patients with SSc compared to healthy controls in all 8 domains of SF-36 (p<0.001), the finding similar to other studies (Table 1). There was no statistically significant difference in mean scores in any domain between patients with dcSSc [56 patients (59.6%) and lcSSc [38 patients (40.4%)]; between patients with disease duration ≤5 yrs [43 patients (45.7%)] and >5 years [51 patients (54.3%)] and in those with ILD [56 patients (59.6%)] and without ILD [38 patients (40.4%)]. Two most important factors responsible for poor QoL based on Indian SyS-QoL questionnaire score (mean±SD) were feeling of dependency on family (1.4±1.3) and ‘cost of treatment’(1.3±1.2)(Fig 1).

Table 1: SF-36 Scores in SSc patients among different studies:

<table>
<thead>
<tr>
<th>Present study</th>
<th>Frantz et al</th>
<th>Georges et al</th>
<th>Daniel et al</th>
<th>Cossetta et al</th>
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<tr>
<td>N</td>
<td>94</td>
<td>1902</td>
<td>89</td>
<td>76</td>
</tr>
<tr>
<td>SF-36v2</td>
<td>mean±SD</td>
<td>mean±SD</td>
<td>mean±SD</td>
<td>median±SD</td>
</tr>
<tr>
<td>Domain</td>
<td>(Range)</td>
<td>(Range)</td>
<td>(Range)</td>
<td>(Range)</td>
</tr>
<tr>
<td>Physical function</td>
<td>55.2±25.4</td>
<td>52.7±28.3</td>
<td>50±31</td>
<td>57.5 (35-80)</td>
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<tr>
<td>Mental health</td>
<td>55.7±23</td>
<td>61.0±23.5</td>
<td>-</td>
<td>56 (36-68)</td>
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<tr>
<td>Social function</td>
<td>60.5±33.9</td>
<td>58±26.2</td>
<td>58±28</td>
<td>87.5 (56-66)</td>
</tr>
<tr>
<td>Pain</td>
<td>58.4±31.2</td>
<td>50.8±25.5</td>
<td>47±28</td>
<td>61 (41-76.5)</td>
</tr>
<tr>
<td>General health</td>
<td>45.7±22.9</td>
<td>36.1±22.0</td>
<td>39±22</td>
<td>50 (35-60)</td>
</tr>
</tbody>
</table>

Discussion: This maiden study from India showed that QoL was significantly affected in patients with SSc compared to the general population; but there was no significant difference in QoL in patients with different subsets of SSc; disease duration ≤ 5 yrs and > 5 yrs, and presence or absence of ILD. The new graded scale devised to assess the impact of SSc on QoL using a simple patient-reported questionnaire showed ‘feeling of dependency’ and ‘cost of treatment’ as the 2 most important factors affecting QoL in Indian patients with SSc. This would help direct more resources to support the patients both mentally and financially.

REFERENCES


Disclosure of Interests: None declared


SAT0279

MULTICENTER DOUBLE-BLIND, PROOF-OF-CONCEPT, RANDOMIZED PLACEO-CONTROLLED TRIAL OF RIOCIUGAT IN SYSTEMIC SCLEROSIS-ASSOCIATED DIGITAL ULCERS (RESCUE)

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Background: The soluble guanylate cyclase stimulator riociguat (RIO) is a vasodilator and has antifibrotic effects in animal models and efficacy in patients with pulmonary arterial hypertension associated with connective tissue diseases.

Objectives: We present results from a randomized placebo-controlled trial (NCT02915835), which evaluated the efficacy and safety of RIO in patients with systemic sclerosis-associated digital ulcers (SSc-DU).

Methods: Eligible subjects (with active or painful indeterminate DU) were randomized in 1:1 ratio to either placebo (PLA, n = 8) or RIO (n = 9) in individualized doses (maximum of 2.5 mg three time daily) during an 8-week titration period, followed by an 8-week stable dosing period. PDE5 inhibitors were not allowed. The primary end point was the change from baseline to week 16 in net ulcer burden (NUB), analyzed using an ANCOVA model, accounting for baseline NUB. Other outcome measures included change from baseline to week 16 in the Raynaud’s Condition Score (RCS), RP attack number, symptom severity during RP attack, patient global assessment, and proportion of subjects with treatment-emergent adverse events (AEs). Eleven plasma biomarkers were measured by ELISA and changes were tested using ANCOVA, after testing for normality.

Results: We randomized 17 participants with SSc-DUs between January 2017 and March 2018. Baseline characteristics were comparable between treatment groups, except participants randomized to PLA were older (mean 61 vs. 43 yrs) and had longer disease duration (mean 17.5 vs. 7.1 yrs). At baseline, the mean (SD) NUB was 2.5 (2.0) in the PLA and 2.4 (1.4) in the RIO. No significant difference was observed between RIO and PLA in change from baseline to 16 weeks in NUB [p=0.70; Table]. No significant treatment effect was observed in the secondary outcome measures. All 17 participants reported ≥1 adverse event, with the vast majority being mild or moderate. There were 4 SAEs, 3 in RIO (worsening DU, NSTEMI, and non-Hodgkin’s lymphoma) and 1 in PLA (digital ischemia; none of SAEs were related to the study medication). Statistically significant elevation of cGMP was observed at 16 weeks [p<0.05]; no other biomarkers showed statistically significant changes.

Conclusion: In participants with SSc-DU, treatment with RIO did not reduce the number of NUB compared with PLA. The safety profile of RIO was similar to that previously reported. There is evidence of target engagement. The negative results may reflect small number of patients, low number of NUB at baseline, moderate-to-severe vasculopathy with long-term disease, and difficulty to recruit patients in the era of widespread use of PDE5 inhibitors.

Acknowledgement: The trial was funded by Bayer, Inc as an investigator-initiated trial to the University of Michigan.

Disclosure of Interests: Dinesh Khanna Shareholder of: Elios Sciences, Inc, Grant/research support from: Bayer, BMS, Pfizer, Horizon, Consultant for: Actelion Acceleron, Arena, Bayer, BI, BMS, CSL Behring, Corbus,

<table>
<thead>
<tr>
<th>Placebo</th>
<th>Riociguat</th>
<th>Treatment Difference (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Net Ulcer Burden, mean±SD</td>
<td>-0.98</td>
<td>-1.22</td>
<td>-0.24</td>
</tr>
<tr>
<td>Severity of RP (0-10)</td>
<td>-1.41</td>
<td>-3.47</td>
<td>-2.06</td>
</tr>
<tr>
<td>Severity of DU (0-10)</td>
<td>-4.00</td>
<td>-4.63</td>
<td>-0.63</td>
</tr>
<tr>
<td>Pain during RP attack (0-10)</td>
<td>-7.01</td>
<td>-0.30</td>
<td>6.71</td>
</tr>
<tr>
<td>Numberness during RP attack, mean (SD) (0-10)</td>
<td>-15.44</td>
<td>-19.73</td>
<td>-4.28</td>
</tr>
<tr>
<td>Tinting during RP attack, mean (SD) (0-10)</td>
<td>-7.49</td>
<td>1.18</td>
<td>8.67</td>
</tr>
<tr>
<td>Raynaud’s Condition Score, mean (SD) (0-10)</td>
<td>-0.82</td>
<td>-1.15</td>
<td>-0.33</td>
</tr>
<tr>
<td>Number of Raynaud’s attacks per day, mean</td>
<td>-0.96</td>
<td>-1.24</td>
<td>-0.28</td>
</tr>
</tbody>
</table>

Plasma Biomarkers, mean±SD (nM):

- cGMP: 41.2±198.5
- cGMP: 157.3±311.5
- A higher number denotes worse symptoms

*Disclosure of Interests: None declared


SAT0280 ESOPHAGEAL DYSMOTILITY AND PULMONARY DISEASE IN PATIENTS WITH SCLERODERMA: A RETROSPECTIVE STUDY

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Background: Systemic sclerosis (SSc) is a connective tissue disease with pulmonary involvement seen in 75% of patients and esophageal involvement in 90% of the patients. Pulmonary disease has overtaken renal disease as the leading cause of death (1). There is conflicting evidence about the association between esophageal dysmotility and lung involvement (Interstitial Lung Disease (ILD) and Pulmonary Artery Hypertension (PAH)).

Objectives: Our aim was to evaluate the relationship between esophageal dysmotility and lung disease by correlating the results of Echocardiogram and Pulmonary Function Test (PFT) with Esophageal Transit Study (ETS).

Methods: Charts of SSc patients fulfilling 2013 ACR/EULAR classification criteria seen in Rheumatology clinic from 2004 to 2015 were reviewed. Patient demographics, ETT result, FVC and DLCO data from PFT as well as pulmonary pressures from echocardiogram were collected at baseline, years 1, 3, 5 and 10. Patients were divided based on their initial ETT findings into normal and abnormal ETT groups. Using logistic regression models, we compared elevated PASP with ETT status at baseline, and years 3 and 5. Linear mixed effects model was used to adjust for covariates (disease subtype, smoking, obesity, use of immunomodulator) when analyzing PFT outcome with time period and ETT status.

Results: 130 patients were identified with either Limited Cutaneous SSc (109) or Diffuse Cutaneous SSc (21) with a mean age of 52.65 years ± 12.59. ETT was normal in 67(52%) and abnormal in 63(48%) patients. Number of patients with abnormal PASP was not statistically different between the two groups (p values 0.104, 0.178, 0.653 at baseline, years 3 and 5 respectively). Likewise, the odds ratio for abnormal PASP was 2.75 in patients with abnormal ETT compared to normal ETT, but the results were not statistically significant (p: 0.428), and the odds ratio did not vary with time (p: 0.731). Sample size was too small to conduct separate longitudinal analysis for adjusted models. The mean DLCo was statistically worse in abnormal ETT patients [p value <0.0001 and 0.0004 for unadjusted and adjusted models] as were the progression rates per year for DLCo at -1.95 (p-value: 0.023) and -2.25 (p-value: 0.019) for unadjusted and adjusted models respectively. The Mean FVC was not statistically different between the two groups, although it’s progression rate per year was statistically worse only in the adjusted model (p value: 0.018).

Conclusion: Esophageal dysmotility was associated with increased pulmonary involvement in the form of abnormal DLCo with worsening progression rates per year. Interestingly, neither PASP nor FVC were statistically different even though progression rate for FVC was worse in adjusted models. We postulate that the small sample size for Echo and differences in the factors determining DLCo vs. FVC and PASP explains the disparity in the results. Larger prospective trials are needed to investigate if there is a causal relationship between esophageal dysfunction and pulmonary involvement.

REFERENCE


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SAT0281 RELATIONSHIP BETWEEN AUTOANTIBODIES AND CYTOKINE PROFILES IN PATIENTS WITH MYOSITIS

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Background: By(auto)antibodies, myositis is recently classified into subgroups with distinctive clinical features. Cytokines play critical roles in the development of the clinical features. However, it is not fully unknown whether myositis subgroups defined by autoantibodies have unique cytokine profiles.

Objectives: To clarify the relationship between cytokine profiles and autoantibodies in myositis.

Methods: Subjects were myositis patients who admitted Dokyo Medical University and whose serum before starting therapy were available. Serum cytokine levels (IL-1α, 1b, 2, 4, 5, 6, 10, 12, 13, 15, 17, 23, IFN-g, TNF-a, IFN-a, b, IP-10 and MCP-1) in sera from the patients and controls were measured using Q-Plex™ Mplex Arrays. Demographic and clinical data were obtained by reviewing medical record retrospectively.

Results: Subjects were 45 myositis patients with male/female: 22/23 and age 36.1±12.5 years. ETT was normal in 67(52%) and abnormal in 63(48%) patients. Antibodies were anti-MDA5+ in 21, anti-ARS+ in18 and anti-TIF1g+ in 5 cases. ILD and malignancy was complicated in 39 and 5 cases, respectively. Serum cytokine levels were measured. As shown in Fig.1, IP-10 levels were increased in all types of myositis patients, but not in controls. In anti-MDA5 Ab+ myositis, IL-6, IL-10, IL-15, TNF-a, IFN-a and MCP-1 levels were increased. In anti-ARS Ab+ cases, IFN-b levels were elevated as well as TNF-a and MCP-1. Through the correlation analysis between cytokine levels, cytokine groups were identified (Fig.2). In anti-MDA5 Ab+ cases, 2 cytokine groups were identified: one includes IFN-a, IL-15, TNF-a and IL-10, and the other involved IL-6, MCP-1. Both groups connected with IP-10. In In anti-ARS

Figure 1. Serum cytokine levels in myositis

Figure 2. Cytokine networks in a-ARS ab+ and a-MDA5 ab+ myositis

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SA10283

CLINICAL AND SEROLOGICAL FEATURES OF SYSTEMIC SCLEROSIS IN ITALIAN AND EGYPTIAN PATIENTS

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Background: Clinical and serological variations exist in the severity of Systemic Sclerosis (SSc) patients, according to different geographic areas.

Objectives: To evaluate clinical and serological features in 2 cohorts of Italian and Egyptian SSc patients and to identify factors associated with Interstitial lung disease (ILD), a leading cause of mortality, by using multivariate logistic regression analysis.

Methods: An Italian center and 3 Egyptian centers participated in SSc patient recruitment in 2017. The cross-sectional demographic, clinical, and laboratory data were collected and defined according to severity score and activity index, previously developed [1, 2]. The database included 152 consecutive Italian patients, 135 women (88.8%) and 17 men (11.2%) and 197 consecutive Egyptian SSc patients, 177 women (89.8%) and 20 men (10.2%), all of whom fulfilled the classification criteria proposed by LeRoy and Medsger [3].

Results: We found that Egyptians SSc patients were younger (41.18±12.5 vs 58.59±12.6 yrs), had an earlier onset of the first non Raynaud’s Phenomenon symptom (7.28±5.69 vs 14.99±11.11) and a more severe Modified Rodnan Skin Score (MRSS=14) (79.27% vs 13.6%). A greater percentage of Egyptian patients presented the active form of the disease (33.3% vs 15.5%) and had a Pulmonary Arterial Pressure (PAPs) estimated by echocardiography ≥40mmHg (37.5% vs 9.5%) in the Italian patients. Furthermore, Egyptian patients affected from the limited form of the disease (lcSSc), presented a higher MRSS (67.2% vs 2.6%), higher PAPs levels (34.5% vs 9.2%), an active form (41.7% vs 7.8%) and history of past/current ulcers (62.2% vs 30.6%) than Italian lcSSc patients.

Conclusions: Clinical and serological comparisons between Italian and Egyptian patients, point to different factors associated with ILD, which should be further investigated.

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CD123+ PLASMACYTOID DENDRITIC CELLS (pDCs) FROM SYSTEMIC SCLEROSIS PATIENTS ARE SUSCEPTIBLE TO THE CYTOTOXIC ACTIVITY OF TAGRAXOFUSP, A CD123-TARGETED THERAPY

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Background: Tagraxofusp is a novel targeted therapy directed to the interleukin-3 receptor (CD123). Tagraxofusp is comprised of human IL-3 recombinantly fused to a truncated diphtheria toxin (DT) payload engineered such that IL-3 replaces the native DT receptor-binding domain. In this way, the IL-3 domain of tagraxofusp directs the cytotoxic DT payload to cells expressing CD123. Upon internalization, tagraxofusp irreversibly inhibits protein synthesis and induces apoptosis of the target cell.

Tagraxofusp was recently approved by the FDA for the treatment of patients with blastic plasmacytoid dendritic cell neoplasm (BPDCN), a malignancy derived from the plasmacytoid dendritic cell (pDC) precursor. pDCs are immune cells that express CD123, secrete IFN-α, and play a role in inflammation and disease pathogenesis observed in systemic sclerosis (SSc) patients.

Objectives: To assess the ability of tagraxofusp to selectively deplete pDCs from SSc patients ex vivo.

Methods: Patients fulfilled the 2013 ACR/EULAR classification criteria for SSc4. PBMCs from either SSc patients or healthy volunteers (HV) were prepared using Ficol-Paque density gradient from fresh blood. pDCs were isolated from PBMCs as previously described and used to enrich the frequency of pDCs in an additional draw of PBMCs. pDC-enriched PBMCs (3-16% pDCs) were cultured at 2x10^4 cells per well in the presence of absence of CpG-274 (0.5 μM) to activate pDCs and then incubated with tagraxofusp (0.01-100 ng/ml, 0.17 pM-1.7 nM) at 37°C, 5% CO2, and 95% humidity. After 24 h of culture, pDC survival was assessed by flow cytometry (CD14, CD3, BDCA4, CD123+), and supernatants were collected for cytokine quantification by a multiplexed Luminex assay.

Results: Tagraxofusp was cytotoxic towards pDCs from both HV (n=5) and SSc donors (n=5) to a similar extent. The ED50 of tagraxofusp in pDCs from HV and SSc was 4.3 and 3.2 ng/ml (74.4 and 55.4 pM), respectively; no effect was observed on B or T cells across the tagraxofusp dose range tested (Fig.1A). Tagraxofusp-mediated pDC depletion was further accompanied by a 68-fold reduction in secreted IFN-α and a 3-fold downregulation of GBP, a type 1 IFN-induced gene (Fig.1B).

Conclusion: Tagraxofusp is a novel CD123-targeted therapy that is cytotoxic towards pDCs from SSc patients. These data present a novel approach of targeting pDCs in the treatment of SSc, and a clinical trial is under design.

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Evaluation of Chronic Pain in Patients with Systemic Sclerosis Compared to Those with Chronic Headache and Rheumatoid Arthritis

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Background: Systemic Sclerosis (SSc) is a chronic systemic disease frequently leading to disability and low quality of life. Chronic pain (CP), due to severe disease complications and internal organs involvement, is often underestimated. Based on available data around a 60-70% of patient with SSc suffer of chronic pain but we still lacking of fire tools to better evaluate it and follow up patients.

Objectives: Evaluate pain in SSc patients, in terms of its intensity, sensory and affective components, the interference with physical and social activities, impact on quality of life and correlation with main SSc clinical manifestations.

Methods: From January 2013 to January 2018 we retrospectively evaluated 98 patients with a diagnosis of SSc [F/M=47/11; Limited/Diffuse SSc 63/35 anti-Scl70/ACA/ANA nuclear positivity 45/39/14; mean age 55.6 ± 12.6 DS; mean disease duration 9.9 ± 7.6 DS] according to 2013 ACR/EULAR criteria: 47 patients with a diagnosis of chronic headache (CH) as defined by the International Classification for Headache Disorders, Third Edition beta version (ICHD-3 beta) criteria [F/M=37/10; mean age 52.6 ± 14.2 DS; mean disease duration: 7 ± 2 yrs DS] and 46 patients with Rheumatoid Arthritis [F/M=36/10; mean age 41±13, mean disease duration 10±2 yrs, DS]. All patients fulfilled self-completing questionnaires for the evaluation of pain and quality of life: Visual Analogic Scale (VAS), Generic Rating Scale (NRS), Short Form-McGill Pain Questionnaire (SF-MPQ), Brief Pain Inventory Score (BPI) e Health Assessment Questionnaire (HAQ).

Results: SSC patients started to suffer of CP in younger ages compared to AR/CH cohort but patients suffering of CH have higher mean scores in all questionnaires compared to AR/SSc. CH patients, have higher mean score in SFMPQ-sensory and affectory. Hundred percent (100%) of AR patients suffered of chronic pain. They, generally, had higher scores than SSc patients with a prevalence of the affectory component. The 83.9% (67/79 pts) of SSc patients experienced chronic pain [SF-MPQ PRI: 6.2±5.8;SF-MPO PPI: 1.69±1.34DS; BPI-factor1: 13.37 ±1.28DS; VAS: 40.7±29.6DS; NRS: 4.08±2.98DS] and in a great majority (84%) that pain interfered with their working activities and social lifes. Fortyeight percent of SSC patients had digital ulcers and 41.3% had musculoskeletal involvement. Pain used to correlate with both of them [p>0.004; p=0.041]. In patients with DUs, affectory component of pain overruled on the sensory one.

Conclusion: SSC patients frequently experience chronic pain and particularly those who have a history of active DUs and musculoskeletal involvement. By the way, it seems that the BPI questionnaire could be more suitable than VAS or NRS in assessing DUs involvement. By the way, it seems that the BPI questionnaire could be more suitable than VAS or NRS in assessing DUs involvement. In fact, FESS could help the identification of different problems leading to dysphagia occurrence and to related dysphagia problems. Thanks to these characteristics, FESS for ENT specialists is the gold standard technique for evaluating swallowing functions. However, no studies so far have investigated the role of FESS in the assessment of IIMs and we are completely lacking a semiotic description of FESS findings in these patients.

Objectives: To provide the first semiotic description of swallowing alterations in patients with idiopathic inflammatory myopathies.

METHODS: We retrospectively reviewed the FEES findings of IIMs patients performed at our hospital.

Results: We enrolled 19 patients with a diagnosis of IIMs (10 patients were positive for a myositis specific antibody), of these 16 (84%) reported symptomatic dysphagia. We divided patients into 3 groups based on levels of peripheral muscle strength. Six patients (32%) had no clinical sign of active muscle disease (MRC scale 4, median CK 51 mU/ml, IQR 35-235), 5 patients (26%) had a mild reduction in muscle strength (MRC scale 3, median CK 150 mU/ml, IQR 62-618). The 67% of patients without muscle disease activity showed an impairment in the oral phase of swallowing for solids and fluids; 40% showed signs of penetration, aspiration or pharyngeal phase of swallowing for both solids and fluids; 40% of patients showed signs of penetration, aspiration or pharyngeal residue for both solids and fluids. In the group of patients with moderate muscle activity, 80% of patients showed impairment in the oral phase of swallowing for solids and 40% for fluids; 60% had a reduction in the activation of the pharyngeal phase of swallowing for solids while 40% for fluids; 40% of patients showed signs of penetration, aspiration or pharyngeal residue for both solids and fluids. Finally, in the group of patients with severe muscle disease activity, 88% of patients showed an impairment in the oral phase of swallowing for solids and 50% for fluids; 63% had a reduction in the activation of the pharyngeal phase of swallowing for solids while 50% for fluids; 75% of patients showed signs of penetration, aspiration or pharyngeal residue for both solids and fluids. The 15% of all patients (3 cases, 1 from each group of muscle activity) showed a dysfunction in the upper esophageal sphincter. Of note, 3 patients (15%; 1 with moderate and 2 with severe muscle disease activity) required nutrition through nasogastric tube.

Figure 1: swallowing alteration for solids and fluids in patients divided by muscle disease activity regarding muscle disease activity (green), moderate muscle disease activity (blue) and severe muscle disease activity (red).

Conclusion: We showed that FESS study identified swallowing dysfunctions in both the oral and pharyngeal phases of swallowing. Swallowing dysfunctions were more prevalent in patients with greater muscle involvement; however, alterations were not rare also in patients with no clinical signs of muscle activity and, in particular, in the few patients without reported symptoms of dysphagia. FESS appears as a useful tool for the evaluation of dysphagia in IIMs.
outcome of PM/DM-ILD. High levels of serum IL-6, IL-8, IL-10, IL-18, CCL2, CXCL10, TNF-α, and IFN-α were detected in PM/DM-ILD cases, suggesting the pathological involvement of activated macrophages, type 1 T helper (Th1) cells, and neutrophils (ref 1, 2). However, investigation of the pathomechanism using serum cytokines remains insufficient in PM/DM-ILD. We hypothesised that multiple inflammatory cytokine pathways related to the above inflammatory cells would be involved in the pathomechanism of PM/DM-ILD.

Objectives: We measured serum cytokine levels before and during treatment of patients with PM/DM-ILD and examined the associated pathomechanism.

Methods: Serum cytokines were collected from 40 PM/DM-ILD patients. Principal components analysis (PCA) and cluster analysis were used to classify patients into subgroups. We compared cytokine profile of the survivors and dead patients as well as anti-MDAS antibody-associated ILD and anti-ARS antibody-associated ILD. We also examined the association of various cytokines with disease activity indicators and prognosis of ILD.

Results: PCA revealed that the diversity of cytokines was driven by three groups: (1) neutrophilic and M1-macrophage-driven cytokines, (2) Th1 cell-driven and M2-macrophage-induced cytokines, and (3) M2-macrophage-driven cytokine. Based on cluster analysis, patients were classified into two subgroups according to the cytokine levels of all groups (Figure A). Ninety percent of patients who died of ILD were included in clusters with high cytokine levels (Figure B). Serum cytokine levels of all groups were significantly higher in the anti-MDAS antibody-positive patients than in the anti-ARS antibody-positive patients. Factors of poor prognosis in PM/DM-ILD correlated significantly with serum cytokine levels of groups 1 and 2. Among the 3 groups, serum cytokine levels of group 1 were significantly higher initially and at 2 and 4 weeks in the death group.

Conclusion: These findings suggest that the activation of monocytes, macrophages, and Th1 cells, and neutrophils plays a role in the pathomechanism. Group 1 cytokines could be efficient biomarkers for predicting prognosis of PM/DM-ILD.

Disclosure of Interests: None declared


A SYSTEMATIC REVIEW OF SYSTEMIC SCLEROSIS CLINICAL TRIALS SINCE 2005. LACK OF EARLY DISEASE TARGETING, CONFUSION RELATED TO DISEASE DURATION DEFINITION AND LOW LEVEL OF INCORPORATION OF THE NEW CLASSIFICATION CRITERIA

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Background: It is still unknown whether treatment in very early systemic sclerosis (SSc) can affect long term outcomes. 

Objectives: To systematically review clinical trials in SSc during the last 14 years aiming at answering the following questions: 1) how many clinical trials in SSc have targeted early disease and whether treatment of patients with early disease leads to better clinical outcomes, 2) how is disease duration defined in SSc clinical trials and whether data on duration since Raynaud’s onset are provided and 3) whether the new 2013 ACR/EULAR SSc criteria have been incorporated in clinical trials throughout the last 5 years.

Methods: A search in published studies indexed in MEDLINE was performed from Jan-2005 to Dec-2018. The Clinical Trial filter was activated and the terms “systemic sclerosis treatment” used. Studies were included if they evaluated adult patients with systemic sclerosis, concerned systemic treatments, presented data for clinical endpoints assessing fibrosis and were prospective in design.

Results: Seventy-three studies with a total number of 3078 patients met the inclusion criteria and were subjected to data extraction. The total weighted mean disease duration (adjusted to the number of patients in each study) was 38.55 months which is more than 3 years, the usual threshold for defining early disease. Baseline total weighted mean mRSS was 21.54 indicating that most patients had full blown fibrotic disease. Only 24 studies (32.9%) recruited early (<36 months disease duration) cohorts, with only 4 studies among them concerning very early disease (<18 months disease duration). We next focused on studies that did not specifically target early disease (n=49) and explored whether disease duration associated with clinical outcomes. We identified such an analysis only in 13 studies. In 8/13 studies there was no difference regarding outcomes according to disease duration. Nevertheless, in 4/13 studies investigators reported better outcomes in patients with shorter disease duration with only one study showing the opposite. Significant heterogeneity was found regarding disease duration definition. Four separate definitions were identified: 1) “From first non-Raynaud’s symptom” (49.3%), 2) “From disease diagnosis” (11%), 3) “From skin thickening onset” (5.5%), 4) “From first symptom” (11%). The remaining studies (23.3%) presented no clear definition in their manuscript for disease duration in their cohorts. The stratification of the studies according to year of publication showed a tendency for greater consistency regarding the definition used in recent years since most studies published from 2015 and onwards use the definition “From first non-Raynaud’s symptom”. Data regarding the duration since Raynaud’s onset were available only in 9 studies (12.3%). A separate analysis of all articles published from 2014 until 2018 was performed to explore the incorporation of the new 2013 ACR/EULAR criteria. Only 6 studies (25%) incorporating the new criteria were identified.

Conclusion: 1) The majority of patients recruited in clinical trials throughout the last 14 years do not have early disease, 2) Only one third of the studies were specifically designed to target early disease, 3) The question of whether early implementation of therapy may lead to better clinical outcomes cannot be definitely answered based on existing data, 4) there is confusion related to disease duration definition across SSc clinical trials but an obvious trend towards improvement was evident throughout the last few years and 5) there is still a very low level of incorporation of the new classification criteria in SSc trials.

Disclosure of Interests: None declared


THE ROLE OF CAPILLAROSCOPY IN THE EARLY DIAGNOSIS OF SYSTEMIC SCLEROSIS

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Background: Systemic Sclerosis is a multisystem autoimmune disease characterized by fibrosis of the skin and internal organs and vascular damage. The diagnosis is usually made in the late stages, when irreversible damage has already occurred. Recently, we have established new criteria to detect early cases of the disease. Performing capillaroscopy and its findings are crucial in the diagnosis of early systemic Sclerosis or “prescleroderma” and there may be changes seen in capillaries of patients without skin manifestations.

Objectives: To analyze the nailfold capillaroscopy findings in patients with anti-centromere or anti-topoisomerase antibodies and evaluate their usefulness for the diagnosis of systemic sclerosis.

Methods: Of a total of 255 capillaroscopy performed in our Rheumatology department, those patients with positive anti-centromere or anti-topoisomerase ase were selected. In all cases, capillaroscopy was performed in eight fingers, always by the same observer. The following findings were considered pathological or scleroderma pattern: Local or global capillary loss (> 20%), hemorrhages: two or more in at least two fingers and enlarged capillaries: two or more capillary with double or more caliber in at least two different fingers. Statistical analysis was performed with SPSS 19.0 program.

Results: The study included 69 patients: 5 (7.2%) males and 64 (92.8%) women, 14 (20.3%) smokers, 47 (68.1%) non-smokers and 8 (11.5%) quitters. The characteristics of the patients included in the study were as follows: 20 patients (30%) were previously diagnosed of systemic sclerosis (19 limited and one diffuse), of which 4 patients had concomitant primary biliary cirrhosis Syndrome (Reynolds), 1 patient with

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primary biliary cirrhosis and positive anti-centomere without the presence of Raynaud, one patient diagnosed with Sjögren’s syndrome with positive anti-centromere without presence of Raynaud, 26 patients with suspected early systemic sclerosis and 21 patients with disease-specific autoantibodies in the absence of Raynaud. Nailfold capillaroscopy was normal in 32 patients (46.4%) and pathological (scleroderma pattern) in 37 patients (53.6%); we detected limited enlarged capillaries in 26.2%, generalized enlarged capillaries also in 26.2%, giant capillaries in 37.7%, local loss of capillaries in 27.9%, global loss of capillaries in 8.2%, hemorrhages in small claims in 29.5% and abundant hemorrhages in 9.8%. All patients previously diagnosed of systemic sclerosis had a pathological capillaroscopy except one. However, no changes were observed in capillaroscopy in patients who had only disease-specific autoantibodies in the absence of Raynaud’s phenomenon. While, the 26 patients who were referred for suspected systemic sclerosis (at least with the presence of Raynaud and autoantibodies) in 18 (69.9%) of these scleroderma pattern was observed with subsequent diagnosis of early systemic sclerosis or “prescleroderma”.

Conclusion: Nailfold capillaroscopy is a useful and inexpensive tool for the diagnosis of systemic sclerosis. The scleroderma pattern is very specific of this disease and we can make an early diagnosis even in patients who only have autoantibodies and Raynaud’s phenomenon, without the presence of other severe manifestations. We have also observed that the absence of Raynaud’s phenomenon is associated with a normal result on capillaroscopy.

REFERENCE


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TRADITIONAL AND DISEASE-RELATED RISK FACTORS FOR ARTERIAL AND VENOUS THROMBOTIC EVENTS (TE) IN IDIOPATHIC INFLAMMATORY MYOPATHIES (IIM)

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Background: Thromboembolic cardiovascular diseases (CVD), affecting both arterial and venous sides, are one of the leading causes of death in patients with Idiopathic Inflammatory Myopathies (IIM), with highest peak of mortality within the first year after diagnosis (1).

Objectives: To assess the prevalence of traditional and disease-related risk factors for arterial and venous thrombotic events (TE) in patients with IIM by comparing those reporting TE (cases) with those without history of TE (comparators). To compare clinical characteristics, autoantibody profile inclusive antiphospholipid antibodies (aPL) and serum levels of adhesion molecules (VCAM, ICAM and e-selectin) between cases and comparators as well as between cases reporting arterial vs venous TE.

Methods: Using national and international registries, and medical charts, we identified 58 cases and 195 comparators with IIM followed at Karolinska University Hospital between 1993 and 2014. Information on gender, age at the time of diagnosis, IIM subgroup, presence of interstitial lung disease (ILD), myositis specific antibodies (MSAs), was retrospectively collected. Information on traditional risk factors for arterial and venous TE (essential hypertension, diabetes, dyslipidemia, smoking, malignancy) was retrieved for both groups. Serum levels of aPL and adhesion molecules were analyzed in stored sera from the time of diagnosis in both groups, before TE in cases and in 40 age and gender matched healthy controls (HC).

Results: One out of 5 IIM patients (22.92%) had suffered from at least one TE, which was observed especially during the first 5 years after diagnosis. Myocardial infarction was the most frequent TE, followed by pulmonary embolism and deep venous thrombosis. In the multivariate analysis, male gender and older age were independent risk factors for TE. Essential hypertension had statistically significant higher prevalence in cases than comparators. Arterial TE was more common in polymyositis, while venous TE occurred more frequently in patients with dermatomyositis, history of malignancy and in those with MSAs. At time of IIM diagnosis, the prevalence of aPL was 6% with no difference between cases and comparators. Significantly higher levels of VCAM and ICAM were obtained in IIM patients compared to HG (Fig.1 and Fig.2). ICAM levels were found significantly higher in comparators than cases (Fig.2). Lower levels of e-selectin were associated with higher odds of developing TE, especially in males and older patients, with no difference between arterial and venous TE (Fig.3).

Conclusion: A high risk of arterial and venous TE should be taken into account in patients with IIM, particularly close to time of diagnosis, with extra attention in male patients and older individuals. Preventive measures should be considered especially in patients with concomitant essential hypertension and malignancy. Lower serum levels of e-selectin might predict TE in IIM patients but the mechanism for this risk factor is not known.

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SAT0291  PULMONARY INVOLVEMENT AND FUNCTIONAL LIMITATION IN SYSTEMIC SCLEROSIS

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Background: Pulmonary involvement is the main cause of death in Systemic Sclerosis patients (SS). However, there is little information whether its presence is capable of affecting the functional capacity of patients and if this influences the quality of life perceived by them.

Objectives: To determine whether the presence of pulmonary involvement in patients with SS (Interstitial Lung Disease and or Pulmonary Arterial Hypertension) is related to greater functional disability.

Methods: Observational and cross-sectional study, with a prospectively performed protocol, of patients diagnosed of SS according to ACR/EULAR 2013 criteria. Demographic, clinical, analytical, activity (EUSTAR index), severity (Medsger scale and modified Rodnan index), health perception (SF36) and disability (HAQ and Cochin test) variables were collected. Moreover, Videocapillaroscopy (VCL) and Respiratory Function Test were made. All the patients had pulmonary TCMD and echocardiography in order to describe pulmonary features.

Results: 42 patients were included (95.4% women), with an average age of 59.2 (SD 12.9) years. The median of years of diagnosis was 4, and 6 from the first not Raynaud symptom. Out of them, 20 were SS limited, 20 patients SS diffuse, and 2 patients SS sine scleroderma. Pulmonary hypertension (HTP) was found in 11.9% of patients, as well as EPID in 33.3% (IUP 16.7%, NSIP 14.3%, bronchiolitis 2.3%). Analyzing the subgroup of patients with EPID, we can highlight a higher score of HAQ, Cochin and activity index EUSTAR, with less influence in Rodnan index and without differences in SF36.

Table 1. Answers to Raynaud’s phenomenon International Consensus Criteria questionnaire according to mode of administration

<table>
<thead>
<tr>
<th>Item</th>
<th>Yes, N (%)</th>
<th>p-value</th>
<th>Measure of individual agreement – Kappa coefficient (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Item 1. Are your fingers unusually sensitive to cold?</td>
<td>79 (94.0%)</td>
<td>0.549 (0.330–0.915)</td>
<td></td>
</tr>
<tr>
<td>Item 2. Occurrence of biphasic colour change during the vasospastic episodes (white and blue)</td>
<td>43 (50.0%)</td>
<td>0.762 (0.623–0.900)</td>
<td></td>
</tr>
<tr>
<td>Item 3. RP disease score</td>
<td>53 (63.1%)</td>
<td>0.640 (0.460–0.815)</td>
<td></td>
</tr>
<tr>
<td>Presence of RP according to RPQc</td>
<td>30 (36.9%)</td>
<td>0.777 (0.640–0.915)</td>
<td></td>
</tr>
</tbody>
</table>

*RP – Raynaud’s phenomenon; RPQc – International Consensus Criteria for the Diagnosis of Raynaud’s Phenomenon questionnaire; ** Fisher-exact test

Conclusion: Overall, there was a substantial level of agreement between self-administered and interview-based application of International Consensus Criteria for the Diagnosis of Raynaud’s Phenomenon questionnaire. However, we observed that the patients were inclined to score the severity of their RP lower than the physicians.

REFERENCE

Disclosure of Interests: None declared

SAT0293  SPECIFIC ALTERATIONS OF NAILFOLD CAPILLARIES MIGHT ANTICIPATE THE APPEARANCE OF THE EARLY CAPILLAROSCOPIC SCLERODERMA-PATTERN IN SYSTEMIC SCLEROSIS PATIENTS

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Background: Non-specific abnormalities (i.e. capillary enlargements) are usually found at the nailfold videocapillaroscopy (NVC) analysis in patients affected by primary Raynaud’s phenomenon (PRP). We have previously demonstrated that capillary diameter is an independent predictor for development of systemic sclerosis (SSc) associated secondary Raynaud’s phenomenon (SRP), so that progression to SRP is unlikely for subjects affected by RP when average nailfold capillary diameter is under 30 µm [1]. However, until now these findings have not been clearly classified in a defined pattern able to really predict the evolution to a sclerodema-pattern.

Objectives: This pilot study aimed to identify in a cohort of SSc patients a “very early” NVC pattern at high risk of evolution in the already defined NVC sclerodermat-patterns.

Disclosure of Interests: None declared

SAT0292  SELF-ADMINISTERED VERSUS INTERVIEW BASED INTERNATIONAL CONSENSUS CRITERIA FOR THE DIAGNOSIS OF RAYNAUD’S PHENOMENON QUESTIONNAIRE – A SINGLE CENTRE EXPERIENCE

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Background: International Consensus Criteria for diagnosing Raynaud’s Phenomenon (RP) have been proposed recently (1). These criteria are based on the three-step conditional approach (i.e. a screening question, assessment of colour changes and an item of disease score calculation). It is unclear whether differences exist between the self-administered and interview-based way of questionnaire fulfilment.

Objectives: We aimed in our study to evaluate the two approaches in patients with suspected RP.

Methods: This cross-sectional study was conducted at our secondary/tertiary-rheumatology centre between 1 October 2018 and 31 December 2018. Each patient referred for the video capillaroscopy was asked to complete the RP questionnaires on the day of the referral. The same questionnaire was applied as an interview by the rheumatologist before the video capillaroscopy. Differences in answers and level of individual agreement on individual three items, as well as the result of the questionnaire, between the two ways of questionnaire completion were assessed with Fisher exact test and Kappa coefficient, respectively.

Results: During the 3-month period we included 84 consecutive patients (88.1% female, median age (IQR) 49.5 (41.9–56.5) years). Results of answers to each item, final outcome of the questionnaire and the level of individual agreement for each item are presented in Table 1.

Table 1. Answers to Raynaud’s phenomenon International Consensus Criteria questionnaire according to mode of administration

<table>
<thead>
<tr>
<th>Item</th>
<th>Yes, N (%)</th>
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<td>Item 1. Are your fingers unusually sensitive to cold?</td>
<td>79 (94.0%)</td>
<td>0.549 (0.330–0.915)</td>
<td></td>
</tr>
<tr>
<td>Item 2. Occurrence of biphasic colour change during the vasospastic episodes (white and blue)</td>
<td>40 (47.6%)</td>
<td>0.762 (0.623–0.900)</td>
<td></td>
</tr>
<tr>
<td>Item 3. RP disease score</td>
<td>53 (63.1%)</td>
<td>0.640 (0.460–0.815)</td>
<td></td>
</tr>
<tr>
<td>Presence of RP according to RPQc</td>
<td>31 (36.9%)</td>
<td>0.777 (0.640–0.915)</td>
<td></td>
</tr>
</tbody>
</table>

*RP – Raynaud’s phenomenon; RPQc – International Consensus Criteria for the Diagnosis of Raynaud’s Phenomenon questionnaire; ** Fisher-exact test

Conclusion: Overall, there was a substantial level of agreement between self-administered and interview-based application of International Consensus Criteria for the Diagnosis of Raynaud’s Phenomenon questionnaire. However, we observed that the patients were inclined to score the severity of their RP lower than the physicians.

REFERENCE

Disclosure of Interests: None declared
Methods: We selected the NVCs of 273 patients affected by SSc (according to 2013 ACR criteria) who presented one of the validated NVC scleroderma patterns (81 with “Early” pattern, 84 with “Active” pattern, 92 with “Late” pattern, 16 with “scleroderma-like” pattern) (2). Among the 273 SSc patients with an established NVC scleroderma-pattern, a number of 54 subjects who had previously NVC analyses performed before the development of the scleroderma-pattern were enrolled. Time of evolution was calculated, and a detailed pilot study of capillaroscopic characteristics was random executed on 10 of those patients. The analysis included the number and the limbs diameters (arterial, venous, and apical) of capillaries with a diameter over 30 μm, together with the total number of capillaries and microhemorrhages, in 16 images per subject.

Results: All the 54 patients (100%) showed enlarged capillaries with an average diameter over 30 μm in their previous NVC. At the follow up, thirty-one patients (57%) developed an “Early” scleroderma pattern in the following 3 years, 6 patients (11%) developed an “Active” pattern in 4 years, 3 patients (6%) evolved in “Late” NVC pattern in 5 years, whereas 14 patients (26%) developed a “scleroderma-like” pattern in 4 years. The average time of evolution in a scleroderma-pattern was 4 years. The detailed pilot morphological analysis conducted on 10 patients revealed an average total number of capillaries of 6.8/mm² at last non-specific NVC analysis; among these 2.66 (31%) capillaries showed a diameter over 30 μm. The mean value diameter of the most dilated capillary was 35.74 μm (arterial limb 33.34 μm, apical limb 43.94 μm, venous limb 30 μm); the mean value for microhemorrhages was 0.6/mm². The number of capillaries reduced from 8.6±0.8 to 6.9±2.2/mm² (p=0.01) during follow-up (4 years).

Conclusion: Present detailed pilot study demonstrates that SSc patients showed a significant increase of nailfold capillary diameter over 30 μm before development of a validated NVC scleroderma-pattern at follow up. Even if this is an independent predictor for development of SSc as previously demonstrated, the data could help in intercepting patients with RP at higher risk of evolution in a validated SNC NVC pattern.

REFERENCE


Disclosure of Interests: None declared


SAT0294

ANALYSIS OF POLIAUTOIMMUNITY IN THE DIFFERENT SUBSETS OF SCLERODERMA

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Background: Coexistence of different connective tissue diseases based on their common autoimmune base is a feasible circumstance, which is known as poliautoimmunity (PAI). Objectives: Evaluation of the occurrence of PAI in systemic sclerosis (SSc) according to subtypes in the patients included in the Spanish SSc Registry (RESCLUE). Causes of death were also analyzed.

Methods: A nationwide, cross-sectional study was carried out. All participating centers had obtained local ethics committee approval. Results: PAI was present in 46% out of 1911 patients, of whom, 33% had more than one association. Most of these patients were women (93%, p<0.001), with no significant differences regarding first manifestation: Raynaud’s phenomenon, puffy hands, arthralgia or skin sclerosis.

Table 1. Prevalence of PAI according to subsets.

<table>
<thead>
<tr>
<th>Isolated SSc</th>
<th>PAI</th>
<th>P-VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>lcSSc</td>
<td>588 (57%)</td>
<td>554</td>
</tr>
<tr>
<td>dcSSc</td>
<td>268 (29%)</td>
<td>176</td>
</tr>
<tr>
<td>ssSSc</td>
<td>121 (12%)</td>
<td>86 (7.9%)</td>
</tr>
<tr>
<td>earlySSc</td>
<td>28 (2.7%)</td>
<td>16 (1.8%)</td>
</tr>
<tr>
<td>preSSc</td>
<td>85 (8.2%)</td>
<td>36 (4.1%)</td>
</tr>
</tbody>
</table>

Conclusion: A rather higher prevalence than reported was observed, although distribution of the associated disorders was similar. No remarkable differences were found regarding SSc subsets, either PAI prevalence, initial manifestations or causes of death.

Disclosure of Interests: None declared


SAT0295

ABSTRACT WITHDRAWN

SAT0296

FAST TRACK ALGORITHM: HOW TO DIFFERENTIATE A SCLERODERMA PATTERN FROM A NON-SCLERODERMA PATTERN

Vanessa Smith1,2,3, Amber Vanhaecke2,3, Miguel Guerra4, Rossella De Angeles1, Ellen Deschepper1, Christopher Denton5, Oliver Disler6, Ivan Foeldvari7, Eric Hachulla8, Francesca Ingegno1,2,9,10,11,12, Ulf Müller-Ladner11,12, Yes Piette1,12, Valeria Riccioni1,13, Barbara Ruano1,14, Alberto Sulli1,15, Jacob M. van Laar1,16, Ariane Hericck17,18, Maurizio Cutolo15,16, Ghent University, Department of Internal Medicine, Ghent, Belgium; 2Ghent University Hospital, Department of Rheumatology, Ghent, Belgium; 3VIB Inflammation Research Center, Unit for Molecular Immunology and Inflammation, Ghent, Belgium; 4Cathedral Hospital Villa Nova de Gaia/Espinho, Vil Nova de Gaia, Portugal; 51University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy; 6University of Manchester, Salford Royal Hospital NHS Foundation Trust, Division of Musculoskeletal and Dermatological Sciences, Manchester, United Kingdom; 711University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy; 8ASST G. Pini, Division of Rheumatology, Milan, Italy; 9Justus-Liebig University of Giessen, Kerckhoff Klinik, Department of Rheumatology and Clinical Immunology, Bad Nauheim, Germany; 10Sapienza University of Rome, Department of Internal Medicine and Medical Specialties, Rome, Italy; 11RRCSS San Martino Polyclinic Hospital, University Of Genoa, Research Laboratory And Academic Division Of Clinical Rheumatology, Department Of Internal Medicine, Genoa, Italy; 12Ghent University, Department of Biostatistics, Ghent, Belgium; 13University College London, Royal Free Hospital, Department of Rheumatology, London, United Kingdom; 14University Hospital Zurich, Department of Rheumatology, Zurich, Switzerland; 15Centre for Pediatric and Adolescent Rheumatology, Hamburg, Germany; 16Univ. Lille, CHU Lille, Department of Médecine Interne et Immunologie Clinique, Centre de Référence des Maladies Systémiques et Auto- Immunes Rares du Nord-Ouest (CERAINO), LIRIC, INSERM, Lille, France;

1University of Milan, Department of Clinical Sciences and Community Health, Milan, Italy; 2ASSST G. Pini, Division of Rheumatology, Milan, Italy; 3Justus-Liebig University of Giessen, Kerckhoff Klinik, Department of Rheumatology and Clinical Immunology, Bad Nauheim, Germany; 4Sapienza University of Rome, Department of Internal Medicine and Medical Specialties, Rome, Italy; 5RRCSS San Martino Polyclinic Hospital, University Of Genoa, Research Laboratory And Academic Division Of Clinical Rheumatology, Department Of Internal Medicine, Genoa, Italy; 6Ghent University, Department of Biostatistics, Ghent, Belgium; 7University College London, Royal Free Hospital, Department of Rheumatology, London, United Kingdom; 8University Hospital Zurich, Department of Rheumatology, Zurich, Switzerland; 9Centre for Pediatric and Adolescent Rheumatology, Hamburg, Germany; 10Univ. Lille, CHU Lille, Department of Médecine Interne et Immunologie Clinique, Centre de Référence des Maladies Systémiques et Auto-Immunes Rares du Nord-Ouest (CERAINO), LIRIC, INSERM, Lille, France.

Background: The European League Against Rheumatism Study Group on Microcirculation in Rheumatic Diseases is a non-profit international network of expert centres. Its main research focus is to investigate the...
morphology and function of the microcirculation with different non-invasive techniques such as nailfold videocapillaroscopy (NVC). NVC is of paramount importance for the differential diagnosis of primary and secondary Raynaud's phenomenon [1], and is part of the 2013 ACR/EULAR classification criteria for systemic sclerosis. As there is a wide variety of non-sclerodema patterns, the categorisation of capillaroscopic images as non-sclerodema patterns may be a challenge to the capillaroscopist.

Objectives: This study was designed to propose a simple fast track algorithm to differentiate sclerodema patterns from non-sclerodema patterns and to assess its interobserver reliability.

Methods: During the 8th EULAR course on capillaroscopy held in Genoa, September 2018, a lecture on teaching the fast track algorithm to categorise an image as non-sclerodema (category 1) or sclerodema pattern (category 2) (see figure) was given to all attendees (from 43 different countries): 6 experts, 68 novices, 53 moderately experienced (< 5 years of experience with capillaroscopy) and 14 experienced physicians (> 5 years of experience with capillaroscopy). Immediately after training, an examination was performed on 30 images. Classification of the images was defined by the presenter (VS) as the gold standard. Interobserver reliability was assessed by the calculation of kappa coefficients and proportion of agreement versus the gold standard.

Results: The light kappa was 1 for the independent experts (n=6) and 0.92 for the attendees (n=135). When comparing with the gold standard, an equal mean kappa of 0.96 (95%CI 0.95 – 0.98) was found for both independent experts and attendees. Analyses according to the reported level of experience on capillaroscopy revealed a mean index of reliability of 0.98 (95%CI 0.96 – 0.99) for novices, 0.96 (95%CI 0.93 – 0.99) for moderately experienced raters and 0.93 (95%CI 0.85 – 1.01) for experienced raters.

Conclusion: For the first time a fast track algorithm has been developed that was trainable within an hour to non-experienced capillaroscopists and has an excellent reliability to discern a non-sclerodema from a sclerodema pattern by medical doctors with varying levels of expertise in capillaroscopy.

REFERENCE
the clinical utility of the antibody and help deciphering the pathogenesis of this complex disease.

REFERENCE

Disclosure of Interests: Ho SO: None declared. Tak Lung Victor Wong: None declared, Maryam Dastmalchi: None declared, Valerie Leclair: None declared, Fabrício Espinosa-Ortega: None declared, Ingrid E. Lundberg Grant/research support from: Dr. Lundberg has received honoraria from Bristol Myers Squibb and Medimmune and is currently receiving a research grant from Bristol Myers Squibb and from Astra Zeneca., Consultant for: She is a scientific advisor for Bristol Myers Squibb, and aTyr

SAT0299 DIAGNOSIS OF SYSTEMIC SCLEROSIS: HOW AND WHEN
Cristina Sobrino, Carlos De la Puente Bujidos. Rheumatology Department, Ramón y Cajal University Hospital, Madrid, Spain
Background: Systemic sclerosis (SSc) is a heterogeneous disease regarding its clinical expression, evolution and forms of presentation. In spite of the lack of a disease modifying therapy, there are effective treatment options to control complications such as pulmonary arterial hypertension (PAH), interstitial lung disease (ILD) or digital ulcers (DU). Early diagnosis is crucial and allows the physician to start these treatments as soon as possible. To know how and when we diagnose SSc and its clinical manifestations will help us to detect potential improvement areas.
Objectives: To study the main clinical manifestations that lead to diagnosis of SSc, the delay of the diagnosis after the beginning of the first symptom, and to analyze the role of the different clinical features in the diagnosis.
Methods: A retrospective and descriptive study was conducted, which included patients with SSc from our Rheumatology Department. Clinical data and specific autoantibodies profile (ACA, Scl-70, RNP) were recorded, paying special attention to the clinical manifestations that led to diagnosis. We classified them in eight categories: secondary Raynaud’s phenomenon (SRP), digital ischemia or DU, musculoskeletal symptoms, skin induration, ILD, PAH, specific autoantibodies detection, and others.
The date of starting of Raynaud’s phenomenon (RP), of the first non-Raynaud symptom and the date when the diagnosis was established were registered. Analysis were conducted using STATA.
Results: The sample included 149 patients with SSc, meeting the 2013 ACR/EULAR criteria. RP appeared several years prior to the diagnosis (median of 3 years, IQR 0-8), and typically before the first non-Raynaud symptom. 141 out of 149 patients (94.6%) presented RP prior to the diagnosis. However, SRP was the manifestation that led to diagnosis in only 42/149 patients (41.6%), followed by skin induration (18.1%) and DU (12.7%). Surprisingly, 30/149 patients (20.1%) were diagnosed after the appearance of severe complications such as DU, ILD or PHA. Most patients started symptoms related to SSc several years before diagnosis (details in Table 1). 40/48 patients (83%) that were diagnosed due to RP, presented abnormalities in nailfold capillaroscopy as well as specific autoantibodies (Table 2). Presenting telangiectasia, calcinosis, ILD or PAH was not associated with an early diagnosis, nor was ACA, Scl-70 or RNP positivity.
Conclusion: An early approach of RP with capillaroscopy and specific autoantibodies would avoid delays to SSc diagnosis, allowing a close follow-up and an early treatment if necessary. SSc must always be considered as a differential diagnosis in patients with DU, ILD or PAH. An adequate referral of patients from primary care physicians to rheumatologists, and a multidisciplinary approach with Vascular Surgery, Pneumology and Cardiology Units would advance the diagnosis of this complex and potentially severe disease.

Table 1.
<table>
<thead>
<tr>
<th>CLINICAL MANIFESTATION THAT LEADS TO DIAGNOSIS</th>
<th>PATIENTS n (%)</th>
<th>YEARS FROM FIRST SYMPTOM TO DIAGNOSIS</th>
<th>YEARS FROM RAYNAUD’S PHENOMENON TO DIAGNOSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Raynaud’s Phenomenon</td>
<td>62 (41.5)</td>
<td>3 (1-10)</td>
<td>3 (1-9)</td>
</tr>
<tr>
<td>Skin induration</td>
<td>27 (18.1)</td>
<td>1 (0-4)</td>
<td>1 (0-4)</td>
</tr>
<tr>
<td>Digital Ischemia/UL</td>
<td>19 (12.7)</td>
<td>2 (0-12)</td>
<td>2 (0-12)</td>
</tr>
<tr>
<td>Musculoskeletal symptoms</td>
<td>18 (12.1)</td>
<td>3 (0-6)</td>
<td>3.5 (0-6)</td>
</tr>
<tr>
<td>ILD</td>
<td>8 (5.3)</td>
<td>2.5 (1-4)</td>
<td>3 (0-4)</td>
</tr>
<tr>
<td>Specific autoantibodies</td>
<td>6 (4)</td>
<td>5.5 (4-9)</td>
<td>3 (0-9)</td>
</tr>
<tr>
<td>Others</td>
<td>6 (4)</td>
<td>5.5 (0-10)</td>
<td>5.5 (0-10)</td>
</tr>
</tbody>
</table>

Table 2.
<table>
<thead>
<tr>
<th>PACIENTES WITH SECONDARY RAYNAUD’S PHENOMENON</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>With abnormal capillaroscopy</td>
<td>48/59 (81)</td>
</tr>
<tr>
<td>... and only ACA+</td>
<td>36 (75)</td>
</tr>
<tr>
<td>... and only anti-Scl-70+</td>
<td>3 (6.2)</td>
</tr>
<tr>
<td>... and only anti-RNP+</td>
<td>2 (4.1)</td>
</tr>
<tr>
<td>... and ACA+ and/or Scl70+ and/or anti-RNP+</td>
<td>40 (83.3)</td>
</tr>
<tr>
<td>... without autoantibodies</td>
<td>8 (16.6)</td>
</tr>
</tbody>
</table>

Disclosure of Interests: None declared

SAT0299 PREVALENCE OF PERIPHERAL EOSINOPHILIA AND CLINICAL ASSOCIATIONS IN THAI SYSTEMIC SCLEROSIS PATIENTS
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Background: Eosinophilia has been reported in systemic sclerosis (SSc) and localized scleroderma, so it might be part of the immune response in the pathogenesis of the disease.
Objectives: To determine the prevalence and clinical associations with peripheral eosinophilia in Thai SSc patients.
Methods: A cross-sectional study was conducted among Thai adult SSc patients, followed up at the Scleroderma Clinic, Khon Kaen University, Thailand, between November 1, 2016 and November 30, 2017. We excluded patients who had clinical overlap with another connective tissue disease, coexisting with localized scleroderma, eosinophilic fasciitis, or eosinophilia myalgia syndrome, and other diseases that cause eosinophilia. Peripheral eosinophilia is defined when total eosinophil count (TEC) is greater than 500 cells/μL. Clinical, laboratory tests for tissue parasite, cytokines, and others for evaluation the cause of eosinophilia were done on the study date.
Results: A total of 185 SSc patients were enrolled. Fifty-seven cases (10.1%) were peripheral eosinophilia of which 21 had the causes of eosinophilia identified by laboratory without clinical symptoms (viz. 9 adrenal insufficiency, 2 tuberculosis, and 10 parasitic infection). The total prevalence of the unknown causes of peripheral eosinophilia in SSc was 21.9% (95%CI 15.9-29.1) (36 of 164 cases). Five of the patients had TEC above 1500 cells/μm3. Of the 164 SSc patients, the majority (70.6%) had diffuse cutaneous SSc, and the female to male ratio was 2.3:1. The respective median age and median duration of the disease was 57.0 years (IQR 52.2-63.9) and 6.5 years (IQR 2.9-10.5). According to a multivariate analysis, being male and duration of disease increasing
every year were significantly associated with peripheral eosinophilia in SSc patients (OR 3.46 (95%CI 1.11-10.73) and 1.16 (95%CI 1.03-1.30), respectively), while Raynaud’s phenomenon had a significantly negative correlation with peripheral eosinophilia in SSc (OR 0.27: 95%CI 0.09-0.84). Other parameters—such as SSC subset, severity of skin tightening, serology, cytokines (transforming growth factor-β), interleukin-5)—were not correlated with peripheral eosinophilia.

Conclusion: Peripheral eosinophilia of unknown cause can be detected in 1 in 5 SSc patients. The factors associated with peripheral eosinophilia are longer disease duration and being male while vasculopathy has a negative association.

REFERENCES

Disclosure of Interests: None declared

SAT0302 SINGLE-PORT THORACOSCOPIC SYMPATHICOTOMY IS VERY EFFECTIVE FOR TREATMENT RESISTANT RAYNAUD’S PHENOMENON: A ONE MONTH FOLLOW-UP
Annie van Roon1, Michiel Kuipers2, Saskia van de Zande1, Amaal Eman Abdulle1, Arie Van Roon1, Reinhard Bus3, Wobbe Bouma1, Theo Klinkenberg2, Hendrika Bootsma4, Mike Dejongste5, Massimo Mariani2, Andries Smit1, Douwe J. Mulder1.
1University of Groningen, University Medical Center Groningen, Internal Medicine, division Vascular Medicine, Groningen, Netherlands; 2University of Groningen, University Medical Center Groningen, Thoracic surgery, Groningen, Netherlands; 3Medical Center Leeuwarden, Rheumatology, Leeuwarden, Netherlands; 4University of Groningen, University Medical Center Groningen, Rheumatology and Clinical Immunology, Groningen, Netherlands; 5University of Groningen, University Medical Center Groningen, Cardiology, Groningen, Netherlands

Background: In some patients, Raynaud’s Phenomenon (RP) symptoms prove resistant to conventional vasodilatory treatment. Thoracic sympathectomy is shown to be effective as treatment of RP, but is associated with surgical burden. During this procedure, the sympathetic nerve traversing to the upper extremity is dissected, subsequently leading to vasodilatation. In our centre, single-port thoracoscopic sympathectomy (SPTS) has been developed, a minimally invasive technique, extensively limiting surgical burden. [1]

Objectives: To evaluate SPTS feasibility and efficacy after one month in patients with treatment resistant RP.
Methods: In this study RP patients were their own controls, as they received an unilateral left sided sympathectomy. The effects of the SPTS was assessed at baseline and one month after the procedure. Perfusion of the hand was assessed using a cooling and recovery procedure, and laser speckle contrast analysis (LASCa) at room temperature of 23 degrees Celsius. The number and duration of RP attacks was reported over a two week period prior to reassessment by standard questionnaire.

Results: Eight patients were included in the study, 6 male/2 female, with a median (IQR) age of 45.2 (30.2–55.3) years, body mass index of 23.9 (23.4–26.8) kg/m², and RP duration of 7.0 (2.5–14.3) years. Five patients suffered from primary RP, and three patients had RP secondary to connective tissue disease (CTD) [mixed CTD (n=2) and limited cutaneous systemic sclerosis (n=1)]. All patients were very satisfied with the results and the number of attacks in the left hand decreased (p=0.018). After surgery an unilateral improvement in left hand perfusion was observed.
during the cooling and recovery procedure (p=0.008, figure 1), and in the fingertips with LASCA (p=0.023). No serious adverse events occurred.

Figure 1: Mean number of fingers per hand with normal perfusion during a cooling and recovery procedure before and after left-sided SPTS

Conclusion: SPTS, a minimally invasive technique, appears to be feasible and effective in improving hand perfusion in patients with RP after one month. Although these results are promising, long-term efficacy needs to be established and therefore follow-up is on-going.

REFERENCE

Disclosure of Interests: Anniek van Roon: None declared, Michiel Kuipers: None declared, Saskia van de Zande: None declared, Aamal Emran Abbule : None declared, Arie Van Roon: None declared, Reinhard Bos Grant/research support from: SUN Pharma, Wobbe Bouma: None declared, Theo Klinkenberg: None declared, Hendrika Bootsma Grant/ research support from: Unrestricted grants from Bristol-Myers Squibb and Roche, Consultant for: Roche, Bristol-Myers Squibb, Novartis, Medimmune, Union Chimique Belge, Speakers bureau: Bristol-Myers Squibb, Novartis, Mike DeJongste: None declared, Massimo Mariani: None declared, Andries Smit Shareholder of: Has been co-founder, and is still shareholder of Diagnoptics Technologies, the company which developed the AGE reader., Douwe J Mulder Grant/research support from: My University has received speakers fee from: Sanofi


SAT0303 DESIGN OF PHASE 3 STUDY OF LENABASUM FOR THE TREATMENT OF DERMATOMYOSITIS

Victoria Werth1,2, Chester V. Oddis2, Ingird E. Lundberg3, David Fiorentino3, Caitlin Cornwall4, Nancy Degtjark6, Scott Constantine6, Barbara White6

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Background: To date, there has not been a Phase 3 study evaluating efficacy and safety of a new chemical entity solely in subjects with dermatomyositis (DM). There is no precedence for design of such a pivotal study, including selection of patients or efficacy outcomes.

Objectives: Develop a Phase 3 study design

Methods: Lenabasum is a synthetic, non-immunosuppressive, selective cannabinoid receptor type 2 agonist that activates resolution of innate immune responses. Lenabasum had acceptable safety and tolerability and improved multiple physician-reported and patient-reported efficacy outcomes in a 16-week double-blinded, randomized, placebo-controlled Phase 2 trial in DM subjects with refractory, skin-predominant involvement, as well as in the open-label extension of that study. The Phase 3 trial design was based on Phase 2 data, input from a steering committee of experts in DM clinical trials, and recommendations made by regulatory authorities in the US, EU, Sweden, and Japan.

Results: A global, double-blind, randomized, interventional design was chosen to provide an unbiased assessment of the efficacy, safety and tolerability of lenabasum 20 mg bid and 5 mg bid compared to placebo in the treatment of DM. A 52-week treatment duration was selected to provide safety and efficacy data adequate to support chronic treatment. Subjects with DM were classified by Peter and Bohan criteria or the 2017 EULAR/ACR classification criteria for DM (both amyopathic DM and classic DM). Subjects will be required to have active disease, as assessed by an expert and based on a range of muscle, skin, and other disease manifestations. Subjects must be on stable doses of current DM treatments with any background immunosuppressive medications allowed except prednisone ≥ 20 mg per day or equivalent. This inclusivity allows testing of efficacy and safety of lenabasum in the setting of current treatment practice and reduces risk of disease flare early in the study. The primary efficacy outcome is change from baseline in 2016 ACR/EULAR Total Improvement Score (TIS) for DM and polymyositis. This composite outcome has six domains that broadly capture improvement in disease activity, is relevant to the range of manifestations in DM, and is applicable to the assessment of efficacy in the target patient population. Secondary efficacy outcomes were chosen to assess how the subject functions (Short Form – 36 physical functioning domain), major organ involvement (MMT-8, CDASI activity score, and a new Investigator Global Assessment scale of skin activity designed specifically for this study), and lung function (FVC). Change in oral corticosteroid dose also will be captured.

Conclusion: To our knowledge, this is the first Phase 3 study in DM with a new molecular entity. As such, agreement with experts and regulatory authorities on design represents a step forward in the development pathway of new treatments for DM.

Disclosure of Interests: Victoria Werth: None declared, Chester V Oddis Grant/research support from: Support of clinical research from Roche/Gene-entech and BMS, Consultant for: Corbus: Previous Steering Committee consultation; No longer being paid as a Corbus consultant, Ingird E. Lundberg Grant/research support from: Dr. Lundberg has received honoraria from Bristol-Myers Squibb and is currently receiving a research grant from Bristol Myers Squibb and from Astra Zeneca., Consultant for: She is a scientific advisor for Bristol Myers Squibb, and aTyr, David Fiorentino Grant/research support from: Pfizer - to support analysis of human tissue from patients with dermatomyositis, Consultant for: Pfizer—design and operation of clinical trial in DM

Corbus—design of clinical trial in DM 23 and me—ad hoc consulting

Adimayx—ad hoc consulting

Janssen—SAB for PSOLAR database


Nemanja Damjanov—ad hoc consulting

Corbus—Shareholder of: Corbus Pharmaceuticals, Inc., Employee of: Corbus Pharmaceuticals, Inc., Nancy Degtjark—ad hoc consulting

Caitlin Cornwall—ad hoc consulting

Bos Grant/research support from: SUN Pharma, Wobbe Bouma: None declared, Theo Klinkenberg: None declared, Hendrika Bootsma Grant/research support from: Unrestricted grants from Bristol-Myers Squibb and Roche, Consultant for: Roche, Bristol-Myers Squibb, Novartis, Medimmune, Union Chimique Belge, Speakers bureau: Bristol-Myers Squibb, Novartis, Mike DeJongste: None declared, Massimo Mariani: None declared, Andries Smit Shareholder of: Has been co-founder, and is still shareholder of Diagnoptics Technologies, the company which developed the AGE reader., Douwe J Mulder Grant/research support from: My University has received speakers fee from: Sanofi


SAT0304 RELATIONSHIP BETWEEN INTERLEUKIN-23 AND GASTROINTESTINAL INVOLVEMENT IN PATIENTS WITH SYSTEMIC SCLEROSIS

Ana Žeković1, Misa Vreća2, Vesna Špasović2, Vesna Skodrić-Trifunović3, Ljiljana Marković-Denic4, Marina Andjelković5, Sonja Pavlović4, Nemanja DamjanovichNemanja Damjanovich1, Institute of rheumatology, Belgrade, Serbia, 2Institute of Molecular Genetics and Genetic Engineering, Belgrade, Serbia, 3Clinic for Pulmonary Diseases, Belgrade, Serbia, 4Institute of Epidemiology, Belgrade, Serbia

Background: Growing evidence suggests that T-cell proliferation and cytokine secretion play an important role in the pathogenesis of systemic sclerosis (SSc). Gut involvement is the leading cause of morbidity in patients with SSc. In this study we evaluated interleukin-23 (IL-23) protein expression profiles and investigated its association with gastrointestinal involvement in SSc patients.
Spondyloarthritis - clinical aspects (other than treatment)

**Objectives:** To define IL-23 expression profiles and to explore association between IL-23 and gastrointestinal involvement in SSc patients.

**Methods:** Study included 31 SSc patients. The expression level of IL-23 mRNA was determined by qRT-PCR method and Enzyme-Linked Immunosorbent Assay (ELISA) was used for analysis of IL-23 serum protein level. We used UCLA GIT 2.0 questionnaire to assess gastrointestinal (GIT) involvement in SSc patients.

**Results:** We found a positive correlation between disease duration and expression levels of IL-23 mRNA (r = 0.49, p < 0.05). Nine SSc patients with high IL-23 levels (cut off point 6.8 pg/ml) had significantly higher UCLA GIT 2.0 score, compared to 22 SSc patients with normal IL-23 levels (p < 0.05). Serum level of IL-23 positively correlated with total GIT score (r = 0.35, p < 0.05) and distension scale score (r = 0.5, p < 0.05).

**Conclusion:** High IL-23 serum levels significantly correlated with gastrointestinal involvement (higher UCLA GIT 2.0 score) in patients with SSc.

**REFERENCES**


**Disclosure of Interests:** Ana Zekovic: None declared, Vesa Vreca: None declared, Vesa Spasovski: None declared, Vesna Skodric-Trifunovic: None declared, Ljiljana Markovic-Denic: None declared, Marina Andjelkovic: None declared, Sonja Pavlovic: None declared, Nemanja Damjanov: Grant/research support from: AbbVie, Pfizer and Roche, Consultant for: Abbvie, Gedeon Richter, Merck, Novartis, Pfizer and Roche, Speakers bureau: Abbvie, Gedeon Richter, Merck, Novartis, Pfizer and Roche.

SAT0306
COMPARISON OF MEN AND WOMEN WITH AXIAL SPONDYLOARTHRITIS IN THE US-BASED CORRONA PSORIATIC ARTHRITIS/SPONDYLOARTHRITIS (PSPA) REGISTRY

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Background: Axial spondyloarthritis (AxSpA) is a chronic inflammatory rheumatic disease that primarily affects the axial skeleton and frequently affects the peripheral joints and entheses. AxSpA encompasses ankylosing spondylitis and nonradiographic AxSpA. Sex differences have been described for patient reported outcomes (PROs) in SpA; however, more research is needed to better understand the overall clinical burden of AxSpA in women, particularly in the United States.

Objectives: To compare the patient demographics, clinical characteristics, treatment profiles, disease activity, quality of life, and work productivity between men and women with AxSpA in the US-based Corrona PsA/SpA Registry.

Methods: This study included patients aged ≥ 18 years with AxSpA enrolled in the Corrona PsA/SpA Registry between March 2013 and November 2018. Patients who were concurrently diagnosed with PsA were excluded. Patient demographics, clinical characteristics, treatment profiles, disease activity, quality of life, and work productivity were characterized for all patients with AxSpA at enrollment and were compared between men and women using t tests or Wilcoxon rank-sum tests for continuous variables and χ2 or Fisher’s exact tests for categorical variables.

Results: Of 498 patients with AxSpA who were included in the study, 307 (61.6%) were male and 191 (38.4%) were female. Compared with men, women were less likely to work full time, were more likely to be normal weight/underweight, had a shorter disease duration, and were more likely to have depression, fibromyalgia, and prior csDMARD and prednisone use (Table 1; all P < 0.05). At enrollment, women with AxSpA had a shorter occiput-to-wall distance, but also had worse disease activity compared with men, as reflected by higher BASDAI and BASFI scores, higher enthesis and tender/swollen joint counts, worse pain and fatigue, worse physical function (HAQ-S) and health state today (EQ-5D), and more severe work and activity impairment (Table 2; all P < 0.05).

Conclusion: In this US registry of patients with AxSpA, women had an increased overall burden of disease compared with men, including higher patient reported symptoms, higher disease activity, and greater work productivity impairment. Women also had lower scores for spinal mobility with increased signs of peripheral arthritis (eg, higher tender/swollen joint and enthesis counts), suggesting that conventional definitions of AxSpA centered around axial symptoms may not be representative of the female population with disease. Improved awareness of sex differences in presentation of AxSpA may aid physicians in earlier identification and improved management of the disease.

Acknowledgement: This study was sponsored by Corrona, LLC. Corrona is supported through contracted subscriptions with multiple pharmaceutical companies. The abstract was a collaborative effort between Corrona and Novartis, with financial support provided by Novartis.

Table 1. Demographic and Clinical Characteristics and Treatments in Men and Women With AxSpA at Enrollment

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Men (N = 307)</th>
<th>Women (N = 191)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>49.9 (13.0)</td>
<td>52.7 (12.0)</td>
<td>0.05</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; White</td>
<td>276 (90.1)</td>
<td>171 (89.5)</td>
<td>0.76</td>
</tr>
<tr>
<td>&gt; Black</td>
<td>3 (1.0)</td>
<td>2 (1.0)</td>
<td></td>
</tr>
<tr>
<td>&gt; Other</td>
<td>11 (3.6)</td>
<td>2 (1.0)</td>
<td></td>
</tr>
<tr>
<td>Full time work, n (%)</td>
<td>190 (61.8)</td>
<td>102 (53.3)</td>
<td>0.01</td>
</tr>
<tr>
<td>Disease duration, mean (SD), years</td>
<td>10.3 (6.0)</td>
<td>13.6 (13.0)</td>
<td>0.02</td>
</tr>
<tr>
<td>Present count of tender points, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 9</td>
<td>120 (39.2)</td>
<td>36 (18.8)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>&gt; 12</td>
<td>110 (35.9)</td>
<td>45 (23.4)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Prior biologic use, n (%)</td>
<td>89 (29.6)</td>
<td>63 (32.8)</td>
<td>0.36</td>
</tr>
<tr>
<td>Prior nonbiologic use, n (%)</td>
<td>216 (70.8)</td>
<td>128 (67.2)</td>
<td>0.62</td>
</tr>
<tr>
<td>Prior psoriasis, n (%)</td>
<td>84 (27.6)</td>
<td>53 (27.8)</td>
<td>1.00</td>
</tr>
<tr>
<td>Prior IBD, n (%)</td>
<td>8 (2.6)</td>
<td>10 (5.2)</td>
<td>0.58</td>
</tr>
<tr>
<td>Prior pregnancy, n (%)</td>
<td>10 (3.3)</td>
<td>9 (4.7)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Conclusion: In this US registry of patients with AxSpA, women had an increased overall burden of disease compared with men, including higher patient reported symptoms, higher disease activity, and greater work productivity impairment. Women also had lower scores for spinal mobility with increased signs of peripheral arthritis (eg, higher tender/swollen joint and enthesis counts), suggesting that conventional definitions of AxSpA centered around axial symptoms may not be representative of the female population with disease. Improved awareness of sex differences in presentation of AxSpA may aid physicians in earlier identification and improved management of the disease.

Acknowledgement: This study was sponsored by Corrona, LLC. Corrona is supported through contracted subscriptions with multiple pharmaceutical companies. The abstract was a collaborative effort between Corrona and Novartis, with financial support provided by Novartis.
SAT0307 LONG-TERM ASSOCIATION BETWEEN DISEASE ACTIVITY MEASURED BY ASDAS AND PHYSICAL FUNCTION IN A LARGE EARLY AXIAL SPONDYLOARTHRITIS COHORT

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1Centro Hospitalar do Algarve – Hospital de Faro, Faro, Portugal; 2Algarve Biomedical Center, Faro, Portugal; 3Le centre Hospitalier Universitaire de Toulouse, Toulouse, France; 4University College London, London, United Kingdom

Background: The Ankylosing Spondylitis Disease Activity Score (ASDAS) has been progressively replacing the Bath Ankylosing Spondylitis Disease Activity Score (BASDAI) as the main disease activity measure to assess patients with axial spondyloarthritis (axSpA), both in the research context as well as in clinical practice. However, further evidence is needed to show its meaningfulness regarding the longitudinal relationship with physical function.

Objectives: To study the long-term association between disease activity and physical function in axSpA.

Methods: DESIR is a prospective observational cohort of patients with recent onset (<3 years) inflammatory back pain, suggestive of axSpA. We analysed data collected during the first five years of follow-up and selected patients with a definite diagnosis of axSpA according to the treating rheumatologist. Physical function was assessed using the Ankylosing Spondylitis Health Assessment Questionnaire (HAQ-AS). Disease activity was measured using the ASDAS C-reactive protein (ASDAS-CRP) and BASDAI. In a first step, associations between HAQ-AS (dependent variable) and disease activity (defined by ASDAS or BASDAI), clinical and demographic variables were tested in univariable models. Multivariable models were then built adjusting for potential confounding factors found to be significant in the univariable analysis.

In a second step, additional multivariable analysis was conducted using the Chi-square Automatic Interaction Detector (CHAID) method, with HAQ-AS as dependent variable. The following independent variables were tested: ASDAS/BASDAI, enthesitis score, arthritis, employment status, gender, symptom duration, body mass index (BMI), HLA-B27 status, treatment with non-steroidal anti-inflammatory drugs (NSAID), conventional disease modifying anti-rheumatic drugs (cDMARD) and TNF-blockers. The final model fixed as criteria: 70 parent nodes and 20 child nodes to create new generations in the decision tree.

Results: Data from 644 patients and 4944 visits were analysed. There was a significant independent association between HAQ-AS and gender, employment status, peripheral arthritis, ASDAS-CRP/BASDAI enthesitis, NSAID and anti-TNF treatment (Table 1). The decision tree revealed ASDAS as the first variable with discriminative power on HAQ-AS, according to the following cut points: 1.3, 2.2 and 2.4. In addition, for ASDAS values above 3.5 the model yield a higher number of explanatory variables setting different patients’ profiles regarding their functional status, namely: gender, anti-TNF and NSAID treatment. Notably, the ASDAS cut-offs that separated different patient profiles largely mimicked the cut-offs previously defined for ASDAS disease activity states (inactive, low, high and very high disease activity). According to this hierarchical model, gender, anti-TNF treatment and enthesitis score were the next variables explaining HAQ-AS variation, followed by employment status and NSAID treatment.

Conclusion: We have shown that disease activity contributes longitudinally to physical function and that it is hierarchically superior to any other variables or disease domains. Previously defined ASDAS-CRP disease activity categories identified different patient profiles on the hierarchical analysis.

REFERENCE

Table 1. GEE models for HAQ-AS (dependent variable) in axSpA

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Univariable analysis, OR (95% CI)</th>
<th>Multivariable analysis, OR (95% CI)</th>
<th>Multivariable analysis, OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>1.00 (1.00-1.00)</td>
<td>1.00 (1.00-1.00)</td>
<td>1.00 (1.00-1.00)</td>
</tr>
<tr>
<td>Height, cm</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>1.10 (1.00-1.20)</td>
<td>1.10 (1.00-1.20)</td>
<td>1.10 (1.00-1.20)</td>
</tr>
<tr>
<td>ASDAS</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>BASDAI</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>ESR, mm/h</td>
<td>1.00 (1.00-1.00)</td>
<td>1.00 (1.00-1.00)</td>
<td>1.00 (1.00-1.00)</td>
</tr>
<tr>
<td>CRP, mg/L</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>ASDAS-CRP</td>
<td>1.15 (1.10-1.20)</td>
<td>1.15 (1.10-1.20)</td>
<td>1.15 (1.10-1.20)</td>
</tr>
<tr>
<td>BASDAI</td>
<td>1.15 (1.10-1.20)</td>
<td>1.15 (1.10-1.20)</td>
<td>1.15 (1.10-1.20)</td>
</tr>
<tr>
<td>ESR, mm/h</td>
<td>1.00 (1.00-1.00)</td>
<td>1.00 (1.00-1.00)</td>
<td>1.00 (1.00-1.00)</td>
</tr>
<tr>
<td>CRP, mg/L</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>ASDAS-CRP</td>
<td>1.15 (1.10-1.20)</td>
<td>1.15 (1.10-1.20)</td>
<td>1.15 (1.10-1.20)</td>
</tr>
<tr>
<td>BASDAI</td>
<td>1.15 (1.10-1.20)</td>
<td>1.15 (1.10-1.20)</td>
<td>1.15 (1.10-1.20)</td>
</tr>
<tr>
<td>ESR, mm/h</td>
<td>1.00 (1.00-1.00)</td>
<td>1.00 (1.00-1.00)</td>
<td>1.00 (1.00-1.00)</td>
</tr>
<tr>
<td>CRP, mg/L</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>ASDAS-CRP</td>
<td>1.15 (1.10-1.20)</td>
<td>1.15 (1.10-1.20)</td>
<td>1.15 (1.10-1.20)</td>
</tr>
<tr>
<td>BASDAI</td>
<td>1.15 (1.10-1.20)</td>
<td>1.15 (1.10-1.20)</td>
<td>1.15 (1.10-1.20)</td>
</tr>
<tr>
<td>ESR, mm/h</td>
<td>1.00 (1.00-1.00)</td>
<td>1.00 (1.00-1.00)</td>
<td>1.00 (1.00-1.00)</td>
</tr>
<tr>
<td>CRP, mg/L</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

* Not selected for this model; NA – not applicable; ** Model adjusted with the cofounders considered significant in the proposed multivariable model for ASDAS (previous column)

Disclosure of Interests: Pedro Carvalho: None declared, Ana Marreiros: None declared, Adeline Ruyssev-Witrand: None declared, Pedro Machado Consultant for: Abbvie, BMS, Celgene, Janssen, MSD, Novartis, Pfizer, Roche and UCB, Speakers bureau: Abbvie, BMS, Celgene, Janssen, MSD, Novartis, Pfizer, Roche and UCB

manifestations (B for both)\(^1\). Those cluster-based SpA phenotypes could correspond to different levels of disease severity.

**Objectives:** To assess whether cluster-based SpA phenotypes defined at baseline are conserved over time and might predict disease outcome at follow-up.

**Methods:** We analysed longitudinal data from the 586 patients who completed all follow-up visits until 5-year (mo 6, 12, 18, 24, 36, 48 and 60) out of the 679 patients included in the DESIR cohort used to define clusters at baseline. We performed a linear mixed-effect analysis for quantitative variables (using Ime4 R package) and a generalized linear mixed-effect analysis for qualitative variables (using glmer R package) with cluster and follow-up visits as fixed effects and subjects as random effect. P-values were obtained by likelihood ratio tests of the full model with cluster against the model without cluster as fixed effects.

**Results:** Over the time, both clusters continued to show sustainable consistent differences characterized by higher frequency of peripheral involvement, higher disease activity, worse patient-reported outcome, higher frequency of conventional DMARDs and TNF blockers usage in cluster B, and higher frequency of radiographic and MRI sacroilitis at 2 and 5 years in cluster A (Table).

**Conclusion:** Cluster-based SpA phenotypes defined at baseline in the DESIR cohort were predictive of severity outcome after 5 years. Patients from cluster B were more prone to develop sacroilitis despite lower disease activity over the time, whereas those from cluster B had poorer clinical outcome and higher need for conventional DMARDs and TNF blockers.

**REFERENCE**


**Disclosure of Interests:** Felicie Costantino: None declared, Philippe Aegerter: None declared, Anna Mollö: None declared, Maxime Breban Grant/research support from: Pfizer, UCB, Novartis, MSD, Consultant for: UCB, Pfizer, Abbvie, deposited into the eular database.  

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**SA10309**

**CLINICAL, IMAGING AND BIOLOGIC FEATURES OF SPONDYLOARTHRITIS IN AN AT-RISK POPULATION: DATA FROM THE PRE-SPA COHORT**

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**Background:** Diagnosis in axial spondyloarthritis (axSpA) is challenging and often delayed by several years, resulting in a delay in treatment. Previously we reported presence of spondyloarthritis (SpA) features and imaging abnormalities in first-degree relatives (FDRs) of HLA-B27 axSpA patients, who are at risk of developing axSpA [1]. Follow up of these at risk individuals could help to identify clinical signs, imaging abnormalities or biomarkers that are predictive of development of axSpA.

**Objectives:** To investigate imaging, biologic and/or clinical signs of SpA at baseline and after 1 year follow up, as well as development of clinically manifest axSpA after 1 year follow up in at risk individuals.

**Methods:** The Pre-Spa cohort[1] is a prospective inception cohort in which FDRs of HLA-B27 positive axSpA patients are included and followed for 5 years. The main exclusion criteria were: a diagnosis of SpA at baseline and back pain with a previous non-rheumatic diagnosis, such as spinal disc herniation. Clinical and biologic characteristics were collected at baseline and after 1 year. Imaging was performed at baseline including MRI of the sacroiliac joints (SIJ) and X-rays of the cervical and lumbar spine and SIJ. MRIs were scored according to the ASAS definition for a positive MRI by two readers. X-rays were scored according to the modified New York (mNY) criteria for ankyllosing spondylitis by two readers.

**Results:** In the current study we report the characteristics of 201 participants at baseline and 123 participants after one year of follow-up. 126 (82.7%) participants reported back pain, of which 39 (19.4%) fulfilled criteria for inflammatory back pain. Median (IQR) VAS total back pain (0-100mm) was 11 (0-28). Six (2.9%) were previously diagnosed with arthritis by a physician, nine(4.4%) with enthesis and one(0.5%) with dactylitis. In none of these participants a diagnosis of SpA was made. Seven participants were previously diagnosed with an extra-articular manifestation possibly related to SpA: four with psoriasis and three with anterior uveitis. Three (1.5%) participants fulfilled the mNY criteria for sacroilitis on radiography. Ten (5%) participants had bone marrow edema on MRI of the SIJ suggestive of SpA. Fifty-six (27.8%) participants would have fulfilled ASAS classification criteria for axSpA if they would have had a clinical diagnosis of axSpA. After one year patient-reported disease activity variables remained stable; median (IQR) VAS total back pain (0-100mm) was still low: 4(0-24). During one year of follow-up, in total seven participants developed symptoms and were clinically diagnosed with axSpA.

**Conclusion:** Imaging signs and clinical signs of SpA are present in a substantial proportion of seemingly healthy FDRs of HLA-B27 positive AxSpA patients. Twelve (6.0%) participants had imaging suggestive of SpA, but a clinical diagnosis of axSpA was still rare after one year of follow up (5.7%). Future follow-up will increase numbers of individuals diagnosed with axSpA and help us identify early symptoms and signs of SpA in this at risk population.

**REFERENCE**


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IDENTIFICATION OF FACTORS ASSOCIATED WITH MAGNETIC RESONANCE IMAGES CHANGES SUGGESTIVE OF AXIAL SPONDYLOARTHRITIS IN THE AXIAL SKELLET OF INDIVIDUALS <45 YEARS – EVALUATION OF DATA FROM A LARGE COMMUNITY STUDY

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Background: Active (bone marrow edema, BME) and structural (fatty lesions, FL) MRI lesions in the spine and the sacroiliac joints (SIJ), as assessed by magnetic resonance imaging (MRI), have been described in patients with axial spondyloarthritis (axSpA) but may also occur in non-axSpA patients and healthy individuals (1,2).

Objectives: Identify factors associated with the occurrence of BME and FL in spinal- and SIJ-MRIs in the population-based Study of Health in Pomernania (SHIP).

Methods: All available spinal- (sagittal T1/T2 sequences) and SIJ- (semi-coronal STIR sequences) MRIs were evaluated by two trained readers blinded to clinical data. BME (SIJ and spine) and FL (spine) suggestive of axSpA were recorded. Disagreements were resolved by consensus. BME was quantified using Berlin MRI scores. Information was available for age (increase per decade), sex, smoking (ever vs. never), prevalence of spinal pain (NRS≥4/10 in last 3 months), CRP, HLA-B27 status and body mass index (BMI) categories (WHO definition of underweight (cat. 1), normal (cat. 2) or overweight (cat. 3)). Associations between clinical factors and MRI lesions were analyzed (a) by modeling of number and size of lesions using negative binomial count regression and (b) for presence/absence of lesions using univariate logistic regression.

Results: MRIs of 793 volunteers, 392 male (49.4%), 45 CRP-positive (5.7%), 67 HLA-B27+ (8.4%), 497 smokers (62.7%) were evaluated. BME lesions were found in 136 SIJ-MRIs (17.2%) and in 218 (27.5%) spinal MRIs, while FL were found in 645 spinal MRIs (81.3%).

A higher number and larger sized SIJ-BME lesions were associated with (wp (β, 95% CI)) with HLA-B27 (2.8, 1.5-4.9), spinal pain (1.7, 1.2-2.6), and higher BMI (cat. 1 vs 3, 1.7, 1.0-3.0). In the spine, higher number and larger sized BME were associated with age (1.5, 1.2-2.0), while FL were associated with higher BMI, (cat. 1 to cat. 3 (1.9, 1.5-2.2), age (1.6, 1.5-1.8) and male sex (1.4, 1.2-1.6).

Presence (odds ratio, 95% CI) of spinal BME (1.3, 1.0-1.7) and/or FL (1.7, 1.3-2.3) was associated with age, while FL alone were associated with a higher BMI (cat. 1 to cat.3, 3.3, 1.6-6.1).

In total, 22 subjects (16.2%) had large (>33% of surface involvement) and 114 small (<33% of surface involvement) SIJ-BME lesions. Large SIJ-BME lesions were found in 4.5% HLA-B27-positive vs. 2.6% HLA-B27-negative subjects (p=0.40). Out of 167 quadrants with BME lesions in SIJ, the majority (n=66, 35-3%) was located in the upper sacral quadrant. Most SIJ lesions (n=156, 83.4%) were small. Out of 362 spinal segments with BME, the majority n=152, 42% was located in the lower (T7/8-T11/12) thoracic spine. Most spinal lesions (n=299, 90.9%) were small.

Conclusion: In this large population-based study, higher numbers of large and small SIJ-BME lesions were significantly associated with HLA-B27, back pain and BMI. In some contrast, spinal BME and FL were associated with older age, male sex and BMI but not HLA-B27. The association for HLA B27 was only shown on the quadrant but not on the patient level. These findings are in accordance with previously published hypotheses that question the specificity of sacroiliitis and spondylitis in axSpA (3).

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DISCLOSURE OF INTERESTS: Xenon Banilack: Grant/research support from: AbbVie, Pfizer, Merck Sharp & Dohme, UCB Pharma, Novartis, Consultant for: AbbVie, Pfizer, Boehringer Ingelheim, Celgene, Janssen Biologics, Novartis, Pfizer, UCB Pharma, Galapagos, Speakers bureau: AbbVie, Chugai, Janssen, Novartis, Pfizer, UCB Pharma, Adrian Richter: None declared, Daniel Feldmann: None declared, Anne Ott: None declared, Robin Bülow: None declared, Carsten Schmidt: None declared, Juergen Braun Shareholder of: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, Grant/research support from: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, Grant/research support from: Abbott, Bristol Myers Squibb, Celgene, Celtrion, Chugai, Johnson & Johnson, MSD, Novartis, Pfizer, Roche, UCB Pharma, Grant/research support from: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, Grant/research support from: Abbvie (Abbott), Amgen, Baxter, Biogen, BMS, Boehringer, Celgene, Celtrion, Centocor, Chugai, Hexal, Janssen, Lilly, Medac, MSD (Scherping-Plough), Mylan, Mundipharma, Novartis, Pfizer (Wyeth, Hospira), Roche, Sanofi-Aventis and UCB, Consultant for: Abbvie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, Consultant for: Abbott, Bristol Myers Squibb, Celgene, Celtrion, Chugai, Johnson & Johnson, MSD, Novartis, Pfizer, Roche, UCB Pharma, Speakers bureau: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, Speakers bureau: Abbvie (Abbott), Amgen, Baxter, Biogen, BMS, Boehringer, Celgene, Celtrion, Centocor, Chugai, Hexal, Janssen, Lilly, Medac, MSD (Scherping-Plough), Mylan, Mundipharma, Novartis, Pfizer (Wyeth, Hospira), Roche, Sanofi-Aventis and UCB, Speakers bureau: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB.


DIAGNOSTIC UTILITY OF INDIVIDUAL INFLAMMATORY BACK PAIN PARAMETERS IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: A recent study in German chronic back pain (CBP) patients (pts) with a suspicion of axial spondyloarthritis (axSpA) report on the performance of, among others, the ASAS inflammatory back pain (IBP) criteria and the individual IBP parameters. Pts were diagnosed by a rheumatologist blinded for all clinical features but IBP and by a rheumatologist with all diagnostic tests available as in daily practice (reference standard). Data show high sensitivity but low specificity of the ASAS IBP criteria.

Figure. Performance of individual parameters of the ASAS IBP criteria

SAT0310

SAT0311
GENDER CONTRASTS IN PATIENT REPORTED OUTCOMES DON'T ALTER THE DISEASE ACTIVITY SCORE IN AXIAL SPONDYLOARTHRITIS PATIENTS

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Background: Disease activity in axial spondyloarthritis (axSpA) is often quantified by the Axial Spondyloarthritis Disease Activity Score (ASDAS), a composite index which combines 4 patient reported outcome (PRO) parameters and C-reactive protein (CRP) as an acute phase reactant. ASDAS commonly acts as a target in treat-to-target approaches in axSpA patients.

Objectives: To identify the impact of gender on ASDAS in newly diagnosed axSpA patients and to determine whether possible differences are PRO- or CRP-driven.

Methods: Patients originate from the Be-Giant cohort, a Belgian observational registry of newly diagnosed axSpA patients (expert opinion). Included patients fulfill the Assessment of SpondyloArthritis International Society (ASAS) classification criteria for axSpA and are anti-TNF naïve prior to inclusion. An extensive patient description was performed at baseline, including PRO and laboratory investigations with CRP (mg/L). ASDAS was calculated for each patient and subdivided in a PRO-component (ASDAS-PRO) and a CRP-component (ASDAS-CRP) (1).

Results: By January 2019, 291 axSpA patients were included (138 male, 153 female). At baseline, ASDAS could be calculated in 262 patients. ASDAS-PRO was significantly higher in women compared to men (1,66 vs. 1,48, p = 0,04), while ASDAS-CRP did not differ significantly (0,90 for both genders, p = 0,96). No significant difference was found between the total ASDAS of women and men (2,54 vs. 2,38, p = 0,09) (Figure 1). When categorizing the score into 4 disease activity states (2), 60,8% (76/125) of men show high or very high disease activity (ASDAS > 2,1) at baseline compared to 67,2% (92/137) of women (p = 0,35).

Concerning the 5 ASDAS components, the discrimination between male and female axSpA patients was most pronounced for patient global scores (Figure 2). Men reported a baseline patient global score of 4,3 (95% CI 3,8 – 4,8), compared to a score of 5,1 (95% CI 4,7 – 5,6) in women (p = 0,01).

Conclusion: Female axSpA patients report a significantly higher patient global score compared to men. This contributes to a significantly higher ASDAS-PRO in women. However, neither the ASDAS itself nor the ASDAS disease activity categories are significantly affected by gender contrasts in PRO.

REFERENCES
ILEAL BUT NOT COLONIC INFLAMMATION IS LINKED TO FATTY LESIONS ON MRI OF THE SACROIACIAL JOINTS IN SPONDYLOARTHRITIS PATIENTS

Background: Gut and joint inflammation in spondyloarthritis (SpA) are closely intertwined. About 50% of axial SpA patients display microscopic signs of inflammation in ileum and/or colon, a risk factor to develop Crohn’s disease over time. It is currently not known if presence of microscopic gut inflammation in new onset SpA is associated with more structural lesions on magnetic resonance imaging of the sacroiliac joints (MRI-SIJ) and whether these lesions relate to the localization of gut inflammation.

Objectives: To assess whether structural lesions on MRI-SIJ (A) are associated with microscopic gut inflammation in SpA patients and (B) are preferably related to colon or ileum inflammation in case of gut involvement.

Methods: We analyzed baseline information from the Be-Giant cohort, a registry of SpA patients fulfilling the Assessment of SpondyloArthritis international Society (ASAS) classification criteria for axial or peripheral SpA. MRI-SIJ was scored by 3 readers, blinded for subject characteristics. Six consecutive slices were assessed for structural lesions: sclerosis, erosions, fatty lesions and (partial) ankylosis. MRI sum scores were analyzed as 2 out of 3 (median) scores. Colon and ileum biopsies were evaluated for microscopic signs of inflammation. The effect of gut inflammation (colon and/or ileum) on MRI-SIJ lesions was investigated by general linear models (GLM), adjusted for age and gender and stratified for the SpA phenotype.

Results: By January 2019, baseline data were available on 105 patients (95 axial and 10 peripheral SpA). Gut inflammation was present in 35 patients (17 ileum, 8 colon, 10 both). Table 1 shows the slope (β1) of the GLMs for erosions, fatty lesions, sclerosis and (partial) ankylosis and the p-value for the SpA phenotype as an interaction term. Erosions, sclerosis, nor ankylosis show a significant association with gut inflammation in general. If present, colon inflammation has no significant relationship with each individual structural lesion. In contrast, presence of ileum inflammation was associated with an increase in the number of fatty lesions by 0.68 (95%CI 0.04 – 1.38). All results are independent of the SpA phenotype (p = 0.05).

Conclusion: Ileal but not colonic inflammatory gut lesions are linked to more fatty lesions on MRI-SIJ in newly diagnosed SpA patients. Baseline microscopic gut inflammation was not associated with erosions, sclerosis nor ankylosis. These data support the concept that microscopic gut inflammation was not associated with erosions, sclerosis and (partial) ankylosis. These data support the concept that microscopic gut inflammation in new onset SpA is associated with more structural lesions on magnetic resonance imaging of the sacroiliac joints (MRI-SIJ) and whether these lesions relate to the localization of gut inflammation.

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SAT0313

SAT0314

IMPLEMENTATION OF AN ASSESSMENT CHECKLIST FOR PATIENTS WITH SPONDYLOARTHRITIS IN DAILY PRACTICE

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Background: Nowadays, despite international and national guidelines on the evaluation and management of spondyloarthritis (SpA), several studies have depicted a sub-optimal assessment of these diseases.

Objectives: To analyze the feasibility and changes in the collection of clinical measures after the implementation of a checklist designed for an optimal evaluation and monitoring of patients with SpA, including psoriatic arthritis (PsA).

Methods: An observational prospective study was performed. The feasibility of the assessment checklist (paper/on-line format) for patients with SpA was tested (time to complete the checklist, simplicity, amenability, clarity, usefullness). Through a medical files review, changes in the number of the checklist variables collected were analyzed previously to the implementation of the checklist and 6 months later. A descriptive and bivariate analysis was performed.

Results: A total 6 hospitals and 11 rheumatologists participated. The median time to checklist completion was 15 (12-20) minutes, and the mean scores for the rest of variables of the feasibility test were in general positives, 6.9±1.1 (simplicity) and 6.9±0.8 (amenity), to 7.5±1.2 (clarity) and 7.5±1.4 (usefullness). A total of 83 and 68 medical files pre-implementation and post-implementation were reviewed respectively. Patient’s features were similar. Mean age at diagnosis was 42.3±1.6 and 40.3±1.3 years respectively. In both study samples around a half of patients were men, and 20% (extra-articular symptoms) to 30% (diabetes mellitus, hyperlipidemia, gout/hyperuricemia and renal failure). Other checklist variables increased but not significantly. However, some of them like the HLA-B27 and signs or arterial hypertension) to 30% (diabetes mellitus, hyperlipidemia, gout/hyperuricemia and renal failure). Other checklist variables increased but not significantly. However, some of them like the HLA-B27 or work status were already recorded (before the implementation of the checklist) in the 82.3% and 95.2% of medical files respectively. Changes were observed irrespecitively of SpA classification.

Conclusion: The implementation of an assessment checklist in daily practice is feasible and improve the assessment of SpA patients.

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Disclosure of Interests: RAQUEL ALMODOVAR: None declared, Beatriz Joven-Ibarzéz Speakers bureau: Celgene, Novartis, MSD, Pfizer, Abbvie, and Janssen, Esther Rodríguez Almaraz: None declared, Sheila Melchor: None declared, Erieta Rabadán: None declared, Virginia Villaverde: None declared, Mª Teresa Navio: None declared, Laura Cebrian: None declared, Laura González: None declared, Álvaro García Martos: None declared, Victoria Navarro-Complejo: None declared, Estíbaliz Loza: Research support from: Roche, MSD, Pfizer, Abbbvie, BMS, UCB, Actelion, Celgene, Genentuchel and Sanofi, Pedro Zarco-Montejo: None declared


Table 1: Association between MRI-SIJ structural lesions and gut inflammation in SpA patients.

<table>
<thead>
<tr>
<th>Structural lesion</th>
<th>Gut inflammation</th>
<th>β1</th>
<th>95% CI</th>
<th>p-value</th>
<th>p-value interaction term*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon and/or ileum</td>
<td>0.02 (0.39 – 0.53)</td>
<td>0.92</td>
<td>0.03</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Erosions</td>
<td>0.08 (0.56 – 0.75)</td>
<td>0.45</td>
<td>0.03</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatty lesions</td>
<td>0.22 (0.04 – 0.88)</td>
<td>0.22</td>
<td>0.01</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sclerosis</td>
<td>0.05 (0.38 – 0.60)</td>
<td>0.03</td>
<td>0.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Partial)</td>
<td>0.27 (0.02 – 0.60)</td>
<td>0.04</td>
<td>0.02</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ankylosis</td>
<td>0.10 (0.04 – 0.30)</td>
<td>0.22</td>
<td>0.01</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*SpA subtype (axial versus peripheral SpA) as an interaction term.
Background: Ankylosing spondylitis (AS) is an inflammatory disease resulting in progressive disability due to structural damage in the spine. The identification of predictors of progression would allow treating physicians to personalize treatments but requires an approach accounting for a relatively short follow-up of clinical studies, large between-patient variability, and low sensitivity of X-ray images which generate intra-patient variability when repeated measurements are taken.

Objectives: 1) To identify patient characteristics predicting faster structural damage progression. 2) To quantify the progression over four years of secukinumab treatment, depending on dose/exposure.

Methods: Data came from the phase 3 randomized placebo-controlled trial MEASURE 1 (NCT01358175) in which patients were treated with secukinumab (intravenous loading of 10 mg/kg at weeks 0, 2, and 4, followed by secukinumab subcutaneously at a dose of either 75 mg or 150 mg every 4 weeks) over 208 weeks. Only patients treated with secukinumab with at least two assessments of structural damage were included. We explored the effect of multiple baseline demographic traits, disease stage, severity, bone cartilage biomarkers as well as prior and current treatment on change in noninvolved Spine Spondylitis Score (mSASSS) using a longitudinal Bayesian mixture model with random effects, which accounted simultaneously for the probability of progression, magnitude of progression, and inter-patient variability. Posterior predictive check was performed.

Results: Out of 249 patients randomized to secukinumab, 167 had their structural damage assessed at least twice. These patients contributed in total 409 assessments of change in structural damage between weeks 0, 52, 104 and 208. Of the factors tested, a higher baseline BASMI score was associated with faster progression rate in a statistically significant way (0.60 in mSASSS/year for each additional standard deviation of baseline BASMI (SD=1.74), 95% interval 0.03 to 1.14). Trends were also detected for association between faster mSASSS progression and younger age, prior exposure to TNF inhibitor, HLA-B27 positivity, and higher osteocalcin levels. Increased exposure to secukinumab was associated with slower structural damage progression (-0.23 in mSASSS/year for each additional standard deviation in exposure, 95% interval -0.58 to 0.10). Model estimation suggested that secukinumab 150 mg was associated with a yearly progression of -0.2 (95% interval -1.2 to 0.8) in the first two years of treatment and 0.1 mSASSS (95% interval -0.3 to 1.0) in the third and fourth year of treatment. Analogously, secukinumab 75mg (currently not approved for clinical use) was associated with a progression of -0.2 mSASSS/year (95% interval -1.3 to 0.9) in the first two years of treatment and 0.5 mSASSS/year (95% interval -0.5 to 1.6) in the third and fourth year of treatment.

Conclusion: Potential predictors of structural progression suggested by the model were higher baseline BASMI, younger age, prior exposure to TNF inhibitor, HLA-B27 positivity, and higher osteocalcin at baseline, although only baseline BASMI showed statistical significance. Further analyses using larger, deeper and real-world data are needed to confirm these findings and to estimate progression rates in AS patients in daily practice.

REFERENCE
INCIDENCE OF EXTRA-ARTICULAR MANIFESTATIONS IN ANKYLOSING SPONDYLITIS, PSORIATIC ARTHRITIS AND UNDIFFERENTIATED SPONDYLOARTHRITIS – RESULTS FROM A NATIONAL REGISTER-BASED COHORT STUDY

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Background: Spondyloarthropathies (SpA), including ankylosing spondylitis (AS), psoriatic arthritis (PsA) and undifferentiated SpA (uSpA), are all to varying degrees associated with extra-articular manifestations (EAMs).

Objectives: To estimate incidence rates (IRs) for EAMs (anterior uveitis, inflammatory bowel disease and psoriasis) in patients with AS, PsA and uSpA, respectively.

Methods: In this nationwide cohort study, three separate cohorts of patients aged 18 to 69 years with AS (n=8517, 66% men, mean age 47 ±13 years), PsA (n=22667, 46% men, mean age 49±12 years) and uSpA (n=10245, 44% men, mean age 42±13 years) were identified 2001-2015 in the Swedish National Patient Register (NPR). The follow-up began 1 January 2006 and ended at the first date of EAM, death, emigration or 31 December 2016, respectively. Patients with a prior EAM in NPR before start of follow-up were excluded from that specific analysis.

Results: The IRs for each EAM are presented in Table 1. The overall highest IRs were noted for anterior uveitis in patients with AS (14.4 (13.2-15.5) per 1000 person-years at risk). Patients with PsA had considerably lower IRs for anterior uveitis (1.7 (1.5-1.9) per 1000 person-years at risk) and slightly lower IRs for IBD than patients with AS and uSpA. The IRs for anterior uveitis were significantly higher in men than in women in both AS and uSpA.

Conclusion: IRs for EAMs clearly differed between the SpA subtypes, and especially for anterior uveitis where the IRs were by far highest in patients with AS and uSpA compared to patients with PsA.

Disclosure of Interests: Karin Bengtsson: None declared, Helena Forsblad-Delia Consultant for: Unrestricted grants from Novartis outside the submitted work, Consultant for: Advisory board fees from SANDOZ, Novartis and Abbvie, Speakers bureau: Lecturing fees from Novartis, Eva Klingberg Consultant for: Karolinska Institutet had research agreements with the following pharmaceutical companies, mainly in the context of the ATRIS national safety monitoring programme for rheumatology biologics: Abbvie, BMS, MSD, Eli Lilly, Pfizer, Roche, Samsung Bioepis, and UCB, Consultant for: Karolinska Institutet has received remuneration for JA participating in ad boards arranged by Lilly, Novartis, and Pfizer., Lennart T.H. Jacobsson Consultant for: LJ has received lecture and consulting fees from Pfizer, Abbvie, Novartis, Eli-Lilly and Janssen

pattern (41.3% and 34.9%), fatigue (35.3% and 28.6%), and loss of interest in sex (21.7% and 21.9%), for AS and PsA, respectively. In univariate analysis (Table 1), female gender (OR=1.73), unemployment due to disability (OR=3.06) or other reasons (OR=2.38), increased BASDAI (OR=1.53), increased BASFI (OR=1.17), and increased morning stiffness (OR=1.01) were significantly associated [all P<0.001 except gender (P=0.009)] with baseline depression among AS patients. For PsA, significantly associated parameters included female sex (OR=2.35; P=0.001), unemployment due to disability (OR=3.57; P=0.001), increased TJC (OR=1.05; P=0.009), increased PGA (OR=1.03; P=0.001) and increased morning stiffness (OR=1.01; P=0.010). Weak correlations (P<0.05) were observed between the BDI score and BASFI (r=0.425), BASDAI (r=0.375), morning stiffness (r=0.285), and number of EAMs (r=0.014) for AS; and TJC (r=0.155), MDGA (r=0.132), and PGA (r=0.451) for PsA. In multivariate regression analysis for AS, higher BASFI (OR=1.32; P=0.001), female sex (OR=1.89; P=0.007) and being unemployed due to other reasons (OR=1.91; P=0.017); and, for PsA, lower baseline disease duration (OR=0.97; P=0.018), and higher PGA (OR=1.04; P=0.001) were identified as significant independent predictors of baseline depression.

Conclusion: Depression in AS and PsA patients was common in this real-world cohort. Female sex, unemployment, and higher disease activity for AS, and shorter disease duration along with higher PGA for PsA were significant independent predictors of depression.

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SAT0319

OBESITY AND ASSOCIATED FACTORS IN NORWEGIAN AXIAL SPONDYLOARTHRITIS PATIENTS. RESULTS FROM THE EUROPEAN MAP OF AXIAL SPONDYLOARTHRITIS SURVEY

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Background: Obesity increases the risk of developing chronic inflammatory diseases, including axial spondyloarthritis (axSpA). Information about how obesity correlates with disease activity in axSpA patients is limited.

Objectives: The objective of this survey was to investigate the association between body mass index (BMI) and patient reported disease activity in Norwegian axSpA patients.

Methods: The European Map of Axial Spondyloarthritis (EMAS), conducted from July 2017 to February 2018, was a cross-sectional on-line survey of 2,846 unselected patients with self-reported axSpA from 13 European countries (Austria, Belgium, France, Germany, Italy, Netherlands, Norway, Russia, Slovenia, Spain, Sweden, Switzerland, and the UK). Participants were recruited through an on-line panel and patient organizations. This analysis is based on data from the 509 Norwegian respondents. Sociodemographic variables (age, gender, BMI, comorbidity), and disease related variables (Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) (0-10), self-reported spinal stiffness (3-12) and General Health Questionnaire (0-12) (GHQ-12) were reported.

Results: Out of the 509 Norwegian participants with axSpA, 69.7% (N=355) were women. The mean age was 48±12 years, mean disease duration was 5.3±2.0 years, 82.3% were HLA-B27 positive, and 55.2% (N=281) were university educated. In total, 35% (N=180) of the participants were normal/underweight (BMI < 25) and 65% (N=329) were overweight/obese (BMI ≥ 25). The mean (sd) disease activity, as measured by BASDAI (0-10), was 5.3±2.0. Overweight/obese patients reported significantly higher disease activity (BASDAI 5.5±1.9) compared to normal weight patients (BASDAI 5.0±2.1). Moreover, being overweight/obese was associated with a significantly higher degree of spinal stiffness, number of comorbidities and a numerically, but not significantly, higher GHQ-12 score. There was no significant differences in alcohol consumption, smoking, or prevalence of inflammatory bowel disease (Crohn’s disease or ulcerative colitis).

Conclusion: Norwegian overweight/obese axSpA patients from the EMAS survey reported significantly higher disease activity, spinal stiffness and number of comorbidities. The results highlight the serious impact of overweight and obesity on the health status of axSpA patients. Therefore, obesity should be considered as a preventable risk factor and within the disease management of axSpA.

REFERENCES


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Disclosure of Interests: Christian Bindsøe: Employee of: I currently work in Novartis Pharma AG Norway as listed in my affiliations, Marco Garrido-Cumbraa Consultant for: Honoraria from Novartis as steering committee member for this survey, Hanne Solvag Dagnærud Consultant for: Honoraria from Novartis as a steering committee member on this survey


SAT0320

FREQUENCY AND CHARACTERISTICS OF INFLAMMATORY BOWEL DISEASE IN SPONDYLOARTHRITIS WITH BIOLOGICAL THERAPY. STUDY OF 270 PATIENTS FROM THE SAME CENTER

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Background: Inflammatory bowel disease (IBD) is an extra-articular manifestation that can appear in spondyloarthritis (SpA), as well as uveitis and psoriasis. Its prevalence is 5-10%, although subclinical intestinal inflammation has been found in up to 60%. Biological therapy (BT) can be the treatment for IBD or produce it paradoxically. Fecal calprotectin (FC) is an intestinal inflammation marker, useful for early diagnosis and monitoring disease activity.

Objectives: To describe the frequency and characteristics of IBD in SpA with BT.

Methods: Descriptive and retrospective study (January 2003-January 2019) of patients with SpA that develop IBD in a single center. Epidemiological variables, type of SpA, presence of IBD and its characteristics, levels of FC, presence of BT at IBD onset and treatment received were registered. For the analysis, frequencies and percentages were used in qualitative variables and mean/standard deviation (SD) in quantitative. Statistical analysis was performed with IBM SPSS v.23.

Results: We studied 270 patients with SpA, 70.4% male with a mean age of 39.9±12 years. The subtypes of SpA were: ankylosing spondylitis (AS) (n=133; 49.3%), psoriatic arthritis (PsA) (n=116; 43%), undifferentiated SpA (n=16; 5.9%), SpA non-Rx axial (n=3; 1.1%) and reactive arthritis (n=2; 0.7%).

IBD was observed in 25 patients (9.26%), 80% male. At the time of IBD onset, they had a mean age of 39.1±9.8 years, the mean ESR was 31.15±24mm/1hr, CRP 2.7±2mg/dl and BASDAI 4.6. 16 patients had AS, 6 PsA and 3 undifferentiated SpA. TABLE 1.

Regarding SpA diagnosis, IBD appeared after in 15 patients with an average time of development of 8.39±2 years, before in 7 and was simultaneous in 3. The subtypes of IBD were: Crohn’s disease (CD) in 7 patients, ulcerative colitis (UC) in 1 and indeterminate colitis (IC) in 3. The FC was > 200µg/g in 17 patients (68%), normal (<50µg/g) in 1 and between 50-200µg/g in 7. The incidence rate adjusted for follow-up of the 25 cases was 7.7 cases/1000 patients-years.

At the time of the IBD onset, 6 patients were with BT: Etanercept (ETN) (n=2), Infliximab (IFX) (n=1), Adalimumab (ADA) (n=1), Secukinumab (SOK) (n=1) and Ustekinumab (UST) (n=1). The BT had been initiated the previous 12 months in 5 of them. The incidence rate adjusted for follow-up of the 6 cases of IBD after BT was 1.83 cases/1000 patient-years. TABLE 2.

The treatment of the 25 patients with IBD was mesalazine (n=15), oral corticoid (n=5), methotrexate (n=7) and BT in all cases. The BT was:
CARDIOVASCULAR EVENTS IN SPONDYLOARTHRITIS: AXSPA PATIENTS WITH SYMPTOM ONSET <30 YEARS

In Ah Choi.

To compare risks for cardiovascular disease including myocardial infarction (MI), ischemic heart disease (IHD), stroke and mortality of patients with SpA compared to general population using large-scale data. These findings support the reduction of inflammation as well as the management of traditional cardiovascular disease risk factors may reduce CV risk in patients with spondyloarthritis.

TABLE 1. CHARACTERISTICS OF ISD IN SPA SUBTYPES

- **Method:** A systematic search was performed in MEDLINE, EMBASE with additional manual searches for studies associated with spondyloarthritis including 13 anklyosing spondylitis (AS) studies, 3 psoriatic arthritis (PsA) studies and 1 undifferentiated spondyloarthritides study. A meta-analysis result showed a significant increase in the risk of MI (RR= 1.38; 95% CI 1.18 to 1.61), and stroke (RR= 2.04; 95% CI 1.11 to 3.78) in spondyloarthritis patients compared to general population. However, mortality related with cardiovascular disease (RR=1.19; 95% CI 0.96 to 1.48) and total mortality (RR= 1.31; 95% CI 0.8 to 2.15) results did not show significant increases in spondyloarthritis patients.

Conclusion: Our meta-analysis results showed that the risk of MI and stroke significantly increased although mortality associated with cardiovascular (CV) disease and overall mortality did not increase in spondyloarthritis compared to general population.

REFERENCES

Disclosure of Interests: None declared

SAT0322
AXSPA PATIENTS WITH SYMPTOM ONSET <30 YEARS HAVE MORE STRUCTURAL LESIONS ON MRI OF THE SACROILIAC JOINTS WHEN FULLFILLING THE MODIFIED NEW YORK CRITERIA

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Background: The modified New York criteria (mNY) combine clinical symptoms with radiographic sacroiliitis on conventional pelvic radiographs (X-SI) classifying radiographic axial SpA patients (r-axSpA). AxSpA is known to typically start in the third era of life but there is a diagnostic delay of ±7 years. As the mNY criteria classify the most typical and severe expression of axSpA it is suggested that the mNY criteria are less useful in younger patients.

Objectives: To explore the diagnostic utility of the mNY criteria in newly diagnosed axSpA patients with a symptom onset <30 years. In addition, describe the extent of lesions on MRI of the sacroiliac joints (MRI-SI) in mNY positive (mNY+) patients with a symptom onset <30 years.

Methods: This study involved newly diagnosed axSpA patients, age ≥18 years, from a Belgian (Be-Giant) cohort. Patients underwent diagnostic tests involving clinical examination, lab tests, and imaging assessment containing an X-SI and an MRI-SI. mNY criteria was assessed on X-SI, MRI-SI reads contained the assessment of inflammatory lesions according to the Spondyloarthritides Research Consortium of Canada (SPARCC) scoring method and erosions, fatty lesions (FL), sclerosis, ankylosis using an adapted method of the SPARCC. Also, the ASAS definition of a positive MRI-SI was evaluated. T1-weighted and STIR images were viewed simultaneously. X-SI and MRI-SI were evaluated independently by 3 trained readers who were also blinded for clinical features. Imaging scores (X-SI grading according to the mNY criteria and MRI-SI grading, and MRI-SI lesion scores) were calculated as 2 out of 3 reader scores.

Results: In the 173 patients available X-SI, the average age at symptom onset was 27.4 years old. In 114/173 (65.9%) patients, the symptom onset was below 30 years. Of those, 11 (9.6%) patients fulfilled the mNY criteria. Seven of the 11 (63.6%) patients that were mNY+ were male, which was slightly lower than in the mNY- patients (n=55; 53.4%). The presence of MLA-B27 was comparable between mNY+ and mNY- patients: 8 (72.7%) patients and 82 (79.6%) patients, respectively. Average X-SI grading in mNY+ patients was 4.7±1.3 (on a scale from 0-8) and in mNY- negative (mNY-) patients (n=103) the average X-SI grading was 1.1±1.1. When looking at the MRI-SI assessment, 8/11 mNY+ patients.
Hepatocyte growth factor is a predictor of development of new syndesmophytes in men with ankylosing spondylitis. A five-year prospective study

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Background: Patients with ankylosing spondylitis (AS) have an increased risk of new bone formation characterized by the development of syndesmophytes. Knowledge of predictors for development of syndesmophytes is limited. Hepatocyte growth factor (HGF) has regulatory effects on a variety of cells in many different organs. HGF signaling can affect both osteoclast and osteoblast lineages and has been shown to promote osteogenesis. Cross-sectional association between increased HGF and increased modified Stoke Ankylosing Spine Score (mSASSS) has previously been shown [1], whereas knowledge of HGF as a predictor for new bone formation is lacking.

Objectives: To study serum HGF as a predictor for development of new syndesmophysetes in patients with AS followed for five years.

Methods: Serum levels of HGF was analyzed using ELISA in patients with AS (modified NY criteria) and in healthy controls (HC) at baseline. Spinal lateral radiographs were obtained at baseline and at the 5-year follow-up in patients with AS followed for five years.

Results: Serum HGF and radiographs at baseline and follow-up were available for 163 patients, 88 men and 75 women, baseline mean age 50±12 years. AS patients had higher serum HGF than HC (n=80), p=0.005. In the AS group, 36 patients (22%) developed ≥1 syndesmophytes after 5 years. The baseline serum HGF of patients with ≥1 new syndesmophyte differed between those who developed ≥1 new syndesmophyte and those who did not progress, p=0.13. The baseline serum HGF of patients with ≥1 new syndesmophyte and those who did not progress, nor did it predict development of ≥1 new syndesmophyte in the univariate analysis, p=0.25. Interestingly, men who developed ≥1 new syndesmophyte had higher serum HGF than the non-progressors (1706±145 vs 1420±338 pg/mL, p=0.001) and increased serum HGF at baseline predicted development of ≥1 syndesmophyte (OR per 1 SD HGF 2.39, 95% CI 1.31 to 4.36) in the univariate analysis. Serum HGF did not predict new syndesmophysetes in women, p=0.13. Multivariable analysis for men including age, smoking, baseline syndesmophysete and serum HGF showed high HGF (OR per 1 SD 1.90, 95% CI 1.01 to 3.59) and ≥1 baseline syndesmophyte (OR 3.48, 95% CI 1.09 to 11.07) to independently predict development of ≥1 new syndesmophyte. If baseline CRP was included in the multivariable model, serum HGF and baseline syndesmophysete remained the significant predictors.

Conclusion: High baseline serum HGF was shown to independently predict the development of at least one new syndesmophyte over five years in men with AS.

References


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Scientific Abstracts

SAT0324 ARTICULAR MANIFESTATIONS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE TREATED WITH VEDOLIZUMAB

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Background: Vedolizumab (VDZ) is a humanized IgG1 monoclonal antibody anti-a4β7 integrin agent used in inflammatory bowel disease (IBD). It has been incriminated in occurrence of articular manifestations but, as it is given in most cases after anti-TNF therapy, it is not known if these articular manifestations are linked to IBD-associated arthritis and unmasked by withdrawal of anti-TNF or are more directly linked to VDZ.

Objectives: The purpose of this study is to describe articular manifestations occurring in patients treated by vedolizumab, and to highlight risk factors for inflammatory manifestations.

Methods: In this retrospective monocentric study, we collected all the cases of incident articular manifestations occurring in the follow-up of the patients treated by VDZ for IBD.

Results: Between February 2013 and June 2017, 112 patients were treated with vedolizumab (56 women, age 39.9 ± 16 years, disease duration ≥ 9.1 ± 7.8 years). IBD cases were distributed into59 (52.7%) Ulcerative Colitis (UC), 49 (43.8%) Crohn’s disease (CD), and 4 (3.6%) Undetermined Colitis. Four patients (3.6%) had a history of spondyloarthritis and 13 (11.6%) of peripheral arthralgia associated with IBD. 102 (91.1%) patients previously received anti-TNFα. At initiation of vedolizumab, 55 (49.1%) received an associated DMARD (azathioprine in 19.6%, methotrexate in 7.1%).

After a mean follow up duration of 11.4 ± 8.6 months, 32 (28.6%) patients presented 35 types of articular manifestations, mechanical (n = 18) (mostly osteoarthritis and tendinosis) or inflammatory (n = 17). Inflammatory articular manifestations were: early reversible arthralgia mostly occurring during perfusion (n = 5), manifestations linked to IBD (n = 11), axial spondyloarthritis, n = 3, peripheral spondyloarthritis, n = 3,
SAT0325 REDUCED STRAIN AND INCREASED STIFFNESS OF COMMON CAROTID ARTERIES IN PATIENTS WITH ANKYLOSING SPONDYLITIS
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Background: Ankylosing spondylitis (AS) is associated with an increased risk of cardiovascular disease (CVD) which also contributes to the increased mortality observed in AS. It is therefore important to develop non-invasive, accurate methods for early detection of atherosclerotic vascular changes.

Objectives: The aim of the present study was to compare arterial stiffness and distensibility in patients with AS and age-sex-matched controls. The arterial stiffness can be examined by ultrasound. The arterial distensibility is defined by the linear regression of the radial arterial pressure and the corresponding change in arterial radius (distensibility index).

Methods: Three hundred and sixty-six patients were enrolled in the study from the Department of Rheumatology at Umeå University, Sweden during the years 2017-2019. The control group consisted of 60 age- and sex-matched patients. The mean age was 50.4 ± 10.2 years in AS patients and 52.9 ± 9.9 years in controls (p = 0.002).

Results: The circumferential systolic strain was measured and the beta stiffness index was calculated. The patients with AS had lower mean systolic circumferential strain and lower stiffness index with p < 0.05.

Conclusions: Our findings suggest that ultrasound methods can be used to evaluate the arterial wall at an early stage of AS. This may be used in the clinical setting to diagnose subclinical CVD.

SAT0326 PLANS FOR MOTHERHOOD ARE CHANGED AFTER DIAGNOSING ANKYLOSIS SPONDYLITIS (AS), AS FEMALE PATIENTS’ ATTITUDE TO THE USE OF AS MEDICATIONS DURING PREGNANCY PLANNING AND CONCEPTION
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Background: Plans for motherhood are changed after diagnosing ankylosis spondylitis (AS). AS female patients’ attitude to the use of AS medications during pregnancy planning and conception.

Objectives: To describe the impact of diagnosis of AS on women’s plans to have children, and patients’ attitude to continuing AS therapy while planning pregnancy or after definite conception.

Methods: 302 AS female patients participated in the survey conducted from May to November 2018. Patient’s mean age was 32.4±5.0 years, average AS duration from onset of symptoms was 10.2±7.4 years. 224 (74.2%) respondents had higher education, 68 (22.5%) college education and 10 (3.3%) vocational college education.

Results: 206 women (68.2%) have changed their attitude to potential pregnancy occurring during AS: – 12 (5.8%) were firmly set to terminate an unplanned pregnancy; – 21 (10.2%) were against getting pregnant, although they yet haven’t had children; – 164 (79.6%) accepted potential pregnancy, although recognizing they would experience continuous emotional discomfort and fear for their own health and health of the unborn child. – 42 (13%) women were distinctly against getting pregnant in case they have AS.

There was a weak inverse correlation between AS status and changing patients’ attitude to pregnancy (R=0.14, p<0.05). 150 (49.7%) respondents discussed pregnancy planning with a rheumatologist. Women with university degree were more likely to consult a rheumatologist before trying for a baby compared to subjects with vocational college and secondary education (55.5%, 35.3% and 40%, respectively; p=0.02), 53 (35.3%) patients failed to receive a comprehensive answer to their questions related to AS and pregnancy mutual influence, the probability of AS inheritance by a child, safety of AS therapy at conception.
and during pregnancy; moreover, in 4 cases AS was interpreted as con- 
traindication to pregnancy. 107 (35.4%) respondents believe that AS medications should be discon- 
tinued during pregnancy planning and conception, 75 (24.8%) subjects 
accepted possible use of AS therapy during this period, while 120 
(39.8%) didn’t know the answer. 15.2% of respondents were ready to 
continue on NSAIDs, 20 (6.6%) – on glucocorticoids and sulfasalazine, 
and 21 (7%) – on biological drugs (GEBD). Of those who are ready to 
continue on AS medications at conception, 46 women (61.3%) consulted 
pregnancy planning with a rheumatologist. Respondents with higher edu- 
cation were slightly more likely to continue on AS therapy at conception 
(29%) compared to women with vocational college education (11.8%). 
Age, duration of disease, presence of spondylitis, attitude of patients’ attitude 
towards AS therapy during pregnancy planning and conception.

Conclusion: The majority of surveyed female patients changed their atti- 
tude to pregnancy after establishing AS diagnosis, although only 13% of them 
were recommended to AS therapy. No more than 50% of respondents were consulted a rheumatologist before planning pregnancy, 
and up to one third of them were not receive all expected answers to 
their questions and recommendations. Only 1/4 of participants accept the idea of continuing AS therapy during pregnancy planning and conception.

Disclosure of Interests: None declared


SAT0327 SEGMENタル RELATIONSHIP BETWEEN MOBILITY, 
STRUCTURAL DAMAGE AND DISEASE ACTIVITY IN 
AXIAL SPONDYLOARTHRITIS

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Background: Axial Spondyloarthritis (axSpA) is characterised by progres- 
sive loss of spinal mobility, due to inflammation and structural damage. Conventional mobility tests have been used alongside radiographic struc- 
tural damage and disease activity scores in order to explore the overall 
relationship between spinal mobility, structural damage and disease activ- 
ity. This has rarely been done at the segmental level e.g. at the level of the 
lumbar spine only. The ViMove inertial motion sensor-based system 
allows segmental spinal mobility to be directly measured, namely at the 
lumbar spine level.

Objectives: To analyse the relationship between mobility, structural dam- 
age and disease activity in the lumbar spine of patients with axSpA.

Methods: Lumbar spinal mobility was measured using the the ViMove 
system with a pair of sensors located at L1 and the sacrum. Lumbar ROM in the three planes (anterior flexion - LFF, extension - LFE, lateral 
flexion – LL, and rotation - LR) was measured. Radiographs were 
obtained to calculate the lumbar part of the mSASSS (LmSASSS). Other 
outcome measures were: BASMI, Schober and lateral flexion (measured 
with a tape), BASDAI and ASDAS-CRP. Subgroups of patients with high 
and low levels of lumbar structural damage were defined, by dichotomis- 
ing the population based on the median LmSASSS (5.5). Pearson corre- 
lations between measures, Student T tests for significant differences 
between models and fitted values (RMSE) were 3.8 units for 
LmSASSS and 7.7° for LFF.

Conclusion: Other studies have shown a relationship between mobility, 
structural damage and disease activity using a more global assessment.

Other studies have shown a relationship between mobility, 
structural damage and disease activity using a more global assessment.

Sociodemographic, disease outcomes and psychological 
associations with sociodemographic, disease outcomes and psychological 
distress were not significantly different between these groups. LmSASSS corre- 
lated (p<0.001) with all mobility measures obtained by IMU system and 
conventional metrology, especially with LFF, but not with activity indexes. 
Only a weak relation between BASDAI and LFE was found (p<0.05). A linear 
regression for analysing relationship between LmSASSS and LFF 
including as variables: age, sex, disease activity, BMI, LFE, LFF, 
therefore a LmSASSS linear regression using only LFF obtained an adjusted R2 of 0.72 (Figure-A). Introducing the rest 
of variables, the most significant for LmSASSS was LFF (p<0.001) and 
the other mobility measures (LL, LR with p<0.05) and age, PCR and 
ASDAS (p<0.01) with an adjusted R2 of 0.81(Figure-B). For LFF, 
LmSASSS was the most significant (p<0.001), with Sex (p<0.01) and 
PCR (p<0.05) included, obtaining an adjusted R2 of 0.76 (Figure-C). 
Differences between models and fitted values (RMSE) were 3.8 units for 
LmSASSS and 7.7° for LFF.

Conclusion: Other studies have shown a relationship between mobility, 
structural damage and disease activity using a more global assessment.

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lada Concepcion Aranda-Valera: None declared. Cristina Gonzalez-Navas: 
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vie, BMS, Celgene, Janssen, MSD, Novartis, Pfizer, Roche and UCB, 
Philip Gardiner: None declared, Joan Condell: None declared, Eduardo 
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SAT0328 PATIENT-REPORTED ATTITUDES TOWARDS AXIAL 
SPONDYLOARTHRITIS: RESULTS FROM THE EMAS 
SURVEY

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Rheumatism, Nicosia, Cyprus; 8Hospital Universitario La Paz, IDIAP, Madrid, Spain; 9Cardiff 
University, Cardiff, United Kingdom; 10Ankylosing Spondylitis International Federation (ASIF), 
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Background: Understanding patient disease-related attitudes plays an 
important role in effective management of axial spondyloarthritis (axSpA).

Nevertheless, the patient perspective remains insufficiently explored.

Objectives: To describe patients’ axSpA-related fears and hopes and their 
associations with sociodemographic, disease outcomes and psychological 
distress.

Methods: The European Map of Axial Spondyloarthritis (EMAS), 
conducted from July 2017 to February 2018, was a cross-sectional on-line 
survey of unselected patients with self-reported axSpA from Austria, Bel- 
gium, France, Germany, Italy, The Netherlands, Norway, Russia, Slovenia, 
Spain, Sweden, Switzerland, and the UK. Participants were recruited 
through an online panel and patient organizations. Participant’s axSpA- 
related fears and hopes were freely expressed through open-ended ques- 
tions (except in France where multiple-choice items were used). Thematic 
analysis, using the French categories and data-driven codes, was per- 
formed and frequencies of specific fears and hopes were subsequently 
calculated. Associations between disease-related fears and hopes with 
sociodemographic characteristics, disease outcomes (BASDAI, self-reported 
spinal stiffness and functional limitation), and psychological distress (Gen- 
eral Health Questionnaire, GHQ-12; with a cut-off point of ≥5) were 

<table>
<thead>
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<th>N</th>
<th>Flexion</th>
<th>Extension</th>
<th>Lateral</th>
<th>Rotation</th>
<th>LmSASSS</th>
<th>BASMI</th>
<th>ASDAS</th>
<th>BASDAI</th>
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<td>10.5(13.4)</td>
<td>42.7(17.0)</td>
<td>24.8(8.8)</td>
<td>8.0(9.7)</td>
<td>3.0(1.9)</td>
<td>1.9(1.1)</td>
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<tr>
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<td>22</td>
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<td>12.7(16.9)</td>
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<tr>
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<td>22</td>
<td>39.6(13.7)</td>
<td>7.7(9.1)</td>
<td>35.1(12.0)</td>
<td>21.1(8.4)</td>
<td>14.2(10.5)</td>
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</tbody>
</table>
Axial Spondyloarthritis (axSpA) has an impact on daily life, but data in the biologics era are scarce.

Objectives: To assess the patient-reported impact of axSpA on social and family life.

Methods: Between December 2017 and February 2018, patients followed for axSpA by their rheumatologists or affiliated to the French patients association AFLAR, and self-reporting axSpA, participated in the European Map of Axial Spondyloarthritis (EMAS) cross-sectional patient survey in France. Socio-demographics and disease characteristics were collected and the impact of axSpA on personal life was evaluated through a questionnaire established by an international committee on social interactions (better/worse), frequency of social activities (less or more frequent), patient fears and the impact of flares on 10 aspects of daily life evaluated as no/low to moderate/severe. No imputation of missing data was performed and the analyses were descriptive.

Results: Data from 638 persons, mean age 41.5±11.1 years, 77% women, mean disease duration 6.9±9.2 years, 19.1% on biologics, were analyzed. The disease (axSpA) was often active (mean BASDAI: 5.9±1.7). Social interactions were reported as worse or much worse since axSpA: with friends (43%), work colleagues (39%), spouse (35%), and family (31%). AxSpA had also an impact on the frequency of social and sport activities, which were «much less frequent than before» for sport activities, «less frequent» for sport activities, and «less frequent than before» for social activities. The most frequent fears of patients were «fear of disease progression» (32.9%), «suffering pain» (30.5%), and «loss of mobility» (30.0%). Accordingly, the most frequent hopes were «improving mobility» (33.2%), «eliminating pain» (32.5%), and «effective treatment» (23.3%).

Conclusion: Axial Spondyloarthritis (axSpA) on social and family life, in a context of fears for the future. These data are important to take into account for shared decision-making.

REFERENCE

Background: Axial Spondyloarthropathies (SpA) are chronic, systemic, inflammatory diseases which affect the axial skeleton, limit chest mobility and cause serious impairments in pulmonary functions.

Objectives: In this cross-sectional study, as a new approach; diaphragm thickness is assessed by ultrasound in patients with axial SpA to determine possible relationships with pulmonary functions and disease activity.

Methods: 49 axial SpA patients enrolled in the study were assessed by Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Metrology Index (BASMI), Erythrocyte Sedimentation Rate (ESR), serum C-Reactive Protein levels (CRP) and chest expansion (cm). 15 patients with lung diseases other than axial SpA pulmonary involvement, neuromuscular diseases, scoliosis and congenital chest deformity were excluded. Dynamic pulmonary function tests (PFT) and 6 min walk (6MW) tests were done and physical activity levels were evaluated by short form International Physical Activity Questionnaire (IPAQ). Diaphragm thickness was measured at end expiration (dFRC) and deep inspiration (total lung capacity (dTLC)). Thickness ratio (dtr: dTLC/dFRC) and thickness change (dtc: dTLC-dFRC) were calculated.

Results: The descriptive data of the patients are presented in Table 1. Patients had a moderate disease activity and all the patients were category 1 (inactivity) according to IPAQ. Mean value of dtr and PFT seem significantly correlated with dynamic pulmonary function tests, yet negatively correlated with ESR and BASMI. The CT and MR images were reviewed for the presence of erosions by 2 musculoskeletal radiologists blinded to clinical findings. After a follow-up of 2 years, 2 experienced rheumatologists confirmed or excluded the diagnosis of SpA. Diagnostic utility of erosions for diagnosis of SpA was determined by calculating sensitivity, specificity, positive and negative likelihood ratio with final clinical diagnosis made by rheumatologists as gold standard.

Conclusion: To the best of our knowledge, this is the first study evaluating the relationship between diaphragm thickness and pulmonary functions with disease activity. Even though, there was no limitation in PFT and expected values were obtained in dtr, the negative correlation with ESR makes us think about the possible effect of disease activity on dtr. With these preliminary results, it is early to conclude, but dtr assessment may be supplementary to PFT and early measures to improve diaphragm function with specific exercises should be implemented in patients with axial SpA.

Disclosure of Interests: None declared


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Background: In the light of new therapeutic strategies, it has become essential to detect spondyloarthritis (SpA) in its earliest stages in order to institute treatment as early as possible. Magnetic resonance imaging (MRI), with its ability to detect active lesions, is usually considered as a key tool for early recognition of sacroiliitis. However, a growing number of studies reported the lack of specificity of bone marrow edema (BME) leading sometimes to a false “positive MRI” of sacroiliac joints (SIJ). In addition, many recent studies have pointed out the utility of detecting structural lesions, especially erosions, reported as the earliest structural change on SIJ in the course of sacroiliitis.

Objectives: We aimed to assess the reliability of early recognition of erosions in patients with suspected SpA.

Methods: Consecutive patients, aged 16 and over, consulting from February 2014 to February 2017 for symptoms suggestive of SpA (inflammatory back pain, enthesitis or dactylitis...) were enrolled in this cohort. They were referred for computed tomography (CT) and MRI of the SIJ. The CT and MR images were reviewed for the presence of erosions by 2 musculoskeletal radiologists blinded to clinical findings. After a follow-up of 2 years, 2 experienced rheumatologists confirmed or excluded the diagnosis of SpA. Diagnostic utility of erosions for diagnosis of SpA was determined by calculating sensitivity, specificity, positive and negative likelihood ratio with final clinical diagnosis made by rheumatologists as gold standard.

Results: Fifty-four patients were included, 13 men and 41 women. The mean age was 39 years [17-71]. The mean duration of symptoms was 75 months (6 years). Cervical, thoracic, lumbar and buttock pain were noted respectively in 46.3%, 37%, 87%, and 57.4% of the studied patients. Morning stiffness was noted in 55.5% of patients. The prevalence of HLA-B27 was 23.4%. After a follow-up of 2 years, the referring rheumatologists made a diagnosis of SpA in 77.8% of patients, whereas SpA was excluded in 22.2%. Among the 42 patients classified as having a confirmed SpA, erosions were detected on MRI or CT in 64.3% (n=27) and by MRI in (n=18) 42.85% of patients. Among the 12 patients in whom SpA was excluded, erosions were detected on MRI by CT in 25% (n=3) of patients and were not detected by MRI in any patient. Sensitivity, specificity, positive and negative likelihood ratio of erosions detected by CT were respectively estimated at 64.3%, 75%, 90% and 37.5%. Those of erosions detected by MRI were estimated at 42.9%, 100%, 100%, 33.33%. A statistically significant association was observed between erosions and rheumatologists’ diagnosis of SpA (p< 0.05 for CT and p = 0.012 for MRI). The likelihood ratio was estimated respectively for CT and MRI at 3.8 and 7.6.

Conclusion: In our study, detection of erosions showed a high specificity for recognition of sacroiliitis, especially when detected by MRI. This study highlights the utility of structural SIJ lesions, particularly erosions, to reduce the number of false positives.

Disclosure of Interests: None declared


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TABLE 1. Baseline descriptive data characteristics of patients

| Age (y) | 46±10.7 |
| Female (n, %) | 26 (76.5) |
| Male (n, %) | 8 (23.5) |
| Disease duration-month | 50 (3.30) |
| dFRC (cm) | Female Male | 0.1±0.4 0.4±0.18 ±0.3 |
| dTLC (cm) | 0.34±0.9 0.43±0.11 |
| dtr | 1.9±0.3 2.4±0.35 |
| BASDAI | 4.7±0.8 (8.5) |
| BASMI | 3.5 (1.9) |
| MASES | 42±10.5 |
| VCMAX | 3.2±0.8 (90.37%) |
| FEV1 | 2.5±0.6 (90.3%) |
| PEF | 6±0.1±6 (87.4%) |
SAT0332 GENDER DIFFERENCES IN DISEASE STATUS, QUALITY OF LIFE AND TREATMENT PATTERNS AMONG AXIAL SPONDYLOARTHRITIS PATIENTS: FINDINGS FROM A GLOBAL SURVEY

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Background: Axial spondyloarthritis (AxSpA) is a chronic inflammatory disease of the axial skeleton associated with impaired health-related quality of life (HRQoL) and disability.1,2 Gender differences in clinical and quality of life (QoL) measures have been demonstrated in axSpA (ankylosing spondylitis (AS) and non-radiographic axSpA (nr-axSpA)), but not well quantified in a real-world clinical setting.

Objectives: To compare the clinical characteristics, QoL and treatment patterns of male and female AS and nr-axSpA patients from a multinational survey.

Methods: Data from a cross-sectional, multinational survey conducted in Australia, Canada, France, Germany, Italy, Japan, Spain, United Kingdom and the United States were analyzed. Demographics, disease status and medication use were reported by the patient, while work disability and QoL measures were reported by the patient. Gender comparison analyses were conducted for AS and nr-axSpA subgroups.

Results: Data from 432 physicians (407 rheumatologists, 13 orthopedists, 2 internists) 2,300 AS patients (male: 1,673 [72.74%]; female: 627 [27.26%]), and 2,099 nr-axSpA patients (male: 1,146 [54.60%]; female: 953 [45.40%]) were included in this analysis. Male AS and nr-axSpA patients were more likely to be younger (AS: p<0.0141; nr-axSpA: p=0.0127), smokers (AS: p<0.0001; nr-axSpA: p=0.0001), have full-time employment (AS: p=0.0001; nr-axSpA: p=0.0001), and currently be in remission (AS: p<0.0001; nr-axSpA: p=0.0001) when compared to female AS and nr-axSpA patients. Male AS patients were more likely to be prescribed biologic treatment when compared to female AS patients (p=0.0070); however, rates of biologic use between male and female nr-axSpA patients were comparable (p=0.2148). Male AS and nr-axSpA patients also had lower Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) scores than female AS patients (AS: p<0.0001; nr-axSpA: p<0.0001), and male AS and nr-axSpA patients had more activity impairment, as assessed by the Bath Ankylosing Spondylitis Quality of Life (ASQoL) (AS: p=0.0001; nr-axSpA: p=0.0001), Assessment of SpondyloArthritis international Society Health Index (ASAS HI) (AS: p<0.0001; nr-axSpA: p<0.0001), and Work Productivity and Activity Impairment (WPAI) (AS: p=0.0006; nr-axSpA: p=0.0002).

Conclusion: Male AS patients were more likely to be prescribed biologics when compared to female AS patients, despite females experiencing worse QoL and greater activity impairment. This study highlights an unmet need among female patients for more appropriate treatment approaches.

REFERENCES


SAT0333 THE DIFFERENCES OF CLINICAL MANIFESTATIONS BETWEEN FAMILIAL AND SPORADIC ANKYLOSING SPONDYLITIS PATIENTS

Yutong Jiang, Li Xiaomin, Dongfang Lin, Yanli Zhang, Mingcan Yang, Zetao Liao, Jieruo Gu. The Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China

Background: Ankylosing spondylitis (AS) is a chronic inflammatory rheumatic disease which could lead to pain, functionally limitation and even less life expectancy. Morning stiffness often occur in the patients. Familial aggregation has been found due to genetic susceptibility of the disease. There are certain difference in the patients with or without familial AS. For example, familial AS patients were reported to show a lower frequency of oligoarthritis [1].

Objectives: Our study was to investigate the difference of morning stiffness in the patients with familial AS or sporadic AS.

Methods: Study participants were recruited from Department of Rheumatology in the Third Affiliated Hospital of Sun Yat-sen University. Each patient was assessed by at least two qualified rheumatologists, and the diagnosis was made according to 1984 Modified New York Classification Criteria for AS. Through detailed family history, AS patients with 2 or more patients in his/her family who firstly went to our clinic were included as a possible proband. Then the probands brought the affected relatives to our clinic for further examination. Of three rheumatologists and two nurses drove to the places where a possible proband’s family member lived. Baseline assessments were completed by trained by using identical questionnaires including demographic information (age, gender), disease related characteristics (back pain, morning stiffness, peripheral arthritis, uveitis, etc.), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), and Bath Ankylosing Spondylitis Functional Index (BASFI). The Statistical Package for Social Sciences (SPSS) software version 21 was used for all data management and analysis. The difference between familial and sporadic AS patients were examined by using Independent T test or M-U test.

Results: Of the 264 AS patients, 175 (66.3%) were males and 89 (33.7%) were female patients. Mean age was 31.0±9.5 years, and disease duration was 7.3±6.7 years. Mean age of disease onset was 23.4±8.5 years. There was no difference between familial and sporadic AS patients in the aspects of age, sex, age of onset and disease duration. However, age of onset of male familial AS patients was significantly lower than that of female patients (21.9±8.4 VS 26.3±8.2, p<0.004), while no such sex difference was detected in sporadic patients (22.6±8.1 VS 25.3±8.6, p=0.08). Familial patients were inclined to have hip joint involvement, compared with sporadic patients (58.6% VS 9.6%, p<0.01). 186 (70.5%) patients suffered from morning stiffness with median time of 61.6 minutes. Degree of morning stiffness was 3.5±3.0. Sporadic patients had more morning stiffness than familial patients (p=0.007). There was no difference in the presentation of peripheral arthritis (p=0.05). Mean BASDAI score was 3.6±2.0, and mean BASFI score was 1.4±1.8. The BASDAI score was slightly higher in sporadic group (p=0.027).

Conclusion: Familial AS patients had more hip joint involvement, less morning stiffness and an earlier disease onset, especially in male patients, compared with sporadic patients.

REFERENCE

Disclosure of Interests: None declared

SAT0334 DOES DEPRESSION PREDICT FUTURE DISEASE STATUS AND IMPROVEMENTS IN DISEASE PARAMETERS? RESULTS FROM THE COMPLETE STUDIES, A CANADIAN REAL WORLD OBSERVATIONAL COHORT

Majid Khraja1, Valenica P. Remige2, Louis Bessette3. 1Memorial University of Newfoundland, St. John’s, Canada; 2AbbVie Corporation, Montreal, Canada; 3Laval University, Centre Hospitalier de l’Université Laval, Quebec, Canada

Background: Depression is a common comorbidity in rheumatic diseases such as Psoriatic Arthritis (PsA) and Ankylosing Spondylitis (AS), whereby it is associated with increased disease activity, decreased functionality, and lower persistence with treatment.

Objectives: The objective of this analysis was to assess if baseline depression in Canadian patients with PsA or AS predicts future disease status and improvement in disease parameters.

Methods: COMPLETE is a Canadian observational cohort of anti-TNFα naïve adults with PsA and AS, who require a change in their treatment. Separate analyses were performed for each disease group. Depression was defined as BDI score ≥20 (or use of anti-depressants and/or anxiolytic medication). Multivariate logistic regression was used to assess the
baseline predictors of achievement of low disease activity (LDA) in BAS- 
DAI (<4) and BASFI (<4) for patients with AS; or DAPSA LDA (≤13), 
DAS28 LDA (≤3.2), DAPSA remission (≤4), DAS28 remission (≤2.6) and 
BSA <3% for patients with PsA. The maximum improvement (highest 
change in score) at either 6 or 12 months was observed in BASDAI. BASFI, 
DAPSA, DAS28 was assessed for using multivariate linear regression and 
the least square means (LSMs). The maximum improvement in HAQ-DI 
and SF-12 physical component scale (PCS) and mental component scale 
(MCS) were also assessed among PsA patients.

Results: A total of 492 patients with AS and 333 with PsA had BDI 
assessments (or criteria for depression) at baseline and were included in 
the analysis; mean (SD) age was 42.7 (13.2) and 51.5 (12.2) years, 
respectively. Patients with AS were mostly male (54.1%) and initiated 
adalimumab treatment (70.9%) with mean (SD) disease duration of 5.4 
(9.1) years; for PsA, sex was evenly distributed (female 50.5%), 66.4% 
initiated treatment with adalimumab and mean (SD) disease duration was 
14.7 (13.7) years. The prevalence of depression at baseline was 24.6% 
and 25.5% in patients with AS and PsA, respectively.

Upon adjusting for potential confounders, presence of depression in 
patients with AS was associated with significantly lower odds of achiev- 
ing BASDAI LDA (OR: 0.51, p=0.021) and BASFI LDA (OR: 0.52, 
p=0.045) during treatment. In the treatment arm, presence of depression 
was also identified as a significant positive predictor of either outcome 
(ORBASDAI: 1.91, p=0.016; ORBASFI: 1.98, p=0.029), while older age 
was identified as a negative predictor of BASFI LDA achievement (OR: 0.98, p=0.044). Similarly, patients with depression experienced sig- nificantly lower improvements in BASDAI LDA (LSM: -1.72 vs. -2.44; 
p=0.007), and BASFI scores (-1.46 vs. -2.02; p=0.029) compared to 
those without depression.

Among patients with PsA, presence of depression appeared to be asso- ciated with lower odds of achieving DAPSA remission (OR: 0.35, 
p=0.070). No association was observed between presence of depression 
and DAPSA LDA, DAS28 LDA or remission, and BSA<3%. In terms of 
disease improvement, significant lower improvement in DAPSA score 
(LSM: -11.00 vs. -14.66; p=0.047) and SF-12 MCS (LSM: -3.01 vs. 
4.36; p=0.007) were observed among patients with depression.

Conclusion: A significant proportion of AS and PsA patients suffer from 
depression. Baseline depression seems to negatively affect treatment 
outcomes in both AS and PsA patients. Whether this is due to differences 
in the assessment of patient-reported outcomes or due to physiological 
differences remains to be confirmed.

Disclosure of Interests: Majed Khraishi Consultant for: AbbVie, Louis Bessette Grant/research support from: AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, Research for statistical analysis, medical writing and editorial assistance

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Disclosure of Interests: Majed Khraishi Consultant for: AbbVie, Speakers bureau: AbbVie, Valencia P. Remple Shareholder of: AbbVie, Employee of: AbbVie, Louis Bessette Grant/research support from: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, Consultant for: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis, Speakers bureau: Amgen, BMS, Janssen, Roche, UCB, AbbVie, Pfizer, Merck, Celgene, Sanofi, Lilly, Novartis. DOI: 10.1136/annrheumdis-2019-eular.6084

SA20335

CLINICAL COURSE OF ANKYLOSING SPONDYLITIS (AS) IN PREGNANCY: INTERIM DATA FROM PROSPECTIVE STUDY

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Objectives: To study the dynamics of clinical signs, AS activity and patients' functional status during gestation.

Methods: 19 pregnant females with confirmed AS based on modified NY criteria (1984) were included. Patients' mean age was 32.2±1.1 years; mean age at AS onset was 22.6±3.1 years; mean disease duration was 147.0±27.7 months. Control visits were scheduled at 10-11, 20-21 and 31-32 weeks of pregnancy. BASDAI and ASAS-ERP calculators were used to assess AS activity, while patients' functional status was assessed using BASFI and BASMI scores, and MASES score was used for evaluation of enthesitis.

Results: Pregnancy outcomes included 18 full-term births at 37.6±1.1 weeks of gestation, and a non-developing pregnancy at 18 weeks in one case. Newborns' weight = 3518±67 g.

Inflammatory low back pain at conception was reported by 78.9% of participants, with mean pain intensity 2.2±0.4 scores by NRS. Pain during pregnancy was observed in 95% of all patients. Its intensity increased by the II trimester (4.6±0.7) and persisted at the same level in the III trimester (p<0.05 between conception and II & III trimesters). Patients reported changing pain patterns by the III trimester: 55.6% noticed pain improvement at rest, and 61.1% indicated exacerbation of pain after physical exercise. Enthesitis rates and intensity were also increasing in the course pregnancy: MASES score was higher in the III trimester (2.3 ±0.5) vs I trimester (0.4±0.22, p<0.05). Meanwhile the rates of AS others non-axial and non-skeletal manifestations were not changing during gestation.

BASDAI score was increasing from the moment of conception (1.7±0.3) until the III trimester (3.3±0.5, p<0.05), staying thereafter at the same level in the III trimester. Multivariate regression revealed BACDAI score (R²=0.7) and low back pain (R²=0.9) at conception, as well as biological therapy at 3 months prior to conception (R²=0.7) as orchestrated predictors of relevant BASDAI score in III trimester. During all pregnancy the BASDAI score was predetermined by assemblage of low back pain intensity (β=0.6), fatigue (β=0.6), and enthesitis-associated pain (β=0.3). Increasing fatigue (by 68.5%), and low back pain (by 24%) genent ASADAS-CRP score by the end of the I trimester. While during the II trimester further increase in BASDAI score was provided by exacerbation of enthesitis (20.7% increment), and back pain (27% increment). ASADAS-CRP score was relatively stable with some trend to increase in the II trimester (3.3±0.3) as compared to baseline at conception (1.7 ±0.2); CRP also showed some increase in the II trimester (9.7±2.9 mg/ml) vs I trimester (6.7±2.4 mg/ml, p<0.05).

BASMI score insignificantly changed during all 3 trimesters (1.3±0.9; 1.8 ±0.2; 2.1±0.3 – in I, II and III trimesters, correspondingly). BASFI score showed increase in the III trimester (3.9±1.0) as compared to I trimester (1.4±0.3, p<0.05). Score increase in the III trimester was due to increased AS activity interfering with habitual physical performance, and also due to pregnancy (forward bend, questions 1,2,4).

Conclusion: AS clinical activity increases by the II trimester of pregnancy and persists at moderate and high levels afterwards during all gestation period. AS activity at conception can determine AS activity during all pregnancy. 50% of pregnant patients are likely to experience low back pain in the III trimester due to increasing pressure of a growing fetus on the spine. Functional disability increases with progress in pregnancy, being caused in the III trimester by both – AS activity and pregnancy per se.


SA20336

CLINICAL DIAGNOSES OF AXIAL SPONDYLOARTHRITIS SHOW A HIGH OVERALL CONCORDANCE WITH CLASSIFICATION CRITERIA FULFILMENT, BUT ARE LESS CONSISTENT FOR DIFFERENTIATION BETWEEN SUBTYPES IN ESTABLISHED AXIAL DISEASE: RESULTS FROM THE SPARTAKUS COHORT

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Background: The ASAS axial SpondyloArthritis (axSpA) criteria encompass radiographic (r-axSpA) and non-radiographic (nr-axSpA) disease to enable classification early, while the modified New York criteria (mNY) for Ankylosing Spondylitis (AS) require radiographic sacroiliitis. Studies of agreement between clinical diagnoses of axSpA and classification criteria are sparse, especially for nr-axSpA.

Objectives: To study the concordance between clinical axSpA diagnoses and classification criteria fulfilment (mNY and ASAS axSpA) disease to enable classification early, while the modified New York criteria (mNY) for Ankylosing Spondylitis (AS) require radiographic sacroiliitis. Studies of agreement between clinical diagnoses of axSpA and classification criteria are sparse, especially for nr-axSpA.

Methods: Patients with clinical diagnoses (ICD-10) of AS (M45.9) or undifferentiated spondyloarthropathy (M46.0, M46.1, M46.8, M46.9)
followed at Skåne University Hospital, and living in a defined area of southern Sweden were assessed in a cross-sectional study. USpA patients had to report back pain ≥3 months before age 45, by telephone screening, to be eligible. To enable classification, included patients underwent clinical assessments, a classification questionnaire, blood testing (including HLA-B27), and scoring of plain X-rays and MRI scans of the sacroiliac joints by an experienced radiologist.

**Results:** Out of 233 patients with clinical AS or axial USpA, 196 (85%) fulfilled either mNY or ASAS axSpA classification criteria, while 35 (15%) met neither criteria set. Among 118 patients with a clinical AS diagnosis, 89 fulfilled ASAS axSpA criteria, while a higher number was classified as AS (n=48) than nr-axSpA (n=36); PPV of clinical USpA diagnosis for fulfilling mNY criteria was 71% and for ASAS nr-axSpA 69%. For 115 patients with a clinical USpA diagnosis, 89 fulfilled ASAS axSpA criteria, while a higher number was classified as AS (n=48) than nr-axSpA (n=36); PPV of clinical USpA diagnosis for fulfilling nr-axSpA criteria was 31% (Figure 1). Comparing characteristics between patients classified as radiographic axSpA (AS [mNY] or ASAS axSpA vs. ASAS nr-axSpA, few differences were observed; the former were older, more often men, had longer disease duration and worse spinal mobility (Table 1).

**Table. Clinical characteristics and outcome measures**

<table>
<thead>
<tr>
<th></th>
<th>Radiographic axSpA*</th>
<th>nr-axSpA*</th>
<th>Radiographic SpA vs. nr-axSpA</th>
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<tbody>
<tr>
<td>n</td>
<td>141</td>
<td>57</td>
<td>29</td>
<td>115</td>
</tr>
<tr>
<td>Age, years</td>
<td>58 (14)</td>
<td>45 (12)</td>
<td>&lt;0.001</td>
<td>49 (12)</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>88 (62)</td>
<td>18 (32)</td>
<td>0.20</td>
<td>10 (29)</td>
</tr>
<tr>
<td>Symptom duration, years</td>
<td>29 (14)</td>
<td>19 (11)</td>
<td>&lt;0.001</td>
<td>20 (13)*</td>
</tr>
<tr>
<td>HLA-B27 positive, n (%)</td>
<td>115 (84)</td>
<td>48 (84)</td>
<td>0.83</td>
<td>4 (11)*</td>
</tr>
<tr>
<td>ASDAS-CRP</td>
<td>1.9 (1.0)</td>
<td>1.9</td>
<td>0.94</td>
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</tr>
<tr>
<td>BASDAI</td>
<td>3.1 (2.3)</td>
<td>3.2</td>
<td>0.77</td>
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</tr>
<tr>
<td>BASFI</td>
<td>2.3 (2.4)</td>
<td>2.1</td>
<td>0.51</td>
<td>2.8 (2.3)</td>
</tr>
<tr>
<td>BASMI</td>
<td>3.4 (1.8)</td>
<td>2.1</td>
<td>&lt;0.001</td>
<td>2.7 (1.0)</td>
</tr>
</tbody>
</table>

Mean (SD) unless indicated. Missing data 0-14%.

*Statistical comparisons by Student’s t-test or Chi-Square test

**Conclusion:** The overall concordance between clinical diagnoses and fulfilment of axSpA classification criteria was good, with >4/5 meeting any criteria. For disease subtypes, however, the agreement was substantially weaker, and a large group of patients with USpA in this established cohort fulfilled the mNY criteria for AS. The results indicate that in studies aiming to compare radiographic and non-radiographic axSpA, classification according to defined classification criteria is important.

**Disclosure of Interests:** Elisabet Lindqvist: None declared, Tor Olofsson: None declared, Anna Jöud: None declared, Mats Geijer Consultant for: Consultant for AbbVie, Novartis, and Pfizer., Johan K Wallman Consultant for: Consultant for AbbVie, Celgene, Eli Lilly, Novartis, and UCB Pharma, Elisabeth Mogard: None declared

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the time between symptom onset and physician diagnosis is 5-7 years. Diagnosis delay is attributed to nonspecific presentation of chronic back pain, requiring clinical experience to recognize early AS.

**Objectives:** To identify obstacles to early diagnosis of AS by assessing the knowledge of nonrheumatology health care providers (HCPs) on inflammatory back pain (IBP) and possible barriers to referral to a rheumatologist.

**Methods:** Survey content was first conceptualized based on concept elicitation interviews with HCPs, and questionnaires were developed by the study investigators to identify clinical characteristics, symptom presentation, and diagnostic measures that lead an HCP to suspect IBP and their perspectives on the referral process. The survey was then cognitively tested with HCPs from 10 specialties (family medicine, internal medicine, dermatology, gastroenterology, ophthalmology, orthopedics, chiropractic, pain management, physical therapy, and physiatry), revised, and finalized. HCPs from these 10 specialties were invited to participate in the cross-sectional web-based survey hosted by Survey Sampling International between June 27 and July 20, 2018. HCPs who were currently licensed, actively practicing in the US, and had referred a patient with suspected IBP (except ophthalmology) or referred a patient with uveitis/iritis (ophthalmology only) within the past 12 months were eligible to participate. Descriptive statistics were used to analyze the data.

**Results:** Of 2395 HCPs screened, 1690 were eligible and included in our study. Overall, HCPs saw a median of 100 patients with chronic back pain within the past 12 months of the survey. Regarding criteria leading to suspicion of IBP, 61% of HCPs indicated morning stiffness > 30 minutes, 29% sleep disturbance due to back pain, 28% pain that improves with activity, and 16% alternating buttock pain. Among HCPs who would order diagnostic blood work, ~ 90% selected C-reactive protein, erythrocyte sedimentation rate, and rheumatoid factor (RF), while 76% selected HLA-B27 (Figure 1). Most HCPs suspected underlying conditions of rheumatoid arthritis (RA; 94%), AS (90%), and psoriatic arthritis (81%) as related to IBP. Almost 40% of HCPs would treat patients with suspected IBP themselves; of these, ~ 80% would recommend nonsteroidal anti-inflammatory drugs and physical therapy (Figure 2). Regarding referrals, 57% of HCPs would refer patients with suspected IBP to another physician, but only 13% would refer immediately; 49% would perform further evaluations, 24% would wait until initial treatment response, 11% would monitor patient for some time, and 3% would consult with another physician before referring. Upon referral, 90% of HCPs estimated a wait time of up to 2 months for their patient to see another specialist. Of 1670 HCPs queried, 80% indicated that the specialist’s expertise in treating autoimmune disease is the most important factor influencing their referral.

**Conclusion:** Most HCPs did not recognize IBP criteria in patients with chronic back pain. As most considered RA to be the underlying condition, ANA and RF were ordered as diagnostic workup. Many HCPs opted to treat and monitor patients with suspected IBP before referral, and most reported a wait time of up to 2 months for their patients to see an expert.

**Acknowledgement:** This study was sponsored by Novartis Pharmaceuticals Corporation, East Hanover, NJ.

**Disclosure of Interests:** Marina Magrey Grant/research support from: M. Magrey received research funding from AbbVie and UCB for clinical trials, served as a consultant for Novartis, and was a member of advisory boards for Eli Lilly, Novartis, and UCB. Consultant for: M. Magrey received research funding from AbbVie and UCB for clinical trials, served as a consultant for Novartis, and was a member of advisory boards for Eli Lilly, Novartis, and UCB. Daniel Wolin Employee of: D. Wolin is an employee of RTI Health Solutions.

Characterization of Patients with Axial Spondyloarthritis by Presence of Enthesitis

Methods: This study included patients aged ≥ 18 years with AxSpA enrolled in the Corrona PsA/SpA Registry between March 2013 and August 2018. Enthesitis at enrollment was assessed via the Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index.

Results: Of 477 patients with AxSpA, 121 (25.4%) had enthesitis. Symptom and disease duration were similar between patients with and without enthesitis using fisher's exact tests for categorical variables.

Conclusions: AxSpA is common in the general population. The prevalence of enthesitis in AxSpA and its impact on disease burden was similar regardless of presence of enthesitis; however, patients with enthesitis were more likely to have prior csDMARD and biologic use, as well as current methotrexate use. Patients with enthesitis had worse disease activity and quality of life compared to patients without enthesitis.

Table 2: CHARACTERIZATION OF PATIENTS WITH AXIAL SPONDYLOARTHRITIS BY PRESENCE OF ENTHESITIS: DATA FROM THE CORRONA PSORIATIC ARTHRITIS/SPONDYLOARTHRITIS (PSA/SPA) REGISTRY

<table>
<thead>
<tr>
<th>Stage of global assessment</th>
<th>Data source</th>
<th>axSpA YES</th>
<th>axSpA NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 246</td>
<td>Clinical plus radiography</td>
<td>141 (57.3%)</td>
<td>105 (42.7%)</td>
</tr>
<tr>
<td>N = 246</td>
<td>Clinical plus radiography after central reader assessment</td>
<td>79 (32.1%)</td>
<td>167 (67.9%)</td>
</tr>
<tr>
<td>N = 149</td>
<td>Clinical plus radiography plus MRI</td>
<td>70 (47.0%)</td>
<td>79 (53.0%)</td>
</tr>
<tr>
<td>N = 149</td>
<td>Clinical plus radiography plus MRI after central reader assessment</td>
<td>45 (30.2%)</td>
<td>104 (69.8%)</td>
</tr>
</tbody>
</table>

Table 1: DEMOGRAPHIC AND CLINICAL CHARACTERISTICS AND TREATMENT PROFILES OF PATIENTS WITH AXSpA STRATIFIED BY PRESENCE OF ENTHESITIS AT ENROLLMENT

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No Enthesitis (N = 326)</th>
<th>With Enthesitis (N = 121)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>43.6 (14.2)</td>
<td>42.7 (13.1)</td>
<td>0.59</td>
</tr>
<tr>
<td>Sex, male (%)</td>
<td>184 (56.5)</td>
<td>57 (46.9)</td>
<td>0.43</td>
</tr>
<tr>
<td>Depression, %</td>
<td>16 (8.0)</td>
<td>15 (12.4)</td>
<td>0.43</td>
</tr>
<tr>
<td>Active disease, %</td>
<td>92 (28.3)</td>
<td>59 (48.9)</td>
<td>0.003</td>
</tr>
</tbody>
</table>
| Activity, quality of life, and work productivity were compared between patients with and without enthesitis using t tests or Wilcoxon rank-sum tests for continuous variables and χ2 or Fisher's exact tests for categorical variables.

Results: Of 477 patients with AxSpA, 121 (25.4%) had enthesitis. Symptom and disease duration were similar between patients with and without enthesitis. In patients with enthesitis, a higher proportion were female, were more likely to have non-radiographic AxSpA and a history of depression, serious infections, and fibromyalgia vs those without enthesitis (all P < 0.05; Table 1). Current treatment with biologies or conventional synthetic disease-modifying antirheumatic drug (csDMARD) monotherapy was similar regardless of presence of enthesitis; however, patients with enthesitis were more likely to have prior csDMARD and biologic use, as well as current methotrexate use. Patients with enthesitis had worse disease activity (ASDAS, BASDAI, and BASFI scores; tender and swollen joint counts; physician global assessment; and DAPSA and cDAPSA scores), spinal mobility measures, quality of life (pain, fatigue, HAQ scores, and EQ VAS scores), and greater work impairment than patients without enthesitis (all P < 0.05; Table 1).

Conclusion: Among patients with AxSpA in this US real-world study, the presence of enthesitis was associated with worse disease activity and quality of life compared to patients without enthesitis. External validity outside of US real-world settings.

Table 2: DISEASE ACTIVITY, QUALITY OF LIFE, AND WORK PRODUCTIVITY IN PATIENTS WITH AxSpA STRATIFIED BY PRESENCE OF ENTHESITIS AT ENROLLMENT

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No Enthesitis (N = 326)</th>
<th>With Enthesitis (N = 121)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASDAS, mean (SD)</td>
<td>3.6 (2.0)</td>
<td>4.6 (2.4)</td>
<td>0.001</td>
</tr>
<tr>
<td>BASDAI, mean (SD)</td>
<td>5.3 (2.4)</td>
<td>6.3 (2.1)</td>
<td>0.001</td>
</tr>
<tr>
<td>BASFI, mean (SD)</td>
<td>2.0 (1.5)</td>
<td>3.0 (1.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>HAQ, mean (SD)</td>
<td>0.6 (1.1)</td>
<td>1.0 (1.4)</td>
<td>0.001</td>
</tr>
<tr>
<td>EQ VAS, mean (SD)</td>
<td>74.5 (13.8)</td>
<td>71.7 (16.4)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Background: Enthesitis is a common extra-axial manifestation in patients with axial spondyloarthritis (AxSpA) 1,2; however, not much is known about the prevalence of enthesitis in AxSpA and its impact on disease burden in US real-world settings.

Objectives: The study describes characteristics of patients with AxSpA who had enthesitis vs patients without enthesitis.

Methods: This study included patients aged ≥ 18 years with AxSpA enrolled in the Corrona PsA/SpA Registry between March 2013 and August 2018. Enthesitis at enrollment was assessed via the SPARCC Enthesitis Index.

Results: Of 477 patients with AxSpA, 121 (25.4%) had enthesitis. Symptom and disease duration were similar between patients with and without enthesitis using t tests or Wilcoxon rank-sum tests for continuous variables and χ2 or Fisher’s exact tests for categorical variables.

Results: Of 477 patients with AxSpA, 121 (25.4%) had enthesitis. Symptom and disease duration were similar between patients with and without enthesitis. In patients with enthesitis, a higher proportion were female, were more likely to have non-radiographic AxSpA and a history of depression, serious infections, and fibromyalgia vs those without enthesitis (all P < 0.05; Table 1). Current treatment with biologies or conventional synthetic disease-modifying antirheumatic drug (csDMARD) monotherapy was similar regardless of presence of enthesitis; however, patients with enthesitis were more likely to have prior csDMARD and biologic use, as well as current methotrexate use. Patients with enthesitis had worse disease activity (ASDAS, BASDAI, and BASFI scores; tender and swollen joint counts; physician global assessment; and DAPSA and cDAPSA scores), spinal mobility measures, quality of life (pain, fatigue, HAQ scores, and EQ VAS scores), and greater work impairment than patients without enthesitis (all P < 0.05; Table 1).

Conclusion: Among patients with AxSpA in this US real-world study, the presence of enthesitis was associated with worse disease activity and quality of life compared to patients without enthesitis.
The prevalence of renal failure in a prospective axial spondyloarthritids cohort and possible associated factors

Xabier Michela-Vegas, Carla Marco Pascual, Xavier González Giménez, Maribel Moro, J Lluch Pons, Jesús Rodríguez, Joan Miquel Nolla, Xavier Juangola-Roura, Department of Rheumatology, Bellvitge University Hospital (IDIBELL), Barcelona, Spain

Background: Extra-articular manifestations and comorbidities are significant complications in the evolution of patients with spondyloarthritids (SpA). The presence of renal failure (RF) is a multifactorial comorbidity that has been shown to be associated with this disease, and its prevalence has been reported around 5% (COMOSPA 1). There are no prevalence studies in our environment.

Objectives: To determine the prevalence and possible factors associated with RF in patients with axial spondyloarthritids (axSpA).

Methods: Data was retrieved from a prospective database designed for the monitoring of patients with SpA from a large teaching hospital. We only included patients with axSpA. Demographic and clinical data were recorded, as well as possible risk factors associated with RF: arteral hypertension (AH), smoking status, diabetes (DM), Dyslipidemia (DL), NSAIDs use and renal function from last test available (we considered RF when eGFR<60 mL/min).

Continuous data were compared with Student t-test if the variables presented normal distribution (previous Shapiro-Wilk test) or Mann Whitney U test otherwise. Chi-square or Fisher test was performed if the variable was categorical.

Results: 339 patients were included. 73.2% were male with a mean age of 56.68 ± 14.8 years and a mean age of onset of 32.0 ± 11.4 years. The mean disease duration was 32.8 ± (IQR 11.4) years. 83.7% were HLAB27+. The clinical variables for the whole cohort were: BASDAI 3.56 ± (2.13), BASFI 5.2 ± 2.56, ASDAS-CRP 2.57 ± 0.87, ASDAS-ESR 2.66 ± 0.93, CRP median (IQR) 19.6 ± 6.65, ESR median (IQR) 15 ± 23.3.

Chi-square or Fisher test was performed if the variable was categorical.

Conclusions: There is a substantial prevalence of RF in patients with axSpA in our cohort. We should maximise our awareness of RF in old patients, those suffering from AHT and DLP, as well as subjects with high BASFI, ASDAS and ESR values.

Reference


References

Matts classification, follow up period, presence of other EIMs and ileal pouchitis. Follow up period [OR 1.17 (95% CI 1.03-1.33, p < 0.05)], Matts classification [OR 2.61 (95% CI 1.19-5.74, p < 0.05)] and ileal pouchitis [OR 2.65 (95% CI 1.16-6.07, p < 0.05)] were significantly associated with an increased risk of developing arthropathy of UC patients after colectomy.

Table 1. The risk factors for developing arthropathy in patients with ulcerative colitis after undergoent colectomy by multivariate logistic regression analysis.

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Odd ratio</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at operation, years</td>
<td>1.02</td>
<td>0.99-1.04</td>
<td>NS</td>
</tr>
<tr>
<td>Sex (female vs male)</td>
<td>1.81</td>
<td>0.84-3.91</td>
<td>NS</td>
</tr>
<tr>
<td>Follow-up period, years</td>
<td>1.17</td>
<td>1.03-1.33</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Matts Classification (grade 3-4 vs 1-2)</td>
<td>2.61</td>
<td>1.19-5.74</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Ileal pouchitis</td>
<td>2.65</td>
<td>1.16-6.07</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Extraintestinal manifestations</td>
<td>2.74</td>
<td>0.85-8.87</td>
<td>NS</td>
</tr>
</tbody>
</table>

Conclusion: About one fifth patients with UC who underwent colectomy developed arthropathy presenting predominantly peripheral type. Long follow-up period, high disease activity by endoscopic classification, and ileal pouchitis were risk factors of onset PsA, arthropathy in UC patients after total colectomy. The frequency and risk factors for developing arthropathy even after colectomy was demonstrated in this study for the first time.

REFERENCES

Disclosure of Interests: Kentaro Noda: None declared, Yuki Mizutani: None declared, Naohiro Sugitani: None declared, Yasuo Suzuki: None declared, Toshimitsu Araki: None declared, Masato Kusunoki Grant/research support from: Novartis, Pfizer, Grant/research support from: Novartis, Pfizer, Grant/research support from: Novartis, Pfizer. Disclosure of Interests: Kento Noda: None declared, Yuki Mizutani: None declared, Naohiro Sugitani: None declared, Yasuo Suzuki: None declared, Toshimitsu Araki: None declared, Masato Kusunoki Grant/research support from: Chugai Pharmaceutical Co., Shionogi Pharmaceutical Co., Taiho Pharmaceutical Co., and Mitsubishi Tanabe Pharma Co., Akoya Nakajima Grant/research support from: Asahi Kasei Pharma co., Chugai Pharmaceutical, Daiichi Sankyo Co., Pfizer, Kissel Pharmaceutical Co., and Mitsubishi Tanabe Pharma Corporation.


SA10343 BURDEN OF DISEASE AT TREATMENT INITIATION AMONG BIOLOGIC-NAIVE PATIENTS WITH OLIGOARTICULAR VERSUS POLYARTICULAR PSORIATIC ARTHRITIS/SYNOVIALTHEMIA ARTHRITIS REGISTRY

Alexis Ogdie1, Mei Liu2, Meghan Glynn2, Kelechi Emeanu2, Leslie Harold2, Sven Richter2, Benoit Guerette3, Philip J. Mease4. 1University of Pennsylvania, Philadelphia, United States of America; 2Corrona, LLC, Waltham, United States of America; 3Celgene Corporation, Summit, United States of America; 4Swedish Medical Center and University of Washington School of Medicine, Seattle, United States of America.

Background: Oligoarticular PsA accounts for ~50% of PsA worldwide, but only a paucity of data describes disease burden among patients with this subtype. The Corrona PsA/SpA Registry, a prospective, US-based, observational cohort study, collects real-world data on characteristics and treatment of PsA patients, including those with oligoarthritis.

Objectives: To characterize demographics, clinical characteristics and patient-reported outcomes (PROs) at treatment initiation in biologic-naive patients with oligoarticular patients (≤4 swollen and ≤4 tender joints) vs. polyarticular patients (>4 swollen or >4 tender joints).

Methods: Biologic-naive patients ≥18 years of age diagnosed with PsA and enrolled in the registry who initiated apremilast, biologics and/or csDMARDs for PsA from March 2013–December 2018 were included. Data on patient demographics, disease activity, treatment history, comorbidities and PROs were analyzed at treatment initiation; comparisons between oligoarticular and polyarticular PsA patients were performed using t-tests or Wilcoxon rank-sum tests for continuous variables and chi-square tests or Fisher’s exact tests for categorical variables, as appropriate.

Results: 330 biologic-naive PsA patients initiating apremilast, biologics and/or csDMARDs were included (oligoarthritis: n=149; polyarthritis: n=181). Demographics and clinical characteristics were mostly similar for patients with oligoarthritides and polyarthritides, including mean age (51.6 vs. 54.3 years; P=0.068), proportion of females (51.0% vs. 59.7%; P=0.117), mean disease duration (3.0 vs. 3.1 years; P=0.789) and prior use of csDMARDs (13.4% vs. 21.0%; P=0.072). History of comorbidities was similar between the 2 groups, but the proportion of patients with fibromyalgia was higher in the polyarthritides group (2.0% vs. 8.8%; P=0.008).

Table 1. History of Comorbid Conditions Among Biologic-naive Patients With Oligoarthritides vs. Polyarthritides

<table>
<thead>
<tr>
<th>Condition</th>
<th>Oligoarthritides</th>
<th>Polyarthritides</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma</td>
<td>24.8%</td>
<td>24.6%</td>
<td>NS</td>
</tr>
<tr>
<td>COPD</td>
<td>11.6%</td>
<td>12.1%</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes</td>
<td>11.9%</td>
<td>13.7%</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension</td>
<td>27.3%</td>
<td>27.1%</td>
<td>NS</td>
</tr>
<tr>
<td>Heart disease</td>
<td>4.7%</td>
<td>4.7%</td>
<td>NS</td>
</tr>
<tr>
<td>Migraine</td>
<td>17.0%</td>
<td>19.0%</td>
<td>NS</td>
</tr>
<tr>
<td>Depression</td>
<td>32.8%</td>
<td>35.7%</td>
<td>NS</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>17.2%</td>
<td>17.8%</td>
<td>NS</td>
</tr>
<tr>
<td>History of obesity</td>
<td>20.5%</td>
<td>23.6%</td>
<td>NS</td>
</tr>
<tr>
<td>History of stroke</td>
<td>0.7%</td>
<td>1.2%</td>
<td>NS</td>
</tr>
</tbody>
</table>

Conclusion: This Corrona PsA/SpA Registry analysis showed similar overall disease burden and comorbidity burden in biologic-naive patients with oligoarthritides and polyarthritides. However, patients with oligoarthritides vs. polyarthritides had lower scores on disease activity and PRO measures at treatment initiation.

Table 2. Disease Characteristics of Biologic-naive Patients With Oligoarthritides vs. Polyarthritides

<table>
<thead>
<tr>
<th>Disease Characteristic</th>
<th>Oligoarthritides</th>
<th>Polyarthritides</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease Activity</td>
<td>3.9 (3.4-4.4)</td>
<td>4.0 (3.5-4.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Pain VAS</td>
<td>63.3 (58.9-67.1)</td>
<td>64.2 (59.8-68.7)</td>
<td>NS</td>
</tr>
<tr>
<td>Fatigue VAS</td>
<td>41.9 (37.5-46.4)</td>
<td>54.3 (50.0-58.7)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Sleep disturbance, %</td>
<td>13.4%</td>
<td>16.0%</td>
<td>NS</td>
</tr>
<tr>
<td>History of anxiety, %</td>
<td>10.2%</td>
<td>13.7%</td>
<td>NS</td>
</tr>
<tr>
<td>History of depression, %</td>
<td>13.4%</td>
<td>16.0%</td>
<td>NS</td>
</tr>
</tbody>
</table>

Acknowledgement: This study was sponsored by Corrona, LLC. Corrona is supported through contracted subscriptions with multiple pharmaceutical companies. The abstract was a collaborative effort between Corrona and Celgene with financial support provided by Celgene.

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**SAT0344**

**STRUCTURAL RADIOLOGICAL DAMAGE MSASSS SCORE: ASSOCIATION WITH THE PRESENCE OF SUBCLINICAL CARDIOT ATHEROMATOSIS IN PATIENTS WITH AXIAL SPONDYLARTHRITIS**

Sonia Peris Montoya1, Hernandez Vanessa1, Delgado Frías Esmeralda1,2, Herrera García Ada1, Juan Carlos Quevedo-Abelado2, Iván Ferraz-Amaro2,1
1Hospital Universitario de Canarias, Rheumatology, San Cristobal de la Laguna, Spain; 2Hospital Universitario de Canarias, San Cristobal de la Laguna, Spain; 3Hospital Universitario Doctor Negrín, Rheumatology, Las Palmas de Gran Canaria, Spain

**Background:** Axial spondyloarthropathies (SpA) are associated with an increase in cardiovascular morbidity and mortality, showing an increase of 20% to 40% in the risk of cardiovascular events compared to the general population and constituting the main cause of death. The presence of subclinical atheromatosis, in the form of carotid plaques, is more frequent in patients with SpAn than in healthy controls. Axial structural radiological damage in SpA is a consequence of the inflammatory activity of the disease.

**Objectives:** To analyze whether axial radiological damage by mSASSS (Modified Stoke Ankylosing Spondylitis Spine Score) is related to cardiovascular risk factors or the presence of subclinical atheromatosis in patients with SpA.

**Methods:** 195 patients diagnosed with SpA according to ASAS criteria were included. At the level of the neck and thorax, the presence of subclinical atheromatosis was assessed by image study. Axial structural damage by mSASSS was analyzed by multivariate regression analysis.

**Results:** 36% of patients with SpA showed presence of carotid plaque and a cIMT of 0.651 ± 0.121 mm. log mSASSS disclosed a positive uni- or multivariable relationship with age (beta coefficient 0.07 [95% CI 0.06-0.08], p = 0.000) and classic cardiovascular risk factors such as abdominal waist, hypertension (0.73 [95% CI 0.31-1.16], p = 0.001), smoking (0.33 [95% CI 0.08-0.59], p = 0.010), SCORE (0.33 [95% CI 0.24-0.42], p = 0.000) and levels of C-reactive protein, glucose and C-peptide. Similarly mSASSS showed a positive relationship with the BASFI (0.18 [95% CI 0.11-0.26], p = 0.000) and BASMI (0.31 [95% CI 0.23-0.38], p = 0.000) scores, but not with ASDAS- CRP or BASDAI. The presence of carotid plaque (0.51 [95% CI 0.09-0.93], p = 0.018) and a higher cIMT (4.1 [95% CI 2.4-5.7], p = 0.000) were also significantly and positively related to a higher mSASSS. When these analyses were performed in a multivariate analysis adjusting for age and sex, the relationships of log mSASSS with cardiovascular risk factors were lost, although the relationship of the former with BASFI, BASMI and SCORE remained statistically significant. With regard to sub-clinical atheromatosis, the relationship between log mSASSS and cIMT was not significant after the multivariable analysis; however, the presence of plaque showed an almost significant relationship after adjustment for age, sex and cardiovascular risk factors (0.34 [95% CI 0.02-0.67], p=0.031).

**Conclusion:** Radiological damage by mSASSS is independently related to cardiovascular risk SCORE. A tendency to an independently significant relationship with the presence of carotid plaque was observed.

**Disclosure of Interests:** None declared.

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**SAT0345**

**PREGNANCY RATES AND OUTCOMES IN EARLY AXIAL SPONDYLOARTHRITIS: ANALYSIS OF THE DESIR COHORT**

1,2Marion Pons, Nathalie Costedoat-Chalumeau2, Karine Briot1,2, Philippe Goupille2, Christian Roux1,2, Maxime Dougdos1,2, Anna Molto1,2
1Université Paris Descartes, Cochin Hospital, Paris, France; 2Inserm U1153, CRESS Paris-Sorbonne, Paris, France; 3Tour Eiffel University, Paris, France

**Background:** Only scarce data is available on regarding pregnancy rates and pregnancy outcomes in early axial Spondyloarthritis (axSpA).

**Objectives:** a) to estimate the probability of achieving a clinical pregnancy over time and its associated factors in early axSpA; b) to estimate the probability of presenting an unfavorable pregnancy outcome over time and its associated factors in this population.

**Methods:** Observational prospective French cohort (DESIR) with 6y of follow-up, including 381 of TNFi-naive women with early axSpA. Study visits were scheduled every 6 months in the first two years of follow up then yearly up to 6 years. Data on pregnancy were collected both retrospectively (before cohort inclusion) and prospectively (since inclusion) up to 6 years of follow up. Baseline characteristics of nulligravidae and uni/multi-gravidae patients where compared. The probability of achieving at least one pregnancy over time was estimated (Kaplan Meier). Associated factors were estimated by multivariable Frailty Shared Models and mixed models taking into account the correlation between several pregnancies from the same women. The probability to present an unfavorable pregnancy outcome over time (i.e a miscarriage or pre-term delivery or an elective termination of pregnancy) was estimated only during the prospective follow-up period (Kaplan Meier) since associated factors were collected also prospectively. Associated factors to an unfavourable pregnancy outcome were estimated by multivariable Frailty Shared Models and mixed models.

**Results:** Of the 381 women included in the analysis, 276 (72.4%) and 105 (27.6%) women were respectively nulligravidae and multigravidae at the end of the 6y follow-up. Multigravidae women were significantly older (37.2±8.0 vs 27.6±7.1, p<0.01), less educated (56.7% vs 71.2% university studies, p=0.01), reported higher fatigue levels (6.3±2.1 vs 5.7±2.4, p=0.02), higher BASDAI (4.9±1.9 vs 4.4±1.9, p=0.03), and higher BASFI (3.6±2.4 vs 2.8±2.2, p=0.003) scores at baseline. The probability to have at least one pregnancy throughout life was 61.8% [55.1-67.5]. The mean age at the first pregnancy was 27.3 years old. One hundred and twenty-four pregnancies occurred during follow-up. The probability to have at least one clinical pregnancy during this period was 28.5% [2.0-0.3]. Lack of TNfi use in the 6 months preceding the pregnancy outcome (HR=2.0 [95%CI 1.1-3.3], p=0.01) and a CRP >6mg/L (HR=1.79 [95%CI 1.2-2.5] p=0.01) were found to be associated with a pregnancy outcome over follow-up.

Among the 80 pregnancies occurring after inclusion with data available on the outcome, 60 (75%) presented a full-term delivery while 12 (15.0%) presented an unfavorable pregnancy outcome (6 (7.5%) and 6 (7.5%) had a miscarriage or a pre-term delivery, respectively). 2(2.5%) had a voluntary interruption of pregnancy and 6 (7.5%) were pregnancies still ongoing at the end of follow-up. Only NSAID use (HR=2.59 [95%CI 1.1-5.0], p=0.02) within 6 months of delivery was associated with an unfavorable outcome. TNfi use during pregnancy (6 patients) was not associated with an unfavorable outcome (HR= 2.29 [95%CI 0.8-5.0], p=0.10).

**Conclusion:** More than 70% patients within this early axSpA had at least one pregnancy. A favorable pregnancy outcome (i.e. full-term delivery) was observed in 75% of patients, which is comparable to the general population data. Patients who achieved a pregnancy were more likely to have stopped their TNfi 6 months prior to the pregnancy outcome and increased their CRP, probably reflecting clinical practice from 10 years ago, when recommendation was to withdraw TNFi before pregnancy. NSAID use within 6 months of delivery was independently associated with an unfavorable pregnancy outcome, while TNfi use was not.

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**SAT0346**

**EARLY RECOGNITION OF AXIAL SPONDYLOARTHRITIS IN PATIENTS WITH ACUTE ANTERIOR UVEITIS:**

**COMPARISON OF TWO REFERRAL STRATEGIES**

1,2Judith Radenscher, Hildrun Haberl1, Susanne Lüders1, Burkhard Mucche1, Fabian Profi1, Mikhail Protopopov1, Valeria Rios Rodriguez2, Laura Spiller1, Sabrina Sron1, Anne Katrin Weber1, Uwe Peyerl3, Denis Podubnyy1,4, Chantele – CBF Medizinische Klinik für Gastroenterologie, Internistische u. Rheumatologie, Reumaklinik, Martin Institute of Health, Berlin, Germany; 2Charité Campus Virchow Klinikum, Ophthalmology, Berlin, Germany; 3Deutsches Rheuma-Forschungszentrum (DRFZ), Berlin, Germany

**Background:** Diagnostic delay in axial spondyloarthritis (axSpA) remains with 5 to 9 years very high. Extraarticular manifestations like acute anterior uveitis might occur as first manifestations. Up to 40% of patients with acute anterior uveitis have an undiagnosed SpA. Recently, the Dublin Uveitis Evaluation tool (DUET) was proposed as a SpA screening tool by Systematic Coronary Risk Evaluation (SCORE) and axial radiological damage (mSASSS score) were analyzed. The presence of plaques and intima-media thickness (cIMT) was determined by carotid ultrason. The relationship between mSASSS and subclinical atheromatosis was analyzed by multivariate regression analysis.

**Results:** 36% of patients with SpA showed presence of carotid plaque and a cIMT of 0.651 ± 0.121 mm. log mSASSS disclosed a positive uni-

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**Disclosure of Interests:** None declared.

**DOI:** 10.1136/annrheumdis-2019-eular.6451
instrument for ophthalmologists [1]. At the same time, the ASAS referral tool [2] can also be used on the level of ophthalmologists.

**Objectives**: The objective of the study was to compare the performance of the DUET and the ASAS referral tools for recognition of SpA in patients with acute anterior uveitis.

**Methods**: A total of 100 consecutive patients with acute anterior uveitis of an ophthalmology clinic were included. 87 had completed a standardized rheumatological examination (including MRI of sacroiliac joints) allowing for a definite conclusion on the presence/absence of SpA. The sensitivity, the specificity and the positive predictive value of both referral tools were calculated.

**Results**: Out of the 87 patients with acute anterior uveitis 54 (62%) were diagnosed with SpA (51 with axSpA, one with peripheral SpA, one with reactive arthritis and one with psoriatic arthritis), in 36 cases the diagnosis was made for the first time. The performance of both referral tools is presented in Table 1. The ASAS referral tool showed higher sensitivity (that was especially evident in the previously undiagnosed population) but somehow lower specificity compared to the DUET. The positive predictive value was comparable for both tools indicating that approximately 2 patients with uveitis should be referred in order to diagnose one case of SpA.

In our study, MRI scans were performed on all patients including those without back pain. We thereby diagnosed axial spondylarthropathy in 5 patients, even though they did not fulfill the ASAS classification criteria as they never reported back pain (1 patient) or their back pain did not start prior to the age of 45 years (4 patients).

**Conclusion**: We revealed a high prevalence of undiagnosed SpA in patients with acute anterior uveitis. As anticipated, the more complex DUET including also psoriasis and HLA-B27 positivity showed higher specificity for recognition than the ASAS referral tool. However, the ASAS tool has a higher sensitivity (especially in undiagnosed population) and a better feasibility (purely clinical tool, does not include HLA-B27 testing and evaluation of psoriasis by an ophthalmologist).

### REFERENCES


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**Table 1. Impact of comorbidity on disease activity (BASDAI) and functional impairment (BASFI) in patients with axial spondylarthritis (N=1,776): Results from multivariable linear regression models.**

<table>
<thead>
<tr>
<th>Reference</th>
<th>BASDAI (95% CI)</th>
<th>BASFI (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elixhauser Index*</td>
<td>0.12 (0.07, 0.17)</td>
<td>0.10 (0.04, 0.17)</td>
</tr>
<tr>
<td>Number of pharmaceuticals**</td>
<td>-0.62 (0.04, 0.19)</td>
<td>0.03 (0.01, 0.06)</td>
</tr>
<tr>
<td>Uveitis, present</td>
<td>-0.14 (-0.74, -0.09)</td>
<td>0.51 (0.42, 0.60)</td>
</tr>
<tr>
<td>Sex, female</td>
<td>0.55 (0.37, 0.73)</td>
<td>-0.02 (-0.24, 0.21)</td>
</tr>
<tr>
<td>Body mass index, kg/m²</td>
<td>0.02 (0.00, 0.04)</td>
<td>0.07 (0.05, 0.10)</td>
</tr>
<tr>
<td>Smoking (current)</td>
<td>-0.29 (-0.09, 0.50)</td>
<td>0.60 (0.37, 0.82)</td>
</tr>
<tr>
<td>Suffering from stress</td>
<td>0.76 (0.75, 0.79)</td>
<td>0.23 (0.01, 0.46)</td>
</tr>
<tr>
<td>NSDAs</td>
<td>0.43 (0.24, 0.62)</td>
<td>-</td>
</tr>
<tr>
<td>Opioids</td>
<td>0.47 (0.2, 0.49)</td>
<td>0.47 (0.20, 0.73)</td>
</tr>
<tr>
<td>Physical therapy</td>
<td>0.43 (0.14, 0.51)</td>
<td>0.37 (0.15, 0.59)</td>
</tr>
</tbody>
</table>

*excluding rheumatic diseases; **except axSpA-related medication.

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; bDMARDs, biological disease-modifying anti-rheumatic drugs; NSDAs, non-steroidal anti-inflammatory drugs.
Conclusion: Comorbid conditions are common in axSpA patients and are independently associated with higher disease activity and higher level of functional impairment. Higher disease activity and a higher level of functional disability might be indicators of a severe disease resulting in the development of comorbid conditions.

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SAT0348 HOW FREQUENT IS NEUROPATHIC PAIN COMPONENT IN PATIENTS WITH SPONDYLOARTHRITIS?

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Background: Criteria to define inflammatory back pain in Spondyloarthritis (SA) are multiple. Although neuropathic pain component was known to be part of disease symptoms, it has been rarely assessed.

Objectives: The aim of this study was to determine the prevalence of the neuropathic pain component in SA patients and secondarily, to detect correlation with the disease duration, activity scores and functional impairment.

Methods: A cross-sectional study including patients with radiographic axial SA defined by ASAS criteria was conducted. Patients were questioned about their neuropathic pain using painDETECT questionnaire and Douleur Neuropathique en 4 Questions (DN4) interview. Further information about their neuropathic pain using painDETECT questionnaire and Douleur Neuropathique en 4 Questions (DN4) interview. Further information about disease characteristics, activity (BASDAI, ASDASCRP) and functional impairment (BASFI) scores were assessed the same day.

Results: Forty patients were included. The average age was about 41 years old (±12.9) and the sex ratio was 12.3 (H/F). The mean disease duration was 10.7±6.9 years. Most of patients suffered from back pain and the visual analogic scale pain scale was about 3.7±2.5. The mean BASDAI score was 2.7±2.3 and the mean ASDASCRP was 2.2±1.07. The average BASFI score was 2.57±2.5. Neuropathic pain component was noted only in 7.5% of patients by DN4 interview (≥4/10) and in 10% of patients by pain DETECT questionnaire. As expected, patients with DN4≥4 were correlated to the visual analogic scale pain (p=0.04) and female gender (p=0.07). But no relation was found with the type of SA or the disease activity or the functional scores.

Conclusion: Neuropathic pain component was noted only in 10% of SA in our work. Positive correlation was found with visual analogic scale pain and female gender. Larger studies are needed to assess this type of pain since therapeutic strategy may be affected.

Disclosure of Interests: None declared


SAT0349 HIGHER DISEASE ACTIVITY IS ASSOCIATED WITH MORE SPINAL RADIOGRAPHIC PROGRESSION IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

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Background: The association between disease activity and spinal radiographic progression in spondyloarthritis (axSpA) has been previously shown in a cohort of patients (pts) not being treated with TNFi inhibitors (TNFi).1

Objectives: To test the possible association between disease activity and spinal radiographic progression in r-axSpA in a real-life cohort, also including patients treated with TNFi.

Methods: Pts with axial spondyloarthritis (axSpA) fulfilling the modified New York criteria (mNY) were included in this prospective, observational cohort (ALBERTA FORCAST). Clinical and imaging data were collected at baseline and every 2 years up to 10 years of follow-up. Radiographs of the spine were independently scored by 2 central readers and one adjudicator (if disagreement), with known chronological order but blinded to clinical data, using the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS). To be included, pts had to have >1 two-year interval with data on mSASSS from ≥1 reader available as well as complete data on ASDAS and TNFi exposure at the start of the interval. The association between ASDAS at the start of the interval (t) and mSASSS 2 years later (t+1) was tested in two types of longitudinal GEE models: a 2-level (2 readers) model with the individual reader scores as outcome (2-level models); ii. Using as outcome averaged scores between readers (1-level models). Both type of models were adjusted for mSASSS at t (autoregression) and for a set of potential confounders defined a priori on clinical grounds. (Figure).

Results: In total, 314 pts (442 intervals) were included [74% males, mean symptom duration 17.8 (SD 11.7) years, 83% HLA-B27 positive and 7% previously treated with ≥1 TNFi]. At baseline the mean ASDAS was 2.7 (1.3) and the mean mSASSS 13.8 (18.8). During follow-up 213 (68%) pts received treatment with TNFi in ≥1 visit. Overall, the average 2-year progression was 1.33 (2.68) mSASSS-units per 2-year interval. In the 2-level multivariable model, 1 ASDAS-unit increase at t was associated with an increase of 0.25 mSASSS-units at t+1 [β (95% CI): 0.25 (0.08; 0.43)] (Figure). Results were similar using the averaged mSASSS as the outcome [β (95% CI): 0.25 (0.08; 0.43)].

Conclusion: These data add to previous evidence by showing that a higher ASDAS is associated with higher spinal radiographic progression in pts with r-axSpA independent of prior treatment with TNFi.

REFERENCE

THE IMPACT OF FIBROMYALGIA ON SLEEP DISTURBANCE AND QUALITY OF LIFE IN PATIENTS WITH ANKYLOSING SPONDYLITIS

Iryna Shapoval, Mykola Stanislavchuk, Larysa Perebetiuk. National Pigov Memorial Medical University, Vinnytsya, Ukraine, Rheumatology, Vinnytsya, Ukraine

Background: Sleep disturbance is a very frequent symptom in patients with diseases associated with pain syndrome [1, 2]. Prevalence of sleep disorders in ankylosing spondylitis (AS) patients varies in a range of 35% to 90% [2]. One of the most common comorbid condition in patients with AS is fibromyalgia (FM), that can significantly worsen quality of life and sleep quality in patients with AS.

Objectives: The aim of this study was to evaluate the impact of FM comorbidity on sleep disturbance and quality of life in patients with AS.

Methods: One hundred and nineteen patients with AS according to modified New York criteria (mean age (M±SD) 42.23±11.5 years; 21 women and 98 men) were enrolled in the study. FM was diagnosed based on the 1990 American College of Rheumatology classification criteria. All patients were asked to complete self-report questionnaires, including the Pittsburgh Sleep Quality Index (PSQI) and Ankylosing Spondylitis Quality of Life Questionnaire (ASQoL) to assess sleep disturbance and quality of life.

Results: Of the AS patients, 23 (19.3%) met the criteria for FM. The patients were divided into two groups in terms of having or not having FM. Groups were representative for age and disease duration. Patients with AS and concomitant FM showed significantly increased frequency of sleep disturbance according to the PSQI. Only 26 patients with AS (27%) scored <5 and indicated as “good sleepers”, whereas all patients with AS and concomitant FM has poor sleep quality. In group with AS patients mean scores (M±SD) of PSQI were 7.52±3.96 and in group with AS+FM - 11.04±3.5 (P=0.01). Table 1 shows detailed information on the sleep quality of patients with and without FM.

Table 1. Sleep Disturbances in patients with Ankylosing Spondylitis and Concomitant Fibromyalgia according to Pittsburgh Sleep Quality Index (sleep component scores)

<table>
<thead>
<tr>
<th>Component</th>
<th>AS with FM</th>
<th>AS without FM</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=23)</td>
<td>(n=96)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>M ± SD</td>
<td>M ± SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sleep quality</td>
<td>1.78±0.74</td>
<td>1.49±0.74</td>
<td>&lt;</td>
</tr>
<tr>
<td>Sleep latency (time to fall asleep)</td>
<td>2.00±0.85</td>
<td>1.31±1.03</td>
<td>0.05</td>
</tr>
<tr>
<td>Sleep duration (hours of sleep)</td>
<td>1.61±1.08</td>
<td>1.16±1.02</td>
<td>&lt;</td>
</tr>
<tr>
<td>Sleep efficiency (percentage of time asleep while in bed)</td>
<td>1.83±1.19</td>
<td>0.85±1.15</td>
<td>0.05</td>
</tr>
<tr>
<td>Sleep disturbances</td>
<td>1.87±0.46</td>
<td>1.32±0.55</td>
<td>0.05</td>
</tr>
<tr>
<td>Use of sleep medication</td>
<td>0.30±0.70</td>
<td>0.15±0.53</td>
<td>NS</td>
</tr>
<tr>
<td>Daytime dysfunction</td>
<td>1.65±0.93</td>
<td>1.23±0.91</td>
<td>0.05</td>
</tr>
</tbody>
</table>

In general, for each of the component scores, patients with AS scored lower than patients with AS+FM, with statistically significantly less severe sleep problems on all domains except for use of sleep medication.

Patients with AS and concomitant FM showed poorer quality of life according to ASQoL compared to patients with alone AS (13.8±2.35 vs. 8.6±1.31; P< 0.01).

Conclusion: Sleep disturbance is a frequent condition in patients with AS. Our study results demonstrate the significant impact of FM comorbidity on sleep disturbance and quality of life in patients with AS.

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Disclosure of Interests: Iryna Shapoval: None declared, Mykola Stanislavchuk Grant/research support from: AstraZeneca, Celgene, Galapagos, Genentech, GlaxoSmithKline, Human Genome, Lilly, MedImmune, Pfizer, Roche and UCB, Larysa Perebetiuk: None declared


SAT0351 IBIS-Q (IBD IDENTIFICATION OF SPONDYLOARTHRITIS QUESTIONNAIRE): A NEW TOOL TO DETECT SPONDYLOARTHRITIS IN INFLAMMATORY BOWEL DISEASE PATIENTS

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Background: Extra-intestinal manifestations (EIM) are frequent in IBD with peripheral and axial spondyloarthritis (SpA) being the commonest EIM, being reported in up to 23% of subjects. Early detection of SpA is clinically relevant to drive the therapeutic management including the right treatment at the right time to prevent disability and improve the quality of life. In the literature there are few validated Rheumatology referral models for SpA for gastroenterological use.

Objectives: The aim of this study was to develop a questionnaire to identify peripheral and axial SpA in a cohort of IBD patients (setting: IBD Unit of Sacro Cuore-Negrar Hospital Verona in a rheumatological-gastroenterology clinic).

Methods: During a preliminary meeting a group of experts in SpA-IBD (6 rheumatologists and 4 gastroenterologists) generated a list of 42 items thought to cover all possible SpA manifestations including spinal, articular and enthesal involvement. Consecutive patients referred to the IBD Unit were then enrolled from January to May 2018 without excluding patients affected by IEM. Rheumatologic assessment was performed in the same day by a Rheumatologist blinded to the medical story and to the questionnaire results in order to collect data about the 66 swollen joint count (SJC) and 68 TJC. MASEI, LEI, presence of ASAS criteria for axial and peripheral SpA, presence of diagnostic criteria for fibromyalgia (FM) and non-specific low back pain (NSLB) pain mainly due to OA. If the patient presented a tender/swollen entheses, a US imaging patients affected by EIM. Rheumatologic assessment was performed during a preliminary meeting a group of experts in SpA-IBD (6 rheumatologists and 4 gastroenterologists) generated a list of 42 items thought to cover all possible SpA manifestations including spinal, articular and enthesal involvement. Consecutive patients referred to the IBD Unit were then enrolled from January to May 2018 without excluding patients affected by IEM. Rheumatologic assessment was performed in the same day by a Rheumatologist blinded to the medical story and to the questionnaire results in order to collect data about the 66 swollen joint count (SJC) and 68 TJC. MASEI, LEI, presence of ASAS criteria for axial and peripheral SpA, presence of diagnostic criteria for fibromyalgia (FM) and non-specific low back pain (NSLB) pain mainly due to OA. If the patient presented a tender/swollen entheses, a US

Results: A final 38-items questionnaire was tested in 210 patients (excluding 17 patients for presence of other rheumatic diseases and 12 for incomplete evaluation). The psychometric analysis of the questionnaire was done on data of 181 patients. 58 patients of the enrolled patients met the ASAS criteria for SpA (13 axial, 5 both axial and peripheral 40 peripheral). The SpA prevalence in our cohort was 32% with 10 new patients identified.

Table 1

| 1. Have you ever had pain in your heels? |
| 2. Have you ever had back pain lasting at least 3 months that was not injury related? |
| 3. Have you ever had a swollen wrist without having any trauma? |
| 4. Have you ever had a swollen joint which goes down to your knee and not beyond? |
| 5. Do you wake up at night and walk because of low back pain? |
| 6. In the morning is your back stiff for more than 30 minutes? |
| 7. Have you ever had a stiff neck for some weeks or months? |
| 8. Have you ever had a pain in your thigh which goes down to your knee and not beyond? |
| 9. Is it difficult to pick things up from the floor without flexing your knees? |
| 10. Have you ever had a swollen finger like a "sausage" for some days? |
| 11. Do you find it difficult to walk because of foot pain? |
| 12. Do you feel pain when people shake your hand? |
| 13. Have you ever had swollen and painful hands? |
| 14. Have you ever had swollen and painful feet? |

In general, for each of the component scores, patients with AS scored lower than patients with AS+FM, with statistically significantly less severe sleep problems on all domains except for use of sleep medication.

Patients with AS and concomitant FM showed poorer quality of life according to ASQoL compared to patients with alone AS (13.8±2.35 vs. 8.6±1.31; P< 0.01).

Conclusion: Sleep disturbance is a frequent condition in patients with AS. Our study results demonstrate the significant impact of FM comorbidity on sleep disturbance and quality of life in patients with AS.

REFERENCES

Disclosure of Interests: Iryna Shapoval: None declared, Mykola Stanislavchuk Grant/research support from: AstraZeneca, Celgene, Galapagos, Genentech, GlaxoSmithKline, Human Genome, Lilly, MedImmune, Pfizer, Roche and UCB, Larysa Perebetiuk: None declared

include in the final questionnaire (named IBIS-Q; Table 1) having a sensitivity 84.4% and specificity 80% to detect SpA (AUC 0.8803 with CI 95% 0.8305-0.9301). We propose as cut-off of 4 positive questions of the IBIS-Q for SpA patient identification.

Conclusion: IBIS-Q seems to be a useful and simple tool to use in our IBD clinic for the detection of SpA, with a good statistical performance. Further studies are needed to validate this questionnaire.

Disclosure of Interests: Ilaria Tinazzi: None declared, Angela Variol: None declared, Antonio Marchetta: None declared, Andrea Geocchi: None declared, Pierluigi Macchioni: None declared, Dennis McDonagle Consultant for: Lilly, Novartis UCB, Speakers bureau: Lilly, Novartis UCB


SAT0352

THE FREQUENCY OF OCULAR MANIFESTATIONS IN PATIENTS WITH ADULT VS. CHILDHOOD SPONDYLOARTHRITIS

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1University of Western Ontario, London, Canada; 2University of Toronto, Toronto, Canada

Background: Adult spondyloarthritis (SpA) is characterized by abnormal bone overgrowth and inflammatory erosive osteopenia in the spine. SpA may be associated with psoriasis and psoriatic arthritis (PsA), inflammatory bowel disease, reactive arthritis, enthesitis, and ocular features such as acute anterior iritis, and chronic uveitis. Juvenile SpA onsets in children under 16 years old and may present with more peripheral enthesopathies and arthritis than adult SpA.

Objectives: This meta-analysis investigated the frequency and type of ocular involvement in childhood and adult SpA. The difference in frequency between childhood and adult SpA was also investigated.

Methods: Medline, Web of Science and Cochrane databases were searched to September, 2018 to identify publications related to spondyloarthropathy (SpA), and ankylosing spondylitis (AS) with ocular conditions (OC) (conjunctivitis, keratoconjunctivitis sicca, xerophthalmia, uveitis, eye hemorrhage, optic neuritis, papilledema, orbital disease, retinal artery/vein occlusion, macular edema, retinitis, choroiditis, xerophthalmia, choroid hemorrhage, blindness and amaurosis fugax). The rates of OC were extracted and random effects models estimated their frequency. Heterogeneity was evaluated using I². Inclusion criteria were studies in SpA of either children or adults that included a frequency of OC. Differences in frequencies of OC between childhood and adult disease were compared using chi square tests.

Results: The search process identified 3164 articles, of which 41 were eligible for inclusion. A pooled random effects model showed the prevalence of uveitis was 24% [20%-27%] in adult AS (23 studies, N= 11943 patients), 10% [7%-14%] in adult PsA (9 studies, N=1817), and 17% [10%-21%] in adult AxSpA (23 studies, N=50). In juvenile AS, the prevalence of uveitis was 27% [16%-38%] (8 studies, N=927 patients). In child onset PsA, uveitis occurred in 16% [10%-21%] (5 studies, N=498), and in juvenile undifferentiated SpA, uveitis had a frequency of 7% [1%-12%] (2 studies, N=1531). The differences in frequency of uveitis in adults vs. child onset SpA spectrum diseases were not significantly different between AS and JAS (p=0.891), PsA and JPsA (p=0.732) and between SpA and JSpA.

Conclusion: This meta-analysis compares the frequency of ocular involve- ment in seronegative spectrum diseases in adults and children where it appears that the frequency of uveitis is not statistically different in adult vs. child onset SpA and the subsets.

REFERENCES

Disclosure of Interests: Matthew Turk: None declared, Jacqueline Hayworth: None declared, Tatiana Nevskaya: None declared, Janet Pope Consultant for: Eli Lilly and Company


SAT0353

HIGH PREVALENCE OF NEWLY DIAGNOSED AXIAL SPONDYLOARTHRITIS IN PATIENTS WITH ACUTE ANTERIOR UVEITIS AND CHRONIC BACK PAIN – PRELIMINARY RESULTS OF THE SP-EYE STUDY

Rianne van Bentum1, Frank Verbraak2, Sanne Wolf3, Jenny Ongkosuwito3, Stevie Tan2, Irene van der Horst-Bruinsma4.

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Background: One third of the axial spondyloarthritides (axSpA) patients suffers from acute anterior uveitis (AAU). Correspondently, AAU can be the first sign of axSpA and previous studies described undetected axSpA in up to 40% of the patients with noninfectious AAU.

Objectives: To study whether referral of all patients with AAU and chronic back pain results in a high prevalence of newly diagnosed axSpA patients.

Methods: Between 1 March 2016 and 1 March 2017, including all patients with noninfectious AAU and a history of back pain (≥3 months, started < age of 45 years), referred from six Ophthalmology clinics to the Rheumatology Outpatient Clinic of the VU medical center. Patients with a known systemic disease associated with AAU were excluded. Patient characteristics, laboratory (HLA-B27, C-reactive

Table 1. Patient characteristics at referral.

<table>
<thead>
<tr>
<th>Overall (N=50)</th>
<th>Definite AxSpA (N=13)</th>
<th>Suspicion of early axSpA (N=21)</th>
<th>No suspicion of axSpA (N=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 42(±13) 44(±15) 38(±9) 45(±15)</td>
<td>Gender, men 26(52) 10(77) 11(52) 5(31)</td>
<td>Back pain 15(5.27) 14(5.27) 9(4.24) 21(15.32)</td>
<td>Inflammatory duration, years 21(42) 9(70) 9(43) 3(19)</td>
</tr>
<tr>
<td>Inflammatory back pain 26(52) 9(69) 12(57) 5(31)</td>
<td>HLA-B27 positive 27(54) 11(85) 12(57) 4(25)</td>
<td>AxSpA features 3(1) 4(1) 3(1) 2(1)</td>
<td></td>
</tr>
<tr>
<td>SI joint 16(32) 9(69) 6(29) 1(6)</td>
<td>Abnormality Sacroilitis, mNY criteria 9(18) 7(54) 2(10) 0(0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BASMI 2.4(2.3-4.2) 4.2(4.0-4.0) 1.6(1.0-5.7) 2.0(1.0-3.3)</td>
<td>BASDAI 3(2.5) 2(2.4) 3(2.5) 3(2.5)</td>
<td>ASDAS-CRP 21(42) 6(46) 10(48) 5(31)</td>
<td></td>
</tr>
</tbody>
</table>

Legend: Numbers are depicted as mean (±SD), median (Q1-Q3) or number of patients (%).

SAT0353

HIGH PREVALENCE OF NEWLY DIAGNOSED AXIAL SPONDYLOARTHRITIS IN PATIENTS WITH ACUTE ANTERIOR UVEITIS AND CHRONIC BACK PAIN – PRELIMINARY RESULTS OF THE SP-EYE STUDY

Rianne van Bentum1, Frank Verbraak2, Sanne Wolf3, Jenny Ongkosuwito3, Stevie Tan2, Irene van der Horst-Bruinsma4.

1Amsterdam Rheumatology and Immunology Center, location Amsterdam University Medical Center VUmc, Amsterdam, Netherlands; 2Amsterdam University Medical Center, location VUmc, Ophthalmology, Amsterdam, Netherlands; 3Onze Leve Vrouwe Hospital, Ophthalmology, Amsterdam, Netherlands; 4Amsterdam Rheumatology and Immunology Center, location Amsterdam University Medical Center VUmc, Amsterdam, Netherlands.

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Objectives: To study whether referral of all patients with AAU and chronic back pain results in a high prevalence of newly diagnosed axSpA patients.

Methods: Between 1 March 2016 and 1 March 2017, including all patients with noninfectious AAU and a history of back pain (≥3 months, started < age of 45 years), referred from six Ophthalmology clinics to the Rheumatology Outpatient Clinic of the VU medical center. Patients with a known systemic disease associated with AAU were excluded. Patient characteristics, laboratory (HLA-B27, C-reactive
CARDIOVASCULAR RISK IN YOUNG PATIENTS WITH LOW AXIAL SPONDYLOARTHRITIS ACTIVITY: PROMISING SCORING TOOLS

Elizaveta Vasilenko1, Olga Nikolaeva1, Anna Dadalova1, Maxim Korolev2, V Mazurov1, Inna Gaydukova1, 1North-Western State Medical University named after I.I. Mechnikov, Department of Therapy, Rheumatology, Examination of Cytology and Genetics, The Siberian Branch of the Russian Academy of Science, Novosibirsk, Russian Federation

Background: Patients (pts) with axial spondyloarthritis (axSpA) have increased cardiovascular morbidity and mortality, compared to the general population. However, assessment of cardiovascular risk (CVR) in axSpA is complicated, as in age < 40 years conventional CVR scales (SCORE, etc.) are not recommended, as conventional risk factors do not completely determine an increased CVR. The QRISK3 Cardiovascular Risk Algorithm (QRISK) is the only scale of measuring probability of major cardiovascular events in pts aged 25 to 40.

Objectives: To measure CVR in young pts with low activity of axSpA, and to evaluate the interrelation between CVR, measured with QRISK and gene predisposition.

Methods: The study included 46 pts 25-40 years old with axSpA (ASAS criteria 2009), achieved inactive disease on TNF-α inhibitors. AxSpA activity was measured with ASASDAS and BASDAI. CVR was calculated with the modified QRISK (QRISK3) [https://qrisk.org/three/]. All parameters of QRISK3 were collected: smoking and diabetes statuses, angina or heart attack in a 1st degree relative ≤60, chronic kidney disease (3-5 stage), atrial fibrillation, blood pressure, migraines, rheumatoid arthritis, systemic lupus erythematosus, severe mental illness, atypical antipsychotic medication, regular steroid tablets usage, erectile dysfunction, cholesterol/HDL ratio, systolic blood pressure, Standard deviation (SD) of at least two blood pressure measurements, systolic blood pressure, smoking, and gene polymorphisms in IL-6, IL17F, CC IL6-174, table 1. Interrelation of CVR with another gene polymorphisms was not significant (data are not present).

To identify the relationship between genetic factors and clinical characteristics an exploratory factor analysis was performed.

Results: Mean age ± SD of included pts was 32.5±3.87 years (26% of pts aged 25 – 30, 28.3% – 30-35, 28.3% – 35-40 years), 36 (78.3%) patient were male, symptoms duration 8.7±4.72 years, duration of TNF-α inhibitor treatment 3.1±2.4 years, ASASDAS 1.95±1.23, BASDAI 1.4±0.8. All three age groups were comparable (p>0.05). Out of the 46 pts 25 – 40 years old 34 (75.6%) had a low CVR and 11 (23.9%) had increased CVR (fig.1). Average QRISK3 score of all the patients was 1.18±1.64%. In the 25-30 year old age QRISK3 was 1.51±0.25%, in pts 30-35 years old – 1.09±0.6%, in 35-40 years old-2.31±1.0% (p<0.05 for the inter-group difference).

All patients with increased CVR had a direct associations with homozygous in CC allele IL17F-11139 gene, heterozygous in GA allele of TNF-308 and heterozygous in GG allele IL6-174. Negative associations were found between CVR and heterozygosity in His/Arg and homozygous in His/His of IL17F7, homozygosity in GG allele TNF-308, homozygosity in CC IL6-174, table 1. Interrelation of CVR with another gene polymorphisms was not significant (data are not present).

Table 1. Interrelation of QRISK 3 and Gene polymorphisms - exploratory factor analysis with ‘varimax’ rotation.

<table>
<thead>
<tr>
<th>Gene Polymorphism</th>
<th>CVR Score</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL17F-11139 CC</td>
<td>1.22</td>
<td>0.05</td>
</tr>
<tr>
<td>IL17F7 GA</td>
<td>1.18</td>
<td>0.05</td>
</tr>
<tr>
<td>TNF-308 CC</td>
<td>1.29</td>
<td>0.05</td>
</tr>
<tr>
<td>IL6-174 CC</td>
<td>1.31</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Conclusion: A quarter of young axSpA pts had an increased 10-year probability of cardiovascular events. Gene polymorphisms in IL-6, IL17F, and TNF-α locuses are strongly associated with increased CVR, QRISK3 and gene polymorphisms could be promising tools in CVR assessment in axSpA.

Further larger studies are needed for evaluation of CVR factors in axSpA.

REFERENCE

Disclosure of Interests: Elizaveta Vasilenko: None declared, Olga Nikolaeva: None declared. Anna Dadalova: None declared, Maxim Korolev: None declared, V Mazurov Grant/research support from: JSC BIOCAD, Inna Gaydukova Grant/research support from: JSC BIOCAD, Speakers bureau: payment from Pfizer, Novartis, Abbvie, Biocad, Selgene, MSD, Sanofi does not exceed 10 000 euros.

SAT0355  IRRITABLE BOWEL SYNDROME SYMPTOMS IN AXIAL SPONDYLOARTHRITIS AND HEALTHY CONTROLS, AND THEIR RELATION TO DISEASE CHARACTERISTICS – IS IT AN OVERLOOKED COMORBIDITY?

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Background: While inflammatory bowel disease (IBD) is a well-known comorbidity in axial spondyloarthritis (axSpA), little is known about the prevalence, drivers and impact of irritable bowel syndrome (IBS). In the general population, the IBS prevalence has been estimated to ~11%.[1] Objectives: To compare the frequency of gut symptoms meeting IBS criteria between axSpA patients and controls, and to examine how such symptoms relate to disease characteristics.

Methods: Consecutive axSpA patients were examined and classified as non-radiographic axial SpA (nr-axSpA; ASAS criteria; n=63), ankylosing spondylitis (AS; modified New York criteria; n=119), excluding cases with known IBD. Proportions reporting gut symptoms meeting the Rome III IBS criteria were compared between axSpA patients and sex and age matched controls (without rheumatic disease or IBD; n=50) by logistic regression.[2] Within the axSpA group, separate logistic regression models were also applied to examine whether the presence of IBS symptoms differed according to disease subtype (nr-axSpA/AS), sex, disease activity, level of systemic and gut inflammation, NSAID and DMARD use, and comorbid fibromyalgia (according to the 1990 fibromyalgia criteria).[3] Finally, we analysed associations between the presence of IBS symptoms and standard patient-reported axSpA outcomes and evaluator’s VAS global assessment of disease activity. All analyses were sex and age adjusted.

Results: Symptoms meeting IBS criteria were significantly more common among axSpA patients (30%) than controls (16%; OR 2.5 [95%CI 1.1-5.7]; Figure 1A). Within the axSpA group, no difference was observed between nr-axSpA and AS (Figure 1B). Furthermore, no associations were observed with markers of systemic or gut inflammation, whereas the presence of IBS symptoms was significantly more frequent among patients with higher disease activity (OR 2.2 [95%CI 1.1-4.4] for ASDAS-CRP >2.1 vs. ≤2.1), in females (OR 3.0 [9.5-5.8] vs. men), among NSAID users (OR 2.3 [1.1-4.6] vs. non-users), and in patients fulfilling fibromyalgia criteria (OR 3.0 [1.0-8.6] vs. not; Figure 1B). All patient-reported outcomes, but not evaluator’s VAS global, were significantly worse in patients reporting IBS symptoms (Table).

Conclusion: In axSpA patients without an IBD diagnosis, gut symptoms meeting IBS criteria were twice as common as in healthy controls. While IBS symptoms do not appear to be driven by subclinical gut inflammation or systemic inflammation, the associations with criteria-assessed fibromyalgia, female sex, and worse levels of patient-reported outcomes indicate a link to central pain sensitization, although side effects of NSAIDs may also play a role.

REFERENCES

SAT0356  DACTYLITIS IN EARLY SPONDYLOARTHRITIS. DATA FROM THE DESIR COHORT

Daniel Wending1, Clément Prati1, Alian Saraux², Anna Molti³, Thao Pham³, Maxime Dougados¹, Xavier Guillot¹, ¹CHRU, Rheumatology, Besançon, France; ²CHU, Rheumatology, Brest, France; ³Hôpital Cochin, Rheumatology, Paris, France; ⁴CHU, Rheumatology, Marseille, France; ⁵CHU de la Réunion, Rheumatology, Saint Denis de la Réunion, France

Background: Dactylitis is a particular feature shared across the several phenotypical forms of spondyloarthritis (SpA), part of the classification criteria. There are only few data available about impact of dactylitis in early stage of SpA, and factors associated with the presence/history of dactylitis.

Objectives: To study, at baseline and after 5 years in the DESIR cohort, the presence/history of dactylitis in an attempt to evaluate frequency of dactylitis in SpA and to look at the factors associated with presence of dactylitis.

Methods: DESIR is a prospective observational cohort of patients with recent onset (less than 3 years) inflammatory back pain, beginning before 50 years, suggestive of axial SpA, all available factors in the database (clinical, biological, imaging and medico economic) were compared between patients with and without past or present dactylitis at baseline (for categorical variables : odds-ratio +/- 95% CI and chi-square/Fisher tests, for continuous variables : unpaired t-tests/Mann-Whitney), by univariate and then multivariate analysis(logistic regression). Significance: p less than 0.05.

Results: At baseline, 708 patients were analyzed. 97 had a past history or a concomitant dactylitis [prevalence 13.7% (CI 95% : 11.6 – 16.2)]. Dactylitis occurred before axial symptoms in 41.3% and before any other symptom in 14.1% of the cases. By univariate analysis, dactylitis was significantly associated with history of arthritis, enthesitis, psoriasis, with elevated CRP and ESR, enthesitic and arthritis scores, BASDAI, ASDAS,BASFI, SF-36, HAQ, ASQoL, shorter disease duration, systemic and local steroids use, and with lower structural damage (sacro iliac, spine). Table shows the result of the multivariate analysis at baseline.
After 5 years, 138 cases were recorded in 480 patients with complete follow-up: prevalence 28.75% [CI 95% 24.75-32.75], with estimated incidence of 1.71/100 patient-years. At 5 years, dactylitis was significantly associated (multivariate analysis) with Achilles enthesitis (OR : 3.3), history of psoriasis (OR: 3.9), cumulative number of ASAS criteria (OR: 7.2), modified New York criteria fulfillment (OR: 0.35), DMARD use (OR: 2.7) and elevated CRP (OR:0.9).

Conclusion: In the DESIR cohort of patients suspected for early SpA, history of dactylitis is present in 13.7% of the cases at baseline and an estimated incidence of 1.7/100 p-y over 5 years. It is an early feature associated with peripheral involvement, and associated with more burden of the disease, more frequent use of DMARDS and steroids, but with less structural damage.

Disclosure of Interests: Daniel Wendling: None declared, Clément Pratil: None declared, Alain Saraux Consultant for: Roche SAS, Speakers bureau: Chugai Pharma France, Anna Moltó: None declared, Thao Pham: None declared, Alain Saraux Consultant for: Roche SAS, Speakers Disclosure of Interests: CATHERINE VAN RALBREGT Consultant for: Abbvie, Pfizer, MSD, Roche and Novartis.


SAT0358 EROSION MIGHT INCREASE PROBABILITY OF POSITIVE AXIAL SPONDYLOARTHRITIS (SPA) DIAGNOSIS IN PATIENTS WITH EARLY INFLAMMATORY BACK PAIN(IBP), A PROSPECTIVE 3.5 YEAR FOLLOW UP OF 133 PATIENTS

Liliya Yankova Komsalova1, Pilar Martinez2, Jose Fermín Gomez2, Antonio Valdavía2. 1Hospital Marina Salud, Denia, Rheumatology, Denia, Spain; 2Hospital Marina Salud, Denia, Rheumatology, Denia, Spain.

Objectives: To analyse sensitivity, specificity and predictive values of inflammatory back pain (IBP), positive HLA B27 antigen, increased C-reactive protein (CRP), clinical features (CF) such as peripheral arthritis, dactylitis, psoriasis, uveitis, inflammatory bowel disease and enthesitis, familial history (FH) of SPA and assess probabilities to develop SPA. To evaluate the impact of chronic (T1) MRI lesions in early diagnosis of SPA.

Methods: We prospectively collected and followed up 133 patients referred to our department with suspicion of SPA from September 2014 to March 2018. Data such as IBP, HLA B27 antigen, increased CRP, CF, FH and sacroiliac X-rays were collected for each patient. STIR and T1 MRI imaging were separately and independently evaluated by a rheumatologist and two radiologists. In case of disagreement, agreement between two readers was regarded as conclusive. MRI STIR sacroiliac joints (SI) assessment was done in a semi-qualitative way as follows: 1) strongly positive MRI imaging(SPMRI): patients with at least 2 highly specific bone marrow oedema(BME) lesions, easily classifiable as SPA. 2) Weakly positive MRI imaging (WPMRI): patients with at least 2 tiny BME lesions, suggestive, but not easily classifiable as SPA. 3) Clearly negative MRI imaging: patients without any of those features. T1 SI MRI images were assessed for erosion, fat metaplasia, backfill and sclerosis in a qualitative way as positive, if there were 1 or more than one, or negative, if there were none of those lesions.

Results: The average age in our study was 38.9 years. 47(35.3%) patients received diagnosis axial SPA. Radiographic sacroiliitis had 8 (17%), Sensitivity (Sn), specificity (Sp) and predictive values of inflammatory back pain (IPB) were found as follows for each item (p=0.001): IBP: 83% SI, 81.4% SI, 71%PPV, positive HLA B27: 49% SI, 80% SI, 57.5% PPV, increased CRP: 40.4% SI, 93% SI, 76% PPV, and CF: 36.2% SI, 91% SI, 68%PPV, Multivariate logistic regression binary analysis adjusted to the group of patients with non-radiographic SPA showed Odds Ratios for positive diagnosis, 64.8 for IBP (p<0.000), 9.4 for increased CRP (p=0.005) and 11.9 for CF (p=0.006). For the total group of patients the Odds Ratios were as follows: 49.2 for IBP.
Table 1. Agreement analysis between CT and bone scintigraphy

<table>
<thead>
<tr>
<th>Structures/locations</th>
<th>Involvement frequency on CT</th>
<th>Involvement frequency on bone scintigraphy</th>
<th>Measure of agreement, k value</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical vertebral</td>
<td>14/68</td>
<td>2/68</td>
<td>0.209</td>
<td>0.055</td>
</tr>
<tr>
<td>Thoracic vertebral</td>
<td>29/68</td>
<td>15/68</td>
<td>0.103</td>
<td>0.343</td>
</tr>
<tr>
<td>Lumbar vertebral</td>
<td>3/68</td>
<td>19/68</td>
<td>0.464</td>
<td>0.001</td>
</tr>
<tr>
<td>Sacral vertebral</td>
<td>20/68</td>
<td>3/68</td>
<td>0.199</td>
<td>0.006</td>
</tr>
<tr>
<td>Sternal angle</td>
<td>27/68</td>
<td>24/68</td>
<td>0.593 &lt; 0.001</td>
<td></td>
</tr>
<tr>
<td>Clavicle</td>
<td>3/68</td>
<td>4/68</td>
<td>0.248</td>
<td>0.039</td>
</tr>
<tr>
<td>Left sternoclavicular joint</td>
<td>27/68</td>
<td>36/68</td>
<td>0.274</td>
<td>0.019</td>
</tr>
<tr>
<td>Right sternoclavicular joint</td>
<td>26/68</td>
<td>40/68</td>
<td>0.209</td>
<td>0.06</td>
</tr>
<tr>
<td>Left sternocostal joint</td>
<td>40/68</td>
<td>6/88</td>
<td>0.024</td>
<td>0.683</td>
</tr>
<tr>
<td>Right sternocostal joint</td>
<td>39/68</td>
<td>8/68</td>
<td>0.075</td>
<td>0.283</td>
</tr>
<tr>
<td>Left sacral joint</td>
<td>8/68</td>
<td>14/68</td>
<td>0.145</td>
<td>0.208</td>
</tr>
<tr>
<td>Right sacral joint</td>
<td>9/68</td>
<td>18/66</td>
<td>0.415 &lt; 0.001</td>
<td></td>
</tr>
</tbody>
</table>

The two tests have comparable detection rates for the involvement of sternal angle with a higher kappa value (0.593). However, there were huge differences at other structures with extremely low kappa value, which suggests the routine bone scintigraphy for diagnosis cannot replace a CT scan in terms of evaluating osteoarticular lesions.

Conclusion: The agreement between CT and bone scintigraphy was poor, indicating an importance of implementing routine CT tests in Sapho syndrome.

REFERENCES

Disclosure of Interests: None declared

Psoriatic arthritis

SAT0359

THE AGREEMENT BETWEEN CT AND BONE SCINTIGRAPHY IN DETECTING OSTEOARTICULAR LESIONS IN SAPHO SYNDROME

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Background: Computed tomography (CT) and 99mTc-MDP bone scintigraphy are commonly used to detect osteoarticular lesions and the typical bull’s head sign of the anterior chest in the diagnosis of Sapho syndrome. Since bone scintigraphy visualizes high radioactive uptake which basically indicates inflammatory lesions, and CT demonstrates the structural lesions in bones and joints, the findings of the two modalities usually do not correspond with each other. However, little is known about the agreement between CT and bone scintigraphy on the findings of osteoarticular lesions in the patients of Sapho syndrome.

Objectives: To determine the agreement between CT and bone scintigraphy on the findings of osteoarticular lesions in Sapho syndrome.

Methods: A total of 68 patients who met the standard criteria of Sapho syndrome proposed by Kahn and Khan [3] with simultaneous (the interval <1 month) whole spine CT scan and bone scintigraphy were recruited in Peking Union Medical College from 2015 to 2016. Every CT or scintigraphy result was evaluated by at least two specialists independently and blindly. CT scan and scintigraphy results of all patients were evaluated for whether the following osteoarticular structures were involved: the clavicle, sternoclavicular joints, sternocostal joints, sacroiliac joints and all vertebrae. The respective involvement frequencies and the kappa value of agreement were calculated.

Results: Involved vertebra on the CT scan present as corner lesions or endplate lesions. Involved vertebra on the CT scan present as narrowed articular spaces or damaged articular facets. CT scan is more sensitive to detect the involvement of vertebra and sternocostal joints, but less sensitive to sternoclavicular and sacroiliac lesions than bone scintigraphy. Kappa value was calculated to assess the agreement between CT and bone scintigraphy (Table 1). It ranges from 0.103 to 0.593 over different structures, indicating a slight to moderate agreement between the two tests.
Cardiovascular risk factors and comorbidities in patients with PsA, RA and the general population

Anton Landgren1, Lennart T.H. Jacobsson2, Mats Dehlin3, Ulrika Bergsten2, Anton Landgren1, Lennart T.H. Jacobsson2, Mats Dehlin1, Ulrika Bergsten2, Ker-Ai Lee4

Background: Patients with psoriatic arthritis (PsA) have previously been reported to have increased cardiovascular morbidity and mortality compared to psoriasis, rheumatoid arthritis (RA) and the general population (GP). Obesiy has been linked to an increased risk of developing PsA and to be higher in patients with PsA compared to those with psoriasis, RA and GP. Furthermore, obese patients with PsA are more likely to have high disease activity and a reduced response to treatment. Few studies have reported on lifestyle data in combination with traditional cardiovascular risk factors in patients with PsA compared to GP and RA in the same setting.

Methods: We performed a cross-sectional study in the Western Sweden Health Care Region (WSHCR). All individuals who were ≥18 and had at least one ICD-10 diagnosis for PsA (ICD-10 codes M073) or RA (ICD 10 codes M059 and M060), at a visit at any of three rheumatology clinics in the WSHCR during a two-year period (Jan 2015 through Feb 2017) were identified. From these we randomly selected PsA patients (n=1200) and RA patients (n=1246), with equal sex distribution and they were sent a postal questionnaire. Data for non-responders were limited to age and sex.

The questionnaire included questions on demographics, comorbidities, smoking, alcohol consumption, physical activity, medications and disease specific entities. The National public health survey from 2015, “Health on equal terms”, which was sent to randomly selected citizens in Sweden aged 16-84, was used as a sex- and aged matched reference population with five controls matched per RA and PsA case. Obesity was defined according to WHO standards as BMI >30. Daily smoking, alcohol consumption (>5 standard drinks of alcohol per week) and physical activity (>3 hours per week) were also analyzed.

Results: Response rates were n=687 (57.3%) for PsA and n=742 (59.6%) for RA. After age- and sex matching there were 432 individuals with PsA, 431 with RA and 4314 matched subjects from the general population left for analyses. Mean age was 61.1 (SD 12.0) years and 42% males in all three groups. Patients with PsA were more frequently obese, compared to both GP (p<0.001) and RA (p=0.012). Smoking was more prevalent in RA and PsA than in GP. In addition, hypertension was more common in PsA compared to RA (p=0.044) and GP (p<0.001). Diabetes was also more prevalent in PsA than in GP (p<0.007), as was hyperlipidemia (p=0.039). Patients with PsA drank more often ≥5 standard drinks of alcohol per week than patients with RA did (p=0.046).

Conclusion: In PsA, obesity and comorbidities related to CVD were increased above what was seen for both RA compared to the GP. This highlights the need to address these partly modifiable factors in particular for patients with PsA.

Disclosure of Interests: Anton Landgren: None declared, Lennart T.H. Jacobsson Consultant for: LJ has received lecture and consulting fees from Pfizer, Abbvie, Novartis, Eli-Lilly and Janssen, Mats Dehlin: None declared, Ulrika Bergsten: None declared, Eva Klingberg Grant/research support from: Unrestricted grant from Roche, Consultant for: Novartis, Speakers bureau: Speakers fee from Lilly


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Table 1. Characteristics of PsA, RA and GP subjects

<table>
<thead>
<tr>
<th></th>
<th>PsA, n=432</th>
<th>RA, n=431</th>
<th>GP, n=4314</th>
<th>p-value (PsA vs RA)</th>
<th>p-value (RA vs GP)</th>
<th>p-value (PsA vs GP)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI, mean (kg/m²)</td>
<td>27.4</td>
<td>26.3</td>
<td>26.4</td>
<td>0.001</td>
<td>0.705</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (≥30, %)</td>
<td>98 (22.7)</td>
<td>69 (16.0)</td>
<td>73 (17.1)</td>
<td>0.012</td>
<td>0.555</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Daily smoker, n(%)</td>
<td>37 (8.6)</td>
<td>55 (12.8)</td>
<td>N/A</td>
<td>0.046</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>≥5 standard drinks of alcohol per week, n(%)</td>
<td>92 (21.3)</td>
<td>69 (16.0)</td>
<td>N/A</td>
<td>0.046</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Physical activity ≥3 hours per week, n(%)</td>
<td>224 (51.9)</td>
<td>205 (47.6)</td>
<td>235 (54.6)</td>
<td>0.208</td>
<td>0.005</td>
<td>0.289</td>
</tr>
<tr>
<td>Diabetes, n(%)</td>
<td>52 (12.0)</td>
<td>42 (9.7)</td>
<td>356 (8.3)</td>
<td>0.167</td>
<td>0.301</td>
<td>0.007</td>
</tr>
</tbody>
</table>

SAT0361

Cardiovascular risk factors and comorbidities in patients with PsA, RA and the general population

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Background: Patients with psoriatic arthritis (PsA) have previously been reported to have increased cardiovascular morbidity and mortality compared to psoriasis, rheumatoid arthritis (RA) and the general population (GP). Obesiy has been linked to an increased risk of developing PsA and to be higher in patients with PsA compared to those with psoriasis, RA and GP. Furthermore, obese patients with PsA are more likely to have high disease activity and a reduced response to treatment. Few studies have reported on lifestyle data in combination with traditional cardiovascular risk factors in patients with PsA compared to GP and RA in the same setting.

Methods: We performed a cross-sectional study in the Western Sweden Health Care Region (WSHCR). All individuals who were ≥18 and had at least one ICD-10 diagnosis for PsA (ICD-10 codes M073) or RA (ICD 10 codes M059 and M060), at a visit at any of three rheumatology clinics in the WSHCR during a two-year period (Jan 2015 through Feb 2017) were identified. From these we randomly selected PsA patients (n=1200) and RA patients (n=1246), with equal sex distribution and they were sent a postal questionnaire. Data for non-responders were limited to age and sex.

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DEPRESSIVE SYMPTOMS ARE ASSOCIATED WITH A GREATER CARDIOVASCULAR RISK IN PATIENTS WITH PSORIATIC ARTHRITIS.

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Background: Cardiovascular (CV) events are the leading cause of death in patients with psoriatic arthritis (PsA) but current cardiovascular risk prevention strategies in these subjects appear to be inadequate. The prevalence of depressive symptoms, even in the absence of a diagnosed depressive disorder, is greater in patients with PsA than in the general population.

Objectives: The objective of the study is to evaluate the association between CV risk factors and depressive symptoms in a cohort of patients with PsA.

Methods: We enrolled consecutive patients with PsA (CASPAR criteria) without a diagnosis of major depression or history of major CV events. The presence of significant depressive symptoms was defined by the Hospital Anxiety and Depression Scale (HADS) for scores ≥8. The subjects were characterized by disease phenotype, duration and activity (according to the DAPSA index) and immunosuppressive, antihypertensive, glucose-, urate- and lipid-lowering therapy. In order to assess the prevalence of traditional CV risk factors, patients were characterized by BMI, waist and hip circumference, blood pressure (BP), smoking habits, physical activity and familiarity for myocardial infarction, lipid, glucose and serum urate. The predictive risk of CV events was calculated by the American Heart Association (AHA) Risk Score (FRS). Atherosclerotic Cardiovascular Disease (ASCVD) score and Systematic Coronary Risk Evaluation (HeartSCORE) risk charts.

Results: One-hundred patients with PsA were enrolled (males 47.0%; mean age 54.9±12.5 years, duration of illness 9.1±10.6 years) of which 20.6% were in remission, 43.3% in low disease activity, 28.8% in moderate disease activity and 10.3% in high disease activity according to DAPSA. 38% had significant depressive symptoms according to the HADS questionnaire. Patients with depressive symptoms had a higher mean age (57.8±12.3 vs 52.1±11.2 years, p=0.002) compared to patients with significant depressive symptoms but were comparable according to BMI, waist and hip circumference, blood pressure (BP), smoking habits, physical activity and familiarity for myocardial infarction, lipid, glucose and serum urate. The predictive risk of CV events was calculated by the AHA Frailty Risk Score (FRS), Atherosclerotic Cardiovascular Disease (ASCVD) score and Systematic Coronary Risk Evaluation (HeartSCORE) risk charts.

Conclusion: The presence of depressive symptoms is associated with a higher incidence of modifiable CV risk factors and a higher predicted risk of CV events in patients with PsA. Systematic research of depressive symptoms in patients with PsA could contribute to the correct assessment of CV risk, helping to implement more effective prevention strategies.

Disclosure of Interests: Gerlando Natalello: None declared, Enrico De Lorenzis: None declared, Dario Bruno: None declared, Giacomo Tanti: None declared, Maria Rosana Magraro: None declared, Barbara Tolusso: None declared, Giuse Peluso: None declared, Elsa Grezeme Consultant for: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Sanofi, UCB, Roche, and Pfizer, Speakers bureau: BMS, Speakers bureau: Roche, Speakers bureau: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Sanofi, UCB, Roche, and Pfizer


ENTHESITIS BUT NOT DACTYLITIS CONTRIBUTES TO BURDEN OF DISEASE IN PSA PATIENTS: DATA FROM THE BEPAS REAL LIFE COHORT

Kurt de Vlam1, Rik Lories1, Serge Steinfeld2, Filip van den Bosch3, Adrien Nzeusuou Toukap3, Hermine Leroi3, BEPAS working group. 1University Hospitals Leuven, Rheumatology, Leuven, Belgium; 2Clinical St Jean, Rheumatology, Gent, Belgium; 3UCL St Luc, Rheumatology, Brussels, Belgium; 4MSD Belgium, Medical Affairs

Background: Psoriatic arthritis (PsA) significantly impacts physical function and quality of life. Limited data are available to specifically evaluate the impact of the different disease domains such as arthritis, axial involvement, skin disease, enthesis and dactylitis. The BEPAS cohort, a prospective daily life cohort of PsA patients allows to study the impact of enthesitis and dactylitis on disease activity, disability and quality of life in PsA patients.

Objectives: 1) to measure the impact of enthesitis and dactylitis on health-related quality of life in PsA patients in Belgium.

Methods: At the inclusion visit, a cross-sectional analysis of dactylitis and enthesitis was performed among 462 patients from the BEPAS cohort and impact of enthesitis and dactylitis was studied. Patients were evaluated for the demographics, clinical disease manifestations, disability, disease global assessment and inflammatory markers at inclusion. Differences of tested variables between patients with and without dactylitis and/or enthesitis were evaluated by T-test or Chi-square testing.

Results: 462 patients (273 males and 189 females) with a mean disease duration of 8.53 years (SD: 9.25yrs) were recruited in 17 BEPAS centers from December 2012 to July 2014. 111 patients had enthesitis and 63 patients had dactylitis at inclusion. 17 patients had both enthesitis and dactylitis. Results are summarized in the table below.

Conclusion: Enthesitis has a larger impact on Quality of Life and Health Status than dactylitis in PsA. Patients with enthesitis and dactylitis have higher joint scores but not higher markers of systemic inflammation than those without.

Acknowledgement: This study is financially supported by MSD Belgium

Disclosure of Interests:

Kurt de Vlam Consultant for: Pfizer Inc, Consultant for: Johnson & Johnson; Rik Lories Consultant for: AbbVie, BMS, Celgene, Janssen, Lilly, Merc, Novartis, Pfizer and UCB. Kurt de Vlam Consultant for: Pfizer records.

Enthesitis

<table>
<thead>
<tr>
<th>Disease duration</th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FtD</td>
<td>7.97 (8.87)</td>
<td>8.17 (9.37)</td>
<td>5.12 (8.30)</td>
<td>9.07 (8.63)*</td>
</tr>
<tr>
<td>BMI</td>
<td>27.98 (4.94)</td>
<td>27.30 (4.95)</td>
<td>27.35 (4.97)</td>
<td>27.74 (4.94)</td>
</tr>
<tr>
<td>TJ&lt;8</td>
<td>7.71 (10.34)</td>
<td>23.49</td>
<td>8.57 (11.99)</td>
<td>3.36 (5.89)*</td>
</tr>
<tr>
<td>SF36</td>
<td>2.94 (4.80)</td>
<td>1.96 (4.51)</td>
<td>6.33 (7.42)</td>
<td>1.45 (3.41)*</td>
</tr>
<tr>
<td>PTGAVAS</td>
<td>5.11 (13.22)</td>
<td>2.85 (6.87)</td>
<td>3.18 (5.74)</td>
<td>3.44 (9.20)</td>
</tr>
<tr>
<td>CRP</td>
<td>4.8 (6.06)</td>
<td>6.17 (11.14)</td>
<td>6.04 (16.16)</td>
<td>5.82 (10.64)</td>
</tr>
<tr>
<td>RTS</td>
<td>47.04 (19.88)</td>
<td>32.92 (24.39)</td>
<td>45.42 (28.76)</td>
<td>35.33 (22.62)*</td>
</tr>
<tr>
<td>PSA</td>
<td>32.86 (21.23)</td>
<td>21.26 (20.12)</td>
<td>39.22 (23.63)</td>
<td>21.16 (15.79)*</td>
</tr>
<tr>
<td>DAS28/CRP</td>
<td>3.42 (1.14)</td>
<td>2.66 (1.06)</td>
<td>3.55 (1.39)</td>
<td>2.73 (1.03)*</td>
</tr>
<tr>
<td>DAPSA/DAREA</td>
<td>24.11 (15.66)</td>
<td>17.27 (16.65)</td>
<td>19.03 (16.65)</td>
<td>17.71 (13.99)*</td>
</tr>
<tr>
<td>HAQ</td>
<td>0.91 (1%)</td>
<td>164.39 (47%)</td>
<td>103.63 (16%)</td>
<td>163.87 (41%)*</td>
</tr>
<tr>
<td>MDA</td>
<td>6.93 (0.60)</td>
<td>0.65 (0.83)</td>
<td>0.69 (0.82)</td>
<td>0.70 (0.62)</td>
</tr>
<tr>
<td>HAQ score status</td>
<td>1161 (14%)</td>
<td>1359 (38%)</td>
<td>196 (32%)</td>
<td>332 (39%)</td>
</tr>
</tbody>
</table>

* p<0.05, §p<0.001

Disclosure of Interests:

Kurt de Vlam: None declared, Filip van den Bosch: Consultant for: AbbVie, BMS, Celgene, Janssen, Lilly, Merck, Novartis, Pfizer and UCB, Speakers bureau: Abb-Vie, BMS, CMS, Galapagos, Janssen, Lilly, Merck, Novartis, Pfizer and UCB., Adrien Nzeusuou Toukap: None declared, Hermine Leroi Employee of: HL is a employee of MSD Belgium

EFFECT OF ACHIEVING DAPSA-LDA ON THE PROGRESSION OF BONE EROSION AND ENTHESIOPHYES IN PATIENTS WITH PSORIATIC ARTHRITIS: A LONGITUDINAL HR-pQCT STUDY

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1) The Prince of Wales Hospital, The Chinese University of Hong Kong, Department of Medicine and Therapeutics, Hong Kong, China; 2)The Prince of Wales Hospital, The Chinese University of Hong Kong, Department of Imaging and Interventional Radiology, Hong Kong, China; 3)The Prince of Wales Hospital, The Chinese University of Hong Kong, Research Centre for Medical Image Computing, Department of Imaging and Interventional Radiology, Hong Kong, China; 4)The Chinese University of Hong Kong, Bone Quality and Health Centre, Department of Orthopaedics and Traumatology, Hong Kong, Hong Kong (SAR)

Background: Psoriatic arthritis (PsA) is characterized by structural bone damage with bone erosions and enthesiophytes. Whether achieving low disease activity (LDA) according to Disease Activity in Psoriatic Arthritis (DAPSA-LDA) limits progression of structural bone damage, as assessed by high resolution-peripheral quantitative computed tomography (HR-pQCT), is uncertain.

Objectives: To investigate the progression of structural bone abnormalities at the metacarpal head in patients with PsA over a 5-year period.

Methods: HR-pQCT examination was performed in 60 PsA patients at baseline and after 5 years. Baseline-indexed image registration and slice matching were performed to acquire precisely matched baseline and follow-up volumes of interest (VOI) at the 2nd and 3rd metacarpal heads (MCH2 & 3). A semi-automated method was used to calculate bone erosion and enthesiophyte volume [1]. Erosion and enthesiophyte progression was defined as change exceeding the smallest detectable change (SDC).

The primary objective of this study was to investigate the degree of bone erosion and enthesiophyte progression in PsA patients receiving routine care. Secondary objectives were to compare changes in bone erosion and enthesiophyte volume between patients who 1) received TNFi group or did not receive TNFi throughout the 5-year period. Comparable changes in bone erosion and enthesiophyte volume were found between the TNFi and the non-TNFi groups. After 5 years, 26 (43%) patients achieved sDAPSA-LDA. Less erosion progression (12/51 [23.5%] vs 25/60 [41.7%], P=0.047) was observed those who did rather than did not achieve sDAPSA-LDA. Similarly, enthesiophyte volume change (0.28±0.67 vs 0.61±0.80 mm³; P=0.048) and total enthesiophyte volume change (0.42±0.69 vs 1.05±1.29 mm³; P=0.019) were lower in those who did rather than did not achieve sDAPSA-LDA.

Conclusion: Once DAPSA-LDA is achieved, it should be maintained for a long period so as to minimize progression of structural bone damage in patients with PsA.

REFERENCE

Disclosure of Interests: None declared
Conclusion: Across the Nordic countries the prescription pattern for biological therapies for PsA has changed significantly over time. The decreasing levels of both CRP scores and SJC suggest that PsA patients who initiate bDMARD treatment have changed towards a less active inflammatory phenotype from 2006-2017. Collaboration across registers will allow for robust assessment of the uptake of newer biological therapies. Overall the number of prescribed therapies increased during the observational period, indicating a previously unmet need for biological therapies in the Nordic population.

REFERENCES

Acknowledgement: This study was partly funded by a grant from Nordforsk and FOREUM

Disclosure of Interests: Rebekka L. Hansen: None declared, Tanja Schjødt Jørgensen Consultant for: Abbvie, Roche, Novartis, UCB, Biogen, Eli Lilly., Speakers bureau: Abbvie, Roche, Novartis, UCB, Biogen, Eli Lilly., Lane Dreyer Consultant for: MSD, UCB and Janssen Pharmaceuticals, Speakers bureau: MSD, UCB and Janssen Pharmaceuticals, Speakers bureau: UCB, MSD, Eli Lilly and Janssen Pharmaceuticals, Bjørn Gudbjornsson: None declared, Johan Askling Consultant for: Received reimbursment from Celgene for speaking about guidelines for the treatment of psoriatic arthritis, Lars Erik Kristensen Consultant/research support from: UCB, Biogen, Janssen Pharmaceuticals, and Novartis, Consultant for: Consultant for Abbvie, Amgen, Biogen, UCB, Novartis, Eli Lilly, and Janssen Pharmaceuticals.

Background: The impact of gender on tumor necrosis factor inhibitors (TNFi) effectiveness has been poorly studied in Psoriatic Arthritis (PsA) patients.

Table 1. Baseline characteristics of PsA patients from Reuma.pt, treated with a 1st TNFi, according to gender.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Population (n=760)</th>
<th>Female (n=377)</th>
<th>Male (n=373)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at 1st TNFi, years (mean ± sd)</td>
<td>47.6 ± 11.6</td>
<td>48.5 ± 11.7</td>
<td>46.7 ± 11.5</td>
<td>0.030†</td>
</tr>
<tr>
<td>Obese (BMI&gt;30Kg/m²), n (%)</td>
<td>104 (21.8%)</td>
<td>64 (16.9%)</td>
<td>40 (10.9%)</td>
<td>0.008†</td>
</tr>
<tr>
<td>Clinical subtype, n (%)</td>
<td>401 (62.3%)</td>
<td>228 (60.6%)</td>
<td>173 (47.5%)</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>Asymptomatic polyarthritis, n (%)</td>
<td>29 (4.4%)</td>
<td>9 (2.7%)</td>
<td>20 (5.8%)</td>
<td>-</td>
</tr>
<tr>
<td>Arthritis distal</td>
<td>6 (0.9%)</td>
<td>4 (1.1%)</td>
<td>2 (0.6%)</td>
<td>0.710</td>
</tr>
<tr>
<td>ESR mm/1 st h (mean ± sd)</td>
<td>35.0 ± 15.1</td>
<td>35.8 ± 15.8</td>
<td>35.2 ± 15.4</td>
<td>0.822</td>
</tr>
<tr>
<td>CRP mg/l (mean ± sd)</td>
<td>10.4 ± 6.5</td>
<td>10.3 ± 6.2</td>
<td>10.5 ± 6.8</td>
<td>0.691</td>
</tr>
<tr>
<td>Tender joints (mean ± sd)</td>
<td>5.3 ± 5.5</td>
<td>6.2 ± 6.3</td>
<td>4.4 ± 4.4</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>Predominant axial</td>
<td>128 (18.3%)</td>
<td>42 (11.9%)</td>
<td>86 (11.5%)</td>
<td>0.033†</td>
</tr>
<tr>
<td>Women years since diagnosis at 1st TNFi (mean ± sd)</td>
<td>6.6 ± 6.7</td>
<td>7.1 ± 6.9</td>
<td>6.0 ± 6.6</td>
<td>0.033†</td>
</tr>
</tbody>
</table>

SAT0366 GENDER DIFFERENCES IN PSORIATIC ARTHRITIS – IMPACT ON TUMOR NECROSIS FACTOR INHIBITORS PERSISTENCE AND RESPONSE

Elsa Vieira-Sousa1, Monica Eusebio2, Pedro Ávila-Ribeiro3, Nikita Khmelinskii1, Ana Rita Cruz-Machado1, Teresa Martins-Rocha1, Miguel Bernardes3, Danielia Farís4, Joana Silva5, Helena Santos6, Claudia Miguel7, Pedro Carvalho8, Tiago Costa9, Lídia Teixeira10, Tiago Meirinhos10, Patricia Nero10, João Euroco Fonseca11, Maria Jose Santos11, Hospital de Santa Maria, CHULN; Instituto de Medicina Molecular, FMUL, Academic Medical Centre, Rheumatology Department, Lisbon, Portugal. 2Portuguese Society of Rheumatology, Lisbon, Portugal. 3CHUL: FMUP, Rheumatology Department, Porto, Portugal. 4ULSAM, Rheumatology Department, Ponte de Lima, Portugal. 5Instituto Português de Reumatologia, Lisboa, Portugal. 6CHUC and CHUA, Rheumatology Department, Faro, Portugal. 7CHLO, Rheumatology Department, Lisbon, Portugal. 8HGO, Rheumatology Department, Almada, Portugal. 9CHBV, Rheumatology Department, Aveiro, Portugal. 10Hospital Cuf Descobertas, Lisboa, Portugal.
PSAID9 in Patients With Active Psoriatic Arthritis Treated With Filgotinib vs Placebo: Results From EQUATOR, a Randomized, Phase 2 Study

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Background: Filgotinib (FIL) is an oral, selective Janus kinase 1 inhibitor that, compared with placebo (PBO), significantly improved patient-reported outcomes in active psoriatic arthritis (PsA) in the phase 2 EQUATOR randomized controlled trial (RCT; NCT03101670) [1]. PsA Impact of Disease (PsAID) is a validated, EULAR-developed, PsA-specific questionnaire for measurement of health-related quality of life (HRQoL) [2]. PsAID is less complex than generic HRQoL tools, such as the 36-item Short Form Survey (SF–36). To our knowledge, this is the first RCT reporting efficacy results using PsAID9.

Objectives: To determine the effect of FIL vs PBO on PsAID9 in participants of EQUATOR.

Methods: EQUATOR was a multicenter, double-blind study in which patients were randomized 1:1 to FIL 200 mg or PBO once daily for 16 weeks [1]. HRQoL was assessed at weeks 4 and 16 with PsAID9 (total and individual domain scores [each scored 0–10]) and, for comparison, with the Physical Component Summary (PCS) and Mental Component Summary (MCS) of SF-36. Higher PsAID scores correspond to greater impact of PsA [2]. Analysis of covariance was used to compare outcomes between groups.

Results: There were 131 participants in EQUATOR (FIL: n=65; PBO: n=66). Mean (standard deviation [SD]) age was 49 (12.2) and 50 (10.9) years and mean (SD) baseline PsAID9 scores were 5.8 (1.6) and 5.7 (2.0) for FIL and PBO, respectively. Effects of FIL on PsAID9 total scores vs PBO; at week 16, PsAID9 total scores were 3.5 (2.3) vs 4.9 (2.2) for FIL and 4.9 (2.2) for PBO. Mean change (SD) from baseline at week 16 was −2.3 (1.8) vs −0.8 (2.2), respectively (Figure 1a); least-squares (LS) mean of group difference (95% confidence interval) was −1.48 (−2.12, −0.84), p < 0.0001. At week 16, significant improvements were observed in all nine individual domains compared with baseline in FIL vs PBO (Figure 2; p < 0.0001; **p < 0.001; ***p < 0.0001; between-group difference in change from baseline scores at week 16).

Disclosure of Interests: Elsa Vieira-Sousa Grant/research support from: MSD, Novartis, Monica Eusébio: None declared, Pedro Ávila-Ribeiro: None declared, Nikita Khmelinskii: None declared, Ana Rita Cruz-Bernardes: None declared, Daniela Faria: None declared, Joana Silva: None declared, Teresa Martins-Rocha: None declared, Mónica Eusébio: None declared, Pedro Ávila-Ribeiro: None declared, Maria Jose Santos: None declared

PsAID9 domains for FIL vs PBO, including pain (p<0.0001; Figure 1b). A significant improvement in SF–36 PCS, but not in MCS, with FIL vs PBO was observed. The mean change (SD) from baseline in PCS at week 16 was 7.4 (6.6) vs 2.4 (6.6) for FIL vs PBO, respectively (L5 mean of group difference: 4.67 [2.58, 6.76], p<0.0001).

Conclusion: Compared with PBO, FIL significantly improved disease impact in patients with active PsA, as measured by the PsA-specific PsAID9 total score and individual domain scores. Significant improvement in SF–36 PCS score was also seen with FIL.

REFERENCE

Disclosure of Interests: Not applicable

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GO-DACT: A RANDOMIZED DOUBLE-BLIND PLACEBO-CONTROLLED PROOF-OF-CONCEPT TRIAL OF GOLIMUMAB PLUS METHOTREXATE (MTX) VERSUS MTX MONOTHERAPY, IN IMPROVING DACTYLITIS, IN MTX NAÏVE PSORIATIC ARTHRITIS PATIENTS

Elsa Vieira-Sousa1, Pedro Alves2, Ana Maria Rodrigues3, Filipa Teixeira4, José Tavares-Costa4, Alexandra Bernardo5, Sofia Pimenta5, Fernando Pimentel dos Santos6, João Lagoa Gomes7, Renata Aguilar8, Tacialina Videira9, Patricia Pinho9, Carolina Costa10, Helena Santos10, Joana Borges10, Graça Sequeira11, Célia Ribeiro11, Lidia Teixeira12, Pedro Ávila-Ribeiro12, Ana Maria Reis12, Maria Teldeira12, Filipa Teixeira12, Ana-Maria Orbai1, M Elaine Husni2, Dafna D. Gladman3, Ying Ying Leung4, Philip J. Mease9.

Objective: To evaluate the efficacy of golimumab plus MTX versus placebo plus MTX for active dactylitis in PsA patients, in a phase 3b trial.

Method: GO-DACT was a proof-of-concept multicentric, investigator-initiated randomized, double-blind, placebo-controlled, parallel-design trial, conducted in 13 Portuguese Rheumatology Centers. PsA patients, naïve for MTX and biologic disease modifying anti-rheumatic drugs (bDMARDs), with active dactylitis, were randomly allocated to either golimumab in combination with MTX or MTX monotherapy. The primary endpoint was the change from baseline in the dactylitis severity score (DSS) assessed at week 24. Key secondary endpoints included DSS response and the magnetic resonance imaging (MRI) dactylitis score, as well as composite indexes of PsA activity.

Results: 44 patients were centrally randomized, 21 to golimumab plus MTX and 23 to placebo plus MTX, for 24 weeks, and 1 patient from each arm dropped out. Due to favorable results on a planned interim analysis recruitment was halted. The median MTX dose in the golimumab plus MTX group was 15mg/week and in the MTX monotherapy group 20mg/week. The median baseline DSS was 6 in each arm. Patients treated with golimumab plus MTX experienced significantly greater improvements in the DSS at week 24 (median change of 5) as compared to the MTX group (median change of 2) (p<0.026). At week 24, 12 (60.0%) patients treated with golimumab plus MTX and 4 (18.2%) with MTX, achieved the DSS70 response (p<0.05). Significant differences were also observed in the median changes from baseline to week 24 in MRI dactylitis score, Disease Activity Score 28 (DAS28), Disease Activity Index for PsA (DAPSA), PsA Disease Activity Score (PASDAS) and Target Nail Psoriasis Severity Index (NAPSI), favoring the golimumab and MTX association arm. Likewise, higher proportions of patients treated with golimumab plus MTX achieved DSS50 responses and the American College of Rheumatology 20/50 responses, at week 24. There were no new safety issues for golimumab during this trial.

Conclusion: GO-DACT suggests additional benefits from the combination of golimumab and MTX as first-line bDMARD therapy versus MTX monotherapy, in the treatment algorithm of PsA active dactylitis.

REFERENCE
Not applicable

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GO-DACT: A RANDOMIZED DOUBLE-BLIND PLACEBO-CONTROLLED PROOF-OF-CONCEPT TRIAL OF GOLIMUMAB PLUS METHOTREXATE (MTX) VERSUS MTX MONOTHERAPY, IN IMPROVING DACTYLITIS, IN MTX NAIVE PSORIASIC ARTHRITIS PATIENTS

Elsa Vieira-Sousa1, Pedro Alves2, Ana Maria Rodrigues3, Filipa Teixeira4, José Tavares-Costa4, Alexandra Bernardo5, Sofia Pimenta5, Fernando Pimentel dos Santos6, João Lagoa Gomes7, Renata Aguilar8, Tacialina Videira9, Patricia Pinho9, Carolina Costa10, Helena Santos10, Joana Borges10, Graça Sequeira11, Célia Ribeiro11, Lidia Teixeira12, Pedro Ávila-Ribeiro12, Fernando M. Martin13, Helena Carrião13, Ruy M. Ribeiro13, Joao Eurioc Fonseca13, Hospital de Santa Maria, CHSJ; Instituto de Medicina Molecular, FUMUL; Centro Académico de Medicina de Lisboa, Serviço de Reumatologia; Lisboa, Portugal, ¶CHLC, Serviço de Radiologia, Lisboa, Portugal, ¶HSEIT, FMUL, Centro Académico de Medicina de Lisboa, Unidade de Reumatologia, Lisboa, Portugal; ¶ULSAM, Serviço de Reumatologia, Ponte de Lima, Portugal; ¶CHSU, Serviço de Reumatologia, Porto, Portugal; ¶CHLC, Serviço de Reumatologia, Lisboa, Portugal; ¶CHEV, Serviço de Reumatologia, Aveiro, Portugal; ¶CH/VNG, Serviço de Reumatologia, Vila Nova de Gaia, Portugal; ¶Hospital Particular do Algare, Faro, Portugal; ¶Instituto Português de Reumatologia, Lisboa, Portugal; ¶CH S da Universidade de Lisboa, Portugal; ¶CHF, Serviço de Reumatologia, Faro, Portugal; ¶ICM, Almada, Portugal; ¶CHCM, Faculdade Portuguesa de Reumatologia, Lisboa, Portugal; ¶CEDOC, NOVA Medical School, UNL, EpDoC UnL, Lisboa, Portugal; ¶FMUL, Laboratório de Biomatematática, Lisboa, Portugal

Background: Psoriatic arthritis (PsA) dactylitis is associated with an increased risk of erosions and higher disease activity. Dactylitis treatment strategies are however controversial due to the absence of evidence from randomized controlled trials studying dactylitis as a primary outcome.

Objectives: To assess the efficacy of golimumab plus MTX versus placebo plus MTX for active dactylitis in PsA patients, in a phase 3b trial.

Method: Difference 4.67 [2.58, 6.76], p<0.0001. Analysis recruitment was halted. The median MTX dose in the golimumab plus MTX group was 15mg/week and in the MTX monotherapy group 20mg/week. The median baseline DSS was 6 in each arm. Patients treated with golimumab plus MTX experienced significantly greater improvements in the DSS at week 24 (median change of 5) as compared to the MTX group (median change of 2) (p<0.026). At week 24, 12 (60.0%) patients treated with golimumab plus MTX and 4 (18.2%) with MTX, achieved the DSS70 response (p<0.05). Significant differences were also observed in the median changes from baseline to week 24 in MRI dactylitis score, Disease Activity Score 28 (DAS28), Disease Activity Index for PsA (DAPSA), PsA Disease Activity Score (PASDAS) and Target Nail Psoriasis Severity Index (NAPSI), favoring the golimumab and MTX association arm. Likewise, higher proportions of patients treated with golimumab plus MTX achieved DSS50 responses and the American College of Rheumatology 20/50 responses, at week 24. There were no new safety issues for golimumab during this trial.

Conclusion: GO-DACT suggests additional benefits from the combination of golimumab and MTX as first-line bDMARD therapy versus MTX monotherapy, in the treatment algorithm of PsA active dactylitis.

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Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) and endorsed by Outcome Measures in Rheumatology (OMERACT), aims to improve and standardize the assessment of PsA outcomes.

Objectives: To report the efficacy of secukinumab vs placebo across individual PsA core domains at week 16 in patients naive to tumor necrosis factor (TNF) inhibitors or who were inadequate responders (TNF-IR), using pooled data from 4 phase 3 FUTURE studies.

Methods: Patients with active PsA participated in the phase 3 FUTURE 2, 3, 4, and 5 trials. Data were pooled for secukinumab 150 mg (load vs. no load), 300 mg, or placebo at the end of the 16-week double-blind period. Efficacy was assessed using multiple clinical and laboratory measures to evaluate the updated GRAPPA-OMERACT PsA core domain set for disease activity, pain, function, and quality of life (Table 1).

Results: A total of 2049 patients were included (1436 TNF naive and 613 TNF-IR). Baseline demographics and disease characteristics were broadly similar in all treatment groups. Efficacy results for the core disease domains are shown in Table 1.

Conclusion: Secukinumab demonstrated efficacy compared with placebo across GRAPPA-OMERACT PsA core domains in the phase 3 clinical trials program, regardless of prior TNF inhibitor use.

REFERENCE

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SAT0370 IMBALANCE OF TH17 AND REGULATORY T CELLS IN PATIENTS WITH PSORIATIC ARTHRITIS AND REBALANCE BY LOW-DOSE IL-2

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Background: Psoriatic arthritis (PsA) is an T lymphocytes-mediated inflammatory condition [1]. Although regulatory T cells (Tregs) isolated from blood and psoriatic skin have been showed a functional deficiency in suppressing effector T-cells in PsA[2], absolute quantitative status of peripheral Treg or Th17 cells is still unclear. On the other hand, recent studies have revealed that low-dose IL-2 alleviates some of autoimmune disease activity by upregulating Treg cells [3, 4], which is expected to control the development of PsA.

Objectives: To assess the absolute numbers of peripheral lymphocyte subpopulations and the efficacy and safety of low-dose IL-2 therapy in PsA patients.

Methods: Total 95 PsA patients and 106 age-and sex-matched healthy controls were recruited. Of them, 22 cases received the treatment of low-dose IL-2 at 0.5 million IU per day for 5 days subcutaneously. The absolute numbers of lymphocyte subgroups and CD4+T subsets in peripheral blood were measured by flow cytometry. The clinical manifestations and laboratory indicators as well as the levels of peripheral lymphocyte and CD4+T subsets were compared before and after the treatment.

Conclusion: Secukinumab demonstrated efficacy compared with placebo across GRAPPA-OMERACT PsA core domains in the phase 3 clinical trials program, regardless of prior TNF inhibitor use.

REFERENCE

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Figure 1: Comparison of absolute numbers of peripheral CD4+ T cell subsets between PsA patients (n=95) and healthy controls (n=106). The level of Th17 was significantly increased while that of Tregs reduced in patients with PsA. Data were calculated and compared with Mann-Whitney U test. *P<0.05, **P<0.01, ***P<0.001.

Figure 2: Comparative analysis of the changes of CD4+ T cell subsets in patients with PsA between pro- and post-treatment (n=22). Low-dose IL-2 markedly raised the absolute numbers of Treg and moderately increased the level of Th17 cells in PsA patients. *P<0.05, **P<0.01, ***P<0.001.
Results: Notably, the absolute numbers of lymphocyte subpopulations in peripheral blood such as NK, CD4+T, Th17 and Tregs in PsA patients were lower than those of healthy controls (P<0.05). The absolute number of Treg was significantly and negatively correlated with the levels of disease indicators, including DAS28, the number of tender joints, visual analogue scale, physician’s global assessment, dermatology quality index, and health assessment questionnaire (P<0.05). After low-dose IL-2 treatment, compared with the baselines, there was a significant increase in the absolute numbers of NK (P<0.05), CD4+T (P<0.01), Th17 (P<0.01) and Treg cells (P<0.001). Interestingly, IL-2 markedly raised the number of Tregs in PsA patients even higher than that of healthy donors (P<0.001), leading to re-balance of Th17 and Tregs. Further, low-dose IL-2 treatment rapidly reduced the disease activity such as DAS28, the number of tender joints, visual analogue scale, physician’s global assessment, dermatology life quality index, and health assessment questionnaire (P<0.05).

Conclusion: Patients with PsA had an imbalance between pro- and anti-inflammatory cells, particularly the reduction of the absolute numbers of Tregs. Low-dose IL-2 combination treatments restored the decreased number of Treg cells and lowered disease activity indicators of these patients without over-treatment and evaluable side effect. Further studies are needed to evaluate the long-term immunoregulatory ability of IL-2 treatment.

REFERENCES

Disclosure of Interests: None declared

SAT0371 CARDIOVASCULAR IMPACT OF HYPERURICEMIA IN PATIENTS WITH PSORIATIC ARTHRITIS
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Background: Inflammatory joint diseases (IJD) such as psoriatic arthritis (PsA) have an increased risk of cardiovascular disease (CVD) since inflammation plays a pivotal role in the pathogenesis of coronary artery disease (CAD), heart failure (HF) and atrial fibrillation (Afib). Additionally, patients with PsA have a prevalence of hyperuricemia (HUC) of 32%, 3 times greater as compared with the general population, which may be related to increased cell turnover as well as the release of pro-inflammatory cytokines and tumor necrosis factor.

Conclusions: Prolonged exposure to high levels of uric acid (UA) has been shown to result in oxidative stress causing endothelial dysfunction, ion channel changes, atrial and ventricular remodeling. There is experimental evidence indicating that uric acid stimulates renin-angiotensin-aldosterone system (RAAS), and it is associated with an increase in cardiac tissue xanthine oxidase activity, all of which induce cardiomyocyte hypertrophy, myocardial oxidative stress, interstitial fibrosis and impaired diastolic relaxation.

Objectives: The aim of this study is to assess the correlation of HUC and the clinical expression of CVD in patients with PsA.

Methods: This is a retrospective cohort study using the 2016 National Inpatient Sample (NIS) of adults diagnosed with PsA based on ICD-10 codes to detect the prevalence of cardiovascular (CV) conditions such as CAD, Afib, and HF with preserved ejection fraction (HFpEF) in patients with concomitant HUC or gout versus age matched controls. Chi square was used for point prevalence and multivariable linear regression adjusted for age, gender, race, CAD, diabetes mellitus, HTN, hyperlipidemia (HLD), smoking, chronic kidney disease (CKD) and Charlson comorbidity index for prevalence odds ratio (POR). We used STATA-15 for statistical analysis.

Results: We identified 37,315 patients with PsA, of whom 2,165 had concomitant HUC or gout (5.80%). Mean age was 61 years, 57% were females. Our results showed that PsA with concomitant HUC or gout compared to PsA without HUC or gout was associated with a higher rate of Afib (17.8% vs 6.1%, p < 0.001), CAD (35.1% vs 19.4%, p < 0.001) and HFpEF (7.2% vs 3.1%, p < 0.001). Furthermore, patients with PsA and HUC/gout appeared to have more risk of developing Afib (POR 1.78; 95%-CI 1.31-2.45; p < 0.001) and HFpEF (POR 1.56; 95%-CI 1.08-2.26; p=0.018), compared to patients with normal uric acid after multivariate-adjustment for risk factors. No statistical difference in CAD was identified between the two groups (POR 1.21; 95%-CI 0.94-1.55; p=0.131) after multivariate linear regression adjustment for confounders.

Conclusion: This study showed that HUC is independently associated with CVD, mainly with Afib and HFpEF in patients with PsA. It remains to be seen if a treat to target approach with normalization of UA in patients with PsA will result in improved CV outcomes. We believe that our findings merit further investigation and that this study adds weight to the hypothesis of UA as a potential risk factor for CVD. Prospective studies are needed to establish the role of serum uric acid level as a biomarker or predictor for CVD, including CAD, Afib and HFpEF in patients with PsA.

REFERENCES

Disclosure of Interests: None declared
ABSTRACT

Our results showed that there was a significant impact of ΔFMD% found to be moderately correlated with the pain visual analog scale (VAS), Patient-Specific Index (PSI), and Chronic Illness Therapy-Fatigue scale (FACIT-F) were assessed at week 16. Analysis of covariance was used to compare changes from baseline in outcomes between groups. Proportions of patients achieving normative PRO scores or minimal clinically important differences (MCIDs) were compared using Cochran-Mantel-Haenszel tests [2, 3].

RESULTS: FIL significantly improved multiple PROs vs PBO at week 16 (Table). Proportions of patients reaching normative PRO values for FACIT-F and SF-36 PCS (+40 or 50, respectively), and achieving MCIDs in HAQ-DI and SF-36 PCS, were significantly greater for FIL vs PBO (Table). Significant improvement in 6/8 SF 36 domains was observed at week 16 with FIL vs PBO (Fig a). Improvement in most individual FACIT-F items was also observed (Fig b).

Conclusion: In EQUATOR, FIL-treated patients with active PsA reported greater and clinically meaningful improvements in most PROs at week 16 vs PBO, mirroring improvements previously reported with FIL in disease activity measures [1].

Table

<table>
<thead>
<tr>
<th>Table</th>
<th>Week 16</th>
<th>FIL (n=65)</th>
<th>PBO (n=65)</th>
<th>Treatment difference (95% CI)</th>
<th>p</th>
</tr>
</thead>
</table>

| Change from baseline | | | | |
| PIGAEDA (mm) | | | | |
| Pain (VAS) | | | | |
| Fatigue (FACIT-F) | | | | |
| HAQ-DI | | | | |
| SF-36 PCS | | | | |
| SF-36 MCS | | | | |

| Response rate, % (N = %) | | | |
| HAQ-DI | | | |
| SF-36 PCS | | | |
| SF-36 MCS | | | |

<table>
<thead>
<tr>
<th>Stress mean</th>
<th>VAS, FACIT-F</th>
<th>FACIT-F</th>
<th>FACIT-F</th>
<th>FACIT-F</th>
</tr>
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<tbody>
<tr>
<td>FIL vs PBO</td>
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REFERENCES

**IXEKIZUMAB, WITH OR WITHOUT CONCOMITANT METHOTREXATE, IMPROVES THE SIGNS AND SYMPTOMS OF PsA FOR UP TO 52 WEEKS OF TREATMENT**

**Bernard Combe**, Tsen-Fang Tsai, Salish Odhav, J. Eugene Huftstutter, Aubrey Trevelin Sprabery, Chen-Yen Lin, So Young Park, Matthew Hufford, Peter Nash, University of Montpellier, Montpellier, France; National Taiwan University, Taipei, Taiwan, Republic of China; Arthritis Clinic, Jackson, United States of America; Arthritis Associates, Hisson, United States of America; Eli Lilly and Company, Indianapolis, United States of America; University of Queensland, Brisbane, Australia

**Background:** Ixekizumab (IXE) is a high affinity monoclonal antibody selectively targeting interleukin (IL)-17A. It was previously demonstrated that IXE, with or without concomitant methotrexate (MTX), was superior to placebo (PBO) in improving the signs and symptoms of patients with psoriatic arthritis (PsA) for up to 24 weeks. The current study evaluated the efficacy of IXE with or without concomitant MTX therapy, for up to 52 weeks of treatment in patients with active PsA.

**Methods:** Patients with active PsA who had prior inadequate response or intolerance to tumour necrosis factor inhibitors (SPIRIT-P1; NCT0195239) or had prior inadequate response or intolerance to tumour necrosis factor inhibitors (SPIRIT-P2; NCT02349295) were randomised to PBO (N=224), 80 mg IXE every 4 weeks (IXEQ4W, N=229) or every 2 weeks (IXEQ2W, N=226), after a 160 mg starting dose. In this post-hoc analysis, efficacy was assessed up to Week 52 for the following two subgroups: (i) patients who were treated with IXE as monotherapy i.e. no concomitant conventional disease-modifying anti-rheumatic drugs and (ii) patients who received constant dose of MTX from Week 0 to 52.

**Conclusion:** In this post-hoc analysis, IXE treatment showed sustained efficacy in patients with PsA up to one year of treatment, with or without concomitant MTX therapy.

**REFERENCES**


**Table 1. Efficacy Outcomes at Week 52**

<table>
<thead>
<tr>
<th>Concomitant Medication</th>
<th>IXEQ4W N=229</th>
<th>IXEQ2W N=226</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACR 20</td>
<td>66.3%</td>
<td>55.3%</td>
</tr>
<tr>
<td>ACR 50</td>
<td>48.4%</td>
<td>48.8%</td>
</tr>
<tr>
<td>DAPSA LDA*</td>
<td>52.6%</td>
<td>52.9%</td>
</tr>
<tr>
<td>MDA</td>
<td>38.9%</td>
<td>36.5%</td>
</tr>
</tbody>
</table>

* score ≤ 14

**Disclosure of Interests:** Bernard Combe Consultant for: Abbvie, Bridstow-Myers Squibb, Galapagos, Eli Lilly, MSD, Novartis, Pfizer, Roche-Chugui, Sanofi, UCSB, Tsen-Fang Tsai Consultant for: Abbvie, Boehringer Ingehelm, Celgene, EIlilly, GSK-Stiefel, Janssen-Cilag, Novartis, Pfizer, Speakers bureau: Abbvie, EIlilly, Janssen-Cilag, Novartis, Pfizer, Salish Odhav Grant/research support from: Abbvie, Ardea Biosciences, AstraZe neca, BMS, Celgene Corporation, Centocor, Eli Lilly and Company, Galapagos, Genentech, GSK, Human Genome Sciences, Janssen, Merck, Mesoblast, Novartis, Novo Nordisk, Pfizer, Roche, Sanofi-Aventis, Takeda Pharmaceuticals, UCB, and Vertex Pharmaceuticals, Consultant for: Abbvie, Ardea Biosciences, AstraZeneca, BMS, Celgene Corporation, Centocor, Eli Lilly and Company, Galapagos, Genentech, GSK, Human Genome Sciences, Janssen, Merck, Mesoblast, Novartis, Novo Nordisk, Pfizer, Roche, Sanofi-Aventis, Takeda Pharmaceuticals, UCB, and Vertex Pharmaceuticals, Speakers bureau: Abbvie, Ardea Biosciences, AstraZeneca, BMS, Celgene Corporation, Centocor, Eli Lilly and Company, Galapagos, Genentech, GSK, Human Genome Sciences, Janssen, Merck, Mesoblast, Novartis, Novo Nordisk, Pfizer, Roche, Sanofi-Aventis, Takeda Pharmaceuticals, UCB, and Vertex Pharmaceuticals, J. Eugene Huftstutter Consultant for: Eli Lilly, Speakers bureau: Janssen, Genentech, Pfizer, Lilly, Regeneron, Aubrey Trevelin Sprabery Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company, Chen-Yen Lin Shareholder of: Eli Lilly and Company, Employee of: Eli Lilly and Company,

SA70375 MILD COGNITIVE IMPAIRMENT IN PSORIATIC ARTHRITIS: PREVALENCE AND ASSOCIATED FACTORS

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Background: A growing body of data demonstrated that systemic inflammation is a predisposing condition for developing cognitive impairment. Different studies highlighted that psoriasis (PsO), a multisystem chronic inflammatory disorder, is associated with cognitive impairment. No data are available regarding psoriatic arthritis (PsA).

Objectives: To assess the prevalence and the factors associated with mild cognitive impairment (MCI) in patients suffering from PsA.

Methods: Consecutive PsA patients, classified as suffering from PsA with the Classification criteria for Psoriatic Arthritis (CASPAR), were enrolled in this study. For each patient were collected the sociodemographic data (age, gender, years of school attendance, years of articular disease duration, years of cutaneous disease duration, treatment), the values of C-reactive protein (CRP) and the following clinical variables: 68 tender joint count (TJC), 66 swollen joint count (SJC), the Leeds Enthesitis Index (LEI), the dactylitis digit count, the Psoriasis Area and Severity Index (PASI), 10 cm numerical rating scale (NRS) for pain and for assessment of disease activity (PsGA), the Dermatology Life Quality Index (DLQI), the 12-item Psoriatic Arthritis Impact of Disease (PsAID-12), the Health Assessment Questionnaire (HAQ), and the Self-administered Comorbidity Questionnaire (SCQ). Cognitive impairment was assessed through the Montreal Cognitive Assessment (MoCA). The exclusion criteria were represented by the presence of: age older than 70 years, major depressive disorder, dementia, Parkinson’s disease, active skin disease other than PsO, concomitant inflammatory joint conditions (such as gout or calcium pyrophosphate deposition), and comorbid fibromyalgia.

Results: The study involved 96 PsA patients, with a mean age of 52.8 years. Twenty (20.8%) patients were suffering from PsA sine PsO. The mean articular disease duration was 9.9 years, and the mean cutaneous disease duration was 14.5 years. The mean Disease Activity Index for Psoriatic Arthritis (DAPSA) was 11.8, and the mean PASI was 0.95. MCI (defined as a MoCA score <26/30) was detected in 47 (48.9%) patients, with a mean value of MoCA of 25.1±3.1. Short-term memory was the most affected domain (mean value 2.6 on 0-5 point scale). The variables under investigation significantly correlated with a worsening cognitive performance (Spearmann’s Rho) were functional capacity (MoCA vs HAQ, r = -0.227, p = 0.026) and fatigue (MoCA vs PsAID item 2, r = -0.22, p = 0.029).

Conclusion: MCI is present in a significant proportion of PsA patients, and is present in a relative young age. MCI occurrence is associated with the presence of a worse functional capacity and a greater fatigue. Short-term memory is the more frequently affected domain. Although not predominantly of rheumatological interest, the MCI presence should be carried out in all patients with PsA.

Disclosure of Interests: Marco Di Carlo: None declared, Andrea Becciolini: None declared, Antonella Incorvaia: None declared, giacomo beci: None declared, Martina Biggioggero: None declared, Ennio Giulio Favalli: None declared, Fausto Salaffi: Grant/research support from: AbbVie, Roche, Novartis, Pfizer, Sanofi, Speakers bureau: AbbVie, Roche, Novartis, Pfizer, Sanofi, Pfizer, BMS DOI: 10.1136/annrheumdis-2019-eular.4695

SA70376 MAKING THE NEXT STEPS IN PSORIATIC ARTHRITIS MANAGEMENT: DOMAIN DRIVEN, TREAT-TO-TARGET, TAILORED MANAGEMENT APPROACH

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Background: The diverse clinical picture of psoriatic arthritis (PsA) suggests the need to identify suitable therapies to address the different combinations of clinical manifestations and comorbidities. The current treatment paradigms recommend early diagnosis and treatment, and a strategic, target orientated approach, aiming at a low disease activity status. The introduction of new treatment modalities highlighted the need for guidelines to prioritize these options for doctors and patients.

Objectives: To develop an evidence-based recommendation for the management and treatment of PsA. The management paradigm should cover all domains of psoriatic disease and provide a stepwise tailored treatment options giving clear advice on treatment from the initial diagnosis, including inclusion/exclusion criteria for treatment, monitoring requirements and how to quantity response to treatment.

Methods: A Steering Committee formulated a set of overarching principles for the management of PsA based on evidence derived from a systematic literature review. These were subsequently discussed, amended and voted on by a Task Force of 20 rheumatologists, dermatologists and patient research partners. Using the nominal group technique and Delphi method, 7 domains were identified (peripheral arthritis, axial disease, enthesitis, dactylitis, skin and nails as well as comorbidities including uveitis). A multidisciplinary, evidence- and consensus-based treatment recommendations for PsA were developed for each of the domains based on three consensus discussions. A set of recommendations for a sequential DMARD/biologic treatment algorithm for patients with PsA was also set.

Results: Literature review provided evidence regarding an optimised domain specific, treat-to-target approach to management. The guidelines addressed both drug and non-drug interventions. 20-statements regarding diagnosis, disease activity scoring, US/MRI scanning, and drug therapy were generated. Percentage of positive votes ranged between 86-100%; whereas mean±SD level of agreement was 9.6±0.3.

The main treatment outcome is to achieve remission status or at least low disease activity state, which should be based on a shared decision with parents/patients. Treatment should be adapted according to disease activity. Treatment should be also adapted if the remission state got lost.

Conclusion: Although no clear correlation exists between joint inflammation and the skin in every patient, the skin and joint aspects of the disease often must be treated simultaneously. Treatment recommendations for the cardinal physical manifestations of PsA were developed based on a literature review and consensus between rheumatologists, dermatologists and patients. It is anticipated that periodic updates will take place using this framework as new data become available.

DISCUSSION: Differences in clinical characteristics, quality of life, disability, and work productivity in Psoriatic Arthritis patients by gender: findings from a cross-sectional survey in the US and Europe.

Background: Psoriatic arthritis (PsA) prevalence is equal in men and women, although gender may play a role in driving mechanisms of PsA leading to differences in manifestations of clinical disease (1).

Objectives: Assess key differences in clinical characteristics, disability, quality of life, and work productivity by gender in real-world practice.

Methods: Cross-sectional survey of rheumatologists and dermatologists and their patients in France, Germany, Italy, Spain, UK, and US. Data were collected from Jun-Aug 2018 via physician-completed patient record forms and patient self-completed forms. Data were analyzed by gender. Demographic characteristics, treatment use, and clinical characteristics ( Tender Joint Count [TJC], Swollen Joint Count [SJC]. Body Surface Area [BSA] psoriasis) were reported by physicians, while quality of life (EQ5D and PsAID12), disability (HAQ-DI), and work productivity (WPAI) were reported by patients. Men and women were compared using parametric tests and non-parametric tests where appropriate.

Results: Data were collected for 2270 patients (95 US, 1675 Europe). Demographic characteristics, time from first symptoms to diagnosis, diagnostic treatment, and clinical characteristics were comparable between women and men (Table 1). More women reported worse quality of life, disability, and work activity impairment than men (Table 2).

Conclusion: In women and men with similar PsA disease activity and treatment rates, women experienced worse quality of life, greater disability, and greater work impairment, despite a lower burden of comorbidities.

REFERENCE


SAT0378 Drivers of discordance in Psoriatic Arthritis when analyzing the link between patient-perceived good status and the disease activity in Psoriatic Arthritis (DAPSA) composite score: An analysis of 436 patients from the International REFLAP observational study

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Background: In Psoriatic arthritis (PsA), the objective of treatment is remission or low disease which can be defined using the Disease Activity in Psoriatic Arthritis (DAPSA) (ref1). We previously showed DAPSA was associated to patient-perceived good status (i.e., self-assessed remission or low disease, yes/no) (ref2). However, some discordance was noted between patient-perceived status and the composite score. This discordance may be related to demographic elements (such as age, gender or country), disease activity components (such as skin involvement which is not assessed in DAPSA) or patient-reported outcomes (such as fatigue or depressive affects). A better understanding of this discordance would be helpful in the context of shared decision-making.

Objectives: To explore the drivers of discordance between patient-perceived remission or low disease and DAPSA-defined remission or low disease.

Methods: This is an analysis of the first visit of ReFlap (NCT03119805, ref2), an observational study in 14 countries of consecutive adult patients with definite PsA >2 years of disease duration. Discordance in assessment of remission/low disease status was defined as a disagreement between a specific patient question (are you in remission or low disease, yes/no) and DAPSA-defined remission/low disease (i.e., score <=14, yes/no). Potential drivers of this discordance were analysed through univariable then stepwise multivariable logistic regression. Variables analysed were demographic (age, gender, disease duration, gross domestic product of country of origin), disease-related (joint counts, psoriasis BSA, enthesitis, CRP) and patient-reported outcomes (pain, fatigue, depressive affect and anxiety). There was no imputation of missing data.

Results: Among 436 patients, mean age 52.3 (SD 12.5) years, mean disease duration 10.1 (8.1) years, 218 (50.8%) male; 259 (63.5%) were taking prednisone. Discordance between patient-reported status and DAPSA-defined remission or low disease was moderate: 36.1% had no current psoriasis skin lesions and mean swollen joint count was 2.2 (7.1). Remission or low disease was frequent both using the patient question (N=286, 65.6%) and using DAPSA (N=246, 56.4%). Discordance between patient-reported status and DAPSA was 12.7% (95% CI 8.4-17.3%).
Conclusion: Remission or low disease appears to be an attainable outcome in PsA. Patients widely self-reported themselves as being in a similar status as the status indicated by the DAPSA score. Discordance in assessment concerned 25.7% patients and was mainly related to CRP (driving higher DAPSA), pain and fatigue (driving patient assessment).

When faced with discordance in assessment, the health professional should assess these elements carefully.

REFERENCE

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SA10379 SUBCUTANEOUS VERSUS ORAL METHOTREXATE IN ACHIEVING MINIMAL DISEASE ACTIVITY IN PSORIATIC ARTHRITIS. CLINICAL PRACTICE: RUSSIAN PSORIATIC ARTHRITIS REGISTRY (RU-PSART) DATA
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Background: The aim of psoriatic arthritis (PsA) therapy is to achieve minimal disease activity (MDA) or clinical remission. Methotrexate (MTX) is the first-line treatment; however, the extent of the disease-modifying effect of MTX on PsA is a matter of debate. It has been shown that the MTX treatment achieves MDA in 6 months in <20% of patients (pts) (1). It has been demonstrated that parenterally administered MTX results in rapid and complete absorption, higher serum levels, and less variable exposure than the oral dosing (2). Clinical practice data on the results of the use of MTX for treating PsA are contradictory.

Objectives: To show the efficacy of MTX in PsA pts in clinical practice and to compare the effectiveness of oral and subcutaneous (SC) MTX treatments.

Methods: 256 pts out of RU-PSART received synthetic disease-modifying antirheumatic drugs (sDMARDs), of whom 182 (71.1%) pts (MTF=68/114) received MTX, and were included in the study according to CASPAR criteria. Their median age 42 [Min 19-Max 73] years (yrs). Pts underwent standard clinical examination of PsA activity at the baseline and the follow-up visits. All pts were biological-naïve. They all were treated with MTX monotherapy: 80 received SC and 102 oral MTX. The main purpose was to determine the cumulative frequency of achieving MDA after the MTX therapy onset. MDA is defined as: the presence of at least 5 out of the following 7 domains: tender joint count ≤1, swollen joint count (SJC ≤3, tender entheseal points ≤3, patient global disease activity measured by Visual Analogue Scale (VAS) score ≤20, and patient pain VAS ≤15. Medians and quartiles [Me (Q25; Q75)], [Min; Max], ORs with 95% CI, Breslow, Long Rank, Tarone-Ware tests were performed. Cumulative frequency was computed using the Kaplan-Meier method. All CI >1, p <0.05 were considered to indicate statistical significance.

Results: Only 16.5% of all 182 pts treated with MTX, both orally and SC, achieved MDA. In the SC MTX group 25 pts (31%) achieved MDA, while 97 (95%) did not achieve it. In the oral MTX group 5 pts (5%) achieved MDA, while 55 (69%) did not achieve it. SC MTX treated pts significantly more often achieved MDA compared with those orally treated (OR 24.3 [1.5; 265.9], p = 0.025).

Conclusion: The results of the present study confirm previous clinical practice data, that SC formulation of MTX significantly increase the cumulative frequency of achieving MDA after the MTX therapy onset. Further comparative clinical trials are needed to elucidate the MTX treatment effect on PsA.
FIBROMYALGIA IS THE STRONGEST NEGATIVE PREDICTOR FOR THE ACHIEVEMENT OF EITHER REMISSION AND MINIMAL DISEASE ACTIVITY IN NAIVE PSORIATIC ARTHRITIS PATIENTS STARTING BIOLOGIC DRUGS

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Background: There is evidence that fibromyalgia (FM) can increase the burden of disease in patients affected with psoriatic arthritis (PsA) and interfere with the assessment of clinical disease activity, but studies focusing on the impact of FM on long-term clinical outcomes are lacking.

Objectives: We aimed at evaluating the impact of FM on the achievement of clinical remission or minimal disease activity (MDA) in naive PsA patients on treatment with a first biologic drug in real life settings.

Methods: We retrospectively assessed PsA patients, fulfilling CASPAR criteria, from 1st January 2010 through 30th June 2017, starting a first biologic drug or apremilast. At baseline and at each visit thereafter, DAPSA, PASI, MDA, ASDAS-CRP, and HAQ were evaluated. Rate of patients achieving DAPSA based low disease activity (LDA) was assessed at 3 months, and MDA or DAPSA-remission at 12 months. LOCF method was carried out for those patients who did not reach 12 months follow-up or discontinue the treatment before 12 months. The persistence on the first treatment was evaluated by Kaplan-Mayer survival curves. Estimated hazard ratios (HRs) of discontinuing therapy or achieving remission or MDA at last observation were assessed by a multivariate stepwise backward Cox regression model, adjusting for patient demographics (gender, age, BMI, comorbidities) and disease characteristics (co-therapy with MTX or glucocorticoids, DAPSA).

Results: Upon excluding pure axial PsA without peripheral involvement, 238 patients (126 female) with mean age 51 years (95% CI, 40-59), BMI 26 (95% CI, 23-30), disease duration 24 (95% CI, 10-60) months were analyzed. At baseline, 120 had polyarticular involvement (> 5 joints), 118 had oligoarticular pattern, and 64 had concomitant spine involvement. One hundred-fifteen begun a treatment with anti-TNF-receptor, n.106 with anti-TNF-mAb, n.9 with ustekinumab, n.6 with apremilast, and n.2 with secukinumab. FM was diagnosed, according to both 1990 and 2019 ACR classification criteria, in 58 (female 74%) patients. Crude drug survival rate was significantly lower in FM-PsA patients (50%) (mean survival time (MST, 95% CI) 32 (25-38) months than in PsA patients without FM (74%) MST 42 (38-45) months (log rank=15.6, p=0.001) (Figure 1a). This large difference was also seen estimating drug survival by inefficacy, FM-PsA 56.6% (MST 35 (28-42) months) vs PsA 82% (MST 45 (42-48) months) (log rank=18.5, p=0.001) (Figure 1b), but not by adverse events (data not shown). LDA at 3 months was reached by 78% of PsA patients and by 21% of FM-PsA patients (p>0.001). At 12 months, MDA was achieved by 62% of PsA and only by 2% (1 out of 58) of FM-PsA (p=0.001), and likewise remission was seen in 47% of PsA and in 2% of FM-PsA (p=0.001) Figure 2. FM was the only independent factor associated to drug discontinuation (HR 2.5, 1.6-4.1 (95% CI)), or to the achievement of either MDA (HR 0.23, 0.1-0.5 (95% CI)) and clinical remission (HR 0.26, 0.1-0.6 (95% CI)), with the first biologic drug within the time span of the study.

Conclusion: Our findings clearly demonstrate the FM has a striking negative impact on clinical outcomes in PsA, as early as 3 months of treatment. Clinicians should be aware that treating PsA patients with comorbid FM is demanding, and appropriate patient shared strategies should be adopted in these settings.
All components of PSAID12 were associated with MDA achievement on univariate logistic regression but only pain remained an independent variable on multiple logistic regression. Disease duration, age and sex were not associated with achievement of MDA.

Patients in MDA had significantly lower PSAID12 than those not in MDA (mean 2.1 ± SD 1.9 vs. 5.8 ±1.9. We also looked at individual components of PSAID (Figure1, mean values for numerical rating scales). Patients in MDA continue to report pain and discomfort despite good clinical outcomes, albeit far lower than patients not in MDA. PSAID12 of less than 4 is considered a good outcome. All components of MDA assessment were associated with low PSAID12 on univariate analysis, but only pain VAS and HAQ remained independent predictors on multiple regression analysis.

Patients with active but not severe arthritis (SJ or TJ 2.3) continued to have high PSAID (one way ANOVA p<0.001), driven by other psoriatic disease manifestations including skin and enthesis.

Conclusion:
- MDA is a relevant treatment target in psoriatic arthritis, with markedly lower PSAID12 in patients in MDA
- Patients with even low numbers of tender or swollen joints continue to have significant impact of disease, supporting the use of a multidimensional treatment target
- Pain and fatigue are dominant symptoms in patients with psoriatic arthritis, even in those in MDA

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Disclosure of Interests: None declared

SA0382
THE RISK FACTORS RELATED TO MENTAL HEALTH PROBLEMS IN PATIENTS WITH PSORIATIC ARTHRITIS IN A LARGE MULTICENTER STUDY: DATA FROM TLAR-NETWORK

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Background: Psoriatic arthritis (PsA) can lead to significant mental burden affecting several aspects of life in majority of patients. Mental health problems, such as depression and anxiety may result in poor treatment adherence and difficulty in coping with disease burden.

Objectives: The aim of this study is to determine the risk factors associated with clinically significant depression and anxiety in patients with PsA.

Methods: The data from 1128 patients with PsA who met American College of Rheumatology (ACR) criteria enrolled by Turkish League Against Rheumatism (TLAR)-Net-work derived from 25 investigating centers. All of the patients underwent clinical, radiological and also laboratory assessment by using standardized protocol. The associations between psychological variables and clinical parameters were assessed by univariate and multivariate analyses.

Results: Of the 1128 patients with PsA (the mean age 46.9 ±12.2%, 64%), 574 (%50.9) had high risk for depression (HADS-D score ≥7) and 270 (%23.9) for anxiety (HADS-A score ≥10). By univariate analysis, the highest odds ratio (OR) associated with both depression and anxiety were PSF6-MCS≤50 (OR 6.9, [95%CI:5.3–9.]) and OR 9, [95%CI:6.5–12.6], respectively. The lowest OR associated with depression belong to PASI total score (OR 1.1, [95%CI:1–1.1]), while the lowest OR associated with anxiety belong to BASMI (OR 1.2, [95%CI:1.1–1.3]). Multivariate logistic regression analysis of potential risk factors for mental health revealed that BASFI (OR 1.9, [95%CI:1.3–2.9], BASDAI (OR 1.6, [95%CI:1.2–2.3], BASRI (OR 1.1, [95%CI:1–1.2]), SF36 MCS≤50 (OR 4.7,[95%CI:3.4–6.4)), unemployment (OR 1.9, [95%CI:1–1.9]) were factors that influence the risk of depression whereas the BASDAI (OR 1.6, [95%CI:1–2.4]), SF36 MCS≤50 (OR 6, [95%CI:4–9.2], BASMI (OR 1.2, [95%CI:1–1.3]) and FIRST2e5 (OR 3, [95%CI:2–4.5]) were factors that influence the risk of anxiety.

Conclusion: This large nationwide database indicated that higher disease activity, functional disability, fibromyalgia (FMS), poor health related quality of life as well as structural damage were estimated as the important risk factors for mental disorders in PsA.

Disclosure of Interests: None declared

SA0383
COMPARISON OF THE EFFICACY AND SAFETY OF TOFACITINIB AND APREMILAST IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS: A BAYESIAN NETWORK META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Background: The therapeutic options for psoriatic arthritis (PsA) include conventional disease-modifying antirheumatic drugs and biologics. However, an unmet need exists for PsA therapies owing to drug intolerance, non-respondiveness, and therapeutic resistance. Therefore, there is a need for additional treatment options with novel mechanisms of action. Tofacitinib is an orally administered JAK inhibitor and apremilast is a novel oral phosphodiesterase 4 inhibitor that regulates inflammatory mediators.

Objectives: The aim of this study is to assess the relative efficacy and safety of tofacitinib and apremilast at different doses in patients with active PsA.

Methods: We conducted a Bayesian network meta-analysis to combine evidence from randomized controlled trials (RCTs) for examination of the efficacy and safety of tofacitinib 10 mg, tofacitinib 5 mg, apremilast 30 mg, and apremilast 20 mg in PsA.

Results: Eight RCTs including 3,086 patients met the inclusion criteria. There were 10 pairwise comparisons including 6 direct comparisons of 5 interventions. All the interventions achieved a significant American College of Rheumatology 20 (ACR20) response compared with placebo. Tofacitinib 10 mg and apremilast 30 mg were among the most effective treatments for active PsA, followed by tofacitinib 5 mg, and apremilast 20 mg. The

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rankinig probability based on the surface under the cumulative ranking curve (SUCRA) indicated that tofacitinib 10 mg had the highest probability of being the best treatment in terms of the ACR20 response rate (SUCRA = 0.785), followed by apremilast 30 mg (SUCRA = 0.670), tofacitinib 5 mg (SUCRA = 0.596), apremilast 20 mg (SUCRA = 0.448), and placebo (SUCRA = 0.001). No significant differences were observed in the incidence of serious adverse events after treatment with tofacitinib 10 mg, apremilast 30 mg, tofacitinib 5 mg, apremilast 20 mg, or placebo.

Conclusion: In active PsA patients, tofacitinib 10 mg and apremilast 30 mg were the most efficacious interventions and not associated with a significant risk of serious adverse events.

REFERENCES

Disclosure of Interests: None declared

SA0384 COMPARATIVE ANALYSIS OF FREQUENCY AND TIMING OF MINIMAL DISEASE ACTIVITY (MDA) ATTAINMENT IN EARLY AND LONG-TERM PSORIATIC ARTHRITIS (PSA) PATIENTS (PTS) AFTER BIOLOGICAL (B) DMARD TREATMENT INITIATION IN CLINICAL PRACTICE: RUSSIAN PSA REGISTRY (RU-PSART) DATA

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Background: MDA is a treatment target of PsA. There is limited data about the frequency and the time of MDA achievement by the use of bDMARD therapy in early and long-term PsA in clinical practice. RU-PSART collected data from 25 rheumatology clinics in the Russian Federation.

Objectives: to investigate the cumulative frequency and timing of MDA attainment in early and long-term PsA after starting bDMARDs in clinical practice.

Methods: 140 (MF=77/63) bDMARD-naive PsA pts according to CASPAR criteria were included in the RU-PSART, after signing consent participation forms; median age 42 [Min 19-Max 73] years (yrs). All patients were divided into two groups based on PsA duration at the time of bDMARDs initiation: early PsA≤2 yrs (67pts) and long-term PsA>2 yrs (73pts). All pts underwent standard clinical examinations of PsA and psoriasis activity and were treated with the following bDMARDs: Infliximab (26pts), Etanercept (25pts), Adalimumab (37pts), Ustekinumab (33pts), Golimumab (19pts), Sekukinumab (4pts), Certolizumab pegol (1pts). MDA was defined as ≥ 5 of the following criteria: tender joint count ≤1, swollen joint count ≤1, PASI≤1 or BSA≤3, patient pain global assessment VAS≤15, patient’s global disease activity VAS≥20, HAQ<0.5, enthesitis count ≤1. The cumulative frequency and the time of MDA attainment were calculated in both groups. Kaplan-Meier cumulative analysis, Mean (95%CI), Min-Max,%, Breslow, Tarone-Ware, Log Rank tests were performed. All Cl>1, p<0.05, were considered to indicate statistical significance.

Results: MDA has been achieved after bDMARDs initiation in 33 out of 67 (49%) pts with early PsA and in 23 out of 73 (32%) pts with long-term PsA. The mean time of MDA achievement was significantly shorter in early PsA in comparison to long-term PsA pts: 21 (CI 95%:13.1-28.9) months and 58 (CI95%:0-118.1) months of bDMARD therapy accordingly (p<0.05 for all tests) (Fig.1).

Conclusion: Comparative analysis has shown that cumulative frequency of MDA achievement after bDMARDs initiation was significantly higher (49% vs 32%) and faster (21 vs 58 months) in early PsA than in long-term PsA. That confirms the benefit of bDMARD therapy initiation at the early stage of PsA.

Disclosure of Interests: : Elena Loginova Speakers bureau: Novartis, Celgene Corporation, Biocod, Janssen, AbbVie Inc, Taliya Korsakova Speakers bureau: Novartis, Celgene Corporation, AbbVie Inc, Biocod, Janssen, Pfzer, UCBy, Lilly, Anastasia Kofaltakova: None declared, ELENA GUBARE: None declared, Yulia Korsakova Speakers bureau: Celgene Corporation, Janssen, Maria Sedunova: None declared, Igor Pristavsky: None declared, Irina Umnova: None declared, Irina Bondareva: None declared, Snezana Kudishina: None declared, Evgeny Nasonov Speakers bureau: Pfzer, Inc., MSD, Novartis, AbbVie Inc, Celgen Corporation, Biocod, Janssen, UCB, Inc.


SAT0385 ASSOCIATION OF SUBCLINICAL MYOCARDIAL DEFORMATION AND DISEASE ACTIVITY IN PSORIATIC ARTHRITIS

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Background: Subclinical impaired myocardial deformation is common in patients with PsA, even with no clinical evidence for CV disease (1). Recent evidence supports the link between the extent of inflammation and CV risk in patients with PsA (2). Elevated levels of inflammatory biomarkers and high activity of joint inflammation were associated with a higher burden of atherosclerosis (2). It is suggested that patients with active disease may have an impaired myocardial deformation (3). But it is unclear if the patients with higher activity of PsA have higher grade of myocardial impairment than the patients without activity of inflammatory rheumatic disease. Speckle-tracking echocardiography (STE), an angle-independent technique, was proposed as a reliable and sensitive method for assessment of subclinical myocardial dysfunction (4).

Objectives: The aim of the study was to assess if there is an association of disease activity of PsA assessed by DAPSA with subclinical myocardial deformation measured by Specleck-tracking echocardiography (STE).

Methods: 48 PsA patients (28 females, 20 males) who fulfilled Caspar criteria, with no clinically evident CV disease or concomitant diseases, were included in the study. Patients who had classic CV risk factors or had experienced CV or cerebrovascular events were excluded. Upon clinical and laboratory evaluation, all subjects underwent conventional echocardiography and 2-dimensional speckle tracking echocardiography (STE).

Results: The results of STE analysis showed that patients with higher DAPSA result have average global longitudinal strain AM ± SD -19.44 ± 0.92, relative to patients without activity of PsA measured by DAPSA result -19.37 ± 0.98 (p=0.0036). In addition, patients with active PsA showed lower value of the variable GLS (R=0.368; p=0.016) and higher DAPSA result and lower values of the variable GLS (R=0.368; p=0.016). Global longitudinal strain of MDA achievement after starting bDMARDs in early and long-term PsA.

Conclusion: Subclinical impaired myocardial deformation is common in patients with PsA, even with no clinical evidence for CV disease (1). Recent evidence supports the link between the extent of inflammation and CV risk in patients with PsA (2). Elevated levels of inflammatory biomarkers and high activity of joint inflammation were associated with a higher burden of atherosclerosis (2). It is suggested that patients with active disease may have an impaired myocardial deformation (3). But it is unclear if the patients with higher activity of PsA have higher grade of myocardial impairment than the patients without activity of inflammatory rheumatic disease. Speckle-tracking echocardiography (STE), an angle-independent technique, was proposed as a reliable and sensitive method for assessment of subclinical myocardial dysfunction (4).

REFERENCES


Disclosure of Interests: None declared

SAT0386 PREVALENCE OF SUBCLINICAL CARDIOVASCULAR DISEASE IN PSORIATIC ARTHRITIS: A MULTICENTRIC STUDY

Maria Paz Martinez-Vidal1, José Andrés Lorenzo Martín2, Mariano Andres1, Vega Jovani1, Carlos Santos Ramirez2, Cinia Romera Lopez2, Cristina Fernández-Carballedo2, Rubén Queeró Silva2, Hospital General Universitario Alicante, Alicante, Spain; 3Hospital Central Universitario Asturias, Oviedo, Spain; 2Hospital Virgen de los Lirios, Alcoy, Spain; 3Hospital del Vinalopó, Elche, Spain; 4Hospital Universitario San Juan, Alicante, Spain

Background: There are scarce data regarding subclinical vascular disease in psoriatic arthritis (PsA)(1). Similarly to rheumatoid arthritis, the real CVR could also be underestimated by clinical risk charts (2).

Objectives: To study the prevalence of subclinical vascular atheromatosis in patients with PsA; to analyze the association of carotid plaques with PsA characteristics; to study the presence of CVR factors and to evaluate the effect on the probability of plaque in PsA.

Methods: Descriptive, transversal and multicentric study, of patients with clinical diagnosis of PsA followed in 4 Spanish hospitals. Demographic data, classic CVR factors and clinical characteristics were recorded. The probability of a 10 years fatal cardiovascular event was calculated by SCORE charts adapted for Spain (3), and afterwards a systematic bilateral common carotid ultrasound (4) was conducted. The intima-media thickness of the carotid wall and the presence of atheroma plaque were registered. Patient’s characteristics were described using descriptive analysis techniques. For univariate comparisons we used Chi2 and Anova. Multivariate analyses were conducted by logistic regression. The probability of plaque according to the age and the presence of CVR factors was calculated for patients with clinical intermediate or high risk who present any classical CVR factor.

Results: 309 patients were included. The characteristics of the sample and the prevalence of CVR factors are depicted in Table 1. Patients were stratified by SCORE as follows: low risk 41 patients (13.3%), intermediate or high risk by means of logistic regression. The study was approved by the Hospital General Universitario de Elda Ethic Committee (RCV-PS-MC/26/02/2016).

Results: 309 patients were included. The characteristics of the sample and the prevalence of CVR factors are depicted in Table 1. Patients were stratified by SCORE as follows: low risk 41 patients (13.3%), intermediate or high risk by means of logistic regression. The study was approved by the Hospital General Universitario de Elda Ethic Committee (RCV-PS-MC/26/02/2016).

Disclosure of Interests: None declared

SAT0387 CONSISTENT EFFICACY IN PATIENT SUBGROUPS ACROSS BASELINE DEMOGRAPHICS AND DISEASE CHARACTERISTICS: RESULTS FROM A PHASE 2 STUDY OF GUSELKUMAB IN PATIENTS WITH ACTIVE PSORIATIC ARTHRITIS

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Background: Gusekumab (GUS) is a monoclonal antibody targeting interleukin-23 that has demonstrated efficacy in a phase 2 trial of psoriatic arthritis (PsA)(1).

Objectives: Here subgroup analyses were conducted to evaluate the consistency of efficacy on the primary endpoint, ACR20 response. Patients with active PsA (/>3 swollen joints, C-reactive protein >3 mg/L, body surface area [BSA] of plaque psoriasis) were randomized 2:1 to subcutaneous GUS 100 mg (n=100) or placebo (PBO, n=49) at Wk0, Wk4, and every 8 wks (q8w) through Wk44. At Wk16, pts with <5% improvement in both swollen and tender joints could escape early to open-label ustekinumab. Pts continuing BVO crossed-over to receive GUS 100mg at Wk 24, 28 then q8w through Wk44. The primary analysis was performed in a modified Intent-to-Treat (mITT) population which included all randomized subjects who received at least one administration of study agent based on their assigned treatment regardless actual treatment received. Pts who met treatment failure criteria, escaped early, or had missing data at Wk24 were considered non-responders for ACR20 at Wk24. Pre-planned subgroup analyses by demographic and disease characteristics at baseline and PsA medication use were performed, using the same data handling rules as in the primary analysis.

Results: At Wk24, 58/100 (58.0%) of pts in the GUS vs 9/49 (18.4%) in the PBO group achieved an ACR20 response (p<0.001). Efficacy was consistently observed in subgroups defined by demographics (gender, age, weight, region), disease characteristics at baseline (disease duration, PsA subtype, tender/swollen joint counts, HAQ-DI, CRP, presence of dactylitis or enthesitis, PASI, and BSA) or PsA medication use (prior use of DMARDs or anti-TNFs, concomitant use of MTX, oral corticosteroids, or NSAIDs) (Table). The treatment effect was statistically significant in the majority of subgroups with the lower bound of the 95% confidence interval of the difference between GUS and PBO exceeding 0 in favor of GUS. There are a few exceptions where small sample sizes of the subgroups limited the interpretation. All enrolled subjects were white; therefore, the effect of gusekumab in other racial groups could not be assessed. Among GUS-treated pts, pts with enthesitis, dactylitis, PASI >12, BSA >10%, tender joint count <10 or swollen joint count <10 appeared to have numerically higher ACR20 response rate than those corresponding subgroups defined otherwise, although the sample size is small and the data should be interpreted with caution.

Disclosure of Interests: None declared

Table 1. Clinical characteristics

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age</th>
<th>Type of PsA</th>
<th>Treatment</th>
<th>PsA duration</th>
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</thead>
<tbody>
<tr>
<td>Women 149 (48.2%), Men 160 (51.8%)</td>
<td>54.8 (SD 12.5), median 55</td>
<td>Axial: 94 (30.4%) Only axial: 18 (5.8%) Peripheral: 290 (39.9%) Only peripheral: 215 (69.6%)</td>
<td>cDMARDs 124 (40.1%) dDMARDs 151 (48.9%) Others (AzA, cyclosporin) 21 (6.6%)</td>
<td>125.1 months (SD 110.5)</td>
</tr>
</tbody>
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Note: | Hypertension | Diastolic | Prevalent CV events | BMI >/=30 | Treatment | Presence of CVR factors |
<table>
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<tr>
<td>89 (28.8%)</td>
<td>45 (14.6%)</td>
<td>12 (3.9%)</td>
<td>110 (35.6%)</td>
<td>73 (23.6%)</td>
<td>26 (8.1%)</td>
<td>107 (34.6%)</td>
</tr>
<tr>
<td>1 factor</td>
<td>108 (35%)</td>
<td>66 (19.4%)</td>
<td>34 (11%)</td>
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</table>
Conclusion: In this phase 2 trial of patients with PsA, GUS demonstrated efficacy consistently across subgroups of pts according to baseline demographics, disease characteristics, and PsA- medication use. The relationship between baseline characteristics and clinical outcome will be further explored in phase 3 studies with a larger PsA population.

REFERENCE


DISCLOSURE OF INTERESTS

**INHIBITION OF RADIOGRAPHIC PROGRESSION WAS ACHIEVED WITH INTRAVENOUS GOLIMUMAB IN ACTIVE PSA PATIENTS REGARDLESS OF CHANGES IN COMPOSITE INDICES OF DISEASE ACTIVITY IN A PHASE III TRIAL**

**Philip J. Mease**,¹ M Elaine Husni,² Shelly Kafka,² Soumya D, Chakravarty,²,4 Diane D. Harrison,⁵ Kim Hung Lo,⁶ Stephen Xu⁷, Elizabeth C. Hsia⁸,⁹

Arthur Kavanaugh¹. ¹Swedish Medical Center and Univ of Wash School of Med, Seattle, United States of America; ²Cleveland Clinic, Cleveland, United States of America; ³Janssen Scientific Affairs, LLC, Horsham, United States of America; ⁴Drexel Univ College of Med, Philadelphia, United States of America; ⁵Janssen Research and Development, LLC, Spring House, United States of America; ⁶Univ of Penn Medical Center, Philadelphia, United States of America; ⁷Univ of CA San Diego, San Diego, United States of America

**Background:** GO-VIBRANT is a Phase 3 trial of intravenous (IV) golimumab (GLM), an anti-tumor necrosis factor alpha (TNFα) monoclonal antibody, in adult patients (pts) with active psoriatic arthritis (PsA).

**Objectives:** To assess if changes in Disease Activity in PsA (DAPSA), PsA Activity Score (PASDAS), Minimal Disease Activity (MDA), Very Low Disease Activity (Vlda), and Clinical Disease Activity Index (CDAI) measures correlate with X-ray progression.

**Methods:** In this multicenter, randomized, double-blind, placebo (PBO)-controlled trial, 480 bionaive PsA pts with active disease (>5 swollen & >5 tender joints, C-reactive protein <50mg/dL, active plaque psoriasis or documented history despite treatment w/csDMARDs &/or NSAIDs) received IV GLM 2mg/kg (N=241) at Wks0/4 then q8wks or PBO (N=239) at Wks0/4/12/20 with crossover to GLM at Wk24. In a post-hoc analysis, association of disease activity measures DAPSA, PASDAS, MDA, Vlda, & CDAI with X-ray progression was examined. Total modified van der Heijde-Sharp (vdH-S) score assessed X-ray progression X-ray progression vs PBO -0.41 vs 1.27).

**Results:** Changes in all disease activity measures appeared to correlate with X-ray progression (Table). GLM-treated pts had less X-ray progression regardless of disease activity measure. GLM treated pts in remission or with low disease activity tended to have less X-ray progression at Wk52 vs pts with moderate or high disease activity (mean change in vdh-S: GLM pts. GLM: DAPSA remission or low disease activity -0.97 vs 1.38, moderate activity -0.48 vs 1.38, high disease activity -0.88 vs 1.49, moderate activity -0.48 vs 1.38, high disease activity -0.88 vs 1.49).

**Conclusion:** In this analysis, all disease activity measures generally correlated with X-ray progression from baseline to Wk24 and to Wk52. Higher disease activity was associated with increased X-ray progression. GLM-treated pts not achieving MDA & Vlda at Wk52 tended to have less X-ray progression vs PBO-GLM pts. GLM’s ability to inhibit X-ray progression, despite pts not being in clinical remission or low disease activity, illustrates an example of “disconnect” between clinical outcomes & X-ray progression seen in other studies.

**Disclosure of Interests:** Philip J Mease Grant/research support from: AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, SUN and UCB. Consultant for: AbbVie, Amgen, BMS, Celgene, Janssen, Lilly, Novartis, Pfizer, SUN, UCB,

None declared, Blessing Dube Employee of: B. Dube is an employee of Corrona, LLC. Meghan Glynn Employee of: M. Glynn is an employee of Corrona, LLC, Alexa Ogdie Grant/research support from: (To my university) Novartis, Pfizer, Grant/research support from: Novartis, Pfizer, Grant/research support from: Novartis, Pfizer, Consultant for: Abbvie, Bristol-Myers Squibb, Celgene, Corrona, Eli Lilly and Company, Novartis, Pfizer, and Takeda, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Corrona, Eli Lilly, Novartis, Pfizer Inc, Takeda, Consultant for: Abbvie, Amgen, BMS, Celgene, Corrona, Lilly, Novartis, Pfizer, Takeda, Consultant for: Abbvie, Amgen, BMS, Celgene, Corrona, Lilly, Novartis, Pfizer, Takeda, Consultant for: AbbVie, Amgen, BMS, Celgene, Corrona, Lilly, Novartis, Pfizer, Takeda, Consultant for: Abbvie, Amgen, BMS, Celgene, Corrona, Lilly, Novartis, Pfizer, Takeda, Consultant for: Abbvie, Amgen, BMS, Celgene, Corrona, Lilly, Novartis, Pfizer, Takeda, Consultant DoI: 10.1136/annrheumdis-2019-eular.1038
SAT0390

GUSELKUMAB WAS MORE EFFECTIVE THAN SECUKINUMAB IN PATIENTS WITH PLAQUE PSORIASIS AND THE SUBSET OF PATIENTS WITH SELF-REPORTED PSORIATIC ARTHRITIS IN THE RANDOMIZED, DOUBLE-BLIND, HEAD-TO-HEAD COMPARISON STUDY ECLIPSE OVER 1 YEAR

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Background: Gusekumab (GUS, an antibody against IL-23) and secukinumab (SEC, an antibody against IL-17A) are both approved for the treatment of psoriasis (PsO). Up to 30% of patients with PsO may have psoriatic arthritis (PsA).

Objectives: The ECLIPSE study compared efficacy and safety of GUS vs SEC in patients with plaque PsO. Post hoc analyses examined outcomes in the subgroup of patients with self-reported psoriatic arthritis (PsA).

Methods: ECLIPSE was a randomized, double-blind trial of adults with moderate-to-severe plaque PsO who received GUS 100 mg at Weeks 0, 4, then every 8 weeks, or SEC 300 mg at Weeks 0, 1, 2, 3, and 4, then every 4 weeks, both through Week 44. The primary endpoint was the proportion of patients achieving ≥90% improvement compared to baseline in the Psoriasis Area and Severity Index (PASI) score at Week 48. Cochran-Mantel Haenszel chi-square testing stratified by investigator was used to compare treatment-group responses.

Results: Overall, treatment groups [GUS (n=534), SEC (n=514)] were comparable at baseline: weight 89kg, 24% body surface area PsO, and Investigator Global Assessment (IGA) moderate (76%) or severe (24%). These characteristics were similar to those of subgroups with self-reported PsA [GUS (n=97), SEC (n=79)]. In the overall population, the primary endpoint of PASI 90 response at Week 48 was achieved by 84.5% of GUS vs 70.0% of SEC patients (treatment difference 14.2 [95% CI=8.6%,18.8%], P<0.001). Among patients with PsA, the primary endpoint of PASI 90 response at Week 48 was achieved by 82.5% of GUS vs 63.3% of SEC patients (treatment difference 19.2% [95% CI=5.0%, 33.4%]). Beyond week 20, in both the overall study population and the PsA subgroup, GUS-treated patients maintained the PASI 90 response while SEC-treated patients had a reduction in response through week 48 (Figure). In the overall population, results of the first major secondary endpoint (proportion of patients with a PASI 75 response at both Week 12 and 48) showed non-inferiority of GUS vs SEC (GUS-84.6% vs SEC-80.2% of patients, p<0.001). Superiority was not demonstrated (p=0.062). Adverse events observed in the overall population and PsA subgroup were generally consistent with the established safety profiles for GUS and SEC.

Conclusion: In the subset of patients with self-reported PsA in the ECLIPSE study, GUS demonstrated better maintenance of response and higher efficacy at approximately one year compared with SEC in the treatment of moderate to severe plaque PsO. These findings were consistent with those for the overall study population of patients with plaque PsA. AEIs observed were generally consistent with the established safety profiles for GUS and SEC.


SAT0391

REMISSION AND DRUG RETENTION RATES OF SECUKINUMAB IN 1549 PATIENTS WITH PSORIATIC ARTHRITIS TREATED IN ROUTINE CARE – POOLED DATA FROM THE OBSERVATIONAL EUROSPA RESEARCH COLLABORATION NETWORK

Brigitte Michelsen, Cecilie Heegaard Brahe, Lennart T.H. Jacobsson, Michael Nissen, Manuel Pombo-Suarez, Helman Mann, Ziga Rotar, Joe Sexton, Maria Jose Santos, Dan Nordström, Catalin Codreanu, Björn Gudbjornsson, Carlos Sánchez-Piedra, Karel Pavelka, Matija Tomsic, Eirik Kristianslund, Helena Santos, Anna-Mari Hokkanen, Ruxandra Ionescu, Thorvardur Jon Love, Yvespehlivan, Mario Sebastiani, Gareth T. Jones, Irene van der Horst-Bruinsma, Lisa Hyldestrup, Niels Steen Krogh, Merete L. Hetland, Mikkel stergaard, EuroSA Research Collaboration, on behalf of DANBIO (Denmark), ARTIS (Sweden), SCCM (Switzerland), NOR-DMARD (Norway), ATTRA (Czech Republic), Reuma.pt (Portugal), BIOBADASER (Spain), ROB-FIN (Finland), bioi.si (Slovenia), ICEBIO (Iceland), TURKBIO (Turkey), RBBR (Romania), ARC (Netherlands), BSRBR-AS (UK), GISEA (Italy), Denmark

Background: There is a lack of data on exposure, treatment outcomes and retention rates of secukinumab in patients with psoriatic arthritis (PsA) treated in routine care.

Objectives: Primary objective: To assess the proportion of PsA patients in remission after 6 months of secukinumab treatment across Europe. Secondary objectives: To compare baseline clinical and demographic characteristics, 6-month crude and LUNDEx adjusted remission rates, 6-month remission rates and median time to secukinumab withdrawal (due to loss of efficacy/adverse events) between bDMARD naïve and non-naïve patients as well as across the participating European registries.

Methods: PsA patients starting secukinumab in routine care and followed for at least 6 months were included from 12 European registries within the European Spondyloarthritis Research Collaboration (EuroSpA). Independent t-test, Mann-Whitney U test, ANOVA, Kruskal-Wallis and Chi-square test were used for group comparisons as appropriate, and Kaplan-Meier plots with log rank test for comparison of secukinumab drug survival.

Results: A total of 1549 PsA patients starting secukinumab were included (Table). 6-month remission and retention rates were significantly different between the registries (Table). Biologic DMARD (bDMARD) naïve compared with non-naïve patients had significantly higher 6-month remission rates and a trend towards better 6-month retention rates (Table, Figure 1a-b).

Conclusion: This study of >1500 patients in 12 European countries provides real-world data on the effectiveness of secukinumab in patients with PsA, adding evidence to existing RCTs. A majority of the patients had long disease duration and was previous bDMARD users. DAS28CRP, SDAI and DAPSA28 remission at 6 months were achieved by 35%, 12% and 12%, respectively. The overall remission rate was 86%, with significant differences across the registries. bDMARD naïve compared with non-naïve patients had significantly better 6-month remission rates and a trend towards better secukinumab retention rates.

Acknowledgement: Novartis Pharma AG and IQVIA for supporting the EuroSpA collaboration

Disclosure of Interests: Brigitte Michelsen Grant/research support from: Unrestricted grant: Novartis, Consultant for: Novartis, UCB, Cecilie Heegaard Brahe Grant/research support from: Unrestricted grant: Novartis, Lennart T.H. Jacobsson Consultant for: LJ has received lecture and consulting fees from Pfizer, Abbvie, Novartis, Eli-Lilly and Janssen, Michael Nissen Consultant for: AbbVie, Lilly, Novartis, and Pfizer, Manuel Pombo-Suarez: None declared, Helman Mann Consultant for: Pfizer, Eli Lilly, Sanofi, Speakers bureau: AbbVie, Roche, Pfizer, MSD, Eli Lilly, Sanofi, Ziga Rotar: None declared, Joe Sexton: None declared, Maria Jose Santos: None declared, Dan Nordström Grant/research support from: MSD, Pfizer, Consultant for: AbbVie, BMS, MSD, Novartis, Roche, Pfizer, UCB, Speakers bureau: Novartis, UCB, Catalin Codreanu: None declared.
IMPLEMENTING THE PSORIATIC ARTHRITIS DISEASE ACTIVITY SCORE (PASDAS) IN ROUTINE CLINICAL PRACTICE: (IM)POSSIBLE?

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Background: Psoriatic arthritis (PsA) is a heterogeneous disease, with involvement of at least five health domains: peripheral joint disease, enthesitis, dactylitis, axial involvement, and skin and nail psoriasis. Because of the heterogeneity of the disease, assessment of disease activity is challenging. One of the many single or composite outcome measures that has been developed is the Psoriatic Arthritis Disease Activity Score (PASDAS). The PASDAS is a comprehensive measure that takes arthritis (66/68 joint score), dactylitis, enthesitis, CRP, physician disease activity VAS score and patient-reported outcomes into account.

Furthermore, it is a continuous outcome measure in contrast to the Minimal Disease Activity criteria (MDA), facilitating the longitudinal follow-up of disease activity. The PASDAS also has better parametric distribution and discriminative capacity compared to other outcome measures such as the Disease Activity for Psoriatic Arthritis score (DAPSA). However, feasibility of PASDAS use in routine clinical care has been questioned due to its complexity. It requires a CRP and filled-out SF36 form at time of assessment, does not include a formal skin assessment, is difficult to calculate and is time consuming for both patient and physician.

Objectives: To implement PASDAS measurements and skin assessments in routine clinical care for all 1300 PsA patients treated at our centre.

Methods: The implementation consisted of the following stages: 1) assessment of patients’ acceptability of measurement burden; 2) implementation of mathematical calculations of the PASDAS in our electronic health record; 3) PASDAS and skin assessment training of rheumatology nurses and rheumatologists; and 4) (logistic) adjustments to the outpatient visit.

Results: Our patient partners preferred comprehensive clinical assessment of skin and joints above a limited assessment (such as the DAS28-CRP), although the latter would be less time consuming. For the assessment, and to comply with international guidelines, we decided to also add assessment of skin disease, by using the Body Surface Area (BSA) and Physician Global Assessment score (PGA). Furthermore, research demonstrated that for the PASDAS calculation the physical component score (PCS) of the SF36 could be substituted by the SF12-PCS.

As the SF12 is more concise, minimizing patient burden, we chose to implement the SF12 instead of the SF36. The SF12-PCS, together with the other separate component scores and corresponding mathematical calculation of the PASDAS, was implemented in our electronic health record. Lastly, we set-up a three phase consultation that consists of laboratory tests and consultation with a rheumatology nurse who performs the physical measurements before each visit with the physician.

Conclusion: Standardized and routine measurement of the PASDAS and skin involvement at each outpatient visit of all our PsA patients before consultation with the treating rheumatologist was successfully implemented, underscoring the feasibility of this approach. In addition to improving clinical care, routine outcome measurements can be used for a variety of clinical studies.

REFERENCES


EFFECTIVENESS AND SAFETY OF INFliximab, Golimumab and Ustekinumab in Psoriatic Arthritis Patients from a Prospective Observational Registry


Background: Long-term registries are essential to evaluate new therapies in a patient population that differs from clinical trials and usually varies over time.

Objectives: To describe the profile of psoriatic arthritis (PsA) patients selected for treatment with infliximab (IFX), golimumab (GLM) or ustekinumab (UST) treatment in Canadian routine care and to describe the long-term real-world effectiveness and safety of these agents.

Methods: 462 PsA patients treated with IFX, GLM or UST were enrolled into the Biologic Treatment Registry Across Canada (BioTRAC) registry between 2009-2015, and 2010-2017 and 2014-2017. Study visits occurred at baseline and every 6 months thereafter. Effectiveness was assessed with changes in TJC28, SJC28, skin, enthesis, dactylitis, pain, HAQ, acute phase reactants. Safety was evaluated with the incidence of adverse events (AES) and drug survival rates.

Results: Of the 111 IFX, 281 GLM and 70 UST-treated patients, the proportion of males were 52.3%, 46.3% and 37.1%, the mean age was 48.4, 52.8 and 53.1 years and the mean disease duration was 5.8, 6.1 and 5.7 years, respectively. Most patients were bio-naïve (85.6%, 77.9% and 50.0% and 55.7% for IFX, GLM and UST, respectively (p<0.001). A reduction in mean baseline duration of morning stiffness was observed in the IFX cohort (from 69.8 to 42.6 to 23 min in 2006-2008 to 2009-2012 to 2013-2015 (p<0.001). Most other baseline disease parameters remained similar over time in all three cohorts. However, UST-treated patients had lower mean baseline DAS28 CRP (3.4 vs 3.9; p=0.003), SJC (3.8 vs 5.3; p=0.0046) and higher PASI (4.8 vs 2.2; p=0.0061) compared to patients treated with GLM or UST.

Treatment with IFX, GLM and UST was associated with significant improvements in all disease parameters over time (>P<0.001) from baseline up to 84, 40 and 36 months, respectively with similar efficacy between agents. The only exception was the proportion of patients in minimal disease activity at 12, 24 and 36 months which reached 40.7%, 50.0% and 55.7% for IFX, GLM and UST, respectively (p<0.001). A reduction in mean baseline duration of morning stiffness was observed in the IFX cohort (from 69.8 to 42.6 to 23 min in 2006-2008 to 2009-2012 to 2013-2015 (p<0.001). Most other baseline disease parameters remained similar over time in all three cohorts. However, UST-treated patients had lower mean baseline DAS28 CRP (3.4 vs 3.9; p=0.003), SJC (3.8 vs 5.3; p=0.0046) and higher PASI (4.8 vs 2.2; p=0.0061) compared to patients treated with GLM or UST.

Conclusion: Differences in baseline characteristics between patients treated with an anti-TNF agent over an anti-IL12/23 agent suggest that the level of joint to skin involvement might be driving physician choice when the time comes to choose a biologic agent. IFX, GLM and UST treatment significantly reduced disease activity and improved functionality in a similar fashion and were well tolerated in patients with PsA.

Disclosure of Interests: Proton Rahman: None declared, Regan Arendse Grant/research support from: Janssen Sponsored Study, Isabelle Fortin Grant/research support from: ABBVIE, AMGEN, ASTRAZENECA, BMS, CELGENE, GSK, JANSSEN, PFIZER, SANOFI, UCB, Consultant for: LILLY, NOVARTIS, SANOFI, Speakers bureau: NOVARTIS, PFIZER, Andrew Chow Grant/research support from: Abbvie, Celgene, EliLilly, GSK, Janssen, Novartis, Pfizer, UCB, Consultant for: Abbvie, BMS, Celgene, EliLilly, GSK, Janssen, Novartis, Pfizer, Roche, UCB, Speakers bureau: Abbvie, BMS, Eli Lilly, Janssen, Novartis, Pfizer, Majed, Kronkhotz, Rashidkhani Grant/research support from: Novartis, Consultant for: Amgen, Celgene, Gebro, Janssen, Novartis, Pfizer, Lilly, Merck, Suneil Kapur Grant/ research support from: Abbvie, Merck, Janssen, Novartis, Eli Lilly, Amgen, Michel Zummer: None declared, Jon Chan Grant/research support from: Janssen, UCB, Novartis, Pfizer, Celgene, Consultant for: Amgen, Celgene, Eli Lilly, Janssen, Amgen, Abbvie, Novartis, Pfizer, UCB, Sandoz, Merck, Larissa Lissnevskia Grant/research support from: Janssen Sponsored Study, Raheem Kherani Grant/research support from: Janssen, BMS, Abbvie, Consultant for: Abbvie, Amgen, BMS, Janssen, Lilly, Merck, Pfizer, Roche, Sandoz, Speakers bureau: Abbvie, BMS, Eli Lilly, Janssen, Novartis, Pfizer, Majed, Kronkhotz, Rashidkhani: None declared, Odalis Asin Milian Employee of: Employee of Janssen, Allen Lehman Employee of: Employee of Janssen, Meagan Racine Shareholder of: Employee of Janssen, Francois Nantel Shareholder of: Employee of Janssen.

POSSIBLE POTENTIAL INTERACTIONS BETWEEN OSTEOPOROSIS, QUALITY OF LIFE, PSYCHOLOGICAL STATUS AND CLINICAL PARAMETERS IN PSORIATIC ARTHRITIS


Background: Psoriatic arthritis (PsA), a chronic rheumatic disease associated with reduced quality of life. Obesity is an important clinical problem which may interfere with loss of functioning and quality of life. Obesity is usually an overlooked entity in patients with PsA. Several studies were involved in prevalence and the impact of obesity on disease activity in patients with PsA, however relationship between psychological status and quality of life have not been evaluated comparatively.

Objectives: To assess the impact of obesity on quality of life, psychological status and clinical parameters in patients with PsA.

Methods: Patients with PsA were recruited who met CASPAR classification criteria enrolled by Turkish League Against Rheumatism-NETWORK (TLAR-NETWORK) derived from 24 different centers of our country. Patients with BMI >30 kg/m2 were considered obese. Disease status and health related quality of life measures [SF-36; HAQ; Psoriatic arthritis quality of life (PsAQOL); Hospital Anxiety and Depression Scale], FACIT-Fatigue, DAS28, BASDAI, BASFI, BaMSI, Maarlyck arthritis Spondylitis Enthesitis Score (MASES) and Psoriasis area severity index (PASI) scores were compared between this groups.

Results: A total 1130 patients with PsA (36.0% male, 64.0% female) included in this cohort 37.6% obese and 62.4% non-obese. The presence of peripheral arthritis, enthesis, dactylitis, ulnae and spine involvement, PASI scores as well as MASES scores were quite similar between patients with and without obesity. Obese patients had significantly higher scores in VAS fatigue and disease activity, poorer QoL and physical functions compared to non-obese patients (p<0.05). Obese patients had high risk for anxiety and depression (p<0.05).

Conclusion: Obesity associated with the risk of depression and anxiety, fatigue, poorer QoL and higher disease activity. These findings suggest that obesity should be considered while assessing patients with PsA.

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Disclosure of Interests: Keusor Gok: None declared, Kermal Nas: None declared, Erkan Kilic: None declared, Betul Sargin: None declared, Sevtap Acer Kasman: None declared, Hakan Alkan: None declared, Nilay Sahin: None declared, Gizem Cengiz: None declared, Nihan Cizdan: None declared, Ikknur Albak Gezer: None declared, Dilek Keskin: None declared, Cevriye Mükkoğlu: None declared, Halice Resorku: None declared, Ismihan Sunar: None declared, Ajda Bal Hasurk: None declared, Mehmets Tuncay Durduz Grant/research support from: Abbvie, Spanglers bureau: Novartis, AMGEN, Abdi Ilyahim, Iko, Okan Kucukak: None declared, Ozan Volkan Yurdakul: None declared, Meltem Alkan: None declared, Yildiray Aydin: None declared, Figen Ayhan: None declared, Halice Bodur: None declared, Mustafa Calis: None declared, Ertugrul Capkin: None declared, Gul Devrimsel: None declared, SAMI HIZMETLI: None declared, Ayhan Kamarli: None declared, Yasar Keskin: None declared, Hilal Kocabas: None declared, Ozur Kutuk: None declared, Nesrin Şen: None declared, Omer Faruk Sendur: None declared, Ibrahim tekeoglu: None declared, Murat Toprak: None declared, Senol Toy: None declared, Ting Tung: None declared


SAT0395 RESPONSIVENESS AND CLINICAL TRIAL DISCRIMINATION OF SWOLLEN AND TENDER JOINT COUNTS FOR THE MEASUREMENT OF MSK DISEASE ACTIVITY IN PSORIATIC ARTHRITIS

Ali Duarte-Garcia1, Lihi Eder2, Nill Goel3, Maarten de Welt4, Dafna D. Gladman5, Oliver FitzGerald6, Philip J. Mease7, Ying Ying Leung8, Anna-Maria Ordi9, Bev Shea10, Vibeke Strand11, Philip Helliwell12, Alisa Stephens-Shields13, William Tillett14, Laura C. Coates15, Ali Duarte-Garcia1, Lihi Eder2, Nitigoe3, Maarten de Witt4, Dafna D. Gladman5, Oliver FitzGerald6, Philip J. Mease7, Ying Ying Leung8, Anna-Maria Ordi9, Bev Shea10, Vibeke Strand11, Philip Helliwell12, Alisa Stephens-Shields13, William Tillett14, Laura C. Coates15, Ali Duarte-Garcia1, Lihi Eder2, Nitigoe3, Maarten de Witt4, Dafna D. Gladman5, Oliver FitzGerald6, Philip J. Mease7, Ying Ying Leung8, Anna-Maria Ordi9, Bev Shea10, Vibeke Strand11, Philip Helliwell12, Alisa Stephens-Shields13, William Tillett14, Laura C. Coates15


Background: While tender and swollen joint counts (TJC and SJC) are key instruments for the assessment of peripheral arthritis in PsA, little is known about the psychometric properties of TJC and SJC in randomized controlled trials (RCTs) and how these properties differ among patient subgroups.

Objectives: To assess the responsiveness and discrimination of TJC and SJC in PsA using RCT datasets and evaluate subgroups of patients with early vs. established disease and 3 or less vs 4 or more active joints.

Methods: Patient-level data from 8 phase III RCTs and the TIght COntrol of Psoriatic Arthritis (TICOPIA) trial were analyzed. The standardized response mean (SRM, mean difference between baseline and follow up divided by the standard deviation (SD) of the mean difference) and standardized mean differences (SMD, mean difference in the treated group minus the mean difference in the placebo group divided by the pooled SD for the change) were used to address responsiveness and discrimination respectively. TJC28, SJC28, TJC68, and SJC66 were the pooled SD for the change) were used to address responsiveness and discrimination respectively. TJC28, SJC28, TJC68, and SJC66 were the 3 or less vs 4 or more active joints.

Results: In traditional phase III RCTs, TJC and SJC were responsive and had good clinical trial discrimination. SRMs were similar and ranged from -0.8 to -0.4 (‘moderate’ responsiveness) (Figure 1). SMDs were similar among SJC28 and SJC66 and likewise between TJC28 and TJC68 but mostly within the small effect range (-0.2 to -0.5; not shown). PhGA and PIGA had higher SMDs than the joint counts. SRMs were substantially lower for joint counts (and also PIGA) among the low compared with the higher joint count groups (Figure 2). There were no substantial differences in SRMs between patients with early and established disease.

Conclusion: Joint counts are responsive to change and have reasonable discrimination in RCTs among patients higher disease activity at baseline. However, joint counts may not be ideal outcome measures in oligoarticular disease and have lower responsiveness and discrimination in this subgroup.

REFERENCES

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### IMPROVEMENT IN THE SIGNS AND SYMPTOMS OF PSORIATIC ARTHRITIS WITH IXEKIZUMAB COMPARED TO PLACEBO IN PATIENT SUBGROUPS DEFINED BY BASELINE DISEASE CHARACTERISTICS

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**Background:** Ixekizumab (IXE), a high-affinity monoclonal antibody that selectively targets interleukin-17A, was superior to placebo (PBO) in two randomized Phase 3 studies in patients (pts) with active psoriatic arthritis (PsA).1,2

**Objectives:** To assess the consistency of response of IXE across subgroups of pts defined by specific baseline disease characteristics.

**Methods:** Data were analyzed from an integrated database of 2 randomized, double-blind, Phase 3 studies in pts who were either biologic Disease Modifying Anti-Rheumatic Drug (bDMARD)-naïve (SPIRIT-P1) or who had prior inadequate response or intolerance to TNF inhibitors (SPIRIT-P2). Analyses included pts randomly assigned to the approved dosing regimen of IXE (80 mg IXE every 4 wks [IXE Q4W] with a starting dose of 160 mg IXE) or to PBO through Week 24. Efficacy was measured as the percentage of pts achieving ≥20%, 50%, or 70% improvement from baseline in the American College of Rheumatology criteria (ACR20/50/70) or minimal disease activity (MDA) in subgroups of pts defined by baseline presence of enthesitis, presence of dactylitis, percentage of psoriasis body surface area (BSA) involvement (<3% or ≥3%), and c-reactive protein (CRP >6 or ≤6 mg/L).

**Results:** Clinical response rates at Week 24 in each subgroup are summarized (Table). Significantly (p<0.05) more patients achieved ACR20, ACR50, ACR70, and MDA with IXE compared to placebo across patient subgroups defined by presence of enthesitis, presence of dactylitis, percentage of psoriasis BSA involvement, and by CRP levels at baseline.

**Conclusion:** At Week 24, IXE was superior to placebo for the treatment of PsA signs and symptoms regardless of baseline presence of dactylitis or enthesitis, BSA involvement, or CRP levels.

**REFERENCES**


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### DESCRIPTIVE COMPARISONS OF THE IMPACT OF APRIMELAST AND METHOTREXATE MONOTHERAPY ON PATIENTS WITH OLIGOARTICULAR PSORIATIC ARTHRITIS/SPONDYLOARTHRITIS REGISTRY

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**Background:** Therapeutic effectiveness has rarely been studied in a subpopulation of patients with oligoarticular PsA.

**Objectives:** To examine baseline characteristics and 6-month clinical assessments of PsA patients with oligoarthritis (≤5 swollen joints) who initiated apremilast (APR) or methotrexate (MTX) monotherapy in the Corrona PsA/SpA Registry, a prospective, US-based, observational cohort study. Patients initiating bDMARD monotherapy were also examined as a point of reference.

**Methods:** Patients >18 years of age with PsA and oligoarthritis in the registry who initiated APR, MTX or a bDMARD (reference group) monotherapy and had a 6-month follow-up visit between June 2014 and March 2018 were included. Descriptive statistics were calculated for patients’ clinical characteristics and disease assessments at treatment initiation and at the 6-month follow-up visit.

**Results:** The analysis included 150 patients initiating therapy (APR: n=34; MTX: n=15; bDMARD: n=101). Among APR and MTX initiators, 79% and 20% received at least 1 prior bDMARD, respectively. APR initiators, compared with MTX initiators, were younger (mean [SD]: 55.7 [12.6] vs. 61.5 [16.6] years), had longer disease duration (mean [SD]: 8.0 [6.7] vs. 5.4 [7.6] years), and had higher levels of disease activity

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#### Clinical responses at Week 24 in subgroups defined by baseline disease characteristics (NRI)

<table>
<thead>
<tr>
<th>Clinical parameter</th>
<th>PBO (N=224)</th>
<th>IXE Q4W (N=229)</th>
<th>PBO (N=224)</th>
<th>IXE Q4W (N=229)</th>
<th>PBO (N=224)</th>
<th>IXE Q4W (N=229)</th>
<th>PBO (N=224)</th>
<th>IXE Q4W (N=229)</th>
<th>MDA (N=229)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Enthesitis Present</strong></td>
<td>29/142 (20)</td>
<td>59/159 (37)†</td>
<td>2/142 (1)</td>
<td>3/159 (2)†</td>
<td>6/142 (4)</td>
<td>1/159 (2)†</td>
<td>21/70 (30)</td>
<td>25/70 (36)</td>
<td></td>
</tr>
<tr>
<td><strong>Enthesitis Absent</strong></td>
<td>26/81 (32)</td>
<td>39/70 (55)†</td>
<td>10/81 (12)</td>
<td>28/70 (40)†</td>
<td>4/81 (5)</td>
<td>21/70 (30)</td>
<td>14/81 (17)</td>
<td>25/70 (36)</td>
<td></td>
</tr>
<tr>
<td><strong>Dactylitis Presence</strong></td>
<td>12/59 (20)</td>
<td>55/60 (90)</td>
<td>6/59 (10)</td>
<td>38/41 (92)</td>
<td>2/59 (3)</td>
<td>24/59 (42)</td>
<td>5/59 (9)</td>
<td>33/59 (56)</td>
<td></td>
</tr>
<tr>
<td><strong>Dactylitis Absent</strong></td>
<td>43/164 (26)</td>
<td>72/137 (53)†</td>
<td>16/164 (10)</td>
<td>48/137 (35)</td>
<td>4/164 (2)</td>
<td>28/137 (20)</td>
<td>15/164 (9)</td>
<td>33/137 (24)</td>
<td></td>
</tr>
<tr>
<td><strong>BSA &lt;3%</strong></td>
<td>20/85 (24)</td>
<td>44/80 (55)†</td>
<td>8/85 (9)</td>
<td>29/80 (36)</td>
<td>2/85 (2)</td>
<td>17/80 (21)</td>
<td>6/85 (7)</td>
<td>21/80 (26)</td>
<td></td>
</tr>
<tr>
<td><strong>BSA ≥3%</strong></td>
<td>35/134 (26)</td>
<td>77/141 (55)†</td>
<td>14/134 (10)</td>
<td>55/134 (41)</td>
<td>4/134</td>
<td>34/141 (24)</td>
<td>13/134 (10)</td>
<td>42/141 (29)</td>
<td></td>
</tr>
<tr>
<td><strong>CRP ≤6 mg/L</strong></td>
<td>29/100 (29)</td>
<td>45/97 (46)†</td>
<td>11/100 (11)</td>
<td>31/97 (32)</td>
<td>2/100</td>
<td>16/97 (17)</td>
<td>11/100 (11)</td>
<td>25/97 (26)</td>
<td></td>
</tr>
<tr>
<td><strong>CRP &gt;6 mg/L</strong></td>
<td>26/122 (21)</td>
<td>80/129 (62)</td>
<td>11/122 (9)</td>
<td>54/129 (42)</td>
<td>4/122</td>
<td>36/129 (28)</td>
<td>9/122</td>
<td>41/129 (32)</td>
<td></td>
</tr>
</tbody>
</table>

Data are provided as n/Ns (%) where n=number of responders and Ns=number of patients in each subgroup.

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**DOI:** 10.1136/annrheumdis-2019-eular.1659

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**NOTE:** The above text contains the abstracts of scientific research articles. For a comprehensive understanding of the research, it is recommended to read the full articles. The tables provide a summary of clinical responses at Week 24 in subgroups defined by baseline disease characteristics.
at baseline, including greater skin involvement (mean body surface area affected [SD]: 7.1% [17.6%] vs. 4.8% [9.4%]), swollen joint count (mean [SD]: 1.5 [1.5] vs. 1.0 [1.1]) and Clinical Disease Activity for Psoriatic Arthritis (cDAPSA) moderate and high disease activity (50% [APR] vs. 20% [MTX]), mean score [SD]: 14.0 [8.5] vs. 11.5 [4.9]). APR initiators also had greater disease impairments at baseline, represented by numerically higher scores on patient-reported outcome (PRO) measures, including the Health Assessment Questionnaire-Disability Index (HAQ-DI) [mean [SD]: 1.0 [0.7] vs. 0.5 [0.4]). Patient's Global Assessment of Disease Activity–Psoriasis (PIGA-PsO; mean [SD]: 47.1 [29.4] vs. 28.4 [16.6]; Patient's Global Assessment of Disease Activity–Psoriasis (PIGA-PsA; mean [SD]: 47.1 [29.6] vs. 32.5 [26.3]), fatigue (mean [SD]: 55.9 [35.0] vs. 37.3 [31.9]) and overall pain (mean [SD]: 50.5 [31.1] vs. 46.7 [26.5]). Taken together, results suggest that APR initiators had more refractory oligoarthritis compared with MTX initiators. Clinical assessments at the 6-month follow-up indicate that patients who initiated APR experienced numerically higher improvements in disease activity and various PRO measures compared with MTX, as well as achievement of ≤1 swollen joint, HAQ-DI minimal clinically important difference and cDAPSA remission or low disease activity (Table). Of note, results associated with bDMARDs were more comparable to that of APR.

Conclusion: In this analysis of the Corona PsA/SpA Registry, APR monotherapy was more often used in patients with refractory oligoarthritis compared with MTX monotherapy. Despite this, the APR treatment group experienced numerically greater improvements in disease activity measures. Improvements observed with APR treatment in patients with longstanding disease and refractory oligoarthritis were comparable to that of bDMARDs.

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**Clinical Disease Assessments of Corrona PsA/SpA Registry Patients With Oligoarthritis at the 6-Month Visit**

<table>
<thead>
<tr>
<th>Disease Characteristic</th>
<th>APR (n=56)</th>
<th>MTX (n=56)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Swollen joint count</td>
<td>12.9 [7.4]</td>
<td>6.3 [4.6]</td>
<td>0.003</td>
</tr>
<tr>
<td>Mean (SD) change</td>
<td>-9.4 [3.9]</td>
<td>6.0 [2.9]</td>
<td>0.006</td>
</tr>
<tr>
<td>Achieved patient’s joint count ≤ 8 (%)</td>
<td>79%</td>
<td>71%</td>
<td>0.003</td>
</tr>
<tr>
<td>(cDAPSA ≤ 11)</td>
<td>84%</td>
<td>75%</td>
<td>0.014</td>
</tr>
<tr>
<td>(cDAPSA ≤ 31)</td>
<td>67%</td>
<td>59%</td>
<td>0.043</td>
</tr>
<tr>
<td>Mean (SD) change</td>
<td>-1.5 [2.8]</td>
<td>-0.2 [1.9]</td>
<td>0.004</td>
</tr>
<tr>
<td>(cDAPSA category ≤ 5)</td>
<td>67%</td>
<td>59%</td>
<td>0.043</td>
</tr>
<tr>
<td>Mean (SD) change</td>
<td>2.1 [2.9]</td>
<td>0.4 [2.5]</td>
<td>0.001</td>
</tr>
<tr>
<td>Remission (ax)</td>
<td>3.3 [1.4]</td>
<td>2.5 [1.0]</td>
<td>0.001</td>
</tr>
<tr>
<td>Mean (SD) change</td>
<td>3.6 [2.9]</td>
<td>1.9 [1.5]</td>
<td>0.001</td>
</tr>
<tr>
<td>Patient-reported fatigue (VAS 0-100)</td>
<td>84%</td>
<td>75%</td>
<td>0.006</td>
</tr>
<tr>
<td>Mean (SD) [change]</td>
<td>-1.5 [2.9]</td>
<td>0.4 [2.5]</td>
<td>0.001</td>
</tr>
<tr>
<td>Mean (SD) change</td>
<td>2.1 [2.9]</td>
<td>0.4 [2.5]</td>
<td>0.001</td>
</tr>
<tr>
<td>Patient-reported pain (VAS 0-100)</td>
<td>84%</td>
<td>75%</td>
<td>0.006</td>
</tr>
<tr>
<td>Mean (SD) change</td>
<td>3.6 [2.9]</td>
<td>1.9 [1.5]</td>
<td>0.001</td>
</tr>
<tr>
<td>Achieved DAS44 DMC (DAS &lt; 3.5 point decrease)</td>
<td>84%</td>
<td>75%</td>
<td>0.006</td>
</tr>
</tbody>
</table>

*P<0.001 among patients with ≤1 swollen joint at baseline. **P<0.001 among patients who did not have criteria for either cDAPSA remission or low disease activity at baseline. Change ≥6 months was used in patients ≤1 swollen joint at baseline. Values reflect the baseline value minus the baseline value. DMC: minimal clinically important difference; DAS: disease activity score.

EVALUATION OF THE PREDICTIVITY OF THE THERAPEUTIC RESPONSE ACCORDING TO THE PRESENCE OF METABOLIC COMORBIDITIES IN PATIENTS WITH PSORIATIC ARTHRITIS: OBSERVATIONAL RETROSPECTIVE STUDY

Simone Parisi1, Davide Mohammad Reza Beigi2, Marta Priora3, Maria Chiara Ditto4, Chiara Lisa Peroni5, Angela Lagani6, Enrico Fusaro7, 1.A.O.U. Città della Salute e della Scienza, Rheumatology, Turin, Italy

Background: Psoriatic Arthritis (PsA) is a systemic chronic inflammatory disease, which leads to an increased oxidative stress and to endothelial alterations, with increased cardiovascular and metabolic risks. These conditions explain the high prevalence of myocardial infarction, cerebrovascular accidents, diabetes mellitus, obesity, steatohepatitis, alterations of lipid set and an increased prevalence of metabolic syndrome in patients with PsA. The results of other studies suggest that these comorbidities could negatively influence the disease activity and the therapy response in patients with PsA.

Objectives: The aim of the study is to evaluate a population of patients with PsA treated with biological drugs (bDMARDs) and the achievement of MDA during the observation.

Methods: Ninety-eight patients with PsA treated by DMARDs from January 2016 to January 2018 were enrolled. Data were collected for 24 months of treatment, related to the check-ups performed every three months. Demographic and clinical characteristics, cardiovascular risk factors and cardio-metabolic comorbidities, disease joint involvement at baseline and the assumed therapy were analyzed. The association with the presence of MDA at 0 months and 24 months was evaluated for each of these parameter. Age and gender were adjusted. Cardiovascular risk factors and cardio-metabolic comorbidities were analyzed at baseline and after 24 months. The aim of the study was to evaluate the population of patients with PsA treated with biological drugs (bDMARDs) and the achievement of MDA at 0 months and 24 months.

Results: Male sex was more associated with the condition of MDA both at baseline (p = 0.01) and at 24 months (p = 0.04). A statistically significant association was found between the presence of cardio-vascular accidents (stroke and TIA) and the disease status was found at baseline: amongst patients with such comorbidity, 75% were not found in MDA at time 0 (p = 0.03). The same result was not found in relation to MDA after 24 months. No other cardio-metabolic comorbidity was associated with a worse outcome. There was no association with a better outcome for any of the two classes of biological drugs considered (anti-TNF-α and not anti-TNF-α). Polycarticular involvement was associated with a worse disease status, both at baseline (p = 0.01) and after 24 months of therapy (p = 0.04).

Conclusion: In the current study, the polycarticular form of PsA present at baseline was the most associated factor (OR 0.44) with a worse outcome in a population of patients with cardio-metabolic comorbidities on bDMARDs. Cerebro-vascular accidents appeared as the only morbidity condition associated with a worse state of disease at the beginning of the observation, but this correlation disappears after 24 months. This result can be justified by the immunosuppressive treatment, which decreases the risks related to the inflammatory condition characteristic of PsA.

**Disclosure of Interests:** Simone Parisi: Speakers bureau: Chesi, Janssens, Pfizer, Celgene, Abbvie, Lilly., Davide Mohammad Reza Beigi: None declared, Marta Priora: Grant/research support from: Sanofi SpA, Maria Chiara Ditto: None declared, Clara Lisa Peroni: None declared, Angela Lagani: None declared, Enrico Fusaro: Grant/research support from: Abbvie, AboIgen, Actelion, Amgen, Biogen, BMS, Celgene, Grunenthal, GSK, Janssen, Lilly, MSD, Mundipharma, Novartis, Pfizer, Roche. SANOCTI, SOIB, UCB

SAT0399

EFFECT OF DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS ON BONE STRUCTURE AND STRENGTH IN PSORIATIC ARTHRITIS PATIENTS


Background: In contrast to rheumatoid arthritis, little is known about the effect of disease modifying anti-rheumatic drugs (DMARDs) on bone structure and bone biomarkers in psoriatic arthritis (PsA).

Objectives: To address whether the use of methotrexate (MTX) and biologic DMARDs (bDMARDs) impacts bone structure and biomechanical properties in PsA patients.

Methods: Cross-sectional study in PsA patients receiving no DMARDs, MTX or bDMARDs. Volumetric bone densities (vBMD), microstructural parameters and biomechanical properties (stiffness/failure load) were determined by high-resolution peripheral quantitative computed tomography (HR-pQCT) and micro-finite element analysis. Bone parameters were compared between PsA patients with no DMARDs and those receiving any DMARDs, MTX or bDMARDs, respectively.

Results: 165 PsA patients were analyzed, 79 received no DMARDs, 86 received DMARDs, of them 52 bDMARDs (TNF, IL-17- or IL-12/23 inhibitors) and 34 MTX. Groups were balanced for age, sex, comorbidities, functional index and bone-active therapy, while disease duration was longest in the bDMARD group (7.8±7.4 years), followed by the MTX group (4.6±7.4) and the no-DMARD group (2.9±5.2). No difference in bone parameters was found between the no-DMARD group and the MTX group. In contrast, the bDMARDs group revealed significantly higher total (p<0.001) and trabecular vBMD (p=0.005) as well as failure load (p=0.012) and stiffness (p=0.012). In regression models age and bDMARDs influenced total vBMD, while age, sex and bDMARDs influenced failure load and stiffness.

Conclusion: Despite longer disease duration bDMARDs treated PsA patients benefit from higher bone mass and better bone strength than PsA patients receiving MTX or no DMARDs. These data support the concept of better control of PsA-related bone disease by bDMARD.

Disclosure of Interests: David Simon Consultant for: Lilly, Speakers bureau: Janssen, Sara Bayat: None declared, Koray Tascilar: None declared, Eleni Kampylafka: None declared, Timo Meineerink: None declared, Louis Schuster: None declared, Anna-Maria Liphardt Grant/research support from: Novartis Pharma GmbH, Jürgen Rech Grant/research support from: Bristol-Myers Squibb and Celgene (greater than $10,000), Axel Hueber, Georg Schett: None declared, Arnd Kleyer Grant/research support from: Lilly, Consultant for: Lilly, Speakers bureau: Abbvie


SAT0400

REAL-WORLD SWITCH RATES AMONG BIOLOGIC-NAIVE PSORIATIC ARTHRITIS PATIENTS INITIATING APREMILAST, TUMOR NECROSIS FACTOR INHIBITORS OR INTERLEUKIN INHIBITORS

David Kaplan1, Brian Ung2, Corey Pelletier2, Chuka Udede2, Marc Tian2, Adult and Pediatric Dermatology, Overland Park, United States of America; 1Celgene Corporation, Summit, United States of America

Background: Psoriatic arthritis (PsA), an inflammatory arthritis, manifests in joints and surrounding tendons and ligaments. As PsA progresses, patients may switch from 1 therapy to another, discontinue medication or use agents in combination. Previous real-world studies have demonstrated that treatment adherence and biomarker treatment rates for biologic-naive PsA patients initiating apremilast or biologics (ie, tumor necrosis factor [TNF] and interleukin [IL] inhibitors) are not different.3,4 Treatment switching is common among PsA patients.

Objectives: This study compares the rate of treatment switching among adult patients initiating treatment with apremilast, TNF inhibitor or IL inhibitors.

Methods: Adult patients with PsA were identified if they newly initiated treatment with apremilast, a TNF inhibitor (adalimumab, certolizumab, etanercept, golimumab, infliximab) or an IL inhibitor (ixekizumab, secukinumab, ustekinumab) between January 1, 2015, and December 31, 2016, and had a minimum of 12 months pre-index and post-index continuous enrollment in the Truven Health (now IBM Watson) MarketScan® Commercial and Medicare Supplemental Database. Propensity score matching, based on available demographic and clinical characteristics, up to 1:2, was utilized between apremilast and biologic patients. Switch was defined as a claim for a new PsA treatment after initiation of the index medication. Days to switch was defined as the number of days between the index date and date of switch. Adherence was assessed utilizing the proportion of days covered (PDC). Outcomes were assessed every 3 months, up to 24 months. 7,802,000 members with baseline and linkage availability were included. 2,793,604 members were included in the Truven Health Truven Health (now IBM Watson) MarketScan® Commercial and Medicare Supplemental Database.

Results: 471 biologic-naive PsA patients initiating apremilast were matched to 890 biologic-naive PsA patients initiating biologics (TNF: n=804; IL: n=86). Patient characteristics were similar between the 3 cohorts (mean age: 50 years; Charlson Comorbidity Index: 0.58 [apremilast], 0.55 [TNF] and 0.56 [IL]). There was a greater proportion of females in the apremilast vs IL cohorts (55% vs 42%; P=0.0249) and a lower proportion of patients with prior PsA systemic treatment (59% vs 79%; P=0.0048). In the TNF cohort, 64% patients received adalimumab, 29% etanercept, 4% infliximab, 2% certolizumab and 1% golimumab. In the IL cohort, 78% of patients received ustekinumab, 21% secukinumab and 1% ixekizumab. At 12 months, significantly fewer patients initiating apremilast switched treatment compared with those initiating TNF inhibitors (15.5% vs 26.6%; P=0.0001), while no significant differences were observed for apremilast vs IL patients (15.5% vs 14%; P=0.714). Similar switching trends were observed at 24 months for patients initiating apremilast vs TNF (25.0% vs 36.5%; P=0.0109) or those initiating apremilast vs IL (25.0% vs 26.7%; P=0.8465). Among those switching by 12 months, mean days to switch was similar between biologic and apremilast patients (199 vs 200 days; P=0.9759) and between IL patients (199 vs 227 days; P=3.602). Patients initiating apremilast had a similar treatment adherence rate as patients initiating a TNF inhibitor (PDC: 0.81 vs 0.84; P=0.0749) and a higher treatment adherence rate than patients initiating an IL inhibitor (0.81 vs 0.79; P=0.0071).

Conclusion: Biologic-naive PsA patients initiating apremilast demonstrated lower switch rates vs biologic-naive PsA patients initiating TNF inhibitors in a large US administrative claims database. No difference in rates of switching was observed between apremilast and IL patients.

REFERENCE


Disclosure of Interests: David Kaplan Consultant for: Celgene Corporation, Speakers bureau: Celgene Corporation, Abbvie, Pfizer, Brian Ung Shareholder of: Celgene Corporation, Employee of: Celgene Corporation, Corey Pelletier Shareholder of: Celgene Corporation, Employee of: Celgene Corporation, Chuka Udede Shareholder of: Celgene Corporation, Employee of: Celgene Corporation, Marc Tian Shareholder of: Celgene Corporation, Employee of: Celgene Corporation


SAT0401

USE OF AND RESPONSE TO METHOTREXATE IN EARLY PSORIATIC ARTHRITIS: RESULTS FROM THE REAL WORLD COHORT, DEPAR STUDY

Kim Wervers1, Hannah den Braanker1, Jolanda Luime1, Ilja Tchetverikov2, Andreas Gerards3, Cathelijne Appels4, Webo van der Graaff5, Hans van Groenendaal5, Linda-Anne Korswagen5, Josien Verla-Verdier7, Johanna Hantes1, Marc Kof1, Marj Vin1, CICERO, Erasmus MC, Rotterdam, Netherlands; 2Albert Schweitzer Hospital, Dordrecht, Netherlands; 3Franciscus Gasthuis and Vlietland, Schiedam, Netherlands; 4Amphia Hospital, Breda, Netherlands; 5Rivus Hospital, Gorinchem, Netherlands; 6Rehausing Zuid West Nederland, Roosendaal, Netherlands; 7Background: Methotrexate (MTX) is the preferred drug of most rheumatologists for treating psoriatic arthritis (PsA). Despite its widespread use in

Scientific Abstracts
clinical practice, scientific evidence of methotrexate on the different manifestations of psoriatic disease is limited. Specifically, data of MTX use in usual care and in early PsA patients are lacking.

Objectives: To describe the response to MTX for patients with PsA and an oligoarthritis or polyarthritis phenotype in usual care in the first year after diagnosis, and its impact on different aspects of the disease, including patients not achieving minimal disease activity (MDA) despite continuous exposure to MTX.

Methods: Data collected in the Dutch southwest Early Psoriatic Arthritis cohort (DEPAR) study were used. Patients with a new diagnosis of PsA who have not started disease-modifying antirheumatic drugs (DMARDs) for PsA were eligible to participate. In this analysis, only patients with a phenotype at time of diagnosis of oligoarthritis or polyarthritis (resp. 2-4 joints involved or 5 or more joints, as defined by the rheumatologist), and at least one year follow up were included. Research nurses collected clinical data and data on medication use every three months in the first year after diagnosis. The following outcomes were used to evaluate disease activity: MDA, EULAR active disease (at least one tender and swollen joint), disease activity index for PsA low disease activity (DAPSA-LDA: DAPSA<14), and disease activity score 28 low disease activity (DAS28-LDA: DAS28<3.2). Disease activity at six months of patients who started MTX within six months after diagnosis and have continued using MTX until one year after diagnosis was analyzed.

Results: In April 2018, 219 patients had a phenotype of oligoarthritis (n=134; 61%) or polyarthritis (n=85; 39%) at time of diagnosis, and at least one year follow up. In 183 (84%) patients, MTX monotherapy was started within six months after diagnosis. Within the first year, 23 of these used MTX intermittently, 25 switched to a different DMARD, and 45 started a different DMARD while remaining on MTX therapy. The remaining 90 patients used MTX monotherapy throughout the first year and of these we assessed disease activity at 6 months after diagnosis. At 6 months, 38 patients out of these 90 were not in MDA despite continuous MTX treatment, while 44 achieved MDA. Major differences amongst the two groups included tender joint count, physical function, evaluation of pain and global disease activity and impact on health-related quality of life scores (Table 1). Conversely, 18% of all patients started MTX monotherapy were in sustained MDA at one year while continuing MTX monotherapy.

Conclusion: The majority of patients with a new diagnosis of PsA with a phenotype of oligoarthritis or polyarthritis started MTX within a year after diagnosis. MTX is maintained as monotherapy in half of these patients, with 18% of them achieving sustained MDA using MTX monotherapy at one year. Interestingly, approximately half of the patients who had continued methotrexate monotherapy were not achieving MDA after six months and they report higher impact of disease on clinical and patient reported outcomes, suggesting need to consider improvement of therapy for these patients.

Disclosure of Interests: Kim Wervers: None declared, Hannah den Braaniker: None declared, Jolanda Luime: None declared, Ilja Tchetverikov: None declared, Andreas Gerards: None declared, Cathelijne Appels: None declared, Wiebo van der Graaff: None declared, Hans van Groenendael: None declared, Lindy-Anne Korswagen: None declared, Josien Venis-van Dieren: None declared, Johanna Hazes: None declared, Marc Kok: None declared, Marijn Vis Grant/research support from: Novartis.


Crystal diseases, metabolic bone diseases other than osteoporosis

Table 1. Disease activity and health-related quality of life at six months after diagnosis, of patients on MTX monotherapy in the first year after diagnosis

<table>
<thead>
<tr>
<th>Metric</th>
<th>MDA at 6 months (n=18)</th>
<th>MDA at 6 months (n=49)</th>
</tr>
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<tbody>
<tr>
<td>Swollen joint count 0</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Swollen joint count &gt; 1</td>
<td>8 (21)</td>
<td>3 (7)</td>
</tr>
<tr>
<td>Tender joint count 0</td>
<td>2 (0-4)</td>
<td>0 (0-0)</td>
</tr>
<tr>
<td>Tender joint count &gt; 1</td>
<td>23 (35)</td>
<td>1 (7)</td>
</tr>
<tr>
<td>Leeds enthesis index 0</td>
<td>0 (0-0)</td>
<td>0 (0-0)</td>
</tr>
<tr>
<td>Leeds enthesis index &gt; 1</td>
<td>16 (26)</td>
<td>1 (2)</td>
</tr>
<tr>
<td>PASI &gt; 10</td>
<td>22 (58)</td>
<td>19 (34)</td>
</tr>
<tr>
<td>VAS pain &gt; 15</td>
<td>36 (95)</td>
<td>10 (21)</td>
</tr>
<tr>
<td>VAS global &gt; 20</td>
<td>33 (88)</td>
<td>7 (14)</td>
</tr>
<tr>
<td>HAQ &gt; 0.5</td>
<td>27 (73)</td>
<td>7 (15)</td>
</tr>
<tr>
<td>PsAQoL</td>
<td>3.8 ± 2.3</td>
<td>3.0 ± 1.1</td>
</tr>
<tr>
<td>PsAQoL1</td>
<td>7.6 ± 4.0</td>
<td>7.2 ± 1.6</td>
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<table>
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<th>Short Form 36</th>
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<tbody>
<tr>
<td>Physical functioning</td>
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<tr>
<td>Physical role functioning</td>
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<tr>
<td>Bodily pain</td>
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<tr>
<td>General health</td>
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<td>Social functioning</td>
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<tr>
<td>Emotional role functioning</td>
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<tr>
<td>Mental health</td>
</tr>
<tr>
<td>Physical component scale</td>
</tr>
<tr>
<td>Mental component scale</td>
</tr>
</tbody>
</table>

Data shown as x (SD), median (interquartile range) or mean ± standard deviation. MDA: minimal disease activity; MTD: methotrexate; PASI: psoriasis area and severity index; VAS: visual analog scale; HAQ: health assessment questionnaire; PsAQoL: psoriatic arthritis impact of disease; PsAQoL1: psoriatic arthritis specific quality of life.
SEX DIFFERENCES ARE PRESENT IN CLINICAL CHARACTERISTICS, BUT NOT IN RESPONSE TO DIFFERENT URATE LOWERING THERAPIES IN PATIENTS WITH GOUT

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Background: Clinical characteristics of gout differ between women and men. Little however is known about the association between these differences and response to treatment. As women seem to have lower mean uric acid excretion compared to men, response to uricosuric agents might be better compared to xanthine oxidase inhibitors.

Objectives: To identify sex differences in clinical characteristics and response to urate lowering therapy (ULT) in patients with gout and in women difference in response to allopurinol or benzbromarone.

Methods: Patients with clinical diagnosis of gout, a first outpatient visit between January 2010 and March 2018 and a follow-up of at least 6 months were included in a retrospective cohort study, with ongoing recruitment, conducted in two rheumatology centres in the Netherlands. From this cohort, patients who started ULT were selected. Clinical characteristics and treatment outcomes of allopurinol and benzbromarone were compared between women and men, including drug survival (corrected for age and renal function) and cumulative incidence of achieving target serum uric acid (<0.36 mmol/l). In women, difference in cumulative incidence of achieving target serum uric acid while using allopurinol or benzbromarone was compared.

Results: From a total of 519 (105 women/414 men) patients, 513 (104 women/409 men) and 74 (18 women/56 men) patients were included in the allopurinol and/or benzbromarone group, respectively. Clinical characteristics are described in Table 1. Drug survival was similar for women and men for allopurinol (hazard ratio 1.08, 95% confidence interval (CI) 0.71-1.64) as well as for benzbromarone (hazard ratio 0.66, 95% CI 0.26-1.66) (Figure 1a and b). Cumulative incidences of achieving target serum uric acid while using allopurinol or benzbromarone was compared.

Disclosure of Interests: Sophie Wanten: None declared, Minke ter Stal: None declared, Wing-Yee Kwok: None declared, Frank van den Hoogen: None declared, Marcel Fiendrie: Grant/research support from: Research grants from Grünenthal, Menarini, Consultant for: Yes, advisory board for Grünenthal in 2017, Paid instructor for: Yes, for Menarini, Noortje van Herwaarden: None declared

REFERENCES

Table 1. Clinical characteristics

<table>
<thead>
<tr>
<th></th>
<th>Women (n = 105)</th>
<th>Men (n = 414)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), median (IQR)</td>
<td>73.9 (54-71.6)</td>
<td>62.9 (54-71.6)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Current alcohol use, n (%)</td>
<td>34 (45)</td>
<td>275 (79)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Comorbidities, n (%)</td>
<td>71 (68)</td>
<td>200 (48)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Hypertension</td>
<td>41 (39)</td>
<td>76 (18)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Renal impairment</td>
<td>36 (34)</td>
<td>80 (19)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diuretics use, n (%)</td>
<td>67 (64)</td>
<td>137 (33)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Joint involvement, n (%)</td>
<td>14 (13)</td>
<td>68 (17)</td>
<td>0.38</td>
</tr>
<tr>
<td>Monoarthrits</td>
<td>64 (62)</td>
<td>220 (62)</td>
<td></td>
</tr>
<tr>
<td>Oligoarthritis</td>
<td>26 (25)</td>
<td>120 (29)</td>
<td></td>
</tr>
<tr>
<td>Polyartrits</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>History or presence of tophi, n (%)</td>
<td>39 (37)</td>
<td>94 (23)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Crystal proven gout, n (%)</td>
<td>89 (85)</td>
<td>348 (89)</td>
<td>0.86</td>
</tr>
<tr>
<td>Baseline serum uric acid (mmol/L), mean (SD)</td>
<td>0.43 (0.13)</td>
<td>0.43 (0.12)</td>
<td>0.73</td>
</tr>
</tbody>
</table>

*P-values for categorical variables were calculated by chi-square analysis, for continuous variables the appropriate (non)parametric analysis was used based on Gaussian distribution.
failed maximal medical management, typically with xanthine oxidase inhibitors (XOI). Studies have shown a complete responder rate of 42% when defined as repeat serum uric acid (sUA) levels <6.0 mg/dL for >80% of the time during months 3 and 6 of treatment. Patients that do not maintain a low uric acid while on pegloticase therapy are presumed to have developed anti-drug antibodies (ADA) which rapidly clear the pegloticase molecule. As is routinely utilized in the treatment of other rheumatologic diseases, coadministration of immunomodulatory medications, such as methotrexate, could potentially temper the development of these ADAs (as defined by maintenance of sUA response) in patients treated with pegloticase for refractory gouty arthropathy.

Objectives: The aim of the current case series was to identify and clinically evaluate patients in a real-world practice setting in order to investigate the use of adding methotrexate to a pegloticase regimen to increase the durability of response.

Methods: In this prospective, proof-of-concept, observational case series, 10 sequential patients with refractory tophaceous gouty arthropathy being started on treatment with pegloticase 8 mg every two weeks (as per the label) were identified from 3 separate infusion centers. No inclusion/exclusion criteria were implemented or prescreening performed. Methotrexate (MTX) 15 mg orally once weekly and folic acid 1 mg orally once daily was started one month prior to the initial administration of pegloticase and continued throughout pegloticase treatment. Any infusion pre-medication, which were consistent with standard practices, were administered per the individual physician’s discretion as well as management of any gout flares which occurred during the treatment course. As per standard of care, sUA was measured every two weeks, prior to each subsequent infusion. At the completion of pegloticase treatment for all patients, the number and percentage of patients able to maintain an sUA at goal <6.0 mg/dL was recorded.

Results: Ten patients ranging in age from 35-80 were identified, from 3 separate infusion centers. There were 143 total pegloticase infusions performed within the observation period. All 10 patients received at least 10 infusions (5 months), 9 patients at least 12 infusions (6 months), 5 patients at least 16 infusions (8 months), 2 patients at least 18 infusions (9 months), and 1 patient received 19 infusions. All 10 patients completed a full course of pegloticase treatment. All patients stayed on MTX 15 mg/week. There were no dose adjustments made in the MTX doses of patients were responders as defined by >80% of sUA levels being maintained at goal <6.0 mg/dL during the observation period. None of the 10 patients stopped pegloticase therapy due to increased sUA or loss of response and there were no infusion reactions in any of the 143 infusions or safety concerns identified. Gout flares did occur, primarily following the initial infusion, with less severity/prevalence with subsequent infusions. No patients discontinued treatment because of flares.

Conclusion: In this proof-of-concept case series of 10 sequential patients, pretreatment and co-administration of methotrexate 15 mg orally once weekly and folic acid 1 mg orally once daily with pegloticase resulted in a 100% maintenance of pegloticase sUA response with no infusion reactions. Although additional studies would be needed to corroborate these results, these data support a potential paradigm shift in treatment of refractory gout with pegloticase.

REFERENCE

Acknowledgement: Research sponsored by the Alaska Rheumatology Alliance.


SA0406
COMPUTED TOMOGRAPHIC MAPPING OF SPINAL AND VASCULAR URATE DEPOSITION IN THE ABDOMEN WITH CORRELATION TO URIC ACID LEVEL

Juvel Lee1, Waheed Abdelfattah2, Sunghan Jung1, Ahmed Neiga3, Bo Gong4, Savvas Nicolaou1, Faculty of Medicine, University of British Columbia, Vancouver, Canada; 2University of British Columbia/Vancouver General Hospital, Radiology, Vancouver, Canada; 3Faculty of Medicine, Zagazig University, Zagazig, Egypt; 4Vancouver General Hospital, Vancouver, Canada; 5University of British Columbia/Vancouver General Hospital, Vancouver, Canada

Background: Gout is characterized by accumulation of monosodium urate (MSU) in joints and soft tissues. Gout prevalence is about 1-5% in the general population, predominantly in elderly men. Accurate diagnosis of gout is paramount in managing disease progression and guiding treatment. A meta-analysis in 2018 showed that Dual-Energy CT (DECT) has high sensitivity, specificity and diagnostic accuracy in MSU detection. MSU...
deposition outside ‘classic’ extremities has been scarcely investigated yet may be a potential indicator of tophus burden and impending clinical deterioration.

**Objectives:**
1. Anatomical mapping of gout deposition in the abdomen (vessels, solid organs and lumbosacral spine).
2. Determine correlation between uric acid level and vascular, solid organ and spinal MSU deposition.

**Methods:** Retrospective analysis of all DECT abdomen and pelvis scans done in our institution (from January 2007 to July 2018). The inclusion criteria were: males > 50 years with high or normal uric acid levels who were asymptomatic for gout. Validated dual-energy gout analysis software was used.

**Results:** 235 DECT cases met the inclusion criteria. Medical Record document review showed no diagnosis of gout in any patient in the sample. By the time this abstract was submitted, 166 cases were reviewed. The analyzed sample (n = 166), showed MSU deposits (1 or more deposits) in the abdominal aorta (n = 48/166; 28.92%), abdominal vessels other than aorta (n = 57/166; 34.34%) and lumbosacral spine (n = 15/166; 9.04%). No deposits were detected in the solid abdominal organs (n = 0/166; 0%). There was a statistically significant positive correlation between uric acid level and spinal deposits (r= 0.22, P= 0.004). Regression analysis showed uric acid levels can’t significantly predict the presence of aortic, vascular or spinal deposits.

**Conclusion:**
Computed tomographic mapping of MSU deposits was positive in the abdominal aorta, other abdominal vessels and lumbosacral spine in patients with normal or high uric acid levels who were asymptomatic for gout. Uric acid level was positively correlated with spinal gout, but not with aortic or vascular gout. Interestingly, uric acid levels can’t significantly predict the presence of aortic, vascular or spinal gout. Larger sample size, wider variation in uric acid levels are still needed.

**REFERENCES**

<table>
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<tr>
<th>Table 1. Correlation Analysis.</th>
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<td>Uric Acid Levels</td>
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<th>Table 2. Regression analysis</th>
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<tr>
<td>Uric Acid Levels</td>
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<td>Spine</td>
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**Disclosure of Interests:** Juvel Lee: None declared, Waleed Abbassall: None declared, Sunghan Jung: None declared, Ahmed Negida: None declared, Bo Gong: None declared, Savvas Nicolaou Grant/research support from: The Department of Radiology, Vancouver General Hospital has a Master Research Agreement with Siemens Healthcare, Forcheim, Germany (non-pharmaceutical company). DOI: 10.1136/annrheumdis-2019-eular.5217
comorbidities. Not believing in medication may impact on the success of achieving these treatment goals.

Objectives: To study which factors were associated to and predictive of beliefs about medicines during one year in patients with a recent gout attack and a need for ULT.

Methods: Baseline data from a prospective observational study were used in patients with crystal-proven gout after a recent gout flare and insufficiently treated serum urate (sUA) level (>360 μmol/L)/>6 mg/dl. In these patients a treat-to-target approach was planned to meet the treatment target (sUA <360 μmol/L, or <300 μmol/L if clinical tophi). Assessments included demographic and clinical data, baseline serum urate levels, medication, comorbidities, physical function (HAQ), and SF-36 mental (MCS) and physical component summary scores. The Beliefs in Medicines Questionnaire (BMQ) (1) queries patient beliefs about medicines on four subscales (necessity and concerns specific for the patient, generally on overuse and harm). Respondents indicated their degree of agreement with each individual statement about medicines on a 5-point Likert scale, (1=strongly disagree to 5=strongly agree). Scores within the four subscales were summed (ranges 5-25 for necessity and concern, 4-20 for overuse and harm). Calculation of the difference within the four subscales were summed (ranges 5-25 for necessity and concern, 4-20 for overuse and harm). Respondents indicated their view on taking medication, and was grouped as high and low relative to the median.

Using multivariate analysis with logistic regression, baseline variables were explored as predictors of high beliefs in the relative importance of medication after 12 months.

Results: 202 patients were included at baseline, 94.1% men, 90.3% Caucasian, mean (SD) age 56.6 (14.2) years, disease duration 8.0 (7.7) years. Mean sUA level was 494 (SD 86.8) μmol/L at baseline, body mass index 28.9 (4.6) kg/m², and physical function (HAQ) 0.36 (0.57), 18.8% (n=28) had tophi, and 30.4% (n=55) were previous users of allopurinol.

During the first year the beliefs in necessity of medication and the perceived importance of medication increased, while the concerns decreased.

Table: Beliefs in Medicines Questionnaire (BMQ) subscales. *=p<0.05, **=p<0.01 vs. baseline

<table>
<thead>
<tr>
<th>Month</th>
<th>0 (195)</th>
<th>3 (158)</th>
<th>6 (144)</th>
<th>12 (126)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Necessity (SD)</td>
<td>17.1 (4.5)</td>
<td>18.2 (3.4)*</td>
<td>18.4 (3.4)**</td>
<td>18.5 (3.3)**</td>
</tr>
<tr>
<td>Concern (SD)</td>
<td>13.7 (4.6)</td>
<td>13.3 (4.5)</td>
<td>13.3 (4.6)*</td>
<td>13.1 (4.6)**</td>
</tr>
<tr>
<td>Nic – Conc (SD)</td>
<td>3.4 (6.2)</td>
<td>4.9 (5.4)*</td>
<td>5.1 (5.5)**</td>
<td>5.4 (5.5)**</td>
</tr>
<tr>
<td>Overuse (SD)</td>
<td>10.6 (2.8)</td>
<td>10.8 (2.5)</td>
<td>10.6 (2.8)</td>
<td>10.6 (2.7)</td>
</tr>
<tr>
<td>Harmful (SD)</td>
<td>9.4 (2.4)</td>
<td>9.5 (2.5)</td>
<td>9.6 (2.5)</td>
<td>9.2 (2.7)</td>
</tr>
</tbody>
</table>

Bivariate comparisons studying demographic, medication and clinical variables did not show consistent cross-sectional associations with beliefs in the importance of medication. However, after 12 months, bivariate comparisons revealed statistically significant differences in mental health (SF36 MCS), physical function (HAQ) and self-efficacy for symptom control. In logistic regression analyses, adjusting for age, gender, BMI and comorbidities, prediction of high beliefs in the relative importance of medication after 12 months were independently associated with baseline self-efficacy for symptom control (OR 1.04 per unit, 95% CI 1.01-1.06).

Conclusion: During one year of treat-to-target strategy in patients with gout, perceived necessity of medication and higher importance of medication increases. Self-efficacy for symptom control at baseline was an independent predictor of high beliefs in importance of medication after 12 months. These findings support that patients increase their perception of the necessity of beliefs in medication during a treat-to-target approach with ULT.

REFERENCE

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SAT0408 BODY FAT MEDIATES THE CORRELATION BETWEEN FRUCTOSE-CONTAINING BEVERAGES CONSUMPTION AND SERUM URIC ACID IN MALE GOUT PATIENTS

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Background: Fructose-containing beverages (FCB) consumption has been recognized as a promoter of hyperuricemia and gout in recent years. FCB consumption also contributes to the development of obesity which is an important risk factor of gout. However, data about the associations among FCB consumption, obesity and the level of serum uric acid (sUA) is limited.

Objectives: To investigate the associations among FCB consumption, obesity and sUA level in gout patients.

Methods: Consecutive gout patients who fulfilled the 2016 ACR/EULAR classification criteria were recruited. Demographic information, clinical characteristics and comorbidities of gout were collected. A 10-items food frequency questionnaire was developed which included alcohol, red meat, animal offal, seafood, hotpot, slow-cooking soup, FCB, tea, coffee and milk/milk products. Patients were asked to report the average consumption frequency over the one year prior to the first gout attack. Body composition was assessed by bioelectric impedance analysis and overweight was defined by body fat percentage (BF%) as ≥25% for men and ≥35% for women.

Results: 1) Among 331 recruited gout patients, 96.1% were male, so only male patients were further analyzed. The median age of male patients was 37.5 (30, 49) years and median sUA was 9.5 (7.8, 10.5) mg/dl with 18.9% presented tophi. The mean BF% was 25.6±6.2% and 54.7% male patients were overfat. The prevalence of hypertension, diabetes, dyslipidemia, metabolic syndrome and fatty liver were 34.6%, 8.5%, 62.9%, 44.3% and 46.9% respectively. 2) There were no significant differences of food intake frequency between overweight patients and normal fat patients. Spearman correlation analysis results showed that FCB consumption was positively correlated with BF% (r=0.176, P=0.002), while milk/milk products consumption was negatively correlated with BF% (r=-0.117, P=0.038). After adjusted by age, duration, family history, eGFR, hypertension, diabetes mellitus, dyslipidemia, metabolic syndrome, fatty liver and the other nine dietary factors, multivariable linear regression showed that FCB consumption was positively correlated with BF% (compared with <1 time/w, 3-4 times/w: coefficient β=2.4619, 95%CI 0.3580~4.5657, P=0.022; 4 times/w: coefficient β=2.6696, 95%CI 0.8266~4.5726, P=0.0049), and BF% was positively correlated with sUA (coefficient β=0.0784, 95%CI 0.0228~0.1239, P=0.001). However, FCB consumption was not correlated with sUA after adjusted by above confounders and BF% (P=0.079). 3) Further mediation analysis were performed to evaluate whether BF% mediated the correlation between FCB consumption and sUA. After adjusted by the confounding factors mentioned above, the total effect of FCB consumption on sUA was significant (compared with <1 time/w, >4 times/w: coefficient β=0.8813, 95%CI 0.1457~1.6169, P=0.019), BF% produced indirect effect on the correlation between FCB consumption and sUA (compared with <1 time/w, >4 times/w: indirect effect coefficient β=0.2115, 95%CI 0.0453~0.4032).

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Conclusion: Our data show that body fat mediates the correlation between FC8 consumption and SUA in male gout patients, which imply the importance of body composition assessment.

Acknowledgement: The present study was supported by Guangdong Natural Science Foundation, China (Grant no. 2014A030310086) to Qian-Hua Li.

Disclosure of Interests: None declared

SAT0410

RADIOPHARMACEUTICAL EROSION SCORE IMPROVED WITH TARGETED URATE-LOWERING THERAPY IN A PROSPECTIVE GOUT VIETNAMESE COHORT

Thomas Bardin1; Quang Dinh Nguyen2; Khoi Minh Tran3; Nghia Hieu Le3; Duc Minh Do5; Valerie Bousson4; Pascal Richelet1; Matthieu Resche-Rigon4; Hippar Larboisire, Rheumatology, Paris, France; 1Vien Gu Medical Center, French-Vietnamese research center on gout and chronic diseases, H0 Chi Minh City, Vietnam; 2University of Medicine and Pharmacy, Molecular Biology, Ho Chi Minh City, Vietnam; 3Hippar Larboisire, Radiology, Paris, France; 4Hôpital Saint Louis, Biostatistics, Paris, France

Background Urate deposition in joints of patients with neglected gout leads to destructive arthropathy, with subchondral bone erosion, bone construction, and late joint space narrowing. Gouty erosions are believed to improve under urate lowering drugs (ULDs), but their course has been little studied. We therefore performed a systematic prospective study of a Vietnamese cohort started on allopurinol at inclusion.

Objective: To characterize radiographic outcome of gouty erosions under serum urate-targeted ULDs, but their course has been little studied. We therefore performed a systematic prospective study of a Vietnamese cohort started on allopurinol at inclusion.

Methods: 120 male Sprague-Dawley rats were randomly divided into 3 groups: After establishment of acute gouty arthritis model, rats were given P2X7R agonist ATP, P2X7R inhibitor BBG and PBS, respectively. The clinical manifestations of the ankle joints were evaluated at 6h, 12h, 24h, 48h and 72h before the rats were sacrificed, and rat ankle synovial slices for H&E staining. IL-1β, IL-6 and TNF-α, suggest-

Disclosure of Interests: None declared

SAT0409

P2X7R PROMOTE THE ATTACK OF ACUTE GOUTY ARTHRITIS IN RATS FROM CLINICAL TO PATHOLOGY

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1The First Affiliated Hospital of University of Science and Technology of China, Rheumatology and Immunology, Hefei, China; 2The First Affiliated Hospital of University of Science and Technology of China, Rheumatology and Immunology, Hefei, China


Objectives: The aim of this study was to activate P2X7R signaling pathway through changes in extracellular ATP concentrations, leading to the development of acute gouty arthritis and the production of pro-inflammatory.

Methods: 120 male Sprague-Dawley rats were randomly divided into 3 groups: After establishment of acute gouty arthritis model, rats were given P2X7R agonist ATP, P2X7R inhibitor BBG and PBS, respectively. The clinical manifestations of the ankle joints were evaluated at 6h, 12h, 24h, 48h and 72h before the rats were sacrificed, and rat ankle synovial slices for H&E staining. IL-1β, IL-6 and TNF-α, in the synovial tissue of the right ankle joint of rats, at 12h, and 24h, the infiltration of mononuclear cell in ATP group was significantly higher than that in BBG group and control group (P=0.000, 0.007; P=0.000, 0.001); The neutrophils infiltration in ATP group was the highest among the three groups at 24h (P=0.001, 0.001), and the control group was higher than BBG group (P=0.04).

Conclusion: Activation of P2X7R can significantly promote the attack of acute gouty arthritis and the production of IL-1β, IL-6 and TNF-α, suggesting that P2X7R affects the development of acute gouty arthritis and regulates the secretion of pro-inflammatory cytokines.

REFERENCE


Disclosure of Interests: None declared

SAT0410

RADIOPHARMACEUTICAL EROSION SCORE IMPROVED WITH TARGETED URATE-LOWERING THERAPY IN A PROSPECTIVE GOUT VIETNAMESE COHORT

Thomas Bardin1; Quang Dinh Nguyen2; Khoi Minh Tran3; Nghia Hieu Le3; Duc Minh Do5; Valerie Bousson4; Pascal Richelet1; Matthieu Resche-Rigon4; Hippar Larboisire, Rheumatology, Paris, France; 1Vien Gu Medical Center, French-Vietnamese research center on gout and chronic diseases, H0 Chi Minh City, Vietnam; 2University of Medicine and Pharmacy, Molecular Biology, Ho Chi Minh City, Vietnam; 3Hippar Larboisire, Radiology, Paris, France; 4Hôpital Saint Louis, Biostatistics, Paris, France

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Methods: 120 male Sprague-Dawley rats were randomly divided into 3 groups: After establishment of acute gouty arthritis model, rats were given P2X7R agonist ATP, P2X7R inhibitor BBG and PBS, respectively. The clinical manifestations of the ankle joints were evaluated at 6h, 12h, 24h, 48h and 72h before the rats were sacrificed, and rat ankle synovial slices for H&E staining. IL-1β, IL-6 and TNF-α, in the synovial tissue of the right ankle joint of rats, at 12h, and 24h, the infiltration of mononuclear cell in ATP group was significantly higher than that in BBG group and control group (P=0.000, 0.007; P=0.000, 0.001); The neutrophils infiltration in ATP group was the highest among the three groups at 24h (P=0.001, 0.001), and the control group was higher than BBG group (P=0.04).

Conclusion: Activation of P2X7R can significantly promote the attack of acute gouty arthritis and the production of IL-1β, IL-6 and TNF-α, suggesting that P2X7R affects the development of acute gouty arthritis and regulates the secretion of pro-inflammatory cytokines.

REFERENCE


Disclosure of Interests: None declared
p=0.004), -1.4 at 12 months (n=47, p=0.0001) and -4.2 at 24 months (n=14, p=0.001). Complete radiographic erosion healing was observed in only one foot joint in which a small baseline erosion disappeared on M33 radiograph. Erosion score decrease correlated with decrease of double contours at 12 months (rho=0.45, p=0.001) and with mean SUA between M3 and M12 (rho=0.59, p=0.03). A total of 41 joints (hand and foot DIPs, foot II-V PIPs) could not be scored due to score specifications. Prominent diaphysis erosions were seen in 6 patients and were not allowed scoring despite improvement. Bone construction and reappearance of bone contours were striking features of improved radiographs that were not measured by the score. Ankylosis of a toe joint was observed in 4 patients. Shrinking of 3 toes developed during dissolution of massive joint space/subchondral bone urate deposits.

Conclusion: Urate-lowering improved gouty erosion score, in correlation with decrease of uricemia and urate crystal load. However, complete erosion recovery was seldom observed during a median follow-up of 12 months. Increased bone production and massive urate dissolution under ULD occasionally led to 2 undescribed features of gouty arthropathy: joint ankylose and shrinking of involved toes respectively.

REFERENCES


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Disclosure of Interests

Chlo Yokose1, Lee Lu2, Michael Chen-Xu3, Yuqing Zhang4, Hyon Choi4. 
1Massachusetts General Hospital, Division of Rheumatology, Allergy, and Immunology, Boston, United States of America; 2Arthritis Research Canada, British Columbia, Canada; 3Harvard T.H. Chan School of Public Health, Boston, United States of America

Background: Gout is associated with many metabolic and cardiorenal comorbidities. Several previous studies investigated the comorbidity patterns by cluster analysis; however, no such study has been based on the entire general population. As such, the generalizability, which is essential to these pattern analyses, remains unknown.

Objectives: We used cluster analysis on a large, representative general population sample of the United States to identify discrete phenotype patterns comorbidities observed in gout patients.

Methods: We used data from 8,607,137 participants in the 2007-2016 National Health and Nutrition Examination Survey (NHANES), a nationally representative sample of adults in the United States. Diagnosis of gout was based on survey of physician- or health professional-diagnosed gout. We used cluster analysis to identify subgroups among participants with gout with distinct comorbidity subgroups based on 9 variables: obesity, hypertension, diabetes, hypercholesterolemia, hypertriglyceridemia, coronary heart disease (CHD), heart failure (HF), chronic kidney disease (CKD), and liver disease.

Results: Cluster analysis identified 5 different subgroups (C1-C5) (Table 2). C1 had the highest proportion of patients with CKD (97%), C2 consisted of patients with gout but few other comorbidities. All patients in C3 had diabetes, but no HF, CHD, or CKD. C4 consisted primarily of patients with liver disease (85%), with high prevalences of lipid abnormalities and obesity. C5 had the highest proportion of patients with CHD and HF.

Conclusion: These findings from a nationally representative data of US adults indicate that gout comorbidities have 5 distinctive phenotypic patterns. These subgroups may have implications in pathogenesis of gout and/or for personalized care in the management of gout and comorbidities.

Disclosure of Interests: None declared

Background: Gout is a frequent and curable arthritis affecting 0.9% of adults in France. Its management remains suboptimal and less than one third of patients have efficient urate-lowering treatment (ULT). However, when individualized information were given and patients engaged in their care a treat-to-target strategy permits to achieve serum urate level (SU) at target (SU < 360 μmol/L) in more than 95% of patients. Therapeutic education sessions (TES) may improve patient knowledges, gout flare and ULT management.

Objectives: To assess the percentage of patients achieving SU target at 1 year after a TES.

Methods: TES was set up in the department since January 2014. Patients willing to participate to TES responded to a questionnaire and were interviewed with a nurse assessing their knowledges, believes and gout representations. Each TES included 5 to 8 patients and was conducted according to participants needs. We retrospectively included all patients who had attended one TES between 1st January 2014 and 31st December 2017 and who had at least one visit between 9 and 15 months later.

TES patients were matched in 1:1 with no-TES patients regarding age, sex and referent practitioner. For all patients were collected: demographics, disease duration, SU, treatments and comorbidities (type 2 diabetes, chronic kidney disease, hypertension, and cardiovascular diseases).

Results: Overall, 54 TES patients were included and matched with 54 non-TES patients. Patients’ characteristics (demographics, disease duration, SU, treatments and comorbidities) were similar at baseline except for the body mass index (BMI) and the follow-up. BMI was higher (31.0 ± 5.7 vs 28.4 ± 5.0 kg/m², p<0.03) and the final visit shorter (11 ± 3.6 vs 14.4 ± 4.8 months, p<0.001) in no-TES patients than in TES patients, respectively.

At final visit, 36 TES patients (67%) and 34 no-TES patients (63%) reached the SU target (< 360 μmol/L) (p=0.84) (Table 1). Moreover, 22 (41%) TES patients and 18 (33%) no-TES patients had a final SU < 300 μmol/L (p=0.43). There were no differences between groups (TES vs no-TES patients respectively) for: final SU (342 μmol/L ± 94 vs 338 ± 10.1136/annrheumdis-2019-eular.4032

Table 1: Patient’s characteristics for gout at the end of the follow-up

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<th>Baseline</th>
<th>End of follow-up</th>
<th>p value</th>
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<tbody>
<tr>
<td></td>
<td>TES No-TES</td>
<td>TES No-TES</td>
<td></td>
</tr>
<tr>
<td>Patient with serum urate &lt; 360</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0.84</td>
</tr>
<tr>
<td>μmol/L, n (%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Patient with serum urate &lt; 300</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0.43</td>
</tr>
<tr>
<td>μmol/L, n (%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Serum urate concentration (μmol/L), mean (SD)</td>
<td>533 (105)</td>
<td>324 (97)</td>
<td>0.84</td>
</tr>
<tr>
<td>Taking ULT</td>
<td>21 (39%)</td>
<td>19 (35%)</td>
<td>0.16</td>
</tr>
<tr>
<td>(μmol/L)</td>
<td>24 (41%)</td>
<td>28 (49%)</td>
<td></td>
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<tr>
<td>Allopurinol, n (%)</td>
<td>16 (30%)</td>
<td>22 (41%)</td>
<td>0.89</td>
</tr>
<tr>
<td>FEB (mg/day)</td>
<td>5 (9%)</td>
<td>7 (13%)</td>
<td>0.84</td>
</tr>
<tr>
<td>ULT dose</td>
<td>186 (160)</td>
<td>284 (102)</td>
<td></td>
</tr>
<tr>
<td>Allopurinol (mg/day), mean (SD)</td>
<td>106 (102)</td>
<td>86 (102)</td>
<td>0.32</td>
</tr>
<tr>
<td>FEB (mg/day)</td>
<td>30 (90)</td>
<td>82 (133)</td>
<td></td>
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<tr>
<td>Taking hyperuricemia therapy, n (%)</td>
<td>13 (24%)</td>
<td>6 (15%)</td>
<td>0.77</td>
</tr>
<tr>
<td>Aspirin, n (%)</td>
<td>6 (24%)</td>
<td>8 (4%)</td>
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<tr>
<td>Thiazide diuretics, n (%)</td>
<td>5 (9%)</td>
<td>6 (3%)</td>
<td>0.49</td>
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<tr>
<td>Furosemide, n (%)</td>
<td>6 (7)</td>
<td>6 (7)</td>
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</tr>
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</table>

Conclusion: The percentage of patients achieving SU target after one single TES was high compare to literature data. However, it was not different from usual care achieved in our department: a tertiary care center expert in gout management. The diffusion of our savoir-faire and the TES will improve gout management.

REFERENCE

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Background: Patients with gout typically present to the hospital when their disease is acutely flared. It is therefore important to educate patients on the disease so that they become more aware of the importance of adhering to therapy. This can be achieved through Therapeutic Education Sessions (TES) which are patient centered, interactive, educational sessions that provide the patient with knowledge about their disease and the importance of adhering to therapy.

Objectives: The primary objective is to assess if TES will improve gout management.

Methods: TES were set up in the department since January 2014. TES was set up in the department since January 2014. Patients willing to participate to TES responded to a questionnaire and were interviewed with a nurse assessing their knowledges, believes and gout representations. Each TES included 5 to 8 patients and was conducted according to participants needs. We retrospectively included all patients who had attended one TES between 1st January 2014 and 31st December 2017 and who at least had one visit between 9 and 15 months later.

TES patients were matched in 1:1 with no-TES patients regarding age, sex and referent practitioner. For all patients were collected: demographics, disease duration, SU, treatments and comorbidities (type 2 diabetes, chronic kidney disease, hypertension, and cardiovascular diseases).

Results: Overall, 54 TES patients were included and matched with 54 non-TES patients. Patients’ characteristics (demographics, disease duration, SU, treatments and comorbidities) were similar at baseline except for the body mass index (BMI) and the follow-up. BMI was higher (31.0 ± 5.7 vs 28.4 ± 5.0 kg/m², p<0.03) and the final visit shorter (11 ± 3.6 vs 14.4 ± 4.8 months, p<0.001) in no-TES patients than in TES patients, respectively.

At final visit, 36 TES patients (67%) and 34 no-TES patients (63%) reached the SU target (< 360 μmol/L) (p=0.84) (Table 1). Moreover, 22 (41%) TES patients and 18 (33%) no-TES patients had a final SU < 300 μmol/L (p=0.43). There were no differences between groups (TES vs no-TES patients respectively) for: final SU (342 μmol/L ± 94 vs 338 ± 10.1136/annrheumdis-2019-eular.4032

Table 1: Patient’s characteristics for gout at the end of the follow-up

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>End of follow-up</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TES No-TES</td>
<td>TES No-TES</td>
<td></td>
</tr>
<tr>
<td>Patient with serum urate &lt; 360</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0.84</td>
</tr>
<tr>
<td>μmol/L, n (%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Patient with serum urate &lt; 300</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0.43</td>
</tr>
<tr>
<td>μmol/L, n (%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td></td>
</tr>
<tr>
<td>Serum urate concentration (μmol/L), mean (SD)</td>
<td>533 (105)</td>
<td>324 (97)</td>
<td>0.84</td>
</tr>
<tr>
<td>Taking ULT</td>
<td>21 (39%)</td>
<td>19 (35%)</td>
<td>0.16</td>
</tr>
<tr>
<td>(μmol/L)</td>
<td>24 (41%)</td>
<td>28 (49%)</td>
<td></td>
</tr>
<tr>
<td>Allopurinol, n (%)</td>
<td>16 (30%)</td>
<td>22 (41%)</td>
<td>0.89</td>
</tr>
<tr>
<td>FEB (mg/day)</td>
<td>5 (9%)</td>
<td>7 (13%)</td>
<td>0.84</td>
</tr>
<tr>
<td>ULT dose</td>
<td>186 (160)</td>
<td>284 (102)</td>
<td></td>
</tr>
<tr>
<td>Allopurinol (mg/day), mean (SD)</td>
<td>106 (102)</td>
<td>86 (102)</td>
<td>0.32</td>
</tr>
<tr>
<td>FEB (mg/day)</td>
<td>30 (90)</td>
<td>82 (133)</td>
<td></td>
</tr>
<tr>
<td>Taking hyperuricemia therapy, n (%)</td>
<td>13 (24%)</td>
<td>6 (15%)</td>
<td>0.77</td>
</tr>
<tr>
<td>Aspirin, n (%)</td>
<td>6 (24%)</td>
<td>8 (4%)</td>
<td>1</td>
</tr>
<tr>
<td>Thiazide diuretics, n (%)</td>
<td>5 (9%)</td>
<td>6 (3%)</td>
<td>0.49</td>
</tr>
<tr>
<td>Furosemide, n (%)</td>
<td>6 (7)</td>
<td>6 (7)</td>
<td>1</td>
</tr>
</tbody>
</table>

Conclusion: TES will improve gout management.

REFERENCE

Disclosure of Interests: Omar Al Tabaa: None declared, Etienne Gaix-Fontaine: None declared, Julia Herrou: None declared, Frederic Liote Grant/research support from: institutional grants from Grunenthal, Ipsen, Menarini, Novartis, SUA. TES will improve gout management.
Thus patients with smaller deposits were more likely to completely resolve the deposits.

Conclusion: We show that both life-style intervention and conventional urate lowering drug therapy reduce the volume of monosodium urate deposits. The size of MSU deposits, but not serum urate level, was the main factor that influenced complete resolution of deposits. This finding reemphasizes that the burden of deposits essentially defines the likelihood and time for complete resolution of gout.

REFERENCES


Disclosure of Interests: Sara Bayat: None declared, Hanna Ellemann: None declared, Elizabeth Araujo: None declared; Bernard Manger: None declared, Melanie Hagen: None declared, Amir Kleyer Grant/research support from: Lilly, Speakers bureau: Abbvie, Alexandeer Cavallaro: None declared, Michael Leil: None declared, Hannah Schenker: None declared, David Simon Grant/research support from: Novartis, Consultant for: Lilly, Speakers bureau: Janssen, Korsay Tascilaci: None declared, Herbert S.B. Baraf: None declared, Georg Schett: None declared, Jürgen Rech Grant/research support from: Bristol-Myers Squibb and Celgene (greater than $10,000), Consultant for: Bristol-Myers Squibb, Celgene, Chugai, GlaxoSmithKline, Janssen, Eli Lilly, Novartis, Roche, Sanofi Aventis, and UCB (in total more than $10,000), Speakers bureau: Bristol-Myers Squibb, Celgene, Chugai, GlaxoSmithKline, Janssen, Eli Lilly, Novartis, Roche, Sanofi Aventis, and UCB (in total more than $10,000)


Disclosure of Interests: Sara Bayat: None declared, Hanna Ellemann: None declared, Elizabeth Araujo: None declared; Bernard Manger: None declared, Melanie Hagen: None declared, Amir Kleyer Grant/research support from: Lilly, Speakers bureau: Abbvie, Alexandeer Cavallaro: None declared, Michael Leil: None declared, Hannah Schenker: None declared, David Simon Grant/research support from: Novartis, Consultant for: Lilly, Speakers bureau: Janssen, Korsay Tascilaci: None declared, Herbert S.B. Baraf: None declared, Georg Schett: None declared, Jürgen Rech Grant/research support from: Bristol-Myers Squibb and Celgene (greater than $10,000), Consultant for: Bristol-Myers Squibb, Celgene, Chugai, GlaxoSmithKline, Janssen, Eli Lilly, Novartis, Roche, Sanofi Aventis, and UCB (in total more than $10,000), Speakers bureau: Bristol-Myers Squibb, Celgene, Chugai, GlaxoSmithKline, Janssen, Eli Lilly, Novartis, Roche, Sanofi Aventis, and UCB (in total more than $10,000)

CLINICAL PRESENTATION OF PAGET DISEASE OF BONE: IS IT CHANGING? A RETROSPECTIVE ANALYSIS ON 368 PATIENTS

Chiara Crofti, Francesca Zucchi, Andrea Becciolini, Luigi Sinigaglia, Massimo Varenna. ASST-Gaetano Pini-CTO, Division of Rheumatology, Milan, Italy

Background: In the last few years, it has been reported a secular change of Paget disease of bone (PDB), expressed as a reduction of prevalence and severity, assessed by disease extent.

Objectives: To retrospectively evaluate the baseline clinical and demographic characteristics of a contemporary cohort of patients affected by PDB, compared with a cohort of a previous decade.

Methods: Data were retrospectively extracted from a monocentric registry, which included PDB patients at their first evaluation in a tertiary rheumatology Center between January 2000 and September 2018. Descriptive data of baseline characteristics included demographics, presenting manifestation and diagnostic procedures (diagnosed by chance or by investigations requested for specific clinical manifestations), extent of PDB, and biochemical data. Patients were divided into two groups according to the year of first evaluation: group 1 before July 2007, group 2 after July 2007. Comparisons between the two groups were performed by T test and chi-square test; logistic regression was used to analyze the association between disease extent and other collected variables.

Results: The overall population included 368 patients (males (M) 57.6%, mean age at diagnosis [± standard deviation, SD] 62.0±12.4 yrs). Diagnosis was made by chance in 43.8% cases, 54.3% patients had symptoms at disease onset: 49.5% was monostotic, mean serum alkaline phosphatase at presentation (sALP) was 196.5±167.5 UI/L.

Group 1 included 217 patients (M 56.2%, mean age at diagnosis 61.0±11.6 yrs, 6.5% family history of PDB; 45.6% diagnosed by chance, 51.2% had symptoms at disease onset, mean sALP 218.9±11.7, 43.3% monostotic). Group 2 included 151 subjects (M 59.6%, mean age at diagnosis 64.3±11.1 yrs, 7.3% family history of PDB; 41.1% diagnosed by chance, 62.9% had symptoms at disease onset, mean sALP 162.7±14.2, 58.3% monostotic).

Poliostotic disease was significantly higher in Group 1 vs Group 2 (p=0.007), and the odd to have a poliostotic disease was higher in Group 1 (OR 1.82 (IC 1.2-2.8), p<0.005) sALP was significantly higher in Group 1 vs Group 2 (218.9±11.7 vs 162.7±14.2; p<0.003). No differences were found in sex, age at diagnosis, presence of family history of PDB between patients diagnosed incidentally or by symptoms.

Conclusion: Our data confirm the reduction of clinical severity, assessed by the proportion of skeleton involved, and the decrease of biochemical markers over time. The reduction of the disease extent is consistent with a serological biomarker of the disease, such as mean sALP levels.

REFERENCES


Disclosure of Interests: Chiara Crofti: None declared, Francesca Zucchi: None declared, Andrea Becciolini: None declared, Luigi Sinigaglia: Speakers bureau: Yes, I’ve been invited speaker by Amgen, Eli Lilly, UCB, Abbvie, Roche and BMS., Massimo Varenna: None declared DOI: 10.1136/annrheumdis-2019-eular.4832

SAT0414

HIGH BODY FAT OF TRUNK IS POSITIVELY CORRELATED WITH SERUM URIC ACID IN MALE GOUT PATIENTS

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Background: Obesity is an important risk factor of gout which is defined by body mass index (BMI). However, BMI has been challenged for the limitation of failure to differentiate comprising tissues of the body. More accurate body composition (BC) has been frequently recommended to assess metabolic status.

Objectives: To investigate the characteristics of BC in gout patients and its clinical significance.

Methods: Consecutive gout patients who fulfilled the 2016 ACR/EULAR classification criteria were recruited between June 2017 and December 2018. BC was assessed by bioelectric impedance analysis including body fat percentage (BF%), the mass and distribution of muscle and fat in trunk and appendicular extremities. Demographic information, clinical characteristics and comorbidities were collected. Overfat was defined by BF% >25% for male and >35% for female.

Results: Among 362 recruited gout patients, 96.1% were male and the median age was 38 (30, 50) years, mean serum uric acid (sUA) was 9.2±2.9mg/dl. 18.0% presented toplhi. The mean BF% was 25.8±6.4% with 53.6% overfat. Male gout patients with overweight (53.7%) showed more affecting joints, higher sUA and higher prevalence of comorbidities than those without overweight (p<0.05, Figure 1). Their BF%, trunk BF% and limb BF% were positively correlated with count of affecting joints, sUA, hypertension, metabolic syndrome and fatty liver in Spearman correlation analysis, respectively (r=0.133-0.424, a p<0.05). The male patients with overweight also presented higher BMI and waist circumference (WC), higher trunk/limb BF% ratio (p<0.05, Figure 1). Their BF%, trunk BF% and limb BF% were also positively correlated with BMI and WC, respectively (r=0.604-0.755, all p<0.05). After adjustment for age, duration, family history, eGFR, hypertension, diabetes mellitus, dyslipidemia, metabolic syndrome, fatty liver, coronary heart diseases, urolithiasis, BMI and WC, multivariable linear regression showed that BF% (β=0.072, 95%CI


SAT0417 HOW EFFECTIVE IS GOUT EDUCATION PROGRAMME TO IMPROVE GOUT KNOWLEDGE AMONG PRIMARY CARE DOCTORS?

Hadyra Bahanaudini1, Nur Ani Eddy Warmi2, Habbab Mohd Yusof3, Ing Soo Lau4, Shelyn Suajin Cheng5, Malyza Mohd Zaini6. Universiti Teknologi MARA, Department of Medicine, Sungai Buloh, Malaysia; 2Hospital Selayang, Department of Medicine, Batu Caves, Malaysia

Background: Gout is a potentially curable disease with simple pharmacological treatment, although its management remained suboptimal. A disconnection between primary care doctors who treat gout most frequently, and rheumatologists who lead the development of gout management guidelines, is one of the challenges in managing gout in primary care. A concerted effort is needed to improve the quality of care of patients with gout and this includes physician education.

Objectives: To determine the effectiveness of gout educational programme in improving gout knowledge among primary care doctors.

Methods: A gout education programme consisted of five 20-minute presentations on gout (challenges in gout, principles of gout management, treat to target, disease burden and gout diet) and a session on case discussion of two gout cases was conducted for primary care doctors. Participants were invited to complete the same set of questions distributed before (pre-test) and after (post-test) the programme. A set of 10 true/false multiple choice questions (MCQ) based on a clinical scenario of a patient with gout was constructed and vetted by two rheumatologists. Comparison between the pre-test and post-test scores were analysed using paired t-test.

Results: Forty-four primary care doctors who attended gout educational programme, answered pre-test and post-tests and the scores are shown in Table 1. The scores for recall questions were higher than application questions. The mean scores for recall questions in post-test were significantly higher compared to pre-test (4.35±0.73 vs 3.51±0.47, p<0.01) but not significant for application questions (2.91±0.71 vs 2.79±0.62, p=0.56). Less than half of participants obtained correct answers for 13 out of 50 options in the pre-test mainly in questions 2, 3, 4, 6 and 7 (Table 1).
Conclusion: Gout educational programme for primary care doctors was effective in improving recall knowledge but not in application knowledge. Some specific areas of deficiency in knowledge identified were features of gout and management of acute and stable gout.

REFERENCES

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Disclosure of Interests: None declared


SA1041B
ASSOCIATION BETWEEN ANEMIA AND HYPERURICEREMIA: KOREAN NATIONAL HEALTH AND NUTRITION SURVEY 2016

Yeonghee Eun1, Eun-Jung Park2, Ji-Young Cha2, Hoon-Suk Cha3, Eun-Mi Koh4, Hyungjin Kim1, Jaejoon Lee1.

Background: Hyperuricemia and anemia may be related in terms of shared comorbidities such as chronic kidney disease and cardiovascular disease. However, to our knowledge, no studies have been conducted on the relationship between these two conditions. For the association of gout and anemia, there was a previous cohort study reporting that patients with anemia had a 2-fold higher risk of gout compared to patients without anemia. And the risk of gout was significantly higher after adjusting for serum urate levels and kidney function. However, there is a lack of data on the relationship between anemia and hyperuricemia.

Objectives: The purpose of this study was to investigate the association between hyperuricemia and anemia using data from Korean National Health and Nutrition Examination Survey (KNHANES VII; 2016), which is representative of the Korean population.

Methods: The present study included 5887 participants aged ≥ 19 years from KNHANES VII. Logistic regression was used to examine the association between anemia and hyperuricemia. Subgroup analysis was performed to confirm whether the association between two conditions varies according to participant characteristics.

Results: In an adjusted model that corrected for body mass index, smoking, drinking, physical activity, income, and education levels, hyperuricemia was 1.4 times more than that those without anemia (HR 1.41, 95% CI 1.01-1.98). The association of anemia with hyperuricemia was not seen under 65 years of age (HR 2.68, 95% CI 1.60-4.48). In addition, this association was not clear in women, but was significant in men (HR 2.62, 95% CI 1.47-4.70). In the results of subgroup analysis according to comorbidities, the association of anemia with hyperuricemia was significant only in subgroups with chronic kidney disease, diabetes, hypertension, metabolic syndrome, and cardiovascular diseases. There was no association between anemia and hyperuricemia in obese subjects, but hyperuricemia risk was higher in non-obese subjects with anemia compared to those who did not have anemia.

Conclusion: In a Korean representative sample, the risk of hyperuricemia was higher for anemia. The association of anemia with hyperuricemia was more pronounced in subjects with older age, male population, and other comorbid conditions.

Disclosure of Interests: None declared


SAT0419
HAS THE INTRODUCTION OF A PRIMARY CARE GOUT GUIDELINE RESULTED IN SERUM URIC ACID (SUA) TARGETS BEING ACHIEVED?

Rashid Farid1,1, Leanne Gray2, Dean John3, Daniel Holtehouse4, Lesley Oettle5.

1 Royal Lancaster Infirmary, Rheumatology, Lancaster, United Kingdom; 2 Bay Medical Group, Morecambe, United Kingdom

Background: Gout is the most common inflammatory arthritis thought to affect 2.4% of the UK population. A local primary care audit in 2012 suggested suboptimal gout management. In an attempt to improve gout management we introduced a local guideline which was supported by an increase in gout education to our local primary care physicians.

Objectives: To assess the impact of a local primary care gout guideline (introduced in 2015) by comparing pre-guideline audit data (2012) to post guidelines audit data (2019). To identify if the introduction of this guideline translated into a reduction in secondary care referrals for advice on gout management.

Methods: Retrospective analysis of primary care data covering all patients with active diagnosis of gout since 2015 in a large primary care medical group (list size of 30,000 patients). This data was then compared to the results of a previous audit carried out prior to introduction of guideline (2012). As well as assessing primary care data, we carried out a secondary care audit pre and post guideline introduction.

Results: Out of a population list of 30,000 patients, 650 (2.1%) cases were coded as gout. 521 (80%) were male and 129(20%) were female. 429(66%) were on ULT. 407 (94.8%) were on Allopurinol, 21(4.8%) were on Febuxostat and only 1 patient on sulfinpyrazone. Of those on Allopurinol, 24 (5.9%) had no documented monitoring of SUA levels. Out of the remaining 383 (94.1%), 179 (46.7%) achieved target SUA levels of <360, compared to 204 (53.3%) in the previous audit. 184 (46.4%) did not achieve the target SUA levels. 178 (46.4%) patients had a previous SUA levels checked in the last year compared to 23.5% in the previous audit. 177 (28%) had SUA levels checked in last 3 years compared to 40% in the previous audit. SUA levels were not checked in the last 3 years in 98(25.6%) compared to 36.4% in the past.

Of those on febuxostat, 14 (67%) achieved target SUA levels. 7 (33%) did not achieve target SUA levels. 10 (47%) patients had their SUA levels checked in the last year. 7(33%) had their SUA levels checked within the last 3 years and 4 (20%) had not had their SUA levels checked within the last 3 years.

No patient was prescribed more than 300mg allopurinol daily by their primary care physician despite the recommended dose being up to 900mg daily.

We found a 70% reduction in the number of referrals to secondary care for gout management over the same period of time.

Conclusion: The introduction of a local primary care gout guideline and associated education appears to have improved the number of patients achieving target serum uric acid levels as well as leading to a reduction in secondary care referrals for gout.

1Royal Lancaster Infirmary, Rheumatology, Lancaster, United Kingdom; 2Bay Medical Group, Morecambe, United Kingdom

Disclosure of Interests: None declared


Table 1. The pre-test and post-test mean scores for all participants of gout education programme.

<table>
<thead>
<tr>
<th>Question type</th>
<th>Areas of knowledge tested</th>
<th>Mean scores, n=30</th>
<th>Post-test</th>
<th>Pre-test</th>
<th>Difference</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Recall Gout diagnosis</td>
<td>3.47, 5.33</td>
<td>-0.77±1.02</td>
<td>0.72 ±0.83</td>
<td>4.50 ±1.07</td>
<td>0.01</td>
</tr>
<tr>
<td>2</td>
<td>Recall Interpretation of investigation</td>
<td>2.73, 2.3</td>
<td>0.43±0.73</td>
<td>-0.01 ±0.74</td>
<td>3.90 ±1.12</td>
<td>0.01</td>
</tr>
<tr>
<td>3</td>
<td>Recall Treatment of acute gout</td>
<td>1.97, 2.27</td>
<td>-3.01±1.01</td>
<td>0.14 ±0.85</td>
<td>1.22 ±1.05</td>
<td>0.01</td>
</tr>
<tr>
<td>4</td>
<td>Recall Treatment of stable gout</td>
<td>3.47, 3.07</td>
<td>0.40±1.52</td>
<td>0.16 ±0.74</td>
<td>1.22 ±1.05</td>
<td>0.01</td>
</tr>
<tr>
<td>5</td>
<td>Recall Indication of urate lowering therapy</td>
<td>4.87, 3.87</td>
<td>0.47±0.90</td>
<td>&lt;0.01 ±0.94</td>
<td>3.77 ±1.09</td>
<td>0.01</td>
</tr>
<tr>
<td>6</td>
<td>Recall Allopurinol mechanism</td>
<td>3.17, 2.77</td>
<td>0.40±1.19</td>
<td>0.08 ±0.94</td>
<td>1.77 ±1.10</td>
<td>0.01</td>
</tr>
<tr>
<td>7</td>
<td>Recall Allopurinol dose initiation</td>
<td>5.00, 3.53</td>
<td>1.47±1.14</td>
<td>&lt;0.01 ±0.46</td>
<td>1.53 ±1.14</td>
<td>0.01</td>
</tr>
<tr>
<td>8</td>
<td>Recall Allopurinol side effects</td>
<td>3.97, 4.1</td>
<td>0.87±0.9</td>
<td>&lt;0.01 ±0.10</td>
<td>1.14 ±1.04</td>
<td>0.01</td>
</tr>
<tr>
<td>9</td>
<td>Recall Non-pharmacological management</td>
<td>4.00, 3.6</td>
<td>0.41±1.25</td>
<td>0.09 ±0.94</td>
<td>3.6 ±1.10</td>
<td>0.01</td>
</tr>
<tr>
<td>10</td>
<td>Recall Medication which can aggravate anemia</td>
<td>4.07, 3.23</td>
<td>0.83±1.51</td>
<td>&lt;0.01 ±0.74</td>
<td>3.23 ±1.46</td>
<td>0.01</td>
</tr>
</tbody>
</table>
IS THERE LIFE TO GOUT TREATMENT AFTER RHEUMATOLOGY IS OUT OF THE EQUATION?

Paula García, Boris Anthony Blanco Cáceres, Fernando Perez-Ruiz. Hospital Universitario Cruces, Barakaldo, Spain

Background: Previous studies show a low persistence rate to urate-lowering therapy (ULT), in patients diagnosed with gout, after being discharged back to primary care from Rheumatology consultations.

Objectives: To assess persistence and adherence to ULT in patients with gout, previously evaluated in specialized care, who have been discharged from Rheumatology consultations to their primary care physician.

Methods: A transverse study of primary care patients with gout included in an inception cohort and followed in a tertiary care centre. Patients were selected according to their status of discharge or loss, in case they had been referred back to their primary care centre from specialized care, or “loss”, in case they had stopped coming to Rheumatology consultations.

Data, including active prescription of ULT, time since suspension of ULT (if applicable), last serum uric acid (sUA) levels and time for that determination, were procured by electronic history. General data of patients and follow-up were obtained from the database of such cohort. Patients lacking data or deceased were dismissed from the study.

Results: A total of 518 patients, classified either as “discharge” or “loss”, with available data accessed by electronic history, followed in specialized consultations during an average time of 52 months (36, 18-72) were studied. Average time since their last visit to Rheumatology services was 90 months (76, 36-132). 88% of them had, at least, one determination of sUA; 80% within the last 12 months, with no differences between the patients with or without active treatment. 376 patients (72.6%) out of 518 had an active prescription of ULT, 338 of them ordered by primary care and 38 by specialized care.

Patients lost during follow-up showed a lower rate of ULT prescription and a higher requirement of specialized attention after than those who were discharged from Rheumatology.

<table>
<thead>
<tr>
<th>Loss (172)</th>
<th>Discharge (346)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Follow-up (number of months)</td>
<td>31±34</td>
<td>64±49</td>
</tr>
<tr>
<td>Time since follow-up (number of months)</td>
<td>113±72</td>
<td>80±55</td>
</tr>
<tr>
<td>Prescription (%)</td>
<td>64</td>
<td>73</td>
</tr>
<tr>
<td>sUA w/o prescription (mg/dl)</td>
<td>7.44±2.02</td>
<td>7.07±1.33</td>
</tr>
<tr>
<td>sUA &lt;6 mg/dl w/o prescription (%)</td>
<td>29</td>
<td>27.5</td>
</tr>
<tr>
<td>sUA w/ prescription (mg/dl)</td>
<td>6.26±2.59</td>
<td>5.66±1.59</td>
</tr>
<tr>
<td>sUA &lt;6 mg/dl w/ prescription (%)</td>
<td>55</td>
<td>58</td>
</tr>
<tr>
<td>Adherence (% average TPM)</td>
<td>76±30</td>
<td>85±24</td>
</tr>
<tr>
<td>Adherence (% TPM &gt;80%)</td>
<td>64</td>
<td>79</td>
</tr>
<tr>
<td>Need of specialized care after (%)</td>
<td>11</td>
<td>6</td>
</tr>
</tbody>
</table>

Conclusion: Patients discharged from Rheumatology consultations maintain good persistence to long-term treatment with ULT, higher than those who were lost during consultation follow-up. Nevertheless, persistence and adherence in the latter group show a higher rate than the ones obtained in patients being followed by primary care, which does not exclude a beneficial influence of the previous assistance provided by Rheumatology services.

REFERENCES
REFERENCES


Disclosure of Interests: Paula García: None declared, Boris Anthony Blanco Cáceres: None declared, Fernando Perez-Ruiz Grant/research support from: Asociación reumatólogos de Cruces, Consultant for: Grünenthal Horizont Menarini, Speakers bureau: Grünenthal, Menarini, Fundación Española Reumatología

URATE VOLUME AND DISTRIBUTION BY DUAL ENERGY CT: CLINICAL AND RADIOLOGICAL CORRELATION IN GOUT PATIENTS

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Background: Dual-energy CT (DECT) has shown tremendous potential as a novel non-invasive method of urate detection in patients with gout.

Objectives: Our aim was to determine the concordance between urate volume and distribution measured on DECT with clinical presentation among patients with gout.

Methods: We conducted a retrospective descriptive study of patients with gout who were referred by a rheumatologist for gout DECT scans between January 2008 and February 2018. At our institution, routine DECT scans for gout consist of four sets of images with limbs scanned in pairs: the hands/wrists, elbows, knees and ankles/feet. We obtained volumetric measurements for all four anatomical regions, and assessed the concordance with clinical presentation as retrieved from patient electronic health record.

Results: A total of 182 patients were included in this study; 96 patients (52%) were male, age range: 27-90, mean age: 62) had urate deposits on DECT scans. Among urate-positive patients, the mean total volume of deposits was 2.45 cm³ (hands/wrists: 0.17 cm³, 7%; elbows: 0.62 cm³, 25%; knees: 0.70 cm³, 22%; ankles/feet: 0.96 cm³, 39%). The average number of urate-positive joints was 2.5, higher than that of clinically symptomatic joints (1.9). Discordance between DECT results and clinical symptoms were seen more often in elbows (46 urate-positive vs. 22 symptomatic) and knees (68 vs. 43), compared with hands/wrists (31 vs. 30) and ankles/feet (90 vs. 87). Only in 25 (26.0%) patients, the distribution of symptomatic joints fully matched the distribution of urate deposits. In 6 patients (6.3%), there was no overlap between these two distribution patterns.

Conclusion: On DECT scans, most urate deposits in gout patients occur in the ankles/feet, followed by knees, elbows, and hands/wrists. DECT scans can reveal urate deposit in asymptomatic joints, especially in elbows and knees. Assessing the concordance of urate distribution with clinical presentation in all limb joints in gout patients, our results can help understand the pathophysiology of urate deposition in gout, and guide the development of DECT protocols for the screening, assessment and follow-up management of gout patients.

REFERENCES

Disclosure of Interests: Bo Gong: None declared, Mark Warwas: None declared, Michael O’Keefe: None declared, Nicole Tsao: None declared, Mary De Vera: None declared, Kamaran Shojaania Shareholder of: Stock options in Augurex – biotech company., Grant/research support from: Doing a vasculitis study with BMS, Faisal Khosa: None declared, Savvas Nicolaou Grant/research support from: The Department of Radiology, Vancouver General Hospital has a Master Research Agreement with Siemens Healthcare, Forchheim, Germany (non-pharmaceutical company).
Table 1. Patient characteristics between early onset and common gout

<table>
<thead>
<tr>
<th>Variable</th>
<th>Early onset gout (N=39)</th>
<th>Common gout (N=174)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at inclusion (years), (mean ± SD)</td>
<td>40.2 (12.2)</td>
<td>62.2 (11.8)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>38 (97.4%)</td>
<td>145 (83.3%)</td>
<td>0.02</td>
</tr>
<tr>
<td>BMI (kg/m²), (mean ± SD)</td>
<td>29.6 (5.8)</td>
<td>28.9 (4.9)</td>
<td>0.49</td>
</tr>
<tr>
<td>Family history (n,%)</td>
<td>20 (60.6%)</td>
<td>30 (24.6%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Age at first flare (years), (mean ± SD)</td>
<td>24.8 (6.2)</td>
<td>55.4 (12.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Disease duration (years) (mean ± SD)</td>
<td>15.4 (12.6)</td>
<td>9.6 (17.6)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Tophi (n,%)</td>
<td>24 (61.5%)</td>
<td>58 (36.9%)</td>
<td>0.005</td>
</tr>
<tr>
<td>Urate amyloidosis (n,%)</td>
<td>21 (56.5%)</td>
<td>61 (49.6%)</td>
<td>0.11</td>
</tr>
<tr>
<td>Number of flares last 12 months (mean ± SD)</td>
<td>4.7 (2.9)</td>
<td>3.0 (2.82)</td>
<td>0.009</td>
</tr>
<tr>
<td>Baseline SUL (μmol/l) (mean ± SD)</td>
<td>495.9 (147.4)</td>
<td>521.1 (109.1)</td>
<td>0.23</td>
</tr>
<tr>
<td>CV diseases (n,%)</td>
<td>6</td>
<td>21 (13.2%)</td>
<td>0.02</td>
</tr>
<tr>
<td>HT (n,%)</td>
<td>9 (23.7%)</td>
<td>107 (84.9%)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Type 2 diabetes (n,%)</td>
<td>3 (7.9%)</td>
<td>41 (25.3%)</td>
<td>0.02</td>
</tr>
<tr>
<td>NAFLD (n,%)</td>
<td>11 (61.1%)</td>
<td>14 (24.1%)</td>
<td>0.003</td>
</tr>
<tr>
<td>Dyslipidemia (n,%)</td>
<td>13 (33.3%)</td>
<td>70 (45.5%)</td>
<td>0.17</td>
</tr>
<tr>
<td>Chronic kidney disease stage 3-5 (n,%)</td>
<td>8 (25.8%)</td>
<td>58 (40.6%)</td>
<td>0.12</td>
</tr>
<tr>
<td>Final SUL (μmol/l) (mean ± SD)</td>
<td>360.7 (135.5)</td>
<td>336.6 (109.9)</td>
<td>0.26</td>
</tr>
<tr>
<td>SUL at target (&lt;360 μmol/l) (n,%)</td>
<td>22 (62.8%)</td>
<td>110 (67.9%)</td>
<td>0.56</td>
</tr>
<tr>
<td>ULT final (n,%)</td>
<td>36 (92.3%)</td>
<td>148 (92.5)</td>
<td>0.97</td>
</tr>
</tbody>
</table>

Conclusion: In conclusion, EOG is more severe and EOG pts have less CMs. Moreover, EOG has a higher inheritability trait than CG patients suggesting different pathological mechanisms.


Disclosure of Interests: Hilde Berner Hammer Grant/research support from: AbbVie, Pfizer and Roche, Paid instructor for: AbbVie, Pfizer, UCB, Novartis, Roche, Speakers bureau: AbbVie, Pfizer, UCB, Novartis, Roche, Lars Fridtjof Karoliussen: None declared, Lene Terslev Speakers bureau: tophi or ulceration(s) over tophi were patients with gout and determine risk factors associated with ulceration. To describe clinical characteristics of ulceration over tophi in patients with gout and improve the management for such challenge problem. Will allow us to better understand the fact of ulceration over tophi and why this is becoming increasingly common in gout patients in our department between 2014 and 2018, and who had at least one visit between 9 and 15 months after first visit. At baseline, ineffective ULT was defined by a serum urate level (SUL) above target (> 360 μmol/L). Demographic characteristics, gout history and CMs, treatments were systematically recorded. Results: Among 213 pts, 39 (18.3%) had experienced a first gout flare before 30 years old. Pts and gout characteristics are summarized in table 1. Mean age of first flare in EOG was 24.8 (± 5.5) years. Familial history of gout was more frequent in EOG than in CG (60.6 vs 24.6%). First flare involved the 1st metatarsophalangeal joint in 70% of EOG pts. EOG pts had more severe gout than CG pts: CV diseases, hypertension, T2D, dyslipidemia and kidney transplantation. Non-alcoholic fatty liver disease was more frequent in EOG than CG (61.1 vs 24.1%). At final visit, 62.8 and 67.9% of EOG and CG patients, respectively, achieved SUL target (p=0.56). Proportion of pts taken ULT was similar in both groups as well as proportion of pts treated with allopurinol or FBX. Comparison of clinical characteristics and risk factors associated with ulceration were analyzed between groups.

Conclusion: In conclusion, EOG is more severe and EOG pts have less CMs. Moreover, EOG has a higher inheritability trait than CG patients suggesting different pathological mechanisms.

Results: A total of 105 patients were enrolled. 33 patients with ulcerations were older, with prolonged duration with gout and tophi, a higher rate of obesity, greater number of tophi, lower level of GFR, and higher level of serum creatinine, ESR and CRP. The mean duration of ulceration was 1.63 ± 2.32 months. The ulcerations mainly located in ankle (34.21%) and MTP (39.47%), with a mean size of 32.37 × 22.76 mm. The majority of ulcerations were categorized as stage I (42.4%) and stage II (51.5%). In univariate regression analysis, age, glucocorticoid abuse, tophi duration, tophi number and GFR were associated with ulceration. In the multivariable model, significant differences were demonstrated in glucocorticoid abuse, tophi duration, tophi number.

Conclusion: Gout patients with ulceration(s) over tophi present several different aspects of clinical characteristics compared with those without ulceration. Glucocorticoid abuse, prolonged duration with tophi and greater number of tophi are risk factors for ulceration over tophi. Avoiding indiscriminate use of glucocorticoid needs to be emphasized, and prevention of tophi formation via initiate effective urate-lowering therapy is highly recommended in patients with gout.

REFERENCES

Disclosure of Interests: None declared

SAI0426  TOPHI, THE PREDICTIVE FACTOR OF ARTERIAL STIFFNESS IN PATIENTS WITH GOUT AND HYPERURICEMIA

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Background: Gout is the most common form of inflammatory arthritis and its prevalence is increasing in recent decades. Many studies have reported that gout and hyperuricemia are associated with an increase in all-cause mortality and cardiovascular mortality. Increased arterial stiffness is an independent marker of cardiovascular diseases and risk predictors. Many studies have shown a significant correlation between uric acid levels and arterial stiffness. Augmentation Index (AI) is an indirect measure of arterial stiffness. Tophi is formed when gout is left untreated for a long time.

Objectives: The aim of this study is to determine whether the presence of tophi could predict an increase in arterial stiffness.

Methods: Between June 2017 and June 2018, augmentation index was measured using Sphygmocor for patients who visited Jeju National University Hospital in South Korea with gout or hyperuricemia. Medical records, laboratory and AI data were retrospectively analyzed.

Results: One hundred twenty two patients participated in the study and AI was measured. Most (96.7%) of the patients were male. At the time of the examination, 99 patients (81.1%) were treated with uric acid lowering agent and the mean duration of the disease was 6.9 years. When the patients were divided into two groups according to the presence or absence of Tophi, the average age (60.2±11.6 vs. 53.4±15.2, p=0.023) of the patients with Tophi was significantly higher, duration of disease (13.0±6.5 vs 5.4±5.4, p=0.000) was longer and the AI (28.7±10.4 vs 20.7±10.4, p=0.001) was higher. When multiple linear regression analysis was performed to exclude the effects of other variables (DM, HTN, hyperlipidemia, age, BMI, total cholesterol, creatinine), tophi was a predictor of high AI (β = 5.478; 95% CI, 0.343-10.613; p=0.037). Multiple logistic regression analysis was performed to determine the predictors of tophi. The duration of disease and AI @ 75 values were significantly predictive of the presence of tophi (Odds ratio 1.113; 95% CI, 1.024-1.209; p=0.012)

Conclusion: This study suggests that the presence of tophi is an independent predictor of increased arterial stiffness in patients with gout and hyperuricemia.

REFERENCES
RISK OF MALIGNANCIES IN PATIENTS WITH GOUT: A COMORBIDITIES IN AN EARLY DIAGNOSED COHORT

Analysis of the prevalence and timing of malignancy in the early diagnosed cohort

Methods: We conducted a retrospective cohort study using Korean National Health Insurance Service-Medical check-up Cohort Database, which composed of qualified individuals as of 2002 in the age of 40-79 in 2002-2003 who received general medical check-up (Approximately 510,000). We included patients newly diagnosed with gout, based on the diagnostic code and relevant medication history, who were between 40 and 65 years of age at the time of diagnosis between 2003 and 2007 (we washed out first year for newly detected cases). The gout patients (case group) were matched by 1:2 propensity score matching using confounding variables (age, sex, income group, region of residence, smoking status, alcohol intake, exercise habit, comorbidities including diabetes mellitus, hypertension and dyslipidemia, body mass index, blood pressure, serum glucose level, total cholesterol, and hemoglobin) and survival analysis was performed to estimate the risk of malignancy.

Results: A total of 4991 cases and 419992 controls were identified. The prevalence of Gout was 4991 (1.17%, male 4093 (82.01%); female 898 (17.99%)). During a mean follow-up of 12 years, malignancy was newly diagnosed in 30262 patients (7.12% of the total cohort). Gout was associated with increased risk of malignancy in the multivariable Cox proportional hazard regression analysis before propensity score matching (hazard ratio (HR) 1.248, 95% confidence interval (CI) 1.130-1.379, p<0.001), as well as after matching (HR 1.369, 95% CI 1.209-1.549, p<0.001). Conclusion: A total of 4991 cases and 419992 controls were identified. The prevalence of Gout was 4991 (1.17%, male 4093 (80.01%); female 898 (17.99%)). During a mean follow-up of 12 years, malignancy was newly diagnosed in 30262 patients (7.12% of the total cohort). Gout was associated with increased risk of malignancy in the multivariable Cox proportional hazard regression analysis before propensity score matching (hazard ratio (HR) 1.248, 95% confidence interval (CI) 1.130-1.379, p<0.001), as well as after matching (HR 1.369, 95% CI 1.209-1.549, p<0.001).

Disclosure of Interests: None declared


ANALYSIS OF THE PREVALENCE AND TIMING OF GOUT CO-MORBIDITY IN PATIENTS UNDERGOING KIDNEY TRANSPLANT

Background: Patients receiving kidney transplants are at increased risk for the development of hyperuricemia and gout compared to the general population, which is generally attributed to the frequent use of calcineurin inhibitors (cyclosporine and tacrolimus). However, the precise proportion of renal transplant patients that develop gout and the time period post-transplant in which this occurs is less established.

Objectives: To analyze a large, multi-insurance, US population database to determine gout prevalence and timing in the renal transplant population.

Methods: A retrospective review of Humana Healthcare claims data (private and Medicare) from 2007 to 2017 was undertaken to identify kidney transplant patients with at least 6 months in plan prior to transplant and at least 6 months in plan post-transplant. Diagnosis of gout (ICD 10/ICD 9 code) was evaluated in relationship to the time of kidney transplant.

Results: The database contained 6,082 patients with a kidney transplant and at least 6 months in plan both pre and post-transplant. Of the 6,082 kidney transplant patients, 1,505 (25%) had a gout diagnosis: 908 (15% of transplant patients) with gout before and after transplant and 597 (10% of transplant patients) with a gout code only after transplant. In patients developing gout post-transplant, the mean time between transplant and gout diagnosis was 1.79 ± 1.85 years.

Conclusion: As expected, gout was a common comorbidity in renal transplant patients. 15% of the patients receiving renal transplants had gout prior to the transplant, and another 10% developed new-onset gout a mean of 1.79 years after receiving a renal transplant. This retrospective analysis demonstrates that kidney transplant patients commonly suffer from gout both before and after their transplant. In addition to more research on this topic, an increased focus on screening and treatment of gout in the renal transplant population may be warranted.


COMORBIDITIES IN AN EARLY DIAGNOSED COHORT OF UNCONTROLLED VERSUS CONTROLLED GOUT: ANALYSIS OF A LARGE US PAYER DATABASE

Background: Gout is a prevalent progressive systemic inflammatory arthritis. The pathogenic cause of gout is elevated serum uric acid or hyperuricemia, and appropriate treatment of gout involves reduction of uric acid levels to a minimum goal of less than 6 mg/dL. Patients who do not achieve uric acid goals are generally described as uncontrolled gout patients and tend to do worse in terms of clinical outcomes such as occurrence of flares and persistence/worsening of tophi. Gout patients often suffer from specific comorbidities, though whether uncontrolled gout patients have a different comorbidity profile is unclear.

Objectives: The objectives of this evaluation were to compare the comorbidities and hospitalizations in uncontrolled versus controlled gout patients from a large de-identified US payer database.

Methods: A retrospective review of Humana Healthcare data from 2007 to 2016 in private pay and Medicare patients was performed to identify...
patients with at least 1 gout ICD 10/ICD 9 diagnosis code (N=539,802) and 90 days of continuous urate-lowering therapy within 1 year of diagnosis. Two cohorts of patients were categorized according to their sUA levels (≥ 1 test) after at least 90 days of gout therapy: sUA<6.0 mg/dL (controlled) and sUA ≥ 8 mg/dL (uncontrolled).

Results: The controlled gout group (sUA<6 mg/dL) included 5,473 patients and the uncontrolled gout group (sUA≥8 mg/dL) had 1,358 patients. The two groups were comparable in terms of demographic features. Chronic kidney disease (CKD) was a common comorbidity overall in this gout population with higher prevalence in the uncontrolled gout cohort (49.4% of uncontrolled vs. 32.4% of controlled population; OR 2.04; 95% CI of 1.808 to 2.301, p<0.001). The most frequent hospitalization codes were similar between the uncontrolled and controlled patients with the exception of congestive heart and acute kidney failure. 20% of uncontrolled patients were hospitalized for congestive heart failure vs. 7% in controlled (OR 3.16, 95% CI: 2.674 to 3.739, p<0.001), and 20% of uncontrolled patients were hospitalized for acute kidney failure vs. 8% in controlled (OR 2.95, 95% CI: 2.497 to 3.480, p<0.001).

Conclusion: Gout patients frequently suffer from cardiovascular and renal diseases. This large retrospective analysis suggests that when divided based on uric acid levels attained, uncontrolled gout patients are more likely to suffer from CKD and also more likely to be hospitalized for acute renal failure than controlled gout patients. Whether hyperuricemia in uncontrolled gout causes the development of specific cardiovascular and renal comorbidities, or if specific cardiovascular and renal diseases lead to hyperuricemia and uncontrolled gout is not fully established.

REFERENCES


SAT0430 IMPACT OF GOUT ON ALL-CAUSE MORTALITY AMONG MEDICARE BENEFICIARIES WITH A HISTORY OF KIDNEY TRANSPLANTATION: A RETROSPECTIVE COHORT STUDY

Li Justin1, Marissa Suh1, Mark Brigham1, Jeff Kent2, Brian LaMereaux2, Richard J. Johnson3, Brian Mandell1, Nandini Hadker1, Herman Sanchez1, Kevin Francis1, Gavin Miyasato1. 1 Trinity Partners, New York, United States of America; 2 Horizon Pharma USA, Inc., Lake Forest, United States of America; 3 University of Colorado, Denver, United States of America; 4 Cleveland Clinic, Cleveland, United States of America

Background: Gout is a frequent comorbidity among kidney transplant recipients. A recent analysis estimated that 13% of kidney transplant recipients had an active diagnosis of gout. The clinical impact of comorbid gout in this population is not well understood, including if gout as a comorbidity associates with higher mortality rates among kidney transplant recipients.

Objectives: This retrospective patient claims analysis was performed to determine whether an association between gout and mortality exists in the prevalent kidney transplant population.

Methods: A retrospective study using administrative claims from the Medicare fee-for-service (FFS) Limited Data Set (LDS) was conducted. Multi-variable Cox proportional hazards regression assessed the relationship between gout and all-cause mortality. Given the ambiguity of the causal relationship between gout and comorbidities that make up the Charlson Comorbidity Index (CCI), three analyses were conducted assuming: 1) gout and certain comorbib conditions are associated by way of a common pathogenetic root, 2) gout is a precursor for developing these comorbid conditions, and 3) these conditions modify the effect of gout on mortality.

Results: Gout was associated with higher adjusted risk of all-cause mortality (hazard ratio, HR: 1.44, 95% CI: 1.27-1.63). After adjusting for baseline demographics and time from transplantation, the HR risk with gout was attenuated but still statistically significant (HR: 1.16, 95% CI: 1.02-1.32). Further adjustment for baseline CCI found gout was not a significant risk factor (HR: 1.03, 95% CI: 0.90-1.17). Stratified models show gout among baseline CCI=0 score was associated with a 3.5-fold increased risk of all-cause mortality (HR: 3.48, 95% CI: 1.27-9.57).

Conclusion: The presence of gout was not an independent predictor of all-cause mortality among Medicare beneficiaries with a history of kidney transplantation. That gout in a subset of beneficiaries without baseline comorbidities was a predictor may suggest that gout serves as an early indicator of declining health in the larger prevalent kidney transplant population. Further research is needed to understand the relationship of gout and mortality in the kidney transplant population.

REFERENCES


SAT0431 RED GINSENG EXTRACTS SUPPRESS MONOSODIUM URATE CRYSTAL INDUCED NLRP3 ACTIVATION

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Background: It is well known that red ginseng extracts (RGE) has anti-inflammatory properties.

Objectives: We aimed to investigate if RGE could suppress monosodium urate crystal (MSU) - induced NLRP3 activation and thus could be a potential therapeutic for gout.

Methods: Acute air-pouch model was used to investigate in vivo effect on acute gouty inflammation of RGE in mice. Human monocyte cell line –THP-1 was stimulated with MSU in the presence of RGE and expression of NLRP3, ASC, caspase-1, IL-1β was measured by PCR, immuno-blotted and ELISA. Twenty four gout patients in intercritical period were randomized either to red ginseng tablet or placebo receiving group in a double-blind manner. After 3 months of taking red ginseng tablets (RGT)/ placebo, expression of NLRP3 and inflammatory cytokines of peripheral blood mononuclear cell was addressed by PCR.

Results: RGE sufficiently inhibited acute gouty inflammation in air-pouch mouse model, represented by reduced number of white blood cells in air pouch lavage fluid. In vitro, RGE dose-dependently suppressed MSU-induced IL-1β production of THP-1 cells. RGE did not affect NLRP3 or pro IL-1β expression. However, ASC oligomerization was inhibited and suppressed NLRP3 inflammasome assembly. Patients taking RGT for 3 months showed significantly reduced NLRP3 expression compared to baseline, which was not observed in the control group.
Conclusion: RGE successfully suppressed MSU-induced acute inflammation in mouse model. Also, RGT reduced NLRP3 expression in intercritical gout patients. These results suggest that red ginseng can be implicated as a therapeutic agent for gout.

REFERENCES

Disclosure of Interests: None declared

SAT0432 GOUTY ARTHRITIS AND DRUG-INDUCED LIVER INJURY AFTER THE TREATMENT WITH NSAIDS
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Background: In order to relieve the pain during acute gout attacks, most patients take high doses of nonsteroidal anti-inflammatory drugs (NSAIDs), which can provoke the hepatotoxicity, or DILI (drug-induced liver injury).

Objectives: To define the timing of DILI formation after the treatment with NSAIDs and its severity in patients with gouty arthritis (GA).

Methods: 738 patients with GA from our database who meet the criteria of the ACR (1977) were included into the study. NSAIDs-induced liver damage is known to be mainly hepatocellular. The dynamic ALT concentration in blood before the start of NSAIDs and during the treatment has been assessed. Hepatocellular toxicity was determined according to the DILI classification criteria based on the blood ALT level increased > 2 times to the upper limit of norm (42 U/l for men and 35 U/l for women). Inclusion criteria for the study group (n = 88): normal ALT before the treatment with NSAIDs, its increase during the treatment and return to the norm after the treatment. Exclusion criteria: chronic hepatitis of any etiology, the comparison group (n = 650) consisted of patients with normal blood ALT level throughout the treatment.

Results: Among 738 patients with GA, 11.9% (n = 88) developed the hepatotoxicity following the NSAIDs therapy. No significant differences in age (54 (59.5) and 57 (52-63) years; p> 0.05) and gender (men 93.3% and 87.6%; p > 0.5) between the study and comparison groups were found. In the study group, the duration of NSAIDs administration was 10 (6-14) days, which did not differ from that in the comparison group — 9.5 (7-12) days (p>0.05).

In patients with DILI, the elevated ALT was observed as follows: 2-3 times in 74 patients (84.1%); 3 to 5 times in 10 (11.4%); more than 5 times in 4 patients (4.5%). So, minimal cytolysis was presented more frequently than more severe forms (p < 0.05).

In the subgroup with the ALT concentration > 5 times (n = 10), 6 patients received Diclofenac in high doses, 2 patients were treated with Nimesulide, 1 patient with Etodolac and 1 with Dexamgion during the observation period. The elevation of ALT concentration 5 times was observed in 3 patients taking Diclofenac i/m and Nimesulide per os, simultaneously, and in 1 patient taking Diclofenac in high doses.

Patients with DILI were taking the following medications: Diclofenac 48.9% (n = 43); Nimesulide 18.2% (n = 16); Meloxicam 5.7% (n = 5), the combination of NSAIDs 20.5% (n = 18) without statistical differences (p > 0.05).

The number of patients who abused alcohol in DILI and control groups did not differ significantly — 53.4% and 48.2%, respectively (p>0.05).

Conclusion: In patients with GA, the hepatocellular DILI was observed in 11.9% cases after the treatment with NSAIDs during 10 days (from 6 to 14 days). Among patients with DILI, 84.1% (n = 74) had NSAIDs-induced hepatitis with minimal cytolysis. Mild cytolysis was seen in 10 (11.4%), moderate in 4 patients (4.5%). In our study, no severe or fatal DILI has been noted. No significant differences for particular drugs in the hepatotoxicity incidence have been found (p > 0.05).

Disclosure of Interests: None declared

SAT0433 AN ANALYSIS OF PRESCRIPTION RECORDS OF GOUT PATIENTS IN EUROPE: EVIDENCE OF SUBOPTIMAL MANAGEMENT AND CLINICAL INERTIA
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Background: Urate-lowering therapy (ULT) should be prescribed to people with recurrent gout flares and tophi, and offered to people with first-onset gout. Despite effective drugs, gout flares are common. Reasons for this include lack of prescription of ULT, under-dosing of ULT by physicians (clinical inertia), and poor adherence to ULT.

Objectives: To ascertain the quality of gout care delivered by general practitioners (GPs), prescribing patterns for ULT were analysed in 4 western European countries.

Methods: Data for this retrospective study were obtained from IQVIA’s Real-World Data Longitudinal Prescription databases of GPs from France, Italy, Spain and United Kingdom (UK). The databases contain anonymised patient prescription records, including demographics, dispensing details (pharmacy, prescription date), and medication (name, dose, therapy duration). Data for patients with gout with or w/o ULT were analysed from July 2015 to June 2016.

Results: Crude prevalence of gout was 0.7% (UK) to 1.1% (France, Italy, and Spain) (Table 1). Only about half (France, Italy, UK) to 1/3 (Spain) of diagnosed patients were on ULT. Between 19.9% (France) and 56.4% (Spain) of patients on ULT had serum urate (sUA) measurements recorded within the year. Only 26.6% (Italy) to 45.6% (France) of patients with a recorded sUA level at target (<6.0 mg/dL). The most common 1st-line treatment was allopurinol (ALLO), almost always at a dose ≥300 mg/d. Febuxostat (FBX) was prescribed as a 1st-line alternative in France and Italy. Switch to 2nd-line ULT, such as FBX, was uncommon, especially in Spain and UK. Uricosurics in monotherapy were not used. Average time on ULT ranged from 57.3% (Italy) to 72.6% (France) of the assessment year. At least one comorbidity (CM) was present in >78% of patients, the most common being hypertension, dyslipidemia, diabetes, chronic kidney disease, and obesity.

Conclusion: In the study period, management of patients with gout in 4 EU countries was suboptimal. Nearly half of diagnosed patients were not prescribed ULT. sUA levels were not being monitored regularly and mean sUA levels were above target. ALLO as the most common 1st-line ULT was generally prescribed at sub-therapeutic doses. Initiation of 2nd-line therapy was infrequent indicating a status quo and/or other reasons and medication adherence was poor indicating low patient self-management.


SAT0434 A TRANSIENT DECREASE IN SERUM URATE CHANGES THE CLINICAL TRAJECTORY OF SUBJECTS WITH ADVANCED GOUT

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Background: The standard approach to monitor subjects with gout is to measure serum urate. The assumption is that the signs and symptoms of disease will improve if serum urate is maintained below the target level of 6 mg/dL. However, there has been little emphasis on whether lowering urate transiently would have a prolonged impact on the clinical manifestations of advanced gout.

Objectives: Assess the clinical benefit in patients with advanced gout who had transient lowering of serum urate resulting from treatment with pegloticase, a pegylated recombinant uricase.

Methods: A post hoc analysis was carried out using the results from two randomized controlled trials (RCTs) of 6 months duration to assess the efficacy of treatment with 8 mg of pegloticase every 2 weeks (q2w). Serum urate was measured before each infusion and the serum urate area under the curve (AUC) was calculated as described2 for the first and second three-month periods of time in the RCTs. The following clinical outcomes were assessed: gout flares, tophus reduction, patient global assessment (PGA), tender and swollen joints (TJC and SJC), pain measured with a 100-mm visual analog scale (VAS) and a variety of patient-reported outcomes (36-item Short Form Health Survey [SF-36] Physical Component Score [PCS] and Arthritis-Specific Health Index Score [ASHIS]).

Results: The analysis included 85 subjects treated with q2w pegloticase and 43 patients who received placebo. Of the 85 pegloticase-treated subjects, 49 had only a transient decrease in serum urate owing to the development of anti-pegloticase antibodies. The mean length of time these subjects experienced a serum urate <6 mg/dL was approximately 6 weeks.3 Despite the transient reduction in serum urate, the serum urate AUC for the first and second 3 months of the RCTs was significantly (p=0.008) decreased compared to placebo-treated subjects. However, it was significantly (p<0.0001) less reduced compared with those with persistent urate lowering throughout the 6 month RCTs (Table 1). Results for both the subjects with persistent and transient lowering of serum urate to <6 mg/dL indicated significant reduction in tophi and improvements from baseline in PGA, TJC, SJC, pain, and ASHIS after 6 months of the RCT. No significant improvements were observed in the patients who received placebo.

Conclusion: A transient reduction in serum urate resulting from pegloticase therapy can result in significant clinical benefit lasting through the 6 months of the RCTs. These results suggest that transient lowering of urate can alter the trajectory of the clinical manifestations of advanced gout. Moreover, estimates of serum urate AUC may be more helpful in assessing the impact of urate lowering therapy than individual measurements of serum urate.

REFERENCES


SAT0435 MANAGEMENT OF ADVANCED GOUT: A CLAIMS-BASED ANALYSIS FROM THE UNITED STATES

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1University of Florida, Gainesville, United States of America; 2Rutgers Robert Wood Johnson Medical School, New Brunswick, United States of America; 3AMPEL BioSolutions, LLC, Charlottesville, United States of America

Background: Gout is one of the most common inflammatory arthropathies. Despite available urate lowering therapies (ULT), many patients progress to chronic or advanced gout, characterized by the development of tophi, chronic inflammatory arthritis, and other manifestations resulting from persistent urate depositions. While numerous guidelines exist for the management of gout, there is little information on the frequency of their implementation, especially in patients with advanced gout.

Objectives: To evaluate the real-world practice patterns in patients diagnosed with advanced gout using a large administrative claims database from the United States.

Disclosure of Interests: Peter Lipsky Consultant for: Consult-
Methods: We carried out a retrospective analysis of the Symphony Integrated Dataverse to identify patients with advanced gout over an approximately 6-year period from October 2012 to August 2018. Patients were identified as having advanced gout if they were >18 years of age and had at least two medical claims for the diagnosis of gout on different days, separated by at least 3 months. Patients with advanced gout were identified and stratified based on their diagnosis as either chronic gout (ICD-9: 274.02, 274.03, ICD-10: M1A.x.x) or tophaceous gout (ICD-9: 274.03, 274.81, 274.82, ICD-10: M1A.xxx.x). A third category designated "uncontrolled gout" was clinically defined as any patient with at least three primary diagnoses of idiopathic gout (ICD-10: M10.0.x, M1A.0x) along with at least three urate tests (CPT 84550, 84560). Percent and frequency of urate testing, rheumatology specialist visits, and administration of ULT (allopurinol, febuxostat, probenecid, and lesinurad) were evaluated for each diagnostic group.

Results: We identified 191,097 advanced gout patients, including 177,610 (93%) with chronic gout, 31,475 (16.5%) with tophaceous gout, and 20,943 (11%) with uncontrolled gout. 35,992(18.8%) were coded in more than 1 diagnostic category. The median age was 67 (range: 19-80), 24.7% were female and 75.3% male, with an average of 5.4 years of claims history in the database. As shown in Tables 1 and 2, despite the diagnosis of advanced gout, urate testing, rheumatology, and ULT were inconsistent. Urate testing was definitional for uncontrolled advanced gout patients, but was done in less than 65% of patients with the diagnosis of chronic or tophaceous gout and then less than once per year. Similarly, less than 60% of subjects with advanced gout received care by a rheumatologist and less than 80% received ULT and for less than 50% of the year.

Table 1. Percentage of patients with urate testing, rheumatologist visits, and urate lowering therapy

<table>
<thead>
<tr>
<th>Population</th>
<th>N</th>
<th>Urate testing (% of patients)</th>
<th>Rheumatologist visit (% of patients)</th>
<th>ULT* (% of patients)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic Gout</td>
<td>177,610</td>
<td>61.72%</td>
<td>34.32%</td>
<td>76.54%</td>
</tr>
<tr>
<td>Tophaceous Gout</td>
<td>31,475</td>
<td>63.74%</td>
<td>57.86%</td>
<td>76.98%</td>
</tr>
<tr>
<td>Uncontrolled Gout</td>
<td>20,943</td>
<td>100.00%*</td>
<td>59.57%</td>
<td>81.32%</td>
</tr>
</tbody>
</table>

*Urate lowering therapies

Table 2. Frequency of urate testing, rheumatologist visits, and urate lowering therapy in advanced gout

<table>
<thead>
<tr>
<th>Population</th>
<th>N</th>
<th>Mean urate test/year</th>
<th>Mean rheumatologist visits/year</th>
<th>Mean ULT* prescriptions per patient</th>
<th>Mean days with active ULT* prescriptions/year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic Gout</td>
<td>177,610</td>
<td>0.73</td>
<td>2.00</td>
<td>7.5</td>
<td>160.27</td>
</tr>
<tr>
<td>Tophaceous Gout</td>
<td>31,475</td>
<td>0.98</td>
<td>3.72</td>
<td>9</td>
<td>160.14</td>
</tr>
<tr>
<td>Uncontrolled Gout</td>
<td>20,943</td>
<td>2.25*</td>
<td>4.18</td>
<td>7.1</td>
<td>169.36</td>
</tr>
</tbody>
</table>

*Urate lowering therapies

Conclusion: The subset of patients with advanced gout, identified either as chronic, tophaceous or uncontrolled, received suboptimal care compared to current guidelines. As this group of advanced gout patients is the most affected by urate deposition, added attention should be paid to optimizing their care.


CROWNED-dens syndrome: a recent case series in a single centre in the United Kingdom


Background: The crowned dens syndrome is a rare presentation of calcium pyrophosphate deposition disease. It is characterised by severe acute or recurrent neck pain associated with headache, fever and elevated inflammatory markers. CT usually demonstrates calcium pyrophosphate crystal deposition in the suspensory ligaments adjacent to the atlanto-axial joint. We are reporting a series of four patients presenting with sudden onset of neck pain and increased inflammatory markers over a 9 month period.

Objectives: To raise awareness of crowned-dens syndrome, its clinical presentation, radiographic findings and management.

Methods: Four patients’ electronic patient records including history, clinical findings and treatment were reviewed. Imaging was discussed at a rheumatology/radiology multi-disciplinary meeting.

Results: Four patients (2 female, 2 male) aged between 64 and 86 years presented with severe neck pain and stiffness. In all cases the onset of symptoms was less than a week prior to presentation and was associated with a restricted neck movement. 2 patients had associated headache, arthralgia and myalgia. All patients had normal tone, power, reflexes and sensation on neurological examination. There was no pyrexia. Inflammatory markers were markedly raised with CRP ranging from 90-343 mg/L at presentation (Table 1). One patient had a neutrophilia. CT scan of the head was performed in each case and showed no evidence of subarachnoid haemorrhage, space occupying lesion or meningeal enhancement. PET-CT scan in all patients showed intense uptake around the atlanto-axial joint as well as calcification of the ligaments. All patients were commenced on a reducing regime of prednisolone starting at 40mg daily, tapering to 0mg over 6 weeks. Symptoms and inflammatory markers reduced on induction of steroids. Two patients suffered a relapse on reducing steroids and required further higher doses of steroid.

Table 1. Patient demographics

<table>
<thead>
<tr>
<th>Patient Age</th>
<th>Gender</th>
<th>CRP on presentation (mg/L)</th>
<th>ESR on presentation (mm/hr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>64</td>
<td>Male</td>
<td>90</td>
<td>77</td>
</tr>
<tr>
<td>74</td>
<td>Male</td>
<td>247</td>
<td>-</td>
</tr>
<tr>
<td>81</td>
<td>Female</td>
<td>133</td>
<td>120</td>
</tr>
<tr>
<td>86</td>
<td>Female</td>
<td>343</td>
<td>112</td>
</tr>
</tbody>
</table>

Figure 1. Image from PET-CT scan of Patient 4 showing increased tracer uptake around the odontoid peg (arrow)

Conclusion: Patients presenting with acute neck pain, headache and raised inflammatory markers require evaluation for an infective aetiology. Pyrophosphate disease of the atlanto-axial joint however, appears to be an increasingly recognised cause of this presentation. Awareness by acute physicians, rheumatologists and radiology colleagues is important, as the condition can be misdiagnosed as Giant Cell Arteritis, Polymyalgia Rheumatica or meningitis; in order to avoid unnecessary investigations and delay in initiating the appropriate treatment. The condition is steroid responsive.

REFERENCES

SAT0437 ABSTRACT WITHDRAWN

SAT0438 TO SCREEN OR “WAIT AND SEE” – CAN HLA GENE TESTING PREVENT ALLOPURINOL RELATED SEVERE CUTANEOUS ADVERSE REACTION? AND WHO ARE AT RISK?

Pui Shan Julia Chan, Sin Nga Ng, Moon Ho Leung. Hong Kong, Department of Medicine, Queen Elizabeth Hospital, Hong Kong, Hong Kong (SAR)

Background: Allopurinol is one of the most common causes of drug-induced severe cutaneous adverse reaction (SCAR). HLA-B*58:01 gene positivity is shown to be the strongest risk factor. However, local data on HLA-B*58:01 test and allopurinol-related SCAR is scanty. Moreover, there is no consensus on routine checking of HLA-B*58:01 before starting allopurinol in Hong Kong and this test is performed according to physicians’ clinical judgement.

Objectives: This study review the use of HLA-B*58:01 in daily practice, included the clinical characteristics and its implications in patients who developed allopurinol allergy in a tertiary internal medicine and rheumatology referral center.

Methods: This is a retrospective study of patients who had HLA-B*58:01 checked in Queen Elizabeth Hospital from January 2008 to December 2017. Patients’ demographic data, clinical characteristics, laboratory findings, gene profile, drug allergy records were retrieved from Clinical Data Analysis and Reporting System and outcomes were reviewed.

Results: Within 10 years, 432 patients had HLA-B*58:01 checked - 23% (N=99) were positive (Figure 1). Among patients who were HLA-B*58:01 positive, 86% had clinical and/or crystal proven gout and 68% were male (M:F=67:32). Gene testing was performed as screening in 56% (57/99) and after skin reaction in 42% (42/99). Alternative urate lowering therapy was considered for patients who screened positive for HLA-B*58:01 and none developed SCAR (Febuxostat 16 patients, probenecid 3 patients). For those who reported skin reaction after allopurinol, 50% had minor rash while 50% (each 21 patients) developed SCAR. In SCAR-group, 52% was male, 76% were chronic kidney disease (CKD) stage 3 or older, 60 years, with mean age 71.2±14.2 and mean estimated glomerular filtration rate 57.1±30.7 mL/min/1.73m² (Figure 2 and table 1). The mean time interval to SCAR was 44.8±52.1 days and the mean starting dose of allopurinol was 154.6±90.7 mg/day. SCAR was associated with substantial morbidity and mortality: 71% (15/21) required steroid and/or intravenous gammaglobulin in addition to supportive care and 17% (4/21) died in the same admission due to sepsis including pneumonia. For patients who were tested negative for HLA-B*58:01, although 12% reported skin reaction, these were self-limiting and all recovered after allopurinol was stopped. Renal impairment was less pronounced in this group, yet 38% were CKD stage 3.

Conclusion: In our cohort, HLA-B*58:01 can identify most of the high risk patients who prompt to develop SCAR. Thus in routine practice, clinicians should consider screening HLA-B*58:01, especially in patients with CKD stage 3 or age ≥60 year, before starting allopurinol, and consider alternatives if positive, to prevent allopurinol-related SCAR.

REFERENCES

Objectives: To assess the effect of XO1 therapy in gouty patients with moderate CKD, in terms of eGFR changes.

Methods: In this multicenter, retrospective study, we included patients from 4 centers diagnosed with gout (EULAR/ACR criteria) and stage-3 CKD according to Cockroft-Gault formula (eGFR 30-59 ml/min/m²) who from 4 centers diagnosed with gout (EULAR/ACR criteria) and stage-3 CKD according to Cockroft-Gault formula (eGFR 30-59 ml/min/m²) who have been in treatment with XOI for at least 6 months. Within the adjusted model we obtained significant differences in eGFR between baseline and 6 months (p=0.0081), and between baseline and 12 months (p=0.0028). eGFR decreased significantly between baseline and 6 months (p=0.0161) and 12 months (p=0.0188).

Conclusion: Reduction of sUA levels in gouty patients with XO1 therapy is significant different between eGFRs in stage-3 CKD. These findings suggest that the response to urate lowering therapy take place in the first 6 months, leading to an improvement in eGFR in this period. From 6 months to 1 year, sUA levels are stabilized and so is eGFR. Conclusion: There is an expected increased electron density (μe) in monosodium urate (MSU) crystal deposition in gout patients with MSU deposition, even though DECT measures do not reach statistical significance. Partial attention will be given to patients with high MU burden (large DC signs on US).

CALCIUM PYROPHOSPHATE CRYSTAL ARTHRITIS DURING HOSPITALIZATIONS: A PROSPECTIVE, CRYSTAL-PROVEN CASE SERIES

Laura Rantet, Francisca Sivera, Mariano Andrés, Alicante, Hospital General Universitario, Alicante, Spain

Background: Despite having passed more than fifty years after its initial description, essential questions for calcium pyrophosphate (CPP) crystal disease, such as clinical spectrum, diagnosis or management schemes, remain unsolved. Acute flares often occurred during hospitalizations. Scant reports have addressed this common setting for CPP crystal disease, and whether these patients behave similarly to ambulatory cases is unknown.

Objectives: The aim of this work was to describe in a prospective way a crystal-proven case series of patients developing acute CPP crystal arthritis during hospitalizations for another conditions.

Methods: An observational, cross sectional descriptive study was conducted in two Spanish centers from November 2013 to December 2018. A prospective convenience sampling was employed to select patients with crystal-proven CPP acute arthritis seen during hospital admissions. Demographic, clinical and CPP-related variables were collected, and X-rays (pelvis, knees, hands, affected joint when different) and laboratory tests (to rule out associated metabolic conditions) were systematically requested. A descriptive analysis is present.

Results: 90 episodes of acute CPP arthritis in 87 patients were seen in the study period, with an average age of 81.8 years (SD 7.7). 50.6% of them men. Approximately 26% of patients reported prior episodes of arthritis, most of them (68.4%) as outpatients. Only three patients were on preventive treatment for CPP arthritis (two on colchicine and one on low dose glucocorticoids). Regarding the acute CPP arthritis during admissions, they were predominantly monoarticular (81.0%) and the main involved joints were knee (46.0%), wrist (13.8%) and ankles (6.9%). The reasons for admission were diverse, with a mean of 7.7 days (SD 9.1) from admission to flare. About X-rays, 23.8% showed no chondrocalcinosis (CC) in the evaluated joints [61/80]. In 57.1% of patients there was chondrocalcinosis in the affected joint [44/77] and regarding usual joints: 74.3% in knees [55/74], 51.5% in triangular carpal ligament [34/66], 25.4% in metacarpophalangeal joints [17/67], 20% in public symphysis [14/70] and 17.6% in coxofemoral joints [12/68]. A secondary form of osteoarthritis was only seen in 10 patients (12.5%). About associated metabolic diseases, one case of primary hyperparathyroidism-related hypercalcemia and five cases of hypomagnesemia at the time of the flare were detected. In all six patients with a polyarticular presentation, laboratory tests for rheumatoid factor and ACPA were negative.

Conclusion: From the findings of this prospective, crystal-proven series of CPP crystal arthritis in an intrahospital setting, we can remark:

- 1. The low numbers of previous ambulatory flares may suggest a different clinical entity of CPP disease.
- 2. Radiological CC was absent in around a quarter of patients despite a extensive assessment, so synovial fluid analysis remains essential for diagnosis.
- 3. The rarity of associated metabolic diseases seen runs against ruling out secondary causes of CPP disease in this setting.

Disclosure of Interests: None declared

SA70443 RECONCILIATION OF URATE LOWERING THERAPIES DURING HOSPITALIZATION AND THE IMPACT OF RHEUMATOLOGIC CONSULTATION ON MANAGEMENT OF INPATIENT GOUT FLARES

Maia Seg, Emory University, Rheumatology, Atlanta, United States of America

Background: Hospitalizations complicated by gout flares may have an impact on patient care. Delayed diagnosis and suboptimal management can lead to prolonged discomfort, impair chronic outcomes of the disease and lengthen the hospitalization. Patients on urate lowering therapy (ULT) are frequently admitted to the hospital for unrelated causes but there is variability in inpatient medication management of the urate lowering agent and acute management of the flare.

Objectives: In this descriptive study, we analyse the variability of reconciliation of ULT on admission and discharge and the impact of rheumatologic consultation on acute and chronic management of gout.

Methods: Patients- above the age of 18- admitted to our tertiary care hospital from 01/01/2010 to 01/01/2016 with an ICD-9 or an ICD-10 diagnosis of gout were reviewed. The first 200 patients underwent a retrospective chart review as a pilot study for an ongoing project. We reviewed patient demographics, laboratory testing, and co-morbid conditions; medications on admission and discharge, incidence of gout flare diagnosis and management during hospitalization, rheumatology consultation and discharge plan for these patients.

Results: Of the 200 patients reviewed, 2.69 admissions per person. We further described the patients who had a gout flare during hospitalization (n =54, 27%). 66% of these patients were males, mean age 69.8 years and BMI 31.78kg/m². A majority of patients had hypertension, renal disease, and dyslipidemia (Table 1). 70% of the patients were on chronic medications for gout (Table 2). 29.6% of these patients were continued on these agents upon admission and only 64.8% of these patient was eventually discharged on these drugs.

Rheumatology consulted for 68.5% of the patients. Arthrocentesis was more frequently performed when rheumatology was consulted (70% vs.17.6%; p<0.001). Rheumatology consultation did not decrease length of stay in the hospital. 78.5% of the patients managed by primary team were discharged on a ULT or colchicine compared to 100% in the group managed by rheumatology consult team (100% vs 78.5%; p=0.0431). Outpatient rheumatology follow up was documented in discharge papers for 62% of the patients managed with rheumatology consult compared to 11.7% in the comparison group. (62% vs.11.7%; p=0.002).

Conclusion: Rheumatology consultation improved adherence to guidelines in diagnosis and management of gout flare and improved the discharge planning and follow up.
REFERENCES

TABLE 1

<table>
<thead>
<tr>
<th>BASELINE DEMOGRAPHICS</th>
<th>TOTAL PATIENTS (n=200)</th>
<th>PATIENTS WITH A GOUT FLARE (n=175)</th>
<th>RHEUMATOLOGY CONSULT (n=37)</th>
<th>PRIMARY TEAM (n=17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>70.99 ± 7.33</td>
<td>69.89 ± 11.28</td>
<td>70.62 ± 11.94</td>
<td>68.25 ± 9.82</td>
</tr>
<tr>
<td>RACE (%)</td>
<td>12.33</td>
<td>15.8</td>
<td>12.5 (3.7)</td>
<td>10.8</td>
</tr>
<tr>
<td>African-American/ Caucasian/Others</td>
<td>164(82)</td>
<td>39(22.2)</td>
<td>22(12.8)</td>
<td>12(7)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>31.39 ± 5.21</td>
<td>31.79 ± 8.83</td>
<td>31.71 ± 7.75</td>
<td>31.9 ± 7.75</td>
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<tr>
<td>Hypertension</td>
<td>177(88.5)</td>
<td>48 (88.9)</td>
<td>32 (84)</td>
<td>16 (94)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>84 (42)</td>
<td>25 (46)</td>
<td>18 (46.9)</td>
<td>7 (41)</td>
</tr>
<tr>
<td>Renal dysfunction</td>
<td>139 (69.5)</td>
<td>43 (76.9)</td>
<td>29 (78)</td>
<td>14 (41)</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>119 (59.5)</td>
<td>25 (46.3)</td>
<td>17 (46)</td>
<td>8 (47)</td>
</tr>
</tbody>
</table>

TABLE 2

<table>
<thead>
<tr>
<th>TOTAL PATIENTS (n=200)</th>
<th>PATIENTS WITH A GOUT FLARE (n=54)</th>
<th>RHEUMATOLOGY CONSULT (n=8)</th>
<th>PRIMARY TEAM (n=17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No of patient on chronic Gout medications N (%)</td>
<td>169 (84.5)</td>
<td>38 (70)</td>
<td>24 (44.8)</td>
</tr>
<tr>
<td>Allipurinol/Febuwatstat (1)</td>
<td>139 (69.5)/2</td>
<td>23 (42.6)/2</td>
<td>15 (40.0)/2</td>
</tr>
<tr>
<td>Colchicine</td>
<td>50 (25)</td>
<td>25 (46.3)</td>
<td>15 (40.0)</td>
</tr>
<tr>
<td>Combination of drugs</td>
<td>22 (11)</td>
<td>12 (22.2)</td>
<td>8 (18.9)</td>
</tr>
<tr>
<td>Inpatient</td>
<td>117 (58.5)</td>
<td>16 (29.6)</td>
<td>10 (27)</td>
</tr>
<tr>
<td>Medications on discharge</td>
<td>153 (76.5)</td>
<td>35 (64.8)</td>
<td>24(46.8)</td>
</tr>
<tr>
<td>Length of Hospitalization (days)</td>
<td>5.00 ± 4.83</td>
<td>5.06 ± 2.56</td>
<td>4.73 ± 2.34</td>
</tr>
</tbody>
</table>

Disclosure of Interests: None declared

SAT0445 ADEQUATE URATE LOWERING THERAPY FOR GOUT IS RARE IN CLINICAL PRACTICE BUT PRESERVES RENAL FUNCTION WHEN EFFECTED

Valgerdur Sigurdardottir1,2, Lena T.H. Jacobsson3, Anna Svärd4, Mats Dehlin2.
1Center for Clinical Research (CKF) Dalarna, Uppsala University, Falun, Sweden;
2Salghirka Academy, University of Gothenburg, Department of Rheumatology and Inflammation Research, Gothenburg, Sweden

Background: Optimal urate lowering therapy (ULT) as defined by most guidelines requires monitoring of serum urate (SU) and titration of the medication dose to achieve a target level of SU. In Sweden, allopurinol is the most widely used ULT and most patients with gout are managed in primary care. As a first step towards implementation of gout treatment guidelines in the Swedish region of Dalarna, we undertook a register study to assess how allopurinol is prescribed and to what extent monitoring of SU takes place.

Objectives: To determine the proportion of patients with gout that receive a) ULT and b) adequate ULT and to determine to what extent SU is monitored. A secondary aim was to explore the effects of adequate ULT on SU and estimated glomerular filtration rate (eGFR) over time.

Methods: Data was retrieved from the electronic healthcare record database of the region. The database holds records of all diagnoses at visits to physicians, prescriptions made in primary care as well as results of laboratory tests. We searched the database from 1997-2012 for individuals with a first diagnosis of gout during 2000-2012 and retrieved data for all prescriptions of allopurinol for the identified patients. Results and dates of SU and creatinine measurements after gout diagnosis were retrieved. MDRD eGFR was calculated from s-creatinine, sex and the age of the patient at the time of measurement. The value nearest in time before initiation of ULT was defined as the baseline measurement for both urate and creatinine. Duration of therapy was defined as number of days from first to last prescription adding 365 days (the usual period for which chronic medication is prescribed in Sweden). The mean daily dose of allopurinol was estimated from prescription data.

Disclosure of Interests: None declared
Adequate ULT was defined as a mean daily dose of at least 300 mg of allopurinol and a duration of therapy of at least 2 years. Patients that had received adequate ULT were matched using propensity score on the basis of baseline eGFR and length of follow-up time to patients that received non-adequate ULT. Change from baseline in SU and eGFR was calculated and compared between groups.

Results: We identified 5433 patients with an incident gout diagnosis during 2000-2012 (and no gout diagnosis or prescription for ULT during 1997-1999). Of these, 2393 (44%) received at least one prescription for allopurinol. SU was measured at some time point after initiation of ULT in 58% of patients. Adequate ULT as defined above was prescribed for 154 patients (3%), of these, 112 (73%) had a SU measurement at some time point after initiation of therapy and 35 (23%) had such a measurement done within 6 weeks of starting treatment. Matched controls could be identified for 109 of the patients with adequate ULT. Mean urate and eGFR at the start of therapy and end of follow up for the group with adequate ULT treatment and the controls are shown in table 1.

### Table 1. Values are mean (SD) or n (%)

<table>
<thead>
<tr>
<th>Adequate ULT, Matched controls, p-value</th>
<th>n=109</th>
<th>n=109</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>66 (14)</td>
<td>66 (13)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>25 (23)</td>
<td>38 (35)</td>
</tr>
<tr>
<td>Allopurinol daily dose in mg</td>
<td>359 (61)</td>
<td>119 (63)</td>
</tr>
<tr>
<td>Baseline s-urate, μmol/L</td>
<td>511 (111)</td>
<td>509 (100)</td>
</tr>
<tr>
<td>Baseline eGFR, ml/min</td>
<td>66 (21)</td>
<td>66 (21)</td>
</tr>
<tr>
<td>Length of follow up, years</td>
<td>4.2 (3.5)</td>
<td>5.2 (3.9)</td>
</tr>
<tr>
<td>Δ s-urate, (baseline compared to last available value)</td>
<td>-168 (-173)</td>
<td>-78 (-125)</td>
</tr>
<tr>
<td>Δ e-GFR (baseline compared to last available value)</td>
<td>-1 (15)</td>
<td>-5 (16)</td>
</tr>
<tr>
<td>Last eGFR worse than baseline measurement, n (%)</td>
<td>50 (46)</td>
<td>67 (61)</td>
</tr>
</tbody>
</table>

Conclusion: ULT was prescribed to less than half of the patients identified. Adequate ULT was rare in clinical practice during the time period studied. Urate monitoring occurred in less than half of ULT-treated patients. The patients with adequate ULT achieved greater lowering of serum urate than matched controls and were more likely to maintain unchanged renal function over time.

Disclosure of Interests: Valgerdur Sigurdardottir: None declared, Lennart T.H. Jacobsson Consultant for: LJ has received lecture and consulting fees from Pfizer, Abbvie, Novartis, Eli-Lilly and Janssen, Anna Svärd: None declared, Mats Dehlin: None declared

Methods: Audit criteria were derived from the latest BSR gout guideline (Hui et al; 2017). A randomised sample of adult patients with a read code for the diagnosis of gout from Jan 2006-Jan 2018 was chosen from six large general practices in Leicestershire County of the United Kingdom. The data collected included demographics, provision of patient information, management of acute attacks and prophylactic treatment, screening of appropriate co-morbidities, dosing of urate-lowering therapy (ULT) and titration of doses against measurement of uric acid levels.

Results: Data was obtained for 861 patients. The mean age was 60 years and 91% were male. 21.5% were recorded as being provided with written information about gout and 65.0% of patients were treated with NSAIDs and COXIBs for acute attacks of gout. When colchicine was prescribed to patients, 71% had no dose recorded in their clinical records. 323 (37.5%) of patients were prescribed a ULT and the recorded starting dose of allopurinol was 100mg daily for 73.8%. Titration of subsequent allopurinol doses was recorded in only 21% of patients. 539 patients (62.6%) had no record of a serum urate level check after starting ULT.

Conclusion: Clinical records indicate that the management of gout in UK General Practitioners in Primary Care is suboptimal in concordance with the BSR guidelines. It was clear that general practices did not employ the treat to target strategy. There is a clear need for increased GP awareness and adherence to the BSR guidelines in order to optimise deficient areas of care, particularly in patient education, initiation and titration of ULT and monitoring of serum urate levels in gout patients. Appropriate patient recording templates are needed so that key information is captured during a patient consultation in order to enable medicines optimisation for those with gout. Most aspects of gout management in primary care did not concord well with published BSR guidelines.

REFERENCES

Disclosure of Interests: None declared
DOI: 10.1136/rheumdis-2019-eular.8137

SAT0446 ATP IS THE SECOND KEY SIGNAL OF GOUT FLARE BEYOND MSU
Hong-Liang Zhang1,2*, Zi-Wen Zhu1, Jinhui Tao3,3, Yu-Jie Tang1, Li Xin-Ya1, Li Lin1, Xian-Feng Wu1,2,3,4. This work was supported by grants from the National Natural Science Foundation of China (81771774) and the Anhui Provincial Natural Science Foundation (1708085MH191)

Disclosure of Interests: None declared
DOI: 10.1136/rheumdis-2019-eular.7510
Sensitivity of Dual-Energy CT Scanning, Ultrasond, and X-Ray for Crystal-Proven Pseudogout

Sara Tedeschi¹, Daniel Solomon¹, Kathleen Vannì¹, Neal Suh¹, Stacy Smith²
¹Brigham and Women’s Hospital, Rheumatology, Boston, United States of America; ²Brigham and Women’s Hospital, Musculoskeletal Radiology, Boston, United States of America

Background: Advanced imaging modalities such as ultrasound (US) and dual-energy CT (DECT) can help diagnose crystalline arthritis. DECT is highly sensitive and specific in gout and has not been well studied in pseudogout.

Objectives: To compare the sensitivity of DECT, US, and x-ray (XR) in pseudogout.

Methods: We prospectively enrolled patients with crystal-proven pseudogout at a tertiary care center, 3/2018-11/2018. We searched the electronic medical record for synovial fluid crystal lab orders and reviewed the record to identify candidates. Eligible patients were 18 years old with acute monoarthritis, joint aspiration, and synovial fluid calcium pyrophosphate (CPP) crystals on polarized microscopy. Patients with both monosodium urate and CPP crystals were excluded. Subjects provided informed consent and underwent DECT, US, and XR of the aspirated joint and standardized joint (right wrist). All images were interpreted by a musculoskeletal radiologist and a rheumatologist trained in US; consensus was reached on each image. DECT images were post-processed using Siemens Syngo.via software, applying color-coded overlay indicating volume and location of CPP deposits. We considered two volume thresholds to identify candidates. Eligible patients were 18 years old with synovial fluid CPP crystals as the gold standard. Larger studies testing DECT sensitivity and specificity in pseudogout vs. other arthritis and establishing a volume threshold are needed.

Disclosure of Interests: Sara Tedeschi: None declared, Daniel Solomon Grant/research support from: Abbvie, Amgen, Genentech, Janssen, and Pfizer, Kathleen Vannì: None declared, Neal Suh Grant/research support from: Pfizer, Stacy Smith: None declared

Gout Flares Become Infrequent During a Treat-to-Target Strategy Over One Year: Data from the Nor-Gout Study

Till Uhlig, Lars Fridjip, Karolussels, Espen A. Haavardsholm, Tore K. Kven, Hilde Berner Hammer, Dønkerhenmøet Hospital, Rheumatology, Oslo, Norway

Background: Urate lowering therapy (ULT) is expected to prevent new gout flares. Treat-to-target ULT is however often not performed, and we need more evidence on how often patient become flare-free during ULT.

Objectives: Urate lowering therapy (ULT) is expected to prevent new gout flares. Treat-to-target ULT is however often not performed, and we need more evidence on how often patient become flare-free during ULT.

Methods: In a prospective observational study, patients with crystal-proven gout with a recent gout attack and insufficiently treated serum urate (sUA) level (>360 µmol/L/4 mg/dl) were included. They received ULT with drug escalation during monthly follow-up until the target sUA level was met (sUA <360 µmol/L, or <300 µmol/L if clinical tophi). Assessment in this ongoing data collection included demographic and clinical variables, serum urate levels, previous medication with allopurinol, colchicine and NSAIDs, co-morbidities, and health related quality of life (SF-36). Flares during the last six months of one year with “treat-to-target” were recorded. Bivariate analyses and logistic regression analyses examined factors associated with and prediction (odds ratio with 95% confidence intervals) of a flare-free period during months 6-12.

References

Table 1. Presence and location of imaging abnormalities in 10 pseudogout subjects

<table>
<thead>
<tr>
<th>Subject</th>
<th>Aspirated joint</th>
<th>DECT color-coded changes (cm³)</th>
<th>Hypercholecyst deposition</th>
<th>XR chondrocalcinosis</th>
<th>Standardized joint (right wrist)</th>
<th>DECT color-coded changes (cm³)</th>
<th>Hypercholecyst deposition</th>
<th>XR chondrocalcinosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>PF, PSFC, M, TF (0.48)</td>
<td>M</td>
<td>M</td>
<td>IC, IP1, MCP3, IFCC</td>
<td>TFCC</td>
<td>TFCC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>ICN, M (0.73)</td>
<td>FC</td>
<td>M</td>
<td>MCP1, TFCC</td>
<td>none</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>3</td>
<td>ICN, M, PF, TF (2.85)</td>
<td>FC</td>
<td>ICN, M, PF</td>
<td>CMC1, CMN3, IFCH</td>
<td>TFCC</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>4</td>
<td>ICN, M, PF, PSFC, Pop, D (1.03)</td>
<td>FC</td>
<td>M</td>
<td>IC (0.10)</td>
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<td></td>
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<td></td>
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<tr>
<td>5</td>
<td>M, PSFC, Q (0.50)</td>
<td>FC</td>
<td>M, PF</td>
<td>IC, TFCC</td>
<td>(0.04)</td>
<td>TFCC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>M, PF (0.67)</td>
<td>FC</td>
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<td>TFCC</td>
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<tr>
<td>7</td>
<td>M, PF, PSFC (1.33)</td>
<td>FC</td>
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<tr>
<td>8*</td>
<td>IC (0.02)</td>
<td>IC, TFCC</td>
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<td>(0.02)</td>
<td>IC, TFCC</td>
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<tr>
<td>9</td>
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<td>IC (0.05)</td>
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<td>10</td>
<td>CMC1, TFCC</td>
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<tr>
<td></td>
<td>IC, MP1, MCP1-2, MCP1-4, MCP1-5, TFCC</td>
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<tr>
<td>5</td>
<td>TFCC</td>
<td>(0.84)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>


Disclosure of Interests: Till Uhlig, Lars Fridjip, Karolussels, Espen A. Haavardsholm, Tore K. Kven, Hilde Berner Hammer: Dønkerhenmøet Hospital, Rheumatology, Oslo, Norway
VITAMIN D INSUFFICIENCY AND DEFICIENCY ARE ASSOCIATED WITH A HIGHER LEVEL OF SERUM URIC ACID: A SYSTEMATIC REVIEW AND META-ANALYSIS

Niph Charoengnam1, Ben Ponvilawan2, Patoompong Ungprasert2, 1Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, 2Faculty of Medicine Siriraj Hospital, Mahidol University, Clinical epidemiology unit, Bangkok, Thailand

Background: Several studies have revealed a relationship between vitamin D deficiency and a number of non-skeletal health conditions such as insulin resistance, metabolic syndrome, cardiovascular diseases, inflammatory diseases, infection and malignancy. The interaction between serum uric acid and vitamin D has also been observed. A study found that uric acid can suppress 1-alpha-hydroxylase in vitro and in vivo, leading to the reduction in the conversion of the storage form of 25-hydroxyvitamin D into the active form of 1,25-dihydroxyvitamin D [1]. In fact, several epidemiological studies have suggested that patients with vitamin D insufficiency and deficiency tend to have a higher level of serum uric acid compared to those with adequate vitamin D level although the results were inconsistent across the studies.

Objectives: To compare serum uric acid level between individuals with normal vitamin D level versus patients with vitamin D deficiency and vitamin D insufficiency.

Methods: A systematic review was conducted using MEDLINE and EMBASE database from inception to October 2018 to identify all studies that compared the level of serum uric acid between individuals with normal vitamin D level and patients with vitamin D insufficiency/deficiency. Eligible studies must be cohort or cross-sectional studies that consisted of two groups of adult participants, one with normal level of vitamin D (vitamin D level >30 ng/ml) and one with vitamin D insufficiency (vitamin D level 20-30 ng/ml) or vitamin D deficiency (vitamin D level <20 ng/ml). Mean serum uric acid level and standard deviation of participants in each group were extracted from each study to calculate mean difference (MD) between the groups. Pooled MD was then calculated by combining MDs of each study using random-effects model.

Results: A total of seven cross-sectional studies were eligible for the meta-analyses. Individuals with normal vitamin D level had a significantly lower serum uric acid level than patients with vitamin D insufficiency with the pooled MD of -0.33 mg/dL (95% CI, -0.61,-0.04) (figure 1) and also had a significantly lower serum uric acid level than patients with vitamin D deficiency with the pooled MD of -0.45 mg/dL (95% CI, -0.82,-0.08) (figure 2). The funnel plots had a certain degree of asymmetry. Funnel plots both meta-analyses were fairly symmetric which did not suggest the presence of publication bias.

Conclusion: Both patients with vitamin D insufficiency and patients with vitamin D deficiency had a significantly higher level of serum uric acid compared to individuals with normal vitamin D level.

REFERENCES

Figure 1. Forest plot of the meta-analysis of vitamin D insufficiency versus normal vitamin D level

Figure 2. Forest plot of the meta-analysis of vitamin D deficiency versus normal vitamin D level


Infection-related rheumatic diseases

JONI MANIFESTATIONS OF WHIPPLE’S DISEASE: CLINICAL AND RADIOLOGICAL PRESENTATION OF 19 PATIENTS

Marie Desmurs1, Hélène Petit2, Jacques-Eric Gottenberg3, 1Hôpital Émilie Muller, Mulhouse, France, 2Centre hospitalier René Pleven, Dinan, France, 3Hôpitaux Universitaires de Strasbourg, Strasbourg, France

Background: Whipple’s disease (WD) is a rare chronic systemic bacterial infection caused by Tropheryma whippelii. It affects middle-aged men with diarrhea, weight loss, fever and joint manifestations. It usually develops as oligoarthritis or polyarthritis of large joints. WD may mimic chronic inflammatory rheumatisms. Some studies and case reports show that immunosuppressive treatment can worsen WD.

Objectives: Clinical and radiological (radiograph, ultrasound (US), MRI) presentation of joint manifestations of WD.

Methods: This retrospective monocentric observational study was led in Strasbourg University Hospital, Reference Center for Rare Diseases and included patients with WD diagnosed between 2006 and 2017. Patients were included if they had joint manifestations, positive T. whippelii polymerase chain reaction in stools or/and saliva, positive T. whippelii polymerase chain reaction on duodenal biopsy and/or positive periodic acid-Schiff performed on duodenal biopsy and good evolution with antibiotics.

Results: Nineteen patients including fifteen men were included. The median age at diagnosis was 57. The median time from first symptoms to diagnosis was 60 months. Before the diagnosis of WD, 13 patients had immunosuppressive therapies.

Clinical presentation of joint manifestations: 11 polyarthritis, 3 oligoarthritis, 1 monoarthritis and 4 inflammatory polyarthritis including 3 with axial pain. Wrists (15/19), ankles (11/19) and knees (10/19) were the most affected. The metacarpophalangeal joints were affected in 8 patients. Eight patients had diarrhoea and weight loss.
Its principal clinical significance is causing carditis at the acute phase of the disease, and valvular impairment, leading to a significant hemodynamic disturbance, as a late sequela.

Despite being a completely preventable disease, Rheumatic fever continues to be the most common cause of acquired heart disease among children in developing countries. In developed countries, a sharp decline in ARF was seen in the last decades.

**Objectives:** To examine the number of cases of Rheumatic fever in Schneider Children’s medical center, and to find whether it has declined during the years of its existence. In addition, to characterize the patient population during that period, determine the clinical characteristics of ARF. Its risk factors and assess the course of the disease and its treatment. In addition, we will address the relapse rates, with an emphasis on cardiac relapses, with a correlation to preventive treatment.

**Methods:** A retrospective cohort study was conducted, by collecting data from medical records of patients with rheumatic fever who were admitted to the Schneider Medical Center from 1993 to 2017. A database was built based on these medical records in order to assess the incidence of rheumatic fever and rheumatic heart disease, and the relapse rates, by use of descriptive and survival analysis.

**Results:** A 402 cases with relevant diagnostic codes were examined during the follow-up period, of which 307 patients met the inclusion criteria. During the acute phase, 197 of the patients (64%) presented with arthritis, 159 patients (52%) with carditis, 47 patients (15%) with chorea, 16 patients (5.2%) with erythema marginatum, and 2 patients (0.7%) with subcutaneous nodules. Carditis was found in higher rates among Jewish patients than among Arabs. 31 patients (19.5%) developed severe carditis, 21 patients (13.2%) of whom developed heart failure signs, 5 were hospitalized in intensive care, and one died. There was a decrease in incidence of rheumatic fever and rheumatic heart disease during the study period. Thirty-two patients (12% of all patients with rheumatic fever) developed a relapse of the disease and 11 of whom (4% of all patients) developed a cardiac relapse.

Median follow-up time was 49 months, and relapse rate was 13.9% after 5 years of follow-up. 15% of the patients who received oral prophylaxis experienced relapse, compared to 9% of those who received intramuscular injection therapy.

The rate of recurrence among all patients with rheumatic fever was 2.8% after 2 years of follow-up, 8% after 5 years of follow-up, and about 7% after 8 years of follow-up. 10 (90.9%) of the 11 patients with cardiac recurrence were present with carditis during the initial disease, with 7 of them (63.6% of patients with cardiac recurrence) having isolated carditis and 3 of them had a combined involvement of arthritis and carditis (27.3% of Cardiac relapses). Only in one case (9.1% of patients with cardiac recurrence) was an isolated occurrence of arthritis in the initial presentation. It was found that chorea is more common among females.

**Conclusion:** Despite the reduction in incidence of rheumatic fever and rheumatic heart disease during the study period, the disease remains a significant cause of general and cardiac morbidity among children despite being completely preventable, therefore. It should remain in the mind of every doctor, pediatricians in particular.

**Disclosure of Interests:** None declared. DOI: 10.1136/annrheumdis-2019-eular.4981

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**References**

Simultaneously, we introduced staff education sessions, point-of-care paper “Arthritis and Infection Worksheets” and “Vaccination Advice Letters”. In 2018, the clinic was re-assessed.

**Results:** 163 patients met inclusion criteria in 2017 and 262 in 2018. Patients were typical of an IA clinic (74% women, 45.4%;60 years old, 72.7% had RA, 61.1% on cDMARDs, 53.6% on methotrexate, 46.6% on bDMARDs, 23.1% on CDMA RD plus bDMARD).

In 2017, 104 (65.4%) knew of the increased infectious risk of IA. In 2018, 168 (65.6%) were aware. Awareness of infection risk with medications increased from 111 (69.8%) to 172 (66.9%).

Table 1 shows vaccination rates. PPSV23 rates increased from 41.0% to 47.2% (P value=0.29, Pearson Chi squared), and influenza from 61.8% to 62.1% (P value=0.95, Pearson Chi squared).

**Table 1. Vaccination Rates**

<table>
<thead>
<tr>
<th></th>
<th>Adequate Vaccination</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2017</td>
</tr>
<tr>
<td><strong>% vaccinated</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Influenza</strong></td>
<td>128 (80.0%)</td>
</tr>
<tr>
<td><strong>Pneumococcal</strong></td>
<td>60 (38.0%)</td>
</tr>
<tr>
<td><strong>Adequate frequency</strong></td>
<td>133 (99.3%)</td>
</tr>
<tr>
<td><strong>Source of awareness</strong></td>
<td>92 (73.0%)</td>
</tr>
<tr>
<td><strong>GP</strong></td>
<td>29 (23.0%)</td>
</tr>
<tr>
<td><strong>Hospital</strong></td>
<td>0 (12.5%)</td>
</tr>
<tr>
<td><strong>Clinical Nurse Specialist</strong></td>
<td>0 (0.0%)</td>
</tr>
<tr>
<td><strong>Public Health/Ward Nurse</strong></td>
<td>6 (4.8%)</td>
</tr>
<tr>
<td><strong>Radio</strong></td>
<td>5 (4.0%)</td>
</tr>
<tr>
<td><strong>Television</strong></td>
<td>93 (76.8%)</td>
</tr>
<tr>
<td><strong>Site of last vaccine</strong></td>
<td>149 (77.2%)</td>
</tr>
<tr>
<td><strong>GP</strong></td>
<td>7 (5.9%)</td>
</tr>
<tr>
<td><strong>Work</strong></td>
<td>6 (5.1%)</td>
</tr>
<tr>
<td><strong>Pharmacy</strong></td>
<td>6 (5.1%)</td>
</tr>
<tr>
<td><strong>Public Health Nurse</strong></td>
<td>6 (5.1%)</td>
</tr>
<tr>
<td><strong>Hospital</strong></td>
<td>2 (1.7%)</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td>18 (36.7%)</td>
</tr>
<tr>
<td><strong>Unaware</strong></td>
<td>12 (24.5%)</td>
</tr>
<tr>
<td><strong>Fear of side effects</strong></td>
<td>6 (12.5%)</td>
</tr>
<tr>
<td><strong>Too busy</strong></td>
<td>2 (4.1%)</td>
</tr>
<tr>
<td><strong>Cost</strong></td>
<td>13 (26.5%)</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td>98 (90.7%)</td>
</tr>
</tbody>
</table>

**Table 2. Vaccination awareness, provision and reasons for non-compliance**

<table>
<thead>
<tr>
<th></th>
<th>2017</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aware required</strong></td>
<td>128</td>
<td>212</td>
</tr>
<tr>
<td><strong>Aware of frequency</strong></td>
<td>133</td>
<td>219</td>
</tr>
<tr>
<td><strong>Source of awareness</strong></td>
<td>92</td>
<td>146</td>
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<tr>
<td><strong>GP</strong></td>
<td>29</td>
<td>44</td>
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<tr>
<td><strong>Hospital</strong></td>
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<td>6</td>
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<tr>
<td><strong>Radio</strong></td>
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<td>6</td>
</tr>
<tr>
<td><strong>Television</strong></td>
<td>93</td>
<td>149</td>
</tr>
<tr>
<td><strong>Site of last vaccine</strong></td>
<td>149</td>
<td>53</td>
</tr>
<tr>
<td><strong>GP</strong></td>
<td>7</td>
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<tr>
<td><strong>Work</strong></td>
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<tr>
<td><strong>Pharmacy</strong></td>
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<td>10</td>
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<tr>
<td><strong>Public Health Nurse</strong></td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td><strong>Hospital</strong></td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td>18</td>
<td>12</td>
</tr>
<tr>
<td><strong>Unaware</strong></td>
<td>12</td>
<td>18</td>
</tr>
<tr>
<td><strong>Fear of side effects</strong></td>
<td>6</td>
<td>10</td>
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<tr>
<td><strong>Too busy</strong></td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td><strong>Cost</strong></td>
<td>13</td>
<td>22</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td>98</td>
<td>96</td>
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</table>

**Conclusion:** This study shows suboptimal vaccination awareness and uptake. Our interventions increased PPSV23 and influenza vaccination rates. There is debate about who is responsible for vaccinations. Guidelines advocate specialists sharing responsibility with GPs. 57% of rheumatologists considered GPs responsible (2). Perhaps, we should take a more active approach.

**REFERENCES**


Disclosure of Interests: Kieran Murray Grant/research support from: Newman Research Fellowship (Abbbie), Francis Young: None declared, Candice Low: None declared, Anna O’Rourke: None declared, Ian Callanan: None declared, Eoin Feeney: None declared, Douglas Veale: None declared.

In areas where Lone Star ticks are present, and in patients with risk factors for tick exposure, alpha gal IgE reactivity should be considered and tested for as part of a “tick panel” in patients who present with symptoms of potential rheumatologic diseases.

REFERENCES


Table 1. Clinical presentation of the patients at onset (n=142)

<table>
<thead>
<tr>
<th>Characteristics of joint involvement at onset</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monarthrits</td>
<td>7(4.9)</td>
</tr>
<tr>
<td>Oligoarthrits</td>
<td>36(25.4)</td>
</tr>
<tr>
<td>Polyarthrits 99(69.7)</td>
<td></td>
</tr>
<tr>
<td>Symmetrical joint involvement</td>
<td>120(84.5)</td>
</tr>
<tr>
<td>Joint swelling</td>
<td>67(47.2)</td>
</tr>
<tr>
<td>Morning stiffness</td>
<td>116(81.7)</td>
</tr>
<tr>
<td>Skin involvement</td>
<td>90(63.4)</td>
</tr>
<tr>
<td>Erythematous rash 24(16.9)</td>
<td></td>
</tr>
<tr>
<td>Erythematous rash and itching</td>
<td>66(46.5)</td>
</tr>
<tr>
<td>Myalgia 46(32.4)</td>
<td></td>
</tr>
<tr>
<td>Ultra-sonographic findings</td>
<td>(n=32)</td>
</tr>
<tr>
<td>Tenosynovitis</td>
<td>22(15.8)</td>
</tr>
<tr>
<td>Synovial hypertrophy</td>
<td>11(15.4)</td>
</tr>
<tr>
<td>Tendinitis</td>
<td>8(5.6)</td>
</tr>
<tr>
<td>Median nerve involvement (CTS)</td>
<td>4(12.5)</td>
</tr>
<tr>
<td>Joint effusion</td>
<td>3(9.4)</td>
</tr>
</tbody>
</table>

Figure 1: Distribution of patients by functional disability using HAQ

Figure 2: Type of Chikungunya arthritis

Disclosure of Interests: None declared

with CHIKV IgM positive. In the EQ-5D (Figure 1), between 72% and 92% of patients didn’t report problems on the mobility, self-care, usual activities, anxiety and depression dimensions. In contrast pain and discomfort dimensions were affected from moderate to extreme (44.7% and 86.6%). There weren’t significant differences between true positives, true false, false negative within all the variables, except on the anxiety and depression dimensions where the false positives had a higher significant score in comparison to the other groups (n: 10, 38.5%; p=0.00; OR:4.17, IC:1.8-9.57). In the EQ-5D-VAS, media for VAS was 75.56 (SD±21.18) where the highest scores of VAS were found on the false negatives. In pain VAS, false positives as well as the duration greater than 7 weeks where associated with several pain (n: 10, 2.9%; OR: 0.2; IC 1.25-6.33; y n: 27, 21.3%; p=0.016; OR 2.02, IC 1.12-3.66 respectively).

Conclusion: In general, the disability of CHIKV infected patients was mild to moderate, finding the most affected dimensions to be pain, discomfort, anxiety and depression. The false positives and the population with anxiety and depression are related with higher score of disability.

Disclosure of Interests: None declared

SAT0459 DIAGNOSIS AND MANAGEMENT OF ACUTE HOT JOINTS AT A TERTIARY RHEUMATOLOGY CENTRE OVER A 7-MONTH PERIOD
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Background: The acute hot joint presentation is common in clinical practice, often due to crystal arthritis or non-inflammatory conditions. The most serious diagnosis is septic arthritis (SA), which can destroy cartilage within days, and therefore must be promptly diagnosed or excluded. The mortality rate for SA is 7-15%, despite antibiotic use [1]. Crystal arthropathies and SA are difficult to distinguish clinically, requiring arthrocentesis and synovial fluid (SF) analysis, in keeping with national guidelines.

Objectives: 1. Quantity number of acute hot joint presentations to our hospital over 7 months, including incidence of SA and crystal arthropathy. 2. Determine clinical features and outcomes (including morbidity/mortality) in SA. 3. Compare clinician diagnosis with laboratory diagnosis (gold-standard diagnostic test; crystal microscopy and culture). 4. Determine the correlation between WCC and crystal arthropathy or SA.

Methods: We retrospectively analysed laboratory diagnostic data and electronic clinical records, for patients presenting to a tertiary rheumatology centre in Northwest England with an acute hot joint, February-August 2018. For crystal arthropathy and SA, sensitivity, specificity, likelihood ratio. In the EQ-5D-VAS, media for VAS was 75.56 (SD±21.18) where the highest scores of VAS were found on the false negatives. In pain VAS, false positives as well as the duration greater than 7 weeks where associated with several pain (n: 10, 2.9%; OR: 0.2; IC 1.25-6.33; y n: 27, 21.3%; p=0.016; OR 2.02, IC 1.12-3.66 respectively).

Conclusion: In general, the disability of CHIKV infected patients was mild to moderate, finding the most affected dimensions to be pain, discomfort, anxiety and depression. The false positives and the population with anxiety and depression are related with higher score of disability.

Disclosure of Interests: None declared

SAT0460 HCV-RELATED MIXED CRYOglobulinemia in the DIRECT-antiviral agents era: is there Advantage in Sequential Therapy with Rituximab?
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Background: Mixed Cryoglobulinemia (MC) is a small vessel vasculitis characterized by the presence of a monoclonal rheumatoid factor (RF) and polyclonal immunoglobulins that precipitate at cold temperature, with a large spectrum of clinical manifestations. MC is strongly associated with hepatitis C (HCV) infection. 90% of the direct-acting antivirals (DAA) against HCV, which can eradicate the virus in >95% of patients, are supposed to have benefits on clinical manifestations of MC, nonetheless the amount of data is still limited. Patients with severe vasculitis may require anti-CD20 agent Rituximab (RTX) over DAA. However, despite the strong rationale, the advantage of dual therapy is still debated and the optimal therapeutic schedule unknown.

Objectives: To investigate the impact of DAA treatment on clinical manifestations and biochemical parameters of disease activity in HCV-related MC patients who reached complete viral eradication, and if pre-treatment with RTX was able to define a subset of patients with a different prognosis.

Methods: Data was collected from 31 patients with MC, mean age 68 yrs, female 80%, mean disease duration 10 yrs who were treated with
Vertebral Osteomyelitis (VO) is an infectious disease that requires specific treatment management. The treatment includes long-term antibiotic therapy, which can be guided by imaging studies. The objectives of this study were to evaluate the interest of follow-up imaging examinations in patients with pyogenic vertebral osteomyelitis (PVO) in order to improve the clinical and biological follow-up and the management of these patients. We conducted a retrospective cohort analysis of patients with PVO who had both baseline and follow-up imaging results available in a French university hospital during the period of 2010-2018. We identified the follow-up images into two groups, improvement/stability and deterioration, compared with the baseline findings. For each patient, we compared their imaging follow-up to their clinical-biological condition assessed at the same time.

Results: We have collected 80 patients. The median age was 71 years (32-89), 46 men, 13 patients had a history of spinal surgery. The most frequently reported germ was methicillin-sensitive staphylococci and the level of spinal involvement was predominantly lumbar. A Computerized Tomography (CT) was performed in 64% and a Magnetic Resonance Imaging (MRI) in 85% at the time of diagnosis. We identified 89 follow-up images, 58 MRIs, 31 CTs. The median delay of realisation was 85 days [11-364]. Soft tissue infiltration was observed in 50 patients compared to 26 on follow-up images but 3 were new. Similarly, 24% of the initial images had epiduritis compared to 16% during follow-up, 3% had compression (61.11% versus 26.92% respectively, p=0.05). Fifteen patients underwent CT-guided biopsy (83.33%) with prior antibiotic exposure in 11 of them. Median exposure was 4.5 days (3, 8.75). Delay from admission to procedure had a median value of 6 days (3.5, 9). Culture was positive in 53.33% of cases. In 10 patients, the picture was attributed to Gram+ (55.56%), in other 2 cases Gram- (11.11) and 1 case of tuberculosis (5.56). In 5 cases (7.88%) final pathogen was unknown. Four patients (22.22%) required further surgical surgery and 2 patients (11.11) died, similar than non-IS group, 11.54%.

Conclusion: In general terms, data about imaging is worse in IS patients and higher proportion of cervical spine involvement was also noted. Although, early intervention (diagnosis, puncture guided biopsy and treatment) seems to be protective against a bad outcome, since IS patients showed similar prognosis (further surgical procedures and death) than non IS patients. To sum up, new onset back pain in a IS patient, should be thoroughly studied so as to consider a VO as soon as possible.

Disclosure of Interests: None declared


SAT0462 INTEREST OF FOLLOW-UP IMAGING EXAMINATIONS IN PATIENTS WITH PYOGENIC VERTEBRAL OSTEOMYELITIS: A RETROSPECTIVE STUDY

Sophie Hequeuot, Kevin Boullier, Frank Verhoeven, Clément Prat, Daniel Wendling, Catherine Chirouze, Centre hospitalier régional universitaire de Besançon, Besançon, France

Background: Systematic follow-up imaging in patients with pyogenic vertebral osteomyelitis (PVO) is widespread. However, it is discussed, and there is no recommendation.

Objectives: Evaluate the interest of follow-up imaging examinations in patients with pyogenic vertebral osteomyelitis

Methods: We conducted a retrospective cohort analysis of patients with PVO who had both baseline and follow-up imaging results available in a French university hospital during the period of 2010-2018. We have classified the follow-up images into two groups, improvement/stability and deterioration, compared with the baseline findings. For each patient, we compared their imaging follow-up to their clinical-biological condition assessed at the same time.

Results: We have collected 80 patients. The median age was 71 years (32-89), 46 men, 13 patients had a history of spinal surgery. The most frequently reported germ was methicillin-sensitive staphylococci and the level of spinal involvement was predominantly lumbar. A Computerized Tomography (CT) was performed in 64% and a Magnetic Resonance Imaging (MRI) in 85% at the time of diagnosis. We identified 89 follow-up images, 58 MRIs, 31 CTs. The median delay of realisation was 85 days [11-364]. Soft tissue infiltration was observed in 50 patients compared to 26 on follow-up images but 3 were new. Similarly, 24% of the initial images had epiduritis compared to 16% during follow-up, 3% had appeared secondarily. There were 12 initial erosions described compared to 25 at follow-up. Of the 33 patients with clinical and biological recovery, 67% of follow-up images were classified as improving/stable and 13% as worsening (new abscesses (n=3), extension of soft tissue infiltration (n=2) and/or epiduritis (n=2) or appearance of new locations (n=2)). Among the 37 patients considered as unhealed, 87% of follow-up images were classified as improving/stable and 13% as worsening (new abscesses (n=1), extension of soft tissue infiltration (n=1) and/or epiduritis (n=1) or appearance of new locations (n=1)).
Conclusion: Our study showed that there was no correlation between the clinical condition of patients and their follow-up imaging in the context of PVO. Clinical and biological evaluation seems sufficient to determine whether or not the patient is cured. Many images are made during the follow-up with a questionable cost/effectiveness ratio. A standard radiograph may be sufficient to provide a basic structural condition at the end of antibiotic therapy.

Disclosure of Interests: None declared


SAT0463 BRUCELLAR SPONDYLODISCITIS: CLINICAL, RADIOLOGICAL AND THERAPEUTIC FEATURES

Aïcha Ben Tekaya1, Khouloua Zouaouli1, Ines Mahmoud1, Olfa Saida1, Mohamed Ben Hammamia2, Rawdha Tekaya1, Leïla Abdelmoula1,1. Charles Nicole Hospital, Tunis, Tunisia;2 la rabta hospital, Tunis, Tunisia

Background: Brucellosis is an endemic disease around the Mediterranean and especially in Tunisia and Brucellar spondylodiscitis is the most common systemic manifestation of the disease in our reality.

Methods: It is a retrospective descriptive study, conducted over 20 years (1999-2019) at a Rheumatology Department. We collected cases of Brucellar spondylodiscitis. We studied the clinical, radiological features and therapeutic outcomes.

Results: We included 23 patients, 15 men and 8 women, with a mean age of 53.21 years [31.79]. Contact with livestock or consumption of raw milk was noted in 16 cases. The diagnosis time was, on average, 3.8 months [1.9]. Spiné pain was present in all cases, with lumbar seat in 16 cases and was inflammatory in 20 cases. At the examination, 19 patients had a limitation of spinal mobility and 4 had neurological abnormalities. A motor deficit with a horsetail syndrome was objectified in one case. We noted a biological inflammatory syndrome in 19 cases. Wright’s serology was positive in 21 cases. Standard radiographs showed disc narrowing in 10 cases. 21 patients had spinal magnetic resonance imaging showing the abnormalities of the disc and adjacent vertebrae. We found abscess in four patients and epiduritis associated with the abscess in six patients. MRI showed spinal compression in 2 patients. Disco-vertebral biopsy was performed in 11 cases and helped to make the diagnosis in 3 cases. The patients had received antibiotic therapy with a combination of doxycyclin and rifampicin with a mean total duration of 4.9 months [2.12]. Evolution was favorable in 19 cases. Complications were mainly neurological (n=3) or related to the toxicity of the treatment(n=3).

Conclusion: Brucellar spondylodiscitis can be serious because of the neurological complications that it can cause. At the slightest diagnostic doubt, we should perform an MRI. And antibiotic treatment must be urgent and well-adapted with careful monitoring of patients.

Disclosure of Interests: None declared


SAT0466 HEPATITIS SAFETY OF ANTI-TUBERCULOUS TREATMENT IN SPONDYLODISCITIS

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Background: Tunisia is considered as a country with high tuberculosis endemicity. The anti-tuberculous treatment is quite long and binding and requires close hepatic monitoring.

Objectives: The purpose of this study was to highlight the hepatic safety of anti-tuberculosis treatment in tuberculous spondylodiscitis.

Methods: This is a retrospective descriptive study, over 20 years (1999-2019) collating cases of tuberculous spondylodiscitis in a rheumatology department. We studied the epidemiological, clinical, radiological and therapeutic aspects.

Results: Our study included 62 patients, 35 women and 27 men. Mean age was 56 years [16-86]. The diagnosis delay averaged 5.59 months [0.23-24]. Tuberculous contact was noted in 11.3% of the cases. Neurological abnormalities were noted in 16.1% of cases with spine compression in 3.2%. The tuberculosis skin test was positive in 29 cases and the Koch bacillus investigations in the sputum and the urine were positive in only 3 patients. Magnetic resonance imaging was performed in 71% of the patients, and mainly showed images of disc destruction with images of abscess, epiduritis and epidural extension. Infectious spondylodiscitis affected the lumbar spine in 66.1% of the cases, the dorsal spine in 14.51% of the cases and the cervical spine in 6.55% of the cases. It was bi-staged in 19.35% of the cases and bifocal in 17.74% of the cases.

Conclusion: Brucellar spondylodiscitis can be serious because of the neuropathy it can cause. The diagnosis delay averaged 5.59 months. Following the initial 4-drug regimen, most patients continued to receive a two-drug regimen with RMP and INH for a mean duration of nine months. Hepatotoxicity was seen in 13%: 11.4% of the patients had a history of cholestasis due to TB treatment, Only 2% of the patients had cytolysis. We needed to modify the treatment in 3.22%, and switch to triple anti-TB therapy based on Isoniazid, Rifampicin and ethambutol with a favorable evolution. No cases of hepatic insufficiency were noted.

Disclosure of Interests: None declared


SAT0465 VALUE OF SERUM PROCALCITONIN FOR THE DIAGNOSIS OF BACTERIAL SEPTIC ARTHRITIS IN DAILY PRACTICE IN RHEUMATOLOGY

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Background: Septic arthritis is a diagnostic and therapeutic emergency because of a high morbidity and mortality. Nevertheless, the etiologic diagnosis is often difficult.

Objectives: The aim of our study was to determine if serum procalcitonin was a discriminatory biomarker in case of arthritis of undetermined etiology.

Methods: Patients were separated in 5 groups: gouty arthritis, calcium pyrophosphate deposition arthritis, osteoarthritis or post-traumatic arthritis (“mechanical” arthritis), chronic inflammatory rheumatic arthritis, and septic arthritis. Levels of serum with blood cells, C-Reactive Protein and procalcitonin were measured.

Results: 98 patients were included: 18 in the “gout” group, 26 in the “calcium pyrophosphate deposition arthritis” group, 16 in the “mechanical” group, 18 in the “chronic inflammatory rheumatic” group and 20 in the “septic” group. The area under the receiver operating characteristic curve of with blood cells, C-Reactive Protein and procalcitonin levels to diagnose a septic arthritis were 0.69 (IC95% 0.55-0.83), 0.82 (IC95% 0.73-0.91), and 0.87 (IC95% 0.76-0.98) respectively. For a cut-off of 0.5 ng/ml, procalcitonin sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio and negative likelihood ratio were 65%, 91%, 65%, 91%, 7.2 and 0.4, respectively. Serum C-Reactive Protein and procalcitonin levels were correlated, were not different in septic arthritis with poly-arthritis than with mono-arthritis (p=0.05).

Conclusion: Serum procalcitonin is a useful biomarker in arthritis management with diagnosis performances higher than those of other biomarkers (with blood cells, C-Reactive Protein).

Disclosure of Interests: None declared


SAT0466 PNEUMOCCOCAL CELLULITIS AND FASCIITIS IN SYSTEMIC LUPUS ERYTHEMATOSUS: A SYSTEMATIC REVIEW

Martin Greci1, Iligo Rua-Figueroa1, Antonio Narango1, Sabrina Ghiglione2, Maria Celia Erausquin1, Juan Carlos Quevedo-Abeldeo1, Carlos Rodriguez-Lozano1, Cristina Almeida1, Paola Leon1, Estibaliz Loza2; 1Hospital Universitario de Gran Canaria Dr. Negrín., Las Palmas, Spain;2Complejo Hospitalario Universitario de Jaén - Materno Infantil – CHUIM. Las Palmas, Spain;3Instituto de Salud Musculoesquelética Innusac, Madrid, Spain

Background: Streptococcus pneumoniae (SPN) is an encapsulated gram-positive bacterium that can be found in the nasopharynx as part of the normal flora. However, it is the most common cause of community-acquired pneumonia in adults and can also cause invasive diseases such as bacterial meningitis, and otitis media. Pneumococcocal cellulitis and fasciitis...
are uncommon. Several factors are associated with a predisposition to infections in patients with Systemic Lupus Erythematosus (SLE).

**Objectives:** To describe and analyze all documented cases of cellulitis or fasciitis caused by SPN in SLE patients.

**Methods:** In the framework of the study of a 24-years-old woman that during the SLE onset presented left tight cellulitis and fasciitis caused by SPN, a systematic review was conducted (until September 2018). The search included terms to identify any SPN infection in SLE patients and all those articles that reported cellulitis or fasciitis were selected (Table 1).

Table 1. Flow chart.

| Total searched articles: 313 | - Medline 72, Embase 241, Cochrane 0. |
| - Selected: 8 | - Selected: 8 |
| Manual included articles: 1. |

**Results:** A total of 313 articles were obtained. Eight of them (1-8) and 1 article identified in a manual search (9) described a total of 15 cases presenting SLE and cellulitis or necrotizing fasciitis caused by SPN; our case is the 16th described.

Documented infections (n=16):

- Cellulitis (n=8): neck, face or chest (n=5, 62.5%); extremities (foot or hand) (n=2, 25%); breast (n=1, 12.5%).
- Fasciitis (n=8): neck, face or chest (n=5, 62.5%); tights (n=3, 37.5%).

**Description of the documented cases:**

- Demographic characteristics (n=13): female sex (n=11, 85%); <30 years of age at the moment of the infection (n=11, 85%).
- Time of SLE evolution at the moment of the infection (n=9): ≤ 1 month (n=3, 33.3%); ≤ 3 years (n=3, 33.3%); ≤ 8 years (n=3, 33.3%).
- Associated conditions (n=12): previous high doses of prednisone (n=5, 45%); recent respiratory symptoms (n=4, 33.3%); renal insufficiency (n=2, 16.6%); previous SPN infections (n=1, 8.3%); recent surgery in the affected area (n=1, 8.3%).
- Microbiological diagnosis (n=12): blood cultures (n=11, 91.6%); other cultures (n=1, 8.3%).
- Treatment (n=12): beta-lactams (n=12, 100%); intensive care support (n=6, 50%); surgical debridement (n=5, 41.6%).
- Outcome (n=15): death (n=3, 20%); recurrent SPN infections (n=2, 13.3%).

**Conclusion:** * - Pneumococcal cellulitis and fasciitis in SLE were predominantly presented in young women and in a high rate of cases during the disease onset.
- Almost half of the cases were previously treated with high doses of steroids. Nevertheless, no other potential predictors of pneumococcal cellulitis or fasciitis were identified; in addition, only one patient presented a previous surgery in the affected anatomical area, previous trauma were not described in any case, and a low number of cases reported associated respiratory symptoms. This supports the importance of the intrinsic immune dysregulation in SLE patients.
- Pneumococcal cellulitis and fasciitis in SLE patients present poor prognosis, requiring intensive care support and surgical debridement in a high rate of cases, and presenting a fatal outcome in a fifth of them.

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**Disclosure of Interests:** Martin Greco: None declared, Irigo Rua-Figueroa: None declared, Antonio Naranjo Grant/research support from: Amgen, Consultant for: UCB, Speakers bureau: Amgen, UCB, Sabrina Ghiglione: None declared, Maria Celia Erausquin: None declared, Juan Carlos Quevedo-Abeledo: None declared, Carlos Rodríguez-Lozano: None declared, Cristina Almeida: None declared, Paola León: None declared, Estibaliz Loza Grant/research support from: Roche, MSD, Pfizer, Abbvie, BMS, UCB, Actelion, Cenegene, Guntheral and Sanofi.

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**SAT0468** INFECTIOUS SPONDYLODISCITIS IN A SPANISH REGIONAL HOSPITAL BETWEEN 2000 AND 2018: 66 CASES

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**Background:** Spondylodiscitis have a large spectrum of clinical manifestations. The early diagnosis and treatment of this condition are essential to give the patient the best chance of a good outcome.

**Objectives:** To analyze the clinical characteristics, most frequent diagnostic methods and different treatments used in spondylodiscitis (SD) in our sanitary area.

**Methods:** Descriptive and retrospective study of patients with the diagnosis of infectious SD (clinical or microbiological) from 2000 to 2018. In each case we studied the presence of underlying diseases, an episode of infection in the previous 6 months, way of presentation, location, diagnostic methods, treatment and evolution, comparing among different etiologies.

**Results:** 66 patients were diagnosed of spondylodiscitis, 44 men (24-90 years: mean 71.7). 62 were pyogenic, 3 tuberculous (TBC) SD, and 1 candida. The patients with TBC were younger (mean age: 45.3; <0.05). An underlying disease was observed in 51 patients, specially Diabetes Mellitus (DM) (53% of SD). 4 patients were Rheumatoid Arthritis patients. A previous episode of bacteremia or a primary source of infection was identified in a 34.8% of the cases, obtaining a microbiological isolation in 50/66 (75.7%) SD (46 bacterial, 3 TBC and 1 Candida). The most frequent pathogens were Gram + (G+) (51% of the total SD) being S. aureus and S epidermidis responsible of 23/66 cases (34.8%). In the 94% of SD caused by G+, hemocultures positive were obtained, in comparison to a 55% of SD caused by G- (p=0.016).

The most frequent presentation symptoms were: lumbar pain (90%), fever (53%) and neurological deficit (19%). Leucocytosis was present in only a third of the SD, observing an increase of ESR and CRP in the pyogenic etiology (p no significative for low number of patients in SD group caused by TBC) and lower levels of hemoglobin, cholesterol and albumin. Lumbar area was affected in the 75.7% of SD (77% in G+ and 50% in G-). In a 13.6% of patients, more than one intersomatic space was affected, being visible the presence of an abscess in 47/66 cases (71.2%). It was necessary surgical treatment in 10/47 (21.2%). 5 patients died due to pathology related to SD (7.5%), without any correlation with a risk factor and other 5 presented a relapse in the subsequent months.

**Conclusion:** - The bacterial SD are the predominant group, being DM the most frequent risk factor.
  - The incidence of SD due to TBC and fungi is scarce in our environment, being absent the Brucella etiology.
  - The G+ SD usually have a previous associated bacteremia.
  - The majority of the patients had pain in the presentation, but only half of them had associated fever.
  - The most frequent location of SD was lumbar.
  - We established a 7.5% of mortality rate in our sanitary area.

**Disclosure of Interests:** None declared

REFERENCES

**Disclosure of Interests:** None declared DOI: 10.1136/annrheumdis-2019-eular.6234

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**SAT0469** THE IMPACT OF CHIKUNGUNYA VIRUS INFECTION ON QUALITY OF LIFE, FUNCTIONAL STATUS AND WORK ABILITY

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**Background:** Chikungunya virus (CHIKV) is a re-emergent arbovirus from the Alphavirus genus transmitted by Aedes species mosquitoes. The frequent feature of CHIKV disease is severe polyarthralgia, which is reported in more than 90% of cases. Musculoskeletal symptoms may persist in the subacute (> 3 weeks) and chronic (> 12 weeks) phases, causing critical physical impairment and significantly impacting the quality of life of patients.

**Objectives:** To assess the impact of CHIKV on pain, functional status, work ability and health-related quality of life (HRQoL) in the subacute and chronic phases of the disease.

**Methods:** Patients with a diagnosis of CHIKV disease (confirmed by PCR or serology) with persistent musculoskeletal symptoms after 4 weeks were referred to the Rheumatology outpatient clinic and followed up from April 2018 to January 2019. Evaluation questionnaires of pain (visual analogue scale – VAS), disability (Health Assessment Questionnaire – HAQ), HRQOL (Short-form 12 – SF-12) and work ability (Work Productivity and Activity Impairment-WPAI) were applied. The assessments were divided into 3 stages according to the time of disease: subacute from 4 to 12 weeks, chronic from 12 to 24 weeks and chronic with more than 24 weeks.

**Results:** Of the 69 patients analyzed, 76.81% were women, mean age 49.78 ± 14.24 years, 49.27% had some comorbidity (such as hypertension and diabetes), 26 were obese and 37.68% presented a previous musculoskeletal condition. Fifty-eight patients initiated follow-up in the subacute phase, in which the average pain was 6.84±1.9, mean HAQ of 1.59±0.57, mean Physical Health Composite Scale Score (PCS) of 26.81 ±14.3 and Mental Health Composite Scale Score (MCS) of 36.77±15.9. Of the 58 patients, 35 were employed and of these, 54.25% were absent from work during the previous week. Women presented higher scores in the mental component of SF-12 (<p=0.0215) and the presence of comorbidity related to higher values reported in the pain VAS (p = 0.026).

In the chronic phase of 12-24 weeks, 50 patients were evaluated, with mean pain 5.27 ± 2.22, HAQ 1.16 ± 0.81, PCS of 38.82±17.26 and MCS 43.72±17.13. Thirty-two patients were employed, of which 25% were absent the previous week. During this stage, women presented lower values of MCS (<p = 0.0245) and the presence of obesity was related to higher values in HAQ (p=0.0157). Finally, in the evaluation of the chronic phase after 24 weeks of evolution, we included 25 patients with the mean of pain 5.64 ± 2.3, HAQ 1.11 ± 0.49, PCS 36.72±19 and MCS 41.56±17.74. Fifteen of the 25 patients were employed and 33% were absent from work as the previous week. There was no significant difference between the groups evaluated after 6 months of evolution.

**Conclusion:** In this study, we demonstrated that the impact of chikungunya persist after 1 month of evolution in a large number of patients. The incapacity for work caused by the disease, represented by persistent rates of absenteeism at work in an economically active age group, further aggravates the magnitude of the problem.

**REFERENCES**

**Disclosure of Interests:** None declared DOI: 10.1136/annrheumdis-2019-eular.6234

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**SAT0470** RISK OF HOSPITAL ADMISSION DUE TO INFECTION IN PATIENTS UNDERGOING TREATMENT WITH BIOLOGICAL THERAPY: CASE-CONTROL STUDY

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**Objectives:** To know risk of admission due to infection in patients treated with biological drugs (DMARDs).

**Methods:** Case-control study, in patients admitted for infection, treated with DMARDs, from 2000-2018. As a control group, patients included, in treatment with conventional synthetic DMARDs (DMARDcs). General data (age, gender), disease (diagnosis, time evolution, DMARD, time in DMARDs, DMARDcs); and infection (time in DMARDs to infection, location of infection, more than one admission).

**Results:** Of 384 patients, 48 (13%) had DMARDcs. 51% had DMARDs and 49% had infection. Absent of SD, 4 patients, 48 (13%) and 32 (9%) treated with DMARDs and DMARDcs alone. When comparing patients admitted vs who do not, RA predominates and no differences in the treatment with DMARDs and/or DMARDcs, corticosteroids, type of DMARD or the infection.

**REFERENCES**
SAT0471 HIGH-RESOLUTION MELTING CURVE ANALYSIS: A RAPID AND PRAGMATIC APPROACH FOR SCREENING OF MULTIDRUG RESISTANT OSTEOARTICULAR TUBERCULOSIS (OATB)

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Background: Emergence of MDR in extrapolummary tuberculosis (EPTB) is a major concern in endemic areas. Timely diagnosis and screening of multidrug resistance in patients of Osteoarticular Tuberculosis (OATB) is a challenge.

Objectives: To evaluate the rpoB gene real time PCR (RT PCR) in synovial fluid/pus samples and its comparison with MPB64 and IS6110 RT PCR for diagnosis of OATB.

Methods: Real time PCR using IS6110, MPB64 and rpoB genes was carried out in 150 cases of OATB and in100 non TB control group. Out of these, 20 OATB cases were culture confirmed and 130 were clinically suspected cases. Phenotypic susceptibility testing for culture isolates was performed by standard proportion method. DNA extracted from samples of the culture confirmed cases and the suspected OATB cases confirmed by RT PCR were subjected to rpoB and katG HRM analysis for screening of MDR.

Results: The sensitivity of rpoB RT PCR, MPB64 RT PCR and IS6110 RT PCR was 86.5%, 86.5% and 76.5% respectively. All RT PCR were negative in the control group thus the specificity was 100%. HRM analysis detected rifampicin resistance in 10 cases of which, 8 (80%) were MDR while 2 (20%) were isolated rifampicin resistance. Of the 13 cases of isoniazid resistance detected by HRM analysis, 8(61.5%) were MDR while 5(38.46%) were isolated isoniazid resistant. HRM analysis detected an additional 4 MDR cases directly from the samples which were negative by culture. Subsequently, results of HRM analysis were confirmed by rpoB sequencing and mutation were observed at codon 531 (60%); 533 (16%); 516 (12%) and 526 (12%). KatG sequencing revealed mutation at codon 315(100%). There was 100% concordance in the results of phenotypic DST, sequencing results and HRM analysis.

Conclusion: rpoB and katG HRM analysis is a promising method in reliable and rapid screening of drug resistance in OATB cases in 90 minutes.

Disclosure of Interests: None declared


SAT0472 THE CONTRIBUTION OF MRI IN THE DIAGNOSIS OF INFECTIOUS SPONDYLODISCITIS

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Background: Infectious spondylodiscitis is a diagnostic and therapeutic emergency, and if there is any doubt, an MRI should be performed to support the diagnosis.

Objectives: The aim of our study is to highlight the role of MRI in the diagnosis of infectious spondylodiscitis.

Methods: This is a 20-year retrospective study (1999-2019) performed at a rheumatology department, collecting cases of infectious spondylodiscitis. We have identified the epidemiological, clinical, and radiological characteristics.

Results: Our study included 106 patients, 57 men and 49 women. The average age was 55 [16; 86]. Mean disease duration averaged 4.54 months [0.23; 24]. All patients had spinal pain: lumbar in 65.09% of cases, dorsal in 17% of cases and cervical in 6% of cases. Standard X-rays showed abnormalities suggestive of spondylodiscitis in 88.67% of cases. Magnetic resonance imaging was then performed in 76.41% patients and was pathological in all cases. The abnormalities found were paravertebral abscess in 23.58% of cases, epiduritis in 10.37% of cases and association of abscess and epiduritis in 32.07% of cases. The rest of the abnormalities noted were vertebral osteolysis (8.49%), spinal cord compression (9.43%) abnormalities of the intervertebral disc with narrowing and/or signal modification (4%). The abnormalities were monofocal in 82.07% of cases and bilocular in 13.2% of cases. 78.57% of bilocular lesions were objectified in tuberculosis spondylodiscitis. 82.07% of the spinal injuries were single-stage and 15.09% were bi-staged. 75% of these were of tuberculous origin. There were 2.63% of spondylodiscitises up to 3 stages and all were tuberculous.

Conclusion: MRI is a great diagnostic aid during infectious spondylodiscitis. It also allows to orient towards the etiological diagnosis.

Disclosure of Interests: None declared


SAT0473 MUSCULOSKELETAL STIFFNESS IN CHIKUNGUNYA DISEASE: DISTINCT FROM PAIN AND RELEVANT TO QUALITY OF LIFE

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Background: Musculoskeletal stiffness is reported to be frequent following chikungunya infection and can persist for many months after infection. However, stiffness severity and its impact is not well characterised in this disease. A stiffness patient reported outcome instrument has been developed for use in rheumatoid arthritis.

Objectives: Our objective was to assess the use of this questionnaire and importance of musculoskeletal stiffness in a cohort of chikungunya patients.
patients with chronic joint symptoms in the Atlántico Department of Colombia.

Methods: Sixty-seven patients with chronic arthralgia and 15 patients without arthralgia were followed up a mean of 40 months after chikungunya infection. The patients came from a larger cohort of 500 patients previously followed up 20 months after infection. Those consenting to a 40-month in-person follow-up were included here. Tender joint counts, a pain intensity visual analogue scale (VAS), Health Assessment Questionnaire-Disability Index (HAQ-DI) and the EuroQol overall health VAS (EQ-VAS) were completed. A 21-item musculoskeletal stiffness questionnaire (MSQ) was completed and summarized as percentage scores for overall stiffness and its components: stiffness severity, physical impact and psychosocial impact.

Results: The 82 patients (12 male and 70 female) had a mean age 51±14 years. Forty-two out of sixty-seven patients with arthralgia and 3/15 patients without arthralgia reported musculoskeletal stiffness. Stiffness in those patients had a median severity of 28% (IQR 0–42). An impact of their stiffness on physical activities was reported by 39/45 patients (87%) and psychosocial impact by 32/45 patients (71%). Overall MSQ score was a median of 16% (IQR 0–34). Mean tender joint count in patients reporting arthralgia was 6.2±7.1, mean pain intensity 65±20 out of 100, mean HAQ-DI = 0.54±0.52, and a mean EQ-VAS = 61±26 out of 100. Overall stiffness scores were poorly correlated with tender joint counts (r²=0.17) and pain intensity (r²=0.22). Stiffness scores were more strongly associated than arthralgia with overall health and disability indicators in patients with chikungunya disease. The MSQ is a potentially useful instrument for assessing symptoms in chronic chikungunya disease.

Conclusion: Musculoskeletal stiffness following chikungunya infection is distinct from the persistent arthralgia usually reported. It does not necessarily occur in the same patients and is poorly correlated with joint pain severity. Stiffness, as measured by this questionnaire, may be more strongly associated than arthralgia with overall health and disability indices in patients with chikungunya disease. The MSQ is a potentially useful instrument for assessing symptoms in chronic chikungunya disease.

Disclosure of Interests: Hugh Watson Shareholder of: Sanofi, Employee of: Sanofi, Sarah Tritsch: None declared, Liliana Encinales: None declared, Andres Cadena: None declared, Carlos Cure: None declared, Alejandro Rico Mendoza: None declared, Aileen Chang: None declared


SEPARATE POLICY STATEMENT

Echinococcosis and Auto-Immune Inflammatory Arthritis; Report of 8 Cases AND REVIEW OF THE LITERATURE

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Background: The prevalence of Echinococcosis in Western Europe and Switzerland has been rising in the past 20 years: <30 cases per year have been reported since 2005 (1). A few case reports (2) and some experimental animal studies (3) have suggested that the immunosuppression linked to inflammatory arthritis and their treatments could favor the development and the growth of parasitic lesions. On the other hand, a recent French study (4) has shown that the prevalence of Echinococcosis in arthritis patients was closer to the normal population. The characteristics of the parasitic disease were quite similar whether inflammatory arthritis was present or not.

Objectives: To evaluate the yearly recent incidence of this disease among patients with inflammatory arthritis in Switzerland and to search

REFERENCES


Acknowledgement: Thanks to my colleagues who help me in writing the paper and analyzing all the data.

Disclosure of Interests: None declared


SAT0474 AUTOIMMUNE MANIFESTATIONS OF VISCERAL LEISHMANIASIS IN CHINESE PATIENTS

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Background: Visceral leishmaniasis (VL), caused by the protozoan Leishmania species, is the most severe form of leishmaniasis. The parasite migrates to the internal organs such as the liver, spleen, and bone marrow, and if left untreated, will almost always cause the host to die [1]. Due to polyclonal B cells activation, VL may present signs and symptoms resembling those of rheumatic diseases, especially systemic lupus erythematosus (SLE) [2–4]. This can sometimes lead to mis-diagnosis and treatment of corticosteroids.

Objectives: To analyze 27 Chinese VL patients retrospectively and focused on their autoimmune findings that could help clinicians to differentiate VL from SLE.

Methods: 27 in-hospitalized VL patients in our hospital from 2006 to 2015 were analyzed. VL was diagnosed by the presence of high titers of parasitic disease were quite similar whether inflammatory arthritis was present or not.

RESULTS: The basic characteristics and laboratory findings of the 27 patients were summarized in Table 1. All patients had hepatitis and the liver was more than 130%.

All of the patients had positive anti-Sm antibody and only 1 had anti-dsDNA antibody. 85.5% had increased IgG level and none had decreased C3 or C4.

All patients were cured with sodium stibogluconate, and ANA titers decreased C3 or C4.

None of the patients had positive anti-Sm antibody and only 1 had anti-dsDNA antibody. 89.5% had increased IgG level and none had decreased C3 or C4.

None of the patients had positive anti-Sm antibody and only 1 had anti-dsDNA antibody. 89.5% had increased IgG level and none had decreased C3 or C4.
for any interaction between arthritis, the treatment of arthritis and development and evolution of the echinococcosis.

Methods: We collected all the cases with the diagnosis of echinococcosis among the patients regularly followed and treated for inflammatory arthritis in three different tertiary rheumatology centers of Westen Switzerland (1.7 million inhabitants, 5000 arthritis pts).

Results: Between 2012 and 2018, 8 cases of echinococcosis (1.3 case/year/5000pts) could be found. The estimated yearly incidence among this arthritis population appears therefore to be significantly higher (p=0.0001) than the one reported in the general population in Switzerland (30/8000000 inhabitants). Figure summarized the relation between the parasitic and the inflammatory disease. Different types of inflammatory arthritis were implicated. Previous and ongoing arthritis treatments comprised also different types of biologics. In 6/8 cases, the parasitic disease was asymptomatic and limited to a single organ, a proportion much higher than what is usually found in the general population. In 2 of them, the discovery was very close in time to the diagnosis of arthritis and treatment initiation (<8 months), 4 pts could be treated by surgery alone. 6 continued their treatments for arthritis. No evidence of relapses after surgery (4 pts) or progression under albendazole (4 pts, median follow-up: 44 months) was found.

Conclusion: The incidence of echinococcosis in autoimmune arthritis appears to be higher than in general population but remains very low. Outcome seems not to be affected by inflammatory arthritis and their treatments but the long-time effects of the combination between arthritis treatments and albendazole need to be further evaluated.

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4: Gauchet A, et al; Clinical Infectious Diseases (2014),1095–104

Disclosure of Interests: Pascal Zufferey: None declared, Zambaz camille: None declared, Rudiger Muller: None declared, Boillat-Blanco Noemie: None declared, Thomas Huguele Grant/research support from: AbbVie, Lilly, Novartis and Pfizer, Speakers bureau: AbbVie, Lilly, Novartis and Pfizer, Hasler paul: None declared, Peter Villiger: None declared


Paediatric rheumatology

SAT0476 JUVENILE IDIOPATHIC ARTHRITIS IN SINGAPORE: A 10-YEAR CLINICAL EXPERIENCE

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Background: Juvenile Idiopathic Arthritis (JIA) is the commonest inflammatory arthritis of childhood worldwide.

Objectives: To describe the incidence, clinical characteristics and experiences with JIA in Singapore over a 10-year period.

Methods: A prospective study was conducted in KK Women’s & Children’s Hospital and National University Hospital, Singapore from Jan 2009-Dec 2018. JIA was defined and classified according to ILAR criteria1. Demographics and clinical information were collected for every patient diagnosed with JIA.

Results: 379 children were diagnosed with JIA (60.2% male, 71.2% Chinese). Average estimated incidence was 5.8 per 100000yr. Clinical characteristics and treatment used are summarized in Table 1. Table 1, “Median (IQR), Rest expressed in (%).

Disease modifying anti-rheumatic drugs (DMARD) were used in 67.8%, and younger age of diagnosis (p=0.002), longer lag time (p=0.004), males (p=0.018) and ERA (p=0.043) predicted their use. 36.3% required biologics, and males (p=0.047), longer lag time (p=0.037) and HLA-B27 positivity (p=0.030) were associated with their use. Uveitis incidence was 2.9%; 54.5% had oligoarthritis, 36.4% ERA, 9.1% polyarthritis (RF+). Younger age at JIA diagnosis was associated with uveitis (p=0.030).

Conclusion: ERA is the commonest subtype of JIA in our cohort, explaining the male predominance and higher HLA-B27 positivity as compared to the West2. Longer lag time was associated with DMARD and biologic use, likely due to more severe disease at presentation. HLA-B27 association with biologic use may predict ineffectiveness of DMARD. Uveitis incidence was low as compared to Western literature that cites a prevalence of 11-30%3,4. Young age at diagnosis is a risk factor for uveitis. Interestingly, ANA-positivity and female gender were not associated with uveitis cases.

REFERENCES

Disclosure of Interests: Poh Lin Pauline Chan Ng: None declared, Pei Ling Ooi: None declared, Elizabeth Ang: None declared, Lee Keen Lin: None declared, Sook Fun Hoh: None declared, Lena Das: None declared, Yen Xin Book: None declared, Thaschawee Arkachaisri Speakers bureau: Abbvie Pte, Ltd


SAT0477 QUALITY OF LIFE IN SUBJECTS WITH PRE-PUBERTAL ONSET SYSTEMIC LUPUS ERYthematosus

Brand Stevens, Martha Rodriguez, Amy Rakeshw, Kathleen O’Neil. Indiana University Health, Pediatrics, Indianapolis, United States of America

Background: Systemic Lupus Erythematosus (SLE) can be a severe disease, especially when diagnosed in childhood. Onset prior to puberty (Tanner stage II) is rare, and less is known about the impact SLE has on this pediatric population. We assessed clinical and quality of life (QOL) measures in a prepuberal SLE onset cohort to better globally understand the burden of this disease in this group.

Overall Systemic Oligoarticular Polyarticular (RF -) Polyarticular (RF +) Psoriasic ERA Undifferentiated

<table>
<thead>
<tr>
<th></th>
<th>Overall</th>
<th>Systemic</th>
<th>Oligoarticular</th>
<th>Polyarticular (RF -)</th>
<th>Polyarticular (RF +)</th>
<th>Psoriasic</th>
<th>ERA</th>
<th>Undifferentiated</th>
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<tr>
<td>N</td>
<td>379 (100)</td>
<td>32 (8.4)</td>
<td>133 (35.1)</td>
<td>47 (12.4)</td>
<td>13 (3.4)</td>
<td>10 (2.6)</td>
<td>137 (36.1)</td>
<td>79 (21.1)</td>
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<tr>
<td>Onset age, yr</td>
<td>10.4</td>
<td>6.6</td>
<td>8.5</td>
<td>7.9</td>
<td>9.9</td>
<td>13.3</td>
<td>12.2</td>
<td>9.7</td>
</tr>
<tr>
<td>(6.6-13.3)</td>
<td>(4.5-10.1)</td>
<td>(5.1-12.1)</td>
<td>(3.5-12.8)</td>
<td>(7.1-13.3)</td>
<td>(6.2-14.3)</td>
<td>(10.0-14.3)</td>
<td>(6.2-13.5)</td>
<td></td>
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<tr>
<td>Diagnosis age, yr</td>
<td>10.9</td>
<td>6.4</td>
<td>9.0</td>
<td>8.6</td>
<td>10.2</td>
<td>13.8</td>
<td>12.6</td>
<td>11.2</td>
</tr>
<tr>
<td>(7.1-14.0)</td>
<td>(4.1-10.2)</td>
<td>(6.0-13.4)</td>
<td>(3.7-13.3)</td>
<td>(7.4-15.7)</td>
<td>(10.7-15.3)</td>
<td>(10.7-15.4)</td>
<td>(9.2-15.1)</td>
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<tr>
<td>Lag time, mth</td>
<td>2.9</td>
<td>0.7</td>
<td>3.1</td>
<td>2.6</td>
<td>5.0</td>
<td>3.6</td>
<td>8.3</td>
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<tr>
<td>(1.0 – 7.4)</td>
<td>(0.3-1.2)</td>
<td>(1.1-7.6)</td>
<td>(1.6-9.0)</td>
<td>(2.1-4.6)</td>
<td>(1.2-2.4)</td>
<td>(1.2-8.1)</td>
<td>(1.6-8.5)</td>
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</tr>
<tr>
<td>ANA</td>
<td>124</td>
<td>11 (34.2)</td>
<td>50 (40.3)</td>
<td>23 (48.9)</td>
<td>5 (38.5)</td>
<td>8 (50.0)</td>
<td>27 (20.0)</td>
<td>0 (0.0)</td>
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<tr>
<td>Positive</td>
<td>32 (253)</td>
<td>0 (0.0)</td>
<td>4 (3.1)</td>
<td>2 (4.3)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>104 (2)</td>
<td>2 (28.6)</td>
</tr>
<tr>
<td>Negative</td>
<td>23 (6.1)</td>
<td>5 (17.2)</td>
<td>2 (1.5)</td>
<td>0 (0.0)</td>
<td>13 (100.0)</td>
<td>0 (0.0)</td>
<td>2 (1.5)</td>
<td>1 (4.3)</td>
</tr>
<tr>
<td>HLA-B27</td>
<td>112</td>
<td>0 (0.0)</td>
<td>4 (3.1)</td>
<td>2 (4.3)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>104 (2)</td>
<td>2 (28.6)</td>
</tr>
<tr>
<td>Positive</td>
<td>28 (396)</td>
<td>0 (0.0)</td>
<td>6 (4.5)</td>
<td>1 (2.1)</td>
<td>0 (0.0)</td>
<td>0 (0.0)</td>
<td>4 (2.9)</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Negative</td>
<td>257 (67.8)</td>
<td>21 (8.6)</td>
<td>47 (17.8)</td>
<td>40 (15.1)</td>
<td>13 (100.0)</td>
<td>10 (100.0)</td>
<td>121 (88.3)</td>
<td>57 (17.4)</td>
</tr>
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<td>145 (38.3)</td>
<td>17 (53.1)</td>
<td>17 (53.1)</td>
<td>17 (53.1)</td>
<td>9 (62.9)</td>
<td>3 (30.5)</td>
<td>79 (57.7)</td>
<td>3 (42.9)</td>
</tr>
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AFTER 24 MONTHS OBSERVATION PERIOD THE PATIENTS RELATED OUTCOMES IMPROVE SIGNIFICANTLY IN THE JUVENILE SCLERODERMA INFECTIONS COHORT. WWW.JUVENILE-SCLERODERMA.COM


Support: NIAMS RO3AR52345, Michael Jan Barlin Foundation, NIAID R56, The University of Indiana Department of Pediatrics and the CARRA-AF 2018 Large Research Grant


SAT0478

School functioning domain had the worst QOL measure with the greatest number of children impacted (Table). Active arthritis was associated with lower mean scores in Physical health (p=0.007), PedsQL Core total (p=0.048), Pain and Hurt (p=0.002), Daily Activities (p=0.003), Treatment (p=0.002), Worry (p=0.036), and PedsQL Rheumatology total (p=0.001). There was no association with QOL measures for rash, alopecia, or laboratory markers. Disease damage on SLICC/ACR DI was associated with greater impact on the Worry domain (mean 64.3 vs 88.1, p=0.02).

Conclusion: Children with pre-pubertal SLE onset report significant impacts on QOL regarding school. The disease manifestation affecting the most QOL domains was arthritis, whereas skin manifestations, while common, did not demonstrate an impact on QOL. This is the first study to specifically address quality of life for children who develop SLE prior to pubertal development.

REFERENCES
**UPDATE FROM THE JUVENILE SCLERODERMA CHRONIC KIDNEY DISEASE IN PATIENTS WITH**

Anjali Patwardhan, Yosef Uziel, Nicola Helmus, Kathryn Torok, Valda Stanevicha, Filivio R. Sztajnbok, Maria T. Teren, Ekaterina Alexeeva, Jordi Anton, Maria Katsiks, Vanessa Smith, Tadej Avcin, Rolando Cinaz, Mikhail Kostik, Thomas Lehman, Walter Alberto Silveutenes-Giraldo, Simon Appenzeller, Mahesh Janarthanan, Monika Molf, Dana Nemcova, Maria Jose Santos, Dienneke Schonenberg, Cristina Battagliotti, Lillemor Bernstoff, Blanca Bica, Juergen Brunner, Patricia Costa Reis, Despina Eleftheriou, Lora Harel, Gerd Horneff, Tilmann Kallinich, Dragana Lazarevic, Kirsten Minden, Susan Nieman, Farzana Nuruzzaman, Anjali Palwardhan, Yosef Uziel, Nicola Helmus, Hamburger Zentrum für Kinder-und-Jugendrheumatologie, Hamburg, Germany, Deutsches Rheuma-Forschungszentrum (DRFZ), Berlin, Germany, JSSc Collaborative Group, Hamburg, Germany

**Background:** Juvenile systemic sclerosis (JSSc) is an orphan disease with a prevalence of 3 in 1,000,000 children. There are limited data regarding the clinical presentation of JSSc. The Juvenile Systemic Sclerosis Inception Cohort (JSSIC) is a multinational registry that prospectively collects information regarding patients with this disease in a standardized manner.

**Objectives:** Evaluation of the JSSc patients at the time of inclusion in the JSSIC.

**Methods:** Patients were included in the JSSIC if they fulfilled the adulthood classification criteria, if they presented the first non Raynaud symptom before 16 years old and if they were younger than 18 years old at the time of inclusion. Patients’ characteristics at time of inclusion were evaluated.

**Results:** Currently, the cohort includes 120 patients, being 89% Caucasian and 80% female. The majority had diffuse subtype (74%) and 18% had overlap features. The mean age of onset of Raynaud phenomenon was 9.7 years in the diffuse subtype (dJSSc) and 10.7 years in the limited subtype (lJSSc). The mean age of non-Raynaud's symptoms was 10.0 years in the dJSSc and 11.4 years in the lJSSc. Mean disease duration time of inclusion was 3.4 years in the dJSSc and 2.4 years in the lJSSc group. Mean Modified Rodnan skin score was 17.5 in the dJSSc and 7.3 in the lJSSc (p=0.002). Gotton papulea were significantly more common in the dJSSc compared to lJSSc group (29% vs 6%, respectively) (p=0.011). History of ulceration was significantly more common in the dJSSc than in the lJSSc group (57% vs 30%, respectively) (p=0.004). FVC<80% occurred in 31% in the dJSSc and 24% in the lJSSc group (p=0.55). Pulmonary hypertension assessed by echocardiogram occurred around 7% in both groups. No systemic hypertension or renal crisis was reported. Gastrentestinal involvement occurred in 39% in the dJSSc and in 26% in the lJSSc (p=0.176). Number of joints with decreased range of motion was observed in approximately half of patients in both groups. Muscle weakness with joint contractures was present in 18% in the dJSSc and 38% in the lJSSc group (p=0.271). Tendon friction rub was present in 11% in dJSSc and 4% in the lJSSc group. dJSSc patients had significantly worse scores for physician global disease activity (VAS 0-100) (41 vs 30) (p=0.020) and for physician global disease damage (VAS 0-100) (37 vs 18) (p=0.001). Patient judgment of disease activity and damage was similar in both subtypes. ANA positivity was 88% in both groups. Anti-Scl70 was positive in 33% in dJSSc and 37% in the lJSSc group. Anticentromere positivity occurred in 3% in the dJSSc and 10% in the lJSSc group. ESR was elevated in 30% in dJSSc compared to 18% in the lJSSc group. DMARDs were used in 86% of the patients.

**Conclusion:** In this large cohort of JSSc patients there were surprisingly not many significant differences between dJSSc and lJSSc. According to the physician global scores the dJSSc patients have a significantly more severe disease.

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**SAT0480 CHRONIC KIDNEY DISEASE IN PATIENTS WITH JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS: EVIDENCE FROM A SINGLE CENTRE**

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**Background:** Estimated 10–20% of all patients with systemic lupus erythematosus (SLE) develop clinical disease before the age of 18 years and are therefore classified as juvenile-onset SLE (JSLE). JSLE is characterised by a higher prevalence of lupus nephritis, compared to adult-onset SLE (1). Chronic kidney disease (CKD) refers to a state of irreversible kidney damage and/or reduction of kidney function that is associated with progressive loss of function over time. Lupus nephritis does not always lead to CKD. However, when it does it is associated with increased morbidity and mortality (2).

**Objectives:** We aimed to identify clinical and laboratory predictors of CKD development in JSLE patients by comparing the baseline characteristics of JSLE patients with and without CKD to ascertain if there are any significant differences between the two groups.

**Methods:** This is a single-centre retrospective study, who included patients reviewed in our young adult and adolescent clinics. All data were analyzed descriptively. Mann-Whitney U or Chi-square test were performed to compare the characteristics between the patients with and without CKD. We used the Pearson’s (r) or Kendall’s τ (tau) correlation to examine if there is any association between the CKD and the baseline characteristics.

**Results:** We identified 44 JSLE patients, out of which 17 (39%) fulfilled the diagnostic criteria for CKD at their last clinical review. The stages of CKD varied from 2 to 5. All patients with CKD also had lupus nephritis, compared to patients without CKD. The baseline characteristics are detailed in the table below. There were statistically significant differences in the treatments used for patients with and without CKD. As expected, the highest dsDNA levels were higher in patients with CKD (p=0.03). There was also a positive correlation between raised levels of dsDNA and the development of CKD (p=0.008). We also found a negative moderate correlation (r=-0.439) between the presence of RF and CKD (p=0.04).

**Conclusion:** Acknowledging the limitations posed by this small study, we identified a negative moderate correlation between the presence of RF and CKD, which has also been reported in the literature before (3). We cannot conclude that RF exerts a protective effect against renal disease in SLE, because of the many confounders that might account for a decreased RF in JSLE. Further research using a large JSLE cohort enabling multivariate logistic regression is recommended. dsDNA antibody levels are a measure of disease activity in lupus nephritis and therefore this might explain why patients who developed CKD were noted to have higher anti-dsDNA levels, in comparison with the patients who did not develop CKD.

**REFERENCES**

Disclosure of Interests: None declared

SAT0482 TREAT-TO-TARGET STUDY FOR IMPROVED OUTCOME IN POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS
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Background: Evidence suggests that early effective treatment is important to minimize the burden of Juvenile idiopathic arthritis (JIA). We hypothesize that a guided-treat to target (T2T) approach as recommended by the German Society for Pediatric Rheumatology (1) is superior to routine care in polyarticular JIA (pJIA) in terms of reaching minimal disease activity and remission after 12 months of treatment.

Objectives: To assess the clinical benefit in subjects with pJIA treated in compliance with national recommendations measured by rates of patients reaching JADAS remission (<1), JADAS minimal disease activity (MDA) (<3.8), JADAS acceptable disease status (<5.4).

Methods: After informed consent, patients with early disease (diagnosis ≤12 months) and active (JADAS ≥3) pJIA were enrolled. Initially, all patients received methotrexate (MTX). Targets for treatment were defined by the level of improvement and are progressively more rigorous with ongoing treatment. Failure to meet a defined target required treatment modification of specified intervals. The choice of biologic was made by shared decision between the investigator and the patient/parent and not influenced by the protocol. Minimal treatment target defined as recognizable improvement of disease activity (2) was demanded after 3 months, JADAS acceptable disease status at month 6, JADAS MDA at month 9 and JADAS-remission at month 12. T2T Patients were 1:4 matched to a pJIA cohort with unguided therapy documented by the BIKER-registry.

Results: Altogether 62 patients (16 males, 26% with non-systemic JIA (46/9 RF negative/positive polyarthritis, 3 extended Oligoarthritis, 1 ERA, 1 PsA) were included (mean age 9.4±4.8 years, disease duration 0.5+/−0.6 years). At month 3; 49 (79%) patients showed JADAS improvement. In 13 (21%) treatment with a biologic was started. At month 6, 45/56 (80%) reached JADAS acceptable disease. In 6 (11%) a biologic agent was started. At month 9, 41/48 (85%) reached JADAS acceptable disease and 38/48 (79%) reached JADAS MDA. In 4 (10.6%) a biologic agent was started and the two patients switched biologics.

So far, 52 patients completed 12 months of observation. 4 patients did not start a biologic although mandatory according to protocol and were excluded. JADAS MDA was reached by 39/48 (81%) and JADAS remission was reached by 22/48 (46%). Compared to the matched control cohort, upon T2T guidance significant more patients reached JADAS MDA (81% vs. 60%; odds 2.9[1.3-6.3]; p=0.0006) and more patients reached JADAS remission (46% vs. 34%; odds 1.6[0.9-3.0]; p=0.15). During the first 12 months of treatment, the T2T approach lead to a significant increase of use of biologics (46% vs. 21%; odds 3.2[1.7-6.3]; p=0.004).

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remission after 12 months of treatment. Interestingly, about half of patients did not need to be treated with a biologic to reach predefined T2T (2). Thus, the early treatment escalation seems advantageous indicating a window of opportunity to successfully treat polyarticular JIA.

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SAT0483
COMPARISON OF THE CLINICAL DIAGNOSTIC CRITERIA AND RESULTS OF THE NEXT GENERATION SEQUENCE GENE PANEL IN PATIENTS WITH PERIODIC FEVER

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Background: Autoinflammatory diseases (AID) are a group of hereditary diseases characterised by inflammation periods accompanied with clinical findings such as fever, skin rash, lymphadenopathy, abdominal pain, musculoskeletal symptoms, and with sign of inflammation in the blood. Each disease has own typical clinical findings and they are associated with mutations in specific genes such as in MEFV gene in familial Mediterranean fever (FMF), MVK gene in mevalonate kinase deficiency (MKD), TNFRSF1A gene in TRAPS and NLRP3 gene in cryopyrin associated periodic fever syndrome (CAPS). There are also patients exhibit the incomplete phenotype of a disease or overlap signs of more than one AID. The diagnosis of these patients have difficult and may not be possible by a single target gene analysis. Screening of the periodic fever syndromes (PFS) genetic panel including various AID genes may be beneficial to define the atypical cases.

Objectives: The aim of this study was to compare the phenotypic diagnoses of the genotypic results obtained from the PFS genetic panel, which studied in patients with phenotypic findings of AIDs except the FMF, such as MKD, TRAPS and CAPS.

Methods: This is a prospective study and conducted between June 2016 and December 2018. Patients who met ‘The Eurofever clinical diagnostic classification criteria’ for MKD, TRAPS and CAPS were included in the study. Next-generation sequencing (NGS) analysis was performed including 8 genes (MEFV, MVK, NLRP3, NLRP12, TNFRSF1A, TNFRSF1A1, LPIN2 and PSTPIP1) in 37 patients with phenotypic findings of MKD, TRAPS or CAPS. The patients phenotypic preliminary diagnoses and genotypic results were compared.

Results: Thirty seven patient included in the study who met the clinical diagnostic criteria for MKD, TRAPS or CAPS. As a result of clinical signs: 19 patients were diagnosed with MKD, 10 were TRAPS and 8 were CAPS.

In the PFS genetic screening panel of 19 patients with phenotypic diagnosis of MKD, disease causing mutation was found in 8 patients in MVK gene, in 3 patients in MEFV gene, in 2 patients in NLRP12 gene and in 1 patient in TNFRSF1A gene. No pathogenic mutation was shown in 3 patients and genetic variants of uncertain significance (VUS) in different genes were shown in two patient.

In the result of PFS panel of 10 patients with phenotypic diagnosis of TRAPS, disease causing mutation was found in 5 patients in MEFV gene and in 2 patients in TRAPS gene. No pathogenic mutation was identified in 3 patients. In 8 patients who were diagnosed phenotypically as CAPS; disease causing mutation was found in 3 patients in NLRP3 gene, in 2 patients in NLRP12 and in one patient in MEFV. No mutation was detected in remaining two patient.

The final diagnosis was made by both phenotypic and genotypic data. In 37 patients (phenotypically 19 MKD, 10 TRAPS, 8 CAPS), respectively; 8 had MKD, 9 had FMF, 3 had CAPS, 3 had TRAPS, 4 had FCAS2 and 10 had undifferentiated PFS.

Conclusion: In our study, we have shown that clinical diagnostic criteria may not always be sufficient to establish the correct diagnosis. In case of clinical suspicion or in the presence of more than one autoinflammatory disease findings, NGS analysis may help to determine the diagnosis.

Disclosure of Interests: We are grateful to all participating children and their families. Ethics committee approval was received from the Institutional Review Board of Umraniye Training and Research Hospital. All the participants and their legal guardians were informed, and their written consent was obtained. Disclosure of Interest: None Declared

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SAT0484
QUALITY OF LIFE IN JUVENILE IDIOPATHIC ARTHRITIS PATIENTS ASSOCIATED UVEITIS: DO WE NEED A NEW ASSESSMENT QUESTIONNAIRE?

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Background: Uveitis, the most common extra-articular manifestation in juvenile idiopathic arthritis (JIA), occurs in 10-20% of patients. Although presence of uveitis within JIA-U (JIA-U) improved, complications still cause severe impairment of visual function in 25-33% of children that affects their psychophysical and psychosocial development and quality of life (QoL).

Objectives: To study the QoL and its dimensions in children suffering from JIA-U as well as to investigate is there any difference in childhood’s and parent’s perception of disease between the group of children with JIA-U and children with JIA without uveitis.

Methods: The study included 42 children with JIA and their parents. Patients were divided into two groups. The first consisted of 21 children with JIA-U and the second of 21 children with JIA and no uveitis. Both groups of patients and their parents filled the Juvenile Arthritis Multidimensional Assessment Report questionnaire (JAMAR) for monitoring and assessing the health status of children with JIA. The variables used to test differences were: QoL, functional ability, pain level, disease activity estimation, and current emotional state of the child. The significance of differences between groups of children and parents was verified by the independent-samples t-test. The Pearson correlation coefficient was used for measurement of the strength of the linear relationship between variables.

Results: There were no statistically significant differences in the JIA-U group and the control group in either of the examined variables. Although there is a tendency of higher scores in children with JIA-U, which indicates their worse functioning, higher pain intensity and worse current emotional state, these differences were not statistically significant. Two groups did not differ significantly in the assessment of their own overall functional ability, which was associated with experienced pain intensity. Stronger pain intensity was associated with dysfunction (r = 0.642, p
<0.01) while a lower level of QoL was associated with more intense pain (r = 0.542, p <0.01) and poor current emotional state (r = 0.401, p <0.05). The activity of the disease in children was not significantly related to any determinant of the QoL. In contrast to children, parents of children with JIA estimated current emotional state of their children significantly worse (t = 2.05, p <0.05) and the overall level of functioning significantly lower than parents whose children did not have uveitis (t = 2.03, p <0.05).

Conclusion: Since children with JIA evaluated the QoL equally well, whether they had uveitis or not, we can conclude that they are psychologically well adapted to their health status and cope well with different levels of pain. Unlike children with uveitis, their parents evaluated the current emotional state and overall functionality significantly worse compared to parents of children who did not have uveitis. These results support a need for the development of new uveitis specific questionnaires that will enable us better identification of patient’s requirements. It is necessary to implement a holistic and multidisciplinary approach to assess the emotional functioning of the children and their families, and to devise appropriate psychosocial interventions for continuing support for ill children and their families.

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treatment of systemic-onset and polyarticular course juvenile idiopathic arthritis (JIA), and is used off-label in other treatment refractory inflammatory diseases. Real-world data regarding tolerance of TCZ in children are scarce.

**Objectives:** To assess the incidence rate and type of serious adverse events in children treated with TCZ.

**Methods:** A single-center retrospective review of all consecutive patients receiving TCZ in the pediatric rheumatology division from 01/2007 to 12/2018 was performed. Inclusion criteria were a diagnosis of inflammatory rheumatic disease and treatment with at least one dose of TCZ. Patients with missing data were excluded. Serious adverse events (SAE) were defined as a life-threatening event and/or an event requiring hospital admission, leading to permanent disability or treatment discontinuation.

**Results:** A total of 70 children (39 females) were included. Thirty children had systemic JIA, 25 polyarticular course JIA, 14 systemic inflammatory disorders such as autoinflammatory syndromes and one patient severe refractory idiopathic uveitis. Median age at diagnosis was 4.2 years (IQR 2.9 – 7.3). The majority of children had received prednisone (n=56), and/or at least one biologic agent (n=63) prior to TCZ initiation. At TCZ start, children had a median age of 8.9 years (IQR 4.9 – 12.3) and disease duration of 3.2 years (IQR 0.9 – 7.4). TCZ was initiated at a 2-week interval in 44 children, 28 children received TCZ every 4 weeks. Fifty-eight children received concomitantly another immunosuppressive agent (prednisone (n=47) and/or methotrexate (n=20) and/or various other drugs (n=5)). A median of 26 TCZ doses were given per child (IQR 7 – 48). TCZ exposure was 146.8 patient years. Twenty-two SAE were observed in 18 (26%) children (SAE 14.9/100 patient years): 8 severe infusion reactions, 7 serious infections, 3 cutaneous reactions (toxic epidermal necrolysis, cutaneous vasculitis, scleroderma-like skin thickening with fasciitis), two macrophage activation syndromes, and one abnormal hepatic function and severe dizziness each. Infusion reactions occurred most frequently during the first few infusions (median during 4th infusion, IQR 3 – 5). All patients with infusion reactions had either systemic JIA (n=4) or another autoinflammatory disease (n=4). At time of infusion reaction, all children (8/8) had active disease, 7/8 had a concomitant treatment with prednisone and 2/8 additionally with cyclosporine. At last follow up, 35 (50%) children were still on TCZ, the other 35 had discontinued TCZ: 4 for remission, 13 because of inefficacy, 12 because of side effects, 3 because of both inefficacy and side effects, and 3 for other reasons. No death occurred during TCZ treatment; two patients with systemic inflammatory disease, in whom TCZ had been inefficient, died from uncontrollable disease 13 and 15 months after TCZ discontinuation, respectively.

**Conclusion:** In this cohort, serious adverse events were observed in a quarter of children with half of them having severe infusion reactions. Higher incidence rates of severe infusion reactions were observed in children with systemic JIA or autoinflammatory diseases. Ongoing careful monitoring of patients treated with TCZ, especially those with important systemic inflammation is required.

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THE FRENCH PAEDIATRIC COHORT OF CASTLEMAN DISEASE

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Background: Castleman disease (CD) is a very rare non-malignant lymphoproliferation of undetermined origin. CD diagnosis is difficult and often delayed because of insidious onset, low awareness and clinical heterogeneity. Two major disease phenotypes can be distinguished: unicentric CD (UCD) and multicentric CD (MCD). Diagnosis confirmation is based on histopathological findings on an involved lymph node.

Objectives: We attempted to survey all cases of paediatric CD identified in France so far, in order to set up a national registry aimed to improve CD early recognition, treatment and follow-up, within the context of a new reference centre (http://www.castleman.fr).

Methods: In 2016, we e-mailed a questionnaire to members of the French paediatric immuno-haematology society, the French paediatric rheumatology society and the French Reference Centre for Castleman Disease to retrospectively collect cases of paediatric CD (first symptoms before age 18 years). Anatomopathological confirmation was mandatory.

Results: We identified 23 patients (12 girls and 11 boys) diagnosed with CD before age 18 years). Anatomopathological confirmation was mandatory. Two major disease phenotypes can be distinguished: unicentric CD (UCD) and multicentric CD (MCD). Diagnosis confirmation is based on histopathological findings on an involved lymph node.

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SAI0489 PREVALENCE OF AUTOIMMUNE DISEASES IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Juvenile idiopathic arthritis (JIA) is one of at least 80 different types of autoimmune diseases, and is the most common paediatric rheumatic disease. After cancer and heart disease, autoimmune diseases are the most common type of disease in the US. The estimated prevalence of autoimmune diseases is 3.2% and 5.9% in the US and Europe, respectively, with a corresponding increase in mortality. Many autoimmune diseases share a common pathogenic mechanism. There are few published studies quantifying the occurrence of other autoimmune diseases in patients with JIA.

Objectives: To estimate and compare the prevalence of 38 co-existing autoimmune diseases in patients with JIA and in a general paediatric population.

Methods: This was a retrospective cohort study conducted using registry data from the Cincinnati Children’s Hospital Medical Center (CHMC; Cincinnati, OH, USA) from Jan 2010 to Oct 2018. Patients <21 years old who had at least one clinic visit at the CHCMC were included in the general patient (GP) cohort, excluding pts with JIA. The JIA cohort consisted of patients <21 years old who had one of the International Classification of Diseases (ICD)-9 or ICD-10 diagnosis codes for JIA. No exclusion criteria were applied. Cases for each of 38 autoimmune conditions (AICs) were identified using ICD9/10 codes. Comparisons were made between the JIA and the GP cohorts for each of the 38 AICs in crude prevalence (reported as X cases per patient-year) for each year up to the end of the study period. A Bayesian Poisson regression model was used for estimating and comparing prevalence rates for the JIA and GP cohorts at the end of study period. The rate and corresponding 95% confidence limits of the two cohorts on their prevalence rates are reported.

Results: There were 2,026 and 41,572 patients included in the JIA and GP cohorts, respectively. Out of 38 AICs, 26 showed significantly higher prevalence in the JIA cohort compared with the GP cohort (Figure). Of the 38 ICD9/10 codes assessed, 14 (36.8%) showed a more than 20-fold greater prevalence in the JIA cohort than in the GP cohort. There

Figure: Significant results from Bayesian Poisson analysis on point prevalence comparisons: JIA cohort vs GP cohort

National Arthritis Foundation of Singapore

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were statistically significant differences in 26 conditions (Figure), with the most striking differences comparing the GP cohort with the JIA cohort in: serum amyloid A (0.001% vs 0.98%), psoriatic arthritis (0.01% vs 4.4%), systemic sclerosis/scleroderma (0.004% vs 0.6%), uveitis (0.07% vs 7.82%) and sarcoidosis (0.003% vs 0.3%). Only alopecia areata was more frequent in the GP cohort than in patients with JIA (4.5% vs 0.2%).

Conclusion: Patients with JIA have more pronounced autoimmune prevalence than the general paediatric population, especially for ankylosing spondylitis, psoriatic arthritis, uveitis, systemic sclerosis/scleroderma and sarcoidosis.

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Lipoprotein lipase is a key enzyme in lipid metabolism, ensuring the hydrolysis of plasma triglycerides found in chylomicrons and very low density lipoproteins. An increase in the catalytic activity of lipoprotein lipase leads to a decrease in the level of TG and an increase in the level of HDL in the blood. According to the results of the survey in children with JIA, the concentration of lipoprotein lipase was 13.9 [7.1; 25.3] μg/l, with obesity 27.5 [9.9; 47.8] μg/l. A direct relationship was established between its content in blood serum and the concentration of LDL (r = 0.37; p < 0.05) and the inverse with the level of LDL (r = -0.4; p < 0.05). There was a significant difference (p < 0.05) by gender: the level of lipoprotein lipase in the blood serum in girls was 25.8 [16.7 - 54.4] μg/l, in boys - 15.6 [7.8 - 29.0] μg/l. A correlation was also established between the level of lipoprotein lipase and body mass index (r = 0.35; p < 0.05).

According to the results of the study, a significant (p < 0.05) increase in the level of primary (DK233) and secondary (DK278 and MDA) LPO products in the blood serum of children with JIA was found in comparison with the control group. During the correlation analysis, a positive correlation was established between the levels of DK233, DK278 in serum and ESR (r = 0.587, p < 0.01). The results obtained indicate the intensification of lipid peroxidation processes. A significant (p < 0.05-0.01) decrease in the content of water-soluble (ACW) and fat-soluble (ACL) antioxidant capacities of substances in the blood serum of children with JIA was found when compared with similar indicators in the control group. During the correlation analysis, a negative correlation was established between the level of CRP and the content of ACL in serum (r = -0.346, p < 0.05), between the content of ACW and CRP in serum (r = 0.54, p < 0.01).

Conclusion: It can be concluded that the activation of lipid peroxidation and the failure of the antioxidant system play a significant role in the development and progression of JIA in the examined children, as well as in the formation of attherosclerotic disorders by the lipid peroxidation mechanism. In addition, children with JIA have abnormalities in the lipid spectrum, acquiring an atherogenic orientation, which, together with hemostatological changes, can be regarded as a risk factor for attherosclerosis.

Disclosure of Interests: None declared


GASTROINTESTINAL MANIFESTATIONS IN CHILDHOOD BEHÇET’S DISEASE

Fatih Demir1, Nergin Gererli2, Seval Sismeke1, Belgül Sözen1. University of Health Sciences, Ümraniye Training and Research Hospital, Pediatric Rheumatology, Istanbul, Turkey; 1University of Health Sciences, Ümraniye Training and Research Hospital, Pediatric Gastroenterology, Istanbul, Turkey

Background: Behçet’s disease (BD) is an idiopathic, chronic, inflammatory systemic vasculitis characterized by recurrent oral and genital aphthous ulcers, skin lesions, and ocular involvement. It can also affect multiple visceral organs and system such as heart, lung, blood vessels, gastrointestinal (GI) system, and central nervous system (1). The etiology of the disease is still unknown. New diagnostic criteria for pediatric Behçet’s disease (2). Two major disturbances in the examined children, as well as in the formation of attherosclerotic disorders by the lipid peroxidation mechanism. In addition, children with JIA have abnormalities in the lipid spectrum, acquiring an atherogenic orientation, which, together with hemostatological changes, can be regarded as a risk factor for atherosclerosis.

Disclosure of Interests: None declared


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Disclosure of Interests: None declared


SAT0493

THE CHALLENGE OF TREATING PULMONARY VASCULITIS IN BEHÇET’S DISEASE: TWO PEDIATRIC CASES

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Background: Behçet’s Disease (BD) is a multisystemic autoinflammatory disease and the most severe complication of BD is pulmonary artery involvement (PAI). Data regarding treatment and outcomes of pediatric patients with PAI is very limited.

Objectives: Herein, we report two pediatric patients with BD presenting with PAI and treated successfully with aggressive immunosuppressive treatment.

Methods: Demographic data, clinical manifestations, laboratory and radiological findings, and treatments of patients were documented from patient charts retrospectively.

Results:

Case 1: A 15-year-old boy was admitted with abdominal pain and fever. An abdominal Doppler ultrasonography (USG) showed stenosis of vena cava inferior (VCI) with a thrombus. Transesophageal echocardiography (TEE) detected that the thrombus extended from VCI to the right atrium. When he started to have hemoptysis, he was referred to our hospital. TTE showed a mass in RV. The computed chest and abdominal tomography angiography (CTA) showed bilateral aneurysmatic dilatation with thrombi in the pulmonary arteries and thrombosis in vena hepatica. The paternity test was negative and the HLA B5 was negative. According to the ICBJD, the patient had been diagnosed as BD due to genital ulcers and vascular involvement. He was given pulse methylprednisolone (MP) 500 mg 3 days along and followed by oral prednisolone 1 mg/kg/day, intravenous cyclophosphamide at a dose of 15 mg/kg every 3 weeks for a total of 6 cycles, and Interferon-02a (IFN-02a) 3 times a week. Within one month, hemoptysis and fever disappeared, and CRP values normalized. After a three-month treatment, TTE and CTA revealed that thrombi shrank significantly. The dosage of prednisolone was tapered gradually and stopped 2 years later. Immunosuppressive treatment was continued with adalimumab. The patient has been followed in remission for nearly 6 years.

Case 2: A fifteen-year-old boy was referred to our hospital for the evaluation of fever for over 4 months and a thrombus in his right ventricle. He had a medical history with cough, fever, intermittent hemoptysis and weight loss for the past 3 months. Physical examination revealed acene-like rashes over face and back, oral ulcers. A CTA confirmed the inflammation. The endoscopic findings shown in the patients are: gastric inflammation in 100% (7/7), esophageal inflammation in 57% (4/7), duodenal inflammation in 42% (3/7), colonic erythema and inflammation in 83% (5/6), polyps in 50% (3/6), ulceration in 66% (4/6), and hemorrhoids in 16% (1/6). Upper GI ulceration was not observed. Pathology specimens were taken in 7 upper endoscopies and 6 colonoscopies within our patients. The findings of pathology specimens were vascular congestion and inflammation in 100% (7/7) of upper GI biopsies and 83% (5/6) of colonic biopsies, cryptitis in 66% (4/6) of colonic biopsies. Acute colitis in pathology specimens was shown in 83% (5/6) of the patients. Three of the patients with colitis had punch ulcers, and these patients were evaluated as BD-associated colitis. The other two patients were diagnosed and treated as Crohn’s colitis accompanying BD.

Conclusion: The GI system is one of the most frequently affected organ by the BD. It may cause the inflammation and ulceration in the GI tract. Inflammatorily bowel diseases can also cause GI inflammation similar to BD. In patients with symptoms of GI inflammation, upper and lower GI endoscopic examination and pathological analysis may be helpful in determining the underlying etiology.

REFERENCES

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Disclosure of Interest: None Declared

thrombus in RV and showed bilateral multiple aneurysms along the pulmo-
mary artery and its branches. According to ICBD, the patient was diag-
nosed with BD due to having aphthous ulcers, pseudofolliculitis, and vascular involvement. IV MP (500 mg/day) for 3 days was followed by oral prednisolone 1 mg/kg/day, which was subsequently tapered. IV cyclo-
phosphamide at a dose of 500 mg was also given every 3 weeks for a total of 6 cycles, followed by oral azathioprine (AZA). Concomitant sub-
taneous IFN-α2a was given two times per week for 6 months. Within two weeks, cough and fever disappeared, CRP values normalized. After 1 year the pulmonary artery aneurysm disappeared and cardiac thrombo-
sis resolved. We have been following the patient with AZA for four years without recurrence.

Conclusion: We present two pediatric patients with pulmonary involvement of BD. PAI is a life-threatening condition and should be managed with more aggressive medical therapy. Early diagnosis and aggressive immu-
nosuppressive treatment are very important in PAI. We strengthened our treatment with IFN-α2a. There is no data in the literature regarding the use of IFN-α2a in PAI treatment along with low dose cyclophosphamide. There were no mortality or recurrences within the 6 and 4 years follow up period. An aggressive immunosuppressive therapy leads to better prognosis in this most dreadful complication of BD.

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Disclosure of Interests: Selcan Demir: None declared, Erdal Sag: None declared, Ummusen Kaya Akca: None declared, Tuncay Hazirolan: None declared, Yelda Bilginer: None declared, Sezay Ozen Consultant for: Seza Ozen is receiving consultancy fees from Novartis, Speakers bureau: Roche


SAT0494 HOME MONITORING OF INACTIVE DISEASE IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS: PREDICTIVE VALUE OF EQ-5D-5L-Y

Martin J.H. Doeleman1, Sytze De Roocok1, Nathan Buijsse1, Mark Klein1, Gouke J. Bonsel2, V. Seyfert3, Nico Wulffraat1, Joost F. Swart1.

1University Medical Center Utrecht, Pediatric Rheumatology, Utrecht, Netherlands; 2University Medical Center Utrecht, Obstetrics and Gynaecology, Utrecht, Netherlands; 3MyOwnMed, Bethesda, United States of America

Background: In recent years, juvenile idiopathic arthritis (JIA) research has shifted towards treat-to-target therapy based on clinical assessments and patient-reported outcomes (1). A well-known measurement of quality of life is the EQ-5D-5L (2). Herewith, we report preliminary results of a retrospective study using the child-friendly ‘EQ-5D-5L-Y’ with an E-health application (Reuma2GO) to monitor children with JIA in an outpatient setting.

Objectives: To assess the relationship between dimensions of the health-related quality of life ‘EQ-5D-5L-Y’ questionnaire and conventional assessments for children with JIA, including the Juvenile Arthritis Multidimensional Assessment Report (JAMAR) and active joint count (AJC), and to investigate the potential of the EQ-5D-5L-Y score as instrument for outpatient management.

Methods: The study was designed as a monocentric retrospective cohort study. Data from October 2017 to January 2019 were available for 70 patients with JIA. The relationships between individual dimensions of the EQ-5D-5L-Y, JAMAR and several clinical assessments were investigated. Furthermore, dimensions of the EQ-5D-5L-Y were investigated as possible predictors for binary disease activity using AJC > 0 as reference standard for active disease.

Results: Seventy patients with JIA completed 115 EQ-5D-5L-Y and JAMAR questionnaires within two weeks before a clinical visit. Moderate to high correlations were found between the EQ-5D-5L-Y and JAMAR. Moreover, the best possible EQ-5D-5L-Y score, with and without health-related visual analogue scale (EQ-VAS), demonstrated high sensitivity (81.1%) and negative predictive value (84.8%) for active disease (Table 1). The few patients who were incorrectly classified as having inactive disease (false-negatives) did not have their medication changed at the clinical visit and experienced little to no impact of disease activity on their quality of life, as indicated by the JAMAR questionnaire.

CONCLUSION: The results indicate the potential of ‘EQ-5D-5L-Y’ as an instrument for outpatient management with an E-health application. The EQ-5D-5L-Y score could be a valuable tool in monitoring children with JIA in an outpatient setting which could aid physicians with deciding whether a clinical visit is necessary or not.

REFERENCES


Disclosure of Interests: Martin J.H. Doeleman: None declared, Sytze De Roock: None declared, Nathan Buijsse: None declared, Mark Klein: None declared, Gouke J. Bonsel: None declared, V. Seyfert Shareholder of: VS is CEO and founder at MyOwnMed, Inc., Employee of: VS is CEO and founder at MyOwnMed, Inc., Nico Wulffraat: None declared, Joost F. Swart: None declared


Table 1. Predictive value of EQ-5D-5L-Y dimensions for active disease using AJC > 0 as reference standard.

<table>
<thead>
<tr>
<th>Dimension</th>
<th>Accuracy (%)</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EQ-5D Mobility &gt; 1</td>
<td>74.0% (65.8-86.0)</td>
<td>59.5%</td>
<td>82.1%</td>
<td>61.1%</td>
<td>81.0%</td>
</tr>
<tr>
<td>EQ-5D Self Care &gt; 1</td>
<td>68.0% (57.7-78.3)</td>
<td>90.0%</td>
<td>82.1%</td>
<td>81.0%</td>
<td>75.8%</td>
</tr>
<tr>
<td>EQ-5D Usual Activities &gt; 1</td>
<td>67.8% (58.5-76.2)</td>
<td>73.0%</td>
<td>65.4%</td>
<td>50.0%</td>
<td>83.6%</td>
</tr>
<tr>
<td>EQ-5D Pain/Discomfort &gt; 1</td>
<td>62.6% (53.1-71.5)</td>
<td>62.2%</td>
<td>62.8%</td>
<td>44.2%</td>
<td>77.8%</td>
</tr>
<tr>
<td>EQ-5D Anxiety/Depression &gt; 1</td>
<td>73.9% (64.9-81.7)</td>
<td>51.4%</td>
<td>84.6%</td>
<td>61.3%</td>
<td>78.6%</td>
</tr>
<tr>
<td>EQ-5D EQ-VAS &lt; 85</td>
<td>60.0% (50.4-69.0)</td>
<td>64.9%</td>
<td>57.7%</td>
<td>42.1%</td>
<td>77.6%</td>
</tr>
<tr>
<td>EQ-5D Total Score &gt; 5</td>
<td>60.0% (50.4-69.0)</td>
<td>81.1%</td>
<td>50.0%</td>
<td>43.5%</td>
<td>84.8%</td>
</tr>
<tr>
<td>EQ-5D Score &gt; 5 &amp; EQ-VAS &lt; 85</td>
<td>92.2% (82.7-96.6)</td>
<td>83.8%</td>
<td>37.2%</td>
<td>38.6%</td>
<td>82.9%</td>
</tr>
</tbody>
</table>

PPV: positive predictive value; NPV: negative predictive value.

PPV: positive predictive value; NPV: negative predictive value.

Conclusion: These results demonstrate the discriminatory value of the EQ-5D-5L-Y between active and inactive disease in our cohort of patients with JIA. High negative predictive value was found for the total EQ-5D-5L-Y score, with and without EQ-VAS. In conclusion, the EQ-5D-5L-Y could be a valuable instrument for monitoring children with JIA in an outpatient setting which could aid physicians with deciding whether a clinical visit is necessary or not.

REFERENCES


Disclosure of Interests: Martin J.H. Doeleman: None declared, Sytze De Roock: None declared, Nathan Buijsse: None declared, Mark Klein: None declared, Gouke J. Bonsel: None declared, V. Seyfert Shareholder of: VS is CEO and founder at MyOwnMed, Inc., Employee of: VS is CEO and founder at MyOwnMed, Inc., Nico Wulffraat: None declared, Joost F. Swart: None declared


SAT0495 PHENOTYPE OF PATIENTS WITH JUVENILE DERMATOMYOSITIS ASSOCIATED WITH ANTI-FACTOR H AUTO-ANTIBODY: A SEVERITY FACTOR?

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Background: Juvenile Dermatomyositis (JDM) is a rare, autoimmune and highly heterogeneous paediatric-onset myopathy, characterized by skin and muscles inflammation. Development of vasculopathy is associated with the severe extra-muscular manifestations of JDM, and portends a poor prognosis. Impaired function of JDM vasculature includes immune complex and complement deposition.

Objectives: The aim of our study is to describe the clinical and paraclinical phenotype of patients with anti-factor H autoantibody (Ab) associated with JDM and overlap myositis.

Methods: Patients with a diagnosis of JDM or overlap myositis and presence of anti-FH auto-antibody, followed in two Parisian tertiary centers over the last twelve years, were retrospectively selected. Besides demographic data, clinical features (cutaneous lesions, severity of muscle involvement, extra-muscular manifestations), treatment options and their outcome were retrieved for each patient. Biological data and presence of myositis-specific autoantibodies were collected, muscle MRI were examined, and data from muscle biopsies were assessed using a validated score tool when available.

Results: Eleven female patients were included in the study, with a median age at diagnosis of 8.8 years [2.8 – 13.1], and a median follow-
up of 3 years [1 – 11.7]. Apart typical cutaneo-muscular presentation, seven developed calcinosis, and six presented with subcutaneous oedema (of which 5 were anti-NXP2 positive). Median CMAS was 24/52 [1 – 47], and median MMT was 52/80 [2 -76]. Gastro-intestinal involvement was found in 10 patients (91%), 4 presented a pulmonary impairment, and 3 girls had psychiatric symptoms. Six patients had a severe form (54%), one of them led to death (after 2.8 years of evolution).

MSA were found in 9 patients (anti-NXP2 = 1, anti-fibrillarine = 2, anti-MDA5 = 1 and anti-TIF1γ = 1). IFN-signature was positive in 9 patients. Complement exploration was normal in all patients, and median positive rate of Anti-Factor H Ab was 260 U/L [115 – 2800]. Muscle biopsy was performed in all patients but one with a median total score severity of 20. All patients received corticosteroids, and one to six other lines of treatment to achieve remission, obtained in 8 patients, with a median time to remission of 2 years [0.5; 4.8]. Use of plasmapheresis/immunoabsorption and/or Ruxolitinib was necessary in 3 of them (27%).

Conclusion: Presence of anti-factor H auto-antibodies in JDM or overlap myositis patients seems associated with more frequent gastro-intestinal involvement, and a more severe phenotype, requiring more aggressive treatment.

REFERENCES

Disclosure of Interests: None declared

SAT0495

THE FREQUENCY OF JOINT HYPERMOBILITY IN TURKISH SCHOOLCHILDREN: EFFECTS TO PHYSICAL ACTIVITY, BALANCE, PAIN AND QUALITY OF LIFE

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Background: Recent studies have focused on the joint hypermobility (JH) to show the association with musculoskeletal pain, functional disability, motor development and psychological distress (1). In contrast, in some publications, the negative effects of JH in childhood were not observed (2).

Objectives: The aim of this study was mainly to determine the frequency of JH in Turkish schoolchildren and to investigate whether relationship between JH and pain, physical activity level and the balance. In addition, the study aimed whether JH has an impact on the quality of life.

Methods: This cross-sectional school-based study evaluated 737 children (52.5% girls) from 8 to 14 years of age, and the data were collected in 2018 in the city of Denizli, Turkey. Firstly, each of the participants was individual assessed by a clinician on the Flamingo Balance Test for stability and Brighton for the diagnosis of JH. According to Brighton, children who scored ≥5 were accepted as hypermobile. Secondly, all participants completed the self-reported measures for the screening of physical activity level and quality of life. The Physical Activity Questionnaire (PAQ) and the Pediatric Quality of Life Inventory (PedsQL) tests were used to determine the level of physical activity and the quality of life. Also, pain severity was quantified by the Visual Analogue Scale (VAS) that is ranging from no pain (score: 0 mm) to worst pain (score: 100 mm) in the last month.

Results: The prevalence of JH in schoolchildren was 19.7% in Turkish population (Table 1). The mean pain severity was 1.29±2.024 in all children. Significant differences were found between hypermobile and non-hypermobile groups in social and school functioning (p<0.05), but no significant differences were found in pain, physical activity level (p>0.05) (Table 2). Brighton score was not significant correlated with pain severity, physical activity, quality of life and balance in childhood (p>0.515, p>0.986, p>0.512, p=0.362 respectively).

Conclusion: As a result, the existence of hypermobility in children had an impact on school and social functions. However, it has been observed that hypermobility does not have a negative effect on these children’s pain, balance, physical activity level, and physical and emotional functions.

REFERENCES


Table 1. Demographic findings of 737 Turkish Schoolchildren

| Table 2. Comparison of the results of children with and without hypermobility |
|---|---|---|---|---|
| Age (year)| With Hypermobility (n=145) | Without Hypermobility (n=592) | P |
| 11.13 ± 1.35 | 11.55 ± 1.28 | 0.000 |
| Weight (kg)| 42.42 ± 11.85 | 45.58 ± 12.3 | 0.004 |
| Height (cm)| 148.8 ± 10.7 | 151.76 ± 10.19 | 0.002 |
| Brighton Score| 6.2 ± 1.14 | 1.9 ± 1.42 | 0.000 |
| Pain severity (During Motion)| 1.04 ± 1.8 | 1.35 ± 2.07 | 0.148 |
| Pain severity (During Rest)| 0.91 ± 1.86 | 1.16 ± 1.9 | 0.063 |
| Balance| 28.13 ± 9.44 | 30.04 ± 9.45 | 0.062 |
| PedsQL 4.0| 27.13 ± 7.7 | 26.18 ± 7.4 | 0.102 |
| Physical functioning| 85 ± 12.74 | 96.21 ± 33.71 | 0.068 |
| Emotional| 77.05 ± 18.18 | 75.37 ± 20.04 | 0.533 |
| functioning| 91.67 ± 13.1 | 90.44 ± 29.14 | 0.049 |
| School functioning| 83.72 ± 13.71 | 80.32 ± 16.09 | 0.030 |

Disclosure of Interests: None declared

SAT0497

CLINICAL PICTURE OF 7 PAPA PATIENTS FOLLOWED IN A SINGLE PEDIATRIC RHEUMATOLOGIC CENTER

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Background: Pyogenic sterile arthritis, pyoderma and acne (PAPA) syndrome is an autosomal dominant inflammatory disorder caused by mutations in the PSTPIP1 gene primarily affecting joints and skin. The E250K mutation cause the hyperzincaemia/hypercalprotectinemia syndrome termed PSTPIP1-associated-related proteinemia inflammatory (PAMI) syndrome in which a bone marrow involvement is reported

Objectives: To describe the clinical presentation of 7 PAPA patients followed at a single pediatric rheumatology center.

Methods: For each patient clinical and laboratory data were collected from medical charts. PSTPIP1 was sequenced through Sanger Sequencing or targeted resequencing using a customized panel, and analyzed with the NextSeq® platform (Illumina).

Results: We describe 7 patients from 4 unrelated families with the E250K mutation in a mother and 2 siblings, the A230T variant in a father and his son and the R405C and D266N respectively in the last 2 unrelated patients. Disease onset occurred within the 7th year of life in all patients. Patients 3 and 4 (Table) presented since the 1st year of life recurrent episodes of fever without any cutaneous or articular symptoms. In both patients inflammatory markers were elevated during fever episodes, but persistently negative during wellbeing not requiring any therapy. The variants described in these patients were not previously reported. However their pathogenic role is supported by the detection of markedly high serum calprotectin levels (>10.000 microg/ml). The predominant feature of patients 1 and 2 was articular involvement with recurrent episodes of arthritis associated to acne. Patient 1 was initially treated
with prednisone with good clinical response but relapse of arthritis at discontinuation followed by the development of a sterile muscle abscess. An anti-TNF drug was started in both patients with complete clinical response. Patient 5 reported severe acne and psoriasis, and recurrent epistaxis and a sterile arthritis. She presented a persistent elevation of acute phase reactants with severe anemia and leukopenia not resolving after splenectomy. Her son (pts 6) presented with recurrent episodes of sterile arthritis, hepato-splenomegaly, anemia and neutropenia. Zinc and ciprofloxacin serum levels resulted respectively 728 microg/ml and 2600 microg/ml. IL-1 inhibition determined a complete normalization of inflammatory parameters with no effects on anemia and neutropenia. In patient 6 zinc decreased to almost normal value after 4 months of therapy. Patient 7 presented at the age of 4 years a sterile lymphnode abscess. She also presented with splenomegaly and neutropenia with persistent elevation of acute phase reactants. Anakirna was proposed but not administered for poor compliance.

**Conclusion:** The clinical picture of patients carrying PSTPIP1 mutation may be heterogeneous. In our cohort TNF-inhibitors were successfully used in PAPA patients preventing new arthritis episodes and resolving cutaneous manifestation where present. In 2 patients the clinical picture was mild not requiring continuous treatment. One PAMI patient had a good response to IL-1 inhibition, which however, had no effect on hematological manifestations.

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**SAT0499**

**THE IMPACT OF OVERWEIGHT ON THE OUTCOME OF JUVENILE IDIOPATHIC ARTHRITIS**

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**Background:** Overweight and obesity are considered to have a negative impact on Rheumatoid Arthritis in adults and there is less information regarding the correlation in juvenile idiopathic arthritis (JIA).

**Objectives:** To assess the effect of overweight on the activity of JIA as well as the stability and ability to achieve a remission using the cJADAS10 score.

**Methods:** This is a longitudinal retrospective study design. We collected data of 164 patients suffering from JIA from three consecutive visits. Treatment was conducted between 2012 and 2015 at our centre in accordance to current guidelines. Remission was defined by cJADAS10 score ≤0.5 in Oligoarthritis and ≤0.7 in Polyarthritis. Patients were categorized by weight-for-age percentiles as heavily underweight (less than 3rd percentile), underweight (4th up to 10th percentile) healthy (11th up to 90th percentile) overweight (91st up to 96th percentile) and obese (97th up to 100th percentile). We compared the cJADAS10 of normal-weighted children with the cJADAS10 of the overweight and the obese patients, respectively.

**Results:** Of all patients, 13 were "underweight" (7.9%), 109 were defined as "normal weight" (66.5%) and 42 patients were categorized as "overweight" (25.6%) of which 16 children (9.8%) were 'obese'. 95 (57.9%) reached a remission during follow-up visits. Overweight was associated with higher disease activity compared to healthy weight children at the first visit (mean 9.5 vs. 8.5) and a wider range of the cJADAS10 score (0-22 vs.0-20.5). Results from the 3-months-follow-up revealed an overall good response to the prescribed medication. At 6-months-follow-up, overweight children couldn’t stabilize the improvement since cJADAS10 range rises while it stays stable in healthy weight children. At the same time, while interpreting the disease activity of "overweight" and "obese" children separately, obese children show significantly less disease activity than overweight children, especially at the 3- and 6-months-follow-ups.

**Conclusion:** Overweight seems to have a negative influence on the disease activity and remission of JIA patients but it is most likely not the only influencing factor since obese patients show a better result regarding the cJADAS10 score than overweight patients. In the future, factors like socioeconomic status, BMI of the parents or physical activity level of the patient should be included in the evaluation. Also, the 7 subtypes of JIA should be analyzed individually since they show heterogeneous etiology, phenotype and prognosis.


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**SAT0498**

**ORAL MICROBIOME IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS RELATION TO DISEASE STATUS, TEMPOROMANDIBULAR JOINT ARTHRITIS AND MEDICATION: A NORWEGIAN 2-YEAR PROSPECTIVE STUDY**

Paula Frid1, Josefine Habbig2, Divyashri Baraniya3, Veronika Rydafi4, Nils Thomas Sangstad5, Anriika Rosen6, Johanna Rykke7, Bent Fiala8, Tuule Chen9, Nezar Noor Al-Hebshi10, Ellen Nordal11, Mohammad Al-Harbi11,12, Norwegian multicenter NorJIA cohort study, 1UIT The Arctic University of Norway, Tromsø, Norway, Department of Otohinolaryngology, Division of Oral and Maxillofacial Surgery, University Hospital North Norway and Public Dental Service Competence Centre North Norway and Department of Clinical Medicine, Tromsø, Norway, 2UIT The Arctic University of Norway, Tromsø, Norway, Public Dental Service Competence Centre North of Norway and Department of Clinical Dentistry, Tromsø, Norway, 3Temple University, Philadelphia, PA, USA, Oral Microbiome Research Laboratory, Maurice H. Kornberg School of Dentistry, Philadelphia, United States of America, 4UIT The Arctic University of Norway, Tromsø, Norway, Department of Clinical Medicine and Department of Pediatrics, Tromsø, Norway, 5UIT The Arctic University of Norway, Tromsø, Norway, 6University of Bergen, Department of Clinical Dentistry and Haukeland University Hospital, Bergen, Bergen, Norway, 7University of Oslo, Department of ENT and Oral and Maxillofacial Surgery, Oslo University Hospital, Oslo, Oslo, Norway, Oslo, 8University of Oslo, Department of Rheumatology, Oslo University Hospital, Oslo, Norway, Oslo, Norway, 9Forsyth Institute, Cambridge, USA, Department of Microbiology, Cambridge, United States of America, 10Temple University, Philadelphia, PA, USA, Oral Microbiome Research Laboratory, Maurice H. Kornberg School of Dentistry, Philadelphia, United States of America, 11UIT The Arctic University of Norway, Tromsø, Norway, Department of Clinical Dentistry, Tromsø, Norway

**Background:** Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in children, with an annual incidence of 1-2 per 1000 children. The temporomandibular joint (TMJ) is involved in 40-70%. The human microbiome might be a potential contributing factor to the development of JIA.

**Objectives:** To describe the oral salivary microbiome in children with JIA and relate this to disease activity, TMJ arthritis, and systemic medications.

**Methods:** 83 children: JIA (n=59), Healthy (n=34) were recruited. Demographics, disease activity, presence of TMJ-arthritis and type of medication was collected in this Norwegian prospective study (www.norjia.com). 116 saliva samples were analyzed using Next Generation Sequencing, V1-3 region of the 16S rRNA gene, coupled with BLASTn-based, species-level taxonomy assignment algorithm. Downstream bioinformatics analysis was performed with QIIME and LEfSe.

**Results:** Mean age for healthy group (n=34; 27 females) is 12.3 ±3.0 years while for the JIA group (n=59; 43 females) the mean age is 12.6 ±2.7 years. A total of 541 bacterial species belonging to 111 genus and 10 phyla were identified, with Prevotella, Streptococcus, Actinomyces, Rothia Haemophilus and Veillonella accounting for the bulk of the average microbiome. There were no significant difference between JIA and healthy subjects in species richness and alpha diversity. However, differ- entially abundant analysis revealed genera TM7-G1, Solobacterium and Mogibacterium to be associated with JIA, while Haemophilus and Lactobacillus to be overabundant in healthy subjects.

**Conclusion:** It seems that taxa associated with chronic inflammation were found to be enriched in the saliva of JIA patients.
JUVENILE RECURRENT PAROTITIS: A RARE MANIFESTATION OF RHEUMATIC IMMUNE-MEDIATED DISEASES

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Background: Juvenile recurrent parotitis (JRP) is the second most common childhood disease of the salivary glands after mumps and mainly affects children between the ages of 3 and 6. There is a male predominance, often with spontaneous resolution at puberty. However, in some cases, it can be the first manifestation of a rheumatic immune-mediated disease.

Objectives: To analyze the clinical, laboratory and imaging profile of children with JRP and investigate the prevalence of rheumatic immune-mediated diseases in these patients.

Methods: Retrospective study from 2008 to 2018 including all cases of recurrent parotitis with juvenile onset at our center. Parameters evaluated included gender, age, laterality, number of recurrences, symptoms of presentation, associated conditions, imaging details, blood tests, treatment, outcome and follow-up.

Results: 40 patients were identified over a 10-year period, with a female to male ratio of 5:3; 62.5% females. The youngest child was nine months old and the eldest was 16 years old with median age at presentation of 5 years. The median (min-max) follow-up period was 3 (0.04-33) years. 29 children (72.5%) only ever reported unilateral symptoms, while the rest had both glands affected, although not usually at the same time. Pain and swelling were the most common presenting symptoms, seen in all cases. Fever in 15 (37.5%) and whitish discharge from Stenson’s duct in one (2.5%), 14 (35%) had palpable cervical lymphadenopathy and 4 (10%) had dental caries. The average reported frequency was 1.25 episodes per year, with a range of 0.43-5 episodes. Numbers of recurrences were in range of one to 15 with average of 3 times. Younger age at first episode didn’t increase the likelihood of recurrences in our sample (p=0.123). Sonography was performed in 34 cases as primary investigation. Reports showed multiple hypoechoic lesions with enlarged intraglandular lymph nodes and enlarged gland. MRI was performed in 10, CT in 4, scintigraphy in 2 and biopsy of minor salivary glands in 1.

The median level of C-reactive protein and erythrocyte sedimentation rate measured, 6 of them having hypergammaglobulinaemia. One patient had a marginally low serum Immunoglobulin A (50; normal variation 55-210).

Conclusion: The clinical, laboratory and imaging profile of our sample is in accord with the literature, except for sex predilection. Although recurrent juvenile parotitis is more common, primary juvenile SS should be considered. A high suspicion is crucial mainly because of a lower incidence of xerostomia and xerophthalmia in this population.
Efficacy and Safety of Adalimumab in Juvenile Idiopathic Arthritis – 10 Year Experience Using Data of the BIKER Registry

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Background: Since 2008, Adalimumab is approved for polyarticular juvenile idiopathic arthritis (JIA) and approval has been extended to other JIA categories and for uveitis.

Objectives: To evaluate efficacy and safety of Adalimumab in clinical practice in JIA patients in comparison to a biologic-naïve JIA cohort using the German Biologics registry (BIKER). Methods: Baseline demographics and disease activity parameters have been documented. Efficacy was determined using the JADAS10. Safety assessments were based on adverse events (AE) reports processed according to MedDRA.

Results: Until October 1, 2018, 951 JIA patients treated with Adalimumab were registered in BIKER, representing 1519 patient-years (PY) of exposure. The total observation time (from date of first dose until last follow-up, censored, if another biologic was started) was calculated with 1709 PY. At baseline, the cohort treated with Adalimumab had experienced disease with a disease duration of 5.4–3.9 years (mean±SD). 849 patients (89.3%) were pretreated with methotrexate, 525 (54.2%) with Etanercept. Concomitantly, 584 (61.4%) received methotrexate, 529 (55.5%) NSAIDs and 255 (26.8%) systemic corticosteroids. In the control cohort, 1517 biologic naïve JIA patients started methotrexate.

Upon treatment, the median (IQR1-3) JADAS10 score decreased from 9.8 (4.7-15.5) to baseline at 3.9 (0.9-9.7) at the last follow-up. With respect to patients with ongoing treatment, approximately 43% achieved a JADAS defined minimal disease activity while 2.2% reached a JADAS defined remission at last follow-up.

904 AE have been observed during exposure or up to 90 days follow-up (58.4/100 exposure years (EY) [95% CI 54.7-62.3]). 66 qualified as serious AE (SAE) [4.3/100 EY [3.3-5.4]]. These figures were compared to 1294 AE reported in the control cohort (34.8/year [32.9-36.8]) and 52 SAE (1.4/100 EY [1.1-1.8]). Adverse events of special interest were serious/medically important infection (n=33), opportunistic infection (n=6), all H. cesteri, malignancy (n=2), anaphylaxis/hypersensitivities (n=3), thrombotic disorders (n=2), autoimmune diseases (n=91, including 12 cases with psoriasis and 53 reports of uveitis), bleeding (n=3), cytopenias (n=4), pregnancies (n=2). Macrophage activation syndrome, demyelination, cardiac or cerebral infarction, or death were not observed. However, 2 malignancies were reported in patients who had ever been exposed to Adalimumab before. Both events were judged as unrelated.

A total of 449 patients (48.5%) discontinued Adalimumab, 188 (19.8%) due to lack of efficacy, 111 (11.7%) due to remission and 76 (8.2%) because of intolerance.

Conclusion: The current analysis adds to the established safety profile of Adalimumab and demonstrates that the rate of SAEs was comparable and consistent with the overall AE profile in paediatric patients. As expected, infections were the most frequent SAE. Uveitis, as well as psoriasis, are likely associated with JIA. Of notice, only one patient developed a chronic inflammatory bowel disease. No new safety signals specific to the paediatric population were identified in this large cohort of JIA patients.

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Development of Malignancies in JIA Patients Exposed to Biologic Agents: A Single Centre Retrospective Study

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Background: Over the last two decades, the usage of biological agents in the treatment of Juvenile Idiopathic Arthritis (JIA) has been a successful and promising approach in controlling the disease activity and preventing chronic sequelae. However, since Food and Drug Administration (FDA) has drawn attention to the possible association between the use of biological agents and the development of malignancy in 2008, there are ongoing concerns about the long-term safety data and side effect profile of the drugs with the contradictory study results.

Objectives: We aimed to present preliminary data on the incidence of malignancy in patients with JIA treated with biological agents versus the general population rates in Turkey.

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Scientific Abstracts
Methods: A retrospective single-center hospital-based cohort study was performed to analyse cancer occurrence among JIA patients treated with biologic agents over the observation period between January 2004 and January 2018. The medical patient records were reviewed to obtain information about the clinical follow-up. As reference data for direct standardization; age, sex, and calendar-year-specific incidence rates from Turkish cancer registry were used. The standardized incidence ratio (SIR, ratio of cancers observed to expected) was generated, with 95% confidence intervals.

Results: The study sample consisted of 504 JIA patients, who had been started their first biologic treatment between 2004 and 2018. Mean age was 17.1 years (SD 5.6) with 56% of female proportion. The mean disease duration was 10.3±5.1 years. Median time from baseline to start of the first biological was 17.5 (IQR:43) months. Mean age of initiation of biologic treatment was 9.8 ± 4.2 years. Etanercept was most commonly preferred drug to initiate as first-line biologic treatment (n=361,72%). 172 (34.1%) patients in the cohort required a switch to a second biologic agent. Main reason for switching to another biologic agent was due to lack of response (16.6%). Median duration of biologic use was 35 (IQR:41) months. One cancer occurred within observation period, compared with 0.095 expected (SIR:10.53, 95% CI 0.526 to 51.91). The patient was a 18-year-old male, who had previously received etanercept and tocilizumab up until diagnosis of the hematological malignancy.

Conclusion: In our JIA cohort, patients treated with biologic agents appeared to have an increased rate of incident malignancy compared to children and age group in the population in Turkey. However, before mentioning a clear causal relationship, other potential contributing factors such as inflammatory process of the underlying disease itself and the use of concomitant immunosuppressants should be taken into consideration. Additional long-term studies with larger populations are needed to be able to draw definite conclusions.

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Disclosure of Interests: None declared


SA10504 IG4 RELATED DISEASE IN CHILDREN: A SINGLE CENTRE EXPERIENCE FROM NORTH-WEST INDIA

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Background: Immunoglobulin G4 related disease (IgG4RD) is a multisystemic disorder characterized by elevated serum IgG4 levels and infiltration of IgG4 positive plasma cells accompanied by fibrosis. It is mostly considered a disease of adults and elderly people. There is paucity of literature on pediatric IgG4RD. A recent systematic review has found only 25 pediatric cases.

Objectives: To report broad patterns of organ involvement in IgG4RD in children and also to create awareness among treating pediatricians about this new entity.

Methods: The study is based on a review of the hospital records of children with IgG4RD at tertiary centre from North-West India. Diagnosis was based on clinical features, IgG4 levels and characteristic histopathology findings.

Results: Six patients had IgG4RD. Pt-1: 10-year-old boy presented with fever for 3 months and significant hepatomegaly. Investigations showed anemia, thrombocytopenia, elevated erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP). Ultrasonography (USG) revealed a hepatic mass (10x5x6 cm) that was confirmed on computed tomography. Liver biopsy showed increased plasma cells (>50 IgG4 positive plasma cells/HPF) and perisinusoidal fibrosis suggestive of IgG4 related hepatic mass. Serum IgG4 level was 420 mg/dl (N: 5-28). Pt-2: 12-year-old girl presented with an abdominal lump. Upper gastrointestinal endoscopy showed an intragastric mass with exophytic component. Histopathology of abdominal mass was consistent with IgG4RD. Serum IgG4 level was > 170 mg/dl (N: 6-28). Pt-3: 21-year-old male symptomatic since age of 14 years with recurrent erythematous swellings over dorsum of the left hand, forearm and chest. Investigations showed anemia, elevated ESR, CRP, and hypergammaglobulinemia. IgG4 levels were 211 mg/ml (N: 7-57). Histopathology from left hand showed lymphoplasmacytic infiltrates, storiform fibrosis, obliterative phlebitis and increased IgG4 plasma cells (>50/HPF). Pt-4: 18-year-old girl presented with fever and weight loss. She had anemia, thrombocytosis, elevated ESR and CRP. USG abdomen showed omental thickening. Serum IgG4 level was 215 mg/ml (N: 7-57). Peritoneal and omental biopsy showed fibrosing stage of IgG4RD. Pt-5: 7-year-old girl presented with fever, oliguria, and anasarca. Investigations revealed anemia, elevated CRP, ESR, deranged renal functions and nephrotic proteinuria. Renal biopsy showed plasma cell infiltrate, storiform fibrosis, and 10-16 IgG4 plasma cells/HPF; consistent with IgG4 related tubulointerstitial nephritis. Serum IgG4 was 68 mg/dl (N: 7-26). Pt-6: 14-year-old, boy presented with painful protrusion of right eye for 8 months. MRI orbit showed bulky and enhancing extra-ocular muscles of the right eye with lacrimal gland involvement. Serum IgG4 was 119 mg/ml (N: 7-26). Histopathology of mass showed extensive fibrosis, obliterative phlebitis and lymphoplasmacytic cells infiltrate with IgG4 plasma cells >30/HPF, consistent with IgG4RD. All patients showed good clinical response to oral prednisolone (1-2 mg/kg/day and subsequently tapered). Four patients required maintenance therapy with azathioprine.

Conclusion: We report 6 cases of pediatric IgG4RD with varied organ involvement and clinical manifestations. Some of the cases presented as space-occupying lesions that can sometimes be confused with neoplastic lesions. It is important to suspect these disorders early and start immunosuppressive therapy promptly to halt end-organ damage due to fibrosis.

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polyomavirus rash was in 244 pts (91.4%), conjunctivitis in 229 (85.8%), mucositis in 224 (83.9%), extremities abnormalities in 196 (73.4%) and lymphadenopathies in 165 (61.8%). The average duration of fever was 7 days (range 1-25 days), CAL were detected in 73 pts (20.2%); 58% (16) had CE, 15 (4.1%) had CAn. Median long-term follow-up was 10 years and 2 months (range 1 year – 36 years). The variance analysis in the different groups of CAL showed a significant difference as regard age at disease onset (F= 2.77, p= 0.025), duration of fever (F=16.32, p=0.0001), CRP value (F=6.94, p=0.001) and day of first administration of IVIG (F=7.963 p<0.001) (Table). A significant correlation between CAL and disease onset at <6 months (p=0.137, p=0.009), the need to administer 2 IVIG doses (p=0.305, p< 0.001), and male (p=0.109, p=0.038) has been highlighted. At the last follow-up, in the group of no-CAL (261 pts), cardiological visit, echocardiography and ergometric test (performed 177/261 pts) were normal in all pts. At the last available follow-up, 53 pts with CE had normal cardiological visit, echocardiography and ergometric test (performed 39/53 pts). Conversely, all 13 pts with CAn showed a normal cardiological visit, whilst ECG was abnormal in 1 patient (7.69%) and echocardiography showed persistent CAn in 8 (61.53%). Ergometric test was performed in 9/13 pts showing abnormal results in one pt (11.11%).

Conclusion: Our long-term follow-up in a large, even monocentric, cohort reports possible risk factor of CAL according to current literature. Our long-term follow-up assesses, in real life, the benign course of KS in children without CAL after 6-8 weeks from onset. According to recent guidelines, stopping cardiologic assessment in no risk pts results economically advantageous, timesaving and able to reduce emotional discomfort in children and their families.

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KAWASAKI DISEASE AND CARDIOVASCULAR OUTCOMES IN THE LAST 25 YEARS. STUDY OF 55 PATIENTS FROM A REFERAL HOSPITAL IN THE NORTH OF SPAIN

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Background: Kawasaki disease (KD) or “mucocutaneous lymph node syndrome” is a systemic vasculitis in children that involve medium-sized vessels with predilection for coronary arteries. Due to the high probability of cardiovascular complications, an early diagnosis and treatment is required.

Objectives: A) To describe demographic, clinical and analytical features in a cohort of patients with KD diagnosis from northern Spain. B) To assess the rate of long-term cardiovascular outcomes.

Methods: We set up an observational study of patients with KD in a University Hospital between Jan-94 and Dec-18. Classic classification criteria were used for diagnosis. Diagnosis of aneurysms was made by serial echocardiography and/or coronary-CT. Results are expressed as mean±SD or as median and interquartile range (IQR) as appropriate.

Results: 55 patients (28 women/27 men), with a mean age at diagnosis of 3.6±2.8 years, 60% presented a previous infection prior to administration of any antiinflammatory doses. 2 required endovenous corticosteroid, and in 1, an anti-TNF drug (infliximab) was needed. At the last follow-up of 13.9±7.0 months, only 1 of them maintained coronary involvement. 98.2% received intravenous immunoglobulin (IVIG) according to international recommendations (2 g/kg). All patients received anti-inflammatory doses of acetylsalicylic acid at diagnosis and subsequently antiplatelet doses.

Conclusions: Although the incidence of KD in our population is lower than other territories, it is still the most frequent cause of acquired heart disease in childhood. Early recognition and treatment with IVIG improve prognosis leading to a decrease in the rate of long-term cardiovascular outcomes.

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EVALUATION OF THE NEW CLASSIFICATION CRITERIA FOR PFAPA SYNDROME

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Background: Modified Marshall criteria used for PFAPA syndrome have never been validated and are little used by the experts because the symptoms of monogenic fevers often overlap with PFAPA ones. A new set of classification criteria based on an international survey and a consensus conference in Genoa was developed in 2017.

Objectives: Evaluate the performance of the new criteria in a real-life setting.

Methods: This is a multicentric, prospective and descriptive cohort study, through the recurrent fever module of the JIRCochort platform. 417 patients diagnosed with PFAPA (187), monogenic fever syndromes (167) or unclassified recurrent fever syndrome (UPF=63) from Swiss and French centers were enrolled in the study. The new classification criteria were applied to this cohort and we calculated their performance. We then analyzed which of the criteria performed the less well.

Results: One hundred fourteen from 187 (61%) PFAPA patients met the new criteria, as well as 20/230 non-PFAPA patients (FMF: 3, MKD: 4, other: 13); 73 PFAPA patients did not meet the criteria. We calculated a specificity of 91.3% and a sensitivity of 60.9%. The least satisfied criterion among PFAPA patients not meeting the criteria was “absence of skin rash”. By removing this criterion, the sensitivity improved (81.2%), but the specificity decreased slightly to 86%.

Conclusion: Genoa 2017 classification criteria for PFAPA syndrome showed a good specificity but an insufficient sensitivity. Excluding the less satisfied criterion, the set reaches a sensitivity and specificity around 80% which could be a fair compromise for PFAPA classification criteria. Our study highlights the difficulty in establishing classification criteria due to the lack of gold standard for PFAPA diagnosis.

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Disclosure of Interests: Fabio Crimi: None declared, Manel Mejbri: None declared, Véronique Henriksen Consultant for: SOBI, Novartis, Abbvie, Speakers bureau: Novartis, Glory Dingulu: None declared, Isabelle Koné-Paule Grant/research support from: SOBI has supported drug product (anakinra) for the presented study, Consultant for: SOBI, Novartis, Pfizer, Abbvie, UC, CHUGAI, ROCHE, Sophie Georgin-Lavalette Consultant for: novartis, sobi, Speakers bureau: novartis, sobi, Pascal Pilliet: None declared, michael hofer Grant/research support from: novartis, SOBI, Consultant for: Novartis, SOBI DOI: 10.1136/annrheumdis-2019-eular.8057

AN INTERNATIONAL SURVEY ON APPROACHES TOWARDS IMMUNISATION IN CHILDREN WITH RHEUMATIC DISEASES: A REPORT OF THE PRES VACCINATIONS WORKING GROUP

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Background: Data on immunisation practices in Paediatric Rheumatology are scarce. EULAR recommendations for vaccination in paediatric patients with rheumatic disease (RD) were published in 2011. In some countries national recommendations for vaccination of immunocompromised patients are available.

Objectives: To ascertain the opinion and current practices of paediatric rheumatologists with regards to immunisation of children with rheumatic diseases (RD), and to establish their confidence to immunise the patients with RD on immunosuppressive medication with live vaccines in light of the evidence available.

Methods: An online survey of practices and opinions towards immunisation of patients on lower grade immunosuppression with MMR or varicella vaccines was conducted with a focus on immunisation of the immunocompromised child with RD was distributed to paediatric rheumatologists across the globe. Responses were collected via SurveyMonkey and descriptive analysis was performed. Responses were anonymous with the exception of identification of the country and length of practice.

Results: 289 responses were received from 53 countries in Europe, North and South America, Australia and Asia. 35% of the responders had over 15 years of practice in Paediatric Rheumatology, while 42% had 5-15 years.

57% responded that all immunisations or at least part of them are given in their paediatric rheumatology unit, and 60% that the vaccinations are mandatory in their country. 93% of responders support the immunisation of paediatric patients with RD, 6.9% responded that they are either not supportive/not sure/support only vaccinations with inactivated vaccines.

53% reported that national recommendations for immunisations of immunosuppressed child are available but not specific to Paediatric Rheumatology. 41% of responders inform their practice on immunisation of patients with RD based exclusively on the EULAR recommendations, 37.5% based on national guidelines, 8.5% on local guidelines and 10% on combinations of the above. 48% of clinicians would postpone vaccinations in all cases if disease is active.

In terms of immunisations with live vaccines of patients with JIA on immunosuppressive treatment, 41% of responders would recommend the first dose of MMR or Varicella vaccines to patients with stable disease on Prednisolone < 1 mg/kg/day (maximum 20 mg) for less than 1 month or higher dose up to 2 mg/kg/day for less than 14 days, 14% would also recommend these vaccines if the above steroid dose was given in combination with Methotrexate (MTX) < 15mg/kg/week, 30% would recommend these vaccines if the patient was on MTX monotherapy. Comparably percentages reported confidence to also recommend booster doses of the two vaccines for the above drug combinations (45%, 15.7%, 37%, respectively), whilst up 10% of respondents would recommend them to patients on anti-TNF agent alone, and up to 7% for other biologics. For patients with SLE and quiescent disease on similar medications as above, 41%, 15%, 31%, respectively, of clinicians reported confidence to recommend MMR or Varicella booster doses.

48% of the respondents identified the reluctance of other health professionals involved in the process of immunisations as the main reason hampering the vaccination of paediatric patients with RD, whilst 22% indicated parental refusal or hesitancy.

Conclusion: There is variation in practice and opinions worldwide with regards to immunisations in paediatric patients with RD, and this likely reflects the discrepancies between national guidelines for immunisation of immunosuppressed child and also national policies. More studies are required, but there is an increasing vote of confidence towards immunisation of patients on lower grade immunosuppression with MMR or varicella vaccines.

BODY MASS INDEX AND DISEASE ACTIVITY IN PORTUGUESE AND BRAZILIAN JUVENILE IDIOPATHIC ARTHRITIS PATIENTS: RESULTS FROM RHEUMATIC DISEASES PORTUGUESE REGISTER – REUMA.PT

Background: The influence of body mass index (BMI) on Juvenile Idiopathic Arthritis (JIA) disease activity is poorly understood. In adults with Rheumatoid Arthritis, obesity has been associated with higher disease activity, while in JIA patients, a previous study has failed to find any association.

Objectives: To investigate the relationship between BMI and JIA disease activity.

Methods: This is an international, multicenter, observational, cross-sectional study. JIA patients (according to ILAR criteria) aged < 18 years, registered at Reuma.pt in Portugal and Brazil were included. Data was analysed upon records from the first registered visit. Age- and sex-specific BMI percentiles (P) were calculated based on WHO growth standard charts and categorized into underweight (P≤85), normal weight (85<P<97) and obesity (P≥97). Disease activity was assessed by Juvenile Arthritis Disease Activity Score (JADAS-27). Univariate linear regression was used to examine the association of JADAS-27 with BMI categories. Two multivariate regression models were performed a) adjusting for age, gender, race, country, disease duration and JIA category (model 1); b) adjusting for those covariates plus use of DMARDs (model 2).

Results: 255 patients included, mean age 10.1±4.7 years, mean disease duration 6.3±4.9 years; 62% female; 85% Caucasian. Thirty-two percent were persistent oligoarticular, 9% extended oligoarticular, 34% polyarticular RF+, 6% systemic, 13% enthesitis-related arthritis, 5% psoriatic arthritis. The influence of body mass index (BMI) on Juvenile Idiopathic Arthritis (JIA) disease activity is poorly understood. In adults with Rheumatoid Arthritis, obesity has been associated with higher disease activity, while in JIA patients, a previous study has failed to find any association.

Conclusion: Importantly, these results suggest that active disease can impair child’s weight gain. Further studies are needed to confirm these findings and understand the underlying mechanisms of this association.


NON-BACTERIAL OSTEITIS IN CHILDREN: PROGNOSTIC FACTORS

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Background: The incidence of non-bacterial osteitis (NBO), a rare autoinflammatory disease in childhood, has increased over the past few years. Early diagnosis and treatment, as well as an adequate follow-up, are necessary to prevent sequelae and complications. However, prognostic factors of the disease are unknown.

Objectives: To establish the prognostic factors of NBO.

Methods: A retrospective study of NBO, according to Jansson criteria, in children (<14 years) at a tertiary hospital from 2009 to 2018. Descriptive statistics were performed to examine clinical features, diagnoses, treatments and progress of the disease. Furthermore, bivariate analysis was performed in order to investigate factors involved in the remission of the disease (without treatment), the number of relapses and sequelae. We considered p<0.1 as significance level due to the small sample size.

Results: We reviewed 15 cases. Table shows the descriptive data. The likelihood of remission was found to be associated with the presence of X-ray findings apart from sclerosis/lysis. (80% vs 40%, p=0.07), a high white blood cell count (mm3) (11988.7 ± 3004.9 vs 8915.7 ± 3310.3, p=0.08) and ESR (mm) (58.3 ± 36.3 vs 26.8 ± 17.4, p=0.05) at diagnosis

Table: Descriptive analysis

Epidemiologic data

<table>
<thead>
<tr>
<th>Variable</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male)</td>
<td>11 (73)</td>
</tr>
<tr>
<td>Age (years), mean (SD)</td>
<td>9.6 (±1.7)</td>
</tr>
<tr>
<td>Delayed diagnosis (months), median (IQR)</td>
<td>3 (1–6)</td>
</tr>
<tr>
<td>Clinical presentation, n (%)</td>
<td>15 (100)</td>
</tr>
<tr>
<td>Pain</td>
<td>15 (100)</td>
</tr>
<tr>
<td>Limited movement</td>
<td>9 (60)</td>
</tr>
<tr>
<td>Swelling</td>
<td>9 (60)</td>
</tr>
<tr>
<td>No. of joints, median (IQR)</td>
<td>11 (4–6)</td>
</tr>
<tr>
<td>Bone lesion sites (n=4), n (%)</td>
<td>8 (53.3), 8 (53.3), 20 (66.6)</td>
</tr>
<tr>
<td>Radiology</td>
<td>12 (80), 5 (33.3), 3 (20.0)</td>
</tr>
<tr>
<td>Periarticular reaction</td>
<td>3 (20.0)</td>
</tr>
<tr>
<td>Bone biopsy (n=12), histopathology, n (%)</td>
<td>9 (75.0), 3 (25.0)</td>
</tr>
<tr>
<td>Inflammation</td>
<td>9 (75.0), 3 (25.0)</td>
</tr>
</tbody>
</table>

Biological tests

<table>
<thead>
<tr>
<th>Variable</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood test</td>
<td>15 (100)</td>
</tr>
<tr>
<td>White blood cells (mm3), mean (SD)</td>
<td>10946.7 ± 3428.8</td>
</tr>
<tr>
<td>CRP (mg/l), mean (SD)</td>
<td>41.0 ± 18.1</td>
</tr>
<tr>
<td>ESR (mm), mean (SD)</td>
<td>43.7 ± 32.5</td>
</tr>
<tr>
<td>MRI (n=4), findings, n (%)</td>
<td>10 (60), 5 (33.3), 3 (20.0)</td>
</tr>
<tr>
<td>Edema</td>
<td>12 (80), 5 (33.3), 3 (20.0)</td>
</tr>
<tr>
<td>Synovial fluid, n (%)</td>
<td>10 (60), 5 (33.3), 3 (20.0)</td>
</tr>
<tr>
<td>Periarticular reaction</td>
<td>3 (20.0)</td>
</tr>
<tr>
<td>Bone biopsy (n=12), histopathology, n (%)</td>
<td>9 (75.0), 3 (25.0)</td>
</tr>
</tbody>
</table>

Treatment

<table>
<thead>
<tr>
<th>Variable</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibiotics, n (%)</td>
<td>8 (53.3)</td>
</tr>
<tr>
<td>Duretine, mean (SD)</td>
<td>50.5 ± 15.9</td>
</tr>
<tr>
<td>NSAIDs, n (%)</td>
<td>7 (46.7)</td>
</tr>
<tr>
<td>Duretine, median (IQR)</td>
<td>72 (65.5–121.5)</td>
</tr>
<tr>
<td>Corticoids, n (%)</td>
<td>9 (60)</td>
</tr>
<tr>
<td>Duretine, median (IQR)</td>
<td>10 (60–195)</td>
</tr>
<tr>
<td>Methotrexate, n (%)</td>
<td>2 (13.3)</td>
</tr>
<tr>
<td>Duretine, median (IQR)</td>
<td>347.5 (185–547.5)</td>
</tr>
<tr>
<td>Folic acid therapy, n (%)</td>
<td>1 (6.7)</td>
</tr>
<tr>
<td>Duretine, median (IQR)</td>
<td>9 (60), 5 (33.3)</td>
</tr>
<tr>
<td>No. of cycles, median (IQR)</td>
<td>3 (2–3)</td>
</tr>
<tr>
<td>TNF inhibitors, n (%)</td>
<td>1 (6.7)</td>
</tr>
<tr>
<td>Duretine, median (IQR)</td>
<td>480 (300–800)</td>
</tr>
</tbody>
</table>

Outcome

<table>
<thead>
<tr>
<th>Variable</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of relapses, median (IQR)</td>
<td>2 (0–4)</td>
</tr>
<tr>
<td>Follow-up time (years), mean (SD)</td>
<td>4.5 (±2.8)</td>
</tr>
</tbody>
</table>

Current status, n (%) | REMission without treatment | REmission with treatment |
<table>
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<tr>
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</thead>
<tbody>
<tr>
<td>8 (53.3)</td>
<td>7 (46.7)</td>
</tr>
</tbody>
</table>

Sequelae, n (%) | Localized deformation | 2 (13.3) |
and a longer duration of disease (months) (5.7 ± 1.6 vs 3 ± 1.2, p = 0.06). In addition, fewer relapses were found among patients with peroneal involvement a 0 (0-5) v 5 (1-6.7), p = 0.05, a high white blood cell count at diagnosis (r = 0.569, p = 0.02) and those who were not treated with pamidronate at diagnosis (r = 0.5) v 5 (1.2-6.7), p = 0.07. Finally, the lack of sequelae was related to the administration of pamidronate (100% vs 57.1%, p = 0.07), younger age at diagnosis (years) (9.08 ± 1.4 vs 11 ± 2, p = 0.07) and lesser CRP level at diagnosis (mg/L) [2.9 (2.9-2.9) vs 3.8 (2.9-3.8), p = 0.005].

Conclusion: Advanced cases of NBO, without radiological signs of sclerosis or lysis, were more likely to achieve remission. Elevation of acute phase reactants was related to a better response to treatment and a lower relapse rates, but with a greater probability of sequelae. As described in the literature, bisphosphonates achieve higher rates of clinical and radiological remission. In our study, they are also associated with a lower relapse rates and the lack of sequelae. The last is the main reason to be considered the first treatment choice in NBO.

REFERENCES

Disclosure of Interests: Nuña Heredia Torres: None declared, Esmeralda Nuña: Quarter research support from: NOVARTIS, ABBI Vie, ROCHE (ALWAYS AS SPEAKER), Speakers bureau: NOVARTIS, ABBVIE, ROCHE, Rocío Galindo Zavala Grant/research support from: NOVAR TIS, ABBVIE (ALWAYS AS SPEAKER), Speakers bureau: NOVARTIS, ABBVIE, ROCHE, Laura Martín Pedraz: None declared, Antonio Urda Cardona Grant/research support from: PFIZER (ALWAYS AS SPEAKER), Speakers bureau: PFIZER


SAT0511 CANAKINUMAB IN SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS: CLINICAL INACTIVE DISEASE RATE AND SAFETY IN ITALIAN PATIENTS

Manuela Pardeo1, Claudia Bracca1, Anna Lucia Piscitelli1, Arianna De Matteis1, Jessica Tibaldi2, Maria Alessio1, Silvana Martino1, Giovanni Filocamo1, Francesca Orlando2, Silvana Martino2, Rolando Cimaz2, Giovanna Pardeo1, Claudia Bracca1, Anna Lucia Piscitelli1, Arianna De Matteis2,

Background: Systemic juvenile idiopathic arthritis (sJIA) is a polygenic autoimmune inflammatory disease. The innate immune mechanisms play a central role with overproduction of inflammatory cytokines. The increased knowledge on the role of these cytokines has provided a change in the natural history of the disease with the introduction of the targeted treatments. Remarkable results has been observed with canakinumab, an anti-interleukin-1β monoclonal antibody, in two clinical trials but little information are recorded in our population.

Objectives: To evaluate clinical inactive disease rate and safety of canakinumab in Italian patients with sJIA.

Methods: We have collected retrospectively clinical and laboratory data of patients with sJIA treated with canakinumab in 9 Italian Pediatric Rheumatology centers. Clinically inactive disease (CID) at 6 months was defined according to Wallace criteria. We analyzed the effect of canakinumab on fever, rash, number of active joints, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and physician’s global assessment of disease activity score.

Results: Forty seven patients (26 F) were included in the analyses. The median age (range) at the beginning of treatment with canakinumab was 7.6 (1.1-4.7) and 10.2 (1.7-22.2) years, respectively. Twenty seven patients (57.4%) had been previously treated with other biologic agents (18 with anakinra, 1 with tocilizumab, 6 with both and 2 with etanercept), withdrawn for inefficacy in 15/27 (55.5%). Thirty patients (63.8%) were receiving concomitant treatment with glucocorticoids at the median dose (range) of 0.69 (0.02-2.75) mg/kg/die. Thirty nine of 47 patients had > 6 months of follow-up. Among these 39 patients, 27 (69.2%) achieved CID at 6 months and 5/27 (18.5%) were still on glucocorticoids. Of the 30 patients who received concomitant glucocorticoids at baseline, 24 achieved 6 months of follow-up and 12 (50%) of these were able to withdraw glucocorticoids. Minor adverse events were reported in 5/30 (16.6%) patients: upper respiratory tract infections in 4 and transient injection site reaction in 1. No cases of macrophage activation syndrome was reported.

Conclusion: Our results provide initial real world evidence of the efficacy of treatment with canakinumab in patients with sJIA. In our study the median age of patients at the end of 27 months treatment (69.2%) than reported at the end (from 3 months to one year) of the 2 published randomized trials (60%). No serious adverse events were recorded in our population.

Disclosure of Interests: : Manuela Pardeo: None declared, Claudia Bracca: None declared, Anna Lucia Piscitelli: None declared, Arianna De Matteis: None declared, Jessica Tibaldi: None declared, Maria Alessio: None declared, Achille Marino: None declared, Giovanni Conti: None declared, Maria Cristina Maggio: None declared, Clotilde Alizzi: None declared, Francesco Liccardi: None declared, Anna Nunziola: None declared, Giovanni Filocamo: None declared, Francesca Orlando: None declared, Silvana Martino: None declared, Rolando Cimaz: None declared, Angela Ravelli: Fabrici De Benedetti: ABBVIE, ROCHE, Garcia-Díez-Cordero: Grant/research support from: ABBVIE, ROCHE (ALWAYS AS SPEAKER), Speakers bureau: ABBVIE, ROCHE, Laura Martín Pedraz: None declared, Antonio Urda Cardona Grant/research support from: PFIZER (ALWAYS AS SPEAKER), Speakers bureau: PFIZER


SAT0512 LONG-TERM FOLLOW-UP OF CARDIOVASCULAR OUTCOMES IN KAWASAKI DISEASE. OBSERVATIONAL STUDY FROM A SINGLE CENTER

D. Pijo-Peña, José Luis Martín-Varillas, Lara Sánchez Bilbao, Eva Peña Sainz-Pardo, Monica Calderón-Goerke, Natalia Palmou-Fontana, María Teresa Viadero, María Jesús Cabero, Miguel A. González-Gay, Ricardo Blanco, Marqués de Valdecilla University Hospital, Santander, Spain

Background: Kawasaki disease (KD) is an acute systemic vasculitis of unknown aetiology which can lead to coronary aneurysm (CA) formation in 15-20% of patients. Long-term rates of adverse cardiac events are not well-known.

Objectives: a) to compare demographic, clinical and laboratory features of patients who developed coronary aneurysm with patients who did not. b) to assess long-term cardiovascular outcomes in the subgroup of patients who developed cardiac aneurysms.

Methods: Single center study of 55 patients with KD who were diagnosed between 1994-2009. KD diagnosis was based on the classic criteria2. We considered two groups: a) patients who presented CA at diagnosis, b) patients who did not present CA. Statistical analysis was performed with SPSS. Student’s t test or Mann-Whitney U test was used to compare continuous variables, and Chi-squared test or Fisher’s exact test for categorical variables as appropriate.

Results: Out of 55 patients with KD, 8 patients (3 men/5 women) presented CA at diagnosis. Differences between the two groups mentioned above are shown in Table 1. Mean age at diagnosis was lower in patients who presented CA (1.74 vs 3.88 years; p = 0.04). The duration of symptoms was longer in patients with CA vs 14.1 vs 9.20 days; p = 0.015, however there were no qualitative differences in the symptomatology. Regarding laboratory markers, C- reactive protein (CRP) levels were significantly higher in patients who developed CA (17.0 vs 10.8 mg/L; p = 0.047). There was also a tendency to higher levels of erythrocyte sedimentation rate (ERS) and higher platelet count. All patients received intravenous immunoglobulin (IVIG) and antiplatelet agents at the time of...
**THERAPEUTIC APPROACH IN JUVENILE IDIOPATHIC ARTHRITIS: EMPIRICAL PAIN MEDICATION AND NEWLY INITIATED DISEASE MODIFYING ANTI-RHEUMATIC DRUGS**

Katarina Rebane1, Kristiina Aalto1, Maji Häapasää2, Kari Puolakkia3, Lauri Virta4, Hannu Kautiainen5, Heini Pohjankoski6.

1Children’s Hospital, Helsinki University Hospital, Helsinki, Finland
2National Pensions Insurance Company, Helsinki, Finland
3South Karelia Central Hospital, Lappeenranta, Finland
4Social Insurance Institution of Finland, Turku, Finland
5Department of General Practice and Unit of Primary Health Care, University of Helsinki and Helsinki University Hospital, Helsinki, Finland
6Päijät-Häme Central Hospital, Lahti, Finland

**Background:** Pain relief remains an important aspect in treating patients with juvenile idiopathic arthritis (JIA) despite of the new advanced therapeutic options. Nonsteroidal anti-inflammatory drugs (NSAIDs) are recommended providing symptomatic relief in JIA1. There is evidence of increased opioid use in adults with rheumatoid arthritis2, the use of opioids in children with JIA is poorly studied.

**Objectives:** Aim of the study was to describe patterns in using of pain medication and newly initiated anti-rheumatic drugs in outpatients with JIA. Methods: Data on 1507 patients (<16 years) with newly diagnosed JIA from 1 Jan 2010 to 31 Dec 2014 were collected from the register of the Finnish Social Insurance Institution. The index day was the date when reimbursement for JIA medication was admitted. The study period included 12 months pre- and post-index date. All patients were without disease modifying anti-rheumatic drugs (DMARDs) before the index day. For each patient three age-, gender- and residence-matched controls (altogether 4511) were identified from the National Centre for Population. Drug purchases were assessed in 3-month periods. Co-morbidities were evaluated.

**Results:** 20-fold more JIA patients purchased NSAIDs, 10-fold more paracetamol, and 10-fold more opioids (mostly tramadol and codeine) compared to controls. 648 patients (43%) purchased NSAIDs during 0-3 months before and after the index day, and 165 patients (11%) 10-12 months after the index day.

28 patients (2%) purchased opioids 12 months before the index-day, and 14 patients (1%) 12 months after. Paracetamol was purchased by 83 patients (5.1%) and by 59 patients (3.9%), respectively. Methotrexate (n = 1361 (90.3%)) was most commonly prescribed conventional DMARD, followed by prednisolone (n = 368 (24.4%)), hydroxychloroquine (n = 194 (12.9%)), sulfasalazine (n = 107 (1.9%)), and biological DMARDs (n = 41 (2.7%)). 26 patients (1.7%) were without antirheumatic treatment at 3-months after index-day.

JIA patients had significantly more comorbidities and traumas (p<0.001), compared to controls. 648 patients (43%) purchased NSAIDs during 0-3 months before and after the index day, and 165 patients (11%) 10-12 months after the index day.

**Conclusion:** Purchases of pain medication reduced after DMARDs were started. Only small proportion of JIA patients purchased opioids, despite of having more traumas and surgical procedures.

**REFERENCES**


**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.3653
Background: Therapeutic patient education (TPE) is widely recommended in the health care pathway of patients with chronic inflammatory rheumatism (CIR) but few pediatric programs are currently available. MIRAJE is a program for children and adolescents with CIR. It has been developed within a French health network (RESRIP (Réseau Rhumatismes Inflammatoires Pédiatriques)) to improve patient care for paediatric patients with CIR living in the Ile de France region.

The originality of the program was to design cross-cutting TPE using common issues to different pathologies: the experience of chronic illness, the management of daily life, inflammatory attacks, long-term treatments, physical activity.

Objectives: Assessment of acquisition of coping, self-care and safety skills.

Methods: After signing a written consent, an educational assessment is conducted in an individual interview with the patients and/or parents (for children under 6 years old), by a member of the multidisciplinary team. Five group sessions and one self-injection session are offered to patients. During the collective sessions, patients and parents are reappointed according to 4 groups: the group of parents, that of adolescents (12-18 years), that of children (6-11 years) and that of toddlers (<6 years).

To investigate the cognitive and behavioral impact of TPE on our patients and parents, a pre-post assessment was performed using a skill/knowledge questionnaire, based on three educational objectives: adaptation (8 skills), self-care (5 skills) and safety (1 skill), before and after the intervention.

Results: We present the results of the first year of implementation of our TPE program (2017). Nineteen children and 20 parents attended at least one group session. Ten participants (6 children aged 6 to 17 and 4 parents) completed the TPE program. The diseases covered were juvenile idiopathic arthritis (7), systemic lupus (2) and mevalonate kinase deficiency (1). All participants improved their knowledge and skills following TPE with greatest improvement in management of inflammatory attacks (self-care) (4 skills), self-care (5 skills) and safety (1 skill) before and after the intervention.

Conclusions: MIRAJE is the first French cross-cutting TPE program for children suffering from CIR and their parents. Although the number of participants having benefited from a full TPE program is relatively low, the first results are very encouraging. Indeed, TPE has allowed improving coping skills (6.8 versus 2.6 skills) and 8 security skills. Regarding self-injection workshop, most patients (4/5) have acquired skills in subcutaneous self-injection.

Background: TPE allows a better acceptance of the disease and fosters patient knowledge and skills for most children and parents.

The originality of the program was to design cross-cutting TPE using common issues to different pathologies: the experience of chronic illness, the management of daily life, inflammatory attacks, long-term treatments, physical activity.

Objectives: Assessment of acquisition of coping, self-care and safety skills.

Methods: After signing a written consent, an educational assessment is conducted in an individual interview with the patients and/or parents (for children under 6 years old), by a member of the multidisciplinary team. Five group sessions and one self-injection session are offered to patients. During the collective sessions, patients and parents are reappointed according to 4 groups: the group of parents, that of adolescents (12-18 years), that of children (6-11 years) and that of toddlers (<6 years) who completed TPE program. A pre-post comparison was performed using a skill/knowledge questionnaire, based on three educational objectives: adaptation (8 skills), self-care (5 skills) and safety (1 skill), before and after the intervention.

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Disclosure of Interests: Linda Rossi-Semeraro Grant/research support from: Roche, Perrine Dusser: None declared, Margarite Lima: None declared, Isabelle Marie: None declared, Fatima Benleulmi: None declared, William Fahy: None declared, Isabelle Kone-Paul: Grant/research support from: SOBI, Novartis, Pfizer, Abbvie, UCB, CHU, GAI, ROCHE, Chrystelle Hascoet: None declared

Acute Rheumatic Fever (ARF) and Post-streptococcal reactive arthritis (PSRA) are well known as post-streptococcal syndromes with arthritis in children. ARF have been declining in developed nations and it is generally thought to be a disease of the past. Despite decreasing incidence between 2010 and 2018 in Japan, focal outbreaks have been reported in developed nations.

The aims of this study were to assess ARF and PSRA incidence, the ratio was 13/21. Manifestations including; carditis, 26 (78.8%); arthritis, 26 (78.8%). The mean age of ARF was 8.0 years (3-15 years), and female/male ratio was 13/21.

Results:

From a total of 63 hospitals (58% response rate), 34 cases of ARF and 32 cases of PSRA were reported. For the research activities of the hospital in fully independent manners the industries listed in this section. This money has been reinvested for drug trials supported by Bristol-Myers Squibb, Pfizer, Novartis, Genentech, Roche, and AbbVie. I have received research support from Janssen. All of the support for these studies was paid to my institution, the University of Utah, and not directly to me.

Acknowledgement:

Professional medical writing: Lola Parfitt, MRes, Caudex; funding: Bristol-Myers Squibb.

Disclosure of Interests: Nicolinor Ruperto Grant/research support from: The Gaslini Institute for the research activities of the hospital in fully independent manners besides any commitment with third parties.

The money received for these activities are directly transferred to the Gaslini Institute’s bank account. Before March 2016, I was the head of the Pediatric Rheumatology Department at the G. Gaslini Hospital, where the PRINTO Coordinating Centre is located. For the coordination activity of the PRINTO network, the Gaslini Hospital received contributions from the industries listed in this section. This money has been reinvested for the research activities of the hospital in fully independent manners besides any commitment with third parties.

Background: Acute Rheumatic Fever (ARF) and Post-streptococcal reactive arthritis (PSRA) are well known as post-streptococcal syndromes with arthritis in children. ARF have been declining in developed nations and it is generally thought to be a disease of the past. Despite decreasing incidence, focal outbreaks have been reported in developed nations. Despite its importance, ARF and PSRA epidemiology has not been reviewed recently.

Objectives: The aims of this study were to assess ARF and PSRA incidence between 2010 and 2018 in Japan.

Methods: This retrospective Study examined ARF and PSRA incidence in 2010-2018, using medical record included in a total of 108 hospitals.

Results: From a total of 63 hospitals (58% response rate), 34 cases of ARF and 32 cases of PSRA were reported.

The mean age of ARF was 8.0 years (3-15 years), and female/male ratio was 13/21. Manifestations including: carditis, 26 (78.8%); arthritis, 26 (78.8%).

REFERENCES


(78.8%); Erythema marginatum in 7 (21.2%); Sydenham chorea, 4 (12.1%); Subcutaneous nodules, 2 (6.1%), respectively. And minor criteria were; fever, 27 (81.8%); first degree heart block, 7 (21.2%); elevated inflammatory markers (ESR, CRP), 30 (90.9%). ARF patients were treated with antimicrobial agent prophylaxis. On the other hand, the mean age of PSRA was 8.0 years (3-14 years), and female/male ratio was 17:14. Three patients (9.4%) had monoarthritis, 15 patients (46.9%) had oligoarthritis, and 14 patients (43.6%) had polyarthritis. Two patients had arthritis and enthesitis. And fever in 24 (75.0%) and Elevated inflammatory markers in 29 (90.6%). PSRA patients were treated with antimicrobial agent therapy 25 (78.1%); NSAIDs 27 (84.4%); and glucocorticoids therapy 3 (9.4%). During the follow up, there was no patient with carditis. 18 (56.3%) patients with PSRA were prescribed with antimicrobial agent prophylaxis.

Conclusion: In this study, ARF is rare in the Japanese pediatic population, but ARF has not yet disappeared. We observed high incidence of arthritis, carditis and erythema marginatum. No PSRA case was complicated with carditis. General pediatrician need to have updated information about ARF and PSRA even in industrialized countries.

REFERENCES


SAT0517 MANAGEMENT OF RISK OF VARICELLA INFECTION IN IMMUNOCOMPROMISED CHILDREN: WHAT IS THE EVIDENCE?

Maria Seago 1, Kate Armon 2, 1 Cambridge University, School of Clinical Medicine, Cambridge, United Kingdom; 2 Addenbrookes Hospital, Department of Paediatrics, Cambridge, United Kingdom

Background: Varicella-naive children on methotrexate are at risk of severe infection if they encounter varicella. Current guidance advises that management of children on higher doses or combination immunosuppression is challenging as there is no consensus about their management. Acyclovir and varicella-zoster immune globulin (VZIG) are commonly used as post-exposure prophylaxis (PEP).

Objectives: Assess the evidence for use of acyclovir and/or VZIG as PEP in the management of varicella exposure in susceptible children taking methotrexate.

Methods: A literature search using PubMed, the Cochrane Library and EMBASE was conducted from November to December 2017, using the terms methotrexate, immunocompromised, varicella, child, prophylaxis, acyclovir, VZIG and their variations. Only full papers, in English language, studying children were analysed (63 abstracts read for relevance, 28 papers obtained, 11 papers included).

Results: There have been no randomised controlled trials (RCTs) analysing the effectiveness of acyclovir and/or VZIG as PEP in immunocompromised children. The studies that do exist (see table for key publications) are small and uncontrolled and have largely been carried out in oncology rather than rheumatology patients. While they suggest that acyclovir and VZIG are effective at reducing historical infection rates of >70%, a significant proportion of recipients still get varicella.

Conclusion: There is only level 3 evidence for the use of acyclovir and/or VZIG as PEP in susceptible children on methotrexate. The literature indicates acyclovir is more effective, but this is a grade 3 recommendation only. A RCT to compare the effectiveness and acceptability of VZIG and acyclovir is needed, however the difficulty of randomising a cohort of similarly immunocompromised patients should not be underestimated.

REFERENCES

Disclosure of Interests: Maria Seago: None declared, Kate Armon Speakers bureau: Abbvie, but the fee was paid into Addenbrookes charitable account. DOI: 10.1136/annrheumdis-2019-eular.996

SAT0518 READINESS FOR TRANSITION – CROATIAN VERSION AND PILOT EVALUATION OF THE TRANSITION READINESS ASSESSMENT QUESTIONNAIRE (TRAQ) IN RHEUMATOLOGIC PATIENTS

Marina Šeršnik Perica 1, Miroslav Mayer 2, Lana T. Bukovac 3, 1 Srebrnjak Childrens Hospital, Department of Pediatric and Adolescent Rheumatology, Zagreb, Croatia; 2 University Hospital Centre Zagreb, University of Zagreb School of Medicine, Division of Clinical Immunology and Rheumatology, Department of Internal Medicine, Zagreb, Croatia; 3 Srebrnjak Childrens Hospital, Department of Pediatric and Adolescent Rheumatology, Zagreb, Croatia

Background: Rheumatic diseases of childhood extend to adulthood as an active disease in 30-70% of patients, which is the reason for requiring transition of rheumatologic care into adulthood. Transition should be individualized based on patient’s readiness, and good transition readiness analysis tools should be available at the time of transition.

Objectives: As systematic review of the available assessment tools for transitional readiness in adolescents with chronic diseases has shown that only the Transition Readiness Assessment Questionnaire (TRAQ) has proven reliability in its key measurement components, we have decided to use the TRAQ in pediatric rheumatology patients.

Methods: English version of TRAQ was translated to Croatian, afterwards a back-translation to English was done. Due to difference in the insurance policy in Croatia (health care is free for children under 18 years of age), question 9 was modified into: “Are you aware of the fact that after 18 years of age you have to start paying for the additional health insurance?”

A pilot study was performed in order to validate translated TRAQ by applying questionnaire to pediatric rheumatology patients at the time of transition.

Results: A total of 41 patients at the median age of 18.25 years (range 17.8-21.1 years) were enrolled, 28 female and 13 male patients. Most of them were under 18 years of age. The mean age of patients was 17.6 years (range 13-21 years), 56% female and 44% male. Most of the patients (85%) were on methotrexate treatment. 32 patients (78%) had history of immunosuppressive treatment.


Authors No. of Patients & VZV Status Cause of immunosuppression Treatment Outcomes

<table>
<thead>
<tr>
<th>Authors</th>
<th>No. of Patients &amp; VZV Status</th>
<th>Cause of immunosuppression</th>
<th>Treatment</th>
<th>Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Evans et al.</td>
<td>102 immunosuppressed children, 80 of whom were known to be seronegative for VZ IgG antibodies</td>
<td>Variable</td>
<td>Zoster immune globulin (ZIG) as a single dose - up to 1 year: 100 mg; 1-5 years: 250 mg; 6-10 years: 500 mg; 11-14 years: 750 mg; 15-16 years: 1000 mg</td>
<td>24/80 became infected; 17 with symptoms</td>
</tr>
<tr>
<td>Zaia et al.</td>
<td>164 immunocompromised children</td>
<td>Variable</td>
<td>81 given VZIG</td>
<td>VZIG: 49/81 became infected</td>
</tr>
<tr>
<td>Shinjoh et al.</td>
<td>65 immunocompromised children (some with a history of varicella); 76 immunocompetent children; 11 immunocompetent controls</td>
<td>Variable</td>
<td>Oral aciclovir (10 mg/kg/dose; 400 mg max dose; 4 times daily). Minimum of 7 days treatment, starting from 7 days after exposure</td>
<td>2/65 immunocompromised children developed varicella, 1/76 immunocompetent children developed varicella, 2/11 controls developed varicella</td>
</tr>
</tbody>
</table>
the patients had juvenile idiopathic arthritis (28 patients, 68.3%), 7 (17.1%) had mixed connective tissue disease, 3 (7.4%) had Raynaud's syndrome and there was one patient (2.4%) with each of the following diagnosis: SLE, fibromyalgia, and polyarteritis nodosa. The mean follow up time before the transition was 5.3 years (3 months - 14 years).

In general, the TRAQ was well understood and was completed in a short time by the study participants. No major difficulties were observed and all the patients were able to read and answer the questionnaire.

OBJECTIVES:
The aim was to compare the clinical characteristics, treatment outcomes of ERA in one of tertiary medical center in Taiwan and risk factors help to predict the development of active and non-active remission off medication.

REFERENCES:


Disclosure of Interests: Marjia Šenjug Perica: None declared, Miroslav Mayer Speakers bureau: Novartis, Sandoz, Abbvie, Pfizer, Alveogen, Roche, MSD, Octapharma, Lana Tambić Bukanov: None declared


SAT0519

CLINICAL CHARACTERISTICS, TREATMENT AND OUTCOMES OF ENTHESIS-RELATED ARTHRITIS IN TAIWAN

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Background: Juvenile idiopathic arthritis (JIA) has been categorized into seven different subtypes according to International League of Associations for Rheumatology system (ILAR) criteria [1]. Enthesitis-related arthritis (ERA) has represented the largest subtype in Taiwanese cohort study [2].

Objectives: The aim was to compare the clinical characteristics, treatments and outcomes of ERA in one of tertiary medical center in Taiwan to other subtypes of JIA. Further, to determine patients’ characteristics and risk factors help to predict the development of active and non-active treatment outcomes in ERA.

Methods: Retrospective review of patients diagnosed with JIA between March 1993 and December 2018 at a pediatric rheumatology clinic in National Taiwan University Hospital (NTUH), Taipei, Taiwan were enrolled. The outcome assessments were based on Wallace criteria to categorize patient into active and non-active (inactive, remission on medication and remission off medication) group.

Results: One hundred and eighty-three patients were included for 8 years mean follow up duration. Distribution of JIA subtypes in Figure 1 showed ERA was the single largest category of JIA (39.8%) in Taiwan. The demographic details of ERA patients in Table 1 revealed: male predominated (86%), late onset age (11.1±3.2 yrs), majority with HLA-B27 positive (92%), sacroiliac join or lumbosacral involvement (16%) and anterior uveitis (10%). Category specific outcomes in Table 2 showed ERA and extensive oligoarthritides were less likely to achieve non-active treatment response compared to persistent oligoarthritides. Among risk factors contributed to poorer treatment response in ERA were any clinical signs of sacroiliitis with P value of significant (0.0057).

Disclosure of Interests: None declared


Table 1. ERA patients and disease characteristic, n=73

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>n=73</th>
<th>Persistent Oligo n=33</th>
<th>Extensive Oligo n=22</th>
<th>Polyarticular RF(+) n=9</th>
<th>Polyarticular RF(-) n=19</th>
<th>Systemic n=25</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at onset, mean ±SD years</td>
<td>11.1±3.2</td>
<td>15 (48)</td>
<td>15 (68)</td>
<td>7 (37)</td>
<td>10 (53)</td>
<td>14 (56)</td>
</tr>
<tr>
<td>Male sex</td>
<td>63 (86)</td>
<td>46 (92)</td>
<td>14 (64)</td>
<td>10 (37)</td>
<td>10 (53)</td>
<td>14 (56)</td>
</tr>
<tr>
<td>Presence of HLA B27 antigen</td>
<td>67 (92)</td>
<td>54 (93)</td>
<td>18 (75)</td>
<td>6 (33)</td>
<td>8 (42)</td>
<td>8 (32)</td>
</tr>
<tr>
<td>Disease characteristic lumbosacral pain</td>
<td>68 (93)</td>
<td>62 (94)</td>
<td>10 (43)</td>
<td>3 (17)</td>
<td>2 (11)</td>
<td>2 (11)</td>
</tr>
<tr>
<td>Disease duration at follow up visit, mean ±SD years</td>
<td>6.5±5.0</td>
<td>7 (8)</td>
<td>1 (5)</td>
<td>5 (26)</td>
<td>10 (53)</td>
<td>14 (56)</td>
</tr>
<tr>
<td>Age at follow up, mean ±SD years</td>
<td>17.6±5.4</td>
<td>14 (42)</td>
<td>2 (9)</td>
<td>0 (0)</td>
<td>5 (26)</td>
<td>8 (32)</td>
</tr>
<tr>
<td>Pain follow up</td>
<td>3 (4)</td>
<td>1 (3)</td>
<td>2 (9)</td>
<td>0 (0)</td>
<td>2 (10)</td>
<td>2 (10)</td>
</tr>
<tr>
<td>Expir</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>1 (5)</td>
<td>1 (5)</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Active/Non-active (P)</td>
<td>46/24</td>
<td>14/18</td>
<td>15/5</td>
<td>7/2</td>
<td>10/8</td>
<td>14/8</td>
</tr>
</tbody>
</table>

*Comparison to Persistent Oligoarthritides. **P<0.05 with significant

Conclusion: ERA has represented the most common subtype of JIA in Taiwanese cohort study and has poorer treatment responses when compared to other JIA subtypes. To identify risk factors that contributing to poorer ERA treatment response might help more aggressive therapeutic strategy and improve outcome of ERA.

REFERENCES
DEFINING OUTCOME MEASURES IN JUVENILE IDIOPATHIC ARTHRITIS ASSOCIATED UVEITIS BY A SYSTEMATIC REVIEW ANALYSIS. DO WE NEED A CONSSENSUS?

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Background: Juvenile Idiopathic Arthritis associated Uveitis (JIA-U) represents its most frequent extra-articular manifestation and the main cause of childhood uveitis in in developed countries. The broad variety of outcome measures utilized makes the comparison of the disease course risk for complications, impairment in visual function, and responses to treatment quite difficult.

Objectives: Our aim was to define related and unified outcome measures in JIA-U.

Methods: A systematic review between January 2000 and December 2018 was performed to identify studies investigating outcome measures used in JIA-U.

Results: The initial search identified 8252 articles of which 29 were potentially eligible. Eighteen eligible articles remained in the analysis. A total of 27 studies, including 2 RCTs, were included. Among these studies 12 outcome measures for JIA-U use have been identified (grade of cells in the AC, grade of flare in the AC, VA, amblyopia, structural complications, use and sparing of oral corticosteroids and immunosuppressive drugs, surgery requirement, biomarkers, bilateral disease, JIA persistence, quality of life assessments, uveitis subtype). As regards primary outcome measures, 44% among studies included one or more variables related to disease activity (i.e. grade of flare, grade of cells); 56% included visual function performance (i.e. visual acuity); 68% (17/25) included one or more variables of disease-associated tissue damage or complications (i.e. cataract, amblyopia); 24% included disease features (i.e. bilateral disease; uveitis subtype); 44% included laboratory features (i.e. biomarkers); 8% included JIA features (i.e. persistence of disease); 12% included quality of life (i.e. EYE-Q); 44% included management (i.e. use and sparing of oral corticosteroids and other immunosuppressive drugs; surgery requirement).

Conclusion: Our systematic review surveys the heterogeneity around outcome measures related to JIA-U in children, even in RCTs. It does not provide the solution to overcome the heterogeneity in uveitis studies, but it does provide an estimate of the scale of the problems and provides data to inform this important debate; highlighting the requirement to obtain a new consensus regarding a common approach to identify suitable and efficient outcome measures in JIA-U.

Disclosure of Interests: Legend. N= number of identified studies.

REFERENCES


Disclosure of Interests: None declared

Comparison of Children Carrying E148Q Variant with Children Carrying Homozygous Pathogenic Variants

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Background: Familial Mediterranean Fever (FMF) is the most frequent autoinflammatory disease. Nearly 300 MEFV variants have been reported and recorded in INFEVERS database. The most common disease-associated variants are mapped on exons 2 and 10 of chromosome 16. Although E148Q variant is the most common one among carriers, its role as a disease causing mutation is still debate (1).

Objectives: The aim of our study was to evaluate and compare the demographic, clinical data, features and severity scores of children carrying only E148Q variant with the patients homozygous for pathogenic MEFV mutations (M694V, M694I, M680I, V726A). One of our objective was to test and compare these two groups for the diagnostic utility of 2 adults and 1 pediatric MEFV diagnostic criteria (Tel Hashomer, Livneh and Pediatric Rheumatology) (2-4).

Methods: The medical records of 1685 children diagnosed and followed up as FMF were reviewed retrospectively. The demographic, clinical and genetic data of children carrying only E148Q variant (either heterozygous or homozygous carriers) (group 1) and children with pathogenic mutations (M694V, M694I, M680I, V726A) (group 2) were collected. All patients were evaluated for three diagnostic criteria.

Results: Children with E148Q variant were 128 and children with pathogenic homozygous variants were 429. Male to female ratio was 1.13 in group 1 and 1.15 in group 2 (p>0.05). The mean age of patients in group 1 was 12±1.5 years, in group 2 14±5.9 (p<0.001). The mean age of symptom onset was 5.4±4.1 in group 1, 4.3±3.6 in group 2 (p<0.01). Consanguinity was significantly higher in group 2 (29% vs 53%, p<0.01). In group 1 17.9% had a sibling with FMF, while in group 2 27% had a sibling with FMF (p=0.03). Clinical features like pleuritis, synovitis, recurrent fever, erysipelas-like erythema and monoarthritis were significantly more common in group 2 than group 1 (31.7% vs 9%; p<0.001, 55.9% vs 32%; p<0.001, 86.9% vs 78.9%; p<0.03, 31.2% vs 7%; p<0.001, 51.7% vs 28.1%; p<0.01, respectively). Incomplete attacks were significantly more common in group 1 than group 2 (16.4% vs 7.4%; p<0.005). Moderate and severe PRAS scores were significantly higher in group 2 (93.9% vs 71.9%; p<0.001). Laboratory values like C-reactive protein, erythrocyte sedimentation rate, serum amyloid A were found significantly higher in group 2 than group 1 (3.6±6.3 vs 0.8±1.2; p<0.001, 13±10 vs 7.3±6; p<0.001, 6.9±22.5 vs 2.9±2.2; p<0.007, respectively). The percentage of children diagnosed according two Tel Hashomer and pediatric criteria was significantly higher in group 2 than group 1 (88.5% vs 77.3%; p=0.002, 95.3% vs 84.3%; p<0.001, respectively). But both groups show similar diagnostic utility according to Livneh criteria.

Conclusion: Although children carrying E148Q variants meet the three validated diagnostic criteria of FMF. They had milder course of disease than children homozygous for pathogenic MEFV variants both clinically and in laboratory means.

REFERENCES

Disclosure of Interests: None declared

Evaluation of Coexisting Diseases in Children with Familial Mediterranean Fever

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Background: Familial Mediterranean Fever (FMF) is the most common periodic fever syndrome in childhood. It is characterized by fever attacks, abdominal pain lasting between 6 - 72 hours, serositis and erysipelas like erythema. Since FMF is inherited in autosomal recessive manner, it has higher frequency in populations that have higher rate of consanguineous marriages. As it is a lifelong chronic disorder, it is important to understand its clinical course for preventive medicine. Despite the higher incidence of variety of disorders showed studies among adult FMF patient, there is not enough data from pediatric populations.

Objectives: The objective of the study is to evaluate the comorbidity disorders in a large pediatric familial Mediterranean fever cohort.

Methods: Six hundred and eighty-six children with FMF were interviewed by the same investigator between October 2018 and January 2019 in our pediatric rheumatology department. Demographic features and MEFV gene mutations were recorded from patients charts. Patients and/or their parents were asked about characteristics of their fever episodes, presence of arthralgia, arthritis, abdominal pain, chest pain in the course of fever attack and coexistence of any other disease confirmed by a physician.

Results: Female-male ratio of our cohort was 0.85. Mean age of the patients was 12.8 ± 7.4 years. Mean age of patients at disease onset and at the time of diagnosis was 4.38 ± 3.46 years and 6.55 ± 3.67 years, respectively. Sixty-five and a half percent of patients had family history of FMF. Consanguineous marriage rate was 29.8%. Most common MEFV mutations were: M694V homozygotes (18.8%), M694V heterozygotes (17.7%), R202Q heterozygotes (13.1%), R202Q homozygotes (5.5%) and V726A homozygotes (4.9%), respectively. Resistance to colchicine treatment was present in 43 (6.2%) patients. Number of patients that underwent tonsillectomy were 9 (1.3%) and number of patients that had appendectomy was 11 (1.6%). Detected coexisting diseases are listed in Table 1.

Table 1.

<table>
<thead>
<tr>
<th>Disease</th>
<th>n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyarticular</td>
<td>13(4.8)</td>
</tr>
<tr>
<td>Oligoarticular</td>
<td>4 (0.5)</td>
</tr>
<tr>
<td>Systemic</td>
<td>11(2.4)</td>
</tr>
<tr>
<td>Juvenile</td>
<td>5 (0.7)</td>
</tr>
<tr>
<td>Enthesitis Related Arthritis</td>
<td>1 (0.1)</td>
</tr>
<tr>
<td>Juvenile Spondylitis</td>
<td>13 (1.8)</td>
</tr>
<tr>
<td>Asthma/Reactive Airway Disease</td>
<td>26 (3.7)</td>
</tr>
<tr>
<td>Henoch Schonlein Purpura</td>
<td>18 (2.6)</td>
</tr>
<tr>
<td>Uveitis</td>
<td>10 (1.4)</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>9 (1.3)</td>
</tr>
<tr>
<td>Periodic fever, aphthous stomatitis, pharyngitis, cervical adenitis (PFAPA)</td>
<td>7 (1)</td>
</tr>
<tr>
<td>Acute Rheumatic Fever</td>
<td>7 (1)</td>
</tr>
<tr>
<td>Migraine</td>
<td>7 (1)</td>
</tr>
<tr>
<td>Allergic Rhinitis</td>
<td>6 (0.8)</td>
</tr>
</tbody>
</table>

Conclusion: In this study, we have reported increased frequency of juvenile idiopathic arthritis, asthma- reactive airway disease, Henoch Schonlein purpura, uveitis, inflammatory bowel disease, PFAPA syndrome and acute rheumatic fever in a large pediatric FMF cohort. Those findings consistent with data from literature. It is important to be alert about these diseases that may develop in patients with FMF for preventing them from the potential morbidities.

REFERENCES
THE ROLE OF MEFV GENE SEQUENCING ON PREDICTING THE RISK AND DISEASE SEVERITY OF SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS

Linqing Zhong, Hongmei Song. Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, China

Background: Genetically susceptibility was essential in pathogenesis of systemic juvenile idiopathic arthritis (SJIA). Objectives: To find out whether MEFV mutations contributed to the occurrence of SJIA and study the association of MEFV mutations with systemic juvenile idiopathic arthritis (SJIA) patients’ disease severity. Methods: SJIA children diagnosed based on the ILAR criteria and followed up for at least 6 months between January 2011 and July 2016 were enrolled. Meta-analysis was performed to evaluate the contribution of MEFV mutations to SJIA susceptibility. All included children were divided into three groups by presence and number of MEFV mutations, namely, those without MEFV mutation, the one mutation group, and those with more than one mutation. Demographic and clinical characteristics, as well as disease severity were compared among these groups. Disease severity was evaluated with the following three items, i.e., average duration of use of each drug, the proportion of disease activity duration and relative relapse rate. Kaplan-Meier curves and log rank test were used to estimate the probability of the first relapse.

Results: Eighty-nine patients met the ILAR criteria, among which 55 patients were eligible for further analysis. The MEFV mutations of our subjects primarily existed in exons 2 and 3. No significant difference were found in frequency of each mutation between SJIA children and healthy controls. Meta-analysis demonstrated that M694V was a risk factor for SJIA (pooled OR: 7.13, 95% CI: 3.01-16.89). Comparing with the one mutation group, biologics were used more frequently in those without or with more than one mutation in MEFV (p<0.017). Moreover, the proportion of disease activity duration was significantly lower in the one mutation group than the other two groups (p=0.028 and 0.002 respectively).

Conclusion: The mutation M694V in MEFV contributed to occurrence of SJIA. SJIA patients carrying one heterozygous mutation in MEFV tend to be less severe, which might be attributed to E148Q.

REFERENCES

Disclosure of Interests: None declared

THE HETEROGENEITY OF JUVENILE PSORIATIC ARTHRITIS: EVIDENCE FROM A LARGE MULTINATIONAL COHORT

Hala Etyar1, Arūne Rama-naukiene2, Alessandra Alongi3, Yaryna Boyko4, Yosef Uziel5, Tadej Avcina6, Pierrot Quartier7, Nicoline Ruperto8, Angelo Ravelli9, Alessandro Consolaro10, Tripoli Children Hospital, Pediatric Rheumatology, Tripoli, Libya; 2Research Council, University of Lithuania, Kaunas, Lithuania; 3Instituto Gianna Gaslini, Pediatrica Rheumatologia, Genoa, Italy; 4Western Ukrainian Specialised Children’s Medical Centre, Pediatric Rheumatology, Lviv, Ukraine; 5Meir Medical Center, Kefar Sava, Israel; 6Necker-Enfants Malades Hospital, Pediatric Rheumatology, Paris, France

Background: Despite being considered as a distinct diagnostic category in the current ILAR classification criteria, Juvenile Psoriatic Arthritis (JPsA) is known to be a heterogeneous clinical entity, with growing evidence suggesting at least two age-based distinct subgroups (1)

Objectives: To identify and characterize subgroups of patients classified as JPsA according to the ILAR criteria and their possible differences in laboratory features at onset and outcomes measures collected at visit, namely JADAS scores, VAS-measured Pain, Overall Well-Being (PGA) Pediatric Rheumatology Quality of Life Scale (PROLL). In patients with disease duration more than 2 years (n=233), the relation with Articular and Extraarticular Juvenile Arthritis Damage Index (JADI) was also assessed.

Results: LCA revealed 5 classes: 1) late-onset patients with psoriasis, characterized by higher frequency of axial involvement at visit (n = 121); 2) early-onset patients with psoriasis, more likely to be ANA-negative (n = 66); 3) young females with dactylitis at onset and family history of psoriasis, more likely to present with symmetric joint involvement (n = 62); 4) subjects with nail changes and family history of psoriasis (n=34); 5) group of patients exhibiting dactylitis and nail changes at onset, mostly males, with higher rates of HLA-B27 positivity, small joint involvement and enthesis at visit (n = 25). Class 1 is associated with higher scores of JADAS10, pain, PGA and J2; these group also shows higher JADI-A than Class 3. Extraarticular damage is worst for Class 2 subjects.

Conclusion: The data driven clustering approach revealed several subgroups, confirming the heterogeneity of JPSA in a multinational cohort. Later-onset subjects with psoriasis have more aggressive disease, being clearly distinct from early-onset ANA-positive patients with psoriasis. The results suggest the need to revise the current classification in order to identify groups that may benefit from different therapeutic choices.

REFERENCES

Disclosure of Interests: Hala Etyar: None declared, Arūne Rama-naukiene: None declared, Alessandra Alongi: None declared, Yaryna Boyko: None declared, Yosef Uziel: None declared, Tadej Avcina: None declared, Pierrot Quartier Consultant for: AbbVie, Chugai-Roche, Lilly, Novartis, Novimmune, Sanofi, and SOBI, Consultant for: AbbVie, Chugai-Roche, Lilly, Novartis, Novimmune, Sanofi, and SOBI, Speakers bureau: AbbVie, BMS, Chugai-Roche, Novartis, Pfizer, and SOBI, Speakers bureau: AbbVie, BMS, Chugai-Roche, Novartis, Pfizer, and SOBI, Nicolino Ruperto Grant/research support from: The Gaslini Hospital, where NR works as full-time public employee, has received contributions (> 10.000 USD each) from the following industries in the last 3 years: BMS, Eli-Lilly, GlaxoSmithKline, Hoffmann-La Roche, Novartis, Pfizer, and SOBI, funding has been reinvested for the research activities of the hospital in a fully independent manner, without any commitment with third parties., Consultant for: Received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, AbbVie, Astre neca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sinergie, Sobi and Takeda., Speakers bureau: Received honoraria for consultancies or speaker bureaus (< 10.000 USD each) from the following pharmaceutical companies in the past 3 years: Ablynx, AbbVie, Astre neca-Medimmune, Biogen, Boehringer, Bristol-Myers Squibb, Eli-Lilly, EMD Serono, GlaxoSmithKline, Hoffmann-La Roche, Janssen, Merck, Novartis, Pfizer, R-Pharma, SanofiServier, Sinergie, Sobi and Takeda., Angelo Ravelli Grant/research support from: Angelini, AbbVie, Bristol-Myers Squibb, Johnson & Johnson, Novartis, Pfizer, Reclitt Beniker, and Roche, Consultant for: Angelini, AbbVie, Bristol-Myers Squibb, Johnson & Johnson, Novartis, Pfizer, Reclitt Beniker, and Roche, Consultant for: Angelini, AbbVie, Bristol-Myers Squibb, Johnson & Johnson, Novartis, Pfizer, Reclitt Beniker, and Roche, Alessandro Consolaro Grant/research support from: AbbVie, Pfizer, DOI: 10.1136/annrheumdis-2019-eular.6209
IMMUNOSCINTIGRAPHY OF SACROILIAC JOINTS SHOWS VERY GOOD AGREEMENT WITH INFLAMMATION ON MRI IN AXIAL SPONDYLOARTHRITIS PATIENTS

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Background: Currently MRI is the preferred imaging method to detect bone marrow edema (BME), the hallmark of sacroiliitis. MRI plays an important role in the early diagnosis of axial Spondyloarthritis (axSpA). Biological disease-modifying anti-rheumatic treatment has revolutionized the therapeutic armamentarium of axSpA. With drugs targeting TNF, 50% of axSpA patients achieve a clinically important response. Therefore, we hypothesized that if we would be able to demonstrate in vivo expression of TNF in sacroiliac joints by scintigraphy with 99mTc-radiolabeled certolizumab pegol (99mTc-CZP), this might lead to more evidence-based biological therapy.

Objectives: To investigate the agreement between BME on MRI-SIJ and tracer uptake on immunoscintigraphy with 99mTc-CZP in the same location in patients with axSpA.

Methods: CZP was conjugated with S-HYNIC and subsequently radiolabeled with approximately 740 MBq Tc99m and injected intravenously. Static images with single photon emission tomography (SPECT)/computed tomography (CT) of SIJ were acquired 4-6h post injection. Uptake of the tracer was scored semi-quantitatively, per quadrant of the SIJ: 0=no uptake, 1=faint uptake or 2=clear uptake. BME on MRI was scored per quadrant over 6 slices as absent or present, providing a maximum score of 6 per quadrant. Agreement between MRI-SIJ and immunoscintigraphy was calculated (kappa; percentage agreement) for all quadrants separately. To calculate the agreement a cut-off of ≥1 was used for MRI scores as well as immunoscintigraphy scores. In addition, depth and intensity of BME lesions on MRI-SIJ (as defined in the Spondyloarthritis Research Consortium of Canada (SPARCC) method) were assessed per slice per SIJ.

Results: 7 axSpA patients (mean age 36±5.7 years) had both MRI-SIJ and immunoscintigraphy available. The mean score for BME lesions seen on MRI was 12.9±7.9 and 4.8±5.4 for tracer uptake observed on the immunoscintigraphy. In 2 out of the 7 patients there was no BME on MRI and in the same 2 patients there was no tracer uptake seen on scintigraphy. In table 1 kappa coefficients and percentage agreement for every quadrant are shown. The mean and median of agreement for all quadrants was k=0.80 and k=0.86, respectively. Clear tracer uptake (score 2) was correlated to deep BME lesions on MRI-SIJ (extending over the depth of at least 1cm from the articular surface); the observed Spearman’s rho correlations were 0.986 (p<0.00) and 0.956 (p<0.00) for left and right SIJs, respectively. Regarding intensity, no significant correlation with clear tracer uptake was found. Interestingly, in one additional patient with complete ankylosis of the SIJs on radiographs no tracer uptake could be detected, suggesting that in vivo detection of TNF does not correlate with bone formation.

Table 1. Agreement on presence of BME on MRI-SIJ in a quadrant and tracer uptake on the immunoscintigraphy in that same quadrant.

<table>
<thead>
<tr>
<th>Location of the SIJ quadrant</th>
<th>Kappa (CI)</th>
<th>Percentage agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right upper iliac quadrant (RQ1)</td>
<td>0.720 (0.21-1)</td>
<td>85.7%</td>
</tr>
<tr>
<td>Right upper sacral quadrant (RQ2)</td>
<td>0.66 (0.14-1)</td>
<td>85.7%</td>
</tr>
<tr>
<td>Right lower sacral quadrant (RQ3)</td>
<td>0.417 (0-1)</td>
<td>71.4%</td>
</tr>
<tr>
<td>Right lower iliac quadrant (RQ4)</td>
<td>1 (1-1)</td>
<td>100%</td>
</tr>
<tr>
<td>Left upper iliac quadrant (LI1)</td>
<td>1 (1-1)</td>
<td>100%</td>
</tr>
<tr>
<td>Left upper sacral quadrant (LQ2)</td>
<td>0.588 (0-1)</td>
<td>85.7%</td>
</tr>
<tr>
<td>Left lower sacral quadrant (LQ3)</td>
<td>1 (1-1)</td>
<td>100%</td>
</tr>
<tr>
<td>Left lower iliac quadrant (LQ4)</td>
<td>1 (1-1)</td>
<td>100%</td>
</tr>
</tbody>
</table>

Conclusion: Inflammation on MRI-SIJ can be detected with immunoscintigraphy with 99mTc-CZP. The immunoscintigraphy showed good correlation with BME lesions on MRI in patients with axSpA. Deep lesions, considered specific for axSpA, showed an almost perfect correlation.

Disclosure of Interests: : Philippe Carron: None declared, Manouk de Hooge: None declared, Thomas Renson: None declared, Bleie Lambert: None declared, Kathia De Man: None declared, Dirk Elewaut: None declared, Filip van den Bosch Consultant for: AbbVie, BMS, Galapagos, Janssen, Lilly, Merck, Novartis, Pfizer and UCB, Speakers bureau: AbbVie, BMS, Janssen, Lilly, Merck, Novartis, Pfizer and UCB.

THE COURSE OF ABERRANT FINDINGS ON MRI OF THE SACROILIAC JOINTS OVER 6 MONTHS IN POSTPARTUM WOMEN

Anais Depecic1, Thomas Renson1,2, Ann-Sophie De Craene1,2, Manouk de Hooge1,3, Thomas Renson1,2, Filip van den Bosch1,2, Ghent University Hospital, Rheumatology, Gent, Belgium; 2Ghent University Hospital, VIB Inflammation Research Center, Gent, Belgium; 3Ghent University Hospital, Obstetrics, Gent, Belgium

Background: Sacroiliac bone marrow oedema (BME) on magnetic resonance imaging (MRI) can have different causes. Besides spondyloarthritis (SpA), other more rare causes as stress fractures, mechanical stress, infections or malignancies can be identified. There are limited data regarding the specificity of MRI lesions in a non-SpA population. Prenancy and vaginal delivery might induce the presence of inflammatory and/or structural MRI lesions by mechanical stress.

Objectives: To assess aberrant findings on MRI features of the sacroiliac joints (SIJ) in postpartum women and describe the course after a 6 month time period.

Methods: Twenty-five women underwent an MRI of the SIJ within 10 days after childbirth; delivery by caesarean section was excluded. The scan was repeated after 6 months. One subject was lost to follow-up. Three trained readers systematically scored inflammatory and structural SpA-like lesions (not reported here) and qualitatively described other aberrant findings. Both time points were scored on T1-weighted and short tau inversion recovery (STIR) MRI images. Readers were blinded for time sequence and clinical and demographic information on the subjects.

Results: In 16 out of 25 (64%) subjects there were aberrant MRI findings at baseline. Thirteen out of 25 (52%) showed BME at the symphysis pubis on the baseline MRI (fig. 1). After 6 months, 6 out of 24 (25%) subjects still showed BME; in 1 subject BME of the symphysis pubis was increased at 6 months. Two out of 25 (8%) displayed a sacral fracture on the baseline MRI. Both these fractures were asymptomatic and resolved completely after 6 months (fig. 2). One out of 25 subjects (4%) showed degenerative disc disease at level L5-S1 in the form of Modic type 2; vertebral and endplate related replacement of bone marrow with fat deposition. As expected, the presence of Modic type 2 did not decrease at follow-up. No other aberrant findings were seen.

Figure 1. BME of the symphysis pubis on STIR sequence.
**SA70527**

**DOPPLER IN ENTHESIES: A POTENTIAL USEFUL OUTCOME IN ACTIVE SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS**

Juan Molina Collada1, Cristina Macía-Villa1, Chaimada Plasencia1, Diana Peiteado1, Laura Nuño1, Irene Moro1, Alejandro Villalva1, Carolina Tornero1, Patricia Bogas1, Luis Coronel1, Gabriela González1, Diego Benavent1, Elisa Fernández1, Pablo Rodríguez-Merlos1, Gerardo Napky1, Alejandro Balsa1, Eugenio de Miguel1, Hospital Universitario La Paz, Madrid, Spain; Hospital Universitario Severo Ochoa, Madrid, Spain; Hospital Universitario Nuestra Señora de la Candelaria, Tenerife, Tenerife, Spain

**Background:** The assessment of activity in spondyloarthritis (SpA) and psoriatic arthritis (PsA) involves several domains, including entheses. Clinical enthesitis has shown low sensitivity, specificity and reliability. The inclusion of ultrasound (US) could be an objective outcome in the assessment of the disease.

**Objectives:** To assess the prevalence of peripheral US enthesitis using an US score, at patient level, among active SpA and PsA patients.

**Methods:** A cross-sectional study in patients with SpA and PsA active disease, are observed when assessing MRI-SIJ of postpartum women for SpA-like lesions. BME at the symphysis pubis was often seen shortly after birth and half of those lesions persisted at follow-up after 6 months.

**Disclosure of Interests:**: None declared.

**Conclusion:** Aberrant findings, like sacral fractures and degenerative disc disease, are observed independently of SpA subtype and activity. Presence of PD enthesitis is found in 80% of patients with active SpA and PsA. This finding is independent of SpA subtype and support the usefulness of PD US in the assessment of enthesitis.

**Table 1. Baseline characteristics of active SpA patients**

<table>
<thead>
<tr>
<th>Total nr</th>
<th>AS n=19</th>
<th>PsA n=10</th>
<th>nr-axSpA n=7</th>
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<tbody>
<tr>
<td>Age</td>
<td>49±13</td>
<td>50±14.5</td>
<td>51±12.9</td>
</tr>
<tr>
<td>Sex</td>
<td>Female</td>
<td>18 (50%)</td>
<td>9 (47.4%)</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>11.5</td>
<td>13±11.4</td>
<td>11±17</td>
</tr>
<tr>
<td>DAS28</td>
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<td>4±1.4</td>
</tr>
<tr>
<td>ASDAS</td>
<td>3.7±0.9</td>
<td>3.7±1</td>
<td>4.1±0.6</td>
</tr>
<tr>
<td>BASDAI</td>
<td>5.7±2.2</td>
<td>5.3±2.5</td>
<td>5.4±0.8</td>
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<tr>
<td>MASEI score</td>
<td>15 (78.9%)</td>
<td>9 (90%)</td>
<td>5 (71.4%)</td>
</tr>
<tr>
<td>Mean number of enthesiopathy with PD</td>
<td>1.7±1.3</td>
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<tr>
<td>Mean number of enthesiopathy with PD OMERACT</td>
<td>1.8±1.4</td>
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**Table 2. Inter-reader reliability**

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<tr>
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**Disclosure of Interests:** Juan Molina Collada: None declared, Cristina Macía-Villa: None declared, Chaimada Plasencia: Speakers bureau: Pfizer, MSD, MD, Diego Benavent: None declared, Laura Nuño: None declared, Irene Moro: None declared, Alejandro Villalva: None declared, Carolina Tornero: None declared, Patricia Bogas: Grant/research support from: non restricted grant from Sanofi, Luis Coronel: None declared, Gabriela González: None declared, Diego Benavent: None declared, Elisa Fernández: None declared, Pablo Rodríguez-Merlos: None declared, Gerardo Napky: None declared, Alejandro Balsa: Grant/research support from: Abbvie, Pfizer, Novartis, BMS, Nordic, Sanofi, Consultant for: Abbie, Pfizer, Novartis, BMS, Nordic, Sanofi, Consultant for: Pfizer, Speakers bureau: Pfizer, Novartis, UCB, Nordic, Sanofi, Sandoz, Lilly, Paid instructor for: Pfizer, Speakers bureau: Pfizer, Novartis, UCB, Nordic, Sanofi, Sandoz, Lilly, Eugenio de Miguel: None declared

**SA70528**

**DETECTION OF FACET JOINT ANKYLOSIS ON WHOLE SPINE LOW-DOSE CT IN RADILOGraphic AXIAL SPONDYLOARTHRITIS: DATA FROM THE SENSITIVE IMAGING OF AXIAL SPONDYLOARTHRITIS (SIAS) COHORT**

Rosalinde Stal1, Floris A. van Gaalen1, Désirée van der Heijde1, Xenofon Baraliakos2, Rosalinde Stal1, Désirée van der Heijde1, Xenofon Baraliakos2, LUMC, Leiden, Netherlands; Rheumazentrum Ruhrgebiet, Herne, Germany

**Background:** In radiographic axial spondyloarthritis (r-axSpA), whole spine low-dose CT (ldCT) is superior in detecting syndesmophytes to conventional radiography (CR), which is limited to the lumbar and cervical spine. As facet joints are difficult to visualize on CR, CT has been used to study facet joint ankylosis in r-axSpA in parts of the spine. However, facet joints in the whole spine have never been studied.

**Objectives:** To assess visibility and interreader reliability of facet joint ankylosis as detected by whole spine ldCT and to describe the prevalence of facet joint ankylosis in patients with r-axSpA.

**Methods:** In an observational cohort, 60 r-axSpA patients with 1-18 syn- desmophytes on CR and at least one inflammatory lesion on spinal MRI, underwent ldCT (approximately 4 mSV) of the whole spine. Images were assessed independently by two trained readers and left and right C2-C3 to L5-S1 facet joints were scored as ankylosis present (1) or absent (0). The percentages of missing joint scores per reader were calculated.

**Disclosure of Interests:** Juan Molina Collada: None declared, Cristina Macía-Villa: None declared, Chaimada Plasencia Speakers bureau: Pfizer, MSD, MD, Diego Benavent: None declared, Laura Nuño: None declared, Irene Moro: None declared, Alejandro Villalva: None declared, Carolina Tornero: None declared, Patricia Bogas: Grant/research support from: non restricted grant from Sanofi, Luis Coronel: None declared, Gabriela González: None declared, Diego Benavent: None declared, Elisa Fernández: None declared, Pablo Rodríguez-Merlos: None declared, Gerardo Napky: None declared, Alejandro Balsa: Grant/research support from: Abbvie, Pfizer, Novartis, BMS, Nordic, Sanofi, Consultant for: Abbie, Pfizer, Novartis, BMS, Nordic, Sanofi, Consultant for: Pfizer, Speakers bureau: Pfizer, Novartis, UCB, Nordic, Sanofi, Sandoz, Lilly, Paid instructor for: Pfizer, Speakers bureau: Pfizer, Novartis, UCB, Nordic, Sanofi, Sandoz, Lilly, Eugenio de Miguel: None declared

**DOI:** 10.1136/annrheumdis-2019-eular.4854

**Figure 2.** STIR image of sacral fracture at baseline (A) and after 6 months (B).

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Facet joint ankylosis progression in patients with radiographic axial spondyloarthritis (r-axSpA).

**Objectives:** To study facet joint ankylosis progression in the whole spine and per segment.

**Methods:**
- In an observational cohort, r-axSpA patients who had between 1-18 syndesmophytes on CR and ≥1 inflammatory lesion on spinal MRI underwent lCT of the whole spine (approximately 4 mSv) with a repeated lCT after two years. Paired lCTs were assessed by two trained readers independently blinded to chronology. Left and right C2-C3 to L5-S1 facet joints were scored as ankylosis present (1) or absent (0).
- Change scores, intraclass correlation coefficients (ICCs; two-way average, absolute agreement) and smallest detectable change (SDC) were calculated for the whole spine and per segment. Joints C2-C3 to L5-S1 were included in the analysis, with the exception of the cervicothoracic junction.

**Results:**
- 60 r-axSpA patients were analyzed (mean age 47.7 years, 85% male, 80% HLA-B27+). Reader 1 had between 0% and 18.3% missings per joint, reader 2 had between 0% and 51.7% missings per joint (figure). Most missings occurred in the cervicothoracic junction for both readers and mostly at both left and right facet joints of the same level. Means (SD) of sum-scores for the whole spine and cervical, thoracic and lumbar segments for both readers as well as ICCs are presented in the table. The lowest ICC was found in the cervical segment. After excluding facet joints with more than 15% missings (C5-C6 to T1-T2), ICCs were 0.93, 0.84 and 0.91 for the whole spine and cervical and thoracic segments, respectively. A striking finding was that while patients with >18 syndesmophytes were excluded from our study, very high scores of ankylosis were reported, suggesting that facet joint ankylosis may occur without syndesmophytes at the same level.

**Conclusion:**
- In patients with r-axSpA and at least one syndesmophyte, facet joint ankylosis was detected in all spinal segments. Facet joints around the cervicothoracic junction were difficult to score in a relatively high percentage of patients. The interreader reliability of the remaining levels was good to excellent. These results show that lCT can be used to study facet joint ankylosis in r-axSpA in all segments of the spine except the cervicothoracic junction.

**Disclosure of Interests:** Rosalinde Stal: None declared, Floris A. van Gaalen: None declared, Alexandre Sepriano: None declared, Juergen Braun Shareholder of: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Celltrion, Chugai, Johnson & Johnson, MSD, Novartis, Pfizer, Roche, UC Pharma, Speakers bureau: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UC Pharma, Galapagos, Speakers bureau: AbbVie, Chugai, Janssen, Novartis, Pfizer, UCB Pharma, Roche, Sanofi-Aventis and UCB.

**Funding:**
- The funding source had no role in the design and conduct of the study.
- Désirée van de Heijde Consultant for: Abbvie, Amgen, Astellas, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Novartis, Pfizer, Regeneron, Roche, Sirtris, Sobi, Takeda, Union Chilﬁth. Xerofon Baraliakos Grant/research support from: Abbvie, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Centocor, Chugai, Janssen, MSD, Novartis, Pfizer Inc, Roche and UCB, Grant/research support from: Abbvie, Pfizer, Merck Sharp & Dohme, UCB Pharma, Novartis, Consultant for: Abbvie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Chugai, Janssen Biologics, Novartis, Pfizer, UCB Pharma, Galapagos, Speakers bureau: Abbvie, Chugai, Janssen, Novartis, Pfizer, UCB Pharma.

**DOI:** 10.1136/annrheumdis-2019-eular.4128

**SAT0529**

**TWO-YEAR PROGRESSION OF FACET JOINT ANKYLOSIS ON WHOLE SPINE LOW-DOSE CT IN PATIENTS WITH RADIOPHGRAPHIC AXIAL SPONDYLOARTHRITIS: DATA FROM THE SENSITIVE IMAGING OF AXIAL SPONDYLOARTHRITIS (SIAS) COHORT**

Rosalinde Stal1, Floris A. van Gaalen1, Alexandre Sepriano1, Juergen Braun2, Monique Reinijerse1, Désirée van de Heijde1, Xerofon Baraliakos1, LUMC, Leiden, Netherlands; 2Rheumazentrum Ruhrgebiet, Herne, Germany.

**Background:** Facet joints are difficult to visualize on conventional radiography (CR). As an alternative, CT has been used to study facet joint ankylosis in radiographic axial spondyloarthritids (r-axSpA) of the spine. In the SIAS study we have shown that, with the exception of the cervicothoracic junction, which is difficult to visualize, low-dose CT (lCT) can be used to study facet joint ankylosis in the whole spine.

**Objectives:** To study facet joint ankylosis progression in the whole spine over two years in patients with r-axSpA.

**Methods:** In an observational cohort, r-axSpA patients who had between 1-18 syndesmophytes on CR and ≥1 inflammatory lesion on spinal MRI underwent lCT of the whole spine (approximately 4 mSv) with a repeated lCT after two years. Paired lCTs were assessed by two trained readers independently blinded to chronology. Left and right C2-C3 to L5-S1 facet joints were scored as ankylosis present (1) or absent (0).

**Change scores, intraclass correlation coefficients (ICCs; two-way average, absolute agreement) and smallest detectable change (SDC) were calculated for the whole spine and per segment. Joints C2-C3 to L5-S1 were included in the analysis, with the exception of the cervicothoracic junction, which were excluded in all patients due to high levels of missing joint scores as previously reported. For change score calculations, segments of individual patients with >25% missings were excluded. Remaining missings were imputed with the segment change score mean. Total scores were calculated using only patients with no excluded segments.**

**Results:** Baseline and 2-year follow up lCT were available in 53 r-axSpA patients (mean age 48.3, 85% male, 79% HLA-B27+). For reader 1, 17%, 5.7% and 3.8% of segments were excluded from the cervical, thoracic and lumbar spine for change score analysis, respectively, and 20.7% of patients were excluded for the whole spine change score analysis. For reader 2 the percentages were 15.1%, 1.9% and 1.9% and 17%, respectively. Therefore, the numbers of patients differed per reader and segment. Mean scores for baseline and follow up, mean change scores,
SDCs and ICCs are presented in Table 1. ICCs for mean status scores are good to excellent, with the lowest ICCs occurring in the cervical segment. ICCs for change scores vary greatly, the lowest ICCs being in the lumbar segment where little progression was seen. Over two years, a fair number of patients had progression of facet joint ankylosis with most progression occurring in the thoracic spine. These results show that using whole spine IDCT, progression of facet joint ankylosis can be studied in r-axSpA patients.

**Disclosure of Interests:** Rosalinde Stal: None declared, Floris A. van Gaalen: None declared, Alexandre Sepriano: None declared, Juergen Braun Shareholder of: AbbVie, Pfizer, UCB, Consultant for: AbbVie, BMS, Celgene, Chugai, Hexal, Janssen, Lilly, Medac, MSD, Pfizer, UCB, Speakers bureau: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, Monique Reijnierse Grant/research support from: Funding from the Dutch Arthritis Foundation.

The funding source had no role in the design and conduct of the study. Désirée van der Heijde Consultant for: AbbVie, Amgen, Astellas, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, Union Chimique Belge, Xenoanon Baraliakos Grant/research support from: AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Centocor, Chugai, Janssen, Lilly, Medac, MSD, Pfizer, UCB, Speakers bureau: AbbVie, BMS, Celgene, Chugai, Merck, Novartis, Pfizer, UCB, Monique Reijnierse Grant/research support from: Funding from the Dutch Arthritis Foundation.

**Background:** Standardized imaging scores in MRI are barley used in daily clinical practice whereby the high expenditure (in terms of time and staff) is often given as a reason.

**Objectives:** To develop and evaluate a simplified version of the OMERACT Psoriatic Arthritis Magnetic Resonance Imaging Score (PsAMRIS).

**Methods:** 19 patients with PsA according to CASPAR classification criteria with inadequate methotrexate response received anti-TNF treatment and were assessed by 3T MRI of the clinically dominant hand at baseline and after 6 months. Scoring was according to PsAMRIS. Items were reduced based on standard response mean (SRM) resulting in sPsAMRIS, which was compared to PsAMRIS by calculation of the total SRM and relative efficiency (RE) after bootstrapping.

**Results:** PsAMRIS subscore of MCP3, 4, and PIP4 resulted in the highest SRM (-0.07 each) and were therefore included in sPsAMRIS. sPsAMRIS had higher SRM compared to PsAMRIS (-0.13 vs. -0.02) and a higher RE (29.46). PsAMRIS and sPsAMRIS highly correlated at baseline (r = 0.75; p < 0.01) and follow-up (r = 0.64; p = 0.01). Evaluation time was reduced from 471 to 142 seconds at baseline and from 478 to 133 seconds at follow-up (p < 0.001).

**Conclusion:** The abbreviated MRI scoring system for PsA-related changes in hands, sPsAMRIS, showed a strong correlation with the well-evaluated PsAMRIS. Hence, sPsAMRIS can be considered as a time and resource saving alternative for detection and monitoring of disease-related joint changes.
COLLAGEN IMAGING USING DUAL-ENERGY COMPUTED TOMOGRAPHY CAN DETECT SOFT-TISSUE INVOLVEMENT OF THE INTERVERTEBRAL DISC IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS

Torsten Diekhoff1, Kay-Geert Hermann1, Fabian Prof1, Mikhail Protopyopov2, Marcus R. Makowski1, Denis Podubryny2, Arthritis Imaging Research Group - Berlin, 1Charité – Universitätsmedizin Berlin, Department of Radiology, CCM, Berlin, Germany; 2Charité – Universitätsmedizin Berlin, Department of Rheumatology, CBF, Berlin, Germany

Background: Based on the unique physical properties of collagen, dual-energy computed tomography (DECT) is able to detect pathological changes in fibrous structures. This has been demonstrated for the Achilles tendon (1) and traumatic disc injury in elderly patients (2).

Objectives: The purpose of this study was to assess the diagnostic potential of DECT collagen imaging for the detection of intervertebral disc involvement in patients with axial spondyloarthritis (axSpA) in correlation with osseous lesions in MRI.

Methods: Sixteen patients with suspicion of or known axSpA and back pain were included. All patients underwent a 1.5-Tesla-MRI including T1 and STIR sequences and an ultra-low-dose DECT of the spine using two sequential helical acquisitions. DECT images were reconstructed in 120 kV-equivalent standard CT images and collagen maps with 1.0 mm slice thickness in sagittal reconstructions. MRI and CT images (D1 to S1) were scored for transdiscal ankylosis, Andersson lesions, syndesmophytes, spondylitis anterior and fatty corner lesions (when applicable) as well as for degenerative findings. DECT images were scored for a loss of collagen density affecting the nucleus pulposus or the annulus fibrosus. Sensitivity (SE) and specificity (SP) values were calculated. All analyses were performed on the level of the disco vertebral units.

Results: Twelve male and four female patients with a mean age of 46.6 ± 11.6 years were included. Eleven were finally diagnosed with axSpA, 3 with degenerative spine disease and 2 with diffuse idiopathic skeletal hyperostosis (DISH). MRI detected 73 lesions in 274 discovertebral units (61 SpA related, 12 degenerative; 26 affecting the disc and 35 affecting the vertebral corner) and CT 68, whereas DECT identified pathologically decreased collagen content in 60 discs (35 in the nucleus and 25 in the annulus). DECT showed high diagnostic accuracy when compared to SpA-related and degenerative changes (MRI and CT combined; SE: 67%; SP: 99.5%) and for SpA-lesions only (SE: 72%; SP: 94.2%), however, was less susceptible for degeneration (SE 60%; SP 81.9%). When comparing disc lesions in SpA as detected by MRI (transdiscal ankylosis and Andersson lesions) with nucleus-pulposus changes in DECT, it showed an SE of 88.5% and an SP of 95.1%. However, the diagnostic accuracy was inferior when comparing anterior spondylitis and fatty corner lesions in MRI with annulus fibrosus changes in DECT (SE 51.4% and SP 97%), although the SE was markedly higher for active inflammatory corner lesion (92.3%) than for fatty marrow lesions (23.3%). The mean radiation exposure was 8.1 ± 3.4 mSv.

Conclusion: DECT is able to demonstrate soft-tissue involvement of the disc, especially for transdiscal ankylosis, Andersson lesions and active anterior spondylitis. This can be achieved with considerably low radiation exposure. While measuring the collagen density, it provides additional information to conventional CT and MR images. Thus, it has high potential to develop into a useful tool to further enhance our understanding of pathological soft-tissue changes in axSpA patients outside the bone and bone marrow.
MRI ASSESSMENT OF HIP JOINTS INVOLVEMENT IN EARLY AXIAL SPONDYLARTHROPATHY PATIENTS

Ekaterina Agafonova, Tatiana Dubinina, Daria Rumiantceva, Anastasiya Demina, Shandor Erdes.

Background: Based on available data from epidemiological studies in Russia different degree of hip involvement was found in 46% of ankylosing spondylitis (AS) patients, but only 7% of all cases resulted in total hip replacement procedures.

Objectives: To describe whether cartilage defects, bone marrow lesions (BMLs), effusion-synovitis, and meniscal pathologies at baseline are associated with TKR over 13 years and to estimate the additive effect of these measures for risk prediction of TKR. To compare the ultrasound (US) manifestations of hip arthritis (coxitis) with the results of magnetic resonance imaging (MRI) of the hip joints (HJ) in patients with early axial spondyloarthritis (AxSpa).

Methods: We examined 59 patients (mean age 28 ± 5.92 years) with a diagnosis of AxSpa (ASAS criteria 2009), with prescription inflammatory spondylitis (AS) patients, but only 7% of all cases resulted in total hip replacement procedures.

Results: All patients in addition to ultrasound signs of coxitis had MRI signs of inflammation of the HJ. Pain in the HJ was determined in 33 (5%). In 15% of cases, coxitis is asymptomatic at early stages, which requires a thorough examination of patients with AxSpa. In addition to clinical and radiological examination, all patients were subjected to MRI with T1 and T2 images. An increase in cervical-capsular distance (CCD) more than 7 mm. Pain in the HJ was determined in 33 (5%).

Conclusion: Ultrasound allows you to detect changes in H in the early stages of the disease. It is possible to use ultrasound as a screening method to determine the presence of synovitis in the TBS. MRI HJ with AxSpa, allows to determine whether the patient has inflammatory changes, including in the absence of radiological changes in these joints. In 15% of cases, coxitis is asymptomatic at early stages, which requires a thorough examination of patients with AxSpa. In addition to clinical and radiological examination, all patients were subjected to MRI with T1 and T2 images.

Disclosure of Interests: Ekaterina Agafonova: None declared, Tatiana Dubinina: None declared, Daria Rumiantceva: None declared, Anastasiya Demina: None declared, Shandor Erdes: Consultant for: Development of research concepts, Speakers bureau: Educational meetings organized or supported by companies.


Table 1. MRI-detected enthesitis versus clinical examination

<table>
<thead>
<tr>
<th>Enthesitis</th>
<th>Normal, no (%)</th>
<th>Clinically suspect, no (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hip</td>
<td>72 (97)</td>
<td>3 (60)</td>
<td>0.41</td>
</tr>
<tr>
<td>Achilles</td>
<td>2 (3)</td>
<td>24 (40)</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1. Planter fascia (A & B) and Achilles tendon (C & D) with increased T2 signal reflecting edema (arrowhead) and contrast enhancement (arrow) around the enthesis.
Semi-quantitative MRI measures such as cartilage defects significantly improve the model performance for prediction of TKR over 13 years, and hence could be utilized in prediction/decision making of TKR.

**SAT0535**

**ANTI-CARBAMYLATED ANTIBODIES IN DISCRIMINATION BETWEEN RHEUMATOID ARTHRITIS AND CHRONIC HEPATITIS C INDUCED ARTHROPATHY PATIENTS**

Asmaa Beltagy1, Ragaa Mahmoud1, Ibtessam Abd-Elhamid1, Akram Deghady2, Nevine Mohannad3.

**Background:** Rheumatoid arthritis (RA) is an autoimmune disease presenting by chronic joint inflammation. Early diagnosis and therapy of RA are crucial for avoiding joint damage and functional disability. HCV related arthropathy (HCVA) is one of the RA mimics that is detected in around 52.2% of HCV patients. The discrimination between HCVA and RA is a challenge especially in early onset RA because of their similar manifestations. Detection of certain serologic markers in sera of arthritis patients could be helpful to differentiate between both types of arthritis. Besides RF and ACPA, anti-Carbamylated Protein (anti-CarP) antibodies were described for their role in early identification of RA. Antibodies were described for their role in early identification of RA. They can be found in up to 45% of early RA patients. Moreover, they can be detected in around 52.2% of HCV patients. The discrimination between HCVA and RA is a challenge especially in early onset RA because of their similar manifestations. Detection of certain serologic markers in sera of arthritis patients could be helpful to differentiate between both types of arthritis. Besides RF and ACPA, anti-Carbamylated Protein (anti-CarP) antibodies were described for their role in early identification of RA.

**Objectives:** To determine the role of anti-CarP antibodies in the differentiation between RA and HCVA.

**Methods:** This study was carried out on 4 groups:

- **Group I:** 20 Patients with chronic HCV infection, **group II:** 20 Patients with HCVA, **group III:** 20 Patients with RA fulfilling the 2010 (ACR/EULAR) classification criteria and **group IV:** 20 Patients with both chronic HCV infection and RA.

All patients were subjected to detailed history taking and musculoskeletal examination. Routine laboratory investigations were done for all patients in addition to ESR, CRP, RF, ACPA and anti-CarP antibodies. Plain X-ray hands and feet were performed to all patients with arthritis.

**Results:**

- **Anti-CarP antibodies were detected in the sera of 12.5% of HCV patients (10% with and 15% without arthritic symptoms) in comparison to 75% of RA patients. The difference between the two groups was statistically significant (p<0.001).**

- **ACPA were detected at low titers in 15% of HCV patients (with and without articular involvement).**

- There was a significant positive correlation between RF and anti-CarP antibodies (r=0.386) and between ACPA and anti-CarP antibodies in the total sample studied (r=0.393).

**Conclusion:** The presence of anti-CarP antibodies together with clinical features could discriminate RA patients from HCVA patients. The detection of ACPA and anti-CarP antibodies in few HCV patients should be interpreted with caution. Simultaneous detection of both anti-CCP and anti-CarP antibodies could be of great value in differentiating RA from other mimicking conditions like HCVA.

**REFERENCES**


**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.646
SAT0537  THE REMS TECHNIQUE IS NOT AFFECTED BY ARTHROSIIS ARTIFACT, WHICH CAN HINDER THE DENSITOMETRIC RECOGNITION OF OSTEOPOROSIS

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Background: the measurement of bone mineral density (BMD) with dual-energy X-ray absorptiometry (DXA) is the current “gold standard” for diagnosing and monitoring osteoporosis, any errors in demographic information, improper patient positioning, incorrect scan analysis or interpretation can lead to erroneous results and decisions [1]. Moreover, a common condition represented by osteoarthritis, by modifying the joint soft tissues composition, can alter the values of BMD [2]. In patients affected by discarthrosis, in fact, osteoporotic T-score values at femoral neck can lead to erroneous results and decisions [1].

Objectives: To evaluate the predictive value of an innovative densitometric technique, the Radiofrequency Echographic Multi Spectrometry (REMS) [3], in detecting bone fragility in patients affected by osteoarthritis.

Methods: The T-score values of 35 postmenopausal women with clinical and/or radiological signs of osteoarthritis (mean age 71 years, average BMI 24.2) obtained by DXA at lumbar spine and femoral neck were compared with those obtained by REMS technique performed in the same bony sites.

Results: In all the subjects, LS T-score resulted significantly higher than the FN one according to DXA measurement. However, REMS outcomes in both the sites were significantly lower than the corresponding DXA measurement (significant difference between DXA and REMS T-score for both LS (p = 0.006) and FN (p = 0.010), and spinal REMS T-scores resulted more similar to femoral REMS (average REMS T-score LS: -2.6 ± 1.6 vs T-score FN: -2.4 ± 0.6) and to femoral DXA values.

Conclusion: These preliminary data suggest that REMS technique, which has been shown to have high sensitivity, specificity and accuracy when compared with DXA in diagnosing and monitoring osteoporosis [3], is not affected by the presence of altered soft tissues composition. It would therefore be particularly useful for the evaluation of bone fragility in subjects at risk of osteoarthritis.

REFERENCES

Disclosure of Interests: None declared
DUAL ENERGY CT FINDINGS IN GOUT WITH RAPID KILOVOLTAGE-SWITCHING SOURCE WITH GEMSTONE SPECTRAL IMAGING

Elin Svensson1, Yva Aurell2, Lennart T.H. Jacobsson2, Anton Landgren2, Hassan Bassiouoni1, Khaled Zaky2, Harry Edén3, Ibrahim Elsakka1, Al-Azhar, Cairo, Egypt; Al-Azhar University, Rheumatology, Cairo, Egypt

Background: The gold standard for diagnosis of gout is the demonstration of monosodium urate(MSU) crystals in the synovial fluid or in tophi. However, joint aspiration is seldom performed and most patients do not have visible tophi. Dual energy CT( DECT) has been shown capable of detecting MSU crystals with high precision in many studies but the vast majority of these studies were performed using CT scanners with two X-ray tubes(dual source) while the performance of other technical CT solutions are much less investigated.

Methods: Patients with incident/prevalent gout who had been examined with DECT with rapid kilovoltage-switching source with Gemstone Spectral Imaging(GSI) to identify MSU crystals and validate these results only were seen in 31% (table 1). Beam hardening was only found in the MTP-joints but also present in ankle/midfoot joints and tendons(table 1). The total urate deposit score was significantly higher in the presence of clinically identified tophi(Wilcoxon Mann-Whitney, p=0.0005) and correlated strongly to disease duration(Spearman corr. coefficient 0.64, p<0.0001) while no association or correlation was seen to age, sex, erosive disease, urate levels, BMI, diuretic or ULT use or renal function. The majority of patients displayed nail artefacts while skin artefacts only were seen in 31% (table 1). Beam hardening was only found in one patient and noise was not seen at all(table 1).

Disclosure of Interests: None declared


SAT0540 CLINICAL AND ULTRASONOGRAPHIC ASSESSMENT OF STERNOCLAVICULAR JOINT IN PATIENTS WITH RA

Hassan Bassiouoni1, Khhaled Zaky2, Harry Edén3, Ibrahim Elsakka1, Al-Azhar, Cairo, Egypt; Al-Azhar University, Rheumatology, Cairo, Egypt

Background: The sternoclavicular (SC) joint is a real diarthrodial joint that can be affected during the route of RA; but, its scientific implications appear to remain underestimated through the rheumatology network, (1) ultrasound (US) is right extensively common imaging approach in each clinical exercise and in rheumatology studies to visualize joints and tendon tissues. To date, there is a regular frame of evidence assisting its validity, reliability, and feasibility inside the evaluation of persistent inflammatory arthritis and its higher sensitivity than scientific exam in the analysis of synovitis, enthesitis, and tenosynovitis in these patients (2).

Objectives: To describe the prevalence of sternoclavicular (SC) joint involvement and the relationship between clinical and ultrasound (US) findings in patients with rheumatoid arthritis.

Methods: 120 subjects with age range from 20 to 50 years were recruited from Physical Medicine, Rheumatology and Rehabilitation department of Sayed Galal and Al-Hussein Al-Azhar University Hospitals, during the period from April 2018 to October 2018. All the patients were informed about the study and signed an informed consent.

Subjects were divided into two groups: Group A: 60 patient known as RA fulfilling ACR criteria for classification of rheumatoid arthritis (1987) (3). Group B: 60 normal control subjects. All subjects have been clinically evaluated and t blinded US examinations of the SC joint were performed bilaterally in both groups. The presence of gray-scale synovitis, erosions, and intraarticular power Doppler (PD) was recorded.

Results: A total of 240 SC joints were evaluated: 120 from patients with RA and 120 from healthy controls. In the RA group, 21 joints (17.5%) were found to be clinically involved (pain/swelling), in contrast to only 6
(5%) in the control group (P = 0.002). In the RA group, US abnormalities were recorded in 62 SC joints (51%) compared with 3 (2.5%) in the healthy control group (P = 0.0001), comprising synovitis in 28 (23.3%) versus 3 (2.5%) (P < 0.001), erosions in 27 (22.5%) versus none (P < 0.001), and intraarticular PD in 7 (5.8%) versus none (P = 0.031). Furthermore, a correlation between the presence of US synovitis (P < 0.001) and intraarticular PD (P < 0.0001) with a higher Disease Activity Score in 28 joints (DAS28) was found.

Figure (1) showing erosions of clavicular head of sternoclavicular joint.

Conclusion: US is extra sensitive than medical examination for detecting SC joint involvement in RA. The correlation amongst US synovitis, intraarticular PD, and the DAS28 show that SC joints actively participate within the systemic inflammatory manner of RA. The precise position of US within the assessment of the SC joint in suffers with RA is but to be mounted firmly in the rheumatologic examination.

REFERENCES


Acknowledgement: Prof. Dr. Sameh Elzayyat

Disclosure of Interests: None declared


SAT0541 MULTIDRUG TRANSPORTERS OF PERIPHERAL LYMPHOCYTES SERVE AS BIOMARKERS TO BDMARD RESPONSE IN RHEUMATOID ARTHRITIS (RA)

Gergely Toldi1, Peter Kraics2, Peter Szeremy1, Kata Filter1, 1MDQuest Ltd., Szeged, Hungary; 2QOL-VO Biotechnology, Szeged, Hungary

Background: Multidrug resistance transporters (MDR-ABC transporters, namely MDR1, MRP1 and BCRP) play essential role in the homeostasis of a variety of endogenous molecules, proinflammatory mediators among them [1]. When the regulation of this phenomenon is disturbed, cell migration, proliferation and inflammatory processes are over activated which finally results in the pathogenesis of RA. Moreover, enhanced function of MDR proteins leads to multidrug resistance [2].

Objectives: In our multicenter, multinational clinical trial we aimed to assess the predictive value of flow cytometry-based multidrug resistance activity measurement of the previously mentioned MDR proteins for bDMARD response in RA in CD3+ and CD19+ lymphocytes before and as well as 4 to 6 and 12 weeks after initiation of bDMARD therapy.

Methods: Peripheral blood samples were collected from 27 bDMARD responders and 12 non-responders RA patients at the indicated time points. Multidrug activity factors (MAFs) were measured from CD3+ and CD19+ lymphocytes by using SOLVO MDQ kit™. Cut-off values were determined by using ROC curve analysis.

Results: Before starting bDMARD therapy, MAFCD3 and MAFCD19 values of CD3+ cells were higher in non-responders as compared with responders. Six weeks after starting therapy, the same pattern was detected in case of MAFCD3, MAFMRP1, and MAFBCRP in both investigated cell types. ROC analysis revealed that when MAFCD3 value is higher than 21.3 in CD3+ cells before starting bDMARD therapy are likely to be non-responders. At later time points, MAFCD3 values above 20.3 and MAFMRP1 above 6.0 and MAFBCRP values above 13.9 in CD3+ cells also predict unfavourable treatment response. Of note, these cut-off values are all below the respective reference ranges in healthy individuals established in our earlier study [3].

Conclusion: Importantly, little is known about the relation of MDR activities and therapeutic success to bDMARDs. Proinflammatory mediators and cytokines may serve as an interface between pharmacological activity of bDMARDS and MDR transporters [4-6].

REFERENCES


Disclosure of Interests: None declared


SAT0542 DETECTION OF SUBCLINICAL LV MYOCARDIAL DYSFUNCTION IN RHEUMATOID ARTHRITIS PATIENTS BY SPECKLE TRACKING ECHOCARDIOGRAPHY

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Background: Patients with rheumatoid arthritis (RA) have shorter life expectancy and their risk of cardiovascular (CV) death is more than 50% higher than the rest of the population. Early myocardial dysfunction may be detectable more precisely and sooner using speckle tracking echocardiography.

Objectives: This study was designed to assess myocardial (LV) systolic function by STE (speckletracking) Echocardiography) strain imaging in patients with RA and to correlate the findings with characters of the disease.

Methods: Cross-sectional observational study enrolled 60 patients with RA (mean age 46.22 ± 8.14 years) without known CVD and 20 healthy controls. All subjects underwent a standard echocardiographic examination as well as the speckle tracking assessment of left ventricle strains.

Results: Speckle-tracking assessment of LV systolic function revealed decreased GLS among the patients group (-16.80% vs. -22.35%, P < 0.001). There was a negative correlation between the duration of RA and the GLS (r = - 0.301). Receiver operating characteristics (ROC) curve was used to define the best cut off value of GLS which was -20, with sensitivity of 76.7%, specificity of 80%, positive predictive value of 92%, negative predictive value of 63% with diagnostic accuracy of 83.9%.

Conclusion: The speckletracking method for myocardial strain analysis showed unambiguously systolic impairment of longitudinal strain parameters. So, patients with RA should undergo a full comprehensive echocardiographic study for assessment of LV systolic function.

REFERENCES


Kentaro Doi3,6, Yuki Iwai3,6, Jun Inamo1, Yuichiro Ota1, Nobuhiko Kajo1, Jun Kikuchi1, Komei Sakata1, Satoshi Takenashi1, Chihiro Takahashi1, Hiroshi Takei1, Hiroya Tamai1, Kazuoto Hiramoto1, Yuko Kaneko1, Masahiro Jinzaki2, Shigeru Ko2, Tsutomu Takeuchi3,3, Keio University School of Medicine, Division of Rheumatology, Department of Internal Medicine, Tokyo, Japan; National Hospital Organization Tokyo Medical Center, Division of Connective Tissue Diseases, Tokyo, Japan; Keio University School of Medicine, Medical AI Center, Tokyo, Japan; Fujitsu Laboratories Ltd., Kanagawa, Japan; Keio University School of Medicine, Division of Radiology, Tokyo, Japan; Fujitsu Ltd., Tokyo, Japan; Keio University School of Medicine, Department of Systems Medicine, Tokyo, Japan

Background: Artificial intelligence (AI) techniques including deep learning have been rapidly evolving and have yielded appreciable benefits in many fields in recent years. In rheumatology field, however, these techniques have not been used often.

Objectives: In an early phase of development of an AI-based automatic radiographic evaluating system for bone destruction, we aimed to develop learning-based models to automatically detect hand joint region, ankylosis and subluxation in radiographic images.

Methods: A total of 130 radiographic image sets of both hands were randomly obtained from rheumatoid arthritis patients who had visited our division at Keio University Hospital in 2015. Well-trained rheumatologists determined the boundaries of regions of MP and PIP/IP joints and evaluated the presence of ankylosis and subluxation of each joint in radiographs. These evaluations of hand joints were performed using our developed annotation software tool [1].

In learning phase, joint images were randomly divided into five sets for 5-fold cross validation. As deep learning models, we utilized Single Shot Multibox Detector (SSD) method [2] with ensemble learning for detecting ankylosis and subluxation of MP and PIP/IP joint regions.

Results: Our model showed 100% detection rate of MP and PIP/IP joint regions. As a performance of detecting hand joint ankylosis and subluxation, our model presented precision values of 0.85 and 0.73, recall values of 0.94 and 0.79, and F-measure values of 0.90 and 0.76, respectively.

Conclusion: Deep learning-based models to automatically detect hand joint region, ankylosis and subluxation in radiographic images were developed with relatively small samples, which suggests that the predictive performance may increase by collecting more training dataset. Next, we are elaborating a plan for a deep learning-based evaluating system for erosion and joint space narrowing.

REFERENCES


Acknowledgement: Keisuke Izumi and Kanata Suzuki are contributed equally.


Disclosure of Interests: None declared.

Scientific Abstracts

Coronary Plaque Progression in Rheumatoid Arthritis: Role of Inflammation, Cardiovascular Risk Factors, Medications and Impact on Event Risk

George Karpouzas1, Sarah Ormseth, Elizabeth Hernandez, Matthew Budoff2,1 Harbor UCLA Medical Center, West Carson, United States of America, 2 Harbor UCLA Medical Center Cardiology, Torrance, United States of America

Background: Patients with Rheumatoid Arthritis (RA) exhibit higher prevalence, burden and different composition of occult coronary plaque compared with age and gender-matched controls. More specifically, plaque burden on coronary computed tomography angiography (CCTA) predicted long-term cardiovascular events (CCE) in RA beyond cardiac risk factors or scores.

Objectives: To evaluate change in coronary plaque burden and composition, predictors thereof and its impact on CCE risk in RA.

Methods: One hundred-one participants with a baseline CCTA underwent a follow-up evaluation in 83±3.6 months. Plaque load was reported as segment involvement score (SIS-number of segments with plaque); segment stenosis score (SSS-cumulative stenosis over all evaluable segments) and total plaque score (TPS-collective plaque amount over all segments). Plaque composition was defined as non-calcified (NCP), mixed (MP) or calcified (CP). Coronal artery calcium (CAC) was quantified by the Agatston method. Robust regression was used to evaluate predictors of increased plaque burden compared to non-progression.
A COMPARATIVE STUDY OF NAILFOLD IL-17A IS UPREGULATED IN SYSTEMIC SCLEROSIS

Rheumatology and Clinical immunology, New Delhi, India

Objective: To study the various patterns on Nailfold Capillaroscopy in microvascular changes in patients with ILD.

Methods: A comparative study was conducted on 50 patients each of IIP and IPAF who fulfilled ERS/JRS/ALAT 2011 revised diagnostic criteria for IIP demonstrating a higher frequencies of abnormalities (microhemor-

Results: Total plaque burden increased in 42% of patients; progression was predicted by older age, higher cumulative inflammation (TA-CRP) and higher total prednisone dose (table 1).

Discussion: The study showed that Nailfold Capillaroscopy is a useful tool in the diagnosis and follow-up monitoring of patients with IPAF.

Conclusion: This study provides valuable insights into the role of nailfold capillaroscopy in the evaluation of microvascular changes and disease progression in IPAF patients.

Disclosure of Interests: None declared


IL-17A IS UPREGULATED IN SYSTEMIC SCLEROSIS PATIENTS WITH MIXED ANA IMMUNOFLUORESCENT PATTERN AND MORE THAN ONE POSITIVE ANTINUCLEAR ANTIBODY TO THE SERUM

Ekatierina Kupteva1,2, Ekaterina Ivanova-Todorova2,3, Kalina Tumangaleva-Yuzevi2,

Methods: We enrolled 31 patients who fulfilled the 2013 ACR/EULAR Classification Criteria for SSc at mean age of 47±3 were recruited in the study. 17 with diffuse SSC and 14 patients with localized SSC, respectively.

Results: Our study consisted of 23 (46%) female patients and 27 (54%) male patients for IPAF group and 19 (38%) female patients and 31 (62%) male patients for IIP group. The mean capillary density was significantly reduced in IPAF group and also had presence of abnormal capillary morphologic patterns (microhemorrhages, neangiogenesis and megacapillaries).

Conclusion: This single centre study found that Nailfold Capillaroscopy (NFC) is an important adjunct to differentiate between patients of IPAF and IIP demonstrating a higher frequencies of abnormalities (microhemor-

References


Disclosure of Interests: None declared


A COMPARATIVE STUDY OF NAILFOLD CAPILLAROSCOPY CHANGES IN IDIOPATHIC INTERSTITIAL PNEUMONIA WITH IDIOPATHIC INTERSTITIAL PNEUMONIA AUTOMMUNE FEATURES

Kurali Kishore1, Vivek Vasudev2, 3Army hospital research and Referral, Rheumatology and Clinical immunology, New Delhi, India; 4Army Hospital Research and Referral, Rheumatology and Clinical Immunology, New Delhi, India

Background: Lung involvement especially interstitial lung disease (ILD), can be the first manifestation of an underlying connective tissue disorder (CTD). About 25% of ILD occurs in the context of an "undiagnosed" CTD, characterized by signs and symptoms that are not specific for any of the described CTD entities, now known as IPAF. Nailfold capillaroscopy (NFC) is an important tool, which helps us in early recognition of microvascular changes in patients with ILD.

Objectives: To study the various patterns on Nailfold Capillaroscopy in patients of Interstitial Pneumonia with autoimmune features (IPAF) and compare them with those having idiopathic Interstitial Pneumonia (IIP).

Methods: The study population consisted of 50 patients each of IIP and IPAF who fulfilled ERS/JRS/ALAT 2011 revised diagnostic criteria for IIP and ERSATS classification criteria for Interstitial pneumonia with autoimmune features respectively. The study also included 50 age and sex matched controls, having normal respiratory examination clinically, normal CXR and normal PFTs. All patients underwent NFC at room temperature and the following parameters were recorded: capillary density, presence of megacapillaries, tortuosity, avascular areas, disarrangement and neoangiogenesis.

Results: Our study consisted of 23 (46%) female patients and 27 (54%) male patients for IPAF group and 19 (38%) female patients and 31 (62%) male patients for IIP group. The mean capillary density was significantly reduced in IPAF group and also had presence of abnormal capillary morphologic patterns (microhemorrhages, neangiogenesis and megacapillaries).

Conclusion: This single centre study found that Nailfold Capillaroscopy (NFC) is an important adjunct to differentiate between patients of IPAF and IIP demonstrating a higher frequencies of abnormalities (microhemor-

References


Disclosure of Interests: None declared


Table 1. Coronal plaque progression in RA: Role of inflammation, risk factors and medications

<table>
<thead>
<tr>
<th>Model</th>
<th>Predictors OR (95% CI)</th>
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<tbody>
<tr>
<td>SIS Total</td>
<td>Age 1.05 (1.04-1.15)**</td>
</tr>
<tr>
<td></td>
<td>time-averaged CRP 2.04 (1.33-3.13)**</td>
</tr>
<tr>
<td>SSS Total</td>
<td>Age 1.07 (1.02-1.12)**</td>
</tr>
<tr>
<td></td>
<td>time-averaged CRP 1.82 (1.30-2.77)**</td>
</tr>
<tr>
<td>TPS Total</td>
<td>Age 1.08 (1.03-1.14)**</td>
</tr>
<tr>
<td></td>
<td>Cumulative prednisone dose 1.01 (1.00-1.02)**</td>
</tr>
<tr>
<td></td>
<td>Time-averaged CRP 1.68 (1.02-2.71)**</td>
</tr>
<tr>
<td>CAC</td>
<td>Age 1.14 (1.05-1.23)**</td>
</tr>
<tr>
<td></td>
<td>Hypertension 4.98 (1.46-16.94)**</td>
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<td></td>
<td>Waist-to-hip ratio 1.10 (1.02-1.17)**</td>
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<tr>
<td></td>
<td>a-b2GPI IgA (+) 4.67 (1.22-17.34)**</td>
</tr>
<tr>
<td></td>
<td>Time-averaged CRP 1.68 (1.02-2.84)**</td>
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</table>

* p<0.1, ** p<0.05, *** p<0.01

Disclosure of Interests: None declared


Scientific Abstracts

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sena with mixed AC pattern. Regarding the Tregs and Th17 cells, we identified a reduced percentage of the CD25+Tregs at a marginal trend toward significance in the patients with mixed AC pattern versus the group with simple AC pattern [5.9 [3.2 – 10.6] vs 11.2 [6.1 – 14.3], p = 0.06].

Conclusion: Although the pathogenetic contribution of ANA in SSc remains unclear, ANA play an important role in the differential diagnosis, risk stratification and assessment of disease activity in SSc. Further research is warranted to clarify the interconnection between the disregulated Th17/Tregs axis and the production of high-high-titer specific ANA in SSc. In the future, rheumatologists could benefit from ANA in order to apply the most accurate therapeutic strategy for each patient.

Disclosure of Interests: None declared.


SAT0547

ULTRASONOGRAPHIC FOLLOW UP OF ENTHESOPHYTE GROWTH IN A CONSECUTIVE SERIES OF IBD PATIENTS

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1Arcispedale S Maria Nuova, RCCS, Reggio Emilia, Italy; 2Policlinico GB Rossi, University of Verona, Verona, Italy; 3University of Modena and Reggio Emilia, Modena, Italy

Background: Previous studies have found an interconnection between inflammatory intestinal diseases (IBD), particularly Crohn disease (CD) and Ulcerative Colitis (UC), and spondyloarthritides.

Objectives: We prospectively evaluate the pattern and predictive factors of enthesophyte growth in a cohort of patients with IBD.

Methods: A total of 68 IBD consecutive patients (31 CD, 36 UC, 1 ID, M/F 37/31, mean age 40.2 ± 13.2 years, mean disease duration 107.5 ± 129 months) were enrolled. Rheumatological examination included 66 peripheral joint count, MASES and Leides entheseal indexes, BASDAI, BASFI and evaluation of spine mobility. US examination was done at baseline and at 24 months using an Esaote MyLabClass, 18-6 MHz linear multifrequency transducer both in B-mode and PD-mode. The follow-up sites were blindly evaluated bilaterally: lateral epicondylear of the humerus, distal quadrupital insertion at the patella, superior and inferior pole of the patella, Achilles tendon insertion, and plantar aponeurosis insertion. Quadriceps, patellar, Achilles and plantar fascia entheses were scored according to the 0-36 Glasgow Ultrasound Enthesitis Scoring System (GUESS) and power Doppler (PD). The presence of enthesophytes were scored dichotomously as present (=1) or absent (=0) for each site and summed up to generate the ARE score (ARES). Enthesophytes was also scored semiquantitatively in a 0-3 scale (0 = absent, 1 = minimal, 2 = discrete, 3 = massive) for each site and summed up to generate RES score (RESS).

Results: Eighteen patients showed no increase of the RESS, 13 pts had 1 point increase, 12 pts less than 4 and 25 pts more than 4 points increase of the RESS at the end of follow-up. Baseline factors associated with RESS progression were age > 50 years, male sex, BMI ≥ 25, CRP > 0.50 mg/dl, and alcohol consumption. As far as the number of sites involved only 8 patients showed no increase of ARES, while 25 pts had ARES increased more than 4. Baseline factors predicting ARES increase were pre-existing presence of enthesophytes at quadriceps tendon insertion at superior patellar pole, age > 50 years, male sex, and alcohol consumption. Progression of ARES and RESS was not associated with type of IBD, use of corticosteroid, biological agents or immunosuppressive drugs nor with the concomitant presence of cutaneous psoriasis smoke habit, diabetes, dyslipidemia.

Conclusion: US examination of selected entheseal area demonstrates the increase of number and size of enthesophytes during a 2 years follow-up of IBD patients. Alcohol consumption and the presence at baseline of enthesophytes are the most important predictive factors for RESS and ARES progression respectively.

Disclosure of Interests: None declared.


SAT0548

TRACKING RESIDUAL INFLAMMATION USING ULTRASOUND IN PATIENTS WITH RHEUMATOID ARTHRITIS IN CLINICAL REMISSION

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Background: With current treatment strategies, achieving a state of remission has become a realistic goal in rheumatoid arthritis (RA). Several composite scores and indices are available to assess remission based on clinical and biological parameters. None of the European League Against Rheumatism or American College of Rheumatology current recommendations include ultrasonography (US) findings as a parameter to define whether or not a patient is in remission.

Objectives: Describe and compare clinical and ultrasonographic findings in RA patients in clinical remission.

Methods: We included RA patients who were in clinical remission by the Disease Activity Score (DAS28-cv2.6) for at least three months. B mode and Power Doppler (PD) US examination were performed by an experienced rheumatologist, blinded to clinical data. Twenty-two joints of both hands (wrist, metacarpophalangeal (MCP) and proximal interphalangeal joints (PIP)) were assessed. A binary score (absence or presence) of synovial hypertrophy/effusion (SH) and power Doppler (PD) signals was applied for each joint. The sonographic Remission was defined by the absence of PD signals.

Results: Thirty patients were recruited (25 female and 5 male). The mean age of our population was 48 ± 8.98 years-old. All patients were in remission according to DAS28. The mean DAS28 was 2.03 ± 0.40 ranged from 1.13 to 2.6. Average length of remission was 16 months [3-72 months]. On clinical examination, nine swollen joints were identified, represented by wrists in all cases. On B mode, synovial hypertrophy was detected in 80% of patients. Among the 660 joints examined, synovitis was identified in 89 cases. A wrist synovitis was detected in 55% of cases (33 out of 60 wrists studied) making it the most affected joint, followed by the second and third PIP in 14 and 12 cases out of 60 studied, respectively. PD signal, as a sign of active disease, was observed in 78% of patients and detected in 43% of the total wrists examined (26/60) [Table 1]. Among the swollen joints found on clinical examination, only one had no synovial hypertrophy in B mode. However, subclinical synovitis was detected in 81 joints (12% of total joints) with prediction for PIP joints (47% of subclinical synovitis). In PD mode and subclinical synovitis, PD signals were found in 38 joints (47%). Thus, the sensitivity of the clinical examination to identify swollen joints compared to US was 9%, its specificity of 99%, its PPV of 89% and its VPN of 88%.

Conclusion: Subclinical joint inflammation detected by US might explain the structural deterioration in RA patients despite clinical remission. Our findings support the use of US for the accurate evaluation of disease status before concluding to remission or otherwise to adjust treatment.

REFERENCES


Table 1. Clinical and Ultrasonographic synovitis distribution in B mode and PD mode

<table>
<thead>
<tr>
<th>Examined joint</th>
<th>Wrist</th>
<th>MCP1</th>
<th>MCP2</th>
<th>MCP3</th>
<th>MCP4</th>
<th>MCP5</th>
<th>IP1</th>
<th>PIP2</th>
<th>PIP3</th>
<th>PIP4</th>
<th>PIP5</th>
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<tbody>
<tr>
<td>Swollen joints</td>
<td>9</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Synovial hypertrophy</td>
<td>33</td>
<td>5</td>
<td>5</td>
<td>6</td>
<td>4</td>
<td>3</td>
<td>1</td>
<td>13</td>
<td>3</td>
<td>14</td>
<td>12</td>
</tr>
<tr>
<td>Active synovitis on PD</td>
<td>26</td>
<td>1</td>
<td>5</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>4</td>
<td>3</td>
<td>2</td>
<td>0</td>
</tr>
</tbody>
</table>
SARCOPENIA IN RHEUMATOID ARTHRITIS FEMALE  
THROMBIN GENERATION ASSAY AND GLOBAL  
TRABECULAR BONE SCORE

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Background: Rheumatoid arthritis (RA) is associated with muscle loss, osteoporosis and an increased risk of fractures. Sarcopenia is a syndrome in which muscle mass loss is linked to functional loss. Trabecular Bone Score (TBS), is an index extracted from the dual-energy X-ray absorptiometry (DXA) that provides an indirect measurement of bone microarchitecture and allows to get information about bone quality [1-3].

Objectives: The aims of this study were to examine associations between bone mineral density, bone quality, fat mass and lean mass in the whole body in female patients with RA and healthy controls (CNT).

Methods: 55 female patients (mean age 58±12 years) affected by RA and 55 CNT (mean age 52±16 years) were enrolled. Bone Mineral Density (BMD, g/cm²) of the lumbar spine (L1-L4) and whole body and the Bone Score (TBS), is an index extracted from the dual-energy X-ray absorptiometry (DXA) that provides an indirect measurement of bone axial microarchitecture and allows to get information about bone quality [1-3].

Results: The mean BMI±SD compared by RA and CNT was 26.1 ± 3.92 kg/m2 and 5.94 ± 0.42 kg/m2 respectively, compared by CNT (23.7±5.5 kg/m2 and 5.5 kg/m2 on women.

Discussion: In this study 55 female patients (mean age 58±12 years) affected by RA and 55 CNT (mean age 52±16 years) were enrolled. Bone Mineral Density (BMD, g/cm²) of the lumbar spine (L1-L4) and whole body expressed by Relative skeletal mass index (RSMI) was analyzed using a DXA scan (GE, Lunar Prodigy). Lumbar spine TBS was derived for each patient with APS compared to patients treated with warfarin and no APS, APS patients had significantly lower ILag (13.3 ±5.9 min; p= 0.003; p= 0.008, respectively) and TPeak (21.3 ±9.2 min; p= 0.006; p= 0.014, respectively) with lower Peak (99.1 ±71.8 nM; p< 0.001; p= 0.005, respectively) and AUC (1150.5 ±637.4 nM; p< 0.001; p= 0.004, respectively).

Conclusion: This study show that sarcopenia is frequent in RA patients, mostly on those classified as normal or overweight according to BMI. Therefore TBS and BMD values, as demonstrated could have a key role in a bone-muscle feedback in chronic systemic inflammatory rheumatic diseases, such as RA.

REFERENCES

Disclosure of Interests: None declared


THROMBIN GENERATION ASSAY AND GLOBAL ANTIPHOSPHOLIPID SCORE (GAPSS) FOR RISK STRATIFICATION IN ANTIPHOSPHOLIPID SYNDROME

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Background: Thrombin generation assay (TGA) is a simple and reproducible technique, that could potentially be used in coagulation laboratories, that measures the concentration of generated thrombin after plasma recalcification. The clinical usefulness of TGAs in assessing thrombotic risk has been a matter of growing interest, however, it has not been applied on a large scale to a large cohort of patients with antiphospholipid syndrome (APS).

Objectives: The aim of our study was to assess the potential use of TGA in monitoring the pro-coagulant state in APS patients and its role in predicting the relative risk score in developing APS clinical manifestations, by comparing its parameters to the validated global antiphospholipid score (GAPSS).

Methods: After chart-reviewing all APS patients that presented at San Giovanni Bosco Hospital in the last 5 years, we enrolled 4 groups of patients for the sake of this study, matched for age and sex. Clinical and laboratory characteristics were retrospectively collected. Inclusion criteria were as follows:

Group A) Fulfilled the diagnosis of Thrombotic APS defined as per Sidney criteria [1]: 60.
Group B) Patients with aPL positivity, but with no clinical manifestations of APS defined as per Sidney criteria [1]: 30.
Group C) Patients treated with Warfarin (target INR 2-3), negative for aPL and other autoimmune conditions: 60.
Group D) Healthy Controls: 60.

Results: Figure 1 resumes the representative TGA profiles between groups. Healthy controls and patients with aPL positivity, but no APS clinical manifestations, had similar TGA profiles [mean ILag (min) 9.6 ±2.9 v.s. 8.6 ±3.2; mean TPeak (min) 16.2 ±4.7 v.s. 13.7 ±5.8; mean Peak (nM) 209.2 ±103.8 v.s. 265.4 ±106.2; mean AUC (nM) 2057.1 ±571.8, respectively).

When analyzing the TGA profile of the patient with APS compared with healthy controls and aPL positive patients with no clinical manifestations of APS, we observed a statistically significant higher ILag (13.3 ±5.9 min; p= 0.003; p= 0.008, respectively) and TPeak (21.3 ±9.2 min; p= 0.006; p= 0.014, respectively) with lower Peak (99.1 ±71.8 nM; p< 0.001; p= 0.005, respectively) and AUC (1150.5 ±637.4 nM; p< 0.001; p= 0.004, respectively).

Furthermore, also when analyzing the TGA profile of APS patients compared to patients treated with warfarin and no APS, APS patients had significant higher ILag (13.3 ±5.9 min v.s. 8.2 ±2.1; p= 0.001), TPeak (21.3 ±9.2 min v.s. 13 ±2.8; p= 0.001), Peak (99.1 ±71.8 nM v.s. 62.3 ±21.5; p= 0.018) and AUC (1150.5 ±637.4 nM v.s. 605 ±148.8; p< 0.001).

When analyzing a correlation model between GAPSS and TGA parameters, we observed a statistically significant correlation for ILag (Pearson
INCIDENTAL FINDINGS OF TEMPOROMANDIBULAR
JOINT DISORDERS ON STANDARD BRAIN MRIS: A CROSS-SECTIONAL STUDY

Tatiana Reitblat1, Azaria Simonovich2, Svetlana Kolontaevsky3, Leonid Kalichman4.

Background: The temporomandibular joints (TMJ) changes is quite often ignored as a differential diagnosis in the evaluation of patients with suspicion on rheumatic and musculoskeletal disease such as temporal arteritis, fibromyalgia, rheumatoid arthritis. To understand whether TMJ changes have to be included in routine workup of patient’s evaluation with the suspect to rheumatic disease, we assessed the prevalence of TMG changes incidental findings in standard brain MRI scan. In our experience, numerous incidental findings are found on a standard brain MRI scan, especially the elderly. A literature search revealed that no studies have reported the prevalence of these findings and their clinical relevance.

Objectives: To evaluate the prevalence of incidental TMJ findings on standard brain magnetic resonance imaging scans and assess if these findings are associated with symptoms.

Methods: Our sample comprised 65 males (47.1%) and 75 females (52.9%), mean age 54.75±17.45 (range: 18-87). Data collected from each TMJ included articular displacement, articular effusion, condyle flattening, condyle erosions, capsule enhancement, and bone marrow edema. Dichotomous data as to TMJ-related symptoms such as headaches, earaches, dizziness, clicking or grating sound, pain or soreness of the joint, limited mouth opening, locking of the jaw, facial muscle pain, unexplained teeth pain, neck pain or stiffness and difficulty swallowing, were acquired during telephone interviews.

Results: The most frequent finding was disc displacement (39.9% on the right side and 47.8% on the left), followed by condyle flattening (33.3% on the right side and 44.2% on the left). All findings, except bone marrow edema, were significantly more frequent on the left side than the right (Table 1). Significant associations were found between incidental findings in the TMJ and earaches (odds ratio 2.759, P=0.043), dizziness, clicking or grating sound, pain or soreness of the joint, limited mouth opening, locking of the jaw, facial muscle pain, unexplained teeth pain, neck pain or stiffness and difficulty swallowing, were acquired during telephone interviews.

Conclusion: Incidental findings of TMJ degenerative features were commonly found on standard brain magnetic resonance imaging. The high frequency of the findings and strong association with facial pain requires performing TMJ assessment in all patients who undergo medical inquiry for suspected rheumatic and musculoskeletal disease.

Disclosure of Interests: None declared

SAT0551

INCIDENTAL FINDINGS OF TEMPOROMANDIBULAR JOINT DISORDERS ON STANDARD BRAIN MRIS: A CROSS-SECTIONAL STUDY

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Objectives:

1. To describe lacrimal gland biopsy results in children, Ophthalmology, London, United Kingdom
2. To describe the largest paediatric cohort of biopsy proven non-infectious dacryoadenitis (4,5).

Methods: We identified 72 children who had lacrimal gland biopsy at GOSH between 25/09/2000 and 12/04/2018 using two key-words: “lacrimal” and “dacryoadenitis”. We excluded patients with infectious dacryoadenitis, benign tumors or malignancy. We retrospectively reviewed the medical notes, laboratory and histopathology results.

Results: Twenty six patients had non-infectious dacryoadenitis with or without soft tissue involvement. All cases manifested as upper lid swelling. 19 (73.1%) patients had unilateral involvement. 12 (46.2%) patients were male. Mean age at time of biopsy was 10.5 years and median 13 years (range 1 – 17.7).

Four patients had GPA (granulomatous polyangiitis), 4 patients sarcoidosis, 1 patient IgG4-related disease, 1 patient Sjögren with secondary anti-phospholipid syndrome and 16 patients non-specific chronic inflammation (NSCI). 2/4 patients with sarcoidosis had extra-ocular involvement. One patient with sarcoidosis had NO2 mutation without Blau phenotype. One patient with GPA had extra-ocular involvement.

4/13 children tested had raised ACE including 2 sarcoidosis and 2 NSCI. 7/17 had raised amylase (2 sarcoidosis, 1 Sjögren, 4 NSCI). 7/20 had elevated CRP and 4/20 had raised ESR. 22/24 had raised IgG (range 0.6-3.3 g/L). 7/20 had raised IgA (range 0.2-1.8 g/L).

We describe the largest paediatric cohort of biopsy proven non-infectious dacryoadenitis (4,5).

Objectives: 1. To describe lacrimal gland biopsy results
2. To report associated clinical, laboratory features and treatment

SAT0552

PAEDIATRIC NON-INFECTIONOUS DACRYOADENITIS: THE GOSH EXPERIENCE

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2Great Ormond Street Hospital for Children, Ophthalmology, London, United Kingdom

Background: Dacryoadenitis is an inflammatory enlargement of the lacrimal gland and the most common orbital inflammatory condition in the paediatric population, although only 6 to 17% of orbital inflammatory disorders occur in children (1-4). Dacryoadenitis may be idiopathic or associated with infections or inflammatory diseases. Systematic inflammatory disorders are more typically associated with chronic than acute dacryoadenitis (3).

We describe the largest paediatric cohort of biopsy proven non-infectious dacryoadenitis (4,5).

Table 1: Frequencies of incidental findings in TMJs on standard brain MRI (n=138).

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>B</th>
<th>p-value</th>
<th>Odds ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>0.475</td>
<td>0.220</td>
<td>1.607</td>
</tr>
<tr>
<td>Earaches, stuffiness or ringing</td>
<td>1.015</td>
<td>0.043</td>
<td>2.759</td>
</tr>
<tr>
<td>Dizziness, lightheadedness</td>
<td>0.844</td>
<td>0.031</td>
<td>3.298</td>
</tr>
<tr>
<td>A clicking or grating sound</td>
<td>1.871</td>
<td>0.002</td>
<td>6.492</td>
</tr>
<tr>
<td>Pain or soreness of the TMJ</td>
<td>0.753</td>
<td>0.424</td>
<td>2.123</td>
</tr>
<tr>
<td>Pain in facial muscles (cheeks)</td>
<td>2.421</td>
<td>0.003</td>
<td>11.255</td>
</tr>
<tr>
<td>Unexplained teeth pain</td>
<td>1.736</td>
<td>0.169</td>
<td>5.676</td>
</tr>
<tr>
<td>Neck pain or stiffness</td>
<td>0.602</td>
<td>0.147</td>
<td>1.826</td>
</tr>
<tr>
<td>Difficulty swallowing (ore)</td>
<td>1.559</td>
<td>0.057</td>
<td>4.752</td>
</tr>
</tbody>
</table>

*Results of logistic regression analysis (d.f.=1) with the symptom as a dependent variable and TMJ- incidental findings, age, and sex as independent predictors. A significant association (p<0.05) is marked in bold.
SAT0553  HIGH FEASIBILITY AND ACCEPTANCE OF A MUSCULOSKELETAL ULTRASOUND PROGRAM TO IMPROVE DMARDs ADHERENCE IN RHEUMATOID ARTHRITIS

York Kit Tan1,2,3, Julian Thumboo2. 1Singapore General Hospital, Department of Rheumatology and Immunology, Singapore, Singapore; 2Duke-NUS Medical School, Singapore, Singapore; 3Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore

Background: Disease modifying anti-rheumatic drugs (DMARDs) non-adherence is a widespread issue in rheumatoid arthritis (RA) which needs to be urgently addressed as it can lead to suboptimal therapy with poor disease outcomes. The subsequent need for more aggressive therapy, treatment of disease related complications and increased consultations can translate into increased healthcare utilization and costs.

Objectives: To describe the feasibility and patient’s acceptance of a Musculoskeletal Ultrasound Program (MUSP) developed to improve DMARDs adherence in RA patients who are non-compliant to their conventional DMARDs (Methotrexate, Leflunomide, Sulfasalazine and/or Hydroxychloroquine) therapy.

Methods: The MUSP is a standardized approach (i.e. each patient given the same standardized intervention) which synergises (1) the patients’ direct visualization of their joint pathologies (inflammation and/or erosions) using real-time ultrasonography and (2) a Rheumatologist’s simultaneous reinforcement of the need for medication adherence, thereby improving patient’s understanding of their joint disease and motivating them to adhere to their DMARDs therapy. Joints utilized to demonstrate joint pathologies real-time using ultrasonography.

Results: 62 RA patients (baseline characteristics: majority Chinese, 40/62 (64.5%); 55/62 (88.7%) female; mean (SD) age, 49.2 (12.0), mean (SD) DAS28, 3.27 (1.39); mean (SD) disease duration, 6.1 (5.4) years) completed the MUSP. The mean (SD) time taken to complete the MUSP was 18 (8.7) minutes. All patients had at least one joint pathology demonstrable to them on real-time ultrasonography. Specifically, 62/62 (100%), 14/62(22.6%) and 25/62 (40.3%) had demonstrable synovial hypertrophy, power Doppler synovial vascularity and bone erosions, respectively. Figure 1 shows the frequency distribution of the joint sites utilized to demonstrate joint pathologies real-time using ultrasonography. The majority of patients reported that the MUSP had moderately or very much improved their understanding of their underlying joint condition (i.e. 44/62 (71.0%) patients) and the importance of regularly taking their RA medication (i.e. 49/62 (79.0%) patients) (figure 2). Most patients (i.e. 56/62 (90.3%) patients) will also recommend the MUSP to another RA patient.

Conclusion: Our results demonstrated high feasibility and acceptance of a MUSP developed to improve DMARDs adherence in RA patients. Further studies are required to establish the clinical impact and cost-effectiveness of the MUSP in this population.

Disclosure of Interests: None declared


References


Disclosure of Interests: None declared

Objectives: To retrospectively summarize 50 cases of mesenteric panniculitis/MP diagnosed by CT to improve the clinicians’ understanding of the disease.

Methods: The patients with MP diagnosed by abdominal CT were collected from the hospital of Shari Medical University from January 2013 to May 2017. The demographic characteristics, clinical features, auxiliary examination, treatment and prognosis were analyzed and summarized.

Results: The proportion of men and women was 1:0.92, the age of onset was 25 - 85 years old, the average age was (59.1±14.0) years old. Most of the patients presented with abdominal pain, fever, hematuria, and lymphadenopathy. 22 cases with tumor, the most common type is lymphoma, 16 cases with abdominal surgery history. There were no special laboratory tests, no patients had mesenteric pathologic biopsy. 6 cases had abdominal CT review. 1 case of who used hormone treatment showed the lesion was significantly absorbed, the remaining 5 cases no significant changes.

Conclusion: MP is common in the elderly, the clinical manifestations are diverse, easy to merge tumor, lymphoma more common, abdominal CT is its most important diagnostic means, when found MP, should pay attention to whether the merger with malignant tumors.

REFERENCES

Disclosure of Interests: None declared


Public health, health services research, and health economics

SAT0555 LOSING FOLLOW-UP IN REGISTRIES OF RHEUMATIC PATIENTS TREATED WITH BIOLOGICS: A POTENTIALLY VALUABLE HIDDEN REAL-WORLD DATA THAT IS BEING OVERLOOKED?

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Hospital Egas Moniz, Serviço Reumatologia, Centro Hospitalar de Lisboa Ocidental, Lisboa, Portugal

Background: The information associated with loss to follow-up (LFU) patients (Pts) may affect a real-world data evaluation of the use of biologics (Bio) that is not being adequately captured in registries.

Objectives: To identify the reasons for LFU in rheumatic patients treated with biologics in our center.

Methods: We identified all Pts treated with Bio in our center who had no registered visits in Reuma.pt for more than 6 months. We retrieved baseline information from Reuma.pt and from the hospital electronic clinical record. We then performed a telephonic interview to characterize the reasons for LFU up at our day care unit. For Pts unable to be contacted by telephone a letter of invitation to an appointment at the hospital was sent.

Results: From a total of 790 Pts registered in Reuma.pt at our centre with active Bio therapy (BioTx) 227 did not have any information registered in last 6 months. Of this, 36 Pts were on BioTx prescribed by other Department (Dermatology, GEA) and maintain follow-up in these departments. 102 Pts had suspended BioTx by medical indication, and this information was registered in the hospital electronic clinical records but not updated in Reuma.pt. For 89 Pts (47%) no information could be retrieved from either the hospital electronic clinical record or Reuma.pt and we classified these Pts as true LFU. Reasons of LFU were: being followed in other Rheumatology centres (n=28; 31.4%), death (n=26; 29.2%), adverse effects (AE) (n=11; 12.4%), other (n=5, 5.6%) and clinical remission (n=4; 4.5%). 15 Pts (16.9%) could not reach us by telephone or attend the appointment.

28 of these LFU Pts were being followed up in another Rheumatology center. The most frequent reasons for this change were: 15 (16.9%) decided to move the follow-up to a newly created and closer Rheumatology Department; 6 (6.7%) moved to another city; 5 patients (5.6%) had administrative problems related to our Department/Hospital and 2 (2.3%) patients referred socio-economic reasons that were interfering with travelling.

26 of the LFU Pts died, at a mean age of 66.3 years. The mean disease duration was 14.3 years and 20 Pts (76.9%) had RA. The mean duration of Bio was 5.9 years and 53.8% were under anti-TNF therapy, 16% under Anti-CD20 therapy and 12% under interleukin-6R inhibitors. Cause of death was identified in only 3 patients: 1 had a myocardial infarction, 2 had surgery complications. None of these Pts was on BioTx at the moment of death.

11 Pts of the LFU had stopped BioTx and abandoned follow-up by their own decision after suffering AE attributed by the patient to the use of Bio. 6 patients (6.7%) had infections: cutaneous (n=3, 3.4%) or urinary tract related (n=3, 3.4%), with need of hospital admission in 2 of the cases (2.2%). The remaining Pts stopped the drug because of cutaneous reactions (n=5, 5.6%).

4 Pts of the LFU were in remission and decided to stop the drug and the medical follow up. All of them believed that the disease was inactive without the need of medical drugs.

Conclusion: Identifying LFU Pts and clarifying the reason for the loss of data in a register contributes to a better knowledge on strategies to discontinue Bio in stable Pts, to a better pharmacovigilance of adverse effects and to more efficiency in data capture by registries. The authors of this study are now making additional efforts to contact the 15 still missing Pts and obtaining access to death certificates in order to further clarify the cause of death of 23 Pts.

Disclosure of Interests: None declared


SAT0556 EVALUATING RESEARCH PARTICIPANT EXPERIENCE IN A RHEUMATOID ARTHRITIS OBSERVATIONAL STUDY

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1The University of Manchester, School of Medicine, Manchester, United Kingdom; 2The University of Manchester, Manchester, United Kingdom

Background: Patient and public involvement (PPI) in research is increasingly common (1), but the experience of research participants is rarely evaluated, missing opportunities to gain insights for improving future studies. (2) Observational studies are often used to study natural progression and treatment response in chronic diseases like rheumatoid arthritis (RA).

Objectives: We aimed to pilot a participant experience questionnaire in an observational study of RA patients, to gain feedback on the study and evaluate the questionnaire as a feedback tool.

Methods: The Rheumatoid Arthritis Medication Study (RAMS) is a large UK prospective observational study of patients with RA or undifferentiated polyarthritis starting methotrexate (MTX) for the first time. Participants were recruited prior to initiation of MTX and followed-up at 3, 6 and 12 months. At visits, disease activity is measured and participants complete a study questionnaire including patient reported outcomes. Participants also complete a weekly diary about their MTX use. (3) A subset of RAMS participants were given a feedback questionnaire at their final visit. The questionnaire was designed by researchers and study coordinators with feedback from patients. Questions addressed the value of participation, study conduct and priorities for future research. Multiple-choice question responses were summarised and key themes were identified in the free-text responses.
OUTPATIENT READMISSION IN RHEUMATOLOGY: A MACHINE LEARNING PREDICTIVE MODEL OF PATIENT’S RETURN TO THE CLINIC

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Background: Readmissions can be defined as the return of a patient to a healthcare setting after a discharged. Attention has been mainly focused on readmissions following inpatient hospitalizations. In the outpatient setting, readmissions have been far less studied. Premature outpatient discharges can have negative impacts at multiple levels, as they may prolong disability, and increase the chance of disease chronification, the demands to the immediate patient’s support system, and healthcare resources utilization. As the first step in preventing outpatient readmission, the assessment of the individual patient’s risk could be useful to help identify those subjects at greatest risk, so, in a further step we could focus the delivery of an intervention in those patients to reduce their risk.

Methods: Patients stored in a departmental electronic health record from April 1st, 2007 to November 30th, 2016, and followed-up until November 30th, 2017, were included in this study. Only readmissions taking place between 3 and 12 months after discharge were analyzed. Discharge episodes were split into training, validation and test datasets. Clinical and demographic variables, including diagnoses, treatments, quality of life, and comorbidities, were used as predictors. Models were developed using Random Forest.

Results: 17,473 patients (18,117 discharges episodes) were analyzed and 1,960 (10.8%) discharges episodes were classified as outpatient readmissions. 46,654 models were finally developed. The best final model showed an AUC-ROC of 0.674 a sensitivity of 0.330 and a specificity of 0.867. The most relevant variables in the model were the number of diagnoses given at discharge, follow-up duration, age, number of previous discharges, previous corticosteroids use and disability.

Conclusion: We have developed a predictive model for outpatient readmission in a rheumatology setting. Clinical, demographical characteristics as well as medication and disability were the most important predictors.

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SAT0560 A QUALITATIVE STUDY EVALUATING NEAR-PATIENT TOOLS INCLUDING A MOBILE APPLICATION FOR EARLIER RA REFERRAL; POTENTIAL TO REDUCE CHRONIC DISEASE BURDEN

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Background: Rheumatoid arthritis (RA) is a chronic, debilitating autoimmune disease. Patients who are treated with disease modifying therapy within 6-12 weeks of symptom onset have better outcomes which leads to a reduced economic burden of disease. 1 Technology that enables near-patient blood testing coupled with digital health applications may increase the proportion of patients treated within this window. Objectives: This study aimed to assess the perceived unmet need for early treatment amongst clinicians and patients as well as their perceptions of a near-patient blood test and digital health mobile application. Methods: 74 participants, approximately half from each of Canada (n=18) and the US (n=20) participated in a combination of in-depth interviews and surveys for 40-50 minutes. 38 of the 74 subjects, consisted of 16 rheumatologists, 14 primary care physicians (PCPs) and 8 RA patients. To supplement the patient study-sample, 36 additional patients completed an online survey of quantitative and open-ended questions focused on diagnosis and perspectives of a described near-patient blood test and mobile application. Rheumatologists who were in full-time practice and PCPs who see at least 15 RA patients a month were included. Patients were between 18 and 60 years old, had an RA diagnosis and experience using apps for health management. Results: Almost all Rheumatologists and PCPs indicated that the time between symptom onset and treatment initiation (currently 6-18 months) could be improved and agreed that difficulty diagnosing is still one of the biggest unmet needs. Referrals to a Rheumatologist range from 6 weeks to 3 months. Patients indicated that it took 8 months to 2 years before treatment initiation. Most Rheumatologists said the longest delay is due to inconclusive PCP clinical exacerbations and blood work, leading to repeated visits before patients are referred. Most clinicians and patients welcomed new tools with 33% of patients willing to pay for the near-patient blood test and mobile application. Clinicians had few concerns about a near-patient blood test and indicated that it should be available in the clinic, not the pharmacy. Patients reported the appeal of an easy to use near-
patient blood test that could have meant an earlier diagnosis over a traditional laboratory blood test.

Conclusion: RA is difficult for PCPs to identify for early referral and treatment within 6-12 weeks of symptom onset. The clinicians and patients we surveyed reported positive perspectives regarding near-patient blood tests and mobile applications and welcome their use to assist with earlier referral and treatment.

With the emergence of innovative near-patient technologies, opportunities exist to intervene earlier and potentially reduce the social and economic burden of chronic diseases.

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REFERENCES


Disclosure of Interests: Norma Blin Shareholder of: Amgen, Employee of: Pfizer, Amgen and Abbott, Simran Chahal: None declared


SAT0561 DIAGNOSTIC ACCURACY OF GOUT IN ELECTRONIC HEALTH RECORDS AND THE ROLE OF RHEUMATOLOGY ELECTRONIC CONSULTS

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Background: Gout is the most prevalent inflammatory arthritis globally. Despite treatment advances, it still has a significant effect on quality of life and healthcare costs. There have been inconsistent studies on administrative coding as an accurate marker of true diagnosis. Although gout can be solely managed by primary care physicians (PCPs), complex cases often require rheumatology consultation. The wait time for an initial rheumatology clinic visit ranges from 38 days to 47 weeks. However, electronic consults (e-consults) allow for swift two-way communication between PCPs and rheumatologists (pre-consult exchange) to facilitate coordination of care among providers.

Objectives: To determine the accuracy of gout diagnosis based on ICD 9 and 10 coding, and the differences in gout outcomes based on PCP management, e-consult or rheumatology clinic visits at two Veterans Affairs Medical Centers.

Methods: A retrospective cohort study was created from 2009-2014 including 101 e-consult patients and a control group of 176 patients. In the e-consult group, 76 patients were ICD 9 or 10 coded for gout; in the control group, 116 were ICD 9 or 10 coded for gout. A blinded abstractor determined the accuracy of gout coding based on chart review and EULAR criteria.

A second random sample of 183 gout patients from 2009-2014 was identified and stratified to 3 modes of management: PCP only (48), e-consult (68), and rheumatology clinic visit (67). Data was reviewed for 24 months following initial gout diagnosis or e-consult. Management was evaluated based on frequency of flares and related ED visits, creatinine clearance, and serum uric acid levels (sUA).

Results: The sensitivity and specificity of ICD coding for accurate gout diagnosis was 94% and 79% in the control (PPV 88%, NPV 90%). For e-consult patients, the sensitivity and specificity was 100% and 70% (PPV 87%, NPV 100%). E-consult patients were more accurately diagnosed with gout by PCPs than in the control group (p=0.03). 83% of e-consults were resolved electronically and 17% were converted to rheumatology clinic visits. The mean wait time for e-consult recommendations was 1.8 days. The mean clinic visit wait after pre-consult exchange was 22.9 days compared to an average of 43.1 days for direct rheumatology clinic visits. Both e-consult and rheumatology clinic patients had more gout flares and related ED visits at diagnosis compared to PCP care; however, at 12 months, both groups had significantly fewer gout-related ED visits, decreased sUA, and improved creatinine clearance (p<0.05).

Conclusion: VA databases are an accurate source of gout patients based on ICD coding. When viewing e-consults, rheumatologists can rely on accurate PCP gout diagnoses, confidently answer clinical questions, and triage more efficiently. E-consult serves as an effective alternative in managing gout with shorter wait times for recommendations and appointments while still reimbursing physicians at a reasonable rate. Therefore, complex gout management can be enhanced by e-consults to improve clinical outcomes, decrease gaps in care and optimize healthcare resources.

REFERENCES


Disclosure of Interests: None declared


SAT0562 BURDEN OF RHEUMATIC DISEASE AMONG KOREAN WOMEN IN CHILDBEARING YEARS BASED ON THE NATIONAL HEALTH INSURANCE SERVICE

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Background: Many rheumatic diseases (RDs) predominantly affect women in their reproductive years, and have a significant impact on childbearing, but its burden remains incompletely understood.

Objectives: The study aimed to identify the prevalence and incidence of RDs among Korean women in childbearing years, and the effect of the diseases on prevalence of comorbidities, medication use, and pregnancy rate.

Methods: From National Health Insurance Service data during 2009-2016, we identified 9,217,119 women aged between 20-44 years. Among these women, we estimated the prevalence and incidence of RDs including rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and ankylosing spondylitis (AS). Prevalence of chronic diseases such as cancer (Ca), hypertension (HT), hyperlipidemia (HLD), and diabetes mellitus (DM) was compared in women with or without RDs. The prescription prevalence of medications including NSAIDs and corticosteroids were compared according to the presence of RDs. We also investigated pregnancy rate in women with rheumatic or chronic diseases, and control subjects without rheumatic or chronic diseases.

Results: Overall prevalence of RDs was 56.3 per 100,000 20-44 aged females, and overall incidence was 7.68 cases per 100,000 person-years. Women with RDs had increased risk for overall chronic diseases (OR 1.90, 3.0, and for Ca (OR 1.3), HT (OR 1.4), HLD (OR 2.9), and DM (OR 2.8), respectively (p<0.0001). The prescription of NSAIDs and steroids was significantly more frequent in women with RDs than those without (81.62% vs 21.79% in NSAIDs, 77.83% vs 4.28% in steroids, p<0.0001). Pregnancy rate was significantly lower in women with RDs compared with the controls (15.92% vs 19.30%, p<0.0001). Among women with RDs, women with RA were less likely to become pregnant (OR 0.80, p<0.0001), whereas women with SLE and AS showed no significant difference in pregnancy rate compared with the normal controls.

Conclusion: RDs are a significant burden for women in childbearing years causing increased co-morbidities and medication use and causing reduced pregnancy rate.

REFERENCES


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Efficacy of Etanercept over a Period of 12 Months in the Routine Treatment of Patients with RA, AxSpA, PsA or Pso: Final Results of a German Non-Interventional, Prospective, Multi-Center Study (Adequate)

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Background: Patients with chronic autoimmune diseases such as rheumatoid arthritis (RA), axial spondyloarthritis (axSpA), psoriatic arthritis (PsA) or plaque psoriasis (PsO), the treat-to-target concept requires attaining remission or at least low disease activity and is defined by the corresponding guidelines. The achievement of these targets affects radiological progression and functional measures. If treat-to-target has not been achieved after 3 months, current treatment could either be continued with an expected increased response over time or could be switched to another treatment option.

Objectives: The primary goal of this non-interventional study was to determine the proportion of patients achieving the treat-to-target criteria with Etanercept at month 3, 6 and 12 in a real-life setting. Secondly, the proportion of patients achieving the treat-to-target criteria at month 6, even if it has not yet been fully attained until month 3, was determined.

Methods: Into this German non-interventional, prospective, multi-center cohort study, adult patients with confirmed diagnosis of RA, axSpA, PsA or Pso without prior Etanercept treatment were included. Planned recruitment number was 2,100 RA patients, and 300 patients each with axSpA, PsA or Pso. Criteria for remission and minimal clinical efficacy were defined according to recommendations of the respective treatment guidelines and the study protocol. The analyses were based on the number of patients completing the respective study period (3, 6 and 12 months).

Results: Overall, 1,465 patients were included (treated set), i.e. 901 females (61.5%) and 564 males (38.5%); patients mean ± SD age was 54.9 ± 14.5 years. Patients’ median disease duration ranged across the rheumatic indications from 3.4 years in PsA to 5.5 years in RA, and was markedly longer in Pso (median: 15.3 years). At week 12, the proportion of patients reached remission was 24.4% in RA, 19.0% in axSpA, 38.3% in PsA and 7.1% in Pso. Further increases were seen up to week 24 in RA (30.6%), PsA (50.7%) and Pso (18.6%), while axSpA rates remained similar (18.4%). In all indications, these proportions continued to increase from week 24. At the end of the observational period, a total of 702 patients (47.9%) experienced at least one treatment emergent adverse event (TEAE). However, serious drug-related AEs were only reported in 41 patients (2.8%).

Conclusion: A considerable proportion of patients attained the target of remission or low disease activity at week 12 under daily routine practice conditions, proving a reliable protective therapeutic effect of Etanercept in a real life setting. These percentages further increased up to week 24 except for axSpA patients. With regard to the safety profile of Etanercept, the incidence numbers and types of AEs were in an expected range and in-line with documented safety profile according to the SmPC. 

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SAT0565  COST EVOLUTION OF BIOLOGICAL AGENTS FOR THE TREATMENT OF RHEUMATOID ARTHRITIS IN A TERTIARY HOSPITAL INFLUENTIAL FACTORS IN PRICE

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Background: The availability of biological therapy has changed the approach to treating rheumatoid arthritis. Spending on biological agents has risen due to the drugs' high cost and the increased prevalence of rheumatoid arthritis.

Objectives: To evaluate the annual cost-per-patient and cost for each biological drug for in patients with rheumatoid arthritis from 2009 to 2017, and to calculate factors that affect at treatment cost, such as optimized therapies by monitoring drug serum levels, the use of biosimilars-TNF inhibitors, and discounts or negotiated rebates in biologicals acquired by pharmacy department.

Methods: Retrospective, observational study in a Spanish tertiary hospital. Main outcome: Annual cost-per-patient and per drug. Influential factors that affected the costs and demographic parameters and disease activity were also analyzed.

Results: A total of 320, 270, and 389 patients were treated in 2009, 2013, and 2017, respectively. Annual cost-per-patient decreased: € 10,798 in 2009, € 7,491 in 2013 to € 7,116 in 2017. The introduction of new drugs drives economic competition leading to discount savings from original infliximab, etanercept, adalimumab, certolizumab, golimumab and tocilizumab respectively, while rebates for biosimilar-infliximab reached 43.1% in 2017. Patients with optimized therapies reached 35.2% in 2017, which lead in cost savings of € 458,535 and savings from optimized therapies of € 830,000 in 2017.

Conclusion: The cost of biological treatments declined after official discounts, negotiated rebates, and optimized therapies, leading to a significant decrease in the annual cost per patient. The greatest contribution to economic savings in biological therapy according to our study was biological therapy optimization.

REFERENCES

Disclosure of Interests: Mª Angéles González-Fernández: None declared, Elena Villamañán Bueno: None declared, Irmaculada Jiménez-Nácher: None declared, Chamaida Plasencia: None declared, Alicia Herreño Ambrosio: None declared, Alejandro Balsa Grant/research support from: Abbvie, Pfizer, Novartis, BMS, Nordic, Sanofi, Consultant for: Abbvie, Pfizer, Novartis, BMS, Nordic, Sanofi, Sandoz, Lilly, Paid instructor for: Pfizer, Speakers bureau: Pfizer, Novartis, UCB, Nordic, Sanofi, Sandoz, Lilly.


SAT0566  LIVING WITH CHRONIC INFLAMMATORY AUTOIMMUNE DISEASE IN BRAZIL: THE PATIENT’S PERSPECTIVE

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Background: The patient’s journey is a complex phenomenon. It includes all the stages, perceptions, and experiences that the patient goes through since the identification of the first symptoms of a given disease. Therefore, it is crucial to understand this journey as it may help to optimize the patient’s quality of life, especially for those who live with chronic inflammatory autoimmune diseases such as Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA) and Axial Spondyloarthritis (axSpA).

Objectives: The aim of this study was to understand the journey of people living with rheumatic disease in Brazil and its impact on several different areas of the patient’s life, including family planning, use of medications, and access to health care services and professionals.

Methods: The data were extracted from an exploratory, descriptive and quantitative research, with primary data collection. It was performed between May 09, 2018 and August 01, 2018. The survey had 58 questions and it was available online for public participation through the GRU-PARU PETRÔPOLIS website.

Results: The survey was accessed by 1223 participants. The proportion of patients with RA, PsA, and axSpA were 70.97%, 17.42% and 11.61%, respectively. Most participants were female (87.64%) and 59.21% of all attendees were between 18 and 54 years old. Only 38.72% of the participants declared that they were working, while 32.34% admitted to being retired or on sick leave. About 60% of the attendees have taken more than a year to visit a rheumatologist and 48.08% received their diagnosis after at least one year of the first symptoms. Nevertheless, once they started to visit a rheumatologist, more than two thirds do not have difficulty to schedule a visit with this specialist. In addition, participants are satisfied with the health care they receive and feel well informed about their treatment. At least half of the attendees used synthetic disease-modifying antirheumatic drugs to control their disease, 41.73% also used corticoids and 33.87% are on biologic drugs. Nevertheless, 37.24% and 17.35% of the participants classified their disease activity as moderate or high, respectively, thus not achieving the target of treatment from their own perspective. This may affect the patient’s quality of life as reflected in the percentage of respondents suffering from emotional problems (46.62%) as well as in the proportion of patients having some or many difficulties to do daily activities. This scenario is impacted by the fact that more than half of the participants do not have access to another health care provider other than the rheumatologist to help manage their condition. This survey has also delved on the topic of family planning. With regards family planning, 50% of the women indicated an unplanned pregnancy (n=142). Moreover, 48.59% (n=69) of these women had never discussed with their rheumatologist about the desire to be pregnant. Furthermore only 13.38% (n=19) affirmed that their treatment during pregnancy was discussed between the rheumatologist and the gynecologist/ obstetrician.

Conclusion: Although most of the participants in this survey indicated a good level of satisfaction with the health care they receive, data also indicate opportunities for improving the patient’s quality of life. Patients are satisfied with the access to the rheumatologist, drug treatment as well as the information they receive on physician’s appointments. This work illustrates the complexity of these chronic inflammatory autoimmune disease and the importance of multidisciplinary treatment to manage it to impact positively the patient journey.

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Background: As part of the IOF recommendations and the “Capture the fracture” program a Multidisciplinary and focused on Primary Medicine Fracture Liaison Prevention Unit (FLS) was created in May of 2018 in the Hospital Universitario Virgen Macarena, in Seville, Spain. In previous reports, the rate of osteoporosis treatment prescription after the fragility fracture was as low as 20%, with a poor communication between the medical specialties involved in the attention of this patients.

Objectives: To improve the medical attention and treatment of patients with a FF. To create a multidisciplinary FLS with the collaboration of Primary Care Medicine, Internal Medicine, traumatology, Emergency Room, Rheumatology, Rehabilitation Service and the Medicine Department of the Seville University.

Design: A prospective, observational study in the setting of usual clinical practice and with approval of the local ethics committee. The Multidisciplinary FLS started to work at may, 2018 connecting primary care with medical specialties. The FLS has 3 weekly consultations (11 first visits, 4 second visits and email consultation, each day) attended by 2 internal medicine physicians, one Rheumatologist and one nurse. All medical specialties involved in the attention of patients with FF can refer patients and the inclusion criteria is the history of a FF in the past 18 months. In a single medical visit, the doctor and the nurse make a clinical history, assesses the risk of FF according to FRAX, the risk of falls (J.H. Downton scale), they evaluate malnutrition (Mini Nutritional Assessment Elderly) and sarcopenia (hands dynamometry and Short Physical Performance Battery). Complete blood count and blood and urine biochemistry in order to evaluate secondary causes of osteoporosis and vertebral radiographs are done. A treatment plan agreed and discussed with patient is started. The plan advice on diet and exercises, drugs, and a written report and medical prescription. And a phone follow-up is programmed. The data are entered and stored in a database (OpenClinica) real time.

Results: From May to October of 2018, 170 patients have been included: 135 (89%) women. The mean (standard deviation) age was 73 ± 11.8 years old; 25% of them with ages between 83 to 94 years. The patients were defined by a series of screening questions in the CCHS-MH and included all rheumatic diseases. The rate of receiving adequate treatment for their comorbid mental disorders. The outcome of interest was utilization of mental health treatments in the previous 12 months, including: 1) medications; 2) professional services (e.g. physician, psychiatrist, nurse); or 3) non-professional services (e.g. family, self-help group, internet). The explanatory variable was self-reported doctor-diagnosed arthritis and included all rheumatic diseases. Multivariable binomial logistic regression was used to evaluate utilization of mental health treatment differs among those with and without arthritis, adjusting for the confounding factors of age, sex, race/ethnicity, and household income.

Methods: We used nationally representative data from the 2012 Canadian Community Health Survey – Mental Health (CCHS-MH) to draw a sample of 1,810 participants with depression, anxiety, or bipolar disorder. Depression, anxiety, and bipolar disorder (bipolar I, bipolar II, or hypomania) were defined by a series of screening questions in the CCHS-MH derived from the World Health Organization version of the Composite International Diagnostic Interview. The outcome of interest was utilization of mental health treatments in the previous 12 months, including: 1) medications; 2) professional services (e.g. physician, psychiatrist, nurse); or 3) non-professional services (e.g. family, self-help group, internet). The explanatory variable was self-reported doctor-diagnosed arthritis and included all rheumatic diseases. Multivariable binomial logistic regression was used to evaluate utilization of mental health treatment differs among those with and without arthritis, adjusting for the confounding factors of age, sex, race/ethnicity, and household income.

Results: A total of 447 (20.5%) participants from our study sample reported having arthritis (66.9% female). Utilization of mental health treatments in the previous 12 months was reported by 82.4% individuals with arthritis and 79.5% without arthritis. The most common treatment utilized by those with arthritis was professional services (66.5%), followed by medication (61.8%) and non-professional services (51.5%). Participants without arthritis most often received mental health treatment in the form of non-professional services (67.3%), followed by professional services (58.1%) and medication (45.6%). The point estimate of the adjusted analysis suggested a positive association between arthritis and utilization of at least one type mental health treatment (odds ratio [OR] 1.41, 95% confidence interval [CI] 0.85, 2.34), though not statistically significant. In the sub-analysis, the ORs for the association between arthritis and specific mental health treatments were: medication (OR 1.30, 95% CI 0.86, 1.99) and for professional services (OR 1.27, 95% CI 0.83, 1.93), but decreased for non-professional services (OR 0.81, 95% CI 0.52, 1.27).

Conclusion: These nationally representative data show that a high proportion of individuals with arthritis seek treatment for their comorbid mental disorders. Findings of this study may also suggest a positive association between having arthritis and seeking care for comorbid mental disorders, which may be explained by an already established connection with the healthcare system to manage arthritis. Opportunities to improve mental health treatment among those with arthritis include optimizing access to non-professional services.
Objectives: We sought to: (i) describe trends of prescribed opioids for non-cancer pain in the UK primary care setting over a 10-year period (ii) assess the sequential transition of opioid strength from index date over a 2-year period.

Methods: We conducted a retrospective observational study over a 10-year period from 1/1/2006 to 31/12/2015 using the Clinical Practice Research Datalink (CPRD). CPRD collects de-identified patient data from a network of GP practices across the UK. New users of opioids, 18 years or over, without cancer in the 2 years prior to index date were included. The number of prescriptions for each drug were calculated by each calendar year accounting for the number of eligible patients registered in CPRD for that year. Sunburst plots were created to evaluate the sequential transition of opioids over time. A 4-state hidden Markov model was used to estimate the transition probability for individuals escalating to more potent opioids over a 2-year period. States were defined as (i) no drug (ii) weak opioid (codeine, dihydrocodeine) (iii) moderate opioid (tramadol) (iv) strong opioid (all others in CPRD). Methadone prescriptions were excluded for the purposes of this analysis.

Results: 1,026,955 opioid users were included: mean age (SD) was 55 (18) years; 58% being female. New users of opioids were most commonly prescribed codeine (n=723,102; 70.8%), followed by dihydrocodeine (n=179,831; 17.6%), tramadol (n=93,338; 9.1%) with n=94,808 (2.4%) strong opioid prescriptions. The rate of prescribing strong opioids/10,000 population increased 12 fold from 2006-2013, followed by a gradual decline till 2015 (Figure 1). This trend was most marked with certain opioids: morphine, oxycodone, buprenorphine and fentanyl (28.5 prescriptions per 10,000 population to a peak of 353.0 prescriptions per 10,000 population in 2013 and 303.1 prescriptions per 10,000 population in 2015). Using sunburst plots, of the new users prescribed weak opioids as their first prescription at index date, 5.5% transitioned to moderate opioids, 4.1% to strong opioids over 2 years (Figure 2). Transition probability of staying on a strong opioid (if first prescription at 2 years remained high if prescribed first as a new user.

Disclosure of Interests: None declared


**Table 1. Patients characteristics of our cohort**

<table>
<thead>
<tr>
<th></th>
<th>RA (n=424)</th>
<th>axSpA (n=145)</th>
<th>PsA (n=132)</th>
<th>SLE (n=41)</th>
<th>Other diseases (n=233)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>60.7 (13.4)</td>
<td>43.7 (12.4)</td>
<td>51.3 (12.7)</td>
<td>48.4 (10.6)</td>
<td>56.1 (16.9)</td>
</tr>
<tr>
<td>Gender, male, n (%)</td>
<td>137 (36.4)</td>
<td>95 (65.5)</td>
<td>55 (41.7)</td>
<td>9 (48)</td>
<td>64 (27.5)</td>
</tr>
<tr>
<td>Current use of bDMARDs, n (%)</td>
<td>103 (38.4)</td>
<td>76 (71.0)</td>
<td>57 (68.3)</td>
<td>9 (22.0)</td>
<td>59 (25.3)</td>
</tr>
<tr>
<td>Physical function*</td>
<td>1.30 (0.76)</td>
<td>4.0 (2.59)</td>
<td>1.28 (0.68)</td>
<td>1.12 (0.67)</td>
<td>1.03 (0.69)</td>
</tr>
<tr>
<td>CRP (mg/dl), median (IQR)</td>
<td>0.3 (0.1-0.2)</td>
<td>0.1 (0.1-0.2)</td>
<td>0.1 (0.0-0.2)</td>
<td>0.3 (0.1-0.6)</td>
<td>0.4 (0.1-0.6)</td>
</tr>
<tr>
<td>Vaccination card available</td>
<td>230 (54.2)</td>
<td>76 (52.4)</td>
<td>66 (50.0)</td>
<td>28 (68.3)</td>
<td>140 (60.1)</td>
</tr>
<tr>
<td>Received information about vaccination</td>
<td>273 (64.4)</td>
<td>101 (69.7)</td>
<td>81 (61.4)</td>
<td>28 (68.3)</td>
<td>146 (62.7)</td>
</tr>
<tr>
<td>Complete pneumococcal vaccination status</td>
<td>129 (33.2)</td>
<td>33 (22.8)</td>
<td>26 (19.7)</td>
<td>12 (26.8)</td>
<td>66 (28.3)</td>
</tr>
<tr>
<td>Complete influenza vaccination status</td>
<td>85 (20.0)</td>
<td>11 (7.7)</td>
<td>20 (15.2)</td>
<td>9 (19.5)</td>
<td>50 (21.5)</td>
</tr>
<tr>
<td>Complete hepatitis B vaccination status</td>
<td>36 (8.5)</td>
<td>26 (17.9)</td>
<td>13 (9.8)</td>
<td>10 (24.4)</td>
<td>37 (15.9)</td>
</tr>
</tbody>
</table>

**Figure 1. Strong opioid prescribing trends over 10 years**

**Figure 2. Sunburst diagram demonstrating opioid prescribing pathways over 2 years**

**Conclusion: Strong opioid prescribing increased till 2013-14 gradually decreasing following UK initiatives to improve monitoring and use of controlled drugs. Although less potent codeine prescriptions made up the majority of first prescriptions, the transition probability of staying on a strong opioid at 2 years remained high if prescribed first as a new user.**

**Disclosure of Interests: None declared**

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SAT0571 IDENTIFYING DETERMINANTS OF PRESENTEEISM IN WORKERS WITH INFLAMMATORY ARTHRITIS
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1The University of British Columbia, Vancouver, Canada; 2Arthritis Research Canada, Richmond, Canada

Background: Work disability (WD) and presenteeism (decreased at-work productivity) are often caused by arthritis, leading to major impact on individuals’ quality of life and cost to society.

Objectives: Our study objective was to identify the determinants of presenteeism in workers with inflammatory arthritis.

Methods: Baseline data from the randomized controlled trial of an employment intervention, the Making-it-WORK program, were used. Participants were recruited from British Columbia, Alberta and Ontario. Inclusion criteria: diagnosis of inflammatory arthritis, currently employed, age 18-59, and having concerns about arthritis affecting ability to work. The primary outcome, presenteeism, was assessed using the ‘In’ impaired while at work, importance of working. Variables correlated with WPAI-SHP were selected for inclusion. The independent variables included: 1) sociodemographic variables: age, gender, ethnicity, marital status, education, children under age 19; 2) disease variables: IA diagnosis, disease duration, number of limiting comorbidities, global assessment of disease activity (VAS), joint pain (VAS), Disease activity [Rheumatoid Arthritis Disease Activity Index (RADAI)], physical function (HAQ II), Fatigue [VAS, Global Fatigue Index from the Multidimensional Assessment of Fatigue (MAF)], Sleep quality [Insomnia Severity Index (ISI)], Depression [Patient Health Questionnaire – PHQ-9]; 3) work variables: physical demand, job autonomy, difficulty commuting to/from work, job spillover, job strain, psycho-social work characteristics [Job Content Questionnaire (JCC) decision latitude, physical and psychological job demands, social support at work], self-employment, family support of decision to work, economic situation of working. Variables correlated with WPAI-SHP at p ≤ 0.20 were selected for inclusion in the multivariable linear regression analysis, using stepwise selection with alpha of 0.15.

Results: The sample included 585 participants [49% with RA, 17% PsA, 14% SLE, 20% AS] with median (IQR) arthritis duration of 7(3-15) years, mean (SD) age 45.6 (10) years; 43% were 50 years or older; 78% were females; 76% had completed post secondary education; 17% were self-employed. Multivariable linear regression analyses revealed that age < 30 (vs.age 30-49, p=0.067; vs. age ≥ 50, p=0.266), having more fatigue (GFI-MAP) (p<0.001), job strain (p=0.011), job spill over (p=0.002), disease activity (RADAI) (p=0.001), poor family support for working (p=0.049), poor physical function (HAQ II) (p=0.077) and commuting difficulty (p=0.081) were associated with greater impairment in work productivity.

Conclusion: This study identified important sociodemographic, disease and work-related factors associated with reduced productivity at work in people with inflammatory arthritis. These results provide useful information to health professionals counselling patients on dealing with employment issues.

Table: Multivariable linear regression modeling determinants of presenteeism

<table>
<thead>
<tr>
<th>Variable</th>
<th>Estimate</th>
<th>P Value 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue (MAP-GF)</td>
<td>0.74</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RADAI</td>
<td>0.06</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Job strain</td>
<td>0.09</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Commuting difficulty</td>
<td>0.10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MAR</td>
<td>0.09</td>
<td>0.001</td>
</tr>
<tr>
<td>HAQ-II</td>
<td>0.08</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Physical function (HAQ-I)</td>
<td>0.11</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

REFERENCES

Disclosure of Interests: André Luquini: None declared, Diane Lacaille Grant/research support from: Bristol-Myers Squibb and Eli Lilly Canada, Eric C. Sayre: None declared, Rebecca Schnurr-Howsam: None declared


SAT0572 ANTI NUCLEAR ANTIBODIES IN PRIMARY CARE SETTING: IS IT WORTH IT?
Mariana Luís, Luisa Bites, Ana Rita Prata, Tânia Santiago, José Antonio P. Da Silva, Catia Duarte. Centro Hospitalar e Universitário de Coimbra, Rheumatology, Coimbra, Portugal

Background: Antinuclear antibodies (ANA) are the most frequently used screening tests for connective tissue diseases. However, their diagnostic value depends on the pre-test probability of such conditions.

Objectives: To evaluate the usefulness, clinical correlates and associated direct costs of ANA testing in the primary care setting in an Early Arthritis Clinic (EAC) referral cohort.

Methods: A retrospective study of consecutive patients referred to the EAC between 2011 and 2018 was conducted. Referral is based on the fulfillment of specific criteria: presence of arthritis or clinically suspected arthralgia beginning in the previous 12 months, plus suggestive laboratoro abnormalities (rheumatoid factor, C-reactive protein or erythrocyte sedimentation rate). Many general practitioners also performed ANA testing (ANA-GP) and all patients underwent ANA testing, per protocol, in EAC (ANA-EAC). All patients having these 2 separated ANA results were included in the analysis. ANA-GP titers and pattern were assessed by indirect immunofluorescence (Hep2, positive–fitter≥1:160). Direct associated costs of ANA-GP were calculated, based on the mean charge of 3 different local labs. Positive (PVV) and negative predictive values (NPV) of ANA-GP for the diagnosis of inflammatory rheumatic disease, ANA-related rheumatic disease (ARD) and for the presence of ANA-EAC were estimated.

Results: 207 patients were referred to the EAC Clinic during this period (84.3% female, aged 53.9 ± 18.2 years-old). Fifty eight percent of these patients (n=120) had their ANA previously determined in primary care setting. Of the 18% (n=11) patients testing positive in both settings, 2 had no rheumatic disease, 2 had an ARD and 4 had another type of inflammatory rheumatic disease.

Disclosure of Interests: André Luquini: None declared, Diane Lacaille Grant/research support from: Bristol-Myers Squibb and Eli Lilly Canada, Eric C. Sayre: None declared, Rebecca Schnurr-Howsam: None declared


Scientific Abstracts
ANA-GP PPV and NPV were: i) 18.2% and 92.7% (LR 2.44) for ARD.; ii) 63.6% and 27.5% (LR 0.74) for inflammatory rheumatic disease and 72.7% and 23.9% (LR 0.124) for a positive ANA-EAC result. The referral criteria with the highest PPV for the diagnosis of inflammatory rheumatic disease were: positive rheumatoid factor (76.2%), high erythrocyte sedimentation rate (71.6%) and clinical signs of arthritis (70.8%). The direct cost associated with duplicate ANA testing was estimated in 2.160 €.

Conclusion: ANA testing in the primary care setting had a poor predictive value in this cohort, which can be explained by its application in patients with low pretest probabilities for ARD. Although the direct costs may not seem impressive, we speculate the real cost to be much higher since ANA test rarely is requested solo but, instead, along with a lot of other autoantibodies in a “trawl fishing” attempt to diagnosis. ANA evaluations are not recommended for the study of putative arthritis cases in primary care and local campaigns should be promoted in order to improve referral quality avoiding unnecessary, costly and lengthy lab tests as ANA.


SAT0573 HEALTHCARE RESOURCE UTILISATION AMONG PATIENTS DIAGNOSED WITH SYSTEMIC SCLEROSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE IN ENGLAND

Alicia Gaye1, Nils Schoof2, Margarida Alves3, Deborah Clarke1, Christina Raabe3, Prithwiraj Das4, Toby Maher5, Boehringer Ingelheim Ltd, Bracknell, United Kingdom; 2Boehringer Ingelheim International GmbH, Ingelheim am Rhein, Germany; 3National Heart and Lung Institute, Imperial College and Interstitial Lung Disease Unit, Royal Brompton Hospital, London, United Kingdom

Background: Systemic sclerosis-associated interstitial lung disease (SSc-ILD) is a substantial burden on patients and on healthcare services. Despite this, assessments of healthcare resource utilisation and costs incurred during the management of SSc-ILD are limited.

Objectives: To assess healthcare resource utilisation and costs among patients with SSc-ILD compared with SSc overall and patients with SSc and other organ involvement (SSc-OI).

Methods: This was a population-based cohort study. Routinely collected healthcare data were extracted from medical records (dated 1 January 2005 to 31 March 2016) in the Clinical Practice Research Datalink (CPRD) and the Hospital Episode Statistics (HES) databases. Patients with SSc, with or without ILD and/or OOI, were identified from primary and secondary care records in combination with modified European League Against Rheumatism (EULAR) classification criteria. Patients were included in the OI cohort if their SSc affected cardiac, gastrointestinal, renal or oral function. Eligible patients were aged at least 18 years at first diagnosis, were diagnosed within the study period, and had at least 12 months of available data in CPRD/HES before and after diagnosis. All-cause healthcare resource utilisation (inpatient stays; A&E attendances; outpatient visits, A&E attendances, and general practitioner visits per patient per year). Each patient with SSc-ILD had, on average, 10 outpatient visits, A&E attendances, and general practitioner visits per year. Inpatient stays alone accounted for >60% of the total healthcare costs among SSc patients with ILD (median cost >€3,600 per patient per year). Each patient with SSc-ILD had, on average, 10 outpatient visits per year, at a total yearly median cost of >€840. In comparison, patients with SSc-OI averaged 7 outpatient visits at a total yearly median cost of €915. Characteristics significantly associated with higher yearly healthcare costs among SSc patients were: older age at diagnosis, diagnosis of anaemia, and number of comorbid diseases.

Conclusion: The annual healthcare cost for a patient with SSc-ILD is substantial (€2,986–13,905), with inpatient stays the major cause of costs, and is much higher than for patients with SSc-OI (without ILD). Healthcare costs are also higher among older SSc patients and those with more comorbidities. These results highlight the economic burden of SSc-ILD in a real-world setting, which will be useful when evaluating the cost-effectiveness of new treatment options for SSc-ILD. There is an unmet need for effective therapies for SSc-ILD.

Acknowledgement: Funding: Boehringer Ingelheim International GmbH, Germany

Disclosure of Interests: Alicia Gayle Employee of: Employee of Boehringer Ingelheim, Nils Schoof Employee of: Employee of Boehringer Ingelheim, Margarida Alves Employee of: Employee of Boehringer Ingelheim, Deborah Clarke Employee of: Employee of Boehringer Ingelheim, Christina Raabe Employee of: Employee of Boehringer Ingelheim, Prithwiraj Das Employee of: Employee of Boehringer Ingelheim, Toby Maher Grant/ research support from: Received funds from BI advisory board participation and conference travel. Received research funding and/or consulting fees or other remuneration from GSK, UCB, AstraZeneca, Roche, Bayer, Biogen Idec, Cipla, Prometic, and Sarunmed. Toby Maher has, via his institution, received industry-academic funding from GlaxoSmithKline R&D and UCB. Consultant for: Toby Maher has received consultancy or speakers fees from Apellis, AstraZeneca, Bayer, Biogen Idec, Boehringer Ingelheim, Galapagos, GlaxoSmithKline R&D, Indalo, Pliant, ProMetic, Roche, Sarunmed and UCB; and has received consultancy fees from Galexco.


SAT0574 A SYSTEMATIC LITERATURE REVIEW OF HEALTHCARE BURDEN IN PATIENTS WITH BEHÇET’S DISEASE

Oriol Sola-Mongès1, Shields Nahta2, Sarah Ronnebaum2, Dipen Patel3, Tara Nazareth4, Angela Paduk4, 5Health Institute for Technology Transfer (HITT), Barcelona, Spain; 2Celgene Corporation, Summit, United States of America; 3Pharmint International, LP, Bethesda, United States of America; 4Pharmint International, Bethesda, United States of America; 5Celgene Corporation, Summit, United States of America; 6San Carlo Hospital of Potenza, Rheumatology Department of Lucania, Potenza, Italy; 7Madonna delle Grazie Hospital of Matera, Potenza, Italy

Background: Behcet’s disease (BD) is a chronic, multisystem, inflammatory disorder primarily characterized by recurrent oral ulcers (OU) and other key features, such as genital ulcers, skin lesions and articular and ocular inflammation. The prevalence of BD is typically reported as higher in Silk Road countries (e.g., Turkey, Jordan); however, it has increased in developed countries (e.g. Europe), likely due to migration. Given the diagnoses across geographic regions, we sought to understand the prevalence of BD manifestations, related symptoms and the impact on comorbidities, treatments, and quality of life (QoL).

Objectives: To understand the clinical and humanistic burden among patients (pts) with BD based on a systematic literature review (SLR).

Methods: An SLR was performed to identify real-world BD studies reported between 2005 and 2016. BD studies were selected if they were published in English, published from January 2005 to 2016, and were included in the Embase/MEDLINE databases. Studies were excluded if they did not report on the prevalence of BD, or if they were not published in English, or if they were not published in English. The following key terms were used: BD, Behcet's disease, BD prevalence, BD manifestations, BD symptoms, BD QoL. The inclusion criteria were: publications published from January 2005 to 2016, and were included in the Embase/MEDLINE databases. Studies were excluded if they did not report on the prevalence of BD, or if they were not published in English, or if they were not published in English. The following key terms were used: BD, Behcet's disease, BD prevalence, BD manifestations, BD symptoms, BD QoL.

Results: A total of 2146 citations were identified, of which 66 citations (55 manuscripts; 11 abstracts) describing >21,000 pts with BD were included. For categorical outcomes, the number (#) of studies, median, interquartile range (IQR) and/or min-max range of prevalence are reported; for continuous outcomes, the # of comparisons with significance (P<0.05) are reported.

Results: A total of 2656 citations were identified, of which 66 citations (55 manuscripts; 11 abstracts) describing >21,000 pts with BD were reviewed. The most common manifestation was OU, with 19 of 27 studies reporting 100% prevalence (IQR: 84%-100%). One study reported an average of 12.7 OU per patient per year; in another study, OU were the only manifestation currently or previously experienced by all pts. Frequently reported symptoms included fatigue/sleep-related issues (7; 70%), pain (4; 59%), and headache (5; 58%); skin lesions were also common (19; 58%). Several comorbidities, e.g. emotional issues (4; 24%-44%), fibromyalgia (4; 8%-24%), hearing loss (3; 10%-59%), etc. were significantly
RACIAL DIFFERENCES IN PRESCRIPTION PATTERNS OF DISEASE MODIFYING ANTI-RHEUMATIC DRUGS, NARCOTICS AND GLUCOCORTICOIDS AMONG MIDDLE-AGED PATIENTS WITH DISABILITY AND RHEUMATOID ARTHRITIS

Iris Navarro-Millan1,2, Mangala Rajan3, Gayanne Liu4, Lisa Kern1, Laura Pinheiro1, Monika Safford1, Jeffrey Curtis2, Well Connell Medicine, New York, United States of America, 2Hospital for Special Surgery, New York, United States of America; 3University of Alabama at Birmingham, Birmingham, United States of America.

Background: Many patients with rheumatoid arthritis (RA) become disabled. While racial/ethnic differences in RA treatment have been described in RA patients without disability, less is known about racial/ethnic differences in RA treatment among middle-aged individuals with RA receiving disability benefits.

Objectives: To determine if racial/ethnic differences exist in the prescription patterns of conventional synthetic (CS) and biologic (B) disease modifying anti-rheumatic drug medications (DMARD), glucocorticoids, and opioids.

Methods: We conducted cross-sectional analyses in the calendar year 2014 using Medicare and Medicaid claims data of individuals receiving Social Security Disability Insurance (SSDI). To be included, patients had to be continuously enrolled over one year, aged <65 years, eligible for both Medicare and Medicaid, and have RA, defined as: 1) two RA diagnoses (ICD9-714.xx) by a rheumatologist between 7 to 365 days apart; or 2) one RA diagnosis by a rheumatologist and at least 1 prescription for a DMARD. We examined the proportion of patients with CS-DMARD, B-DMARD, glucocorticoid (>7.5 mg prednisone daily for >30 days), or opioid (either a prescription for opioids with 3 refills or at least one 90 day supply) prescriptions in each year by race/ethnicity. Generalized estimating equation (GEE) models were used to report adjusted differences in prescription rates for Blacks, Hispanics, and Other using Whites as the reference group, adjusting for age, gender, and medical comorbidities.

Results: The were 9,265 patients in 2014 out of which 60% were White, 21% were Black, 15% were Hispanic, and 5% were Other race. The proportion of female patients by race/ethnicity was >75% for each group. Hispanics had a 6.6% point higher rate of B-DMARD prescriptions and a 10.7% point lower rate of opioid prescriptions compared to Whites. Blacks had a 3.4% point higher rate of glucocorticoid prescriptions, and a 3.3% point lower rate of opioids prescriptions compared to Whites.

Conclusion: We observed racial differences in arthritis-related treatment patterns, among disabled RA patients, with Blacks receiving less biologic treatment and Whites receiving more opioids. Hispanics received the highest prescription rates of biologics and the Other race received lowest prescription rates of opioids among the three racial/ethnic groups. Further studies are needed to examine the reasons for such differences.

Table 1: Adjusted differences (95% CI) in rates of prescription for CS-DMARD, B-DMARD, glucocorticoids or opioids among Blacks, Hispanics, and Other compared to Whites *

<table>
<thead>
<tr>
<th>Drug Type</th>
<th>Black vs. White</th>
<th>Hispanic vs. White</th>
<th>Other vs. White</th>
<th>Adjusted Reference Percentage (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CS-DMARD</td>
<td>4.3 (1.8, 6.8)</td>
<td>2.4 (0.5, 4.5)</td>
<td>2.2 (0.6, 3.8)</td>
<td>61.9% (60.5 – 63.4)</td>
</tr>
<tr>
<td>Any B-DMARD</td>
<td>4.6 (2.7, 6.6)</td>
<td>2.8 (0.9, 4.7)</td>
<td>2.0 (0.9, 3.1)</td>
<td>53.7% (52.1 – 55.2)</td>
</tr>
<tr>
<td>Any SQ B-DMARD</td>
<td>-5.2 (-7.7, -2.7)</td>
<td>1.5 (-1.3, 4.3)</td>
<td>4.4 (0.3, 8.4)</td>
<td>35.6% (34.5 – 37.5)</td>
</tr>
<tr>
<td>Any IV B-DMARD</td>
<td>0.3 (-1.8, 2.3)</td>
<td>6.8 (4.5, 9.2)</td>
<td>3 (-0.9, 6.9)</td>
<td>17.3% (16.1 – 24.1)</td>
</tr>
<tr>
<td>Glucocorticoids</td>
<td>3.4 (1.7, 5.2)</td>
<td>-0.2 (-2.2, 0.4)</td>
<td>-2.3 (-0.9, 6.9)</td>
<td>13.5% (12.5 – 14.6)</td>
</tr>
<tr>
<td>Opioids</td>
<td>-3.3 (-4.8, -1.8)</td>
<td>-10.7 (-13.5, -8.0)</td>
<td>-10.4 (-12.1, -7.8)</td>
<td>64.1% (62.7 – 65.6)</td>
</tr>
</tbody>
</table>

*Adjusted for age, sex and Charlson comorbidity index. CS-DMARD = conventional synthetic disease modifying anti-rheumatic drug; B-DMARD = biologic disease modifying anti-rheumatic drug; SQ = subcutaneous

SAT0576  ETANERCEPT BIOSIMILAR SWITCH: CAN IT BE SUCCESSFUL WITHOUT CLINIC REVIEW?

Muhammad Khurram Nisar, Luton and Dunstable University Hospital, Rheumatology, Luton, United Kingdom

Background: Since the introduction of anti-TNF biosimilars in routine clinical practice, there has been a drive to implement the switch program for all biosimilars at the point of availability. Etanercept biosimilar (SB4) was granted marketing authorisation by the EMA in January 2016. Our Trust was one of the leading centres to switch all patients within one year of the drug’s availability. The aim of the non-medical switch was to obtain significant savings for the NHS whilst achieving similar clinical outcomes.

Objectives: We report patient experience after a year of completing the switch program.

Methods: A list of all patients prescribed etanercept was extracted through our database. The original strategy included a ‘switch’ letter sent to all patients including SB4 information sheet. Patients were given the opportunity to contact nurse helpline for information or if disease control worsened/adverse effects developed. We reviewed all relevant records and collected data on any adverse events and disease outcome on either side of the switch.

Results: 84 patients were prescribed reference etanercept. 41 (49%) had RA, 17 (20%) had PsA, 18 (21%) had AS and remaining eight had JIA. 84 patients were prescribed reference etanercept. 41 (49%) had RA, 17 (20%) had PsA, 18 (21%) had AS and remaining eight had JIA.

Conclusion: Overall patient experience following etanercept biosimilar switch has been positive. 90% continue with SB4 originator a year later with no adverse outcomes. All were happy to switch after receiving a
letter and having the opportunity to contact if necessary. This made the process quite smooth, easy to administer and avoided costs associated with face-to-face review. Substantial annual cost savings of nearly £100,000 were achieved once the switch process completed. Only six patients (7%) encountered adverse effects, two of whom had uncontrolled disease despite switching back to the originator. We support the routine switching from originator to biosimilar etanercept in view of good patient experience and disease outcomes. This can be achieved with minimal contact in a cost-efficient manner.

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References

Disclosure of Interests: None declared

others are dedicated to primary immunodeficiencies and autoinflammatory diseases (respectively 15 registries, 28%, and 12 registries, 23%). Fifteen registries (28%) enrolled patients with a single specific disorder; in particular, three registries are devoted to systemic lupus erythematosus, two registries to Kawasaki disease or Behcet disease, and single registry to juvenile dermatomyositis, juvenile systemic sclerosis, juvenile idiopathic arthritis (JIA)-related uveitis, systemic JIA, Blau syndrome, sarcoidosis, Guillain-Barre syndrome, and myasthenia gravis. More than 55000 patients with RID are enrolled. The majority of registries (36; 68%) enrol only patients from national territories. Among the international, six collect data on autoimmune disorders (Pharmachild, BrainWorks, EuroMyoBis, EULAR web library, UKIVAS registry and JIR cohort), five on primary immunodeficiencies (ESID, EBMT, SCETIDE, PCID and HLH registry), and three are devoted to autoinflammatory diseases (Eurofever, Infevers, and ImmuN.AI), despite also ESID registry and JIR cohort collect data on autoinflammatory diseases. Data usually collected in these registries are demography, diagnosis, clinical manifestations, laboratory tests and treatment, while genetic and imaging data are less frequently reported (respectively in 38% and 9% of registries). A treatment safety profile is reported in 29 registries (55%). Collectively, fifteen biobanks are counted.

Conclusion: The survey highlighted the pivotal role of national and international registries in Europe to collect and organize clinical data on immune diseases, allowing the rapidly growing knowledge on these rare disorders, creating research networks and providing significant numbers of data to support new discoveries in the field. RITA network could improve the coordination of these numerous entities, supporting initiatives of collaboration. As a first attempt, the present survey revealed that the collection of key parameters about patient safety, as well as outcome data and quality of life measures should be improved among the registries of RITA network.

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SAT0579

AN ELECTRONIC MDHAQ (MULTIDIMENSIONAL HEALTH ASSESSMENT QUESTIONNAIRE) GIVES SIMILAR RESULTS TO A PAPER VERSION

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Background: A self-report multi-dimensional health assessment questionnaire (MDHAQ) is used in many routine care rheumatology settings as a pragmatic tool to recognize efficacy and adverse events. The MDHAQ is available in all rheumatic diseases in which it has been studied. An electronic version of the MDHAQ (eMDHAQ) could offer several advantages, including completion at home rather than in the waiting area and completion from any site between visits to report possible change in status and/or adverse events of a medication. Furthermore, the 4-page-“new patient” eMDHAQ can allow a patient to store a full medical history at a password-protected, secure website. Reports of the patient history can be available for an electronic medical record (EMR) without dictation or typing by the doctor, although interaction with the EMR vendor is required, which often has proven difficult. Implementation of eMDHAQ software requires documentation that eMDHAQ responses are similar to responses on a paper MDHAQ.

Objectives: To compare scores on an eMDHAQ vs paper version of MDHAQ.

Methods: All patients with all diagnoses complete a paper MDHAQ at all visits in the waiting area and part of routine clinical care in one setting. Consecutive patients completed MDHAQ in paper and in an iPad at the same visit. The MDHAQ includes 0-10 scores for physical function, pain and patient global visual analog scales (VAS), compiled into 0–30 Rapid3, as well as a 0–48 self-report painful joint count, and 0–20 symptom checklist. For this study, at the conclusion of the visit, the rheumatologist asked a patient if she/he would volunteer to complete an eMDHAQ on an iPad indicating no problem if a patient declined for any reason. Patients who agreed to participate completed the an eMDHAQ, with identical content to the paper MDHAQ. The patient also completed a 3-query questionnaire, with 2 VAS concerning the value of the MDHAQ to the patient or the doctor (0= no value, 10= great value), and a query of her/his preference for the eMDHAQ vs paper MDHAQ or no preference. Test-retest reliability was examined by intraclass correlation coefficients (ICC).

Results: 65 patients completed the study. The ICC for physical function, patient global VAS, and RAPID3 was >0.9 indicating excellent reliability between the electronic and paper versions, while the ICC for pain, self-report painful joint count, and symptom checklist was >0.75, indicating good reliability. Differences between the 2 versions were within variation on the paper questionnaire. The mean rating for the value of MDHAQ was 8.8±10 to the patient, 8.8±10 to the doctor. Among the 65 patients, 43 (66%) indicated a preference for the eMDHAQ, 7 (11%) for the paper MDHAQ, and 15 (23%) indicated no preference.

Conclusion: An eMDHAQ appears to have similar performance compared to a paper MDHAQ version. A high percentage of patients prefer the digital version to paper, although about 20% of patients are likely to require a paper MDHAQ. An eMDHAQ offers remote completion at home, before and/or between visits, to report issues concerning efficacy and adverse events. Expanded eMDHAQ software can allow a doctor to develop flow-sheets and a database for all patients, a full patient medical history, and interfacing with any electronic medical record (EMR), although that requires interaction with the EMR vendor, which is often difficult. The eMDHAQ appears useful independent of the EMR.


SAT0580

HEALTHCARE BURDEN AND COST OF ILLNESS OF GIANT CELL ARTERITIS IN THE ITALIAN REGION OF FRIULI VENEZIA GIULIA: A 17-YEAR INTEGRATIVE ANALYSIS OF DIGITAL ADMINISTRATIVE DATABASES

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Background: Giant cell arteritis (GCA) is the most common systemic vasculitis in persons aged 50 and above (1). Data on incidence and prevalence of GCA are welcomed. Further information is also needed on the healthcare burden and resource consumption. The use of multiple digital administrative databases with the integration of clinical data from a formalized network of specialists is needed.

Objectives: To estimate incidence, prevalence and costs of GCA by an integrative analysis of multiple administrative databases of the healthcare system of the Italian Region of Friuli Venezia Giulia (about 1.2 millions of inhabitants), cooperating with the existing local Rheumatology Network.

Methods: A 17-year retrospective study was conducted through the following administrative health regional digital databases of the Friuli Venezia Giulia Regional Health Services, the Friuli Venezia Giulia Regional Health Services, and the Friuli Venezia Giulia Regional Health Services.
Giulia Region: the Database of Regional Potential health Care Beneficia-
ries, the Hospital Discharge Database, the Ambulatory Care Database, the
Pharmaceutical Prescription Database, the Emergency Department
Database, the Mortality Database, the Anatomical Pathology Database, the
Database of Exemptions from Medical Charges, and the Regional
Rare Disease Registry. All the databases were integrated at the individual
patient level using a univocal stochastic key.

Results: From 2001 to 2017, 208 patients with GCA were registered.
The crude identification rate of patients identified with GCA until 2017 in
the population >45 years of age was 3.8/100,000 person-years (95%CI:
2.5-5.5). The maximum incidence rate was observed in the age group
70-74 years. The prevalence of GCA in the population >45 years of age
as of December 31st, 2017 was 27.2/100,000 (95%CI 23.5-31.4). The
mean medical observation was 4.5±3.6 years per patient, totaling
940.8 years of observation.

192 patients had at least one ambulatory specialist visit, resulting in a
total of 3162 specialist visits (338 per 100 patient-years). The most fre-
quent medical specialties involved were Rheumatology (N=610, 19.2%),
Internal Medicine (N=564, 17.7%), Ophthalmology (N=292, 9.2%), and
Orthopedics (N=191, 6%). 108 (52%) patients had at least one hospitalization, resulting in 287 hos-
apitalizations (30 per 100 patient-years). Circulatory Cardiovascular diseases
were the most common discharge diagnoses, followed by musculoskeletal
conditions.

199 subjects were prescribed medications for a total of 9588 prescriptions
(91 per 100 patient-years). Notably, an immunosuppressive drug, usu-
ally methotrexate, was prescribed in more than half of the patients. Car-
diovascular medications were prescribed to 154 (74%) patients; bisphosphonates or other anti-osteoartropenic drugs to 123 patients (59%).
The average annual direct cost of GCA was 2374 Euros per patient-year
(81 for outpatient visits, 1661 for hospitalizations, 312 for prescribed med-
ications and 340 for medications directly dispensed by the hospital phar-
cacies). The overall estimated direct healthcare cost for 940.8 patient-
years was 2,234,070 Euros.

Conclusions: Novel epidemiologic data in GCA are reported after a very
long-term observation, and by integrating data from multiple databases
with clinical data from a Regional network of specialists (Rheumatology
being the major contributor to disease clinical follow-up).

Cost of illness is high in GCA. Both the diseases itself and cardiovascu-
lar manifestations, and, possibly, the complications of glucocorticoids, may
contribute to the healthcare burden of GCA. Despite a high use of
immunosuppressors in our region, new drugs (2) and novel treatment strategies are required.

References

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Luca Quartuccio: None declared, Milena Bond: Speakers
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SAT0582 POOR HEALTH-RELATED QUALITY OF LIFE (HRQOL) AND FATIGUE ARE ASSOCIATED WITH A HIGHER WORK PRODUCTIVITY IMPAIRMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) PATIENTS

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Background: Because most patients with SLE are in their productive-age
years, the ability to maintain a gainful employment is fundamental for both
the patient and society at large. It is thus quite important to
determine the work and non-work factors that are associated with work
productivity impairment in these patients.

Objectives: To determine the factors associated with absenteeism (per-
centage of the time missed from scheduled work-time over the preceding
7 days, due to SLE), presenteeism (percentage of time from scheduled
work-time where productivity was impaired while patient was at work,
over the preceding 7 days, due to SLE) and overall work impairment
(combination of absenteeism and presenteeism) in patients with SLE.

Methods: The study included a cohort of 133 consecutive (1997 American College of Rheuma-
tology (ACR) criteria) working patients with SLE were assessed between
October 2017 and December 2018, using a standardized data collection
form. Sociodemographic, disease and work-related variables were col-
lected. Disease activity was assessed with the Systemic Lupus Erythe-
matosus Disease Activity Index (SLEDAI); disease damage with the
Systemic Lupus International Collaborating Clinics/ACR Damage Index
(SDII); health-related quality of life was assessed with the LupusQol and
fatigue with the FACIT-Fatigue (Functional Assessment of Chronic Illness
Therapy-Fatigue). Work Productivity and Activity Impairment (WPAI) was
assessed with the respective questionnaire; absenteeism and presentee-
ism due to overall health and symptoms during the past 7 days were
scored. Linear regression models were performed to determine the factors
associated with absenteeism, presenteeism, and overall work impairment.
Potential factors included were age at diagnosis, gender, socioeconomic
status, educational level, SLEDAI, SDII, FACIT- Fatigue and the compo-
nents of the LupusQol.

Results: The mean age at diagnosis was 32.2 years (11.8); 121 (91.7%)
were female. Nearly all patients were Mestizo. Mean years of education
was 14.1 (2.6). The mean disease duration was 11.9 (7.5) years. Mean
SLEDAI was 2.9 (4.0), and mean SDII was 1 (1.4). The mean percent of
time for absenteeism was 5.0 (12.9), it was 28.5 (26.4) for presenteeism,
and it was 31.3 (27.2) for overall work impairment. In the multiple regres-
sion analysis, factors associated with absenteeism were disease duration
(B=-0.34; p<0.001), daytime sleepiness (B=0.14; p=0.007) and pain (B=0.14;
p<0.001); night-time sleepiness (B=0.14; p=0.006), presenteeism were physical health (B=-0.43;
p=0.002) and FACIT (B=0.87; p<0.001) and with overall work impairment were pain (B=0.40;
p=0.001) and FACIT (B=0.74; p<0.001) and presenteeism were physical health associated with a higher percentage of absenteeism, presenteeism and overall work
impairment in SLE patients. Addressing the factors related to HRQol and Fatigue may have significant impact on work performance among SLE patients.

Disclosure of Interests: None declared.


SA2575 THE LATIN AMERICAN RHEUMATOLOGY SURVEY: LARS STUDY

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Background: Currently, Latin America does not have detailed information
of rheumatologists in the region based on: education, working conditions,
productivity, distribution of time between work activities and job
satisfaction.

Objectives: The purpose of this survey was to provide more information
on the rheumatology community in Latin America

Methods: A digital survey was created using the Google Forms platform,
it was approved and endorsed by the scientific committee of PANLAR
and later sent to the different rheumatology associations of the region.
The data was analyzed in the statistical programSPSS v.23.

Results: 456 surveys of rheumatologists from 23 countries were received.
The majority were females (64%). The mean age was 47.18 ± 11.79 [20-78] years, with a majority of mixed race 58%, 63% are married, 23% are single, 8% are divorced, 5% in free union and 2% are widowed. The mean number of children was 2 [0-7]. Birthplaces included Argentina (27%), Brazil (16%). The selection of the professional practice after obtain-
ing the title of specialists was: public hospital (35%), private (25%), pri-
ivate/teaching in a university hospital (12%), public/teaching in a university
hospital (14%), and industry (1%). The main place of work was in public/
government hospitals by 30% followed by private practice 31%, private
hospital 23%, university hospital 15% and nonprofit organization of Rheu-
matics. The average of weekly working hours was 39.12 ± 27.53, 89% of the sample
practices adult rheumatology, 17% pediatric rheumatology, 2% immunology

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and 3% another specialty. 30% had an early arthritis care center at their workplace, 71% had an infusion unit, 17% had ultrasound, 23% had a densitometer, 17% had a resonator and 9% had X-rays, however, most work in collaboration. 30% have training in ultrasound and 9% are in training period. 75% have training in reading densitometry and 2% in training period. 54% have training in resonance reading and 11% in training period. The average satisfaction with practice as a rheumatologist was 5/7, career options/professional growth 4/7, geographic location 5/7, income 4/7, security 4/7, colleagues and co-workers 5/7. 33% had an annual compensation of <19,000 US dollars. Only 58% have malpractice insurance and 87% have medical insurance. 40% present at least one clinical comorbidity.

Conclusion: The majority of rheumatologists in the region who responded were female and felt satisfied with their clinical practice. This survey shows a low level of income for the region, however, more data should be obtained. This is the first study of its kind in Latin America, being an initiative for similar projects.

Disclosure of Interests: None declared

DEVeLOPMENT AND TESTING OF A SMARTPHONE APPLICATION TO SELF-MONITOR DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS

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Background: Several mobile applications (apps) exist to monitor symptoms of rheumatoid arthritis (RA), but high-quality apps are lacking.1 We developed an app with patients, following the Medical Research Council (MRC) sub-model.2 It focused on self-monitoring and self-initiated care.

Objectives: To evaluate the users' satisfaction, usability and engagement of the app, as a first and preparatory step toward the ultimate goal of telemonitoring and self-initiated care.

Methods: In a first, one month pilot study 42 RA patients used the app. User's satisfaction was measured using an 11-point Likert scale. Usability was measured using the three concepts of the Technology Acceptance Model (TAM).3 According to TAM, perceived usefulness (PU), perceived ease of use (PEOU), (behavioral) intention to use (ITU) predict how and when a product will be used. The PU and PEOU were measured using the system usability scale (0-100). A score of 68, or higher, indicates sufficient system usability.4 The ITU was measured on a 11-point Likert scale. Engagement was measured by the percentage of patients completing all weekly questionnaires. General feedback was collected and implemented.

In a second, one month pilot study, the improved app was evaluated in 24 RA patients using 5 themes derived from the Mobile App Rating Score5: 'engagement', 'functionality', 'aesthetics', 'information' and 'subjective quality.' Participants rated the questions on a 5 - point Likert scale. All responses were categorized into three categories: negative (1-2), neutral (3) and positive (4-5). Afterwards, nine participants (three users, three dropout users, and three non-users) agreed to participate in a semi-structured interview to get feedback on the App.

Results: In the first study, the ReumaMeter scored an overall median score of 8.0 (interquartile range (IQR) 7.0-9.0), a mean system usability score of 76 (SD 14.8) and participants intended to keep using the ReumaMeter in the future (median 7.0, IQR 5.0-9.0). Engagement decreased to 61% in week 4. During the second study, the number of positive responses for each category was at least twice as high as the number of negative responses (Figure 1). Feedback that emerged during the interviews matched these responses. In addition, several participants stated that app usage declined due to low disease activity.

Conclusion: The participants' overall feedback was positive in terms of users' satisfaction and usability. Engagement dropped, which may be due to lack of internal triggers to measure disease activity when patients are in remission. To assess the overall impact of the app on RA patient care, a randomized controlled trial is planned.

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Figure 1. Qualitative results of app-evaluation - 79% of participants responding

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PATIENTS WITH LUPUS

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Background: Hip osteonecrosis and hip osteoarthritis are common causes of severe hip disease in lupus (1), both treated successfully with a total hip arthroplasty (THA). A recent systematic review of arthroplasty outcomes reported that the risk of overall complications post-THA was higher than in patients with lupus compared to those without lupus (2). However, no analyses were provided for specific outcomes such as infection, revision or associated health care utilization.

Objectives: To assess the risk of specific post-THA outcomes, i.e., infection, transfusion, revision and mortality and associated health care utilization, associated with lupus.

Methods: We used the 1998-2014 U.S. National Inpatient Sample data. Multivariable-adjusted separate Cox proportional hazard regression models assessed the association of lupus with post-operative complications (infection, transfusion, THA revision and mortality) and health care utilization outcomes (total hospital charges, discharge to inpatient facility, length of hospital stay) post-THA, adjusting for demographics, underlying diagnosis, comorbidity, insurance payer, and hospital characteristics, using hazard ratios (HR) and 95% confidence intervals (CI).

Results: Among 4,116,485 primary THA hospitalizations, 22,557 (0.5%) were in lupus patients. Patients with lupus were younger, more likely to be female, African-American or Hispanic and, have higher comorbidity, Medicaid insurance payer, lower income, or living in the South. In multi-variable-adjusted analyses, lupus was associated with a significantly higher risk of infection, transfusion, hospital charges above the median

POORER OUTCOMES AND HIGHER HEALTHCARE UTILIZATION AFTER TOTAL HIP ARTHROPLASTY IN PATIENTS WITH LUPUS

SAT0584

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Knee osteoarthritis (OA) is a painful, disabling condition with increasing prevalence. The concept of spondyloarthritis (SpA) comprises several chronic inflammatory joint diseases. SpA patients can be distinguished as having SpA with predominantly peripheral SpA (pSpA) or with predominantly axial SpA (axSpA) according to their clinical presentation. AxSpA primarily affects the axial skeleton and the sacroiliac joints. Within axSpA patients, a subdivision based on the radiographic changes of the sacroiliac joints can be made: radiographic axSpA, which corresponds to ankylosing spondylitis (AS), and non-radiographic axSpA (nr-axSpA). SpA occurs typically in young and professionally active patients. Since 2000, important improvements have been made in the management of SpA, both on a pharmacological (introduction of biological disease-modifying antirheumatic drugs (bDMARD)) and a non-pharmacological (holistic approach) level. As a result of early diagnosis followed by adequate treatment, the majority of patients achieve a state of clinical remission allowing them to function without significant problems. However, many of these persons still experience problems such as exclusion clauses, additional premiums and even contract refusals when contracting private insurances because mostly risk contracts refusals when contracting private insurances because mostly risk contract refusals when contracting private insurances because mostly risk

**SAT0586 THE INFLUENCE OF THE NEW PHARMACOLOGICAL AND NON-PHARMACOLOGICAL TREATMENTS IN AXIAL SPONDYLOARTHRITIS ON WORK PARTICIPATION: A SYSTEMATIC REVIEW**

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**Background:** The concept of spondyloarthritis (SpA) comprises several chronic inflammatory joint diseases. SpA patients can be distinguished as having SpA with predominantly peripheral SpA (pSpA) or with predominantly axial SpA (axSpA) according to their clinical presentation. AxSpA primarily affects the axial skeleton and the sacroiliac joints. Within axSpA patients, a subdivision based on the radiographic changes of the sacroiliac joints can be made: radiographic axSpA, which corresponds to ankylosing spondylitis (AS), and non-radiographic axSpA (nr-axSpA). SpA occurs typically in young and professionally active patients. Since 2000, important improvements have been made in the management of SpA, both on a pharmacological (introduction of biological disease-modifying antirheumatic drugs (bDMARD)) and a non-pharmacological (holistic approach) level. As a result of early diagnosis followed by adequate treatment, the majority of patients achieve a state of clinical remission allowing them to function without significant problems. However, many of these persons still experience problems such as exclusion clauses, additional premiums and even contract refusals when contracting private insurances because mostly risk assessments are solely based on historical data.

**Objectives:** The aim of this systematic literature review was to investigate whether the work participation in patients with axSpA has improved since the introduction of the bDMARD and the non-pharmacological treatment modalities. This would provide arguments for a more accurate and updated risk assessment of the expected personal and economic incapacity of axSpA patients by private insurance companies.

**Methods:** A systematic literature review from January 1997 until November 2017 was performed using Pubmed, Embase and Web of Science. Different search terms were used in each database: absenteeism, presenteeism, employment, sick leave, work disability and work participation. All studies assessing one of the search terms were analysed.

**Results:** In total, 33 studies out of 603 retrieved citations were included. Overall, the results were highly heterogeneous because of the different study designs and different use of definitions regarding work outcomes. Patients with AS were significantly confronted with restrictions on work participation compared to the general population before the availability of bDMARD. In addition, our literature review showed that, since the introduction of the bDMARD and other non-pharmacological treatments, there is no evident improvement in work disability in AS patients. In contrast, a significant improvement could be observed on absenteeism, presenteeism and work productivity. Only 6 studies included patients with nr-axSpA. In most of these studies a positive tendency towards work productivity was detected. In addition, contextual factors such as the type of job, support from employers and colleagues, adjustments in workplace, and so forth were also considered. Further research into treatment patterns and characteristics of knee OA patients treated by rheumatologists is warranted.
Epidemiology, risk factors for disease or disease progression

SAT0587 THE ART OF IMPUTING MISSING DATA OF DISEASE AND FUNCTION ACTIVITY IN RHEUMATOID ARTHRITIS REGISTRIES

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Background: Large observational studies become more common in rheumatoid arthritis (RA). Disease registers [1] allow to analyse the effectiveness and safety of RA treatments in real-world populations, but observational studies suffer from missing data. To minimise bias, it has been shown that imputing missing data is superior to the use of complete case analysis [2]. Although some imputation methods have been studied in clinical trials of rheumatic diseases [3] and in small registers [4], the various imputation techniques have never been systematically compared in large registers.

Objectives: To compare the effects of available imputation methods on the estimated values and on RA remission rate for missing disease activity measures in large registers.

Methods: We used 1000 patients with complete data for disease activity (Disease Activity Score (DAS28) and Clinical Disease Activity Index (CDAI)) at baseline (treatment initiation), 6, 12, and 24 months after initiation of abatacept or a tumor-necrosis factor inhibitor (TNFi) from an existing register collaboration (PANABA). Simulation procedure: Values were deleted randomly and imputed with three types of imputation methods: (1) methods imputing forward in time, such as Last Observation Carried Forward (LOCF) or Linear Forward Extrapolation (LFE); (2) methods considering data both forward and backward in time, such as Nearest Available Observation (NAO), Linear Extrapolation (LE) or Polynomial Extrapolation (PE); and (3) methods using computer-intensive multi-individual imputations, such as Linear Mixed Effects cubic regression (LME3) and Multiple Imputation by Chained Equation (MICE).

We conducted a simulation study by performing this procedure 1000 time and computing the mean difference between the true and the imputed values, and between the true remission rate (CDAI and DAS28) and the imputed ones.

Results: Results are summarised in Fig. 1. At baseline, all methods underestimated the true values by up to 20%. Despite this, LME3 and MICE were able to provide estimates of baseline remission rates with less than 15% of error. For follow-up data, missingness at 6, 12, or 24 months, NAO, LE and PE led to relative bias of the mean values ≤15% and almost unbiased remission rate. LOCF and LFE respectively over- and underestimated the mean imputed values up to 20%, leading respectively to a non-negligible under- and over-estimation of the remission rate. Although LME3 and MICE had low bias in estimating the mean values, they narrowed the distribution of the imputed values and thus strongly underestimated remission rate.

Conclusion: When imputing disease activity in rheumatoid arthritis register data, researchers should prefer Linear Mixed Effects cubic regression (LME3) for baseline and nearest available observation (NAO) for follow-up data.

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SAT0588 COMPARATIVE EFFECTIVENESS RESEARCH IN OBSERVATIONAL SETTINGS: EVALUATING TWO NEW METHODS TO ANALYSE RESPONSE RATES

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Background: Researchers typically report the proportion of patients reaching a defined clinical threshold (e.g. EULAR response, low disease activity (LDA) rates) after a set time. Comparing response rates (%rr) in observational settings is hampered by two major threats. 1. Confounding: Patient, disease, and treatment characteristics often differ for each drug. 2. Attrition bias: Assessing %rr after a set time excludes patients who discontinued their treatment, which may overestimate drug effectiveness. Currently, no proposed method accounts for both confounding and attrition.

Conclusion: Most of the patients included in the selected studies had longstanding AS with significant structural damage. The great heterogeneity between the studies in patient populations, study design and evaluation methods impeded the formation of a uniform conclusion. However, since the introduction of the new treatment modalities, a positive tendency in work productivity in AS and nr-axSpA patients could be observed. More observational, cross-sectional and prospective studies are needed - especially in nr-axSpA patients - to evaluate the effect of both pharmacological and non-pharmaceutical treatment on the work outcome in SpA patients.

Disclosure of Interests: None declared
Objectives: To propose two new methods (3 and 4) to adequately compare %rr in patients with different baseline characteristics, while accounting for attrition and compare them to established methods (1 and 2).

Methods: 1. Complete case (CC) for attrition and compare them to established methods (1 and 2).

1. LUNDEX: %rr is computed as the percentage of responders on total patients still on treatment at the given time point.

2. PSM LUNDEX: Propensity Score (PS) Matching LUNDEX

Step A: Select patients in both exposure groups using propensity score matching.

Step B: Use the LUNDEX to compute the %rr.

3. CARRAC: Confounder-Adjusted Response Rate with Attrition Correction by reason for drug discontinuation.

Step A: Compute estimates of drug survival for the main reasons of drug discontinuation (e.g., ineffectiveness, adverse events, remission, other reasons).

Step B: Estimate %rr using random effect IPD meta-analysis with estimates for each reason of drug discontinuation.

Step C: Combine %rr estimates using weights of step A.

The methods will be illustrated using CDAI LDA (%10) rates in data from a collaboration of registries.

Results: We used 3,448 patients treated by a biologic, either intravenously (IV: n=2,414) or subcutaneously (SC: n=1,034). Before matching, the population differed in terms of body mass index, function (Health Assessment Questionnaire, HAQ), concomitant treatments and erythrocyte sedimentation rate (ESR). Adjustment was done using these potential confounders. For PSM LUNDEX, PS matching was done on a 1:1 basis, yielding 561 patients in each group with similar characteristics. Estimated %rr differed by more than 20%, depending on the method used (Figure). Compared to CC %rr, both PSM LUNDEX and LUNDEX methods yielded much lower %rr, while the CARRAC method estimated %rr was in between these estimates.

Conclusion: Both LUNDEX methods certain underestimate the true response rates by considering all patients stopping treatment as non-responders, while complete case method certainly overestimates the %rr by considering patients stopping as having a similar %rr to patients continuing treatment. As expected, the CARRAC method, which accounts for attrition by reason for drug discontinuation, obtained %rr estimates in between complete-case and LUNDEX corrections. Simulation studies are needed to assess the most accurate estimation method.
PPV>=0.90 for all medication except golimumab, which had a low prevalence in our dataset.

**Conclusion:** We developed and validated an algorithm enabling a highly accurate automated extraction of RA medication from format-free fields of Electronic Medical Records.

**REFERENCES**


Disclosure of Interests: Tjardo Maarseveen: None declared, Thomas Huizinga Consultant for: Merck, UCB, Bristol Myers Squibb, Biostat AG, Pfizer, GSK, Novartis, Roche, Sanofi-Aventis, Abbott, Crescendo Bioscience Inc., Nycomed, Boeringer, Takeda, Zydus, Epirus, Eli Lilly, Erik van den Akker: None declared, Rachel Knevel: None declared

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**SAT0590** AUTOMATED DIAGNOSIS EXTRACTION FROM ELECTRONIC MEDICAL RECORDS WITH MACHINE LEARNING CLASSIFIERS

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**Background:** While Electronic Medical Records (EMR) constitute a rich resource for research into various diseases, their unstructured format often poses practical challenges. For instance, retrieval of the records belonging to all patients with a particular outcome is often accomplished with naive methods such as exact word matching. A more advanced alternative is to employ methods of Machine Learning (ML) for text classification. Rather than requiring a set of rules, an ML-model extracts these rules by itself given sufficient example records with known annotations.

**Objectives:** To build a reliable classifier with machine learning techniques that can identify Rheumatoid Arthritis (RA) cases in provided EMR entries.

**Methods:** Data was acquired from the HI-X-EMR database consisting of 2,771 patients that visited the rheumatology outpatient clinic of the Leiden University Medical Centre between 2007 and 2018. This database featured a total of 38,216 entries. The first visit entry (if available) was selected per patient for annotation, resulting in a total of 1,361 entries.

The annotated sample was then randomly split into an equally sized training and test set. Both sets were preprocessed and then classified with the following methods: Exact word-matching, Naive Bayes (NB), Decision Tree, Gradient Boosting (GB), Neural Networks and Support Vector Machines (SVM), see table 1 for more information. Classification of the naive word-matching model was based on the presence of the Dutch RA-defining terms ‘Reumatoïde Artritis’ and ‘RA’. Default Scikit-learn implementations [1] were used to create the ML-models. Finally, the performance of the models was evaluated with a receiver operating characteristic (ROC) curve analysis via the pROC R-package [2]. The Delong test was used to assess the 95% confidence intervals (CI) and to determine the difference in performance between the word-matching method and the ML-models.

**Results:** The exact word-matching approach resulted in an area under the curve (AUC) of 0.76 (CI: 0.7265-0.7783), see figure. Likewise, the ML-models resulted in relatively high AUC-scores (CI) as well: NB =0.83 (0.80-0.86), SVM=0.91 (0.89-0.93), Neural Networks=0.92 (0.90-0.94) and the GB-method with a 0.94 (0.92-0.96). The Decision Tree showed the worst performance with an AUC-ROC of only 0.51 (0.49-0.56). In comparison to the exact word-matching ROC-curve, all the ML-models showed a significant difference: Decision Tree (p<2.2e-16), NB (p= 0.004), Neural Networks (p<2.2e-16), GB (p<2.2e-16) and the SVM (p<4.0e-16).

**Conclusion:** The Gradient Boosting, Neural Networks, SVM and Naive Bayes models all showcased a significantly better performance than a naive exact word matching, which establishes these ML-methods as an efficient approach for data extraction from EMR.

**REFERENCES**


Disclosure of Interests: Tjardo Maarseveen: None declared, Thomas Huizinga Consultant for: Merck, UCB, Bristol Myers Squibb, Biostat AG,
A CLINICAL TOOL FOR AUTOMATED PREDICTION OF HIP AND MAJOR OSTEOPOROTIC FRACTURES USING ELECTRONIC MEDICAL RECORDS DATA: THE EPIC STUDY

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Background: With increasing availability of patient data in healthcare, there is an unprecedented opportunity for prediction tools that can be automatically implemented in electronic medical records systems.

Objectives: We aimed to develop and validate a fracture prediction tool that leverages patient data as routinely available in primary care computerized records.

Methods: We conducted a population-based cohort study. Data was extracted from all subjects registered in the SIDIAP database on 1/1/2012, with data for 1+ years, and aged 50 years or older on that date. SIDIAP contains primary care records linked to pharmacy dispensations for >6 million people, equivalent to >80% of the population of Catalonia. Participants were followed up until the earliest of death, transfer out/immigration, or end of 2017. Two models were developed to predict hip fracture (main outcome) and major osteoporotic (hip, clinical vertebral, wrist/forearm, and proximal humerus) fracture risk over 5 years. Potential predictors were pre-specified based on previous literature and combined in Cox models to derive prediction tools. Internal validation was performed using c-statistic for discrimination, and observed vs predicted plots for calibration. Multiple imputation with chained equations was used to minimize the impact of missing data on body mass index, smoking, and alcohol consumption. Bootstrapping methods were used to select key predictors to be combined in the final resulting models.

Results: A total of 1.76 million people (9.76 million person-years) were included, 50.7% women, of average age 65.4 years old. A 10.1% and 7.4% were lost to follow-up over 5 years due to mortality and migration respectively.

Fracture rates were 3.57/1000 person-years [95% CI 3.53-3.60] for hip and 11.61 [11.54-11.68] for major fracture. Key predictors of increased fracture risk included age, female gender, history of falls or previous fractures, specific medication/s use (insulin, GnRH inhibitors, anticonvulsants, sedatives, SSRI, antipsychotics), and a history of diabetes mellitus (type 1/type 2), cerebrovascular disease, ischemic heart disease, COPD and anorexia nervosa. Variables associated with lower fracture risk included use of statins, thiazidic diuretics, and overweight/obesity. Combined, these resulted in a c-statistic of 0.84.9% for hip and 72.9% for major fracture. Calibration was excellent for both outcomes.

Conclusion: We have developed and validated a clinical prediction tool for 5-year hip and major osteoporotic fracture risks. The algorithm has excellent performance and can be installed in electronic primary care record systems for automated risk calculations at the population level. More research is needed on the transportability and external validity of this prediction tool.

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and all of them are associated with a high burden of comorbidities. Incidence of these diseases and of their comorbidities are unknown in Belgium.

**Objectives:** To determine incidences of disease and comorbidities in patient populations of RA, PSA and SPA in a General Practitioners (GP) setting.

**Methods:** Data were obtained from Intego over a 13-year time interval from 1999 to 2012. Intego is a Flemish GP-based morbidity registration network hosted at the Academic Center for General Practice of KU Leuven, covering 2% of the Flemish general population. Patients classified under the International Classification of Primary Care codes L88 (rheumatoid/seropositive arthritis) and L99 (musculoskeletal disease other) were selected for this study. Experienced rheumatologists verified if the keywords mapped to these codes corresponded to a diagnosis of RA/SPA/PSA. The entry date of these diagnoses in Intego was considered "baseline". Yearly disease incidence and comorbidity incidence over 3 years are presented. The following comorbidities with high impact on outcomes like disability, costs, hospitalization and death were considered: lung disease, cardiovascular disease including myocardial infarction, stroke or other heart condition, hypertension, fracture of the spine/hip/leg, depression, diabetes mellitus, digestive disease including ulcers and stomach disorders and malignancies [1].

**Results:** Over a 13-year period, 817, 258 and 190 patients were included with a diagnosis of RA, SPA or PSA, respectively. The average incidence of RA was 0.47, of SPA 0.15 and of PSA 0.11 per 1000 person years. Fig1 gives the yearly incidence per disease. The RA cohort had a mean(SD) age of 57.7(17.2) with 68% being women. The SPA cohort had a mean(SD) age of 40.6(15.1) with 50% being women. The SPA cohort had a mean(SD) age of 47(13.2) with 48% being women.

The comorbidity with the highest prevalence (23%) and incidence (29.6/1000 person years) in RA was hypertension. In the SPA cohort, digestive disease was most common at baseline (14%) and during follow-up (21.0/1000 person years) in RA was hypertension. In the SPA cohort, digestive disease was most common at baseline (14%) and during follow-up (21.0/1000 person years) in RA was hypertension. In the SPA cohort, digestive disease was most common at baseline (14%) and during follow-up (21.0/1000 person years).

**Conclusion:** The incidence of RA appears to remain stable while incidence of PSA - and to a lower extent SPA - seem to increase over a 13-year interval. A control cohort will be formed to improve comparability of comorbidity presence, yet from these preliminary results we can determine that an important subgroup of patients with rheumatic diseases already presents with significant comorbidities at baseline, or during 3-year follow-up. This study highlights the growing issue of multimorbidity in patients with musculoskeletal diseases and the importance of a holistic approach to manage these patients.

**References**
with IAEs, for which immunotherapy was not suppressed. However, the medication was suppressed in the remaining 40% of the cases. Exceptionally, one patient underwent a severe IAE (pneumonitis) that resulted in death. In terms of the occurrence of IAEs, there was no difference between sexes (men 6.3%, women 6.4%). The rheumatic IAEs responded well to treatment with corticosteroids without further biological treatments or DMARDs.

**Conclusion:** Immunotherapy is changing the typology of side effects in cancer patients, including IAEs. The cases analysed showed a relatively small number of rheumatic events that were easily solved with corticosteroids (nor the immunotherapy treatment was suppressed or immunosuppressive treatment was necessary). The study highlights the benefits of involving multidisciplinary medical teams to manage oncologic patients treated with immunotherapy towards the early detection and treatment of IAEs.

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**Disclosure of Interests:** None declared

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**SAT0595**

**DIRECT COMPARISON OF CERTOLIZUMAB PEGOL, ABATACEPT AND BIOSIMILAR INFlixIMAB IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED IN ROUTINE CARE. OBSERVATIONAL DATA FROM THE DANISH DANBIO REGISTRY ANALYZED LIKE A RANDOMIZED CLINICAL TRIAL.**

**Kathrine Gøn1, Bente Glinthøj1, Mette Nørgaard2, Frank Mehnert2, Mikkel Stergaard1, Lene Dreyer1, Niels Steen Krog1, Jakob B. Bjørner3, Merete L. Hetland1,2, DANBIO and the Danish Departments of Rheumatology, Copenhagen, Denmark; 2Department of Clinical Epidemiology, Aarhus University Hospital, Aarhus, Denmark; 3Department of Public Health, University of Copenhagen, Copenhagen, Denmark**

**Background:** Nationwide Danish guidelines regarding RA patients (pts) initiating bDMARDs are issued approximately annually. For bio-naïve pts on concomitant methotrexate (MTX) the recommended drugs (year, recommended compliance) were: certolizumab pegol (CTZ) (2013-2014, 80%)/abatacept (ABA) (2014-2015, 80%)/biosimilar infliximab (CT-P13) (2015-2016, 50%). We hypothesized that the guidelines could be perceived as a surrogate randomization tool where calendar-time rather than patient-specific factors defined choice of bDMARD.

**Objectives:** To assess compliance to guidelines (justifying the assumption of surrogate randomization) and compare effectiveness of CTZ/ABA/CT-P13 in Danish RA patients treated according to guidelines.

**Methods:** Observational cohort study analyzed like a randomized clinical trial (RCT, intention-to-treat). RA patients were identified in DANBIO. Compliance in each calendar period was defined as number of pts adherent to guideline/numbers of all bio-naïve pts initiating bDMARD + MTX. Outcomes were DAS28-remission-rates (at 6 and 12-months) and one-year retention rates, compared across treatments (confounder-adjusted multivariable logistic and Cox regression analyses).

**Results:** Compliance to guidelines was 70%/85%/59%, and 776 patients were included (CTZ/ABA/CT-P13: 336/215/225). Baseline characteristics were similar across drugs. DAS28-remission-rates after 6 and 12 months were: 37%/34%/44% and 37%/33%/36%, respectively. Adjusted odd ratios for achieving DAS28 remission were at 6 months: 0.96 (95% CI: 0.6;1.5) for ABA and 1.38 (0.9;2.1) for CT-P13; 12 months: 0.74 (0.5;1.2) and 0.96 (0.6;1.5), CTZ reference drug (figure). The adjusted hazard ratios for withdrawal were 1.16 (95% CI: 0.84;1.60) for ABA and 0.83 for CT-P13 (0.59;1.17) (table).

**Table.** RA patients starting first bDMARD according to Danish national guidelines during the three calendar periods. Baseline characteristics and adjusted hazard ratios (HR) for withdrawal during the first year of treatment (Cox regression analyses).

<table>
<thead>
<tr>
<th></th>
<th>N=336</th>
<th>N=215</th>
<th>N=225</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calendar time periods</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jan 2013 - July 2014</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>July 2014</td>
<td>Jul 2015</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Expected compliance to guideline</td>
<td>80%</td>
<td>80%</td>
<td>50%</td>
</tr>
<tr>
<td>Actual compliance to guideline</td>
<td>70%</td>
<td>65%</td>
<td>59%</td>
</tr>
<tr>
<td>Age, years</td>
<td>57 (48-65)</td>
<td>57 (48-65)</td>
<td>59 (50-66)</td>
</tr>
<tr>
<td>Female</td>
<td>71%</td>
<td>72%</td>
<td>68%</td>
</tr>
<tr>
<td>Hazard ratio for withdrawing from treatment 0-90 days</td>
<td>HR (95% CI)</td>
<td>HR (95% CI)</td>
<td>HR (95% CI)</td>
</tr>
<tr>
<td>Adjusted for age and gender</td>
<td>1.0 (ref)</td>
<td>0.78 (0.45 to 1.36)</td>
<td>0.63 (0.35 to 1.13)</td>
</tr>
<tr>
<td>Fully adjusted*</td>
<td>1.0 (ref)</td>
<td>0.70 (0.39 to 1.27)</td>
<td>0.58 (0.33 to 1.10)</td>
</tr>
<tr>
<td>91-365 days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adjusted for age and gender</td>
<td>1.0 (ref)</td>
<td>1.15 (0.85 to 1.56)</td>
<td>0.74 (0.53 to 1.04)</td>
</tr>
<tr>
<td>Fully adjusted*</td>
<td>1.0 (ref)</td>
<td>1.16 (0.84 to 1.60)</td>
<td>0.83 (0.59 to 1.17)</td>
</tr>
</tbody>
</table>

*Variables are median (IQR) unless otherwise mentioned. *age, gender, DAS28, HAQ, smoking, CCI Abbreviations: CCI: Charlson Comorbidity Index; CI: confidence intervals; DAS28: Disease Activity Score of 28 joints, HAQ: Health assessment questionnaire

**Conclusion:** Compliance to guidelines was high. Direct comparison showed that remission and retention rates were highest for CT-P13, intermediate for certolizumab and lowest for abatacept. Results should, however, be interpreted with caution due to wide CIs and risk of residual confounding.

**Acknowledgement:** Thanks to Laura Köcher from Karolinska Institutet, Stockholm, Sweden for help with the figure

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SAT0596

RISK OF MAJOR ADVERSE CARDIOVASCULAR EVENTS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS AND A LOW-INTERMEDIATE A PRIORI RISK OF CORONARY ARTERY DISEASE AFTER INITIAL CT-BASED DIAGNOSIS AND TREATMENT A REGISTRY-BASED FOLLOW-UP STUDY USING DATA FROM THE WESTERN DENMARK HEART REGISTRY

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Background: Rheumatoid arthritis (RA) is a known risk factor for developing coronary artery disease (CAD). The influence of RA on the prognosis after initial diagnosis and treatment of CAD is however largely unknown.

Objectives: To examined the risk of major cardiovascular events among RA and non-RA patients with chest pain referred to cardiac computed tomography (CCT).

Methods: This was a follow-up study, using data from the Western Denmark Heart Registry[1]. Information on RA diagnosis and co-variables were identified through nationwide administrative registers. The primary outcome was a combined outcome including myocardial infarction, ischemic or unspecified stroke, coronary artery bypass grafting, percutaneous coronary intervention, and all-cause mortality. In the studied region, RA-fares are controlled through escalation of disease modifying drugs and intra-articular or intramuscular glucocorticoid injections (GGI). Hence, the number of times a patient had received GCS 3 years prior to the CCT were used as a surrogate marker of disease activity. Analyses were performed for overall RA and the serological subtypes: ‘seropositive RA (ICD-10: M05) and ‘other RA (ICD-10: M06).

Median time until events or censoring was 3.5 years (min/max: 0.0-9.2). Cox proportional hazard models were used to examine the association between RA/non-RA patients and outcomes.

Results: Among 42,257 patients, referred from 2008 and 2016, we identified 358 (0.8%) with RA. An increased risk was seen in RA compared to non-RA (adjusted hazard ratio (HR) 1.35 (95% CI: 0.93; 1.36)). An additional risk was found among patients who had received flare treatment more than once prior to CCT (adjusted HR 1.80 (95% CI: 1.08; 3.00)), and in patients with sero-positive RA (adjusted HR: 1.42 (95% CI: 0.93; 2.16)).

Conclusion: In patients with low-intermediate a priori risk of CAD, we found an association between RA and the combined primary outcome, supporting that RA per se, but in particular sero-positive and active RA, increase the risk of cardiovascular events even after initial CAD diagnosis and treatment.

REFERENCES


Disclosure of Interests: None declared

SAT0597

RISK OF HEART FAILURE FOLLOWING EXPOSURE TO NON-TNFİ COMPARED TO TNFİ BIOLOGICS IN US PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Biologic disease modifying drugs including TNF inhibitor (TNFi) and non-TNFi agents have become cornerstone of rheumatoid arthritis (RA) management. Case reports on new-onset heart failure (HF) following TNFi initiation led to an FDA black box warning released in October 2001. Subsequent observational studies have shown no association or even a protective effect of TNFi for HF, but the black box warning is still in place. There is a lack of knowledge regarding the risk of HF following exposure to the newer non-TNFi biologics.

Objectives: We aimed to assess the risk of incident HF following exposure to non-TNFi compared to TNFi biologics.

Methods: Using US claims data from Truven MarketScan (2004-2016), we conducted a cohort study of RA patients who initiated a ‘TNFi (adalimumab, certolizumab pegol, etanercept, golimumab, infliximab), or non-TNFi biologic or targeted synthetic DMARD (abatacept, anakinra, tocilizumab, tofacitinib). Patients were excluded if they were <18 years old, had previous HF, an implantable cardiologic device, or a loop-diuretics prescription. Patients were followed from the day after treatment initiation until the earliest event of the following: death, insurance disenrollment, treatment switching or discontinuation. The primary outcome of incident HF was defined based on primary inpatient diagnosis. Cox proportional hazards regression compared risk of HF among new users of non-TNFi compared to TNFi. To control for confounding, we used multivariable adjustment as well as propensity score (PS) adjustment by decile with trimming.

Results: A total of 13,290 non-TNFi patients were included, primarily consisting of abatacept (65%), tocilizumab (17%), and tocilizumab (15%). For the TNFi group, we identified 67,892 patients, primarily consisting of etanercept (42%), adalimumab (37%), and infliximab (15%). More patients treated with non-TNFi were female, older, had higher proportion of comorbidities and number of rheumatologist visits; lower proportion of NSAID/Coxib use. Table 1. The crude hazard ratio (HR) of HF after initiating a non-TNFi was 1.28 (95%CI 0.75-2.18) versus TNFi. After confounding adjustment in a multivariable model, the HR was attenuated to 1.08 (95%CI 0.57-2.05). The PS adjusted analysis showed consistent results (Table 2).

Conclusion: In this large US-based cohort of 81,182 RA patients, we found no difference in the risk of incident HF after initiation of non-TNFi biologic or targeted synthetic DMARD versus TNFi.

Table 1. Patient characteristics in 1 year prior to treatment initiation.

<table>
<thead>
<tr>
<th>Non-TNFi</th>
<th>TNFi</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients, n</td>
<td>13,290</td>
</tr>
<tr>
<td>Number of person-years</td>
<td>102,425</td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>66.0±10.0</td>
</tr>
<tr>
<td>Number of events</td>
<td>89</td>
</tr>
<tr>
<td>Crude HR (95% CI)</td>
<td>1.08 (0.98-1.19)</td>
</tr>
<tr>
<td>Adjusted HR (95% CI)</td>
<td>1.08 (0.98-1.19)</td>
</tr>
<tr>
<td>Number of rheumatologist visits, mean (SD)</td>
<td>13.8±39.9</td>
</tr>
</tbody>
</table>

Table 2. Risk of HF in non-TNFi versus TNFi initators.

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>Number of person-years</th>
<th>Number of events</th>
<th>Incidence rate per 1,000 person-years</th>
<th>Crude HR (95% CI)</th>
<th>Adjusted HR (95% CI)</th>
<th>Full adjusted HR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-TNFi</td>
<td>13,284</td>
<td>14,821</td>
<td>16</td>
<td>1.08</td>
<td>1.28 (0.75-2.18)</td>
<td>1.08 (0.57-2.05)</td>
</tr>
<tr>
<td>TNFi</td>
<td>67,860</td>
<td>102,425</td>
<td>89</td>
<td>0.87</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Covariates included in adjusted and PS models: year of cohort entry, age, gender, region, comorbidities, prior drug-use, and health utilization.

Disclosure of Interests: Thomas Bo Jensen: None declared, Nicole Tsao: None declared, Ajinkya Pawar: None declared, Rishi J Desai Grant/ research support from: RJD has received research grants to the Brigham and Women’s Hospital from Merck, Bayer and Vertex for unrelated projects., Seoyeong Kim Grant/research support from: Pfizer, Bristol-Myers Squibb, Roche/Genentech and AbbVie.

RHEUMATIC IMMUNE RELATED ADVERSE EVENTS ASSOCIATED WITH CANCER IMMUNOTHERAPY: A NATIONWIDE MULTI-CENTER CANADIAN COHORT FROM THE CANADIAN RESEARCH GROUP OF RHEUMATOLOGY IN IMMUNO-ONCOLOGY (CANRIO)

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Background: Immune checkpoint inhibitors (ICI) have revolutionized cancer therapy by harnessing the immune system to fight cancer. As the indications for ICI continue to expand, their success in advanced stage malignancies is tempered by the development of autoimmune toxicities, referred to as immune-related adverse events (irAE). Rheumatic irAE (Rh-irAE), particularly arthralgias and arthritis are common and optimal management remains unknown.

Objectives: The Canadian Research Group of Rheumatology in Immun-oncology (CanRIO) is an emerging network of Canadian rheumatologists with an interest in Rh-irAE secondary to ICI. We describe the clinical presentation and management of Rh-irAE associated with ICI in patients seen at 9 CanRIO sites.

Methods: Patients presenting with rheumatic symptoms associated with ICI therapy between 2013 and January 2019 at participating CanRIO sites were identified. Cases were stratified based on the presence or absence of pre-existing autoimmune disease (PAD). Standardized data were extracted by chart review. The data were pooled and analyzed descriptively.

Results: 118 patients without PAD who developed 140 Rh-irAE were identified, 59% were male with a mean age of 62 years. Common indications for ICI were melanoma (n=57, 43.8%), lung (n=30, 23.4%), and genitourinary cancer (n=19, 16.1%). ICI included nivolumab (n=30, 25.6%), pembrolizumab (n=38, 32.5%), ipilimumab (n=1, 0.9%), durvalumab (n=3, 2.6%), atezolizumab (n=4, 3.4%) or combination therapy (n=29, 24.8%). Common Rh-irAE included symmetric polyarthritis (n=45, 32%), arthralgias/myalgias or acute flare of osteoarthritis (n=20, 14.3%), polymyalgia rheumatica-like presentation (n=17, 12%), tenosynovitis/enthesitis (n=17, 12%), sicca syndrome (n=11, 7.9%) and myositis (n=5, 6.4%). 20 patients with PAD were identified, 70% of whom were in remission prior to starting ICI. 50% (n=10) had flares, 15% (n=3) developed a new Rh-irAE and 20% (n=6) developed O-irAE. 53% experienced at least one other non-rheumatic irAE (O-irAE) (n=63). Mean time from first ICI exposure to onset of Rh-irAE was 6.8 months. In 65% ICI was held or discontinued (n=77). Despite this, 68.6% (n=81) had favorable tumor response, while 12% (n=14) had tumor progression. There were no deaths related to Rh-irAE. The majority of patients without PAD had partial or complete response to mono or combination therapy with oral prednisone (n=77; maximum dose 60 mg/d), nonsteroidal anti-inflammatories (NSAID; n=52), intra-articular corticosteroids (n=29), hydroxychloroquine (n=26), methotrexate (n=17), or tumor necrosis factor alpha inhibitors (n=8).

Conclusion: This is the largest multi-centered cohort of Rh-irAE described to date. Seronegative inflammatory irAE was the most common Rh-irAE although a broad range of conditions were identified. The most common first-line treatment was systemic corticosteroids followed by NSAID and intra-articular steroid injections. Prednisone was effective, however higher doses were required. Disease-modifying anti-rheumatic drugs (DMARD) and biologic therapy were well tolerated and effective, with hydroxychloroquine being the most commonly used DMARD. Despite moderate to high doses of immunosuppression, the majority of patients had favorable tumor responses.

Disclosure of Interests: Daniel Ennis: None declared, Shahin Jamali Consultant for: Consultant for Abbvie, Amgen, BMS, Eli Lilly, Pfizer, Janssen, Merck, UCB, Marie Hudson Grant/research support from: Unrestricted research funds from Bristol-Myers Squibb, Carrie Ye: None declared, Alexandra Saltman: None declared, Meghan Himmel: None declared, Janet Pope Consultant for: Eli Lilly and Company, Sabrina Hoa: None declared, Annalise Tisseverasinghe: None declared, Aurore Fill-Mah Grant/research support from: Roche, Abbvie, Janssen, BMS, Speakers bureau: Roche, Abbvie, Janssen, BMS, Pfizer, Nancy Maltez: None declared, Janet Roberts: None declared

controlled, longer RA duration) sustained the lowest mean SJC throughout follow-up. Cluster 4 patients ("health low, moderate, moderate RA") exhibited the highest improvement in mental health (FSMHI; Figure). Cluster 5 patients ("health low, RA uncontrolled, longer RA duration") exhibited the highest CDAI scores (Figure) and maintained baseline line of therapy the longest.

Conclusion: Five patient clusters identified by data-driven PC analysis of the BRASS registry exhibited distinct patterns of clinical outcome and management over a 4-year follow-up period. The clinical outcomes data suggest the clusters represent clinically meaningful categories of RA and illustrate the potential of data-driven patient profiling as a tool to support personalized medicine in RA. Validation in an independent dataset is ongoing.

Acknowledgement: Study funding and medical writing support (Matt Lewis, Adelphi) provided by Sanofi and Regeneron Pharmaceuticals, Inc.


**COMPARATIVE CARDIOVASCULAR SAFETY OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDS) IN PATIENTS WITH OSTEOARTHRITIS: FINDINGS FROM PROVINCIAL PRESCRIPTION CLAIM RECORDS IN BRITISH COLUMBIA, CANADA**

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**Background:** Osteoarthritis (OA) has been reported as an independent risk factor for cardiovascular diseases (CVD) (1). Furthermore, mediating role of NSAIDs in the observed OA-CVD association has also been noted (2). Thus, a substantial proportion of the total risk of CVD among OA patients compared to non-OA controls was attributable to NSAIs use (1). This is particularly worrisome as there is no cure for OA, and NSAIDs are the mainstay of treatment in controlling the primary symptoms of pain and inflammation among OA patients. However, only a handful of observational studies evaluated the risk of a specific NSAID among OA patients for a specific CVD event such as myocardial infarction (MI) (3). The overall cardiovascular safety of NSAIDs used in treating OA in the real-world therefore remains unknown.

**Objectives:** To evaluate the comparative safety of various NSAIDs against CVD when treating patients with OA.

**Methods:** We used linked health administrative data (HAD) of a previ- ously assembled, population-based cohort of 720,055 British Columbians from Canada. We identified individuals with OA who received at least one NSAID prescription from January 1996 to December 2013. Eligible study subjects were at least 20 years old, did not have CVD and had not received an NSAID prescription within the last 90 days from their OA diagnosis date. We defined composite CVD outcome from hospital discharge abstract database, payment information file of Medical Services Plan and vital statistics deaths data file using ICD-9 or ICD-10 codes. We created an NSAID exposure variable in a time-dependent fashion in which individuals were considered at risk for the duration of NSAID pre- scriptions. We used time-dependent Cox regression analysis to estimate CVD risk associated with NSAID use overall as well as four unique groups of NSAIDs, i.e., coxibs, naproxen, ibuprofen and other conven- tional NSAIDs.

**Results:** Our cohort included 3,806 OA individuals. There were 1,147 CVD events. After adjusting for age, sex, SES, COPD, diabetes, hyper- tension, hyperlipidemia, peptic ulcer disease and Romano comorbidity score, the hazard ratio (HR) and 95% confidence interval (CI) from the time-dependent Cox regression model was 1.48 (1.27, 1.73). When expo- sure to different groups of NSAID was compared with unexposed person- time, CVD risk were similar among coxibs and naproxen followed by other conventional NSAIDs and ibuprofen, adjusted HR (95% CI) were 1.58 (1.24, 2.00), 1.58 (1.11, 2.24), 1.39 (1.10, 1.75) and 1.36 (0.75, 2.47), respectively.

**Conclusion:** Our study is the first retrospective cohort study using BC HAD that looked at the overall CVD risk of NSAID use in treating OA in a real-world setting. After modelling exposure to NSAIDs as time-depend- ent, we found that exposure to NSAIDs substantially increased overall CVD risk compared to non-exposed periods. We also found that coxibs and naproxen may increase CVD risk more than conventional NSAIDs including ibuprofen.

**REFERENCES**


Disclosure of Interests: Mohammad Atiquzzaman: None declared, Ehsan Karim: None declared, Hubert Wong: None declared, Jacek Kopec: None declared, Mary De Vera: None declared, Aslam Anis Grant/research sup- port from: Not related to the research presented in this abstract, Consul- tant for: Not related to the research presented in this abstract DOI: 10.1136/annrheumdis-2019-eular.1145

**MORTALITY RATE IN PATIENTS TREATED WITH BIOLOGICS: DATA FROM THE ROMANIAN REGISTRY OF RHEUMATIC DISEASES**

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**Background:** Rheumatoid arthritis (RA) is associated with increased mor- tality, with longitudinal studies averaging a standardised mortality ratio of
1.5 (95%CI 1.2 to 1.8) for RA patients compared to the general population [1]. In contrast, information on mortality in ankylosing spondylitis (AS) is scarce, whereas there are conflicting reports of the mortality risk among patients with psoriatic arthritis (PsA), but it is accepted that patients with PsA do not have a significantly elevated risk of mortality [2].

Objectives: To estimate the Mortality Rate in RA, SA and PsA for patients (pts) treated with biologics in Romania.

Methods: Data were gathered from the Romanian Registry of Rheumatic Diseases (RRRB), which comprises all patients treated with biologics in Romania for RA, AS and PsA. We have studied demographic data, disease duration, exposure to biologics in person-years (PY), and all-cause mortality until 01.07.2018.

Results: The cohort included 9577 pts (35596.83 PY) as following: 5224 RA pts (18676.75PY), 3469 AS pts (12680.63PY) and 884 PsA pts (4212.45PY). The mean age of the cohort was 54.86 yrs (62.87 yrs for RA pts, 56.54 yrs for AS, 56.18 yrs for PsA); 3196 pts (33.57%) were men: 79 (1.5%) RA pts, 2681 (77.28%) AS pts and 436 (49.3%) PsA pts. Mean disease duration for the cohort was 16.46 yrs for RA, 11.46 yrs for AS and 10.99 yrs for PsA. The number of all-cause deaths was 89 (74 deaths in RA, 11 in AS and 4 in PsA group). The mortality rate for the entire cohort was 0.25/100PY, and the rate varied across the diseases: 0.39/100PY in RA pts, 0.08/100PY in AS pts and 0.09/100PY in PsA. Infections were the major mortality cause in RA (0.09/100PY) and AS (0.04/100PY). Cardiovascular fatal events occurred in 0.06/100PY in RA population, significantly higher than 0.007/100PY in AS pts. Rate of solid neoplasm death in RA cohort was 0.04/100PY, compared to 0.007/100PY in AS; non-Hodgkin lymphoma was recorded only in RA pts (0.005/100PY). All deaths reported in PsA cohort (4 deaths) were of unknown cause.

Conclusion: This is the first report on mortality rate in biological treated patients in Romania. These data support data from the literature, showing that RA patients have a higher mortality risk compared to AS and PsA.

REFERENCES

Disclosure of Interests: None declared

SAT0602 SHOULD ALL PATIENTS WITH ANTI-CENTROMERE ANTIBODIES BE REFERRED FOR A RHEUMATOLOGY ASSESSMENT?

Hoda Alkoty, Mark Lazarus. Southend University Hospital, Rheumatology, London, United Kingdom

Background: Anti-centromere antibodies (ACA) are commonly associated with systemic sclerosis (SSc). The presence of ACAs in patients with SSC is known to increase the likelihood of developing Pulmonary Hypertension, which has a high mortality rate. ACAs are also seen in patients with other connective tissue diseases (CTD) and can sometimes be identified after testing for antinuclear antibodies in patients who have not reported any rheumatological symptoms. It is possible that connective tissue diseases are being under diagnosed due to a lack of awareness by physicians of the clinical significance of ACAs.

Objectives: To investigate whether patients with ACAs are being appropriately referred to the Rheumatology service.

Methods: All patients who were positive for ACAs in Southend university hospital between April 2016 and October 2018 were included in this single centre retrospective observational study. We identified patients’ demographics, diagnosis, ANA titre, additional diagnosis and immunosuppressive therapy. We also captured their monitoring with pulmonary function testing and echocardiography.

Results: A total of 75 patients were identified with ACAs. The average age was 65 years, 61 females, 14 Male. Fifty-six patients were referred to rheumatology team and were found to have the following diagnosis. LCsSc (21), Sjogren’s syndrome (SS) (10), undifferentiated connective tissue disease (UCTD) (6), Rheumatoid arthritis (RA) (5), ANA associated vasculitis (AAV) (3), Raynaud’s phenomenon (3), Lupus (2), Antiphospholipid syndrome (APS) (1), Primary biliary cirrhosis with Sjogren’s syndrome (SS) (1), Autoimmune hepatitis (1) and osteoarthritis (1). Of those 33 patients had a routine screening with an Echocardiogram and 26 had pulmonary function tests. One patient with lqScs developed pulmonary hypertension. The remaining 19 patients were not referred and did not have the appropriate screening for pulmonary hypertension. ANA titre was 1:30 in one patient, 1:320 for 4 patients, unknown for three and 1:640 for the remaining 67. 11 patients were treated with Hydroxchloroquine (4 SS, 4 UCTD, 1 lupus, 1 APS and 1 lc SSc), 5 on Methotrexate (4 RA and 1 AS), 2 on MMF and steroid (AAV).

Conclusion: Nearly all patients with ACAs that were seen in the Rheumatology clinic had an autoimmune rheumatic disease. However, we found that 25% of people with ACAs were not referred to the Rheumatology service. The reasons for this are unclear. It is possible that patients did not report symptoms that would have prompted a referral. Some of the CTDs in which ACAs are typically found (lqScs and SS) are associated with symptoms that can be mild and might not be reported by the patients or general physicians do not associate them with rheumatological disorders (e.g. sicca symptoms, gastro-oesophageal reflux and Raynaud’s phenomenon). Early diagnosis might enable earlier treatment and prevent complications from these diseases. General physicians should therefore be made aware of these antibodies and the disorders that they can be associated with.

Disclosure of Interests: None declared

SAT0603 SENSITIVITY TO PHENYLTHIOCARBAMIDE IN RHEUMATOID ARTHRITIS PATIENTS

Natalia Dostanko¹, Viktor Yagui², Tatiana Zybalkova³, Valery Andreashov¹, Viktoria Dostanko². Belarusian State Medical University, 2nd Department of Internal Medicine, Minsk, Belarus; ²PMUE Infomed, Minsk, Belarus

Background: Sensitivity to phenylthiocarbamide (PTC) as the ability to taste this bitter compound is a genetic marker ranked alongside eye color and blood groups [1,2]. Almost 90 years have passed since the first publication of A.L. Fox on the relationship of the “chemical constitutio- tion” and sensitivity to PTC [3] and 35 years later, J. Stepan et al. (1965) analyzed the sensitivity to PTK in patients with joint diseases. According to the literature [4,5] sensitivity to PTK is associated with the peculiarities of clinical manifestation and the course of these diseases.

Objectives: To estimate the sensitivity to PTC in RA patients and its influence on the prognosis of the disease.

Methods: The physiological parameter of sensitivity to PTC was determined by H. Harris et al. [8]. The total number of dilution thresholds was 15 (PTC<1), Patients were considered as non-tasters (not able to taste PTC) in the case of PTC<4 sensitivity thresholds and as tasters in the case of PTC≥4 sensitivity thresholds. Sensitivity to PTC was assessed in 140 RA patients, 110 women and 30 men, at Minsk clinical hospital No9 and we used the data on the PTC sensitivity of the mixed population of Minsk as a control [7].

Results: The frequencies of tasters (PTC+) and non-tasters (PTC-) as well as allele frequencies (T and t) of the PTC sensitivity gene among RA patients and controls are presented in the table.

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Phenotypes</th>
<th>Allele frequencies</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA, t</td>
<td>110</td>
<td>32</td>
<td>78</td>
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<tr>
<td>RA, T</td>
<td>140</td>
<td>40</td>
<td>98</td>
</tr>
<tr>
<td>Control, t</td>
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<td>40</td>
<td>90</td>
</tr>
<tr>
<td>Control, T</td>
<td>119</td>
<td>41</td>
<td>78</td>
</tr>
</tbody>
</table>

There were no significant differences between general groups of PTC tasters and non-tasters among RA patients and the controls (two-way Fisher exact test, two-way FET, p<0.01) while the sensitivity threshold of PTC<4 was revealed 2 times less in RA patients than in the control group 10.7% and 22.1%, respectively (two-way FET, p=0.0057). Operating characteristics of PTC<4 are the following: OR=0.43 Cl95:0.23-0.78, LR+=0.49 Cl95:28-0.81, LR−<1.15 Cl95:0.95-1.23, that means that a taste threshold of PTC<4 decreases the chance of RA by 2.0 times.

Seronegative RA was significantly more common in non-tasters vs tasters in the case of PTC<4 sensitivity thresholds and as tasters in the case of PTC≥4 sensitivity thresholds. Sensitivity to PTC was assessed in 140 RA patients, 110 women and 30 men, at Minsk clinical hospital No9 and we used the data on the PTC sensitivity of the mixed population of Minsk as a control [7].

Results: The frequencies of tasters (PTC+) and non-tasters (PTC−), as well as allele frequencies (T and t) of the PTC sensitivity gene among RA patients and controls are presented in the table.

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<td>41</td>
<td>78</td>
</tr>
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</table>
advanced stages of RA (3-4 stages by O. Steinbrocker) (two-way FET, p=0.0024) with the same duration of RA.

Conclusion: The taste threshold of PCTC decreased the chances of RA by 2.0 times and non-sensitivity to PCTC was associated with seronegative RA, especially in men, and more benign course of the disease.

REFERENCES

Disclosure of Interests: None declared

SAT0604 ANALYSIS OF INFECTIOUS SPONDYLODISCITIS: 20-YEARS DATA: EPIDEMIOLOGY, CLINICAL FEATURES, DIAGNOSIS AND TREATMENT

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Background: Infectious spondylodiscitis is defined as an infectious disease involving intervertebral disks and adjacent vertebral bodies. It is rare and difficult to diagnose due to its non-specific clinical features.

Objectives: To study the clinical, microbiological, radiological, therapeutic and evolving of infectious spondylodiscitis.

Methods: Retrospective monocentric study including patients diagnosed as spondylodiscitis and hospitalized in our department between January 1999 and December 2018. The diagnosis was based on clinical, biological, radiological and bacteriological data.

Results: We included 107 patients. There were 58 men (54.2%) and 49 women (45.8%) with a mean age of 55 years [16-86]. Predisposing factors were found in 59 patients (55.1%). This was diabetes in 21.49% of cases, spinal cord compression in 9.3% and vertebral ostelysis in 8.4% of cases. The lumbar spine was most affected (54.2%), followed by the dorsal spines in 31.7%.

Conclusion: Early diagnosis is needed to avoid neurological complications and to reduce the duration of antibiotic treatment. Early diagnosis is needed to avoid neurological complications and to reduce the duration of antibiotic treatment.

Disclosure of Interests: None declared

SAT0605 BODY MASS INDEX AND SYSTEMIC CORTICOSTEROID USE AS INDICATORS OF DISEASE BURDEN AND THEIR INFLUENCE ON THE SAFETY PROFILE OF CERTOLIZUMAB PEGOL ACROSS INDICATIONS

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Background: Certolizumab pegol (CZP) is an anti-TNF drug approved for rheumatoid arthritis (RA), axial spondyloarthritis (axSpA), psoriatic arthritis (PsA), ankylosing spondylitis (AS) and Crohn’s disease (CD). Older age, comorbidity burden and corticosteroid (CS) use have been linked to increased risk of serious infectious events (SIEs) in CZP-treated patients (pts) with RA. However, the impact of overall disease burden on the risk of serious adverse events (SAEs) has not been fully examined for other CZP indications. High body mass index (BMI) has been associated with systemic inflammation and greater comorbidity risk. Greater disease burden in these pts may lead to increased CS use – a known risk factor for SAEs.

Objectives: To examine the contribution of BMI and CS use to the risk of SIEs, malignancies and major adverse cardiovascular events (MACE) in CZP-treated pts across indications.

Methods: Safety data were pooled across 49 CZP clinical trials (27 RA, 1 axSpA, 1 PsA, 5 PSU, 15 CD). SAEs of potential concern were medically reviewed by an external expert committee using predefined case rules. Incidence rates (IR) were calculated per 100 pt-years (PY). Multivariate Cox modeling was used to estimate relative risk (hazard ratio [HR]) of time to first SIE, malignancy or MACE by baseline BMI (<18.5, 18.5–25, 25–30, >30 kg/m²) and CS use (yes, no). The model was adjusted for baseline age, sex, disease duration, methotrexate (MTX) use, prior anti-TNF drug use, and CZP indication.

Results: Across indications, 11,317 pts received CZP (21,695 PY total exposure; max: 7.8 years [yrs]; exposure for RA: 13,542 PY; axSpA: 978 PY; PsA: 1,316 PY; PSU: 1,481 PY; CD: 4,378 PY). Mean BMI was 27.8 kg/m² in RA, 27.6 kg/m² in axSpA, 29.8 kg/m² in PsA, 30.1 kg/m² in PSU, and 24.0 kg/m² in CD. Overall, 4,132 pts (37%) took CS at baseline, more so in RA (46%) and axSpA (51%). Across indications, IRs were 0.82/100 PY for all malignancies (IR for malignancies excluding non-melanoma skin cancer [NMSC] was 0.66/100 PY), 0.47/100 PY for serious infectious events, and 0.70/100 PY for major adverse cardiovascular events.
MACE, and 3.6/2/100 PY for SLEs. According to the Cox model, age ≥45 yrs, disease duration <1 yr (compared with ≥5 yrs), and no MTX use were risk factors for malignancies (including NMSCs); BMI and CS use did not have a detectable impact (Table). MACE risk was higher in RA and PsA; BMI >30 kg/m² was a risk factor for MACE, in addition to age ≥45 yrs and male sex (Table). Compared with RA, SIE risk was higher in CD and lower in PSO and PsA; key risk factors included age ≥65 yrs, disease duration ≥10 yrs and CS use. Without CS use, BMI did not impact SIE risk, but among CS users, SIE risk was higher for obese pts (Table).

Conclusion: In CZP-treated pts across indications, malignancy risk was not influenced by BMI or CS use. As expected, obesity and CS use increased the risk of MACE. The SIE risk associated with CS use was compounded in obese pts, which may reflect the contribution of comorbidity, disease activity or other factors not examined here.

REFERENCES


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INCIDENCE AND SEVERITY OF FRACTURE FRAILTY

Bernard Cortet1, Pierre Chauvin2, Jean-Marc Feron3, Laurent Grange4, Alan Coulomb5, Robert Lauonis6, Francoise Alliot Launois7, Rahima Sellami8, Chantal Touboul9, Benoit Vincent9, Jean-Michel Joubert9, Karine Briot10.

Background: Certain fragility fractures (for example of the hip and femur) are the most frequent falling-related injuries in the elderly and are considered major since they are associated with increased mortality and morbidity.1

Objectives: To describe the characteristics of adults aged ≥50 years in France experiencing fragility fractures according to the site of fracture.

Methods: A postal questionnaire was sent to 15,000 individuals aged ≥50 years in order to identify and characterise subjects with a history of fragility fracture. Subjects were asked whether they had experienced a fracture in the previous 3 years and, if so, how many. Fractures were classified according to site into major (shoulder, vertebrae, pelvis, hip or femur and ≥3 ribs) or minor (other sites).1

Results: Of the 13,914 subjects returning the questionnaire, 425 (3%) reported ≥1 fragility fracture. The fracture rate history in the previous year was 1.4% [95%CI: 1.2–1.6], this rate was higher in women (2.0%) than in men (0.7%) and increased with age. 147 subjects reported major fractures and 287 subjects minor fractures. Most fractures (82.4%) resulted from falling over. The most frequent major fracture sites were the humerus (10.6% of all fractures), vertebra (8.1%) and hip (7.1%). The most frequent minor fracture sites were the forearm/wrist (24.7%) and ankle (17.7%). 25 subjects reported ≥1 fractures and were excluded from further analyses. Subjects with a history of major fractures were older (<p>0.01) than those with minor fractures (72:61±13 vs. 67:1±10.6 years; <p>0.01). Distribution of gender, body mass index and comorbidities did not differ between fracture type groups. Current obesity was, however, associated with a higher rate of previous fracture of the lower limb. Subjects with a history of major fractures reported a significantly greater loss in height since the age of 20 (p<0.01) than those with a history of minor fractures (-3.9±2.35 vs. -2.7±2.02 cm). Subjects who reported lifetime corticosteroid use for ≥3 months more frequently reported major fractures than minor fractures (odds ratio: 1.90 [1.13;3.18], as did post-menopausal women (odds ratio: 4.64[1.06;20.43]) and women using oestrogen-based hormone replacement therapy (odds ratio: 1.86 [1.06;3.29]). Parental fracture history, a history of falls, excess alcohol consumption or active smoking, and use of drugs that may increase risk of falls (antidepressants, antiepileptic drugs) were not associated with the type of fracture.

Conclusion: Extrapolated to the total French population, >340,000 people aged ≥50 years would be expected to experience a fragility fracture each year. One third of these fractures are major. Characteristics found to be associated with the severity of the prior fracture were older age, corticosteroid use, post-menopausal status and use of oestrogens. Limitations of the study include retrospective data collection, risk of recall bias, lack of ascertainment of fracture history and failure to capture subjects in residential care or who had died since the fracture.

REFERENCES


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Disclosure of Interests: Bernard Cortet Consultant for: Bernard Cortet has received consultancy honoraria of speaker’s fees from Amgen, Expanscience, Ferring, Lilly, Medtronic, MSD, Novartis, Roche diagnostics, Theramex and UCB. Pierre Chauvin: None declared, Jean-Marc Feron Consultant for: Jean-Marc Feron has received consultancy honoraria and conference fees from UCB, Amgen and Lilly, LAURENT GRANGE Consultant for: Laurent Grange has received honoraria from Amgen, Lilly and UCB and research support from Lilly, Amgen, UCB, Expanscience, Mylan, Roche diagnostics and TEVA, Alain Coulomb: None declared, Robert Lauonis: None declared, Francoise Alliot Launois: None declared, Rahima Sellami: None declared, Chantal Touboul: None declared, Benoit Vincent: Employee of: Benoit Vincent is an employee of UCB Pharma, France, Jean-Michel Joubert Employee of: Jean-Michel Joubert is an employee of UCB Pharma, France, Karine Briot Consultant for: Karine Briot has received consultancy honoraria and conference fees from UCB, Amgen, Lilly and MSD.


THE PREVALENCE OF RHEUMATOID ARTHRITIS IN CHILE, A STUDY PERFORMED AS PART OF THE NATIONAL SURVEY HEALTH (ENS 2016-17)

Joselina Duran1, Loreto Massaró2, Carolina Llanos3, Sergio Iacobelli4, Paula Burgos5, Raquel Arquilla6, Maria Eugenia Martinez7, Natalia Cristostomo7, Alvaro Cisternas3, Paula Margozzini8, ENS2017, Pontificia Universidad Católica de Chile, Santiago, Chile; Universidad San Basilio, Santiago, Chile; Pontificia Universidad Católica de Chile, Santiago, Chile; Clínica Santa María, Santiago, Chile; Universidad de la Frontera, Temuco, Chile.

Background: Genetic and environmental backgrounds influence the development of rheumatoid arthritis (RA) and its frequency has regional variations. In Latin America epidemiologic data are scarce.

Objectives: We aimed to determine the prevalence of RA in Chile as part of the National Health Survey (ENS, Encuesta Nacional de Salud).

Methods: ENS was a cross-sectional household survey with a stratified multistage probability sample of 6,233 participants performed between August 2016 and March 2017. A screening instrument for RA was applied to a random sample of 3,700 subjects >30 years old.1 Positive screening was defined by at least one of the following: (i) 2 swollen joints for at least 4 consecutive weeks (past or present) and/or (ii) a diagnosis of arthritis in the past. Individuals with positive screening had Rheumatoid Factor, Anti-citrullinated protein antibodies, and C-reactive protein measured and clinical examination was performed by a rheumatologist. Self-report of doctor-diagnosed RA was also performed.

Results: The screening questionnaire was applied to 2,998 subjects. Seven hundred and thirty-eight (22.1%) had a positive screening. Among the subjects with a positive screening 493 (66%) had consulted a rheumatologist. Thirty-one subjects had RA according to the ACR/EULAR 2010 classification criteria, which corresponds to 0.6% (95%CI 0.3, 1.2). Two point three per cent reported having RA. Prevalence was higher in women and in high SES.

Conclusion: According to this national population-based study RA prevalence in Chile is 0.6% (0.3, 1.2). This is similar to the prevalence previously reported in developed countries, which is noteworthy given the differences in sociodemographic characteristics which exist compared to Chile. Self-reporting leads to an important overestimation of RA. Our study suggests there is a higher risk of RA in subjects with high SES in this region.

REFERENCES


Disclosure of Interests: Joselina Duran: None declared, Loreto Massaró Speakers bureau: Werfen, Carolina llanos: None declared, sergio iacobelli: None declared, Paula Burgos: None declared, Raquel Arquilla: None declared, maria eugenia martinez: None declared, marcela cisternas: UCB Lilly, None declared, Maria Eugenia Martinez: None declared, macarena armstrong: None declared, mirentxo iruretagoyena: None declared, carlos cardona: None declared, alvaro cisternas: None declared, lucero hagedorn: None declared, natalia cristostomo: None declared, alvaro cisternas: None declared, paula margozzini: None declared.

SAT0609 WOMEN WITH METABOLIC SYNDROME AND GENERAL OBESITY ARE AT HIGHER RISK FOR SIGNIFICANT HYPERURICEMIA THAN MEN: RESULTS FROM THE 2016 KOREAN NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY

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Background: Hyperuricemia is emerging as a potential biomarker and a predictor for metabolic syndrome (MetS) and its related complications.

Objectives: We aimed this study to investigate the risk factors of hyperuricemia, particularly, the association of hyperuricemia with MetS and general obesity.

Methods: We performed multivariate logistic regression analyses using the 2016 Korea National Health and Nutrition Examination Survey (KNHANES) data collected in a representative sample of Korean adults. Hyperuricemia was defined by serum uric acid level >7.0 mg/dl for men and >6.0 mg/dl for women. General obesity was based on body mass index (BMI) >25 kg/m².

Results: Among a total of 5,591 Korean adult participants, 685 (12.3%) individuals were classified as having hyperuricemia. Hyperuricemia was significantly associated with MetS in men (Odd ratio (OR): 1.74, 95% CI: 1.29-2.34) and women (OR: 2.47, 95% CI: 1.55-3.93) after adjustments for age, sex, smoking, alcohol, exercise, BMI and estimated glomerular filtration rate (eGFR). General obesity was also independently related to hyperuricemia in both sex (OR: 1.70, 95% CI: 1.31-2.19 in men, OR: 3.73, 95% CI: 2.57-5.41 in women). Among the components of MetS, elevated blood pressure, elevated triglyceride and reduced HDL-cholesterol in men, and increased waist circumference, hyperglycemia, elevated triglyceride in women were risk factors for hyperuricemia. In subgroup analyses, the presence of concomitant MetS and general obesity posed strikingly higher risk for hyperuricemia among women (OR: 7.24, 95% CI: 4.56-11.50 in women, versus, OR: 2.90, 95% CI: 2.12-3.96 in men) when compared to individuals free of neither conditions (OR: 1.00, referent). In addition, the risk of hyperuricemia has increased up to 6-fold by the presence of MetS and general obesity among young adults aged less than 40 years old.

Conclusion: Hyperuricemia was independently associated with MetS and general obesity, regardless of sex. These increases in risk of hyperuricemia were more prominent in women. Among women, those who had both MetS and general obesity were at nearly 7-fold increased risk for hyperuricemia compared to those without both conditions. It may be considered to incorporate hyperuricemia as one of the components of MetS.

REFERENCES

Disclosure of Interests: None declared

SAT0610 THE DELPHI METHOD IN RHEUMATOLOGY RESEARCH: ARE WE DOING WELL?

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Background: Delphi method is an iterative process, designed to combine the opinion of a group of experts within a consensus. It is a structured methodology to systematically collect expert judgments about a problem, process the information and finally build a general group agreement. It has 4 defining characteristics: iterative, anonymous process, generates feedback and generates a consensus.

Objectives: To evaluate the methodology and application of the Delphi method in rheumatology research.

Methods: Search of the literature was performed in the MEDLINE, EMBASE, Clinical key and Scielo databases. MESH terms “Delphi Technique”, “Rheumatology” and “Rheumatoid arthritis” were used, finding 404 articles. A total of the abstracts of these studies was read, discarding duplicates, articles of consensus methodology different from the Delphi technique and articles from studies of other specialties. The consultation was held on 30-10-18.

Results: 109 articles were found. Journal with highest number of publications was Clinical Rheumatology (30 articles), followed by Journal of Rheumatology (11 articles), Rheumatoid arthritis was the first rheumatic diseases studied in 21.1% (n=23), followed by psoriatic arthritis in 11% (n=12). Only 16.5% (n=18) of the studies met the 4 characteristics of the Delphi method, 31.2% (n=34) met 3 characteristics, 18.3% (n=20) met 2 characteristics and 39.9% (n=37) meets only one of the defining characteristics of the method. Feedback was made in 43.1% (n=47) of the studies. Process was iterative in 64.2% (n=70) of papers. The coordinating group of the exercise was only reported in 27.5% (n=30), with an average of 8 (± 3.14) coordinators for each study. The group of experts was reported in 90.6% (n=102) of the studies, with a median of 28 (interquartile range: 54) experts per study. In 30.4% (n = 45) of the studies, the way in which communication with the group of experts was established was not reported. The modification of the Delphi technique was declared in 14.9% (n = 22) of the studies, however, in 18 of these studies it is not explained what was the modification of the technique; in 4 studies, the modification consisted of holding a face-to-face meeting of the group of experts after the consultation rounds; one of the studies clarifies having made a "RAND/UCLA" method without explaining in more detail what this method consists of. To refer to the modified versions of the method, terms such as "informal Delphi" or "Delphi like study" are coined, without further considerations or clarifications to what these mean.

Conclusion: Use of Delphi technique in rheumatology has not been carried out following the original methodology in most of the evaluated works, which puts at risk the validity of the results of these studies. Propening for the correct use of the technique, will improve the validity of the results obtained with this type of qualitative research. It is necessary to establish and validate minimum compliance criteria, so that an expert consensus exercise through the Delphi method achieves its purpose in a valid way. This context allows to open a line of methodological research in evaluation of the application of the Delphi methodology in the health area.

REFERENCES


Disclosure of Interests: None declared

SAT0611 PREVALENCE OF HYPOTHYROIDISM WITH THERAPEUTIC INDICATION IN PATIENTS WITH RHEUMATOLOGICAL DISEASES

Sho Fukugi, Yukihiko Ikeda, Haruki Sawada, Mitsuhiro Watanabe, Ayako Kido, Rui Imai, Masei Suda, Haruyuki Yanaska, Hisanori Shimizu, Ryo Rokutanda, Hiroshi Tamaki, Tokutaru Tsuda, Kenichi Yamaguchi, Mitsumasa Kishimoto, Masato Okada. St. Luke’s International Hospital, Immuno-Rheumatology Center, TOKYO, Japan

Background: Hypothyroidism is known as a common complication of rheumatological diseases(RD). Thyroid hormone supplementation is important not only in clinical hypothyroidism but subclinical one for cardiovascular events in the future. But the data about prevalence of hypothyroidism requiring treatment and it’s changes with follow up in patients with RD is limited.

Objectives: To reveal the prevalence and risk factors of hypothyroidism, especially which requires thyroid hormone supplementation, in patients with RD and compare it with that of general population.

Methods: We retrospectively reviewed charts of RD patients and healthy controls in preventive medicine center, at St. Luke’s International Hospital from January 2004 to July 2018. We investigated basic demographics, underlying diseases, blood tests including thyroid functions and treatment with thyroid hormones. We compared the number of hypothyroidism requiring treatment (Thyroid stimulating hormone: TSH ≥10 μIU/mL or physician started treatment) and it’s changes in follow up using univariate analysis and Kaplan–Meier method with log rank test. Cox proportional hazard model was performed for evaluating the risk of hypothyroidism which needs treatments in all patient and only RD patients.

Results: 2307 RD patients and 78251 controls without past medical history of hypothyroidism with therapeutic indications are included. Newly-detected hypothyroidisms requiring treatments are significantly frequent in
Table 1. Comparison of RD patients and control

<table>
<thead>
<tr>
<th>Parameter</th>
<th>RD patients (n = 2307)</th>
<th>Control (n = 78251)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>53.7 (16.3)</td>
<td>46.1 (11.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FEMALE (%)</td>
<td>1826 (79.2)</td>
<td>38632 (49.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI</td>
<td>22.7 (3.9)</td>
<td>22.4 (3.3)</td>
<td>0.03</td>
</tr>
<tr>
<td>Hb (g/dl)</td>
<td>12.1 (1.6)</td>
<td>13.9 (1.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MCV (fl)</td>
<td>88.9 (5.7)</td>
<td>91.0 (4.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cre (mg/dl)</td>
<td>0.61 (0.29)</td>
<td>0.73 (0.21)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>L-CHO (mg/dl)</td>
<td>107.2 (29.1)</td>
<td>115 (30.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RF positive (%)</td>
<td>961 (41.7)</td>
<td>6734 (8.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypothyroidism requiring treatment (%)</td>
<td>159 (6.9)</td>
<td>1573 (20.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Time of TSH check</td>
<td>2 [1-175]</td>
<td>5 [1-28]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of TSH follow up (days)</td>
<td>258.00 (9-4999)</td>
<td>1992.00 (1-5230)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Baseline TSH Level (μU/mL)</td>
<td>1.76 [0.01-110.8]</td>
<td>1.74 [0.01-735.7]</td>
<td>0.137</td>
</tr>
<tr>
<td>4.5 (%)</td>
<td>170.7 (4)</td>
<td>4051 (5.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>10 (%)</td>
<td>22.0 (1)</td>
<td>365 (0.5)</td>
<td>0.003</td>
</tr>
<tr>
<td>TSH in follow up</td>
<td>378 (16-42)</td>
<td>11099 (14-22)</td>
<td>0.003</td>
</tr>
<tr>
<td>4.5 (%)</td>
<td>85 (3.7)</td>
<td>1228 (1.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Supplementation Treatment (%)</td>
<td>129 (5.6)</td>
<td>718 (9.9)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 2. Multivariate analysis in RD patients

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Adjusted HR [95%CI]</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.01 [1.00-1.03]</td>
<td>0.047</td>
</tr>
<tr>
<td>ANA 80</td>
<td>1.91 [1.19-3.06]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cre</td>
<td>1.78 [1.13-2.80]</td>
<td>0.013</td>
</tr>
<tr>
<td>Baseline TSH</td>
<td>1.12 [1.10-1.15]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Baseline TPO-Ab or Tg-Ab</td>
<td>2.21 [1.25-3.93]</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Conclusion: Hypothyroidism with therapeutic indication is more frequent in RD patients, even if screening TSH is within normal range. We encourage active routine measurement of thyroid function tests in patients with RD, especially with above risk factors.

REFERENCES

Disclosure of Interests: Sho Fukui: None declared, Yukihiko Ikeda: None declared, Haruki Sawada: None declared, Mitsuji Watanabe: None declared, Ayako Koido: None declared, Rui Imai: None declared, Masei Suda: None declared, Haruyuki Yanaoka: None declared, Hisanori Shimizu: None declared, Ryoko Kutunaka: None declared, Hiromichi Tamaki: None declared, Tokutarou Tsuda: None declared, Kenichi Yamaguchi: None declared, Mitsumasa Kishimoto Consultant for: Kyowa Hakko Kirin Co., Ltd., Masato Okada: None declared


FREQUENCY OF POLYAUTOIMMUNITY IN A TERTIARY HOSPITAL

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Background: Polyautoimmunity (PAI) is the presence of more than one Autoimmune Disease (AID) in one patient. PAI have been reported in different AIDs as systemic lupus erythematosus (SLE) (33-45%), rheumatoid arthritis (RA) (13-23%), systemic sclerosis (SSc) (10-43%) or Sjögren Syndrome (SS) (32-52%). On the other hand, Multiple Autoimmune Syndrome (MAS) where three or more AIDs coexisting in one patient has been reported.

Objectives: To determine PAI frequency in the context of AIDs reported in a tertiary hospital.

Methods: Cross-sectional observational study with systematic revision of patients’ electronic clinical records with AIDs (from 2014 to 2018). We selected those patients who had two or more diagnosis of AIDs. Demographic, clinical and immunological data were collected.

Results: Of 1854 patients with AIDs, 96 (5.17%) had PAI. Mean age was 56±15 years and 93.75% were female. 7 patients from the 96 (0.4%) also had MAS.

The mean age at diagnosis of the first AID was 39.03±15.93 years and median age at diagnosis of the second AID was 48.16±15.04 years. A mean difference of 9.17±10.18 years between first and second AIDs debut was observed.

The most frequent AIDs registered are shown in table 1.

<table>
<thead>
<tr>
<th>DISEASES</th>
<th>TOTAL CASES</th>
<th>POLYAUTOIMMUNITY CASES</th>
<th>FREQUENCY (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>APS</td>
<td>70</td>
<td>23</td>
<td>32.86</td>
</tr>
<tr>
<td>SLE</td>
<td>154</td>
<td>42</td>
<td>27.27</td>
</tr>
<tr>
<td>SS</td>
<td>261</td>
<td>15</td>
<td>15.71</td>
</tr>
<tr>
<td>SSc</td>
<td>88</td>
<td>5</td>
<td>5.68</td>
</tr>
<tr>
<td>RA</td>
<td>926</td>
<td>46</td>
<td>4.97</td>
</tr>
<tr>
<td>Vasculitis</td>
<td>83</td>
<td>4</td>
<td>4.82</td>
</tr>
<tr>
<td>PsA</td>
<td>371</td>
<td>7</td>
<td>1.89</td>
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</table>

Table 3. Frequency of Polyautoimmunity by diseases

Conclusion: A 5.17% frequency of patients with PAI in our group of AID diseases in PAI cases were RA-SS, APS-SLE and SS-SLE. We also observed the coexistence of a MAS in 0.4% of patients.

REFERENCES
found a rather lower frequency compared with those published in the literature, possibly due to the putative bias of retrospective studies and the geographical differences of PAI patients.

Disclosure of Interests: None declared

SAT0613 CHANGING TREATMENTS AND OUTCOMES FOR JUVENILE IDIOPATHIC ARTHRITIS: INITIAL FINDINGS FROM A NEW CANADIAN INCEPTION COHORT
Jaime Guzman, Michelle Battish, Roberta Berard, Roxana Bolaria, David Cabral, Gaëlle Chédeville, Ciaran Duffy, Kerstin Gerhold, Tommy Gerschman, Adam Huber, Jean-Philippe Proulx-Gauthier, Alan Rosenberg, Dax Rumsey, Heinrike Schmeling, Natalie Shiff, Gordon Soon, Lori Tucker. Canadian Alliance of Pediatric Rheumatology Investigators, Vancouver, Canada

Background: Treatments for juvenile idiopathic arthritis (JIA) are changing rapidly. Healthcare providers and families require up-to-date knowledge of current treatment practices and expected outcomes to inform their decisions.


Methods: A new investigator-driven Canadian Alliance of Pediatric Rheumatology Investigators (CAPRI) JIA Registry was started in February 2017 to prospectively collect information on children enrolled within 3 months of JIA diagnosis. Information about disease activity, treatments, outcomes and adverse events is collected at all clinic visits. Registry data were extracted in October 2018 and clinical characteristics at presentation, use of anti-rheumatic medications, attainment of inactive disease, cJADAS10 scores and adverse events were described. Selected findings were compared to those observed in the ReACCh-Out cohort. The proportion of patients (cumulative incidence) receiving various treatments and their outcomes were estimated with Kaplan Meier survival methods.

Results: A total of 166 patients enrolled a median of 6 weeks after diagnosis at 10 centres were included. Median age at diagnosis was 9 years (IQR 3, 13), 61% were female and 51% had oligoarthritis. At enrolment, subjects had a median of 2 active joints (IQR 1, 3), a Physician Global Assessment of 3 (1.5, 4) and a Parent Global Assessment of 1 (0, 3). The median cJADAS10 score was 6.5 (4, 10). Table 1 compares baseline characteristics and the cumulative incidence of medication use and inactive disease at one year after diagnosis with those observed in the ReACCh-Out cohort, diagnosed on average 10 years earlier. Figure 1 shows the Kaplan Meier curves for attainment of inactive disease.

Conclusion: In Canada, treatments for newly diagnosed patients with JIA have intensified in the last 10 years, and 35% will now start their first biologic within 1 year of diagnosis. Short-term outcomes have improved, 81% of current patients now attaining inactive disease within one year of diagnosis. Funding: The Arthritis Society, Canada.

REFERENCES

Figure 1. Time to inactive disease across Canada in the new CAPRI cohort (2017-2018) and the ReACCh-Out cohort (2005-2010)

Table 1:

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Previously reported ReACCh-Out findings</th>
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<td>Age at diagnosis (median (25th, 75th centiles))</td>
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<td></td>
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<tr>
<td>Female sex (%)</td>
<td>64</td>
<td>61</td>
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<tr>
<td>JIA categories (%)</td>
<td>38</td>
<td>51</td>
</tr>
<tr>
<td>Oligoarthritis</td>
<td>21</td>
<td>14</td>
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<tr>
<td>RF-negative polyarthritis</td>
<td>14</td>
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<tr>
<td>Enthesitis-related arthritis</td>
<td>7</td>
<td>5</td>
</tr>
<tr>
<td>Systemic arthritis</td>
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<td>5</td>
</tr>
<tr>
<td>Psoriatic arthritis</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>RF-positive polyarthritis</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Undifferentiated</td>
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</tr>
<tr>
<td>Active joint count at enrolment</td>
<td>3 (1, 7)</td>
<td>2 (1, 3)</td>
</tr>
<tr>
<td>PGA at enrolment</td>
<td>3 (1.7, 5.2)</td>
<td>3 (1.4, 4.0)</td>
</tr>
<tr>
<td>CUMULATIVE INCIDENCE 1y AFTER DIAGNOSIS:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Started a NSAID (%) (95% CI)</td>
<td>&gt;88</td>
<td>96 (90-99)</td>
</tr>
<tr>
<td>Received a joint injection</td>
<td>37</td>
<td>59 (49-69)</td>
</tr>
<tr>
<td>Started a first DMARD</td>
<td>48</td>
<td>70 (58-81)</td>
</tr>
<tr>
<td>Started a biologic medication</td>
<td>5</td>
<td>35 (21-55)</td>
</tr>
<tr>
<td>Started systemic corticosteroids</td>
<td>20</td>
<td>25 (18-35)</td>
</tr>
<tr>
<td>Attained inactive disease</td>
<td>45</td>
<td>81 (71-90)</td>
</tr>
<tr>
<td>PGA at enrolment</td>
<td>5 (0.9, 13)</td>
<td>9 (6, 13)</td>
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<tr>
<td>PGA at 1 year</td>
<td>3 (1.7, 5.2)</td>
<td>3 (1.4, 4.0)</td>
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Acknowledgement: Funding: The Arthritis Society, Canada.

Disclosure of Interests: Jaime Guzman: None declared, Michelle Battish: Speakers bureau: Novartis, Abbvie, Roberta Berard: None declared, Roxana Bolaria: None declared, David Cabral: None declared, Gaëlle Chédeville: None declared, Ciaran Duffy: None declared, Kerstin Gerhold: None declared, Tommy Gerschman: None declared, Adam Huber: None declared, Jean-Philippe Proulx-Gauthier: None declared, Alan Rosenberg: None declared, Dax Rumsey: None declared, Heinrike Schmeling: Grant/research support from: F. Hoffmann-La Roche Ltd, Natalie Shiff: None declared, Gordon Soon: None declared, Lori Tucker: None declared

SAT0614 DOES DRUG EFFECTIVENESS OF 2ND AND 3RD TNF INHIBITORS IN PATIENTS WITH PSORIATIC ARTHRITIS DEPEND ON THE REASON FOR WITHDRAWAL FROM THE PREVIOUS TREATMENT? – RESULTS FROM THE EUROSPA RESEARCH COLLABORATION
Cecile Heegaard Bråth1, Lykke Ømbjerg1, Lennart T.H. Jacobsson2, Michael Nissen1, Eirik Kristianslund3, Helmaan Mann1, Maria Jose Santos1, Manuel Pombo-Suarez1, Dan Nordström1, Ziga Rotar1, Björn Gudbjornsson1, Ediz Dakili1, CataloniaCODEan1, Anne Gitte Loft1, Ulf Lindström1, Burkhard Moeller2, Joe Sexton1, Karel Pavek1, Anabela Barcelos1, Carlos Sánchez-Piedra1, Karl Eklund1, Malija Tomić1, Thovardur Jon Love1, Ismaili Sari1, Ruxandra Ionescu1, Marleen van de Sande1, Irene van der Horst-Bruinsma1, Gareth T. Jones1, Florenzo Iannone1, Brigitte Michelsen1, Lisa Hyldstrup1, Niels Steen Krogh1, Mikkel Stergaard1, Merete L. Heiland1

1EuroSpA Research Collaboration, On behalf of the DANBIO (Denmark), ARTIS (Sweden), SCQM (Switzerland), NOR-DMARD (Norway), ATTRA (Czech Republic), Reuma.pt (Portugal), BIOBADASER (Spain), ROB-FIN (Finland), biorx.si (Slovenia), ICEBIO (Iceland), TURKBIO (Turkey), RRBR (Romania), ARC (Netherlands), BSRBR-AS (United Kingdom), GISEA (Italy), Denmark

Background: Tumour necrosis factor inhibitors (TNFi) are efficacious in patients with psoriatic arthritis (PsA), but some patients switch to a different TNFi because of adverse events (AE) or lack of effect (LDE). The EuroSpA Collaboration has previously demonstrated a 1-year retention rate of 77% and 6 months LUNDEX adjusted 28-joint count Disease Activity Score (DAS28) remission rates of 45% in patients with PsA initiating the first TNFi treatment. Little is known about the effectiveness of switching to a second and third TNFi in patients with PsA.

Objectives: Firstly, to investigate retention and remission rates at 6, 12 and 24 months in patients with PsA initiating the 2nd and 3rd TNFi in clinical practice across Europe. Secondly, to investigate whether the outcomes are associated with the reason for withdrawal (AE or LDE) from the previous TNFi-treatment.

Methods: Prospectively collected data on PsA patients in routine care from 12 European registries were included. Kaplan-Meier estimation was used to investigate TNFi retention rates. LUNDEX adjusted remission rates were calculated for DAS28<2.6 and 28 joint Disease Activity index

<table>
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Acknowledgement: Funding: The Arthritis Society, Canada.

Disclosure of Interests: Cecile Heegaard Bråth: None declared, Lykke Ømbjerg: None declared, Lennart T.H. Jacobsson: None declared, Michael Nissen: None declared, Eirik Kristianslund: None declared, Helmaan Mann: None declared, Maria Jose Santos: None declared, Manuel Pombo-Suarez: None declared, Dan Nordström: None declared, Ziga Rotar: None declared, Björn Gudbjornsson: None declared, Ediz Dakili: None declared, CataloniaCODEan: None declared, Anne Gitte Loft: None declared, Ulf Lindström: None declared, Burkhard Moeller: None declared, Joe Sexton: None declared, Karel Pavek: None declared, Anabela Barcelos: None declared, Carlos Sánchez-Piedra: None declared, Karl Eklund: None declared, Malija Tomić: None declared, Thovardur Jon Love: None declared, Ismaili Sari: None declared, Ruxandra Ionescu: None declared, Marleen van de Sande: None declared, Irene van der Horst-Bruinsma: None declared, Gareth T. Jones: None declared, Florenzo Iannone: None declared, Brigitte Michelsen: None declared, Lisa Hyldstrup: None declared, Niels Steen Krogh: None declared, Mikkel Stergaard: None declared, Merete L. Heiland: None declared.

The overall retention rates for 2nd and 3rd TNFi at 12 months were 69% (67-70%) and 66% (64-68%), (2nd vs 3rd p=0.053), respectively (Figure). Corresponding retention rates for the individual registries ranged from 48-100% and 49-91%, respectively. If patients had stopped the 1st TNFi due to AE or LOE, 12-month retention rates for the 2nd TNFi treatment were 66% and 65%, respectively. In patients who stopped the 2nd TNFi due to AE or LOE, 12-month retention rates for the 3rd TNFi treatment were 65% and 63%, respectively.

For the 2nd and 3rd TNFi, 6 months LUNDEX adjusted DAS28 remission rates were 35% and 27% (p<0.001), respectively, and for DAPSA28 remission 14% and 10% (p=0.008) (Table).

Conclusion: The EuroSpA Collaboration demonstrated decreasing retention and remission rates with increasing number of previous TNFi, although with only minor difference between 2nd and 3rd. Patients who had withdrawn from the previous TNFi due to LOE had retention rates and remission rates similar to those who had withdrawn due to AE.

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Have received research grant (current) from the British Society for Rheumatology, who received the funds from Celgene., Florence Iannone Consultant for: F Iannone has received consultancy fees and/or speaker honoraria from Pfizer, AbbVie, MSD, BMS, Novartis, Lilly, UCB outside this work, Speakers bureau: F Iannone has received consultancy fees and/or speaker honoraria from Pfizer, AbbVie, MSD, BMS, Novartis, Lilly, UCB outside this work, Brigitte Michelsen: None declared, Nils Steen Krogh: None declared, Mikkel Stergaard Consultant for: Abbvie, Celgene, Centocor, Merck, Novartis, Consultant for: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, Speakers bureau: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron, Roche, and UCB, Merete L. Hetland Consultant for: BMS, Abbvie, Roche, Novartis, Biogen, Pfizer, Consultant for: Eli Lilly, Speakers bureau: Orion Pharma, Biogen, Pfizer, CellTrion, Merck, Samsung Bioepis


for Psoriatic Arthritis (DAPSA28) c4. Group comparisons were performed by Chi-square test.

Results: A total of 4971 patients initiating their 2nd TNFi and 1768 patients initiating their 3rd TNFi were included. Baseline characteristics are shown in the Table.
THE DIFFERENT EFFECTS OF CIGARETTE SMOKING ON ANTI-CITRULLINATED CYCLIC PROTEIN ANTIBODY AND RHEUMATOID FACTOR FORMATION IN RELATION TO SHARED EPITHE AL ALLELES IN JAPANESE RA PATIENTS

Yuki Ishikawa1, Katsunori Ikari2, Motomu Hashimoto3, Koichiro Ohmura4, Masao Tanaka5, Hiromi Itō6, Atsuo Taniguchi2, Hisashi Yamanaka2, Tsuneo Mimori7, Chikashi Terao7.

1 Joslin Diabetes Center, Harvard Medical School, Immunology, Boston, United States of America; 2Tokyo Women's Medical University, Institute of Rheumatology, Tokyo, Japan; 3Graduate School of Medicine, Kyoto University, Department of Advanced Medicine for Rheumatic Diseases, Kyoto, Japan; 4Graduate School of Medicine, Kyoto University, Department of Rheumatology and Clinical Immunology, Kyoto, Japan; 5Graduate School of Medicine, Kyoto University, Department of Orthopaedic Surgery, Kyoto, Japan; 6RIKEN, Center for Investigative Medical Sciences, Yokohama, Japan; 7Shizuoka General Hospital, Clinical Research Center, Shizuoka, Japan. The School of Pharmaceutical Sciences, University of Shizuoka, Department of Applied Genetics, Shizuoka, Japan

Background: In rheumatoid arthritis (RA), cigarette smoking affects both rheumatoid factor (RF) and anti-citrullinated cyclic peptide/protein antibody (ACPA) formation, but its association related to HLA-DRB1 alleles, especially shared epitope (SE) alleles, have been controversial among different races. Furthermore, the impact of cigarette smoking and its cessation on levels of RF and ACPA have not been well documented.

Methods: A total of 6,239 subjects from two independent Japanese cohorts were enrolled. Their precise smoking histories both before and after the onset of RA were collected in questionnaires. The latest RF and ACPA levels were used (mean disease duration 15.6 years). We defined top quadrant of levels of RF or ACPA as high levels. Associations between smoking status and positivities or high levels of ACPA or RF as well as effects of HLA-DRB1 alleles on the associations were investigated by multiple logistic regression models.

Results: Smoking at onset was an independent risk factor of not only RF and ACPA, odds ratios (OR) 1.31, 95% CI 1.22-1.41, but also high levels of these autoantibodies, especially RF (OR 2.06, 95% CI 1.26-1.85, p = 1.8 x 10^-5; ACPA, OR 1.39, 95% CI 1.09-1.76, p = 6.8 x 10^-3), but their odds ratios decreased over time. The risk of RF positivity and its high level was apparent only in the presence of SE alleles (Table below).

Conclusion: Cigarette smoking especially at RA onset is a significant risk factor of future high levels of ACPA and RF preferentially in males, and RF is more sensitive to smoking status than ACPA. The effect of cigarette smoking was significantly larger in males than in females. The patients who quit smoking before onset had no longer significant risks of high autoantibody levels compared to subjects who had never smoked (RF, OR 1.33, p = 0.059; ACPA, OR 1.19, p = 0.013) and the risk was gradually attenuated depending on cessation years (RF, 0-10 years OR 1.34, 10-20 years OR 1.21, > 20 years OR 1.06; ACPA, 0-10 years OR 1.38, 10-20 years OR 1.01, > 20 years OR 1.12). The effect of smoking on ACPA positivity and its high level was apparent only in the presence of SE alleles, while the effect on RF positivity and its high level was apparent despite the presence of SE alleles (Table below).

DIETARY HABITS OF SIX AUTOIMMUNE DISEASES IN THE SPANISH POPULATION: A CROSS-SECTIONAL STUDY

Antonio Juliá1, Sergio Hilario Martínez2, Jesús Tomero3, Juan D. Cañete4, Antonio Fernando Nebro5, Francisco Blanco6, Jesús Rodríguez7, Francisco J. López-Longo8, Íñigo Fernández-Quitrid9, Jordi Gratacos10, José Javier Pérez Venegas11, Carolina Pérez12, Rubén Quiroga Silva13, Alejandro Oliver14, Mercedes Alperó-López15, Carlos A. Montilla-Morales16, Jose Luis Andreu17, Juan Carlos Toro-Alonso18, M. Angélica Aquínez-Zamorano19, Hector Cornominas20, Paloma Vela-Casasempere21, Victor Martínez Taboada22, Sara Manrique Arija23, Joan Miquel Nolla24, Isidoro González-Álvaro1, Antonio Zea25, Marta López Lasarta26, Daniel Roig27, Jose M. Pego-Reigosa28, Mireia Lopez Cortet29, Pedro Zarco-Monfort30, Mercedes Freire Gonzalez31, Alba Era32, Elvira Diez Alvarez33, Santos Castañeda24, Esther Rodriguez Almarza34, Alicia García35, Patricia Carreira36, Georgina Salvador Alarcon37, Cesar Diaz Torre38, Ricardo Blanco39, Alfredo Willich Dominguez40, José Antonio Mosquera Martínez41, Simon Sánchez Fernández42, Julio Ramírez43, Sara Marseal44, Maire Gabaldon45, Humke Van Hebrón46, Barcelona, Spain; 47Guadalajara, Guadalajara, Spain; 48H Clinic, Barcelona, Spain; 49Málaga, Málaga, Spain; 50A Coruña, La Coruña, Spain; 51Bellvitge, Barcelona, Spain; 52Madrid, Madrid, Spain; 53San Carlos, Madrid, Spain; 54Virgen Macarena, Sevilla, Spain; 55Virgen del Mar, Barcelona, Spain; 56Asturias, Oviedo, Spain; 57HJUGTP, Badalona, Barcelona, Spain; 58H Salamanca, Salamanca, Spain; 59Puerta de Hierro, Madrid, Spain; 60H Monte Narón, A Coruña, Spain; 61H Reina Sofia, Córdoba, Spain; 62Moisés Broggi, Sant Joan Despi, Barcelona, Spain; 63Hyal, Alicante, Alicante, Spain; 64Marqués Valdecilla, Santander, Spain; 65H La Princesa, Madrid, Spain; 66H Infanta Sofia, Madrid, Spain; 67Virgen Valme, Seville, Spain; 68H Ramón y Cajal, Madrid, Spain; 69FHI Alcorcon, Madrid, Spain; 70H León, Leon, Spain; 71H 12 Octubre, Madrid, Spain; 72CS Virgen de los Reyes, Seville, Spain; 73H M Terrassa, Terrassa, Barcelona, Spain; 74H Sant Pau, Barcelona, Spain; 75CH Ourense, Orense, Spain; 76CHP Pontevedra, Pontevedra, Spain; 77H La Mancha, Ciudad Real, Spain

Background: In the last years multiple genetic variants have been associated with autoimmune disease (AD) risk. However, much less is known about the association with important environmental factors like diet.

Objectives: The objective of the present study is to characterize the dietary patterns of six prevalent ADs, including rheumatoid arthritis (RA), psoriatic arthritis (PsA) and systemic lupus erythematosus (SLE).

Methods: A cross-sectional cohort of 11,621 individuals from Spain encompassing 1,949 RA, 2,186 Psoriasis (PS), 1,437 PsA, 699 SLE, 1,415 ulcerative colitis (UC), 1,952 Crohn’s disease (CD) and 1,983 atopic dermatitis (AD) cases were recruited. Together with presenting demographic data, lifestyle factors and smoking status, lifestyle factors were grouped into comprehensive dietary patterns using a novel approach combining multiple linear regression analyses to identify a few groups among 116 available dietary variables. The resulting dietary patterns were tested for association with disease status using multivariate linear models.

Results: Patients with AD targeting the digestive system showed the largest differences in comparison to controls. In the rheumatic ADs several food categories were also found to be consumed differently compared to controls. In PsA the dietary pattern differences with controls

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PROGRESSION IN RHEUMATOID ARTHRITIS INFLAMMATORY BURDEN ON CORONARY PLAQUE ANTIBODIES MODERATES THE EFFECT OF

Antonio Julià1, Sergio Hilario Marín2, Marc'el Reinert3, Daniel Roig4, Carmen Gómez1, Ana Bolaños5, Miguel A. Carrasco1, Antonio Julià1, Sergio Hilario Marín2, Marc’el Reinert3, Daniel Roig4, Carmen Gómez1, Ana Bolaños5, Miguel A. Carrasco1

Background: Beta2-glycoprotein-1 (b2GPI), an apolipoprotein abundant in human plasma, is readily expressed in human atherosclerotic plaques. High frequencies of anti-b2GPI-IgA antibodies have been previously reported in both Rheumatoid arthritis (RA) patients and controls; their presence has been independently predictive of cardiovascular events in general populations.

Objectives: We explored the role of a-b2GPI-IgA presence and their interaction with inflammatory load on occult coronary plaque progression in patients with RA.

Methods: One hundred-one participants with a baseline plaque evaluation with coronary computed tomography angiography (CCTA) underwent follow-up assessment within 23±3.6 months. Coronary artery calcium (CAC) was quantified by the Agatston method. Subclasses (IgG, IgM, and IgA) of a-b2GPI Ab, antiradiliprotein-Ab (ACL) and lupus anticoagulant (LA) were assessed on the day of baseline CCTA and reconfirmed 12 weeks later, if positive. Serum interleukin-6 (IL-6) was measured at baseline scan, while CRP was assessed on every clinic visit from baseline through follow-up scan. Multivariate linear regression models evaluated predictors of CAC progression; predictors entered as continuous variables included baseline CAC, age, waist-to-height ratio (obesity index), cumulative prednisone dose, years exposure to bDMARDs, statins and baseline IL-6 or time-averaged CRP. Gender, diabetes, hypertension, dyslipidemia, and a-b2GPI-IgA positivity were entered as dichotomous independent variables. Specific interactions between a-b2GPI-IgA presence (predictor) and time-averaged CRP or baseline IL-6 (moderator) where explored; the conditional effects of the predictor at values of the moderator and significant CAC regions were defined with the John-Neyman test.

Results: A-b2GPI-IgA antibodies were highly prevalent (34.7%) in contrast to other antiphospholipid-Ab subclasses (<4%). A-b2GPI-IgA presence predicted incident CAC [OR=3.69 (1.02-13.32), p=0.046] as well as greater CAC change from baseline, after adjustments for age, baseline CAC score and significant covariates [mean change (95%CI) = 93.2 (69.8-116.6) vs. 56.0 (39.0-73.0) units, p=0.012]. A significant interaction between a-b2GPI-IgA positivity and time-averaged CRP as well as baseline IL-6 on CAC progression was observed [beta=-0.19, p=0.048 for time-averaged CRP and beta=-0.26, p=0.029 for IL-6 respectively]; higher baseline IL-6 and time-averaged CRP associated with significant CAC progression exclusively in a-b2GPI-IgA positive patients but not in negative ones (figure 1).

Conclusion: A-b2GPI-IgA antibodies independently contributed to occult coronary plaque progression in RA and specifically moderated the effect of inflammation on progression of atherosclerotic burden. Tight control of inflammation may be particularly important in Ab positive patients in order to prevent coronary plaque progression; additionally, a-b2GPI-IgA presence may serve as a predictive biomarker for atherosclerosis progression, especially in the context of higher inflammatory state.


SA0618 BASELINE CHARACTERISTICS AND TREATMENTS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS: THE CREDIT STUDY IN CHINA, 2016-2018

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Background: Rheumatoid Arthritis (RA) has been a huge public health issue among the Chinese population, but little is known about the current treatments among RA patients, especially with different disease activity levels.

Objectives: To describe the baseline characteristics among all RA patients registered in the Chinese Registry of rhEumatoID arthritis (CRedit) and the treatment patterns by patients’ disease status.

Methods: A total of 25,191 RA patients registered in CREDIT from Nov, 2016 to Apr, 2018 were enrolled. Patients’ baseline characteristics of demographics, disease characteristics, comorbidities, as well as treatment agents for RA were abstracted for analysis.

Results: The mean age of patients was 53.0 years and 79.9% of them were female. The median disease duration from diagnosis was 2.0 years. The proportions of moderate/high disease activity according to the Disease Activity Score 28 (DAS28-CRP<3.2) and Clinical Disease Activity Index (CDAI>10) were 76.1% and 87.1%, respectively. Among those patients with treatment records, a similar conventional systematic disease-modifying antirheumatic drugs (cDMARDs) usage was observed in remission/low activity patients and

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SA0617 PRESENCE OF ANTI-BETA2-GLYCOPROTEIN-1 IG A ANTIBODIES MODERATES THE EFFECT OF INF LAMMATORY BURDEN ON CORONARY PLAQUE PROGRESSION IN RHEUMATOID ARTHRITIS

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Background: Beta2-glycoprotein-1 (b2GPI), an apolipoprotein abundant in human plasma, is readily expressed in human atherosclerotic plaques. High frequencies of anti-b2GPI-IgA antibodies have been previously reported in both Rheumatoid arthritis (RA) patients and controls; their presence has been independently predictive of cardiovascular events in general populations.

Objectives: We explored the role of a-b2GPI-IgA presence and their interaction with inflammatory load on occult coronary plaque progression in patients with RA.

Methods: One hundred-one participants with a baseline plaque evaluation with coronary computed tomography angiography (CCTA) underwent follow-up assessment within 23±3.6 months. Coronary artery calcium (CAC) was quantified by the Agatston method. Subclasses (IgG, IgM, and IgA) of a-b2GPI Ab, antiradiliprotein-Ab (ACL) and lupus anticoagulant (LA) were assessed on the day of baseline CCTA and reconfirmed 12 weeks later, if positive. Serum interleukin-6 (IL-6) was measured at baseline scan, while CRP was assessed on every clinic visit from baseline through follow-up scan. Multivariate linear regression models evaluated predictors of CAC progression; predictors entered as continuous variables included baseline CAC, age, waist-to-height ratio (obesity index), cumulative prednisone dose, years exposure to bDMARDs, statins and baseline IL-6 or time-averaged CRP. Gender, diabetes, hypertension, dyslipidemia, and a-b2GPI-IgA positivity were entered as dichotomous independent variables. Specific interactions between a-b2GPI-IgA presence (predictor) and time-averaged CRP or baseline IL-6 (moderator) where explored; the conditional effects of the predictor at values of the moderator and significant CAC regions were defined with the John-Neyman test.

Results: A-b2GPI-IgA antibodies were highly prevalent (34.7%) in contrast to other antiphospholipid-Ab subclasses (<4%). A-b2GPI-IgA presence predicted incident CAC [OR=3.69 (1.02-13.32), p=0.046] as well as greater CAC change from baseline, after adjustments for age, baseline CAC score and significant covariates [mean change (95%CI) = 93.2 (69.8-116.6) vs. 56.0 (39.0-73.0) units, p=0.012]. A significant interaction between a-b2GPI-IgA positivity and time-averaged CRP as well as baseline IL-6 on CAC progression was observed [beta=-0.19, p=0.048 for time-averaged CRP and beta=-0.26, p=0.029 for IL-6 respectively]; higher baseline IL-6 and time-averaged CRP associated with significant CAC progression exclusively in a-b2GPI-IgA positive patients but not in negative ones (figure 1).

Conclusion: A-b2GPI-IgA antibodies independently contributed to occult coronary plaque progression in RA and specifically moderated the effect of inflammation on progression of atherosclerotic burden. Tight control of inflammation may be particularly important in Ab positive patients in order to prevent coronary plaque progression; additionally, a-b2GPI-IgA presence may serve as a predictive biomarker for atherosclerosis progression, especially in the context of higher inflammatory state.

SAT0619 ATTITUDES AND PERCEPTIONS OF PHYSICAL ACTIVITY IN PATIENTS WITH SPONDYLOARTHRITIS: A SYSTEMATIC REVIEW

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Background: Patients with arthritis are less likely to adhere to physical activity recommendations than are individuals in the general population. In contrast to rheumatoid arthritis (RA), which affects predominantly peripheral joints, axial spondyloarthritis (axSpA) affects predominantly the axial skeleton and may result in restricted spinal mobility. Both RA and axSpA are associated with an increased risk of cardiovascular disease, the development of physical disability, and decreased levels of physical activity. However, the extent to which the distinct joint distributions in these forms of inflammatory arthritis might differentially affect physical activity behaviors is not known. Several studies have addressed the relationship between “physical activity behavior” and “disease-specific outcomes” among patients with RA, but information about this among patients with axSpA is more limited.

Objectives: To review systematically and synthesize qualitatively the literature about perceived facilitators and barriers to physical activity in patients with axSpA and identify the types of physical activity preferred by these patients.

Methods: PubMed and Scopus and reference lists were searched for quantitative and qualitative studies reporting on beliefs towards exercise activity among patients with axSpA. Searches were limited to studies published from 2000 through 2018. The PRISMA guidelines were followed. Systematic searches identified 125 publications which underwent a title, abstract, or full-text review. Studies were excluded if articles were not in English or did not include original data. We summarized the methodologic quality using modified criteria for quantitative and qualitative studies.

Results: Eight quantitative and three qualitative studies met eligibility criteria, with variable study quality. Based on self-reported data, 50% to 68% of patients with axSpA have engaged in swimming or water exercise, while most common forms reported, intrinsic factors such as motivation and improvement in symptoms and health were commonly reported as facilitators associated with physical activity/exercise. Barriers included lack of time, fatigue, and symptoms such as pain.

Conclusion: Up to half of patients with axSpA do not meet established physical activity recommendations. Given the potential for regular physical activity to reduce symptom burden in this patient population and the recent 2018 EULAR recommendations for regular physical activity as part of the management of these patients, more rigorous studies of physical activity behaviors and attitudes will be useful to inform interventions and promote exercise among individuals with axSpA.

REFERENCES

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SAT0620 INCIDENCE AND TREND OF HIP FRACTURE IN SPAIN, FACTORS ASSOCIATED WITH THE VARIABILITY OBSERVED

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Background: It is known that in Spain there is a great variability between Autonomous Communities (CCAA) in the incidence and trend of hip fracture, with rates in certain regions that can double those of others. Although it is speculated with different hypotheses that explain it, there are no studies that demonstrate the reasons for this variability.

Objectives: 1.- To analyze the incidence and trend of hospital admissions for hip fracture, in Spain, during the period between 1999 and 2015. 2.- Analyze factors/risk markers (genetic, demographic, level and living conditions, health indicators, cohort effect centered on the period of the civil war, climatology and environment) that could explain the variability in incidences and trend between different CCAA.

Methods: Part 1: retrospective observational study, nationwide, based on the exploitation of an administrative database (MBDS) that collects hospital admissions from 1/1/1999 to 12/31/2015. Hip fractures were identified through the presence of ICD-9-CM 820.0 to 820.9 as primary or secondary diagnosis. Only those that the patient was 50 or older were selected. The crude rates and adjusted for age of incidence of hip fracture were calculated, by sex, age groups and by CCAA. The population census issued by the National Institute of Statistics (INE) was used to calculate this rate. The trend over the 17 years covered in the study was analyzed using Poisson regression and negative binomial models.

Part 2: ecological study, based on the analysis of the results obtained in part 1, with different risk markers obtained from the INE (except the 4), by CCAA. The analyzed factors were: 1.- Genetic; 2.- Demographic; 3.- Level and conditions of life; 4.- Health; 5. Impact of the civil war. 6.- Environment; 7.- Climatological. This analysis was performed using bivariate correlations and univariate and multivariate linear regression.

Results: There were 744,848 patients diagnosed with hip fracture: 182,205 (24.4%) men and 562,643 (75.5%) women p <0.001. (Ratio M: V of 3.07). The mean age was 81.7 years (SD 8.9), 79.3 years (SD 10.3) in men and 82.5 years (SD 8.2) (p <0.001). In-hospital mortality was 27%. The average of the Charlson Index was 0.71 (SD1.14). The rate adjusted for the age of incidence of global hip fracture at the national level was 315.38/100,000 inhabitants * year (95% CI 312.36-317.45), 196.59 (95% CI 166.26-172.39) in men and 434.89 (95% CI 430.66-438.17) in women. By CCAA the incidence of hip fx varied from 213.97 in the Canary Islands to 363.13 in Comunidad Valenciana and Cataluña.

The trend for both sexes was -0.67% (95% CI 0.9990-0.9957) (p <0.001); in men it was -0.06% (95% CI 0.9975-1.0013) (p = 0.537) and
Impact of hindfoot coronal/sagittal alignment on metatarsus primus elevatus in rheumatoid foot deformities

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Background: Typical foot deformity patterns of patients with rheumatoid arthritis (RA) include hallux valgus, claw toes, splay foot, flat foot, and hindfoot valgus deformities. However, some patients show deformities different from a typical pattern, including metatarsus primus elevatus, described as dorsal elevation of the first metatarsal in relation to the lesser metatarsals, as we reported previously. In the report, we speculated that metatarsus primus elevatus might be associated with calcaneal inclination and hindfoot varus alignment. However, there are no studies on the association of hindfoot alignment with metatarsus primus elevatus in patients with RA.

Objectives: To elucidate the impact of hindfoot coronal/sagittal alignment on metatarsus primus elevatus in patients with RA.

Methods: A retrospective study was performed of standing anteroposterior and lateral radiographs of 81 feet in 53 patients who underwent surgical treatment for metatarsalgia in our hospital. The distance between the dorsal cortical bones of the first and second metatarsals (MPE) was measured using a two-dimensional coordinate system on the lateral radiographs of 81 feet in 53 patients who underwent surgical treatment for metatarsalgia in our hospital. The distance between the dorsal cortical bones of the first and second metatarsals (MPE) was measured.

Results: Median MPE was 1.7 mm (interquartile range: 0-5.2 mm). The first metatarsal head, first metatarsal-cuneiform and posterior talocalcaneal joint were shifted dorsally (r=0.70, p<0.01; r=0.57, p=0.01; r=0.42, p=0.01, respectively). No correlation MPE with HVA and M1M5A were observed (r=-0.26, p=0.05; r=-0.25, p=0.07, respectively), however, M1M2A showed correlation with MPE (r=0.52, P<0.01). On the other hand, MPE showed a high degree of correlation with talar declination angle, calcaneal pitch, and NC overlap ratio (r=0.45, p<0.01; r=0.35, p=0.01; r=-0.45, p=0.01, respectively).

Conclusion: In patients with RA, the hindfoot joints shifted dorsally in metatarsus primus elevatus. Moreover, hindfoot varus alignment and high-arched foot affect metatarsus primus elevatus. The results of the present study suggest the importance of evaluating hindfoot alignment when determining surgical treatment procedures for rheumatoid foot deformities.

Disclosure of Interests: None declared


References


SERUM URIC ACID LEVELS WERE INDEPENDENTLY ASSOCIATED WITH AORTIC ARCH CALCIFICATION IN MIDDLE-AGED AND ELDERLY CHINESE POPULATION

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Disclosure of Interests: None declared, Carlomaurizio Montecucco Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Roche, Genzyme, Lilly, MSD, Pfizer. UCB, Vittorio Grosso: None declared, Barbara Vitolo: None declared, Silvana Quaglini: None declared, Carlon-switzerland Montecucco Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Roche, Genzyme, Lilly, MSD. Pfizer. UCB, Vittorio Grosso: None declared.

Background: Aorta calcification are considered markers of subclinical atherosclerotic disease that are independent predictors of subsequent cardiovascular events. A growing number of studies have shown that serum uric acid is associated with the development of cardiovascular diseases.

Objectives: The main purpose of this study was to investigate the prevalence of aortic calcification and to determine the relationship between the levels of serum uric acid and aorta calcification in the middle-aged and elderly population.

Methods: From Jan 2018 to Dec 2018, totally 6152 consecutive participants aged ≥50 years old underwent annual health survey were included in this study. Detailed physical examination was performed as well as a thorough review from structured questionnaires, which in baseline demographics and medical history including alcohol consumption, smoking and physical activity status, BMI, blood pressure, blood glucose and serum lipid were all collected and recorded. Aortic calcification was analyzed by chest X-ray. All data were analyzed retrospectively.

Results: The prevalence of aortic arch calcification was 13.9% in these 6152 participants with age >50 years and was equally common in men and women. Aortic arch calcification prevalence was significantly increased in populations with hyperuricemia (defined as serum uric acid ≥ 420 umol/L), as compared with populations with normal serum uric acid levels (defined as serum uric acid ≤ 420 umol/L) (83.39% vs. 16.61%, p < 0.001). Participants were divided into three groups according to their uric acid levels: A more prevalent aortic arch calcification was identified in high uric acid level group than those in middle or low uric acid level group (p < 0.05). On logistic regression analysis, serum uric acid levels were found to be independently associated with aortic calcification (OR=1.469, 95%CI: 1.199-1.800, P<0.01) in these participants.

Conclusion: Serum uric acid levels were independently associated with aortic arch calcification in middle-aged and elderly Chinese population. These results may suggest the need for more aggressive actions for urate lowering therapy in middle-aged and elderly hyperuricemia patients, especially in patients coexist with other cardiovascular disease risks.

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effects of these metabolites. Diminished metabolic diversity may be a feature of active AAV and potential biomarker to predict disease activity in AAV.

REFERENCES

Disclosure of Interests: None declared


SAT0624 VALIDATION PROCESS OF CASES OF RHEUMATOID ARTHRITIS IN A LARGE PROSPECTIVE COHORT OF FRENCH ADULT WOMEN: THE E3N COHORT

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Background: Rheumatoid arthritis (RA) is a complex multifactorial autoimmune disease in which genetic and environmental factors interact in the pathogenesis of the disease to trigger autoimmunity. Except for tobacco smoking, the role of environmental factors has been suggested yet poorly investigated, and results were rarely reproducible. More observational studies are requested to address the question. Cohort studies offer the advantage over case-control studies of having a prospective collection of environmental factors before disease onset, thus avoiding recall bias. However, collected information about disease phenotypes is usually limited, and a rigorous process of case validation is needed.

Objectives: To detect RA cases in a large prospective cohort of healthy French adult women and to assess the performance of the validation methods.

Methods: The French E3N cohort included 98,995 healthy women prospectively followed since 1990. Self-administered questionnaires were sent every 2–3 years to collect medical events, and general, lifestyle, and environmental characteristics. Potential cases of inflammatory rheumatic diseases (IRD), including RA cases, were identified through self-reports in three consecutive questionnaires. Self-reported RA cases were validated with two methods including sending of a specific validation questionnaire and the use of the reimbursement database. The sensitivities and specificities of each method were calculated using as a reference the analysis of available medical records reviewed by a panel of expert rheumatologists.

Results: Among the 3,192 identified potential IRD cases, 964 RA cases were validated, including 698 incident cases and 266 prevalent cases. Of them, 314 (32.6%) had unknown antibody status. Mean age at diagnosis was 57.4 ± 13.9 years (40.9 ± 10.4 years for prevalent cases, and 63.8 ± 9.0 for incident cases). Sensitivities and specificities of the validation methods were 92.2 and 83.7% for the specific validation questionnaire and 69.8 and 97.0% for the reimbursement database.

Conclusion: This study enabled us to detect a large number of RA cases in a large general population prospective cohort of women with acceptable sensitivity and specificity. This will allow investigating a large number of potential endogenous and exogenous risk factors of RA in women.

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SAT0625 TREATMENT RESPONSE AND DRUG RETENTION RATES IN 23,956 BIOLOGIC-NAÏVE PATIENTS WITH AXIAL SPONDYLOARTHRITIS INITIATING TNFI TREATMENT – ROUTINE CARE DATA FROM 12 REGISTRIES IN THE EUROSPA COLLABORATION

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Background: The efficacy of Tumour Necrosis Factor Inhibitor (TNFi) in patients with axial spondyloarthritis (axSpA) has been investigated in randomized controlled trials (RCTs) with strict inclusion and exclusion criteria. Patients treated in routine care are more heterogeneous and only ~20-30% of patients receiving TNFi in routine care would have been eligible to be enrolled in the RCTs. This emphasizes the need for real-world observational data as a valuable supplement to RCTs. Studying large patient groups from several European countries would increase the external validity of the results. Particularly, large data sets from patients with non-radiographic axSpA (nr-axSpA) are lacking.

Objectives: To investigate TNFi retention rates at 12 months (primary objective), 6 and 24 months, and response rates at the same time-points in biologic-naïve patients with axSpA from the EuroSpA Research Collaboration. Furthermore, to investigate if findings vary between patients with nr-axSpA and ankylosing spondylitis (AS).

Methods: Data from 12 European quality registries in rheumatology, prospectively collected in routine care, were anonymized and uploaded through the secure Virtual Private Network pipelines to the EuroSpA server. Baseline characteristics were investigated with non-parametric descriptive statistics. TNfi retention rates (Kaplan-Meier statistics), and Ankylosing Spondylitis Disease Activity Score (ASDAS) Inactive disease (<1.3) and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) ≤4 were assessed, including LUNDEX adjustment1. For patients initiating 1st TNFi after January 1st 2009, the following sub-cohorts were also included: patients starting 1st TNFi after January 1st 2009, patients starting 1st TNFi after 2009, patients receiving TNFi after 2009, patients with nr-axSpA and AS, patients with nr-axSpA and AS, and patients with nr-axSpA and AS.

Results: Among the 23,956 biologic-naïve patients, 1,492 patients with nr-axSpA and 22,464 patients with AS were included in the analysis. The efficacy of TNFi in axSpA and AS was comparable. However, patients with nr-axSpA had a lower retention rate compared to AS. Retention rates for AS patients were ~70% at 12 months, ~55% at 6 months, and ~45% at 24 months. In contrast, retention rates for nr-axSpA patients were ~60% at 12 months, ~45% at 6 months, and ~35% at 24 months.

Conclusion: TNFi retention rates in biologic-naïve patients with axSpA are lower compared to AS. Further research is needed to investigate factors influencing TNFi retention in nr-axSpA.

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studied: patients fulfilling the ASAS criteria for axSpA, the modified New York criteria for AS and ASAS criteria for nr-axSpA.

Results: First TNFi treatment was initiated in 23,956 axSpA patients. Baseline characteristics of the pooled population are shown in the Table. The 12-month retention rate was 83.2% (95%CI: 81.5%-84.7%) across registries (Figure). At 6 months, overall ASAS Inactive disease/ BASDAI<4 scores were: 35% (LUNDEX adjusted: 27%-59%). Percentage of patients initiating 1st TNFi after 2009 and registered with fulfillment of axSpA (ASAS) was 6,087. Ankylosing Spondylitis (modified New York Criteria) was 2,935 and non-radiographic axSpA (nr-axSpA) was 1,178. We observed lower retention rate and marginally lower LUNDEX adjusted response rates in nr-axSpA patients (Table).

Table: Baseline characteristics, treatment and response status of all patients in the axial subgroup (ASAS criteria, modified New York criteria and nr-axSpA).

Table

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Available</th>
<th>ASAS (n=4971)</th>
<th>Modified New York (n=6087)</th>
<th>Nr-axSpA (n=1178)</th>
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<tr>
<td>Age (years)</td>
<td>49.5%</td>
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<td>35%</td>
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<tr>
<td>Disease duration, yrs</td>
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<td>3.2%</td>
<td>3.7%</td>
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<tr>
<td>ESR</td>
<td>35.5%</td>
<td>35.5%</td>
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Conclusion: In routine care ~1/3 of patients with axSpA initiating 1st TNFi treatment were in ASAS inactive disease after 6 months, while 1/3 achieved BASDAI<4. Four out of five patients continued treatment after 1 year. Results were slightly inferior in nr-axSpA as compared to AS.

REFERENCES

Acknowledgement: Novartis Pharma AG and IQVIA for supporting the EuroSpA collaboration.

The influence of Mediterranean diet in rheumatoid arthritis: a monocenter cross-sectional study

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Background: Mediterranean diet (MD) is considered a well-balanced and potentially anti-inflammatory diet characterized by high consumption of olive oil, unrefined cereals, fresh or dried fruit and vegetables, fish, dairy, meat and with a moderate amount of red wine. Currently, there is conflicting data for the benefits of MD in RA, and no enough evidence to support a role of MD in the prevention and treatment of rheumatoid arthritis (RA) [1].

Objectives: The aim of our study was to evaluate the association between MD adherence and disease activity, general health (GH) and comorbidities in patients with RA.

Methods: Consecutive patients with RA (ACR/EULAR Criteria 2010) were enrolled in this cross-sectional study. For each patient, Disease Activity Score on 28 joints (DAS28), Simple Disease Activity Index (SDAI), patient GH and a self-reported questionnaire called MD score [2] were recorded. The association between MD score and the above mentioned variables was assessed through univariate regression models (MD score as response variable and the variables of interest as independent variables).

Results: From each model were reported in terms of: 1) test of association (Likelihood Ratio test, with a Chi-square distribution); 2) for categorical independent variables, estimated differences of mean MD score between groups, with respective 95% CI; 3) for numerical independent variables, estimate of correlation coefficient and regression slope coefficient, with respective 95% CI. All analyses were performed using the R software.

Results: 205 patients (197 Italian) were enrolled: median age at visit 53 (IQR 47-61); age at onset of disease 38 (IQR 31-45); disease duration 12 (IQR 8-17). A high proportion of patients had a low MD score (41% had a MD score <15). Patients with a lower MD score had a significantly higher disease activity (DAS28 >5.1; p=0.007). A significantly lower DAS28 and SDAI were observed in the highest tertile of MD score (p=0.029). Moreover, a significant negative correlation was observed between MD score and DAS28 (r=-0.2; p=0.05). A significant positive correlation was observed between MD score and patient GH (r=0.23; p=0.02). A significant positive correlation was observed between MD score and a self-reported questionnaire called MD score [2] (r=0.22; p=0.03).

Conclusion: Mediterranean diet (MD) is considered a well-balanced and potentially anti-inflammatory diet characterized by high consumption of olive oil, unrefined cereals, fresh or dried fruit and vegetables, fish, dairy, meat and with a moderate amount of red wine. Currently, there is conflicting data for the benefits of MD in RA, and no enough evidence to support a role of MD in the prevention and treatment of rheumatoid arthritis (RA) [1].

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**Table 1:** presents the number and percentage of patients with rheumatic diseases accompanied by anxiety or depression. The ratio of probable anxiety was 12% in RA, 14% in SLE, 15% in SS, 16% in AS, 10% in Gout, 11% in OA, 12% in MCTD, 14% in UCTD and 10% in PM/DM. The prevalence of probable depression was 19% in RA, 21% in SLE, 20% in SS, 21% in AS, 17% in Gout, 19% in OA, 21% in MCTD, 18% in UCTD and 16% in PM/DM.

**Conclusion:** SSDM can be used for HADS self-assessments by patients with rheumatic diseases. RA was recorded as the most prevalent condition, followed by SLE. 10% to 20% patients could be classified as probable case of anxiety or depression according to HADS scores. The prevalence of anxiety was usually lower than that of depression in patients with rheumatic diseases in this study.

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.6652

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**Validation of outcome measures and biomarkers**

**SAT0626**

**VALIDATION OF METHODS FOR PREDICTING LONG-TERM OUTCOME IN JUVENILE IDIOPATHIC ARTHRITIS: RESULTS FOR CANADIAN AND NORDIC PREDICTION MODELS IN THE NORDIC COHORT**

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**Background:** Models predicting outcome in juvenile idiopathic arthritis (JIA) have recently been proposed by Guzman et al. and Rydal et al. Guzman et al. constructed a model for predicting severe disease course derived from the ReACCh-Out study, and Rydal et al. constructed models for prediction of non-remission, functional disability and joint damage.

**Objectives:** To validate methods for prediction of long-term outcome in JIA by testing the ability of Guzman’s model and Rydal’s model to predict severe disease course (the ReACCh-Out outcome) in the Nordic cohort.

**Methods:** The Nordic cohort is a prospective longitudinal multicenter cohort from defined geographical areas of 4 Nordic countries. Children with a baseline and an 8-year study visit were included. Missing data were imputed using low rank matrix factorization3 and a K-medoids algorithm4 was used to identify clusters corresponding to severe disease course in the ReACCh-Out study. With this outcome, the prediction model of Guzman et al. was tested with no re-estimation of parameters. A Receiver operating characteristic (ROC) curve and the corresponding area

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**SAT0627**

**PSYCHOLOGICAL PROFILE IN PATIENTS WITH RHEUMATIC DISEASES IN CHINA: A STUDY OF HADS SELF-ASSESSMENT USING SMART SYSTEM OF DISEASE MANAGEMENT (SSDM)**

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**Background:** The patients with chronic diseases such as rheumatic diseases suffer from physical pain and/or disability. In addition, psychological morbidities have also been found in patients with rheumatic diseases. Hospital Anxiety and Depression Scale (HADS) is commonly applied to assess the mental health of patients with rheumatic disease. A Smart System of Disease Management (SSDM) is a mobile application which has two application systems for both patients and doctors for rheumatic diseases management. The patient application system provides functions including self-assessment, medication management, adverse events management and laboratory records. After input by patients, all the data will be synchronized to the mobile terminal for further analysis. The HADS self-assessment data could be extracted from the mobile terminal for further analysis. The HADS self-assessment results can be shared with the rheumatologists. Based on these data, rheumatologists can evaluate and follow up with their patients and provide consultation service through SSDM in text or voice method. The rheumatologists can also adjust therapeutic regimens based on patients’ profiles.

**Objectives:** The purpose of this study is to explore the profile of psychological morbidities in patients with rheumatic diseases.

**Methods:** The patients were educated and trained to perform HADS assessments using SSDM by the rheumatologists. The HADS self-assessments data could be extracted from the mobile terminal for further analysis. The HADS scale consists of two subscales for anxiety (HADS-A) and depression (HADS-D) which have 7 items, respectively. Both subscales range from 0 to 21, with higher scores indicating greater anxiety and depression. A score between 11 and 21 indicates a probable case of anxiety or depression according to HADS scores.
under the curve (AUC) were computed. For the same outcome, prediction models were built using the method of Rydhal et al. on randomly sampled training sets, and tested on disjoint validation sets.

Results: In the Nordic cohort 98/440 (22%) patients were identified with a severe disease course. This ratio is similar to the 125/610 (20%) found in the ReACCh-Out study. Characteristics of groups of patients with severe and non-severe disease course are similar in the two cohorts. The model of Guzman et al. had an AUC of 0.85 for prediction of severe disease course and an AUC of 0.66 for predicting remission off medication. In repeated cross-validations, the model of Rydhal et al. had a median AUC of 0.90 (IQR 0.86-0.92) for prediction of severe disease course, and a median AUC of 0.78 (IQR 0.72-0.82) for remission off medication.

Conclusion: Tests in the Nordic cohort validate the ability of the model of Guzman et al. to predict severe disease course. Repeated cross-validations of the model of Rydhal et al. indicate that validation results are highly dependent of the chosen outcome, and that prediction of long-term remission status is more challenging than prediction of a severe disease course.

REFERENCES


Disclosure of Interests: Veronika Rydhal: None declared, Jaime Guzman: None declared, Andrew Henrey: None declared, Thomas Loughin: None declared, Mia Glerup: None declared, Anders Fasth: None declared, Ellen Nordal: None declared, Troels Herlin: None declared, Martin Rypdal: None declared, Marite Rygg: None declared, Kristiina Aalto: None declared, Susan Nielsen: None declared, Marek Zak: None declared, Mia Glerup: None declared, Kristiina Aalto: None declared, Troels Herlin: None declared, Martin Rypdal: None declared, Ellen Nordal: None declared


SA10629 THERE ARE 4 MAIN QUESTIONNAIRES TO ASSESS ADHERENCE IN INFLAMMATORY ARTHRITIS BUT NONE OF THEM PERFORM WELL: A SYSTEMATIC LITERATURE REVIEW

Déborah Puyniamond-Zemmour1, Xavier Romand2, Matthieu Lavieille3, Anna Moltó3, Rene-Marc Filpo4, Christophe Richez4, Alain Saraux5, Loraine Gutermann5, Maryse Mezière6, Maxime Dougdos7, Laure Gosses1, Rencontreurs d’Experts 2017 Working Group, Paris France. 1 Sorbonne University, Rheumatology, Paris, France; 2 Grenoble Hospital, Grenoble, France; 3 Cochin Hospital, Paris, France; 4 Lille Hospital, Lille, France; 5 Bordeaux Hospital, Bordeaux, France; 6 Brest Hospital, Brest, France

Background: Insufficient patient adherence to treatments in inflammatory arthritis (IA) including rheumatoid arthritis (RA), spondyloarthritis (SpA), psoriatic arthritis (PsA), crystal-induced arthritis and connective tissue diseases (CTD) may lead to complications, unnecessary treatment switches, and increased costs. Patient adherence to treatment should be assessed, however how to evaluate it has not been determined.

Objectives: To assess the psychometric properties of questionnaires to measure adherence to treatment in IA.

Methods: We performed a systematic literature review (SLR) using three central databases (Pubmed, Cochrane, Embase) and several websites in January 2019. The scope was limited to IA (i.e., RA, SpA, PsA, CTD, crystal-induced arthritis, vasculitis, and auto-inflammatory diseases), and disease-modifying drugs (i.e., mainly conventional DMARDs, biologics and targeted synthetic DMARDs). All questionnaires used to assess adherence were collected, then a specific search using the questionnaire name was run to obtain data on their psychometric properties including overall validity (sensitivity (Se), specificity (Sp) and Cronbach coefficient (CC), reliability, and sensitivity of change, following the OMERACT filter. These properties were analyzed semi-quantitatively.

Results: After screening 1209 publications and 194 other documents, 242 relevant papers were analyzed for measuring adherence (63.6% in RA, 8.7% in SpA, 6.6% in PsA, 14.5% in CJD and 19.0% in CTD). The number of articles using adherence questionnaires by disease was: 69/154 in RA, 14/21 in SpA, 27/40 in systemic lupus erythematosus (SLE), 9/16 in PsA, 8/35 in crystal induced arthritis and 4/6 in other CTD. Four questionnaires were used to evaluate drug adherence (Table1). The most used questionnaire was the MMAS in all diseases except in RA where the CQR was more used. The CQR was validated in 85 patients with IA against as external standard, electronic medication monitoring (Se 62 to 98%, Sp 67 to 97% and CC of 0.71 to 0.85). The MARS was validated in 55 patients with SLE against adherence based on pharmacy refill information (Se 87%, Sp 86% and CC of 0.70). The MMAS was validated in 91 patients with gout against medication possession ratio Se 81 to 93%, Sp 44 to 53% and CC of 0.54). The MARS was validated in 108 patients with RA (Se 13 to 53%, Sp 57 to 94% and CC 0.60 to 0.75). Reproducibility was correct but copyright posed issues (Table).

Table 1. Questionnaires performances to assess adherence in IA

<table>
<thead>
<tr>
<th>Questionnaire</th>
<th>Compliance</th>
<th>Medication</th>
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<tr>
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<td>Questionnaire</td>
<td>Questionnaire</td>
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<td>Inventory</td>
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The + represents a semi-quantitative summary of the available literature with more + meaning higher/better results (from - to +++)

Conclusion: Four questionnaires are being used to measure medication non-adherence in IA; the most used is the MMAS which is unfortunately copyrighted and not fully validated in rheumatology. The CQR and MASRI questionnaires were the most validated in rheumatology, but the CQR is long and the MASRI only used for SLE. Thus it appears that to date, a simple, reliable and valid questionnaire to assess drug adherence is lacking.

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DUTCH TRANSLATION AND PSYCHOMETRIC PROPERTIES OF A PATIENT REPORTED EXPERIENCE MEASURE (PREM) FOR PATIENTS WITH RHEUMATOID ARTHRITIS AND SPONDYLOARTHRITIS

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Background: Evaluating the quality of care provided as perceived by patients can be helpful in order to reveal areas for improvement, identify best practices and stimulate interventions to further improve these. This can be done with a patient reported experience measure (PREM). Such a PREM, containing 23 questions in 7 domains has been developed and validated specifically for patients with rheumatic conditions, including rheumatoid arthritis (RA) and spondyloarthritis (SpA), in the United Kingdom (box 1) (1). Until now, no translated and validated Dutch questionnaire is available for patients with SpA or RA in the Netherlands.

Objectives: To translate the PREM into Dutch and to study its psychometric properties in patients with SpA or RA.

Methods: The PREM was independently translated into Dutch by two researchers fluent in the English language (one rheumatologist and one healthcare scientist) and a consensus version was generated which was checked by two other researchers (one rheumatologist and one methodologist). The final version was piloted in two Dutch real-life quality registries for patients with SpA or RA: SpA-Net and DREAM-RA, respectively. Patients completed the PREM annually starting from December 2016. For the current cross-sectional analysis, the most recently completed PREM from each patient was included. Feasibility was assessed by the median and interquartile ranges (IQR) of completion times. Reliability was assessed by internal consistency (Cronbach’s α) and homogeneity (corrected item-total correlations r p)) within each domain. Content validity was assessed by floor- and ceiling effects (>15%) for each question. Divergent validity was assessed by Spearman rank correlation coefficients (rs) between the average score of each domain and outcome measures for disease activity (BASDAI, ASDAS or DAS28), daily functioning (BASFI, HAQ or HQAG-S), health status (ASAS-HI) and quality of life (SF-36).

Results: The PREM was completed by 282 patients with SpA and 378 patients with RA. The average age and the proportion of female patients with SpA was lower compared to patients with RA (54.2 (SD 12.2) versus 65.1 (SD 11.9) years and 47.9% versus 65.1% female patients, respectively). Average disease activity was high in patients with SpA but low in patients with RA (mean ASDAS 2.2 (SD 0.9), mean DAS28 2.3 (SD 1.2)). The median time to complete the PREM was 5.5 minutes (IQR 2.7) in SpA-Net and 5.4 minutes (IQR 2.3) in DREAM-RA. Internal consistency of all domains was considered good for patients with SpA or RA (0.70 ≥ α ≥ 0.95), except for the domain Daily living and physical comfort in patients with RA (α=0.65). In both populations, thresholds for homogeneity were exceeded within three domains (rs > 0.7) suggesting possible item redundancy. Ceiling effects were found in 75% (SpA) and 90% (RA) of the questions. As expected, correlation coefficients showed that nearly all domains of the Dutch PREM were independent of scores on outcome measures in both patients with SpA and RA (0.3 ≤ r p ≤ 0.3).

Conclusion: The Dutch PREM has acceptable psychometric properties to assess perceived quality of care in patients with SpA or RA. The homogeneity within three domains could be improved. The results for perceived quality of care are not affected by scores on outcome measures for disease activity, physical functioning, health status and quality of life.

REFERENCES

Disclosure of Interests: None declared

SAT0631 CRITERION VALIDITY AND CUT-OFFS OF THE FLARE ASSESSMENT IN RHEUMATOID ARTHRITIS (FLARE-RA) QUESTIONNAIRE: INTERNATIONAL COLLABORATION

Elena Myasoedova1, Annette de Thurn2, Marie-Line Erpelding2, Emilie Schneeberger3, Thomas Maribo4, Gustavo Citera5, John Davis6, Eric Matteson7, Cynthia S. Crowson8, Bruno Fautrel9, Francis Guillerm9, Mayo Clinic, Rochester, MN, United States of America; 2Aarhus University Hospital, Aarhus, Denmark; 3University of Lorraine, Nancy, France; 4Instituto de Rehabilitacion Psicosocial, Buenos Aires, Argentina; 5DEFACTUM, Aahus, Denmark; 6University Pierre et Marie Curie, Paris, France.

Background: Flares are inherent to the rheumatoid arthritis (RA) disease course and associated with poor clinical outcomes. The self-administered Flare Assessment in Rheumatoid Arthritis (FLARE-RA) questionnaire was devised and validated for detection of current and recent flares in RA, taking into account both patient and provider perspectives [1, 2]. The FLARE-RA questionnaire includes arthritis-related subscale and general subscale. The overall score for the questionnaire is defined as the global scale, with scoring from 0 (no flare) to 10 (maximum flare).

Objectives: To define the cross-cultural criterion validity of the FLARE-RA questionnaire and cut-off(s) for definition and decision in four different countries, using different anchor items in patients with RA.

Methods: This cross-sectional study included adult patients with prevalent RA (per 2010 ACR/EULAR criteria) attending outpatient rheumatology clinics in France (n=138), Denmark (n=253), USA (n=75), and Argentina (n=105). Flare occurrence over the past 3 months was assessed using the FLARE-RA questionnaire. The cut-offs for the FLARE-RA score were defined using the following anchor items obtained at the same encounter: 1) Patient report of flare; 2) DAS28-ESR>3.2; 3) Change of anti-rheumatic treatment. Detection of the optimal cut-off for the FLARE-RA questionnaire was performed with distance (0,1) method, based on the area under the receiver operating characteristic curve (AUC).

Results: The study included 571 patients with RA (mean age 56.9 years, 75.3% female). The discrimination for the FLARE-RA was acceptable-to-excellent: AUC for the global FLARE-RA score ranged from 0.71 to 0.92. The summary of optimal cut-offs for the FLARE-RA questionnaire is presented in the Table. The cut-offs for the FLARE-RA score were overall lowest using “patient’s report of flare” and highest using “change of anti-rheumatic treatment” as an anchor item: cut-offs for the global score for patients with RA duration 2-5 years: 1.82 and 4.35, respectively; for patients with RA duration >5 years – 2.18 and 3.18, respectively. The cut-offs corresponding to DAS28-ESR>3.2 were lower in patients with RA disease duration >5 years than in those with RA duration 2-5 years.

Table: Summary of FLARE-RA optimal cut-offs by RA disease duration using different anchor selection methods

<table>
<thead>
<tr>
<th>Anchor Item</th>
<th>Disease duration 2-5 years</th>
<th>Disease duration &gt;5 years</th>
</tr>
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<tbody>
<tr>
<td>Flare</td>
<td>Arthritis subscale</td>
<td>General subscale</td>
</tr>
<tr>
<td>Patient report of flare</td>
<td>2.80</td>
<td>1.00</td>
</tr>
<tr>
<td>DAS28 CRP &gt;3.2</td>
<td>4.40</td>
<td>3.67</td>
</tr>
<tr>
<td>Change of anti-rheumatic treatment</td>
<td>4.00</td>
<td>4.50</td>
</tr>
</tbody>
</table>

Conclusion: The FLARE-RA questionnaire has acceptable-to-excellent discriminative capacity across the tested anchor items. Patient report of flare corresponds to a lower FLARE-RA cut-off score than DAS28-ESR and change of anti-rheumatic treatment, suggesting the hierarchy of flare recognition from flare self-perception to its detection by DAS28 to treatment change by the rheumatologist. More studies are needed to ensure the early recognition of flares and the appropriate alignment between flare and the adjustment of anti-rheumatic and other medications.

REFERENCES

Disclosure of Interests: None declared
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SAT0632 NEUTROPHIL ACTIVATION IDENTIFIES PATIENTS WITH ACTIVE POLYARTICULAR GOUT – A NOVEL BIOMARKER?

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Background: Neutrophils are key immune cells participating in host defense through several mechanisms, including the formation of neutrophil extracellular traps (NETs). Although beneficial from a host-pathogen perspective, excessive neutrophil activation has been linked to inflammation and autoimmunity, including systemic lupus erythematosus (SLE) and gout.(1) In gout models, uric acid crystals induce NETosis. Though NETs are known to induce marked inflammation through TLR9- and cGAS-dependent pathways, as well as partake in induction of tissue damage and thrombotic events, the role of NETs in human gout has not been carefully investigated.

Objectives: Our objective is to investigate evidence of systemic neutrophil activation, and the clinical utility of neutrophil-derived biomarkers in gout. We hypothesize that uric acid crystals will activate neutrophils to undergo NET formation, with these processes contributing to immune cell activation and local joint destruction.

Methods: Plasma samples from 75 gout patients participating in the ‘Readys gout cohort Amsterdam’ were compared with 30 healthy controls (HC). Levels of NETs, and NET-derived markers (cell-free DNA and peroxidase activity) were analyzed using a MPO-DNA ELISA, as well as fluorimetry.(2) Levels of calprotectin (S100A8/A9) were analyzed by ELISA. Mitochondrial (mt, COXII), as well as genomic (n, RPLP0) DNA levels orimetry.(2) Levels of calprotectin (S100A8/A9) were analyzed by ELISA. Mitochondrial (mt, COXII), as well as genomic (n, RPLP0) DNA levels orimetry.(2) Levels of calprotectin (S100A8/A9) were analyzed by ELISA. Mitochondrial (mt, COXII), as well as genomic (n, RPLP0) DNA levels. Results: Levels of NETs, as well as other neutrophil biomarkers, were significantly increased in gout patients as compared to healthy subjects (p<0.01, Figure 1A). In contrast to SLE, gout patients did not have elevated levels of circulating mtDNA (p=0.96), but only nDNA (p=0.006). No associations were found between markers of cell death (mtDNA and NETs) and disease activity. Peroxidase activity correlated with disease activity (RAPID score: r=0.43, p<0.01, RAPID function: r=0.24, p=0.001) and inflammation markers (CRP: r=0.40, p<0.01, and ESR: r=0.43, p<0.001). Involvement of ankle and wrist resulted in significant higher peroxidase levels compared to mono-articular disease (p<0.01, and p<0.03, respectively), suggesting peroxidase activity being a marker of polyarticular gout (Figure 1B). Calprotectin (S100A8/A9) correlated with the inflammation markers CRP and ESR (r=0.30, p=0.01, and r=0.30, p=0.001, respectively) and morning stiffness, especially in patients with chronic polyarticular gout (r=0.61, p=0.001).

Conclusion: To our knowledge, this is the first report demonstrating presence of NETs in the peripheral blood of gout patients. Although markedly elevated, levels of NETs did not associate with markers of disease activity or inflammation, possibly due to the lack of inflammatory mitochondrial DNA within the NETs. Even so, our data demonstrate an important role of neutrophils in gout pathogenesis, with neutrophil activation markers associating with characteristics of active, and more pronounced polyarticular disease.

REFERENCES


Disclosure of Interests: Daisy Vedder Speakers bureau: Novartis, Martijn Gerritsen Grant/research support from: Grunenthal has sponsored the Reade Cohort, Michael Nurmohamed Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi and UCB, Consultant for: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi and UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi and UCB, Ronald van Vollenhoven: None declared, Christian Lood: None declared


SAT0633 PREGNANCY SUCCESS RATE AND RESPONSE TO HEPARINS AND/OR ASPRIN DIFFERS IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS ACCORDING TO THE GAPSS SCORE

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Background: Current standard of care (SoC) in pregnancy for patients with Systemic lupus erythematosus (SLE) and/or aPL positivity includes treatment with low dose aspirin (75–100mg/day) and low molecular heparin or unfractionated heparin. However, up to 30% of women continue to have pregnancy complications despite SoC. Therefore, identifying patients that are at greater risk to develop pregnancy complications despite the SoC and might benefit from additional therapeutic approaches, is still an unmet clinical need.

Recently, our group conceived and validated the global antiphospholipid syndrome score (GAPPS) [1], as a risk score for predicting aPL-related clinical manifestations (thrombotic and/or pregnancy morbidity).

Objectives: We aimed to investigate response to SoC in women with SLE and/or aPL positivity when stratifying their risk according to GAPPS Score.

Methods: 143 women ever pregnant treated with SoC therapy with SLE and/or aPL positivity were retrospectively included. Data on cardiovascular risk factors and aPL positivity were retrospectively collected. The individual GAPPS was then grouped according to the patients’ GAPPS low risk (<6), medium risk (6-11) and high risk (≥12).

Results: The analysis included 143 patients (mean age 30.8 ± 6.4) with SLE (122; 85.3%) and/or aPL positivity, for a total of 352 pregnancies.

<table>
<thead>
<tr>
<th>GAPPS ≤6</th>
<th>GAPPS 6-12</th>
<th>GAPPS ≥13</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=72)</td>
<td>(n=68)</td>
<td>(n=9)</td>
</tr>
<tr>
<td>Age, mean (±S.D.)</td>
<td>30.7 ±5.9</td>
<td>30.6 ±6.2</td>
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![Graph](image)

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Overall, we observed a live birth rate of 70.5%, with a total of live birth of 248 out of the 352 pregnancies. Forty-five patients (31%) experienced at least one event of PM, defined as early or late. When considering patients who ever experienced PM while treated with SoC, all patients in the high risk group (GAPSS ≥12) experienced PM, while patients in the medium group (GAPSS 6-11) had a significant higher rate of PM when compared to the low risk group (GAPSS < 6) group [29 (43.9%) patients V.s. 100(62.1%) and 137(82.5%), respectively; p<0.05]. Furthermore, patients with medium risk group also had significantly lower birth rates, when compared to the other groups [11(40.7%) live births V.s. 100(62.1%) and 137(82.5%), respectively; p<0.05]. Regarding the number of pregnancies in the three groups, patients in the high risk group had significantly lower live birth rates, when compared to the other groups [11(40.7%) live births V.s. 100(62.1%) and 137(82.5%), respectively; p<0.05].

Figure 1 resumes the results of PM and live births divided in the three groups.

Conclusion: GAPSS might be a valuable tool for identifying patients with a higher likelihood of response to SoC.

Methods: Baseline data from two phase 3 trials investigating oral salmon calcitonin OA, NCT00486434 and NCT00704847 (total N=2206), was analyzed in a post-hoc cross-sectional analysis. Patients with self-reported current or previous depression, anxiety or post-traumatic stress syndrome (PTSD) were selected and compared to a control group, matched by sex, age, BMI and JSW. Spearman’s correlation coefficient between JSW and WOMAC pain was calculated for both groups. Multiple regression analyses of both groups with WOMAC pain as the outcome variable, and age, sex, body mass index (BMI) and baseline JSW or KL-grade as explanatory variables were performed.

Results: In the AD group, 149 patients had AD in medical history of which 123 reported the condition as ongoing at baseline. The study groups of AD and matched controls (MC) were comparable in terms of age, sex, BMI, JSW, KL-grade and WOMAC pain. Associations between pain and JSW In the AD group, no significant correlation between JSW and WOMAC Pain score was found, while BMI was found to be weakly associated with WOMAC pain (R= 0.19, p=0.02) in the multiple regression analysis. In the MC group, a statistically significant (p=0.004), correlation (R= -0.24) was found between JSW and pain indicating that lower JSW was associated with higher pain, with JSW accounting for approximately 6% of the total natural variation behind reported pain. In addition, a positive significant association between male sex and WOMAC pain (R=0.18, p=0.04) was found. The univariate linear relationship between JSW and pain is illustrated in Figure 1, and multivariate analyses are shown in Table 1.

Table 1. Associations between WOMAC pain, JSW (in red) and other baseline covariates

<table>
<thead>
<tr>
<th>Anx/Depr. group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.04 0.60</td>
</tr>
<tr>
<td>BMI</td>
<td>0.18 0.03</td>
</tr>
<tr>
<td>Male Sex</td>
<td>0.10 0.21</td>
</tr>
<tr>
<td>JSW</td>
<td>0.03 0.75</td>
</tr>
</tbody>
</table>

Associations between pain and KL-Grade In the model evaluating associations between KL-grade and symptoms, there was no correlation between KL-grade and symptoms in the AD group. Similar to the findings relating to JSW, in the MC group, a weak (R=-0.16), borderline...
statistically significant association (p<0.07) was found between KL-grade and WOMAC pain.

Conclusion: A marked structure-symptoms discordance was found in OA patients with AD, while a statistically significant correlation was seen in matched controls without AD. The results suggest that exclusion of trial patients with anxiety and depression in medical history may improve the accuracy of pain reporting in clinical OA trials.


SAT0635 PATIENT-PERCEIVED RESIDUAL BURDEN OF PSORIATIC ARTHRITIS IN PATIENTS IN REMISSION/LOW DISEASE: AN ANALYSIS OF 444 PATIENTS

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Background: The objective of treatment in psoriatic arthritis (PsA) is remission or low disease (ref1). However, there may remain residual patient burden in patients where inflammation is controlled.

Objectives: To explore patient-perceived burden of disease in PsA patients in remission or low disease, when using different definitions of remission.

Methods: RefFlap (NCT03119805, ref2) was an observational study in 14 countries of consecutive adult patients with definite PsA and >2 years of disease duration. Remission/low disease status was defined at the baseline visit using composite scores: Minimal Disease Activity (MDA), and Disease Activity in PSoriatic Arthritis (DAPSA)<14 (both corresponding to a status of remission or low disease). Patient-perceived burden of disease was assessed through the PsA Impact of Disease (PsAID12) composite score and its individual components assessing physical and psychological impact (0-10 where 0 is the optimal status). Mean and median levels of patient-reported symptoms were assessed in remission/low disease status. P-values by Wilcoxon test were computed to compare patients in good status according to both MDA and DAPSA (n=161), versus in good status according to DAPSA only (n=96). There was no imputation of missing data.

Results: Of 446 patients, 444 had disease status and impact available: 220 (50.5%) were male, mean age was 52±12.6 years, mean disease duration was 10.1±8.1 years; 261 (59.5%) were taking a conventional DMARD and 255 (61.3%) a biologic. Disease activity was moderate: 154 (36.2%) had no current psoriasis skin lesions, mean tender joint count was 4.7±9.5, mean swollen joint count (SJC) was 2.2±7.0, and mean DAPSA was 16±17.2. Remission/low disease was more frequent when defined by DAPSA: 251 (56.5%) patients, than by MDA: 171 (38.5%) patients. As expected, objective measures of disease activity were minimal in the good status categories (e.g., SJC was 0.3±0.6 in MDA and 0.4±0.9 in DAPSA-remission/low disease). In remission/low disease, residual disease impact (assessed with PsAID12) was low: most median levels of symptoms were below 1 on a 0-10 scale; 5 aspects of impact had a median level of 1 (figure); only one had a median level of 2, and this was fatigue. Levels of impact were slightly though significantly higher in patients in DAPSA-defined good status than in patients in both MDA and DAPSA-remission/low disease (all p<0.001).

Conclusion: In this unselected population, residual symptoms were of low magnitude using both definitions of good status: DAPSA-based definitions (present in 56%) and MDA (38%), confirming the patient relevance of remission/low disease as a treatment objective. The predominant aspect of impact was fatigue, which is one of the most important domains of impact recognized by patients. Residual burden of disease was lower in the MDA group than in the DAPSA-remission/low disease group, which could indicate that MDA corresponds to a ‘deeper’ form of disease control, though the clinical relevance of the differences observed should be further explored. A holistic approach should be implemented when evaluating people with PsA including when disease control has been obtained.

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SAT0636 A DRUG INDUCED REMISSION SIGNATURE PROMISES PERSONALIZED THERAPY IN RA PATIENTS

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Background: Today the objective for efficient Rheumatoid Arthritis (RA) therapy is not restricted to reduced synovial inflammation but to induce immunological and clinically lasting remission. Despite improvement in therapy of RA, anti-TNF alpha or anti-IL-6 (Tocilizumab) biologics provide less than 20% of clinical remission. Interestingly, the complete remission can last up to 12 months in about 40% of these patients despite discontinuation of the above biologics. In order to set up optimized strategy to obtain persistent clinical remission, new predictive markers of complete remission are needed.

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- **Results**
  - The ROC curve of IgG4 and IgG4/IgG3 ratio.

- **References**

**THE DIAGNOSTIC VALUE OF SERUM IgG4 IN IgG4-RELATED DISEASES**

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**Background:** IgG4-RD is a newly recognized autoimmune disease. Serum IgG4 is an important tool for the diagnosis of IgG4-RD. However, only a few articles have reported the value of serum IgG4 for the diagnosis of IgG4-RD.

**Objectives:** To explore the diagnostic value of serum IgG4 in IgG4-related diseases. Whether 1350 mg/L as the cutoff concentration is suitable for Chinese people to identify IgG4-RD and other rheumatic immune diseases.

**Methods:** From October 2013 to December 2018, 40 patients with IgG4-RD diagnosed in the rheumatic immunology department of people's hospital of Xinjiang Uygur Autonomous Region were collected.

**Results:** The cut off levels were determined by receiver operating characteristic (ROC) curve analysis. The mean serum IgG4 concentration of 40 definite IgG4-RD was significantly higher than that of other rheumatic immune diseases group and healthy control group.

**Conclusion:** Serum IgG4 is an important tool for the diagnosis of IgG4-RD. Whether 1350 mg/L as the cutoff concentration is suitable for Chinese people to identify IgG4-RD and other rheumatic immune diseases.

**Disclosure of Interests:** None declared

**REFERENCES**


**SAI0638**

**INCREASED LEVELS OF CIRCULATING EXTRA CELLULAR LONG NON-CODING RNAs MALAT1, MEG3 AND NEAT1 IN PATIENTS WITH RHEUMATOID ARTHRITIS AND THEIR IMPACT ON DISEASE ACTIVITY MEASURES**

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**Background:** Deregulations of long non-coding RNAs (lncRNA) have been lately implicated in autoimmune diseases(1) including Rheumatoid arthritis (RA). However, their specific roles in disease pathogenesis, extra-cellular manifestations and clinical impact in RA remain largely unknown.

**Objectives:** To identify the intra- and extra-cellular expressions of lncRNAs, MEG3, MALAT1, NEAT1, in RA and their impact on disease activity.

**Methods:** Blood samples were collected from 82 active RA patients (DAS28-CRP: 4.7±0.2) and 15 age-sex matched healthy individuals. Knee synovial fluids (SF) were collected from 24 RA patients (among 82) and 10 osteoarthritis patients (as control). Sera were separated for cytokines.
measurements. RNA, isolated from peripheral blood mononuclear cells (PBMCs), plasma and synovial fluid were quantified by spectrophotometry. Levels of MALAT1, MEG3 and NEAT1 were determined using specific primers and real time PCR, 18S RNA was the endogenous control. Fold changes were calculated using standard $2^{-\Delta\Delta CT}$ method. Multivariate analysis was performed to analyze associations between the dependent variable (DAS28-CRP) and the predictor variables (CRP, MALAT1, MEG3 and NEAT1). Confidence interval of 95% ($p<0.05$) was considered statistically significant for all analyses.

Results: All patients recruited were anti-CCP positive (122.5 ±28.3 IU/mL) and RF positive (166.5 ±37.3 IU/mL). Their systemic inflammation were high compared to controls ($p<0.05$) as reflected in serum CRP (47.4 ±26.2 mg/L), TNFα (140±29 pg/dL) and IL17 (270±33 pg/dL). Levels of MALAT1, MEG3 and NEAT1 were increased in the PBMCs ($p<0.05$) of RA patients compared to controls. Similar increases of these IncRNAs were seen in plasma and in SF. Spearman’s correlation were performed with the fold changes of IncRNAs in PBMC, DAS28-CRP and its components. MEG3 significantly correlated with tender joint count (TJC) ($r=0.75$, $p=0.002$) whereas NEAT1 correlated with both TJC ($r=0.571$, $p=0.002$) and DAS28-CRP ($r=0.943$, $p=0.001$). Multivariate analysis was performed with NEAT1 and MEG3 as the predictors and DAS28-CRP (model 2) as outcome and co-efficient of determinant ($r^2$) was compared to that of CRP as the predictor and DAS28-CRP as the outcome (model 1). Model 1 was made to set a cut-off mark for model 2. The $r^2$ for model 1 (0.862) was greater than that of model 2 (0.656) indicating the expressions of NEAT1 and MEG3 accounted for more variability in DAS28-CRP scores (86.2%) than CRP (65.6%). In model 2, $r^2$ co-efficient of NEAT1 ($β=0.868$) was greater than that of MEG3 ($β=0.397$) suggesting a greater impact of NEAT1 on DAS28-CRP scores. The IncRNAs in plasma and in synovial fluids had shown similar trends.

Conclusion: Increased in IncRNAs in extra cellular fluid suggests their systemic regulation on RA pathogenesis. Increased predictability of DAS28-CRP by NEAT1 and MEG3 compared to CRP indicate their potentiality of being probable markers in monitoring disease activity. However, validation of this finding in larger cohort is necessary.

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Disclosure of Interests: Barbara Drec: None declared, Rusmir Husic Speakers bureau: BMS, UCB, Celgene, MSD, Philipp Bosch: None declared, Angelika Lackner: None declared, Theresa Bruegmann: None declared, Winfried Graninger: None declared, Johannes Fessler: None declared, Martin Stradner Speakers bureau: Novartis, Roche, Lilly, BMS, Pfizer, Shire


SAT0639

ACTIVE JAK/STAT SIGNALING IN CIRCULATING LEUCOCYTES DEFINES DISTINCT IMMUNOLOGIC ENDEOTYPES OF RHEUMATOID ARTHRITIS

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Background: In rheumatoid arthritis (RA) stratification is considered an important step towards the development of patient-tailored therapeutic concepts. The fact that less than 50% of RA patients experience a substantial improvement in response to any single biologic therapy has brought up the idea that yet unidentified subtypes of RA (endotypes) might exist. This concept is in line with distinct microscopic patterns of synovitis found in biopsies of RA joints.[1] Furthermore, a subset of RA patients has leukocytes with interferon driven gene expression, whereas the majority of RA patients does not.[2] Interferons activate receptor associated Janus kinases leading to phosphorylation of STAT1 and STAT2. Other STAT family members are activated by cytokines such as IL-6 (STAT3) or IL-15 (STAT5). Therefore, the phosphorylation pattern of the different STAT molecules in circulating leukocytes might mirror the specific cytokine milieu of a given patient.

Objectives: To define endotypes of RA based on the phosphorylation patterns of the different STAT molecules in circulating leukocytes.

Methods: Cross-sectional study of 63 patients with established RA fulfilling the 2010 EULAR/ACR criteria (mean age: 64.5 ± 1.7 (SEM) years, female ratio: 0.79). Ten healthy subjects served as a control group. Flow cytometry was performed to detect the phosphorylated forms of STAT1-6 in Monocytes, Granulocytes, B cells, naïve-, effector-, and memory-T cells of the CD4+ and CD8+ lineage. All steps from blood draw to cell fixation were performed at 4°C to prevent auto-activation of leukocytes. The mean fluorescence intensity (MFI) of phosphorylated STATs in the different leukocyte populations was used for statistical analysis. MFIs were correlated with disease activity measured by the cDAI. MFIs of populations with elevated STAT phosphorylation not associated with disease activity were used by unsupervised hierarchical clustering. The resulting groups were validated by principal component analysis. Finally, criteria for patient assignment to specific groups by MFI were generated by calculating ROC-curves.

Results: Pronounced ex vivo phosphorylation of STAT1-6 in any leucocyte population was detected in 20 of 63 (48%) RA patients but not in healthy subjects (n=10). Active STAT5 signaling in Monocytes, naïve CD4+ T cells and CD4+ effector T cells was significantly associated with disease activity. Unsupervised hierarchical cluster analysis of RA patients based on STAT MFIs not associated with disease activity resulted in 3 groups: 1) Patients with active STAT1 and STAT3 signal in Monocytes and Granulocytes (n=14/63, 22%), 2) Patients with active STAT5 signal in naïve CD4+ T cells, CD8+ effector T cells and CD4+ memory T cells (n=16/63, 25%) and 3) Patients without active STAT signal in any leucocyte population (n=33/63, 52%). cDAI, CRP, ESR, current treatment, RF and ACPA status did not differ significantly between the groups. To test if the assignment to a group changed over time, we performed a second analysis of STAT phosphorylation after 3-6 months. Eighty percent of the patients tested (12/15) were re-assignment to their initial group.

Conclusion: We identified three distinct RA endotypes based on active STAT signal. Whether patients within different endotypes respond differently to a given therapy will be subject to further research.

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Disclosure of Interests: Barbara Drec: None declared, Rusmir Husic Speakers bureau: BMS, UCB, Celgene, MSD, Philipp Bosch: None declared, Angelika Lackner: None declared, Theresa Bruegmann: None declared, Winfried Graninger: None declared, Johannes Fessler: None declared, Martin Stradner Speakers bureau: Novartis, Roche, Lilly, BMS, Pfizer, Shire


SA	0640

SHEAR-WAVE ELASTOGRAPHY OF SKIN STIFFNESS IN SYSTEMIC SCLEROSIS: A FIVE-YEAR FOLLOW-UP STUDY

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Background: Measurement of skin involvement is essential for diagnosis and assessment of prognosis in systemic sclerosis (SSc). The mRSS is the gold standard measure of skin thickness. The mRSS has been criticised for being associated with high inter-observer variability and being too insensitive to detect relevant changes in skin thickness over time. Previously, our group demonstrated that shear-wave elastography (SWE) offers a potential for objective and quantitative assessment of skin involvement in SSc patients.1 However, no studies have evaluated its sensitivity to change over-time.

Objectives: To assess changes in skin stiffness in SSc patients using SWE, over-time.

Methods: This study included 19 SSc patients [89.5% females; age 57.5 years (10.3), 53% with limited form; disease duration 11.4 years (8.5)] at baseline and, 13 healthy controls [89.2% females; age 53.4 years (11.5)]. Skin stiffness was measured by SWE, using virtual touch image quantification, at the 17 sites corresponding to the mRSS, in each participant, at baseline and follow-up [a mean of 4.9 (I4.6–4.9) years later]. mRSS was performed at both time points. Differences between groups were analysed using the related-samples Wilcoxon Signed Rank test. Results are presented as mean ±SEM (interquartile range [IQR]).

Results: In SSc patients, skin stiffness measured by SWE decreased in a strongly significantly way (p<0.001), over time at all skin Rodnan sites, except the fingers (table 1). Interestingly, the same was observed in controls for all sites, except the leg. The effects of normal ageing correspond to 30 to 60% of the changes observed in SSc. Local Rodnan

scores only decreased significantly at the forearms and fingers of SSc patients. The reduction of mRSS at the fingers did not correspond to improvements in SW. Shear wave velocity (SW) measurements correlated with mRSS both at baseline (r=0.56; p=0.0001) and at follow-up (r=0.74; p=0.0001).

Conclusion: Although preliminary, this study provides the first evidence suggesting that 1. SW of the skin is more sensitive to change over time than mRSS; 2. Skin stiffness reduces significantly over time in normal controls, and 3. Normal skin ageing may contribute to the overall decrease of SW with time in SSc. Our results highlight the discriminant ability of SW in detecting subtle skin changes not identified by mRSS. SW may offer a significant improvement in the evaluation of skin stiffness and may provide relevant insights into the biology of healthy and sclerodermia skin. Studies including a larger number of patients in different phases of skin involvement and data on normal reference values of these ultrasound measurements are needed to reach a definitive validation.

References

Table 1. Comparison between skin stiffness – shear wave velocity measurements – and mRSS at the site of analysis, at baseline and follow-up.

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<thead>
<tr>
<th>SS1 patients (BW &amp; mRSS)</th>
<th>Controls (BW)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>Follow-up</td>
</tr>
<tr>
<td><strong>SWV</strong></td>
<td>3.12 (0.53)</td>
</tr>
<tr>
<td>fSWV</td>
<td>0.03 (0.01)</td>
</tr>
<tr>
<td>SWV</td>
<td>2.94 (0.83)</td>
</tr>
<tr>
<td>fSWV</td>
<td>0.01 (0.01)</td>
</tr>
<tr>
<td>SWV</td>
<td>3.24 (0.79)</td>
</tr>
<tr>
<td>fSWV</td>
<td>0.02 (0.01)</td>
</tr>
<tr>
<td>SWV</td>
<td>3.89 (0.74)</td>
</tr>
<tr>
<td>fSWV</td>
<td>0.02 (0.01)</td>
</tr>
<tr>
<td>SWV</td>
<td>2.55 (1.87)</td>
</tr>
<tr>
<td>fSWV</td>
<td>0.23 (0.20)</td>
</tr>
<tr>
<td>SWV</td>
<td>0.10 (0.21)</td>
</tr>
<tr>
<td>fSWV</td>
<td>0.02 (0.01)</td>
</tr>
</tbody>
</table>

Disclosure of Interests: None declared


SAT0642 PROTEIN BIOMARKERS TO DIFFERENTIATE PSORIATIC ARTHRITIS FROM PSORIASIS

Conor Magee1,2, Yitong Pu3, Anna Kwasnik3, Angela MC Ardle3, Belinda Hernandez4, Flora Farkas4, Natsumi Ikumi1, Agnes Szentpetery1, Looi Shaker4, Phil Gallagher4, Brian Kirby4, Stephen Pemovscek4, Oliver Fitzgerald5, Measuring Outcome in Psoriatic Arthritis (MOPsA) Group. 1St. Vincent’s University Hospital, Rheumatology, Dublin, Ireland; 2University College Dublin, The Conway Institute, Dublin, Ireland; 3Trinity College Dublin, School of Medical Gerontology, Dublin, Ireland; 4St. Vincent’s University Hospital, Dermatology, Dublin, Ireland

Background: The BIOMarkers of COMpofibridities (BIOCOCOM) in Psoriasis (Pso) study is a longitudinal study in which we aim to identify clinical, genetic and protein biomarker features associated with the development of co-morbidities, notably psoriatic arthritis (PsA), in patients with psoriasis (Pso). Pso usually precedes the development of PsA with an average interval of 10 years. Thus, patients with Pso are an ideal group in which to study the early events in the evolution to PsA.

Objectives: To use a targeted proteomics approach to identify a serum protein, or panel of proteins, which can predict the development of PsA in patients with Pso. As a first step, we initially sought to identify serum proteins capable of discriminating between patients with Pso only and patients with established PsA.

Methods: 30 patients with Pso and 30 patients with established PsA were selected from the BIOCOCOM-Pso database. Serum samples from these patients, taken at their initial assessment, were digested using an established in-house standard operating protocol (SOP). Once digested, a targeted proteomics approach using liquid chromatography – mass spectrometry (LC-MS) and a multiple reaction monitoring (MRM) assay called PAPRICA was used to measure candidate biomarker proteins. These 206 proteins (423 peptides) were previously identified as being protein biomarkers in a number of different inflammatory rheumatological conditions.

Results: The demographics of the 2 patient groups are shown in Table 1.

Table 1. Demographic & Clinical Characteristics of the Study Population

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Pso</th>
<th>PsA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean +/- SD years</td>
<td>41.1 +/- 14.6</td>
<td>50.3 +/- 10.6</td>
</tr>
<tr>
<td>Male Sex, number (%)</td>
<td>20 (66.7)</td>
<td>21 (70)</td>
</tr>
<tr>
<td>Duration of Pso, mean +/- SD years</td>
<td>6.5 +/- 2.9</td>
<td>23.3 +/- 12.1</td>
</tr>
<tr>
<td>Duration of PsA, mean +/- SD years</td>
<td>14.8 +/- 10.1</td>
<td></td>
</tr>
<tr>
<td>PASI, mean +/- SD</td>
<td>8.1 +/- 3.7</td>
<td>2.8 +/- 2.7</td>
</tr>
<tr>
<td>CDAI, mean</td>
<td>4.4</td>
<td></td>
</tr>
</tbody>
</table>
Targeted proteomics data from the PsA and Pso patients was subjected to univariate and multivariate analysis using a leave one out cross validation approach. The initial results revealed that the application of the PAPRICA method to the BIOCOM-Pso samples resulted in a dataset in which 88 of the 206 PAPRICA proteins could be reliably measured (CV Area < 20%; Signal to Noise ratio > 5; Library Dot Product > 0.8). This subset of the PAPRICA proteins was not able to discriminate between PsA and Pso and none of the associated peptides were significantly different between the two groups (p value < 0.05).

Conclusion: Analysis of a subset of 88 of the 206 biomarker proteins in the PAPRICA method, in patients with PsA and Pso, did not reveal peptides (proteins) that were statistically different between these two groups. Multivariate analysis generated a model that was unable to discriminate between patients with PsA and Pso. The possibility that the full PAPRICA assay may be able to discriminate between PsA and Pso will be explored, as will supplementing the PAPRICA method with additional biomarkers including proteins that may be identified in an unbiased proteome wide screen of PsA vs Pso serum samples.

Disclosure of Interests: None declared


SAT0643

FACIT-FATIGUE TO PROMIS-FATIGUE CROSS-WALKED DATA FROM MONARCH, MOBILITY AND TARGET RANDOMIZED CLINICAL TRIALS OF SARILUMAB FOR THE TREATMENT OF MODERATELY-TO-SEVERELY ACTIVE RHEUMATOID ARTHRITIS (RA)

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Background: Fatigue is a common symptom in RA and increasingly recognized as an important therapeutic target in disease management. Phase 3 randomized clinical trials (RCTs) have shown significant improvements in fatigue for sarilumab, based on the 13-item Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue measure. In TARGET (n=546) and MOBILITY (n=1197), patients receiving sarilumab 150 or 200 mg subcutaneous (SC) every 2 weeks (Q2W) achieved clinically meaningful improvements in fatigue vs placebo. In MONARCH (n=369), there was a trend towards greater improvement in fatigue scores for sarilumab 200mg SC Q2W vs adalimumab 40mg Q2W. To facilitate a trend towards greater improvement in fatigue scores for sarilumab, based on the 13-item Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue measure, including the subset of 10 FACIT-F items deemed most relevant to RA patients.

Objectives: To describe patient-level, cross-walked PROMIS-fatigue and scoring service 13- and 10-item PROMIS-fatigue scores, patients treated with sarilumab demonstrated statistically greater and clinically meaningful improvement in fatigue vs placebo and a trend towards greater improvement vs adalimumab. Converting FACIT-fatigue scores to PROMIS-fatigue using either the patient level cross-walk or via the PAPRICA method to the BIOCOM-Pso samples resulted in a dataset in which 88 of the 206 biomarker proteins could be reliably measured (CV Area < 20%; Signal to Noise ratio > 5; Library Dot Product > 0.8). This subset of the PAPRICA proteins was not able to discriminate between PsA and Pso and none of the associated peptides were significantly different between the two groups (p value < 0.05).

Conclusion: Consistent with trial results shown for FACIT-Fatigue, follow-up results across all studies (Table) indicate greater improvement in fatigue scores for sarilumab, based on the 13-item Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue measure, including the subset of 10 FACIT-F items deemed most relevant to RA patients.

Disclosure of Interests: None declared


SAT0644

OUTCOME MEASURES IN NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Neuropsychiatric involvement in Systemic Lupus Erythematosus (NPSLE) is one of the most complex and severe expressions of the disease consisting of a variety of neurological and psychiatric syndromes. To identify the NPSLE symptoms and to assist in test new therapeutic strategies or drugs in controlled clinical trials NPSLE is included.

Objectives: To identify the instruments used to assess NPSLE in published studies according to the OMERACT (Outcome Measures in Rheumatology) Filter 2.0 [Ref].

Methods: This systematic review was conducted in accordance with the Preferred Reporting Items for systematic reviews and Meta-analysis (PRISMA) statement. All articles available in English, published from June 1967 to March 1 2018, in Pubmed, EMBASE, PsyCINFO, Cochrane Library and EULAR Library for Outcome Measure were screened as well as extensive hand search. Study selection and data collection were performed by 4 independent reviewers. All data were extracted using a standardized template designed for this review, each outcome was characterized according to the OMERACT Filter 2.0 considering core areas (neurophysiological manifestations, life impact, death, resource use) and domains [Ref].

Results: Of 2,625 abstracts, we included in the review 62 studies of which 1 randomised clinical trial (1.6%, 32 patients), 4 systematic literature reviews (6.4%, 8,024 patients), 21 cohort studies (33.8%, 2,684 patients) and 36 observational studies (58.1%, 1,534 patients), with a total of 12,274 patients. Patients were predominantly female (86.6%) with a mean±SD age of 34.9±5.8 years. The mean disease duration was 5.1±2.2 years (range 1 - 9.6). The most frequent included events were seizures (34 studies, 54.8%), cerebrovascular disease (30 studies, 48.4%), psychosis and myelopathy (29 studies, 46.8%), mood disorders (28...
ANTI-DFS70 AUTOANTIBODIES INDUCED BY ANTI-TNF THERAPY IN RHEUMATOID ARTHRITIS AND SPONDYLOARTHRITIS PATIENTS

Teresa Carboni 1,2, Carmela Esposito 3, Ornella Mercuro 2, Antonio Carriero 1, Valentina Picerno 1, Maria Carmela Padula 1, Angela Padula 1, Vito Pafundi 2

Background: anti-DFS70 antibodies (anti-DFS70ab) were recently described as biomarkers clinically useful to discriminate Systemic Autoimmune Rheumatic Diseases (SARD) from non-SARD patients, especially if no concomitant SARD-specific autoantibodies were found. Several unanswered questions concerning the biological significance of this autoantibodies still remain. Objectives: to evaluate the prevalence of anti-DFS70ab in Rheumatoid Arthritis (RA) and Spondyloarthritis (SpA) patients and the influence of anti-TNF therapy on their development. Methods: sera from adult RA (n=100) and SpA (n=105) patients, included psoriatic arthritis, fulfilling ACR/EULAR 2010 and ASAS 2011 criteria, respectively, were studied for anti-DFS70ab as measured by IIF, then confirmed by immunoblotting. Medical history, demographic and clinical data were collected at enrolment.

Results: the prevalence of anti-DFS70ab was 4.00% (4/100) in the RA and 4.76% (5/105) in SpA cohort. All anti-DFS70ab in RA patients were monospecific, while only 1 sample in SpA showed concomitant anti-centromere positivity. The findings for the anti-DFS70ab positivity revealed no statistical differences between the groups (p>0.05). In RA cohort, there were no differences between anti-DFS70ab positive and negative patients regarding the F/M ratio (F/M, 3/1 vs 84/12, p=0.05), mean age (50.2±12.4 vs 55.6±11.7 yrs, p>0.05) and disease duration (18.8±7.7 vs 19.0±20 yrs, p>0.05) while the mean age of anti-DFS70ab patients was significantly higher than the negatives (66.8±10.4 vs 53.5±15.0 yrs, p<0.05). Serological and clinical data of anti-DFS70ab positive patients were summarized in Table 1. In our cohort, all anti-DFS70ab were negative before initiating biologics.

Conclusion: based on our findings, detection of anti-DFS70ab reactivity cannot completely exclude the suspicion of SARD, especially for RA and SpA. In addition, the rate of anti-DFS70ab positivity resulted higher in RA and SpA patients than previously observed in a cohort of samples from outpatients clinics (2.1%) [1]. Immunogenicity of anti-TNF therapy has been also addressed in this study, showing that all detected anti-DFS70ab were induced by anti-TNF therapy. Further studies are needed to support these preliminary data.

REFERENCES

Disclosure of Interests: Teresa Carbone: None declared, carmela esposito: None declared, ornella mercuro: None declared, antonio carriero: None declared, valentina picerno: None declared, maria carmela padula: None declared, angela padula: Speakers bureau: Lilly Italia EMS, vito pafundi: None declared, salvatore d’angelo: None declared


Table 1. Serological and clinical data of anti-DFS70ab positive patients.

<table>
<thead>
<tr>
<th>Patient n</th>
<th>Diagnosis</th>
<th>ACPA</th>
<th>RF</th>
<th>ENA</th>
<th>Extra-articular manifestations</th>
<th>Comorbidities</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>RA</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>None</td>
<td>AH</td>
</tr>
<tr>
<td>2</td>
<td>RA</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>Lung Fibrosis</td>
<td>OP, AH, HBV, DM, Dyslipidemia</td>
</tr>
<tr>
<td>3</td>
<td>RA</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>4</td>
<td>SpA</td>
<td>na</td>
<td>na</td>
<td>-</td>
<td>Erythema nodosum</td>
<td>Autoimmune thyroiditis</td>
</tr>
<tr>
<td>5</td>
<td>SpA</td>
<td>na</td>
<td>na</td>
<td>-</td>
<td>None</td>
<td>COPD, AH</td>
</tr>
<tr>
<td>6</td>
<td>SpA</td>
<td>na</td>
<td>na</td>
<td>-</td>
<td>Poliomyelitis</td>
<td>DM, AH, diverticulosis</td>
</tr>
<tr>
<td>7</td>
<td>SpA</td>
<td>na</td>
<td>na</td>
<td>-</td>
<td>Poliomyelitis</td>
<td>COPD, autoimmune thyroiditis, allergic asthma</td>
</tr>
</tbody>
</table>

RA, Rheumatoid Arthritis; SpA, Spondyloarthritis; ACPA, anti-Cyclic Citrullinated Peptide Antibody; RF, Rheumatoid Factor; AH, Arterial Hypertension; EM, Endomysiosis; OP, Osteoporosis; DM, Diabetes Mellitus; COPD, Chronic Obstructive Pulmonary Disease; na, not available; , negative; +, positive.

Disclosure of Interests: Teresa Carbone: None declared, carmela esposito: None declared, ornella mercuro: None declared, antonio carriero: None declared, valentina picerno: None declared, maria carmela padula: None declared, angela padula: Speakers bureau: Lilly Italia EMS, vito pafundi: None declared, salvatore d’angelo: None declared

Background: The mechanisms underlying thrombosis and cardiovascular disease (CVD) in antiphospholipid syndrome (APS) are not completely understood, but recent evidence has brought to light the existence of a complex interplay between traditional CV risk factors and disease-specific features, such as the presence of autoantibodies [1]. Recent studies have discovered the existence of a heterogeneous group of autoantibodies specifically directed against lipoproteins and their components [anti-high density lipoproteins antibodies (anti-HDL)]. Anti-HDL showed promising results in predicting the development of CVD, lipoprotein dysfunction and clinical outcomes in autoimmune conditions. Nevertheless, the association between anti-HDL and clinical features of APS remains unclear.

Objectives: The aim of the study was to evaluate the presence of IgG anti-HDL antibodies in a cohort of thrombotic APS patients and to investigate if these antibodies can discriminate between arterial and venous thrombosis.

Methods: This cross-sectional study included 60 patients with persistent antiphospholipid antibodies (aPL) positivity that fulfilled the Sydney criteria for thrombotic APS (venous and/or arterial) [2], and 20 age- and sex-matched healthy donors (HDs). Clinical data were retrospectively collected. Serum levels of total IgG, IgG anti-HDL antibodies and complete aPL profile were assessed, including lupus anticoagulant, anti-cardiolipin, anti-β2-glycoprotein I, and anti-phosphatidylserine/prothrombin both IgG and IgM antibodies.

Results: 43 patients (72%) were primary APS and 17 patients (28%) had a concomitant diagnosis of systemic lupus erythematosus. Thirty APS patients (50%) presented previous arterial events and 37 (61%) venous events (7 patients experienced recurrent thrombotic events, both venous and arterial; the first event was taken as a reference for the analyses). The characteristics of the cohort are displayed in Table 1. Higher levels of IgG anti-HDL were found in APS patients compared to HDs [mean 46 (±70) vs. 14 (±13) AU, respectively; p < 0.001], even after controlling for total IgG levels [anti-HDL/IgG: mean 13.1 (SD ±16.7) vs. mean 9.5 (SD ±6.6); p = 0.046] (Figure 1.1). No association with traditional cardiovascular risk factors, except for smoking habit (p < 0.001) was found. No differences in anti-HDL levels were observed between patients with primary APS and those with a concomitant autoimmune disease (p >0.050). Patients who experienced at least one arterial event had significantly higher levels of anti-HDL antibodies when compared to patients with history of venous thrombosis [mean 53 (SD ±94) vs. mean 34 (SD ±29), respectively; p =0.046]. This difference became stronger when adjusting for total IgG levels [anti-HDL/IgG: mean 13.1 (SD ±16.7) vs. mean 9.5 (SD ±6.6); p =0.007] (Figure 1.2). In addition, patients tested positive for aPS/PT (IgG/IgM) antibodies had significantly higher levels of anti-HDL antibodies [mean 53.1 (SD ±81.1) vs. mean 20.7 (SD ±17.6), p < 0.001] (Figure 1.2). No association with traditional cardiovascular risk factors was found. No differences in anti-HDL levels were observed between patients with primary APS and those with a concomitant autoimmune disease (p >0.050).

Conclusion: Our study demonstrates that thrombotic APS patients have higher levels of IgG anti-HDL antibodies, supporting the emerging role of these autoantibodies in APS setting. Moreover, our findings suggest that anti-HDL represent a promising tool for risk management and assessment and a potential biomarker for lipid dysfunction and arterial thrombotic events.

REFERENCES


Disclosure of Interests: None declared

RELIABILITY OF MAGNETIC RESONANCE IMAGING (MRI)-SCORING OF THE METATARSOPHALANGEAL-JOINTS ACCORDING TO THE RHEUMATOID ARTHRITIS-MRI SCORE (RAMRIS)

Yousra Dakkak1, Xanthe Matthijsen2, Desiée van der Heijde3, Monique Reijnierse2, Annette van der Helm - van Mil1,2,3, Leiden University Medical Center (LUMC), Rheumatology, Leiden, Netherlands; 2 Leiden University Medical Center (LUMC), Radiology, Leiden, Netherlands; 3Erasmus University Medical Center, Rheumatology, Rotterdam, Netherlands

Background: The Rheumatoid Arthritis Magnetic Resonance Imaging Score (RAMRIS) is validated for magnetic resonance imaging (MRI) of the hand. Its reliability when applied to metatarsophalangeal (MTP-1-5)-joints is unknown.

Objectives: To assess the inter-reader and intra-reader-reliability of status scores and the inter-reader-reliability of change scores applied to the MTP-joints for the following MRI-outcomes: bone marrow edema, synovitis, tenosynovitis and erosions.

Methods: Patients underwent 1.5T MRI of MTP(1-5)-joints. Two readers scored bone marrow edema(BME), synovitis, tenosynovitis and erosions. Interreader reliability was assessed of 4-41 consecutive early arthritis patients at baseline, the first 215 by two readers, the remaining 268 by two different readers. Additionally, baseline MRIs of 82 consecutive patients with arthralgia were scored by two readers, a random set of 40 patients by seven additional readers (nine readers in total). Intra-reader reliability was determined on a random set of 15 early arthritis patients, scored twice by two readers. For change-scores, 30 early arthritis patients with baseline and 1-year follow-up MRI were scored by two readers. Intraclass correlation coefficients (ICCs), Bland-Altman (BA)-plots and smallest detectable change (SDC) were determined.

Results: Interreader mean scores and ICCs in early arthritis are presented in Table 1; ICCs were good to excellent (0.85-0.92) in arthralgia-patients mean scores were lower, ICCs were comparable (Table 1). Intra-reader ICCs for MRI-features were good to excellent (0.84-0.98), but for erosions moderate for reader 1 (0.71) and excellent for reader 2 (0.92). Mean change scores and ICCs are presented in Table 2; ICCs were generally excellent (0.90), but moderate for erosions (0.77). SDCs were ≤1.0. BA-plots for status and change scores showed no systematic bias.

Conclusion: Status and change MRI-scores of BME, synovitis, tenosynovi- tis and erosions of MTP-joints can be assessed reliably by the RAMRIS. This is encouraging for the use of MRI of the MTP-joints in trials in early phases of RA.

Disclosure of Interests: None declared.

Table 1. Interreader intraclass correlation coefficients and average status scores according to the RAMRIS in early arthritis patients (n=441 in total) and patients with arthralgia (n=62)

| Region | Mean change scores and ICCs are presented in Table 1; ICCs were good to excellent (0.85-0.92) in arthralgia-patients mean scores were lower, ICCs were comparable (Table 1). Intra-reader ICCs for MRI-features were good to excellent (0.84-0.98), but for erosions moderate for reader 1 (0.71) and excellent for reader 2 (0.92). Mean change scores and ICCs are presented in Table 2; ICCs were generally excellent (0.90), but moderate for erosions (0.77). SDCs were ≤1.0. BA-plots for status and change scores showed no systematic bias.

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Disclosure of Interests: None declared.

Table 2. Intra-reader intraclass correlation coefficients and average status scores according to the RAMRIS in MTP-joints (n=441) from baseline until 12 months of follow-up

SAT0648

RELIABILITY OF MAGNETIC RESONANCE IMAGING (MRI)-SCORING OF THE METATARSOPHALANGEAL-JOINTS ACCORDING TO THE RHEUMATOID ARTHRITIS-MRI SCORE (RAMRIS)

Yousra Dakkak1, Xanthe Matthijsen2, Desiree van der Heijde3, Monique Reijnierse2, Annette van der Helm - van Mil1,2,3, Leiden University Medical Center (LUMC), Rheumatology, Leiden, Netherlands; 2 Leiden University Medical Center (LUMC), Radiology, Leiden, Netherlands; 3Erasmus University Medical Center, Rheumatology, Rotterdam, Netherlands

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Disclosure of Interests: Yousra Dakkak: None declared, Xanthe Matthijsen: None declared, Desiree van der Heijde Consultant for: Abbvie, Amgen, Astellas, AstraZeneca, Bristol-Mysers Squibb, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, Union Chimique Belge, Monique Reijnierse Grant/research support from: Funding from

Disclosure of Interests: Yousra Dakkak: None declared, Xanthe Matthijsen: None declared, Desiree van der Heijde Consultant for: Abbvie, Amgen, Astellas, AstraZeneca, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Daiichi, Eli-Lilly, Galapagos, Gilead, GlaxoSmithKline, Janssen, Merck, Novartis, Pfizer, Regeneron, Roche, Sanofi, Takeda, Union Chimique Belge, Monique Reijnierse Grant/research support from: Funding from
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The funding source had no role in the design and conduct of the study.


SAT0649

DEVELOPMENT AND VALIDATION OF A PATIENT-REPORTED OUTCOME ASSESSING ACTIVITY LIMITATION AND PARTICIPATION RESTRICTION OF PATIENTS WITH SYSTEMIC SCLEROSIS: THE COCHIN 17-ITEM SCLERODERMA FUNCTIONAL SCALE (CSF-17)

Camille Daste1, Hendy Abdou2, Frantz Foissac2, Agathe Papelier1, Sophie Alam1, Marie-Martine Lefève Cola1, Serge Poiraudieu1, François Rannou1, Luc Mouthon1, Christelle Nguyen1, Service de Rééducation et de Réséparation de l’Appareil Locomoteur et des Pathologies du Rachis, Hôpital Cochin, Paris, France, Unité de Recherche Clinique – Centre d’Investigation Clinique Paris Descartes Necker/Cochin, Hôpital Tarnier, Paris, France, Cabinet d’Études Sociologiques Interlis, Paris, France, Service de Médecine Interne, Centre de Référence Maladies Systémiques Auto-innées Rares de l’élla-de-France, Hôpital Cochin, Paris, France

Background: Few patient-reported outcomes measures (PROs) have been specifically designed to assess the functioning of patients with systemic sclerosis (SSc). In addition, the development of currently available instruments did not fully follow current guidelines (1).

Objectives: To develop and validate a PRO assessing activity limitation and participation restriction of patients with SSc.

Methods: A provisional International Classification of Functioning, Disability and Health (ICF)-based 65-item questionnaire previously developed from interviews of SSc patients was submitted online to French patients (n=184) of the Scleroderma Patient-centered Intervention Network e-cohort (2). Items were reduced according to their metric properties, dimensional structure of the questionnaire was assessed by principal component analysis, convergent and divergent validities using the Spearman correlation coefficient (ρ), internal consistency by the Cronbach α coefficient and reliability by a test-retest method using intraclass correlation coefficient (ICC) and Bland and Altman analysis.

Results: Overall, 113/184 (61.4%) patients completed the provisional questionnaire. The item-reduction process resulted in a 17-item questionnaire, the Cronbach α coefficient was 0.94 for section A and 0.95 for section B. The observed convergent validity with global activity limitation, pain, depression and aesthetic burden and divergent validity with anxiety. The Cronbach α coefficient was 0.94 for section A and 0.95 for section B. ICC (n=25 patients) was 0.92 for CSF-17 total score. Bland and Altman analysis did not reveal a systematic trend for the test-retest.

Conclusion: The CSF-17 is a self-administered questionnaire assessing activity limitation and participation restriction of patients SSc with good content and construct validities.

REFERENCES


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Disclosure of Interests: None declared


SAT0650

THE INFLUENCE OF PATIENT DEMOGRAPHICS ON DISEASE ACTIVITY MEASUREMENTS IN RHEUMATOID ARTHRITIS

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Background: Several indexes have been constructed for the measurement of disease activity in rheumatoid arthritis (RA) patients, including the Disease Activity Score 28-joint count, which either includes the Erythrocyte Sedimentation Rate (DAS28ESR) or the C-reactive protein concentration (DAS28CRP), and the Clinical Disease Activity Index (CDAI). The categorization of the results of these three indexes into levels of disease activity (Remission, Low, Moderate and High) is used to assess patient outcomes, and to guide medical decisions regarding treatment. However, the different indexes can lead to somewhat different classification, and hence influence treatment decisions (3).

Objectives: To investigate how DAS28ESR, DAS28CRP and CDAI indexes are associated to age and sex in RA patients. To investigate the agreement between indexes and between categories of disease activity levels.

Methods: We identified a cohort of RA patients, registered in the Swedish Rheumatology Quality Register between January 1**2014 and December 3**2017. The indexes were obtained from the first visit at the time point of RA diagnosis, and at the visit registered at the start of a first ever biological treatment prescription. Linear models were used to investigate the correlation between the indexes, age and sex. The agreement between the indexes was explored with Bland-Altman plots. The agreement between disease activity levels was evaluated through kappa statistics.

Results: Data were analyzed for 3855 RA patients (2576 women, mean age ±SD=60±15) at their first diagnosis visit and for 3062 RA patients (2313 women, mean age ±SD=57±14) at the start of their first biologic. Similar results for all subsequently described analyses were obtained at both time points. The correlation coefficient and 95% confidence interval (95%CI) between the indexes and age were 0.093 (0.063-1.124) for DAS28ESR and 0.055 (0.025-0.085) for DAS28CRP at the first visit, while CDAI was not correlated to age. There was no difference between men and women for CDAI and DAS28CRP, while DAS28ESR presented a mean difference of 0.1 unit between men and women. The agreement between categories of disease activity was moderate: at the RA diagnosis visit, the kappa statistics and 95% CI were: 0.63 (0.61-0.65) between DAS28ESR and DAS28CRP, 0.59 (0.57-0.61) between DAS28ESR and CDAI, and 0.55 (0.53-0.57) between DAS28CRP and CDAI. About 25% of the patients were classified differently. The Bland-Altman plot revealed that the difference between DAS28ESR and DAS28CRP depended on sex and slightly increased with age.

Conclusion: Factors related to patient demographics might influence the results of disease activity indexes. This has a potential to affect clinical decisions, as the definition into disease activity categories can differ depending on the score used. This suggests the need to consider sex and age when defining such categories and interpreting results from these indexes.

REFERENCES
Disclosure of Interests: Bénédicte Delcoigne: None declared, Daniela Di Giuseppe: None declared, Johan Asling Grant/research support from: Karolinska Institutet (JA) has or has had research agreements with the following pharmaceutical companies, mainly in the context of the ATRIS national safety monitoring programme for rheumatology biologicals: Abbvie, BMS, MSD, Eli Lilly, Pfizer, Roche, Samsung Bioepis, and UCB, Consultant for: Karolinska Institutet has received remuneration for JA participating in ad boards arranged by Lilly, Novartis, and Pfizer., Lotta Ljung: None declared

SAT0652

VALIDATION OF A RISK PERCEPTION QUESTIONNAIRE DEVELOPED FOR PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Risk perception (RP) is a multidimensional phenomenon that describes the individual’s judgment of the likelihood of experiencing something unpleasant. RP shapes health-related-behaviors and may be central for rheumatoid arthritis (RA) management, where treatment must be based on shared decisions between the patient and the rheumatologist. Rheumatologists can motivate successful self-care in RA patients with information that brings the physician vision closer to the patient’s perceptions. Assessing patients-perceived risk may help explain how RA patients integrate their ideas concerning the disease and its treatments, and how this understanding drives their self-care management. There is no current validated instrument to assess RP in RA.

Objectives: To assess whether the SENS can discriminate between treatment groups when the treatment contrast is low, using data from the DRESS (Dose REduction Strategy of Subcutaneous TNF inhibitors) trial

Methods: The DRESS study (Dutch trial register, NTR 3216, CMO region Arnhem-Nijmegen, NL 37704.091.11) is an open label non-inferiority randomised controlled trial in which RA patients with low disease activity on a stable adalimumab or etanercept dose were randomised 2:1 to disease activity guided tapering or usual care [4]. Radiographs of hand and feet at baseline and the end of follow up (18 months) were assessed independently in chronological order by 2 blinded trained readers using the SHS. The SENS was determined based on the individual joint scores of the SHS in the COBRA trial, suggesting some discrimination might be lost when using the SENS, especially in more advanced RA populations [2]. This is an important issue, as time savings using SENS are substantial (7 instead of 25 minutes [1,3], but contrast between interventions is in general lower than in the early years of RA research as the standard of care improves and trials are more and more characterized by active controls and disease activity guided treatment strategies that tend to converge.

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Results: Table 1 shows baseline characteristics of the study population. A significant but clinically unimportant mean increase (95% CI) in radiographic progression was found in the early years of RA research as the standard of care improves and trials are more and more characterized by active controls and disease activity guided treatment strategies that tend to converge.

Results: Table 1 shows baseline characteristics of the study population. A significant but clinically unimportant mean increase (95% CI) in radiographic progression was found in the early years of RA research as the standard of care improves and trials are more and more characterized by active controls and disease activity guided treatment strategies that tend to converge.

Table 1. Baseline characteristics

<table>
<thead>
<tr>
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<th>Dose reduction (n=116)</th>
<th>Usual care (n=59)</th>
</tr>
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<tbody>
<tr>
<td>Age, mean (sd)</td>
<td>59 (10)</td>
<td>58 (9)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>78 (61%)</td>
<td>41 (69%)</td>
</tr>
<tr>
<td>Disease duration, median (IQR)</td>
<td>10 (5-16)</td>
<td>10 (6-16)</td>
</tr>
<tr>
<td>Erosive disease, n (%)</td>
<td>65 (61%)</td>
<td>34 (62%)</td>
</tr>
<tr>
<td>Rheumatoid factor, n (%)</td>
<td>91 (83%)</td>
<td>49 (83%)</td>
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<tr>
<td>Anti CCP, n (%)</td>
<td>82 (71%)</td>
<td>45 (76%)</td>
</tr>
<tr>
<td>Baseline SvdH, median (IQR)</td>
<td>23 (6-50)</td>
<td>18 (9-47)</td>
</tr>
<tr>
<td>Baseline SENS, median (IQR)</td>
<td>10 (4-22)</td>
<td>10 (5-20)</td>
</tr>
</tbody>
</table>

Conclusion: The SENS and SHS were equally able to detect a difference in radiographic progression, even with a very low treatment contrast between the two groups and in this relatively advanced RA population.

REFERENCES

Disclosure of Interests: None declared
PATIENT-ACCEPTABLE SYMPTOM STATUS IN RHEUMATOID ARTHRITIS: WEALTH AND AGE MATTER BEYOND DISEASE ACTIVITY AND IMPACT. AN ANALYSIS OF 548 PATIENTS

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Background: Patient Acceptable Symptom State (PASS) represents the maximum level of symptom intensity that patients consider acceptable. Control of disease activity is associated to attainment of PASS1. Recognizing the factors associated with PASS status beyond disease activity, can be helpful in identifying the need for interventions beyond disease-modifying drugs, aimed at improving the satisfaction and well-being of patients with rheumatoid arthritis (RA).

Objectives: To explore the clinical and socio-demographic factors associated with PASS status in RA.

Methods: Data of patients with definite diagnosis of RA from 11 countries (post-hoc analyses of RAID Study2, with additional data from Portugal) were used. PASS was assessed using the anchored method based on patients’ perspective, through the question: “Think about all the ways your RA has affected you during the last week. If you were to remain for the next few months as you were during the last week, would this be Acceptable/Unacceptable?”. Variables analysed for differences across PASS status were (a) disease activity based on DAS28-3v-ESR (joint counts and ESR) categories, (b) impact by the seven patient-reported domains included in the RA Impact of Disease (RAID) score, (c) demographics: age (above or below 50) and gender, and (d) Country gross domestic product (GDP) classified as High GDP (>35.000 USD per capita) and Low GDP. Differences between patients in PASS or not were assessed using t-test for independent samples or Chi-square test, as adequate. Variables with p<0.05, gender and GDP category were included in multivariable logistic regression (Forward Conditional) analysis. A sub-group analysis was performed for patients in DAS28-ESR remission.

Results: In all, 548 patients (80.5% female, mean (SD) age 55.8 (12.8) years, mean (SD) disease duration 13.6 (10.6) years, mean (SD) DAS28-3v 3.6 (1.5), 44.2% in LDA or remission) from 11 European countries (5 (n=230) with NOR-DMARD and 6 (n=318) with low-GDP) were assessed. The majority of patients (65.7%) considered themselves to be in PASS; among them 40% were in remission and 16.7% in DAS28-3v≤2.6 (14.1) years, mean disease duration 13.8 (10.4) years, mean DAS 28-3v-ESR 3.0 (1.4)] were analysed. In all, 14.5% considered themselves as being in a “very good”, 21% as “good” and 33% in an “acceptable” status. Disease activity, RAID global score and all individual seven domains of RAID were significantly different between patients across these 3 symptom states (p<0.001). Patients reporting a “Very Good” symptom status had disease activity in the range of remission (mean DAS28-3v-ESR: 1.99±0.91), while patients in “Acceptable” status were in range of low disease activity (DAS28-3v-ESR: 2.98±1.20) and in moderate disease activity in patients with “Bad” (DAS28-3v-ESR: 3.83±1.44) and “Very Bad status” (DAS28-3v-ESR: 4.10±1.59). Remission according the Boolean ACR/RHU criteria was observed in 70.9% of patients in “Very Good” symptom status (versus 26% in “Good”, 5% in “Acceptable” and inferior to 1% in “Bad” and “Very Bad” symptom status). The cut-off value for “Very Good” status was 0 for most individual RAID items, except for pain and fatigue ≤1 (Figure1).

Conclusion: Being in a “very good” symptom status showed a good correspondence to being in remission and having very low disease impact. This shows promising in identifying a status that patients would actually desire, more than accept for, while corresponding to a level of disease activity consistent with the long-term preservation of structure and function.

REFERENCES

Disclosure of Interests: Calia Duarte: None declared, Eduardo Santos: None declared, Tore K. Kvien Grant/research support from: AbbVie, Biogen, BMS, MSD, Pfizer, Roche and UCB. Consultant for: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Hospira, Merck-Serono, MSD, Novartis, Oktal, Orphan Pharma, Pfizer, Roche, Sandoz, Sanofi, Mylan and UCB. Speakers bureau: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Hospira, Merck-Serono, MSD, Novartis, Oktal, Orphan Pharma, Pfizer, Roche, Sandoz, Sanofi and UCB, Maarten de Wit: None declared, maxime dougados Grant/research support from: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma, Consultant for: Eli Lilly and Company, Pfizer, AbbVie, and UCB Pharma, Laure Gossec Grant/research support from: AbbVie, BMG, Celgene, Janssen, Lilly, MSD, Novartis-Sandoz, Pfizer, Sanofi, and UCB, Consultant for: AbbVie, Biogen, BMG, Celgene, Janssen, Lilly, MSD, Nordic Pharma, Novartis-Sandoz, Pfizer, Roche, Sanofi, and UCB. Consultant for: L Gossec has received honoraria from Celgene as investigator for this study, José Antonio P. da Silva: None declared

SHOULD PATIENTS WITH RHEUMATOID ARTHRITIS (RA) ASK FOR A BETTER DEAL THAN MERELY AN ACCEPTABLE SYMPTOM STATE? AN ANALYSIS OF 1931 RA PATIENTS

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Background: Patients satisfaction with their symptoms state may be considered an acceptable outcome in RA. However, many patients who report being in an Acceptable Symptom State (PASS) have still moderate disease activity.

Objectives: To explore whether it is possible to identify more stringent levels of symptom states in patients’ perspective.

Methods: A cross-sectional analysis of unselected adult patients with the diagnosis of RA from the RA Impact of Disease (RAID) validation study (n~570, from 12 European countries), and from the Norwegian DMARD (NOR-DMARDII) registry (n=1372), was performed. Symptom state was calculated using the anchored method based on the patients’ perspective, taking, as gold standard, the question: “Think about all the ways your rheumatoid arthritis has affected you during the last week. If you were to remain for the next few months as you were during the last week, how would you consider this state?”, with five levels: Very bad/Bad/Acceptable/Good/Very good. Disease activity was assessed based on the DAS28-3v (joint counts and ESR). Impact was evaluated through the seven patient-reported domains included in the RAID score. The threshold levels of DAS28-3v, Individual RAID items and RAID score for Acceptable/Good/Very Good states were calculated using the receiver-operating characteristic (ROC) curve and the optimal cut-off was determined through Youden Index.

Results: Data from 1931 patients [74.5% female, mean (SD) age 54.4 (14.1) years, mean disease duration 13.8 (10.4) years, mean DAS 28-3v-ESR 3.0 (1.4)] were analysed. In all, 14.5% considered themselves as being in a “very good”, 21% as “good” and 33% in an “acceptable” status. Disease activity, RAID global score and all individual seven domains of RAID were significantly different between patients across these 3 symptom states (p<0.001). Patients reporting a “Very Good” symptom status had disease activity in the range of remission (mean DAS28-3v-ESR: 1.99±0.91), while patients in “Acceptable” status were in range of low disease activity (DAS28-3v-ESR: 2.98±1.20) and in moderate disease activity in patients with “Bad” (DAS28-3v-ESR: 3.83±1.44) and “Very Bad status” (DAS28-3v-ESR: 4.10±1.59). Remission according the Boolean ACR/EULAR criteria was observed in 70.9% of patients in “Very Good” symptom status (versus 26% in “Good”, 5% in “Acceptable” and inferior to 1% in “Bad” and “Very Bad” symptom status). The cut-off value for “Very Good” status was 0 for most individual RAID items, except for pain and fatigue ≤1 (Figure1).

Conclusion: Being in a “very good” symptom status showed a good correspondence to being in remission and having very low disease impact. This shows promising in identifying a status that patients would actually desire, more than accept for, while corresponding to a level of disease activity consistent with the long-term preservation of structure and function.
SAT0655
THE SPECTRUM OF MYOSITIS ANTIBODIES: CLINICAL CORRELATION AND PREVALENCE OF ANTI-DFS70
carmela esposito1,2, teresa Carbone3,4, antonio carriero1, valentina picerno1, Maria Carmela Padula2, Angela Padula2, vito pafundi3, salvatore D’angelo3
1Rheumatology Division-Internal Medicine Department, Prato Hospital, Prato, Italy; 2IReL – Rheumatology Institute of Lucania – San Carlo Hospital, Potenza, Italy; 3Department of Immunopathology Laboratory, San Carlo Hospital, Potenza, Italy
Background: Myositis can be a clinical feature of several rheumatic diseases. In inflammatory idiopathic myopathies (IIM), such as Dermatomyositis (DM), Polymyositis (PM), Antisynthetase syndrome (ASS), muscular dystrophies and to connect them to clinical features, cancer history and anti-DFS70ab presence.
Methods: 37 patients with myositis (including IIM, overlap syndrome and myositis related to other rheumatic diseases) were evaluated. Anti-DFS70ab pattern was determined by indirect immunofluorescence on HEp-2000 cells. Detection of anti-DFS70ab specificity (truncated sequence of the DFS70 antigen (residues 349-435)), of MDA (MDA-5, TIF-1, SAE1, SAE2, NXP-2, Jo-1, PL-7, PL-12, EJ, OJ, KS, ZO, HA, SRP, Mi-2), of MAA (U1-RNP, SSA/Ro52/60, PM-Scl100/75, Ku) and of other Scleroderma associated antibodies (Sc-70, CENP-A, CENP-B, RNA Polymerase III, Th/β, Fibrillarin) were performed using immunoblotting assay. Clinical, serological and instrumental data were recorded.
Results: 15 patients had a diagnosis of DM, 8 of PM, 3 of ASS, 5 of overlap syndrome (3 with Systemic Sclerosis (SSc), 1 with Sjogren Syndrome (SSS), 1 with cryoglobulinaemia), 6 of myositis related to other rheumatic disease (1 SSc, 1 Rheumatoid Arthritis, 2 Undifferentiated Connective Tissue Disease, 2 Systemic Lupus Erythematosus). In IIM, overall frequencies of MSA and MAA were 46.1% (12/26) and 38.4% (10/26), respectively, with concomitant expression in 5/26 cases. The 30.7% (8/26) of patients was negative for any type of antibodies. Mi-2 (4/15=26.6%), NXP-2 (3/15=20%) and SRP (2/15=13.3%) were detected in DM subset and were associated with typical skin lesions, muscle weakness, dysphagia and microvascular damage on capillaroscopy, while no interstitial lung disease, cardiac and articular involvement were recorded. Jo-1 was positive in 5/26 patients (2 PM, 2 ASS, 1 DM=19.2%) characterized by interstitial lung disease, arthritis, skin involvement and muscle weakness and by pulmonary hypertension when associated with TIF1-γ (1 DM=6.6%). Autoantibodies profile in overlap syndrome and myositis related to other rheumatic diseases was characterized by prevalence of MAA, more frequently PM-Scl100/75, RNP, Ku, SSA/Ro52/60. Only in 1 patient with an overlap syndrome (SSc) and lung cancer, but to our knowledge no data are present about melanoma. Our preliminary data confirm that, not only in DM but also in PM, anti-DFS70ab were observed with a low frequency; however more studies are needed to establish the possible role of these antibodies.
Disclosure of Interests: : carmela esposito: None declared, teresa Carbone: None declared, antonio carriero: None declared, valentina picerno: None declared, Maria Carmela Padula: None declared, Angela Padula: None declared, vito pafundi: None declared, salvatore D’angelo: None declared

SAT0656
DAPSA OR MDA/VLDA CRITERIA FOR DEFINING THE TREATMENT TARGET IN PSSORIC ARTHRITIS?: CROSS-SECTIONAL ANALYSIS FROM A MULTICENTER ITALIAN COHORT
Ennio Giulio Fava1, luca Idalozzi2, serena Bugatti3, Alberto Baticcioii2, luca Quattrocchi2, Matteo Filippini2, Simone Parisi2, marina Bigigjero2, angelo Fassio2, G Zanfrmundo3, Giuliana Gugino8, Giovanni4, Maria Chiara Dito5, Francesca Ciccia6, Gaetano Pin-C TO Institute, Rheumatology, Milan, Italy; 2University of Verona, UOC Rheumatology, Verona, Italy; 3University of Pavia, IRCCS PoliChieti San Matteo, Rheumatology, Pavia, Italy; 4La Sapienza Universita`, Roma, Italy; 5University of Udine, Rheumatology Clinic, Udine, Italy; 6ASST Spezial Civil, UO Reumatologia, Brescia, Italy; 7UCO Città della Salute e della Scienza, Turin, Italy; 8University of Palermo, DIBIMIS, Palermo, Italy; 9University of Campania Luigi Vanvitelli, Rheumatology, Naples, Italy
Background: According to international recommendations, psoriatic arthropitis (PsA) should be managed by a treat-to-target approach, but the identification of the best tool for defining the target of remission/low disease activity (LDA) is still controversial.
Objectives: To evaluate and compare the rates of remission/LDA by comparing Disease Activity in Psoriatric Arthritis (DAPSA) score with Very Low Disease Activity (VLDA)/Minimal Disease Activity (MDA) criteria in a real-life multicentre cohort of PsA patients.
Methods: We performed a cross-sectional analysis including the first consecutive 500 PsA patients evaluated in 8 Italian rheumatology centres since September 2017. The rates of patients achieving DAPSA remission/ LDA and VLDA/MDA were calculated and compared by a chi-square test. The agreement between the two criteria sets was established by Cohen’s kappa. The proportion of patients with residual disease activity despite remission/LDA and VLDA/MDA was computed for: peripheral arthritis...
MONOCYTE-LYMPHOCYTE RATIO AND PLATELET-LYMPHOCYTE RATIO: ROLE AS BIOMARKERS OF DISEASE ACTIVITY IN PSORIATIC ARTHRITIS PATIENTS

Rafael Ferreira, Sara Garanhão, Bruno Miguel Fernandes, Salomé Garcia, Sofia Pimenta, Miguel Bernardes, Lúcia Costa, São João Hospital Centre, Porto, Portugal

Background: Monocyte-lymphocyte ratio (MLR), neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) have been used to evaluate the inflammatory status in a wide variety of diseases like cardiovascular and autoimmune diseases. Furthermore, some recent data showed relevant association of this haematological parameters with others traditional inflammatory measures as serum c-reactive protein (CRP) levels in rheumatic patients, suggesting their use as a valuable indicator of disease activity.

Objectives: To assess the association between the NLR, MLR, eosinophil-lymphocyte ratio (ELR), basophil-lymphocyte ratio (BLR) and PLR with disease activity and functional parameters in psoriatic arthritis (PsA) patients.

Methods: An observational cross-sectional study was performed in patients with psoriatic arthritis before introduction of a bDMARD, followed at our Rheumatology department until December 2018. Demographic, clinical and laboratory information were collected from the national database (Rheuma.pt). Available data of blood cell counts were consulted and NLR, MLR, ELR, BLR and PLR were calculated by dividing neutrophil, monocyte, eosinophil, basophil and platelet count by lymphocyte count, respectively. The following disease activity and functional scores were assessed: levels, CRP and ESR, DAS28 4V and 3V (ESR and CRP), HAQ, BASDAI, ASDAS-CRP, BASMI, BASFI, swollen and tender joints counts (SJC and TJC), SPARCC index, patient global assessment (PGA) and physician global assessment (PGA) rated on a visual analogue scale (VAS). Correlations between variables were evaluated with Spearman’s test. The statistical analysis was performed using SPSS 21.0 software. Differences were considered statistically significant at p<0.05.

Results: A total of 83 patients were enrolled. Forty-three were females (51.8%) and forty were males (48.2%). The mean age was 47 years (SD 10.9) and the median disease duration at start of biological therapy was 6.9 years (min:1.4; max:32.4). In total, 67.5% of the patients had axial involvement (n=56), 91.6% articular involvement (n=76) and 43.4% enthesopathic involvement (n=36). Almost all patients fulfilled the CASPAP criteria for PsA (n=78; 94%). Thirty patients presented with arthritis (36%). Most were non-smoking (n=48; 57.8%) and most didn’t have history of alcohol consumption (n=55; 66.3%). According to ASDAS criteria, 25 patients (30.1%) had high disease activity and 45 patients (54.2%) very high disease activity. At time of evaluation, 71.1% were receiving csDMARDs. NSAIDs and corticosteroids were prescribed in 80.7% and 54.2% of the patients, respectively. We found statistically significant correlation between MLR values and CRP levels (r=0.278, p=0.014). MLR did not correlate with ESR levels, DAS28 4V and 3V (ESR and CRP), HAQ, BASDAI, ASDAS-CRP, BASMI, BASFI, SJC, TJC, SPARCC, PGA and PGLR values also had weak correlation with ESR (r=0.340, p=0.002), DAS 4V-ESR (r=0.260; p=0.027) and with DAS 3V-ESR (r=0.290, p=0.012). There was no statistically significant correlation between PLR values and others disease parameters. No significant correlation were found between NLR, ELR and BLR and the functional and disease activity scores evaluated.

Conclusion: Our study showed that MLR had a positive association with CRP and PGA with ESR, DAS 4V-ESR and DAS 3V-ESR. Evaluation of this novel inflammatory biomarkers may represent a simple, cost-effective and useful tool in monitoring disease activity in PsA patients.

Disclosure of Interests: None declared


SAT0658 A LONGITUDINAL ANALYSIS OF ANTI-FHL1 ANTIBODIES IN A SWEDISH COHORT OF PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

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Background: Antibodies targeting a novel and muscle-specific autoantigen, the Four-and-a-half-LIM-domain 1 (anti-FHL1), have been identified in patients with idiopathic inflammatory myopathies (IIM). Objectives: The aim of this project was to evaluate when anti-FHL1 auto-antibodies are present in the course of the disease and if autoantibodies titers vary over time.

Methods: The anti-FHL1 antibody status was obtained from a previous serological cross-sectional analysis from where we selected sera from IIM anti-FHL1+ patients (n=26) and sex and age matched sera from IIM anti-FHL1 patients (n=51), and healthy controls (HCs, n=50). Levels of anti-FHL1 autoantibodies were evaluated by ELISA. Patients included in the study had at least one sample available at time of diagnosis and one consecutive serum sample within an interval of 36 months. All patients were followed at the Division of Rheumatology, Karolinska University Hospital from January 1982 to December 2017. HCs sera collected at a single time point were tested.

Results: In the IIM group we included 76 patients with a total of 320 serum samples. Median follow-up time was 108 months, with median of 4 samples available per patient. In total, we identified the presence of anti-FHL1+ antibodies in n=31 IIM patients, corresponding to the group of
APPLYING THE OMERACT TRUTH FILTER TO A NEW PROPOSAL OF CORE OUTCOME DOMAINS IN MIXED KINGDOM

were fluctuating around the cut-off point. Eight of 14 (57%) patients from the intermediate positive and baseline negative groups were seroconverted around the cut-off point. Eight of 14 (57%) patients from the group “baseline negative” seroconverted to anti-FHL1 within the first 36 months. The anti-FHL1 “negative” group presented constant low anti-body titers during the longitudinal follow-up.

Conclusion: Anti-FHL1 antibody positivity was detected in patients with high titers of anti-FHL1 antibody in the first available serum sample or developed within the first 36 months after diagnosis and persisted over many years. A group of patients with intermediate levels had fluctuating positivity over the years. It is still unknown if the anti-FHL1 antibody titer is a marker of prognosis and/or damage in IIM; thus, clinical data needs to be addressed, and in-vitro experiments and biochemical characterization of this autoantibody are still required.

Disclosure of Interests: Angeles Shunashy Galindo-Feria: None declared. Eliad Ya’ari: None declared. César del Moro: None declared. Carina Fernández-Cerqueira: None declared. Maryam Dastmalchi: None declared. Edvard Wigren: None declared. Susanne Gräslund: None declared. Ingrid E. Lundberg Grant/ research support from: Dr. Lundberg has received honoraria from Bristol Myers Squibb and Medimmune and is currently receiving a research grant from Bristol Myers Squibb and from Astrazeneca., Consultant for: She is a scientific advisor for Bristol Myers Squibb, and aTyr.


SAT0659 APPL YING THE OMERACT TRUTH FILTER TO A NEW ELECTRONIC SPINAL MOBILITY INDEX FOR AXIAL SPONDYLOARTHROPSIS BASED ON INERTIAL SENSORS

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Background: Loss of spinal mobility is one of the most characteristic problems for people with axial spondyloarthrits (axSpA) and is predictive of loss of function. Traditional measures such as the BASMI fail to capture many elements of spinal mobility and lack responsiveness to change. Inertial Motion Unit (IMU) sensors can be used to accurately measure spinal movement without requiring significant operator expertise.

Objectives: The primary objective of this study was to test the reliability of these new tools in patients with axSpA and to develop a new composite spinal mobility index. Our secondary objective was to apply the OMERACT ‘Truth’ filter to evaluate the new index for bias, for clinical relevance, and for convergent validity with existing measures.

Methods: Patients with axSpA fulfilling ASAS classification criteria were recruited. A Move system was used to obtain ROM by attaching two IMU sensors at the cervical (Occiput-T3) and lumbar spine (L1-Sacrum). Intrarater, inter-rater and test-retest reliability of IMU tests were assessed by intraclass correlation coefficients (ICC). The maximum range of movement for anterior flexion/extension (AFE), lateral flexion (Left-Right) and rotation (Left-Right) were obtained for the lumbar and cervical region. These six values were used in a composite score (IMU-ASMI) which referenced equivalent ROM values from normal subjects in an earlier criterion validity study. Pearson correlation coefficients with BASFI were calculated for each component as well as the overall score.

Results: The study included 40 patients (12 females, 28 males) with a mean age of 48 (27-41). Subjects had a wide range of severity of axSpA. The mean BASMI was 4.8 (range 0.7 to 8.2, SD 1.9). The mean IMU-ASMI was 4.0 (range 1.9-5.2, SD 2.1). The sensor based measurements had good to excellent reliability (Table 1) and correlated closely with BASMI (r=0.79). The mean BASFI was 4.6 and the IMU-ASMI correlated closely with BASFI (r=0.71).

Face Validity: Each IMU test presents spinal movement in angles and can also be represented as a normalized severity index analogous to BASMI. The mean cervical and lumbar IMU-ASMIs were 3.5 and 4.4 units, respectively.

Construct Validity: Do IMU movements correlate with their corresponding traditional measurements? As expected, the closest correlations were between IMU and goniometer cervical rotation (r=0.85) and between IMU and tape measure lumbar side flexion (r=0.84). Correlations between Schober’s test and IMU lumbar AFE and between tragus to wall and IMU cervical FE were moderate (r=0.62, 0.65).

Do IMU movements correlate with BASFI? Correlation coefficients were as follows: lumbar AFE -0.57; rotation -0.59; side flexion -0.45; cervical AFE -0.55; rotation -0.61; side flexion -0.39. BASFI correlations with BASMI were comparable.

Content Validity/Comprehensiveness: No major ceiling or floor bias issues were found in the composite indices. Intrameasure distance (BASMI) represents hip rather than spinal mobility, but it correlates with BASFI and is not in the IMU-ASMI. IMU-ASMI includes lumbar rotation which accounts for 27% (0-53%) of the lumbar mobility score.

Conclusion: IMU sensors can be used by non-experts to accurately and reliably measure spinal mobility in patients with axSpA. Lumbar rotation is an important new outcome measure.

REFERENCES


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Disclosure of Interests: Philip Gardiner Grant/research support from: Educational support to attend rheumatology conferences from AbbVie, Abbott, MSD, Novartis, Amgen, Pfizer, Roche, UCB., Speakers bureau: Menarini, Dawn Small Employee of: Medical representative - Farmitalia Carlo Erba, Pharmacia, Pharmacia & Upjohn, Yamanouchi/Astellas., Paid instructor for: Medical representative - Farmitalia Carlo Erba, Pharmacia, Pharmacia & Upjohn, Yamanouchi/Astellas., Pedro Machado Consultant for: Abbvie, BMS, Celgene, Janssen, MSD, Novartis, Pfizer, Roche and UCB, Speakers bureau: Abbvie, BMS, Celgene, Janssen, MSD, Novartis, Pfizer, Roche and UCB, Karla Munoz Esquivel: None declared, Joan Condell: None declared, Antonio Cuesta-Vargas: None declared, Juan L. Garrido-Castro: None declared.


SAT0660 PROPOSAL OF CORE OUTCOME DOMAINS IN MIXED CRYOglobulinemic VAScULITIS

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Background: Cryoglobulinaemic vasculitis is immune complex mediated vasculitis of medium and small-size vessels. This vasculitis involves mainly kidneys, peripheral nervous system, skin and joints. Currently, no standardized outcome measures are available for the evaluation of treatments in patients with cryoglobulinemic vasculitis.

Objectives: To identify a core set of outcome measure (what to measure) for clinical studies for mixed cryoglobulinemic syndrome, following the OMERACT filter 2.0. [Ref]Methods: A search was made in Medline (via PubMed) and Embase using a standardized search [filter https://omeracthandbook.org/]. This review considered studies that included patients with Mixed (type 2 and 3) cryoglobulinemic syndrome, any type of outcome measures, articles in

<table>
<thead>
<tr>
<th>Movement</th>
<th>AFE</th>
<th>Lat</th>
<th>Rot</th>
<th>AFE</th>
<th>Lat</th>
<th>Rot</th>
<th>IMU-ASMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intra-rater</td>
<td>0.95</td>
<td>0.87</td>
<td>0.97</td>
<td>0.89</td>
<td>0.84</td>
<td>0.76</td>
<td>0.96</td>
</tr>
<tr>
<td>Inter-rater</td>
<td>0.96</td>
<td>0.96</td>
<td>0.98</td>
<td>0.94</td>
<td>0.94</td>
<td>0.77</td>
<td>0.98</td>
</tr>
<tr>
<td>Test-retest</td>
<td>0.88</td>
<td>0.96</td>
<td>0.85</td>
<td>0.91</td>
<td>0.94</td>
<td>0.81</td>
<td>0.97</td>
</tr>
</tbody>
</table>

Table 1. Results of ICC for different IMU spinal mobility tests
the English language and considered only SLR, RCT, cohort, case control and case series (>5 patients). Data were screened independently by three reviewers, recorded on a prespecified extraction form and summarized qualitatively. Considering core areas and core domain set was drafted. The results were presented and voted by a Consensus Committee including physicians with expertise in rheumatic, kidney and infectious diseases. Specific domains were separately voted and scored from 1 (strongly disagree) to 5 (strongly agree). Agreement was calculated as the percentage of agree/strongly agree. Consensus was reached in case of >70% of agreement.

Results: In the review were included 88 studies of which 4 randomised clinical trial (3%, 144 patients), 3 systematic literature reviews (9%, 401 patients), 25 cohort studies (27%, 1284 patients), and 56 other observational studies (61%, 2871 patients). The most frequent domains were: bio-humoral activity markers (e.g. cryocrit, rheumatoid factor, complementemia), viral infection and liver function, reversible and non reversible manifestation of skin, peripheral nerve, kidney, joint. Only a few studies included as life impact area, survival and safety. No studies analyzed included economical impact. Drafted core domains within core areas and percent agreement from the Delphi survey are reported in Table I. Additional core domains included adverse events and viral infection, considered as contextual factor.

Conclusion: This is the first study aimed at identifying the core outcome measures in cryoglobulinemic vasculitis. Further studies will be needed to evaluate appropriate instruments to measure these outcome domains to be applied in clinical trials and practice.

REFERENCES

Disclosure of Interests: None declared

SAT0662 MXA IS A CLINICALLY APPLICABLE BIOMARKER FOR TYPE I INTERFERON ACTIVATION IN SYSTEMIC LUPUS ERYTHEMATOSUS AND SYSTEMIC SCLEROSIS
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Background: Activation of the type I interferon (IFN) system has been found in large subsets of patients with systemic autoimmune diseases. This is usually assessed with a laborious quantification of IFN-stimulated genes. An easier and cheap biomarker would facilitate implementation of type I IFN measurements in diagnostic laboratories. Previously, we described Myxovirus resistance protein 1 enzyme immunoassay (MXA-EIA) for systemic evaluation of type I IFN activity in primary Sjögren’s syndrome [1].

Objectives: To assess the applicability of the MXA-EIA to detect systemic type I IFN activation in patients with systemic lupus erythematosus (SLE) and systemic sclerosis (SSc).

Methods: Whole blood intracellular MXA protein levels were measured in SLE (discovery cohort n=25; replication cohort retrieved from the CHILL-NL study [2]: n=102), SSc (n=28) and healthy controls (HC) using the MXA-EIA. IFN scores were determined from whole blood gene expression of interferon-stimulated genes IFI44, IFI44L1, IFIT1, IFIT3, and MXA by RT-PCR.

Results: MXA levels were significantly elevated in patients with SLE and SSc compared to HC and highly correlated to IFN scores (r=0.735 to r=0.854, p<0.003). MXA-EIA robustly discriminated (AUC=0.938 to AUC=0.991, p<0.007) between low and high type I IFN activity in SLE and SSc patients with a specificity of 100% and a sensitivity of 67.5 to 94.7%. Patients with autoantibodies against SM, RNP, SSA/Ro, or SSB/La antigens showed higher MXA levels and IFN scores compared to patients without these antibodies.

Conclusion: Intracellular MXA is an easy applicable and clinically relevant biomarker for systemic type I IFN bioactivity in SLE and SSc. MXA-EIA could be used to identify patients eligible for IFN-targeting treatments and potentially to monitor treatment responses.

REFERENCES

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SAT0663 SERUM INFLAMMATORY ANGIogenic AND Tissue REMODELING BIOMARKERS IN PERIPHERAL SpondylOarthritis Before and After IL-17A Blockade
Merlin Kaal1,2, Leontiee van Mens1, Jan Piet van Hamborg1,2, Dominique Baeten1,4, Marleen van de Sande1, Sander W. Tuij2,1. 1Amsterdam UMC, University of Amsterdam, Amsterdam Rheumatology and Immunology Center, Amsterdam, Netherlands; 2Amsterdam UMC, University of Amsterdam, Department of Experimental Immunology, Amsterdam, Netherlands

Background: Spondyloarthritis (SpA) is characterized by extensive angiogenesis, tissue remodeling and inflammation of both the enthesis and the synovial tissue. Several studies have shown a relation between angiogenic/tissue remodeling serum markers and disease progression. Secukinumab, an anti-IL-17A inhibitor, is an effective treatment in SpA, but it’s effects on serum markers of angiogenesis, tissue remodeling and inflammation are largely unknown.

Objectives: The purpose of this study was to analyze several candidate biomarkers of these processes in patients with SpA treated with anti-IL-17A.

Methods: Serum samples from 20 active peripheral SpA patients that were included in a 12 week open-label trial with secukinumab were analyzed for several markers with lumines protein technology. Study design and primary results were previously published (1).

Results: Serum levels of IL-6, MMP-3, osteopontin (all P < 0.001), Vascular Endothelial Growth Factor A (VEGFA), tumour necrosis factor (TNF)-alpha, IL-31, IL-33, S100A8, S100A9 (all P < 0.05) decreased

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significantly upon treatment with anti-IL-17A. These serum level changes correspond with the clinical responses and the published effects on inflamed target tissues of this cohort. Meanwhile, serum levels of DKK-1, ROCB4, sclerostin and CD40L remained unchanged.

Conclusion: These results indicate that anti-IL-17A not only diminishes inflammation, but also impacts on other processes such as angiogenesis and tissue remodeling. Whether these observations are predictive of disease progression or outcome remains to be determined.

REFERENCES

Disclosure of Interests: Merlijn Kaaji: None declared, Leonieke van Mens: None declared, Jan Piet van Hamburg: None declared, Dominique Baeten Employee of: UCB Pharma, Marleen van de Sande Grant/research support from: Research support from Janssen, Novartis, Eli Lilly, Consultant for: Received consultation fees from Abbvie and Novartis, Sander W. Tas: None declared

SAT0663 ABILITY OF THE MULTI-BIOMARKER DISEASE ACTIVITY SCORE TO IDENTIFY RHEUMATOID ARTHRITIS PATIENTS IN REMISSION AT RISK OF RELAPSE AFTER TNF-BLOCKER TAPERING. AN ANCILLARY STUDY OF THE STRASS TRIAL

KOSSI Sandra1, Eric H. Sasso2, Hubert Marotte3, Xinyu Liu2, Florence Tubach1, David Hajage1, Bruno Fautrel1.

Background: Rheumatoid arthritis (RA) patients in sustained remission are candidates for tapering of disease modifying anti-rheumatic drugs (DMARDs). However, no predictors of relapse have been clearly identified so far. The STRASS trial included 137 RA patients in sustained DAS28 remission with TNF blockers (TNFb) who were randomized to 2 strategy arms: maintenance of TNFb at full dose or progressive DAS28-driven spacing of TNFb injections 1. RA relapses were significantly more common with TNFb spacing in STRASS but no baseline characteristics predicted the risk of relapse in either strategy arm. The multi-biomarker disease activity (MBDA) blood test measures 12 serum protein biomarkers and uses a validated algorithm to produce a score for RA disease activity on a scale of 1-100. In some studies, the MBDA score was a significant predictor of flare following DMARD tapering in well controlled RA patients.

Objectives: To test the ability of the MBDA score to identify rheumatoid arthritis patients who will relapse following continuation or tapering of TNF blocker (TNFb) treatment in the STRASS study.

Methods: MBDA scores were determined in a central laboratory (Crescendo Biosciences, San Francisco, USA) for available archived serum samples that had been obtained at baseline from patients in STRASS (N=133). The ability of the MBDA score to predict relapse (defined as DAS28 >2.6 and increased >0.6 from previous study visit) in each arm of the 18-month STRASS trial was assessed by: 1) comparing MBDA scores in relapsing vs. non-relapsing patients by Wilcoxon rank sum and Fisher’s test, and 2) determining the ability of the MBDA score to discriminate relapse, based on receiver operating characteristic (ROC) analysis summarized by C-statistic (i.e., area under the ROC curve [AUC]), and its 95% confidence interval (CI). Analyses were performed for intention-to-treat (ITT) and completer populations.

Results: At 18 months, 48% and 77% of the patients relapsed in the full dose maintenance and the spacing arms, respectively. In each study arm, mean MBDA scores and the percentages of patients with low, moderate or high MBDA scores at baseline were not significantly different in relapsing vs. non-relapsing patients (Table 1). The ROC analyses displayed no statistically significant discriminating ability for the MBDA score in terms of relapse prediction over the 18-month period of the trial in either arm of the ITT population (Figure 1). However, a significant ROC result was obtained in the maintenance group in the complete analysis (AUC 0.638 [95% CI: 0.502, 0.774], p<0.01).

Table 1. MBDA scores at baseline in the STRASS trial

<table>
<thead>
<tr>
<th>Randomization arm</th>
<th>Maintenance</th>
<th>Spacing</th>
</tr>
</thead>
<tbody>
<tr>
<td>MBDA Mean MBDA score (SD) [Median]</td>
<td>29.7 (11.4) [30]</td>
<td>26.8 (10.3) [27]</td>
</tr>
<tr>
<td>MBDA score &lt; 30, N (%)</td>
<td>29 (43.2%)</td>
<td>35 (57.4%)</td>
</tr>
<tr>
<td>30 ≤ MBDA score ≤ 44</td>
<td>33 (48.5%)</td>
<td>25 (41.2%)</td>
</tr>
<tr>
<td>MBDA score &gt; 44</td>
<td>5 (7.4%)</td>
<td>1 (1.64%)</td>
</tr>
<tr>
<td>Outcome at Month 18</td>
<td>No relapse</td>
<td>Relapse</td>
</tr>
<tr>
<td>N (%)</td>
<td>36 (52.2%)</td>
<td>33 (47.8%)</td>
</tr>
<tr>
<td>MBDA scores</td>
<td>Mean MBDA score (SD)</td>
<td>27.28 (11.4)</td>
</tr>
<tr>
<td>MBDA score &lt; 30, N (%)</td>
<td>18 (50%)</td>
<td>12 (35.5%)</td>
</tr>
<tr>
<td>30 ≤ MBDA score ≤ 44</td>
<td>15 (41.7%)</td>
<td>18 (58.1%)</td>
</tr>
<tr>
<td>MBDA score &gt; 44</td>
<td>3 (8.3%)</td>
<td>2 (6.4%)</td>
</tr>
</tbody>
</table>

*Each comparison between No relapse vs. Relapse groups was not statistically significant (p >0.05).

Conclusion: The MBDA score did not display quantification of the risk of relapse in RA patients in remission, when assessed, in the context of the DAS28-driven TNFb tapering strategy in STRASS.

REFERENCES

Disclosure of Interests: Sandra KOSSI: None declared, Eric H. Sasso Shareholder of: Myriad Genetics, Inc., Employee of: Crescendo Bioscience, Inc., Hubert MAROTTE: None declared, Xinyu LIU: None declared, Florence Tubach Grant/research support from: Financial compensation received from MSD on a pro-rata basis for participation in Scientific Committee meetings and functions for this study, David Hajage: None declared, Bruno Fautrel research support from: Abbvie, Lilly, MSD, Pfizer, Consultant for: Abbvie, Biogen, BMS, Celgene, Janssen, Lilly, Medac, MSD, NORDIC Pharma, Novartis, Pfizer, Roche, Sanofi-Aventis, Sanofi Genzyme, SOBI, UCB

SAT0664 RESPONSIVENESS OF PATIENT-REPORTED PHYSICAL FUNCTION OUTCOME MEASURES IN A REAL LIFE INTERNATIONAL COHORT OF 405 PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Physical function (PF) is a core domain to be measured in all trials for psoriatic arthritis (PsA); several instruments can be used but have not been compared.

Objectives: To evaluate the longitudinal construct validities of 3 physical function patient-reported outcome measures (PF-PROMs): HAQ-disability

Figure 1. Discriminative ability of the MBDA test to identify RA patients at risk of relapse during the 18-month follow-up in the STRASS trial, based on ROC analyses of the ITT population.

Disclosure of Interests: Ying Ying LEUNG: None declared, Ana Maria ORBAI: None declared, Maarten DE WIT: None declared, Andra BALANESCU: None declared, Emmanuelle DENIS: None declared, Martin SOUBRIE: None declared, Lihi EDERY: None declared, Joel S. SMOLEN: None declared, Laura C. COATES: None declared, Laure GOSSÉ: None declared, ReFlap study group: None declared.
index (HAQ-DI), physical functioning of SF12 (SF12-PF) and functional capacity of Psoriatic Arthritis Impact of Disease (PsAID-PF).

**Methods:** The Remission/Flare in PsA (ReFlap) study (NCT03119805), is a prospective longitudinal study in 14 countries of consecutive adults with definite PsA collecting validated PsA outcomes. We assessed longitudinal construct validity using correlation between change scores of PF-PROMs with other assessments, according to a priori hypotheses. Responsiveness was assessed using the change of PF-PROMs anchored with patient-defined improvement/worsening at follow-up. We calculated the relative effectiveness statistic (RE=Standardized response mean, SRM$^2$ ratios) for each PF-PROM comparing improved/worsened groups vs. no change at follow-up.

**Results:** Of 466 subjects recruited, 405 completed follow-up (50.8% male, mean(SD) age = 52.7 (12.6) years). After a mean (SD) follow-up of 4.3 (2.7) months, 27.6%, 55.0% and 17.4% reported improvement, no change and worsening. All change scores of the PF-PROMs met the a priori hypotheses (Table 1). PF-PROMs change scores were statistically different for improved and worsened group from the no change group (p<0.001).

All PF-PROMs were more sensitive to worsening than improvement in PsA studies. These data will help to choose outcomes in PsA studies.

**Abstract Table 1.** Correlations of PF change with change in other outcomes, Spearman’s rank correlation

<table>
<thead>
<tr>
<th></th>
<th>Δ HAQ-DI</th>
<th>Δ SF12-PF</th>
<th>Δ PsAID-PF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Δ HAQ-DI</td>
<td>-0.73 **</td>
<td>-0.73 **</td>
<td>0.68 **</td>
</tr>
<tr>
<td>Δ SF12-PF</td>
<td>-0.73 **</td>
<td>-0.73 **</td>
<td>0.68 **</td>
</tr>
<tr>
<td>Δ PsAID-PF</td>
<td>-0.64 **</td>
<td>-0.64 **</td>
<td>0.64 **</td>
</tr>
<tr>
<td>Δ Patient joint OA</td>
<td>0.56 **</td>
<td>0.56 **</td>
<td>0.74 **</td>
</tr>
<tr>
<td>Δ Physician OA</td>
<td>0.28 **</td>
<td>0.28 **</td>
<td>0.42 **</td>
</tr>
<tr>
<td>Δ Tender joint count</td>
<td>0.40 **</td>
<td>0.40 **</td>
<td>0.47 **</td>
</tr>
<tr>
<td>Δ SF12-PF</td>
<td>0.32 **</td>
<td>0.32 **</td>
<td>0.33 **</td>
</tr>
<tr>
<td>Δ PsAID12 total</td>
<td>0.67 **</td>
<td>0.67 **</td>
<td>0.90 **</td>
</tr>
</tbody>
</table>

$^a$ p<0.001; $^b$ change scores; GA: global assessments

**Abstract Table 2.** Responsiveness of PF-PROMs in PsA

<table>
<thead>
<tr>
<th>Sample size</th>
<th>Change score (SD)</th>
<th>SRM (95% CI)</th>
<th>SRM$^2$ ratio$^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAQ-DI (0.3) Improved</td>
<td>-0.20 (0.85)</td>
<td>-0.23 (-0.43, -0.03)</td>
<td>3.56</td>
</tr>
<tr>
<td>No change</td>
<td>-0.10 (0.79)</td>
<td>0.12 (-0.25, 0.03)</td>
<td>-</td>
</tr>
<tr>
<td>SF12-PF (0-100) Improved</td>
<td>4.76 (45.61)</td>
<td>0.10 (-0.09, 0.31)</td>
<td>8.70</td>
</tr>
<tr>
<td>No change</td>
<td>2.43 (40.95)</td>
<td>0.06 (-0.07, 0.20)</td>
<td>-</td>
</tr>
<tr>
<td>PsAID-PF (0-10) Improved</td>
<td>-0.88 (4.12)</td>
<td>-0.21 (-0.40, -0.02)</td>
<td>6.39</td>
</tr>
<tr>
<td>No change</td>
<td>-0.33 (3.91)</td>
<td>0.02 (-0.04, 0.04)</td>
<td>-</td>
</tr>
</tbody>
</table>

$^a$ determined by the best cut-off point using ROC curve; $^b$ comparing to the no change group; $^c$ p<0.001 by Kruskal-Wallis test; SD = standard deviation; SRM = standardized response means.

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**SAT0665**

**PLASMA HS PRO-C2 LEVELS PREDICT RADIOGRAPHIC PROGRESSION IN SYMPTOMATIC KNEE OSTEOARTHRITIS PATIENTS**

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**Background:** There is a lack of objective diagnostic modalities that identify patients at risk for severe osteoarthritis (OA), which complicates the development of disease-modifying OA drugs. The biochemical marker, high-sensitive PRO-C2 (hsPRO-C2), is a measure of the propeptide of type II collagen and a blood measure of cartilage formation.

**Objectives:** The aim of this study was to determine whether hsPRO-C2 could predict radiographic progression in a knee OA population and stratify patients into high and low risk for joint destruction.

**Methods:** Subjects with varying degrees of symptomatic knee OA (n=106) were included from a New York University (NYU) progression cohort. Radiographic progression was assessed by medial joint space narrowing (JSN), based on the change in joint space width (JSW), of the signal knee at baseline and at 24months. Baseline plasma type II collagen formation biomarker (hsPRO-C2) levels were measured. Association between
baseline hsPRO-C2 and JSN was analyzed by Pearson’s correlation, corrected for age, sex, BMI, race, baseline JSW, and non-steroids anti-inflammatory drugs (NSAID) use. Subjects were divided into quartiles of equal size depending on the hsPRO-C2 levels, and the difference in JSN was investigated. The median level of baseline hsPRO-C2 (1.48 ng/ml) was used as a cut-off for stratifying all the subjects. The difference in JSN over 24 months was investigated in patients dichotomized based on median level. The values were compared with two-way analysis of covariates (ANCOVA).

Results: Baseline plasma hsPRO-C2 levels were negatively correlated with the progression of radiographic joint space narrowing over 24 months (r = -0.14, p = 0.009) after adjustment for confounders (Figure 1A). Quartile analysis demonstrated a decreasing trend of hsPRO-C2 in the radiographic progression from quartile 1 to 4 (Figure 1B). One-way ANOVA revealed a significant difference in mean JSN between quartiles 1 and 4 (0.5073 mm versus -0.0691 mm, p = 0.036, Figure 1B). JSN was significantly larger in the low hsPRO-C2 patients (0.3710 mm) compared to the high hsPRO-C2 patients (0.0185 mm) (Figure 2).

Conclusion: These data suggest that symptomatic knee OA subjects with lower levels of hsPRO-C2 at baseline presented more radiographic medial JSN progression compared to the subjects with higher levels of hsPRO-C2. The biomarker hsPRO-C2 may be useful for predicting OA progression.

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Figure 2. Medial joint space narrowing (JSN) on the signal knee over 24 months. The values were compared with two-way analysis of covariates (ANCOVA). Data were adjusted for BMI, sex, age, race, baseline medial JSW and NSAID user. Asterisks indicate the following: *p < 0.05. All values were presented as means and standard error of the mean (SEMs).

Disclosure of Interests: Yunyun Luo Employee of: I’ve been worked in Nordic Bioscience before I started PhD., Jonathan Samuels: None declared, Svetlana Krasnokutsky: None declared, Yi He Employee of: I am a full-time employee in Nordic Bioscience, Morten Kandel Shareholder of: I own shares of Nordic Bioscience, Employee of: I am a full-time employee in Nordic Bioscience, Steven Abramson: None declared, Mukundan Mukundan: None declared, Anne-Christine Bay-Jensen Shareholder of: I own shares of Nordic Bioscience, Employee of: I am a full-time employee in Nordic Bioscience


SAT0666

ASSESSMENT OF INFLAMMATORY AND IMMUNE PATHWAYS IN RHEUMATOID ARTHRITIS PATIENTS USING BIOPRED KIT TO IDENTIFY CANDIDATE BIOMARKERS
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Background: Rheumatoid Arthritis (RA) is a chronic, progressive, inflammatory autoimmune disease associated with articular, extra-articular and systemic effects leading to joint destruction. T cells, B cells and the orchestrated interaction of pro-inflammatory cytokines play key roles in the pathophysiology of RA. Better comprehension of interaction between cytokines and their signaling pathways are key for the development of new strategies with small molecules or biologicals. Today, new technologies allow the specific investigation of inflammatory pathways at mRNA level without extraction step directly from the blood. The BIOPRED panel, Disease activity specific gene enrichment studies in RA & other autoimmune-inflammatory disorders would help pharmaceutical industry tailor target specific therapies and would help clinicians choose optimal & personalized therapy for their patients. Therefore, we have identified active biological pathways in RA patients associated with different disease activity status.

Objectives: By using Firalis’ BIOPRED assay, a targeted gene sequencing panel including 2155 mRNAs from inflammatory and immune pathways, we aimed to identify active biological pathways in function to different disease activity status of RA and Healthy volunteer (HV) subjects.

Methods: Paxgene samples of active RA patients with DAS28>3.2 (n=178) and HV (n=25) are directly profiled without RNA extraction with BIOPRED assay and 2155 mRNA were quantified on HTG EdgeSeq platform, a combination of a nucleic acid protection assay & next generation sequencing (NGS). Subjects are categorized into three groups: High disease activity (HDA) group with DAS28 >5.1, Moderate disease activity (MDA) group with DAS28 between 3.2 and 5.1, and Healthy volunteer (HEV) group.

Results: After transformation and normalization of the gene expression data, 22 mRNA genes are found to be significantly upregulated in RA (p-value < 0.005, fold change > 2) as compared to HV group. After ANOVA analysis on three groups as stated above, 351 mRNA targets are significantly regulated (p-value < 0.005). Pathway analysis based on protein-protein interaction from BioGrid, String and Intact database was used and score were generated based on fold change for 22 pathways to assess modification in HDA and MDA groups versus HV group. Various pathways including Jak/STAT pathway were shown to be significantly upregulated.

Conclusion: Our results identify a list of mRNAs relevant to RA pathology and pathways that have the potential to be candidate biomarkers for disease activity, disease severity or as therapeutic targets. Moreover, BIOPRED panel accurately measures 2155 mRNA (Coefficient of Variation is less than 20% for more than 1100 mRNAs) from inflammatory and immune pathways and can be further used to study pathway analysis in autoimmune-inflammatory disorders such as RA.

Disclosure of Interests: None declared

SAT0667

TREATMENT RESPONSE CRITERIA FOR ANCA-ASSOCIATED VASCULITIS: RESULTS OF A SCOPING REVIEW
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Background: A comprehensive assessment of outcome measures to assess response to treatment in ANCA-associated vasculitis (AAV) is necessary to implement.
Objectives: To perform a review of outcome measures to assess response to treatment in AAV which will help advance methodology for clinical trials in this disease.

Methods: As part of an ongoing international project to develop response criteria, we performed a scoping review to assess the tools used as outcome measures in randomized clinical trials (RCTs) of AAV. Medline, Cochrane Central, and ClinicalTrials.gov were searched from inception until November 2018 to identify RCTs enrolling patients with granulomatosis with polyangiitis and/or microscopic polyangiitis. AAV assessments in RCTs for AAV and the current lack of a composite defined or evaluated. Furthermore, other important outcomes in AAV, such as renal function, were not always reduced to a dichotomous variable (0 or > 0) providing distinction between remission and active disease. Reduction in BVAS and/or achievement of BVAS-0 represented a main study outcome (primary or secondary endpoint) in 20/24 (83%) RCTs; 6 of these trials used the BVAS/WG. Damage, mainly assessed by the Vasculitis Damage Index (VDI), was an outcome for 14/24 (58%) RCTs. Physician global assessment and patient-reported outcomes (PROs) [measures of health-related quality of life (HRQoL) and/or patient global assessment] were assessed in 7 (29%) and 14 (58%) RCTs, respectively. Assessment of renal function or activity was a major outcome or specifically included in definitions of remission/relapse in 23/24 (96%) RCTs. Timing for outcome measure assessment differed substantially, with baseline, 6 months (15/20 RCTs), and 12 months (14/20 RCTs) after enrollment being the most common time points for reporting BVAS and VDI. Assessment of disease state occurred as early as 1-4 weeks after enrollment.

Conclusion: Outcome measures used in RCTs of AAV include the repeated use of vasculitis specific tools to assess disease state, but with heterogeneity in the definitions for remission/relapse and timing of assessment. Intermediate states of disease activity are currently poorly defined or evaluated. Furthermore, other important outcomes in AAV, such as renal function and damage measures, and global assessments are often not included as primary or confirmatory secondary outcomes in RCTs in AAV. This review highlights the need for more homogeneous outcome assessment in RCTs for AAV and the current lack of a composite measure that integrates various endpoints relevant to physicians and patients.

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DISCRIMINANT ABILITY OF THE PARENT VERSION OF THE JUVENILE ARTHRITIS DISEASE ACTIVITY SCORE IN A LARGE MULTINATIONAL COHORT OF PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: The assessment of disease activity plays a pivotal role in the management of children with juvenile idiopathic arthritis (JIA). Most recent recommendations require that parents’ and children’s perception is incorporated in the evaluation of the disease course and of effectiveness of therapeutic interventions. A new disease activity tool, named parent Juvenile Arthritis Disease Activity Score (parJADAS) and based only on parent-centered outcome measures, is currently under development (1).

Objectives: To demonstrate, in a large multinational dataset of JIA patients, the discriminant ability of the parJADAS.

Methods: The parJADAS includes 4 measures: 1) parent assessment of disease activity; 2) assessment of pain intensity; 3) proxy assessment of joint disease; 4) assessment of morning stiffness (MS). Disease activity and pain are assessed on a 21-numbered circle VAS (0 = best and 10 = worst). The active joint count is based on the count of any swollen or painful joint, irrespective of its type, up to a maximum of 10 joints. MS duration is assessed on a Likert scale, ranging from no MS (0 points) to > 2 hours of MS (10 points). Validation was conducted on a dataset of 8,656 children with JIA from 49 countries, enrolled in the study of Epidemiology, treatment and Outcome of Childhood Arthritis (2), who had all the variables included in the parJADAS available. Discriminant ability was evaluated by comparing parJADAS levels (median, IQR) among patients with inactive disease (ID), low disease activity (LDA), moderate disease activity (MDA), and high disease activity (HDA) according to the CJADAS10; patients in remission, continued activity, or flare according to the attending physician; patients whose parents were satisfied or not with current disease state. To assess the possible influence of the articular and extra-articular damage on the parJADAS, the levels of the score in patients with or without damage (Juvenile Arthritis Damage Index > 0) were compared. For this analysis, only subjects in inactive disease and with at least 2 years of disease course were considered (n = 2,423).

Results: The levels of parJADAS in patients in ID, LDA, MDA, and HDA were 0.0 [0.0, 1.0], 3.0 [1.0, 6.0], 6.0 [2.0, 11.5], an 14.5 [8.5, 21.0], respectively (Kruskal-Wallis test, p < 0.001). The levels of par JADAS in patients in remission, continued activity, or flare according to the attending physician were 0.5 [0.0, 3.5], 9.0 [3.5, 17.0], 12.0 [5.5, 20.0], respectively (Kruskal-Wallis test, p < 0.001). Median parJADAS in patients whose parents were satisfied or not satisfied with disease course is 1.5 [0.0, 7.0] and 13.0 [6.6, 20.5], respectively (Mann-Whitney test p < 0.001). ParJADAS was not different in JIA patients in remission with or without damage measured with the JADI (Mann-Whitney test p = 0.08).

Conclusion: The parJADAS showed excellent discriminate ability in a large multinational cohort. The score did not show to be relevantly influenced by disease damage in JIA patients in remission.

REFERENCES

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SAT0670 REDUCING THE IMPACT OF THE PATIENT GLOBAL ON BOOLEAN REMISSION CRITERIA FOR RHEUMATOID ARTHRITIS

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Background: The patient global assessment (PiGA) is a core set variable to assess disease activity in rheumatoid arthritis (RA). It is strongly linked to patient-reported pain and has shown to be a limiting factor for reaching remission in patients with remittent joint inflammation and normal acute phase response, particularly when the ACR/EULAR Boolean criteria are used. In these, the PiGA may not be greater than 10 on a 0-100 scale to reach remission.

Objectives: To analyse the impact of higher cut-offs for or removal of the PiGA applied in the ACR/EULAR Boolean remission on the consistency with the SDAI remission definition, and with respect to long-term structural and functional outcomes.

Methods: We retrieved data from six clinical trials testing the efficacy of tumor-necrosis factor inhibitors vs MTX or placebo/MTX. Three trials depicted early RA: ASPIRE (infliximab), Go Before (golimumab), PREMIER (adalimumab); and three late RA: ATTRACT (infliximab), DE019 (adalimumab) and Go Forward (golimumab). We increased the cut-off of the PiGA gradually by 5mm (mB20015-REM) up to 30mm, and also omitted the criterion completely (Boolean-NO REM, i.e. requiring only CRP, SJC, TJC/C). We assessed frequencies of remission by these definitions at 6 months, and explored clinical characteristics of remission according to each remission definition. Further, we explored functional and structural outcomes 1 year after achievement of a remission.

Results: We included 3263 patients in our study, 2121 in early and 1172 in late RA (mean disease duration: 1.5±3.0 and 9.8±8.6 years, respectively). The rates of patients achieving Boolean remission increased with higher allowance for PiGA from 11.9% to 18.6% in early RA, and from 5.9% to 12.4% in late RA. CRP values across all definitions, including no PiGA, were similar (data not shown).

Conclusion: Increasing the PiGA cut-off to 15mm would provide highest consistency between Boolean with the index based remission, while the integer cut-off of 20mm (or 2/10) would also allow the use on numerical rating scales. This new cut-off would discount the overly stringency of the PiGA in the remission context, while keeping the patient perspective in the core of RA disease activity evaluation.

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SAT0671 SEROCONVERSION OF AUTOANTIBODIES TO UH-RA.21 PEPTIDE IS ASSOCIATED WITH CDAI REMISSION IN RHEUMATOID ARTHRITIS PATIENTS OF THE CARERA COHORT

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Background: Autoantibodies are present in the majority of rheumatoid arthritis (RA) patients and are used clinically as diagnostic serum biomarkers. Insight in their role in prediction of therapy response and disease progression would provide a useful tool for patient stratification and personalized selection of a suitable treatment. In a previous pilot experiment, autoantibody levels to the University of Hasselt (UH) peptide UH-RA.21 were measured in patients continuing the same DMARD during a 17 month follow-up period, which was taken as a proxy for treatment success, persistently positive anti-RA.21 antibody levels showed an overall decrease in titer (p=0.0034).

Objectives: Our aim is to determine the association between autoantibodies to the UH-RA.21 peptide and disease remission in early RA patients from the CareRA cohort.

Methods: In the CareRA trial, different COBRA treatment regimens consisting of synthetic DMARDs combined with a step-down glucocorticoid treatment, have been studied. Disease remission was defined as a DAS28CRP<2.6, CDAI<2.6 or SDAI<3.3. Custom peptide enzyme-linked immunosorbent assays were used to screen for the presence of antibodies to the UH-RA.21 peptide in serum samples of the CareRA cohort. Cut-off for seropositivity was defined by 2 x SD above the mean antibody level of the healthy control group. Antibody reactivity to UH-RA.21 was evaluated in baseline samples, collected before the start of treatment. In 223 early RA patients from the CareRA cohort, patients that were positive for anti-UH-RA.21 antibodies at baseline, follow-up samples collected 16, 40, 52 and 104 weeks after the initiation of treatment were tested.

Results: Antibodies to UH-RA.21 were found in 21% (47/223) of the baseline samples from the CareRA cohort. Compared to baseline levels, combination therapy induced a 50% reduction of anti-UH-RA.21 antibody levels in 30% of patients after 16 weeks and in 47% of patients after 52 weeks. Seroconversion was observed in 16% (7/44) of patients after 16 weeks and 30% (10/34) after 52 weeks. Seroconversion was not correlated with remission according to the DAS28CRP or SDAI remission indices. However, of those patients which were UH-RA.21 positive at baseline, more seroconversion occurred in patients reaching remission (5/14, 36%) than in patients remaining in active disease (2/30, 7%), according to CDAI remission criteria (p=0.025).

Conclusion: A COBRA therapy induces a rapid decrease in anti-UH-RA.21 autoantibody levels in many patients. Moreover, early anti-UH-RA.21 seroconversion is associated with CDAI remission.

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Disclosure of Interests: Josef S. Smolen: Grant/research support from: AbbVie, Pfizer Inc, Roche, Consultant for: AbbVie, Amgen, AstraZeneca, Biovitrum, Celgene, GSK, Lilly, GlaxoSmithKline, ILTOO, Janssen, Medimmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Sanofi, UCB, Speakers bureau: AbbVie, AstraZeneca, Biovitrum, Celgene, GSK, Lilly, GlaxoSmithKline, ILTOO, Janssen, Medimmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Sanofi, UCB, Sandoz, Daniel Atehah: Grant/research support from: AbbVie, Bristol-Myers Squibb, and MSD, Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Medec, Merck, MSD, Pfizer Inc, Roche, and UCB, Satvinder Kaur: None declared, Tanja Stamn: Grant/research support from: AbbVie, Eli Lilly, Janssen, MSD, Pfizer Inc, Roche, Consultant for: AbbVie, Amgen, AstraZeneca, Astro, Celgene, Celtrion, Eli Lilly, GlaxoSmithKline, ILTOO, Janssen, Medimmune, MSD, Novartis-Sandoz, Pfizer Inc, Roche, Sanofi, Sandoz, UCB, Speakers bureau: AbbVie, Eli Lilly, Janssen, Medec, Merck, MSD, Pfizer Inc, Roche, and UCB.


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THE DIAGNOSTIC VALUE OF SERUM KL-6 IN CONNECTIVE TISSUE DISEASE ASSOCIATED INTERSTITIAL LUNG DISEASE

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Background: The connective tissue diseases (CTDs) are a group of inflammatory, immune-mediated disorders. Involvement of the respiratory system, particularly interstitial lung disease (ILD), is common and is an important contributor to morbidity and mortality. Currently, high-resolution computed tomography (HRCT), bronchoscopic examination and surgical lung biopsy (SLB) are the basic methods for the diagnosis of ILD. But these tests require specific inspection machines, are less repeatable and cause considerable discomfort to the subject.

Objectives: To evaluate the diagnosis of the serum Krebs von den Lungen-6 (KL-6) for the interstitial lung disease (ILD) associated with connective tissue diseases (CTD).

Methods: Patients with CTDs who visited our Hospital between January, 2016 and December, 2017, and whose serum KL-6 level was measured were included. We analyzed 175 patients with CTDs, 84 CTDs associated ILD, 91 CTDs patients without ILD. Record age, gender, diagnosis, serum KL-6 levels, pulmonary function tests and performed in parallel were reviewed. Statistical analysis was performed using SPSS (version 20.0) statistical package.

Results: The significantly higher levels of KL-6 were determined in the CTD-ILD group than in the CTDs without pulmonary involvement group (P<0.05) (figure 1). By the ROC curves of serum KL-6 levels in 175 patients. The optimal cutoff value of serum KL-6 for a diagnosis of CTD-ILD was 409 U/ml, and the sensitivity and specificity were 82.1% and 86.8%, respectively. The AUC was 0.905 (figure 2). Serum KL-6 correlated negatively with vital capacity (VC) (%predicted), forced vital capacity (FVC) (%predicted), forced expiratory volume in one second (FEV1%) (%predicted) and diffusing capacity of the lung for carbon monoxide (DLcoSB) (% predicted) (Table 1).

Table 1 Correlation between KL-6 level and pulmonary function

<table>
<thead>
<tr>
<th>Function</th>
<th>KL-6</th>
<th>r</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>VC%</td>
<td>-0.196</td>
<td>0.009</td>
<td></td>
</tr>
<tr>
<td>FVC%</td>
<td>-0.158</td>
<td>0.037</td>
<td></td>
</tr>
<tr>
<td>FEV1%</td>
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<td>0.022</td>
<td></td>
</tr>
<tr>
<td>FEF25%</td>
<td>-0.090</td>
<td>0.237</td>
<td></td>
</tr>
<tr>
<td>FEF50%</td>
<td>-0.058</td>
<td>0.447</td>
<td></td>
</tr>
<tr>
<td>FEF75%</td>
<td>-0.044</td>
<td>0.560</td>
<td></td>
</tr>
<tr>
<td>MMEF%</td>
<td>-0.075</td>
<td>0.323</td>
<td></td>
</tr>
<tr>
<td>DLcoSB</td>
<td>-0.470</td>
<td>0.000</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: The serum KL-6 is a valuable biomarker for CTD-ILD diagnosis, and it is an important serum marker for detection of CTD-ILD activity.

REFERENCES

Disclosure of Interests: None declared


ANTI-C1Q ANTIBODIES HAVE HIGHER CORRELATION WITH LUPUS NEPHRITIS DISEASE ACTIVITY

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Background: Systemic lupus erythematosus (SLE) is the prototype of autoimmune disease and is characterized by the production of a variety of autoantibodies. and lupus nephritis continues to be a principal cause of morbidity and mortality. The focus is to finding biomarkers that can monitor renal activity and predict prognosis for early diagnosis and treatment. Complement C1q is the starter molecule of the classical pathway
of complement activation and plays an important role in the clearance of immune complexes and apoptotic cell debris. Hereditary homozygous deficiency of C1q has been described to be the strongest risk factor for developing SLE. There are some cross-sectional studies on anti-C1q in which the antibody was found to have a significant association with renal involvement but the association of anti-C1q antibodies (antiC1q) with lupus nephritis (LN) still a matter of debate.

**Objectives:** We assessed the association between lupus nephritis disease activity and anti-C1q antibodies

**Methods:** We retrospectively analyzed the medical records of 88 patients with lupus nephritis, aged 35.7±10.8 years on the average, with SLE of average duration 12 (3, 57) years. In all examines the levels of anti-dsDNA and anti-C1q antibodies were measured using the ELISA. C3, C4, 24-hour urinary protein performed in parallel were reviewed. The clinical manifestations of SLE was also collected. Lupus nephritis disease activity was measured by The SLICC Renal Activity Score of 2004. All biopsied tissues were scored based on the to ISN/RPS2003 lupus nephritis pathological typing standards. Acute Index, Chronic Index Score were used to evaluated the activities of lupus. All the analyses were performed by SPSS 20.0 software.

**Results:** Patients with active lupus nephritis had a higher levels of anti-C1q antibodies than inactive lupus nephritis (68.9(34.1, 140.1) vs. 11.6(5.5, 44.1); p<0.001) (Figure 1). Anti-C1q antibody levels were positively correlated with levels of 24-hour urinary protein(r=0.605; P=0.000), AI score (r=0.337; P=0.001), and negatively correlated with serum C3 (r=-0.573; P=0.000) and C4 (r=-0.509; P=0.000). (Figure 2).

**Conclusion:** Anti-C1q antibodies are more closely correlated with renal disease activity.

**REFERENCES**


**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.7816

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**ADIPOKINES AND ENDOTHELIAL DYSFUNCTION IN SYSTEMIC LUPUS ERYTHEMATOSUS**

**ahmed yamany1, Mervat Behiry1, Ahmed Fayed1, Ahmed Soliman2. 1Kasr El Aini Teaching Hospital, internal medicine, cairo, Egypt; 2Kasr El Aini Teaching Hospital, internal medicine, cairo, Egypt**

**Background:** Premature atherosclerosis is clearly described in systemic lupus erythematosus as a main cause of poor outcomes and mortality(1). Pleiotropic adipokines including adiponectin and visfatin are implicated in the inflammatory process of lupus disease that promote cytokines signaling leading accelerated endothelial disruption(2).

**Objectives:** To evaluate the endothelial dysfunction by measuring serum visfatin, adiponectin, leptin and HOMA-insulin Index as reliable biomarkers of atherosclerosis &estimating the FMD of brachial artery among lupus patients and correlating these parameters with clinical characteristics

**Methods:** A case-control study in which 150 systemic lupus patients who were fulfilling American College of Rheumatology revised classification were recruited consecutively from Internal Medicine department at Cairo University. They were compared to 90 age & sex matched healthy controls. Patients who were pregnant, smoker, diabetic, those with hepatic and...
renal dysfunction, hypothyroidism, and familial dyslipidemia were excluded. Adiponectin, leptin, visfatin, and HOMAIR were evaluated. Flow-mediated dilation of brachial artery was calculated as the maximum percent increase in artery diameter after cuff release compared to baseline.

**Results:** Data revealed elevated levels of adiponectin, leptin, visfatin and HOMAIR in lupus cases compared to controls with reduced FMD percent. Clinical and laboratory background are summarized in Table (1).

### Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cases N=150</th>
<th>Controls N=90</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>25.15±5.78</td>
<td>24.84±5.8</td>
<td>0.256</td>
</tr>
<tr>
<td>Female (N,% )</td>
<td>125 (83.3%)</td>
<td>75 (83.3%)</td>
<td>0.34</td>
</tr>
<tr>
<td>Male (N,% )</td>
<td>25 (16.7%)</td>
<td>15 (16.7%)</td>
<td></td>
</tr>
<tr>
<td>Disease duration (months)</td>
<td>10±6</td>
<td>12±7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.56±3.86</td>
<td>22.74±3.12</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Clinical characteristic (N,% )</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Mucocutaneous</td>
<td>123 (82%)</td>
<td>112 (80%)</td>
<td></td>
</tr>
<tr>
<td>- Arthritis/arthralgia</td>
<td>100 (75%)</td>
<td>80 (75%)</td>
<td></td>
</tr>
<tr>
<td>- Renal disease</td>
<td>13 (9%)</td>
<td>8 (9%)</td>
<td></td>
</tr>
<tr>
<td>- Central nervous disease</td>
<td>68 (45.4%)</td>
<td>11 (12%)</td>
<td></td>
</tr>
<tr>
<td>- Cardiovascular disease</td>
<td>49.32(66%)</td>
<td>49.32(66%)</td>
<td></td>
</tr>
<tr>
<td>- Vascular occlusion</td>
<td>97±8</td>
<td>89±9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fasting glucose (mg/dl)</td>
<td>10.6±2.9</td>
<td>12.8±1.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>13±6±9.3</td>
<td>14±1±1.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Triglycerides (mg/dl)</td>
<td>187±44</td>
<td>143±18</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total Cholesterol (mg/dl)</td>
<td>118±33±7</td>
<td>64±6±7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>48±14</td>
<td>49±3</td>
<td>0.13</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>42±11</td>
<td>43±3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ESR (mm/hr)</td>
<td>64.6±7</td>
<td>62±6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HOMA IR</td>
<td>10.6±5.2</td>
<td>4.0±3.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Plasma Adiponectin (ng/ml)</td>
<td>16.5±3.2</td>
<td>12.2±3.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum C-reactive protein (mg/ml)</td>
<td>25.1±10.7</td>
<td>7.8±0.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Serum Visfatin (ng/ml)</td>
<td>18.0±5.6</td>
<td>10.1±1.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FMD of brachial artery (%)</td>
<td>8.8±3.12</td>
<td>11.6±1.2</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

None of adipokines is correlated to age, BMI, disease duration or activity. An inverse correlation between FMD of the brachial artery and total cholesterol, visfatin, adiponectin, leptin and HOMAIR (r-value = -0.52, -0.35, -0.27, -0.45, -0.56 respectively) with P < 0.05. Adipokines and FMD did not differ regarding clinical presentations specially cardiovascular.

ROC curve analyses studied the performance of adipokines. Adiponectin and visfatin are better predictors of atherosclerosis in lupus patients with apparently quiescent disease activity.

### Conclusion:

Endothelial dysfunction is evident in SLE. Reduced FMD of brachial artery and increased adipokines & HOMAIR are noted. Adiponectin and visfatin could be predictors of atherosclerosis in lupus.

### REFERENCES


Acknowledgement: to all participants in this work

**Disclose of Interests:** None declared.
SAT065B  ANTI-MODIFIED PROTEIN AUTOANTIBODIES IN RA: DISPLAY IMPORTANT PEPTIDE CROSS-REACTIVITY BUT YET PROTEIN RECOGNITION SELECTIVITY

Peter Sahlström1,2, Johanna Steen1, Björn Forström3, Philip Titcombe1,4, Ragnhild Stålen1, Ute Nonhoff1, Zoltán Kontur4, Luca Piccoli2, Karin Lundberg2, Holger Bang1, Daniel Mueller1, Anca Catrina4, Lars Krężel1, Karl Skriner2, Vivianne Malmström1, Caroline Grönwall1, Karl Skriner1, Johanna Steen1, Björn Forström3, Philip Titcombe1,4, Ragnhild Stålen1, Ute Nonhoff1, Zoltán Kontur4, Luca Piccoli2, Karin Lundberg2, Holger Bang1, Daniel Mueller1, Anca Catrina4, Lars Krężel1, Karl Skriner2, Vivianne Malmström1, Caroline Grönwall1

Background: The continuing increase of anti-citrullinated protein autoantibodies (ACPAs) litters together with epitope spreading close to onset of disease, suggests that antibody responses to different citrullinated antigens may be critical in rheumatoid arthritis (RA) pathogenesis. Interestingly, monoclonal antibodies demonstrate reactivity to multiple cit-antigens that can even expand to other protein modifications. The width of this cross-reactivity is still not understood.

Objectives: To characterize the targets of monoclonal ACPA in relation to amino acid motif recognition, cross-reactivity with others post-translational modifications, and cellular localization.

Methods: A peptide array ( NimbleGen, Roche) containing 165 amino acid- or lysine in pairs with citrulline- or homocitrulline peptides (53019 and 49211 cognate peptide pairs, respectively) derived from 1610 extracellular proteins and known RA cit-targets was used to screen 12 monoclonal ACPA with CCP2 reactivity. In addition, these ACPA were also screened for reactivity to acetylated-histone peptides and for reactivity to acetylated HeLa cell extracts from cytosol, membrane, nuclear and cytoskeleton fractions. Three of the described mAbs together with polyclonal anti-CCP2 IgG were further evaluated on a macroarray platform (HIXselect, Engine) consisting of 20776 E.coli on-array expressed His-tagged protein fragments from 6909 genes originating from a human cDNA library. The array was enzymatically citrullinated with rabbit PDA and mAb-reactivity was scored from 0-6.

Results: On the peptide arrays, all 12 ACPA displayed low reactivity to unmodified peptides (<0.06%), while reacting to 1,000s of synthetically citrullinated peptides (>3.4% of the peptides). Based on the sequence from the positive peptides, consensus amino acids motifs were created, identifying aa-patterns with only a few critical citrulline-flanking residues (e.g. Cit-Gly; Gly-Cit; Arg-Cit-Asp). Intriguingly, five of the antibodies also reacted with the carboxamidated peptides (>2.2%) and the recognition of certain homocitrulline-motifs also correlated with cross-reactivity to acetylated peptides. Interestingly, these ACPA reacted with acetylated-histones in NETs and apoptotic cells and in the nuclear fraction of in vitro acetylated cell-extracts. Three of the 12 ACPA were further screened on the macroarray and displayed multiple binding to citrullinated proteins and protein fragments identifying primarily previously unknown autoantibody targets (98, 210 or 917 positive hits for the mAbs, scoring 2-3), while limited binding was seen to native proteins.

Conclusion: ACPA display multi-reactivity to citrullinated peptides and proteins to a much greater extent than previously appreciated. Additionally, some ACPA, but not all, show distinct cross-reactivity to other post-translational modifications. Importantly, different autoimmune clones display modified protein recognition patterns dominated by proteins from different cellular structures. These reactivity profiles are likely to have impact on functionality and pathogenesis.

REFERENCES

Disclosure of Interests: None declared

SAT0677 HETEROGENEITY OF STRATEGIES AND METHODS FOR ASSESSMENT OF COMPETENCES IN RHEUMATOLOGY TRAINING: RESULTS OF A SYSTEMATIC LITERATURE REVIEW TO INFORM EULAR POINTS TO CONSIDER
Alessia Alunno, Aurelie Najm, Francisca Sivera, Catherine Haines, Sofia Ramiro, University of Pernigia, Pernigia, Italy; University Hospital and INSERM UMR1238, Nantes, France; Hospital Universitario Elda, Alicante, Spain; King’s College, London, United Kingdom; LUMC, Leiden, Netherlands; Zuyderland MC, Heerlen, Netherlands

Background: The structure and content of Rheumatology training programs vary widely among European countries. Harmonization of assessment methods of competences across EULAR countries could contribute to ensure a minimal standard of care.

Objectives: To identify and review the evidence on competence assessment methods and strategies in postgraduate medical training in rheumatology and other specialties.

Methods: As part of the EULAR project to develop points to consider on assessment of competences in rheumatology training, a systematic literature review (SLR) was performed. Two reviewers (AA and AN) independently identified eligible studies according to the PIM framework: P (population): trainees, fellows; I (instrument of interest): assessment strategies and methods; M (measurement of properties of interest): validity, discrimination, feasibility. Two searches were conducted: (i) for rheumatology, retrieving original studies; (ii) for related medical specialties, retrieving SLRs through which we identified original studies. Risk of bias was assessed using the medical education research study quality instrument (MERSQI) and the tool by Daly et al for qualitative studies. Studies were too heterogeneous to allow for any form of pooling, so descriptive results are presented.

Results: Of the 6276 articles from the rheumatology search, 4 met the inclusion criteria; of the 2,265 SLRs in other specialties, 36 were included, corresponding to a total of 133 original studies included. Studies on the assessment of competences in rheumatology were at variable risk of bias and explored only 2 methods: direct observation of practical skills (DOPS) and objective structured clinical examination (OSCE) (Table 1). Rheumatology OSCEs have been used to assess clinical skills consistently demonstrated a good to very good inter-rater reliability (r=0.60-0.95), while those on OSCEs to assess communication skills consistently demonstrated a good to very good internal consistency (Cronbach’s α=0.70-0.98). Other tools such as multisource feedback (MSF) and mini-clinical evaluation exercise (mini-CEX) showed feasibility and a good to very good internal consistency, but results on validity and reliability were conflicting.

Conclusion: Although there is a consistent body of evidence about assessment of competence in postgraduate medical training in several specialties, data in rheumatology is scarce and this partial picture indicates some conflicting evidence. OSCEs represent an appropriate tool to assess clinical competences and correlate fairly well with other assessment strategies; DOPS, MSF and mini-CEX are other feasible alternatives. A mapping of European countries and a qualitative study will be additionally performed.

SAT0678 DEVELOPMENT AND VALIDATION OF A SELF-ADMINISTERED QUESTIONNAIRE MEASURING ESSENTIAL KNOWLEDGE FOR PATIENTS WITH SPONDYLIOARTHRITIS: THE SpondyloArthritis Knowledge QUESTIONnaire(SPAkE)

Catherine Beauvais, Bruno Pereira, Thao Pham, Christelle Sordeil, Pascal Claudepierre, Françoise Fayet, Daniel Wendling, Felicie Costantino, Laurence Carton, Laurent Grange, Martin Soubrier, Nathalie Legoupil, Aleth Perdriger, Isabel Tavares, Emmanuelle Dernis, Laure Gossec

Background: Patient education is recommended for patients with inflammatory arthritis to enhance self-management. Only one Knowledge coefficient= 0.80-0.95). A fair to moderate correlation (r=0.44-0.52) between OSCEs and other assessment tools, including DOPS, has been found. The study on DOPS but not those on OSCEs provided evidence for feasibility. Studies in other specialties were more heterogeneous for strategy/tools investigated, type and comprehensiveness of the analysis. The majority of studies on OSCEs to assess clinical skills showed a good to very good inter-rater reliability (r=0.60-0.95), while those on OSCEs to assess communication skills consistently demonstrated a good to very good internal consistency (Cronbach’s α=0.70-0.98). Other tools such as multisource feedback (MSF) and mini-clinical evaluation exercise (mini-CEX) showed feasibility and a good to very good internal consistency, but results on validity and reliability were conflicting.

Conclusion: Although there is a consistent body of evidence about assessment of competence in postgraduate medical training in several specialties, data in rheumatology is scarce and this partial picture indicates some conflicting evidence. OSCEs represent an appropriate tool to assess clinical competences and correlate fairly well with other assessment strategies; DOPS, MSF and mini-CEX are other feasible alternatives. A mapping of European countries and a qualitative study will be additionally performed.

Disclosure of Interests: Alessia Alunno: None declared, Aurelie Najm: None declared, Francisca Sivera: None declared, Catherine Haines: None declared, Sofia Ramiro: Grant/research support from: MSD, Consultant for: AbbVie, Lilly, MSD, Novartis, Pfizer, Sanofi, Speakers bureau: AbbVie, Lilly, MSD, Novartis, Pfizer, Sanofi
Questionnaire (KQ) is available in spondyloarthritides (SpA) (ref 1) and needs to be updated according to the recent recommendations for SA and the patients’ needs (ref 2).

Objectives: To develop and validate a new KQ in SpA.

Methods: 4 steps. Step 1. Selection of knowledge considered essential for patients with SpA through Delphi rounds by a working group of rheumatologists, health professionals (HPs) and patients, leading to a list of consensual items (ref2). Step 2. Two rheumatologists and a rheumatology nurse constructed the first version of the KQ, each question of the KQ referring to a selected item on the list. The formulation was then amended by the working group. A new version was elaborated during a face-to-face meeting of 3 health professionals and one patient. Step 3. The KQ was submitted to ten patients for cognitive debriefing, comments were analyzed and a final version was elaborated. Step 4. Multicentric validation in 13 rheumatology departments: acceptability was measured by the rates of missing data per item, reproducibility and sensitivity to change were assessed respectively by test/retest at a 2 weeks interval (Lin’s concordance correlation coefficient) and by testing the KQ before and after patient education sessions.

Results: Step 1 obtained 42 items, 32 considered essential and 10 considered useful, selected respectively by more than 2/3 or more than 50% of participants to the Delphi rounds, leading to the SPAKE: a 42-items questionnaire, with a 32-items short form. The SPAKE contains 6 knowledge domains: disease knowledge (12 items), pharmacological treatment (11), non-pharmacological treatment (8), comorbidities (1), self-care for pain and fatigue (4), adaptive skills to psychosocial, professional issues and health care system (6). The validation included 130 patients, 67 (51.5%) men, mean age 43.5±12.9 years, median disease duration 8 years [3;16]. There were no missing items in the KQ. The SPAKE’s internal validity (Cronbach’s coefficient) was 0.95. Reproducibility (in 61 patients) was 0.81 [95% CI, 0.72; 0.89]. Sensitivity to change was measured in 55 patients. A statistically significant difference in total knowledge score was observed between the two assessment times: 29.1±6.4 vs. 34.7±5.9 (p<0.001), representing an effect size of 0.92 [0.52; 1.31]. The questionnaire’s external validity was confirmed by a significant correlation with the patients’ educational level (p=0.02).

Conclusion: This study enabled the development and the validation of the SPAKE, a knowledge questionnaire for patients with SpA, with a good acceptability, reproducibility and sensitivity to change. This KQ will be helpful to assess the process of knowledge acquisition in patient education approaches.

REFERENCES

Disclosure of Interests: Catherine Beauvais: None declared, Bruno Perreira: None declared, Thao Pham Speakers bureau: Lilly, Novartis, Christelle Sordet: None declared, Pascal Claudel-Peugnet Consultant for: Honoria from Novartis as steering committee of this survey, Francoise Fayet: None declared, Daniel Wendling: None declared, Felicie Costantino: None declared, Laurence Carboni Grant/research support from: AMGEN UCB MYLAN BIOGARAN BIOGENEPI FRIZER LILLY GRENENTHAL TEVA NOVARTIS JANSSEN EXPANSICINE SANOFI THUASNE MSD GEN- EVRIER ABBVIE, LAURENT GRANGE Consultant for: Laurent Grange has received honoraria from Amgen, Lilly and UCB and research support from Lilly, Amgen, UCB, Expanscience, Mylan, Roche diagnostics and TEVA. Martin SOUBRIER: None declared, Nathalie Legoupil: None declared, Aleth Perdriger: None declared, Isabelle Tavernes: None declared, Emmanuelene Denni: None declared, Laure Gossez Grant/research support from: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis-Sandoz, Pfizer, Sanofi, and UCB, Consultant for: AbbVie, Biogen, BMS, Celgene, Janssen, Lilly, MSD, Nordic Pharma, Novartis-Sandoz, Pfizer, Roche, Sanofi, and UCB, Consultant for: L Gossez has received honoraria from Celgene as investigator for this study, Malory RODERE: None declared DOI: 10.1136/annrheumdis-2019-eular.4379 SAT0679 EFFICACY OF A NURSE-LED PATIENT EDUCATION INTERVENTION IN PROMOTING SAFETY KNOWLEDGE AND SKILLS OF PATIENTS WITH INFLAMMATORY ARTHRITIS TREATED WITH BIOLOGICS: A RANDOMIZED CONTROLLED TRIAL Catherine Beauvais1, Francoise Fayet2, Alexandra Rousseau1, Christelle Sordet2, Sophie Poupin1, Yves Maugars3, Rose Marie Polverid4, Caroline Save5, Veronique Segard6, Beatrice Godon7, Christian Lamour8, Aleth Perdrger7, Fabienne Brin7, Patricia Peyraud5, Fabienne Chalier5, Beatrice Pallot Prades6, Isabelle Griffoul1

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Background: Biologic disease modifying drugs (bDMARDs) are highly effective treatments of IA such as rheumatoid arthritis (RA) and axial or peripheral spondyloarthritids (SpA). However, they lead to risks of infections and other side effects. Some of these adverse events may be prevented by patient education (PE) aimed at promoting patients’ safety skills.

Objectives: To investigate the effect of a nurse-led PE on safety skills of patients with IA at the introduction of a first subcutaneous bDMARD.

Methods: Multicentric randomized controlled trial comparing an intervention group (IG) to usual care (UC) at the time of the introduction of a first bDMARD. Inclusion criteria: patients with RA or SpA, biologic naïve, eligible for a subcutaneous bDMARD according to the rheumatologist’s opinion. Intervention: a face-to-face nurse-led PE at baseline (BL) and 3 months later, ie, assessment by the nurse of the patients’ health beliefs and educational needs, education focused on safety skills, self-injections and motivation. The primary outcome was the acquisition of safety skills at 6 months measured by the Biosecure Questionnaire (0-100 scale), a 55 item validated questionnaire assessing competences to deal with fever, infections, vaccination, and other daily life situations (ref). The secondary outcomes were quality of life, severe infections rate, coping, psychological well-being and disease activity. Data were analysed as intent-to-treat using multiple imputations.

Results: 128 patients were included from 9 rheumatology departments between January 2017 and April 2018, 39 (30.7%) with RA, 72 (56.7%) with axial SpA, 16 (12.6%) with peripheral SpA; mean age 47.0 ±12.8 years, mean disease duration 6.1±7.5 years, 120 (94%) completed the study. BL mean self-reported information on RA treatments (0-10 numeric scale) was similar: 7.1±2.0 in IG, 6.8±2.1 in CG. The mean duration of the intervention was 65.5 ±17.9 minutes. The primary outcome was met: the Biosecure score at 6 months was 81.2 ±13.1 versus 75.6±13.0 in the IG and CG respectively (p =0.016), showing better skills in the IG. Secondary outcomes were also favorable.

Conclusion: Safety is an important issue in the management of IA treated with bDMARDs. In this trial, a nurse-led patient education was shown for the first time to be effective in teaching patients the essential safety skills.

REFERENCES
Background: Patient education is an important part of the management of rheumatic and other diseases. Since patients do not have the same needs, it is crucial to assess needs of a targeted group to be able to tailor educational interventions.

Objectives: To assess educational needs of a large cohort of patients with different rheumatic and musculoskeletal diseases attending a health facility in Austria.

Methods: We conducted an online survey with patients attending the Gastein Healing Galleries in Bad Gastein, Austria. Approximately 12,000 patients with a variety of diseases are treated in the centre every year. Of those, 6,465 patients were invited by email to fill out an anonymous online survey. Socio-demographics and health outcomes were collected from all respondents. In addition, the Educational Needs Assessment Tool (Austrian version - OENAT) was administered to a subset of respondents. The OENAT (39 items) assesses 7 domains of educational needs: Managing Pain, Movement, Managing Feelings, Arthritis/Disease process, Treatments, Self Help Measures, Support Systems.

Results: In total 2017 (31%) patients responded of which 516 had data on educational needs: AS (63%), RA (14%), and FM (24%). Their mean (SD) age was 56 (11), and 54% were male. Level of education was: Elementary School (32%), Junior High School (22%), High School (21%), College (12%), and University (14%). Table 1 presents differences in educational needs across disease groups. Across the groups, there were significant differences in following OENAT domains: Managing Pain, Feelings, Treatments, and Support Systems. There were no differences in the level of educational needs in Movements, Disease Process, and Self Help Measures.

Patients with FM had significantly lower needs for managing and higher needs for feeling education, compared to those with AS and RA (p<0.05). The RA group had significantly higher needs than the AS (p<0.05) and FM (p<0.05) groups for treatments education - the AS group had significantly higher needs than the FM group (p<0.05) in the same domain. AS patients had significantly higher needs for support system education than FM (p<0.05) and RA patients (p<0.05).

Conclusion: Educational needs vary by disease groups and depend on the domain under consideration.

Disclosure of Interests: None declared

PATIENT EDUCATION IN THE EUROPEAN REFERENCE NETWORK ON RARE AND COMPLEX CONNECTIVE TISSUE AND MUSCULOSKELETAL DISEASES (ERN RECONNET): UNMET NEEDS FROM THE HEALTHCARE PROVIDERS SIDE AND FROM THE PATIENTS' SIDE

Meryem-Maud Farhat1, Alain Corret2, Chaïtoua Frank3, Ilaria Galetti4, Juergen Grunert5, Vera Guimarães6, Lisa Matthews7, Ana Vieira8, Eric Hachulla4

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SAT0682

NORMATIVE DATA FOR THE DISEASE AND TREATMENT ASSOCIATED KNOWLEDGE SCORE (DATAK-RA) IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Having adequate disease-related knowledge is essential for patients with RA, since it may influence treatment decisions, shared-decision making, and the ability to perform self-management behavior. Patient Knowledge Questionnaires can be used to measure disease-related knowledge. We recently developed and validated the item response theory (IRT) based Disease and Treatment associated Knowledge in Rheumatoid Arthritis (DataK-RA) item bank, containing 42 multiple-choice items. In the present study we establish normative data to facilitate the interpretability of DataK-RA scores.

Methods: Consecutive patients enrolled from three hospitals in the Netherlands were asked to complete a form containing either 27 or 26 DataK-RA items. DataK-RA IRT-scores and standard errors (SEs) were obtained using the weight maximum likelihood estimator. The Dutch Committee on Tests and Testing (COTAN) quality criteria for test norms were followed. DataK-RA IRT scores and the precision of the scores (SE) were summarized using the mean (SD) or median and 1st-3rd quartile in case of non-normal distribution. Scores were compared between male

Conclusion: Based on the EULAR recommendations for PE (Zangi HA et al.), PE should be apply in all EU countries. E-learning on PE for staff members and ePE for patients will be developed by the ERN ReCONNET.

REFERENCE


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and female patients and patients with low, middle and high educational attainment, according to the International Standard Classification of Educa-
tion, using One-way ANOVA with a significance level of α = 0.05.

Results: In total 631 patients participated, most of them were female
(60.9%). Mean age (SD) was 64.0 (11.6) years. Mean (SD) DataK-RA
score was 52.5 (14.1) (range 11.7 – 104.7). Female patients had signif-
ically higher DataK-RA scores compared with men (F = 25.23, p < 0.01).
Mean (SD) DataK-RA-score was 54.6 (15.1) for women, and 48.9
(11.5) for men. The median (1st – 3rd quartile) SE of the IRT-scores
was 4.7 (4.1 – 5.8). Regarding education, higher-educated patients had a sig-
ificant higher IRT-score than middle- and lower-educated patients (p < 0.01),
as well as middle-educated versus lower-educated patients (p < 0.01).
Table 1 shows the percentiles DataK-RA-scores, and DataK-RA
scores stratified by age educational level.

Conclusion: We present normative data for DataK-RA scores generated
from a sample of consecutive patients participating in an ongoing longitudi-

Table 1. Percentiles DataK-RA scores and percentiles DataK-RA scores stratified by age and educational level

<table>
<thead>
<tr>
<th>DataK-RA scores</th>
<th>DataK-RA scores by educational level</th>
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<td>%</td>
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<td>10</td>
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References


SA70684 A UNIQUE FREE EDUCATIONAL RESOURCE FOR RHEUMATOLOGISTS: WWW.RHEUMATOLOGYMINDMAP.COM

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Background: One of the challenges for doctors in training is fast and
easy access to reliable, relevant, and up-to-date clinical information. It

Figure 1

Figure 2搜索，容易修改，能够嵌入文档，链接主题，并使用外部超链接。证据显示，思维导图有助于学习

Objectives: To create a free educational resource in rheumatology using
mind-mapping techniques.

Methods: We used Mindjet MindManager 2017 (mind mapping software
allowing export into HTML5 files that can be published online) to create
the Rheumatology Mind Map website (www.rheumatologymindmap.com). A
wide range of information relevant to adult rheumatology practice in the
United Kingdom has been retrieved from various sources and structured
in accordance with common standards used in medical education. The
mind map embeds infographics currently used in rheumatology (diagnostic
and classification criteria, activity and damage indices, treatment decision
aids, downloadable templates, etc). Appropriate permissions from right
owners have been obtained.

Results: The current version of the website (1.7, January 2019) contains
an expandable mind map with above 1900 subtopics covering all aspects
of adult rheumatology. It works with all modern desktop and mobile
browsers. Examples of structure of the mind map and some subtopics
are shown in figures 1 and 2. The main advantages of the mind map are
the presence of the most up-to-date information, detailed lists of
investigations relevant for each of rheumatic conditions, thorough differen-
tial diagnosis, subtopics on pregnancy issues, extensive information about
medications used in rheumatology practice and treatment options for each
condition. Specific attention is paid at the clinical information relevant
for trainees, e.g., what to ask when you suspect a certain rheumatic illness,
what to look for at the examination, and which investigations to order.
The mind map has direct online links to appropriate NHS, NICE, BSR,
SIGN, EULAR, and ACR guidelines and policies, and various resources
including online calculators, relevant databases, websites providing support
for patients, etc.

Conclusion: The website www.rheumatologymindmap.com is an attempt to
create a unique comprehensive educational resource in rheumatology. It
allows free access and structured approach to clinical information required
by a trainee or an established rheumatologist. It is an up-to-date source
of a wide range of information and is linking hundreds of current online
sources together in one place.

REFERENCES

USE AND IMPACT ON SOCIAL NETWORKS BY RHEUMATOLOGY JOURNALS

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Background: Traditional system for assessing the quality and impact of a scientific journal is based on the number of citations. One of the main forms of measurement is the impact factor, which measures the impact that a journal has on the scientific community. Despite its traditional use, this quality and impact assessment system has been criticized in recent years. The “Alternative Assessment Metrics” initiative (Altmetrics) seeks to define new measures of metrics for scientific publications. Alternative metrics are based on the number of “mentions” of an article in various online sources, including blogs and social networking platforms. The alternative metrics are more dynamic and accumulate quickly in real time. The social networks most frequently used by scientific journals are Facebook, YouTube and Twitter.

Objectives: To evaluate presence, number of followers and activity of rheumatology journals in 3 social networks (Facebook, Twitter and Youtube).

Methods: Platform of scientific journals SCOPUS was consulted, selecting journals classified as rheumatology journals. Scimago Journal Rank (SJR) of 2017 was taken to evaluate the quality of the journal. The social networks Facebook, Twitter and YouTube were consulted, searching for rheumatology journals of those found in SCOPUS with active accounts in these social networks. Date of consultation: 13-11-18.

Results: 51 rheumatology journals in SCOPUS, of which only 8 (13.1%) had an active account in at least one of the social networks consulted. On Facebook the most active and most popular magazine was Nature Reviews, followed by the Journal of Rheumatology and Annals of the Rheumatic Diseases. It should be noted that Nature Reviews includes other journals in their social networks that cover other specialties of medicine such as cardiology, immunology, microbiology, oncology, among others. On Twitter, as on Facebook, magazine with largest number of followers was Nature Reviews, followed by Annals of the Rheumatic Diseases and Journal of Rheumatology. Activity on Twitter, measured as number of twits, had same behavior according to the number of followers. The only journal with channel on YouTube was Annals of the Rheumatic disease with 67 subscribers, 12 videos, of which the most watched has 315 reproductions. See table 1.

Table 1. Characterization of scientific journals in social networks in rheumatology. SJR: Scimago Journal Rank. Facebook: Number of followers. Twitter: Number of followers. Twits: Number of twits reported on the platform

Conclusion: YT and FB are social networks with a high content of false information. The majority of available videos promise to cure different rheumatic diseases (even several simultaneously). This is the first work of a line of research that seeks to highlight the high degree of misinformation. We will continue to analyze other diseases and social networks, to make publications and communications in different media and to alert local regulatory entities.

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Disclosure of Interests: None declared


ONLINE EDUCATION IMPROVES PHYSICIANS’ KNOWLEDGE OF FAMILY PLANNING AND PREGNANCY MANAGEMENT IN WOMEN WITH CHRONIC INFLAMMATORY RHEUMATIC DISEASES

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Background: Chronic inflammatory rheumatic disease (CIRDs) often develop in women during their childbearing years. Preconception counseling and coordinated medical and obstetric care are essential to maintain control of the disease and maximize the chances of a successful pregnancy.

Objectives: This study assessed whether online CME can improve physicians’ understanding of the risks of uncontrolled chronic rheumatic diseases in pregnancy and the benefits of proactive pregnancy planning, and enhance physician confidence in managing such patients.

Methods: Physicians participated in an online CME activity consisting of a 15-minute video discussion between 2 experts with accompanying slides. Educational effect was assessed using a 4-question repeated pairs, pre-/post-assessment. A Chi-square Test of Independence was used to determine if a statistically significant improvement (5% significance level, P <.05) existed in the number of correct responses between the pretest and posttest scores. Cramer’s V was used to estimate the effect of the education. The CME accredited activity launched on August 2 2018, and data were collected through August 30 2018.

Results:
- Rheumatologists (n=47) had a high baseline knowledge of family planning and pregnancy management in women with CIRDs, but the activity had a significant impact (P =.0008) on rheumatologists’ knowledge and the Cramer’s V value of 0.199 indicates a considerable effect of the education
- The average percentage of correct responses for rheumatologists was 91% post–activity compared with 76% pre–activity
- 64% more rheumatologists answered all 3 questions correctly post–activity compared with pre–activity (74% vs. 45%)
- 26% of rheumatologists gained confidence in their ability to manage CIRDs in pregnant patients, with an average confidence shift of 9%
- Obstetricians/gynaecologists (n=40) also had a fairly high baseline knowledge of family planning and pregnancy management in women with CIRDs, but again, the activity had a significant impact (P =.0005) on their knowledge and the Cramer’s V value of 0.226 indicates a considerable effect of the education
- The average percentage of correct responses for obstetricians/ gynaecologists was 83% post–activity compared with 63% pre–activity
- 97% more obstetricians/gynaecologists answered all 3 questions correctly post–activity compared with pre–activity (65% vs. 33%)
- Almost half (45%) of obstetricians/gynaecologists gained substantial confidence in their ability to manage CIRDs in pregnant patients, with an average confidence shift of 22%

Conclusion: This online, 15-minute video discussion between 2 experts significantly improved rheumatologists’ and obstetricians/gynaecologists’ understanding of family planning and pregnancy management in women with CIRDs which may lead to improved outcomes for both women and babies. Both groups would benefit from further education to reinforce knowledge of disease activity on conception and pregnancy and to emphasize the need for collaborative proactive family planning in women with CIRDs.

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Evolving the Management of Rheumatoid Arthritis Through Development of Practical and Educational Tools

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Background: Despite advances in the treatment armamentarium for rheumatoid arthritis (RA) over the last decade, several unmet needs remain within RA management.

Objectives: To enhance scientific knowledge and improve patient care by providing practical tools and evidence-based awareness – in line with EULAR recommendations – on how to implement optimal RA management and address identified needs.

Methods: The eRA (evolving the management of RA) programme convened a Steering Committee (SC) of 17 European and International experts in RA, including representation from rheumatologists, nurses, health professionals and patients. Through literature search and assessment of expert opinion, 4 core areas of unmet need were identified: delays in referral and initiation of disease-modifying anti-rheumatic drugs, inconsistent application of treat-to-target strategy, sub-optimal identification and management of comorbidities, and a growing need to actively engage patients with their care. Several clinical and educational gaps associated with these unmet needs were also identified. To fill these gaps and support application of an optimal approach to RA management, practical and educational tools were developed. A cascade process engaging national leaders in rheumatology was then initiated to disseminate the tools to health professionals across Europe, with tools being updated in participating countries to ensure alignment with local practices and individual country needs. Broader programme dissemination is supported by congress activities and a digital communication plan. The eRA programme is funded by Sanofi Genzyme. Programme direction and content creation are driven by the SC.

Results: A suite of 12 educational tools was developed (Figure 1), including educational slides to raise awareness of unmet needs, self-reflection questionnaires to evaluate personal practice alongside EULAR recommendations, case scenarios outlining the optimal approach to management, and clinical checklists to support daily practice. The process to disseminate these tools commenced in November 2017 with a Multi-Country Workshop, which convened 43 national leaders in rheumatology from countries participating in the programme. Feedback on the eRA tools at this meeting was positive, and in 2018, additional countries were onboarded to the programme. Launch of a digital web-platform aims to further support dissemination of the eRA tools.

Conclusion: The content of the eRA programme has been well-received, largely due to the programme’s flexible approach, which is responsive to individual country needs. As the cascade process continues, it is anticipated that many more health professionals and patients will benefit from the eRA tools. References: Disclosure of Interests: Gerd Rüdiger Burmester Consultant for: Roche, Sanofi-Genzyme, Speakers bureau: Roche, Sanofi-Genzyme, Mart van de Laar Grant/research support from: AbbVie, Eli Lilly, Janssen-Cilag, Merck Inc, Pfizer Inc, Sanofi Genzyme, Speakers bureau: Eli Lilly, Pfizer Inc, Jose-Maria Alvaro-Gracia Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, MSD, Novartis, Pfizer Inc, Roche, Sanofi, and UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, MSD, Novartis, Pfizer Inc, Roche, Sanofi, and UCB, Neil Betteridge Consultant for: Amgen, Eli Lilly, Grunenthal, GSK, Heart Valve Voice, Janssen, Roche, Sanofi Genzyme and Sanofi Regeneron, Speakers bureau: Amgen, Eli Lilly, Grunenthal, GSK, Heart Valve Voice, Janssen, Roche, Sanofi Genzyme and Sanofi Regeneron, Jaime Calvo Consultant for: Bristol-Myers Squibb, Janssen, Celgene, Sanofi Genzyme, Speakers bureau: Bristol-Myers Squibb, Bernard Combe Consultant for: AbbVie, Bristol-Myers Squibb, Gilead, Janssen, Eli Lilly, MSD, Novartis, Pfizer, Roche-Chugai, Sanofi, UCB, Patrick Durez Speakers bureau: Bristol-Myers Squibb, Eli Lilly, Sanofi, Celltrion, Ricardo J.O Ferreira Consultant for: Sanofi Genzyme, Bruno Fautrel Grant/research support from: AbbVie, Lilly, MSD, Pfizer, Consultant for: AbbVie, Biogen, BMS, Celgene, Janssen, Lilly, Medac, MSD, NORDIC Pharma, Novartis, Pfizer, Roche, Sanofi-Aventis, Sanofi Genzyme, SCIBI, UCB, Cem Gabay Grant/research support from: Roche, Pfizer, AB2 Bio Ltd, Consultant for: Roche, Pfizer, Lilly, AbbVie, Sanofi, Regeneron, Bristol-Myers Squibb, Novartis, UCB, AB2 Bio Ltd, Debipharma, Annamaria Iagnocco: None declared, Carlmaurizio Montecucco Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Sanofi, Genzyme, Lilly, MSD, Pfizer, UCB, Mikkel Stergaard Grant/research support from: AbbVie, Celgene, Centocor, Merck, Novartis, Consultant for: AbbVie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orison, Pfizer, Regeneron, Roche, and UCB, Speakers bureau: AbbVie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orison, Pfizer, Regeneron, Roche, and UCB, Sofia Ramiro Grant/research support from: MSD, Consultant for: AbbVie, Lilly, MSD, Novartis, Pfizer, Sanofi, Andrea Rubbert-Roth Consultant for: Chugai, Eli Lilly, Roche, and Sanofi, Speakers bureau: AbbVie, Bristol-Myers Squibb, Chugai, Hexal/Novartis, Janssen, Eli Lilly, Merck Sharp & Dohme, Pfizer, Roche, and Sanofi, Tanja Stamm Grant/research support from: TS has received grant support from AbbVie., Paid instructor for: TS has received speaker fees from AbbVie, Janssen, MSD, Novartis, and Roche., Zoltán Szekanecz Grant/research support from: Pfizer, UCB, Consultant for: Pfizer, AbbVie, Roche, Sanofi, Lilly, Novartis, Speakers bureau: Pfizer, AbbVie, Roche, Sanofi, Lilly, Novartis, Peter C. Taylor Grant/research support from: Celgene, Galapagos, Eli Lilly, UCB, Consultant for: AbbVie, Galapagos, Gilead, Eli Lilly, Pfizer Inc


Figure 1. eRA toolkit

PATIENT STATE OF KNOWLEDGE ON BIOSIMILARS – DO PHYSICIANS NEED TO IMPROVE EDUCATION SKILLS?

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Background: Biosimilars are highly similar to original biological medicines. However, worldwide prescription of biosimilars is still low because of the lack of understanding in manufacturing and approval process together with mistrust in the extrapolation of indication in clinical use. Lack of biosimilar awareness throughout rheumatic patients results in an unjustified underuse.

Objectives: To assess patients’ current knowledge and concerns on biosimilars and to investigate their expectations when receiving such a treatment following the principle of shared-decision making.

Methods: A national cross-sectional survey was conducted in Romanian patients with rheumatoid arthritis (RA), spondyloarthropathies (SpA), psoriatic arthritis (PsA) currently on a bio-originator or biosimilar. 336 patients responded to this survey.
a survey distributed from August to December 2018 mainly topics being patient basic information on biosimilars, their efficacy, safety, price or differences to original drugs.

Results: Out of 336 patients, 47.3% had RA, 39.8% had SpA, 12.5% PsA with a mean age of 50.5 in the study cohort. 13% received approved biosimilars while 87% bio-originators with different mechanisms of action. A yes/no type of question divided patients into those aware or not of biosimilars with further exclusion of those with lack of information. Half of the patients (48.8%) stated they never heard of biosimilars. Surprisingly, four of them were already on this type of treatment. Out of the 172 remaining patients, 28.4% feared the risk of adverse events like infections or cancer while almost 20% expressed either insecurity on drug tolerability or the possibility that the biosimilar might be less efficient that the original drug. Another 19.7% certified they had no concerns related to these products and only 15.1% stated confusion regarding the potentially different in the pharmacological structure of the drugs. Most patients (48.2%) were convinced that the price of a drug should not exceed its efficacy or safety. Half of the respondents say they could accept a switch from an original to a biosimilar if their rheumatologist advises them and 30% might agree but only after being informed. 8.7% are interested in scientific proof of the drug and only 1% would consent to a change directly from the pharmacists. When handling prescription, 37.7% of patients would want to know if it is an original drug or a biosimilar while 20% do not mind if they receive either. Another 30% trust their rheumatologist and 12.7% would feel more secure if receiving a patient card and written information. Most patients (73.2%) say that they feel completely confident in their rheumatologist if they would want to prescribe a biosimilar, 18.6% will have doubts but they will accept the drug and 4% would ask for another medical opinion. After biosimilar initiation, 45.9% would be cautious when administering it, 23.2% would stop the drug if an adverse event occurred and 15% would have no fears.

Conclusion: Study results confirm there is still a significant information gap concerning biosimilars in patient population. Most concerns on biosimilars are related to adverse event occurrence. There is a need to improve patient education on biosimilars involving patients and health professionals. Shared-decision principle is more of a myth since most patients rely on their rheumatologist and only 15% would ask for another medical opinion. After biosimilar initiation, 45.9% would be cautious when administering it, 23.2% would stop the drug if an adverse event occurred, and 15% would have no fears.

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SAT0690 HOW TO REDUCE THE NOCEBO EFFECT WHEN SWITCHING FROM ORIGINATOR INFLIXIMAB TO A BIOSIMILAR: POSITIVE RESULTS OF A MULTIDISCIPLINARY TEAM INTERVENTION

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Background: Non-specific subjective adverse effects (NSAE), usually considered as related to a nocebo effect (NE), have been identified as a barrier to the acceptability of switches from biologic originators (BO) to biosimilars (BS).

Objectives: To assess the efficacy of a multidisciplinary team intervention to reduce the NE among inflammatory arthritis (IA) patients concerned by systematic switch from originator Infliximab (OI) to the biosimilar infliximab (BI) SB2.

Methods: The intervention was part of a multidisciplinary patient education (PE) program. It was developed in 4 steps. Step 1: we conducted first semi-directive qualitative interviews with 5 patients treated by other intravenous (IV) biologics. Interviews showed: fears about efficacy and tolerability of BSs, need for information (particularly on the difference between BSs and generics), importance of sharing their experience of adverse effects (AE) with health practitioners (HP), and having the opportunity to switch back. The wish to discuss the nurses’ own experience of BSs was prominent. Step 2: a meeting with the multidisciplinary team (3 rheumatologists, 1 resident, 1 pharmacist, 3 nurses, 1 peer-patient from a patient’s association) was set up for designing the intervention based on the interviews, on non-systematic literature review about switches and on patients’ perspective regarding NE. Step 3: Consensual agreement on the intervention and the chosen pieces of language to be used by all HPs. The intervention included written and oral information by the nurses; nurse-led PE; if necessary, distribution of an informative leaflet made by the team. Step 4: Implementation of the intervention. The rheumatologist had the entire appreciation for discontinuing the BS or not. Inclusion criteria were all IA patients concerned by OI. The primary outcome was SB2 retention rate (RT) at 34 weeks, secondary outcomes were the number of NSAEs leading to SB2 discontinuation; the comparison of the RT and NSAE rate of the cohort with 1) RT and NSAE rate of a systematic switch from another Infliximab BS (CT-P13) to SB2 made at the same period in the same rheumatology department 2) RT of BS2 and NSAE rate of switches in other published European cohorts (1,2,3).

Results: Forty-five patients were included from March 12th, 2018 to May 25th, 2018, median follow up was 34 weeks, 17 rheumatoid arthritis

SAT07689 A NOVEL METHODOLOGY FOR TEACHING RHEUMATOLOGY TO NEW GENERATIONS

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Background: Teaching rheumatology to undergraduate students is every day more challenging. In order to motivate new generations and use time more efficiently, we explored new methods to incorporate active learning in our rheumatology course. Therefore, we developed a video library and turned the classical lectures into flipped classrooms.

Objectives: To evaluate the impact of this new teaching method of rheumatology in a cohort of medical students at Pontificia Universidad Católica de Chile School of Medicine.

Methods: Fundamental lectures of rheumatology were recorded, edited and uploaded to YouTube, so the students were able to easily access the lessons from different electronic devices. A total of 10 videos were created, with an average duration of 6 minutes. A cohort of 120 fourth-year medical students took the rheumatology course between May 28th and June 11th of 2018. They were asked to watch the videos before the class, and during the classroom time the teacher could work on clinical cases, complement the information about the topic and answer questions. At the end of the course, the students evaluated this new methodology with a final online and anonymous survey. Performance analysis of each video was obtained from YouTube Analytics.

Results: Seventy-two students completed the survey at the end of the course, the students who evoluted the videos before the class was useful for their learning. Moreover, 70 students (97%) would like to continue using flipped classrooms in the future, and 1/3 of them would even use them to replace traditional lectures. Overall, the rheumatology was evaluated with a 6.8 score in a 1 – 7 scale. A 100% of this cohort approved the course. Average view duration of all videos was 4:37 minutes. Twenty-two students added positive comments about the use of flipped classroom in this course, and appreciated the videos were short enough to watch them before attending lectures.

Conclusion: Advances in technology have allowed developing innovating ways to teach. Flipped classroom encourages students to adopt a more active role in the learning process. This new methodology seems to be well accepted by students and shows a promising way to motivate new generations to learn rheumatology.

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Physician–patient agreement in a Rheumatology consultation

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Background: Several aspects of the consultation have already been studied. These usually comprise the patient satisfaction, patient enablement, physician–patient interaction and physician–patient agreement.1 After consultations, the physician’s perceptions differed from the patient’s in the illness level, cause and nature of the problem and the content of the consultation.2 Greater physician–patient agreement on consultations was associated with higher patient global satisfaction.3 Agreement on problems requiring follow-up was associated with a better outcome.4 Objectives: Assessment of physician–patient agreement in Rheumatology consultation.

Methods: A 10 item questionnaire - “Consultation Assessment Instrument” (CAI) - was constructed with the aim of assessing physician-patient agreement. It was anonymously applied, after the consultation, to the patient and physician. The higher the score obtained, the more positive the consultation experience. Patients above 18 years of age, with an established diagnosis of inflammatory joint disease under biological therapy were included. Items were evaluated and index of proportional agreement for the dichotomized answers - agree (Ppos) and disagree (Pneg) - was calculated.

Results: 102 observations were obtained, corresponding to 10 physicians and 102 patients. Most patients were female (53.9%) with a mean age of 51.5 ± 12.7 years old. Rheumatoid Arthritis was the most prevalent diagnosis (40.2%) and more than half of patients were in disease remission (28-joint Disease Activity Score (DAS28) < 2.6) or Ankylosing Spondylitis Disease Activity Score (ASDAS PCR) < 1.0. Higher CAI scores correlated with lower Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) scores (r = 0.376; p < 0.05). Also, patients with mild disease (score < 3.2) by DAS28 had higher CAI scores (low disease = 37.3±8.6; moderate disease = 35.8±4.3; high disease = 35.0±2.3; p = 0.039). It was also found that the more satisfied the patient, the lower the Bath Ankylosing Spondylitis Functional Index (BASFI) (r = 0.334; p < 0.05) and ASDAS PCR scores [low disease = 35.3±4.2; high disease = 30.5±7.8; p = 0.001]. There was no statistically significant association between CAI total score and Health Assessment Questionnaire (HAQ) score, ASDAS PCR or BASFI. Patient’s satisfaction did not show an association with DAS28, HAQ or BASDAI scores.

Conclusion: Both patient and physician tend to show a positive experience towards Rheumatology consultation. Patients with a more positive experience had lower disease activity scores. Physician–patient agreement was high in the majority of the consultation aspects. CAI could be useful as a mental checklist in daily practice or as an educational tool for training consultation skills.

REFERENCES

Disclosure of Interests: None declared

Dealing with comorbidities in rheumatoid arthritis with medical assistants. The patients’ opinion on assessment and education by medical assistants during routine clinical practice

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Background: In 2006 the curriculum for rheumatology health professionals of the Academy of the German Association of Rheumatologists (DGRh) was developed. [1]. Since then more than 1400 health professionals (medical assistants [medizinische Fachangestellte] and nurses) were trained and are currently playing an increasing role in rheumatology practices in Germany.

Objectives: To evaluate the patients’ opinion on the assessment by medical assistants in general and regarding assessment and education on cardiovascular risk and vaccination.

Methods: Patients with rheumatoid arthritis were interviewed by a medical assistant in a rheumatology practice that is part of the primärversorgungssystem with five rheumatologists in Erlangen, Germany. A semi-standardized interview assessed disease activity, pain, medication, general health, and side effects of medication. A part of the patients was also assessed and educated regarding cardiovascular risk or vaccinations. Thereafter they were examined by the rheumatologist and finally asked to complete a questionnaire regarding their visit. The questions were numerical scales ranging from 0 [very good, very satisfied] to 10 [very poor/inaequate].

Results: 293 Patients (mean age 61.3 ± 13.5 years, mean DAS28 2.6 ± 0.9, mean FFUH 76.4 ± 20.6) were documented between August and December 2018. 212 completed the general questionnaire. 34 regarding a structured cardiovascular assessment and education, and 18 regarding a structured assessment of vaccinations.

Table 1 shows patients answers between 0 [very good, very satisfied] to 10 [very poor/inaequate]. Overall rating was excellent with a mean score of 1.0 (SD 1.5). The rating was only slightly different, if patients were assessed by medical assistants for the first time (n=111; mean score 1.2, SD 1.5), between the 2nd to 4th time (n=82; mean score 1.0, SD 1.3) or the 5th time or more (n=19; mean score 0.6, SD 0.6).
ONLINE EDUCATION SIGNIFICANTLY IMPROVED QUALITATIVE ANALYSIS OF MOBILE APPS DIRECTED Candice Yuvienco1.

Methods: Rheumatologists participated in an online CME activity consisting of a 30-minute video roundtable discussion between 3 experts with accompanying slides. Educational effect was assessed using paired, repeated pairs, pre-post-assessment. A chi-square test was used to determine if a statistically significant improvement (P < .05 significance level) existed in the number of correct responses from the pretest and posttest scores. Cramer’s V was used to estimate the level of impact of the education. The CME activity launched on December 20, 2017, and the data were collected through March 6, 2018.

Results: A total of 328 rheumatologists completed the pre- and post activity assessments. Overall the activity had a significant impact (P < .001) on rheumatologists’ understanding of comparative effectiveness data in AS with a Cramer’s V value of 0.189 indicating a considerable effect of the education. The average percentage of correct responses rose from 22% pre-activity to 39% post-activity. A linked learning assessment (each individual tracked pre and posteducation) showed that 24% of learners improved their knowledge and 15% reinforced their knowledge. The change in percentage of correct responses from pre- to post-assessment achieved statistical significance (P < .05) for all 3 questions presented: (i) recommendations for biologic DMARD use in AS according to the ASAS-EULAR 2016 guidelines (34% at baseline rising to 67% post activity; P < .001), (ii) understanding the impact of treatment with biologic DMARDs on radiographic progression in AS (17% at baseline rising to 26% post activity; P < .01), (iii) understanding comparative analysis of RCTs in AS (14% at baseline rising to 24% post activity; P < .001) and (iv) a quarter of rheumatologists gained confidence in their ability to select a biologic DMARD based on comparative data and individual patient needs, with an average confidence shift of 14%.

Conclusion: This online CME activity significantly improved rheumatologists’ understanding of how to compare treatments and interpret comparative effectiveness data in AS which may lead to improved treatment selection and better patient outcomes. However, there is clearly room for further improving physicians’ knowledge of treatments & radiographic progression and comparative analysis of RCTs (since 75% of rheumatologists provided incorrect answers to questions 2 and 3 post-activity) which can be addressed in future education.

REFERENCE

Disclosure of Interests: Adriana Stan: None declared, Elaine Bell: None declared, Peter Schoenheim: None declared, Xenodon Baraliakos Grant/ research support from: AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Centocor, Chugai, Janssen, MSD, Novartis, Pfizer Inc, Roche and UCB, Grant/research support from: AbbVie, Pfizer, Merck Sharp & Dohme, UCB Pharma, Novartis, Consultant for: AbbVie, Bristol-Myers Squibb, Boehringer Ingelheim, Celgene, Chugai, Janssen Biologics, Novartis, Pfizer, UCB Pharma, Galapagos, Speakers bureau: AbbVie, Chugai, Janssen, Novartis, Pfizer, UCB Pharma DOI: 10.1136/annrheumdis-2019-eular.2987

SA10694 QUALITATIVE ANALYSIS OF MOBILE APPS DIRECTED FOR LUPUS PATIENTS
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Background: Systemic lupus erythematosus (SLE) is chronic disease that requires lifelong treatment with a multidisciplinary approach. Increasingly, patients use the internet and associated technology to access health-related information. Smartphone applications (apps) have become essential tools in this age and are widely-accessed by patients. These apps can be very helpful tools to inform patients about their disease and treatment options and help them in their treatment plan, and help them connect with others. Unfortunately, healthcare apps remain largely unregulated.

Objectives: We aim to evaluate the overall quality of patient-directed lupus apps with a focus on the accuracy and appropriateness of the health information contained in these apps.

Methods: The 2 most commonly used app stores are Apple Store and Google Play. These stores were searched for the terms “lupus” and “SLE” during December 2018. The resulted apps (Patient oriented, English language, and free of charge) were analyzed and the following data was collected: app type (informational, tool, or both); features, and

SA10693 ONLINE EDUCATION SIGNIFICANTLY IMPROVED RHEUMATOLOGISTS’ UNDERSTANDING AND INTERPRETATION OF COMPARATIVE TREATMENT DATA FOR AS
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Background: With multiple therapeutic options now available for patients with ankylosing spondylitis (AS), clinicians and payers require evidence to guide their decision-making. Head-to-head randomized controlled trials (RCTs) are considered to provide the best evidence for informing treatment decisions, but in the absence of such trials, physicians often rely on their own experience and clinical trial data from single RCTs. In the absence of head-to-head RCTs, data from comparative studies such as network meta-analysis and matching adjusted indirect comparisons can be useful to help inform treatment choices.

Objectives: This study assessed whether the online CME accredited round-table-discussion with title “Comparing Treatment Alternatives in Ankylosing Spondylitis” improves physicians’ understanding and interpretation of comparative effectiveness data for AS.
content. Tool apps are those used by patients to track symptoms, contained lupus action plan, appointment and medication reminders, and/or quizzes/gameification. App features included connection to external sites (social media, professional societies, online patient communities, healthcare provider), and security features including login/password protection and privacy policy statement. Apps were then rated using (with permission from originator) a published reliable and multidimensional scale: Mobile App Rating Scale (MARS). The study authors were trained on MARS using the recommended slides and reach test with the general health dimension. In addition, quality of health information contained in informational apps was rated using the published DISCERN instrument.

Results: The search terms SLE and Lupus retrieved a total of 471 apps on Google Play store and a total of 196 apps on Apple Store. On Google Play, 14/471 met our inclusion criteria compared to 11/198 on Apple Store. Majority of Google apps were in the tools category representing 44%, followed by apps that are both tools and informational (31%), whereas informational apps were 25%. On the other hand, majority of Apple Store apps were both tools and informational (64%), followed by tools only apps (27%), and finally informational only apps (9%). The most common apps features were email login (37%) and links to external sites including social media platforms (31%). Two apps were identified as a potential source for misleading information claiming that certain homemade herbs/food has anti-inflammatory properties to treat lupus. The average MARS score for Google apps was 2.75/5 indicating poor apps quality. The average MARS score for Apple apps was 3.7 indicating acceptable apps quality. Overall, the functionality score was the highest (3.9/5) while the engagement score was the lowest (2.75/5) for both app stores. For apps that contained information for patients, DISCERN score was 2.15/5 and 3.12/5 for Google and Apple apps respectively indicating potentially important shortcomings in the quality of health information provided in these apps.

Conclusion: Our study demonstrates that a larger need is emerging for designing high-quality apps for patients with lupus. Healthcare organizations, professional societies, rheumatologists, and allied health professionals are encouraged to participate in promoting and creating high-quality apps for lupus patients. These apps are likely to contribute to improving the quality of care provided to these patients and can potentially extend care in the looming global shortage of rheumatologists. This is also an encouraging component of the need to adapt to advancing communications technology as it integrates into many patients’ lives in this digital age.

Disclosure of Interests: None declared

HPR Epidemiology and public health (including prevention).

SAT0695-HPR ASSOCIATION OF PHYSICAL FITNESS WITH HEALTH-RELATED QUALITY OF LIFE IN WOMEN WITH FIBROMYALGIA

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Background: Physical fitness (PF) represents a marker of health and is associated with health-related quality of life (HRQoL). Different components of PF have shown to be consistently associated with lower symptomatology in people with fibromyalgia1,2. Identifying which PF components are associated with HRQoL in people with fibromyalgia may contribute to the development of more specific therapeutic strategies.

Objectives: The aim was to examine the associations of different PF components with HRQoL in women with fibromyalgia.

Methods: This population-based cross-sectional study included 466 women with fibromyalgia. The Senior Fitness Tests battery plus handgrip test were used to assess PF and the 36-item Short-Form Health Survey (SF-36) was used to assess HRQoL. Tendar points, cognitive impairment, anthropometric measurements and medication usage were also measured and used as confounders. Firstly, multivariate linear regression assessed the independent relationship of each PF test with the eight dimensions of the SF-36. Secondly, a standardized composite score was computed for each component of PF (aerobic fitness, muscular strength, flexibility and motor agility). Forward stepwise regression was performed to analyse which components of PF were independently associated with the SF-36 physical and mental component scales.

Results: Overall, higher performance on PF tests was associated with higher levels of HRQoL in all SF-36 dimensions and subscales (all p<0.05 or p<0.001) except for associations between handgrip with social functioning, emotional role, mental health and mental component scale, as well as the chair sit-and-reach test with the general health dimension. The muscular strength composite score was independently (from other fitness components and confounders) associated with the SF-36 physical component scale (p<0.001), while the flexibility composite score and cardiorespiratory fitness were independently (from other fitness components and confounders) associated with the SF-36 mental component scale (both p<0.05).

Conclusion: High PF is consistently associated with better HRQoL in women with fibromyalgia. Muscular strength, flexibility and cardiorespiratory fitness are independent indicators of HRQoL in this population. These results might have implications for future intervention studies because it could facilitate the selection of the most suitable exercise interventions according to the clinical profile of each patient.

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Disclosure of Interests: None declared

SAT0696-HPR THE PREVALENCE OF SEPTIC ARTHRITIS AT A LARGE UNIVERSITY TEACHING HOSPITAL

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Background: Septic arthritis (SA) is a rheumatological emergency requiring early treatment to prevent lasting joint damage. Treatment outcomes depend on prompt diagnosis, which currently rests on clinical suspicion, raised non-specific inflammatory markers and identification of a pathogen from synovial fluid.

Objectives: To establish the prevalence of SA in a large University teaching hospital. To review the microbiology results and identified pathogens in each positive case along with subsequent treatment regimes utilising outpatient parenteral antimicrobial therapy (OPAT) with adherence to local guidelines.

Methods: Retrospective data collection of all samples identified as synovial fluid or joint aspiration sent to microbiology lab between 1 January 2016 and 31st December 2016. Electronic review of microbiology results and treatment outcomes.

Results: There were 364 samples identified as joint aspirate or synovial fluid, 54 of these grew a pathogen. Positive aspirates from native joints totaled 35 in 31 patients. Twenty-three of these patients accounting for 25 of the positive samples were treated clinically as SA. Sub analysis of this group revealed Staph.aureus was the most commonly identified pathogen in 14 cases (56%). There were however 8 other pathogens identified in the 25 positive samples. Fifteen patients (65%) underwent a joint washout in theatre, 7 of these patients had multiple washouts. Duration of antibiotic therapy was 5 weeks in 8 cases; 3 cases had therapy for >5 weeks and 2 cases with SA in the upper limb had treatment for <5 weeks. There were 10 positive samples taken from 8 native joints that grew a pathogen and were not treated as SA. These were identified
on enrichment culture only n=3 or an alternative clinical diagnosis was declared which needs to be taken into account when formulating local antimicrobial guidelines. Current literature reports surgical treatment as not superior to medical\textsuperscript{6}, yet 65% of cases here underwent joint lavage in theatre. This information will be used to inform local clinical practice, and, guide recruitment targets for a large multi-centre study collecting data and samples from patients presenting with a hot swollen joint, with the aim of identifying a specific biomarker for SA.

**REFERENCES**


**SA10969-HPR COMMON COMORBIDITIES IN PATIENTS WITH RHEUMATOID ARTHRITIS IN A UNICENTRIC BIG COHORT**

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**Background:** Rheumatoid arthritis (RA) is a common systemic autoimmune disease characterized chronic joint inflammation. RA and ageing are associated with comorbidities such as cardiovascular disease, malignancies and osteoporosis, these conditions have an important effect on the management of RA. These comorbidities can be associated with higher mortality, poor life quality, and the increasing of costs for the health system.

**Objectives:** To describe the prevalence of comorbidities and characteristics of a Colombian unicentric big cohort that assist to RA specialized centers.

**Methods:** We performed a descriptive analysis; our main goal was to provide real-life data regarding characteristics of patients with RA. We collected sociodemographic information, DAS28, and prevalence of comorbidities regarding hypertension, cerebrovascular disease, diabetes mellitus, osteoporosis, renal chronic disease, or Sjogren’s syndrome. We calculated means, and standard deviations for continuous variables and categorical variables were presented as rates. Rates were estimated the prevalence of comorbidities and performed a bivariate analysis.

**Results:** We reviewed the medical charts of 6541 patients, 82% were female and 18% male; median age was 60 years RIQ (50-67), regarding disease activity, mean DAS28 was 3.34 ± 1.28. The prevalence of comorbidities was 36%, the most common disease was high blood pressure followed by osteoporosis, see table 1. When we compared DAS28 and comorbidities 11% of patients who were in moderate or severe disease activity had one or more comorbidities. The relationship between disease activity and comorbidities was not associated and it was not statistically significant (P=0.05)

**Table 1. Comorbidities in patients with RA**

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Blood Pressure</td>
<td>1589</td>
<td>24</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>804</td>
<td>12</td>
</tr>
</tbody>
</table>

Diabetes Mellitus 319 5
Sjogren Syndrome 262 4
Chronic Renal Failure 54 0.83
Cardiovascular 30 0.46

**Conclusion:** As other studies have shown high blood pressure is the most common disease among patients with RA followed by osteoporosis (1, 3). s. According to these results it is important to consider the patient’s context, medical conditions, and the number of comorbidities in order to understand the complexity of the management of patient with RA. Additionally, it is important to explore barrier and health care services in order to plan a realistic plan where a patient is managed with all comorbidities.

**Disclosure of Interests:** Angie Aza: None declared. Michael Cabrera: None declared. Fernando Rodriguez: None declared. Pedro Santos-Moreno Grant/research support from: Dr Santos has received research grants from Janssen, Abbvie and UCB. Speakers bureau: Dr Santos has received speaker fees from Sanofi, Lilly, Bristol, Pfizer, Abbvie, Janssen and UCB. DOI: 10.1136/annrheumdis-2019-eular.6454

**SAT0698-HPR SYSTEMATIC LITERATURE REVIEW AND META-ANALYSIS OF INFECTION TYPES AND THE EFFECT OF MEDICATIONS ON INFECTION IN SYSTEMIC LUPUS ERYTHEMATOSUS**

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**Background:** The infection incidence rates are high in systemic lupus erythematosus (SLE) patients\textsuperscript{9} and the medical literature documents broad categories of specific bacterial infection risks for SLE patients.\textsuperscript{2,4} However, there has not been a detailed incidence of infection types and infection predictors.

**Objectives:** In a systemic literature review (SLR) and meta-analysis, to describe the types and incidences of infections in SLE patients and to examine the effect of medications used to treat SLE.

**Methods:** An SLR of SLE and infection articles generated through a search of MeSH terms using PubMed and Medline generated 1,211 articles. Using predefined Incl/Excl criteria, data from 32 accepted articles were double-extracted and descriptive and multivariable analyses were conducted. Relative risks between drug classes were estimated using Arm-Based Network Meta-Analysis. Hypothesis tests were two-sided and a p-value <0.05 was statistically significant. Analysis was conducted in the R Statistical Computing Environment (R Core Team; Vienna, Austria).

**Results:** 4,130 patients were considered, 91% females, average age: 36.8 (10.9) years, mean disease duration: 6.9 (6.1) years, SLEDAI mean: 11.7 (4.6). In drug trials, 775 used conventional synthetic DMARDs (csDMARDs), 1,809 used biologic DMARDs (bDMARDs), 691 (16.7%) used placebo and the rest were in non-drug specific observatio

**Table 1. Comorbidities in patients with RA**

<table>
<thead>
<tr>
<th>Disease</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes Mellitus</td>
<td>319</td>
<td>5</td>
</tr>
<tr>
<td>Sjogren Syndrome</td>
<td>262</td>
<td>4</td>
</tr>
<tr>
<td>Chronic Renal Failure</td>
<td>54</td>
<td>0.83</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>30</td>
<td>0.46</td>
</tr>
</tbody>
</table>

**Conclusion:** As other studies have shown high blood pressure is the most common disease among patients with RA followed by osteoporosis (1, 3). s. According to these results it is important to consider the patient’s context, medical conditions, and the number of comorbidities in order to understand the complexity of the management of patient with RA. Additionally, it is important to explore barrier and health care services in order to plan a realistic plan where a patient is managed with all comorbidities.

**Disclosure of Interests:** Angie Aza: None declared. Michael Cabrera: None declared. Fernando Rodriguez: None declared. Pedro Santos-Moreno Grant/research support from: Dr Santos has received research grants from Janssen, Abbvie and UCB. Speakers bureau: Dr Santos has received speaker fees from Sanofi, Lilly, Bristol, Pfizer, Abbvie, Janssen and UCB. DOI: 10.1136/annrheumdis-2019-eular.6454

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infection, compared to 5.6% (CI: 0.1-52.6%) for bDMARDs. The attributable risk for developing gram positive infections when using csDMARDs was 3.9% (CI: 0.2-25%) and 3.5% (CI: 0.1-41.6%) when using biDMARDs.

Conclusion: In this SLR and meta-analysis in SLE, the frequency of infections was bacterial > viral > opportunistic, in that order, although some details were unavailable. csDMARDs were associated with more infections than bDMARDs.

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Acknowledgement: J. Grotts
Disclosure of Interests: None declared

Background: SSc is a chronic, complex and very debilitating disease, involving all the aspects of physical, mental and social life. Thus, the need of a first assessment of the degree of health literacy (HL) is required to develop useful tools for SSc patients to simplify their access to health care services. HL is defined as the ability to acquire, synthesise, and understand health information and services required to make decisions regarding an individual or community’s health.

Objectives: to assess the HL in SSc patients.

Methods: 25 SSc patients classified ACR/EULAR criteria (limited and diffuse subsets) were enrolled in September-October 2018 with the support of the local association of patients (ASSMAF). Patients have been evaluated for socio-demographic variables and the HLS-EU-Q16 questionnaire of the general population (assessed for subscales) were enrolled in September-October 2018 with the support of the local association of patients (ASSMAF). Patients have been evaluated for socio-demographic variables and the HLS-EU-Q16 questionnaire.

Results: Questions 1 to 7 (on health information) are associated with age, educational qualifications and with the number of children; while 8 to 12 (on prevention) are associated with the number of children, but also with the type of employment and marital status; finally, questions 13-16 (on health promotion) are associated with age, educational qualifications and number of children. Moreover, our results show 20% of SSc patients with an inadequate level (0-8) of HL, compared to the 12% of the general population; 40% show a problematic level (9-12) of HL lower than that found in the general population (55%), while 40% of patients show an adequate level (13-16) of HL higher than the 33% of the general population.

Conclusion: Health literacy level is an important parameter to consider and assess in SSc patients to facilitate their access to health care services and their understanding of the disease. Future researches with larger sample size are needed.

Disclosure of Interests: Khadija El Aoufy: None declared, Silvia Basville: None declared, Chiara Lorini: None declared, Lucio Zaccagnino: None declared, Luca Pietrini: None declared, Cosimo Brunii: None declared, Marco Mattucì-Cerinì Grant/research support from: Actelion, MSD, Pfizer, BMS, Chemomab, Sanipedia, Speakers bureau: Actelion, BMS; MSD, Janssen, Laura Rasero: None declared


SAT0699-HPR

ASSESSMENT OF HEALTH LITERACY IN A COHORT OF SYSTEMIC SCLEROSIS (SSC) PATIENTS

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Background: SSc is a chronic, complex and very debilitating disease, involving all the aspects of physical, mental and social life. Thus, the need of a first assessment of the degree of health literacy (HL) is required to develop useful tools for SSc patients to simplify their access to health care services. HL is defined as the ability to acquire, synthesize, and understand health information and services required to make decisions regarding an individual or community’s health.

Objectives: to assess the HL in SSc patients.

Methods: 25 SSc patients classified ACR/EULAR criteria (limited and diffuse subsets) were enrolled in September-October 2018 with the support of the local association of patients (ASSMAF). Patients have been evaluated for socio-demographic variables and the HLS-EU-Q16 questionnaire of the general population (assessed for subscales) were enrolled in September-October 2018 with the support of the local association of patients (ASSMAF). Patients have been evaluated for socio-demographic variables and the HLS-EU-Q16 questionnaire.

Results: Questions 1 to 7 (on health information) are associated with age, educational qualifications and with the number of children; while 8 to 12 (on prevention) are associated with the number of children, but also with the type of employment and marital status; finally, questions 13-16 (on health promotion) are associated with age, educational qualifications and number of children. Moreover, our results show 20% of SSc patients with an inadequate level (0-8) of HL, compared to the 12% of the general population; 40% show a problematic level (9-12) of HL lower than that found in the general population (55%), while 40% of patients show an adequate level (13-16) of HL higher than the 33% of the general population.

Conclusion: Health literacy level is an important parameter to consider and assess in SSc patients to facilitate their access to health care services and their understanding of the disease. Future researches with larger sample size are needed.

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SAT0700-HPR

PHYSICAL AND PSYCHOLOGICAL DETERMINANTS OF FIBROMYALGIA SEVERITY: A STRUCTURAL EQUATION MODELLING FROM THE AL-ÁNDALUS CROSS-SECTIONAL STUDY

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Background: In fibromyalgia, the main aim of therapy is to reduce the severity or impact of the disease [1]. The effectiveness of the most commonly used therapies is modest in fibromyalgia. Therefore, identifying modifiable factors associated with lower fibromyalgia severity is a priority as these modifiable factors may be possible therapeutic targets [2-4].

Objectives: This study examined the determinants of fibromyalgia severity.

Methods: In this observational, population-based cross-sectional study, 569 people with fibromyalgia were assessed on resilience, catastrophizing, active lifestyle, declarative memory, subjective fitness, objective fitness, psychological distress, physical fatigue and disease severity. Structural equation modelling estimation was used to analyse the following hypotheses: (i) resilience, catastrophizing and active lifestyle through subjective fitness, objective fitness, psychological distress, and physical fatigue determine fibromyalgia severity; and (ii) these factors are distributed in two core pathways (one physical and one psychological) that interplay between each other.

Results: We confirmed the above-mentioned hypotheses. Our model explained 83% of fibromyalgia severity, which is a considerably large proportion.

Conclusion: Our findings not only corroborate the importance of the two core (i.e., physical and psychological) pathways but also their interaction in their association with fibromyalgia severity. The understanding of these interconnections between alleged predisposing and perpetuating factors may optimise current approaches for treating fibromyalgia. Although the present research is the most comprehensive model of fibromyalgia severity to date, its cross-sectional design impedes to determine causal relationships. Longitudinal research is warranted.

REFERENCES

Figure 1. Estimated standardised regression and squared multiple regression (R²) coefficients for the final model.

All the coefficients were significant.

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SLE exacerbation predictors in patients of Kyrgyz nationality


Background: Taken into account the wave-like multivariate flow of SLE, there are still difficulties in diagnosing conditions such as ‘remission’ and ‘exacerbation’. The questions of SLE ‘exacerbation’ predictors and their influence on the further nature of the course and outcome of the disease remain little studied.

Objectives: Study of SLE exacerbations predictors in patients living in Kyrgyzstan.

Methods: The study included 150 (26.31%) Kyrgyz patients out of 570 with a reliable diagnosis of SLE, female (96%), young age (median - 34 [26; 44]), Kyrgyz nationality (89.33%), high - 61 (40.66%) and very high activity rate (46) - 20 (13.33%), with the duration of SLE at 1 observation point from 7 months to 10 years, with dynamic observation from 1 year to 3 years. To determine the gradation of the degree of reduction in glomerular filtration rate (GFR) and the severity of proteinuria in patients with lupus nephritis, used the classification of chronic kidney disease (CKD) according to KDIGO (2013).

The characteristic and frequency of SLE exacerbations were assessed by the SFI - R index: mild, moderate or severe.

Results: The results of the study showed that 84 (56%) Kyrgyz patients out of 150 had 192 SLE exacerbations by using the SFI index during 3 years of follow-up, with a frequency of 1 to 4 cases (2.82 ± 2.21) per patient. A mild exacerbation was observed predominantly in 103 patients (55.65%), manifested by skin - mucous syndrome - in 81 (78.64%) and febrile fever - in 22 (21.36%). A moderate exacerbation was noted in 48 (25%) patients in the form of polyserositis - in 18 (37.5%), articulations - in 16 (33.33%) and nephritis with minimal urinary syndrome - in 14 (29.17%) of them. Severe exacerbation was recorded in 41 (21.35%) patients, manifested mainly by kidney damage - in 28 (68.29%), lungs - in 4 (9.76%), central nervous system - in 4 (9.76%) and hematological disorders - in 5 (12.19%).

Severe exacerbations of the kidneys were characterized by nephritis with CKD C1 A1 in 6, CKD C1 A3 in 6, with CKD C2 A3 in 6, severe nephritis with CKD C3 A3 in 3, CKD C3b A3 in 2 and nephritis with nephrotic syndrome - in 5 patients.

SLE exacerbations in most cases resulted from self-withdrawal of glucocorticoids and cytostatic therapy in 44 (52.38%) and activation of the pathological process in 35 (41.67%) patients and in 5 (5.95%) of them were unknown.

Conclusion: On the background of careful dynamic monitoring of patients, predominantly mild SLE exacerbation was observed (53.65%), due to self-withdrawal of glucocorticoids and cytostatic therapy (52.38%) and activation of the pathological process in 44 (52.38%) patients.

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with RA and a SMI experienced significantly greater levels of pain (p=0.04), functional disability (p=0.01), along with poorer disease activity (p=0.03) and poorer quality of life (p=0.03) than those with RA, but without SMI. There was however, no significant difference in the receipt of DMARDs or NSAIDS between the two groups (p=0.12).

Conclusion: Prevalence rates of SMI are no greater in RA than the general population. Those with RA and a SMI do however experience significantly poorer clinical outcomes than people with RA but without SMI despite being in receipt of similar medications. Further research is needed to explore why these health inequalities exist and how best to ensure more positive outcomes for this vulnerable population.

REFERENCES

Disclosure of Interests: None declared

SAT0704-HPR PREVALENCE OF RHEUMATIC PATHOLOGY IN CHILDREN IN THE CENTRAL FEDERAL DISTRICT OF THE RUSSIAN FEDERATION, STRUCTURE OF MORBIDITY AND THERAPY
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Background: Analysis of the incidence of rheumatic diseases in children can help to evaluate the real needs in treatment provision and improve medical service.

Objectives: To analyse the prevalence, structure of morbidity, and therapy of rheumatic pathology in children in the Central Federal District of the Russian Federation.

Methods: Statistical, sociological methods and content analysis were used. The study included generalised information on 3940 patients aged 1-17 years with various rheumatic diseases living in the 13 regions of the Central Federal District of the Russian Federation. The data is provided by the main paediatric rheumatologists of the regions.

Results: 5.999/124 children aged 0 to 17 years live on the territory of 13 regions of central Russia. In these regions, 3.940 patients with rheumatic diseases are observed. Our data allowed us to calculate the prevalence of rheumatic diseases per 100,000 children from 0 to 17 years. The prevalence of juvenile idiopathic arthritis (JIA) is 62.2, systemic lupus erythematosus - 0.7, juvenile dermatomyositis - 0.7, systemic scleroderma - 0.6. The overall incidence of the rheumatic disease is 65.7 per 100,000 children from 0 to 17 years. In the structure of rheumatic pathology, 94.7% are accounted for JIA, 1.1% for systemic lupus erythematosus, 1.0% for juvenile dermatomyositis, 0.9% for systemic sclerosis, 2.2% for other rheumatic diseases. 67.3% of patients receive disease-modifying anti-rheumatic drugs (DMARDs) (n = 2650), of which 80.1% receive methotrexate (n = 2122), 13.5% - sulfasalazine, 0.3% - leflunomide, 0.7% - cyclosporine A, 3.8% - corticosteroids, 0.7% - mycophenolate mofetil, 0.5% - hydroxychloroquine. Biological therapy is received by 27.5% of patients suffering from JIA (n = 1026). The data differs depending on the region. In the Bryansk region, the proportion of patients receive biological therapy is 45.8%, in the Yaroslavl region - 41.2%, in Moscow - 40.7%. More rarely, the biological therapy is initiated in Kostroma - 11.9% and Oryol - 15.3% areas. The structure of biological therapy is dominated by TNF-alpha inhibitors - 71.3%, 41.6% of all children undergoing biologic therapy were prescribed etanercept, 27.2% - adalimumab. 18.1% of patients receive tocilizumab, 7.2% - abatacept, 1% - infliximab, 2.5% - canakinumab, 1.5% of patients receive golimumab.

Conclusion: 1. The overall incidence rate of rheumatic diseases in central Russian regions is 65.7 per 100,000 children from 0 to 17 years old.
2. The prevalence of juvenile idiopathic arthritis is 62.2 per 100,000 children from 0 to 17 years old.
3. 67.3% of patients receive DMARDs. In 80.1% of cases, the drug of choice is methotrexate.
4. 27.5% of patients suffering from JIA receive biological therapy; data vary by region (45.8% - 11.9%). The structure of biological therapy is dominated by TNF-alpha inhibitors - 71.3%.
5. At the level of various regions, countries, it is necessary to conduct research aimed at studying the causes influencing the overall incidence, the detectability of rheumatic diseases, and the structure of therapy.

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HPR Measuring health (development and measurement properties of PROs, tests, devices)

SAT0705-HPR PATIENTS’ EXPERIENCES OF REASONS TO BEING PHYSICALLY ACTIVE IN EARLY RHEUMATOID ARTHRITIS – A MIXED METHODS STUDY
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Background: The importance of physical activity in rheumatoid arthritis (RA) is well known and patients are informed about the importance of being physically active. Despite this knowledge there is a lack of compliance to this advice. Studies comparing physical activity in different groups of patients with RA and reasons influencing physical activity are needed.

Objectives: The objectives were to compare physical activity (PA) in workers, retired and patients with sick-leave with early RA and further to explore reasons to being physically active. Despite this knowledge there is a lack of compliance to this advice. Studies comparing physical activity in different groups of patients with RA and reasons influencing physical activity are needed.

Results: A total of 66 patients with early RA were included in the study. A sequential explanatory mixed methods design was used. The groups were compared with clinical data as: disease activity (DAS28); pain (VAS 0-100, best to worst); health-related quality of life (EQ5D, -0.594-1 worse to best) and a physical function (HAQ, 0-3 best to worst). ESR and CRP. Patients were dichotomized as being active on recommended levels of PA (MVP/Aec; physically active on a moderate level ≥150min/week (MFA) or on an intense level ≥75min/week (VPA)) or not (sedentary). The patients were grouped on self-reported working ability; workers, patients with sick-leave and retired patients. Qualitative data was collected by a questionnaire with open-ended questions about reasons influencing PA. The qualitative data was analysed with a manifest qualitative content analysis to gain a greater understanding of patients’ experiences of PA in early RA.

Results: There were no significant differences between the groups in disease activity, physical function, swollen joints, health-related quality of life
or inflammatory parameters (ESR, CRP). Patients on sick-leave had more tendons (min-max) 9 (2-18) vs. 4 (0-20) and 3 (0-10), p=0.013. Workers reported higher intensity of pain, though not significant. Retired patients fulfilled MVPA criteria to a higher rate (86%) than workers (42%) or patients with sick-leave (40%), p=0.010. The qualitative content analysis resulted in three categories. Reasons to being physically active in patients with early RA were: limitations (pain, physical function, stiffness, limited strength and fatigue), awareness as motivation (fear of movement and health benefits) and external environment (weather, transports to activity, economy and time, especially for workers).

Conclusion: Knowledge of reasons to being physically active in patients with RA is important to facilitate and support the patients. Joint pain seems to be an issue for patients with sick-leave. This could be associated to fear of movement and in this aspect these patients need to be supported. Time could be a limiting issue for working patients, which need to be highlighted and solved for these patients.

Disclosure of Interests: None declared

### SAT0705-HPR THE RELATIONSHIP BETWEEN SUBJECTIVE AND OBJECTIVE METHODS FOR MEASURING PHYSICAL ACTIVITY STATUS OF AXIAL SPONDYLOARTHRITIS PATIENTS: QUESTIONNAIRE VERSUS ACCELEROMETER

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**Background:** Physical activity is getting more attention for the appropriate management of both disease itself and co-morbid conditions in patients with axial spondyloarthritis (axSpA). Many different tools are available for determining physical activity status. Although subjective tools such as questionnaires are quick and easy for gathering data, objective tools such as accelerometers might provide more accurate information.

**Objectives:** To investigate the relationship between a subjective physical activity questionnaire (International Physical Activity Questionnaire Short Form: IPAQ) and an accelerometer (Actigraph wGT3X-BT) for measuring physical activity status of axSpA patients.

**Methods:** Thirty-nine patients with axSpA (age 37.9±11.3 years, body mass index 26.9±5.3 kg/m², disease activity: 3.3±2.3 according to Bath Ankylosing Spondylitis Disease Activity Index, functional status: 2.9±2.8 according to Bath Ankylosing Spondylitis Functional Activity Index, 24 male) according to ASAS criteria were included to assess the subjective and objective physical activity status by using the Turkish version of IPAQ and an accelerometer (Actigraph wGT3X-BT, respectively). The accelerometer was worn by the patients on their waists at their first visit and it provides information about the light, moderate, vigorous physical activity times in minutes. On the seventh day when the accelerometer was removed, patients were asked to complete the IPAQ. The IPAQ inquires the physical activity performed previous week in minutes and categorizes into three sections as vigorous, moderate activity, and walking. The walking section in IPAQ was accepted as equal to light physical activity in Actigraphy. The relationship between measurements was determined by using Spearman’s Rank Correlation Coefficient.

**Results:** No significant correlations were determined between subjective and objective methods (p>0.05), except the time spent during moderate physical activity (rho: 0.457, p<0.05). It was also observed that IPAQ were underestimating the physical activity times for all types of physical activity (Table 1).

<table>
<thead>
<tr>
<th>Objective Activity (min)</th>
<th>Subjective Activity (min)</th>
<th>Spearman’s Correlation</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>2270.26±1016.70 331.03±552.75</td>
<td>243.97±167.9 90.26±241.39</td>
<td>0.457 0.003</td>
<td></td>
</tr>
<tr>
<td>7.23±18.61 248.72±848.93</td>
<td>0.184 0.914</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2521.46±1094.40 670.05±1183.30</td>
<td>0.271 0.095</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** According to our results, IPAQ, short version may not be an appropriate tool for determining physical activity status in axSpA patients. It seems that we need disease specific tools in axSpA.

**REFERENCES**

**Disclosure of Interests:** Deniz Bayraktar: None declared, Tugce Yukel-Karsi: None declared, Derya Ozer Kaya: None declared, Dilek Solmaz: None declared, Gokhan Kabadyay: None declared, Idil Kurut: None declared, Servet Akar Grant/research support from: MSD, Abbvie, Roche, UCB, Novartis, Pfizer, Amgen, Consultant for: MSD, Abbvie, Roche, UCB, Novartis, Pfizer, Amgen, Speakers bureau: Pfizer

### SAT0707-HPR PATIENT AND CLINICIAN PERSPECTIVES USED FOR SURVEY DEVELOPMENT TO INVESTIGATE THE NATURE, EXTENT AND IMPACT OF FOOT PROBLEMS IN PEOPLE WITH PSORIATIC ARTHRITIS

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**Background:** Despite recognition that hallmark features of psoriatic arthropitis (PsA), such as enthesitis, are predominant and persistent in the foot and ankle [1], limited research has focused on the foot. Few published studies have used RA-specific outcome measures unlikely to capture the dermatological impact in PsA and there has been little incorporation of the patient perspective [1]. The importance of patient and clinician involvement as a central component of research design has been identified in PsA [2, 3], and provides a basis for defining what should be measured to represent comprehensively the experience of people with PsA-related foot problems and important domains of impact.

**Objectives:** To develop a survey based on the views of people with PsA and clinicians on foot problems, their impact and the foot care needs.

**Methods:** Interviews of people with PsA-related foot problems and focus groups with clinicians on their understanding of the patient experience were undertaken in Sydney, Australia and Auckland, New Zealand. A representative sample from public and private sector, from lower and higher socioeconomic geographical areas, as well as clinicians with different professional backgrounds was sought. Based on the themes from the qualitative interviews, previous research [1, 3] and clinical experience, survey items were generated by the research team using a consensus based approach. The survey was pre-tested using a 4-stage method that comprised: cognitive de-briefing of people with PsA, expert review panels of people with PsA and clinicians, pilot testing. All focus groups and interviews were audio-recorded, transcribed verbatim and survey items were revised based on comments made.

**Results:** The final 60-item self-administered survey was developed based on feedback from each of the 4-stages, which related to wording, comprehension, timescales, content, repetition, number of survey items and overall survey design. Key survey domains included demographic (10%) and socioeconomic data (10%), global disease information (18%), foot and ankle characteristics (18%), and the impact of foot problems on daily
life including daily routine, footwear choice, family life, work and access-
ing health care (44%). Percentage coverage of items directly reflects the
dominant concerns of people with PsA-related foot problems and clini-
cians. Whilst priorities for clinicians included the diverse expression of
disease and determining the nature of foot symptoms as mechanical or
inflammatory, a key theme from patients was the psychological impact of
foot involvement on daily life coupled with self-management strategies
(coping skills, self-care activities and availability of social support), which
was poorly recognised by clinicians. Consequently, nearly a quarter of
survey content was dedicated to these areas of impact highlight by
patients (23%). Engaging patients and clinicians in the survey develop-
ment methods ensured that face and content validity were confirmed and
cognitive and usability standards were achieved.

Conclusion: By incorporating the views of those with the disease and of
clinicians into the survey development process, good conceptual coverage
of items important to both patients and clinicians was achieved whilst
minimising responder burden. This is the first study to develop a survey
on foot involvement in PsA based on best practice methods in qualitative
survey design, which may have utility in the future development of
assessment or screening tools.

REFERENCES

Disclosure of Interests: None declared


SAT0708-HPR DEVELOPING AN ALLIED HEALTH CORE OUTCOME SET FOR PAEDIATRIC RHEUMATOLOGY MUSCULOSKELETAL CONDITIONS

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Background: Musculoskeletal (MSK) conditions are prevalent within the
general population, including children and young people (CYP) with MSK
pain. There is evidence that MSK pain in CYP is an antecedent of adult
MSK-pain. Paediatric Rheumatology Allied Health Professionals (PRAHPs)
are well placed to manage these CYP, but there is no current standard-
isation in treatment, services or outcomes.

Objectives: To develop a core outcome measure set for clinical use by
PRAHPs to facilitate national collaboration and standardisation of care.

Methods: A modified Nominal Group technique study was undertaken by an
expert panel of PRAHP’s working in 8 Tertiary Paediatric and Ado-
lescent UK centres. Literature search and presentation of findings
informed expert panel discussion with particular reference to the following
criteria: paediatric population specific, ease of clinical use, cost, general
availability to clinicians, reliability, validity, length to administer/perform and
previous research use. Expert panel discussion and ranking identified
eight domains. A survey was sent to the 12 members of the expert
panel asking participants to choose two measures or none, based on cri-
teria above. Consensus was pre-determined as agreement between
experts of 60% or more.

Results: Survey response rate was 83% with consensus achieved for 6
outcome measures- see table. Consensus could not be reached for hand
function, sleep and goal-setting in part due to the large number of mea-
ures and variation in use, lack of paediatric specific measures, length of
time taken to administer or costs involved. Psychological measures were
not included within the scope of this work, but would be a valuable future
addition.

Conclusion: This study informs a pilot outcome measure set for PRAHPs
in clinical settings when time, space, money and ease of use are paramour.

Outcome domain selected by expert panel Measure with consensus
Fatigue Fatigue VAS
Sleep PedsQL pain and fatigue scale
School attendance % attendance rate

References

Disclosure of Interests: None declared


SAT0709-HPR SPINAL MOBILITY IN SPONDYLOARTHRITIS PATIENTS: DO THE BASMI-MEASUREMENTS CORRELATE WITH THE DAVID BACK DEVICES-MEASUREMENTS?

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Background: The BASMI is a common used and well established index to
measure spinal mobility in spondyloarthritis(SpA)-patients, both in the
clinic as well as for research. The David Back Devices (DBD) on the
other hand, are used to measure and exercise lumbar and cervical mobi-
ity and strength in spine patients. The DBD might have the potential
advantage of not being operator dependent in contrast to the BASMI-
measurements.

Hence, the question rose if the BASMI measurements that correspond
with cervical rotation and lumbar lateral flexion movements on the DBD
are correlated with one another.

Objectives: The aim of this study was to measure the spinal mobility in
SpA-patients both by using BASMI measurements and by using the DBD
and determine their relationship.

Methods: SpA-patients of the outpatient rheumatology department of the
Ghent University Hospital (included in the Be-Giant cohort) were consecu-
tively asked to participate in the study. After informed consent, BASDAI,
BASFI and BASMI were evaluated. To measure mobility on the DBD
both trunk and cervical range of motion for flexion, extension, lateral flex-
ion and rotation were assessed. Spearman correlation coefficients were
calculated for cervical rotation and lumbar lateral flexion.

Results: Thirty-one SpA-patients participated of which 18 were male
(58%). Twenty-four (77%) were classified as axial SpA and 7 (23%) as
peripheral SpA. Median time since diagnosis was 5 years. Mean age of
the patients was 41 years (range: 21 – 58 years) and their BMI was on
average 24 (range: 17-33). Averages for BASDAI, BASFI and BASMI
were 2.6, 1.7 and 0.9 respectively.

There was a significant positive correlation between the cervical rotation
measurement obtained by BASMI and DBD (r=0.84 for right and r=0.80
for left) as well as between the lateral flexion measurement obtained by
BASMI and DBD (r=0.72 for right and r=0.65 for left). Due to the sitting
position during testing the lumbar flexion by DBD, the range of motion
was limited when the chest touched the thighs. Therefore, correlation
could not accurately be determined between the modified Schöberindex
and DBD lumbar flexion.

Conclusion: This study demonstrated that in SpA-patients, the BASMI
measurements for cervical rotation and lumbar lateral flexion show high
correlations when compared with the similar measurements on the DBD.
The correlations for cervical rotation were better than those for lumbar
lateral flexion.

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**SAT070-HPR** RADIOfREQUENCY ECHOGRAPHIC MULTI SPECTROMETRY OSTEOPOROSIS DIAGNOSIS ON FEMORAL NECK: A SPANISH CLINICAL EXPERIENCE

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**Background:** Radiofrequency Echographic Multi Spectrometry (REMS) is an innovative echographic technology able to provide the most important densitometric parameters by a fully automatic approach. Its high accuracy with respect to the conventional Dual X-ray absorptiometry (DXA) has been shown in a very recently published multicenter clinical trial [1].

**Objectives:** To evaluate the performance of the REMS technology in osteoporosis diagnosis, with respect to DXA (Clinical Gold Standard), when applied on femoral neck.

**Methods:** DXA and REMS acquisitions were performed on the femoral neck in 324 female patients, aged between 51 and 70 year, recruited at the Department of Internal Medicine of the Hospital del Mar (Barcelona, Spain). REMS technology is based on a automatic integrated processing of the native unfiltered "raw" (RF) signals, which can be employed to assess the bone health status through comparisons with reference spectra modeling osteoporotic patients and by evaluating the correlation between REMS and DXA measurements.

**Results:** The REMS approach is effectively able to discriminate between osteoporotic and non-osteoporotic patients with a sensitivity equal to 93% and a specificity equal to 95%. These data are further emphasized by the obtained Pearson Correlation value \( r = 0.90; p<0.001 \). REMS accuracy was confirmed also by Cohen’s kappa coefficient \( k \) equal to 0.76. Finally, a very low average difference (expressed as bias \( \pm 2 \) SD) between REMS and DXA measured BMD \((-0.006 \pm 0.078 \, \text{g/cm}^2)\) was shown.

**Conclusion:** In conclusion, REMS technology has proven to be an accurate non-invasive approach to detect osteoporosis disease at the femoral neck. The performance of this radiation-free technique opens new perspectives for early diagnosis and screening of osteoporosis in clinical and epidemiological studies.

**REFERENCE**


**Disclosure of Interests:** Diana Ovejero Crespo: None declared, Xavier Nogues Speakers bureau: Amgen and Eli Lilly, Adolfo Diez-Perez Speakers bureau: Lilly, Amgen, GSK and UC

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**SAT0711-HPR** ADDING INFORMATION ON WIDESPREAD PAIN TO THE START BACK SCREENING TOOL WHEN IDENTIFYING LOW BACK PAIN PATIENTSAT INCREASED RISK FOR POOR PROGNOSIS

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**Background:** Early identification of those with the highest risk of developing chronic low back pain (CLBP) is important but difficult. STarT Back Screening Tool (SBST) is reported to capture patients at high risk of developing CLBP, but does not include concurrent pain from other locations, which is a known risk factor for worse outcome.

**Objectives:** To study differences in self-reported health between patients with low, medium and high risk of developing CLBP identified by the combination of SBST and information on widespread pain.

**Methods:** Adults aged 16-67 seeking primary care for LBP in the south-west of Sweden were included. The STarT Back Screening Tool was used to differentiate between three risk levels: low, medium and high risk. When patients were classified as medium risk, information from a pain mannequin on widespread pain and multisite pain were added to further distinguish between high and medium risk. If widespread pain and pain from more than seven locations (multisite pain) were reported, patient was transferred from the medium risk to the high risk group. Differences between the three risk groups with regard to physical function (Roland Morris Disability Questionnaire (RMDQ), 0-24 best, worst), mental health (Hospital Anxiety and Depression scale (HADa and HADd) 0-21 no distress-maximum distress), health related quality of life (EuroQol-5D (EQ5D), 0-1 worst-best), fear avoidance for physical activity (PA) and work (Fear Avoidance Beliefs Questionnaire (FABQ) PA, 0-24, and work, 0-42 worst) were analyzed in an ANOVA.

**Results:** Ninety-five patients (61% women), mean (SD) age 42 years (14) seeking health-care for their LBP were included in the study. Of those scoring low risk on SBST (n=19), 3 also reported multisite CWP. Of those who scored medium risk on SBST were reported multisite CWP and were moved to the high risk group. Of 17 scoring high risk on SBST, 4 simultaneously reported multisite CWP. After constructing three risk groups combining SBST and multisite CWP, there were 19 in low risk group, 45 in the medium risk group, and 25 in the high-risk group. The low, medium, high risk groups identified by the combined method, differed statistically significant in reported RMDQ (low, medium, high mean respectively 7.0, 12.2, 13.4, p<0.001), HADa (3.7, 6.4, 10.1, p<0.001), HADd (2.9, 4.0, 8.4, p<0.001), FABQ PA (9.1, 12.7, 14.4, p=0.005), FABO work (9.9, 16.7, 23.1 p<0.001), EQ5D (0.72, 0.53, 0.38, p=0.001).

**Conclusion:** Adding information on multisite widespread pain to the SBST resulted in classifying more patients in the high risk group as compared to using only SBST. The three groups identified by combining the screening tools differed significantly on all investigated health variables, indicating the combination may be capturing more patients at risk for CLBP.

**Disclosure of Interests:** None declared

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**SAT0712-HPR** VALIDATION OF THE TEST FOR SUBSTITUTION PATTERNS – IN INDIVIDUALS WITH SYMPTOMATIC KNEE OSTEOARTHRITIS

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**Background:** Few tools evaluates quality of movements in individuals with knee osteoarthritis (OA). The Test for Substitution Patterns (TSP) is developed to measure the ability to perform five functional movements regarding postural control and altered movement patterns (1). TSP is validated and reliable in individuals with anterior cruciate ligament injury, but has not yet been evaluated in individuals with knee OA.

**Objectives:** To study the relationships between the OA modified TSP (OA-TSP) and self-reported knee function as measured with the Knee Injury and osteoarthritis Outcome Score (KOOS) and the 30 s chair stand test (30 s CST) in individuals with symptomatic knee OA. A second aim was to study the discriminative ability of the OA-TSP for unilateral knee pain.

**Methods:** Sixty-two individuals with symptomatic knee osteoarthritis were included using consecutive sampling. Health status was assessed with the EuroQol five dimension scale (EQ5D, 0-1 worst-best), and knee function in five subscales for KOOS (pain, symptoms, ADL, quality of life and sport/recreation, 0-100 worst-best). The 30 s CST-test measured the number of rises in 30 seconds. In the OA-TSP, substitution patterns are observed and scored from 0-3 (no substitution pattern-poorly performed) during five standardized functional movements. The maximum score is 54 points/side with score of 108 points. Median and min-max were used for all descriptive data. Spearman’s correlation and Wilcoxon signed rank test were used for analyzes. A correlation coefficient \( r_s \) \( \geq 0.50 \) is considered large, \( r_s < 0.30 \) to \( 0.50 \) and \( 0.30 \) to \( 0.50 \) moderate, \( 0.10 \) to \( 0.30 \) small.

**Results:** The median age was 54 years (30-61), 76% were women. The median Body Mass Index index was 25 (18-48) and EQ5D 0.8 (0.29-1.00). There were no significant differences between the gender regarding BMI and EQ5D. Median OA-TSP total score was 29 (10-70), Median KOOS pain was 75 (36-100), symptoms 71 (21-96), ADL 87 (30-100), and sport/recreation 50 (0-100). In the 30 s CST the median was 16 rises (5-32). Moderate, significant correlations were observed between TSP total score and KOOS pain and KOOS ADL (\( r_s=-0.30 \); \( p<0.03 \), \( r_s=-0.35 \); \( p<0.01 \).
respective) and small correlations between TSP and KOOS sport/recrea-
tive impact of symptomatic knee OA. We also found that pain in one leg was related 
ment and KOOS symptoms (r s=-0.13; p=0.36, r s=-0.22; p<0.11 respec-
tive). There was a moderate, significant correlation between TSP total 
tively). There was a moderate, significant correlation between TSP total 
tive by using accelerometers, which potentially is a feasible method 
Istanbul, Turkey; 2Istanbul Medipol University, Physical Therapy and Rehabilitation, Istanbul, Turkey; 3Istanbul Medipol University, Ergotherapy, Istanbul, Turkey; 4Istanbul University, Istanbul, Turkey

Background: The rate of back pain prevalence and its subsequent nega-
tive psychological effects is quite high in mothers of disabled children. Family caregivers of children with a disability demonstrate higher levels of chronic conditions and are more likely to engage in health risk behav-
ors (1, 2).

Objectives: The purpose of this study was to investigate the effects of home exercise programs on mothers’ back pain, relevant functional influ-
and the depression level (3).

Methods: Forty-two mothers aged 35.71±6.53 were included in this study whom children were diagnosed with cerebral palsy. Back pain level of the mothers was measured with Visual Analogue Scale (VAS), relevant functional disability was measured with Oswestry Disability index and depression level was measured with Beck Depression Scale. Disability level of their children was measured with Gross Motor Function Classification System (GMFCS). Following the assessments, a home exercise program consisting of Dynamic Lumbar Stabilization Exercises was given to mothers. They were asked to perform the exercises for three months and exercises were checked once in a month.

Results: GMFCS average of the children was 3.35±1.57. There was a significant difference in the pain level (VAS) changed from 4.90±2.67 to 3.21±2.50 after the exercise (p<0.000). The difference between the Oswestry Disability Index score before (13.92±8.32) and after the exercise (10.76±8.54) was statistically significant (p<0.001). Also there was a signif-
icant difference in the Beck Depression Scale score decreased from 25.16±10.46 to 17.76±7.50 (p<0.000).

Conclusion: Mothers with disabled children complain about back pain dur-
ing activities such as caregiving their children (4). This study reveals that back pain, relevant functional influence and depression could be reduced in mothers by perform recommended exercises regularly.

REFERENCES

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Disclosure of Interests: None declared

SA0715-HPR] BREAKING BAD: REPORTING OF VERTEBRAL FRAGILITY FRACUTRES AND THE IMPACT TO MANAGEMENT OF BONE HEALTH

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Background: Verterbral fragility fracture (VFF) is the most common osteo-
porotic fracture and a strong predictor for future vertebral fracture(s) and/ 
or hip fracture. A clear reporting of VFF by radiologists offers ample opportunity for early diagnosis and appropriate management of osteoporo-
sis among treating physicians.

Objectives: The objectives of this study were two-fold; to evaluate 1) the 
reporting of VFF by radiologists at one of the largest acute hospitals in 
southern Ireland 2) the management of osteoporosis (adherence to
screening for secondary causes and commencement/switching of anti-resorptive therapy accordingly) for patients with VFF.

**Methods:** We conducted a retrospective cross sectional study involving all patients (n=199) who attended our specialist rheumatology outpatient clinics at University Hospital Kerry during the month of November 2018. Patients who previously had undergone plain radiography of the spine (PRS) in the previous 5 years were identified and reassessed for evidence of VFFs. Basic demographic, drug history, clarification of fragility fracture and previous related trauma, investigations for secondary causes of osteoporosis, and treatment received for osteoporosis were documented.

**Results:** 73 of the 199 patients had undergone previous PRS, 9 of which had evidence for VFFs. Only two patients (22.2%) were reported as having vertebral "fractures", while 7 others had different terms used to describe the fracture(s):2 patients with "wedgeing", 1 with "compression", 2 with "loss of height" and 2 with "collapse". All (2 patients; 100%) with VFF reported as "fracture" had complete clarification of VFF, secondary osteoporotic work-up and treated with anti-resorptive therapy accordingly.

Among the other 7 patients with VFFs but not reported as having "fracture", 1 patient had concomitant report of "osteoporotic" bones and had complete management for osteoporosis. 4 patients had concomitant report of "osteopenia", 3 (75%) of which received complete management for osteoporosis; while only 50% (1 patient) of the 2 remaining patients without further description of bone density received appropriate management.

Further 6 patients with non-VFF were reported to have reduced bone density (1 reported as "osteoporotic" bones; 5 as "osteopenic" bones). Only one of them (16.7%) had further work-up, evaluation and management for osteoporosis.

**Conclusion:** Clear radiological report of PRS with VFFs using the word "fracture" is a strong predictor for appropriate management of bone health. It is essential that other terms used to describe VFFs such as "wedgeing", "compression", "loss of height" and "collapse" not to be used alone without the concomitant use of the word "fracture".

**Disclosure of Interests:** None declared


**SAT0716-HPR**

**SYSTEMATIC REVIEW OF THE PSYCHOMETRIC PROPERTIES OF PATIENT-REPORTED OUTCOME MEASURES FOR FOOT AND ANKLE IN RHEUMATOID ARTHRITIS**

Ana Belen Ortega-Avila1, Gabriel Giljoen-Nogueron1, Christopher Nester2, Pablo Cervera-Garvi1, Laura Ramos-Petersen1.

**Background:** Foot problems and pain are common in patients with rheumatoid arthritis. Patient-reported outcome measures provide a standardized method of capturing patients’ perspectives of their functional status and wellbeing. There are many instruments specific to people with feet affected by rheumatoid arthritis but knowledge of their psychometric validation and methodological quality is lacking.

**Objectives:** To identify patient-reported outcome measures specific to the foot and ankle and rheumatoid arthritis and investigate their methodological quality and psychometric properties.

**Methods:**

**Design:** Systematic review. **Data source:** A search was conducted for psychometric or validation studies on patient-reported outcomes in Rheumatoid Arthritis published in different languages, by examining the PubMed; Scopus, CINAHL; PEDro and Google Scholar databases.

**Review methods:** The systematic review performed was based on the following inclusion criteria: psychometric or clinimetric validation studies on patient-reported outcomes specific to the foot and ankle that included patients with Rheumatoid arthritis. Two authors independently assessed the quality of the studies and extracted data.

**Results:** Of the initial 431 studies, fourteen instruments met the inclusion criteria. Significant methodological flaws were detected in most with only SEFAS met the COSMIN quality criteria.

**Conclusion:** SEFAS had the best quality and was ranked most appropriate for use with patients living with Rheumatoid Arthritis.

**REFERENCES**


**Review registration number:** PROSPERO (CRD42018090594).

**Disclosure of Interests:** None declared


**Table 1. Detailed COSMIN ratings**

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Rating: **+:** Positive rating; **–:** Indeterminate rating; **-:** Negative rating.
CONSTRUCT VALIDITY AND RELIABILITY OF A PORTUGUESE VERSION OF THE ANIMATED ACTIVITY QUESTIONNAIRE (AAQ)

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Background: The AAQ assesses activity limitations in individuals with hip/knee osteoarthritis (HKOA), and consists of video animations of 17 basic daily activities performed with different levels of difficulty (www.myaaq.com). The participants choose the animation that best matches their own performance. The AAQ was developed in the Netherlands, and showed a good overall cross-cultural validity in 6 other languages.

Objectives: The aims of this study were to assess the construct validity and reliability of the Portuguese version of the AAQ.

Methods: In Diamantina, Brazil, men and women (≥45 years) with clinical HKOA were included in the study. The exclusion criteria were: cognitive impairment, visual/auditory deficit, or any medical condition other than HKOA that could hamper activity. This study was approved by the UFVJM Ethics Committee. All participants completed the Portuguese version of the AAQ. Illiterate or functional illiterate participants were assisted by the researchers. The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), to assess pain, stiffness and function was completed by the participants. Performance-based tests were applied to a subgroup of 71 participants: Timed Up and Go (TUG) and Short Physical Performance Battery (SPPB). The first 53 participants completed the AAQ twice. To validate the AAQ, Spearman’s rho coefficients were calculated between the AAQ score, each score of the WOMAC, the SPPB score, and TUG score. To evaluate the influence of education in completing the AAQ, the participants were divided in two groups, 0-3 years of education and ≥4 years of education. To evaluate internal consistency and test–retest reliability of the AAQ, we calculated the Cronbach’s alpha coefficient and the intraclass correlation coefficient (ICC), respectively.

Results: 200 individuals, 85% female, mean age of 64.4 (SD 11.2) years, and a mean of 5.8 (SD 4.4) years of education, participated in the study. 72% of the participants had knee OA, 9% had hip OA, and 19% had both joints affected. The mean values on the different measures were as follows: AAQ = 72.7 (SD 16.1), WOMAC pain = 36.5 (SD 19.3), WOMAC stiffness = 37.1 (SD 26.2), WOMAC function = 39.1 (SD 19.6), SPPB = 8.0 (SD 2.1), and TUG = 16.2 (SD 12.7) seconds. The AAQ showed high internal consistency (Cronbach’s alpha = 0.94) and good test-retest reliability was (ICC = 0.98). The AAQ showed a moderate correlation with WOMAC pain (r = -0.51, 95%CI = -0.61 to -0.39), and WOMAC stiffness (r = -0.46, 95%CI = -0.56 to -0.33), and a high correlation with WOMAC function (r = -0.77, 95%CI = -0.82 to -0.71), SPPB (r = 0.65, 95%CI = 0.48 to 0.77), and TUG (r = -0.71, 95%CI = -0.81 to -0.56). Regarding the level of education, the correlations between the AAQ score and the three domains of the WOMAC were similar when the participants with 0-3 years of education (n = 62) were compared to the participants with ≥4 years of education (n=138) (pain: r = -0.51, 95%CI = -0.68 to -0.29 vs -0.52, 95%CI = -0.64 to -0.39; stiffness: r = -0.54, 95%CI = -0.70 to -0.32 vs -0.41, 95%CI = -0.54 to -0.25; function: r = -0.80, 95%CI = -0.88 to -0.68 vs -0.75, 95%CI = -0.82 to -0.66).

Conclusion: The Portuguese version of the AAQ showed good construct validity and reliability, and also seems to be applicable for patients with low literacy.

REFERENCE

Disclosure of Interests: None declared.

FOOT PRESSURE DISTRIBUTION AND FUNCTIONAL LEVELS: ANKYLOSING SPONDYLITIS VS CONTROLS

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Background: Ankylosing spondylitis (AS) is a chronic rheumatic disease characterized by the inflammation of the pelvis and spine with a tendency to bony ankylosis. The most common AS-related alterations in posture are, the limitation of spinal mobility, head protraction, loss of lumbar lordosis, increased dorsal kyphosis, flexion contracture of the hip and consequent flexion of the knee.

Objectives: The purpose of this study was to investigate the foot pressure distribution and functional levels differences in ankylosing spondylitis and also compare with healthy individuals.

Methods: Eighteen patients with ankylosing spondylitis (median age= 42.2 ±2.4 years, median BMI=25.7±1.27 kg/m²) and 17 controls (median age= 43.1±2.4 years, median BMI=26.78±0.65 kg/m²) were included in the study. Plantar pressure distribution was recorded by Digital Biometry Scanning System and Milletrix software (DIASU, Italy). The static test was used to determine the maximum foot pressure (N/cm²) of the foot, forefoot weight ratio, rarefoot weight ratio, total load and foot angle axis (FAA). When evaluating spinal mobility; lumbar flexion, lateral flexion and trunk to wall distance were used in Bath Ankylosing Spondylitis Mobility Index (BASMI) sub-parameters. The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) was used to determine the disease activity; The Bath Ankylosing Spondylitis Functional Index (BASFI) was used to measure functional impairment; The Ankylosing Spondylitis Quality of Life (ASQoL) Questionnaire was filled out by the patients in an attempt to understand the impact of the disease on the quality of life. Mann-Whitney U test was used to compare AS groups with the control group. Spearman test was used for correlation analysis.

Results: No difference between age (p=0.031) and BMI (p=0.012) in both groups. There were no differences modified Schober (p=0.184), lumbar flexion (p=0.160) and tragus to wall distance (p=0.434). But lower right lateral flexion (p=0.003) and left lateral flexion (p=0.001) in ankylosing spondylitis group when compared to healthy individuals. Rearfoot load higher than forefoot load in ankylosing spondylitis group (p=0.001). There were no differences static and dynamic analysis parameters ankylosing spondylitis group and healthy group. In addition to right lateral flexion (r=0.645 p=0.005) and left lateral flexion (r=0.641 p=0.04) correlated foot angle axis; tragus to wall distance correlated maximum foot pressure (r=0.578 p=0.015) and average foot pressure (r=0.542 p=0.025).

Conclusion: Lumbar spine flexibility was lower and associated with foot pressure distribution in AS patients. In addition, the load distribution between the rare and fore foot was different in these patients. Therefore, the foot pressure distribution as well as the spine flexibility should be monitored closely, when implementing and designing the exercise programs in patients with AS.

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Disclosure of Interests: Nazi Sari: None declared, Hande GUNEY DENIZ: None declared, Umut Kalyoncu: Grant/research support from: MSD, Roche, UCB, Novartis and Pfizer, Consultant for: MSD, Abbvie, Roche, UCB, Novartis, Pfizer and Abdi Ibrahim, Speakers bureau: MSD, Abbvie, Roche, UCB, Novartis, Pfizer and Abdi Ibrahim, Gul Baltaci: None declared DOI: 10.1136/annrheumdis-2019-eular.5381

PULMONARY FUNCTIONS AND RESPIRATORY MUSCLE PERFORMANCE CORRELATE WITH NIGHT PAIN IN PATIENTS WITH ANKYLOSING SPONDYLITIS COMPARED TO CONTROLS

Bilge Taskin1, Naciye Vardar-Yagil2, Umut Kalyoncu1, Gul Baltaci1. Private Guven Hospital, ANKARA, Turkey; Hacettepe University, Ankara, Turkey

Background: In ankylosing spondylitis (AS), chronic systemic inflammation mainly affects the axial skeleton and involvement the costovertebral and costotransverse joints results in limitation of thoracic and spinal mobility (1,2). There is no study published to evaluate the endurance and strength of respiratory muscle and to investigate the relationship with pain.

Objectives: The aim of the study was to investigate the functional status, quality of life, pain, pulmonary function, respiratory muscle strength and endurance patients with AS and compare to healthy controls.

Methods: Standard pulmonary function tests, maximum inspiratory pressure (Pimax), and maximum expiratory pressure (PEmax) for pulmonary volumes and respiratory muscle strength were applied. Respiratory muscle endurance was recorded using sustained threshold loading of 40% maximal inspiratory pressure. AS group were evaluated by using the functional status and quality of life, the Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Ankylosing Spondylitis Quality of Life Questionnaire (ASQoL). The severity of night pain, morning pain and morning stiffness were evaluated by Visual Analog Scale (VAS) in patients with AS. Mann Whitney-U test and Student-t Test were used to compare to groups variables. To evaluate the correlation in AS group Spearman’s Test was used.

Results: A total eleven patients (6 female, 5 male; mean age: 41.9±4yrs, body mass index (BMI): 26.1±6.3kg/m² and duration of disease 22±24.9months) and eleven controls (6 female, 5 male; mean age: 42.9±12.7yrs and BMI: 25±3.6kg/m²) were included in this study. There were no differences in age (p=0.554) and BMI (p=0.923) between the groups. No difference between FEV1% (p=0.069), FEV1/FVC% (p=0.243), PEF% (p=0.490), FEFP25-75% (p=0.297), MVV% (p=0.450), PEmax (p=0.694), PEmax (p=0.358) and respiratory muscle endurance (p=0.341) in both groups. But FVC% (p=0.041) significantly lower in AS group compare to controls. In addition to PImax (r= -0.800, p=0.003), PEmax (r= -0.683, p=0.021) and respiratory muscle endurance (r= -0.683, p=0.021) were correlated the night pain level in AS group. The respiratory muscle endurance (r= -0.675, p=0.023) was correlated the duration of disease. No correlations to the functional status, quality of life indexes and pulmonary functions in AS group.

Conclusion: This study shows that patients with AS have clearly reduced maximal PImax and PEmax, indicating decreased respiratory muscle strength and endurance as night pain levels increased. If indeed the respiratory strength were to be unchanged or even increased the decreased respiratory muscle strength should be due to reduced strength or atrophy of intercostal or accessory muscles, or both. Although the present data do not provide the direct evidence of intercostal muscle atrophy, it is tempting to speculate that immobilization of these muscles due to thoracic rigidity and decreased inspiratory intercostal and accessory activation leading to disuse may be an important factor contributing to it.

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Disclosure of Interests: Bilge Taskin: None declared, Naciye Vardar-Yagil: None declared, Umut Kalyoncu: Grant/research support from: MSD, Roche, UCB, Novartis and Pfizer, Consultant for: MSD, Abbvie, Roche, UCB, Novartis, Pfizer and Abdi Ibrahim, Speakers bureau: MSD, Abbvie, Roche, UCB, Novartis, Pfizer and Abdi Ibrahim, Gul Baltaci: None declared DOI: 10.1136/annrheumdis-2019-eular.5386

Scientific Abstracts

Saturday, 15 June 2019 1461
SAT0721-HPR INVESTIGATION OF FUNCTIONAL OUTCOMES AND QUALITY OF LIFE IN YOUNG ADULTS WITH INTERNAL FIXATION SURGERY OF FEMORAL SHAFT FRACTURE

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Background: Femoral Shaft Fracture (FSF) is a severe injury with incidence 10-21 per 100,000 persons/year. The union rate is reported between 95-99%. Unfortunately, even after union a number of patients still report impairments and limitations in functional outcomes and quality of life (QoL). The literature lacks studies evaluating long-term functional outcome and performance and QoL.

Objectives: The aim of this study was to compare the functional outcomes and quality of life of the young adults who underwent internal fixation (IF) surgery of femoral shaft fracture (FSF) to the healthy individuals.

Methods: Twenty patients who underwent IF surgery of FSF by the same surgeon and 20 healthy individuals were included in this retrospective study. Individuals with secondary osteoporosis risk were not included. Function of both two groups was assessed using Harris Hip Score. To evaluate performance Stair Climbing Test (SCT) is applied. Quality of life was assessed by the EQ-5D-3L HRQoL. The Mann Whitney U-Test was used to compare the results of the function, performance and quality of life of the two independent groups. Statistically, p<0.05 was accepted as a significant difference.

Results: The mean age after surgery was 2.2±0.8 years. Comparing to the healthy group, the EQ-5D-3L VAS and TTO scores of the patient group were significantly lower (p<0.001). When the function results were compared between the groups, the mean total HHS of the patient group were found significantly lower (p<0.001). The results of mean stair climbing time in healthy group were significantly lower (p<0.001). Descriptive outcomes and results details is shown in Table 1.

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Healthy Group</th>
<th>p-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>39.55 ± 11.92</td>
<td>0.43</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>170.70 ± 8.51</td>
<td>0.86</td>
</tr>
<tr>
<td>Body Weight (kg)</td>
<td>75.45 ± 12.68</td>
<td>0.79</td>
</tr>
<tr>
<td>Body Mass Index (kg/m²)</td>
<td>25.85 ± 3.76</td>
<td>0.82</td>
</tr>
<tr>
<td>HHS Overall (point)</td>
<td>71.65 ± 15.42</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td>SCT Overall (sec)</td>
<td>11.58 ± 6.55</td>
<td>0.53 ± 0.89</td>
</tr>
<tr>
<td>EQ-5D-3L VAS</td>
<td>0.527 ± 0.182</td>
<td>0.849 ± 0.147</td>
</tr>
<tr>
<td>EQ-5D-3L TTO</td>
<td>0.513 ± 0.266</td>
<td>0.874 ± 0.131</td>
</tr>
</tbody>
</table>

Mann-Whitney U Test, M±SD: Mean score and Standard Deviatiion

Conclusion: The results of the study showed that there were deficiencies in long-term function, performance and quality of life in young adults after IF surgery compared to healthy individuals. Therefore, we suggest that the assessment of the in long-term functional outcomes and quality of life of the patients with FSF after IF surgery is necessary to plan appropriate rehabilitation programs by determining the patient’s needs.

REFERENCES

Disclosure of Interests: None declared

SAT0722-HPR WHAT IS THE MOST AFFECTED BIOPSYCHOSOCIAL ASPECT IN RHEUMATIC DISEASES?

Edbe Ünal1, Gamze Arın1, Derya Gökmen2, Sedat Kiraz2. 1Hacettepe University Faculty of Physical Therapy and Rehabilitation, Ankara, Turkey; 2Ankara University Faculty of Medicine, Department of Biostatistics, Ankara, Turkey

Background: Rheumatic diseases are chronic illnesses that vary in the extent to different manifestations in musculoskeletal and internal organ systems. In addition to organ involvements, patients with these conditions suffer from biopsychosocial problems such as pain, stiffness, loss of functionality, social isolation, anxiety and depression, fatigue, sleep, and sexual problems due to the chronic nature of these diseases (1). BETY-BQ is a newly developed biopsychosocial questionnaire that can be used in rheumatic diseases and assesses patients in regards to biopsychosocial status.

Objectives: The aim of this study was to investigate the most affected biopsychosocial aspect that rheumatic diseases cause to.

Methods: 343 patients with rheumatic diseases (283 females and 60 males, mean age: 45.9±10.6) who referred to Hacettepe University, Department of Internal Medicine-Rheumatology were included in this study. Biopsychosocial aspects were assessed by using Bilgisel Egzersiz Terapi Yaklaşımı-Biopsychosocial Questionnaire (BETY-BQ)(2). Rasch analysis was used to determine the different biopsychosocial aspects and the most affected one.

Results: It was found that BETY-BQ has 6 categories assessing pain, functionality & fatigue, emotional status, social participation, sexuality, sleep. When the residual correlation matrix was evaluated, substantial local dependency was observed among the items. Consequently, the sets of items within each of the six subscales were treated as one summary item (testlet) and the data fitted to the Rasch model. Following this, all items were found to fit the model (given a Bonferroni adjustment fit level of 0.0083) (Table 1). Overall, the resulting 6-item item bank was well targeted. The most affected biopsychosocial aspect was found to be ‘social participation’ and the less affected was ‘sleep problems’.

<table>
<thead>
<tr>
<th>Items Location</th>
<th>Item Fit</th>
<th>Chi-Square</th>
<th>Test Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subtest of “fatigue” items</td>
<td>0.101</td>
<td>0.017</td>
<td>1.026</td>
</tr>
<tr>
<td>Subtest of “paining” items</td>
<td>0.080</td>
<td>0.011</td>
<td>1.190</td>
</tr>
<tr>
<td>Subtest of “emotional status” items</td>
<td>0.092</td>
<td>0.011</td>
<td>1.730</td>
</tr>
<tr>
<td>Subtest of “social participation” items</td>
<td>0.156</td>
<td>0.021</td>
<td>1.149</td>
</tr>
<tr>
<td>Subtest of “sexuality” items</td>
<td>0.140</td>
<td>0.023</td>
<td>2.201</td>
</tr>
<tr>
<td>Subtest of “sleep problems” items</td>
<td>0.207</td>
<td>0.039</td>
<td>7.199</td>
</tr>
</tbody>
</table>

Conclusion: According to our results, social functioning is the most affected aspect of patients with rheumatic diseases. Following social functioning, sexuality, and emotional status were further affected. This results should be taken into consideration in the multidimensional rehabilitation programs.

REFERENCES

Disclosure of Interests: None declared
INVESTIGATION OF FUNCTIONAL CAPACITY AND AFFECTING FACTORS IN SYSTEMIC SCLEROSIS PATIENTS

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Background: Systemic Sclerosis (SSc) is a rare, systemic connective tissue disease characterized by widespread microscopic damage and by increased production and deposition of extracellular matrix components both in the skin and internal organs (1).

Objectives: The aim of this study was to investigate the functional capacity and affecting factors in SSc patients.

Methods: Twenty-two SSc patients were included in the study. Functional capacities of patients were measured by 6 Minute Walking Test (6MWT). Lung volumes (FVC, FEV1, FEV1/FVC, PEF, VCF) were performed with Pulmonary function tests-PFT. Respiratory muscle strength was evaluated with a muscle inspiratory pressure (MIP)–muscle expiratory pressure (MEP) modulated spirometer known as respiratory muscle strength meter. Peripher- al muscle strength (deltoid, biceps, quadriceps and ilopsoas muscles) were also evaluated with manual muscle strength meter.

Results: The mean age of the patients was 52.0±11.23 years and duration of diagnosis was 7.83±4.86 years. The patients’ mean 6MWT distance was 430.5±105.25 meters, FEV1% were 78.52±22.23 L, FVC% were 80.95±23.02 L, FEV1/FVC% were 102.56±9.58 L, VC% values were 72.95±22.75 L, MCP% were 54.27±34.85 L, and MEP% values were 56.59±33.56. The mean deltoid muscle strength of the patients was 5.88 ±1.26 kg, biceps were 6.48±1.68 kg, quadriceps were 6.06±1.55 kg, iliopsoas were 80.95±23.02 L, FEV1/FVC% were 102.56±9.58 L, VC% values were 72.95±22.75 L, MCP% were 54.27±34.85 L, and MEP% values were 56.59±33.56.

Conclusion: The decrease in the functional capacity of the patients is accompanied by a decrease in pulmonary function, loss of respiratory and peripheral muscle strength in parallel. 6-min walk test showed negative effects in the pulmonary and musculoskeletal system or in the patients’ clinic on SSc patients. To evaluate and improve functional capacity, while performing medical and rehabilitation follow-up, respiratory functions, respiratory and peripheral muscle strengths should be evaluated and improved.

REFERENCE

Disclosure of Interests: None declared

HPR Service developments, innovation and economics in healthcare

SAT0723-HPR

PROMISING OUTCOMES IN PATIENTS WITH RA UNDER A T2T PROGRAM AND A MULTIDISCIPLINARY DISEASE MANAGEMENT MODEL – 5 YEARS RESULTS FROM A RETROSPECTIVE COHORT

Anggie Aza1, Michael Cabrera2, Pedro Santos-Moreno3, Laura Villareal4, Diana Buitrago-Garcia1, 1Biomab – Center for rheumatoid arthritis, Bogotá, Colombia; 2Biomab – Center for rheumatoid arthritis, Psychology, Bogotá, Colombia; 3Biomab – Center for rheumatoid arthritis, Bogotá, Colombia; 4Biomab – Center for rheumatoid arthritis, Bogotá, Colombia

Background: Rheumatoid arthritis (RA) is a common chronic inflammatory disease. It is characterized by progressive, irreversible joint damage, impaired joint function and pain, the disease causes disability and reduced quality of life. Treat-to-target (T2T) is a management strategy for RA. It proposes that the therapeutic goal in RA should be a state of remission, or an alternative goal could be a low disease activity, addition- ally it looks to achieve long-term health quality of life for the patients.

Additionally, multiapproach programs for RA aim to take into account all components that interfere with the course of RA.

Objectives: To describe the effectiveness of a T2T strategy associated to a disease management model with a multidisciplinary approach of patients with RA, according to disease activity measured with Activity Score 28 (DAS28) in a 5-year period in patients who receive conven- tional or biological DMARDs in a Colombian specialized in RA center.

Methods: A descriptive cohort study was conducted. Medical records of patients from specialized in RA center were reviewed during 2015-2017; those patients were followed-up under T2T standards and a multidisciplinary approach. Clinical follow-up was designed by the authors according to DAS28 as follows: every 3-5 weeks (DAS28 > 5.1), every 7-9 weeks (DAS28 > 3.1 and ≤ 5.1), and every 11-13 weeks (DAS28 ≤ 3.1). Tender joint count (TJC), swollen joint count (SJC) and DAS28 were measured on each visit. Therapy had to be adjusted with DAS28 > 3.2 unless patient’s conditions don’t permit it; we considered this follow-up type as an implementation of a T2T strategy in patients with RA. Patients entered into a multidisciplinary program of care with periodic consultations not only to rheumatology but with a psychologist, physiotherapist, occupational therapy nutrition, and, a patient focused program. With a multidisciplinary model of care the patient is seen as a whole, and the expectation is to achieve the best results in the management of RA. We divided patients in four groups: remission (REM), low disease activity (LDA), moderate disease activity (MDA) and high disease activity (HDA) patients and the aim of the study was to look at what percentage of patients who were in moderate or severe disease activity reached a low disease activity or remission. Descriptive epidemiology was done, we calculated means, and standard deviations for continuous variables and categorical variables were presented as rates. We compared disease activity at base line and at the end of follow-up.

Results: We included 4000 patients, 83% were female and 17% male; median age was 60 years RIQ (50-67). Regarding pharmacological ther- apy 77% were receiving conventional DMARDs while 37% were receiving biological DMARDs. At beginning 55% were in MDA, 26% in LDA and 19% and during 5 years 82% of our patients achieved remission. See table 1. We performed a Wilcoxon test in order to compare the mean DAS28 at baseline and at the end showing statistical significance (P<0.05).

ACTIVITY LEVEL

<table>
<thead>
<tr>
<th>BASELINE</th>
<th>5 YEARS FOLLOW-UP</th>
</tr>
</thead>
<tbody>
<tr>
<td>REM</td>
<td>LDA</td>
</tr>
<tr>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>3397</td>
<td>82.40</td>
</tr>
</tbody>
</table>

Conclusion: A T2T strategy associated with a multiapproach disease management model improves considerably disease activity in patients with RA. This evidence from a real-life setting that shows the advantages of treating RA patients with a multidisciplinary team under a T2T model with a low-cost treatment. It is important to explore other predictors that can improve disease activity.

REFERENCES
Disclosure of Interests: Anggie Aza: None declared, Michael Cabrera: None declared, Pedro Santos-Moreno Grant/research support from: Dr Santos has received research grants from Janssen, Abbvie and UCB, Speakers bureau: Dr Santos has received speaker fees from Sanofi, Lilly, Bristol, Pfizer, Abbvie, Janssen and UCB, Laura Villareal: None declared, Diana Buitrago-Garcia: None declared

SAT0725-HPR

A DISEASE MANAGEMENT MODEL TYPE CENTER OF EXCELLENCE IN SPONDYLOARTHRITIS – FIRST PILOT ANALYSIS RESULTS

Anggie Aza1, Fernando Rodriguez2, Pedro Santos-Moreno3, Diana Buitrago-Garcia1, 1Biomab – Center for rheumatoid arthritis, Bogotá, Colombia; 2Biomab – Center for rheumatoid arthritis, Bogotá, Colombia; 3Biomab – Center for rheumatoid arthritis, Patient program coordinator, Bogotá, Colombia; 4Biomab – Center for rheumatoid arthritis, Bogotá, Colombia; 5Biomab – Center for rheumatoid arthritis, Bogotá, Colombia

Background: Ankylosing spondylitis (AS) mainly affects the spine and the sacroiliac joints, it is a chronic inflammatory disease that might be asso- ciated with a variety of extra spinal lesions involving the eyes, bowel,
and skin. In Colombia little is known in regards of this condition. Spondyloarthritis (SpA) is one of the most prevalent musculoskeletal disease in the Americas, with an estimated prevalence of 0.5%. This group of patients present a number of unmet needs for accessibility to the consultation, diagnosis and adequate treatments. That is why in this project it is necessary to develop a program of Centers of Excellence (CoE) in this pathology, which allows answer to these needs and at the same time to add values for our health systems.

Objectives: To describe the characteristics of patients with AS who attend to a specialized in SpA disease management model center.

Methods: We implemented a pilot SpA program under the scheme of CoE, as they are already delineated in projects like REAL-PANLAR for rheumatoid arthritis. We performed a cross sectional study and reviewed the medical charts of patients with AS. All patients had a confirmed diagnosis of AS. We collected demographic data (age, sex, smoking, alcohol consumption); BASDAI, BASFI, DAS, disease specific data treatment with csDMARDs or bDMARDs and comorbidities, evaluation period covered January to December 2018.

Results: During 2018 257 patients with AS entered to our program. 64% were men and 36% were female; mean age was 48 years ±14. 28% of our patients with SA had comorbidities the most common was high blood pressure 19%, followed by diabetes mellitus 4%. Regarding behavioral habits 23% were current smokers and 11% reported to consume alcohol. When we evaluated clinical outcomes BASDAI mean score was 2.95 ± 2.06, BASFI mean score was 3.49 ± 2.36 and, ASDAS mean score was 1.70 ± 1.01. 60% of patients received biological DMARDs and 25% received conventional DMARDs. The remaining 15% received corticoids or pain medications.

Conclusion: Due to the need to develop CESPAs, in order to define treatments for SpA type T2T-SpA, we implemented an innovation program in a low-income country with the aim to improve clinical outcomes and avoid so much disability and health economic costs. This descriptive data is the starting point to collect evidence and demonstrate the impact of the program.

Disclosure of Interests: Annigge Aza: None declared, Fernando Rodriguez: None declared, Pedro Santos-Moreno: Grant/research support from: Dr Santos has received research grants from Janssen, Abbvie and UCB, Speakers bureau: Dr Santos has received speaker fees from Sanofi, Lilly, Bristol-Myers, Abbvie, Janssen and UCB, Diana Buitrago-Garcia: None declared DOI: 10.1136/annrheumdis-2019-eular.7569

SAT0725-HPR EHEALTH CONSULTATIONS IN RHEUMATOLOGY MANAGED BY NURSING. SPANISH NATIONAL DESCRIPTIVE STUDY

Silvia García Díaz1, All the members from the Nursing Working Group from the Rheumatology Spanish Society (GTE-SER), Hospital Sant Joan Despí Moises Broggi-Hospital General de Hospitalet, Consorcio Sanitari Integral (CSI), Rheumatology, Barcelona, Spain Background

The increase in social media applications and electronic technology has made it possible to carry out consultations with patients using an electronic interface. These tools are used in the healthcare environment for the purpose of prevention, diagnosis, treatment, monitoring, and in health management, to save costs to the health system by improving its effectiveness [1-4].

For patients with rheumatic diseases these non-face-to-face eHealth consultations, carried out by specialized nurses have been shown to resolve a large part of the problems that these patients may present with [5-8]. However we do not know how many of these types of consultations are taking place in Spain.

Objectives: The aim of this study was to describe the content of these types of consultations, mostly managed by nursing, in the Spanish national territory.

Methods: A descriptive study of a group of nurses working actively in rheumatology was carried out in November 2018. The data collection was done using a Google-form questionnaire developed for that purpose by the members of the Nursing Working Group from the Rheumatology Spanish Society (GTE-SER). The main variables studied were the socio-demographic details of the group and the content of the activity carried out mainly by them in the eHealth consultations. This instrument had 31 questions, with wide variability of response. Statistical analysis: descriptive statistics was used.

Results: A total of 47 (out of 50) completed surveys were analysed. 94% of the nurses were women, from 15 Spanish Autonomous Communities, with an average age between 51-60yo; 52% had education at postgraduate level (17%) or master’s degree (35%). 47% of professionals had been working in rheumatology for more than 10 years and 77% had received specific training in rheumatology. 37% reported having between 1-5 years experience of using e-Health consultation in rheumatology. The average of monthly consultations was between 50-100 sessions. Further details of the eHealth consultations in Rheumatology: see Table 1.

Table 1:

<table>
<thead>
<tr>
<th>VARIABLES</th>
<th>Nursing professionals%</th>
</tr>
</thead>
<tbody>
<tr>
<td>eHealth consultations ARE managed by nursing professionals</td>
<td>100%</td>
</tr>
<tr>
<td>The type of eHealth consultation is both scheduled and on demand</td>
<td>68%</td>
</tr>
<tr>
<td>The type of access to the consultation is telephone</td>
<td>72%</td>
</tr>
<tr>
<td>The management of the answer to the consultation is IMMEDIATE</td>
<td>68%</td>
</tr>
<tr>
<td>The space where the consultation is handled is in a quiet office</td>
<td>41%</td>
</tr>
<tr>
<td>eHealth consultations ARE always registered</td>
<td>76%</td>
</tr>
<tr>
<td>eHealth consultations ARE registered in the patient’s clinical history</td>
<td>91%</td>
</tr>
<tr>
<td>eHealth consultations are computed as a clinical activity in the nursing agenda</td>
<td>79%</td>
</tr>
<tr>
<td>There are NO standards or protocols on the use of eHealth consultations in rheumatology in your centre</td>
<td>81%</td>
</tr>
<tr>
<td>There has not been any audit on the use of eHealth consultations in rheumatology</td>
<td>98%</td>
</tr>
</tbody>
</table>

Conclusion: EHealth consultations are already established in many Rheumatology services in Europe. However, this has not been described in Spain. The survey showed that there is a great variability in the way the nurses carry out this type of consultations, including the number and type of consultation (on demand and/or scheduled); registration and analysis of the data of this consultation as well as its quality standards.

This study demonstrates a lack of regulated training and standardized protocols in managing this type of consultation at the national level. Therefore standards and protocols should be developed in the near future, so that patients receive a more consistent service from this type of consultation.

REFERENCE


Acknowledgement: Professor Claire Halle and all the participants


SAT0727-HPR CHANGES IN ACHILLES TENDON STIFFNESS IN GOUT MEASURED BY ELASTOGRAPHY – A PRELIMINARY STUDY

Simon Otter1, Catherine Payne2, Anna-Marie Jones2, Nick Webborn2, Peter Watt2.

1University of Brighton, School of Health Sciences, Eastbourne, United Kingdom; 2University of Brighton, Sport and Exercise Science and Sports Medicine Research Group, Eastbourne, United Kingdom; 3Sussex Partnership NHS Foundation Trust, Research and Development, Worthing, United Kingdom

Background: In addition to acute attacks of severe joint pain and swelling, chronic gout has been associated with weaker foot/leg muscles, altered gait patterns and on-going foot pain. Inflammation associated with gout may change tissue elasticity and ultrasound imaging (US) utilising elastography is a non-invasive method of quantifying these changes in tendon stiffness and elastography findings have not previously been reported in individuals with gout.

Objectives: To determine differences in Achilles tendon stiffness in people with chronic gout compared to controls (non gout)

Methods: A cross sectional study comparing people with gout according to 2015 ACR/EULAR criteria and age/sex matched controls. Clinical and demographic data were collated and US imaging used to determine tendon thickness, presence of gouty tophi and/or aggregates and levels of angiogenesis. Previously validated protocols for conventional US imaging [1] and shear wave elastography [2] were used. Prior to data collection, intra-observer error was good (ICC (2) 0.69 (95%CI 0.62-0.89)). Ten elastography measures were taken along a longitudinal section of the mid-point of the Achilles tendon bilaterally. Data were summarised using descriptive statistics and a repeated measures ANCOVA was used to compare elastography outcomes between the two groups for the left and right foot separately after accounting for Body Mass Index (BMI).

Results: A total of 14 people with gout and 13 age/sex matched control subjects participated. Table 1 displays clinical and demographic data. A
small proportion of those with gout presented with intra-tendon aggregates and/or intra-tendon tophi in one or both tendons (n=7 (27%) for both). There was no significant difference in tendon thickness between groups, neo-vascularity was present in n=3 (21%) gout participants. Elastography findings (table 2) demonstrated significantly reduced tendon stiffness in those with gout compared to controls.

Abstract SAT0727HPR Table 1. Clinical & demographic characteristics

<table>
<thead>
<tr>
<th></th>
<th>Gout</th>
<th>Non-gout</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male:Female</td>
<td>11:3</td>
<td>11:2</td>
</tr>
<tr>
<td>Mean age (SD)</td>
<td>71.9 (10.54)</td>
<td>71 (10.8)</td>
</tr>
<tr>
<td>Mean BMI (SD)</td>
<td>30.8 (5)</td>
<td>27.8 (4.54)</td>
</tr>
<tr>
<td>Mean duration gout years (SD)</td>
<td>12.7 (9.88)</td>
<td></td>
</tr>
<tr>
<td>Comorbidities (%)</td>
<td>50</td>
<td>62</td>
</tr>
<tr>
<td>Diabetes</td>
<td>85</td>
<td>70</td>
</tr>
<tr>
<td>Hypertension</td>
<td>64</td>
<td>70</td>
</tr>
<tr>
<td>Dyslipaemia</td>
<td>57</td>
<td>23</td>
</tr>
<tr>
<td>Cardiac disease</td>
<td>36</td>
<td>8</td>
</tr>
<tr>
<td>Chronic Kidney disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gout management n (%)</td>
<td>3 (9)</td>
<td>None</td>
</tr>
<tr>
<td>NSAID (µm)</td>
<td>6 (21)</td>
<td></td>
</tr>
<tr>
<td>Allopurinol</td>
<td>1 (3)</td>
<td></td>
</tr>
<tr>
<td>Chloroquine</td>
<td>2 (7)</td>
<td></td>
</tr>
<tr>
<td>Prednisolone</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: Subjects with chronic gout show reduced Achilles tendon stiffness compared to controls. From a clinical standpoint, our findings were similar to elastography measurements in otherwise healthy subjects with Achilles tendinopathy and who did not have gout [3].

REFERENCES


Disclosure of Interests: None declared


SAT0727-HPR REVISION OF THE DUTCH GUIDELINE FOR PHYSIOTHERAPY IN PATIENTS WITH HIP AND KNEE OSTEOARTHRITIS: RECOMMENDATIONS FOR DAILY PRACTICE

Wilfred F. Peter 1,2, Mitchell van Doormaal 2, Guus Meehoff 3, Thea Vliet Vlieland 1. 1 Leiden University Medical Center (LUMC), Orthopaedics, Rehabilitation and Physiotherapy, Leiden, Netherlands; 2 Amsterdam Rehabilitation Research Center / Reade, Amsterdam, Netherlands; 3 Royal Dutch Society for Physical Therapy, Amersfoort, Netherlands

Background: Until 2018, the most recent update of the Dutch physiotherapy guideline for Hip and Knee Osteoarthritis (HOCA) was conducted in 2010. Since then, scientific developments changed the view on osteoarthritis and could have significant impact on daily practice. An update of the guideline was necessary with more applicable recommendations about the content of exercise therapy.

Objectives: To revise the Dutch guideline for physiotherapists in patients with HKOA.

Methods: To develop more practical and widely supported guidelines, a guideline methodology was developed by the Royal Dutch Society for Physical Therapy (KNGF) in 2016. This methodology was based on GRADE, the most accepted approach in guideline development worldwide. According to the KNGF methodology, a guideline panel was formed out of 22 stakeholders, e.g. physiotherapists, general practitioners, orthopedic surgeons, patient representatives and healthcare insurers. Based on the scientific evidence and other considerations, the guideline panel formulated the recommendations in this guideline.

Results: Recommendations about diagnostics and therapeutic interventions formed the base of the new Dutch physiotherapy guideline for HKOA. Three indications were formulated, based on patient preferences, severity of the functional condition and existence of comorbidity. A fourth indication concerned pre- and postoperative physical therapy before or after a total joint replacement. It was recommended to restrict physical therapy in patients with minor functional limitations by informing and advising about osteoarthritis and how to deal with the disease. In contrast, extensive supervised exercise therapy was recommended in patients with severe functional restrictions and/or comorbidity. Besides informing and advising, supervised exercise therapy is stated as the intervention with the strongest recommendation. Frequency, Intensity, Type and Time (FITT factors) of exercise therapy are described extensively, based on evidence and strongly linked to (inter)national recommendation for physical activity. Besides informing and advising, other non-exercise therapeutic interventions were not recommended.

Conclusion: The new physiotherapy guideline for HKOA provides practical information and guidance to physiotherapists on diagnostics and therapeutic interventions. Extensive implementation is necessary to enhance conservative treatment of osteoarthrosis and achieve uniform health care.

REFERENCE


Disclosure of Interests: None declared

Conclusions: Three indications for PT are distinguished, based on the patients’ health status and abilities of self-management: 1) patient education combined with instructions for mainly unsupervised exercise therapy, 2) patient education combined with exercise therapy with short-term supervision and 3) patient education combined with exercise therapy with intensified supervision. Exercise therapy is recommended for indication 2, and conditionally recommended for indication 1 and 3. Patient education consist of information and advice on RA and promotion of self-management. Specific recommendations concerning the frequency, intensity, type and time (FITT) of the exercise therapy are provided, based on studies performed in patients with RA, recommendations from The Dutch Health Council (2017), EULAR recommendation on Physical Activity (2018), and The American College of Sports Medicine guidelines for exercise testing and prescription (2018). Behavioral interventions to promote physical activity in patients with RA are also recommended. The guideline obtains practical advice for applying tailored behavioral interventions.

Disclosure of Interests: None declared


References


EDevelopment and Design of Smartphone Application for Postural Alignment of Cervical and Thoracic Spine for Young Adults

Eda Tonga, Merve Can, Mine Gilden Polat, Marmara University, Faculty of Health Sciences, Department of Physiotherapy, Istanbul, Turkey

Background: Mobile health (mHealth) technologies offer personal, intelligent, cost-effective, access to health care services. Numerous smartphone applications exist to assist the users for management or prevention of the musculoskeletal disorder. But most of the apps were not designed with both users and experts focus. As our knowledge, there is no health exercise app for neck and upper back musculoskeletal prevention designed by experts with the user-centered method.

Objectives: The aim of our study is to develop a smartphone exercise application (app) for cervical-thoracic postural alignment for young adults.

Methods: We used a combination method of focus groups interviews and user-centered design approach. The mobile application was designed in three phases: (1) we conducted multidisciplinary focus group meetings to compromise the content, feature and design of app in the first phase (prototype smartphone app/MarNeckEx). Focus group consisted of software developers, 3 experienced physiotherapists on musculoskeletal ergonomics, 3 young smartphone users who have neck and upper back problems associated with an excess smartphone using. The focus group members discussed the variety of topics in subgroups (login parameters, self-monitoring, exercises content, video or animation types, exercise diary, reminders, encouragement method etc). We conducted 4 focus group meeting for phase 1. (2) After developing the prototype version of app 30 young adult downloaded the prototype app and used the app for one week, after one week we asked the satisfaction levels, barriers and facilitators of the app design and advice for usability. We conducted 2 focus group meetings for development of the revised application by modifying the errors taking into account feedbacks (revised MarNeckEx).

Results: Major themes identified for development app phase 1 were (a) self-assessment of musculoskeletal problems (b) Choosing the spinal stabilization and postural alignment exercises with well design videos (c) encouraging and notifications for exercise adherence. A second phase themes, (d) education for using the digital app for exercise, (e) positive or negative feedback notifications for improving adherence were added.

Disclosure of Interests: None declared


Triage Ad Hoc Referral by Rheumatology Nurse – An Alternative Path to Clinic Visit

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Background: Rheumatic diseases are chronic conditions characterized by disease flares and remissions. Patients are often referred back from other healthcare providers in between follow-up visits when they seek attention for disease flares or adverse effects from treatment. While prompt attention and assessment is important, the busy rheumatology clinic may not have the coping capacity for these ad hoc needs. Rheumatology nurse (RN) can play a pivotal role in triaging these referrals.
Objectives: The study aims to evaluate the safety of referral triage by rheumatology nurse and the effectiveness in alleviating workload of the rheumatology clinic.

Methods: This was a retrospective study. Data were retrieved from November 2016 till December 2018. Ad hoc referrals to the rheumatology out-patient clinic were screened by rheumatologists and suitable cases were directed to RhN for further handling. The triage process included phone triage or attendance of RhN clinic for assessment and subsequent phone follow-up. Investigations including laboratory and radiography were arranged as indicated. Frequency of phone follow-up after the first contact depended on patients’ needs. Patients would be referred to rheumatologist for further management if the condition worsened at or before the first phone follow-up.

Results: Totally 110 referrals were triaged by rheumatology nurse with 54 arthritis, 28 systemic lupus erythematosus, 10 vasculitis, 8 undifferentiated connective tissue disease and 5 others. Age ranged from 22 to 84 years and 82.7% were female. Sources of referral included general out-patient department (38.2%), emergency department (22.7%), other specialists (33.6%) and general practitioners (5.5%). Reasons for referral included disease flare-up (47.3%), drug-related problems (20.9%), abnormal investigation results (12.7%) and alarming clinical presentation (19.1%). Mean time interval from referral to first phone contact was 3.8 days. Of the 110 cases, 20 patients had follow up advanced; 1 patient was admitted before phone triage and 86 patients could follow original appointments. Two of the 110 patients’ symptoms subsided spontaneously and no intervention was required; 1 patient was arranged admission after discussion with rheumatologist. No record of emergency attendance or admission for the 86 patients who kept the scheduled appointment. Nursing interventions included drug education and advice (64 episodes), disease education (20 episodes), investigation arrangement (50 episodes), counselling and emotional support (12 episodes). Three patients attended RhN clinic for assessment and education. The other 83 patients were managed through phone communication and majority (81.4%) had phone follow up once.

Conclusion: The result of the study showed that referral triage by rheumatology nurse is safe and effective in handling the majority of ad hoc referral requests. The service can promptly address patient needs and reduce clinic visit burden of the rheumatology clinic.

Disclosure of Interests: None declared

Genomics, genetic basis of disease and antigen presentation

AB0001 ASSOCIATION OF MDR1 GENE G2677T POLYMORPHISM WITH METHOTREXATE RESISTANCE IN PATIENTS WITH UZBEK RHEUMATOID ARTHRITIS

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Background: Methotrexate (MTX) is the most widely prescribed disease-modifying antirheumatic drug (DMARD) for treatment of rheumatoid arthritis (RA) [1]. According to different authors, in 25–40% of cases "complete clinical remission" or "low disease activity" is not achieved, by reason of refractoriness to methotrexate and this may be related to the activity of the MDR1 (ABCB1) gene which is involved in its metabolism. According to many studies on the C3435T isoform MDR1 polymorphism CC genotype is associated with methotrexate refractoriness [2]. But a certain interest is also influenced by the other isoform of the MDR1 gene (G2677T) for the presence of resistance to methotrexate.

Objectives: The aim of this research was to study the effect of MDR1 gene polymorphisms G2677T (rs2032582) on resistance to treatment with methotrexate in Uzbek patients with RA.

Methods: The study involved 76 patients with RA of Uzbek nationality and 24 healthy people. The average age of patients was 48.9 ± 15.9 years. RA was diagnosed according to the criteria of the American College of Rheumatology (ACR). 75.6% of patients had high and 24.4% moderate RA activity (DAS28). All patients took methotrexate in monotherapy, at a dose of 7.5-15 mg for 3-6 months. All patients were genotyped by the MDR1 gene G2677T polymorphisms by using the polymerase chain reaction (PSR-Real time).

Results: Genotyping of the G2677T isoform of MDR1 gene revealed the following results: in patients with CC genotype was found in 22 patients (28.9%), CT genotype was found in 31 patients (40.7%) and TT genotype was found in 23 patients (30.2%). In patients treated with methotrexate, the following disease activity was observed: in patients with CC genotype, the disease activity was Das28 -6.2, with CT genotype Das28 3.2-4.5. Patients with the TT genotype had an activity of Das28 5.1. Despite the increase in the dose of methotrexate, the remission was not achieved.

Conclusion: TT genotype G2677T isoform of MDR1 gene is associated with resistance to treatment with methotrexate and this may be related to the activity of this polymorphism with other DMARD preparations. Patients are recommended to conduct genotyping to the MDR1 gene for personal selection of drugs.

REFERENCES

Disclosure of Interests: None declared

AB0002 INCREASED SENSITIVITY TO DNA DAMAGING AGENTS IN HUMAN PERIPHERAL BLOOD MONONUCLEAR CELLS FROM PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic autoimmune disease with not fully elucidated pathogenesis. Rheumatoid arthritis patients have increased risk of developing lymphomas. One of the possible mechanisms of this predisposition is increased genomic instability and impaired DNA repair. It is unclear how this genomic instability contributes to diseases pathogenesis.

Objectives: The aim of this study was to analyze the sensitivity and repair efficiency of mononuclear cells isolated from RA patients to DNA damaging agents.

Methods: The study group consisted of 22 patients with RA (age years – 60,7±13.0, women-17, men-5) hospitalized in the Department of Rheumatology between 2017 and 2018 and 10 healthy controls without autoimmune and oncological diseases in clinical history (age 44.09±16.56; women-5, men-6). The peripheral blood mononuclear cells (PBMC) from all subjects were isolated. Using comet assay the degree of intracellular DNA damage as a result of exposure to standard damage factors: tert-butyl hydroperoxide (TBH), bleomycin, methyl methanesulfonate (MMS) and UV radiation was assessed.

Results: RA patients show a statistically significant higher level of endogenous damage in PBMC DNA than controls (mean RA: 9.64%, vs 4.68% in control; p<0.001). The extent of the DNA damage induced by TBH, MMS as well as UV was significantly higher in PBMC derived from RA patients than in healthy counterparts (p<0.001). The DNA of RA patients treated with TBH was repaired less effectively than in control (p<0.0001). Significantly higher percentage of DNA damage in RA DNA (p<0.0001) under the influence of bleomycin and clearly marked repair processes were observed. Among the healthy controls lower percentage of DNA was damaged, and although the repair process was slower but the final percentage of DNA damage was also lower.

Conclusion: DNA of people with rheumatoid arthritis is significantly more susceptible to damage in baseline and induced. The kinetics of DNA repair from RA patients after the introduction (TBH and bleomycin) was statistically less effective as compared to healthy control. Understanding the etiology of this phenomenon in RA may provide insight into disease pathogenesis and explain the increased susceptibility of patients to malignancies.

Acknowledgement: The project is financed under the funds of the National Science Center (2017/25/B/NZ6/01356).

Disclosure of Interests: None declared

AB0003 GENETICS OF PAIN IN WOMEN WITH FIBROMYALGIA: THE PROMISING ROLE OF REDUCING SEDENTARY BEHAVIOUR

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Background: Fibromyalgia is characterised by chronic pain and a heterogeneous presentation of other symptoms (e.g., fatigue and depression) [1]. It is widely accepted that pain is promoted by both genetic susceptibility and environmental factors such as people’s behaviours [2]. In addition to genotype individual associations with gene-gene interactions, when considering complex phenotypes such as pain, environment interacts with genetic factors in different ways and can affect the development and management of pain. This is particularly important in fibromyalgia, where there is increasing evidence that genetic factors contribute to inter-individual differences in pain experience and help to shape the clinical presentation of fibromyalgia.

Objectives: To test the individual association of 64 polymorphisms (34 candidate-genes) and the gene-gene, gene-physical activity, and gene-sedentary behaviour interactions with pain and pain-related cognitions in fibromyalgia.

Methods: In 274 women with fibromyalgia, saliva samples were collected for extracting DNA. We measured physical activity and sedentary behaviour by accelerometers for a week, pain with algometry and questionnaires, and pain cognitions with questionnaires. Age, body fat, and analgesics and antidepressants consumption were included as covariates. Significance was set at P-values lower than the Bonferroni’s correction or P- and false discovery rate values lower than 0.05.

Results: The rs8311 and rs6313 polymorphisms were individually related to algorimeter scores. The interaction of rs4818 and rs1799971 polymorphisms was related to pain catastrophizing. Five gene-behaviour interactions were significant: the interactions of sedentary behaviour with rs1383914, rs6860, rs46580, rs165599, and rs12994338 polymorphisms were associated with the bodily pain subscale of the SF-36.

Conclusion: The HTR2A gene (individually), COMT and OPRM1 gene-gene interaction, and the interactions of sedentary behaviour with ADRA1A, CHMP1A, COMT, and SCN9A genes were associated with pain-related outcomes in fibromyalgia females. Besides indicating the relevance of genetic background for pain and pain-catastrophizing, the observed genotype-behaviour interactions suggest that the effects of sedentary behaviour on pain may depend on the genotype of women with fibromyalgia. Future clinical experimental research should examine whether reducing sedentary behaviour is particularly beneficial for reducing pain in women with specific genotypes.
DETECTION OF THE SNP-SNP INTERACTIONS IN THE FAVORABLE RESPONSE TO RITUXIMAB IN A PATIENT ASSOCIATION OF HLA-DPB1*16:01 ALLELE WITH PR3-Ro

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Objectives: The aim of the study was to estimate interactions between SNPs of the genes implicated in immune and inflammatory responses: STAT4 (rs7574865), TRAF1/C5 and RUNX3 genes and is characterized by 0.6727 entropy value of 1.12% statistically significant high-order interaction of three polymorphisms: STAT4 – RUNX3 (rs11249215). GT (STAT4 rs7574865) and GG (TRAFC5 rs3761847), OR = 2.92, combined entropy – 4.83%. Separate data analysis for males and females didn’t show any statistically significant model of SNP interactions associated with JIA. However, MIF ns755622 with entropy of 2.92% was more informative in females, while STAT4 rs7574865 with entropy value of 1.12% – in males.

Conclusion: MDR analysis of the JIA-case-control data set identified a statistically significant high-order interaction of three polymorphisms: STAT4 – RUNX3 (rs11249215). GT (STAT4 rs7574865) and GG (TRAFC5 rs3761847), OR = 2.92, combined entropy – 4.83%. Separate data analysis for males and females didn’t show any statistically significant model of SNP interactions associated with JIA. However, MIF ns755622 with entropy of 2.92% was more informative in females, while STAT4 rs7574865 with entropy value of 1.12% – in males.

Disclosure of Interests: None declared


FAVORABLE RESPONSE TO RITUXIMAB IN A PATIENT WITH HYPOCOMPLEMENTEMIC URTICARIAL VASCULITIS ASSOCIATED WITH A HOMOZYGOUS FRAMESHIFT AGBL3 VARIANT

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Background: Last year we described a homozygous AGBL3 variant in a patient with autoinflammatory features and hypocomplementemic urticarial vasculitis. Whole exome sequencing revealed a deleterious homozygous c.768C>T mutation in AGBL3 (ATP/GTP binding protein-like 9) gene, which results in early termination of the protein (p.Gln257Ter) and deletion of the functional carboxy-peptidase domain. This protein belongs to metallocarboxypeptidases that mediate both deglutamylation and deaspartylation of target proteins, and AGBL3 is suspected to catalyze the deglutamylation of polyglutamate side chains.

Results: The index case was 23-year-old male patient of Assyrian origin, who had consanguineous parents. He was evaluated in our clinic because of recurrent attacks of fever, urticarial rash on the extremities and trunk, conjunctival injections and arthralgia, without a trigger or more frequently following an infection. His 2 to 3 days lasting attacks started when he was 13 and recurred more frequently during warm weather conditions or following hot baths. He had highly elevated CRP and ESR during attacks, but his acute phase response did not return to normal values in between the flares. Low C3 and C4 values were also observed during asymptomatic periods. His ANA test became positive during the course of his disease with an increase in titer during the last years. The biopsy of skin lesions revealed findings compatible with urticarial vasculitis. He responded only partially to corticosteroids, canakinumab and anakinra treatments. His treatment was switched to rituximab following the favorable response was observed following the first two infusions. He developed less frequent and milder attacks only after infections, and acute phase response was reduced to near normal values in between attacks.

Conclusion: The AGBL3-metallocarboxypeptidase gene was recently identified as a novel autoinflammatory gene associated with hypocomplementemic urticarial vasculitis phenotype, and it was different from the previously defined variants including DNASE1L3 mutations. The clinical features of the index case included both autoinflammatory and autoimmune findings including autoantibodies; and his inflammatory attacks did respond to rituximab treatment but not IL-1 blockade. Long-term follow-up and search for other patients associated with AGBL3 variation among idiopathic hypocomplementemic urticarial vasculitis are required for better clarification of the AGBL3-associated clinical phenotype.

Disclosure of Interests: None declared


ASSOCIATION OF HLA-DPB1*16:01 ALLELE WITH PR3-ANCA POSITIVE GRANULOMATOSIS WITH POLYANGIITIS IN TURKISH PATIENTS

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Background: ANCA associated vasculitides (AAV) comprise an important subset of small vessel vasculitides with a multifactorial pathogenesis, which is considered to be associated with the interaction of genetic and environmental factors. Certain HLA Class 2 alleles have been reported among the genetic risk factors for AAV from different geographic regions such as Europe and Asia (1,2).

Objectives: In this study, we aimed to analyse the distribution of HLA Class 2 genotypes among a series of Turkish AAV patients in comparison with the healthy Turkish subjects and the previously reported data of AAV cohorts from other countries.

Methods: Ninety-eight patients (aged between 18–75 years) diagnosed with AAV according to 2012 Chapel Hill Consensus Criteria were enrolled into the study. Records of age-at-birth and geographical regions throughout the follow-up period during the last 8 years.

Results: HLA Class 2 genotypes among Turkish AAV patients were compared by Chi-square test, and P value lower than 0.05 was accepted as significant.

Disclosures: None declared


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Disclosure of Interests: None declared

was significantly higher in the GPA-AAV group (%7.14 vs. %0.26 p<0.01, OR=30, 95% CI: 3.8–237). No significant difference was detected between the MPO-AAV and control groups.

**Conclusion:** HLA analysis of this small series of Turkish AAV patients revealed a negative correlation between PR3-ANCA positivity and HLA-DPB1*04:01 and HLA-DPB1*02:01 alleles in opposition to the results reported from different European AAV cohorts (1,3). On the other hand, a significant increase in both GPA and PR3-AAV subgroups for a previously unpublished HLA-DPB1*16:01 allele may suggest that HLA association may show ethnic or regional differences, and further analyses in larger series of AAV patients may reveal the molecular basis of this observation.

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**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.2854

**AB0007**

**IL12B POLYMORPHISMS ARE ASSOCIATED WITH ELEVATED SERUM LEVELS OF IL-12P40, IL-23 AND GENETIC PREDISPOSITION TO RHEUMATOID ARTHRITIS**

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**Background:** Rheumatoid arthritis (RA) is the most common type of autoimmune arthritis in which genetic predisposition in close interaction with environmental triggers seems to play the major role in the disease pathogenesis. Genetic analyses suggest a polygenic inheritance, as the largest genetic contribution to RA susceptibility remains the HLA-DRB1 gene, residing within the HLA gene complex. Since immune dysregulation plays a key role in immune-mediated inflammatory disorders, genetic variations within cytokine loci may contribute to variability in the immune response determining susceptibility or resistance to a certain autoimmune disease.

**Objectives:** We aimed to investigate whether IL12B polymorphisms are involved in causation of RA and in variations of circulating IL-23 and IL-12p40 levels in our Bulgarian population.

**Methods:** A total of 125 RA patients aged from 18 to 79 years in comparison to 239 age- and sex-matched healthy controls (HC) were genotyped for rs17860508 and rs3212227. Both IL12B polymorphisms were investigated by polymerase chain reaction (PCR) - based methods. Serum IL-12p40 and IL-23 concentrations measurement was done using ELISA test in 67 RA patients and 55 age-matched HC.

**Results:** An association between the rs17860508 polymorphism and RA development was established under the allelic model (allele 2 vs allele 1; OR = 2.00, 95% CI: 1.10–3.62, p = 0.022). These results support the hypothesis that the IL12B allele 2 genotype may be predisposing, while 1 genotype might be protective factor for RA susceptibility. No association between the rs3212227 and RA risk was revealed under the same genetic models. Also, a combined two loci model was designed with a referent group - the individuals with the IL12Bpro 1.1 + IL12B UTR AA genotype. We found that the combination of IL12Bpro 1.1 with IL12B 3’ UTR AA genotype is protective factor for RA susceptibility, whereas the carriage of IL12Bpro allele 2 despite hetero- or homozgyosity simultaneously with IL12B 3’ UTR AC/CC genotypes increase the RA risk more than 3-fold. The highest risk for RA susceptibility was established in the carriers of IL12Bpro 1.1 + IL12B 3’ UTR AA genotype. We found that the combination of both loci was significantly associated with a higher production of both IL-12p40 and IL-23 in RA cases, whereas the lowest serum levels were seen in CC genotype carriers. Also, the rs17860508 2.2 genotype, identified as a risk for RA, was associated with a higher serum levels of IL-23 in all patients. Notably, the highest circulating IL-23 levels were observed in carriers of the rs3212227 AA genotype and rs17860508 2.2 genotype compared to the remaining genotypes.

**Conclusion:** IL12Bpro (rs17860508) and 3’ UTR (rs17860508) polymorphisms do confer susceptibility to RA either as an individual or combinatorial effect and might influence the RA occurrence through regulating the expression of the IL-12/IL-23 p40 and production of IL-23.

**Disclosure of Interests:** Mariana Ivanova Goycheva Speakers bureau: Abbvie, Pfizer, UCB, Novartis, Irena Manolova: None declared, Georgi Vasilev: None declared, Lyuba Miteva: None declared, Rumen Stoilov: Speakers bureau: Pfizer, UCB, Abbvie, Pfizer, Amgen, UCB, Novartis, Spaska Stanilova: None declared

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**AB0008**

**CLINICAL AND GENETIC FEATURES OF NON-BACTERIAL OSTEOEMLYTIS IN RUSSIAN FEDERATION**

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**Background:** Chronic non-bacterial osteoelmytitis (CNO) is Data about incidence, prevalence and clinical and genetic features of chronic non-bacterial osteomyelitis (CNO) in Russia is scarce.

**Objectives:** The aim of our study was to evaluate clinical and genetic peculiarities of CNO in Russia.

**Methods:** The diagnosis of CNO was made with criteria, proposed by Jansson [1, 2], after the exclusion of other cause of bone disease. Our cohort consists of three main subtypes: i) early-onset (<5 years) CNO (n=22); ii) CNO, associated with RA (n=20) and iii) not associated (n=59) with rheumatic diseases (RD). Targeted next generation sequencing (NGS) analysis of 302 genes related to primary immune deficiency syndromes and autoinflammatory syndromes was performed.

**Results:** We selected a subgroup of the CNO patients having the following features: 1) early disease onset (<5 years); 2) all children were initially diagnosed as having tuberculosis (TB) due to bone morphology findings (granulomatous, e.g. tuberculosis-like inflammation), but had negative TB culture test; 3) initial treatment with combination of 3-4 anti-MBT drugs during 1-2 years was ineffective, and the patient continued to develop new inflammatory bone foci; 4) patients had very severe clinical (fever and symmetric arthritis) and radiological signs of disease; 5) all patients were from areas with traditionally high prevalence of consanguinity (table).

In the subgroup patients with early onset we performed genetic tests. Rare variants of PI3K genes were detected in 7/22 (32%) patients. Mutations affecting the genes previously associated with CNO were found only in two patients: one of them carried heterozygous variant IL1RN c.170G>T (p.C57F) and another had IL1RN c.517T>C (p.V171A). No mutation of LPN2 was revealed. Other detected variants included one pathogenic MEVF p.M69IV mutation in heterozygous state and number of VUS in CD40LG, NLRP12, CR2, NLRP3, IL12B, PLCG2, SH3BP2, CARD14, IRF8, CASP10 and NFKB1A genes.

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<th>CNO with RD</th>
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**Disclosure of Interests:** M. Koskina, M. Makhova, E. Supsatini, A. Skolenko, V. Zern, E. Iaspova, S. Magomedov, I. Koskina, H. Takayanagi, A. Mushkin, E. Imyanitov: None declared.
Conclusion: We have found the unique regional subtype of CNO with early-onset in North Caucasian region with at least 10 times higher prevalence. We have not yet seen similar patients in other nationalities of Russia. Mutations in known genes were detected only in a minor fraction of CNO patients from Dagestan and Chechnya. This work supported by the Russian Foundation for Basic Research (grant No 18-515-57001) and by Japan Medical Research Foundation (grant No 18mr001).

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Disclosure of Interests: None declared

AB0009
IDENTIFICATION OF A NOVEL POLYMORPHISM OF ERAP1 IN A GROUP OF ITALIAN PATIENTS WITH BEHÇET SYNDROME
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Background: The endoplasmic reticulum aminopeptidase protein 1 gene (ERAP1) was associated to several human diseases, including Behçet syndrome (BS), a multisystemic disorder with unknown etiology. ERAP1 protein is involved in immune response and its role can be influenced by gene single nucleotide variations (SNVs) with an unclear mechanism [1-5].

Objectives: We aim to genotype ERAP1 whole structure searching for SNVs, in 50 consecutive BS patients and 50 sex and ethnically-matched healthy controls (HC) unrelated to each others and to BS patients.

Methods: We used forensic bioinformatics and molecular methodologies. Specific primers for the coverage of all ERAP1 regions were designed using the NCBI Primer Blast tool. Genomic DNA was extracted from whole blood and amplified using in vitro PCR. Good-quality PCR amplicons were directly sequenced using the Mutation Surveyor software and NCBI-Blast Nucleotide on line similarity search tool.

SNV functional impact was predicted using on line PolyPhen-2 [6], while the 3D protein prediction was obtained using 3D Protein server [7].

Results: Our study was performed recruiting an explorative cohort of BS patients from Southern Italy, a population characterized by low disease prevalence. We found a SNV not previously reported in literature in a relatively small group of Italian BS patients. Our data need to be tested in a larger case-control study. In particular, the link between our SNV and the protein stability is to be validated in future functional studies.

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Disclosure of Interests: Nancy Lascaro: None declared, Pietro Leccese: None declared, Salvatore D’Angelo: None declared, Teresa Carbone: None declared, Angela Padula Speakers bureau: Lilly Italia EMS, Giuseppe Martelli: None declared, Maria Carmela Padula: None declared

AB0010
THE ASSOCIATION OF THE LTA AND PTPN22 GENES POLYMORPHIC VARIANTS WITH THE REDUCED IMMUNOGLOBULIN A LEVEL IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS
Liliia Nazarova1, Ksenia Dariiko1, Viktor Malievsky1, Tatiana Viktorova1,2, 1Bashkir State Medical University, Ufa, Russian Federation; 2Institute of Biochemistry and Genetics, Ufa, Russian Federation

Background: Data from a number of studies indicate the presence of a genetic predisposition to the level of immunoglobulins [1]. The aberration in the distribution of serum immunoglobulin A (IgA) concentrations was previously shown in patients with juvenile idiopathic arthritis (JIA) [2].

Objectives: The goal of the study was to determine whether the LTA rs909253 and PTPN22 rs2476601 polymorphic loci variants are associated with the reduced IgA level in JIA patients.

Methods: The study included 234 JIA patients (154 girls and 80 boys) from the Republic of Bashkortostan, Russia. IgA levels were measured in serum by the radial immunodiffusion method and considered reduced when they were less than the lower limit of established age-dependent reference intervals. Genotyping was performed by the real-time PCR method, and statistical processing of the results – using the two-tailed Fisher exact test (p) and the odds ratio (OR) with a 95% confidence interval (CI).

Results: Reduced IgA levels were detected in 10.68% of patients with JIA (n=25), and the majority of them were girls (n=21). There were only four boys with the reduced IgA level, and therefore the isolated analysis was not carried out for them.

The analysis of the LTA rs909253 polymorphic locus in the general JIA group, as well as in girls with JIA, showed that, in the presence of the reduced IgA level, the heterozygous genotype LTA rs909253*AG was significantly less common than in the absence of this IgA level abnormality (the general JIA group: 48.33%, p=0.010, OR=0.286, 95% CI 0.101-0.843, respectively). When studying the PTPN22 rs2476601 polymorphic locus in the general JIA group, the risk markers for the formation of the reduced IgA level were not established (p>0.1). At the same time, it turned out that in girls with JIA with the reduced IgA level, the genotype PTPN22 rs2476601*GG was significantly more common, and the allele PTPN22 rs2476601*A was significantly less common than in girls with JIA with normal or elevated IgA levels (*GG: 95.24% vs. 73.68%, p=0.028, OR=7.143, 95% CI 1.162-76.405; A: 2.38% vs. 14.86%, p=0.025, OR=0.142, 95% CI 0.014-0.865, respectively).

Conclusion: As a result of the study, the association of the LTA rs909253 and PTPN22 rs2476601 polymorphic loci variants with the reduced IgA level in girls with JIA was established.

REFERENCES

Disclosure of Interests: None declared

AB0011 CLINICAL CHARACTERISTICS AND GENETIC EXPRESSION IN A COHORT OF PATIENTS WITH FAMILY MEDITERRANEAN FEVER

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Background: Familial Mediterranean fever (FMF) is the most frequent monogenic periodic fever syndrome and is characterized by recurrent episodes of fever, serositis, arthritis, dermal manifestations and long-term renal complications (arthritis is the most important complication). The genetic mutation of the disease is found in the MEFV gene located on the short arm of chromosome 16 and is inherited in an autosomal recessive manner. It affects the populations of the Mediterranean basin and is diagnosed according to the clinical evaluation.

Objectives: To describe the clinical characteristics of a cohort of patients with FMF and to study the different genetic mutations located in the MEFV gene.

Methods: Retrospective descriptive study of patients treated in our Hospital (2008-2018), with FMF diagnosis and MEFV gene mutation. The data was obtained through the review of medical records.

Results: We included 52 patients (29 men), mean age 41 ± 13 years. The following results have been identified in alleles of the MEFV gene: Non-pathogenic in 34 patients (65%) (p 202Q 73%, p148Q 17%, p. 319K 6% and p339F 3%). Pathogenic in 18 patients (34%) (pr 202Q 22%, eg 148Q 27%, pr 653H 5%, pm 694V 16%, pf 195T 5%).

In 17% of the patients family history was documented. Elevation of acute phase reactants in 41 patients (79%) (C Reactive Protein 75%, Globular sedimentation rate 65%), Echocardiography was performed in 14 patients, with diagnosis of pericardial effusion in 6 of them. Two patients develop renal amyloidosis, one of them (homozgyous for the mutation 148Q) died due to this complication.

54% of patients use colchicine as initial treatment, achieving 50% good response with control of symptoms. 19% undergo treatment with glucocorticoids in 25% of the patients.

Conclusion: The genetic study confirms the diagnosis of FMF, allowing it to be differentiated from other SAs. It also has prognostic value, depending on the mutation detected and if it affects one or both alleles. In our series, the most prevalent symptoms in patients with pathogenic mutations were fever, abdominal pain and arthromyalgia.

Disclosure of Interests: None declared

AB0012 GENETIC EXPRESSION AND CLINICAL MANIFESTATIONS IN A COHORT OF PATIENTS WITH AUTOINFLAMMATORY SYNDROME

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Background: The autoinflammatory syndromes (SAI) encompass a set of diseases in which there is an alteration of the innate immune response, contrary to what occurs in autoimmune diseases, in which the origin is due to pathological changes in the adaptive immune response. These diseases have common symptoms such as fever, skin, joint and lung involvement, among others, so they can be difficult to diagnose and classify.

Objectives: To study the clinical and genetic characteristics of a cohort of patients with autoinflammatory syndromes (SAI).

Methods: Retrospective descriptive study of patients with SAI diagnosed in adulthood. The data was obtained through the review of medical records.

We have included data from patients who present a positive genetic study, both for described and pathogenic mutations, as well as nonpathogenic mutations, but which present a clinical picture according to this pathology.

Results: We included 80 patients (52 men), mean age 41 ± 13 years. Fourteen patients (17.5%) presented family history. Summary of diagnoses (TABLE 1) and associated mutations by order of frequency (TABLE 2).

Disclosure of Interests: None declared

AB0013 GENOMIC PROFILING OF INFLAMMATION-RELATED GENES IN NEURO-BEHÇET SYNDROME: A PRELIMINARY ITALIAN STUDY

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Background: Behçet Syndrome (BS) is a chronic vasculitis characterized by a wide spectrum of clinical manifestations, including the rare nervous system

The most frequent clinical manifestations: Articulargias 77.5%, followed by high fever (> 39) 73.8%, myalgias 72.5%, abdominal pain 56.3%, exanthema 47.5%, arthritis 35%, pericarditis 28.8%, headache 21.3%, pharyngitis 21.3% and canker sores 20%. The onset of the picture was a fever in 59 patients (73.8%) accompanied by cutaneous manifestations in 51.2% of the cases, with the rest of the symptoms being variable depending on the study.

The most affected joints were: Metacarpophalangeal in 18 patients (22.8%), ankles in 15 patients (18.8%), proximal interphalangeal in 8 patients (10%), hips in 2 patients (2.5%) and knees in 2 patients (2.5%).

Elevated acute phase reactants were found in 53 patients (66.8%), with high sedimentation velocity in 56.3% and C reactive protein in 63.3%.

The initial treatment was based on colchicine in 45 of the cases, needing to add corticosteroids in 25% of the patients. 10.1% required drugs modifying the disease, being the most frequent methotrexate (74.25%).

Sixteen patients (20%) required biological therapy, being the most used anakinra (12.5%), followed by etanercept (12.5%) and canakinumab (2.5%).

In the period of time analyzed, 3 patients died due to causes unrelated to the SIA.

Conclusion: The results obtained are consistent with what exists in the medical literature. The most frequent SAI in our center is the family Mediterranean fever, followed by the TRAPS. The most frequent mutation was the MEFV (P.R202Q), followed by the MEFV (p.E148Q).

- With our study we want to reflect the variety of symptoms presented by patients with SAI diagnosed in adulthood. Despite the great variability, the most frequent symptoms are arthralgia, fever greater than 39 °C and myalgias.
- The most used treatment in this type of patients is colchicine and respond to this positively in most cases.
inflammation-related genes.

Methods: NBS patients were extracted from our database and retrospectively studied. Molecular characterization was performed for a subset of 20 NBS patients and 42 sex-matched healthy controls (HC) via: a) bioinformatics consulta-
tion for SNPs selection and primer design; b) SNPs genotyping: DNA extraction, PCR amplification, direct sequencing; c) DNA variant analysis using similarity search tool and specific software. In a second phase of analysis, a group of 30 BS patients without neurological involvement (no-NBS) was also genotyped. The results of this study were used to calculate the strength of BS association for each genotype.

Results: NBS patients subset was formed by 14 males and 6 females with mean age equal to 44.20 (±10.73) years. Six SNPs were considered eligible for molecular analysis and genotyped. Our results underlined the major role of age in the BS disease process. The results of this study were used to calculate the strength of BS association for each genotype.

Conclusions: The findings of this study support the association of SNPs in the MIR146a with BS, and the use of bioinformatics tools for SNP selection and primer design. These findings could be useful for future studies on the genetic basis of BS and its subtypes.

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Disclosure of Interests: Maria Carmela Padula: None declared, Pietro Lecce: None declared, Nancy Lascaro: None declared, Teresa Carbone: None declared, Antonina Rita Limongi: None declared, Rosa Paola Radice: None declared, Angela Padula Speakers bureau: Lilly Italia EMS, Salvatore D’Angelo: None declared, Giuseppe Martelli: None declared


A MIR146A POLYMORPHISM IS ASSOCIATED WITH ANTI-CARBOXYLATED PROTEIN ANTIBODIES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: (SLE) is a chronic autoimmune disease with a complex pathogenesis in which genes and environmental factors interact leading to a protein clinical picture. Joint involvement is one of the most common manifestations in SLE patients, with a prevalence ranging from 69 to 95%. This feature significantly influences the patients’ quality of life, possibly leading to disability and impaired functional performance in daily activities. Identification of prognostic biomarkers, able to identify patients at risk to develop this more aggressive phenotype, is mandatory. Autoantibodies associated with inflammatory arthritis, such as Rheumatoid Arthritis (RA), have been shown to play a role also in SLE arthritis. For instance, ACPA can be found in approximately 16% of SLE patients and, recently, it was demonstrated that anti-carbamylated proteins antibodies (anti-CarP) can be identified in up to 28.3% of SLE patients (1).

Objectives: Thus, our aim was to analyze previously identified loci associated with SLE in a cohort of SLE patients to evaluate their influence on autoantibody production.

Methods: We recruited 52 Italian SLE patients. A panel of 34 SNPs in 19 genes involved in immune response, autophagy and inflammation, was selected. SNPs genotyping was performed by allelic discrimination assay by TaqMan assays (Applied Biosystems, Foster City, CA, USA) and ABI PRISM 7000. The main clinical/laboratory features (including injury index and disease activity) were collected on an electronic platform. The presence of Rheumatoid Factor (RF), ACPA, and anti-CarP antibodies was investigated. All autoantibody assays were done in duplicate, commercial enzyme-linked immunosorbent assay (ELISA) kits were used and the results were evaluated according to the manufacturers’ instructions. Detailed methods are described in (1).

Results: Clinical and demographic data of patients are described in table 1. The variant allele of rs2910164 (MIR146a) (P=0.03) was significantly associated with presence of anti-CarP antibodies in SLE. Specifically, patients carrying the C allele of MIR146a were more likely to have anti-CarP antibodies (P=0.01, OR 5.018, 95% CI 1.414-17.811). Among the clinical and laboratory features, the same polymorphism was associated with presence of arthritis in clinical history (P=0.02), and with anti-dsDNA positivity (P=0.025). In a multilocus logistic regression analysis, MIR146A was independently associated with anti-CarP (P=0.017, Exp(B)=5.433, 95%CI 1.345-21.944).

Conclusion: Carbamylatin is a non-enzymatic process consisting in the addition of a cyanate group on self-proteins determining a modification in the tertiary structure. This change causes the generation of new epitopes and the consequent production of autoantibodies. This study supports that anti-CarP production is genetically driven. Indeed, MIR146a expression is altered in SLE and has been linked with autoantibody production in lupus-prone mice models. Probably, the higher IFNα levels observed in patients carrying the C allele can be responsible for such higher autoantibody production.

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microrna-155 expression in behçet’s disease

nadeen saad3,3,3.

Furthermore, aberrant expression of miR-155 has been reported in human autoimmunity in germinal centers, and greatly affects antibodies and cytokines production. The deletion of miRNA-155 impairs T and B cell differentiation in germinal centers, and greatly affects antibodies and cytokines production. Recent miRNA deletion studies have revealed a central role in the regulation of gene expression in a variety of manners, including translational repression, or more messenger RNA (mRNA) molecules, and their main function is to downregulate gene expression in a variety of manners, including translational repression, miRNA cleavage, and deadenylation. Recent miRNA deletion studies have revealed a central role in the regulation of the immune response. The deletion of miR-155 impairs T and B cell differentiation in germinal centers, and greatly affects antibodies and cytokines production. Furthermore, aberrant expression of miR-155 has been reported in human autoimmune disorders such as rheumatoid arthritis and systemic lupus erythematosus.[1] Whether miR-155 plays a role in the pathogenesis of Behçet’s Disease is not yet known and is therefore the subject of this study.

Objectives: The aim of this work is to study the expression of microRNA-155 as a molecular biomarker in Behçet’s disease.

Methods: Thirty patients with Behçet’s disease and 15 healthy matched controls were included. Patients fulfilled the International Study Group (ISG) diagnostic Criteria of Behçet’s Disease. Exclusion Criteria included other types of primary or secondary vasculitis; reactive arthritis; inflammatory bowel disease; current or past history of cancer, chemotherapy or radiotherapy; current infection; long standing diabetes mellitus; and hypertension. Total RNA, including miRNAs isolation, from peripheral blood mononuclear cells (PBMCs) was extracted by using miRNeasy Mini Kit (QIAGEN, cat. no. 217004). This was followed by reverse transcription into complementary DNA (cDNA). Expression of microRNA-155 was carried out using quantitative real time polymerase chain reaction (RQ_PCR). Relative expression of microRNA155 was calculated using 2−ΔΔct formula. Where ct (ct miRNA− ct miRNA control) and Ct is the fractional cycle number at which the fluorescence passes the fixed threshold.

Results: Our results showed a significantly decreased expression of miR-155 in peripheral blood mononuclear cells (PBMCs) of Behçet’s disease patients with active disease compared to that in patients with inactive disease as well as healthy control (p=0.026).

The level of miR-155 showed a significant positive correlation with patients’ age (p=0.042), and significant negative correlation with BDCAF activity score of the disease (p=0.034), and platelets count (p=0.011) (Table1).

Conclusion: Downregulation of miR-155 expression in active BD patients may be used as a molecular biomarker for increasing activity and severity of Behçet’s disease. This pathway could be a potential target for a new therapeutic strategy.

References:

Disclosure of interests: Carlo Perricone Speakers bureau: BMS; Lilly, Celgene, Sanofi, Cinzia Cicciacci: None declared, Fulvia Cecarelli: None declared, Ilaria Leccese: None declared, Giuseppe Mettola: None declared, Sara Rufini: None declared, Cristina Politi: None declared, Andrea Latin: None declared, Giuseppe Novelli: None declared, cristiano alessandri: None declared, francesca spinelli: None declared, Carlo Perricone Speakers bureau: BMS; Lilly, Celgene, Sanofi, Cinzia Cicciacci: None declared, Fulvia Cecarelli: None declared, Ilaria Leccese: None declared, Giuseppe Mettola: None declared, Sara Rufini: None declared, Cristina Politi: None declared, Andrea Latin: None declared, Giuseppe Novelli: None declared, cristiano alessandri: None declared, francesca spinelli: None declared, Carlo Perricone Speakers bureau: BMS; Lilly, Celgene, Sanofi, Cinzia Cicciacci: None declared, Fulvia Cecarelli: None declared, Ilaria Leccese: None declared, Giuseppe Mettola: None declared, Sara Rufini: None declared, Cristina Politi: None declared, Andrea Latin: None declared, Giuseppe Novelli: None declared, cristiano alessandri: None declared, francesca spinelli: None declared.

AB0016 combined genome-wide association and gene-expression meta-analysis identifies novel psoriasis genes

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Background: Psoriasis (Ps) is a common, inflammatory disorder affecting skin, joints and associated connective tissue, with significant genetic underpinnings. Multiple genome-wide association studies (GWAS) have been conducted with identification of several Ps loci. However, these only explain about a third of Ps genetic risk indicating that additional loci of modest effect remain to be discovered (1).

Objectives: Identify novel psoriasis genes that have functional consequences for psoriasis by altered gene expression

Methods: Association clustering methods such as gene- and locus-based tests are more powerful than single variant analysis for identifying modest genetic effects (2, 3). Here, a dbGAP GWAS dataset (4) for Ps (pha002855: 1348 Ps cases and 1368 controls, genotyped for 448K SNPs) was analyzed using the locus-based algorithm, OASIS (3), to identify 13 highly significant loci other than the HLA-C locus. In these loci 50 genes were identified using SNIPPER, which were then subjected to gene expression analysis in three Ps GEO datasets. Results: This genetic and functional analysis identified a total of 18 genes that were significantly associated and had altered expression in psoriasis skin. The most significant of these were two genes that were two-fold upregulated in Ps, IL12B (P=3x10−11) and TFCGB3 (P=3x10−12) and two genes that were repressed
Comparative analysis of the altered peripheral replicative study of GWAS-associated transcriptomic characterization of single

**Methods:**

To compare the expression levels of miR-146a and miR-155 in the whole PB of SLE samples showed a possibility for the local pathological process and thus to differentiate patients from HCs. The expression of both miRNAs in whole PB of SLE patients with OA were over-expressed in 25 (62.5%) and levels of miR-155 were increased in 20 (50.0%) of the patients (p<0.05).

**Conclusion:** Although miR-146a and miR-155 are involved in key signaling pathways in the pathogenesis of RA their whole PB expression could not fully reflect the local pathological process and thus to differentiate patients from HCs. The expression of both miRNAs in whole PB of SLE samples showed a possibility for discriminating patients from HCs. Further analysis with larger sets is needed to confirm if altered systemic miRNA expression levels could be used in the clinical practice as disease biomarkers.

**Disclosure of Interests:** Mohammad Saeed Shareholder of: Partner at ImmunoCure - laboratory, which performs Autoimmune antibody testing, Grant/research support from: Participation in EULAR 2019 Meeting is sponsored by High-Q Pharma Pak


**AB0018**

**TRANSCRIPTOMIC CHARACTERIZATION OF SINGLE PATHOGENIC MEMORY B CELLS IN RHEUMATOID ARTHRITIS**


**Background:** Autoantigen-specific B lymphocytes are crucial players in the development of rheumatoid arthritis (RA). Despite the fact that ACPA+ autoreactive memory B cells have been observed in the majority of RA patients for a long time, their properties still remain enigmatic.

**Objectives:** In this study, we aimed to reveal transcriptomic nature of single pathogenic memory B cells from RA patients.

**Results:** Single-cell full-length RNAseq data was generated from ACPA+ and control memory B cells from 7 human donors with established rheumatoid arthritis and subjected to transcriptome analyses as well as B cell receptor (BCR) assembly.

**Conclusions:** Transcriptome and BCR data was successfully generated from the majority of the sequenced cells. The success rate depended on chosen sequencing parameters as well as on a BCR assembling algorithm that was used. We observed expression of genes defining memory B cell population in our data as well as pathways crucial for their function.


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**AB0019**

**REPLICATIVE STUDY OF GWAS-ASSOCIATED CANDIDATE GENE LOCI IN PATIENTS WITH OSTEOARTHRITIS FROM THE BASHKORTOSTAN REPUBLIC**

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**Background:** Osteoarthritis (OA) is one of the most common joint diseases and a global socially significant problem. Currently, new methods of early diagnosis of the disease are being developed, before the development of destructive processes in various tissues of the joint. The leading role in determining the pathophysiology of OA is given to the identification of genetic and epigenetic mechanisms.

**Objectives:** The main goal of the study was replicative analysis of the associations of loci associated with OA according to data on genome-wide analysis of associations (GWAS) located near the DOTT1L, ALDH1A, GNL3, GLTB8D1, ASTN2, FILIP1, SENP6, NCOA3, DWA, CHA11 genes with various localization of OA.

**Methods:** DNA samples from 410 women were used (mean age 45.45 ± 2.35). Patients with OA was carried out in accordance with the criteria of the American College of Rheumatology (1990), the debut of the disease before the age of 55 years and radiographic confirmation. For genotyping, PCR–RFLP analysis using KASPR technology was used. As a calculation tool, MS Office Excel 2007 (Microsoft), Statistica v.6.2 (StatSoft), SPSS v.13 (SPSS Inc) software packages are used.

**Results:** We conducted replicative analysis of the 12 loci that were the most significantly associated with OA in the results of GWAS study, among which rs12887244 and rs2302601 (DOTT1L), rs4836732 (ASTN2), rs9305591 (FILIP1 &

**Disclosure of Interests:** The study was supported by Grant 60/2013 and Grant 51/ 2014 and funded by Medical University-Sofia.

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**AB0017**

**COMPARISON BETWEEN THE ALTERED PERIPHERAL BLOOD miRNA EXPRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS**

Pavlina Shumateva, Darina Chakalakova, Radka Kanavova, Zlatimir Kolarov, Simeon Morov.

**Background:** MicroRNAs (miRNAs) are a class of small, non-coding RNAs that negatively regulate gene expression at posttranscriptional level. Altered miRNA expression in the circulation has been described in inflammatory joint diseases such as rheumatoid arthritis (RA) as well as in systemic rheumatic diseases, such as systemic lupus erythematosus (SLE). miR-146a and miR-155 have been found to regulate key signaling pathways involved in the pathogenesis of RA and SLE [1-2].

**Objectives:** To compare the expression levels of miR-146a and miR-155 in peripheral blood (PB) from RA and SLE patients in regard to their use as disease biomarkers.

**Methods:** 63 RA patients and 40 SLE were included in the study. The expression levels of miR-146a and miR-155 in whole PB were determined by qPCR (Sybr-Green technology) and compared to healthy controls (HCs). Relative changes of gene expression levels of the studied miRNAs were calculated by 2−ΔΔCT method. SPSS was used for statistical analysis.

**Results:** 29 (46.03%) of the RA patients showed overexpression of miR-146a in the PB when compared to HCs, but the levels were not statistically significant to differentiate patients from HCs (p=0.365). 34 (53.97%) of the RA patients did not show a statistically significant expression of miR-155 in the PB when compared to HCs and PB expression of miR-155 couldn’t be used for differentiating RA from HCs (p=0.074). In the group of SLE patients the PB levels of miR-146a were over-expressed in 25 (62.5%) and levels of miR-155 were increased in 20 (50.0%) of the patients (p<0.05).

**Conclusion:** This combined genetic and functional meta-analysis elucidated novel genes, functional networks and pathways for psoriasis. These results will lead to important insights into the immunopathogenesis and treatment of psoriasis.

**REFERENCES**


**Disclosure of Interests:** Mohammad Saeed Shareholder of: Partner at ImmunoCure - laboratory, which performs Autoimmune antibody testing, Grant/research support from: Participation in EULAR 2019 Meeting is sponsored by High-Q Pharma Pak


**AB0019**

**REPLICATIVE STUDY OF GWAS-ASSOCIATED CANDIDATE GENE LOCI IN PATIENTS WITH OSTEOARTHRITIS FROM THE BASHKORTOSTAN REPUBLIC**

Anton Tyurin, Daria Shapovalova, Luitza Lukmanova, Rashit Davletshin, Rita Khusanova, 1Bashkir State Medical University, Ufa, Russian Federation; 2Institute of Biochemistry and Genetics, Ufa Scientific Center, Ufa, Russian Federation

**Background:** Osteoarthritis (OA) is one of the most common joint diseases and a global socially significant problem. Currently, new methods of early diagnosis of the disease are being developed, before the development of destructive processes in various tissues of the joint. The leading role in determining the pathophysiology of OA is given to the identification of genetic and epigenetic mechanisms.

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**Disclosure of Interests:** The study was supported by Grant 60/2013 and Grant 51/ 2014 and funded by Medical University-Sofia.

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Adaptive immunity (T cells and B cells) in rheumatic diseases

Table 1. Heritability estimation before and after imputation, including and excluding MHC SNPs

<table>
<thead>
<tr>
<th>Test</th>
<th>PsA</th>
<th>PsC</th>
<th>PsV</th>
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<td>Imp</td>
<td>h2 (sd)</td>
<td>Imp</td>
</tr>
<tr>
<td>PsA</td>
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<td>0.48 (0.09)</td>
<td>0.81 (0.07)</td>
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<tr>
<td>PsC</td>
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<td>PsV</td>
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<td>0.20 (0.03)</td>
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<td>LDAK (all SNPs)</td>
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<td>0.48</td>
<td>0.81</td>
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<tr>
<td>LDAK (non MHC)</td>
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<td>SNPS</td>
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<td>SNPS</td>
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Conclusion: SNP based heritability estimates suggest greater heritability for PsC as compared to PsA. Common environmental factors may need to be considered to account for the strong recurrence rate of PsA over psoriasis among first degree relatives reported in previous epidemiological studies, as this finding is not noted from large SNP based association studies.

REFERENCES
Adaptive immunity (T cells and B cells) in rheumatic diseases

**AB0021 IMMUNOGENICITY OF TNF ALPHA ANTAGONISTS IN RHEUMATIC INFLAMMATORY DISEASES: IMPACT ON CLINICAL RESPONSE**

Selma Bouden1, Lisa Laaadhir2, Imen Ayadi3, Mariam Sallemi1, Rabha hospital, tunis, Tunisia; 2rabha hospital, tunis, Tunisia

**Background:** One of the mechanisms implicated in the loss of response to TNF alpha antagonists in rheumatic inflammatory diseases is the formation of antibodies against these drugs (anti-drug antibodies: ADAb).

**Objectives:** The objective of our study was to determine the incidence of ADAb anti Infliximab (IFX) and anti Adalimumab (ADA) and to evaluate the therapeutic impact of the presence of ADAb, the rate of ADAbr and trough serum concentration of the drug at the time of sampling and six months later.

**Methods:** A cross-sectional study was conducted including patients with rheumatoid arthritis (RA) or spondyloarthritides (SpA) treated with IFX or ADA as a first biotherapy for at least six months. ADAb and trough levels were measured. The evaluation of the therapeutic response was made at the time of sampling and six months later.

**Results:** Fifty patients were included (17 RA and 33 SpA). ADAb were positive in 39% of SpA and 35% of RA. They were positive in 40% of cases for IFX and 25% for ADA. The presence of ADAb was negatively related to the trough levels of IFX and ADA during RA (p=0.01 and p<0.0001) and SpA (p=0.01) and p<0.0001). For the two pathologies, no impact of the presence of ADAb, the rate of ADAbr or the trough levels was noted on the therapeutic response at the time of sampling. However, the presence of ADAb was related to a higher activity of SpA six months after the sampling (p=0.05). Factors that were related to ADAb formation were a high BMI in RA (p=0.05) and a longer duration of evolution of RA (p=0.03).

**Conclusion:** The presence of ADAb and low trough levels seem to not affect the therapeutic response in patients on TNF alpha antagonists. Other tracks than immunogenicity should be investigated to explain the loss of response to these biotherapies.

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.6333

**AB0022 STUDY OF FUNCTIONAL ORIENTATION OF B CELLS IN PHYSIOLOGY AND SJOEGREN’S SYNDROME**

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**Background:** Sjögren’s syndrome (SS) is a chronic systemic autoimmune disease, characterized by mouth and eye dryness, due to irreversible destruction of glandular tissue by infiltrated lymphocytes. It is now well established that B cells play a key role in the physiopathology of SS. Indeed, B cells exhibit various signs of activation and produce excessive amounts of pro-inflammatory cytokines and immunoglobulins (Ig), especially IgG type-antibodies (Abs) (Kroese et al.2014). Currently, it is suggested that the interleukin (IL)-21 (Wang et al., 2018) and immunoglobulins (Ig), especially IgG type-antibodies (Abs) (Kroese et al.,2014). Currently, it is suggested that the interleukin (IL)-21 (Wang et al., 2018) promote the generation of autoreactive IgG-producing B cells. Moreover, this will also enable a further understanding of the impact of ADAb, the rate of ADAbr and trough serum concentration of the drug at the time of sampling and six months later. Conclusions: First results on HC suggest that switched memory B cells differentiate into IgG and IgA-secreting plasmablasts (PB), when stimulated in a TI manner. Moreover, this will also enable a further understanding of the heterogeneity of the distinct effector B cells and their involvement in SS pathogenesis.

**REFERENCES**


**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.6850

**AB0023 IMPACT OF METABOLIC CHANGES DURING AGING ON HUMAN EX VIVO NAIVE AND MEMORY CD4+ T CELL FUNCTION**

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**Background:** Age-related dysfunction in immune cells (immuno-senescence), such as T cell dysfunction, may contribute to the development of rheumatoid arthritis (RA). The aged people, senescent T cells tend to produce low amounts of pro-inflammatory cytokines leading to low-grade inflammation. However, cellular metabolism modulates effector functions such as cytokine production and proliferation in T cells by providing energy and building blocks. Metabolically, naïve and memory CD4+ T cells are relatively quiescent immune cells. Currently, the metabolic phenotype of naïve and memory CD4+ T cells and how metabolism affects functions of naïve and memory CD4+ T cells in aged people are not well understood.

**Objectives:** Therefore, we analysed the differences in the metabolic phenotype of peripheral naïve and memory CD4+ T cells in young and aged healthy donors to explore fundamental processes of immune-aging in the pathogenesis of RA.

**Methods:** Naïve and memory CD4+ T cells were isolated from PBMCs of young donors (18-35 years) and old donors (>50 years) by using MACS® technology. Purification of isolated cell fractions was assessed by flow cytometry. Ex vivo naïve and memory CD4+ T cells were analysed by Seahorse® Technology to determine proton efflux rate (PER) as a measure of glycolysis (glycPER) and oxygen consumption rate (OCR) as a measure of mitochondrial respiration (mitoOCR). Cyto- kine expression and secretion were measured by flow cytometry and multiplex array. Finally, TCR-stimulated memory CD4+ T cell proliferation was determined using CSFE and Ki-67 after 3 and 4 days by flow cytometry.

**Results:** We included 9 young (20-32 years, 25.0±3.4 years) and 9 aged gender-matched donors (52-67 years, 57.8±5.7 years) for PER and OCR measurement. Memory CD4+ T cells demonstrated higher basal glycolysis, compensatory glycolysis as well as basal OCR and spare respiratory capacity than naïve CD4+ T cells. Memory CD4+ T cells from young donors had higher basal glycolysis, and compensatory glycolysis than aged donors, but lower ratio of basal mitoOCR/glycPER. Although we did not observe differences in intercellular cytokine expression measured by flow cytometry after 5h stimulation of memory CD4+ T cells, we determined a significant higher amount of secreted IL-6, IL-9, IP-10, monocyte chemotactic and activating factor in the supernatant of memory CD4+ T cells from young donors as compared to those from young donors. Cell division index, proliferation index, percentage of divided cell, and Ki-67 expression after 3 and 4 days of stimulation showed no statistical differences between both groups.

**Conclusion:** Here, we demonstrate a higher basal glycolysis, basal OCR, mitochondrial and glycolytic capacity of human ex vivo memory CD4+ T cells as compared to naïve T cells. A decrease of basal glycolysis, compensatory glycolysis in memory CD4+ T cells of aged people which results in an enhanced cytokine expression can be assumed to culminate in T cell dysfunction leading to the development of RA during aging.

**Acknowledgement:** The work of Yuling Chen was funded by the Chinese Scholarship Council (201606320324). The work of Timo Gaber was funded by the Deutscher Forschungsgemeinschaft (35314284).

**Disclosure of Interests:** Yuling Chen: None declared, Peit Löwe: None declared, Hao Wu: None declared, Frank Buttgeril: None declared, Timo Gaber: Grant/research support from: Pfizer.
WHOLE BLOOD ENDOGENOUS RETROELEMENT ACTIVITY ASSOCIATES WITH ANTI-CCP TITRES IN EARLY DRUG NAÏVE RA AND IS PREFERENTIALLY INCREASED IN CD5- AND NAÏVE B CELLS

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Background: Endogenous retroelements of which LINE1, Alu and LTR are the main subsets, constitute approximately 50% of the human genome. They are mobile elements derived from the historical genomic integration of retroviruses. Whilst most are inactive, some expression of viral mRNA and subsequent protein is retained. This theoretically could promote immune activation, for example by triggering type I interferon (IFN-I) production and notably Alu has been identified as a target for R06 autoantibody. Retroelements may therefore provide a mechanism whereby tolerance is breached in autoimmune disease.

Objectives: To examine the potential clinical impact of retroelement activity in early drug naïve rheumatoid arthritis (eRA). This stage of disease was chosen to minimise therapeutic confounding.

Methods: Drug-naïve eRA and healthy controls (HC) were recruited and clinical characteristics including disease activity, immunoglobulins (IgA, IgG, IgM), ESR, CRP, rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) auto-antibody titres documented. Serum cytokines (IFN-γ, IL-6, IL-12 p70, TNF-α, IL-1β, IL-2, IL-13, IL-10) were also measured. Whole blood (WB) RNA was extracted and expression of an IFN-I gene signature (IGS: MXa, IFIH1, OAS1, ISG15, IFI44L) and LINE1 5’UTR activity quantified using RT-PCR. In addition anti-CCP and RF positive (double seropositive) eRA peripheral blood plasmacytoid dendritic cells (pDCs), myeloid DCs, CD19+ B cells, monocytes, CD4+ and CD8+ T cells were flow cytometrically sorted. CD19+ B cell subsets were further sorted from double seropositive eRA and disease controls (early, drug naïve, psoriatic arthritis, PsA) into CD5- B cells, age associated B cells (CD19+CD41+CD201), naïve (IgD’CD27’) and memory (IgD’CD27’) B cells. Cell specific expression of LINE1, Alu and LTR was quantified by NanoString nCounter and analysed using R Core Team (2013). WB RNA analysis for continuous and categorical variables included linear regression and Mann-Whitney U tests respectively (GraphPad Prism, significance p<0.05).

Results: WB LINE1 expression for 56 eRA patients (median age 58 [range 30-87], male/female 3:4, 77% seropositive for either RF or anti-CCP) and 23 HC (median age 39 [range 23-62], male/female 1:1) was obtained. WB LINE1 activity was not associated with age or gender and was comparable between cohorts. However in eRA a unique, robust positive association between WB LINE1 and anti-CCP titres was identified (see table and figure). Additionally, when comparing eRA circulating cell subsets, B cells had the highest expression of Alu, LINE1 and LTR (n=8, median age 56 [range 49-64], male/female 1:1). Furthermore, there was significantly increased expression of all retroelement classes in eRA CD5- and naïve B cells compared with PsA (n=4, male/female 1:1 and median age 62 for both with age range [63-78] and [60-80] respectively).

Conclusion: This is the first time peripheral blood retroelement activity has been examined in both HC and RA. It highlights intriguing, IFN-I independent, associations between anti-CCP titres, autoantibody producing B cells (CD5-) and retroelements. Whether such retroelements may play a more extensive role in autoantibody generation and may ultimately provide a novel target in the treatment or prevention of RA.


AB0025 ATYPICAL, ACTIVATED MEMORY B CELLS ARE EXPANDED IN THE SYNOVIAL FLUID OF PATIENTS WITH OLG0ARTHRITIS COMPARISON TO PERIPHERAL B CELLS

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Background: Juvenile idiopathic arthritis (JIA) is an umbrella term used to describe a group of chronic arthritides of unknown cause in children and adolescents. It is the most common rheumatic disease in children and young people under the age of 16, and if left untreated can cause significant morbidity. Oligoarthritis is the most common of the seven different JIA subtypes and is characterized directly to Newcastle University., Catharien Hilken: None declared, Ruchi Shukla: None declared. Disclosure of Interests: Andrew Skelton: None declared, Arthur Pratt Grant/research support from: Pfizer, Research support from: Pfizer, Consultant for: Abbvie, Pfizer, Roche, Galvani, Merck, Gilead, Eli Lilly, Amgen, Janssen, Celltrion, NAPP, Consultant for: Abbvie, Pfizer, Roche, Galvani, Merck, Gilead, Eli Lilly, Amgen, Janssen, Celltrion, NAPP, Speakers bureau: Abbvie, Pfizer, Eli Lilly, Speakers bureau: Abbvie, Pfizer, Eli Lilly.

Disclosure of Interests: None declared


Disclosure of Interests: None declared


Scientific Abstracts

Disclosure of Interests: None declared


Disclosure of Interests: None declared

Disclosure of Interests: None declared

Disclosure of Interests: None declared
LARGE JOINT ARTHRITIS IN SYSTEMIC LUPUS ERYTHEMATOSUS IS CHARACTERISED BY T CELL RATHER THAN B CELL ACUMULATION

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Background: Musculoskeletal involvement is a common clinical feature of systemic lupus erythematosus (SLE), that can present either at the onset or in later disease course. SLE related arthritis is usually non-erosive and non-deforming as opposed to rheumatoid arthritis (RA). While RA synovial pathologies has been extensively studied, little is known about the pathophysiology of arthritis in SLE.

Objectives: to explore the cellular compartments in synovial fluid of SLE patients with arthritic manifestations.

Methods: paired synovial fluid (SF) samples from large joint aspiration and peripheral blood samples (PBMC) obtained at the same time point from five SLE patients were analyzed by microlucor flow cytometry. The patients fulfilled the ACR 1982 classification criteria for SLE [1]. Clinical records were reviewed in order to exclude the presence of comorbidities such osteoarthritis or overlap with RA.

There were three different lineage-specific panels for B cells, T cells (cytotoxic and helper) were developed.

Results: The overall frequency of CD4+ and CD8+ T cells was similar across the SF and PBMC samples. Among the CD4+ T cells, those co-expressingCCR4 showed a much higher frequency in the SF compared to the peripheral blood in 4 out of 5 patients (mean percentage 8.9±7.0% vs 2±1.6%, p>ns). In addition, in 4 out of 5 patients we could identify an increased frequency of CD4+ expressing CCR4+, a marker for Th17 cells in SF as compared to PBMC (mean percentage 35±16.6% vs 12.7±8.9%, respectively, p>ns). In all patients, a higher frequency of EOMES+ Granzyme A + CD4+ T cells was observed in SF when compared to PBMC (9±2±5% vs 4.5±2.5%, p>0.03). Moreover, in all patients, we could observe a higher proportion of regulatory T cells (FOXP3+/CD25+) in the SF (21.5±15.4% vs 8.4±7.8%, p>ns). No relevant differences were observed in the Th1 compartment (CXCR3+), CD19+ cells (B-lymphocytes) were scarcely present in the SF of SLE patients as opposed to the peripheral blood.

Conclusion: Although SLE is usually considered to be a B cell driven disease, its cellular component seems largely to be a T cell driven disease, its cellular component seems largely to be a T cell driven disease.

REFERENCES

Disclosure of Interests: None declared

ARE RHEUMATOID FACTORS AND ANTINUCLEAR ANTIBODIES ASSOCIATED WITH FRAILITY IN ELDERLY TUNISIAN POPULATION?

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Background: An emerging concept is the ‘frailty syndrome’, which may explain diversity in clinical outcomes in the elderly population.

Objectives: The aim of the study was to investigate the possible association between antinuclear autoantibodies, different isotypes of Rheumatoid Factor and frailty in aged individuals.

Methods: Using a validated set of frailty criteria (the SEGA tool), we conducted a cross sectional observational study to evaluate the prevalence of antinuclear antibodies (ANA) (assessed by IFI) and different isotypes of Rheumatoid Factor (RF) (determined by ELISA) in 89 Tunisian individuals aged at least 65 years living in the community. The study population were categorized into three groups: severely frail (n=29), frail (n=31), and non frail (n=29) according to the validated and widely utilized frailty criteria (SEGA tool).

Results: ANA were detected in 36 of the participants. No significant difference was observed between the three groups. Immunofluorescence patterns observed were speckled in 34%, homogeneous in 3.3%, and nucleolar in 3.3% of individuals. Nineteen of the severely frail patients had positive IgA RF compared to 11 from the frail group and 6 only from the non-frail group (p=0.02), RF isotypes showed low correlations with other features. Indeed, the IgG RF was correlated with the age (r= -0.22, p<0.03), the C-Reactive Protein level (r= -0.45, p<0.01), and the nutritional state of the patients assessed by the MNA score (r=0.27, p<0.009). The IgG RF was correlated with hemoglobin (r= 0.22, p<0.03) and creatinin (r= -0.36, p<0.01) levels.

Conclusion: Our study showed no significant difference in the frequency of ANA amongst nonfrail, frail, and frail aged individuals, whereas RF isotypes were found to be slightly correlated with several biological parameters and other features.

REFERENCES

Disclosure of Interests: None declared

SELECTIVE DEPLETION OF PLASMA CELLS IN VIVO BASED ON SPECIFICITY OF SECRETED ANTIBODIES

Qingyu Cheng1,2, Andreas Petz1, Bimba F. Hoyer3, Laleh Khodadadi1,2, Tobias Alexander1,2, Gerd Rüdiger Burmester1, Andreas Radbruch1, Falk Hiepe1,2.


Background: Antibody-mediated diseases like allergies and chronic-inflammator y autoimmune diseases affect more than 10% of the human population, and for most, no cure is available. This is particularly true when pathogenic antibodies are secreted by long-lived plasma cells generated early in pathogenesis, which are refractory to conventional therapies. Therapeutic concepts for the generic ablation of plasma cells are currently being tested in clinical trials. These concepts target both plasma cells secreting pathogenic antibodies and those providing protective antibodies, i.e., humoral immunity. Efficient ablation of pathogenic plasma cells is inevitably accompanied by immunodeficiency and increased susceptibility to infection.

Objectives: We studied the use of an antigen-antibody conjugate to label plasma cell in vivo with the antigen and selectively ablate those secrete antibodies specific for the antigen.

Methods: Balb/c mice were immunized with ovalbumin (OVA) and chicken gamma globulin (CGG), which resulted in the generation of OVA and CGG-specific long-lived plasma cells in the bone marrow. These mice were treated by a single intraperitoneal injection of a conjugate consisting of OVA and a monoclonal anti-CD138 antibody. The effect of this treatment on the long-lived plasma cells and antibody levels was analyzed by flow cytometry and ELISA, respectively.

Results: The single injection of an OVA-anti-CD138 conjugate resulted in a significant depletion of OVA-specific plasma cells while CGG-specific plasma cells were not affected. The selective depletion of OVA-specific plasma cells also led to stable reduction of serum anti-OVA antibody levels; circulating anti-CGG antibody levels decreased by 90%.

Conclusion: The cellular antigen-affinity matrix strategy described here for the ablation of plasma cells in vivo according to the specificity of their antibodies enables a unique causative therapeutic approach in established antibody-mediated diseases without impairment of humoral immunity.

REFERENCES
CITRULLINE REACTIVE B CELLS ARE PRESENT IN THE LUNGS OF EARLY UNTREATED RA

Vijay Joshua1, Malena Lobberg-Haarhaus1, Heidi Wähämäa1, Aase Hensvold1, Magnus Sköld2, Johan Grunewald3, Lars Klareskog1, Vivianne Malmström1, Anca Catrina4, Karolinska Institute and University Hospital, Rheumatology Unit, Department of Medicine, Solna, Stockholm, Sweden; 2Karolinska University Hospital, Department of Respiratory Medicine and Allergy, Stockholm, Sweden

Background: We have previously shown that structural changes, increased tissue citrullination, signs of local inflammation and ACPPA are present in the pulmonary compartment of early seropositive RA. These findings suggest a potential role for the lungs in generation of RA-associated autoimmunity.

Objectives: To identify citrulline reactive B cells in the lung compartment of early untreated RA patients and to generate and characterize the corresponding monoclonal antibodies.

Methods: Bronchoalveolar lavage (BAL) fluid cells (13 and 22.5 million respectively) were obtained from two early untreated non-smoking ACPPA positive RA patients and single CD19+ B cells were sorted by flow cytometry. Immunoglobulin variable region genes were sequenced and expressed to generate recombinant monoclonal antibodies (mAbs). The citrulline reactivity was determined by in-house ELISA against different citrullinated peptides and controls.

Results: Single sorted CD19+ B cells (n=768) from each patient (RA.1 and RA.2) were processed and the variable region amplification and sequencing yielded 192 variable region genes were sequenced and expressed to generate recombinant monoclonal antibodies (mAbs). The citrulline reactivity was determined by in-house ELISA against different citrullinated peptides and controls.

Conclusions: For the first time we demonstrate that citrulline-reactive B cells are present in the lung compartment of early untreated RA. Further analysis and functional characterization are needed and ongoing to understand their role in RA.

REFERENCE


Disclosure of Interests: Vijay Joshua: None declared, Malena Lobberg-Haarhaus: None declared, Heidi Wähämäa: None declared, Aase Hensvold: None declared, Magnus Sköld: None declared, Johan Grunewald: None declared, Lars Klareskog Grant/research support from: Yes, but not for the presented study., Vivianne Malmström: None declared, Anca Catrina Grant/research support from: Yes, but not for the presented study.


QUANTIFICATION OF CD27+ MEMORY B CELLS IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH RITUXIMAB

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Background: Rituximab (RTX) is being increasingly used in treatment of several autoimmune diseases, including Rheumatoid Arthritis (RA). RTX induces a deep depletion of all peripheral B-Cell subsets (memory and naive B-cells). During the B-Cell repopulation phase, occurring approximately 3 months of RTX administration, B-precursors and naïve cells reappear. Several studies have shown that relapsing RA patients are characterized by a relative expansion of memory B cells during the B-cell repopulation phase.

Objectives: The aim of this study was to quantify the memory B-Cell compartment in RA patients with different disease activity scores, evaluated by DAS28, during RTX treatment.

Methods: 28 RA patients under RTX treatment were studied. At the end of the treatment 8/26 showed high-to-moderate activity risk (median DAS28=4.8) and 18 low activity risk or remission (median DAS28=2.69). After a median of 3 months from last RTX infusion, B-Cell subsets (precursors, naïve, memory B cells and plasma cells) were quantified in peripheral blood by flow cytometry, using a panel of 8 markers (CD3, CD4, CD8, CD19, CD20, CD227, CD38 and CD45). B-naïve cells were identified as CD19+ CD20+ CD227-. Memory B cells were identified as CD19+ CD20+ CD227+. Plasma cells were identified as CD19+ CD38++ CD227+. The virtual absence of peripheral B-cell was defined as <0.1 B-cell/µL. In the responder group, 5/18 cases showed absolute B-cell levels <0.1 cell/µL, while only in 1/8 of the non-responder group a similar B-cell depletion was found. The memory B-Cell% was significantly higher in non-responder than in responders (p<0.05); the memory B-Cell level in non-responders was similar to that of the NC group.

Conclusion: We used a sensitive and easily applicable flow cytometric multicolor panel that allowed the accurate and standardized identification and enumeration of peripheral blood B-Cell subsets. As reported by other studies, higher levels of memory B-Cells were found in non-responding RA patients treated by RTX, approaching those of healthy individuals.

REFERENCES


Disclosure of Interests: None declared

IL-2 THERAPY AFFECTS PERIPHERAL BLOOD LYMPHOCYTE LEVEL IN PATIENTS WITH PRIMARY SJÖGREN’S SYNDROME

Wenjuan Niu1, Hong Yan Wen1, Shi Giao1, Yanan Duan1, Yang Liu1, Chong Guo2, Li Xiaofeng1, 1The Second Hospital of Shanxi Medical University, Department of Rheumatology, Department of Pathology, Taiyuan, China; 2Department of Pathology, Brigham and Women’s Hospital, Harvard Medical School, Boston, MA, USA, Department of Pathology, Massachusetts, American Samoa

Background: Primary Sjogren’s Syndrome (PSS) is a chronic inflammatory autoimmune disease that mainly involves exocrine glands. Changes in the number of lymphocytes in PSS due to broken immune balance.

Methods: To observe the quantitative changes of peripheral Th17 cells and regulatory T cells (Tregs) in patients with primary Sjogren syndrome before and after short-term low-dose IL-2 treatment, and to explore the correlation between the level of peripheral blood lymphocytes and clinical indexes in patients with primary Sjogren syndrome.

Methods: Total172 PSS patients were enrolled, and 196 healthy adults were used as normal controls. Of them, 53 cases were treated with low dose IL-2 (5.0×10^12 international units (IU) for 5 days). The median four quantile method was used for statistical description. Multiple samples were compared with Kruskal-Wallis H test, and the correlation between variables was Spearman rank correlation analysis.

Results: (1) The number of Th17 cells were decreased as compared with that in the control group (P<0.05). The number of total T, CD8+ T, Th1, Th17, Treg, and the ratio of Th17/Treg were negatively correlated with CRP (P<0.05). (2) The Th17 cell levels, the ratio of Th17/Treg and CD4+ T/CD8+ ratio of Th17/Treg were negatively correlated with CRP (P<0.05).

Conclusion: The level of CD4+ T cells in peripheral blood of patients with PSS such as Th1, Th17 cells were significantly decreased. Th17/Treg were correlated with ESR, CRP. However, Th1, Th2, Th17 cells levels were increased according to treatment with short term low dose IL-2. Especially Treg cells. It indicated that IL-2 promoted the differentiation of Treg cells, maintained the function of Treg cells.

REFERENCES


Table 1. Comparison of lymphocyte levels sandratios between the two groups (Ng/ml, %)

<table>
<thead>
<tr>
<th>Groups</th>
<th>T (ng/ml)</th>
<th>CD4+ T (ng/ml)</th>
<th>CD8+ T (ng/ml)</th>
<th>CD4+ T/CD8+ T</th>
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<tr>
<td>Case group</td>
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<td>(362.50,867.35)</td>
<td>(275.00,551.00)</td>
<td>(0.99,2.18)</td>
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<td>II-2 treatment group</td>
<td>(927.00,1805.15)</td>
<td>(135.50,367.50)</td>
<td>(2.21,162.60)</td>
<td>(1.16,2.36)</td>
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<td>Healthy control group</td>
<td>(1072.00,569.74)</td>
<td>(550.25,825.12)</td>
<td>(0.99,2.18)</td>
<td>(1.05,1.90)</td>
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<th>Groups</th>
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<td>Case group</td>
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<td>477.01</td>
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<td>Healthy control group</td>
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<td>693.47</td>
<td>510.45</td>
<td>1.58</td>
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Table 2. Correlation of lymphocytes with inflammatory indexes in patients with lymphocytoslevels.

<table>
<thead>
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<th>T</th>
<th>CD4+ T</th>
<th>CD8+ T</th>
<th>CD4+ T/CD8+ T</th>
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<td>ESR</td>
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<td>0.547</td>
<td>-0.098</td>
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<td>CRP</td>
<td>-0.002</td>
<td>0.286</td>
<td>-0.121</td>
<td>0.114</td>
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Table 3. Changes in anti-Ro52 and anti-Ro60 antibody titers.

<table>
<thead>
<tr>
<th>Antibodies</th>
<th>Before PD-1 treatment</th>
<th>After PD-1 treatment</th>
<th>After PSL treatment</th>
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<tbody>
<tr>
<td>Anti-Ro52 titer (positive range: 44.48)</td>
<td>240&lt;</td>
<td>240&lt;</td>
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<tr>
<td>Anti-Ro60 titer (positive range: 31.3)</td>
<td>88.9</td>
<td>72.7</td>
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</tbody>
</table>

Case report: Advanced melanoma patient with favorable response to immune checkpoint inhibitor treatment shows severe erythema circinatum with anti-SS-A/SS-B antibodies

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Background: Immune checkpoint inhibitors (ICI) targeting cytotoxic T lymphocyte-associated protein 4 (CTLA-4) and programmed cell death protein 1 (PD-1) have been efficacious treatments in oncology. However, the use of ICI induces a large spectrum of immune side effects. The prevalence of autoimmune connective tissue diseases and the autoantibody profiles induced by ICI are largely unknown.

The Ro52/TRIM21 antigen is known as a cytosolic Fc receptor that is found in almost all tissues. Its expression is regulated by interferons, and overexpression or hypoexpression has been observed in several cancers.

Objectives: In this study, we investigated autoantibodies produced after ICI treatments and analyzed the clinical characteristics of the patients.

Methods: Sera were collected from patients with unresetable metastatic or recurrent melanoma before and after treatment with ICIs such as ipilimumab, nivolumab or pembrolizumab. Autoantibodies were screened by Western blotting (WB) using A375 and HaCaT cell extracts. Antigenic proteins, which showed differences in reactivities in WB before versus after treatment, were purified by immunoprecipitation and analyzed by time-of-flight mass spectrometry. The identified proteins were tested for serum reactivities with ELISA.

Results: Of the 19 melanoma patients, 1 patient showed high titers of anti-SS-A/Ro52 and anti-SS-A/Ro60 antibodies after treatment. The other 18 melanoma patients were negative for both anti-SS-A/Ro52 and anti-SS-A/Ro60.

Case presentation: An 81-year-old Japanese male patient with multiple metastatic melanomas on the face (Figure 1A) was judged as unresetable, and treatment with pembrolizumab was started. After the fifth pembrolizumab administration, a grade 2 skin rash appeared (Figure 1B). The multiple metastatic lesions and the primary melanoma showed significant reductions, without new cancer lesions (Figure 1C). Pembrolizumab was ceased after the ninth administration with grade 3 skin erythema, and systemic prednisolone (PSON) at 1mg/kg/day was started. No other subjective symptoms, such as sicca, fever or fatigue, were observed. A biopsy specimen of erythema circinatum on the back showed strong liquefaction degeneration, individual cell keratinization and exocytosis. The reactive 52kDa and 60kDa polypeptides in WB (Figure 1D) were presumed to be SS-A/Ro52 and SS-A/Ro60, respectively, and the serum was confirmed to be reactive with these antigens by ELISA. The skin symptoms and anti-SS-A/Ro52 and anti-SS-A/Ro60 antibodies remained after the PSL treatment. Some of the erythema left incomplete degeneration of the skin (Figure 1E, F). Anti-SS-A/Ro52 and anti-SS-A/Ro60 antibody titers increased along with the skin symptom in this melanoma patient who was being treated with an ICI (Table 1).

Conclusion: Anti-SS-A/Ro52 and/or anti-SS-A/Ro60 may have some association with cancer immunity.

REFERENCES


Table 4. Changes in anti-Ro52 and anti-Ro60 antibody titers.

<table>
<thead>
<tr>
<th>Antibodies</th>
<th>Before PD-1 treatment</th>
<th>After PD-1 treatment</th>
<th>After PSL treatment</th>
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<tbody>
<tr>
<td>Anti-Ro52 titer (positive range: 44.48)</td>
<td>240&lt;</td>
<td>240&lt;</td>
<td></td>
</tr>
<tr>
<td>Anti-Ro60 titer (positive range: 31.3)</td>
<td>88.9</td>
<td>72.7</td>
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</table>

Table 5. Changes in anti-Ro52 and anti-Ro60 antibody titers.

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<td>88.9</td>
<td>72.7</td>
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</tbody>
</table>

I2: No patient who was being treated with an ICI (Table 1).

Notes: ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; *P<0.05.
AGE AND GENDER EFFECTS ON PROGRAMMED CELL DEATH-1 EXPRESSION IN HEALTHY DONORS

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Background: Giant cell arteritis (GCA) is the most frequent form of vasculitis affecting the large sized vessels. GCA occurs more frequently in females and exclusively in individuals > 50 years of age but it is unclear how gender and age relate to GCA pathogenesis.

In balancing the immune response and preventing immune dysfunction, immune checkpoints are crucial. Recently, the co-inhibitory checkpoint molecule programmed cell death-1 (PD-1) and its ligand PD-L1 were found to be aberrantly expressed in GCA (1). However, data on age and gender related effects on immune checkpoint expression is limited.

Objectives: To further investigate the contribution of immune checkpoints in GCA pathogenesis and how this relates to ageing and gender differences, we first studied PD-1 expression as a function of age and gender in healthy males and females.

Methods: Whole blood cells of 13 young healthy donors (mean age 25.5 years, female/male ratio 7:6) and 20 elderly healthy donors (mean age 72.7 years, female/male ratio 11:9) were stained for CD3, CD4, CD45RA, CD25 and PD-1 with monoclonal antibodies and expression was measured with flow cytometry. Results: Percentages of PD-1+ cells within CD4+ T cells, memory CD4+ T cells and the subset of non-suppressive regulatory T cells (Tregs) were decreased in (subsets of) CD4+ T cells of post-menopausal females compared to elderly males (Figure 1A-C; p<0.05). Furthermore, the frequency of PD-1+ cells within non-suppressive Tregs was also decreased in post-menopausal females compared to young females (Figure 1C; p<0.05).

Conclusion: PD-1 expression is decreased in (subsets of) CD4+ T cells of post-menopausal females when compared to younger females and elderly males. These findings suggest that post-menopausal status in females can influence PD-1 expression. Further studies on the relation between hormonal changes and immune checkpoint expression may contribute to understanding why elderly females are predisposed to develop GCA.

REFERENCE
with AS, suggesting that hydrogen production in the small intestine may be related to inflammation. In addition, with increasing age of the female, hydrogen and methane produced in the small intestine may increase, with increasing age of the male, small intestine may reduce the production of hydrogen, suggesting a reason why there are more female patients than male in some autoimmune disease.

**REFERENCES**


Disclosure of Interests: None declared

**AB0035**

**THE CHARACTERISTICS OF CIRCULATING FOLLICULAR T LYMPHOCYTE SUBSETS IN PATIENTS WITH RHEUMATOID ARTHRITIS AND THE EFFECT OF TFR/TFH BALANCE ON DISEASE ACTIVITY**

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**Background:** Rheumatoid arthritis (RA) is a highly disabling autoimmune disease. T lymphocyte subsets imbalance causing immune dysfunction is essential stages in the occurrence and development of RA diseases. Recent studies show that the interaction of both follicular helper T (Tfh) cells and follicular regulatory T (Tfr) cells are important frontier scientific direction to maintain autoimmune tolerance, and Tfr/Tfh balance may play a pivotal role in the formation of lymphoid germinial center and the production of autoantibodies.[1-3]

**Objectives:** The aim of this study was to explore the clinical characteristic of peripheral follicular T cell subsets in patients with RA and healthy individuals, and the effects of Tfr/Tfh balance on autoantibodies formation and disease activity. Searching for new immunomodulatory targets from it.

**Methods:** The study included 26 patients with a diagnosis of RA according to the 1987 revised criteria of the American College of Rheumatology and 17 healthy individuals as control group. All follicular T cell subsets from them were assessed by flow cytometry (Figure1). Using isotypic controls to distinguish follicular T cell subsets that were not clearly clustered. In addition, we measured all peripheral lymphocyte subsets in RA patients by Flow Cytometry. IgG, IgA, IgM,RF were measured using Turbidimetric inhibition immuno assay. Anti-CCP was measured using ELISA. We also collected relevant clinical information and made DAS28 score.

**Results:** (1)Compared with healthy controls, the proportions of CD4+ CXCR5+ PD-1high Tfh cells were higher in RA patients (P=0.029), In contrast, patients with RA had much lower level of CD225+CXCR5+Foxp3+ Tfr cells (P=0.010). And there were significant differences of Tfr/Tfh between these two groups (P<0.000). (2) Among 26 RA patients, there was obvious correlation between Tfr/Tfh and the DAS28 value(ρ=0.422, P=0.032). But there was no correlation between Tfr/Tfh and ESR(P>0.05). Correlation between CD4+CD25+Foxp3+ Treg cells and Tfr cells was also analyzed(ρ=0.722, P=0.000) (Figure2). (3) We have not found correlation between Tfr/Tfh and autoantibodies maybe for the small sample content.

**Conclusion:** Treg cells have a negative immunomodulatory effect on inflammatory response, the high correlation between Tfr cells and Treg cells indicates that Tfr cells may come from directional transformation of Treg. There is a Tfr/Tfh imbalance in RA patients, which suggests a potential mechanism of RA disease severity. However, more samples are needed to confirm whether it is related to the production of autoantibodies to affect disease activity.

**REFERENCES**


Background: Ankylosing Spondyloarthritis (AS) is a progressive, chronic, inflammatory skeletal disorder affecting the spine and sacroiliac joints. To date, the disease etiology remains unclear. Some studies have shown that lymphocytes play important roles in the inflammatory process of AS. However, the roles of comprehensive subtype lymphocyte subset imbalance in AS was rarely mentioned.

Objectives: In the present study, the correlation of lymphocyte subset changes with the progression of AS was investigated.

Methods: Flow cytometry analyses were carried out to detect the levels of a series of lymphocytes including different stages of differentiation CD4+ T cells, CD8+ T cells, helper T cells (Th), cytotoxic T cells (Tc), regulatory T cells (Treg), B lymphocytes and so on. Evaluation of hip joint disease were by using Bath Ankylosing Spondylitis forty X-ray index. Ankylosing Spondylitis Disease Activity Score (ASDAS) was used to assess disease activity and AS patients were divided into inactive disease group (ASDAS<1.3) and active disease group (ASDAS ≥1.3).

Results: The percentage of circulating follicular T lymphocyte subsets in patients with RA and healthy controls (\(p<0.05\), ***\(p<0.001\)). Correlation between Treg cells and Th1 cells, and correlation between Th1/Th2 and the DAS28.

Disclosure of Interests: None declared

AB0036B LYMPHOCYTE SUBSET IMBALANCES IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Ankylosing Spondyloarthritis (AS) is a progressive, chronic, inflammatory skeletal disorder affecting the spine and sacroiliac joints. To date, the disease etiology remains unclear. Some studies have shown that lymphocytes play important roles in the inflammatory process of AS. However, the roles of comprehensive subtype lymphocyte subset imbalance in AS was rarely mentioned.

Objective: To investigate the role of Treg and CD4+ T cells of different differentiation stages on the pathogenesis of active AS, and to study the mechanism of TNFα blocker on the treatment of active AS by detecting the number of Treg cells and CD4+ T cells before and after the treatment.

Methods: Ankylosing Spondylitis Disease Activity Score (ASDAS) was used to assess disease activity. AS patients who fulfilled the Assessment in Ankylosing Spondylitis Criteria in 1984 and ASDAS≥1.3 were enrolled in this study. The percentage of Th2 cells, Th17 cells, Th2 cells, inactive phase-specific CD8+ T cells and B cells were found to be significantly higher in the AS groups compared with the healthy individuals (\(p<0.05\)). In addition to the above differences, the percentage of Treg cells were significantly lower in the AS groups compared with the healthy individuals (\(p<0.05\)). AS patients with family history have significantly higher percentage of Th1 cells, Tc1 cells, Th1 cells, Th1 cells, continuous expression of virus-specific terminally differentiated CD8+ T cellsplasma cells, memory B cells and convertable B cells were significantly lower in the AS groups (\(p<0.05\)). As a result, the percentage of Th1/Th2 and (Th1+Th17)/Th2 ratios were significantly lower in AS patients (\(p<0.05\)).

Disclosure of Interests: None declared
Conclusion: Imbalances in the numbers and functions of specific lymphocyte cell subsets are key pathogenic derangements in AS, and these insights are leading to changes in clinical practice. The present study provided further evidence on the function and underlying mechanism of lymphocyte subsets, which may be useful in the diagnosis and treatment of ankylosing spondylitis.

REFERENCES

Disclosure of Interests: None declared

AB0036C IMMUNOPHENOTYPIC CHARACTERIZATION OF T-CELL IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH GOLIMUMAB

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Background: Golimumab is a human anti-TNF monoclonal antibody that has shown efficacy in RA. In the RA pathophysiology, the elevation of TNF modulates the cellular immune response, which leads to a sustained activation of T-cell response; however, it is unknown whether anti-TNF interferes with the immunophenotype of T-cell.

Objectives: To evaluate activation (CD25, CD69) and exhausted (PD-1, TIM-3, LAG-3, CTLA-4) markers of T-cells in RA patients treated with Golimumab.

Methods: We included 14 patients with RA diagnosis (Criteria ACR/EULAR 2010), with moderate to severe activity; 11 non-responders to synthetic DMARDs (NR-DMARDs) and 3 responders to synthetic DMARDs with pharmacological toxicity (R-DMARDs). All patients were treated with Golimumab during 24 weeks. The questionnaire SF-36, DAS28-CRP, power Doppler signal and expression of CD25, CD69, PD-1, TIM-3, LAG-3 and CTLA-4, in T-cell were evaluated at 0 and 24 weeks.

Results: Clinical variables evaluated in patients with Rheumatoid Arthritis are shown in tables 1 and 2.

Table 1. Clinical variables evaluated in patients with Rheumatoid Arthritis

<table>
<thead>
<tr>
<th>Clinical variables</th>
<th>Cases n=14</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>13 (92.9%)</td>
</tr>
<tr>
<td>Male</td>
<td>1 (7.1%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>52 ± 8.91</td>
</tr>
<tr>
<td>Time of evolution</td>
<td>10 ± 5.51</td>
</tr>
<tr>
<td>Extra-articular</td>
<td>4 (28.6%)</td>
</tr>
<tr>
<td>Rheumatoid factor</td>
<td>307 ± 700</td>
</tr>
<tr>
<td>Anti CCP (U/ml)</td>
<td>351 ± 699</td>
</tr>
<tr>
<td>DAS28-CRP</td>
<td>0.40 ± 0.20</td>
</tr>
<tr>
<td>Week 0</td>
<td>2.8 ± 2.1</td>
</tr>
<tr>
<td>Week 24</td>
<td>2.4 ± 0.71</td>
</tr>
<tr>
<td>Power Doppler signal (score)</td>
<td>2.1 ± 4.1</td>
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</tbody>
</table>

The frequency of LAG-3+ on CD4+ T-cells increased after 24 weeks of treatment with Golimumab (p = 0.013) (figure 1). The expression of LAG-3 in CD4+ T-cells (r = -0.586, p = 0.028) (Figure 2) and CD8+ T-cells (r = -0.617, p = 0.019) (Figure 3) inversely correlated with DAS28-CRP after treatment. At the beginning of treatment NR-DMARDs patients showed higher expression of CD25 in CD8+ T-cells and lower expression of TIM-3 in CD4+ and CD8+ T-cells with respect to R-DMARDs. After 24 weeks of treatment, a lower frequency of CD69+ and LAG-3+ T-cells was found and increased of CD25+ T-cells compared to R-DMARDs.

Conclusion: Golimumab treatment increased the expression of LAG-3 in T-cells, suggesting a negative regulator of antigen presentation of T-cells.

REFERENCES

Disclosure of Interests: None declared

Innate immunity in rheumatic diseases

AB0037 NEUTROPHIL GRANULOCYTES ARE PRIMED IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS (JIA)

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Background: The adaptive as well as innate immunity is involved in JIA pathology. Neutrophils are key mediators of the innate immune response and is the most abundant cell type found in JIA synovial fluid. Studies of neutrophils in JIA have shown transcriptional abnormalities and neutrophil-derived S100A proteins have shown a potential role as biomarkers. Still, studies of neutrophils in JIA are scarce.
Human neutrophil lipocalin (HNL), also known as neutrophil gelatinase-associated lipocalin (NGAL), is a protein found in the secondary granules of neutrophil granulocytes. HNL can be found in epithelial cells as well, but only in its monomeric form. The dimeric form is only produced by neutrophil granulocytes. HNL resides in the secondary granules and is released upon stimulation, making HNL a unique marker of primed and activated neutrophil granulocytes, compared to myeloperoxidase (MPO) that resides in the primary granules and is released when neutrophils are activated, but also found in monocytes.

Objectives: To examine levels of the dimeric form of human neutrophil lipocalin (dHNL), to reveal if neutrophil granulocytes are primed in JIA, also analysis of myeloperoxidase MPO to reveal neutrophil activation. We aimed to compare the analyses to healthy controls and correlate the results to established measures of disease activity.

Methods: Blood samples from 75 patients with JIA (68% females) and 16 healthy controls were analyzed regarding HNL using a dimer ELISA assay (Diagnostics Development, Uppsala, Sweden) specifically detecting the dimeric form of HNL (dHNL). We also analyzed MPO (Diagnostics Development, Uppsala, Sweden), white blood cell count, neutrophil granulocyte cell count, ESR and CRP. All categories of JIA except the systemic category were included. Patient/parent and the physician filled out a global health assessment on a VA-scale (0–10). The number of active joints at sampling was collected and patients were classified according to the JIA criteria. The participants with JIA had a median age of 12.1 (IQR: 7.7–15.3) years, the control group 5.3 (IQR: 2.9–9.5) years.

Results: The serum levels of dHNL and MPO were significantly elevated compared to healthy controls, (p < 0.001; p = 0.002), and correlated significantly with each other (rs = 0.68, p < 0.001). The levels of dHNL correlated best to the count of neutrophil granulocytes (rs = 0.54, p < 0.001), total leucocyte count (rs = -0.43, p <0.001) and less well to CRP (rs = 0.42, p < 0.001) and ESR (rs = 0.35, p < 0.002) and not at all to the scoring system for disease activity, JADAS27 (rs = 0.06, p > 0.65).

Conclusion: The increased levels of the dimeric HNL in serum confirmed the involvement of neutrophil granulocytes in JIA although dHNL did not correlate with disease activity. The mechanisms by which neutrophils are primed and activated in JIA, however, still remain an enigma.

Disclosure of Interests: Lillemor Berntsson Consultant for: AbbVie, Speakers bureau: AbbVie, Ulrika Kihlb erg: None declared, Per Venge: None declared

References:
AB0041

DO FUNCTIONAL INTERACTIONS BETWEEN MACROPHAGES AND SYNOVIAL FIBROBLASTS DRIVE SYNOVIAL PATHOLOGY OR RESOLUTION OF INFLAMMATION?

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Background: We recently uncovered heterogeneity in human synovial tissue macrophages during inflammation and resolution of inflammation (remission) in rheumatoid arthritis (RA). The transcriptomic profiles of distinct macrophage sub-populations suggest distinct functions, ranging from inflammatory to regulatory. Prior studies propose reciprocal interactions between macrophages and synovial fibroblasts (FLS) exist in the joint; however, the exact contribution of these interactions to synovial pathology or resolution of inflammation remains unknown.

Objectives: The aim of this study was to examine the functional interactions between different macrophage phenotypes and synovial fibroblasts.

Methods: To model different macrophage phenotypes, monococyte-derived macrophages (MOMD) were pre-stimulated (16h) with LPS (100ng/ml) to model inflammatory; or with dexamethasone (Dex, 1μM) to model regulatory macrophage. After extensive washing, MOMD were co-cultured with FLS for different periods of time. Prior to co-culture, FLS and MOMD were labelled with CellTraceTM-Violet and CellTraceTM-Red, respectively. After 24 & 48 hours of co-culture, FLS and MOMD were sorted based on positivity for CellTraceTM-Violet (FLS) or Red (MOMD) using FACS ARIA III, and expression of IL-6 and MMP1 in FLS analysed by ultrasensitive qPCR. In addition, the levels of IL-6 and MMP3 proteins were evaluated in co-culture supernatants by ELISA.

Results: FLS co-cultured with MOMD showed an increased mRNA expression of IL-6 at both 24 and 48h, and MMP1 at 48h, compared to FLS cultured alone. This expression pattern was decreased when MOMD were pre-treated with Dex and significantly upregulated when MOMD were pre-treated with LPS. Consistently with mRNA expression, IL-6 protein was significantly increased when FLS were co-cultured with MOMD (119±2.137pg/ml) as compared to FLS cultured alone (445±7.83pg/ml). This production was significantly augmented when MOMD were pre-treated with LPS (1985±25 pg/ml) and decreased when MOMD were pre-treated with Dex (729±63pg/ml). Similarly, MMP3 protein level was increased when FLS were co-cultured with MOMD (256±10pg/ml) as compared to FLS cultured alone (123±1 pg/ml). This production was significantly augmented when MOMD were pre-treated with LPS (1860±34pg/ml) and decreased when MOMD pre-treated with Dex (164±22pg/ml). These distinct effects of MOMD phenotypes on FLS function were associated with different dynamics of their interactions. Our preliminary data reveal that MOMD are quiescent on FLS monolayers unless MOMD are pre-treated with Dex, which induced a patrolling behaviour.

Conclusion: Macrophages can actively increase or limit activity of FLS, depending on their inflammatory or regulatory phenotypes, respectively. These observations indicate the potential for different subsets of synovial tissue macrophages to drive or resolve synovial inflammation by influencing the stromal compartment.

REFERENCES


AB0042

PRECLINICAL EVALUATION OF JAK1 SELECTIVE INHIBITORS INCB039110 AND INCB054707 AS TARGETED THERAPY OF CUTANEOUS LUPUS ERYTHEMATOSUS

Tanja Fetter1, Paul Smith2, Tugce Gül3, Thomas Bieber1, Jörg Wenzel1 on behalf of Prof. Wenzel lab group. 1University of Bonn, Department of Dermatology and Allergy, Bonn, Germany; 2Incyte Corporation, Wilmington, United States of America

Background: Cutaneous lupus erythematosus (CLE) is an autoimmune disease with heterogeneous subtypes presenting with inflammatory skin lesions, a histological pattern called “interface-dermatitis” and enhanced type-1-interferon (IFN)-regulated JAK/STAT (Janus kinase/signal transducers and activators of transcription) pathway signaling. Despite deeper understanding of the pathogenesis still no specifically approved drugs for CLE exist.

Objectives: The aim of our study was to investigate the effect of JAK1 selective inhibition as potential therapeutic approach for CLE in established preclinical models of cutaneous autoimmunity.

Methods: The expression of IFN-regulated proteins and genes after JAK1 inhibitor treatment was analysed in cultured, stimulated immortalized and primary human epidermal keratinocytes. In addition the impact of JAK1 inhibition on CLE-like skin lesions in lupus prone MRL/lpr- and TREX1-knockout-mice was determined.

Results: In vitro investigation revealed a significantly decreased gene- and protein expression of proinflammatory cytokines, in particular CXCL10 as key driver of CLE in established preclinical models of cutaneous autoimmunity.

Conclusion: Our findings indicate that inhibition of JAK1 results in a decreased chemokine expression, subsequent less cytotoxic T cell induced keratinocytic cell death leading to an improvement of lesional skin. By breaking the vicious inflammatory cycle JAK1 inhibitors appear to be promising agents as targeted therapy of CLE. Further investigation has to be performed in clinical trials.

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Acknowledgement: The authors thank Nadine van Holt (University Hospital Bonn) for her most valuable support in preparation of the manuscript and Sandra Ferring-Schmitt and Sonja Sternberg for their great helpfulness in the laboratories.

Disclosure of Interests: Tanja Fetter: None declared. Paul Smith Shareholder of: The author is an employee and/or shareholder of Incyte Corporation., Employee of: The author is an employee and/or shareholder of Incyte Corporation., Tugce Gül: None declared. Thomas Bieber: None declared. Jörg Wenzel Grant/research support from: GSK, Incyte, Consultant for: Biogen, Leo, Paid instructor for: Novartis

AB0043  EFFECT OF IN VIVO HYDROXYCHLOROQUINE AND EX VIVO ANTI-BDCA2 TREATMENT ON PDC IFNα PRODUCTION FROM PATIENTS AFFECTED WITH CUTANEOUS LUPUS ERYTHEMATOSUS

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Background: BIIB059 (aka 24FA4) is a monoclonal antibody that targets BDCA2, an inhibitory receptor expressed on pDCs. Plasmacytoid dendritic cells (pDCs) are a major source of Type-I Interferon (IFN-I), which is considered to be a key pathogenic driver in Cutaneous Lupus Erythematosus (CLE). Recent results from a Phase I clinical trial suggest that BIIB059 may ameliorate skin lesions in CLE patients. BIIB059 is currently evaluated in Phase II clinical trial for CLE with or without SLE.

Objectives: Given that Hydroxychloroquine (HCQ), a widely-used CLE therapy, and BIIB059 are both able to inhibit pDC-derived IFN-I production; this study aimed to determine whether BIIB059 would show an additional inhibitory effect on pDC response after ex-vivo or in-vivo treatment with HCQ.

Methods: The effect of BIIB059 on pDC-derived IFNα was measured from peripheral blood mononuclear cells (PBMC) either from healthy donors in presence or absence of HCQ or from CLE patients clinically exposed to various levels of HCQ. TLR7/9 and TLR9 agonists (ssRNA, R848, and CpG-A) were used for pDC stimulation.

Results: PDCs were the only producers of IFNα in response to CpG-A, R848, and ssRNA stimulation in PBMC cultures. CLE patients with high blood HCQ levels showed lower ex-vivo pDC responses to CpG-A, but not R848 or ssRNA. In contrast, BIIB059 reduced the amount of IFNα produced by pDCs from CLE patients in response to all TLR agonists, irrespective of the blood HCQ level. This effect was observed in patients with low or high blood IFN signature and in patients with or without concomitant SLE diagnosis.

Conclusion: Clinically-relevant HCQ concentrations partially inhibit the pDC response to TLR9 and weakly affect the response to TLR7/9 stimulation. BIIB059 robustly inhibits pDC responses even in the presence of HCQ, highlighting its unique potential to disrupt pDC disease relevant biology, which could provide additional benefit for CLE patients.


AB0044  PHARMACOLOGICAL MANIPULATION OF SIRTUIN 1 ACTIVITY IN EXPERIMENTALLY INDUCED ARTHRITIS

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Background: Sirtuin 1 (Sirt1) is a member of the sirtuin family of NAD+ dependent protein deacetylases. This nuclear enzyme with deacetylase activity serves as a metabolic sensor and transcriptional regulator, and exerts its beneficial effects by promotion of cell viability, tissue regeneration, and inhibition of inflammation.

Objectives: 1) To investigate the effect of pharmacological modulation of Sirt1 enzymatic activity on disease outcomes of experimental rheumatoid arthritis in mice; and 2) To characterize surface marker and pro-inflammatory cytokine expression in neutrophils following Sirt1 activation or inhibition.

Methods: Arthritis was induced by intra-peritoneal administration of a cocktail of monoclonal antibodies against collagen type II in Balb/c mice (CAIA). We utilized synthetic compounds which specifically activate or inhibit Sirt1 activity - SRT2183 and EX527, respectively. We investigated the effect of Sirt1 activity modulation on clinical scores of arthritic mice after subcutaneous seven-day treatment initiated at Day 7 of CAIA. We used flow-cytometry for phenotyping and functional analysis of blood, and bone marrow (BM) derived neutrophils stimulated in vitro, and in vivo. The effects of the two compounds on Sirt1 activity and on cell viability were assessed using ELISA-based colorimetric assays.

Results: Activation and inhibition of Sirt1 activity led to CD11b down-regulation and CXCR2 up-regulation on healthy blood and BM neutrophils, suggestive of neutrophil mobilization from the BM to the periphery following treatment in vivo. Both SRT2183 and EX527 had a positive effect on clinical scores in CAIA mice. However, in EX527-treated mice the re-emergence of signs of joint inflammation was observed 14 days after cessation of treatment. Administration of SRT2183 was able to up-regulate IL-1beta in healthy and CAIA mice, which we also observed in un-stimulated neutrophils in vitro. Iso-nicotinamide, a compound which activates sirtuins via an alternative mechanism, had a similar effect on IL-1beta expression in vitro. Finally, Parp1 cleavage, a marker for cell death, was reduced in purified BM neutrophils following Sirt1 activation.

Conclusion: Sirt1 activity modulation, whether activation or inhibition, improved clinical scores in arthritis. This corresponds to the mobilization of neutrophils from the BM to the periphery. The selective increase of IL-1beta following Sirt1 activation indicates that while activation or inhibition achieves a similar outcome, this is done through different molecular pathways. Our results underscore that systemic pharmacological modulation of Sirt1 activity for a complex disease, such as rheumatoid arthritis, is complicated and attention should be paid to the schedule and duration of treatment, as well as to the progressive involvement of various cell types, in order to maximize the beneficial effects.

Disclosure of Interests: This study was funded by the Bulgarian National Science Fund (DN 5/11-2017 to P.D.).

AB0045  MESENCHYMAL STEM CELLS INHIBIT THE ACTIVATED COMPLEMENT C5 BY CLUSTERIN IN LUPUS NEPHRITIS

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Background: Dysregulation of clusterin (CLU) and over-activated complement C5 were involved in the development and progression of lupus nephritis (LN). Allogeneic mesenchymal stem cells (MSCs) transplantation has achieved good clinical efficacy for refractory LN, however, the exact mechanisms remain to be elucidated.

Objectives: To investigate the clinical effect of MSCs on SLE model mice (B6. lpr), and explore the mechanisms of MSCs inhibiting the activated complement C5 in vivo and in vitro.

Methods: 26-week-old female B6.lpr mice were randomly allocated in three groups, which were given the following treatments, CTX (200mg/kg), MSCs (1 x 10^7), and an equal volume of PBS. 24 hours urinary and peripheral blood were collected periodically. All mice were sacrificed at 40 weeks of age. Urine protein to creatinine ratio and plasma creatinine were quantified to evaluate renal disease. Levels of C3, soluble C5b-9 (SC5b-9), CLU, and anti-dsDNA antibody were determined in the plasma by ELISA. Histopathological evaluation of renal lesions was undertaken by HE, PAS, PASM and Masson staining under light microscopy. Podocyte foot processes were assayed by the transmission electron microscopy. Accumulation of immunocomplexes (IC), C3, C5b-9, and CLU were detected in renal specimens by immunofluorescence or immunohistochemistry. Expressions of CLU in MSCs were detected by real-time PCR and ELISA. MSCs-derived CLU and anti-dsDNA antibody were determined in the plasma by ELISA. Histopathological evaluation of renal lesions was undertaken by HE, PAS, PASM and Masson staining under light microscopy. Pathological analysis showed that the proliferation of glomerular cells and foot process fusion were significantly alleviated in MSCs treated mice. Immunofluorescence and immunohistochemistry showed that depositions of IC, C1q, C3 and C5b-9 were significantly decreased in the MSCs group, although the expression of CLU was obviously increased in these mice. Mechanistically, interferon-α promoted the secretion of functional CLU by MSCs in vitro.

Conclusion: Allogeneic MSCs transplantation can effectively improve the clinical outcome of lupus mice. Possible mechanisms of MSCs might be related to inhibit the activated C5 via clusterin, which would be a potential treatment target in the future.

Disclosure of Interests: None declared
COMPARATIVE ANALYSIS OF TLRS AND INFLAMMASOMES GENES EXPRESSION IN DIFFERENT ETHIOLOGY ARTHRITIS AFTER STIMULATION WITH INFLAMMATORY STIMULI AND VITAMIN D

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Background: It has been shown that a variety of environmental and genetic factors, as well as deficiency of vitamin D plays a key role in outcomes of arthritis. Many studies have shown that the central feature of synovitis in rheumatoid arthritis (RA) is activated synovium fibroblasts (SF) that play a key role in expression and secretion of distinct patterns of inflammatory factors. Recent studies demonstrated that nucleotide-binding oligomerisation domain-like receptor (NLR) containing a PYRIN domain 1 (NLRP1) and NLRP3 inflammasomes as well as Toll-like receptors (TLR), may be important in pathogenesis of chronic autoimmune joint diseases such as RA and potentially in development of osteoarthritis (OA). Therefore, better understanding of the role of SF, TLRs and inflammasomes inflammatory pathways in different ethiology joint damage could make a significant contribution to the early disease prognosis, monitoring, and therapy.

Objectives: A pilot study, to evaluate the effects of tumour necrosis factor α (TNFα), lipoteichoic acid (LTA), lipopolysaccharide (LPS), vitD on expression levels of TLRs and inflammasomes genes expression levels in SF. Downregulation of TLR2 expression and upregulation of NLRP3 accompanied by enhanced secretion of distinct patterns of inflammatory factors. Recent studies demonstrated that nucleotide-binding oligomerisation domain-like receptor (NLR) containing a PYRIN domain 1 (NLRP1) and NLRP3 inflammasomes associated with TNFα receptor (VDR) in human SF different ethiology knee damage: OA, RA, early arthritis (EA) (duration <12 months), healthy controls (HC) (after meniscus tear due to trauma).

Methods: Synovial tissue and blood samples for viD analysis were collected from patients undergoing joint replacement/arthroscopic synovectomy surgery, following informed consent according to the permission Lithuanian Ethics Committee. The isolated cells were expanded in a monolayer and used between passages 2 and 4. The expression of TLR, TLR1, TLR2, TLR4, NLRP1, NLRP3 inflammasomes was analysed by qRT-PCR after 24h of stimulation with LPS, TNFα, vitD, vitD.

Results: Analysis of gene expression results revealed that TNFα, LPS or LTA have no effect on TLR4 and TLR1 genes expression levels in SF. Downregulation of NLRP1 expression and upregulation of NLRP3 accompanied by enhanced expression of TLR2 was determined after stimulation with all factors, particularly TNFα. Highest upregulation of TLR2 was observed in RA and early arthritis patients, levels of other genes showed high variation between all patients, disrespectfully to diagnosis. Stimulation with TNFα resulted in 8-fold downregulation of VDR gene expression only in RA group, but not in OA, EA or HC. Stimulation with vitD had no effect on expression levels of studied genes in SFs in vitro, while the blood levels of vitD were neither associated with the endothelitis of arthritis nor with VDR responses to stimulation with TNFα, LPS, LTA.

Conclusion: We demonstrated downregulated expression of NLRP1, associated with increased levels of NLRP3 and TLR2 upon inflammatory stimuli in human articular SF from patients with arthritis of different ethiology. These data further support active involvement of those cells in inflammatory responses. Downregulated expression of VDR by TNFα in SF of RA patients implies altered signalling of vitD in the disease.

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CHARACTERIZING THE ROLE OF NET-DERIVED IL-33 IN SLE PATHOGENESIS

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Background: Interleukin (IL)-33 is a cell necrosis-derived alarmin with immunostimulatory properties which depend on the context of immune cells and the inflammatory milieu (1). In Systemic Lupus Erythematosus (SLE), extracellular DNA (as in extracellular chromatin traps [NETs] or immune complexes [ICs]) combined with alarmins stimulate innate immunity receptors (such as Toll-like receptors [TLRs]) and the production of IFNs by plasmacytoid dendritic cells (pDCs) (2, 3, 4).

Objectives: We propose that IL-33 is a potential NET-decorating protein and we want to investigate its pro-inflammatory properties. Additionally, NETs could also act as a platform mediating IL33’s bioactivity taking into consideration the excessive accumulation of proteases on extracellular traps. We hypothesize that NET-derived IL-33 might enhance the interferogenic capacity of pDCs.

Methods: Peripheral blood polymorphonuclear cells (PMNs) were isolated from healthy and SLE individuals and their ability to form IL33-decorated NETs was assayed by confocal microscopy. Renal sections from active lupus nephritis patients were immunostained to observe any IL-33 decorated NETs. NET-supernatants from untreated and IC-treated SLE PMNs were administrated to healthy pDCs and type I IFN production was monitored by qPCR and ELISA. The contribution of IL-33 to the interferogenic capacity of NETs was assessed by pre-treating pDCs with a specific mAb against IL33-receptor (anti-ST2L). The effect of proteases on the IL33-mediated interferogenic potential of NETs was investigated by pharmacological inhibition of elastase and Cathepsin G.

Results: Spontaneous-released NETs from peripheral blood PMNs of active SLE patients were decorated with IL-33 to larger extent as compared to healthy PMNs. NETs from untreated and IC-treated SLE PMNs were administrated to healthy pDCs and type I IFN production was monitored by qPCR and ELISA. The contribution of IL-33 to the interferogenic capacity of NETs was assessed by pre-treating pDCs with a specific mAb against IL33-receptor (anti-ST2L). The effect of proteases on the IL33-mediated interferogenic potential of NETs was investigated by pharmacological inhibition of elastase and Cathepsin G.

Conclusion: NET-derived IL-33 is a novel mediator of the nucleic acid-driven aberrant type I IFN response which exacerbates SLE disease. NET structure may want to investigate its pro-inflammatory properties. Additionally, NETs could also act as a platform mediating IL33’s bioactivity taking into consideration the excessive accumulation of proteases on extracellular traps. We hypothesize that NET-derived IL-33 might enhance the interferogenic capacity of pDCs.

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DISCLOSURE OF INTERESTS: None declared.


REDUCED FCR R III AND ENHANCED FCR R III EXPRESSION ON MONOCYTES IN PATIENTS WITH BEHÇET DISEASE

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Background: Behçet’s disease (BD) is a systemic inflammatory disease without clear pathogenesis. Previous studies have shown the association between FcγRII gene polymorphisms and BD. FcγRs, the receptor of IgG, has both activatory and inhibitory subtypes, and the imbalance of them on immunocytes has been illustrated to have significant pathogenic roles in many autoimmune diseases.

Objectives: This study was aimed to investigate the potential abnormal expression of FcγRs in BD patients.

Methods: We recruited 27 newly-onset treatment-naïve BD patients (according to 2014 International Criteria for BD) and 23 gender-and age-matched healthy controls (HC). Flow cytometry was used for detecting the expression of the inhibiting receptor (FcγRIIB) and activating receptors (FcγRI and FcγRII) on the neutrophils, monocytes, B cells, natural killer cells, dendritic cells, and T cell from the whole blood of BD and HC. The correlation between the expression of FcγR and disease activity index of BD was evaluated.

Results: BD patients had increased numbers of monocytes (60.14±3.87% vs. 47.56±4.92%, p=0.0365) compared with HC. FcγRIIB expression on monocytes, rather than other immunocytes (p>0.05), was significantly lower in BD patients (4.87±0.61% vs. 7.67±1.10%, p=0.0199). FcγRIIB expression on monocytes was negatively correlated to ESR (r=-0.576, p=0.031) and CRP (r=-0.539, p=0.047), positively correlated to serum IgA (r=-0.785, p=0.001) and uncorrelated to serum IgG, IgM and PLT (p>0.05). FcγRIIB expression on monocytes was higher in BD patients (19.61±3.046% vs. 9.349±1.107%, p=0.0091). FcγRII expression on monocytes was positively correlated to ESR (r=0.2551, p=0.0274) and CRP (r=0.2354, p=0.0352), and uncorrelated to serum IgG, IgM, IgA and PLT (p>0.05). Furthermore, FcγRIIB expressions of monocyte were comparable between BD patients in active disease or remission, while FcγRII expression was significantly decreased (p=0.0158) after 3-month of treatment.

Conclusion: Our research demonstrated, for the first time, that the decreased expression of inhibitory receptor FcγRIIB and increased expression of activatory receptor FcγRII on monocytes in BD. Furthermore, the abnormal expression was correlated with disease activity. These findings suggested that FcγRs ratio imbalance may play a role in the pathogenic role of BD.

REFERENCES

Disclosure of Interests: None declared.


CHANGES OF INNATE LYMPHOCYTE CELLS IN PERIPHERAL BLOOD OF PATIENTS WITH PRIMARY SJÖGREN’S SYNDROME AND ITS CORRELATIONS WITH CLINICAL MARKERS

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Background: Innate Lymphoid Cells (ILCs) are a novel group of innate immune cells, according to the cytokine profile, they were divided into three major subtypes:
Objectives: Our purpose is to explore the function and role of ILC in the pathogenesis of Primary Sjögren’s Syndrome (primary SS).

Methods: 20 patients with pSS and 15 age-matched healthy non-immune-related diseases controls were enrolled. The frequency of ILCs, B cells, CD4+ and CD8+ T cells from PBMCs was detected by flow cytometry. Analysis the subsets of ILCs in each group which compared with B cells and T cell subsets respectively and correlation with clinical serologic markers. Analyze the levels of IL-4, IL-9, IL-33, IL-22 and IFN-γ in each group by ELISA.

Results: Compared with the control group, the percentage of ILC was decreased significantly in primary SS (P<0.0001). Meanwhile ILC1 was significantly increased in primary SS (P=0.0001). ILC2 was decreased significantly in primary SS (P=0.0009) and ILC3 has no significant difference in the primary SS (P>0.05).

The frequency of ILCs in all patients positively correlated with antinuclear antibody titer (ANA(D)) (r=0.295, P=0.0133). Moreover, the frequency of ILC2 in primary SS was positively correlated with B cells (r=0.389, P=0.05), and the serum IgG was negatively correlated with ILC2 of all patients (r=0.2091, P=0.0427). Compared with Healthy control group, the level of IL-22 was significant higher in primary SS (P<0.0003), however, the levels of IL-4, IL-9, IL-33 and IFN-γ were not significant different with ILC2.

Conclusion: The frequency of ILCs is related to ANA(D) of primary SS patients and ILCs play a critical role in the pathogenesis of primary SS. Its function and mechanism are worth further exploration.

References:

Disclosure of Interests: None declared

AB0050
DETECTION OF SERUM AND SYNOVIAL FLUID LEVELS OF VISFATIN DURING FLARE-UPS AND REMISSION OF PRIMARY OSTEOARTHRITIS OF THE KNEES
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Background: OA is the most common form of joint disease and a major contributor of disability in older people. OA is a chronic joint disease characterized by cartilage breakdown, bone remodeling, osteophyte development and synovial inflammation [1]. Adipose tissue expresses and secretes a large number of proteins that often share functional and structural properties of cytokines and are there classified as adipokines [2]. These include leptin, adiponectin, resistin, visfatin, and others. These factors are associated with inflammation and immune response. Visfatin is an adipokines identified in 2004 and was identified first as Pre B cell Colony Enhancing Factor [3]. Visfatin is a potent inducer of PGE2 release in both human and immature mouse articular chondrocytes, as a result of increased messenger prostaglandin E synthase and decreased 15 Prostaglandine dehydrogenase synthases [4].

Objectives: The aim of the study was to measure the level of visfatin in serum and synovial fluid from patients with knee osteoarthritis in flare-up and after they enter in remission.

Methods: to achieve the target of our study 20 patients with OA of the knee in flare-up were selected from out-patients clinic. The patients were followed up every two weeks after the first setting until they entered into remission. Twenty normal controls age, sex and body mass index (BMI) matched were recruited. In the first setting all patients had their sera, and synovial fluid measured for Visfatin, in the second setting sera and synovial fluid (if any) was drawn for visfatin measurement. Measurement of Visfatin by (ELISA) for quantitative determination of human visfatin in biological fluids.

Results:
1: serum visfatin of patients and control groups:

<table>
<thead>
<tr>
<th>P value</th>
<th>T</th>
<th>Control ng/ml</th>
<th>Patients ng/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0001</td>
<td>42.29</td>
<td>216.600±30.25</td>
<td>547.359±59.96</td>
</tr>
<tr>
<td>0.001</td>
<td>23.6</td>
<td>216.60±30.25</td>
<td>542.45±59.60</td>
</tr>
</tbody>
</table>

Flare up: Remission

Patients recorded higher VIII-S readings than the controls with high significant difference in both situations.

2: serum and SF visfatin of patients during flare-up and remission:

<table>
<thead>
<tr>
<th>P value</th>
<th>T</th>
<th>Serum ng/ml</th>
<th>Remission ng/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0001</td>
<td>847.90±59.86</td>
<td>542.45±59.60</td>
<td></td>
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</table>

Visfatin vistsin:

<table>
<thead>
<tr>
<th>P value</th>
<th>T</th>
<th>Serum ng/ml</th>
<th>Remission ng/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.0001</td>
<td>694.60±77.35</td>
<td>384.00±30.61</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: Visfatin was elevated both systemically and locally in the patients with knee OA, was elevated during flare-ups and decrease during remission, was higher in serum than in synovial fluid of patients and There was no difference in the level of visfatin in relation to aging or gender difference.

References:

AB0040C
INFILTRATING NATURE DRIVES RELEASE OF MITOCHONDRIAL DNA ENCLOSED IN EXTRACELLULAR MEMBRANE VESICLES AND PROPAGATION OF INFLAMMATION IN BEHÇET’S DISEASE
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Background: It has been reported that mitochondrial DNA (mtDNA) is released into the cytosol by mitochondrial stress and induces pro-inflammatory cytokine production via inflammasome and intracellular DNA sensors. Also, mtDNA in the extracellular space is known to result in sterile inflammation. However, the molecular mechanism of mtDNA release and its pathological significance in autoimmune diseases (ADs) has not been elucidated.

Objectives: To clarify the molecular mechanism of mtDNA release and its pathological significance in ADs.

Methods: We collected the serum from various AD patients and analyzed the levels of mtDNA in serum. We digested mtDNA in serum by DNase treatment. We purified the extracellular membrane vesicles (EMVs) and evaluated their inflammation-inducing potential. Also, we investigated the molecular mechanism behind mtDNA-induced inflammation by using inflammasome gene Knock out cell lines.

Results: We first measured the levels of mtDNA in serum of the various ADs by quantitative PCR and found that serum mtDNA levels were significantly high in BD. Moreover, mtDNA in BD serum could not be digested by DNase treatment and was detected in the extracellular membrane vesicles (EMVs) purified by ultracentrifugation. Since EMVs are known to deliver various molecules from one cell to another, we stimulated monocytic cells with BD-derived EMVs and found that these EMVs could induce IL-1β production in an NLRP3 inflammasome-dependent manner. We then studied the mechanism of secretion of mtDNA in EMVs and found that both human primary monocyte and monocyte-like cell line released mtDNA-containing EMVs after stimulation with ATP or LPS. Further, BD-derived monocytes secreted more abundant mtDNA in EMVs than monocytes derived from healthy donors. Additionally, the inhibition of caspase-1 activity reduced the secretion of mtDNA in EMVs

Conclusion: We revealed a novel mechanism of inflammation propagation involving inflammasome and mtDNA; activated inflammasome releases mtDNA-containing EMVs and subsequently leads to mtDNA-induced inflammation via NLRP3 inflammasome. Such inflammatory mechanism may contribute to the exacerbation of inflammation in BD.

Disclosure of Interests: None declared

Cytokines and inflammatory mediators
SEMAPHORIN 3A: A POSSIBLE MARKER FOR DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS
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Background: Sema 3A is concerned in the pathogenesis of many autoimmune diseases because it is involved in regulation of immune responses and maintenance of self-tolerance. Regulatory T cells play an important role in maintaining immunological self-tolerance by suppressing autoreactive T cells. Sema3A promotes regulatory T cells by enhancing IL-10 production

Objectives: The current study aimed at testing the possible role of Semaphorin 3A (Sema 3A) in activity and in remission in rheumatoid arthritis patients and to assess whether this level correlates with interleukin 10 (IL-10) level.

Methods: Sixty Egyptian patients with rheumatoid arthritis (RA) were divided into three groups according to modified Disease Activity Score (DAS28), RA in high activity (group II, n=20), RA in moderate activity (group III, n=20) and RA in remission (group IV, n=20) and compared with 20 normal individuals (group I). Serum levels of Sema 3A and IL-10 were measured and correlated with ESR, CRP, TNF-α, IL-10, IL-6, IL-8, MCP-1/CCL2, VEGF, and IL-6.

Results: IL-6 was higher in patient groups, with highest mean among group IV. A significant negative correlation was detected between Sema 3A and each of ESR, CRP, DAS28 and HAQ. Serum IL-10 was higher in patient groups, with highest mean among group IV. Conclusion: reduced serum level of Sema 3A was found to be correlated with disease activity and indicating its usefulness marker for RA disease activity.


GENE POLYMORPHISM TNFAIP3 RS6920220 IS ASSOCIATED WITH A SPECIFIC CYTOKEINE PATTERN IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS
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Methods: 44 eRA patients (36 females; median age 55.0 [46; 60,0]; median disease duration 7.0 [4; 9.11) months; DAS28 5.9 [4.8, 6.4] were included. 89% were positive for IgM rheumatoid, 92% - anti-CCP positive. “Gene candidate” approach was used to search for the following gene polymorphisms (SNPs): TP53N2 (+1685 C/T, rs2476601), CTLA4 (+49A/G, rs213775), TNFAIP3 (rs675520, rs9092020, rs1049914), IL1B (-174G/C, rs1800795), ILEP (-358A/G, rs1800629), MCP1/CCL2 (+358A/G, rs1204611), IL10 (-592A/G, rs1808072, -1082 A/G, rs180896). Serum levels of 27 cytokines/chemokines were measured using the xMAP multiplexing technology at baseline, at 12 and 24 weeks after initiation of therapy. All patients were treated with methotrexate and/or biological therapy in accordance with the treat-to-target strategy (REMARKA study).

Results: Among all studied SNPs only polymorphism rs6920220 of gene TNFAIP3 was associated with a certain cytokine/chemokine production across all time-points: baseline, 12 and 24 weeks. At baseline, the carriers of GG genotype (27 pts) showed significantly higher serum levels of the following mediators, compared to the patients with GA/AA genotypes (17 pts): IL8 (42.8 ± 23.0 pg/ml vs 25.5±8.4 pg/ml, p<0.0001), IL-17 (20.4±15.8 pg/ml vs 11.5±12.1 pg/ml, p=0.017), MIP-1α (19.1±40.5 pg/ml vs 9.8±27.9 pg/ml, p=0.036), MIP-1β (155.4±45.0 pg/ml vs 117.8±47.2 pg/ml, p=0.013), PDGF-BB (6967.5±3257.7 pg/ml vs 4600.6±1826.0 pg/ml, p=0.018). At week 12th, IL-8 serum levels were the only ones to remain associated with polymorphism rs6920220 (p=0.015). At week 24th, the carriers of GG genotype had higher serum levels of several cytokines/chemokines, compared to the patients with GA/AA genotypes: IL-8 (47.9±26.2 pg/ml vs 33.7±19.3 pg/ml, p=0.05), IP-10 (2451.7±1825.2 pg/ml vs 1404.9±941.1 pg/ml, p=0.037), MIP-1β (150.7±68.2 pg/ml vs 89.7±33.8 pg/ml, p=0.004), PDGF-BB (515.9±2667.6 pg/ml vs 3915.4±1343.5 pg/ml, p=0.046). There was no statistically significant difference in production of IL-6, IP-10, MIP-1β, and PDGF-BB prior to and after 24 weeks of therapy.

Conclusion: The results suggest that polymorphism rs6920220 of gene TNFAIP3 is linked to a particular cytokine/chemokine pattern. Biological therapy used according to the treat-to-target strategy for 24 weeks does not lead to the reduced production of IL-6, IP-10, MIP-1β, and PDGF-BB in the carriers of GG genotype.


ACTIVIN A AND FOLLISTATIN AFFECT THE INTERACTION OF ENDOTHelial CELLS AND RHEUMATOID ARTHRITIS SYNOVIAL FIBROBLASTS
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Background: Activin A and its antagonist follistatin are part of an autoregulatory cycle, which is well known in the hypophalamic-pituitary-gonadal axis. Activins also have an important function in autoimmune diseases, such as rheumatoid arthritis (RA). Due to inflammation, activin A is released systemically, causing an induction of its antagonist follistatin. The negative feedback mechanism is well described for hepatocytes, but seems to be inactive in synovial fibroblasts from patients with rheumatoid arthritis (RA). Neangiogenesis, which is mediated partially by local fibroblasts, is increased due to inflammation and tissue hyperplasia in RA synovium. Despite the fact that RASF contribute to cartilage destruction in RA and RASF are able to interact with endothelial cells, less is known about the effect of activin and follistatin in this context.

Objectives: The aim of this study was to examine the effect of activin A and follistatin on the interaction of RASF and endothelial cells.

Methods: Endothelial cells (HUVECs) were commercially obtained and RASF were isolated from synovial tissue of patients with RA undergoing joint replacement surgery. RASF and HUVECs were stimulated in mono-, or coculture with activin A (15 ng/ml), follistatin (500 ng/ml) and/ or IL-1β (1 ng/ml). The concentrations of activin A, follistatin, VEGF and IL-6 were measured by ELISA.

Results: IL-1β induced the release of activin A 8-fold in RASF alone (p<0.01, n=5) as well as in direct coculture with HUVECs 4-fold (p<0.02, n=5). The stimulation with follistatin together with IL-1β reduced the activin A concentration produced by HUVECs 9-fold (p<0.01, n=5) as well as in cocultures (10-fold, p<0.01) in comparison to stimulation with IL-1β alone. This reduction could not be observed in RASF mono-culture. In HUVECs, the IL-6 release was reduced by 37.6% after stimulation with activin A and IL-1β (n=5, p<0.05) in comparison to the stimulation with IL-1β alone. In RASF mono-culture the release of IL-6 was induced by 61.0% after stimulating with activin A combined with IL-1β in comparison to the stimulation with IL-1β alone. In direct coculture neither the induction, nor the reduction of the IL-6 concentration could be detected when stimulated with activin A and IL-1β. The release of VEGF was induced in RASF with IL-1β (89%), activin A (55%), activin A combined with IL-1β (148%), follistatin and IL-1β (84%) compared to unstimulated control. In coculture with HUVECs, the induction was less distinct than in monoculture (IL-1β: 75%), activin A: 22%, activin A and IL-1β: 101%, follistatin and IL-1β: 67%, n=4)

Conclusion: The autoregulatory cycle of activin A and follistatin is active in endothelial cells and inactive in RASF. Due to the interaction of endothelial cells and RASF, the proinflammatory response of the RASF is weakened. This was shown in direct coculture with no induction in coculture compared to stimulation with activin A and IL-1β in RASF monocytes. Interestingly, in direct coculture, the effects of HUVECs appear to dominate resulting in a significant reduction of the activin A concentration in the presence of follistatin and IL-1β in comparison to RASF monocytes.

REFERENCES

**AB0054**

**SEQUENTIAL INTRA-ARTICULAR INJECTIONS OF LINEAR AND CROSS-LINKED HYALURONIC ACIDS IN THE TREATMENT OF GONARTHROSIS**

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**Background:** Sequential intra-articular injections of linear and cross-linked hyaluronic acids in the treatment of gonarthrosis  

**Objectives:** This study evaluates clinical and biochemical effects of sequential intra-articular (IA) injections of two different formulations of hyaluronic acid (HA) in gonarthrosis (GA) patients. The first formulation consists in linear HA (LHA, MW 800-1200kDa; Regenflex Starter, Regenyal Labs, Italy) and the second in an intercalated mixture of cross-linked and linear HAs (CL-LHA, MW 1-2 MDa the crosslinked form and 500kDa the linear, intercalated one; Regenflex BioPlus).  

**Methods:** 39 knee GA patients, 19 adults (50-65 years) and 20 elderly (>65 years), underwent 2 IA injections, i.e. LHA only at baseline and CL-LHA after 1 week. The same injections were repeated after 6 months. Clinical assessment - visual analog scale (VAS) for pain, range of motion (ROM) and WOMAC index for knee functional limitation - was performed at baseline and after 3, 6, 9, 12 months. Blood, collected at baseline, after 1 week and 3 months, was analysed for relevant cytokines and collagen telopeptide II (CTX-II). Synovial fluid (SF) from patients with recurrent knee effusion (GA worse group) was biochemically analysed at baseline and 1 week. SF proteomic analysis was also carried out at specific time points.  

**Results:** This HA-regimen improved joint pain and function independently from the age; plasma and synovial biochemical analyses indicate the attenuation of inflammatory cytokines (IL-1α, IL-6, IL-17) and the stabilization of CTX-II; ultrasonograph data show an improvement of cartilage conditions and thickness at 12 months.  

**Conclusion:** Sequential IA injections of LHA and CL-LHA represent a highly effective treatment especially in low degree GA patients and produce a significant and enduring improvement also in the GA worse group. The efficacy is likely dependent on the sequential administration of LHA and CL-LHA: the pharmacokinetic rationale of this combination will be discussed.  

**References:** E. Barbieri,2 P. Sestili,1 F. Mannello,1 G. Amnabali1, S. Contarini1, L. Vallorani1, A. M. Gioacchini1, D. Ligui1, L. Croce1, Tung Tran Dang Xuan4, C. Bartolucci1, V. Stocchi1 and I. Capparucci1  

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**AB0055**

**INFECTIONS WITH ANTI TNF ALPHA: PROSPECTIVE STUDY OVER 12 YEARS**

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**Background:** Anti Tumor Necrosis Factor alpha (TNFα) has significantly improved the prognosis of some chronic inflammatory diseases (CID). Nevertheless, they carry with them a significant risk of opportunistic infections, imposing a rigorous surveillance and an adequate education of the patients. In a context of endemic tuberculosis, it is imperative to take the appropriate precautions to detect this kind of infection in rheumatisers under anti TNFα.  

**Objectives:** The aim of our work was to study the profile of infectious incidents in patients treated with anti TNFα.  

**Methods:** This is a prospective study of patients treated with anti-TNFα over a 12-year period (2006-2018). We examined all infectious complications for each patient who received an anti-TNFα for CID while assessing the level of severity, the type of infection and the risk factors that may be related to this type of incident.  

**Results:** During the study period, 134 patients were identified, these patients were followed for ankylosing spondylitis (AS) for 58 cases, 36 for enteric rheumatism, 23 for psoriatic arthritis and 17 for rheumatoid arthritis. The mean age was 46.3 years (19-64 years), the mean age of the disease was 44.2 months (8-140). The molecules used were: infliximab, etanercept, adalimumab with a respective number of patients (%): 29 (21), 44 (33), 61 (46). Of the 134 patients evaluated, 71 were diagnosed and treated by a physician (in 47 patients), only 5 were serious: 2 cases of tuberculosis were reported (intestinal and ganglionic tuberculosis), 1 case of chickenpox of the adult, 1 case with perianal abscess, 1 case of erysipelas of the lower limb. The infection was bacterial, viral or mycotic [n (%) = 38 (53), 61 (86), 7 (8)]. A large proportion of the patients were on conventional immunosuppressive therapy. The factors related to the occurrence of infectious incidents were: use of corticosteroids p<0.0001, habit in rural areas p=0.042.  

**Conclusion:** More than a third of patients have infectious complications after TNFα treatment in our study sometimes with serious issue. Thus, with the emergence of these incidents, the physician has to be very vigilant when instituting this biotherapy, and secondly, a rigorous and prolonged monitoring of the patients.


**AB0056**

**CUTANEOUS ADVERSE EFFECTS WITH BIOLOGIC AGENTS**

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**Background:** Biologic agents (BA) are designed to treat chronic inflammatory diseases (CID), however, the adverse effects inherent with these drugs are more and more encountered. Among them are dermatological manifestations: infections, allergic reactions or even skin cancers, which sometimes require stopping treatment temporarily or permanently.  

**Objectives:** The goal of this work consists to identify the cutaneous manifestations (CA) that have been reported to the most commonly used biologics in CID.  

**Methods:** It’s a prospective study in patients received in day hospital and treated with BA for CID during a period of 9 months (October 2017 - June 2018), we recorded all the data on CA after a complete dermatological examination, nor forgetting that we appreciated the phototype of the patients, the level of exposure to the sun and means of photoprotection.  

**Results:** We collected the data of 68 patients under BA for the study (Adalimumab = 21, Etanercept = 17, Tocilizumab = 12, Infliximab = 7, Rituximab = 11) with a clear female predominance 59.4%, the mean age was 39 years. 37 (54%) had cutaneous manifestations, the main CA occurred with TNFs inhibitors 21/68 (30%), with more often skin infections. The other CA encountered were cutaneous rashes and allergic reactions, appearance of psoriasis or eczema and injection site reactions, we did not cross any skin cancer.  

**Conclusion:** Cutaneous manifestations remain frequent and relatively benign with BA. This work confirms the importance of education and dermatological monitoring of patients treated with biologic drugs in the CID. This prospective study needs to be completed over a longer period especially to screen any skin cancer.


**AB0057**

**ASSESSMENT OF MATRIX METALLOPROTEASE 3 (MMP3) AS A POTENTIAL BIOMARKER FOR RHEUMATOID ARTHRITIS IN ALGERIAN PATIENTS**

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**Background:** Matrix metalloproteinase 3 (MMP3) is a protease induced by rheumatoid pannus pro-inflammatory cytokines during rheumatoid arthritis (RA) and degrades many cartilage and bone components. Its serum level is a useful marker for predicting joint destruction and evaluating disease activity.  

**Objectives:** First, compare MMP3 production in RA patients to controls, then try to place this marker in the evaluation of disease activity.  

**Methods:** We subdivided the studied population into three groups:  

- RA: n = 134; sex ratio: 1: 5; age: 50 ± 14 years; disease duration: 7 ± 9 years.  
- Healthy controls: n = 67; sex ratio: 1: 7; age: 38 ± 11 years.  
- Population control: Patients with:  
  - Inflammatory rheumatism: n = 80;  
  - Chronic inflammatory diseases (CID): 18 Connective tissue disease (CTD), 14 chronic hepatitis C and 2 Cohn disease (CD).

- RA: n = 134; sex ratio: 1: 5; age: 50 ± 14 years; disease duration: 7 ± 9 years.  
- Healthy controls: n = 67; sex ratio: 1: 7; age: 38 ± 11 years.  
- Population control: Patients with:  
  - Inflammatory rheumatism: n = 80;  
  - Chronic inflammatory diseases (CID): 18 Connective tissue disease (CTD), 14 chronic hepatitis C and 2 Cohn disease (CD).
The serum MMP3 measurement was performed by ELISA assay.

Results: Serum MMP3 was significantly higher in RA patients vs. healthy controls (p < 0.0001), Inflammatory rheumatism (p < 0.0001) and CID (p < 0.05) and is particularly high in women with high Disease Activity Score 28 joints (DAS28) vs. Moderate DAS28 (p < 0.05). In addition, it is higher if patients have: positive CRP: p < 0.05; positive RF: p < 0.05; ACDA: p < 0.05 and Bone erosion: p < 0.01 compared to other patients. Finally, there is a positive correlation between MMP3 production and RF (p < 0.001, Spearman r = 0.35) and ACDA (p < 0.01, Spearman r = 0.29) but not with DAS28 joining the results published by Mahmood et al.[2013] and Fadda et al.[2016]. Furthermore, in RA patients, there is no significant difference in MMP3 levels according to whether the erythrocyte sedimentation rate (ESR) is accelerated or not, unlike CRP which represents the best marker of inflammation in this disease, according to the literature. Finally, the production of MMP3 is greater in case of erosion and is associated to bone and joint destruction.

Conclusion: MMP3 serum measurement is a particularly useful marker of inflammatory activity in RA and may have potential predictive value in the development of bone and joint destruction.

REFERENCES

Disclosure of Interests: None declared
METHOTREXATE DOWNREGULATES P-GLYCOPEPTIDE EXPRESSION AND INHIBITS THE ACTIVATION OF JAK2/STAT3 PATHWAY IN RHEUMATOID ARTHRITIS PERIPHERAL BLOOD MONOUNCLEAR CELLS

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Background: Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by abnormal synovial hyperplasia, inflammatory cell infiltration, and destruction of cartilage or bone. Early use of disease-modifying anti-rheumatic drugs (DMARDs) can significantly improve the patient's condition. However, many patients had no response after treatment or gradually decreased after treatment for some time. DMARDs Multidrug resistance (MDR1) is an important cause of the above phenomenon. How to reverse MDR in RA patients, and then control the disease is a major problem in RA treatment. The mechanism of MDR is complex. ATP binding cassette transporter super family consists of 48 transporters. ABCB1/P-glycoprotein (P-gp) is one of the major proteins associated with MDR1. The expression of P-gp is induced not only by genotoxic mechanisms, but also by inflammatory cytokines such as IL-2, IL-4, IL-6, and TNF-a in some inflammatory diseases.

Objectives: The multiple drug resistance (MDR) to disease modifying anti-rheumatic drugs (DMARDs) is the key factor in Rheumatoid arthritis (RA) treatment field. P-glycoprotein (P-gp) encoded by multidrug resistance gene (MDR1) is involved in the excretion of numerous DMARDs. We investigated the effects of methotrexate (MTX) alone and combined with interleukin 6 (IL-6) on P-gp expression and examined the signaling pathway involved in peripheral blood mononuclear cells of RA patients.

Methods: The peripheral blood mononuclear cells were extracted from Fifteen RA patients who were without any DMARDs and biological agents treatment. These cells were treated with IL-6, IL-6+MTX(0.1μg/ml), IL-6+MTX (0.1μg/ml), IL-6+MTX (1μg/ml) for 72h. P-gp expression was measured by flow cytometry and real-time polymerase chain reaction (RT-PCR); JAK2 and STAT3 were measured by RT-PCR.

Results: Methotrexate produce a dose-responsive reduction of both P-gp, JAK2 and STAT3 expression induced by IL-6.

Conclusion: Methotrexate downregulates p-glycoprotein expression and inhibits the activation of JAK2/STAT3 pathway in rheumatoid arthritis peripheral blood mononuclear cells.

REFERENCES

Disclosure of Interests: None declared

AB0061 INVESTIGATING THE ROLE OF TGF-B AND FATIGUE IN CHRONIC FATIGUE SYNDROME

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Background: Chronic fatigue syndrome (CFS) is estimated to affect up to 5% of people in Europe and is more common in women than men. It is characterised by unexplained fatigue, post-exertional malaise and a range of other symptoms. Recent studies indicate potential immune dysfunction in CFS, specifically regarding cytokines and the adaptive behavioural response.

Objectives: This study aims to investigate serum transforming growth factor-beta (TGF-B) and the expression of the TGF-B Receptor 1 (TGFBR1) and TGF-B Receptor 2 (TGFBR2) genes, in relation to the fatigue associated with CFS.

Methods: Serum active and total TGF-B concentrations were measured in 117 CFS patients and 40 HCs using a TGF-B specific luciferase bioassay. Expression levels of TGFBR1 and TGFBR2 were analysed using quantitative PCR. Fatigue was assessed using the fatigue impact scale (FIS).

RESULTS
Serum TGF-B concentrations in the CFS group did not differ significantly compared with the HC group (p=0.58). TGF-B concentrations showed no correlation with disease duration but there was a trend towards decreased TGF-B with increasing symptom duration. There were no significant differences between the levels of TGFBR1 and TGFBR2 in any of the fatigue groups, or between HCs. Active TGF-B concentrations were significantly elevated in the ‘severe’ FIS group compared with the ‘mild’ FIS group (p=0.04). Active/total TGF-B levels were significantly higher in the ‘severe’ FIS group than the ‘mild’ and ‘moderate’ FIS groups (p=0.02, p=0.03 respectively).


AB0062 P75NTR IN THE MODULATION OF INFLAMMATORY RESPONSE MEDIATED BY SYNOVIAL FIBROBLASTS

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Background: Our previous studies showed high expression levels of p75NTR, the nerve growth factor (NGF) receptor, in mononuclear cells (MNCs) obtained from blood and synovial fluids of patients with juvenile idiopathic arthritis (JIA) and rheumatoid arthritis (RA). p75NTR binds with high affinity proNGF, the immature form of NGF whose concentration, as we recently demonstrated, is extremely high in the synovial fluids of arthritis patients. In ex vivo experiments we demonstrated that recombinant proNGF increases inflammatory cytokine production in patient MNCs, an effect that was abolished using p75NTR inhibitors.

We also found that synovial fibroblasts (SFs) represent the main source of proNGF in the inflamed synoviae. At present it is not known whether proNGF can influence the activity of SFs that are key effector cells in synovial inflammation producing inflammatory mediators that regulate chondrocytes and osteoblasts activation.

Objectives: To investigate the mechanisms regulating p75NTR expression in synovial fibroblasts of arthritis patients and to evaluate the effects of its inhibition on the inflammatory response.

Methods: SFs from arthritis patients were used to study the activity of proNGF/p75NTR axis. SFs from osteoarthritis patients (OA) and skin fibroblasts from healthy donors (HD) were used as controls. p75NTR, NGF, and cytokine transcripts were evaluated by quantitative PCR (qPCR). Protein expression of p75NTR, NGF, and proNGF were analyzed by Western Blot. ELISAs were used to evaluate NGF, proNGF and cytokine concentration in supernatants and synovial fluids. p75NTR was inhibited using LM1A-31, a synthetic inhibitor that blocks the binding between p75NTR and its specific ligand proNGF.

RESULTS: mRNA and protein expression of p75NTR were up-regulated in arthritis SFs compared to OA SFs and skin fibroblasts. In vitro stimulation with recombinant cytokines (IL-1B, IL-6, IL-1T), LTR-ligands (such as LPS), and TGFβ1 strongly increased p75NTR mRNA expression in arthritis SFs. Interestingly, after stimulation we observed that also OA SFs and HD fibroblasts up-regulated p75NTR transcript, suggesting that p75NTR levels are modulated by the inflammatory mediators. SFs of arthritis patients spontaneously produced proNGF and its release was further enhanced by all the above-mentioned inflammatory stimuli, albeit with different extent. Thus patient SFs can both produce proNGF and bind it through p75NTR. The inhibition of proNGF binding to p75NTR using LM1A-31 in arthritis SFs, activated with inflammatory cytokines or with synovial fluids, significantly reduced the expression and release of pro-inflammatory cytokine.
A SYSTEMS APPROACH TO INVESTIGATE INFLAMMATION RESOLUTION BY MULTICOMPONENT MEDICINAL PRODUCT TR14

Patrick Schopohl1, Suchi Smita1, Faiz Khan1, Tom Gebhardt1, Matti Hoch1, Marco Moneta2, Ivan Caiello3, Luigi Manzo4, Marzia Soligo5, Luigi Manni6, Gian Luciapia Farina7, Gaetana Minnone8

AB0064

SERUM TENASCIN-C LEVELS ARE ELEVATED IN PATIENTS WITH AXIAL SpondyloArthritis

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AB0065

SYSTEMS APPROACH TO INVESTIGATE INFLAMMATION RESOLUTION BY TR14

Patrick Schopohl1, Suchi Smita1, Faiz Khan1, Tom Gebhardt1, Matti Hoch1

REFERENCES

Gliostatin (GLS) is known to have angiogenic and arthritogenic activities. GLS was expressed in inflamed synovial tissues of patients with RA. In cultured fibroblast-like synoviocytes (FLSs), GLS expression was found to be up-regulated by inflammatory cytokines, such as IL-1β, TNFα, IL-6. GLS acted as a cytokine in FLSs, augmenting its own synthesis, and also induced the extracellular secretion of matrix metalloproteinase (MMP)-1, -3, -9, and -13. Therefore, the suppression of GLS production might be an effective therapy in RA. The mechanism of the action of baricitinib had not been determined in fibroblast-like synoviocytes (FLSs).

Objectives: The purpose of this study was to investigate the GLS production effect of interferon (IFN) γ and the inhibitory action of baricitinib in FLSs derived from patients with RA (RA-FLSs).

Methods: RA-FLSs were cultured from synovial specimens of patients with RA and stimulated by IFNy with or without treatment of baricitinib. The expression levels of GLS were determined using reverse transcription-polymerase chain reaction (RT-PCR), enzyme immunosassay and immunocytochemistry.

Results: In cultured RA-FLSs, GLS mRNA and protein were significantly induced by stimulation with IFNy and these GLS inductions were significantly suppressed by treatment of baricitinib in dose-dependent manners.

Conclusion: Our data demonstrated that JAK/STAT activation play a pivotal role in IFNy mediated GLS up-regulation in RA-FLSs. Suppression of GLS production in inflamed synovia has been suggested as one of the anti-inflammatory effects of baricitinib.

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Disclosure of Interests: None declared
Conclusion: The GC genotype of IL-6-174 G/C was suggested by the analyses to be related to low prevalence of vasculitis, especially for large and medium vessels.

REFERENCES

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cytokines and chemokines including IL-12β (P=0.07), IL-6 (P=0.07), IL-10 (P=0.12), IL-18 (P=0.19), and IL-4 (P=0.63).

Conclusion: This study illuminates the downstream effects of neutralizing TNFα not previously investigated. Adalimumab had a pronounced effect on downregulation of the inflammatory CXCL1 subfamily chemokines IL-8, CXCL5, CXCL9, and CXCL10. This helps explain findings of diminished inflammatory cell migration into joints seen in the first trials with TNFα inhibitors.[2] Further characterization of downstream effects of the multiple DMARDs used for the treatment of immune mediated inflammatory arthritis will help guide treatment strategies for these patients.

REFERENCES

Disclosure of Interests: Anne Fauschou Boisen: None declared, Elisabeth Busk Rasmussen: None declared, Tue Wenzel Kragstrup Consultant for: Bristol-Myers Squibb, Speakers bureau: Pfizer, Bristol-Myers Squibb, Eli-Lilly, Novartis, UCB

AB0070
THE RELATIONSHIP BETWEEN THE LEVEL OF NESFATIN-1 AND THE CLINICAL MANIFESTATIONS OF RHEUMATOID ARTHRITIS
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Background: Nesfatin-1 is actively studied in the pathogenesis of metabolic disorders. An excess of this factor in the brain leads to loss of appetite, a feeling of fullness, as well as a decrease in body weight. Similarly, elevated levels of nesfatin are associated with depressive disorders [1]. We studied the level of nesfatin in the serum of patients with rheumatoid arthritis (RA) and found a relationship with systemic inflammation and functional impairment [2].

Objectives: To study the relationship of serum nesfatin-1 levels with the clinical manifestations of RA.

Methods: To identify the relationship between serum nesfatin-1 and the clinical manifestations of rheumatoid arthritis, all patients were divided into 2 groups. The first group - 1 (66 patients) with elevated serum nesfatin (> 37.95 ng/ml). The second group - 2 (44 patients) - with normal values (<37.95ng/ml). In both groups, we studied the clinical manifestations of RA.

Results: A high level of nesfatin in RA patients was typical for patients with a higher degree of activity in DAS28 (χ² = 8.37; p = 0.04), seropositivity for the rheumatoid factor (RF) (χ² = 5.53; p = 0.02), the duration of the disease is more than 10 years (χ² = 9.53; p = 0.01). At the same time, there was no significant correlation between the level of nesfatin and the extra-articular manifestations of RA (χ² = 2.09; p = 0.14) and the degree of radiological damage to the joints (χ² = 4.45; p = 0.21).

Conclusion: This study shows that serum nesfatin-1 levels are significantly higher in patients with more unfavorable RA, than in RA with minimal clinical manifestations. These data confirm the pathogenic role of nesfatin-1 in the development of clinical manifestations associated primarily with RA activity, but to a lesser extent with organ lesions in RA. The relationship of the level of nesfatin with the duration of the disease is of particular interest, since there is no correlation with the degree of X-ray damage to the joints and organ damage. There are literary data on the relationship of depression and late stage of RA [3].

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Disclosure of Interests: Ruth J. Pepper: None declared, Mathew Hutchinson: None declared, S.R. Henderson: None declared, S.K. Todd: None declared, Alan D. Salama: None declared, Philip N. Hawkins: None declared, Helen J. Lachmann: None declared, UCL Division of Medicine and Royal Free Hospital London NHS Foundation Trust, UCL Centre for Nephrology, London, United Kingdom; University College London Hospitals NHS Foundation Trust, Rheumatology, London, United Kingdom; UCL Division of Medicine and Royal Free Hospital London NHS Foundation Trust, National Amyloidosis Centre, London, United Kingdom

Background: Familial Mediterranean Fever (FMF) is caused by mutations in MEFV. The protein product pyrin is expressed in monocytes, neutrophils and eosinophils. Acute inflammatory attacks are accompanied by a dramatic hepatic acute phase response. S100A8/A9 is damage associated molecular pattern and a TLR4 ligand expressed in neutrophils, monocytes and early infiltrating macrophages. We aimed to investigate S100A8/A9 in 39 patients with FMF, 45 healthy carriers and wild type controls.

Objectives: To measure S100A8/A9 in patients with FMF, carriers and healthy controls.

Methods: All patients were genotyped. Patients and healthy controls (HC) serum S100A8/A9 levels, cell surface expression on monocytes and neutrophils as well as intracellular peripheral blood mononuclear cells (PBMC) expression were measured by flow cytometry (FACS). CD14 cells were isolated and following overnight incubation with or without LPS, S100A8/A9 was measured in the supernatants by ELISA. Patient and HC monocyte apoptosis was compared.

Results: Serum levels were measured in 84 samples from 31 patients with homozygous or compound mutations (median 9061ng/ml [range 500-38470], 79 samples from 39 symptomatic patients who were MEFV heterozygotes (median 9394ng/ml [range 1744-38119], 80 samples from 45 individuals with MEFV variants but without clinical features of FMF (median 10939ng/ml [range 2447-40000]. There was no difference in ciprofloxacin concentrations between the different mutations. All the groups described had significantly higher levels than healthy controls (n=16 median 2836ng/ml [range 1058-6175] [p<0.001],Minimal monocyte and neutrophil cell surface expression was detectable. Following LPS stimulation there was significantly more S100A8/A9 detected in the supernatants in patients than healthy control CD14. There was also a trend to an increased intracellular monocyte S100A8/A9 expression.

Disclosure of Interests: Ruth J. Pepper: None declared, Mathew Hutchinson: None declared, S.R. Henderson: None declared, S.K. Todd: None declared, Alan D. Salama: None declared, Philip N Hawkins: None declared, Helen J. Lachmann Grant/research support from: SOBI, Novartis, Consultant for: Novartis, Takeda, Speakers bureau: SOBI, Novartis

Disclosure of Interests: None declared
AB0072 BIOMARKER CHANGES FOR PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING TOFACITINIB WITH METHOTREXATE OR GLUCOCORTICOIDS VS TOFACITINIB MONOTHERAPY

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Background: Tofacitinib is an oral Janus kinase inhibitor for the treatment of RA. Herpes zoster is more common in patients (pts) with RA vs the general population.¹ This risk increases with tofacitinib use² and appears to be further increased with concomitant use of csDMARDs such as methotrexate (MTX), or glucocorticoids (GC).² The mechanism for these increases in risk may be linked to treatment-induced interferon (IFN) suppression,² given that replication of the varicella zoster virus appears to be limited by IFN activity.²

Objectives: To evaluate whether treatment of RA with tofacitinib + MTX or GC suppresses IFN pathway proteins to a greater extent than treatment with tofacitinib monotherapy.

Methods: This was a post hoc analysis of pooled data from 1 Phase (PII) (Japan study [NCT00687193]) and 2 P3 (ORAL Scan [NCT01039688]) tofacitinib studies. Serum samples were collected at baseline (BL), Week (W)12 and/or W24 from pts with RA treated with tofacitinib 5 or 10 mg BD, given as monotherapy (Japan study; ORAL Scan) or with stable doses of MTX (15–25 mg weekly for 26 weeks; ORAL Scan) and/or GC (≤10 mg/day prednisone or equivalent; all studies). A total of 376 proteins associated with cellular and inflammatory processes, including 6 IFN pathway proteins (CXCL10, CXCL9, CXCL11, IL-12, IFNγ and IL-20), were measured using a homogeneous solution-based assay (Olink Proseek® Multiplex Assay, Uppsala, Sweden). Changes in protein levels from BL to W12 (Japan study; ORAL Scan) and/or W24 (Olink Scan, ORAL Scan) were compared for tofacitinib monotherapy vs tofacitinib + MTX or GC using linear regression models. The dependent variable was change from BL in protein levels at W12 or W24. The independent variable was MTX or GC status. Age, gender, GC status (in MTX model) and BL protein levels and tofacitinib dose were covariates. Regressions were performed separately for each study; results for GC were combined via meta-analysis using fixed and random effect models. Significance was considered at p<0.01 after controlling for false discovery rate (FDR). Data quality control included accounting for plate/batch effects and limits of detection, and removal of sample/analyses with excessive missing data.

Results: In total, 659 serum samples were collected from 321 pts. Of the 6 IFN pathway proteins, 2 (IFNγ and IL-20) were below the limit of detection. There was no strong evidence suggesting statistical differences between tofacitinib monotherapy and tofacitinib + MTX or GC in changes in levels of the 4 detectable IFN pathway proteins (CXCL10, CXCL9, CXCL11 and IL-12) from BL and/or W12 and/or W24. Significant differences were observed for 2 of the 570 other proteins: MMP-1 (FDR adjusted p=0.008) and IL1Ra (FDR adjusted p=0.009), where levels decreased from BL to W12 for tofacitinib + MTX to a greater extent than for tofacitinib monotherapy.

Conclusion: The results of this post hoc analysis suggest that tofacitinib + MTX or GC may not suppress circulating serum levels of IFN pathway proteins to a greater extent than tofacitinib monotherapy. Although there were differences at W12 for tofacitinib + MTX vs tofacitinib monotherapy in MMP-1 and IL1Ra, it is not yet clear whether these observations may be attributable to differences in the ethnicities of the study populations receiving these two treatment regimens (global vs Japan). Further analyses of biomarker changes with tofacitinib are ongoing.

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Interrelationship between Nicotinic Acetylcholine Receptor and Cytokine Production Noted Following T-Cell Antigen Recognition and Activation
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Background: T cells express muscarinic and nicotinic acetylcholine receptors (nAChRs, nAChRs) that increase intracellular Ca2+ [1] on stimulation. The expression of these receptors on macrophages and their activation by vagal stimulation has recently been the focus for novel arthritis treatment [2].

Methods: nAChR heterologous subunits were expressed in Xenopus oocytes and the inhibitory activity of various peptides at ACh-evoked currents were assessed. The effect of these peptides on T-cell antigen recognition and subsequent cytokine production was assessed using an antigen presentation assay (APA). Briefly, the 284.11 murine T cell hybridoma recognizes cytochrome c as the antigen was co-cultured with the antigen presenting B cell hybridoma line LK35.2 (I-Ek bearing) and pigeon cytochrome c in the absence or presence of peptide or several nAChRs antagonists, including mecamylamine (broad nAChR antagonist), waglerin-1 (α9β4δ), and β2 δ-bungarotoxin did not affect IL-2 production in the APA. ELISA and real-time PCR were performed to measure cytokine protein levels and nAChRs T-cells mRNA express levels separately.

Results: At 10μM, peptide W32052 had modest 50-55% inhibition of human (h) αβ2 and h4q2 nAChR subtypes, and 35% inhibition at h9q10. W32052 greatly inhibited chimeric rat α1β1δ-μ mouse e (85%) at 10μM. W32052 also inhibited IL-2, IL-6, TNF-α and GM-CSF production at 50μM in the APA. nAChRs antagonists, mecamylamine (100μM), Rag1 (10μM), Vc1.1 (7.5μM) and dihydro-β-erythroidine hydrobromide (d94β and d9β2), ELISA and real-time PCR were performed to measure cytokine protein levels and nAChRs T-cells mRNA express levels separately.

Conclusion: W32052, an antagonist of nAChRs, inhibits cytokine production following antigen recognition suggesting that there is a close link between T-cell antigen activation, ion channel regulation mediated by ACh and cytokine production. Further experiments are in progress.

REFERENCES

Disclosure of Interests: None declared

Effect of Sidaguri Extract (Sidaguri Rhombifolia L.) on Urinary Carboxy-Terminal Telepeptides of Type II Collagen in Osteoarthritic Patients
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Background: Osteoarthritis is one of the most common joint diseases in Indonesia and elsewhere. Assessment of the effectiveness of osteoarthritis therapy with biomarkers should be developed. One of the biomarker that can be used to assess the activity of osteoarthritis is Urinary Carboxy-Terminal Telepeptides of Type II Collagen. Indonesia is the center of world biodiversity, and Sidaguri is one of the traditional plants that is believed to have many benefits including its anti-inflammatory effect and the ability to decrease level of uric acid. The β-sitosterol is an active component in Sidaguri that has anti-inflammatory activity in osteoarthritis.

Objectives: To compare the effect of sidaguri and meloxicam therapy with meloxicam alone in decreasing the levels of Urinary Carboxy-Terminal Telepeptides Of Type II Collagen in osteoarthritic patients.

Methods: This study was conducted on 24 patients with osteoarthritis at H. Adam Malik General Hospital Medan from April to June 2018. Subjects were divided into two groups, namely placebo and Sidaguri group. Levels of uCTX II were assessed before and after intervention. T-test was used to analyze the data using SPSS version 22.

Results: 83.3% of osteoarthritic patients in H. Adam Malik hospital who participated in this study were women with mean age 50.38 ± 9.74 years in the placebo group and 63.08 ± 14.14 years in the sidaguri group. The results showed that subjects receiving Sidaguri showed significant decrease in uCTX II before and after intervention (521.42 ± 369.99 vs 330.75 ± 163.49 ng/mmol, p = 0.003). Meanwhile, in the placebo group also found decreased levels of uCTX II but it was not statistically significant (286.17 ± 163.92 vs. 218.25 ± 75.05 ng/mmol, p = 0.238). In addition, there was a significant difference between the mean of the two groups after the intervention (p = 0.046).

Conclusion: There was a significant decrease in uCTX II levels in osteoarthritic patients who received Sidaguri extract for 30 days compared to the placebo group.

REFERENCES
Results: 152 patients were included. (80 adalimumab-treated and 72 etanercept-treated). No statistically significant difference between mean IL-17A, IL-17AF, IL-17F and IL-10 levels at baseline and 3 month follow-up were observed (figure 1). For IL-17A, those patients classified as good responders demonstrated an increase in mean serum levels of IL-17A from 1.06 pg/ml at baseline to 1.23 pg/ml at 3 months. This came close to significance (p = 0.07). Further analysis was carried out by drug group and also a subgroup analysis by drug group linked to responder status. No statistically significant results were obtained. Adjusting for gender, baseline DMARD use and DAS-28 scores did not alter findings.

Figure 1: Mean interleukin levels at pre-treatment and 3 months

Conclusion: There was a lack of statistically significant data to suggest a correlation between pre-treatment and 3 month IL-17F, IL-17AF and IL-10 concentrations. However, an increase in IL-17 A serum levels between baseline and 3 months may be associated with a good EULAR response status by 6 months. Larger sample sizes are required to confirm this.

References

Disclosure of Interests: None declared

AB0077 THE THERAPEUTIC EFFECT OF GPMB IN A TRAUMATICALLY-INDUCED OSTEOARTHRITIC MODEL

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Background: Osteoarthritis is a severe joint disease that affects millions of people. At this time, the current treatment for osteoarthritis is total joint reconstruction surgery. GPNMB plays a key role in bone remodeling and bone growth. Data from our lab suggested that GPNMB is a positive regulator of osteoblastogenesis and a negative regulator of osteoclastogenesis.

Objectives: The role of GPNMB in cartilage has not been investigated before. In this study we examined the therapeutic effects of GPNMB on damaged cartilage using post-traumatic osteoarthritic mouse model.

Methods: The destabilization of the medial meniscus (DMM) surgery in mice has been found to be an excellent model for studying post-traumatic osteoarthritis. We performed the DMM surgery on 21 C57BL6 mice. These mice were divided into three intra-articular injection treatment groups consisting of a control, low dose GPNMB, and high dose GPNMB. These mice were divided into three intra-articular injection treatment groups consisting of a control, low dose GPNMB, and high dose GPNMB. Moderate to severe osteoarthritis develops around six to eight weeks with this model.

Results: Here we present that damaged human cartilage has significantly higher levels of GPNMB compared to undamaged cartilage. In addition, human osteoarthritic chondrocytes treated with GPNMB showed a protective response to inflammation induced by IL-1-beta. In this study, we examined whether recombinant GPNMB has an anti-inflammatory effect in a model of post-traumatic osteoarthritis.

Conclusions: Our data clearly showed that GPNMB has therapeutic anti-inflammatory effects on protecting cartilage damaged. Hence, future studies will be directed towards examining the therapeutic effects of GPNMB on larger animal models for osteoarthritis. Given the remarkable ability of GPNMB to reduce expression of key inflammatory markers, we conducted this study to reveal GPNMB therapeutic effects in traumatically-induced osteoarthritis.

References

Disclosure of Interests: None declared
AB0079 EFFECT OF HYALURONIC ACID LOCAL INJECTIONS ON ACHILLES TENDINOPATHIES: AN OBSERVATIONAL STUDY ON TENDON VISCOSCELLAR PROPERTIES AND THEIR RELATIONSHIPS WITH CLINICAL OUTCOMES

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Background: Effect of hyaluronic acid local injections on Achilles tendinopathies: an observational study on tendon viscoelastic properties and their relationships with clinical outcomes.

Objectives: Achilles tendinopathy (AT) affects athletes, recreational exercisers and also inactive people, where it is sometimes associated with arthritic phenotypes. The aim of this study was to evaluate the efficacy of a three-local injections regimen of hyaluronic acid (HA) in middle aged patients with a diagnosis of AT; the relationships of the functional, biochemical and clinical outcomes with the viscoelastic properties of the tendon were also studied

Methods: 8 patients previously diagnosed for monolateral AT were enrolled. AT was confirmed before the first local HA injection (T0) by clinical examination, MR and thermography. At T0 patients were assessed for maximal voluntary isometric contraction (MVI) involving Achilles tendon (both injured and healthy), and pain level with a Likert scale; Achilles tendon viscoelastic state, i.e. tone and stiffness, were then measured at relaxed state and at 10% of MVI with MyotonPro (Myoton Ltd, UK). Finally patients received the first HA injection (RegenFlex T&M, a blend of 2 to 1000 KDa HA, Regenyl, IT). All the measurements were repeated at T1 (15 days after the first injections and immediately prior the second), at T2 (15 days after the second injection and prior the third) and at T3 (15 days after the third injection), i.e. over a total of 45 days in which clinical visits were also performed. Furthermore, each injection, injured tendon exudates were collected by needle aspiration and the levels of IL-1β and matrix metalloprotease 3 (MMP-3) were determined with an ELISA test.

Results: At T0, pain score and MVI were significantly higher and lower in injured tendons, respectively. Accordingly, tone and stiffness values were significantly different between injured and contralateral tendons, especially when measured at the relaxed state. Interestingly, the above differences gradually disappeared at T1, T2 and T3. In keeping with these results, tendon exudates volumes also decreased over time, as well as the levels of IL-1β and MMP-3.

Conclusion: RegenFlex T&M promoted a progressive healing of AT, with recovery of clinical, functional and tendon’s viscoelastic state.

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[1] P. Sestili, M. Gervasi, E. Barbieri, I. Capparuccì, G. Annibali, S. Contarini, D. Sisti, S. Amatori and Department of Biomolecular Sciences, Università Urbino Carlo Bo, via A. Saffi 2, 61029 Urbino, Italy

Disclosure of Interests: None declared

AB0080 THE INHIBITION OF IL-25 TO THE EFFECT OF IL-17 TO ERK1/2 AND MMP-3 IN RHEUMATOID ARTHRITIS FIBROBLAST-LIKE SYNOVIALCYTIES

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Background: Rheumatoid arthritis (RA) is a common chronic systemic autoimmune diseases characterized by the inflammation in joint and synovium. Synovitis leads to the destruction of cartilage and bone in joint subsequently joint dysfunction and even disability eventually. Recently, IL-25 has been found to play a role in regulating inflammation through Th1 and Th17 responses in inflammatory diseases[25]. However, the function to fibroblast-like synoviocytes and its signaling pathway are not clear. This study aims to probe the effects of IL-25 on the expression of ERK1/2 and MMP-3 in RA fibroblast-like synoviocytes.

Objectives: To study the function of IL-25 for rheumatoid arthritis (RA) fibroblast-like synoviocytes.

Methods: The effects on ERK1/2 and MMP-3 protein levels were tested in RA-FLS and healthy controls, then IL-17A (10ng/ml), different concentrations of IL-25 (0.01, 0.1, 1 and 10ng/ml) and IL-17A(10ng/ml) to co-stimulate the RA-FLS for 24 hours respectively. The expression of ERK1/2 and MMP-3 protein were detected by the Western blot. The results were expressed by ±s, t test was used for the comparison between different groups.

Results: The expression of ERK1/2 (1.7±1.0±0.1) and MMP-3 (0.5±0.13) proteins in RA-FLS was higher than the healthy controls (0.50±0.15, 0.17±0.05) (t=9.13,P<0.001) and (-4.10,P<0.05), because of the stimulation of IL-17A, the expression of ERK1/2 (0.77±0.22) and MMP-3 (0.59±0.13) proteins in RA-FLS were increased compared with untreated groups (0.18±0.35, 0.04±0.03)(t=constantly.

Conclusion: IL-25 can inhibit the stimulation of IL-17A on ERK1/2 and MMP-3 fractionally, which imply that it may take part in the development of RA through this pathway and may play as a target for the RA treatment on IL-17A.

Disclosure of Interests: None declared

AB0081 NOVEL COOPERATION BETWEEN CCL26 AND CX3CL1 VIA CX3CR1 IN THE INJURY OF SMALL BILE DUCT IN PRIMARY BILARY CIRRHOSIS

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Background: CXCCL1-CX3CR1 pathway has been found to be critically involved in the pathogenesis of primary biliary cholangitis (PBC) 1. As a novel ligand to CX3CR1, CCL26 can promote chemotaxis of CX3CR1+ immune cells but its role in PBC remains elusive 2.

Objectives: This study aimed to explore the role of CCL26, together with CXCL1-CX3CR1 pathway, in the pathogenesis of PBC.

Methods: We recruited 40 patients diagnosed with PBC in the Peking Union Medical College Hospital from Jan 2018 to May 2018 and 18 age and sex-matched healthy controls (HCs). Peripheral blood and liver tissue samples were collected. The plasma level of CX3CL1 and CCL26 were determined by ELISA. Flow cytometry was used to measure the percentage of CX3CR1+ cells in various subsets of PBMCs. The expression of CX3CL1 and CCL26 in liver tissues was revealed by immunohistochemical staining. Using ELISA and flow cytometry, the change of CX3CL1/CCL26-CX3CR1 pathway expression in human intrahepatic biliary epithelial cells (HIBECs) upon stimulation of various cytokines was studied.

Results: The plasma level of CX3CL1 and CCL26 was higher in patients with PBC than HCs with a P value of 0.044 and 0.104 respectively. The increased level of CCL26 was positively correlated with peripheral eosinophils, basophils and CRP level. In comparison with HCs, the expression of CX3CR1 was significantly higher in NKT-like and CD4+ T cells in PBC patients. In liver samples from PBC patients, CXCL1 and CCL26 were significantly over-expressed in intrahepatic bile ducts and CCL26 also tended to be abundant in hepatocytes near portal areas and gradually weakened in distant regions. This distribution pattern was not observed in HCs. Upon stimulation of IFN-y, the expression of CX3CR1 on HIBEC surface and CX3CL1 in culture supernatant was significantly up-regulated, while the expression of CCL26 was increased upon IL-4 and IL-13 stimulation.

Conclusion: CCL26 may cooperate with CX3CR1 to mediate the immune injury of intrahepatic bile ducts via CX3CR1 in PBC.
Reduced Steroidogenic Activity of Repository Corticotropin Injection (RCI) Induces a Distinct Cytokine Response Following T Cell Activation in Vivo

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Background: Melanocortin receptor agonists, such as oMSH, have been shown to reduce inflammation in preclinical models, suppressing the production of proinflammatory cytokines. Natural and synthetic ACTH analogues remain linked to the induction of corticosteroids as their primary mechanism of action, leading to the anti-inflammatory and immunosuppressive responses. Repository Corticotropin Injection (RCI) is a complex mixture containing purified porcine pituitary ACTH-analogue, and is an FDA-approved treatment for several inflammatory diseases. RCI has been shown to be effective in steroid-refractory autoimmune disorders.

Objectives: We hypothesize that Acthar has an immune regulatory response distinct from synthetic ACTH and steroids. These studies sought to explore the differences between RCI and synthetic ACTH on corticosterone levels in rats and cytokine production in a murine T cell activation model.

Methods: RCI (10, 40, or 400 IU/kg) or ACTH (0.6, 1.2, or 2.4 mg/kg) was administered to Sprague Dawley rats, plasma samples collected and analyzed for corticosterone. To determine the effect on T cell cytokine production, Balb/C mice were treated with RCI (10, 40, and 400 IU/kg), ACTH (0.6, 1.2, or 2.4 mg/kg) or prednisolone 1 hour prior to the administration of an anti-CD3. Two hours after anti-body administration, plasma cytokines were measured using Meso Scale multiplex ELISA.

Results: RCI and ACTH peak corticosterone and area under the curve (AUC) were evaluated. RCI-induced corticosterone rapidly peaked between 2-8 hrs. and was dependent on the dose. ACTH displays a delay in the peak time (8-24 hours) and was not dose dependent. When compared to the high dose ACTH, RCI reduced the AUC by 50.0 ± 2.6%, 45.5 ± 5.6% and 27.3 ± 12.5% respectively for 10, 40, and 400 IU/kg. However, there was no significant reduction between any of the ACTH doses tested.

Conclusion: These data show that RCI has a reduced steroidal response compared to synthetic ACTH. RCI has a direct and distinct immunomodulatory response on T cells unique from both synthetic ACTH and steroids. These characteristic effects suggest a mechanism of action for RCI that is steroid-independent and may help explain its benefit in steroid-refractory inflammatory disease.

Disclosure of Interests: None declared

Adiponectin Stimulates Pro-Inflammatory Cytokine Production by Peripheral Blood Mononuclear Cells from Patients with Early Untreated Rheumatoid Arthritis

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Background: The pathogenesis of rheumatoid arthritis (RA) involves the action of immune cells and fibroblast-like synoviocytes (FLS). Adiponectin, an adipokine produced mainly by adipocytes, is elevated in serum of RA patients compared to healthy controls; moreover, synovial fluid from RA subjects has higher levels of adiponectin compared to controls with osteoarthritis. Adiponectin induces the production of pro-inflammatory cytokines, such as interleukin 6 (IL-6) and IL-8, by

Disclosure of Interests: None declared

REFERENCES


AB0082

ADIPONECTIN STIMULATES PRO-INFLAMMATORY CYTOKINE PRODUCTION BY PERIPHERAL BLOOD MONONUCLEAR CELLS FROM PATIENTS WITH EARLY UNTREATED RHEUMATOID ARTHRITIS

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Background: The pathogenesis of rheumatoid arthritis (RA) involves the action of immune cells and fibroblast-like synoviocytes (FLS). Adiponectin, an adipokine produced mainly by adipocytes, is elevated in serum of RA patients compared to healthy controls; moreover, synovial fluid from RA subjects has higher levels of adiponectin compared to controls with osteoarthritis. Adiponectin induces the production of pro-inflammatory cytokines, such as interleukin 6 (IL-6) and IL-8, by
FSL from RA patients. However, it remains unclear whether the response to adiponectin in terms of cytokine production is different in immune blood cells from healthy donors compared to RA patients; moreover, it is not known if FLS from healthy subjects can also produce pro-inflammatory cytokines upon adiponectin stimulation.

**Objectives:** The study aims to analyze if adiponectin induces pro-inflammatory cytokine production by peripheral blood mononuclear cells (PBMCs) from both early RA patients and healthy controls. We also aim to study whether adiponectin induces pro-inflammatory cytokine production by FLS from healthy subjects.

**Methods:** PBMCs were isolated from whole blood obtained from 5 healthy donors and 3 early untreated newly diagnosed RA patients using Ficoll-Paque PLUS. FLS were isolated from synovial tissue obtained from 3 healthy donors after knee surgery due to injury. Healthy FLS were cultured in Dulbecco’s Modified Eagle Medium (DMEM GlutaMAX) supplemented with 10% FBS, 1% Penicillin-streptomycin, and 0.5% Gentamycin. Harvested PBMCs and FLS were resuspended in X-VIVO 15 serum-free hematopoietic cell medium and stimulated with different doses of human recombinant adiponectin (1, 5 and 10 µg/ml), and the culture media were collected at different time points. Concentrations of IL-6, IL-8 and TNF-α were measured with ELISA.

**Results:** Unstimulated PBMCs from early RA patients produced higher levels of IL-6 compared to healthy subjects (P<0.001). In healthy controls, both the production of IL-6 and TNF-α was higher in PBMCs stimulated with adiponectin compared to unstimulated PBMCs (n=5, P<0.01 for IL-6 and P<0.01 for TNF-α). Likewise, the production of both IL-6 and TNF-α was higher in PBMCs from early-RA patients after stimulation with adiponectin compared with unstimulated PBMCs (n=3, P<0.01 for IL-6 and P<0.03 for TNF-α) in a dose- and time-dependent manner. After stimulation with adiponectin, levels of IL-6, but not TNF-α, were higher in PBMCs from subjects with early RA compared to healthy controls (P<0.01). Adiponectin stimulation did not induce IL-8 production from PBMCs from either healthy donors or RA patients.

Adiponectin was able to induce the production of IL-6 and IL-8 by FLS isolated from healthy donors (n=3, P<0.03 for IL-6 and P<0.02 for IL-8), but not TNF-α.

**Conclusion:** Our results show that adiponectin induces the production of IL-6 and TNF-α from PBMCs from both healthy subjects and patients with RA and that adiponectin is able to stimulate the production of IL-6 and IL-8 by FLS isolated from healthy subjects. Those results suggest that adiponectin may play a role in the pathogenesis of RA.

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**Disclosure of Interests:** Yuan Zhang: None declared, Jonathan Aldridge: None declared, Anna-Carin Lundell: None declared, Anna Rudin Granit/research support from: I havereceivedgrants from AstraZeneca (2017-2018), Consultant: I was paid consultant for AstraZeneca (2015-2018), Cristina Maglio: None declared

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**Cartilage, synovium and bone**

**AB0084** ASSOCIATION OF SYNOVITIS VERSUS CARTILAGE LOSS WITH PAIN SEVERITY AND FUNCTIONAL LIMITATION IN PRIMARY KNEE OSTEOARTHRITIS: CLINICAL, ULTRASONOGRAPHY AND MAGNETIC RESONANCE IMAGING

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**Background:** Osteoarthritis (OA) is a common and debilitating condition associated with pain and mobility that undermines quality-of-life. Magnetic resonance imaging (MRI) has become the most important modality for assessment of pathologic changes in knee cartilage, in both clinical and research environments, also Musculoskeletal Ultrasound (MSU) is a valuable tool for imaging musculoskeletal changes in osteoarthritis. It shows early and late changes.

**Objectives:** The aim of the study was to detect the association of MRI and musculoskeletal ultrasound detected synovitis versus cartilage defect with knee pain severity and functional limitation in patient with primary knee osteoarthritis.

**Methods:** This study was carried out on fifty patients of primary osteoarthritis diagnosed as primary osteoarthritis of knee joints according to American College of Rheumatology Radiologic and Clinical Criteria for Knee osteoarthritis all patients were assessed clinically and knee examined for any swelling tenderness, warmth, limitation of range of motion. Pain severity and functional limitation assessed by Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Musculoskeletal ultrasound and M.R.I of osteoarthritic knee joints were done.

**Results:** MSUS synovitis of examined joints was (0.93 ± 0.94) and cartilage thickness(3.95 ± 1.4), MRI synovitis of examined joints was (0.89 ± 0.93) and cartilage thickness (39.9 ± 13.26), There was Correlation between WOMAC pain score and MSU synovitis and cartilage thickness with Significant difference (p<0.01), also there was Correlation between WOMAC pain score and MRI synovitis and cartilage thickness with Significant difference (p<0.01), a positive Correlation between MSU Synovitis and MSU cartilage thickness was detected Significant difference (p<0.01) r(0.38). Also a Correlation between MRI Synovitis and MRI cartilage thickness show Significant difference (p<0.01) r(0.39).

Sagittal an proton density–weighted magnetic resonance imaging shows focal cartilage loss in the lateral tibiofemoral joint

**Conclusion:** The severity of cartilage loss and severity of the synovitis/effusion are the most significant determinants of pain and functional disability. Synovitis has role on increasing cartilage los MRI and MSU are a non-invasive method which allows comprehensive assessment and detection of early structural changes in osteoarthritic joints.

**REFERENCES**


**Disclosure of Interests:** None declared


**AB0085** ULTRASONOGRAPHIC EVALUATION OF THE METACARPAL CARTILAGE THICKNESS IN WEIGHTLIFTERS AND VOLLEYBALL PLAYERS

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**Background:** Articular cartilage is inevitably exposed to impact and loading in different sports play. Despite the fact that it is quite prone to different forms of overloading, the cartilaginous structure has not been looked into in the pertinent literature. Accordingly, in this comparative study, we have assessed the metacarpal cartilage in volleyball players and weightlifters whereby different forms of stress is naturally prevalent in the athletes’ hands.
Objectives: To evaluate the possible effects of impact and loading on the metacarpal cartilage and hand functions in young athletes.

Methods: A total of 42 male athletes (19 weight-lifters and 23 volleyball players) and 46 healthy control subjects were enrolled. Demographic and clinical characteristics (age, height, weight, smoking habit, duration/type of sport, dominant hand) were recorded. The 2nd to 5th finger metacarpal head cartilage thicknesses were measured bilaterally using ultrasonography. Hand grip strength was measured with a Jamar dynamometer. Pinch strengths (lateral, tip to tip and three jaw pinch) were measured using a pinchmeter. Michigan Hand Outcomes Questionnaire was also completed for each and every participant.

Results: Metacarpal cartilage thicknesses of the athletes (more predominant in weightlifters) were found to be thicker than those of the healthy controls (all p<0.001). There were no differences between the dominant and non-dominant hands (all p>0.05). Athletes’ handgrip and pinch strengths were higher than those of the controls. In the weightlifting group, Michigan Hand Outcome Questionnaire work performance and pain scores were worse than the other groups.

Conclusion: The presence of increased cartilage thickness measurements in the athletes suggests that sports activities might affect the metacarpal articular cartilage. Highest pain scores and lowest work performance scores in the weightlifters with highest metacarpal cartilage thickness might suggest that impact and loading during their sports play could lead to cartilage edema.

REFERENCES

Disclosure of Interests: None declared

AB0086

BCP AND CPPD CRYSTALS INFLUENCE THE CHONDROCYTE PHENOTYPE IN DIFFERENT WAYS

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Background: Calcification of cartilage with BCP crystals is a common finding during osteoarthritis (OA) and is directly linked to the severity of the disease and hypertrophic differentiation of chondrocytes. In some OA cartilage samples calcium pyrophosphate dihydrate (CPPD) crystals can be found. The mechanism underlying the formation of the CPPD crystals and their effects on the chondrocytes are not completely understood.

Objectives: The aim of this study was to evaluate the effect of CPPD compared to BCP crystals on the chondrocyte phenotype in OA cartilage.

Methods: Cartilage samples of patients with chondrocalcinosis were used and compared with samples of severe OA patients without chondrocalcinosis and healthy cartilage samples served as control. Radiological presence of chondrocalcinosis was evaluated using standard X-ray pictures, as well as macroscopically inspection. The cartilage samples were stained using von Kossa/Safranin-orange staining. These stainings were used for OA severity scoring using the Charnig-Score. Chondrocyte differentiation markers were evaluated using Collagen-2 and Runx2. mRNA expression of the respective genes after stimulation of C28 chondrocytes with CPPD and BCP crystals was evaluated using qRT-PCR. TUNEL staining was performed to investigate cell death. In vivo results were validated using qRT-PCR for the expression of the respective genes after stimulation of C28 chondrocytes with CPPD and BCP crystals.

Results: Radiologically detectable cartilage calcifications were evident in chondrocalcinosis patients, but absent in OA patients without chondrocalcinosis. Chondrocalcinosis cartilage exhibited an increased collagen 10 expression compared to healthy cartilage, as well as to severe OA cartilage containing BCP calcification. Interestingly, aggrecan and collagen 2 were not reduced in chondrocalcinosis cartilage, but markedly reduced in OA cartilage. TUNEL positive cells were significantly increased in CPPD cartilage compared to OA cartilage, although the histological OA severity was lower. qRT-PCR indicated no relevant influence of CPPD crystals on hypertrophic marker genes, whereas BCP crystals significantly induced hypertrophic differentiation.

Conclusion: BCP and CPPD crystals seem to trigger differential effects on the chondrocyte phenotype. BCP crystals induce hypertrophic differentiation, which is not induced by CPPD crystals.

Disclosure of Interests: None declared

AB0087

DLX5 AND DLX6 PROMOTES THE COMMITMENT OF MSC TO OSTEOBLASTIC LINEAGE AND CORTICAL BONE FORMATION

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Background: Osteoporosis which affects 200 million women worldwide is the consequence of an imbalance of low anabolism to high catabolism, causing a risk of fracture. Impaired anabolism involved reduced osteoblast differentiation. The osteoblast differentiation is mediated by transcription factors, including Dlx5 and Dlx6. Dlx5 is known to have a role in osteoblast/osteoclast couple and as a promoter of osteoblast lineage commitment[1, 2]. Thus, Dlx5 is a transcriptional actor of Runx2[2], a key element of osteoblastic differentiation.

Objectives: The goal of this project is to expand our knowledge about bone formation and cellular precursors of osteoblasts, focusing on Dlx5 and Dlx6.

Methods: We analyze the kinetic expression of Dlx5, Dlx6 and osteoblastic markers during the osteoblast differentiation from murine osteoblastic progenitor derived from calvaria and bone marrow. Same analysis was carried out in osteoblastic precursors from control cells, Dlx5/Dlx6 cells with ex vivo recombination or from KO mice in parallel to human bone marrow cells. We analyzed the bone phenotype of mutated mice in the absence of expression of Dlx5 and Dlx6 under Osx promoter.

Results: Dlx5 and Dlx6 increases at D7 during osteoblastic differentiation in the murine bone marrow and then was stable to D21. The absence of Dlx5/D6 in cells derived from calvaria and bone marrow resulted in decreased levels of osteocalcin and alkaline phosphatase. Dlx5/D6−/− Osx-Cre mice were lethal. Dlx5/D6−/− Oxs Cre mice does not affect cortical and trabecular parameters at 6 weeks but had a significant lower cortical thickness and also lower Tb. Bv/TV and Tb. Th along with a lower BMD at 3 months in both sexes. Moreover, periosteal volume was also lower in mutated mice. The skulls revealed a lack of sutures closures and dental abnormalities at 6 weeks and 3 months in both sexes.

Conclusion: The deletion of these transcription factors under the action of the Osteocalcin promoter generates lethality, in favor of an essential role in bone development. Heterozygous mutation show impaired bone acquisition during growth. To obtain a total deletion of Dlx5 and Dlx6 in osteoblastic precursor cells, a new murine model of conditional induced deletion is generated. Dlx5 and Dlx6 promote osteoblastic differentiation with an effect on late bone markers, in favor of a role in terminal differentiation. Analysis in vitro of Dlx5 and Dlx6 will be confirmed by ongoing in vivo experimentation.

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MECHANICAL STIMULUS INDUCED BY CHIROPRACTIC MANIPULATION REDUCES CARTILAGE, SUBCHONDRAL BONE DAMAGE AND SYNOVIAL INFLAMMATION IN AN EXPERIMENTAL MODEL OF OSTEOARTHRITIS

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Background: Osteoarthritis (OA) is a degenerative joint disease characterized by cartilage degradation, although both subchondral bone deterioration and synovial inflammation are also hallmarks of the disease. Chiropractic manipulation (CM) is a therapeutic approach focused on the diagnosis, treatment and prevention of musculoskeletal disorders. It is essentially manual, allowing the chiropractor to restore the normal range of motion and function of the joints, muscles, and ligaments. Clinical evidences suggest that CM might exert positive effects in OA patients.

Objectives: The aim of this study was to evaluate the effects of CM on cartilage, subchondral bone and synovial state in an OA rabbit model.

Methods: Ten (4 months old) male New Zealand rabbits underwent knee surgery to induce OA by transection of anterior cruciate ligament. One week after the surgery, CM was performed using the chiropractic adjusting instrument ActivatorV as follows: Force 2 setting was applied onto the tibial tubercle of the right hind limb (true manipulation, TM-OA group), at an angle of approximately 90°, from medial to lateral, whereas the corresponding left hind limb received a false manipulation (FM-OA group) consisting of ActivatorV firing in the air and slightly touching the tibial tubercle. These procedures were repeated 3 times a week for 8 weeks. Three healthy animals were used as control. Following sacrifice, μCT and histological damage evaluation (Mankin score) were done in femur and tibia. RANKL/OPG protein expressions were studied by immunohistochemistry in tibia samples. Sirius red was assessed by Krenn score and immunohistochemistry for macrophages (RAM11) and angiogenesis (CD31) were done. Protein expression of VEGF, COX2, TNFa, IL-1β and MMP3 were determined by Western Blot.

Results: In the OA rabbits, subchondral BMD decreased in relation to control, being significantly reversed in the tibia of TM-OA group. When subchondral bone structural parameters were analyzed by microCT, a significant decrease of bone volume trabecular volume (BV/TV), trabecular number (Tb.N) and trabecular thickness (Tb.Th) was observed in the OA rabbits, while trabecular separation (Tb.S) increased compared to control animals. TM-OA group showed a significant improvement of these parameters compared to FM-OA group. FM-OA joint had higher Mankin score (cartilage damage) than control joints, and TM decreased Mankin score compared to FM-OA (p<0.05). The study of RANKL and OPG in cartilage and subchondral bone showed that the significant increase in the RANKL/OPG ratio observed in both tissues respect to controls, was partially reversed in TM-OA group. OA synovial membranes presented a total Krenn synovitis score higher than healthy animals; however, TM-OA rabbits exhibited scores lower than FM-OA (p<0.05). RAM11 immunostaining revealed lower expression in TM-OA synovial membrane compared to FM-OA (p<0.05). Similarly, the significant increase in proinflammatory cytokines (COX2, TNFa and IL-1β) and MMP3 were observed in the synovial membranes of OA rabbits respect to controls, being partially reversed in TM-OA group. Likewise, VEGF and COX31 expression was higher in FM-OA synovium compared to TM-OA.

Conclusion: These results suggest that mechanical stimulus induced by CM may retard the pathologic progression of OA. The beneficial effects of CM might be associated with an improvement in bone and cartilage damage and also inflammatory state.

Disclosure of Interests: None declared.


IN VITRO EFFECT OF FASCIOLA HEPATICA EXTRACT ON SYNOVIAL FIBROBLASTS OF RHEUMATOID ARTHRITIS PATIENTS

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Background: Synovial fibroblasts (FLS) have an aggressive and invasive profile and play a major role in RA[1]. Available therapeutic options are effective for induction and maintenance of disease remission[2], but not all patients respond to treatment and there is no cure. New therapeutic options need to be explored. Studies have shown that products secreted by helminths contain components with anti-inflammatory properties[3,4], capable of suppressing Th1 immune response[5] and the production of inflammatory cytokines[6]. One example is the immunomodulating properties[7] of the extract of Fasciola hepatica.

Objectives: To evaluate the effects of F. hepatica extract in FLS from RA patients.

Methods: Firstly, the cultures of FLS isolated from the synovial fluid of RA patients were exposed at different concentration of F. hepatica extract (60µg/mL, 80µg/mL and 100µg/mL) and analyzed after 24h, 48h and 72h by MTT cell proliferation assay. FLS controls were exposed to standard culture medium. The effect of extract was also evaluated through adhesion and wound healing assay, and TNF-α production after IFNγ stimulation. Statistical analysis was performed with ANOVA or T Test and the p<0.05 were considered statistically significant.

Results: F. hepatica extract decreased the cell proliferation of FLS at concentration of 100µg/ml after 48h (83.8% ± 5.0 extract vs 100.0% ± 0.0 control; p<0.05), and at concentrations of 80µg/ml (84.4% ± 3.0 extract vs 100.0% ± 0.0 control; p<0.05) and 100 µg/ml (89.8% ± 3.8 extract vs 100.0% ± 0.0 control; p<0.05) after 72h, when compared with control group. Based on these results, the concentration of 100µg/ml and the time of 48h were chosen for the following tests.

Results: FLS with extract show with extract compared to control, FLS ± 5µ extract vs 116.3 cells ± 7.9 control; p<0.05) and migratory potential (40.2 inch ± 13.9 extract vs 58.7 inch ± 6.5 control). Moreover, after treatment there was a trend of decreased TNF levels (7.0 pg/mL ± 0.5 extract vs 8.1 pg/mL ± 0.7 control).

Conclusion: Taken together, our results suggest that extract of F. hepatica is able to reduce the aggressive and invasive profile of FLS. However, further analyses are needed for a better understanding the mechanisms of the effect of F. hepatica extract on FLS and its different components, such as cytokin.

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INHERITED DEPITE OF PROTEOGLYCAN MIMICKING SEPTIC ARTHRITIS

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Background: Aggrecanopathies (AP) are a heterogeneous group of skeletal disorders caused by ACAN gene mutations leading to proteoglycan synthesis defect. Inherited called aggrecan that plays a pivotal role in the organization of the extracellular matrix of the growth plate cartilage. Clinically, patients with AP display bone dysplasias ranging from severe spondyloepimetaphysial dysplasia to familial cases of osteochondritis dissecans (OCD) associated with short stature and typical facial dysmorphisms[1].

Objectives: Herein we report a patient with AP referred to our Institute for an inflammatory articular involvement mimicking a septic arthritis.

Methods: Molecular analysis of the ACAN gene was performed using Sanger sequencing method.

Results: A 14-year-old boy displayed pain and swelling at the right elbow. Echo- scan revealed an effusion in both condor and olecranon recess. Acute phase reactants were negative. A month later, since non-steroidal anti-inflammatory drugs were administered without benefit, the patient was admitted in our Institute. On physical examination, acute arthritis at the right elbow was noted: it appeared painful, warm, and not erythematous. Laboratory test showed slight elevation of acute phase reactant (C reactive protein 1.7 mg/dl, normal value <0.5).


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AB0090 INHERITED DEPITE OF PROTEOGLYCAN MIMICKING SEPTIC ARTHRITIS
Arthrocentesis was performed and sterile synovial fluid was found. Magnetic resonance images displayed a bone fragment detachment from the humeral condyle of the right elbow with synovium thickening and persistent effusion: the diagnosis of OCD was pointed out.

The patient showed minor dysmorphisms (i.e. dolicocephaly, hypotelorism, arched palate and brachydactyly of the IV finger of both hands) and parents reported a previous episode of OCD when he was 12: at that time, symptoms resolved with non-weightbearing and non-steroidal anti-inflammatory therapy after few days. Furthermore, the patient went under regular endocrinologist follow-up for short stature since he was 8. At the age of 10, his height was 123 cm, SDS 2.4, and growth hormone (GH) stimulation tests showed partial response to insulin tolerance test (GH peak 6.27 ng/ml). Bone age at the X-ray of right hand and wrist was delayed of 12 months. Human recombinant GH replacement therapy was administered without significant growth-velocity improvement. Although the patient came to observation because of suspected elbow septic arthritis, we re-considered the diagnosis: namely, i. recurrent episodes of OCD; ii. short stature that was poorly responsive to the human recombinant GH treatment, iii. mild skeletal and facial dysmorphism, led us to hypothesize a form of aggrekanopathy.

Molecular analysis of the ACAN gene revealed the novel missense variant c.6970T>C, p.Trp2324Arg in the G3 domain of the protein. Notably, another mutation of the G3 domain (c.7249G>A) has been previously related to aggrekanopathy2. Intra-familial molecular analysis allowed us to detect the same variant in other three subjects (the mother and 2 siblings) affected only by brachydactyly and short stature.

Conclusion: A patient carrying a novel mutation of the ACAN gene presented an atypical form of aggrekanopathy mimicking inflammatory and/or septic arthritis associated with slight short stature and bone dysmorphisms. Further studies are needed to investigate a possible role of this novel ACAN gene variant in the inflammatory articular involvement.

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EFFECTIVENESS AND SAFETY OF PRILOCAINE IN COMBINATION WITH HYALURONIC ACID IN KNEE OSTEARTHRITIS: AN OPEN-LABEL STUDY

Methods: A total of 64 patients with knee OA diagnosed as per the American College of Rheumatology (ACR) criteria were enrolled in the study. Of these patients, 42 had grade 2 and others had grade 3 disease. A single injection of the combination product was administered to all patients. The combination product contained 1 mg hyaluronic acid, 14 mg cross-linked hyaluronic acid, 6.9 mg sodium chloride and 3 mg prilocaine hydrochloride in a 2 ml solution. The combination was injected into a single joint in the painful knee through the anteromedial aspect of the joint. Assessments were performed before the treatment and at 4 and 12 weeks post-treatment by the same physician. The study was designed as an open-label, observational study. The patients were assessed using the Lysholm Knee Scoring Scale. Patient scores were categorized as poor (0-64), fair (65-83), good (84-90) or excellent (91-100). Pain and functional measures were evaluated by this scale. Results: There was a female (n=58) predominance in the study sample. The mean age of the patients was 56.4 ± 15.3 years. As rated by the Lysholm Knee Scoring Scale, the number of patients with good scores rose to 6 at 4 weeks and 16 at 12 weeks. These findings were statistically significant (p<0.05). None of the patients received any additional medication and all continued their daily activities. A home exercise program was followed by the patients throughout the study. Global evaluation of the study physician rated 40 patients in good or excellent condition, whereas 34 patients self-rated themselves in good or excellent condition. Six patients had local symptoms including swelling, pain and redness which were of mild-to-moderate intensity. These symptoms resolved in 1-3 days with simple interventions.

Conclusion: Local hyaluronic acid injections may represent an alternative to systemic medications in the treatment of knee osteoarthritis and they can provide long-term relief with minimal adverse effects when combined with local anesthetics without the need for additional drugs or treatments.

Disclosure of Interests: None declared


DIFFERENTIATION OF ADIPOSE DERIVED MESENCHYMAL STEM CELLS OBTAINED FROM PATIENTS WITH SYSTEMIC LUPUS ERYTHMATOSUS ANKYLOSING SPONDYLITIS AND SYSTEMIC SCLEROSIS

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Background: Cartilage and bone destruction occurs in many rheumatic diseases. While the use of biologic drugs may delay the destruction but still it cannot be averted. Adipose tissue is an easy accessible and rich source of MSCs. Application of mesenchymal stem/stromal cells (MSCs) may be a promising option for successful tissue regeneration in therapy of ankylosing spondylitis (AS) systemic lupus erythematosus (SLE) and systemic sclerosis (SSc) patients.

Objectives: The aim of this study was to compare differentiation potential of ASCs obtained from AS, SLE, SSc patients and ASCs line originating from healthy volunteers (hASCs). The phenotype of these cells has been also analysed.

Methods: ASCs obtained from AS (n=9), SLE (n=10), SSc (n=10) patients and 5 commercially available hASCs lines were used in study. Cells in passage 4 were used in each experiment. Phenotype of ASCs was evaluated by flow cytometry. Differentiation was evaluated by using osteogenic, chondrogenic or adipogenic media. At the end of differentiation process cells were harvested and total RNA was isolated. Relative quantification (RQ) of gene expression level were calculated by the 2-ΔΔct method.

After 4 weeks of chondrogenic differentiation, mRNA level of SOX9 and aggrecan (ACAN) mRNA was evaluated by RT-PCR. Additionally glycosaminoglycan (GAG) deposition was analysed by alcian blue staining. After 2 weeks of osteogenic differentiation, expression of RUNX-2 collagen 1a1 (COL1a1) and osteopontin (OPN) mRNA has been determined. Calcium deposition has been determined by alizarin red staining. After 3 weeks of adipogenic differentiation expression of CCAAT/enhancer-binding protein (C/EBP), peroxisome proliferator activated receptor-γ (PPAR-γ) and fatty acid binding protein 4 (FABP4) was determined.

Results: All ASCs cultured in osteogenic medium showed calcium deposition. The expression of RUNX-2 and OPN mRNA was significantly higher in AS-ASCs. Cells obtained from SLE and SSc revealed significantly lower expression of COL1a1 than hASCs lines.

The results of alizarin blue staining showed chondrogenesis of cells obtained from all patients types. No statistically significant differences between AS, SLE, SSc and hASCs lines were observed in Sox9 mRNA expression. However, all patients derived cells expressed a lower of ACAN mRNA level.

Conclusion: AS, SLE and SSc ASCs have phenotype comparable with hASCs line. The patients derived ASCs highly to differentiate into any of the 3 cell types, although the process is altered.

Disclosure of Interests: None declared


ABO096

A REGULATORY ROLE OF ANTXR1 IN RANKL-INDUCED OSTEOCLAST DIFFERENTIATION AND FUNCTION

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Background: Antrax toxin receptor 1 (ANTXR1) has been known to have relationship with extracellular transmembrane protein deeply associated with the process of bone formation and exert important role in angiogenesis. However, there have been no reports to prove the effects of ANTXR1 on bone metabolism mediated by two types of bone cells, osteoclasts and osteoblasts. The aim of this study is to reveal the role of ANTXR1 in the differentiation and function of osteoclasts and osteoblasts.

Objectives: The aim of this study is to reveal the role of ANTXR1 in the differentiation and function of osteoclasts and osteoblasts.

Methods: To determine the effect of ANTXR1 on osteoclastogenesis or osteoblast differentiation, we examined TRAP staining, F-actin staining and Pit assay, or ALP and Alizarin Red mineralization staining, respectively. The mechanism of ANTXR1 by transfection of retrovirus or siRNA analyzed using real-time PCR and western blot analysis. Also, the effect of ANTXR1 on osteoclast-mediated angiogenesis of endothelial cells assessed by in vitro vascular tube formation assay of human umbilical vein endothelial cells (HUVECs).

Results: Through gaining- and loss-of-function studies, we found that ANTXR1 positively regulated receptor activator of nuclear factor kappa B ligand (RANKL)-induced osteocalcit differentiation and bone resorption with no effects on osteoblast differentiation. During ANTXR1-mediated regulation of osteoclastogenesis, phosphorylation of early signal transducers, c-Jun N-terminal kinase (JNK), Akt, and inhibitor of kappa B (IκB) was affected, which in turn alteration of mRNA and protein levels of c-Fos and nuclear factor of activated T cells cytoplasmic 1 (NFATc1). In addition, genetic manipulation of ANTXR1 in bone marrow macrophages (BMMs) modulated the capillary-like tube formation by HUVECs via two kinds of angiogenic factors, matrix metalloproteinase-9 (MMP-9) and vascular endothelial growth factor-A (VEGF-A). These results explained the important role of ANTXR1 in osteoclast differentiation and functional activity, as well as osteo- clast-mediated angiogenesis of endothelial cells.

Conclusion: Taken together, it was proposed that ANTXR1 might be a promising candidate for gene therapy related with bone metabolic diseases and further, have potential to be served as an important biomarker in the research fields of bone metabolism associated with vascularization.

Disclosure of Interests: None declared

ANALYSIS OF THE GENE EXPRESSION OF URAT-1, ABCG2, GLUT-9, OCT3, IL1B, TL4 AND ALPK1 IN MONONUCLEAR CELLS OF PATIENTS WITH INTER-CRITICAL GOUT

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Background: Gout is a common type of arthritis that has increased in the world due to environmental and genetic factors that associate it with an altered metabolic state. In Mexico, overweight, obesity, diabetes and metabolic syndrome have increased in children and adult population. These alterations are associated with the development of gout in adults.

The gout is characterized by an inflammatory chronic process caused by the deposition of monosodium urate crystals (CUMs) in the joints. The recognition of these crystals by macrophages and neutrophils in the joint activates innate immunity. However, high levels of uric acid (UA) in intercritical phase could activate the expression of urate transporters and inflammation genes in other cell types such as monocytes and peripheral blood lymphocytes.

Objectives: The aim of this project was to analyze the changes in gene expression of SLC22A12, SLC2A9, SLC22A3, ABCG2, ALPK1, IL1β, TL4 and peripheral blood mononuclear cells (PBMC) of Mexican patients with inter-critical gout arthritis and controls without hyperuricemia (HU) comparing it with their metabolic profile.

Methods: The determination of the biochemical parameters was performed by a serum - blood chemical test for uric acid, glucose, triglycerides, cholesterol, HDL, LDL and creatinine. Through the use of UniCiel DxC 600, Synchron Clinical System, the total RNA of the PBMC cells was amplified by qRT-PCR using the GoTaq® 1-Step RT-PCR System real kit (Promega) and the Qiagen Rotor Gene Q kit, using specific primers. The gene expression analysis were performed by the ΔCT and ΔΔCT method and using GAPDH as a reference gene to compare the expression of urate transporter genes and inflammatory genes in the study groups.

The expression results were associated to clinical and biochemical parameters such as levels of uric acid, triglycerides, and weight. All statistical analyses were performed with the SPSS program (IBM 22 version for Windows, SPSS, Inc., Chicago, IL, EU), using student’s t-test or Mann-Whitney test, for the normal and non-normal data, when p <0.05 or p<0.01.

Results: In this study we compared 24 patients with inter-critical gout and 26 controls without HU. It was found that the expression of ABCG2 was higher in the patients than in controls and that the expression of OCT3 was higher in overweight people regardless of whether they had gout or not compared with normal weight people. The expression of ALPK1 was higher among patients and controls while the expression of TL4 and IL1β was not different. The patients had a higher mean in the levels of UA, triglycerides, weight, age and hypertension, but lower HDL than the controls.

Conclusion: Patients with inter-critical gout maintain metabolic alterations associated with the metabolic syndrome although some of them are under treatment. They are also characterized by having overexpression of ABCG2 and ALPK1. These conditions could favor a new attack of gout.

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Disclosure of Interests: None declared

NOVEL EX VIVO MODEL OF SEPTIC ARTHRITIS DEVELOPED TO IDENTIFY BIOMARKERS RELEASED UPON ARTICULAR INFECTION

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Background: Septic arthritis (SA) is most commonly caused by infectious agents such as Staphylococcus aureus. Due to the morbidity and mortality associated with the disease, joint infections are treated as a medical emergency and therefore early diagnosis is essential. Unfortunately, no reliable biomarkers are available to assist diagnosis, beyond serum CRP and synovial fluid culture.

Objectives: To generate a novel ex vivo model of septic arthritis comprised of cartilage matrix, neutrophils and SA-associated Staph. aureus, to identify biomarkers released upon an inflammatory host response to infection.

Critical Methods: Cartilage explants biopsied from human femoral heads were compared to chondrocyte disks differentiated from mesenchymal stem cells (MSC). MSC differentiation into chondrocytes under defined media and growth factor conditions was confirmed by IHC staining for collagen II on the disks. Explants and disks were infected for 48h with 10^5 CFU Staph. aureus (SA patient derived). Structural damage was measured by glycosaminoglycan (GAG) release. Neutrophils were purified from health donor blood samples using the StemCell whole blood isolation kit. 10^5 cell were added in the final 4h of bacterial infection. Disks were stained with eosin to visualise microscopic damage, CMFDA for viability and PI to identify cell death.

Results: Co-culture of MSC-derived chondrocyte disks with neutrophils or Staph. aureus alone resulted in microscopically identifiable structural damage to the disk matrix. The addition of neutrophils in the final 4h of the Staph. aureus co-cultures resulted in enhanced structural damage. Assessment of cellular viability revealed that both neutrophils and Staph. aureus alone induced cell death throughout the disk whilst the combination of both resulted in total abrogation of viable chondrocytes. Subsequent evaluation of GAG release, however, showed no clear differentiation between the conditions and as such this model was judged not to be sufficient for biomarker development. In comparison, femoral head cartilage explants studies demonstrated that Staph. aureus infection in this explant model resulted in significant GAG release after 24h and 48h, which was consistent between donors.

Conclusion: Cartilage explants provide a superior and more physiologically relevant cartilage matrix model for the ex vivo analysis of septic arthritis. Staph. aureus infection resulted in reproducible damage to cartilage matrices that was not emulated in an MSC-derived chondrocyte disk system. These findings suggest that the femoral head cartilage explants are the optimal model to identify biomarkers for joint infections.

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GENE EXPRESSION AND FUNCTIONAL COMPARISON BETWEEN MESENCHYMAL STEM CELLS FROM LATERAL AND MEDIAL CONDYLES OF KNEE OSTEOARTHRITIS PATIENTS

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Background: Osteoarthritis (OA) is the most common degenerative joint disorder, mainly afflicting the weight-bearing joints, and is the leading cause of physical disability worldwide. Despite the identified risk factors, the exact pathogenesis of osteoarthritis remains unclear (1). Formation of mesenchymal stem cells’ (MSC) clusters and their aberrant osteogenic differentiation in OA subchondral bone (SB) has been proposed as a key contributor to progression of OA in animal models (2) and in human hip OA (3). MSCs have a crucial role in joint repair but it remains unknown how OA severity affects MSC numbers or characteristics. Knee OA provides a good model to determine this as in knee OA, distribution of damage is usually asymmetrical and tends to be more severe in the medial (Med) compartment compared to the lateral (Lat) compartment (4).

Objectives: The aim of this study was to determine whether there were differences in MSC numbers, topography and gene expression (GE) between Med and Lat femoral condyles of patients with knee OA.

Methods: Condyles were obtained from OA patients that underwent total knee replacement (n=16). UK Ethics Committee approval. 14/YH0087). Decalcified samples were histologically evaluated for cartilage damage, bone sclerosis and CD271+ MSC distribution (2). MSCs were extracted from SB and sorted using the CD271+CD45- phenotype for GE analysis. Colony forming unit (CFU-F) (3), trilineage differentiation (5) and population doubling (PD) assays were performed. MSC numbers, topography and GE were compared between condyles.

Results: Med condyles presented significantly higher (p<0.05) degree of cartilage damage (median OARSI score 20, range 15-20) compared to Lat condyles

Coculture of Synovial Membrane and Cartilage: A Potential Human Ex Vivo Cartilage Degradation Model

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Objective: To study the potential of synovial membrane and cartilage coculture as a model for cartilage degradation and to identify factors influencing PG synthesis.

Methods: Synovial membrane and cartilage were cocultured for up to 28 days. PG content was analyzed by ELISA and staining with Alcian Blue.

Results: PG content was significantly lower in coculture compared to control (p = 0.0007).

Conclusion: The coculture model can be used to study cartilage degradation and factor influence PG synthesis.

References


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AB0101

SECRETOMES ANALYSIS OF CHONDROCYTES AND SYNOVIAL FIBROBLASTS IN OSTEOARTHRITIS: MODULATION BY VIP

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Background: Osteoarthritis (OA) is a chronic, degenerative and multifactorial disease, and the main cause of pain and dysfunction among elder people. It is characterized by a progressive loss of function of synovial joints (1). The role of chondrocytes in this pathology has been widely studied (2), but other joint cells are also involved, including the synovial fibroblast (SF) (3-5). During joint destruction, inflammatory and degradative mediators are released by joint cells and from the extracellular matrix (ECM), including fibronectin degradation fragments (Fn-f) (3, 4, 6). On the other hand, vasoactive intestinal peptide (VIP) exerts anti-inflammatory and immunomodulatory actions in several autoimmune and inflammatory disorders, including OA (3, 5). The study of the mediators released by joint cells and their modulation by pro- and anti-inflammatory mediators would be useful for the design of novel therapies for OA treatment.

Objectives: To analyse the mediators released from co-cultures of OA chondrocytes and SF, and to elucidate the effect of Fn-fs and VIP on these cells.

Methods: Human articular chondrocytes (HAC) and SF from 4 OA patients were provided by the Rheumatology Service at Complejo Hospitalario Universitario A Coruña. Isolated cells were recovered and plated in SILAC DMEM-Flex lacking Arginine and Lysine. In the case of medium and heavy media, isotope-labeled L-lysine and L-arginine were used. When 100% of labeling was reached, cells were put in co-culture and incubated in serum-free medium with or without Fn-fs (10 μM) or Fn-fs + VIP (10 nM) for 48h. Cell secretomes were separated on a 10% SDS PAGE gel. Gels were stained with Coomassie blue and the resulting lanes were cut into slices and subjected to in-gel digestion. Extracted peptide mixtures were desalted and concentrated via NtuP, subjected to liquid chromatography using a Tempo nano LC equipped with a Sun Collect MALDI Spotter, and analyzed by MALDI-TOF/TOF. Identification of peptides and proteins and relative quantification were performed using Protein Pilot software (Sciox).

Results: Cell secretomes were analysed in 4 OA patients in duplicate. Database search (UniprotKB/Swissprot and Venn’s diagrams drawing tool (Venny 2.1.0) allowed us to identify 79 common proteins in the HACS-SF co-cultures. Among them, VIP was able to modulate 33 different proteins, significantly reducing 9 of them: CH3L1, PTX3, PGS2, MMP2, Complement C1r, Complement C1s, TBA1, QSOX1, and CATB. These proteins include inflammatory and ECM proteins, pro- and complement system proteins among others, which play a main role in the OA pathogenesis.

Conclusion: VIP decreases inflammatory and degradative mediators in HAC-SF co-cultures, potentially slowing the progression of the disease and supporting its therapeutic role in osteoarthritis.

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AB0102

GENERATION OF OSTEOARTHRITIC MESENCHYMAL STROMAL CELL LINES

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Background: Bone-marrow mesenchymal stromal cells (MSCs) are multipotent self-renewal adult cells with high potential to regenerate the damaged tissues in degenerative diseases such as osteoarthritis (OA). Nevertheless, their usefulness for osteochondral Regenerative Medicine research is hampered by their proneness to senescence when in vitro cultured. Currently, MSC lines available are scarce and present limitations regarding their differentiation capacities. In addition, there is no OA MSC line available for research on this disease.

Objectives: The aim of this study was to generate and characterize immortalized human OA and non-OA MSC lines for their use in osteochondral Regenerative Medicine research.

Methods: For the generation of the immortalized MSC lines, SV40LT and GFP-fused human telomerase reverse transcriptase (hTERT) were used. Primary MSCs derived from two hip OA patients and one hip fracture patient without OA were transduced by spinoculation at 800 xg for 45 minutes. Transgene expression was induced by valproic acid. Nuclear expression of SV40LT and GFP was tested by immunofluorescence. Proliferation and senescence were investigated through calculation of population doublings (PDs) at each passage after immortalization and β-galactosidase negative staining. Normal induction of telomerase expression by flow cytometry and self-renewal experiments. Multi-lineage differentiation potential was analysed histochemical, immunohistochemical and molecularly.

Results: Three MSC lines have been generated: two OA and one non-OA. As shown by immunofluorescence, SV40LT is expressed in the nucleolus of these cells, while GFP-fused hTERT is expressed in the nucleoli. A constant proliferation rate throughout subculturing in addition to β-galactosidase negative staining confirms that immortalized MSC lines do not senesce, unlike primary MSCs. Expression of CD29, CD44, CD73, CD90, CD105, CD34 and CD45 was tested by analysis of CD29, CD44, CD73, CD90, CD105, CD34 and CD45 expression by flow cytometry and self-renewal experiments. Multi-lineage differentiation potential was assessed histochemical, immunohistochemical and molecularly.

Conclusion: Both OA and non-OA MSCs are susceptible to immortalization by SV40LT and hTERT. For they increased lifespan combined with keeping of most...
of primary MSC characteristics, these MSC lines are expected to be valuable tools for the research on Regenerative Medicine for OA as part of Tissue Engineering in vitro models.

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Background: Prevalence of knee osteoarthritis (OA) has doubled since the mid-20th century. Interestingly, this increase cannot be explained solely by longer life expectancy and the obesity epidemics (1). Therefore, other environmental factors known to have increased in the recent years could be part of the explanation.

Objectives: We performed a systematic literature review (SLR) to summarize the existing knowledge about associations between OA and pollutants.

Methods: Pubmed database was used to identify studies reporting data on OA and pollutants in humans (examples of MeSH terms: “Polychlorinated Biphenyls (PCB)” or “Lead”). Abstracts from international congresses were reviewed for the past 2 years, combined with manual curation. Studies were classified in epidemiological clinical studies, pollutants assessments in ex vivo OA joint tissues, and in vitro effect on human chondrocyte.

Results: As of January 15, 2019, 193 potentially relevant articles were screened. Among them, 14 were selected. After manual curation, a total of 21 full text articles were analyzed. Ten articles reported epidemiological clinical studies. Four articles underlined the link between PCB and OA: in the 3 articles reporting association with past exposure to PCB, the most robust one showed that risk of OA was significantly increased, at least in men (OR 4.1 [95% CI: 1.8-11.2] for men and 1.3 [95% CI: 0.8-2.3] for women). In the 4th study, the highest serum concentration of PCB was associated with a higher risk of arthritis: maximal adjusted OR (aOR) was 3.2 [95%CI: 1.6-6.7], p<0.01. However, sensitivity analysis of OA patients did not find any significant association in this study. Two articles focused on serum levels of perfluorocarboxanate (PFDA) and perfluorocarboxylate (PFOS): aOR to have OA in the PFDA highest serum level quartile was 1.42 [95%CI: 1.26-1.59], p<0.00001 and 1.55 [95%CI: 0.99-2.43]. Data were conflicting for PFOS: aOR to have OA in the PFOS highest serum level quartile was 1.77 [95%CI: 1.05-2.96], p<0.05 and 0.76 [95%CI: 0.68-0.85], p<0.00001. Two articles showed an association between serum lead levels and knee OA in the general population. In Korea, the risk of radiographic OA was increased in the highest quartile of lead serum level compared to the lowest one (aOR 1.90 [95%CI: 1.09-3.32] for men and 1.81 [95%CI: 1.17-2.77] for women). In the United States, risk kidney radiographic OA correlates with increased lead serum levels. In the last study, household air pollution induced by the cooking heat source was examined: compared to electricity, the risk of OA was increased with the use of liquids (kerosene/paraffin: aOR 1.73 [95%CI: 1.33-2.25]) or solid (coal, wood: aOR 1.73 [1.32-2.27]), (agriculture/crop: aOR 2.0 [1.47-2.72]. Lead and zinc accumulation was reported in 7 articles: 4 of them analyzed the concentration in OA joint obtained during arthroplasty and showed highest concentration in cartilage versus bone. In another, lead serum levels were associated with biomarkers of joint tissue metabolism. Two studies with X-ray fluorescence on cadavers found a high accumulation of lead and zinc in the articular cartilage landmark. Four studies assessed the in vitro effect of pollutants on human chondrocytes: the viability of chondrocytes was reduced in presence of PCB, gold, silver, fluorid acid and bisphenol A. Conclusion: This SLR suggests a possible link between OA and pollutants but the designs of the studies, the populations investigated and the type of pollutants were still too heterogeneous and limited to conclude definitively that pollutants represent a new environmental risk factor for OA. However, this SLR highlights a critical need for novel epidemiological, clinical and basic research studies in order to identify other potential environmental factors in OA.

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Disclosure of Interests: None declared

AB0105  THE EFFECT OF TROMBOSIT RICH PLASMA APPLICATION ON DEGENERATED CARTILAGE: IN VITRO EXPERIMENTAL STUDY
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Background: Osteoarthritis is the most common problem among musculoskeletal system disorders. Platelet-rich plasma (PRP) has been suggested to be
beneficial in the treatment of degenerative musculoskeletal problems. The pur-
pose of this study is to evaluate PRP treatment efficacy on degenerated cartilage.

Objectives: In this study, we aimed to determine the efficacy of platelet-rich plasma (PRP) on mechanically damaged chondrocyte cells by using different doses of calcium, different duration of exposure and different methods of activation of platelet.

Methods: Human source chondrocytes (CHON-001 ATTC CRL-2846) were used in the study. Chondrocyte cells were produced in appropriate medium and an experimental cartilage model was created. The platelet-rich plasma was produced from platelets obtained by apheresis in the laboratory, from blood of volunteer. The platelet-rich plasma was adjusted at five different doses as 4.8x10⁶, 2.4x10⁶, 1.2x10⁶, 6x10⁵, 3x10⁵. The first group of platelet-rich plasma was left intact, the second group was denatured within seven minutes by applying ultrasonic waves in water, the third group was activated with calcium chloride and the fourth group was determined as control group. Using a ten microliter pipette tip, a linear damage to the opposite side was created at the widest part of the well. Cell migration was monitored at 0-4-8-24 and 48 hours at x10 magnification by in vitro microscopy and wound healing was evaluated by photographing. Migration intervals were determined quantitatively using the program named Image J.

Results: When the rates of recovery were compared to the groups, no significant improvement was observed in the intact and denatured platelet groups at 4-8 and 24 hours compared to the control group. In the third group which was activated with calcium, no significant improvement was observed in all doses at 4 and 8 hours compared to the control group. However, at the 48th hours there was a significant improvement in the doses of 1.2x10⁶, 2.4x10⁶ and 4.8x10⁶ compared to the control group (p < 0.0001).

When evaluated in terms of activation, there was a significant improvement in the explanted and intact groups at the 48th hour, compared to the calcium-activated group at doses of 3x10⁶ and 6x10⁵ (p < 0.01).

Conclusion: Cartilage damage is the main pathology in the pathogenesis of osteoarthritis. All doses of PRP used in the study contributed to improvement. Meanwhile, the most critical parameter for platelet migration was timing and significant improvement was started after 48 hours.

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AB0106

CHANGES IN THE miRNA PROFILE AND HYPOXIC BEHAVIOR OF HUMAN CHONDROCYTES BY THERAPEUTIC NUCLEAR MAGNETIC RESONANCE THERAPY (NMRT)

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Background: Therapeutically applied nuclear magnetic resonance (NMRT) is discussed to participate in repair processes regarding cartilage and influences pain signaling. Studies concerning NMRT therapy implemented within the treatment of patients with degenerative rheumatic diseases outlined pain reduction as the main clinical outcome [1]. NMRT is also known to lead to improvements in pain from patients with knee OA due to a chondroprotective effect on the articular cartilage. In spite of this significant reduction in pain, the mechanism of action of NMRT at the cellular level remains to be elucidated.

Objectives: To substantiate the application of NMRT the aim of this work targets the underlying mechanisms at the cellular level. We investigated NMRT induced changes of the miRNA profile of human healthy and OA chondrocytes and studied the respective miRNA targets. Based on the fact that articular cartilage functions as an avascular and hypoxic connective tissue we were further able to demonstrate that NMRT modulation seems to be more pronounced under hypoxic conditions.

Methods: Human primary chondrocytes and the chondrocyte cell line TC28/2a were used for the experiments. RNA was extracted using RNEasy Mini Kit and was used as input for the Thermo Fisher Ion Total RNA-Seq Kit v2. Sequencing was performed on the Ion Proton sequencer using the Ion PI Hi-Q DQ v2 Sequencing 200 system. Signal processing and base calling was performed using Torrent Suite version 5.6. Hypoxic conditions were established and enabled cell growth in presence of 1-5% O2. Expression of miRNAs and target proteins was studied by a standard PCR procedure as well as protein detection by western blot. HDAC activity was measured by HDAC Glo III assay.

Results: Characterization of the miRNA profile showed a slight up regulation of miR-24-1-5p and miR-502-5p while miR-25-5p and miR-365-5p was down regulated. For miR-365a-5p known to directly targeting HDAC and NFκB a decrease of HDAC activity by NMRT was detected. The miR-25-5p target COX2 was changed in expression by NMRT whereas no influence on CDK4 knowing to be controlled by miR-24-1-5p was detected. NMRT treatment of chondrocytes under hypoxic conditions (0.5 - 5 % O2) changed the expression profile with respect to NO3, IGf2, PDGF and IGFBP and a change in the expression of HIF1a under the influence of IL1b was observed. The hypoxic conditions changed apoptotic behavior of the cells, NMRT showed no influence.

Conclusion: A closer look into the mechanism of the NMRT at the cellular level revealed a modulatory effect on miRNA, their regulatory units and chondrocytes under hypoxic conditions. The results underline our former results indicating that NMRT counteracts IL-1b induced changes which mean that pain reduction by NMRT might be due to NMRT holding against inflammatory mechanisms under OA.

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AB0107

S-ALLYL-L-Cysteine attenuates inflammation related oxidative stress parameters and increases adhesion capacity of primary human osteoarthritic articular chondrocytes

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Background: Osteoarthritis (OA) is characterized by progressive destruction of the articular cartilage, and chondrocytes, the only cells in articular cartilage, are in charge of maintaining the homeostasis of articular cartilage via modulating extracellular matrix anabolism and catabolism [1]. Due to the association of the degree of oxidative degeneration of chondrocytes and OA, preventing impaired redox signaling and reactive oxidative death of chondrocyte are suggested as potential targets to relieve OA [2]. In this respect, some photochemicals have been shown to be potential agents for preventing or treating OA due to their antioxidant and anti-inflammatory properties [3].

Objectives: We studied the effects of an antioxidant S-allyl-cysteine (SAC), a major sulphur-containing amino acid component of garlic[4], on the redox system, and its associations with the proliferation rate and index of human OA chondrocytes (OACs).

Methods: Chondrocytes were isolated from the joint cartilages of OA patients (grade 4, mean age= 66 years, BMI= 29.7 ± 4.4 kg/m²). The alterations in cell proliferation (MTT), adhesion profile (RTCA-CELLigence System), reactive oxygen species generation (ROS), lipid hydroperoxides levels (LPO), HNE protein adduct levels (HNE), AGE-protein adduct levels (AGE), 3-nitrotyrosine levels (3-NT),
The role of CD70 in the pathogenesis of Rheumatoid Arthritis

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Background: Rheumatoid arthritis (RA) is characterized by inflammation and cellular proliferation in the synovium. Activated lymphocytes and proinflammatory molecules are important in the pathogenesis of RA.

CD70 belongs to the tumor necrosis factor (TNF) ligand superfamily and is typically present on activated B and T lymphocytes, natural killer cells and mature dendritic cells. CD70 expressing CD4+ T cells are enriched in the peripheral blood and synovial fluid of patients with RA and promote autoimmunity via co-stimulatory CD70-CD27 interaction.

CD70 expression is associated with aggressive phenotype of cancer cells and it is mediated by hypoxia inducible factor 2α (HIF-2α).

Objectives: In this study, we examined the presence of CD70 on the surface of fibroblast-like synoviocyte (FLS) of patients with RA and investigate the role of CD70 in the pathogenesis of RA associated with HIF-2α.

Methods: RA FLS were obtained from 7 patients with RA who were undergone operation like total knee replacement or synovectomy. All patients were fulfilled the 2010 ACR-EULAR classification criteria for RA.

Expression of CD70 and HIF-2α messenger ribonucleic acid (mRNA) were analyzed in RA-FLS by quantitative polymerase chain reaction (qPCR).

Results: SAC increased OAC's proliferation rate and adhesion profile at relatively low concentrations (1, 10 and 100 nM), but inhibited at higher concentrations (1-100 μM). SAC (1 nM-10 μM) inhibited ROS, LPO and 3-NT, but not HNE- and AGE-modified proteins levels. SAC increased Gpx but drastically down regulated ICE/caspase-1, indicating a potential redox regulating and anti-inflammatory effect.

Conclusion: Results suggest that SAC has favorable effects on OA chondrocytes through protecting proliferation capacity and ameliorating redox-mediated inflammatory pathways. Further studies are needed to investigate its therapeutic potential in patients with OA.

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Figure. Cell proliferation of human primary chondrocytes (A) and dynamic monitoring of adhesion profile of human primary chondrocytes during SAC (B) treated with SAC (24 h). ICE/caspase-1, ROS, LPO, HNE, AGE, 3-NT levels after SAC (24 h) treatment (C). *p<0.05, **p<0.01, ***p<0.001 vs OAC. (Bland-Altman Statistics)

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Disclosure of Interests: None declared

Rheumatoid arthritis - etiology, pathogenesis and animal models

AB1019

SYSTEMIC OVEREXPRESSION OF INTERLEUKIN-22 INDUCES EXPRESSION OF THE NEGATIVE IMMUNE-REGULATOR SOCS3 AND POTENTLY REDUCES COLLAGEN-INDUCED ARTHRITIS IN MICE

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Background: High interleukin-22 (IL-22) levels are detected in serum and synovial fluid of rheumatoid arthritis (RA) patients. The increased IL-22 serum levels in RA patients correlated positively with multiple clinical disease parameters like disease activity score (DAS)28 and serum levels of rheumatoid factor. The role of IL-22 in autoimmunity and inflammation appears to be greatly contradictory, being both pro- and anti-inflammatory. Especially the anti-inflammatory properties of IL-22 are not well understood.

Objectives: We aimed to investigate the anti-inflammatory and immune-suppressive effect of IL-22 during experimental arthritis.

Methods: Collagen-induced arthritis was induced in DBA1 mice by immunization and booster with bovine collagen type II (CII). After booster, but before arthritis onset, IL-22 was overexpressed either locally or systemically using adenosine construct (AdIL-22) or Luciferase as control (AdLuc). 1x10⁷ plaque-forming units (PFU) of the adenoviruses were injected intra-articularly for local overexpression or 3x10⁶ PFU was injected intravenously for systemic overexpression in immunized mice, and mice were sacrificed 10 days later. Macrosopic scoring and histological analysis was performed, and mRNA expression and protein production of various pro- and anti-inflammatory mediators was determined in synovial tissue, spleen, and serum.

Results: Local overexpression of IL-22 by injection of AdIL-22 in the knee joint of CII-immunized mice resulted in an unaltered arthritis incidence and severity as compared to the control virus AdLuc. Additionally, no changes in mRNA expression or protein production were observed in CIA mice locally overexpressing IL-22. In contrast, systemic overexpression of IL-22 potentely reduced disease incidence and severity, which was also confirmed by histological analysis. Systemic levels of IL-1β, IL-17, GM-CSF and MCP1 were unaltered in mice overexpressing IL-22 systemically. However, these mice showed significantly lower serum levels of IFNγ, TNFα, MIP1α, and IL-10. Interestingly, the significantly enhanced splenic SOCS3 expression was found to negatively correlate to serum TNFα and MIP1α levels, which is in line with our hypothesis that the observed reduction in the cytokine levels is mediated in a SOCS3-dependent manner.

Conclusion: With this study, we revealed clear anti-inflammatory effects of IL-22 overexpression during collagen-induced arthritis, which are completely dependent on the systemic route of administration. Additionally, we were the first to show that this protective effect of IL-22 during experimental arthritis is likely orchestrated via up-regulation of the negative regulator SOCS3.

Disclosure of Interests: None declared


AB110

RITUXIMAB INDUCED GRANULOMATOUS HEPATITIS WITH A SARCOCIDOSIS LIKE REACTION: A BLINDED TRIAL IN MICE

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Background: Rituximab is useful in patients with rheumatoid arthritis (RA) with persistently active disease despite adequate trials with other disease-modifying antirheumatic drugs (DMARDs).

Objectives: To determine whether the inhibition of the B cell CD20 receptor by rituximab results in acute hepatitis in BALB/c mice.

Methods: Twenty BALB/c mice were studied. Ten mice received subcutaneous (SC) injection of rituximab (0.31mg per 25g body weight per 0.03 ml normal saline) at 0, 1, 2 and 4 weeks. For the control group, 10 mice received a SC injection of normal saline (NS) (0.03 ml). At the 10th week post injection, the mice were sacrificed, and histopathological studies were conducted.

Results: Of the rituximab-treated group, 1/10 mice died. Liver histology for the rituximab-treated group showed that 7/9 displayed histopathological changes in the lobular cellular infiltrates of eosinophils, lymphocytes and histocytes, in addition to granuloma formation. In contrast, only minimal inflammation was observed in 3/10 mice in the control group (p<0.05).

Disclosure of Interests: None declared

Conclusion: To our knowledge this is the first experimental controlled study demonstrating rituximab may play a role in inducing granulomatous hepatitis with a sarcoidosis-like reaction.

REFERENCES

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AB0112 EVALUATION OF A NEW MULTIPLEX TECHNOLOGY ASSAY FOR ANTICITRULLINATED PEPTIDE ANTIBODIES DETERMINATION
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Background: Anti-citrullinated peptides antibodies (ACPAs) are highly specific RA markers. In 2010, experts included them in the ACR/EULAR criteria for disease diagnosis, usually, measured by ELISA. However, a new assay has been developed, recently: Multiplex technology, which allows searching IgG ACPA directed against four citrullinated peptides: Human (HCP1 and 2) and Viral (VCP1 and 2).

Objectives: First, assess ACPA diagnostic performances using Multiplex technology and then compare them to those obtained with the reference technique (ELISA).

Methods: We studied sera of 273 RA patients versus 165 controls (64 healthy controls and 101 patients with other pathologies). We realized ACPA dosage by Multiplex technology and compared them with ELISA assay results. In the end, we looked for a correlation between ACPA production and shared epitope expression in RA patients.

Results: The overall agreement calculated between the two methods was about 91.3%. As to the comparison of diagnostic values of Multiplex technology vs. ELISA, it revealed a sensitivity of 80.2% vs. 82.4% and a specificity of 95.8% vs. 95.5%. Then, for a better evaluation, we plotted ROC curves for ACPA detected by Multiplex technology and ELISA ones. Therefore, we obtained the following areas under the curve (AUC) (p value <0.0001): Anti- HCP1 (0.775), HCP2 (0.798), VCP1 (0.715) and VCP2 (0.837) and ACPA ELISA (0.867). Finally, our results reveal higher serum levels of ACPA detected by Multiplex technology, in case of SE expression (SE (+) vs SE (-): (p value <0.0001).

Conclusion: Diagnostic performance of ACPA detection methods is comparable with relatively good agreement. Our study demonstrated an association between elevated serum levels of anti-HCP and anti-VCP and SE expression, in RA patients.

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Disclosure of Interests: None declared.

AB0113 ARTHRITIS IS ASSOCIATED WITH CEREBROVASCULAR ENDOThelial Dysfunction: MECHANISTIC INSIGHTS IN THE RAT ADJUVANT-INDUCED ARTHRITIS MODEL
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Background: Stroke is the second cause of premature mortality and sudden death in rheumatoid arthritis (RA) after myocardial infarction. The mechanisms involved in the high risk of stroke are currently known, but data from the general population argue for a contribution of cerebrovascular dysfunction.

Disclosure of Interests: Antonio Alvarez de Cienfuegos : None declared, Lucia Cantero-Nieto: None declared, José Alberto García-Gómez: None declared, Gemma Robledo: None declared, Daniel Sánchez-Cano: None declared, Javier Martín Ibanez: None declared, Miguel A González-Gay: Grant/research support from: Prof. MA González-Gay received grants/research supports from Abbvie, MSD, Jansen and Roche., Speakers bureau: Consultation fees/participation in company sponsored speaker’s bureau from Pfizer, Lilly, Sobi, Celgene, Novartis, Roche and Sanofi., Norberto Ortego: None declared.
OBJECTIVES: The aim of our study was to investigate cerebrovascular function in the rat adjuvant-induced arthritis (AIA) model and to unravel the mechanisms involved, with special emphasis on the pathways regulating nitric oxide (NO) vascular availability.

METHODS: Arthritis was induced in 6 weeks-old male Lewis rats by a single injection at the base of the tail of a suspension of Mycobacterium butyricum in Freund’s incomplete adjuvant. A control group received saline. Thirty-three days after induction, middle cerebral artery (MCA) were dissected and mounted on two glass micropipettes in a small vessel arteriograph before being pressurized at 80 mmHg. Endothelial function was evaluated in vessels pre-contracted with serotonin (10^{-5} M) by measuring the relaxant effect of bradykinin (BK, 10^{-6} M), adenosine diphosphate (ADP, 10^{-6} M) and cumulative concentrations of acetylcholine (Ach, 10^{-10} to 10^{-4} M) in the presence or not of a Nitric Oxide Synthase (NOS) inhibitor (L-NAME, 10^{-4} M), an arginase inhibitor (nor-NOHA, 10^{-4} M), a NOS co-factor (BH4, 10^{-5} M), an analog of superoxide dismutase (Tempol, 10^{-4} M). The relaxant response of vascular smooth muscle cells to a NO-donor (SNP, 10^{-10} to 10^{-5} M) was also evaluated.

RESULTS: Vasodilation induced by BK, ADP and Ach were significantly reduced in AIA compared to controls rats (p<0.0001). L-NAME decreased Ach-induced relaxation in controls but not in AIA rats. By contrast, nor-NOHA (p<0.0001), Tempol (p<0.0001) and BH4 (p<0.02) significantly improved Ach-induced relaxation in AIA but not in controls. The response to SNP was not different between the 2 groups.

CONCLUSION: Arthritis is associated with endothelial dysfunction in MCA. These results indicate that this model is relevant for mimicking the cerebrovascular low NOS activity, a high arginase activity and excessive superoxide anions production. Overall data suggest that therapies able to reverse the imbalance in NOS/arginase pathways would be efficient for reducing the incidence of cerebrovascular events in RA.

REFERENCES

Disclosure of Interests: None declared

AB0114 POTENTIAL THERAPEUTIC EFFECTS OF CENTAUREA CYANUS L. ON RHEUMATOID ARTHRITIS THROUGH CD38+ NK CELLS

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BACKGROUND: CD38 catalyzes nicotinamide adenine dinucleotide (Coenzyme I, NAD+) to cyclic ADP ribose (cADPR). We previously reported that CD38 is specifically overexpressed in synovial membrane during rheumatoid arthritis (RA), and CD38+ natural killer (NK) cells are not only highly proportionate in the peripheral blood of RA patients but are also closely related to the disease severity. Cynus CYANUS L. is an inhibitor of CD38 that has anti-inflammatory effects.

OBJECTIVES: This study aimed to determine the roles and mechanisms of CD38 and its inhibitor C3G on RA and provides a basis for C3G to become a potential therapeutic agent for RA.

METHODS: This study employed bovine type II collagen-induced arthritis (CIA) rats, in vitro cultured RA synovial fibroblasts (RASFs) and mononuclear cells (MNCs) as models to explore the potential therapeutic effects and mechanisms of C3G on RA.

RESULTS: Rats following C3G injections showed significantly alleviated CIA, while the concentrations of inflammatory interleukin (IL)-6 and interferon (IFN)-γ and the proportion of CD38+ NK cells decreased, the levels of anti-inflammatory IL-10 and the proportion of regulatory T (Treg) cells increased, in the peripheral blood and synovial fluids (Figure 1). After C3G treatment, the RASF proliferation and the level of IL-6 in the culture medium decreased, apoptosis increased. C3G also increased IL-2 and IL-10 secretion, and decreased IL-6 and IFN-γ level and the proportion of CD38+ NK in MNCs. The coculture of CD38+ NK cells with MNCs depleted of CD38+ NK cells decreased the proportion of Treg cells and the IL-10 levels, meanwhile the coculture in the presence of C3G showed increased the proportion of Treg cells and the IL-10 levels and decreased IL-6 and IFN-γ level. However, C3G did not directly affect the Treg cell proliferation and their cytokine production. C3G treatment also increased sirtuin (Sirt)6 expression, while decreasing the expression of the NK activation receptor natural killer group 2D (NKG2D) in CD38+ NK cells. The expression level of NKG2D in CD38+ NK cells transfected with Sirt6 siRNA was not significantly changed in the presence of C3G. After CIA rats were injected with both C3G and OSS_128176, a Sirt6 inhibitor, the rats remained joint inflammation and the low proportion of Treg cells, although the proportions of CD38+ NK cells decreased in these CIA rats. After C3G treatment, the concentration of tumor necrosis factor (TNF)-α in the CD38+ NK culture medium increased and the concentration of IFN-γ decreased. When cocultured MNC and CD38+ NK cells were treated with C3G and TNF-α or C3G and anti-IFN-γ antibody, the proportion of IL-10+ Treg cells increased significantly, while the proportion decreased when cocultured MNC and CD38+ NK cells were treated with C3G and IFN-γ or C3G and anti-TNF-α antibody. The secretion level of TNF-α decreased sharply, and the concentration of IFN-γ increased significantly in the CD38+ NK cell culture treated with both Sirt6 siRNA and C3G.

CONCLUSION: C3G has therapeutic effects for CIA and RA. C3G decreases the proportion of CD38+ NK cells, and increases the expression of Sirt6 in CD38+ NK cells, which increases TNF-α secretion and decreases IFN-γ secretion and sequentially stimulates MNC differentiation into IL-10+ Treg cells and the secretion of IL-10. This study also suggests that the inhibition of MNC differentiation into Treg cells by CD38+ NK cells is an important cause of immune imbalance in RA and CIA (Figure 2).

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Disclosure of Interests: None declared
**AB0115**

**SEMAPHORIN 4A PERPETUATE SYNOVIAL INTERACTIONS WITH CD4+ T CELLS AND OSTEOCLAST DIFFERENTIATION: IMPLICATION IN RHEUMATOID ARTHRITIS**

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**Background:** Rheumatoid arthritis synovial fibroblast (RASF) and T cells are important contributors in the pathogenesis of RA. Semaphorin 4A has been reported to be elevated in RA patients and play crucial role in promoting inflammation of RA. However, whether semaphorin 4A could facilitate RASF interactions with CD4+ T cells and osteoclastogenesis is less known.

**Objectives:** The present study aims to investigate the role of semaphorin 4A-Plexin B1 axis in RASF interactions with CD4+ T cells and osteoclastogenesis in vitro.

**Methods:** Mouse synovial fibroblasts (SF) were isolated from collagen-induced arthritic mice and cultured in vitro with TNF-α and IL-1β for 24h. Small interfering RNA (siRNA) against Semaphorin 4A and Plexin B1 were constructed and transfected into SF via adenovirus. Spleenic CD4+ T cells isolated from arthritic mice were cocultured with SF under anti-CD3 and anti-CD28. The proportion of Th17 cells was determined at 5 days. BMSC isolated from blood of healthy donors were incubated with 1 μg/ml Plexin D1 neutralizing antibody overnight. Cells were washed for monocyte enrichment and cultivated for 14 days in a MEM supplemented with M-CSF and RANKL. Osteoclast differentiation was evaluated by TRAP staining. Total RNA was extracted and expression of osteoclast markers were examined by quantitative real-time PCR.

**Results:** Adenovirus-Mediated siRNA efficiently inhibited expression of Semaphorin 4A and Plexin B1 in SF. The proportion of Th17 cells was significantly decreased in both Semaphorin 4A and Plexin B1 transfected SF cocultures. The number of TRAP-positive osteoclasts were significantly decreased in cultures that pretreated with Plexin D1. Consistently, blocking of Plexin D1 signaling dramatically downregulated mRNA expression level of Trap, Cathepsin K and NFATc1. Conclusion: Semaphorin 4A perpetuate synovial fibroblasts interactions with CD4+ T cells by promoting Th17 differentiation. Moreover, Semaphorin 4A-Plexin D1 axis promote osteoclastogenesis and therefore might serve as a potential therapeutic target in the treatment of RA.

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**AB0117**

**HOMOCYSTEINYLATED ALPHA 1 ANTI-TRYPSIN AS A POTENTIAL ANTIGENIC TARGET IN RHEUMATOID ARTHRITIS**

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**Background:** Rheumatoid arthritis (RA) is a chronic, inflammatory, autoimmune disorder that primarily affects joints. Beside the well-known rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA) have been reported to be a very useful diagnostic and prognostic marker of RA, recently antibodies against carbamylated (anti-Carb) have been described also in ACPA-negative RA patients. However, more than 20% of RA cases are still defined as seronegative forms. Therefore, the individuation of new antibody specificities in RA could be helpful for diagnostic and prognostic purposes.

**Objectives:** The goal of this study was to identify the and the immunologic characterization of post-translational modified synovial fluid (SF) autoantigens, specifically targeted by autoantibodies from sera of seronegative RA patients.

**Methods:** SFs from 5 seronegative RA patients were collected, pooled and treated with hyaluronidase. After removal of both albumin and IgG, the sample was washed and cleansed, concentrated, separated by 2-dimensional electrophoresis (2-DE) and then transferred by Western blooting to nitrocelluose membrane, for autoantigen detection by immunoassay, using a pool of sera from 5 seronegative RA patients. The antigenic protein spots were identified by peptide mass fingerprint, using a Matrix-Assisted Laser Desorption/Ionization-Time Of Flight (MALDI-TOF) mass spectrometer.

**Results:** This approach revealed Alpha 1 Anti-Trypsin (A1AT) as a target of RA patients autoantibodies. Pooled SFs were also analyzed by reverse-phase nanoliquid chromatography and tandem mass spectrometry, to confirm the presence of A1AT and for the identification of A1AT post-translational modifications.

Homocysteinylated A1AT was immunoprecipitated from pooled SFs of RA seronegative patients, and, after a dilatation and concentration process, was used as an antigen to detect anti-homocysteinylated A1AT antibodies by Enzyme-Linked ImmunoSorbent Assay (ELISA). In order to this, consecutive patients with RA, osteoarthritis (OA), psoriatic arthritis (PsA), and healthy donors were enrolled and sera were collected.

**Results:** Homocysteinylated A1AT was identified as a potential antigenic target not only in ACPA and RF positive RA patients but, more importantly, also in RA seronegative patients. Antibodies anti-homocysteinylated A1AT were found in 66.7% (44/66) RA patients seronegative for ACPA and RF, 88.6% (39/44) RA patients, 15% (3/20) OA patients, 26.3% (5/19) PsA patients and in none (0/41) of healthy donors.

**Conclusion:** Homocysteinylated A1AT was identified as a new potential antigenic target of autoantibodies in sera from RA patients, including RA seronegative patients. This tool may be useful in diagnosis and monitoring of the disease and may contribute to understand the immunopathogenic mechanisms of RA in future studies.

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The mechanism of traditional Chinese medicine prescription Er-miao-san in the treatment of rheumatoid arthritis based on cholinergic anti-inflammatory pathway

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Background: Rheumatoid arthritis (RA) is a chronic progressive autoimmune disease. The traditional Chinese herbal formula Er-miao-san (EMS) has been used to treat RA demonstrating significant clinical efficacy; however, the mechanism of action remains unclear. In view of the important role of α7 nicotinic acetylcholine receptor (α7nAChR) in the cholinergic anti-inflammatory pathway (CAP) for the regulation of inflammation and cytokines. Indeed, we previously found a correlation between CHRNA7 (encoding α7nAChR) expression and EMS, we hypothesized that it may play a role in the anti-inflammatory effects of EMS.

Objectives: The mechanism of EMS in the treatment of RA based on CHRNA7 involved in the regulation of CAP.

Methods: We established a CIA model with female Wistar, and the effects of intragastric administration of EMS on the expression of CHRNA7, arthritis score, inflammatory, and articular cartilage changes, was examined in the joints. The serum levels of TNF-α, IL-6, and IL-1β were determined using commercial ELISA kit.

Results: The CIA model was successfully established. Macroscopic changes of arthritis, such as redness and swelling, were clearly observed in the CIA rats, but were attenuated by the treatment of EMS. The mean arthritis score was markedly lower in the EMS-treated group (EG, P < 0.05). The same results were found in the serum levels of IL-6 and IL-1β. Synovial edema and extensive infiltration of inflammatory cells occurred in the CIA rats, but were repaired by the treatment of EMS. Cartilage tissue was thinning, dissolution and disappearance, as well as extensive inflammatory cell infiltration with plasma cells and lymphocytes, was observed in the articular cartilage of the ankles in CIA group. In contrast, EMS treatment prevented cartilage degeneration and markedly reduced inflammation. Immunohistochemistry (IHC) analysis showed positive signals of CHRNA7 was expressed on fibroblast-like synoviocytes, macrophages, and endothelial cells in the joints. Effect of EMS on the expression of CHRNA7 protein in the joint by Western blot (WB) analysis. IHC and WB relative optical density values of CHRNA7 was significantly higher in EG compared with CIA group (P < 0.05).

Conclusion: EMS can significantly alleviate the symptoms of arthritis in CIA rats by regulating the expression of CHRNA7 in CAP. It provides a scientific research foundation for the further development of EMS and explores more ways to treat RA.

Disclosure of Interests: None declared
there is a lack of relevant reports on their function in chronic, multisystem autoimmune diseases.

**Objectives:** Here, using molecular biology techniques were performed to evaluate the expression of 7 chemokines/chemokine receptors in different tissues and their localization in the joints.

**Methods:** We established a collagen-induced arthritis (CIA) model in female Wistar rats and evaluated the expression patterns of 7 chemokines/chemokine receptors ([CCR3, CCR5, CXCR7, CCL5, CXCR3, CXCR4, and CXCL10]) in different tissues using RT-PCR and western blotting and their localization in the joints using immunohistochemistry.

**Results:** The mRNA expression of CCR3, CCR7, CXCR4, and CXCL10 was significantly higher in the spleen and joints, while that of CCR5 and CCL5 was significantly higher in the liver and that of CXCR5 was significantly higher in the lung, spleen, and joints (Fig. 1). Protein expression patterns largely corresponded to mRNA expression patterns. In the joints, CCR3, CCR5, and CXCR7 were expressed in fibroblast-like synoviocytes (FLS), macrophages, stromal cells, and endothelial cells. CCL5, CXCR3, and CXCR4 were expressed in FLS, endothelial cells, and stromal cells. CXCL10 was expressed throughout the synovium, stromal cells, and endothelial cells (Fig. 2).

**Conclusion:** Seven chemokines/chemokine receptors are widely expressed in different tissues in the CIA rat model, and all are involved in the inflammatory response. Our results provide a basis for investigations into the mechanism of action of RA and suggest that chemokines may become novel targets for RA treatment.

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AB0123  CCL17 IN SYNOVIAL FLUID AND PLASMA OF PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS

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Background: Despite the advancements in management of rheumatoid arthritis (RA) in the last two decades, there are still a significant number of patients who cannot achieve low disease states or remission with the current available therapy. Granulocyte macrophage-colony stimulating factor (GM-CSF) is a key mediator in inflammation and autoimmunity, and has emerged as a novel therapeutic target in RA. However, potential adverse side effects warrant further investigation of a more specific target.

Objectives: Chemokine (C-C motif) ligand 17 (CCL17) is a downstream mediator of GM-CSF and has recently been shown to be regulated by GM-CSF in human monocytes. Significantly, CCL17 has a non-redundant role in inflammatory arthritis and pain. We investigated the expression levels of CCL17 in synovial fluid and plasma from RA patients.

Methods: We recruited RA patients with symptomatic swollen joints, who require joint aspiration for diagnostic and/or therapeutic purposes. Synovial fluid and plasma were collected and CCL17 protein levels were determined by ELISA.

Results: CCL17 protein was measured in synovial fluid and plasma samples from our cohort of RA patients. Levels of secreted CCL17 were higher in plasma [median 240 (40-580) pg/ml] compared to synovial fluid [median 100 (30-300) pg/ml] p<0.05.

Conclusion: Significant levels of CCL17 were detected in RA synovial fluid and plasma. This is a novel study which demonstrates and compares the presence of CCL17 in synovial fluid and plasma from matching RA patients. The expression of CCL17 in plasma can make it a useful potential biomarker for RA, while its expression in synovial fluid suggests that CCL17 may be a therapeutic target for treating RA.

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Disclosure of Interests: Cecil Hor Speakers bureau: Mundipharma, Pfizer, Adrian Achuthan: None declared, Keith Lim Consultant for: Advisor for role of hepatititis and TB in Cimzia, UCB, Speakers bureau: Role of biological in pregnancy UCB, John Hamilton Grant/research support from: GSK


AB0124  IMPACT OF INFLAMMATORY CYTOKINE IL-1β ON THE EXPRESSION OF MULTIPLE DRUG RESISTANCE PROTEIN BCRP/ABCG2 IN SYNOVIOCYTES OF PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease characterized by synovitis and vasospasm27. So far, The biggest challenge on the current field of RA treatment is the production of DMARDS multidrug resistance (MDR) and the most critical mechanism for the production of MDR is the ABC transporter family-mediated increase in target cell drug exclusion, while inflammatory cytokines play an important role in its expression regulation. Our previous research have confirmed that IL-1β, IL-6 and IL-17 are involved in the regulation of P-glycoprotein (P-gp) expression in lymphocytes of RA patients. The breast cancer resistance protein (BCRP/ABCG2) is also a highly efficient efflux pump, which absorbs, distributes, and excretes drugs or exogenous substances in the body22. IL-1β is a cytokine involved in the whole process of RA, which can aggravate the inflammatory response. However, there is no research on the effect of IL-19 on the expression of BCRP in RA Fibroblast-like synovicyes (FLS).

Objectives: To explore the effects of different concentrations of IL-1β on the expression of drug resistance proteins in FLS of RA patients at different time points.

Methods: Synovial tissues of untreated RA patients (n=3) were extracted by Joint surgery. FLS culture system in vitro was established and passed to the 6th generation so or to do the experiments. FLS cells were divided into A, B, C, D four groups randomly with different treatments: Group A was the cell control group. Group B, C, D were respectively co-cultured with low (20ng/ml), middle (50ng/ml), high (100ng/ml) concentrations of IL-1β. They were cultured respectively for 24 hours, 48 hours, and 72 hours. The effect of IL-1β on the expression level of BCRP mRNA was observed at different concentrations and at different time points.

Results:
1. With the proliferation of IL-1βculture, the expression of BCRP mRNA increased. Under the same concentration of IL-1β[20ng/ml or 50ng/ml], the expression of BCRP mRNA in the 72h group was higher than that in the 24h group or 48h group (P<0.05). At the concentration of IL-1β[200 ng/ml, the 48h group showed higher levels of BCRP mRNA expression than the 24h group (P<0.05).
2. The expression of BCRP mRNA increased with the increase of IL-1βconcentration. After 48h of IL-1βculture, the 100 ng/ml group showed high levels of BCRP mRNA expression compared with the 0 ng/ml group (P<0.05). After 72h of IL-1βculture, compared with the 0 ng/ml group, the expression of BCRP mRNA was significantly increased in the 20 ng/ml or 50 ng/ml or 100 ng/ml group (P<0.01); and the 100 ng/ml group showed high levels of BCRP mRNA expression compared with the 20 ng/ml group (P<0.05).

Conclusion: The expression of BCRP mRNA in FLS of RA patients has a certain concentration and time dependence of IL-1β, suggesting that IL-1β is involved in BCRP-mediated multidrug resistance, which lays a foundation for exploring its specific mechanism.

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Disclosure of Interests: None declared

CXCL17 IN RHEUMATOID ARTHRITIS: INTERFERON-ANTI-INFLAMMATORY EFFECTS OF SPLEEN TYROSINE

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Background: CXCL17 is the latest chemokine discovered and was reported to influence angiogenesis and monocyte trafficking. Its role in rheumatoid arthritis (RA) has not been assessed so far.

Objectives: To assess the role of CXCL17 and its putative receptor G-protein-coupled receptor 35 (GPR35) in RA.

Methods: Synovial tissue from joint replacements of RA and osteoarthritis (OA) patients was used for CXCL17 and GPR35 immunohistochemistry and in situ hybridization/immunofluorescence double-stainings. CXCL17 concentration in the synovial fluid of RA and CXCL17 production by synovial fibroblasts and smooth muscle cells after stimulation with TNF-α, INF-γ and IL-1β was quantified by qPCR and ELISA. Angiogenesis was assessed by a human umbilical vein endothelial cell culture assay.

Results: CXCL17 and GPR35 are widely expressed in the synovial membrane of RA compared to OA (p<0.006). Within the synovial membrane CXCL17 mRNA could be located to vascular smooth muscle cells. INF-γ significantly induced CXCL17 mRNA and protein production in RA synovial fibroblasts (19-fold, p=0.019 and 2-fold, p=0.0002 respectively) and rat smooth muscle cells (67-fold, p=0.02 and 3.7-fold, p=0.001). CXCL17 was detected in the synovial fluid of RA (mean 310 pg/ml). In vitro angiogenesis was inhibited by CXCL17. This effect was reversed by specific GPR35 antagonists.

Conclusion: CXCL17 is abundant in RA synovial tissue, localizes to vascular smooth muscle cells and fibroblasts, and is inducible by INF-γ. Antiangiogenic properties are mediated by GPR35. CXCL17 and GPR35 may constitute a hitherto unrecognized regulatory protein in RA pathogenesis and therefore be interesting drug targets.

REFERENCES


ANTI-INFLAMMATORY EFFECTS OF SLEEP TYROSINE KINASE (SYK) INHIBITOR, PICEATANNOL, ON FIBROBLAST-LIKE SYNOVIOTYE IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is an autoimmune disease characterized by chronic inflammation with subsequent cartilage and bone erosion leading to joint destruction. The fibroblast-like synoviocytes (FLS) have a central role in disease pathogenesis and in vitro FLS invasiveness correlates with articular cartilage damage in RA patients. Spleen tyrosine kinase (Syk) is an intracellular protein tyrosine kinase in the cells in tissues such as bone, cartilage, and synovium, where it is involved in tumor necrosis factor (TNF-α) receptor signaling. Piceatannol, a naturally occurring hydroxylated analog of resveratrol, was reported to inhibit Syk.

Objectives: The aim of this study is to evaluate the effects of piceatannol on inflammation and the downstream signaling pathway of Syk in RA FLS.

Methods: FLS isolated from synovium of rheumatoid arthritis (RA) patients were cultured with DMEM supplemented with 10% FBS and 1% penicillin/streptomycin. FLS were stimulated with lipopolysaccharide (LPS) for 24 hr after 1 hr treatment of piceatannol. The cytokines were screened using human inflammatory and matrix metalloproteinase (MMP) antibody array kit (Abcam) in the culture supernatant. Also, IL-6, IL-8 and CXCL10 levels were measured by ELISA and the expression levels of cyclooxygenase-2 (COX-2) and inducible nitric oxide synthases (iNOS) were determined by western blotting.

Results: Protein expression level of Syk was suppressed by piceatannol (50 μM treatment). Piceatannol inhibited the production of cytokines/chemokines such as IL-6, CCL-5, CCL-8 and MMP-1 in RA FLS stimulated with LPS. The levels of IL-6, IL-8 and CXCL10 in RA FLS were dose-dependently decreased. The viability and proliferation of the cells were not affected. Piceatannol significantly suppressed COX-2 and iNOS protein expressions.

Conclusion: Piceatannol had suppressive effects on pro-inflammatory cytokines/chemokines production and had anti-inflammatory effects in RA FLS.

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Disclosure of Interests: None declared

AB0127

VERY STRONGLY POSITIVE RHEUMATOID FACTOR LEVELS (10-FOLD HIGHER THAN THE UPPER NORMAL RANGE) RATHER THAN “RHEUMATOID FACTOR POSITIVITY” PER SE ASSOCIATED WITH SMOKING IN FEMALE RA PATIENTS WITHOUT A HISTORY OF OCCUPATIONAL DUST AND FUME EXPOSURE

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Background: Rheumatoid factor (RF) forms part of the 2010 EULAR/ACR classification criteria1. A weakly positive RF is defined as up to 3-fold higher and a strongly positive RF >3-fold higher than the upper normal range. However, a longitudinal study of individuals with RF levels at least 4-fold higher than the upper range of normal had an adjusted hazard ratio for RA development of 26 (95% CI 15 to 46) compared to only 6.0 (3.4 to 10) for individuals with levels 2 to 4-fold above the upper normal range2. We have recently reported median RFs of greater than 10-fold higher than the upper normal range in nodular RA which is far more prevalent in smokers than non-nodular RA3. We have arbitrarily defined this level of RF as very strongly positive as it defines a disease subtype. Additionally, RF levels are strongly associated with addictive exposures to both smoking and industrial vapours, gases, dust and fumes (VGDF) in male RA, with only 8% having been exposed to neither VGDF or cigarette smoke4. Objectives: Accordingly, we have studied female RA in whom VGDF exposures are less common to compare RF levels in an appreciable number of smokers and non-smokers without the significant confounding effect of VGDF exposures to determine if smoking is specifically associated with a very strongly positive RF.

Methods: Medical record analysis yielded 241 female RA patients seen in clinic between January and June 2018 without exposures to industrial VGDF. These patients were stratified for a history of smoking. RF was measured with Tina-quant Rheumatoid Factors II Test System, by Roche Diagnostics Corporation at the time of RA diagnosis. A value of < 14 IU/ml was considered as negative as per manufacturer guidelines, a RF weakly positive (14-42 IU/ml), RF strongly positive (42-140 IU/ml) and RF very strongly positive (>140 IU/ml).

Results: There were 109 never smokers and 132 smokers with a median RF of 21 IU/ml and 53 IU/ml respectively, p<0.05. In never-smokers significantly more were seronegative 46/109 (42%) vs. 32/132 smokers (24%), odds ratio (OR)=2.22 (95% confidence interval (CI):1.28-3.83, P=0.004). Of never smokers 22/109 (20%) were weakly RF positive and very similar to smokers 28/132 (21%).28/132 (21%) of never smokers were strongly RF positive and a similar proportion of smokers 37/132 (28%) were strongly RF positive. Finally in never smokers, only 12/109 (11%) very strongly RF positive compared to 35/132 (27%) of smokers, OR=2.99 (95% CI 1.41-5.99, p=0.004).

Conclusion: Considering female RA smokers and non-smokers, the difference in RF positivity was exclusively accounted for by an increased prevalence of a very strongly positive RF in female smokers. This suggests that smoking has an impact on very strongly positive RF levels rather than RF positivity per se without the important confounding factor of VGDF exposure.
REFERENCES


Disclosure of Interests: None declared

AB0128 ANTI-OXIDATIVE PROTECTION AND MONOXIGENASE SYSTEM ACTIVITY OF CYTOCHROME P450 (MOG) OF NEUTROPHILIC LEUKOCYTES (NL) FROM SYNOVIAL FLUID (SF) IN RHEUMATOID ARTHRITIS (RA)
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Background: MOG system is present not only in the liver but also in far less quantities in other organs and tissues, including SF.

Objectives: SF in RA patient contains up to 95% of NL that determines the inflammation also by inhibiting MOG.

Methods: SF of knee joints of 8 patients with RA with active synovitis and 4 donors (D) were examined. NL have been isolated by standard methods. After the application of Triton-X-100 0.1% solution, NL have been centrifuged at 25000 g for 30 minutes. The supernatant has been used in the experiment. The activity of MOG has been estimated according to the level of cytochromes P450, P420 and b5 and has been estimated by applying the method of differential spectrophotometry.

Active forms of oxygen have been registered by applying electron paramagnetic resonance (EPR).

The activity of the antioxidant enzymes - Cu-Zn superoxide dismutase (Cu-Zn SOD), Se-glutathione peroxidase (Se-GPO) and catalase (CAT) was estimated by applying classical enzymology methods.

Results: It has been found out that in RA, the level of active oxygen forms increases by 68%. Meanwhile, the enzymes level of antioxidant defense is insufficient.

In RA the activity of SOD, GPO and CAT enzymes is inhibited at 52, 66 and 39% respectively. In RA the activity of MOG (P450 and b5) in NL is 4 times lower than normal. The concentration of the inactive form of cytochrome P420, however, doubles. Nevertheless, their ratio P450/P420 (when normal = 5) in case of RA = 5.8, hardly ever changes.

Cytochrome concentration P450, P420 and b5 (nmol/mg of protein), level of active oxygen forms (Units/mg of protein) and antioxidant system activity (SOD, GPO - Unbinding of protein; CAT - unbinding of protein) in NL in RA

<table>
<thead>
<tr>
<th>NL</th>
<th>P-450</th>
<th>P-420</th>
<th>b5</th>
<th>Level of active forms</th>
<th>Cu-Zn SOD</th>
<th>Se-GPO</th>
<th>CAT</th>
</tr>
</thead>
<tbody>
<tr>
<td>P-450</td>
<td>0.4</td>
<td>0.025</td>
<td>0.43</td>
<td>15.7 ± 4.1</td>
<td>19.7</td>
<td>1.8</td>
<td>10.8</td>
</tr>
<tr>
<td>P-420</td>
<td>0.025</td>
<td>0.029</td>
<td>0.07</td>
<td>19.7 ± 4.1</td>
<td>15.3</td>
<td>3.3</td>
<td>13.1</td>
</tr>
<tr>
<td>b5</td>
<td>(0.027)</td>
<td>(27.1)</td>
<td>(2.1)</td>
<td>(13.1)</td>
<td>(13.3)</td>
<td>(13.1)</td>
<td></td>
</tr>
<tr>
<td>PA</td>
<td>0.054</td>
<td>0.063</td>
<td>0.03</td>
<td>19.7 ± 4.1</td>
<td>15.3</td>
<td>3.3</td>
<td>13.1</td>
</tr>
<tr>
<td></td>
<td>(0.059)</td>
<td>(13.1)</td>
<td>(0.7)</td>
<td>(2.8)</td>
<td>(13.1)</td>
<td>(13.1)</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: A fall in the level of free radical oxidation and antioxidant defense and faster generation of active oxygen forms in RA leads to NL being destroyed and creates favorable conditions for the development of autophagy and apoptosis. The oxidative stress during RA is accompanied by a fall in the activity of MOG and creates favorable conditions for the development of autophagy and apoptosis.

REFERENCE

Disclosure of Interests: None declared

AB0129 ULTRA-MICROSCOPIC ANALYSIS OF NURSING PHENOMENON IN SYNOVIAL TISSUE OF RHEUMATOID ARTHRITIS
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Background: Applying recent advances in electron microscope technology, cells and cell-cell interactions are observable using virtual slides, three-dimensional (3D) imaging, and serial sections of ultrathin thickness. Inflammation in rheumatoid arthritis (RA) is caused by multiple cell types, including infiltrating inflammatory cells, such as lymphocytes, neutrophils, macrophages, and spindle-shaped fibroblasts. Especially, we are focusing on fibroblast-like synoviocytes (FLSs). These cells have been reported to be positive for multiple markers including CD14, CD68, HLA-DR and vimentin, and we have shown that these cells are dendritic cells in our previous study using electron microscopy. Therefore, FLSs are presumed to function as dendritic cells and these cells involved in the nursing phenomenon.

Objectives: The objective of this study is to investigate the chronically mechanism of immunological inflammation in RA by using electron microscopy.

Methods: Synovial tissues collected from RA patients undergoing elbow or knee joint surgery were prepared for this study. Using wide field of view images of the synovial tissue, areas containing the nursing phenomenon were selected by using multiscale electron microscopy. 3D structures of the features were constructed from series of micrographs obtained by using focused ion beam-scanning electron microscopy and those by using transmission electron microscopy with double-axis electron tomography (DA-ET).

Results: From multiscale electron microscopy, many synovial dendritic cells and plasma cells were present in various areas of the lymphnodular infiltration. Serial cross-sectional observation with an FIB-SEM and 3D images revealed that synovial dendritic cells patroonized the plasma cells, wrapping around the plasma cells, by the long slender axes. A tomogram of an ultra-thin sliced section created by using DA-ET revealed that synovial dendritic cells formed a membranous fusion with the plasma cells.

Conclusion: The nursing phenomenon involves characteristic histopathological features, which may be a factor in the chronicity of the inflammation mechanism RA synovial tissue.

REFERENCES

Disclosure of Interests: None declared

AB0130 THE EFFECTS OF METHOTREXATE ON THE VASCULAR ENDOTHELIUM

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Background: Anti-inflammatory therapy has been recently validated as a treatment option for patients with cardiovascular disease (CVD) [1]. The anti-inflammatory drug methotrexate (MTX) reduces cardiovascular risk in patients with systemic inflammatory rheumatic diseases [2]; possibly by improving endothelial function [3]. However, the molecular basis of the drug’s anti-inflammatory and potential anti-atherogenic effects on the vasculature is not well described.

Objectives: Our goal was to characterize the actions of MTX on vascular endothelial cells (EC).

Methods: MTX-treated human umbilical vein (HUVEC) or aortic endothelial cells (HAE) were analyzed by quantitative real-time PCR (qRT-PCR) of pro-angiogenic and pro-inflammatory cytokines. EC viability and cell cycle were evaluated by flow cytometry using Annexin V and/or propidium iodide staining. For selected experiments, EC were exposed to laminar (LSS; 20 dyn/cm²) or oscillatory shear stress (OSS; 0.5 dyn/cm² - 2Hz) using a parallel plate model.

Results: Under static conditions, MTX independently increased the activity of multiple kinases in quiescent and TNFα-activated EC. MTX-activated kinases

Disclosure of Interests: None declared
included the mitogen-activated protein kinase (MAPK) p38 and Akt. MTX did not inhibit TNFα-induced nuclear factor kappa B (NFκB) transcriptional activation, signaling or target gene expression. However, MTX induced pro-inflammatory markers such as vascular cell adhesion molecule (VCAM)-1 in an additive manner with TNFα. Functionally, MTX did not induce apoptosis but caused S-phase cell cycle arrest, which, along with p38 and Akt activation, could be abrogated by supplementation with folic acid.

Findings to date in EC subjected to shear stress are somewhat different. MTX had no or a mild inhibitory effect on kinase signaling in EC under LSS and OSS, respectively. MTX did not affect cell proliferation nor baseline or OSS-induced VCAM-1 expression in EC under shear stress.

Conclusion: In static EC, low-dose MTX caused cell cycle arrest through folate depletion, which is a known mechanism of action in other cell types. Of note, this response was not seen in EC pre-conditioned by shear stress and emphasizes the impact of biomechanical forces on endothelial phenotype and response to exogenous stimulation. This is the first report to study the effects of MTX on EC under shear stress, which will be crucial in understanding its molecular actions on the vasculature.

REFERENCES

Disclosure of Interests: Marie Lang: None declared, Charis Pericleous: None declared, Robert Maughan: None declared, Allan Kiprianos: None declared, Justin Mason Consultant for: Prof Mason has worked as a paid Consultant for Roche/Chugai and Novartis, Speakers bureau: Prof Mason has been a paid speaker for Roche/Chugai


AB0131 THE CORRELATION OF EXPRESSION OF DIFFERENTIAL DRUG-RESISTANT PROTEINS AND INFLAMMATORY CYTOKINES IN COLLAGEN INDUCED ARTHRITIS MODEL

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Background: Rheumatoid arthritis (RA) is a systemic autoimmune disease. The most characteristic patho-logical changes are chronic synovitis. At present, the combination of traditional disease-difying anti-rheumatic drugs (DMARDs) and biological agents DMARDs has improved the therapeutic effect of RA, but some RA patients still have poor response due to Multidrug resistance (MDR) phenomenon. The main mechanism of MDR is resistance (MDR) is related to the ATP-binding cassette (ABC) transporter superfamily members, which increases drug efflux and reduces intra-cellular drug concentration. We will study how cytokines regulate the expression of ABC transporters.

Objectives: By comparing the differential expression of ABC transporter family resistance-related proteins P-gp, BCRP, MRPI and inflammatory cytokines IL-1β, IL-2, IL-6, IL-10, TNFα and IL-17 in CIA model mice, to investigate the correlation between Inflammatory cytokines and drug-resistant proteins.

Methods: Fourteen DBA1 mice were successfully induced by collagen and Freund's Adjuvant. According to the scores of synovial pathology, the CIA group was divided into mild, moderate-to-severe groups, another four mice were selected as control. The mRNA expressions of P-gp, BCRP, MRPI in splenic lymphocyte cells were measured by RT-qPCR. The concentrations of IL-1β, IL-2, IL-6, IL-10, TNFα, IL-17 in serum were determined by Cytometric Bead Array(CBA). Further analyze the correlation between differential inflammatory cytokines and these proteins, then study one of the proteins which is most related with cytokines by target gene expression. 2. In the spleen lymphocytes, there was no significant difference in the mRNA expression level of P-gp and BCRP among the groups, but the mRNA expression level of MRPI was significantly increased (P<0.05). Compared with the mild CIA group, the MRPI mRNA in the moderate-to-severe CIA group was higher, there was significant difference(Z=2.132, P<0.05). There was a correlation between mRNA expression of MRPI and P-gp(r=0.635, P<0.015).

3. The mRNA expression of MRPI was positively correlated with IL-6 level (r=0.711, P<0.004).

4. The expression of MRPI in normal group, low-level IL-6 group and high-level IL-6 group were respectively as follows:1.08±0.65(1.30), 1.40 (1.13.2.07), 1.90(1.68,2.17).

5. Compared with the controls, the cytokiasis/membrane of the knee and ankle joint synovial tissue in the CIA group was yellowish-brown, which proved that MRPI expression was positive.

Conclusion: In the CIA arthritis model, synovial tissue lesion is not only related to inflammatory cytokines, but also related to MRPI expression in the ABC transport resistance protein family, and it is proved that IL-6 is highly correlated to MRPI.

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therefore also our hypothesis 1 that BSSL is a novel target for treatment of inflammatory diseases.

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ANALYSIS OF INTESTINAL MICROBIOME PROFILE OF RA Patients

Statistical analysis: The authors are grateful to Eva-Lotta Andersson for excellent technical assistance.


HUMAN UMBILICAL CORD-DERIVED MESENCHYMAL STEM CELLS AMELIORATE COLLAGEN-INDUCED ARTHRITIS VIA IMMUNOMODULATORY EFFECT ON T LYMPHOCYTES

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Background: Rheumatoid arthritis (RA) is an autoimmune disease that results in cartilage and bone destruction. Overactivation of T lymphocytes and imbalance of T helper (Th1/Th2) are critical factors that contribute to the occurrence and development of RA. These have become important mechanisms of inflammation, immune activation, and bone destruction. RA treatment ideally involves regulation of immune abnormalities and maintenance of immune homeostasis. Mesenchymal stem cells (MSCs) are multipotent adult stem cells with high proliferation, multi-differentiation, and immune regulation. They exert immunoregulatory effects on T lymphocytes to improve RA symptoms, inhibit synovial hyperplasia, and reduce cartilage and bone erosion. However, the specific molecular mechanisms have not been fully elucidated.

Objectives: To investigate the effect of human umbilical cord mesenchymal stem cells (hUCMSCs) on collagen-induced arthritis (CIA) in rats in comparison with that of methotrexate (MTX), a classical drug for RA. It evaluated T lymphocyte proliferation, apoptosis, differentiation, and associated inflammatory factors, and further explored the regulatory mechanism of T lymphocyte differentiation at the gene transcription level. This study elucidated that hUCMSCs play an immunoregulatory role in T lymphocytes of CIA rats through multiple pathways and explored the possible mechanism of hUCMSCs in RA treatment via the immunomodulated T lymphocyte pathway.

Methods: The effects of hUCMSCs on arthritis, radiological and synovial pathological changes in CIA rats were assessed. Flow cytometry was conducted to detect T lymphocyte proliferation, apoptosis, the ratio of Th17 and Treg cells in the spleen, and IL-17 and TGF-β levels in the sera from CIA rats. Further, Foxp3 and ROR-γT expression in the spleen were assessed by immunohistochemistry, Fqox3mRNA and ROR-γTmRNA expression were assessed by reverse transcription-polymerase chain reaction (RT-PCR).

Results: HUCMSCs inhibited proliferation and promoted apoptosis of T lymphocytes, up-regulated Foxp3 mRNA and protein expression, increased the proportion of Treg cells, down-regulated ROR-γT mRNA and protein expression, and decreased the proportion of Th17 cells in the spleens of CIA rats. Correction of the Foxp3/ROR-γT imbalance to regulate the Threg/Th17 ratio, promoted anti-inflammatory factors, TGF-β expression and inhibited pro-inflammatory factor IL-17 expression, thereby improving arthritis in CIA rats, delaying radiological progression, and inhibiting synovial hyperplasia. This effect was similar to that of MTX.

Conclusion: HUCMSCs exert immunomodulatory effects on T lymphocytes in CIA rats through many pathways and are expected to become a new immunomodulatory therapy for RA.

REFERENCES


ANALYSIS OF INTESTINAL MICROBIOME PROFILE OF PATIENTS WITH ESTABLISHED RHEUMATOID ARTHRITIS AND HEALTHY CONTROLS

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Objectives: Describe the intestinal microbiome profile in RA patients and analyze the mechanisms through which intervenes in the pathogenesis RA.

Methods: Design: Controlled, observational, cross-sectional study of established RA cohort. Patients: Forty consecutive RA patients (ACR/EULAR 2010 criteria) >16 years, selected from a prospective inception cohort (2007-2011) and 40 age-sex matched healthy controls. Protocol: Cases and controls were evaluated by a rheumatologist. Clinical data of disease activity were collected during the follow-up and analytical values were determined. Fecal samples were frozen within 24 hours of collection. Main outcome: Fecal samples exam. Microbial DNA was extracted from fecal samples using QIAamp DNA stool Mini Kit. The concentration and quality of DNA was determined by Nanodrop. Secondary Other variables: Demographic, clinical-analytical and therapies (DMARDs), Statistical analysis: Analysis of microbiota profile: Principle Coordinate Analysis (PCoA), was performed with the abundance data of operational taxonomic units (OTU) by means of the variancovance matrix implemented in Quantitative Insights Into Microbial Ecology (QIME). The relative abundance of each OTU (taxa) was compared using a Wilcoxon test. The variations of abundance and diversity were compared by ANOSIM pathway. The calculation of α and β-diversity was carried out using QIME.

Results: Most of subjects were women (75%) (table). In RA patients, the average DAS28 was 3.6. β-diversity data showed that patients tend to differ from healthy subjects according to their microbiota (p < 0.07). Patients with RA exhibited decreased gut microbiome diversity compared with controls, although it was not statistically significant. Regarding species richness, the analysis suggested an increase of the Collinsella aerofaciens species and enterococcus genera in patients compared with controls. Likewise, an increase of arginine deaminase activity was observed, which belonged, in approximately 90%, to the RA genes of the genus Collinsella. The multivariate analysis identified ACPA positive (95% CI), 0.33 [27.4-390], smoking (0.3 [8.8-256.4]) and age (-0.3 [27.4-390.0]) as factors associated with Collinsella. Also, we observed a decrease in other bacterial lineages. On the other hand, RA patients showed a altered metabolic capacity for the transport of zinc and copper.

Conclusion: These observations suggest a dysbiosis in RA patients, resulting from a abundance of certain bacteria (i.e Collinsella) and decrease of other bacterial lineages. These alterations could influence in a significant way in the perpetuation of the autoimmunity of the disease.
Introduction of Details: Natalia Mena-Vázquez: None declared, Patricia Ruiz-Limon: None declared, Isabel Moreno-Indias: None declared, Sara Mariniqe Aria Skeleus bureau: ABBiVie, MSD, Janssen, Lilly, Roche, Pfizer, Novartis., Francisco Jose Tinahones: None declared, Antonio Fernandez-Nebro: None declared

Disclosure of Interests: Natalia Mena-Vázquez: None declared, Patricia Ruiz-Limon: None declared, Isabel Moreno-Indias: None declared, Sara Mariniqe Aria Skeleus bureau: ABBiVie, MSD, Janssen, Lilly, Roche, Pfizer, Novartis., Francisco Jose Tinahones: None declared, Antonio Fernandez-Nebro: None declared

Disclosure of Interests: None declared

Disclosure of Interests: Jordania Miranda de Souza Silva: None declared, Rafaela Cavalheiro do Espírito Santo: None declared, Deborah Negoro Gonçalo Dias: None declared, Nayara Felicidade Thomas Braz: None declared, Érica Leandro Marciano Vieira: None declared, Eduarda Freitas: None declared, Rafaela Mendonça da Silva Chakr: None declared, Adriana Maria Kakehasi: None declared, Ricardo Xavier Consultant for: Abbvie, Pfizer, Novartis., Janssen, Lilly, Roche


AB0136 LEVELS OF MYOKINES AND RADIOGRAPHIC PROGRESSION IN PATIENTS WITH RHETUMATOID ARTHRITIS
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Background: Myokines, such as irisin and myostatin, are cytokines and growth factors mainly expressed in skeletal muscle, which is also their primary target tissue. They are released into circulation and exert a variety of systemic effects promoting crossstalk among different tissues [1]. Irisin is known to retrieve disuse-induced bone loss by stimulating the osteoblast pathways, while myostatin was demonstrated to be highly expressed in the synovial tissues of rheumatoid arthritis (RA) subjects, with direct role in osteoarthritisogenesis [2, 3].

Objectives: To investigate whether myokines serum levels can predict one-year radiographic progression in patients with RA.

Methods: Forty female patients with RA, according to ACR/EULAR 2010 classification criteria, were included in the study. Blood samples were collected, and ELISA was used to measure serum levels of irisin and myostatin. Radiographs of hands and feet, taken within three months of the blood collection and a year later, were evaluated using the Sharp-van der Heijde (SvH) score to verify the one-year radiographic progression. The RA activity was assessed by disease activity score (DAS28-ESR) based on evaluation of 28 joints (DAS28-ESR). Statistical analysis included Mann-Whitney U test and Spearman correlation. A value of p<0.05 was considered significant.

Results: The mean age of RA patients was 53 years old, mean DAS28-ESR was 4.09, mean disease duration was 11.2 years and mean BMI was 27.33 kg/m2. The mean serum levels of irisin and myostatin were respectively 25.61 ± 8.25 ng/ml and 3011.28 ± 1271.11 pg/ml. Considering radiographic progression, the mean values of SvH score were 28.3 and 31.3 in the baseline and after one year, respectively, resulting in a mean ΔSvH of 3. Over one year, 89.2% of the patients demonstrated significant increase in SvH of 3. Over one year, 89.2% of the patients demonstrated significant increase in SvH of 3.

Conclusion: The serum levels of irisin and myostatin were not correlated with one-year radiographic progression. There was a tendency of increased myostatin levels in patients with rapid progression compared to patients with no progression. More studies are needed to investigate whether the myokine levels in the joint environment differ from the circulating concentration.

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AB0137 ROLE OF VIMENTIN AS A TARGET OF ANTI-BODIES AGAINST CARBAMYLATED PROTEINS IN RHETUMATOID ARTHRITIS PATIENTS
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Background: Patients with Rheumatoid Arthritis (RA) have an increased risk of cardiovascular diseases (CVD). Inflammation and autoantibodies independently promote endothelial dysfunction, which is the earliest, reversible stage of atherosclerosis. In vitro studies have demonstrated that antibodies against carbamylated proteins (anti-CarP), recently described in RA patients, can induce the production of proatherosclerotic molecules like Vascular Cell Adhesion Molecule (VCAM-1) and activate Interleukin-1 Receptor-Associated Kinase (IRA-K1), Nuclear Factor KB (NF-KB), inducible Nitric Oxide Synthase (iNOS) in endothelial cells (1,2). Moreover, anti-CarP are associated to endothelial dysfunction and subclinical atherosclerosis in RA patients (3).

Objectives: Aims of the present study were: 1) to analyze the role of vimentin as a target of autoantibody response in the serum of patients with RA and 2) to investigate the expression of vimentin and carbamylated proteins in endothelial cells.

Methods: Consecutive RA patients enrolled in this study. Vimentin was carbamylated and used as an antigen for the detection of anti-Vimentin Carbamylated antibodies (CarVim), through immunoenzymatic methods. Cells were incubated with anti-vimentin and carbamylated antibodies. The presence of vimentin and carbamylated proteins was investigated by immunofluorescence on the immortalized endothelial cell line EA.hy 926.

Results: Eighty-eight (88) RA patients were enrolled in this study (F/M = 79:9, mean age = 56 ± 13 years). Anti-CarVim antibodies were present in 9% of the patients with a mean titre of 442 aU/mL (IQR 303 aU/ml). Vimentin and carbamylated proteins were detected in the endothelial cells by immunofluorescence (Figure 1).


AB0138 EVALUATION OF ANALGESIC ACTIVITY OF ALLOPURINOL AND FEBUXOSTAT IN EXPERIMENTAL ANALGESIC MODELS IN MICE
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Background: Allopurinol and febuxostat are xanthine oxidase inhibitor which are used in the treatment of hyperuricemia and gout. Pain is one of the important symptoms in gout patients.

Objectives: The present study is to evaluate the analgesic activity of allopurinol and febuxostat in two analgesic models in mice.

Methods: The analgesic activity of allopurinol (38 mg/kg) and febuxostat (15.6 mg/kg) was evaluated by using central analgesic model of Eddy’s hot plate and peripheral analgesic model of acetic acid induced writhing. Both drugs were compared with the positive control, piroxicam for hot plate model & aspirin for the Writhing method. Also both allopurinol and febuxostat were compared with each other.

Results: Both allopurinol and febuxostat showed significant increase in reaction time at various time periods in hot plate model & also showed significant delay in onset of writhing as well as decrease in number of writhes in writhing method. As compared to positive control result allopurinol and febuxostat result were lower. Febuxostat shows better analgesic activity as compared to that of allopurinol.

Conclusion: Allopurinol and febuxostat exhibited analgesic activity in both central and peripheral models of pain.

Disclosure of Interests: None declared

Conclusion: The results of this study confirm that Vimentin is one of the antigenic targets of anti-CarP antibodies present in the serum of RA patients. The presence of carbamylated proteins and vimentin in endothelial cells suggests that anti-CarP Vim could bind the modified protein and determine endothelial activation and subsequent endothelial dysfunction.

REFERENCE


REFERENCES


Disclosure of Interests: None declared

ABO138

INDIVIDUALS WITH ACPA POSITIVE RA PRESENTING INITIALLY WITH PALINDROMIC SYMPTOMS ARE SIGNIFICANTLY LESS LIKELY TO BE RHEUMATOID FACTOR POSITIVE THAN CLASSICAL ACPA POSITIVE RA: COULD THE AETIOPATHOGENESIS DIFFER BETWEEN THESE TWO DISTINCT TYPES OF ACPA POSITIVE RA?

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Background: It remains unclear whether ACPA positive RA presenting initially with palindromic symptoms (PRA) has the same underlying pathophysiology as ACPA positive RA presenting without palindromic symptoms (classical ACPA positive RA). The lung is an initiating site in RA development and rheumatoid factor (RF) is generated within bronchial associated lung tissue (1). RF in combination with ACPA immune complexes can induce TNF– from joint macrophages and potentially induce synovitis (2). Unsurprisingly a positive RF is a risk factor for RA development. Alternatively, palindromic rheumatism in the absence of RA occurs commonly in RF negative individuals (58%) (3). Therefore this form of explosive synovitis often occurs independently of RF, but is commonly associated with ACPA positivity (56%) (3).

Objectives: To identify whether classical ACPA positive RA differs in terms of RF positivity compared to ACPA positive PRA.

Methods: A retrospective case note observational study was undertaken to identify ACPA positive RA patients with or without a palindromic onset. All patients fulfilled the RA 2010 EULAR/ACR classification criteria (4). Patients were stratified for a history of smoking. RF was measured with Tina-quant Rheumatoid Factors II Test System, by Roche Diagnostics Corporation at the time of diagnosis. A value of < 14 IU/ml was considered as negative, weakly positive (14-42 IU/ml) and strongly positive (>42 IU/ml) as per EULAR/ACR guidelines (4).

Results: 99 classical ACPA positive RA and 35 ACPA positive PRA were identified. The median RF for PRA was significantly lower than the non-RF onset RA group (25 vs 86 IU/ml, p = 0.001). Comparing classical ACPA positive RA with ACPA positive PRA revealed 8/99 (8%) vs. 8/35 (23%) to be RF negative, 23/99 (23%) vs. 11/35 (31%) to be RF weakly positive and 68/99 (69%) vs. 16/35 (46%) to be strongly RF positive. Classical ACPA RA patients were significantly less likely to be RF negative, odds ratio 0.25 (95%CI 0.09–0.73), P<0.01. RA patients were significantly more likely to be strongly RF positive OR 4.32 (1.88–9.89), P<0.0005.

Conclusions: The majority of ACPA RA patients presenting with palindromic symptoms have either a negative or weakly positive RF (54%). This contrasts with classical ACPA RA (31%) and suggests that a strongly positive RF is more important in the pathogenesis of classical ACPA RA than ACPA PRA. We suggest that a strongly positive RF and palindromic rheumatism is likely to be independent risk factors for ACPA positive RA.

Disclosure of Interests: None declared

ABO140

EFFECT OF THE CO-TREATMENT WITH BACTERICIDAL/PERMEABILITY-INCREASING PROTEIN AND HYALURONIC ACID IN AN IN VIVO MODEL OF ARTHRITIS

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Background: Bacterial/permeability-increasing protein (BPI) is an antibacterial, anti-inflammatory and antiangiogenic glycoprotein which has been detected in synovial fluid of patients with differing arthritis [1].

Objectives: To investigate the effect of BPI alone or in combination with hyaluronic acid (HA) in a mouse model of collagen-induced arthritis (CIA).

Methods: CIA was induced in C57Bl/6 mice (n=12 per condition) by immunization with type II collagen/complete Freund’s adjuvant emulsion at days 0 and 21 [2]. Development and severity of arthritis were monitored by measuring paw swelling with a caliper and scored (0-5) every 2 days. Articular mice (paw score=2) were intraperitoneally injected with 200 μl of BPI (50 μg/ml) in PBS in the presence or absence of HA (0.02%). Treatment and arthritis evaluation were carried out twice a week for 2 months. Untreated mice or animals that received HA alone (0.02%) were used as controls. At the experiment endpoints, mice were sacrificed to collect paw and blood samples. Hind paws were processed for histological analysis to assess inflammation, pannus formation, cartilage damage and bone resorption in ankle joints (score 0-5). CXCL1, TNF, IL-6, IL-1β and VEGF serum levels were determined by ELISA.

Results: All mice reached an arthritis score of 2 after 28-33 days and showed a progressive worsening of clinical signs that picked at day 49-56, and continued during the entire follow-up period only in control groups. At the end of the experiment, hind paw swelling and scores were lower in BPI-mice (paw thickness=4.76 ±0.33 mm; score=4.5±0.5) than in untreated mice (paw thickness=6.39±0.95 mm; score=5). Histological analysis revealed leukocyte infiltration (score 3.00±1.73), synovial proliferation (score 3.50±0.71), cartilage damage (score 2.50±0.71) and mild bone resorption (score 1.50±1.71) in ankle joints of untreated controls. All of these histological changes were decreased (50-80%) in the group that received BPI. CIA induction led to high levels of CXCL1 (834.08±68.8 pg/ml), TNF (277.72±15.24 pg/ml), IL-6 (376.04±46.33 pg/ml), IL-1β (656.80±45.6 pg/ml), and VEGF (347.48±75.58 pg/ml) which were reduced with BPI treatment by 1.9, 14.6, 1.8, 2.9 and 2.7 fold, respectively. Animals injected with HA alone displayed slight improvement of all parameters evaluated but the differences were not significant. The combined use of BPI and HA showed paw swelling (3.65±0.37 mm), arthritis score (0.67±0.75) and histological scores for pannus formation (0.4±0.55), inflammation (0.20±0.45), cartilage damage (0.0±0.0) more remarkably reduced than their separate use. In addition, the lowest levels of CXCL1 (11.44±1.31 pg/ml), TNF (4.46±2.23 pg/ml), IL-6 (129.30±14.25 pg/ml), IL-1β (81.58±17.64 pg/ml), and VEGF (107.80±32.64 pg/ml) were observed in serum of mice co-injected with BPI and HA.

Conclusion: This study shows that BPI attenuates progression of CIA in mice, and this effect is greatly enhanced by co-administration of HA. The combined use of BPI and HA represents an interesting perspective for a new potential intervention in the treatment of arthritis.

Disclosure of Interests: None declared


Disclosure of Interests: None declared
AB0141 THE ROLE OF AIR POLLUTION ON EXTRACELLULAR VESICLES AS A POTENTIAL PRO-INFLAMMATORY STIMULUS IN RHEUMATOID ARTHRITIS
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Background: Rheumatoid arthritis (RA) is an heterogeneous chronic autoimmune disorder potentially leading to a progressive joint damage with great impact on quality of life. RA pathogenesis is complex and involves environmental factors that contribute to the disease in genetically susceptible individuals. Extracellular vesicles (EVs) have been described to play an important role in RA pathogenesis and to modulate autoimmune response following environmental exposures, such as air pollution.

Objectives: Our aim was to evaluate the effects of particulate matter (PM) with aerodynamic diameter ≤10 μm (PM_{10}) and ≤2.5 μm (PM_{2.5}) on EVs in RA and osteoarthritis (OA) as control.

Methods: Plasma EVs were analyzed by Nanosight and flow cytometry: CD14 (monocyte/macrophage), CD61 (platelet), CD25 (T-reg), human endogenous retrovirus w (HERV-w), human leukocyte antigen G (HLA-G). Demographic and clinical data were collected for each patient. Plasma EV concentrations were measured in RA and OA patients and were analyzed by generalized linear regression models. Daily PM concentrations, estimated by Regional Environmental Protection Agency, at municipality resolution, were used to assign short-term exposure (mean of the 7 days preceding the evaluation) to each patient.

Results: 12 consecutive patients with RA (median age 68.1, median disease duration 9.3, 12 female, median DAS28 2.25, 5 positive for anti-citrullinated peptide antibodies) and 12 patients with OA (median age 67.1, median disease duration 9.3, 8 female) were enrolled. Analysis of EVs concentration, according to their dimensions, showed a negative association of exosomes (63-92nm) in RA compared to OA (p<0.05). The increase of PM{sub}2.5 led to a decrease of CD14+ microvesicles (MV) (β=−0.13; p<0.01) and CD25+ (β=−0.08; p<0.05) in RA, and of HERV-w in OA (β=−0.09; p<0.01). Similar results were observed analyzing PM{sub}10 exposure. PM exposure was not observed to modify CD61+ and HLA-G+ MV release both in RA and OA patients (table below). More-over, we compared plasmatic EVs median concentration among patients with RA and OA, and we found a significant difference in the two groups in the HERV-w subpopulations (BRM vs BOX = 0.044 ± 0.091; p = 0.011). In RA patients we also observed a significant association between EVs (CD14+ and HLA-G+ MV) and DAS28 (β=0.13, p<0.03; p=0.04) in RA, and of HERV-w in OA (β=0.09; p=0.01). Similar results were also observed analyzing PM{sub}10 exposure. PM exposure was not observed to modify CD25+ and HLA-G+ MV release both in RA and OA patients (table below). Moreover, we observed a negative association between exosomes and C-reactive protein (CRP) (BRM vs BOX = 0.044 ± 0.091; p = 0.011). In RA patients we also observed a significant association between EVs (CD14+ and HLA-G+ MV) and DAS28 (β=0.13, p<0.03; p=0.04) in RA, and of HERV-w in OA (β=0.09; p=0.01). Similar results were observed analyzing PM{sub}10 exposure. PM exposure was not observed to modify CD25+ and HLA-G+ MV release both in RA and OA patients (table below).

EV count

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<tr>
<th>EV count</th>
<th>β</th>
<th>SE</th>
<th>p-value</th>
<th>β</th>
<th>SE</th>
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<tr>
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<tr>
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<td>-0.02</td>
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Conclusion: The results of this pilot study show that PM exposure modulates the release of EVs carrying HLA-G and/or HERV-w in RA patients. This might be interpreted as an attempt of immune system to counteract the perturbation provoked by a pro-inflammatory environmental stimulus. More research is still needed to tie the genetic, epigenetic and environmental factors together and to determine their role in RA pathogenesis.


AB0142 IMMUNOREGULATORY ROLES OF B2 INTEGRINS IN RHEUMATOID ARTHRITIS
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Background: Evidence is mounting that β2 integrin expression, activation or function in DCs may contribute to the immune dysregulation prevalent in autoimmune disorders such as Rheumatoid Arthritis (RA). To this end, we aimed to characterise β2 integrin expression and activation in antigen-presenting cell (APC) populations from people with RA compared to healthy controls.

Methods: Using flow cytometry, we can detect both total and activated β2 integrin subunits (CD11a, CD11b, CD18) on different APC populations present in human blood and synovial fluid.

Results: Based on our results so far, we found CD11b expression to be equivalent in APC populations between patients with RA and healthy controls. However, expression of both the total and active forms of CD11a was reduced across several APC populations in RA patients compared to healthy controls, with CD2c2 (CD1c+) showing the most striking reduction. Interestingly, we found that CD2c2 from matched RA synovial fluid samples express even lower levels of CD11a than blood CD2c2. Previous studies show that CD2c2s are the DC population primarily involved in the site of inflammation and activate self-reactive T cells2. As CD11a is described to have largely pro-inflammatory effects by contributing to immune cell contacts and recruitment to inflammatory sites, this could suggest that contrary to our initial hypothesis, cells downregulate CD11a as a means of limiting the aberrant inflammation present in the disease.

Furthermore, CD2c2s from RA patients in remission express lower levels of active CD11a compared to those from patients with high disease activity. Upon stimulation with CD2c2s with PMA, cells from patients with active disease decrease their activation of CD11a, while neither healthy controls nor patients in remission show any change in CD11a activation. This might suggest that CD11a activation is differentially regulated in patients with active disease, while remission signifies a return to a state of normal CD11a regulation on CD2c2s. In additional work on exploring monocyte-derived DCs (Mo-DCs) as a potential therapeutic for RA, we did not detect a reduction in CD11a expression in activated Mo-DCs, suggesting that the effect may be specific to settings of chronic inflammation that cannot be easily modelled in vitro.

Conclusion: Further interrogation of our integrin expression data, including disease stratification, together with functional studies on RA patient CD2c2s compared to Mo-DCs, is currently under way to fully investigate the role of this immunoregulatory pathway in autoimmune disorders. In doing so, we will explore β2 integrin subunits and signalling pathways as potential therapeutic targets in RA.

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Disclosure of Interests: Leonie Schittenhelm: None declared, Jamie Robertson: None declared, Arthur Pratt Grant/research support from: Dr. Pratt is in receipt of an externally peer-reviewed Investigator Initiated Research grant from Pfizer ($66,000.), Grant/research support from: Dr. Pratt is in receipt of an externally peer-reviewed Investigator Initiated Research grant from Pfizer ($66,000.), Speakers bureau: Dr. Pratt has received honoraria from Eli Lilly and Janssen-Cilag Ltd. for his time in preparing presentations for non-promotional meetings that have been paid directly to Newcastle University., Researchers bureau: Dr. Pratt has received honoraria from Eli Lilly and Janssen-Cilag Ltd. for his time in preparing presentations for non-promotional meetings that have been paid directly to Newcastle University, Arthritis Research UK: None declared, Vicky L. Morrison: None declared. DOI: 10.1136/annrheumdis-2019-eular.5465
AB0143 PERIODONTITIS AND SALIVA ANTIBODIES TO CITRULLINATED PEPTIDES IN RHEUMATOID ARTHRITIS

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Background: Mucosal immunity, involving antibodies against citrullinated peptides (ACPAs), is a prevailing hypothesis concerning the pathogenesis of rheumatoid arthritis (RA). The oral mucosa is a possible site that is involved. Several epidemiological studies have found an association between RA and periodontitis, and periodontal inflammation has been suggested as a possible pathogenic factor.

In established RA, periodontitis has been associated with ACPA positivity (1) although a recent large study (2) did not find any association between periodontitis and IgG ACPA. Previous studies only evaluate ACPA in serum, and as local mucosal immune responses are likely involved in periodontitis, saliva antibodies are of interest to investigate. Saliva IgA ACPA has in a pilot study of RA patients been associated with lower disease activity and less erosions (3), but has not previously been evaluated in relation to periodontitis.

Objectives: To evaluate if saliva or serum ACPA is associated to periodontitis, in patients with RA.

Methods: In this population-based cohort of patients with RA (n=132), we included all patients with RA older than 61 years, living in Karlskrona in southern Sweden, between October 21, 2013 and January 7, 2015.

The patients underwent a clinical examination by a rheumatologist, a dental clinical examination by a dental nurse and a panorama radiograph of the jaws and teeth. Periodontitis was defined as a distance from the cement-enamel junction (CEJ) to the bone level ≥ 5 mm, as defined by the radiographic assessment, at ≥ 30% of interproximal sites.

We analysed antibodies against second generation cyclic citrullinated peptides (anti-CCP) in enzyme immunoassays in serum and saliva. Saliva samples were analysed in parallel for anti-CCP and anti-CAP, the arginine containing control peptide. Serum ACPA positivity was defined as the 99th percentile of healthy controls. In saliva, a positive test was defined as a difference in optical density (OD) for IgA anti-CCP and IgA anti-CAP (delta OD)> 0.

Results: Saliva IgA ACPA was found in 11% of RA patients with periodontitis and in 24% of RA patients with no periodontitis (p=0.052). There was no difference between the groups concerning IgG or IgA ACPA in serum.

Conclusion: Periodontitis leads to increased formation of IgA ACPA in saliva or serum. Although a recent large study (2) did not find any association between periodontitis and ACPA positivity in serum, our findings do not support the hypothesis that periodontitis leads to increased formation of IgA ACPA in saliva or serum.

REFERENCES


AB0144 EFFECTS OF AB501 (CERTOLIZUMAB MICE EQUIVALENT) IN ARTHRITIS INDUCED BONE LOSS

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Background: Rheumatoid arthritis (RA) is a chronic immune-mediated inflammatory disease, which causes local and systemic bone damage.

Objectives: The main goal of this work was to analyze, how treatment intervention with Ab501 (certolizumab mice equivalent) prevents the disturbances on bone structure and mechanics induced by arthritis.

Methods: Thirty one DBA/1 collagen-induced arthritis (CIA) mice were randomly housed in experimental groups, as follows: arthritis untreated (N=10), preventive intervention with ab501 2 days before arthritis induction (N=10) and treatment intervention upon arthritis onset with ab501 (N=11). A non-induced group (N=5) was used as a control. Mice were monitored during 70 days after disease induction for the inflammatory score, ankle perimeter and body weight. Non-induced mice were used as controls. After 70 days of disease, mice were sacrificed and bone samples were collected for histology, micro-computed tomography (μCT) and 3-point bending analysis. In addition, blood samples were also collected for bone turnover markers quantification. Statistical differences were determined with Mann–Whitney tests using GraphPad Prism (GraphPad, California, USA). Data were expressed as median with interquartile range. Differences were considered statistically significant for p<0.05.

Results: Results showed that Ab501 administration was able to control and abrogate disease development both in preventive and early therapeutic intervention.

μCT results revealed that ab501 was able to preserve bone structure when delivered before arthritis induction. Conclusion: Ab501 preventative administration was able to control inflammation and prevent the degenerative effects of arthritis on trabecular bone structure.

Acknowledgement: This work was supported by UCB in the context of an Investigator Initiated Study where UCB provided financial and product support.


AB0145 THE INHIBITION OF JAK PATHWAY WAS ASSOCIATED WITH REDUCTION OF AUTOFLUHY IN SYNVOYOCITES FROM RHEUMATOID ARTHRITIS PATIENTS

Matís Vorms1, Matía Caliste1, Cristina Barbatí1, Tanis Colesanti1, Francesca Spirelli1, Fulvia Cecarelli2, Carla Perricone1, Annarcaia Finucì1, Mariangela Speziali1, Alessandra Ida Celia1, Michele Bombardieri2, Fabrizio Conti1, Guido Valesini1, Cristiano Alessandri1, 1Unidade de Investigação em Reumatología, Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa, Centro Académico de Medicina de Lisboa, Lisboa, Portugal; 2Research Unit of Medical Imaging, Physics and Technology, Faculty of Medicine, University of Oulu, Oulu, Finland; 3Sapienza University of Rome, Internal Medicine and Medical Specialties, Rome, Italy; 4Queen Mary University of London, London, United Kingdom

Background: The pathway of Janus tyrosine kinases (JAKs) has a central role in the pathogenesis of rheumatoid arthritis (RA) by regulating multiple immune functions and cytokine production. The orally available JAK inhibitor CP-690,550, named tofacitinib, is able to inhibit Jak1, Jak2 and Jak3 and it showed a great clinical efficacy in RA patients not responding to methotrexate or TNF-inhibitors (1). Autoaphagy, a highly conserved mechanism involved in the degradation of intracellular components, was found to be dysregulated in several autoimmune diseases including RA (2). In fact, fibroblasts like synoviocytes (FLS) from RA patients showed a resistance to apoptosis associated with the induction of autophagy (3). Maeshima and colleagues recently demonstrated that tofacitinib suppressed proliferation, but not apoptosis, of CD4+ T cells derived from the synovium (4), but to date there are no data on the effect of inhibition of JAK pathway on autoaphagy.

Objectives: Since hyperactive autoaphagy has been associated with impaired apoptosis of RA FLS, the aim of the study was to investigate the role of tofacitinib in modulating autoaphagy and apoptosis in FLS from RA patients.

Methods: Primary RA FLS isolated from RA biopsies (Figure 1A) were cultured in presence of autoaphagy inducer rapamycin (as control condition) and tofacitinib (1µM). After 24h of culture, autoaphagy was evaluated both by flow cytometry and...
western blot analysis. Apoptosis was analyzing by annexin V (AV) and propidium iodide (PI) apoptosis detection kit by flow cytometry.

Results: As expected tofacitinib inhibited the expression of the phosphorylated form of STAT3 (p<0.01). Rapamycin caused an increase in autophagy, while the levels of autophagy marker LC3-II were reduced after treatment with tofacitinib in vitro (p<0.001 and p<0.02, respectively, Figure 1B). In addition, the analysis of autophagic vacuoles by specific fluorescence dye confirmed the reduction of autophagy in RA-FLS treated with tofacitinib. The percentage of annexin V-positive apoptotic cells was not influenced by the treatment with tofacitinib.

Conclusion: The results of this study elucidated a new mechanism of action of tofacitinib related to autophagy modulation and led to a better understanding of the role of autophagy in RA. This study was supported by an unconditioned Research grant from Pfizer Inc.

REFERENCES

Disclosure of Interests: Marta Vomero: None declared, Mattia Caliste : None declared, cristiana barbati: None declared, Tania Colasanti: None declared, francesca spinelli: None declared, Fulvia Ceccarelli: None declared, Carlo Perricone Speakers bureau: BMS; Lilly, Celgene, Sanofi, Annacarla Finucci: None declared, Mariangela Speziali: None declared, Alessandra Ida Celia: None declared, Michele Bombardieri Grant/research support from: Celgene, Consultant for: Mediimmune, fabricio conti: None declared, Guido Valesini: None declared, cristiano alessandri: None declared DOI: 10.1136/annrheumdis-2019-eular.5445

AB0147 RESEARCH PROGRESS OF MESENCHYMAL STEM CELL-DERIVEDMICROVESICLES BY DELIVERING MICRONA IN RHEUMATIC DISEASES

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Background: Recently, studies have shown that Mesenchymal Stem Cell-Derived Microvesicles (MSC-MVs) can play a role in immune regulation and tissue repair by transporting miRNAs, and their effects are not weaker than that of their mother stem cells. Rheumatoid arthritis is an autoimmune disease characterized by chronic synovitis and progressive cartilage and bone destruction. Current treatments include non-steroidal anti-inflammatory drugs, glucocorticoids, DMARDs, and biological agents. But 30% of patients with rheumatism are ineffective, so there is an urgent need to find a new treatment.

Objectives: To review the research progress of MSC-MVs by delivering microRNA(miRNA) in rheumatic diseases.

Methods: Literatures were searched by using MSC-MVs, autoimmune diseases and miRNA as keywords.

Results: In the field of rheumatology, Chen C showed that after MSCT transplantation, miR-151-5p was transferred through exosomes to damaged bone marrow MSC of systemic sclerosis(SSc) mice, and the activation of IL4/IL10R pathway was down-regulated to improve the osteoporosis of SSc mice [1].Exosomes of human synovial mesenchymal stem cells overexpressing miR-140-5p promoted cartilage regeneration and prevented OA in rat models [2].In the field of autoimmune diseases, Chen L et al. demonstrated that BMSC-derived exosomes containing miR-223 play a important role in liver protection by down-regulating NLRP3 (nod-like receptor family protein) and caspase-1 (caspase-1) in the experimental model of autoimmune hepatitis [3].Human BMSC-derived exosomes transfected with sIgAs and anti-miR-375 plasmids down-regulated Fas and miR-375 in human NOD scid gamma (NSG) mice, thereby protecting islet function and inhibiting immune rejection in islet transplantation [4].

Conclusion: MiRNA targeting therapy with MSC-MVs as vector or the construction of MSC-MVs with overexpression of protective miRNA will provide new, accurate and promising treatment strategies for multiple rheumatic diseases.

REFERENCES
OSTEOBLASTS SECRETE A HIGH LEVEL OF BROMODOMAIN INHIBITOR, I-BET762 INHIBITS PGE2, OCs were not induced. OC precursor cells did not seem to even survive.

Background:
Osteoclasts (OCs) are multinucleated cells of monocyte/macrophage lineage and are the only cells known to resorb bone matrix. Osteoblasts (OBs) have the ability to differentiate bone marrow cells (BMCs) into osteoclasts when co-cultured with BMCs in the presence of Vitamin D3 (1,25(OH)2D3) and prostaglandin E2 (PGE2). OBs produce both M-CSF, a survival factor for OC precursor cells, and RANKL, a differentiation factor. In rheumatoid arthritis (RA), synoviocytes may fulfill the functional role of OBs, since OBs are not observed in the synovium of the joints. Although human BMCs are difficult to obtain, mouse BMCs are known to respond to human M-CSF and RANKL, and differentiate into OCs in the presence of both cytokines.

Objectives: Our aim was to examine whether a co-culture system of human synoviocytes and mouse BMCs might be developed. Through this analysis, we attempted to clarify the characteristics of synoviocytes in the pathogenesis of bone destruction observed in RA.

Methods: Human synoviocytes were prepared from synovium obtained in the course of joint replacement surgical operations performed at Saitama Medical University Hospital. Written informed consent, approved by the ethics committee of the hospital, was obtained from each patient prior to the experiment. Mouse BMCs were obtained from the calvaria of newborn C57BL/6 mice. Mouse BMCs were co-cultured with either synoviocytes or OBs. OCs were detected by tartrate-resistant acid phosphatase (TRAP) staining. The concentrations of M-CSF, RANKL and the decoy receptor for RANKL, OPG, were quantified by ELISA in the culture supernatant of synoviocytes or OBs.

Results: When synoviocytes and BMCs were cultured with 1,25(OH)2D3 and PGE2, OCs were not induced. OC precursor cells did not seem to even survive. Next, we added human M-CSF to the system. This time, OC precursor cells remained, but TRAP-positive multinuclear cells were not observed. It was only in the presence of exogenous M-CSF and RANKL that BMCs transformed into OCs. RANKL was not detected in the culture supernatant of synoviocyte culture, but OPG and M-CSF were detectable at a level comparable to mouse OBs. Finally, we cultured mouse OBs and BMCs that were separated by a poly-carbonate membrane in the presence of 1,25(OH)2D3 and PGE2. In this case, too, BMCs did not survive unless exogenous M-CSF was added, and they did not differentiate into OCs unless both M-CSF and RANKL were added to the system.

Conclusion: These results indicate that the M-CSF derived from OBs or synoviocytes is not sufficient to support the survival of OC precursor cells. Likewise, the soluble RANKL derived from OBs is by itself insufficient for the differentiation of OCs, confirming the importance of a cell-cell interaction between OBs and OC precursor cells. Thus, membrane-bound RANKL seems to play a role more important than soluble RANKL in the co-culture system of OCs in vitro. Soluble RANKL may be neutralized by the OPG that is produced at a fairly high level from both OBs and synoviocytes. We propose that this is the system by which ectopic differentiation of OCs is prevented.

Disclosure of Interests: None declared
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AB0149 ARSENIC TROXIDROPE IMPROVES TREG AND TH17 BALANCE VIA MODULATING STAT3 IN TREATMENT-NAÏVE RA PATIENTS

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Background: We have a long-term interest in novel arsenic trioxide As2O3 (ATO) medical application since some acute promyelocytic leukemia (APL) patients have been cured by first using ATO and survived for more than 45 years successfully treated by Prof. Zhang Tinglong in our institute. Moreover, our previous studies have shown that ATO significantly suppress angiogenesis and induced fibroblast like synoviocytes (FLS) apoptosis in collagen induced arthritis (CIA) model[1, 2]. However, the extract mechanism by which ATO anti-rheumatic and whether this occurs via modulation of immune system are still unclear.

Objectives: To investigated the immunologic mechanism by which ATO may inhibit T helper 17 cells (Th17) differentiation while promote regulatory T cells (Treg) generation via modulating signal transducer and activator transcription 3 (STAT3) in treatment-naive RA patients.

Methods: Naïve CD4+ T cells sorted by fluorescence-activated cell sorting (FACS) from treatment-naive RA patients and healthy controls were used to investigated the effect of ATO on its polarization process and related cytokines. Knockdown or enforced expression of STAT3 transfection experiments were conducted by small interfering RNA (siRNA) and lentivirus STAT3 to verify the mechanism of ATO on Th17/Treg balance in vitro. Collagen-induced arthritis (CIA) model was constructed to detect the clinical score, histopathological change, bone destruction, Th17/Treg proportion and joint tissues immunohistochemistry. Single cell sequencing and other methods have been applied too.

Results: We found that ATO prevented activated naïve CD4+ T-cell differentiates into Th17 cell and reduced cytokine production by activated Th17 cells by downregulating their signature transcription factors, STAT3 and orphan nuclear receptor (RORγt). Notably, ATO reduced Th17 cells frequency while increased Treg cells frequency under specific polarizing conditions from treatment-naïve RA patients by transfecting siRNA STAT3 and lentivirus STAT3. Furthermore, we have noticed that intervention of ATO in CIA model attenuated joint inflammatory infiltration and bone destruction, significantly improved the imbalanced Th17/Treg ratio. In-detail single cell sequencing analysis is ongoing.

Conclusion: ATO may be an immune modulator candidate for treatment-naive RA patients via balancing well Treg/Th17 cell ratio through STAT3 regulation.

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AB0116 BROMODOMAIN INHIBITOR, I-BET762 INHIBITS PRODUCTION OF PRO-INFLAMMATORY MEDIATORS BY DOWN-REGULATING BROMODOMAIN AS AN EPGENETIC READER IN RHEUMATOID ARTHRITIS FIBROBLAST-LIKE SYNOVIOCYTES

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Background: Rheumatoid arthritis (RA) is a chronic autoimmune disorder, characterized by joint inflammation and bone destruction. The fibroblast-like synoviocyte contributes to the pathogenesis of RA through proliferation and production of cytokines. Recently, blockade of the bromodomain and extra-terminal domain
AB0139 ASSOCIATION OF RS17004921 ADORA2A GENE POLYMORPHISM WITH EFFICACY OF MTX TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Adenosine A2A receptors (ADORA2A) are part of the adenosine-mediated antiinflammatory pathway. These receptors are over-expressed in the peripheral blood leukocytes of patients with rheumatoid arthritis (RA). Methotrexate (MTX), the gold standard for therapy, exerts its antiinflammatory effects via increased release of adenosine into the extracellular space. Adenosine binds to ADOR A2 and A3 and initiates an antiinflammatory response. Therefore, ADOR gene polymorphisms could have an impact on MTX therapy outcome.

Objectives: To examine the role of adenosine receptor 2A gene (ADORA2A, rs17004921) polymorphism on outcome of MTX treatment in RA.

Methods: A total of 123 patients with RA (mean age 56.5±10.7; 91 (74%) females), treated with MTX for 6 months (mean dose 12.2±3.20 mg/week) were enrolled in a prospective study. Genotypeisation within ADORA2A gene was performed using the KASP genotyping assays. MTX efficacy assessment was based on the changes in the Disease activity score (DAS28) after 6 months of treatment according to the EULAR response criteria. Patients with good and moderate response were classified as ‘responders’, whereas patients with poor response were considered ‘nonresponders’. Data of adverse effects were collected during this period. MTX efficacy and toxicity were compared among patients with different genotypes. All statistical analyses were performed by SPSS version 16.0.

Results: Median DAS 28 at the beginning of MTX treatment was 7.43±0.89. According to EULAR response criteria, 111 (90.2%) patients with RA were classified as responders. Among all RA patients, 97 (78.9%) had CC, 20 (16.3%) CT and 6 (4.9%) TT genotype. The distribution of ADORA2A genotypes in responders (CC 77.5%, CT 17% and TT 5.4%) was not significantly different from nonresponders (CC 91.7%, CT 8.3%), p>0.05. After 6 months, 26 carriers of T allele (CT +TT) had higher reduction DAS 28 (7.16 vs. 3.88) in comparison to other 97 patients (7.50±4.84, p<0.013). Adverse effects were reported in 24 (19.5%) patients. Most of patients had hepatotoxicity and nausea, 14 (56%) and 9 (37%) respectively. No statistically significant association between ADORA2A genotype and side events has been observed (p>0.05).

Conclusion: According to our results, T allele of ADORA2A rs17004921 polymorphism may have favourable influence on efficacy in RA patients treated with methotrexate.

REFERENCES

AB0150 IMMATURE GRANULOCYTES LEVEL IS A POTENTIAL BIOMARKER IN PERIPHERAL ENTEHISIS

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Background: Immature granulocytes (IG) level in peripheral blood is used as early sign of infection. On the other hand, IG could be elevated in other conditions like inflammatory or cancerous diseases and in pregnancy. Similar to CRP, we have observed a series of cases of peripheral enthesitis associated increased level of IG and correlated with CRP elevation and clinical activity.

Objectives: To test the concept of IG as a biomarker in peripheral enthesitis, this observation might be a reflection to the innate immunity role in pathogenesis of enthesitis.

Methods: We have identified 13 cases over the last 12 months at the Rheumatology clinic in our centre who have shared two features (clinical enthesitis and elevated IG) those 13 cases are mainly presented with recurrent foot and ankle pain and swelling of entheses nature.

Results: The cohort is of equal gender distribution 46/54% respectively and age range 31-53 years (mean age 38.5), only 3 patients are known to have Psoriatic arthritis whilst the rest either undiagnosed or diagnosed Rheumatoid arthritis or gout prior to clinic visit. The rheumatologist clinical diagnoses are of enthesitis of foot, ankle, knee and hip area as shown on the table [1] apart from one patient who has spinal symptoms mainly. 4/13 patients have the history of psoriasis and after their visits we find them fit in the CASPAR criteria for psoriatic arthritis. All these cases are associated with increased absolute number of IG as well as differential (IG) number compare to 10/13 of these cases are having high CRP. The 3 cases with normal CRP do have relatively slight increase in (IG) number. The main correlation is of response to therapy and was seen in 7 cases who have followed up at the time of submission and it shows a 100% correlation between CRP, absolute (IG) and differential (IG) values. There are 3 patients who have elevated (IG) but normal CRP and it would possible indicate (IG) test has a better yield than CRP in peripheral enthesitis.

Conclusion: Immature granulocytes can be elevated in inflammatory disease and more notably in peripheral enthesitis of the lower limbs of inflammatory rather than mechanical nature and do correlate with CRP elevation as well as response to therapy. Larger studies are needed to assess the usefulness and validity of (IG) level in clinical practice.

REFERENCES

Disclosure of Interests: None declared
AB0151 EXPRESSION OF ANXIETY AND DEPRESSION IN PATIENTS WITH ANKYLOSING Spondylitis DEPENDING ON THE STATE OF THE AUTONOMIC NERVOUS SYSTEM AND INTENSITY OF THE PAIN SYNDROME

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Background: Chronic pain syndrome, immanent in the majority of immune-inflammatory processes, is one of the pathophysiological mechanisms of the development of emotional and affective disorders. It has been proven that high levels of “pro-inflammatory” mediators are predictors of depression, and increased anxiety leads to an imbalance in the autonomic nervous system (ANS). It is also known that the pain syndrome worsens the autonomic supply of the organism. However, this problem remains insufficiently studied today.

Objectives: To assess the severity of anxiety and depression in patients with ankylosing spondilitis, depending on the state of the ANS and pain syndrome.

Methods: The study included 75 patients with ankylosing spondylitis (AS), who studied the frequency of anxiety-depressive disorders and their severity on the Spielberger anxiety and Hamilton depression scales. The autonomic state was investigated according to the methods “Wayne-patient” - WP, filled by the patient (more than 15 points - possible autonomic dysfunction (AD)) and “Wayne-doctor” - WD, filled by a doctor (more than 25 points - confirms the presence of signs of AD); we evaluated the indicators of heart rate variability (HRV) - mode (Mo), mode amplitude (Amo), autonomic equilibrium index (AEI), regulatory systems tension index (TI), the standard deviation of the normal RR intervals (SDNN), the square root of the mean squares of the difference between successive RR intervals (RMSSD) and the balance ratio of the activity of the sympathetic and parasympathetic divisions of the ANS (LF/HF). Pain syndrome and the patient's own health index (POH) were assessed by a visual analogue scale (VAS) by patients, and by a physician - by counting the number of painful joints (NPJ), index BASDAI and ASDAS indices.

Results: In 25.3% of patients with AS, a high situational anxiety was observed and in 36% of patients high personal anxiety (PA) was observed. Depressive disorders were found in 57 patients with AS (76%). The severity of pain in the joints and the spine influenced the increase in PA (F = 2.75, p = 0.047; F = 3.54, p = 0.037, respectively) and the level of depressive disorders (F = 3.28, p = 0.03; F = 3.44, p = 0.047, respectively), and the level of depression is also POH (F = 3.49, p = 0.048), 68% patients had an AD (according to WP and WD methods). They constituted the 1st group of observation, and the remaining 24 patients were included in the 2nd group. In group 1, signs of anxiety disorders were identified in 64.3% of cases, and in patients without AD - 45.8% of cases. Depressive disorders were observed in 94% of patients with autonomic disorders (11 cases of psychotic, 37 - non-psychotic depression) and in 37.5% in patients without signs of AD - signs of non-psychotic depression.

In both groups, there was a decrease in SDNN and RMSSD in comparison with normative ones, which indicates an increase in sympathetic regulation. In the 1st group, there was a more significant increase in LF/HF (4.15 ± 0.64) and a decrease in SDNN (22.4 ± 5.6 ms) than in the 2nd (3.0 ± 0.86; 29.1 ± 8.4 ms), which indicates the connection between the strengthening of the sympathetic regulation link and the presence of signs of psycho-emotional disorders. The growth of Amo in the 1st group (47.9 ± 8.4%) reflects the degree of mobilizing influence of the sympathetic division and indicates an increase in the activation of the central contour and the growth of sympathetic regulation in patients with AS and AD.

Conclusion: Patients with AS have a high incidence of clinically significant anxiety and depression, which were affected by the intensity of the pain syndrome. The presence of autonomic imbalance and dysregulation of the sympathetic link of the ANS also contribute to the strengthening of psycho-emotional disorders in this category of patients.

Disclosure of Interests: None declared


AB0153 CLINICAL SIGNIFICANCE OF MONOCYTE TO HEMOGLOBIN RATIO AND PLATELET TO ALBUMIN RATIO IN PATIENTS WITH AXIAL SPONDYLOARTHROPSIS

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Background: Axial spondyloarthropathy (axSpA) is a progressive, chronic, inflammatory skeletal disorder. Platelet to hemoglobin ratio (PHR) and platelet to albumin ratio (PAR) have been recommended as prognostic factor of cancer. However, none of study has focused on the clinical significance of PHR, PAR, neutrophil to hemoglobin ratio (NHR), neutrophil to albumin ratio (NAR), monocyte to hemoglobin ratio(MHR) to albumin ratio(MAR) for axSpA.

Objectives: To study the reason of clinical significance of NHR, NAR, MHR, MAR, PHR, PAR for axSpA.

Methods: A total of 198 axSpA patients and 48 healthy subjects were enrolled in the study retrospectively. Neutrophil, monocyte, platelet, hemoglobin, albumin, CRP, ESR, MHR, NAR, MHR, PAR, NAR, MAR were included. AxSpA patients were divided into remission group (BASDAI<4) and active group (BASDAI≥4). Relationships between the parameters and BASDAI were assessed by the Spearman’s correlations analysis.

Results: Neutrophil, monocyte, platelet, NAR, MHR, MAR, PHR, PAR were higher in active group than those of control group, while albumin and hemoglobin were lower (P<0.05). ROC curve results showed that the AUC value of PHR for axSpA was 0.808 (CI95%: 0.738-0.878), yielding a highest AUC value than other parameters. The optimal cutoff value of MHR for axSpA was 0.002447, with the Youden index of 0.498, sensitivity of 87.4% and specificity of 62.5%. The closely positive correlations were found between MHR, and BASDAI were collected. AxSpA patients were divided into remission group (BASDAI<4) and active group (BASDAI≥4). Relationships between the parameters and BASDAI were assessed by the Spearman’s correlations analysis.

Receiver operation characteristic (ROC) curves were used to discriminate axSpA patients from healthy subjects and active group from remission group.

Results: Neutrophil, monocyte, platelet, NAR, MHR, MAR, PHR, PAR, CRP, ESR in axSpA group were higher than those of control group, while albumin and hemoglobin were lower (P<0.05). ROC curve results showed that the AUC value of PAR for active group was 0.693 (CI95%: 0.610-0.775), yielding a highest AUC value than other parameters. The optimal cutoff value of PAR for active group was 5.967, with the Youden index of 0.354, sensitivity of 83.3% and specificity of 52.1%.
Conclusion: MHR was elevated in axSpA patients with a highest diagnostic value. PAR was elevated in active axSpA patients, showing a significant correlation to the disease activity.

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AB0154 WNT-BETA CATENIN PATHWAY MAY BE UPRERGULATED IN ANKYLOSING SPONDYLITIS
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Background: The Wnt–β-catenin pathway may play a critical role in new bone formation in ankylosing spondylitis. Wnt–β-catenin signaling depends primarily on the activity of glycogen synthase kinase-3β (GSK3β) that plays a key role in controlling β-catenin stability/degradation. It has been clearly established that phosphorylation of serine 9 in GSK3β correlates with the inhibition of its kinase activity and stabilization of β-catenin. Dickkopf-1 (DKK1) and sclerostin (SOST) are both upstream inhibitors of the Wnt/β-catenin pathway. Given that AS is associated with new bone formation we are interested in the molecular pathways that lead to this clinical phenotype.

Objectives: The objective of our studies was to test the hypothesis that “alterations in the Wnt–β-catenin activity may be a contributing factor in the pathogene- sis of AS”.

Methods: 5 healthy donors and 12 patients (mean age 48 y.o., HLA-B27+ 70%) with AS based on New York classification criteria were enrolled. RNA was extracted from whole blood collected in PAX tubes following PreAnalytix method were used to quantify the data (normalized to RPLP0(60S acidic ribo- somal protein P0)). Protein lysates were prepared using NucleoSpin RNA/Pro-tein kit (Takara) from PBMCs isolated from blood collected from the same 12 patients. Equal amounts of protein were loaded on 4–12% SDS gels and trans- ferred to PVDF membranes. Membranes were blocked with 5% milk in TBST and probed at 4°C overnight with primary antibodies [rabbit anti-phos- phoGSK3β (Ser9) (1:500; Cell Signaling, #9336), rabbit anti-GSK3β (1:500; Santa Cruz Biotech- nology, #2859), and ΔΔCt- method were used to quantify the data (normalized to RPLP0(60S acidic ribosomal protein P0)]. Protein lysates were prepared using NucleoSpin RNA/Protein kit (Takara) from PBMCs isolated from blood collected from the same 12 patients. Equal amounts of protein were loaded on 4–12% SDS gels and trans- ferred to PVDF membranes. Membranes were blocked with 5% milk in TBST and probed at 4°C overnight with primary antibodies [rabbit anti-phos- phoGSK3β (Ser9) (1:500; Cell Signaling, #9336), rabbit anti-GSK3β (1:500; Santa Cruz Biotech- nology, #2859), and mouse anti-β-actin (1:1000; Santa Cruz Biotech- nology, sc-7778)}. Appropriate HRP-conjugated secondary antibody was applied at room temperature for 1 hour. Immunoreactive protein bands were visualized using ECL (Pierce) and imaged with VisionWorks Image Acquisition and Analysis Software (Analytik Jena US, Upland, CA). β-actin was used as a loading control.

Results: Compared to healthy controls the mRNA levels of DKK1 and SOST were significantly lower in AS patients (p < 0.01), while the mRNA level of β-catenin was significantly higher in AS patients than in healthy controls (p < 0.05) (Fig 1).

Conclusion: These data indicate that altered Wnt–β-catenin activity may be contributing to the new bone formation in AS patients and thereby contributing to the disease pathogenesis and can be targeted for therapeutic development.

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AB0155 INTESTINAL MICROBIAL SIGNATURE IN ANKYLOSING SPONDYLITIS
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Background: Intestinal microbiota analysis is a current subject because of its important role in the pathogenesis of various autoimmune diseases such as intestinal inflammatory diseases or spondylarthropathies.

Objectives: The objective of this paper was to perform a quantitative determination of the intestinal microbiota in patients with ankylosing spondylitis (AS) and to highlight the main characteristics of intestinal dysbiosis in these cases.

Methods: We conducted a case-control prospective study that included 28 patients with AS and 32 control cases (healthy individuals). Intestinal microbiota analysis was performed by real-time PCR (polymerase chain reaction) in faeces. Intestinal microbiota analysis focused on the following bacterial species: Bacteroides, Bifidobacterium, Clostridium cocoides (XIVa) (C. Cocoides), Clostridium leptum (IV) (C. Leptum), Faecalibacterium prausnitzii (F. Prausnitzii), Lactobaci- lus, Escherichia coli (E. coli).

Results: Intestinal dysbiosis in AS patients was characterized by a significant bacterial decrease compared to the control arm. Some bacterial species showed a numerical growth: Bacteroides, C. cocoides and C. leptum, F. praussnitzii. In other bacterial groups there was a significant decrease: Bifidobacterium, Lactobacillus and E. coli. Statistically significant correlations were observed only for Bifidobacte- rium, significantly increased in the axial form of AS compared to the peripheral form (p = 0.035). Other bacterial groups were numerically elevated in the axial form of AS (except Bacteroides), without statistically significant differences. In all AS cases, a moderate disease activity was evidenced (mean BASDAI = 4.83, mean BASFI = 9.11). BASDAI score inversely correlated with the total bacteria group (p = 0.010, r = -0.606) - intestinal dysbiosis worsens as disease activity increases. Also, direct proportional correlations were highlighted between BAS- DAI and F. prausnitzii (p = 0.000, r = 0.764), respectively Lactobacillus (p = 0.047, r = 0.488). An increase in AS activity is associated with an increase in proinflam- matory bacteria. BASFI score statistically correlated with the total bacterial count (p = 0.000, r = -0.764), F. prausnitzii (p = 0.010, r = 0.606), Bifidobacterium (p = 0.016, r = 0.843) and E. coli (p = 0.016, r = 0.575). An important decrease in the functionality of these patients correlates with a decrease in total bacterial diversity. Improvement of intestinal dysbiosis has been observed in patients on synthetic and biological immunosuppressive therapy compared to the control arm.

Conclusion: The study highlights the characteristics of intestinal dysbiosis in AS patients. There is a direct relationship between the composition of intestinal microbiota and the AS activity scores. Specific treatment for AS leads to a decrease in proinflammatory bacteria, improving gut dysbiosis.

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Disclosure of Interests: None declared

A NOVEL ASSOCIATION OF TLR-2 (23 BPINS/DEL: RS111200466) POLYMORPHISM WITH ANKYLOSING SPONDYLITIS – A POSSIBLE ROLE IN DISEASE SUSCEPTIBILITY: A HOSPITAL BASED CASE-CONTROL STUDY

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Background: Role of innate immunity in pathogenesis of ankylosing spondylitis (AS) has been well documented. Higher expression of TLR2 has been reported in AS patients and associated with clinical severity. Recently, a functional 23bp ins/del polymorphism of 5’UTR of TLR2 gene has been reported and association of variant with elevated TLR2 surface expression and proinflammatory molecules has been elegantly demonstrated. This is associated with high TNF-alpha levels, one of the key molecules in the pathogenesis of AS. In this preliminary study, we investigated the possible role of TLR2 (23bp ins/del) polymorphism with AS in a cohort from Odisha, India.

Objectives: To investigate the role of TLR-2 (23 bp ins/del: rs111200466) Polymorphism in Ankylosing Spondylitis

Methods: AS patients (n = 101), who fulfilled the ASAS classification criteria for peripheral spondyloarthritis or ASAS classification criteria for peripheral spondyloarthritides were enrolled along with 100 healthy age matched controls from similar geographical areas. Patients were examined in detail and BADA/BASFI recorded. TLR2 (23 bp ins/del) polymorphism was genotyped by polymerase chain reaction. Genotype and allele distribution among patients and controls were compared by Fisher’s exact test.

Results: All patients enrolled in the present study were males. The mean age of AS patients and healthy controls was 31.21±11.43 and 28.28±9.62 years, respectively. At the time of enrolment, mean disease duration of patients was 2.07±1.13 years. BASDAI and BASFI scores were above 5. Distribution of TLR2 (23 bp ins/del) polymorphism was in accordance with Hardy-Weinberg Equilibrium. No significant association of TLR-2 polymorphism was observed with disease severity.

Conclusion: TLR2 5’UTR homozgyous mutants (23 bp deletion) were significantly associated with patients of AS in but not with disease severity. Larger sample size and levels of TNF alpha and IL17 in the mutants will further improve the understanding of its role in AS.

REFERENCES

Disclosure of Interests: None declared


SYNOVIAL FLUID PROTEOMICS IN PATIENTS WITH ANKYLOSING SPONDYLITIS

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Background: Ankylosing Spondylitis (AS), affecting 0.5% of the population, is a chronic inflammatory rheumatic disease affecting the axial skeleton and peripheral joints. When peripheral arthritis in ankylosing spondylitis (AS) develops early in the disease course it is a predictor of more aggressive disease. SF is in contact with the primary tissues affected by arthritic diseases and has been implicated in disease pathophysiology. Therefore it is an excellent source for discovery of biomarkers.

Objectives: We used proteomic analysis using SFs from AS patients and other arthritic patients in order to discover novel diagnostic markers for AS. Our aim was to identify differentially expressed protein mediators in synovial fluid of ankylosing spondylitis.

Methods: A Total of 40 SF samples from 10 AS and each 10 controls [Osteoarthritis (OA), Rheumatoid Arthritis (RA), gouty arthritis (Gout)] were collected. Liquid chromatography and tandem mass spectrometry (LC-MS/MS), to identify differentially expressed proteins based on the ratios of the extracted ion current of each protein between the four groups. Among the 9 proteins showing 1.5 fold change, 8 were verified with the exception of the abundant protein Haptoglobin (HP), Matrix metalloproteinase-1(1MMP1) and Matrix metalloproteinase-3(3MMP3) were used as a positive control, and the remaining 6 proteins were subjected to western blot analysis.

Results: We identified 9 proteins that were found to be more than 1.5-fold differentially expressed in SF of AS patients compared to control groups. Proteins such as HP, MMP1, MMP3, Serum amyloid P-component (APCS), Complement factor H-related protein 5(CFHR5), Fumarylacetacetase(FAH), Mannose-binding lectin2(MBL2), Complement component C9(C9) and Complement C4-A(C4A) were found to be upregulated in the SF of AS patients. CFHR5 and C9 were reported in previous studies with AS serum. APCS was reported in SF as well as serum. However, FAH, C4A and MBL2 were newly discovered through this analysis. We were able to verify the unique expression level of C9 and CFHR5 in AS sample using western blot analysis compared to other three diseases.

Conclusion: We performed quantitatively proteomic profiling of the respective SF sample from 4 diseases, i.e., AS, OA, RA, and GOUT, by LC-MS/MS. The systematic comparative proteomic analysis of the four groups together was carried out for the first time, leading to several differentially expressed proteins in AS. Among them, we expect C9 and CFHR5, which expression levels were confirmed by western blot analysis, can be a potential biomarker for AS.

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Disclosure of Interests: None declared


FREQUENCY AND SPECTRUM OF ANEMIC SYNDROME IN PATIENTS WITH ANKYLOSING SPONDYLITIS: PECULIARITIES OF CYTOMETRIC CHARACTERISTICS AND HEMOPOIESIS

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Background: Anemia is one of the most common extraarticular manifestations in patients with ankylosing spondylitis (AS). According to various sources, from 18.5 to 45.8% of patients with AS have anemia. In the pathogenesis of anemic syndrome in the AS, a leading role is given to proinflammatory cytokines (IL-1, IL-6, and TNF-alpha), which is associated with the development of anemia of chronic disease (ACD) in this category of patients. Another type of anemia in patients with AS is iron deficiency anemia (IDA), and the relationship between the latter and the ACD varies significantly according to various literature data. As for other types of anemia in the AS, they are represented by anemia caused by drugs. ACD varies significantly according to various literature data. As for other types of anemia in the AS, they are represented by anemia caused by drugs.

Objectives: The purpose of the work was to investigate the prevalence of anemia in the Ukrainian population of patients with AS and evaluate the hematopoiesis in patients with the main types of it.

Methods: The group with anemia included patients whose haemoglobin levels were below 120 g/l. The diagnosis of AS was determined according to the modified New York criteria (1984). Laboratory methods of research (general analysis of blood, erythrocytes, haemoglobin, color index, serum iron, total iron binding capacity (TIBC) included in the list of standard examinations of patients were performed according to standard methods. To verify the diagnosis of ACD, ferritin (FN) and levels of soluble transferrin receptor (sTfR) were determined.

Results: 118 patients with AS were included into the study, 11 (32.3%) females and 23 (67.7%) males. It was found that 34 patients (28.8%) had anemia. Anemia of mild degree was manifested in 27 (79.4%) patients and with moderate severity - 7 (20.6%) patients. Among 34 patients with anemia, patients with ACD - 15 (44.1%) predominated. In the second place, 10 (29.4%) showed a combination of ACD and iron deficiency anemia, and 2 (5.9%) patients had signs of IDA. Only one of the subjects had signs of scarce anemia. Consequently, anemic
ABO157C
OCULAR CAUSES OF THE INITIATION OF SYSTEMIC THERAPY PATIENTS WITH SPONDYLOARTHROPATHY (SPA) AND UVEITIS
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Background: Uveitis is the most frequent extra-axial manifestation in Spondyloarthritis (SPA). It is a complication that affects patients with SPA and requires treatment with Steroid Therapy (ST). The causes of uveitis in patients with SPA are well defined, they are not when dealing with eye involvement.

Objectives: To evaluate the ocular causes of the initiation of systemic therapy in patients with SPA.

Methods: Retrospectively, we analyzed the ocular causes of the initiation of systemic therapy in patients with SPA. The follow-up of these patients was between 2015 and 2019. The causes of uveitis were divided into: viral, autoimmune, neoplastic, biochemical, infectious and idiopathic.

Results: A total of 32 patients were analyzed. The causes of uveitis were as follows: viral (12%), autoimmune (31%), neoplastic (12%), biochemical (25%), infectious (6%) and idiopathic (4%).

Conclusion: Uveitis is a frequent complication in patients with SPA. The causes of uveitis in patients with SPA are well defined, but they are not when dealing with ocular involvement.

Disclosure of Interests: None declared

SLE, Sjögren’s and APS - etiology, pathogenesis and animal models

ABO158
DECREASING AUTOPHAGY IN SALIVARY GLANDS OF PRIMARY SJÖGREN’S SYNDROME PATIENTS COULD BE ASSOCIATED WITH AN INCREASED EXPRESSION OF INFLAMMATORY MARKERS
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Background: Salivary glands (SG) of primary Sjögren’s syndrome (pSS) patients show high levels of IL-6 and endoplasmic reticulum (ER) stress1. In response to ER stress salivary epithelial cells trigger the unfolded protein response, seeking to alleviate ER stress through several mechanisms, such as autophagy. The autophagy does not only eliminate misfolded protein aggregates, but also decreases the inflammation selectively removing proteins related to TLRs and inflammasomes. Interestingly, the activation of IL-6/STAT3 signaling pathway inhibits the autophagy through an increase in MCL-1 expression2. Given the role of the autophagy as anti-inflammatory mechanism, it is interesting to evaluate if SG from pSS patients show a decrease in autophagy and if this correlates with the increased expression of inflammatory markers.

Objectives: To evaluate the expression of autophagy markers in labial SG (LSG) from pSS patients and 3D-acini deficient in autophagy. In addition, the expression of inflammatory marker IL-6, as well as, autophagy inhibitor MCL-1 was determined in 3D-acini control or deficient in autophagy, evaluating the possible participation of IL-6/STAT3 signaling pathway.

Methods: In LSG of 11 anti-Ro/La seropositive pSS patients and 10 control subjects, mRNA levels of ATG5, mTOR and Beclin-1 were measured by qPCR. ATG5, p62 and LC3B protein levels were measured by Western blot in LSG or 3D-acini deficient in autophagy by knocking down ATG5. HSG cells were transduced with lentiviral vectors expressing shRNAs against ATG5 mRNA or a control vector. Later, 3D-acini were generated from shATG5 and control cells. Acini were incubated with 10 ng/mL recombinant IL-6 in the presence or absence of 1.5 μM of JAK inhibitor tofacitinib for 24 h. The mRNA levels of IL-6 and MCL-1 were measured by qPCR.

Results: A significant decrease in mRNA levels of ATG5, mTOR and Beclin-1 was observed in LSG of SS-patients. In addition, a significant decrease of ATG5 protein levels was observed similar to SS-patients. Although, an increase in mRNA levels of MCL-1 was determined in 3D-acini stimulated with IL-6 and reverted with tofacitinib. Moreover, an increase in mRNA levels of IL-6 was measured in shATG5 3D-acini compared to 3D-acini control.

Conclusion: Our results suggest an attenuation of autophagy in salivary epithelial cells from anti-Ro/La seropositive pSS patients, which could be associated with an increased expression of inflammatory markers. We postulate that a plausible via involved in the autophagy attenuation in LSG from pSS patients could be the IL-6/JAK/STAT3 pathway, which induces MCL-1 expression. Further experiments are needed to elucidate this proposal.

Disclosure of Interests: None declared

REFERENCES
Silent Cerebral MRI Findings in Lupus Nephritis and Non Nephritis Patients

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Background: Lupus nephritis carries high morbidity and mortality and whenever added to neuropsychiatric manifestations lead to more unfavorable prognosis. The current work focused on LN patients comparing them to those without kidney affection, studying their cerebral MRI and its correlation with the histopathological classes of LN and disease activity.

Objectives: To study the effect of renal affection on the brain in SLE and their clinical significance with early detection and management of such lethal comorbidity

Methods: Cerebral MRI and MRA were studied in 40 SLE patients without neuropsychiatric manifestation: 20 LN patients with different histopathological classes and 20 patients without kidney affection. Disease activity was assessed for all patients using SLE disease activity index

Results: Abnormal MRI brain findings were more common in LN patients “though non significant” (P=0.9). The most common lesions were white matter hypointense lesions. Number and size of such lesions were significantly higher in LN patients (1.8 fold that of non nephritis, P=0.003 and 0.03, respectively) and positively correlated with urea, creatinine, urinary albumin/creatinine ratio, SLEDAI, ESF, CRP, and grades of renal biopsy and negatively correlated with c3 and c4, cortical atrophy and preponite space dilatation were also significantly higher in LN patients (P<0.01).

Conclusion: Asymptomatic MRI brain lesions in LN patients, they are usually clinically significant and correlate to laboratory parameters of LN, grades of renal biopsy, and disease activity independent to age, sex and hypertension.

REFERENCES


Disclosure of Interests: None declared


Lupus Podocytopathy–Case Report

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Background: Lupus podocytopathy is a recently recognized new entity of lupus nephritis characterized by diffuse foot process effacement with or without mesangial expansion. Capillary wall immune deposits and glomerular proliferation are lacking in the histopathological analysis. (1) Clinically, it is manifesting as nephrotic proteinuria in the majority of reported cases.(1) Nevertheless, there is insufficient knowledge about the epidemiology, precipitant etiology and choices of management. Here, we describe a case presented with significant proteinuria secondary to podocyte effacement which is unusual underlying pathology.

Methods: 45 years old female diagnosed to have SLE 14 years back in the setting of malar rash, alopecia, arthritis and positive serology (ANA, Ds DNA). She was doing fine on HCQ till a years ago when she presented to the clinic with gradual onset lower limbs swelling.

Laboratory results showed a significant proteinuria 2781 mg/dl/day, urine analysis showed RBC 1-2 cells/microlitter, WBC 2-3 cells/microlitter, normal renal profile and normal C3-C4 counts. Kidney biopsy taken and described a picture of minimal change glomerulonephritis with mild mesangial expansion. In addition, the study was negative for the presence of immunocomplementation deposition with the absence of capillary basement membrane and tubulointerstitial inflammation. Patient was treated with Mycophenolate Mofetil 2 grams twice per day and 1 mg/kg/day oral steroids. 3 months later, protein was noticeably reduced in urine to 731 mg/dl/day but the patients had a side effect of MMF inform of significant weight loss, gastritis, and diarrhea. Azathioprine had been instituted alternatively with low dose prednisolone 10 mg. Proteinuria level had peaked again after 4 months of starting azathioprine to reach 5660 mg/dl. Kidney biopsy performed again which showed minimal light microscopic changes, the ultrastructural study showed extensive podocyte injury and foot process effacement up to 70% by the electron microscope.

Conclusion: Lupus podocytopathy is a recently recognized new entity of lupus nephritis characterized by diffuse foot process effacement without capillary wall immune deposits and glomerular proliferation. This case presentation illustrates an attention toward this new lupus entity. However, the lack of efficient knowledge about the frequency, clinical features and treatment necessitate further investigation.

REFERENCES


Disclosure of Interests: None declared


Clinical Associations and Diagnostic Potential of Regulatory-Like B-Cells in Sjögren’s Syndrome

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Background: Some B-cell subsets contribute to the regulation of immune responses, mainly through the secretion of interleukin-10, which suppresses T-cell responses, mainly through the secretion of interleukin-10, which suppresses T-cell responses, mainly through the secretion of interleukin-10, which suppresses T-cell responses, mainly through the secretion of interleukin-10, which suppresses T-cell responses, mainly through the secretion of interleukin-10, which suppresses T-cell responses, mainly through the secretion of interleukin-10, which suppresses T-cell responses, mainly through the secretion of interleukin-10, which suppresses T-cell responses, mainly through the secretion of interleukin-10, which suppresses T-cell responses, mainly through the secretion of interleukin-10, which suppresses T-cell responses, mainly through the secretion of interleukin-10, which suppresses T-cell responses, mainly through the secretion of interleukin-10, which suppresses T-cell responses, mainly through the secretion of interleukin-10, which suppresses T-cell responses.

Objectives: To evaluate the distribution of regulatory and effector T and B-lymphocytes, in patients with pSS and healthy controls (HC), and the relation between regulatory-like B-cell subsets and the pSS phenotype.

Methods: Fifty-seven pSS patients (2002 AECG criteria) and 24 HC were included. Circulating T and B-lymphocytes were characterized by flow cytometry and groups were compared. Significance was considered for p<0.05.

Results: Compared to HC, pSS patients had lower percentages (19.9 vs 32.0%, p=0.001) and absolute numbers (28 vs 81 cells/µL, p=0.001) of Breg-enriched CD24+CD27- B-cells, and a decrease in CD24−CD38+ B-cells percentages (6.2 vs 7.7%, p=0.09).

Lower frequencies of CD24−CD27− B-cells were found in anti-SSA-positive patients, compared to anti-SSA-negative patients (15.0 vs 19.6%, p=0.170), as well as lower absolute counts (26 vs 31 cells/µL, p=0.173). Anti-SSA-positive patients presented higher CD24−CD38− B-cells percentages (6.2 vs 4.2%.

Disclosure of Interests: None declared

p=0.260) and absolute counts (10 vs 5 cells/µL; p=0.343) compared to anti-SSA-negative patients. Although CD24hiCD27+ B-cells frequencies and absolute counts did not differ between patients with active (n=27) or inactive disease (n=30), (16.9% vs 17.0%, p=0.946; 25 vs 31 cells/µL, p=0.166; 19 vs 24 cells/µL, p=0.179), patient activity (ESSDAI≥5) (n=9) presented lower absolute counts of CD24hiCD27+ B-cells (18 vs 31 cells/µL, p=0.096) and lower CD24hiCD27+ B-cells (4 vs 10 cells/µL, p=0.075), and higher Th1/Breg CD24hiCD27+ ratios (16.2 vs 9.2, p=0.064).

Considering all patients, a negative correlation was found between the ESSDAI score and the absolute numbers of either CD24hiCD27+ B-cells (r=−0.277, p=0.037) and Tregs (r=−0.311; p=0.019).

Correlations with ESSDAI was stronger when looking at patients with ESSDAI≥5: for the percentages of CD24hiCD27+ B-cells, r=−0.705, p=0.023; for CD24hiCD27+ B-cells absolute counts, r=−0.644; p=0.045; and for the absolute counts of Tregs, r=−0.862; p=0.001.

To study the effect of hydroxychloroquine on the level of anti-cardiolipin antibodies, IgM/IgG at 3 and 6 months from the start of therapy. Statistical data processing was performed using non-parametric methods (Wilcoxon Signed Ranks Test). Comparison of dependent samples confirmed APS. All patients were characterized by a history of three or more reproducible positive ANA, and 14% of them were confirmed APS. In patients treated with HC, levels of antibodies to cardiolipin (IgM/IgG) were 30.4% lower (p=0.001) after 6 months of therapy compared to the initial one [Me 21.43 (95% CI 20.2-24.2), p = 0.001]. By the sixth month of therapy, a reduced level of antibodies to cardiolipin remained unchanged; there was no statistically significant difference between the rates after 3 and 6 months of therapy. The level of antibodies to β2GPI (IgM/IgG) after three months from the start of therapy remained at the level of the indicator before inclusion in the study. A statistically significant decrease in the level of antibodies to β2GPI by 28.5% compared to the initial one was determined 6 months after the start of HC administration [Me 19.17 (95% CI 10.8-27.4), p = 0.003].

Conclusion: The study showed that, against the background of additional administration of hydroxychloroquine in patients with APS with low-level SLE, a decrease in the level of antibodies to cardiolipin (IgM/IgG) by 30.4% (p = 0.001) was observed after 3 months of therapy, to β2-glycoprotein I (IgM/IgG) - by 28.5% (p=0.003) after 6 months of therapy.

Disclosure of Interests: None declared


AB0163 THE ROLE OF IMMUNOREGULATORY MOLECULES ON FATIGUE IN PRIMARY SJÖGREN’S SYNDROME

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2Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, United Kingdom

Background: Primary Sjögren’s syndrome (pSS) is a chronic autoimmune rheumatic disease characterized by exocrine gland dysfunction. The clinical presentation of pSS can vary considerably from predominantly sicca symptoms such as dry eyes and dry mouth to systemic manifestations such as arthralgia, vasculitis and fatigue. Previous work from our laboratory has suggested that immunoregulatory pathways might play a role in fatigue development in patients with pSS. The first aim was to measure the serum levels of three candidate immunoregulatory molecules (melatonin, TGF-β and IL-10) and determine any relationship with fatigue severity. The second aim was to compare molecular profiles of the immunoregulatory mediators between pSS patients and healthy controls. The third aim was to identify key predictors of fatigue in pSS.

Methods: Serum levels of the three molecules were measured in 124 patients with pSS and 28 healthy non-fatigued controls selected from the United Kingdom Primary Sjögren’s Syndrome Registry using various assays. IL-10 concentrations were measured using a cytometric bead array-based immunoassay, melatonin levels were determined using ELISA and TGF-β concentrations were quantified using a bioassay in which HKC-8 cells were stably transfected with a TGF-β inducible CAGA-luciferase reporter construct. Patient fatigue levels were evaluated with a validated self-complete questionnaire and the scores were compared with the immunoregulatory molecular levels using analysis of variance. Significance in immunoregulatory mediators between the patients and controls was determined using the Wilcoxon test. Ordinal logistic regression analysis was performed in a smaller subset of patients (N = 75) to identify the key predictors of fatigue in pSS.

Results: IL-10 was significantly higher in the sera of patients with pSS compared to the healthy controls (p<0.0001). Melatonin showed a positive correlation with fatigue levels within the patient cohort (p=0.0164) whereas IL-10 and TGF-β were inversely related to fatigue severity (p=0.1265 and p=0.0643 respectively). The regression model used the three investigated immunoregulatory molecules, disease specific, haematological and clinical parameters as well as patient reported depression, anxiety and pain as predictors. The model was able to predict fatigue levels to a 7% accuracy.

Conclusion: The study suggests that melatonin may play a role in regulating the immune response in pSS and may affect fatigue levels in patients. Dryness, anxiety, pain and melatonin appear to be the most powerful predictors of fatigue in pSS. Further research into the effects of these immunoregulatory molecules is necessary to gain a better understanding of the pathophysiology of fatigue in pSS.

Disclosure of Interests: None declared


AB0162 IMPLEMENTATION OF HYDROXYCHLOROQUINE AT THE PRE-CONCEPTIONAL STAGE IN THE TREATMENT OF ANTIPHOSPHOLIPID SYNDROME ASSOCIATED WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The problem of correcting the antiphospholipid syndrome (APS) at the planning stage of pregnancy of patients with systemic lupus erythematosus (SLE) is an important task of rheumatology.

Objectives: To study the effect of hydroxychloroquine (HC) on the level of antiphospholipid antibodies titer in women with SLE of low degree of activity at the planning stage of pregnancy.

Methods: The study included 7 women aged from 18 to 44 years with a definite diagnosis of low-level SLE (1–5 points according to the SLEDAI2K scale) and confirmed APS. All patients were characterized by a history of three or more reproductive losses in the gestational age of 10 weeks or more. According to standard laboratory tests, the level of antibodies to cardiolipin (IgM/IgG) and/or to β2-glycoprotein I (IgM/IgG) in a titre above 99 percentile was determined twice in a 12-week interval. Before inclusion in the study, patients received methylprednisolone and acetazolamide in the recommended dosages. Other drugs potentially affecting the activity of SLE or hemostasis indicators of the patient during the observation period were not administered. At the time of inclusion, patients were prescribed with hydroxychloroquine (HC) in a dose of 400 mg per day orally, in addition to the therapy received earlier. The level of antibodies to cardiolipin (IgM/IgG) and antibodies to β2GPI (IgM/IgG) was determined at three times: initially, after 3 and 6 months from the start of therapy. Statistical data processing was performed using the MS Excel 2010 statistical software package and MedCalc Version 17.9.7. Data of laboratory parameters are presented in the form of median (Me) and 95% confidence interval (95% CI). Comparison of dependent samples was performed using non-parametric methods (Wilcoxon Signed Ranks Test).

The statistical significance of the hypotheses was accepted at a level of p<0.05.

Results: The initial SLEDAI2K index constituted 4.0±1.0 points. The median of the level of antibodies to cardiolipin is defined as 69.2% [95% CI 57.4 - 80.0] U/ml.

antibodies to β2GPI - 69.24 [95% CI 49.7 - 87.5] U/ml. After 3 and 6 months from the start of HC administration, the SLEDAI2K index did not statistically significantly change (p=0.09). 3 months later, a statistically significant decrease in the level of antibodies to cardiolipin (IgM/IgG) by 30.4% was determined relative to the initial one [Me 21.43 (95% CI 20.2-24.2), p = 0.001]. By the sixth month of therapy, a reduced level of antibodies to cardiolipin remained unchanged; there was no statistically significant difference between the rates after 3 and 6 months of HC therapy. The level of antibodies to β2GPI (IgM/IgG) after three months from the start of therapy remained at the level of the indicator before inclusion in the study. A statistically significant decrease in the level of antibodies to β2GPI by 28.5% compared to the initial one was determined 6 months after the start of HC administration [Me 19.17 (95% CI 10.8-27.4), p = 0.003].

Conclusion: The study showed that, against the background of additional administration of hydroxychloroquine in patients with APS with low-level SLE, a decrease in the level of antibodies to cardiolipin (IgM/IgG) by 30.4% (p = 0.001) was observed after 3 months of therapy, to β2-glycoprotein I (IgM/IgG) - by 28.5% (p = 0.003) after 6 months of therapy.

Disclosure of Interests: None declared


REFERENCES


AB0164  THE EXPRESSION AND CLINICAL SIGNIFICANCE OF DIFFERENT FORMS OF LILRA3 IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: LILRA3 is a member of the LILR family produced as a soluble molecule by monocytes and macrophages. A 6.7-kb deletion in the gene of LILRA3 results in a null allele and an absence of function. The frequencies of the 6.7-kb deletion vary greatly in different populations, considerably higher in Northeastern Asians (0.56–0.84) compared with Africans (0.10) or Europeans (0.17). The homozygous LILRA3 deletion (nonfunctional LILRA3) has been demonstrated to be associated with Sjogren’s syndrome (SS) and multiple sclerosis (MS) in Caucasians. However, in our previous studies, we found that in Chinese Han population, the LILRA3 non-deletion (namely functional LILRA3) contributes to susceptibility and subphenotypes of SLE and SS. With respect to the significant role of LILRA3 in immune-modulatory functions, we studied the role of LILRA3 in SLE.

Objectives: Our previous study has shown that functional LILRA3 contributes to susceptibility and subphenotypes of systemic lupus erythematosus (SLE). However, the mechanism remains unclear. We aimed to evaluate the role of LILRA3 in SLE.

Methods: 126 SLE patients and 48 healthy controls were recruited in this study. Functional studies were performed using intracellular flow cytometry and ELISA.

Results: Both LILRA3 levels in serum and CD14+ monocytes were significantly elevated in SLE patients compared with healthy controls. Elevated LILRA3 level was found positively correlated with SLEDAI. Furthermore, more elevated LILRA3 levels were found in patients with higher SLEDAI, presence of lupus nephritis and thrombocytopenia.

Conclusion: Both LILRA3 levels in serum and CD14+ monocytes significantly increased in SLE and positively correlated with disease activity and severity. The up-regulation of LILRA3 expression may serve as a biomarker of disease activity and severity of SLE.

Table 1. Correlations of LILRA3 levels with the studied parameters in SLE patients

<table>
<thead>
<tr>
<th>Clinical manifestations</th>
<th>LILRA3 in monocytes (MFI) Spearman’s r</th>
<th>P value</th>
<th>LILRA3 in serum (pg/mL) Spearman’s r</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLEDAI</td>
<td>0.398</td>
<td>0.0018</td>
<td>0.257</td>
<td>0.0036</td>
</tr>
<tr>
<td>24h proteinuria excretion</td>
<td>0.328</td>
<td>0.024</td>
<td>0.159</td>
<td>0.09</td>
</tr>
<tr>
<td>Leucocytes</td>
<td>-0.033</td>
<td>0.680</td>
<td>-0.253</td>
<td>0.0037</td>
</tr>
<tr>
<td>Thrombocytes</td>
<td>-0.176</td>
<td>0.213</td>
<td>-0.144</td>
<td>0.11</td>
</tr>
<tr>
<td>Anti-dsDNA Ab</td>
<td>0.066</td>
<td>0.627</td>
<td>-0.061</td>
<td>0.498</td>
</tr>
<tr>
<td>C3</td>
<td>-0.138</td>
<td>0.290</td>
<td>-0.076</td>
<td>0.392</td>
</tr>
<tr>
<td>C4</td>
<td>-0.140</td>
<td>0.282</td>
<td>-0.025</td>
<td>0.777</td>
</tr>
<tr>
<td>IgA</td>
<td>0.068</td>
<td>0.604</td>
<td>0.017</td>
<td>0.852</td>
</tr>
<tr>
<td>IgM</td>
<td>0.107</td>
<td>0.417</td>
<td>0.053</td>
<td>0.557</td>
</tr>
<tr>
<td>IgG</td>
<td>0.143</td>
<td>0.218</td>
<td>0.228</td>
<td>0.01</td>
</tr>
<tr>
<td>CRP</td>
<td>0.164</td>
<td>0.237</td>
<td>0.088</td>
<td>0.339</td>
</tr>
</tbody>
</table>

SLE: systemic lupus erythematosus; SLEDAI: systemic lupus erythematosus disease activity index; LILRA3: Leukocyte immunoglobulin-like receptor A3; ANA: antinuclear antibody; Anti-dsDNA Ab: anti-double strand DNA Antibody; ACP: antithrombin antibody; AruA: antinucleosome antibody; Sm: anti-Smith antibody; SS: anti-SSA antibody; C3 Complement component 3; C4: Complement component 4; CRP: C-reactive protein. *P < 0.05, **P < 0.01. Spearman’s correlation coefficient (r) was applied to detect correlation between two types of numerical data.
THE EUROPEAN REGISTRY ON OBSTETRIC ANTIPHOSPHOLIPID SYNDROME (EUROAPS): A SURVEY OF 1100 CONSECUTIVE CASES

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Background: The obstetric antiphospholipid syndrome (OAPS) is an autoimmune disease defined by the presence of obstetric complications related to antiphospholipid antibodies. EUROAPS project is the biggest published European registry on obstetric antiphospholipid syndrome and it is ongoing.

Objectives: To analyse the clinical features, laboratory data and foetal-maternal outcomes, and follow them up on a cohort of 1100 women with obstetric antiphospholipid syndrome (OAPS).

Methods: Thirty hospitals throughout Europe have collaborated to carry out this registry. Cases with obstetric complaints related to antiphospholipid antibodies (aPL) who tested positive for aPL at least twice were included prospectively and retrospectively. The eight-year survey results are reported.

Results: 1100 women with 3653 episodes were included of which 2553 were retrospectively. The eight-year survey results are reported.

Background: Primary Sjögren’s Syndrome (pSS) is a chronic systemic autoimmune disease that is affecting primarily women near the menopausal age, causing exocrine gland dysfunction, with clinical manifestations varying from dry eye and mouth to multi-systemic disorders [1]. The lack of automated means for data quality improvement in pSS cohorts and the huge time effort needed for manual curation, yield data that are irrelevant and incomplete, introducing undesirable implications in their analysis.

Objectives: To enhance the quality of the clinical data in pSS using automated data curation.

Methods: Anonymized clinical data were recruited from 380 patients with pSS from the University of Athens (UoA) cohort (300 patients, mean age 68.79±14.84) and the Harokopio University of Athens (HUA) cohort (80 patients, mean age 59.2±13.92). The features consist of SS-related measures (see [2] for details). The curation tool produces 3 files: (i) a quality report, including the metadata, the presence of outliers (using the z-score [3]), unknown data types, and missing values, on a feature-basis (data imputation [4] is used to fix features with ≤ 50% missing values), (ii) the curated dataset, where the inconsistencies are marked using color notations, and (iii) a standardization report, where the features that share common terminology with those from a reference model [5] (i.e., a set of parameters that describe the pSS minimal requirements) are identified using lexical matching [6].

Results: For the UoA cohort, out of 167 features, 80 were classified as “bad”, 30 with unknown data type, and 12 were marked for outliers (Fig. 1). An example of an outlier was found for the IgM (1370 mg/dL). For the HUA cohort, out of 204 features, 69 were classified as “bad”, 5 with unknown data type, and 13 were marked for outliers. The standardization process successfully matched 82 out of 88 (93.18%) pSS-related terms for the UoA cohort and 61 out of 69 (88.4%) terms for the HUA cohort.

Conclusion: Our strategy enhances the quality of the pSS clinical data through data curation and reduces the time effort needed for manual curation, yield data that are relevant and complete, introducing undesirable implications in their analysis.
advice them regularly and broadly in the areas of inflammation and infection), David Wofsy Consultant for: GlaxoSmithKline – Member, data safety monitoring board.

Novartis – Member, data safety monitoring board.

Celgene – member, scientific advisory board, Anne Davidson: None declared, Matthias Kretzler: None declared, David Hildeman: None declared, E. Steve Woodle: None declared, Betty Diamond: None declared, Michelle A Petri Shareholder of: Pfizer, Merck, Grant/research support from: AstraZeneca, Exagen, Consultant for: Eli Lilly, GSK, Merck, EMD Serono, Janssen, Amgen, Novartis, Quintiles, Exagen, Inova Diagnostics, AstraZeneca, Blackrock, Glenmark, UCB, and the Annenberg Center for Health Sciences.


AB0167

SINGLE CELL RNA EXPRESSION IN LUPUS NEPHRITIS COMPARING AFRICAN-AMERICAN AND CAUCASIAN PATIENTS IDENTIFIES DIFFERENTIAL EXPRESSION OF TYPE 1 INTERFERON PATHWAY

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REFERENCES


SNP (1513A>C AND 489C>T) OF P2X7 RECEPTOR IN SYSTEMIC LUPUS ERYTHEMATOSUS WITH SEROSITIS

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Background: our preliminary data demonstrated that expression and activity of P2X7R was impaired in Systemic Lupus Erythematosus (SLE) and associated with a reduced production of IL-1β. Serositis is a typical manifestation of SLE characterized by a marked inflammation, which has been suggested to be an “inflammase driven” manifestation.

Objectives: to investigate the role of 1513A>C (rs3751143) and 489C>T (rs208294) Single Nucleotide Polymorphisms (SNPs) which are differently associated with loss or gain of function, respectively, of P2X7R, a potent activator of the NLRP3 inflammasome and IL-1β release in patients with SLE and in a history of serositis (SLE-S).

Methods: DNA was extracted from whole blood and used for evaluation of 2 P2X7R SNPs (1513A>C and 489C>T). Considering the combined action of these two SNPs, the overall activity of P2X7R was divided, into three groups: GOF (gain of function), normal function (NF), and LOF (loss of function). In addition, peripheral mononuclear cells (PBMCs) were isolated from venous blood and employed to evaluate P2X7R and NLRP3 expression by RT-PCR, assess P2X7R activity as Benzoyl ATP (BzATP)-induced intracellular Calcium ([Ca2+]i) increase and evaluate in vitro IL-1β following stimulation with lipopolysaccharide (LPS) and BzATP, either separately or in combination.

Results: 33 SLE patients (pts), 11 with (SLE-S) and 22 without serositis (SLE-NS) were enrolled. Mean age was 49.0±10.9 years and disease duration was 135.3±108.6 months. No significant difference in disease activity and clinical characteristic was found between the two groups (table 1). Evaluating 1513A>C SNP, 20 pts were positive for A/A and 13 for A/C phenotype respectively, while in case of 489C>T SNP, 7 pts presented C/C, 12 C/T and 14 T/T phenotype with a comparable distribution between SLE-NS and SLE-S (table 1). After combination of different phenotypes, 9 pts presented normal function (NF), 22 gain of function (GOF) and 2 loss of function (LOF) with no significant difference between SLE-S and SLE-NS (table 1). P2X7R activity, (evaluated as IL-1β production and [Ca2+]i increments) and expression (evaluated with RT-PCR) were comparable between SLE-S and SLE-NS. No significant difference was found between expression and activity of P2X7R and the two SNPs evaluated (table 2).

Table 1 Comparison between patients with a positive history of serositis (SLE-S) vs patients without history of s (SLE-NS)

<table>
<thead>
<tr>
<th>SLE-NS</th>
<th>SLE-S</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age mean±sd years</td>
<td>48.3±10.9</td>
<td>50.2±10.9</td>
</tr>
<tr>
<td>Disease duration (months)</td>
<td>138.4±108.6</td>
<td>132±107.6</td>
</tr>
<tr>
<td>Ongoing treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steroids (mg/day)</td>
<td>20 (17.5-25)</td>
<td>30 (25-35)</td>
</tr>
<tr>
<td>Nonsteroids (mg/day)</td>
<td>0.01 (0.00-0.03)</td>
<td>0.01 (0.00-0.03)</td>
</tr>
<tr>
<td>Mean immunosuppressive treatment (mg/day)</td>
<td>10 (5-20)</td>
<td>10 (5-20)</td>
</tr>
<tr>
<td>Mean dosage of intravenous ganciclovir (mg)</td>
<td>10 (5-20)</td>
<td>10 (5-20)</td>
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<tr>
<td>Mean dosage of intravenous ganciclovir (mg)</td>
<td>10 (5-20)</td>
<td>10 (5-20)</td>
</tr>
<tr>
<td>Cumulative dosage of intravenous ganciclovir (mg)</td>
<td>50 (25-75)</td>
<td>50 (25-75)</td>
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<tr>
<td>Current immunosuppressive treatment</td>
<td>3.8±1.7</td>
<td>3.6±1.7</td>
</tr>
<tr>
<td>SLEDAI-2K mean±sd</td>
<td>5.3±6.7</td>
<td>5.6±6.7</td>
</tr>
</tbody>
</table>
| DISEASE IN AB0169 AND 489C>T OF P2X7 RECEPTOR IN SYSTEMIC LUPUS ERYTHEMATOSUS WITH SEROSITIS

Conclusion: our data indicate that the 1513A>C and 489C>T SNPs do not seem linked with reduced activity and expression of P2X7R that we previously observed in our cohort of lupus patients. Furthermore, no significant association was found between expression of these SNPs and development of serositis.

REFERENCES

Disclosure of Interests: Federica Furini: None declared, Anna Lisa Giuliani: None declared, Mattia Erminio Parlati: None declared, Marcello Govoni Paid instructor for: Pfizer, Roche, Speakers bureau: Pfizer, Abbvie, MSD, Roche, Eli-Lilly, Celgene, Sanofi, Janssen, Francesco Di Virgilio: None declared, Alessandra Bortoluzzi: None declared


TUBERCULOSIS IN PATIENTS WITH SYSTEMIC RHEUMATIC DISEASES: THE TUNISIAN EXPERIENCE

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Background: The incidence of tuberculosis among patients with systemic rheumatic diseases is much higher than in the general population. The clinical manifestations of both systemic rheumatic disease activity and tuberculosis, (i.e. fever, weight loss, asthma) may overlap or lead to confusion. The immunosuppression of systemic diseases makes the management of patients with tuberculous more complicated.

Objectives: The purpose of our study was to describe the clinical characteristics of patients with systemic rheumatic diseases and tuberculosis.

Methods: A retrospective study, from 1998 to 2018, in the internal medicine service in Fattouma Bourgiba hospital, Tunisia, of 59 patients suffering from connective tissues disease, treated by corticosteroids linked in one or several treatments to immunosuppressors, who subsequently developed tuberculosis.

Results: Fifty nine patients were included (46 women and 13 man) with a mean age of 47 years (range from 18-83 years). Systemic illnesses were: systemic lupus erythematosus (13.6%, n = 8), Gougerot-Sjögren syndrome (secondary or primary) (16.2%, n = 11), systemic scleroderma (5.1%, n = 3), rheumatoid arthritis (n = 1), Takayasu arteritis (n= 2), Behcet’s disease (n = 1), osteoarticular (n = 2) and more than one location in 23.7% of the cases. The localization of the tuberculosis was pulmonary (32.3%, n = 19), ganglionic (33.9%, n = 16), urogenital (20.3%, n = 12), lymphatic (n = 5), abdominal (n=4), cerebral (n=2), ocular (n=2), osteoarticular (n=2) and more than one location in 23.7% of the cases. The diagnosis of tuberculosis was confirmed by bacteriology in 13.6% (n = 8) and in thirteen cases, histologically (22.0%). The systemic rheumatic disease was clinically active at the time of the diagnosis of tuberculosis in 8 patients. The diagnosis of systemic rheumatic diseases was made before that of tuberculosis in 13 patients and concomitantly in 5. Under tuberculosis treatment by four drugs then by two drugs, the evolution of tuberculosis was favourable in most of our patients. Three of the patients developed an allergy in isoniazid. Nine patients have developped hepatotoxicity with pyrazinamide. Retrobulbar neuritis was observed in 3 cases treated with ethambutol.

Conclusion: This study confirms the often extra-pulmonary character of tuberculosis in patients with systemic disease as well as the difficulty of diagnosis and problems multiplied by this association. The screening strategies for tuberculosis should probably be extended in all patients with systemic rheumatic diseases receiving glucocorticoids and/or immunosuppressive therapy.
REFERENCES

Disclosure of Interests: None declared

AB0172 EXPRESSION OF SLAMF6 AND ITS FUNCTIONAL SIGNIFICANCE IN PODOCYTES OF LUPUS NEPHRITIS
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Background: Systemic lupus erythematosus (SLE) is a multisystem disorder whose expression of nephritis (LN) is frequent complication and one of the most serious manifestations of SLE. The expression of nephritis, as podocyte marker, is reduced in various renal diseases that develop into nephrotic syndrome. The alteration of the structural protein in podocytes is known as a mechanism of proteinuria in LN.

Objectives: The signaling lymphocyte activation molecule family (the SLAM family) of type I transmembrane receptors consists of nine related members of the immunoglobulin superfamily and has been reported to mediate important regulatory signals between immune cells through their homophilic and heterophilic interactions. The 1q23 region (Step17 region in mouse) on human chromosome 1 including the SLAMF cluster of genes, containing SLAMF6 has been identified as a lupus susceptibility locus. It has been shown that the expression of signaling lymphocyte activation molecule family 6 (SLAMF6) is enhanced in CD4+ T cells of SLE patients and is involved in IL-17 production. We sought to examine the functional role of SLAMF6 in lupus podocytes.

Methods: We evaluated the co-expression of nephritis in nephritis (LN) and podocytes of normal controls and LN patients, also in B6 and MRL/lpr mice at the age of 6 wk and 10 wk by immunofluorescence analysis. We also examined nephrin positive SLAMF6 expression in isolated podocytes from B6 and MRL/lpr kidneys. Then, we analyzed the expression of SLAMF6 in CD4+ T cells of isolated kidney and spleen in B6 and MRL/lpr mice. We treated human podocytes with IgG from healthy individuals and LN patients for 24 h and 48 h and analyzed the expression of SLAMF6 by real-time PCR.

Results: In the histopathology, the expression of SLAMF6 was increased in nephritis in LN patients and MRL/lpr mice compared to control groups. Among the expression of nephritis in MRL/lpr mice kidney at 16 wk old decreased compared to B6 mice at same age, the expression of SLAMF6 in podocytes increased in diseased MRL/lpr mice compared to B6 mice. Similarly, the expression of SLAMF6 in CD4+ T cells increased in diseased MRL/lpr mice kidney and spleen compared to B6 mice. The level of SLAMF6 mRNA elevated in human podocytes exposed to LN-derived IgG compared to healthy individuals-derived IgG.

Conclusion: The expression of SLAMF6 is enhanced in LN podocytes, suggesting that the possibility of Cooperating with CD4+ T cells contributing to its dysfunction. Further examination is needed to investigate in detail how SLAMF6 is involved in the development of LN in the future.

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Disclosure of Interests: Takashi Iwaga: None declared, Kunihiro Ichinose: None declared, Mizuna Eguchi: None declared, Monoko Okamoto: None declared, Yushiro Endo: None declared, Sousuke Tsuji: None declared, Ayako Takatani: None declared, Toshimasa Shimmizu: None declared, Remi Sumiyoshi: None declared, Tomohiro Koga: None declared, Shir-ya Kawashiri: None declared, Naoki Iwamoto: None declared, Mami Tamai: None declared, Hideki Nakamura: None declared, Tomoki Origuchi: None declared, Atsushi Kawakami Grant/research support from: Astellas Pharma, Consultant for: Astellas Pharma, Speakers bureau: Astellas Pharma

AB0171 THE REGULATION AND PHARMACOLOGICAL MODULATION OF IMMUNE COMPLEX INDUCED PRODUCTION OF TYPE III IFN BY PLASMACYTOID DENDRITIC CELLS
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Background: The type I Interferons (IFN-α) are the most important drivers of the IFN gene signature in Systemic Lupus Erythematosus (SLE). However, both type II and type III IFNs (IFN-λ) can be measured in a proportion of patients with SLE and contribute to the IFN signature. The exact role of type III IFNs in SLE is not completely clear, but serum levels of type III IFN correlate with disease activity and specific organ manifestations, such as arthritis, nephritis and anti-dsDNA antibodies. Type III IFN can be induced in DCs by nucleic acid containing immune complexes (IC), has, to our knowledge, not been investigated before.

Objectives: We asked if RNA containing immune complexes (RNA-IC), which trigger the synthesis of large amounts of IFN-α by plasmacytoid dendritic cells (pDCs), can act as stimuli for type III IFN production, and how this production is regulated by Natural Killer (NK) cells and different cytokines. We also investigated if the type III IFN production could be blocked by hydroxychloroquine (HCQ) and an interleukin receptor 1 associated kinase 4 inhibitor (IRAK4i).

Methods: Peripheral blood mononuclear cells (PBMCs) from SLE patients or healthy individuals were used to isolate PDCs and natural killer (NK) cells, or were depleted of monocytes. Cells were stimulated with RNA-IC, and cytokines were measured by immunoassays. mRNA expression in RNA-IC stimulated pDCs and NK cells was analyzed with a microarray. The effect of HCQ and IRAK4i on IFN-λ1 production was investigated in pDCs and NK cells from healthy individuals.

Results: Type III IFN mRNA expression was strongly upregulated in co-cultures of pDC-NK cells stimulated with RNA-IC. High levels of IFN-λ1 and IFN-λ2 (medians 2000 pg/ml and 100 pg/ml) were detected in supernatants from RNA-IC stimulated pDC-NK cell co-cultures. IFN-κ2 enhanced IFN-λ1 and IFN-α production by purified pDCs. Interleukin (IL) -3, -6, and -10, and GM-CSF significantly enhanced IFN-λ1 production (4-5 fold) by RNA-IC stimulated pDCs. Monocyte depleted PBMCs and pDC-NK cell co-cultures from 15% and 9% of SLE patients produced IFN-λ1 in response to RNA-IC stimulation. Exogenous IFN-α and GM-CSF in pDC-NK cell co-cultures increased the proportion of patients responding to RNA-IC stimulation from 9 to 36%. IFN-λ1 production by RNA-IC stimulated pDCs and pDC-NK cells was significantly inhibited by HCQ (by 99% and 93% respectively) and an IRAK4i (by 98% and 96% respectively).

Conclusion: pDCs produce both type I and type III IFN in response to RNA containing immune complexes. This is promoted by activated NK cells as well as a number of pro-inflammatory cytokines, including IFN type I and type III, considered important in SLE. Consequently, in order to achieve a proper control the IFN driven autoimmune process in SLE, both type I and type III IFN need to be targeted. In this system of stimulated, co-cultivated pDCs and NK cells, HCQ and an IRAK4 inhibitor blocked the type III IFN production.

Disclosure of Interests: None declared
LONG NON-CODING RNA, LINC00487 EXPRESSION IS UPREGULATED IN B CELLS AND CORRELATES TO DISEASE ACTIVITY IN PATIENTS WITH PRIMARY SJÖGREN’S SYNDROME

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Background: Primary Sjögren’s syndrome (pSS) is a systemic autoimmune disease characterized by interferon signature [1] and exocrine gland dysfunction which leads to dryness of the eyes and mouth [2]. B cells are considered to play an important role in the pathogenesis of pSS. Dysregulation of B cells can lead to production of anti-Sjögren’s syndrome-related antigen A (anti-SSA) autoantibodies.

Objectives: We investigated the differential gene expression of peripheral B cell subsets to reveal the precise role of B cells in the pathogenesis of pSS.

Methods: We enrolled pSS patients (n=6) and healthy controls (HC) (n=6), with matching for age and sex. Peripheral B cells acquired from the participants were separated by cell sorting into 4 subsets: CD38-IgD+, CD38+IgD+, CD38highIgD+ and CD38±IgD-. Total RNA was extracted and gene expression was measured using the Human Genome U133 Plus 2.0 Array (Affymetrix). The data were bioinformatically analyzed with reference to the corresponding clinical information.

Results: Using principal component and clustering analyses, we found that transcript expression patterns depended on cell type rather than clinical condition (pSS or HC). Interferon signaling was the most upregulated pathway in many of B cell subsets of pSS patients. As well as HLA and interferon signature genes, LINC00487 was upregulated significantly in all B cell subsets. Its fold changes in CD38-IgD+, CD38+IgD+, CD38highIgD+ and CD38±IgD- were 8.4 (p=0.038), 11.3 (p=0.014), 8.5 (p=0.089) and 6.37 (p=0.078), respectively. In addition, the normalized intensity value of LINC00487 was significantly correlated with disease activity score in all pSS B cell subsets, namely CD38-IgD+ (Figure A, r=0.96, p=0.002), CD38+IgD+ (Figure B, r=0.90, p=0.015), CD38highIgD+ (Figure C, r=0.81, p=0.049) and CD38±IgD- (Figure D, r=0.96, p=0.003). The expression of LINC00487 in B cell lines was regulated by IFNβ.

Conclusion: Compared to HC, patients with pSS showed upregulation of the interferon signaling pathway and LINC00487 gene in all B cell subsets. This upregulation correlated with disease activity and regulated by IFNαs in B cell lines. These results may suggest that long non-coding RNA contributes to B cell dysregulation in patients with pSS and the precise role of LINC00487 in B cell and pathogenesis of pSS requires further study.

REFERENCES

Figure. Correlation between the expression of LINC00487 and disease activity score in each B cell subset.

ESSDAI; EULAR Sjögren’s Syndrome Disease Activity Index


production of pro-inflammatory cytokines were analyzed in urinary myeloid cells of patients with LN.

Results: Myeloid cells were identified by the expression of CD45+ and CD11c+ in the urine of patients with LN. The frequency and absolute numbers of myeloid cells were markedly increased in patients with proliferative LN than non-proliferative LN. In addition, titers of anti-dsDNA antibodies were correlated with the frequency or numbers of urinary CD11c+ myeloid cells. These urinary CD11c+ myeloid cells showed the phenotypes of infiltrated monocyte-derived cells rather than tissue-resident macrophage. In addition, CD11c+ myeloid cells were localized in tubulointerstitial and had capacity to produce pro-inflammatory cytokines including IL-6. Further, we found that there was a significant population of tubule cells in the urine, which is correlated with the frequency of CD11c+ myeloid cells.

Conclusion: Our results indicate that CD11c+ myeloid cells are present in the urine and contribute to tubulointerstitial inflammation in proliferative LN.

Disclosure of Interests: None declared

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AB0175

ABSOLUTE REDUCTION OF PERIPHERAL CD4+CD25+FOXP3+ T REGULATORY CELLS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: T lymphocytes are important contributors to systemic lupus erythematosus (SLE). Regulatory T (Treg) cells, with the capacity to suppress immune responses, effector T cells (Teff), which promote inflammation, have been intensively studied in recent years. However, previous reports describing the respective changes of Treg and Teff, especially T helper cells (Th17) in SLE patients were controversial. Here, we investigated both absolute number and percentage of CD4+CD25+Foxp3+Treg (CD4Treg) cells and effector cells on a large scale and the role of low-dose interleukin-2 (IL-2) in SLE.

Objectives: To investigate both absolute number and percentage of CD4+CD25+Foxp3+Treg (CD4Treg) cells and effector cells on a large scale and the role of low-dose interleukin-2 (IL-2) in SLE.

Methods: Two hundred and thirty-five SLE patients (219 women and 16 men), with mean age of 37.80±14.00 years, were enrolled. The absolute count and percentage of subpopulation of peripheral blood (PB) lymphocyte in these patients were measured by flow cytometry combined with internal microscope standard. And low-dose IL-2 was used among 127 patients at a dosage of fifty IU every day for five days. Immunological and clinical assessments were performed again at the end of IL-2 treatment. Ninety healthy volunteers, matched for patients’ age and gender, were also included for the estimation of lymphocyte subsets.

Results: As compared to healthy controls (median of Treg cells: 33.09 cells/μl), the absolute number of circulating CD4Treg cells were significantly decreased in SLE patients (median: 15.49 cells/μl, P<0.001). The median ratios of Th17/Treg cells in patients were greatly higher than that of healthy volunteers [0.42 (0.19, 0.88) vs. 0.21 (0.15, 0.34), P<0.001], while there was not a significantly different in peripheral Th17 cell between two groups. Besides, Th1, Th2, CD8+T, B cells and their respective ratios to Treg cells were like that of Th17 cells as well. Moreover, CD4Treg cells were negatively correlated with ESR and SLEDAI score (r=-0.198, P=0.01; r=-0.25, P=0.002). While no obvious correlation was seen between Th17 cells and SLEDAI score. After IL-2 therapy in SLE, there was a four-fold increase in circulating CD4Treg cells [43.73 (24.08, 74.22) vs. 11.95 (7.51, 20.34), P<0.001], whereas Th17 cells were increased slightly. The ratio of Th17/Treg was decreased significantly in patients with IL-2 treatment [0.19 (0.09, 0.41) vs. 0.52 (0.23, 0.95), P<0.001], tended to balance and had no difference with healthy individual (P=0.275). Similarly, there were same trends in Th1, Th2, CD8+T, B and NK cells.

Conclusion: The reduction of CD4Tregs but not the elevation of effector cells may be the major reason for imbalance of Teff:Treg, indicating that SLE is an autoimmune disease triggered by the defect of immunotolerance. More importantly, low-dose IL-2 might promote the proliferation of various lymphocyte subpopulation, and mainly modulated the abundance and immunosuppression activity of Tregs, which effectively induced autoimmune tolerance and further improved clinical symptoms.

REFERENCES


Disclosure of Interests: None declared

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AB0176

MITOGEN- AND STRESS-ACTIVATED PROTEIN KINASE-1 (MSK1) AS THE LINK BETWEEN MIR-130A-DYSREGULATION AND CDC2-ACTIVATION IN SJÖGREN’S SYNDROME

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Background: Primary Sjögren’s syndrome (pSS) is a systemic autoimmune disease characterized by lymphocytic infiltration of the exocrine glands and dryness of mouth and eyes. T and B lymphocytes that infiltrate the salivary glands play a central role in local production of autoantibodies and cytokines, associated with dryness and tissue-damage. Type 2 conventional dendritic cells (cDC2) are very potent antigen-presenting cells and have the ability to produce a variety of cytokines involved in T and B cell activation, germinal centres formation and autoantibody production.

Objectives: Considering the critical role of microRNAs (miRNAs) in regulation of cell activation, we investigated their potential dysregulation in circulating cDC2s of patients with pSS compared to healthy controls (HC).

Methods: CD1c-expressing cDC2s were isolated from peripheral blood of pSS patients and controls from two independent cohorts. In the donors from the discovery cohort (15 pSS, 6 HC) the expression of 758 miRNAs was screened; the replication cohort (14 pSS, 11 HC) was used to confirm consistent differential expression of 18 identified miRNAs. A quantitative mass spectrometry-based technique (qPSILAC) in HEK-293T cells was used to identify novel targets of the replicated miRNAs. Target-miRNA interaction was replicated in primary cDC2s. Differences in cytokine production between pSS and HC cDC2s were evaluated by FACS. cDC2s were cultured in the presence of different MSK1-inhibitors to examine their effect on cytokine production.

Results: The expression of miR-130a and miR-708 was consistently decreased in cDC2s from pSS patients compared to HC in both cohorts, and both miRNAs were downregulated upon stimulation via TLR3 and TLR7/8. MSK1 was identified as a novel target of miR-130a and overexpression of miR-130a reduced MSK1 protein expression in both HEK-293T cells and primary cDC2s. In-line with the regulation of MSK1 by miR-130a, MSK1 expression was higher in cDC2s of pSS patients as compared to controls. An increased frequency of cDC2s producing-IL-12 and TNF-α was observed in pSS patients compared to HC, consistent with the central role of MSK1 in regulation of cytokine production. Exposure to either of two different MSK1 inhibitors in vitro reduced cDC2 cytokine production and the production of IL-12, TNF-α and IL-6.

Conclusion: We here provide the first evidence of molecular dysregulation of cDC2s in pSS, including increased expression of miR-708 and miR-130a, which can result from TLR activation, and enhanced production of pro-inflammatory cytokines. In view of its central role in NF-κB signalling, inhibition of MSK1 to decrease cell activation and inhibit pro-inflammatory cytokine production represents a novel therapeutic avenue for treatment of Sjögren’s Syndrome.

Disclosure of Interests: None declared

DOI: 10.1136/annrhumdis-2019-eular.6806
Methods: The study involved 80 (59-f and 21-m) APS patients (pts) 24 pts had PAPS and 56 pts had APS following SLE. In the whole study group the mean age was: 39.3± 12.7 years (range 18-71), the duration of the disease was 8.8 ± 8.3 years (range 0-37).

The presence of aPL was detected in patients’ serum using the commercially available tests: aPL-immunodot assay Anti-Phospholipid 10 Dot, for the qualitative detection of IgG or IgM antibodies. The statistical data analysis was performed using Statistics v13.0

Results: In the study group of 80 patients we have detected the presence of the following aPLs: a-cardiolipin IgM -37%, IgG -50.6%; a-phosphatidic acid IgM -19.7%, IgG -13.3%; a-phosphatidylycholine IgM and IgG -1.2; a-phosphatidy- lethanolamine IgM -1.2% and IgG -5.0%, IgG -12.5%; a-phosphatidylinositol IgM-10.0%, IgG -12.5%; a-phosphatidylserine IgM -31.0%, IgG -50.6%; a-annexin V IgM -20%, IgG -10%; a-β2-GP I IgM 44.5%, IgG -35.0%; a-prothrombin IgM -44.5%, IgG -30%.

Table 1

<table>
<thead>
<tr>
<th>aPL</th>
<th>PAPS n=24</th>
<th>SAPS n=56</th>
<th>P&lt;0.05</th>
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<tbody>
<tr>
<td>aCL IgM aCL IgG</td>
<td>10</td>
<td>20</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(41.6%)</td>
<td>(35.7%)</td>
<td></td>
</tr>
<tr>
<td>a-phosphatidic acid IgM a-phosphatidic acid IgG</td>
<td>8 (32.3%)</td>
<td>14 (51.3%)</td>
<td>0.0651</td>
</tr>
<tr>
<td></td>
<td>(41.6%)</td>
<td>(55.3%)</td>
<td></td>
</tr>
<tr>
<td>a-phosphatidylycholine IgM a-phosphatidylycholine IgG</td>
<td>3 (12.5%)</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(12.5%)</td>
<td>(12.5%)</td>
<td></td>
</tr>
<tr>
<td>a-phosphatidylethanolamine IgM a-phosphatidylethanolamine IgG</td>
<td>0(0%)</td>
<td>1(1.8%)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>(0%)</td>
<td>(1.8%)</td>
<td></td>
</tr>
<tr>
<td>a-phosphatidylcholine IgM a-phosphatidylcholine IgG</td>
<td>0(0%)</td>
<td>1(1.8%)</td>
<td>NS</td>
</tr>
<tr>
<td></td>
<td>(0%)</td>
<td>(1.8%)</td>
<td></td>
</tr>
<tr>
<td>a-phosphatidylinositol IgM a-phosphatidylinositol IgG</td>
<td>2 (8.3%)</td>
<td>2 (3.6%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(12.5%)</td>
<td>(12.5%)</td>
<td></td>
</tr>
<tr>
<td>a-phosphatidylinositol IgM a-phosphatidylinositol IgG</td>
<td>5 (20.8%)</td>
<td>3 (5.4%)</td>
<td>0.0345</td>
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<tr>
<td></td>
<td>(12.5%)</td>
<td>(3.8%)</td>
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</tr>
<tr>
<td>a-phosphatidylserine IgM a-phosphatidylserine IgG</td>
<td>11 (45.8%)</td>
<td>14 (25.0%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(12.5%)</td>
<td>(12.5%)</td>
<td></td>
</tr>
<tr>
<td>a-annexin V IgM a-annexin V IgG</td>
<td>17</td>
<td>12</td>
<td>0.0004</td>
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<tr>
<td></td>
<td>(70.8%)</td>
<td>(28.6%)</td>
<td></td>
</tr>
<tr>
<td>a-β2-GP I a-β2-GPI IgG</td>
<td>6 (25.0%)</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(25.0%)</td>
<td>(12.5%)</td>
<td></td>
</tr>
<tr>
<td>a-annexin V IgM a-annexin V IgG</td>
<td>2 (8.3%)</td>
<td>3 (10.7%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(6.6%)</td>
<td>(3.7%)</td>
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</tr>
</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th>Clinical symptoms</th>
<th>PAPS n=24</th>
<th>SAPS n=56</th>
<th>P=0.0108</th>
</tr>
</thead>
<tbody>
<tr>
<td>stroke</td>
<td>3 (12.5%)</td>
<td>5 (9.0%)</td>
<td></td>
</tr>
<tr>
<td>pulmonary embolism</td>
<td>6 (25.0%)</td>
<td>7 (12.5%)</td>
<td></td>
</tr>
<tr>
<td>thrombosis</td>
<td>14 (58.3%)</td>
<td>19 (34.0%)</td>
<td></td>
</tr>
<tr>
<td>obstetric comp.</td>
<td>3 (18.9%)</td>
<td>12 (28.0%)</td>
<td></td>
</tr>
<tr>
<td>valve defects</td>
<td>4 (16.7%)</td>
<td>8 (14.3%)</td>
<td></td>
</tr>
<tr>
<td>livedo reticulars</td>
<td>4 (28.6%)</td>
<td>7 (12.5%)</td>
<td></td>
</tr>
<tr>
<td>nephropathy</td>
<td>4 (20.8%)</td>
<td>19 (34.0%)</td>
<td></td>
</tr>
<tr>
<td>deep vein thrombus</td>
<td>14 (58.3%)</td>
<td>19 (34.0%)</td>
<td></td>
</tr>
<tr>
<td>hypertension</td>
<td>12 (50.0%)</td>
<td>23 (41.0%)</td>
<td></td>
</tr>
<tr>
<td>convulsions/chorea</td>
<td>0(0%)</td>
<td>5 (9.8%)</td>
<td></td>
</tr>
<tr>
<td>migraine</td>
<td>1(0%)</td>
<td>4 (8.9%)</td>
<td></td>
</tr>
<tr>
<td>depression</td>
<td>(4.2%)</td>
<td>2 (3.6%)</td>
<td></td>
</tr>
</tbody>
</table>

The following clinical symptoms of APS were also present: stroke -10%, arterial/venous thrombosis -34%, pulmonary embolism-16.3%, obstetric complications-25.4%, nephropathy – 30.0%, hypertension-43.8%, valve defects 15.0%, livedo reticulars 11.2%, convulsions/chorea-6.2%, thrombocytopenia- 23.7% of the study group.

During the study we detected statistically significant differences in the frequency of occurrence of aPLs between groups with PAPS and SAPS: a-phosphatidylglycerol p=0.0045; a-β2-GP I IgM p=0.0045; a-prothrombin IgM p=0.0108 a-phosphatidylcholine acid IgG p=0.045 (table 1).

There are no differences in the assessed clinical symptoms between pts with PAPS and SAPS, apart from significantly higher frequency of the deep vein thrombosis in pts with PAPS (p<0.04).

Conclusion: The clinical pictures of PAPS and SAPS are similar. Only deep vein thrombosis occurs more frequently in pts with PAPS. Some classic and novel aPLs occur more frequently in pts with SAPS than in PAPS, and maybe could become a biomarker of PAPS

Disclosure of Interests: Magdalena Drygowska: None declared, Andrzej Majdan: None declared, Maria Majdan: Speakers bureau: MSD, UCB, Abbvie, Roche


AB0178

TRANScriptional profiling of peripheral B cells in antibody-positive primary Sjögren’s syndrome reveals interferon signature and upregulated expression of genes which may be predictive of transformation to lymphoma and correlated to chronic pulmonary non-tuberculous mycobacterial (NTM) infection

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Background: Primary Sjögren’s syndrome (pSS) is the second most common systemic autoimmune disease (after RA), with a prevalence of about 0.5% in the general population and it occurs primarily in women at a ratio of women to men of 9:1. Key features of the disease include infiltration of salivary and lacrimal glands by lymphocytes, production of inflammatory cytokines, and the production of auto-antibodies. Nevertheless, systemic manifestations can arise in a proportion of pSS with pulmonary manifestation and higher incidence of NTM infection. Also, B-cell non-Hodgkin lymphoma (NHL) development represents a severe complication, affecting approximately 5% of patients. The risk of NHL occurrence in the setting of pSS, has been previously estimated to be 7-19 fold higher than the general population. B activation is one of the proposed hypotheses, that accord with the known biological findings, including hypergamaglobulinemia, presence of auto-antibodies including SSA/Ro60/TROVE2, SSA/Ro52/THIM2 and SSB/La48.

Objectives: B cells play a key role in the pathogenesis of pSS. The aim of this study was to analyze the transcriptome of B cells from patients with pSS and healthy controls to decipher the B-cell specific contribution to pSS.

Methods: RNA of negatively selected B cells from 5 ANA, SSA (both Ro60 and Ro 52), SSB and rheumatoid factor positive untreated female patients with pSS and 5 healthy controls was subjected to whole transcriptome sequencing. A false discovery rate corrected threshold of < 0.1 was applied to define differential gene expression.

Results: RNA-sequencing identified 56 and 23 up and down differentially expressed genes, respectively, and hierarchical clustering showed a clear separation between the two groups. Ingenuity Pathway Analysis revealed that these genes may play a role in interferon signaling (IFI35, IFIT1, OA51, MX1, STAT2, IFI35, IFITM1, IFG15, IFI27, IFI44L, IFI44, and PARP9), chronic mycobacterial infection (IFI35,IFI44,IFI44L,IFI44L,IFIT1,IFIT3,IFIT3,IFIT1,MXI,OA51,OA52,OA53,STAT2) and transformation to myeloproliferative disorders, especially B cell lymphomas (CD160, CD38, ENAM, FUT4, GADD45B, IFI35, IFI44, IFI44L, IFIT3, IFIT1, IFITM1, ISG15, JCHAIN, MX1, OA51, OA52, OASL, RG516, RNFP213, RSAD2, SAR52, SATB1, SMAD7, and STAT2).

Conclusion: Upregulated expression of type I and type II interferon (IFN)-induced genes was observed, establishing an IFN signature in pSS B cells. There are also genes that may play a role in other coconcomitant conditions like mycobacterial/NTM infection and higher risk for developing myeloproliferative conditions. This adds insight into the autoimmune process and suggests potential targets for future functional and prognostic studies.

REFERENCES


The transcription factors IKZF1 and IKZF3

**VALIDATION OF COMPLEX IMMUNOPHENOTYPING STRATIFICATION OF PATIENTS WITH LUPUS AND SJÖGREEN’S SYNDROME WITH THERAPEUTIC POTENTIAL**

Lucia Martin-Gutierrez 1,2, Hannah Peolharn 1, George Robinson 1,2, Giulia Varnier 1, Elizabeth Jury 1, Cozana Cunfit 1, UNIVERSITY COLLEGE OF LONDON, Rheumatology, LONDON, United Kingdom; 2UNIVERSITY COLLEGE OF LONDON, Arthritis Research UK Centre for Adolescent Rheumatology at UCLH, UCL and Great Ormond Street Institute of Child Health, LONDON, United Kingdom

Background: There is a current paucity in effective treatments for patients with primary Sjögren’s syndrome (pSS) and systemic lupus erythematosus (SLE). Their overlapping symptoms mean that they are often treated with similar biologic therapies, despite being distinct diagnoses. Our pilot research sought to stratify patients by novel, complex immune signatures, to potentially facilitate a more personalised approach to prescribing medication, irrespective of clinical diagnosis. From a cohort of 40 patient patients with SLE, pSS or combined SS/SLE, and 33 healthy controls; five distinct clusters were originally identified.

**Objectives:**
- Here we aimed to validate the original patient endotypes from our pilot data with a new patient cohort, and refine the identified clusters to be of more realistic clinical benefit.

**Methods:**
- A new cohort of patients with SLE (n=32), pSS (n=31) and SS/SLE (n=15) donated peripheral blood samples while attending appointments at UCLH clinics. None had received B-cell depletion therapy in the preceding 48 months. Complex phenotyping of peripheral T and B-cell subsets was performed by flow cytometry. Unsupervised clustering, statistical comparison to healthy and Receiver Operator Characteristic (ROC) analysis, as per our previous work, were used to stratify patients using immune signatures into distinct endotypes considering only those markers where sensitivity and specificity were above 80% (AUC > 0.80). Clinical diagnoses and symptoms treatment did not differ significantly between clusters.

**Results:**
- Five distinct endotypes across the three disease groups were identified after unsupervised clustering of CD19+ B-cell, CD4+ and CD8+ T-cell subsets. Two of these clusters serve to validate groupings from our original data: one with a distinct B cell fingerprint (BMI, IBr5 and Total CD19+) with AUC>0.87, AUC=0.81 and AUC>0.83 respectively, and another with a T cell fingerprint (Total CD4+, Total CD8+, CD8+ naïve, CD8+ effector memory T cell subsets) with AUC>0.80 for all of them. Clinical diagnoses and symptoms treatment did not differ significantly between clusters.

**Conclusion:**
- Our results demonstrate a novel method to re-classify patients using clustered immune phenotype abnormalities. Two distinct groups demonstrated either B or T-cell immunophenotypes, likely reflective of their underlying immunopathogenesis. Stratification by patient endotype has the potential to facilitate a better-informed selection of biologic therapeutics for individual patients; and highlights pathways for further mechanistic research.

**Acknowledgement:**
- British Sjögren’s syndrome Association and Versus Arthritis

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.5696

**AB0180**

**ASSOCIATION BETWEEN SINGLE NUCLEOTIDE POLYMORPHISMS (SNPs) OF THE BAFF GENE AND FATIGUE IN PRIMARY SJÖGREEN’S SYNDROME**

Christina Maria Flessa 1, Adriano Nezio 1, Evangelia Zampeli 1, Haralampos M. Moutsopoulos 1, 2, 3, 4, Medical School, National and Kapodistrian University of Athens, Department of Physiology, Athens, Greece; 2Medical School, National and Kapodistrian University of Athens, Department of Pathophysiology, Athens, Greece; 3Academy of Athens, Athens, Greece; 4National and Kapodistrian University of Athens, School of Medicine, Joint Academic Rheumatology Program, Athens, Greece

**Background:**
- Primary Sjögren’s Syndrome (SS) is characterized by B lymphocyte hyperactivity with B cell activating factor (BAFF) acting as an important regulator. Single Nucleotide Polymorphisms (SNPs) of the BAFF gene have been implicated in the pathogenesis of several autoimmune diseases including lupus and SS both of which are characterized by heightened fatigue levels, often compromising quality of life.

**Objectives:**
- To explore potential associations between several BAFF gene SNPs and fatigue status experienced by primary SS patients.

**Methods:**
- Fatigue status was assessed by Functional Assessment of Chronic Illness Therapy–Fatigue (FACIT-F) scale in 178 primary SS patients. Five SNPs (rs9514827, rs1041569, rs9514828, rs1224141, rs12583006) of the BAFF gene were tested in DNA extracted from peripheral blood of all patients enrolled in the study using the RFLP-PCR method. A cut-off value of -0.30 was used, which indicated a severe fatigue. Analysis of BAFF SNPs in association with fatigue levels was performed by the online platform SNPStats.

**Results:**
- The frequency of T/T genotype of both rs9514828 and rs1224141 was reduced in primary SS patients with severe fatigue compared to those without
(17.9% vs 36.7%, p=0.0094 and 51.8 vs 69.2%, p=0.027, respectively. The corresponding ORs [95%CI] in the dominant model were 0.38 [0.17-0.82] and 0.48 [0.25-0.92], respectively. No statistically significant associations between fatigue status and other SNPs tested were detected.

**Conclusion:** We report novel associations between genetic makeup and primary SS-associated fatigue with the rs9514828 and rs1224141 BAFF TT genotypes decreasing the likelihood of fatigue development among these patients. These findings need to be validated in multi-center studies.

**REFERENCES**


**Acknowledgement:** This research is co-financed by Greece and the European Union (European Social Fund-ESF) through the Operational Programme «Human Resources Development, Education and Lifelong Learning» in the context of the project “Strengthening Human Resources Research Potential via Doctorate Research” (MIS-5000432), implemented by the State Scholarships Foundation (IKY).

**Disclosure of Interests:** Christina Maria Flessa: None declared, Adrianos Nezos: None declared, Evangelia Zampeli Speakers bureau: Roshe, Astazyme.


**AB0182 RECEPTOR ACTIVATOR OF NUCLEAR FACTOR-KAPPA B LIGAND (RANKL)/RANK AND OSTEOPROTEGERIN (OPG) PATHWAY ACTIVATION IN SJOGREN’S SYNDROME**

Charalampos Skarlis1, Eleni Palli1,2,3, Adrianos Nezos1, Clio Mavragani1,2,3, Michael Koutris2,3, Medical School, National and Kapodistrian University of Athens, Department of Psychology, Athens, Greece, 2Medical School, National and Kapodistrian University of Athens, Department of Pathophysiology, Athens, Greece, 3Joint Academic Rheumatology Program, National and Kapodistrian University of Athens, School of Medicine, Athens, Greece

**Background:** Primary Sjögren’s syndrome (SS) is an autoimmune exocrinopathy characterized by chronic salivary and lacrimal glands dysfunction. Recent studies suggest that activation of the receptor activator of nuclear factor-kappa B ligand (RANKL)/RANK and osteoprotegerin (OPG) pathway is implicated in the development of autoimmunity.

**Objectives:** The aim of this study is to investigate the contribution of RANK/RANKL/OPG pathway in primary SS pathogenesis.

**Methods:** Sixty-six primary SS patients fulfilling the American/European criteria and 13 subjects with oral and/or ocular dryness without satisfying the aforementioned criteria (sicca controls, SC) and 11 healthy controls (HC) have been enrolled. RANKL and OPG serum levels were determined by ELISA in 29 SS patients and 11 HC. Total RNA was extracted from minor salivary glands biopsies (MSG) from 43 SS patients and 13 SC and RANKL mRNA expression was assessed by qRT-PCR. Protein expression of RANKL was determined by Western Blot and immunohistochemistry (IHC) in total protein extract and paraffin embedded tissue respectively, derived from MSG biopsy of 6 primary SS patients and 5 SC. Statistical analysis was performed with SPSS 24.0 package.

**Results:** Increased serum levels (pg/ml) of RANKL (mean±SD=4.197±897.6 vs mean±SD=5±1897.6 vs 495±897.6 vs 2±1897.6, p=0.03) and OPG (mean±SD=173±5 vs 173±8 vs 173±9 vs 173±9, p=0.01) were detected in SS patients compared to HC. Higher RANKL at both mRNA and protein level by IHC were detected, in MSG derived from primary SS patients compared to SC. RANKL protein expression was significantly increased in MSG biopsies from primary SS patients compared to SC by Western Blot (mean±SD=2.46±1.86 vs mean±SD=0.5±0.823, p=0.0335).

**Conclusion:** Increased serum levels, mRNA and protein expression of RANKL in association with increased OPG titers in SS patients compared to controls, suggest that the activation of RANK/RANKL/OPG pathway contributes to SS pathogenesis.

**REFERENCES**


**Acknowledgement:** Research Grant from the Greek Rheumatology Society and Professional Association of Rheumatologists

**Disclosure of Interests:** None declared


**AB0183 THE ROLE OF THE PHOSPHOLIPASE LP-PLA2 ACTIVITY IN SJOGREN’S SYNDROME RELATED LYMPHOMAGENESIS: A NEW SERUM BIOMARKER?**

Eleni Kotsifaki1, Adrianos Nezos1, Anna Pasmou1, Panayiotis Garantziotis2, Michael Koutris1, Clio Mavragani1,2,3, Michael Koutsilieris1, Medical School, National and Kapodistrian University of Athens, School of Medicine, Athens, Greece

**Background:** One of the major complications of primary Sjogren’s syndrome (SS) is the development of B-cell non-Hodgkin’s lymphoma (B-NHL). The contribution of tissue macrophages in the pathogenesis of B-NHL, based on previous histopathological studies, appears to be significant. Extracellular lipoprotein-associated phospholipase A2 (LP-PLA2) is a product of tissue macrophages which is found in the circulation associated with lipoproteins and has been involved in both cardiovascular and malignant diseases, including B-NHL lymphoma.

**Objectives:** The purpose of the current study was to investigate the role of serum LP-PLA2 activity as a potential biomarker for the development of B-NHL in the setting of primary SS.

**Methods:** Extracellular LP-PLA2 activity was determined by measuring [3H]PAF degradation products in liquid scintillation counter in serum samples obtained from 48 primary SS patients, 9 primary SS patients complicated by lymphoma (SS-lymphoma) and 40 healthy controls. Similar results were obtained in an independent cohort of 25 primary SS patients, 17 primary SS-lymphoma and 10 healthy controls, when a commercially available ELISA kit was implemented. Statistical analysis was performed with the Graph Pad software.

**Results:** The activity of LP-PLA2 was statistically significant increased in patients with primary SS-lymphoma compared to primary SS patients without lymphoma [mean±SD (nmol/min/ml): 62±1±3 vs 47±1±4, p=0.003 and 19±7±3 vs 15±7±3, p=0.06, respectively], as well as healthy controls [mean±SD (nmol/min/ml): 62±1±3 vs 52±1±6, p=0.03 and 19±7±4 vs 15±7±3, p=0.06, respectively]. No statistical significant differences in LP-PLA2 activity were detected between primary SS patients without lymphoma development and healthy controls.

**Conclusion:** Evaluation of extracellular LP-PLA2 activity in primary SS patients could be a useful serological biomarker for B-NHL development in the context of primary SS.

**REFERENCES**


**Disclosure of Interests:** None declared

AB0184
FLOWS CYTOMETRIC IMMUNOPHENOTYPING OF SALIVARY GLANDS IN PRIMARY SJÖGREN’S SYNDROME
Paul Milne1, Anastasia Resteu1, Aleksandra Ivovic2, Emmanuella Traianos3, David Storey4, Jessica Tam5, Richard Siegel6, Peter Campbell7, Wan Fai Ng8, Matthew Collin4. 1Newcastle University, Human District Cell Lab, Institute of Cellular Medicine, Newcastle upon Tyne, United Kingdom; 2Wellcome Sanger Institute, Cambridge, United Kingdom; 3Newcastle University, Musculoskeletal Research Group, Institute of Cellular Medicine, Newcastle upon Tyne, United Kingdom; 4National Institutes of Health, Autoimmunity Branch, Bethesda, United States of America

Background: Primary Sjögren’s Syndrome (PSS) is a common autoimmune disease of unknown aetiology. It is characterised by inflammatory infiltration of exocrine glands, development of a sicca syndrome and a 20-fold increase in the risk of developing lymphoma. Standard pathological evaluation is based on a lymphocyte ‘focus score’ but little is known about the composition of the lymphoid infiltrate or its relationship to disease markers such as autoantibodies and the risk of lymphoma.

Objectives: The aim of the study was to use flow cytometry to characterise the lymphoid infiltrate in more detail.

Methods: Salivary glands were collected from 103 subjects attended the Newcastle Sjögren’s clinic who had undergone minor salivary gland biopsy as part of the diagnostic investigations which also include testing for anti-SSA/SSB antibodies, Schirmer’s tests and unstimulated oral salivary flow. 70 with confirmed PSS, 15SLE patients; 20 early-stage PSS and 18 with non-Ss. Salivary glands were digested in collagenase for 3 hours and sort-analysed using a BD Biosciences FACSFusion flow cytometer. Sorted cells from 6 patients were Giemsa stained to observe cell morphology. All subjects have given their written informed consent according to the principles of Helsinki and the project has received local REC approval.

Results: Salivary glands contain multiple lymphoid populations including CD19+ B cells, CD19+CD308+ plasmablasts, CD19-CD308+ plasma cells, and predominately central memory CD4+ and CD8+ T cells. The focus score is associated with an increase in the total number of lymphocytes of up to 10-fold. In particular there is a striking increase CD19-CD308+ cells with restricted kappa light chain expression associated with the most advanced cases. By morphology these cells have the appearance of plasma cells with frequent Russell bodies and occasional binucleated forms.

Conclusion: Flow cytometry of dispersed salivary gland demonstrates and associates between lymphoid cells and the focus score in PSS patients. The dominant B cell population in PSS salivary gland is a CD19-negative tissue plasma cell with evidence of kappa light chain restriction in advanced disease.


AB0185
INTERFERON-γ AMPLIFIES IMMUNE RESPONSE MEDIATED BY TYPE I INTERFERONS IN PAEDIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS AND CORRELATES WITH DISEASE ACTIVITY
Gian Marco Moneta1, Claudia Bracaglia1, Ivan Caiello1, Rafaele Pecoraro1, Chiara Farroni1, Fabio Basta1, Luisa Bracci-Laudiero2, Riletta Carsetti2, Fabrizio De Benedetti3, Emiliano Marsaco4, Babimbo Gesu5, Division of Rheumatology, Rome, Italy; 2Babimbo Gesu, B Cell Physiopathology Unit, Rome, Italy

Background: Paediatric systemic lupus erythematosus (pSLE) is an autoimmune disorder of childhood characterized by the production of autoantibodies against nuclear antigens. In the last decade, several studies showed an up-regulation of genes induced by type I interferons (IFNs) in peripheral blood and tissues of pSLE patients1. It has been reported that the expression of this group of genes, known as the type I IFN signature, correlates with disease activity2. More recently, also the type II interferon (IFNγ) has been implicated in pSLE; however, its precise role has not been clarified yet3.

Objectives: To investigate the role of IFNγ in the pathogenesis of pSLE, IFNγ-induced genes (CXCL9, IDO1) and IFNγ itself were evaluated. Then we analysed cytokines production in supernatants. IFNγ was up-regulated in pSLE patients with active disease (n = 21) compared to healthy donors (HD) and pSLE patients with inactive disease (n = 17). The type II IFN score correlated with the SLEDAI (r = 0.64, P < 0.01). As previously reported, also the type I IFN score correlated with SLEDAI (r = 0.67, P < 0.01). We also found increased serum levels of CXCL9 and CXCL10 in pSLE patients compared to HDs (P < 0.05).

In order to study a possible cross-talk between type I and type II IFNs, we stimulated in vitro HD PBMCs with recombinant IFNα2b and IFNγ for 6 hours: we analysed the expression levels of type I and type II IFN signature and assessed the production of CXCL9 and CXCL10 in the supernatants. IFNα2b strongly up-regulated the expression level of both IFNα and IFNγ. On the other hand, IFNγ induced the expression of the 6 IFNα-related genes. IFNα, but not IFNα2b, induced the release of CXCL9 in supernatants. Both IFNα and IFNα2b produced the induction of CXCL10. IFNα also up-regulated the expression levels of both TLR7 and TLR9, two potent inducer of IFNα. Finally, whole blood of pSLE was incubated with an anti-IFNα neutralizing antibody for 24 hours: the type II signature was significantly downregulated (P < 0.05), whereas the type I signature was reduced without reaching statistical significance.

Conclusion: Our data suggest a potential role of IFNγ in the pathogenesis of pSLE. IFNγ-induced genes in whole blood and CXCL9 in serum are increased in pSLE patients. Type I and type II signatures are not strictly interferon-specific as IFNγ can induce the expression of type I genes. Moreover, blocking of IFNγ in the blood of pSLE patients reduces the type II signature confirming the presence of IFNγ in the blood of pSLE patients. IFNα also induces the expression of TLR7 and TLR9, and IFNα induces the expression of IFNα, thus establishing a positive crosstalk between IFNα and IFNγ that potentiate their reciprocal biological activity in pSLE.

REFERENCES

Disclosure of Interests: Gian Marco Moneta: None declared. Claudia Bracaglia: None declared. Ivan Caiello: None declared, Rafaele Pecoraro: None declared. Chiara Farroni: None declared, Fabio Basta: None declared, Luisa Bracci-Laudiero: None declared. Riletta Carsetti: None declared, Fabrizio De Benedetti: Grant/research support from: Abbvie, Scibi, Novimmune, Roche, Novartis, Sanofi, Pfizer, Emiliano Marsaco: None declared


AB0186
CORRELATIONS BETWEEN RENAL TRANSCRIPTOMIC PROFILES AND OUTCOMES IN A MOUSE MODEL OF SYSTEMIC LUPUS ERYTHEMATOSUS
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Background: Factors contributing to poor renal outcomes in lupus nephritis (LN) are poorly understood. In our previous research, we found an association between the presence of active effector cells in the lupus kidney and disease severity. Here we investigated correlations between patterns of renal genes expression and biological parameters of renal disease activity in a mouse model of systemic lupus erythematosus (SLE).

Methods: We collected blood, urine, kidneys and spleens from 33 B6/Sle1 SLE2.Sle3 congenic mice, before disease onset at 3 months (n=8), and at different stages of disease progression, at 6 (n=7), 9-10 (n=12) and 17-18 (n=5) months. RNA was extracted from kidneys, and hybridized on Mouse Gene 2.0 ST exon arrays. Unsupervised hierarchical clustering studies and pathways analyses were performed on Genespring and DAVID softwares. Spleen and kidney C/D T cell activation and differentiation markers were evaluated by flow cytometry (CD8, CD69, CD62L, CD44, CD122, CD25, CD44, CCR7, CD279, CD152, CD11a, CD103). Plasma urea and albuminuria were measured by immunoassay.

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Results: 712 (out of 33,793) transcripts were overexpressed in kidneys from diseased mice (age > 6 months). These transcripts were significantly enriched in the following pathways: response to type I interferons, antigen processing and presentation, activation and regulation of B cells, complement activation, and regulation of cytokotically mediated by T cells. Proportions of renal CD8 T cells with an effector phenotype were significantly increased in the kidneys from 6 months and older compared to younger mice, and compared to paired spleens. Proportions of renal effector CD8 T cells correlated significantly with transcripts involved in interferon signature, adaptive immune responses, cytotoxic T cell, chemotaxis, and correlated negatively with pathways associated with renal tubular cell functions. Finally, we found a correlation between biological parameters of kidney function (plasma urea, albuminuria) and transcripts involved in pro-fibrotic pathways, chemokines and adaptive immune responses.

Conclusion: Our results confirm the link between the presence of activated immune effectors in the kidney and renal outcomes in a mouse model of SLE, similar to our previous observations in human LN, and warrant further functional studies on the role of kidney-infiltrating T and B cells in this model.

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Disclosure of Interests: None declared


AB0187 CAN ARTIFICIAL INTELLIGENCE REPLACE MANUAL SEARCH FOR SYSTEMATIC LITERATURE REVIEW ON CUTANEOUS MANIFESTATIONS IN PRIMARY SJÖGREN’S SYNDROME?

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Background: Manual systematic literature reviews are becoming increasingly challenging due to the sharp rise in publications. The task is particularly daunting when the study topic is complex.

Objectives: The primary objective of this literature review was to compare manual and in-house computer software retrieval of publications on the cutaneous manifestations of primary Sjögren’s Syndrome (pSS). The secondary objective was to evaluate the prevalence of cutaneous manifestations in pSS.

Methods: We compared manual searching and searching with the in-house computer software BIBOT (1) designed for article retrieval and analysis. Both methods were used for a systematic literature review on a complex topic i.e., the cutaneous manifestations of pSS. Articles published in French or English between 1 January 1990 and 30 May 2018 were sought.

Results: The manual search retrieved 855 articles and BIBOT 1042 articles. In all, 202 articles were then selecting by applying exclusion criteria. Among them, 155 were retrieved by both methods, 33 by manual search only, and 14 by BIBOT only. Further selection was performed by reading the 202 articles, of which 54 were deemed relevant, including 23 providing data on the prevalence of one or more cutaneous signs in a cohort of patients with pSS. Cohort sizes and the nature and prevalence of cutaneous manifestations varied across publications. In all, 52 cutaneous manifestations were reported, of which the most common were cutaneous vasculitis (561 patients), xerosis (651 patients), and annular erythema (215 patients).

Conclusion: Agreement was good between the two methods. BIBOT was faster and automatically classified the articles in a chart. Combining the two methods retrieved the largest number of publications. The prevalence of cutaneous manifestations in patients with pSS varied considerably across studies. The advanced machine learning techniques used in artificial intelligence hold promise for literature reviews.

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AB0188 MOLECULAR NETWORKS IN MONOCYTES FROM SYSTEMIC LUPUS ERYTHEMATOUS PATIENTS RELATED TO THEIR PHYSIOPATHOLOGY. MODULATORY EFFECTS OF ANTI-DSDNA ANTIBODIES AND MOLECULAR MECHANISMS UNDERLYING IN VIVO STATIN TREATMENT

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Objectives: 1. To characterize the miRNAs and microRNA transcripts of monocytes from systemic lupus erythematosus (SLE) patients and their association with the pathophysiology of the disease. 2. To evaluate the role of anti-dsDNA antibodies in the regulation of these processes. 3. To investigate the molecular mechanisms involved in the efficacy of Fluvastatin in preventing the atherothrombotic risk.

Methods: Monocytes from peripheral blood of 81 SLE patients and 40 healthy donors (HD) were purified by negative immunomagnetic selection. Then, gene expression microarray (Agilent G4122F platform) and nCounter microRNA expression arrays (Nanostring) were performed. Functional categorization of altered genes and miRNAs was made using IPA software, and interaction networks were identified. Genes and miRNAs integrating the networks were validated in the whole cohorts by RT-PCR. Predicted miRNA-mRNA interactions were tested by microRNA over-expression or inhibition experiments. Serum and cellular inflammatory and oxidative profiles were evaluated by multiplex assay, PCR and specific commercial kits, respectively; phosphorylation status of intracellular proteins was analyzed by PathScan array. To evaluate the clinical significance of the parameters analyzed, correlation and association studies were performed. Mechanistic studies were developed to typify the specific effects of the anti-dsDNA antibodies on monocytes. Besides, the beneficial effects of ex vivo Fluvastatin treatment on the monocyte molecular profiles were assessed.

Results: Microarray identified 553 altered genes in SLE monocytes. Relevant biofunctions and disorders on which these genes were involved included inflammatory, immunological, cardiovascular, neurological, renal and reproductive diseases. Analysis of miRNA profiles showed altered expression of 35 miRNAs in SLE monocytes. Sixty-one genes were inversely correlated and predicted as CVD-related target genes of 26 differentially expressed miRNAs. Transfection studies confirmed the relationship between specific miRNAs and their identified target genes.

Association of these genes and miRNAs with the anti-dsDNA positivity, early atherosclerosis and nephropathy, along with correlations with disease activity (SLE-DAL), activation of some intracellular signaling proteins, and levels of serum inflammatory and oxidative markers were demonstrated. In vitro studies demonstrated the specific modulation of several genes/miRNAs by anti-dsDNA, along with the increase of prothrombotic and proinflammatory mediators, the induction of apoptosis and the phosphorylation of intracellular proteins participating in renal and CVD-related signaling pathways. Besides, treatment of HD-monocytes with SLE patients’ serum after Fluvastatin supplementation prevented the proinflammatory altered gene/miRNA profiles induced by serum from those patients before treatment.

Conclusion: 1. Gene and microRNA expression profiles allowed the identification of relevant genes and pathways altered in monocytes of SLE patients, associated with the pathogenesis of the disease, and modulated by anti-dsDNA. 2. Specific microRNA-miRNA regulatory networks control the biological processes and factors related to the CV pathology in SLE, which are prevented by Fluvastatin treatment.

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AB0189 DECREASED URINE SEMAPHORIN 3A SECRETION PREDICTS THE EXTENT OF RENAL DAMAGE IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Semaphorins are a family of proteins, involved in axon guidance, malignancy spread and angiogenesis. Semaphorin 3A (sema3A) is recognized also as ‘immune semaphorin’, it is expressed on regulatory T cells and has been
shown to enhance their inhibitory effect of CD4+ T cell pro-inflammatory function and replication. We have reported a decreased serum levels of sE3A in systemic lupus erythematosus (SLE) compared to controls and in correlation with SLE disease activity [1]. sE3A was found to be over expressed in podocytes and epithelial cells in animal models with diabetic nephropathy. Increased urinary sE3A was also detected in diabetic patients with proteinuria and in contrast-induced acute renal injury [2-3].

Objectives: To assess urine sE3A secretion in SLE patients with and without renal involvement compared to rheumatoid arthritis patients as disease control and healthy controls.

Methods: 50 ml of fresh urine samples were collected, centrifuged and the supernatant was then concentrated up to 50 times the initial concentration and subjected to kit. Human sE3A ELISA kit (MBST32622, San Diego, CA, USA).

Results: Thirty-eight lupus patients fulfilling the 2012 SLICC criteria were recruited, 33 (87%) of whom were women, at a mean age of 35±12 years. Eight patients had active nephritis (21%) and additional 5 had a history of nephritis but were in remission. APLA was diagnosed in 13 (34%) of patients. Disease activity was evaluated by the Systemic lupus erythematosus disease activity index 2000 (SLEDAI 2K) and 8.2±7.7.

Sema3A was lower in lupus patients compared to rheumatoid arthritis and healthy controls, 4.9±3.9 ng/mL, 8.5±2.7ng/mL, 9.85±1.7ng/mL, p=0.0006. Sema3A in SLE patients demonstrated lower urine sE3A concentration compared to lupus patients without renal involvement 4.3±3.4 ng/mL, 6.5±3.8 ng/mL, p=0.03. Sema3A reversely correlated with proteinuria r=-0.43 p=0.006 and SLEDIA2K -0.3, p=0.04, but not with creatinine concentration, disease duration and complement concentration. There was no difference in urinary sE3A between SLE patients with or without APLA syndrome.

Conclusion: Urinary excretion of Sema 3A was found to be decreased in the SLE patients with renal disease, reversely correlating with disease activity and proteinuria. These findings are in line with previous reports of decreased serum level of Sema3A in SLE, that may result in reduced efficacy of regulatory T cells, driving autoimmunity and kidney damage. The discrepancy between low sE3A urinary excretion in SLE nephropathy and increased urinary secretion in other "non-auto immune" conditions with renal damage, suggests that sE3A in the kidneys is protective in autoimmune diseases and detrimental in "non-auto immune" conditions. This differential effect of sE3A may have to do with different populations of effector cells and different expression of sE3A receptors (nuropilin1). Further studies should evaluate semaphorin 3A role in lupus nephritis and its potential as a treatment option.

REFERENCES

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AB0190 CROSSTALK BETWEEN SALIVARY GLAND EPITHELIAL CELLS AND B LYMPHOCYTES IN PRIMARY SJÖGREN’S SYNDROME

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Background: Primary Sjogren’s syndrome (pSS) is an auto-immune disorder characterized by lymphoplastic infiltrates and destruction of the salivary glands. Mechanisms leading to B lymphocytes chronic activation remain partially understood and we assumed that salivary gland epithelial cells (SGECs) might play a key role in B lymphocytes activation and differentiation.

Objectives: We aimed to study the interactions between SGECs from pSS patients or controls and B lymphocytes.

Methods: Patients with pSS according to 2016 EULAR/ACR criteria and controls with sicca symptoms were studied. RNASeq analysis was performed on SGECs and B lymphocytes sorted from salivary gland and blood using a FACS ARIA. Enrichment analysis was performed using Ingenuity Pathway Analysis software. Validation of the results was performed by qPCR (Biomark technology).

Cultured SGECs from pSS patients (n=6) and controls (n=6) were co-cultured with B lymphocytes sorted from healthy donors blood and stimulated with or without Polycl, INFα or IFNγ for 5 days. Transwell assays were performed. Survival, activation (CD38 positivity) and differentiation of B lymphocytes were assessed at day 5 by flow cytometry.

Results: The RNASeq analysis of B lymphocytes sorted from salivary gland showed an up-regulation of CD40 and CD48 which are involved in their activation. The analysis of sorted SGECs highlighted IL-7, interferon (IFN) signaling pathways and genes potentially involved in immune responses, including HLA-DR, BST2 (bone marrow stromal cell antigen 2) and BAFF-R. Co-culture experiments showed an increase of B lymphocytes viability when co-cultured with SGECs compared to B lymphocytes cultured alone (p<0.05). Co-culture with SGECs from pSS was more likely to induce higher activation of B lymphocytes compared to SGECs from controls, assessed by the percentage of CD38+ B lymphocytes (significant after stimulation with Polycl (p<0.01) (Figure 1A). Similarly, SGECs from pSS were more likely to induce higher activation of B lymphocytes compared to controls, assessed by the percentage of CD38+ B lymphocytes – percentage of alive cultured alone B lymphocytes) without stimulation or stimulated with Polycl (p<0.01) (Figure 1B). To determine whether the activation of B lymphocytes and SGECs required a direct cell contact, we used transwell experiments. Preliminary results suggested that the increase of B lymphocytes viability could depend mostly on soluble factors that are currently being identified and will be communicated at the congress.

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AB0191 ENDOTHELIN-I LEVEL IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME, ITS ASSOCIATION WITH ENDOTHELIAL DYSFUNCTION AND ATEROSCLEROSIS

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Background: It is known that endothelin-I is one of the leading factors in the development of coronary artery disease, acute myocardial infarction, atherosclerosis of cerebral and peripheral vessels, pulmonary hypertension, ischemic lesion...
of the brain vessels etc. Patients with rheumatic diseases also have an elevation of endothelin-1 in serum. But it remains unclear whether the endothelin-1 level may reflect endothelium dysfunction in patients with antiphospholipid syndrome (APS) and serve as an early marker of atherosclerosis.

**Objectives:** The aim of the study was to evaluate the endothelin-1 concentration, its association with antiphospholipid antibodies and atherosclerotic vascular lesions in patients with APS.

**Methods:** According to our observation, there were 82 patients, among which 34 (41.6%) with primary antiphospholipid syndrome (PAPS) and 48 (58.4%) with secondary antiphospholipid syndrome (SAPS). The control group consisted of 37 practically healthy persons. The groups of patients were comparable by age, sex, and duration of the disease. The APS diagnosis was established according to the international classification criteria (2006). The content of the anticardiolipin antibodies IgG, anti-beta2-glycoprotein-1 antibodies IgG, IgA, IgM and endothelin-1 were determined by the immune enzyme method using commercial sets of Trinity Biotech Capita USA - Ireland, ORGenTec GmbH Germany and «Endothelin-1» (Cormay, England). All patients were assessed for the level of endothelium-dependent vasodilation (EDVD), the thickness of the intima-media complex of the common carotid artery (IMT), the presence of atherosclerotic plaque (AP) and clinical manifestations of vascular involvement.

**Results:** The analysis of endothelin-1 levels has shown that its content was in 2.2 times higher in patients with APS than in the control group. The proportion of people with optimal endothelin-1 content was twice lower, and the proportion of people with extremely high and high rates was 1.6 and 5.3 times higher, respectively, among patients with APS, than in the control group. Also differences in the endothelin-1 level have been established depending on the type of APS. The content of endothelin-1 was significantly higher (1.3 times) in patients with PAPS, than in PAPS. Among the patients with SAPS, the proportion of patients with an optimal level of endothelin-1 was 1.7 times lower, and the proportion of patients with high levels was 1.8 times higher than in patients with PAPS. The significantly lower endothelin-1 level was recorded in patients with highly positive antibodies to cardiolipin and beta-2 glycoprotein-1. Correlation analysis has shown direct correlation between anticardiolipin antibodies of the IgG class and anti-beta2-glycoprotein-1 antibodies and endothelin-1 concentration (n=0.35 and 0.34). High endothelin-1 level was a factor of structural and functional atherosclerotic changes of the heart and blood vessels in patients with APS. IMT increasing and EDVD decreasing were from 1.7 to 6.6 times more frequent among patients with high endothelin-1 level (>10 pg/ml), than patients with optimal endothelin-1 level (≤5.0 pg/ml).

**Conclusion:** Thus, the obtained data has showed that the excess concentration of endothelin-1 is a circulating marker of early atherosclerosis, since it is closely associated with subclinical manifestations of atherosclerotic vascular damage.

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**AB0193**  
**THE EFFECTS OF NON-INVASIVE VAGUS NERVE STIMULATION ON FATIGUE AND IMMUNE RESPONSES IN PATIENTS WITH PRIMARY SJÖGREN’S SYNDROME**

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**Background:** Primary Sjögren’s syndrome (pSS) sufferers have rated physical and mental fatigue ‘brain fog’ as the most important symptoms needing improvement. Previous data from our group suggest that stimulation of the vagus nerve can invoke immunological responses and concurrently an improvement of patient reported symptoms of fatigue.

**Objectives:** This follow up study uses the gammaCore device (electroCore) and a sham device to assess the effects of non-invasive vagus nerve stimulation (nVNS) on patient reported symptoms of fatigue in pSS. In addition, immunoregulatory tests were used to assess the effect of nVNS on short term memory, executive function and attention.

**Methods:** 40 pSS participants were assigned to use active (n = 20) or sham (n = 20) nVNS devices. Participants and research staff were blinded to the active/ sham device assignment. The participants were instructed to use the device twice daily for a study period of 56 days. The following patient reported measures of fatigue and neuropsychological tests were collected at baseline and day 56; Profile of Fatigue (PRO-F, Physical and Mental), visual analogue scale (VAS) of abnormal fatigue, trail making, Digit Symbol Substitution Test (DSST), Stroop test and digit span. 7 subjects were excluded from the analysis due to withdrawal from the study. Changes in fatigue and test scores from baseline to day 56 were compared between devices using t-tests.

**Results:** Physical fatigue was significantly reduced between baseline and day 56 in the active group but not the placebo group (p = 0.047). The mean reduction in physical fatigue was 30% and 6% for the active and sham arms respectively (Figure 1). In both the active and sham subject groups there were no significant changes in the patient reported mental fatigue or neuropsychological test scores. Conclusion: This sham controlled scientific study of vagus nerve stimulation in pSS suggests nVNS may improve patient reported symptoms of physical fatigue, which is consistent with our published data. There were no improvements in the neuropsychological test scores which is consistent with no improvements in patient reported mental fatigue. nVNS has been shown to activate the anti-inflammatory reflex, therefore assessment of peripheral inflammatory markers may help our understanding of nVNS, inflammation and fatigue.

**REFERENCE**


BTLA Expression Is Reduced on SLE B Cell Subsets

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Background: B- and T-lymphocyte attenuator (BTLA/CD272) is a co-receptor constitutively expressed on B cells [1, 2]. Upon B cell activation via the B cell receptor (BCR), BTLA co-localizes with Src homology region 2 domain-containing phosphatase-1 (SHP-1) and thus negatively regulates BCR signaling [2]. A recent study found that CD4+ T cells from SLE patients fail to upregulate BTLA upon activation [3], however, data on BTLA expression and function for B cells in autoimmunity is missing.

Objectives: To assess BTLA expression on conventional naïve (CD20+CD27+), conventional memory (CD20+CD27+) B cells and on CD27+CD38+ expressing plasma cells (PC) in peripheral blood mononuclear cells (PBMCs) of patients with systemic lupus erythematosus (SLE) and healthy donors (HD).

Methods: PBMCs were isolated from EDTA blood taken from 7 female SLE patients (age 38, mean disease activity 5 (SLEDAI)) and 6 female HD (mean age 28) by Ficoll density gradient centrifugation according to the manufacturer’s protocol. Cells have been stained and expression of BTLA was assessed by flow cytometry.

Results: Analysis of BTLA surface expression on B cell subsets in SLE patients and HD revealed decreased expression of BTLA on naïve SLE B cells (p=0.0173, Mann-Whitney U Test (MWU), BTLA median fluorescence intensity (MFI) 9006±1450) compared to naïve HD B cells (11957±941). A similar tendency was found for memory SLE B cells (p=0.0823 MWU) compared to HD memory but not SLE PC and HD PC. Remarkably, an inverse correlation was found for BTLA expression on naïve SLE B cells and SLE PC with Siglec-1 expression on monocytes (p=0.0333 Spearman’s rank correlation (SRC) naïve B cells, p=0.0167 PC), a marker for interferon signature, and the same trend was seen for memory SLE B cells (p=0.0583 SRC). Inverse correlation of BTLA expression was also found with disease activity (SLEDAI) with these B cell populations but did not reach significance (p=0.0583 naïve B cells, p=0.1361 memory B cells, p=0.0833 PC).

Conclusion: Herein, we document that B cell subsets of SLE patients express lower levels of the negative regulator BTLA than HD. Additionally, an inverse correlation between BTLA expression on B cell subsets and Siglec-1 on monocytes were found suggesting its involvement in disease and consideration BTLA as therapeutic target in SLE. We hypothesize that reduced BTLA expression is a feature of post-activated B cells. Further studies need to delineate functional properties of BTLA expression and activation in autoimmune B cells.

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The Impact of Ketogenic Diet and High-Fat-High-Glucose Diet in Pristane Induced Lupus-Like Nephritis Murine Model

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Background: Systemic lupus erythematosus is a chronic systemic inflammatory disease which commonly invokes kidneys[1]. Aside from the use of conventional immunosuppressants, dietary components and metabolites may likely affect our immune system.

Objectives: An interest in the anti-inflammatory property of ketogenic diet (KD) has recently come to attention. It not only alters the balance between Th17 and Treg cells[2], its metabolite, beta-hydroxybutyrate was known to block NLRP3 inflammasome-mediated inflammation[3-6]. High-fat-high-glucose diet (HFGD), on the other hand, was known for a proinflammatory property. Aim to understand the immune modulatory effect of KD and HFGD in cases with systemic lupus erythematosus, a chronic systemic inflammatory disease with glomerulonephritis, pristane induce lupus like nephritis murine model was used.

Methods: Pristane induced lupus nephritis mice were divided in to groups fed with regular chow (CD), KD and HFGD along with healthy controls. The diets were kept for 6 months with regular body weight and urine protein monitoring. Serum samples were collected for metabolic evaluation and immune survey bimonthly. The mice were sacrificed 6 months after diet change. Kidneys, lymph nodes, spleen, blood and guts were collected for evaluation.

Results: KD and HFGD were both well tolerated by experimental mice. Two months after diet change, higher level of beta-hydroxybutyrate and triglyceride but lower sugar level was noted in mice fed on KD when compared to those fed on CD and HFGD (all p<0.05). Mice fed on KD and HFGD have a much lower RBC and platelet count than those fed on CD in the experimental mice group (both p<0.05). Although global lymphocyte counts were much lower in those pristine treated mice, Th17 lymphocytes were significantly higher in the blood as well as kidneys among those fed on HFGD (all p<0.05). This is compatible with their higher serum concentration of anti-dsDNA, anti-nRNP and anti-Sm and the rapid progressing proteinuria. Renal, hepatic and intestinal histopathology was still under analysis at present.

Conclusion: In conclusion, food plays a critical role in immune modification. Despite the reported anti-inflammatory effect of KD, it does not mitigate lupus nephritis progression. HFGD formula, however, accelerated the autoimmune phenotype for cases with lupus like glomerulonephritis.

REFERENCES:

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Vitamin D Protects Podocytes from Autoantibodies Induced Injury in Lupus Nephritis by Reducing Ablerrant Autophagy

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Background: Recent data suggest that vitamin D insufficiency may play a role in the progression of SLE and the nephropathy such as chronic kidney disease[1]. We previously show that severe vitamin D deficiency increases the risk for moderate to severe disease activity[2]. Moreover, vitamin D has been demonstrated a protective effect on podocyte injury via diverse mechanisms in proteinuric glomerular disease[3-7]. However, there is a paucity of data to demonstrated the mechanisms through which the autophagy functions on the protective role vitamin D plays on podocyte in the pathogenesis of lupus nephritis

Objectives: The aim of this study was to investigate whether vitamin D play a protective role in podocyte injury induced by autoantibodies purifyed from lupus nephritis (LN) patients serum via autophagic way.

Methods: Autophagic activities of LN patients renal tissues were evaluated under transmission electronic microscope. IgG from patients with LN were purified to induce human podocyte injury and the role of vitamin D in injury was observed. Podocytes were observed under TEM and autophagic activity was evaluated by western blot analysis and qRT-PCR, mRFP-GFP-LC3B adenovirus were injected into HPC in vitro.

Results: Significantly higher autophagic levels were observed in LN patients(p<0.05) and apparently greater autophagic levels in podocytes were shown (p<0.05). Among different classifications of LN, Class V(n=5), III+V(n=5) and IV+(n=5) gained higher autophagic levels than Class III (n=5) and IV(n=5). Induced autophagy, which was evident by increased LC3B-II and Beclin 1 level, caused consumption of p62, more autophago-somes observed under TEM, and more LC3B dots observed under confo- mercial microscope in IgG group, along with decreased Foxo3a expression, which suggests podocyte injury. Reduction of autophagy as well as alleviated podocyte injury was observed in the IgG+ group.

CONCLUSION: This study demonstrates that vitamin D plays a protective role in podocytes injury induced by autoantibodies from LN patients and that appears to be a novel therapy target in LN.

REFERENCES:

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BENEFIT OF CRITHIDIA TESTS IN DIAGNOSING CONNECTIVE TISSUE DISEASES

Results: Among differentially expressed renal microRNAs in LN, miR-127-3p was reduced in renal tissues of patients with LN. The miR-127-3p suppressed the fluorescein gene expression of ISRE induced by ISRE, and the phosphorylation of STAT1 and STAT2. By microarray analysis, we found that most ISG was inhibited by miR-127-3p in IFN-stimulated Hela cells. The functional deletion of miR-127-3p enhanced the IFN response in human primary mesangial cells, which was manifested by enhanced ISRE mediated reporter gene expression, enhanced STAT2 phosphorylation and increased ISG expression. In addition, we found that JAK1, the upstream tyrosine kinase of STAT1 and STAT2, was a new target molecule for miR-127-3p.

Conclusion: Our study shows that miR-127-3p can inhibit IFN signal transduction by targeting JAK1. The decreased expression of miR-127-3p in the kidney is associated with an overactive IFN response in the renal tissue of patients with LN. Subsequent mouse model studies indicate the therapeutic potential of miR-127-3p in treating lupus associated organ damage.

REFERENCES:

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AB0198

BENEFIT OF CRITHIDIA TESTS IN DIAGNOSING CONNECTIVE TISSUE DISEASES

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Objectives: To assess the construct validity of the Arab Hand Function Index (AHFI), an Arabic and adapted version of the Cochin hand Functional scale (CHFS) and an Arabic version of the Health Assessment Questionnaire (HAQ) in SSc.

Methods: We evaluated 100 patients with SSc followed between 2015 and 2017. All patients were white and fulfilled the American College of Rheumatology/European League Against Rheumatism criteria and/or the Lenier and Medger (2) criteria for SSc. Means±SD age at the time of evaluation was 47.66±12.28 years. The mean±SD disease duration was 6.54±6.23 years. Forty-one (41%) patients had diffuse cutaneous SSC and 59 (59%) had limited cutaneous SSC. Global hand and wrist mobility were evaluated using the hand functional index (HFI) and Kapandji index. Global disability and hand disability were assessed by an Arabic and adapted version of the HAQ and by the Arab hand functional index, an Arabic and adapted version of the CHFS, respectively. Anxiety and depression significant symptoms were assessed with the Arabic version of Hospital Anxiety and Depression Scale (HADS) anxiety and HADS depression. Construct validity was assessed by convergent and divergent validity (Spearman’s rank correlation coefficient) and factor analysis.

Results: The AHFI had correct convergent validity with global disability assessed by the HAQ (0.61) and the HFI (0.55), moderate correlation with the Kapandji index (-0.48: inverse correlation), depression (HADd) (0.45) and anxiety (HADA) (0.42) and no correlation with the disease duration (0.29) and the age (0.19) (Table 1). Factor analysis (Table 2) extracted 2 factors that accounted for 64.45% of the total variance. The AHFI has a good correlation with hand disability (AHF: 0.61), anxiety (0.57) and the HFI (0.51), a moderate correlation with depression (0.47) and Kapandji index (-0.46) and a little correlation with the age (0.28) and the disease duration (0.10) (Table 1). The factor analysis of the HAQ, extracted 1 factor that accounted for 50.64% of the total variance (Table 2).

Conclusion: In patients with SSc, the AHFI and the Arabic HAQ have good construct validity. The total score of the AHFI explained 61% of the variance of the HAQ.

Disclosure of Interests: Nouria Benmostefa: None declared, Samy Simlani: None declared, Samir Raouibia: None declared, Daoud Roula: None declared, Moulaoukh: None declared, Rechid Malek: None declared

Table 1. Convergent and divergent validities of the AHFI and the HAQ for patients with SSc (correlation with other variables)**

<table>
<thead>
<tr>
<th>Scale</th>
<th>Spearman’s correlation Coefficient</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AHFI</td>
<td>Convergent validity</td>
<td></td>
</tr>
<tr>
<td>HAQ</td>
<td>0.61</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HFI</td>
<td>0.55</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Kapandji</td>
<td>0.48</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Divergent validity</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression (HADd)</td>
<td>0.45</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Anxiety (HADA)</td>
<td>0.42</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Disease duration</td>
<td>0.29</td>
<td>0.003</td>
</tr>
<tr>
<td>Age</td>
<td>0.19</td>
<td>0.058</td>
</tr>
</tbody>
</table>

**These tables are not visible in the image.
INHIBITION OF DOT1L ACTIVITY IN HUMAN SKIN FIBROBLASTS: A Transcriptome ANALYSIS

Nathalie Benham1,2, Ellen De Langhe1,2, Rik Lories1,2.

1KU Leuven, Department of Development and Regeneration, Leuven, Belgium; 2UZ Leuven, Division of Rheumatology, Leuven, Belgium.

Background: The pathophysiology of fibrosis, a hallmark of diseases like Systemic Sclerosis, is still not well understood. The role of epigenetic factors is increasingly explored. DOT1L, the unique H3K79-methyltransferase, methylates histone 3 at the Lysine residue at position 79, thereby regulating gene expression programs. Inhibition of DOT1L in cartilage and bone has cell-type specific effects on Wnt signaling, a pathway suggested to play an important role in fibrotic disease.

Objectives: To study the changes in the transcriptome of dermal fibroblasts after DOT1L inhibition.

Methods: Primary human dermal fibroblasts isolated from abdominal skin were treated with DOT1L-inhibitor EPZ-5676 or vehicle and stimulated or not with TGF-β or CHIR99021 (activating Wnt signaling). RNAseq was performed using the NextSeq500 as a platform and TruSeq as library prep kit. The preprocessed reads were aligned to the reference genome of Homo-sapiens (Ensembl.GRC38.88/GRCh38). Statistical comparative analysis for differential expressed genes (DEG) was done using theedge prep kit. The preprocessed reads were aligned to the reference genome of Homo sapiens (Ensembl.GRC38.88/GRCh38). Statistical comparative analysis for differential expressed genes (DEG) was done using the edge prep kit. The preprocessed reads were aligned to the reference genome of Homo sapiens (Ensembl.GRC38.88/GRCh38).

Results: The DOT1L-inhibitor EPZ-5676 effectively reduced H3K79 dimethylation in the treated samples. RNAseq analysis revealed 663 differentially expressed genes in dermal fibroblasts exposed to the DOT1L inhibitor, based on group analysis: 77 genes were downregulated and 556 upregulated. There was no significant interaction between inhibition of DOT1L and stimulation.<span>par</span> of the cells with TGF-β or CHIR99021. Pathway analysis showed involvement of primarily the integrin signaling, the cadherin and Wnt pathway, suggesting a potential impact on the fibrotic process that is leading to pathology in SSc.

Conclusion: More than 600 differentially expressed genes were discovered by RNA sequencing in human dermal fibroblasts exposed to DOT1L inhibition (independent of TGF-β or CHIR 99021 stimulation). These gene lists and their networks indicate that DOT1L activity affects integrin signaling, the cadherin and Wnt pathway, suggesting a potential impact on the fibrotic process that is leading to pathology in SSc.

Acknowledgement: RNA sequencing and analysis was performed by VIB Nucleomics Core (www.nucleomics.be).

Disclosure of Interests: Nathalie Benham: None declared, Ellen De Langhe: None declared, Rik Lories Consultant for: Abbvie, Celgene, Eli-Lilly, Janssen, Merck, Novartis, Pfizer, UCB.


Table 2. Analysis of the differences in the transcriptome of dermal fibroblasts after DOT1L inhibition.

<table>
<thead>
<tr>
<th>ICAM-1</th>
<th>IL-6</th>
<th>IL-8</th>
<th>TGF-β</th>
<th>Collα1</th>
<th>ET</th>
<th>IFN-α</th>
<th>IFN-β</th>
<th>P38MAPK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pol(+)I</td>
<td>***</td>
<td>***</td>
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<td>NA</td>
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<td>***</td>
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<td>NA</td>
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<tr>
<td>AICS-α</td>
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<tr>
<td>ACA-IC</td>
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<tr>
<td>AICS-α</td>
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<td></td>
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<tr>
<td>anti-TGF-β</td>
<td>***</td>
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<tr>
<td>PAPS-IC</td>
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<tr>
<td>SLE-IC</td>
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<tr>
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</tbody>
</table>

*p < 0.05; **= p < 0.001; ***=p < 0.0001

Table 2. Modulation of study mediators in HUVEC.

<table>
<thead>
<tr>
<th>ICAM-1</th>
<th>IL-6</th>
<th>IL-8</th>
<th>TGF-β</th>
<th>Collα1</th>
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<tbody>
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<td></td>
<td></td>
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<tr>
<td>AICS-α</td>
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<td>***</td>
<td></td>
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</tr>
<tr>
<td>ACA-IC</td>
<td>*</td>
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<td>**</td>
<td>**</td>
<td>**</td>
<td>***</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AICS-α</td>
<td>*</td>
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<td>**</td>
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<td>**</td>
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<td></td>
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</tr>
<tr>
<td>anti-TGF-β</td>
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<tr>
<td>SLE-IC</td>
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<td></td>
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</tr>
<tr>
<td>NHS-IC</td>
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</tr>
</tbody>
</table>

*p < 0.05; **= p < 0.001; ***=p < 0.0001
Dysphagia has been reported to occur in 10% to 73% of these patients and can be present at any time during the disease process (1).

Objectives: The primary objective of the study was to evaluate the prevalence of dysphagia in a cohort of patients with idiopathic inflammatory myopathy (IIM) and to evaluate factors associated with the presence of dysphagia. The secondary objective was to evaluate the factors associated with severe dysphagia.

Methods: Retrospective, observational study, which included patients with a diagnosis of IIM according to modified classification criteria of Bohan and Peter (1992-2018). Demographic data, clinical characteristics, laboratory data, autoantibodies, imaging studies, videodensitometry, muscle biopsy and EMG were recorded.

Severe dysphagia was considered: one in which oral feeding was contraindicated and/or which required nasogastric tube feeding (NGT) either by clinical evaluation or by videodensitometry study. The rest of the patients with dysphagia who did not present a contraindication to oral intake during the course of the disease were considered mild/moderate dysphagia.

Results: 94/110 patients were included, 76% female, mean age at diagnosis: 48 years (SD ± 14). Idiopathic dermatomyositis was the most frequent subtype of myopathy (64%). Dysphagia occurred in 53/94 patients (56.4%) and it was presented at the beginning of the disease in 31/94 (32%). Severe dysphagia was found in (22/94) 23%.

When analyzing the clinical features of patients with myopathy and dysphagia, it was found that Idiopathic dermatomyositis was the most frequent IIM in these patients (71%). Patients with dysphagia presented: proximal muscle weakness 90%, neck muscles weakness 47%, and respiratory muscle weakness 27%.

Treatment received: 90/94 (97%) oral glucocorticoids, mean dose 48 mg of prednisone (Range 4 -100 mg.), pulses of Intravenous methylprednisolone was indicated in 25 patients (27.5%). The main steroid sparing agents used were: 72% methotrexate, followed by 33% azathioprine.

The primary objective of the study was to evaluate the prevalence of dysphagia in a cohort of patients with idiopathic inflammatory myopathy (IIM) and to evaluate factors associated with the presence of dysphagia. Both dysphagia in general and severe dysphagia were associated with parameters of severity, high cost and poor prognosis. However, in the analysis of multiple variables, this relationship could not be demonstrated.

Conclusion: All deaths were related to severe dysphagia. Both dysphagia in general and severe dysphagia were associated with parameters of severity, high cost and poor prognosis. However, in the analysis of multiple variables, this relationship could not be demonstrated.

Disclosure of Interests: Ana Carolina Costi: None declared, Claudia Pena: None declared, Pierina Sansinanea:

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>Severe dysphagia (present)</th>
<th>Severe dysphagia (absent)</th>
<th>p</th>
<th>OR IC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weak neck muscles</td>
<td>15 (65%)</td>
<td>18 (25%)</td>
<td>&lt;0.001</td>
<td>8.6</td>
</tr>
<tr>
<td>Weakness of respiratory muscles</td>
<td>10 (45%)</td>
<td>6 (8%)</td>
<td>&lt;0.001</td>
<td>9.5</td>
</tr>
<tr>
<td>Pulses of corticosteroids</td>
<td>17 (77%)</td>
<td>8 (11%)</td>
<td>&lt;0.001</td>
<td>25</td>
</tr>
<tr>
<td>Intravenous gammaglobulin</td>
<td>10 (45%)</td>
<td>7 (9%)</td>
<td>&lt;0.001</td>
<td>7.73</td>
</tr>
<tr>
<td>Intensive care unit</td>
<td>8 (36%)</td>
<td>8 (11%)</td>
<td>&lt;0.001</td>
<td>4.57</td>
</tr>
<tr>
<td>Mechanical ventilation</td>
<td>6 (27%)</td>
<td>5 (7%)</td>
<td>&lt;0.001</td>
<td>5.02</td>
</tr>
<tr>
<td>Death</td>
<td>16 (72%)</td>
<td>10 (14%)</td>
<td>&lt;0.001</td>
<td>16.53</td>
</tr>
</tbody>
</table>

Table 1. Growth factors values (23 patients with SE and 16 controls)

<table>
<thead>
<tr>
<th>Factor</th>
<th>PPP (pg/mL)</th>
<th>PRP (pg/mL)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>TFG-β1</td>
<td>21148.7</td>
<td>237185.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>IL-19</td>
<td>7.7</td>
<td>11.7</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Conclusion: The levels of VEGF-α (intratissue) are lower in patients with SE vs controls (p <0.0001). The intratissue levels of the growth and angiogenic factors are higher than the plasma (patients and controls), finally, the plasma levels of these factors are similar in patients compare with controls. In almost all studies until today the measured levels have been carried out in serum, which are not precise since, in serum, several cells and lysate residues can alter the values, therefore, quantification in plasma is important. The present work is the result of the doctoral thesis of the main author.
Background: Anti-TIF1gamma antibody positive dermatomyositis (TIF1gamma-DM) has greater risk of complication with cancer.

Objectives: We aimed to analyze the clinical features of TIF1gamma-DM and find the difference between cancer-associated TIF1gamma-DM (CA-TIF1gamma-DM) and non-cancer-associated TIF1gamma-DM (nCA-TIF1gamma-DM).

Methods: We investigated the clinical data of idiopathic inflammatory myositis (IM) patients received remission induction therapy in out hospital between January 2006 and December 2018. Results: We treated 148 patients with IM in this period, 9 cases of them were TIF1gamma-DM. Patients with CA-TIF1gamma-DM and nCA-TIF1gamma-DM were 4 and 5 cases, respectively. Average age at onset of 9 patients with TIF1gamma-DM was 63 years old. CA-TIF1gamma-DM was significantly older than nCA-TIF1gamma-DM (average: 78.0 vs 57.4). All of 9 TIF1gamma-DM had distinctive skin rash and muscle weakness. Seven cases of them suffered from dysphagia. Intestinal lung disease was not seen in all patients with TIF1gamma-DM. Serum creatine kinase (CK) levels of CA-TIF1gamma-DM was significantly higher than those of nCA-TIF1gamma-DM (average: 3405.5IU/L vs 719.8IU/L (Fig 1)). Among the TIF1gamma-DM patients, we administrated glucocorticoid (GCs) for 8 cases, immunosuppressants for 4 cases, and intravenous immunoglobulins (IVIG) for 7 cases. All 4 cases of CA-TIF1gamma-DM were treated with GC and IVIG. All TIF1gamma-DM patients, especially 4 CA-TIF1gamma-DM patients, seemed to have good response to treatment in serum CK levels. Although serum CK levels of these 4 cases were normalized within a month (Fig1.), their muscle weakness, skin rash and dysphagia which was associated with quality of life and the prognosis were poorly improved.

Conclusion: In our investigation, the age of onset and serum CK levels were significantly different between CA-TIF1gamma-DM and nCA-TIF1gamma-DM. We report our investigation of the phenotype and treatment of anti TIF1gamma antibody positive dermatomyositis. TIF1gamma-DM with high serum CK levels, we should perform appropriate tests to check for cancer throughout our treatment, and the improvement of serum CK levels is not equal to the success of our treatment.

Disclosure of Interests: None declared

(IVIG), and hydroxychloroquine HCL) was performed, attending to possible differences between IM subtype and the year of diagnosis. T student and Chi square tests were used for quantitative and qualitative variables, respectively.

Results: From 479 patients (74% females, 52% PM, 44±22 y at diagnosis, 10±8 y follow up), 473 (99%) received oral GC, 50/344 (15%) pulses GC, 78 (16%) HCL, 355 (74%) IS (methrotexate MTX 228, leflunomide 10, azathioprine AZA180, cyclophosphamide 44, mycophenolate MP 38, cyclosporine 32), 55 (12%) biologics (rilumixab 45, abatacept 2, atNf 16) and 79 (17%) IVIG. Differences according to IM subtype (1), and to the year of diagnosis (2), are shown in Tables.

Table 1

<table>
<thead>
<tr>
<th>PM (n=251; 52%)</th>
<th>DM (n=228; 48%)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>mean ± SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time (T) initial symptoms- diagnosis (dx) (m)</td>
<td>19±43</td>
<td>11±28</td>
</tr>
<tr>
<td>T initial - any treatment (tt) (m)</td>
<td>15±42</td>
<td>7±15</td>
</tr>
<tr>
<td>T initial - IS (m)</td>
<td>16±49</td>
<td>8±18</td>
</tr>
<tr>
<td>m,%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MTX</td>
<td>10/4±25 (41%)</td>
<td>12/4±28 (54%)</td>
</tr>
<tr>
<td>AZA</td>
<td>11/4±25 (45%)</td>
<td>7/6±27 (33%)</td>
</tr>
<tr>
<td>Mycophenolate</td>
<td>35/3±4 (12%)</td>
<td>8/2±4 (4%)</td>
</tr>
<tr>
<td>HCL</td>
<td>27/2±51 (11%)</td>
<td>5/1±22 (21%)</td>
</tr>
<tr>
<td>GC withdrawal due to improvement</td>
<td>5/2±45 (21%)</td>
<td>10/2±12 (47%)</td>
</tr>
<tr>
<td>Severe infections</td>
<td>7/5±41 (31%)</td>
<td>28/5±71 (17%)</td>
</tr>
</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th>Diagnosis &lt;2000</th>
<th>Diagnosis &gt;2000</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>means SD</td>
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<td></td>
</tr>
<tr>
<td>T initial - dx (m)</td>
<td>22±48</td>
<td>11±26</td>
</tr>
<tr>
<td>T initial - any tt (m)</td>
<td>16±42</td>
<td>8±22</td>
</tr>
<tr>
<td>T initial - GC (m)</td>
<td>17±43</td>
<td>9±24</td>
</tr>
<tr>
<td>T initial - IS (m)</td>
<td>53±82</td>
<td>14±28</td>
</tr>
<tr>
<td>T dx - IS (m)</td>
<td>39±75</td>
<td>1±19</td>
</tr>
<tr>
<td>N° tt</td>
<td>2.3±1.6</td>
<td>2.8±1.3</td>
</tr>
<tr>
<td>N° IS</td>
<td>0.9±1</td>
<td>1.3±0.8</td>
</tr>
<tr>
<td>m,%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any IS</td>
<td>121/208 (64%)</td>
<td>23/47 (1%)</td>
</tr>
<tr>
<td>MTX</td>
<td>69/208 (33%)</td>
<td>159/271 (6%)</td>
</tr>
<tr>
<td>MP</td>
<td>9/205 (4%)</td>
<td>29/263 (11%)</td>
</tr>
<tr>
<td>Any biologic</td>
<td>12/208 (6%)</td>
<td>43/271 (16%)</td>
</tr>
<tr>
<td>RTX</td>
<td>8/208 (4%)</td>
<td>37/271 (14%)</td>
</tr>
<tr>
<td>IVIG</td>
<td>21/204 (10%)</td>
<td>58/271 (21%)</td>
</tr>
<tr>
<td>GC withdrawal due to improvement</td>
<td>75/189 (40%)</td>
<td>77/191 (29%)</td>
</tr>
<tr>
<td>All cause mortality</td>
<td>69/162 (43%)</td>
<td>45/247 (18%)</td>
</tr>
<tr>
<td>Severe infections</td>
<td>61/190 (32%)</td>
<td>52/266 (19%)</td>
</tr>
</tbody>
</table>

Conclusion: The therapeutic management of IM has changed over the last few years, with a clear increase and earlier use of IS in patients diagnosed after 2000. In spite of a more aggressive approach in recent years, severe infections are less frequent, perhaps as a consequence of lower GC doses. The management of PM and DM is similar.

REFERENCE:

Disclosure of Interests: Beatriz Joven-Ibáñez Speakers bureau: Celgene, Novartis, MSD, Pfizer, Abbvie, and Janssen, Laura Nuño: None declared, Francisco J López-Longo: None declared, Julia Martínez-Barrio: None declared, Carmen Larena: None declared, Valentina Maldonado: None declared, Carmen Barbadillo: Paloma García de la Peña: Irene Llorente: Eva Tomero Muriel: Ana Pérez Gómez: Henry Moruno: Tatiana Cobo-Ibáñez: Raquel Almodovar: Leticia Lajo: María Jesús García de Yébenes: Patricia Carreira: University Hospital 12 de Octubre, Madrid, Spain; Hospital La Paz-madrid, Madrid, Spain; Gregorio Marañón Hospital, Madrid, Spain; Hospital Ramón Y Cajal, Madrid, Spain; Hospital Puerta de Hierro-Majadahonda, Majadahonda, Spain; IM University Sanchinarro Hospital, Madrid, Spain; Hospital de la Princesa, Madrid, Spain; 9Hospital Príncipe de Asturias, Alcalá de Henares, Spain; Infanta Sofia University Hospital, San Sebastián de los Reyes, Spain; Fundación Hospital Alcorcón, Alcorcón, Spain; Hospital Infanta Leonor, Madrid, Spain; 10Instituto de salud musculoesquelética, Madrid, Spain

Background: Inflammatory myositis (IM) are heterogeneous autoimmune diseases, characterized by muscular inflammation, which can associate systemic manifestations. In other inflammatory diseases, as rheumatoid arthritis, inflammation is a cardiovascular risk factor (CVRF), with clear influence on cardiovascular events and mortality (CVE, CVM).

Objective: To analyze the influence of IM severity in the development of CVE and CVM in the REMICAM registry.

Methods: All patients from REMICAM were included(1). REMICAM is a retrospective multicentric registry of IM patients (n=479), performed in Madrid between 2003-2014, containing demographic, clinical and outcome data (1). The presence of extra muscular features (cardiac, pulmonary, cutaneous and systemic involvement), number of therapies, immunosuppressants (IS) need, and glucocorticoids (GC) withdrawal due to IM remission defined IM severity. BI and multivariate logistic regression analysis were used to test the association between these factors and CVE. Survival analysis and regression proportional hazard bi and multivariate Cox models were used to determine the effect of these factors on CVM. All factors with p<0.2 in bivariate analysis were included in multivariate models. The entire was controlled for sex and CVRF. CVE: age, sex, CVRF number, diagnosis before year 2000, presence of arrhythmia or Raynaud. CVM: IM severity. CVRF: number, diagnosis after year 2000, presence of arrhythmia or Raynaud (Table 1). Arrhythmia was the only independent risk factor for CVM. GC withdrawal due to IM remission, and a smaller number of therapies, were protective factors for CVM (Table 2).

Conclusion: In the REMICAM registry, extra muscular manifestations such as arrhythmia, were associated to CVE and CVM, as independent risk factors. A smaller number of treatment or GC withdrawal due to remission were protective factors for CVM. Our results support the hypothesis that more severe IM, with extra muscular involvement and persistent inflammation, could favor atherosclerosis and CVE development.

Table 1. Characteristics associated with cardiovascular event (CVE) development

<table>
<thead>
<tr>
<th>Bivariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR (IC 95%)</td>
<td>P</td>
</tr>
<tr>
<td>Sex</td>
<td>1.7 (1.9-2.9)</td>
</tr>
<tr>
<td>Age at diagnosis</td>
<td>1.04 (1.03-1.05)</td>
</tr>
<tr>
<td>CVRF number</td>
<td>2.2 (1.7-2.7)</td>
</tr>
<tr>
<td>Raynaud</td>
<td>2.0 (1.3-3.2)</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>9.7 (5.2-18.1)</td>
</tr>
<tr>
<td>Porcidualis</td>
<td>3.9 (1.8-6.3)</td>
</tr>
<tr>
<td>Diagnosis after year 2000</td>
<td>13 (5.2-31.8)</td>
</tr>
</tbody>
</table>

REFERENCE:

Disclosure of Interests: Beatriz Joven-Ibáñez Speakers bureau: Celgene, Novartis, MSD, Pfizer, Abbvie, and Janssen, Laura Nuño: None declared, Francisco J López-Longo: None declared, Julia Martínez-Barrio: None declared, Carmen Larena: None declared, Valentina Maldonado: None declared, Carmen Barbadillo: Paloma García de la Peña: Irene Llorente: Eva Tomero Muriel: Ana Pérez Gómez: Henry Moruno: Tatiana Cobo-Ibáñez: Raquel Almodovar: Leticia Lajo: María Jesús García de Yébenes: Patricia Carreira: University Hospital 12 de Octubre, Madrid, Spain; Hospital La Paz-madrid, Madrid, Spain; Gregorio Marañón Hospital, Madrid, Spain; Hospital Ramón Y Cajal, Madrid, Spain; Hospital Puerta de Hierro-Majadahonda, Majadahonda, Spain; IM University Sanchinarro Hospital, Madrid, Spain; Hospital de la Princesa, Madrid, Spain; Hospital Príncipe de Asturias, Alcalá de Henares, Spain; Infanta Sofia University Hospital, San Sebastián de los Reyes, Spain; Fundación Hospital Alcorcón, Alcorcón, Spain; Hospital Infanta Leonor, Madrid, Spain; Instituto de salud musculoesquelética, Madrid, Spain
AB0207 RECEPTOR EXPRESSION OF ANGIOTENSIN TYPE-1 AND 2 ARE DECREASED IN PATIENTS WITH SYSTEMIC SCLEROSIS AND PULMONARY ARTERIAL HYPERTENSION (PAH) AND CORRELATED WITH SEROLOGICAL LEVELS OF NT-PROBNP

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Background: Previous studies identified functional autoantibodies against the angiotensin receptor type-1 (AT1R) and the endothelin receptor type A (ETAR) in about 85% of the patients with systemic sclerosis (SSc). The antibodies are cross-reactive, agonistic and functionally active by increasing the effects of the natural ligands as well as by specific activation of the receptors (2, 3). The levels of the antibodies are associated with clinical findings such as pulmonary arterial hypertension (PAH). Patients with highest antibody levels show worst prognosis and do not respond well to receptor blocker therapy (2-4). Several in vitro effects of the antibodies depend on the antibody levels and on the cell type bearing the receptors. Receptor expression of ETAR and AT1R was highest in early disease (3).

Objectives: To determine predictors of PAH, DU and clinical complications by measuring the antibody levels and the receptor expression on peripheral mononuclear cells in patients with systemic sclerosis.

Methods: The current study analyzed the serological levels of anti-AT1R and anti-ETAR antibodies and the extracellular and intracellular expression of AT1R, AT2R, ETAR, ETBR and ETRB on circulating CD4+ T cells, CD8+ T cells, CD14+ Macrophages, CD15+ Granulocytes and CD19+ B cells in SSc (n=41) using sandwich ELISA and flow cytometry. Clinical data (PAH, history of digital ulcers, digital-ulcers score, mRSS, pulmonary fibrosis, RA, antiphospholipid antibodies) were also collected. All samples were obtained at the time of serum sampling and every three-month to 27 months after baseline.

Results: Patients with PAH demonstrated a lower AT1R MFI and AT2R MFI ratio on all PBMC. Levels of NT-proBNP correlated negatively with the AT1R MFI and AT1R/AT2R MFI ratio on all PBMC. The levels of anti-AT1R ab correlated with the NT-proBNP in SSc patients with levels of NT-proBNP >300pg/ml and AT1R MFI on T cells, Granulocytes and Macrophages distinguished between pathological and physiological levels of NT-proBNP. Using Log-rank test and Mantel-Cox proportional hazards model, decreased expression of AT1R MFI on T cells, Granulocytes and Macrophages identified trends of deterioration of NT-proBNP over 50%.

Conclusion: Expression of AT1R and AT2R on PBMC could be of diagnostic value identifying clinical progress and/or subgroups in SSc. Their role in the pathophysiology, e.g. their impact on endothelial damage, has to be further investigated in SSc.

REFERENCES:
A STUDY OF CORRELATION BETWEEN PLATELETS AND LYMPHOCYTE SUBSETS IN SCLEROSIS

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Background: Systemic sclerosis (SSc) is an autoimmune disease characterized by vasculopathy, autoimmunity and widespread dermal and visceral fibrosis. There are existing evidence to support excessive platelet activation and their contribution to vascular function and fibrosis. Now we will focus on the immune role of PLT in SSc.

Objectives: By analyzing the correlation between platelet and lymphocyte subsets, CD4+ T cell subsets and disease activity in patients with diffuse SSc (dcSSc)/limited SSc (lcSSc), and to explore the immune role of PLT in SSc.

Methods: The peripheral blood of 21 stable disease patients, 31 active disease patients and 20 healthy controls (HC) were collected. The clinical data and laboratory indicators of them were enrolled. The T, B, NK lymphocyte subsets and CD4+ T cell subsets were detected by flow cytometry (FCM). The CD4+ T cell subsets contains Th1, Th2, T17, Treg, Th1/Th2 and Th17/Treg. Non-parametric Kruskal-Wallis H test was performed on multiple independent samples. The correlation between variables was used by Spearman correlation analysis.

Results: The PLT, PCT, MPV, PDW in peripheral blood of the stable group and active group were significantly higher than the HC group (P<0.05). The amount of T cells in peripheral blood of active group was [1127.80 (796.66-1393.78)], which was lower than the percentage of HC group [1246.44 (984.81-1497.84)] and stable group [1249.59 (1179.09-2022.88)]. There was significant difference between active disease group and stable group (Z=6.525, P=0.038). The amount of Th cells of the stable group [888.11 (679.55, 1430.70)] and active group [884.20 (385.878)] were higher than the HC group [574.84 (493.22-728.00)]. The Th1/Th2 ratio of the stable group [0.18 (0.10, 0.34)] and active group [0.21 (0.13, 0.28)] were lower than the HC group [0.25 (0.12, 0.31)]. There was significant difference between stable active group and HC group (Z=-6.525, P=0.038). The ESR and CRP were positively correlated with PLT, PCT; The amount of CD4+ T, CD8+ T and Th1/Th2 cells was positively correlated with MPV, and the ratio of Th1/Th2 was negatively correlated with MVP, and the ratio of Th1/Th2 was negatively correlated with MVP. There was significant negative correlation between Th1/Treg and PDW.

Conclusion: In SSc patients, lymphocyte subsets and CD4+ T cell subsets were altered. There was significant negative correlation between Th1/Treg and PDW. Among them, CD4+ T cell subsets was positively correlated with PLT, PCT. Explore the potential function of EXOs in the pathogenesis of SSc.

Disclosure of Interests: Yoshihito Koyama Paid instructor for: Asahi Kasei Pharma, Speakers bureau: BMS, Chugai, Ayumi and Eli Lilly, Soichiro Fuke: None declared, Yoshiharu Sato: None declared, Akemi Senoh: None declared, Toshiie Higuchi: None declared


REFERENCES:

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Disclosure of Interests: None declared


AB0209

THE GLOBAL EXPRESSION OF MIRNAS AND LNCRNAS IN THE EXOSOMES OF SYSTEMIC SCLEROSIS PLASMA AND NEUTROPHIL AND RELATED FUNCTIONS

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Background: Systemic sclerosis (SSc) is a systemic autoimmune disease with unknown pathogenesis. Exosomes (EXOs) are cell-derived vesicles 30-150 nm in size that contain various miRNAs, microRNAs (miRNAs), long non-coding RNAs (IncRNAs) and proteins. Plasma EXOs play wide roles in various diseases, however, little is known in SSc.

Objectives: Investigate the global expression of miRNAs and IncRNAs in the EXOs of SSc plasma and neutrophil. Explore the potential function of EXOs in the pathogenesis of SSc.

Methods: EXOs were respectively isolated from plasma, cultured neutrophils supernatants, and were identified by transmission electron microscopy. Global expression of miRNAs and IncRNAs form 5 SSc and 5 normal controls was analysis by Illumina HiSeq 3000 platform. Differentiated expressed and bioinformatics analysis was performed by edger, limma package, GO, KEGG, and cytoscape. Furthermore, we used the EXOs stimulated human dermal microvascular endothelial cells (HDMECs) and human primary skin fibroblasts, and explore the potential functions of EXOs.

Results: 1. In plasma EXOs, we identified a total of 37 miRNAs and 479 IncRNAs that showed significant differences between the two groups. Among them, 26 of upregulated miRNAs were involved in the E6E7 signaling pathway; 11 of downregulated miRNAs were involved in the MAPK signaling pathway; TGF-b signaling pathway, AMPK signaling pathway, the expression levels of IncRNAs were involved in the PI3K-Akt signaling pathway, p53 signaling pathway, 180 of downregulated IncRNAs were involved in lymphosome.

2. In neutrophil EXOs, we identified a total of 22 miRNAs and 281 IncRNAs that showed significant differences between the two groups. Among them, 12 of upregulated miRNAs were involved in the Wnt signaling pathway; 10 of downregulated miRNAs were involved in the MAPK signaling pathway, AMPK signaling pathway; 119 of upregulated IncRNAs were involved in interferon-23 signaling pathway; 162 of downregulated IncRNAs were involved in the signaling by GPCR, signalling by NOTCH and TRAIL.

3. After stimulated with SSc plasma EXOs, the expression levels of has-miR-324-5p and SP1/SMAD2, has-miR-624-5p and PIK3RCB, has-miR-483-5p and MAPK1 were negatively correlated, the expression levels of ENST00000596255.1 and OSMR, ENST00000801511.1 and HMGB1/ENOS were positively correlated, variably in HDMECs and human primary skin fibroblasts.

4. After stimulated with SSc neutrophil EXOs, the expression levels of has-miR-1268a and PRKCA, has-miR-299-3p and IGF1R were negatively correlated, the expression levels of ENST00000596255.1 and OSMR, ENST00000801511.1 and HMGB1/ENOS were positively correlated, variably in HDMECs and human primary skin fibroblasts.

5. These miRNAs and IncRNAs with consistent expression might be involved in the pathogenesis of SSc EXOs.

Conclusion: Our study identified and confirmed differently miRNAs and IncRNAs in the neutrophil EXOs and plasma EXOs. Those genes may be involved in the pathological mechanism of SSc, such as has-miR-324-5p and SP1/SMAD2, has-miR-624-5p and PIK3RCB, has-miR-483-5p and MAPK1, ENST00000596255.1 and IL23R, ENST00000596255.1 and TDFP2, ENST00000608572.1 and HDAC2 were positively correlated, variably in neutrophil, HDMECs and human primary skin fibroblasts.

Disclosure of Interests: None declared

AB0211 NEUTROPHIL-DERIVED EXOSOME S100A8/A9 INHIBITS ANGIogenesis IN SYSTEMic SCLEROSIS
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Background: Systemic sclerosis (SSc) is an autoimmune disease characterized by vasculopathy, inflammation, and extensive fibrosis of the skin and organs. Exosomes (EXOs) are cell-derived vesicles 30-150 nm in size that contain various mRNAs, microRNAs and proteins.

Objectives: Here, we aimed to investigate the roles of EXOs in SSc pathogenesis, especially in angiogenesis.

Methods: EXOs were respectively isolated from plasma, cultured peripheral blood mononuclear cells (PBMCs) and neutrophil supernatants, and were identified by transmission electron microscopy. The expression of S100A8/A9 was measured by real-time PCR and ELISA. Proliferation, migration and scratch assays in human dermal microvascular endothelial cells (HDMECs) were used to study the influence of neutrophil EXOs and neutrophil EXOs S100A8/A9. We also performed a genome-wide transcriptome analysis on PBMCs from 19 SSc patients and 18 matched normal controls (NC) using Illumina BeadChip arrays. The ingenuity pathway analysis involved regulating both vascular fibrotic, and immune T- and B-lymphocyte-mediated alterations that characterize several SSc manifestations. According to our previous experience with RTX [1], we suggested that neutrophil EXOs S100A8/A9 inhibit the proliferation and migration of HDMECs, and that they might through Toll-like receptor 4 (TLR4) pathway.

Conclusion: S100A8/A9 is one of components of neutrophil EXOs that regulates vascular endothelial cell angiogenesis in SSc patients, most likely by activating the TLR4 signalling pathway.

REFERENCE:

Disclosure of Interests: None declared

AB0212 LONG-TERM TREATMENT WITH RITUXIMAB IN SYSTEMIC SCLEROSIS MANAGEMENT: AN OVERVIEW OF THE CLINICAL EXPERIENCE FROM A REAL-LIFE SETTING
Federica Lumenti1, Annelia Spinella1, Michele Colaci2, Emanuele Ciccodia1, Luca Magnani1, Gianluigi Balocchi1, Clodoveo Ferri1, Carlo Selvaramani1, Dilia Giuggioli2, Luca Magnani3, Gianluigi Baiocchi3, Clodoveo Ferr1, Carlo Salvaramain, Dilia Giuggioli2, Luca Magnani3, Gianluigi Baiocchi3, Clodoveo Ferr1, Carlo Salvaramain

Background: Systemic sclerosis (SSc) is a chronic inflammatory autoimmune disease characterized by vascular, immunologic, and fibrotic alterations of the connective tissue. SSc affects approximately 10-55% of SSc patients and might be associated with chronic kidney disease, reduced renal functional reserves. Furthermore, subclinical renal impairment affects approximately 10-55% of SSc patients and might be associated with other vascular manifestations. However, the available evidence on CKD in patients with SSc residing in low-middle income countries (LMIC) is scarce. Because the health system of LMIC, and especially Peru, could have great differences in access to diagnosis and management of SSc, it is important to identify which clinical factors would be associated with CKD in patients with this autoimmune disease.

Objectives: To identify the associated factors to renal involvement in Peruvian patients with SSc.

Methods: We analyzed the associated factors to renal involvement in SSc patients at Hospital Nacional Edgardo Rebagliati Martins Lima-Peru, a national reference hospital in Peru. Between June 2001 and December 2018, we included ambulatory patients, older than 18-year-old with SSc included in this study. One hundred and five patients with diffuse cutaneous SSc (n=13) showing a significant decrease of mRSS after the first 6 months (from 24.3 ± 17.4 to 17.9 ± 4.3; p = 0.006) and at the end of the follow-up period (17.8 ± 5.7; p = 0.005). Similarly, a valuable improvement of other skin manifestations, namely hypermelanosis (17/20 pts), pruritus (18/21 pts) and tender joints (from 5.2 ± 4.0 to 0.9 ± 2.5; p = 0.0001) in 2024 patients. Final lung fibrosis detected in 19/24 on chest CT remained stable during the entire follow-up, as well as pulmonary function tests (PFTs). These positive clinical changes were mirrored by the subjective improvement of patients well being in all subjects (HAQ from 1.04 ± 0.55 to 0.85 ± 0.38; VAS from 71.0 ± 15.2 to 28.0 ± 10.3; p = 0.0001). No significant side effects were observed during the entire follow-up. Only in one patient a severe urinary tract infection leading to the discontinuation of the treatment was detected.

Conclusion: The present study reinforces the previous trials and our preliminary researches on this topic, showing the efficacy of RTX in the management of SSc with good safety profile. The specific therapeutic role of RTX on B-cell-driven autoimmune, might explain its beneficial effects on some SSc clinical alterations. The improvement of skin sclerosis, arthritic symptoms and the stabilization of lung involvement were identified as the main results. Further exploration of the potential clinical efficacy of RTX in SSc with multicentre, double blind, controlled study is needed.

Disclosure of Interests: None declared
years; 92% were women, and the average time of illness was 8.2 years. The model based on theory showed that age (aPR = 1.03, 95% CI = 0.99-1.07, p = 0.143) and exposure to Penicillamine (aPR = 0.51, CI 95% = 0.19-1.33, p = 0.170) were marginally associated (p <0.02) with CKD, while pulmonary hypertension (aPR = 2.76, 95% CI = 1.29-5.88, p = 0.009) and arterial hypertension (aPR = 3.51, 95% CI = 1.06-11.6, p = 0.04) were significantly associated (<0.05) with CKD. The parsimonious model retained pulmonary hypertension (aPR = 3.74, 95% CI = 1.87-8.36, p <0.001) and arterial hypertension (aPR = 7.45, 95% CI = 3.31-16.7, p <0.001) as significantly associated factors to CKD.

Conclusion: Hypertension, a classic cardiovascular risk factor, and pulmonary hypertension were important factors associated with CKD. The appropriate management of these factors must be taken into account to prevent CKD. Prospective cohort studies should evaluate the influence of these factors in reducing the incidence of CKD.

REFERENCES:

Disclosure of Interests: None declared

AB0214 MUSCLE INVOLVEMENT IN SYSTEMIC SCLEROSIS

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Background: The prevalence of myopathy in systemic sclerosis (SSc) or scleroderma patients varies from 5% to 81% depending on the diagnostic criteria used to define the muscle involvement. The histopathological characteristics found in these patients and their correlation with the clinical features and autoantibody profile has not been fully characterized.

Objectives: To characterize the muscle involvement and histopathology findings in patients with SSc.

Methods: This retrospective cross-sectional study included all patients from the Scleroderma Cohort of Vall d’Hebron General and Hospital Clinic de Barcelona with muscle biopsies available for review performed at the Muscle Research Unit of Hospital Clinic de Barcelona from May 2004 to November 2018. Muscle biopsies were performed, for weakness or raised CK and/or aldolase. Histological sections were independently evaluated by two myopathology experts looking for inflammation in the endomysium, perimysium and perivascular areas. The presence of necrosis, regeneration, fibrosis, necrogenic atrophy, and fiber type grouping as well as perifascicular atrophy were also recorded. Based on the autoantibody profiles patients were classified into five groups, “Scl70”, “PM/ScIi”, “centromere”, “U1-RNP”, and “nucleolar and centromer IFI ANA pattern without specificity for anti-Scl70 or anticentromere”. Demographic and clinical data were obtained by chart review.

Results: 42 subjects were included, 33 (76.6%) of them were women. Considering the immunological profile 12 had Scl70, 12 PM/ScIi, 5 anti-centromere, 2 U1RNP, and 11 had ANA pattern without specificity for anti-Scl70 or anticentromere. Most of patients (90.5%) were Caucasians, 2 (4.8%) were Hispanic, and 2 of other ethnic background. The mean age at the onset of SSc was 42.1 (SD 2.5) years and at the muscular symptoms 50.7 (SD 2.1) years, respectively. Twenty-two (52.4%) patients presented with high aldolase level (mean level of 200 U/L) whereas 38 (90.5%) exhibited high aldolase level (mean 200 U/L). Of note, 17 (40.5%) presented with high CK level (mean level of 1316 ± 353.8 U/L; normal value < 6 U/L). Among the pathological features, 28 (66.7%) biopsies had fibrosis. Neurogenic atrophy was detected in 4 (9.5%) and fiber type grouping was present in 9 (21.4%) muscle biopsies. In near half of the muscle biopsies (45.2%) inflammatory infiltrate was present. Compared to other patients, those positive for PM/ScIi had more perivascular (75%), endomysial (50%) and perineural inflammation (75%) and perifascicular atrophy (42%) (all p<0.05), while a reduced prevalence of inflammatory infiltrates was noted in the Scl70 group (17%) (p<0.05).

Conclusion: In our cohort of SSc patients with muscle involvement, two main histopathological patterns were found, fibrosis and inflammation. Almost half patients presented with elevated aldolase with normal CK values. The muscle disease heterogeneity suggests that a variety of pathologic mechanisms play a role in the scleroderma associated myopathy but those patients with histopathologically inflammatory features deserve to be treated with immunosuppressive therapy.

REFERENCES:

Disclosure of Interests: None declared

AB0215 A LATE ONSET OF SYSTEMIC SCLEROSIS IS ASSOCIATED WITH A MORE RAPIDLY PROGRESSING CLINICAL PHENOTYPE IN LCSSC PATIENTS

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Background: SSc is a heterogeneous multisystem connective tissue disease. The majority of patients (pts) develop initial clinical symptoms between the ages of 30-50 years (yrs). It is not yet known whether the age of onset has an influence on the development of a distinct clinical phenotype.

Objectives: Investigating the relationship between age at disease onset and the development of clinical characteristics using data of the German Network for Systemic Sclerosis.

Methods: We evaluated 2928 patient data, subdivided them into 3 age groups at disease onset (<40 yrs, 40-50 yrs, and >50 yrs) and correlated the age at disease onset with specific clinical characteristics.

Results: Overall, 24% of pts developed first non-RP symptoms at the age of <40yrs, 53% between the age of 40-60yrs, and 23% were older than 60yrs. In particular, SSc pts with disease onset >60yrs developed significantly (p<0.001) more often the lcSSc subtype (64%) as well as ACA antibodies (42%) with a significantly lower mRSS. They, however, also suffered more often from pulmonary hypertension (PH) and developed less often digital ulcers. Especially lcSSc pts were associated with a more rapidly progressing clinical phenotype, i.e., 25% of the elderly lcSSc pts developed PH after five years. In contrast, less than 5% diagnosed with lcSSc at the age of <40yrs suffered from PH after five yrs (p<0.001).

Conclusion: In this registry, approximately one quarter of pts developed SSc at an age above 60yrs, predominantly having a lcSSc subtype. Although these pts have been diagnosed with the mild form of SSc, pts with a lcSSc subtype at a higher age (>60yrs) had more frequent a PH and showed a more rapid disease progression than the youngest pts. These findings may have an important influence on recommendations on
Background: Systemic sclerosis (SSc) is a connective tissue disease of unknown cause. The key points in development of SSc are immune disorders [2]. Autoimmune inflammation is the factor that underlies the enzymatic pattern of purine and pyrimidine metabolism in most patients.

Methods: Fifty SSc patients and 30 healthy controls were investigated with HRCT twice (at first visit and at the end of the study) and according the CT-changes were divided into 3 groups: the 1st group (16 pts) with improvement; 2nd group (39 pts) without any changes and 3rd group (22 pts) with worsening of fibrosis. Disease activity was assessed by the 2001 European Scleroderma Study Group Activity Index (EScSG-AI).

Results: There were no significant differences between groups related to sex, frequency of diffuse form and duration disease. Mean dates of follow up were 58.9±11.4 months. Pts. were investigated with HRCT twice (at first visit and at the end of the study) and according the CT-changes were divided into 3 groups: the 1st group (16 pts) with improvement; 2nd group (39 pts) without any changes and 3rd group (22 pts) with worsening of fibrosis. Disease activity was assessed by the 2001 European Scleroderma Study Group Activity Index (EScSG-AI).

Results: Mean age of patients (Mean±SD) was 42.8±1.3 years, mean SSc duration was 7.9±0.7 years. We revealed substantial changes in enzymatic activities related to both purine and pyrimidine metabolism in lysed red blood cells of SSc patients. The increased ADA (p<0.001), AK (p>0.001), IMPDH (p<0.001), TK (p<0.001), UDH (p<0.001) activities and the decreased DODH (p<0.001), PNP (p<0.001) activities in lysed red blood cells were observed of SSc patients in comparison with healthy controls. AK, IMPDH, TK, UDH activities positively correlated with SSc activity. Negative correlations with SSc activity were revealed for ADA, CDA, DODG, AK, TP activities.

Conclusion: The progression of SSc goes with the imbalance of the purine and pyrimidine enzymes in a regular manner. Activity of the autoimmune inflammation is the factor that underestimates the enzymatic pattern of purine and pyrimidine metabolism.

Disclosure of Interests: None declared. 

REFERENCES:
was significantly higher than in groups 1.2 (p < 0.01 and p < 0.04 accordingly) at the end of the study.

Conclusion: Mean values of EScSG-AI score associated with and were accompanied by progression pulmonary alterations in pts SSC so EScSG-AI score can be used as valuable tool for long-term follow-up studies.

Disclosure of Interests: None declared


AB0219 BIOMARKER EXPRESSION IN MONOCYTE SUBPOPULATIONS IN SSC PATIENTS

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Background: Systemic sclerosis (SSc) is a chronic autoimmune disease characterized by vasculopathy and fibrosis, which can be classified into diffuse cutaneous (dSSc) and limited cutaneous (lSSc) subtypes. Monocytes are key agents in the pathophysiology of systemic autoimmune diseases, including systemic sclerosis (SSc). M1 cells (CD14++CD16--) represent a predominantly pro-inflammatory phenotype and M2 cells (CD14+/CD16+) are more associated to an regulatory/pro-fibrotic phenotype.

Objectives: Our aim was to evaluate circulating blood monocyte subpopulations [classical (M1), intermediate and non-classical (M2)] and analyze the expression of CD163, CD169, CD206 and HLA-DR (function and activation monocytes receptors).

Methods: Fifty consecutive patients fulfilling the 2013 ACR/EULAR classification criteria for SSc were included in a cross-sectional study. Monocyte subpopulations were identified and characterized according to the expression of CD64, CD16, CD14, CD163, CD169, CD206 and HLA-DR. Thirty-eight age- and sex-matched healthy individuals were recruited as a control group.

Results: SSc patients mean age was 57.2 ± 12.8 years (HC 55.2 ± 11.4) and 94% were female. Limited form of disease was present in 72% of SSc patients and SSc patients had an increased number of circulating peripheral blood monocytes compared to healthy subjects (table 1). Absolute counts of CD16+ (intermediary and non-classical) monocyte subpopulations were higher in SSc patients than HC (79.9 (53.4-103.5)x10⁴/mm³ vs. 55.9 (26.8-85.6)x10⁴/mm³, p<0.003). HLA-DR intensity of expression was higher in all monocyte subsets from lSSc and dSSc patients when compared to control. There was a higher percentage of classical [1.56 (0.84-2.98) vs. 0.68 (0.37-1.88); p<0.003] and intermediate monocytes [15.9 (9.5-29.9) vs. 6.1 (3.7-11.5); p<0.001] with CD206 expression in SSc patients compared to HC, and a higher percentage of CD169 expression in lSSc patients compared to control and ISSc groups (p<0.01).

Table 1. Absolute value (x10⁴/mm³) about monocyte subpopulations in all systemic sclerosis (SSc) patients compared to healthy controls (HC) and in limited (lSSc) and diffuse (dSSc) systemic sclerosis subtypes.

<table>
<thead>
<tr>
<th>Monocytes</th>
<th>SSc</th>
<th>HC</th>
<th>p*</th>
<th>ISSc</th>
<th>dSSc</th>
<th>p*</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td>subpopulations</td>
<td>patients</td>
<td>(n=36)</td>
<td>(n=38)</td>
<td>(n=36)</td>
<td>(n=38)</td>
<td>(n=36)</td>
<td>(n=38)</td>
</tr>
<tr>
<td>Classical</td>
<td>346.2</td>
<td>209.8</td>
<td>&lt;0.001</td>
<td>363.2</td>
<td>326.5</td>
<td>0.779</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>monocytes</td>
<td>(260.9-146.1-146.1)</td>
<td></td>
<td></td>
<td>(262.9-231.2-231.2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(451.6-287.1-287.1)</td>
<td></td>
<td></td>
<td>(451.6-272.1-272.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intermediate</td>
<td>38.2</td>
<td>25.4</td>
<td>0.005</td>
<td>38.5</td>
<td>37.1</td>
<td>0.795</td>
<td>0.009</td>
</tr>
<tr>
<td>monocytes</td>
<td>(24.6-12.6-12.6)</td>
<td></td>
<td></td>
<td>(24.7-12.6-12.6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(47.1-47.1-47.1)</td>
<td></td>
<td></td>
<td>(47.1-47.1-47.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-classical</td>
<td>41.2</td>
<td>28.3</td>
<td>0.006</td>
<td>42.5</td>
<td>37.1</td>
<td>0.310</td>
<td>0.005</td>
</tr>
<tr>
<td>monocytes</td>
<td>(20.8-11.5-11.5)</td>
<td></td>
<td></td>
<td>(20.8-20.8-20.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(58.3-46.1-46.1)</td>
<td></td>
<td></td>
<td>(58.3-46.1-46.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data are shown as median (interquartile range - IQR). * Mann-Whitney U test

Conclusion: In our study, SSc patients show greater monocytes counts than HC with a predominantly regulatory/pro-fibrotic phenotype (M2). dSSc seems to be more associated to CD169 than ISSc.

REFERENCES:


Disclosure of Interests: Laiana Schneider: None declared, Natalia Marcondes: None declared, Vanessa Hax: None declared, Isadora Moreira: None declared, Carolina Yuka: None declared, Rafaela Rómeo: None declared, Ricardo Xavier Consultant for: Abbvie, Pfizer, Novartis, Janssen, Lilly, Roche, Rafael Chakr: None declared
**ABO220: ALPHA-SMOOTH MUSCLE ACTIN EXPRESSION ON ENDOTHELIAL PROGENITORS CELLS OF SYSTEMIC SCLEROSIS PATIENTS: POSSIBLE ROLE IN THE ENDOTHELIAL-TO-MESENCHIMAL TRANSITION PROCESS**

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**Background:** Endothelial-to-mesenchymal transition (EndoMT), a newly recognized type of cellular transdifferentiation, seems to be involved in Systemic Sclerosis (SSc) pathogenesis. In this process endothelial cells lose their specific markers, and acquire a mesenchymal phenotype, thus expressing cell products such as alpha smooth muscle actin (α-SMA) (1,2). Circulating endothelial progenitors cells (EPCs) derive from bone marrow stem cells and contribute to de novo vessels formation. Several studies, although with conflicting results, have shown that EPCs in the peripheral blood of patients with SSc are impaired in their number and function (3).

**Objectives:** to assess the expression of α-SMA, possibly associated with a pro-mesenchymal switch (EndoMT) of the circulating Early (CD34+KDR+CD133+) and Late (CD34+KDR+) EPCs in the peripheral blood of SSc patients and of patients with Very Early Diagnosis of SSc (VEDOSS) compared with healthy controls (HC) using flow cytometry.

**Methods:** enrolled 11 patients (7 SSC and 4 VEDOSS), classified according to the classification criteria for SSC (4) and for VEDOSS not fulfilling SSC criteria (5), and 10 HC. Phenotypic characterization was performed as previously described by Vasa et al. using a FACS Calibur (BD Immunocytochemistry Systems). EPCs number was expressed as a percentage of cells within the lymphocyte gate.

**Results:** we found a significantly higher percentage of α-SMA positive Early EPCs (CD34+KDR+CD133+α-SMA+) in all patients respect to HC (0.06%±0.03 vs 0.03%±0.01; p=0.0149) particularly in VEDOSS patients (0.07%±0.01 vs 0.03±0.01; p=0.008). Moreover, in VEDOSS patients, also the percentage of Late EPCs (CD34+KDR+α-SMA+) in all patients respect to HC (0.05%±0.01 vs 0.03%±0.01; p=0.05; 0.07%±0.01 vs 0.04%±0.02; p=0.04; 0.06%±0.01 vs 0.04%±0.02; p=0.05). Besides Early EPCs and α-SMA positive Early EPCs percentages seem to be significantly reduced in patients taking iloprost (p=0.05 and p=0.01 respectively), calcium channel blockers (CCB) (p=0.05 and p=0.03) and DMARDs (p=0.017 and p=0.013).

**Conclusion:** EndoMT seems to be involved in the pathogenesis of SSc and circulating EPCs seem to be impaired in number and function in SSC patients. In our study we found higher levels of EPCs, in particular α-SMA positive Early EPCs in both groups of patients (SSC and VEDOSS) respect to HC. Thus we can hypothesize a predominant pro-mesenchymal phenotype of this kind of EPCs. This could be considered the expression of the involvement of EPCs in EndoMT process and could better explain the controversial role of EPCs in SSc pathogenesis. Very interesting is the finding of a lower percentage of Early EPCs, and could better explain the controversial role of EPCs in SSc pathogenesis.

**REFERENCES:**


**Disclosure of Interests:** Katia Stefanoniti Consultant for: Only 1 scientific advice for Ifalfarmaco in 2016, cristiana barbari: None declared, Carlotta Angelotti: None declared, Greta Pellegrino: None declared, cristiano alessandrini: None declared, Guido Valesini: None declared, Valeria Riccieri: None declared.

**DOI:** 10.1136/annrheumdis-2019-eular.7890
ASSOCIATION BETWEEN CENTROMERE AND TOPOISOMERASE SPECIFIC IMMUNE RESPONSES AND THE DEGREE OF MICROANGIOPATHY IN SYSTEMIC SCLEROSIS

Nina van Leeuwen1, Jaap Bakker1, Corrie Wortel1, Hans Ulrich Scherer1, Rene Toes1, Thomas Huizinga2, Jeska de Vries-Bouwstra2, 1Leiden University Medical Center, Rheumatology, Leiden, Netherlands; 2Leiden University Medical Center, Clinical Chemistry, Leiden, Netherlands

Background: In systemic sclerosis (SSc) more severe microangiopathy has been associated with worse disease outcome. In addition, auto-antibodies are important tools for disease prognostication. To what extent these two biomarkers reflect the same pathophysiological background is not clear. A better understanding of the interaction between the specific auto-immune response and the degree of microangiopathy could not only improve our insight in disease pathophysiology but could also contribute to more reliable disease prognostication. We hypothesized that an ongoing activated immune response, as reflected by higher anticientromere antibody (ACA) or anti-topoisomerase (ATA) specific IgG levels and higher number of ACA or ATA specific isotypes, associates with more severe microvascular damage and with more severe SSc.

Objectives: 1. To evaluate whether ACA and ATA isotype expression associates with the degree of microangiopathy in SSc. 2. To determine the additive value of more activated immune response for prediction of organ involvement.

Methods: ACA and ATA IgG, IgA and IgM levels were measured in serum samples of 129 ACA IgG+ or 102 ATA IgG+ SSc patients, respectively. The degree of microangiopathy was determined based on nailfold videocapillaroscopy (NVC) images, with SSc late pattern reflecting more severe microangiopathy. Associations between ATA and ACA iso-type expression and NVC patterns were evaluated. Logistic regression analyses, with NVC pattern, autoantibodies, isotype expression and IgG levels as independent and disease characteristics as dependent variables were performed, adjusted for age, sex and disease duration.

Results: NVC images were available for 164 patients (n=100 ACA, n=64 ATA). Prevalence of SSc early, active and late pattern did not differ between ACA/ATA IgM- and IgM – patients, nor between ACA/ATA IgA- and IgA – patients. No associations between isotype expression (Figure 1) or IgG levels and NVC patterns were found. Logistic regression confirmed the association of ATA with pulmonary involvement (multivariable Odds Ratio [OR] 9.0 range 2.3-34.5) and of late SSc pattern with digital ulcers (multivariable OR 12.0 range 3.0-48.0) and pulmonary involvement (multivariable OR 5.0 range 1.5-16.1). Of note, higher topoisomerase and centromere specific IgG levels were independently associated with presence of digital ulcers (OR 3.5 range 1.1-11.0).

Conclusion: We did not observe an association between the quality of the anti-centromere specific or the anti-topoisomerase specific immune response and degree of microangiopathy in SSc patients. This might indicate that specific autoantibodies and stage of microangiopathy reflect different processes in the disease. The association between higher ATA or ACA specific IgG levels with digital ulcers, independent of specific autoantibody and NVC patterns suggests that an ongoing, active immune response is associated with more severe organ involvement.

Figure 1. SSc patterns on nailfold videocapillaroscopy (NVC) stratified for number of isotypes expressed.

Disclosure of Interests: Nina van Leeuwen: None declared, Jaap Bakker: None declared, Corrie Wortel: None declared, Hans Ulrich Scherer Grant/research support from: Sanofi, BMS, Rene Toes Grant/research support from: Sanofi, Thomas Huizinga Consultant for: Merck, UCB, Bristol Myers Squibb, Biostest AG, Pfizer, GSK, Novartis, Roche, Sanofi-Aventis, Abbott, Crescendo Bioscience Inc., Nycomed, Boehringer, Takeda, Zydis, Epiris, Eli Lilly, Jeska de Vries-Bouwstra: None declared


AB0223 ASSESSMENT OF DISEASE ACTIVITY IN SYSTEMIC SCLEROSIS: THE COMPARISON BETWEEN REVISED EUSTAR AND EScSG ACTIVITY INDEXES

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Background: Assessment of disease activity in systemic sclerosis (SSc) is challenging and usually hard to distinguish from damage or chronicity. Objectives: We aimed to evaluate disease activity by different indexes and compare them in a SSc cohort.

Methods: Disease activity was evaluated by revised EUSTAR (European Scleroderma Trials and Research group) and EScSG (European Scleroderma Study Group) activity indexes in 131 SSc patients fulfilling ACR/EULAR classification criteria (2013). The patients with the scores of EUSTAR activity index ≥2.5 or EScSG activity index ≥3 were accepted as having active disease.

Table 1

<table>
<thead>
<tr>
<th></th>
<th>ATA Late NVC</th>
<th>ATA Other NVC</th>
<th>ACA Late NVC</th>
<th>ACA Other NVC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, n(%)</td>
<td>13 (72)</td>
<td>34 (74)</td>
<td>14 (93)</td>
<td>75 (88)</td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>60 (14)</td>
<td>50 (15)</td>
<td>64 (11)</td>
<td>57 (13)</td>
</tr>
</tbody>
</table>
| Since non RP, median(IQR) | 6 (0-12) | 2 (1-4) | 15 (8-26) | 4 (1-10) |}

Results: Demographics, disease characteristics and nailfold video-capillaroscopic (NVC) pattern details were summarised in table-1. The scores of EUSTAR and EScSG activity indexes were correlated well (r=0.576, p=0.000) and the agreement between two scores for activity was moderate (cohen kappa:0.407). The percentages of SSc patients described as having active disease or not according to two activity indexes were summarised in table-2. Of the patients, 9.9% had active and 70.9% had inactive disease according to both indexes in this SSc cohort. Twenty-one (for EUSTAR) and 4 patients (for EScSG) were described as active according to one index and not to the other. Revised EUSTAR activity index was found to have 76.5% sensitivity and 81.6% specificity when the activity was defined by EScSG activity index.

Table 1.

<table>
<thead>
<tr>
<th>All SSc Patients</th>
<th>NVC</th>
<th>Clinical Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSc patients: N=121</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>eSD</td>
<td>Gender M/F</td>
</tr>
<tr>
<td>50.3±12.4</td>
<td></td>
<td>56/65</td>
</tr>
</tbody>
</table>

Table 2.

<table>
<thead>
<tr>
<th>EScSG activity index</th>
<th>NVC</th>
<th>Disease Severity Score (IU)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All SSc patients: N=121</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>eSD</td>
<td>Gender M/F</td>
</tr>
<tr>
<td>50.3±12.4</td>
<td></td>
<td>56/65</td>
</tr>
</tbody>
</table>

Conclusion: This SSc cohort predominantly had limited cutaneous disease, digital vasculopathy and late scleroderma pattern. Defining active disease was differed in 19% of the patients according to EUSTAR and EScSG activity indexes, former described higher frequency for activity. This difference might be related to validation procedures of these indexes in patients with different predominant stages of SSc disease, content of the index and the features of the cohort.

Disclosure of Interests: None declared


AB0224 SYSTEMIC SCLEROSIS SINE SCLERODERMA: CHALLENGES WITH VERIFICATION IN PATIENTS WITH PULMONARY ARTERIAL HYPERTENSION

Natalia Yudkina, Alexander Volkov, Ekaterina Nikolaeva, Ildar Kurmukov, Evgeny Nasonov. V.A.Nasonova Research Institute of Rheumatology, Moscow, Russian Federation

Background: Recognizing systemic sclerosis (SSc) in patients without cutaneous involvement is a real challenge due to inapparent clinical picture. 1980 ACR classification criteria for SSc fail to verify the diagnosis in the majority of cases. Therefore, the diagnosis is usually established years and decades after SSc onset at the stage of full-blown visceral disease. Introduction of 2013 ACR/EULAR classification criteria into clinical practice allow early diagnosis of SSc even in cases with skin involvement thanks to the fact, that list of considered criteria includes telangectasia, pulmonary arterial hypertension (PAH), abnormal nailfold capillaries and SSc-related autoantibodies.

Objectives: To identify specific features in the clinical course of SSc sine scleroderma (ssSSc) in patients with PAH.

Methods: 11 patients with verified SSc diagnosis according to 2013 criteria were included; participants did not have any SSc-specific signs of skin involvement, such as puffy fingers, fingers’ skin thickening/induration or skin atrophy. PAH was diagnosed in 11 patients during of right heart catheterization.

Results: Isolated Raynaud’s phenomenon (RP) was along-standing diagnosis (more than 5 years) in all patients, except for one whom, in whom the disease manifested with signs of Sjogren’s syndrome (SjS) (parotitis). Benign, chronic, and gradually progressing during a long time disease was documented in all patients. In 7 patients out of 11 SSc diagnosis was initially suspected by cardiologists, and later confirmed by detection of antinuclear autoantibodies. The following signs were documented in SSc patients as initial manifesting non-Raynaud symptoms: esophageal dysmotility – in 3 patients, digital ulcers – in 2, telangectasia – in 2 patients, and dyspnea (PAH symptom) – in 1 patient. None of the patients ever experienced skin thickening typical for SSc. RP was present in all 100%, but digital ischemic alterations – digital tip ulcers, pitting scars were found only in 3 patients. SSc diagnosis was verified based on abnormal nailfold capillaries (in 100% cases), and based on identification of SSc-specific antibodies (anti-Ro/SSA antibodies – ACA) – in 7 patients. Anti-Ro-antibodies were found in 4 patients, anti-RNP-70 – in 3. SjS was established in 3 out of 4 anti-Ro-antibodies – positive patients and ruled out in one. Myositis was documented in past-medical history in one patient with anti-RNP-70-antibodies positivity. It should be noted, that 3 ACA-negative patients had, nevertheless, a “threshold” score value (9 scores) for SSc diagnosis, exhibiting many clinical features in favor of SSc diagnosis beyond any doubt. Esophageal dysmotility and associated symptoms were found in 10 out of 11 SSc patients. One patient had an SSc-rheumatoid arthritis overlap syndrome (erosive arthritis, joint deformities, positive ACA, rheumatoid factor, anti-CCP).

Conclusion: Introduction of 2013 ACR-EULAR classification criteria for SSc into clinical practice was highly relevant for identification of SSc even in cases without skin involvement, such as puffy fingers, fingers’ skin thickening/induration or skin atrophy. PAH was diagnosed in 11 patients during of right heart catheterization. The earlier PAH-SSc is diagnosed and PAH-specific therapy is initiated, the longer will be patient’s lifespan.


AB0225 CLINICAL SUBTYPE OF PULMONARY ARTERIAL HYPERTENSION ASSOCIATED WITH SYSTEMIC SCLEROSIS

Natalia Yudkina, Alexander Volkov, Ekaterina Nikolaeva, Ildar Kurmukov, Evgeny Nasonov. V.A.Nasonova Research Institute of Rheumatology, Moscow, Russian Federation

Background: Despite the similar pathogenesis and clinical picture, pulmonary arterial hypertension in systemic sclerosis (PAH-SSc) is different from idiopathic pulmonary arterial hypertension (IPAH) is characterized by a more severe course, an unsatisfactory response to PAH-specific therapy, a poor survival and a
disappointing prognosis. In this connection, before doctors of different specialties, first of all before rheumatologists, cardiologists and pulmonologists, there is a need to highlight the characteristics of the flow of PAH depending on the presence of SSc.

**Objectives:** To describe specific symptoms of PAH associated with SSc.

**Methods:** The study included 51 patients with PAH-SSc and 50 patients with IPAH formed the control group. To verify the diagnosis of PAH all patients underwent studies according to the program corresponding to the running recommendations for the diagnostics and treatment of pulmonary hypertension with mandatory right heart catheterization. The diagnosis of SSc was established in accordance with the classification criteria ACR-EULAR 2013. Univariate logistic regression was used to calculate a probability (odds ratio (OR)) of SSc-associated symptoms.

**Results:** We identified 29 symptoms that were associated with PAH-SSc. The most significant of them, increasing the risk of detection of SSc in patients with PAH, were age over 45 years (OR 9.7, 95% CI 3.9-24.3, p <0.00001), serum uric acid level> 387 μmol/L (OR 3.8, 95% CI 1.5-9.6, p = 0.003), diffusion lung capacity (DLCO) >60% (OR 13.8, 95% CI 4.3-44.7, p <0.0001), ratio of forced vital capacity to DLCO <1.7 (OR 13.0, 95% CI 3.9-42.9, p <0.0001), level of C-reactive protein >2 mg/l (OR 12.9, 95% CI 3.96-41.8, p <0.00001), the presence of pericardial effusion (OR 6.1, 95% CI 1.2-30.6, p = 0.04), mean right ventricular pressure > 15.5 mm Hg. (OR 8.9, 95% CI 3.4-23.1, p <0.00001), diastolic right ventricular pressure > 4.5 mm Hg. (OR 4.6, 95% CI 1.9-11.2, p = 0.0003).

**Symptoms that reduce the risk of detecting SSc in patients with PAH include mean pulmonary artery pressure >55 mmHg, (OR 0.4, 95% CI 0.2-0.9, p = 0.03), pulmonary vascular resistance >12 units Wood (OR 0.4, 95% CI 0.2-0.9, p = 0.02), hemoglobin level >146 g/l (OR 0.3, 95% CI 0.2-0.8, p = 0.007), presence of syncope (OR 0.3, 95% CI 0.1-0.9, p = 0.03).

**Conclusion:** The selection of features of the course of PAH that increase the likelihood of detection of SSc will contribute to the timely diagnosis of PAH, will allow to predict the course of PAH, to approach more carefully the selection and monitoring of the effectiveness of PAH-specific therapy. That will contribute to improving the survival and functional status of patients with PAH-SSc.


**AB0226** NEOUTROPHIL EXTRACELLULAR TRAPS ACTIVATE LUNG FIBROBLAST TO INDUCE MYOSISI-RELATED INTERSTITIAL LUNG DISEASES IN MICE

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**Background:** Excessive neutrophil extracellular traps (NETs) formation may contribute to myositis-associated interstitial lung diseases (ILD), but the underlying mechanism is not fully revealed.

**Objectives:** This research aimed to elucidate the mechanism by which NET formation and myositis-associated ILD.

**Methods:** Myositis mice model was established by injecting with the rat skeletal muscle homogenate and pertussis toxin. Expressions of ACTA2, CCN2, ADAM12, miR-7 and Smad2 were detected by quantitative real-time polymerase chain reaction (qRT-PCR). Smad2, CCN2, ADAM12, miR-7 and Smad2 were detected by quantitative real-time polymerase chain reaction (qRT-PCR). Smad2, CCN2 and TLR9 signaling-related proteins were measured by western blot. Soluble collagen I-IV were detected by Sircol collagen assay kit. The proliferation of LF was measured by [3H]-thymidine incorporation assay. The interaction between miR-7 and the Smad2 was confirmed by dual-luciferase reporter gene assay. TLR9 and Smad2 were upregulated in lung tissue of myositis group than control group, and NETs further decreased miR-7 expression. TLR9 and Smad2 were upregulated in lung tissue of myositis group than control group, and NETs further increased TLR9 and Smad2 expressions. In vitro experiments showed that PMA-treated NETs accelerated the proliferation of LF and their differentiation into myofibroblasts (MF), whereas DNase I decreased the promotion effect of NETs. NETs components myeloperoxidase (MPO) and histone 3 also promoted the proliferation and differentiation of LF. In addition, we demonstrated that TLR9 involved in the regulation of NETs on LF proliferation and differentiation, and confirmed the interaction between miR-7 and Smad2 in LF. Finally, miR-7-Smad2 pathway was confirmed to be involved in the regulation of TLR9 on LF proliferation and differentiation.

**Conclusion:** NETs promote myositis-related ILD, and TLR9-miR-7-Smad2 signaling pathway is involved in the proliferation of LFs and their differentiation into MFs.

**REFERENCES:**


**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.4222

**Basic science in paediatric rheumatology**

**AB0227** EXTENSIVE IMMUNOPHENOTYPIC ANALYSIS OF CO-INHIBITORY AND CO-STIMULATORY MOLECULES IN JUVENILE IDIOPATHIC ARTHRITIS (JIA) PERIPHERAL LYMPHOCYTES

Estefania Quesada-Masachs1, Daniel Álvarez de la Sierra2, Antonio Júlía3, Monica Martinez-Galio3, Maria Moreno-Cortés3, Ricardo Pujol-Borrell1, Consuelo Modesto1, Sara Maragà1, Vall d’Hebron University Hospital, Pediatric Rheumatology, Barcelona, Spain; 2Vall d’Hebron University Hospital, Immunology, Barcelona, Spain; 3Vall d’Hebron Research Institute, Barcelona, Spain; 4Vall d’Hebron University Hospital, Rheumatology, Barcelona, Spain

**Background:** In a previous in-depth phenotypic analysis of PBLS in JIA, we detected differences in cell subpopulations dependent on the age and disease activity, and some cellular changes that could be often associated with an exhausted phenotype.

**Objectives:** To analyze the expression of co-inhibitory and co-stimulatory molecules in different cellular subpopulations in Oligoarticular JIA patients stratified by age and treatment.

**Methods:** Exploratory cross-sectional study. 53 patients fulfilling Oligoarticular JIA (ILAR) criteria and 22 controls were included. All of them were children or young adults (2 to 35 years of age). JIA patients were either not treated (n=14) or treated with MTX (n=14), anti-TNF (n=8), or a combination of both (n=16). JIA disease activity was clinically and biologically assessed. Four flow cytometry panels were designed for the analysis of co-stimulatory/co-inhibitory markers, some typical of “exhausted” cells (PD1, TIM 3, TIGIT, CD226, CD137, HVEM, LIGHT, BTLA), assessed in memory, effector and naïve CD4+ and CD8+ T lymphocytes, and also in B lymphocytes and NK cells. Statistical analysis was performed, and FDR correction was applied for p values.

**Results:** No correlation was found among the different exhaustion/activation markers and age or disease activity. However, there were some differential trends in CD8+ compartments in Oligoarticular JIA patients, but stratified by age and treatment.

**Conclusion:** No clear differences were found in PBL subpopulations of oligoarticular-JIA patients regarding co-stimulatory/co-inhibitory molecules.

**Disclosure of Interests:** None declared

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CHILDREN WITH EXTENDED OLOGOARTICULAR
AND MULTARTICULAR JUVENILE IDIOPATHIC ARTHRITIS
HAVE A CYTOKINE PATTERN FAVOURING B CELL
ACTIVITY IN COMPARISON SIMILARLY TO EARLY
AND ESTABLISHED RHEUMATOID ARTHRITIS
PATIENTS

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Background: The majority of polyarticular JIA (pJIA) and a large fraction of extended oligoarticular JIA (oJIA) patients fulfill classification criteria for rheumatoid arthritis (RA) in adulthood. B cells play several important roles in RA pathogenesis, but it is still unclear if the pattern of B cell involvement in pJIA and extended oJIA follows what has been described for adults with RA.

Objectives: The main goal of this study was to determine the concentration of cytokines potentially relevant for B cell activation in serum from children with pJIA and extended oJIA when compared to children with persistent oJIA, adult JIA, early and established RA patients.

Methods: Serum samples were collected from children with extended oJIA (n=8), persistent oJIA (n=6), pJIA (n=6), adult JIA (n=8), untreated early RA (<1 year of disease duration, n=12), established RA patients treated with anti-TNF (n=20), anti-DICARs (n=10) and corresponding groups of age- and sex-matched healthy donors (children, n=4 and adults, n=10). A proliferation-inducing ligand (APRIL), B-cell activating factor (BAFF), interleukin (IL)-6 and IL-21 serum levels were measured by ELISA.

Results: Children with extended oJIA, early and established RA patients had significantly higher IL-6 and IL-21 serum levels when compared to controls, but no significant differences were observed in children with persistent oJIA, pJIA and adult JIA when compared to all groups included. APRIL serum levels were significantly increased in all patient groups when compared to controls, except in adult JIA, who had similar APRIL concentrations in comparison to controls. In addition, children with extended oJIA and pJIA had significantly higher APRIL serum levels when compared to adult JIA. IL-6 serum levels were significantly increased in children with persistent oJIA and adult JIA patients. IL-21 serum levels were significantly increased in early RA when compared to controls, but no significant differences were observed between any of the other groups included.

Conclusion: There is a similarity in B cell cytokine pattern found between extended oJIA, pJIA, and non-classical monocytes in patients with SLE and JSLE. This correlation was lost when JSLE and SLE were grouped together, or when SLE was examined in isolation. Increased percentages of non-classical monocytes were associated with a higher odds of adult onset SLE relative to JSLE, after adjusting for the effects of disease activity (SLE-DAI) (OR= 1.137, 95% CI= 1.021–1.266, p= 0.018).

Disclosure of Interests: None declared


RELATIVE MONOCYTE SUBSET DIFFERENCES
BETWEEN JUVENILE- AND ADULT-ONSET SYSTEMIC
LUPUS ERYTHEMATOSUS

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Background: Inflammation is a mediator and primary driver of joint damage in juvenile idiopathic arthritis (JIA). Musculoskeletal pain can be experienced in the presence or absence of inflammation. Enthesitis related arthritis (ERA) is a subtype of JIA characterised by inflammation of the spine, entheses, and peripheral joints. Cytokines and numerous other regulatory molecules are implicated in pain and inflammation, yet, to date, no reliable biomarkers have been identified.

Objectives: To assess if cytokine profiles correlate with pain or disease activity in well controlled ERA.

Methods: 42 patients, with either a prior diagnosis of JIA or back pain, agreed to have a standard clinical MRI scan of lumbar spine, sacroiliac joints, and pelvis and to donate serum. Serum was also collected from 12 volunteer age matched healthy controls. Serum was analysed using a bead-based multiplex assay (Luminex) for the concentrations of the

Disclosure of Interests: None declared


CYTOKINE SIGNATURE DOES NOT CORRELATE WITH
PAIN OR DISEASE ACTIVITY IN WELL CONTROLLED
ERA

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Background: Inflammation is a mediator and primary driver of joint damage in juvenile idiopathic arthritis (JIA). Musculoskeletal pain can be experienced in the presence or absence of inflammation. Enthesitis related arthritis (ERA) is a subtype of JIA characterised by inflammation of the spine, entheses, and peripheral joints. Cytokines and numerous other regulatory molecules are implicated in pain and inflammation, yet, to date, no reliable biomarkers have been identified.

Objectives: To assess if cytokine profiles correlate with pain or disease activity in patients with ERA.

Methods: 42 patients, with either a prior diagnosis of JIA or back pain, agreed to have a standard clinical MRI scan of lumbar spine, sacroiliac joints, and pelvis and to donate serum. Serum was also collected from 12 volunteer age matched healthy controls. Serum was analysed using a bead-based multiplex assay (Luminex) for the concentrations of the
following analytes: IL-6, IL-12, IL-17, IL-23, TNFα, IFNγ, MIF, OPG, SOST, GM-CSF, VEGF, DKK-1, S100A8, MMP-3 and CRP. To assess pain levels, patients indicated on a scale of 0-10 the amount of back pain experienced at night and separately the amount of back pain experienced at any time during the last week. They also completed a Bath Ankylosing Spondylitis Disease activity Index (BASDAI) questionnaire to assess disease activity. Cytokine concentrations in patients with ERA were compared with those of controls. The levels were also correlated with the two measures of back pain as well as individual questions from the BASDAI questionnaire.

Results: Of all 54 samples tested, 11 patients and 5 controls cross-reacted with the negative control for the assay and thus were excluded from analysis. Based on MRI scan results, 14 patients had ERA, 8 had biomechanical pain, 7 had other subtypes of JIA, and 2 had non-specific features of spinal inflammation. The median overall back pain and the total BASDAI scores for the ERA group were 2.4 (IQR=1.45-5.55) and 2.5 (IQR= 0.75-6.25) respectively, suggesting well controlled disease on treatment and minimal residual symptoms. There was no statistical difference between cytokine levels in the ERA group compared to controls when corrected for multiple testing, with the exception of IL-12 which was significantly higher in controls (p=0.003). No correlation was found between cytokines and pain scores (at night or overall during the last week) or with the overall BASDAI score or any of the sub-component questions of the BASDAI questionnaire.

Conclusion: Well-controlled ERA patients on treatment have similar cytokine profiles as healthy controls and they do not correlate with clinical pain scores or disease activity.

Disclosure of Interests: None declared


ABO2306 STUDY OF CELIAC DISEASE ANTIBODIES IN PATIENTS WITH JUVENILE ONSET RHEUMATOLOGICAL DISORDERS

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Background: Preclinical autoimmunity can be detected in the form of circulating autoantibodies in the peripheral blood many years preceding the onset of the clinical disease. Celiac disease (CD) is an immunological response to gluten in genetically susceptible people. The clinical presentation of CD includes abdominal pain, diarrhea and nutritional deficiencies. However, clinical symptoms could be misleading in most of the patients presenting subclinical forms with only minor gastrointestinal symptoms. Celiac disease will present in older children by atypical presentation. Most celiac disease patients show atypical symptoms and may remain untreated, which makes screening is mandatory in high-risk patients with autoimmune diseases. This collectively highlights the need to check for clinical evidence of celiac disease among patients diagnosed as juvenile onset rheumatic diseases.

Objectives: The aim of this study was to screen for celiac disease antibodies (anti-tissue transglutaminase IgA and IgG auto-antibodies) in the serum of juvenile onset rheumatic diseases patients in comparison with normal subjects.

Methods: Serum anti-ITG (both IgA and IgG) level was detected in 60 juvenile onset rheumatic patients and 20 age and sex matched healthy controls. We also assessed different clinical and laboratory markers of disease parameters; 31 juvenile onset systemic lupus erythematosus (SLE), 21 juvenile onset idiopathic arthritis (JIA), 4 juvenile onset systemic sclerosis and 2 juvenile onset behcet's disease and each disease activity score. We also correlated serum transglutaminase auto-antibodies with each disease activity, Endoscopic examination and histopathologic examination, for the patients with a least one positive anti-ITG Ab was done.

Results: Serum anti-ITG Abs was no statistical significant differences in the patients group than in the control group, and there was no correlation between anti-ITG Abs with positive disease activity score.

Conclusion: The presence of concomitant CD and another rheumatic disorder in the same patient is unlikely.

REFERENCES:


ABO231 PAIN THRESHOLD IN RHEUMATOID ARTHRITIS AND ITS RELATED FACTOR

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Background: Pain remains the most important challenge for rheumatoid arthritis (RA) patients. In order to cope with pain in RA, clinicians firstly need to understand the degree of patients' pain. When self reported measures such as visual analog scale were used, inconsistency between clinicians' and patients' ratings of pain was demonstrated (1). As a result, inability to fully assess the pain will cause the inability to fully assess the impact of pain on disease severity. Measuring pressure pain threshold with pressure algometry may provide additional advantages for the evaluation of pain and disease severity when compared with self-reported measures.

Objectives: The aim of this study was to evaluate the pain threshold and to determine the variables associated with pain threshold in the patients with RA.

Methods: The current study included 100 RA patients and 80 age-sex matched controls with non-inflammatory chronic low back pain. Clinical parameters, functional status, disease activity, pain, fatigue, depression, anxiety, pain catastrophizing and laboratory activity of RA patients were recorded. The pressure pain thresholds on the dominant thumb nail bed, trapezius and wrist of the two groups were measured by the algometer. The pain thresholds of the patients with RA and controls were compared.

Moreover, the relation between pain thresholds and all evaluated parameters in RA patients was analysed.

Results: The mean age of RA patients was 55.93 ± 10.81; the mean age of the controls was 54.50 ± 9.47. The pain thresholds of RA patients and controls were statistically similar in all areas. When the parameters found to be significantly correlated with pain threshold in RA patients were analyzed by regression analysis, depression was the only factor associated with low pain threshold in all areas (Table 1).

Conclusion: We found that depression was the only factor associated with low pain threshold in the patients with RA. The use of pressure algometry in the evaluation of chronic pain could offer an additional method to detect pain/depression overlap.

Table 1. The correlation between pain threshold values and demographic, clinical and laboratory parameters of RA patients

<table>
<thead>
<tr>
<th></th>
<th>Nail PT</th>
<th>Wrist PT</th>
<th>Trapezius PT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>age</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>BMI (kg/m²)</strong></td>
<td>0.351</td>
<td>0.060</td>
<td>0.038</td>
</tr>
<tr>
<td><strong>Duration of disease</strong></td>
<td>0.141</td>
<td>0.082</td>
<td>0.054</td>
</tr>
<tr>
<td><strong>Morning stiffness</strong></td>
<td>0.451</td>
<td>0.082</td>
<td>0.592</td>
</tr>
<tr>
<td><strong>Tender joint counts</strong></td>
<td>0.109</td>
<td>0.161</td>
<td>0.227</td>
</tr>
<tr>
<td><strong>Swollen joint counts</strong></td>
<td>0.361</td>
<td>0.091</td>
<td>0.069</td>
</tr>
<tr>
<td><strong>CRP</strong></td>
<td>0.764</td>
<td>0.044</td>
<td>0.144</td>
</tr>
<tr>
<td><strong>ESR</strong></td>
<td>0.050</td>
<td>0.030</td>
<td>0.098</td>
</tr>
<tr>
<td><strong>VAS</strong></td>
<td>0.056</td>
<td>0.192</td>
<td>0.069</td>
</tr>
<tr>
<td><strong>PCS</strong></td>
<td>0.013+</td>
<td>0.248</td>
<td>0.031-</td>
</tr>
<tr>
<td><strong>Fatigue Intensity Scale</strong></td>
<td>0.107</td>
<td>0.162</td>
<td>0.145</td>
</tr>
<tr>
<td><strong>HADS-Anxiety</strong></td>
<td>0.157</td>
<td>0.143</td>
<td>0.118</td>
</tr>
<tr>
<td><strong>HADS-Depression</strong></td>
<td>0.010</td>
<td>0.256</td>
<td>0.005-</td>
</tr>
<tr>
<td><strong>HADS-Total</strong></td>
<td>0.026</td>
<td>0.232</td>
<td>0.014+</td>
</tr>
<tr>
<td><strong>HAG</strong></td>
<td>0.001*</td>
<td>0.264</td>
<td>0.003-</td>
</tr>
<tr>
<td><strong>DAS28-ESR</strong></td>
<td>0.013</td>
<td>0.248</td>
<td>0.091-</td>
</tr>
<tr>
<td><strong>DAS28-CRP</strong></td>
<td>0.009</td>
<td>0.261</td>
<td>0.066-</td>
</tr>
</tbody>
</table>

PT: pain threshold, BMI: Body mass index, PCS: Pain Catastrophizing Scale, VAS: Visual Analog Scale, HAG: The health assessment questionnaire

*p < 0.05

Disclosure of Interests: None declared


Rheumatoid arthritis – prognosis, predictors and outcome
AB0232 TIGHT CONTROL MANAGEMENT OF EARLY RA ACHIEVES MORE PATIENTS IN REMISSION AT 6 MONTHS AND IMPROVES PAIN, FUNCTION AND FATIGUE AT 24 MONTHS COMPARED TO A CONTROL GROUP

Maria Aronsson1,2, Annika Teleman1, Stefan Bergman2,3, Kristina Forslind4, Maria Andersson1,2. Background: Even with modern antirheumatic treatment, many patients experience chronic pain and loss of function despite less disease activity. The understanding of how this chronic pain development can be prevented is sparse. There is furthermore little knowledge if a tight control management without specific treatment schemes and instructions for the physicians to follow could increase the remission frequency.

Objectives: To determine whether solely a tight control management of patients, without further intervention in the physician’s work, can increase the remission frequency and improve patient reported outcome in early RA.

Methods: In all, 96 patients with early RA were consecutively included in a tight control study group (TCS). Inclusion criteria were early RA patients (<13 month duration) with no previous history of rheumatic disease. A control group, with so far 27 patients receiving standard care, has been analyzed. The tight control management included monthly visits to the physician the first 6 months, followed by visits at 9, 12 and 24 months. If not in remission at 6 months the patients’ monthly visits could continue to 12 months. The study did not include any treatment guidelines for the physicians. Pain, Fatigue and the Patient’s Global Assessment of the General Health (PIGA) were reported on a Visual Analogue Scale (VAS). The 28 tender and swollen joint score, DAS28, C-Reactive protein, Erythrocyte sedimentation rate and Health Assessment Questionnaire (HAQ) were assessed.

Results: There was no significant difference between the groups at baseline in gender, age, smoking, disease duration, disease activity, pain, HAQ, fatigue, RF and ACPA. There was a significant difference between groups in outcome, with 70% of TCS and 37% of control patients in remission (DAS28 <2.6), p=0.010, at 6 months, figure 1A. At 12 and 24 months there was no significant difference in the remission frequency, figure 1A. The TCS group improved more than the control group in Pain, Fatigue and HAQ during follow up, figure 1B-D. The median VAS pain at 24 months was 11 (IQR 2-22) in the TCS group and 22 (IQR 4-42) in the control group, p=0.036. The median VAS fatigue was 13 (IQR 2-38) in the TCS group and 33 (IQR 8-70) in the control group p=0.028 at 24 months. The difference in HAQ reached significant numbers solely at 6 months where the median was 0.13 (IQR 0-0.50) in the TCS group and 0.57 in the control group (IQR 0.16-0.94).

Conclusion: Patients in tight control reached remission faster than patients receiving standard care. They also reported less pain and fatigue, despite the fact that there was no difference in remission frequency at 24 months. The results indicate that a tight control scheme could influence pain development in patients with early RA, but further studies are required.

Disclosure of Interests: None declared
AN INTEGRATED PROTEOMICS AND ANTIBODY ANALYSIS OF THE U-ACT-EARLY TRIAL TO IDENTIFY MARKERS OF TREATMENT RESPONSE AND DISEASE PROGRESSION IN EARLY RHEUMATOID ARTHRITIS

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Background: Predictive markers of treatment response in rheumatoid arthritis (RA) are necessary to stratify patients to devise personalised treatment strategies. The U-ACT-Early trial [1], in which disease-modifying anti-rheumatic drugs (DMARD) naïve early RA patients initiated either methotrexate (MTX) or tocilizumab (TCZ) in monotherapy or in combination, offers a unique opportunity to assess the capacity of many baseline –omics markers (i.e. genomics, transcriptomics, proteomics, metabolomics, auto-antibodies) to predict clinical outcomes.

Objectives: To identify predictive markers of treatment response by developing a statistical machine learning methodology for correlating baseline clinical and –omics variables with clinical response data over time.

Methods: We developed a multi-omics approach that combines longitudinal statistical modelling of clinical data with Bayesian machine learning variable selection to identify the most predictive markers of treatment response. The time course of clinical outcomes was fit using a non-linear mixed longitudinal model, that characterises each patient of the U-ACT-Early trial (n=317) by three parameters: a baseline value, an asymptotic value and a velocity (describing the speed at which the asymptote is reached). Supervised machine learning methods (such as Bayesian sparse regression as well as tree-based algorithms) were subsequently employed to find active markers for each of the longitudinal model parameters. We specifically focused on 85 auto-inflammatory proteins and 450 auto-antibodies markers, including 41 citrullinated-peptides antigens. The analysis was repeated for the three treatment-arms since DAS28-subscores response markers may vary across treatment strategies and clinical outcomes. We finally investigated whether predictions are enhanced by incorporating known networks of protein-protein interactions, rather than –omics variables with clinical response data over time.

Results: Preliminary results are that some proteins (e.g. sCD14, VEGF) were moderately predictive of the disease status at baseline. Specifically, the available inflammatory proteins predicted baseline DAS28, swollen and tender joints and ESR with R² values of 0.25, 0.32, 0.16 and 0 respectively. Surprisingly, these proteins did not improve the prediction of treatment-response (i.e. the velocity and asymptotic parameters) after controlling for the baseline disease status. Protein networks marginally improved prediction when compared to prediction of individual proteins. Citrullinated peptide antigens did not appear predictive of the baseline disease status nor the treatment response.

Conclusion: In our initial investigation inflammatory proteins, especially when considered as part of interaction networks, appear to be predictive of the baseline status of the disease but not of treatment-response. The most predictive marker of treatment response appears to be disease activity at baseline.

REFERENCES:

Disclosure of Interests: Francesco Brizzi Employee of: F. Hoffmann-LaRoche, Suleiman A. Khan: None declared, Marco Prunotto Employee of: F. Hoffmann-La Roche, Jenny Devporton Employee of: F. Hoffmann-La Roche, Attila Pethoe-Schramm Shareholder of: F. Hoffmann-La Roche, Employee of: F. Hoffmann-La Roche, Michelle Born Employee of: An employee of Roche Nederland BV, Johannes W Bijlaard Grant/research support from: The department of the author who included patients (JWJB) in the U-ACT-Early trial received reimbursements from Roche Nederland BV. JWJB reported grants and fees from Roche, AbbVie, Bristol-Myers Squibb, Merck Sharp & Dohme, Pfizer, and UCB University Medical Center Utrecht, Utrecht University, Consultant for: SUN Pharma, Speakers bureau: Lilly, Roche, Johannes W G. Jacobs Grant/research support from: Roche, Consultant for: Roche, Floris Lafeber Shareholder of: Arthro-Save, Grant/research support from: FOREUM; Dutch Arthritis Society, Paco Welsing: None declared, Tero Naltokkio: None declared, Antoine Soubret Employee of: F. Hoffmann-La Roche


THE LIFETIME RISK OF KNEE AND HIP REPLACEMENT FOLLOWING A DIAGNOSIS OF RHEUMATOID ARTHRITIS: FINDINGS FROM ROUTINELY COLLECTED DATA FROM ENGLAND

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Background: Understanding the lifetime risk of knee and hip replacement following a diagnosis of rheumatoid arthritis (RA) would help provide patients and clinicians with an indication of long-term prognosis and future health care utilisation.

Objectives: To estimate the lifetime risk of knee and hip replacement following a diagnosis of RA.

Methods: Routinely collected data from the English NHS was used to inform the analysis. Diagnosis of RA was identified using primary care records, with knee and hip replacement observed in linked hospital records. Parametric survival models were fitted for up to 15 years of follow up, with age, sex, Charlson comorbidity score, socioeconomic status, BMI, and smoking status included as explanatory variables. A decision model was used to combine and extrapolate survival models to estimate lifetime risk. Lifetime risk was estimated for individuals with average characteristics (median for continuous variables and mode for categorical ones). The partial effect of explanatory factors on lifetime risk was assessed by re-running models with participant profiles varying in the explanatory factor of interest, while holding other characteristics constant at their average.

Results: 13,961 study participants with a diagnosis of RA were included. Lifetime risk of knee replacement and hip replacement was estimated to be 22% (95%CI 16% to 29%) and 17% (11% to 26%) following a diagnosis of RA for the average patient profile (non-smoking women aged 64 with no other comorbidities, BMI of 27 and in the top socioeconomic quintile). Risks were higher for younger patients, but broadly similar for men and women. Comorbidities, socioeconomic status, BMI, and smoking status had relatively little impact on lifetime risk.

Conclusion: This study has estimated lifetime risk of knee and hip replacement following a diagnosis of RA, allowing for a better understanding of long-term prognosis and healthcare resource use. These risks are more than double those of the general UK population.

Disclosure of Interests: Edward Burn: None declared, Christopher Edwards Grant/research support from: Abbvie, BMS, Biogen, Cellgene, Fresenius, Janssen, Lilly, Mundipharma, Pfizer, MSD, Novartis, Roche, Samsung, Sanofi, UCB, Consultant for: Abbvie, BMS, Biogen, Cellgene, Fresenius, Janssen, Lilly, Mundipharma, Pfizer, MSD, Novartis, Roche, Samsung, Sanofi, UCB, Grant/research support from: Grants from Zimmer Biomet, Consultant for: Personal fees from Zimmer Biomet, Alan Silman: None declared, Cyril Cooper Consultant for: Personal fees from Alliance for Better Bone Health, Agen, Eli Lilly, GSK, Medtronic, Merck, Novartis, Pfizer, Roche, Servier, Takeda and UCB, Nigel Arden Grant/research support from: Grants from BIOIBERICA, and from MERC., Consultant for: Personal fees from Flexion, from Regeneron, from Fresfield Bruckhaus Deringer, outside the submitted work., Rafael Pinedo-Villanueva: None declared, Daniel Prieto-Alhambra Grant/ research support from: Grants from Agen, UCB Biopharma and Servier outside the submitted work, Consultant for: UCB Biopharma, Speakers bureau: Agen

WHAT FACTORS ARE ASSOCIATED WITH THE EVOLUTION TOWARDS RHEUMATOID ARTHRITIS, USE OF BIOLOGICAL THERAPY AND DEVELOPMENT OF CARDIOVASCULAR EVENTS IN A COHORT OF PATIENTS WITH UNDIFFERENTIATED ARTHRITIS?

Jerusalem Calvo Gutierrez1, Rafaela Ortega Castro1, Clementina López-Medina2, Ladehse Pineda Lourdes3, María del Carmen Castro Villegas4, Alejandro Escudero Contreras4, Eduardo Collantes Estévez5, Reina Sofia University Hospital, Maimonides Institute of Biomedical Research of Córdoba (IMIBIC), University of Córdoba, Rheumatology, Córdoba, Spain; 2Cochin Hospital, Rheumatology, Paris, France

Objectives: To describe the clinical-demographic characteristics and behaviour over time (12, 24 and 60 months) of a cohort of Undifferentiated Arthritis (UA) and to assess which factors are associated with the evolution towards Rheumatoid Arthritis (RA), use of Biological Therapy (BT) and the development of Cardiovascular Disease (CVD).

Methods: Ambispective cohort study of patients with UA evaluated longitudinally from January 2009 to 2019. We analyzed baseline clinical and laboratory variables and a Multivariate Logistic Regression was performed to determine the factors associated with RA development after 5 years of follow-up. To analyze what factors were associated with the use of BT and the presence of CVD the chi-square or Fisher test were used for binary variables, and U-Mann Whitney for continuous variables.

Results: 180 patients were included, 55% women, with an average age of 49.3 (SD 16.1) years. The average duration of symptoms before the first visit was 6.9 (SD 9.9) months. 47.2% were FRR., 41% ACPA+, 20.6% HLA-DRB1 shared epitope. At the end of follow-up, 33.3% evolved to RA, 17.2% remained as palindromic rheumatism, 25% were diagnosed other chronic rheumatic diseases, 21.1% remitted spontaneously and 3.3% remained as UA. Of the 60 AR, 37 were diagnosed in the first year, 13 at second and 10 at 5 years of follow-up. During follow-up, 13 patients with RA started BT, and 12 patients presented CVD (7 of them died).

Table 1: Factors associated with RA after 5 years of follow-up.

<table>
<thead>
<tr>
<th>Baseline data</th>
<th>Total patients</th>
<th>RA</th>
<th>No RA</th>
<th>OR (95% CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (women)</td>
<td>99 (45.7%)</td>
<td>34</td>
<td>65</td>
<td>1.11 (0.69-1.75)</td>
<td>0.719</td>
</tr>
<tr>
<td>duration of symptoms (months)</td>
<td>7.7 (8.8)</td>
<td>7.5 (6.5)</td>
<td>7.8 (9.8)</td>
<td>0.99 (0.96-1.03)</td>
<td>0.33</td>
</tr>
<tr>
<td>Age at diagnosis</td>
<td>49.3 (16.1)</td>
<td>49.4 (14.5)</td>
<td>49.6 (16.2)</td>
<td>1.00 (0.98-1.02)</td>
<td>0.961</td>
</tr>
<tr>
<td>RF+</td>
<td>85 (46.7%)</td>
<td>27</td>
<td>58</td>
<td>2.19 (1.51-3.21)</td>
<td>0.002</td>
</tr>
<tr>
<td>ACPA+</td>
<td>79 (43.9%)</td>
<td>20</td>
<td>59</td>
<td>3.54 (2.36-5.25)</td>
<td>0.00001</td>
</tr>
<tr>
<td>Morning stiffness&gt;1h</td>
<td>43 (23.9%)</td>
<td>21</td>
<td>22</td>
<td>2.73 (1.35-5.52)</td>
<td>0.005</td>
</tr>
<tr>
<td>RF+</td>
<td>85 (47.2%)</td>
<td>47</td>
<td>38</td>
<td>7.3 (3.78-16.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ACPA+</td>
<td>73 (41.0%)</td>
<td>50</td>
<td>23</td>
<td>2.06 (1.01-4.15)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>High ESR</td>
<td>104 (57.8%)</td>
<td>64</td>
<td>40</td>
<td>1.75 (0.92-3.34)</td>
<td>0.089</td>
</tr>
<tr>
<td>Hight CRP</td>
<td>105 (56.6%)</td>
<td>40</td>
<td>65</td>
<td>2.0 (1.05-4.05)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HLA-DRB1 Shared epitope</td>
<td>37 (20.6%)</td>
<td>32</td>
<td>5 (4.2%)</td>
<td>26.3 (9.39-73.55)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HLA-DRB1 Shared epitope</td>
<td>37 (20.6%)</td>
<td>32</td>
<td>5 (4.2%)</td>
<td>26.3 (9.39-73.55)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Table 1 identifies the factors associated with the development of RA. The MDR identified ACPA+ OR (95% CI) = 7.9 (6.09 - 10.69) (4.43 - 25.78), and the HLA-DRB1 shared epitope OR (95% CI) = 9.18 (2.96 - 28.48) p <0.001 as factors associated to the development of AR. We failed to identify factors associated with the use of BT, possibly due to the sample size. The factors associated with the development of CVD, where only the use of glucocorticoids as a factor associated with the presence of CVD shows statistical significance.

Conclusion: 1) Useful clinical and laboratory characteristics have been identified to predict which patients are at risk of developing persistent arthritis. 2) HLADR1 shared Epitope and ACPA are predictive factors of evolution to RA. 3) Possibly the continued use of glucocorticoids, even at low doses, may be related to the development of long-term CVD.

WHAT DO SPANISH RHEUMATOLOGISTS THINK ABOUT THE EFFICACY OF THE DRUGS USED IN THE MANAGEMENT OF PATIENTS WITH RHEUMATOID ARTHRITIS AND POOR PROGNOSIS FACTORS? PROGRESAR-2 PROJECT

Loreto Carmona1, J. Narváez2, Jaime Calvo3, Alejandro Escudero Contreras4, Santiago Muñoz Fernandez5, José M. Rodríguez-Heredia6, Susana Román-Gómez7, Paloma Vela Casasempere8, Jose Luis Baquero9, Sara Lujan Valdés10, Juan J. Sancho Jiménez11, ImMus (Instituto de Salud Musculoesquelética), Madrid, Spain; 2Hospital Universitari de Bellvitge, Barcelona, Spain; 3Hospital Universitario Araba, Vitoria, Spain; 4Hospital Universitario Reina Sofía, Córdoba, Spain; 5Hospital Universitario Infanta Sofia, Universidad Europea, Madrid, Spain; 6Hospital Universitario de Getafe, Madrid, Spain; 7Hospital Universitario de Pontevedra, Pontevedra, Spain; 8Hospital General Universitario de Alicante, Alicante, Spain; 9Scienctia Salus, Madrid, Spain; 10Medical Department, Bristol-Myers Squibb, Madrid, Spain

Background: Currently, patients with rheumatoid arthritis (RA) have a wide range of treatments available to achieve a good control of the disease and avoid progression. However, some patients, especially those with poor prognostic factors, need to switch drugs to achieve remission or low disease activity. If we can predict the response to a drug, given specific prognostic profiles, we may be able to choose the best drug for individual patients.

Objectives: To assess the degree of confidence of rheumatologists regarding the efficacy of biologic therapies and specific targeted synthetic molecules in patients with RA harboring poor prognostic factors.

Methods: A Delphi survey was sent to a group of rheumatologists with the aim to capture the perceived efficacy of a group of drugs (antiTNF, T-cell co-stimulators, B-cells depletors, anti IL6, and JAK inhibitors) given different poor prognostic factors are present at the onset of the disease. These factors were: interstitial lung disease, elevated HAQ, positive rheumatoid factor (RF), presence of anti-citrullinated protein antibody (ACPA), elevated acute phase reagents (APR), and bone erosions observed by simple x-ray/ultrasound. The survey was circulated in two rounds, with agreement on scores were in one of the three levels (correspondingly it would be "neutrality", "agree", and "strongly agree").

Table 1: Agreement of the efficacy of therapy (m SD)

<table>
<thead>
<tr>
<th>Prognostic factor</th>
<th>AntiTNF</th>
<th>T-cell co-stimulators</th>
<th>B-cells depletors</th>
<th>Anti IL6</th>
<th>JAK inhibitors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intestinal Lung Disease</td>
<td>2.5 (1.5)</td>
<td>8.6 (0.7)</td>
<td>7.3 (1.4)</td>
<td>6.2</td>
<td>5.1 (1.6)</td>
</tr>
<tr>
<td>High HAQ</td>
<td>8.1 (0.7)</td>
<td>7.4 (1.0)</td>
<td>7.0 (1.0)</td>
<td>8.1</td>
<td>7.9 (0.9)</td>
</tr>
<tr>
<td>RF positive</td>
<td>7.7 (0.8)</td>
<td>8.1 (0.6)</td>
<td>8.3 (0.5)</td>
<td>7.8</td>
<td>7.6 (0.8)</td>
</tr>
<tr>
<td>ACPA positive</td>
<td>7.8 (0.8)</td>
<td>8.6 (0.5)</td>
<td>8.2 (0.7)</td>
<td>7.5</td>
<td>7.4 (0.7)</td>
</tr>
<tr>
<td>Elevated APR</td>
<td>7.9 (0.7)</td>
<td>7.2 (0.7)</td>
<td>7.0 (0.9)</td>
<td>8.7</td>
<td>7.9 (0.9)</td>
</tr>
<tr>
<td>Bone erosions by</td>
<td>8.1 (0.8)</td>
<td>7.9 (0.6)</td>
<td>7.3 (0.8)</td>
<td>8.2</td>
<td>7.8 (0.8)</td>
</tr>
<tr>
<td>Bone erosions by US</td>
<td>8.2 (0.9)</td>
<td>7.9 (0.7)</td>
<td>7.9 (0.7)</td>
<td>7.4</td>
<td>7.8 (0.8)</td>
</tr>
</tbody>
</table>

Table 1 shows that there is agreement among rheumatologists regarding the efficacy of biologic therapies and specific targeted synthetic molecules in patients with RA with poor prognostic factors. There is agreement among rheumatologists regarding the efficacy of therapy m (SD).
AB0239 EFFECT OF SMOKING ON THE EFFICACY OF TNF INHIBITORS IN THE TREATMENT OF CHRONIC INFLAMMATORY IMMUNE-MEDIATED DISEASES: SYSTEMATIC REVIEW AND META-ANALYSIS

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Background: Chronic inflammatory immune-mediated diseases, as rheumatoid arthritis (RA), psoriatic arthritis (PsA), psoriasis (Ps), ankylosing spondylitis (AS), ulcerative colitis (UC) and Crohn’s disease (CD), have higher risks of morbidity and mortality and a great impact on quality of life of patients1. Drug inhibitors of tumor necrosis factor (TNF) inhibitors have demonstrated an adequate efficacy and safety profile in these patients when classical treatments (as disease-modifying antirheumatic drugs) have been failed or patients were intolerant. TNF inhibitors are used to control inflammatory response and to improve quality of life, pain, functional capacity and progression of the disease2. Studies in RA show that smoking habit is related to more articular and extra-articular damage, worse prognosis, higher basal activity and higher risk of seropositive RA. It has been related also to greater number of different treatments and higher doses needed for patients by pharmacokinetic and pharmacodynamic reasons. Data published until now suggest that smoking habit decreases efficacy of TNF inhibitors3.

Objectives: To analyze the smoking habit influence on the efficacy of TNF inhibitors in patients diagnosed of chronic inflammatory immune-mediated diseases (RA, PsA, Ps, AS, UC, CD).

Methods: It was made a systematic literature search using Cochrane Library, Medline, the Web of Science and Embase databases. Meta-analyses were performed using a random-effects model.

Results: 37 of 9877 identified articles met the inclusion criteria. No documents with GOL were found. The analysis of all the diseases together gives a significant decrease on the response to TNF inhibitors in smoking patients [OR 0.812 (0.662-0.996), p=0.046]. This response also has a significant decrease in IBD maintained response in smoking patients [OR 0.467 (0.257-0.848), p=0.012]. A non-significant decrease in the treatment response of smoking patients with IBD clinical remission was found, in smoking patients versus ex-smoking and never smoking patients with IBD remission, in ex-smoking patients versus never smoking patients with IBD partial response, in current and ex-smoking patients versus never smoking patients with IBD partial response, in current smoking patients versus ex-smoking patients with IBD partial response, in current smoking patients versus never and ex-smoking patients with IBD partial response, in current smoking patients versus never smoking patients with IBD partial response, in patients with AR EULAR and in patients with AR EULAR moderate response.

Conclusion: Smoking habit is a poor prognosis factor in RA, AS, PsA, UC and CD. Its leaving will decrease cardiovascular risk, joint and bowel damage, will increase the efficacy of TNF inhibitors and will benefit the health of patients, not only in their particular disease, and it can be the first step on their treatment.

REFERENCES:

Disclosure of Interests: None declared
ALCOHOL CONSUMPTION AND DEVELOPMENT OF ARTHRITIS AMONG PATIENTS WITH ANTI-CITRULLINATED PEPTIDE ANTIBODIES AND MUSCULOSKELETAL PAIN

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Background: Individuals with anti-citrullinated peptide antibodies (ACPA) and arthralgia are at increased risk of developing rheumatoid arthritis (RA). Predictors of disease development are important within this category of patients in order to improve treatment and follow-up decisions. Although excessive use of alcohol is well-known to cause harmful medical and social consequences, an inverse association between alcohol consumption and RA development has been proposed. Phosphatidylethanol (PEth) has shown to be a reliable biomarker to measure recent (up to four weeks) alcohol consumption with high specificity.

Objectives: The aim of this study was to, in relation to other possible clinical and laboratory predictors, pinpoint the association between biochemically determined alcohol consumption and development of arthritis in ACPA-positive individuals with musculoskeletal pain.

Methods: The study was performed as part of an observational prospective cohort (TIRx), including 104 ACPA-positive individuals with musculoskeletal pain and maximally one arthritis upon clinical examination. Exclusion criteria were >1 clinical arthritis, previous inflammatory rheumatic disease, and oral or intraarticular corticosteroid treatment within 6 weeks prior to screening. Participants were enrolled between 2010 and 2013 and were carefully followed during 72 months in median (range 23-91). The primary outcome measure was development of arthritis upon clinical examination. In baseline samples, we assessed ACPA levels in serum (2nd generation cyclic citrullinated peptides (CCP) as antigen), rheumatoid factor (RF), and the presence of shared epitope. PEth 16:0/18:1 was measured by liquid chromatography coupled with tandem mass spectrometry (LC/MS/MS) in whole blood from baseline, and the results were categorized into three groups: no/low, moderate, or high consumption. Cox regression analyses were performed adjusting for smoking, symptom duration, age, sex, shared epitope, RF, and treatment with disease-modifying antirheumatic drugs (DMARDs) and oral glucocorticoids.

Results: In TIRx, 82 patients had no swollen joints at inclusion, of whom 39 (48%) developed arthritis during follow-up after median 6 months (range 1-71). Of those, 48 (59%) patients were classified according to PEth values with no/low alcohol consumption, 28 (34%) with moderate consumption and 5 (6%) patients with high alcohol consumption. There was no significant difference in PEth values between patients with one baseline arthritis compared to those without (p=0.09). Neither were there any significant differences in arthritis-free survival across PEth categories versus arthritis development (p=0.64). Unadjusted hazard ratios (HRs) were numerically, but not significantly, increased among moderate (HR 1.001 95% CI 1.000-1.002, p=0.007) and higher ACPA levels (adjusted HR 1.001 95% CI 1.000-1.002, p=0.007), respectively. Disease activity remained stable and functional status and QoL had improved significantly over time (Table 1). The majority of the patients (89%) were in Steinerbrocker Class 1 or 2 with only 7 (11%) being in Steinerbrocker Class 3. Of the 7 deceased patients (4 women 3 men; median age: 68.21±12.5 SD years; mean disease duration: 127.61±73.8 SD months) 3 were on Rituximab, 2 were on synthetic DMARDS (one being biologic naive) and 2 were free of RA medications (one was biologic naive) at the time of death. Serious infections were the cause of death in 4 patients followed by hepatic failure due to hepatitis B, abdominal bleeding under anticoagulation and multi organ failure in 3 patients, respectively. Direct costs were higher than indirect costs and made up two thirds of RA related total costs (Table 1).

Conclusion: Disease activity remained stable and functional status and QoL improved among our patients over 6 years. Biologic usage was increased. Cardiovascular events and serious infections were major determinants of morbidity and mortality. Direct costs were the main determinants of RA related cost.

Table 1: RAPID 3, HAQ-DI, EQ5D Scores and annual cost

<table>
<thead>
<tr>
<th></th>
<th>Mean (SD) RAPID3 Score</th>
<th>Mean (SD) HAQ-DI Score</th>
<th>Mean (SD) EQ5D Score</th>
<th>Annual mean (SD) direct costs (€)</th>
<th>Annual mean (SD) indirect costs (€)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous study</td>
<td>4.85±1.64</td>
<td>1.86±0.59</td>
<td>0.57±0.21</td>
<td>NA*</td>
<td>2262±2227</td>
</tr>
<tr>
<td>Current study</td>
<td>4.36±1.54</td>
<td>0.69±0.57</td>
<td>0.68±0.21</td>
<td>0.003</td>
<td>1220±2449</td>
</tr>
</tbody>
</table>

Results: The survey was replied by 41 rheumatologists, representing all regions in the country. Table 1 shows a summary of the results of the second round in terms of m and SD. To summarize, there was an agreement regarding the drugs that might be more adequate for patients with particular prognostic factors, except in the case of pulmonary involvement, in which agreement was only met for T-cell co-stimulation, and for elevated HAQ and acute phase reagents, where the use of B-cell depressant treatments did not reach an 80% of agreement. NA* = not available.
REFERENCES:

Acknowledgement

Supported with an unrestricted grant from Pfizer


AB0242

RADIOLOGICAL EVALUATION OF FOREFOOT INVOLVEMENT IN RHEUMATOID ARTHRITIS

Rym Fakhfakh, Saoussen Znour, Abir Oghais, Hibaltalah Mosbeh, Olfa Jmaa, Grassa Rini, Jijjin Mahboubas, Ismail Bejia, Mongi Touzi, Naceur Bergaoui. CHU Fattouma Bourguiba, Rheumatology, monastir, Tunisia

Background: Severe and often debilitating involvement of the forefoot is seen frequently in patients with rheumatoid arthritis (RA).

Methods: Monocentric retrospective study of 52 consecutive patients with RA, hospitalized in the Rheumatology Department between 2012 and 2018. Radiological measurements included the modified Sharp/van der Heijde method (SHS) for the forefoot.

Results: The average age was 53 ± 15 years and the sex-ratio was 0.21. The average disease duration was 8 ± 10 years and the average disease activity index DASH28 was 5.65±1.12. The prevalence of forefoot erosion and joint space narrowing were 35% and 58%, respectively. In 85% of patients, both >1 forefoot erosion score and >1 forefoot joint space narrowing score were present. Erosions were the most frequent in the 5th metatarsophalangeal joint (MTP) and 1st interphalangeal joint (50% and 47% of eroded joints, respectively) and the least frequent in 4th MTP (27%). The forefoot erosion score was significantly correlated with age, disease duration and hand erosion score and weakly but statistically significantly with titer of ACPA (p<0.05). Obesity was an independent protective factor (OR = 0.25, p < 0.05) of forefoot erosions. Foot deformities were observed in 71% of the patients: Metatarsus primus varus(MV) (56%), hallux valgus(HV) (38.5%) and spaying foot(SF) (13.5%). The HV was significantly correlated with forefoot damage (erosion score r=0.67, joint space narrowing r=0.7, p<0.01), extra-articular manifestations of RA, disease duration and rheumatoid factor titer. Multivariate analysis showed that the extra-articular manifestations was an independent risk factor for HV (OR = 9.39, p <0.05). There was significant correlation between the MV and forefoot damage (erosion score: r=0.4, joint space narrowing: r=0.5, p<0.05). There was no correlation between the spaying foot and the forefoot damage. The spaying foot was associated with the hallux valgus (OR = 5.7, p = 0.05).

Conclusion: In our study, forefoot involvement is common in patients with RA and it isn’t associated with disease severity. Deformities (HV, MV) are associated with forefoot joint damage and spaying foot is associated with hallux valgus.

REFERENCES:


Disclosure of Interests: None declared


AB0243

CYSTEINE RICH 61 (CYR61): A POTENTIAL BIOMARKER ASSOCIATED WITH DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS

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Background: Numerous preclinical studies have revealed a critical role of Cysteine rich 61 (Cyr61) in the pathogenesis of rheumatoid arthritis (RA). However, little is known about the potential value of circulation Cyr61 in clinical RA patients.

Objectives: To compare serum Cyr61 level in patients with RA and healthy controls, and to characterize the potential association between Cyr61 and RA disease activity.

Methods: In training cohort, serum samples were obtained from 177 patients with definite RA and 50 age- and gender- matched healthy controls. Medical records were collected and serum Cyr61 concentration was detected by enzyme-linked immunosorbent assay. Correlations between Cyr61 levels with clinical disease activity were analyzed. Furthermore, a validation cohort consisting of 77 active RA patients who received uniform biologic therapy for 12 weeks was set up (ClinicalTrials.gov identifier: NCT02320630). Paired serum samples were collected at baseline and after 12-week treatment for each individual and prepared for detection of Cyr61. Comparisons between groups were made using Mann-Whitney U test or Wilcoxon matched-pairs signed rank test, as appropriate.

Results: Significant elevation of serum Cyr61 concentration was found in RA patients, demonstrating excellent diagnostic ability to discriminate RA with healthy controls (area under the curve (AUC) = 0.98, P < 0.001). In training cohort, Cyr61 level in active RA patients was significantly lower than that in inactive RA, and it was inversely with measures of clinical disease activity in statistic. Findings were further confirmed in our validation cohort. Active RA patients who had a reduction in disease activity showed a significantly increase of Cyr61 level after effective treatment (in terms of achieving ACR20/50/70 improvement criteria); RA patients who did not achieve ACR response showed no significant difference of Cyr61 level before and after treatment. Multivariate logistic regression analysis revealed that increase of Cyr61 level as well as younger age were independent indicators for achieving ACR20 response.

Conclusion: Serum Cyr61 levels were remarkably increased in RA patients compared with healthy control. More intriguingly, the level of Cyr61 was inversely associated with RA disease activity and increased after effective treatment.

REFERENCES:


Conflict of interest: The authors declare that they have no competing interests.

Disclosure of Interests: None declared


AB0244

THE IMPORTANCE OF TREATMENT STRATEGY FOR THE OUTCOME OF EARLY RHEUMATOID ARTHRITIS PATIENTS NOT RESPONDERS TO THE FIRST LINE THERAPY WITH METHOTREXATE

Anna Laura Fedele, Dario Bruno, Barbara Tolusso, Luca Petricca, Gianfranco Ferraccioli, Elisa Gremese. Fondazione Policlinico Universitario A. Gemelli IRCCS, Division of Rheumatology, Rome, Italy

Background: According to EULAR recommendations for the management of Rheumatoid Arthritis (RA), if the treatment target is not reached with the first conventional synthetic (cs)-disease modifying antirheumatic drugs (DMARDs), addition of another csDMARD or of a biological (b)-DMARD should be considered [1].

Objectives: To evaluate the clinical and radiological outcome under combination therapy of cs-DMARDs or b-DMARDs in our cohort of early rheumatoid arthritis (ERA) patients treated according to the treat-to-target (T2T) strategy.

<table>
<thead>
<tr>
<th>REFERENCE</th>
<th>AUTHORS</th>
<th>TITLE</th>
<th>DOI</th>
<th>ABSTRACT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rym Fakhfakh, Saoussen Znour, Abir Oghais, Hibaltalah Mosbeh, Olfa Jmaa, Grassa Rini, Jijjin Mahboubas, Ismail Bejia, Mongi Touzi, Naceur Bergaoui.</td>
<td>CHU Fattouma Bourguiba, Rheumatology, monastir, Tunisia</td>
<td>Background: Severe and often debilitating involvement of the forefoot is seen frequently in patients with rheumatoid arthritis (RA).</td>
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<tr>
<td>Anna Laura Fedele, Dario Bruno, Barbara Tolusso, Luca Petricca, Gianfranco Ferraccioli, Elisa Gremese.</td>
<td>Fondazione Policlinico Universitario A. Gemelli IRCCS, Division of Rheumatology, Rome, Italy</td>
<td>Background: According to EULAR recommendations for the management of Rheumatoid Arthritis (RA), if the treatment target is not reached with the first conventional synthetic (cs)-disease modifying antirheumatic drugs (DMARDs), addition of another csDMARD or of a biological (b)-DMARD should be considered [1].</td>
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<tr>
<td>Objectives: To evaluate the clinical and radiological outcome under combination therapy of cs-DMARDs or b-DMARDs in our cohort of early rheumatoid arthritis (ERA) patients treated according to the treat-to-target (T2T) strategy.</td>
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</table>
Methods: A total of 384 ERA patients with less than 12 months of disease duration (mean age 54.6±14.6 years, 75% female, 73.3% seropositive) were enrolled in the study. ERA patients fulfilled the 2010 ACR criteria for RA and were followed according to the T2T strategy. At baseline and every three months, the ACERAFLAR core data set variables were recorded. At baseline and every year, hand and foot radiographs were examined according to modified Total Sharp score (mTSS). At each visit, clinical improvement and remission were evaluated according to EULAR criteria. The achievement of Comprehensive Disease Control (CDC) (28-joint Disease Activity Score using C reactive protein <2.6, Health Assessment Questionnaire <0.5 and change from baseline in mTSS ≤0.5) was assessed every year of follow-up (FU). The mean FU duration was 45.5±40.6 months. In patients not reaching the target with methotrexate (MTX) after the 3rd-6th month of FU, the addition of another csDMARD (chloroquine, leflunomide or sulfasalazine) or a bDMARD was considered in order to attain at least a good EULAR response. Results: At the twelfth month of FU, out of the 174 ERA patients (45.3%), not reaching the target with MTX, 97 (23.3%) were in combination therapy with csDMARDs and 77 (20.1%) were treated with csDMARDs in association with bDMARDs. Similar percentages of good EULAR response, DAS remission and CDC were registered in the two groups of patients, both at 12th month of FU and at the last FU. Although not statistically significant, fewer bDMARD treated patients showed 5-year radiographic progression (RP) (21.7%) compared to subjects in combination therapy (36.8%, p=0.13). A higher BMI was observed in ERA patients who started bDMARDs (26.0±4.1) compared to subjects in combination therapy with csDMARDs (24.8±4.2, p=0.02). No differences were found regarding age and disease duration. Autoantibody positivity was comparable between the two groups. Conclusion: Our results support data suggesting that the treatment strategy is more important than the therapy used to achieve remission. In fact, when a strict protocol of tight control is applied, similar clinical and radiological outcome is achieved both in patients treated with csDMARD combination, and in subjects in bDMARD association, regardless of RA prognostic factors. A higher BMI is associated with a major frequency of bDMARD therapy, underlying a possible more csDMARD refractory disease.

REFERENCES:

Disclosure of Interests: Anna Laura Fedele: None declared, Dario Bruno: None declared, Barbara Tolusso: None declared, Luca Petricca: None declared, Gianfranco Ferraccioli: Consultant for: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Sanofi, UCB, Roche, and Pfizer, Speakers bureau: BMS, MSD, Novartis, Sanofi, UCB, Roche, and Pfizer DOI: 10.1136/annrheumdis-2019-eular.8158

Disclosure of Interests: Marco Fornaro: None declared, Fabio Cacciapaglia: None declared, Giuseppe Lopalco: None declared, Daniela Renna: None declared, Gaetana Laselva: Crescenzo Scioscia, Giovanni Lapadula: Florencia Iannone, Giuseppe Apulian Registry (BIOPURE), Policlinico di Bari, Rheumatology Unit, Department of Emergency and Organ Transplantations, Bari, Italy

Background: Thanks to biologic therapies, disease remission in Rheumatoid Arthritis (RA) patients is not a wishful thinking but an achievable goal. Nevertheless, some patients experienced treatment discontinuation after disease remission. EULAR recommendations suggest to suspend steroids as soon as possible[1], but in real life-setting this point is not always hold in esteem. Objectives: The objective of our study was to assess the impact of steroid withdrawal on long-term drug survival and the possible predictors of drug discontinuation in RA patients who achieved Simplified Disease Activity Index (SDAI) remission at 1-year upon treatment with a first biologic disease-modified anti-rheumatic drug (bDMARD).

Methods: Data of RA patients naïve to bDMARDs, registered in Biologic Apulian Registry (BIOPURE) between 1st January 2008 to 31st December 2017, were retrospectively analysed. Demographic and clinical data of all RA patients were acquired at the initiation of first bDMARDs (“screening-time”) and after 1-year follow-up (“baseline-time”). The inclusion criterion in this study was the achievement of SDAI remission (SDAI ≤ 3.3) at 1-year of treatment with the first bDMARD. At “baseline-time”, RA patients on SDAI remission were divided, according to steroid administration, into concomitant “steroid-no” and “steroid-yes” groups. Drug discontinuation rate and mean survival time (MST) were estimated using Kaplan-Meier (K-M) life-table analysis. Estimated hazard ratios (HRks) of discontinuing bDMARD were assessed by performing a multivariate Cox-regression analysis with stepwise backward methods.

Results: 216 RA patients started their first bDMARDs between 1st January 2008 to 31st December 2017. Among these, 86 (39.8%) patients achieved SDAI remission at 1-year of whom 54 (62.8%) were steroid free while 32 (37.2%) were still taking low-dose steroids (mean 3.8 mg/die; SD ±1.4). Considering patients who achieved SDAI remission at “baseline-time”, global drug discontinuation was 81.4% [MST=88.5 (95% CI: 80-97) months], higher for “steroid-no” patients [90.7%, MST=98.2 (95% CI: 89-107) months] than “steroid-yes” ones [68.8%, MST=68.9 (95% CI: 57-81) months] (log rank 7.086, p=0.008) (Figure 1). This difference was also seen when drug discontinuation by inefficacness was calculated [96.1%, MST=103 (95%CI: 96-110) months vs 72.4%, MST= 70.6 (95%CI 57-84) months, long rank 10.101, p=0.001], but not by adverse events. Moreover, no steroid administration (HR = 0.31, 95% CI:0.10-0.93) and concomitant Methotrexate therapy (HR = 0.34, 95% CI:0.12-0.98) were independently associated with low risk of bDMARDs interruption after the achievement of SDAI remission.

Conclusion: This study provided evidence that, among RA patients who achieved SDAI remission, those who stopped steroids and continued combination therapy with MTX had a very long drug survival with just the first bDMARD in a real-life setting. These results can help rheumatologists to precociously select RA patients who might start a tapering or spacing strategy of biologic drug.

REFERENCE:
being a very disabling symptom, the variables that predict it are still unknown.

**Objectives:** To identify potential factors associated with fatigue.

**Methods:** Cross-sectional study. 60 patients were included, patients were being followed up in the rheumatology outpatient clinic of Hospital Clinico San Carlos, Madrid, Spain. Data were collected between July 2018 and January 2019. All patients met the ACR/EULAR 2010 criteria and they were in treatment with Biological agents or Targeted Synthetic DMARDs.

**Main variable:** Fatigue was assessed by the Bristol Rheumatoid Arthritis Fatigue Multidimensional Questionnaire (BRAF-MDQ) and the Bristol Rheumatoid Arthritis Fatigue Numerical Rating Scale (BRAF-NRS).

**Variables:** Sociodemographic, clinical, Disease-related variables and treatment.

**Statistical analysis.** A descriptive analysis was carried out for the different variables. To identify factors independently associated to BRAF-MDQ a multivariable linear regression was applied. Results were expressed as $\beta$ with their corresponding 95% CI. A value of $p < 0.05$ was accepted as statistically significant.

**Results:** A total of 60 patients, comprising of 53 females (88%) and 7 males (12%) with a mean age of 56.45±11.89 years and mean disease duration of 14.11±7.79 years were evaluated. RF was positive in 60% of patients. 65% of the patients were in active on work and 23% were retired. Regarding comorbidities, 43% had dyslipidemia, 42% hypertension, 17% hypothyroidism and 15% depression. The DAS28-ESR and SDAI scores of the patients were 2.68 ± 0.86, 8.56 ± 5.96 respectively. The rest of the clinical, treatment characteristics, and the scores of the fatigue instruments used in the study are shown in Table 1. Physical dimension was the most affected according to patients, who perceive an average severity and affectionation, and insufficient coping. The factors affecting the total BRAF-MDQ was evaluated in multivariate analyze Table 2. We found that patients with Disability (p <0.0001) and those in treatment with Non anti-TNF (p 0.048), experienced more fatigue while a positive RF (p 0.022) decreases overall fatigue.

**Conclusion:** Fatigue is a substantial symptom in RA patients and should be evaluated on the daily clinical practice. The results of our study indicated that disability and type of treatment were the dominant factors in the experience and degree of fatigue. Disease activity (DAS28 and SDAI) was not associated to fatigue. The evaluation and management of fatigue should be one of the objectives in the treatment of patients with RA.

---

**Table 1. Characteristics of the sample**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Descriptive statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucocorticoids mg/day, mean ± SD</td>
<td>4.66 ± 1.65</td>
</tr>
<tr>
<td>Treatment, n (%)</td>
<td>47 (78.33)</td>
</tr>
<tr>
<td>Conventional DMARDs</td>
<td>40 (66.67)</td>
</tr>
<tr>
<td>Anti TNF</td>
<td>16 (26.67)</td>
</tr>
<tr>
<td>Non Anti TNF</td>
<td>4 (6.67)</td>
</tr>
<tr>
<td>Synthetic target DMARD (Jakinibits)</td>
<td>0.86 ± 7.7</td>
</tr>
<tr>
<td>VAS pain mean ± SD</td>
<td>39.3 ± 24.27</td>
</tr>
<tr>
<td>Sleep quality self-report, n (%)</td>
<td>23 (39.66)</td>
</tr>
<tr>
<td>Good</td>
<td>35 (60.34)</td>
</tr>
<tr>
<td>Poor</td>
<td>0.08 ± 3.46</td>
</tr>
<tr>
<td>BRAF-MDQ (0-70), mean ± SD</td>
<td>24.95 ± 15.01</td>
</tr>
<tr>
<td>Physical (0-22)</td>
<td>10.6 ± 5.48</td>
</tr>
<tr>
<td>Living (0-21)</td>
<td>5.08 ± 5.04</td>
</tr>
<tr>
<td>Cognitive (0-15)</td>
<td>3.3 ± 3.38</td>
</tr>
<tr>
<td>Emotional (0-12)</td>
<td>2.96 ± 2.75</td>
</tr>
<tr>
<td>BRAF-NRS, mean ± SD</td>
<td>4.75 ± 2.33</td>
</tr>
<tr>
<td>Fatigue severity (0-10)</td>
<td>4.6 ± 2.43</td>
</tr>
<tr>
<td>Coping with fatigue (0-10)</td>
<td>3.73 ± 2.29</td>
</tr>
</tbody>
</table>

**Table 2. Multivariate analyses of Total-BRAF-MDQ**

<table>
<thead>
<tr>
<th>Total BRAF</th>
<th>Coef.</th>
<th>Std. Err.</th>
<th>t</th>
<th>p</th>
<th>IC 95%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>-0.041</td>
<td>0.141</td>
<td>0.29</td>
<td>0.769</td>
<td>-0.325 to 0.242</td>
</tr>
<tr>
<td>Sex</td>
<td>-6.933</td>
<td>4.985</td>
<td>-1.39</td>
<td>0.170</td>
<td>-16.938 to 3.071</td>
</tr>
<tr>
<td>FR positive</td>
<td>-9.589</td>
<td>3.467</td>
<td>-2.77</td>
<td>0.008</td>
<td>-16.546 to -2.631</td>
</tr>
<tr>
<td>Non Anti TNF</td>
<td>7.348</td>
<td>3.621</td>
<td>2.03</td>
<td>0.048</td>
<td>0.062 to 14.614</td>
</tr>
<tr>
<td>HAG &gt;1.1</td>
<td>15.863</td>
<td>3.290</td>
<td>4.82</td>
<td>0.000</td>
<td>9.259 to 22.467</td>
</tr>
</tbody>
</table>

**Disclosure of Interests:** None declared

respondents, 98% reported asking pts about adherence to RA medication, even though 61% felt there was no way of knowing if pts were taking medications as prescribed and, overall, HCPs responded that 64% of pts did not always take RA medication as prescribed. While 87% of HCPs agreed, 32% of bDMARDs were most effective when taken in combination with csDMARDs and 92% reiterated this to pts, 62% were concerned that pts take bDMARDs without csDMARDs. Pts and caregivers reported that pts often stopped taking csDMARDs; however, HCPs underestimated the number of non-adherent pts (Figure A). The most common reason given by pts and caregivers for non-adherence to RA medication was difficulty in remembering to take medication; however, concerns about feeling ill and potential side effects were also common (Figure B). Despite this, 47% of pts and 51% of caregivers responded that pts often don’t share all side effects caused by their RA medication with HCPs, while 38% of HCPs believed that pts did not inform them of all side effects.

Conclusion: This study from a large, multinational cohort of pts with RA, care providers and caregivers is the first to look at this relationship. This study from a large, multinational cohort of pts with RA, care providers and caregivers is the first to look at this relationship. While 38% of HCPs believed that pts did not inform them of all side effects, extent of pt non-adherence was underestimated by HCPs. These results highlight gaps in communication and understanding of non-adherence between pts, caregivers and HCPs.


Disclosure of Interests: None declared


AB0248 DISEASE ACTIVITY IS ASSOCIATED WITH FATIGUE IN THE FOLLOW-UP OF PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Chronic fatigue negatively impacts on quality of life in Rheumatoid Arthritis (RA) patients. However, the influence of disease activity on fatigue is still under debate. The objective was to determine whether disease activity correlates with fatigue in the following 24 months following bDMARD initiation.

Methods: Prospective study of the RA-Almenara cohort (criteria ACR87/91, EULAR). Patients were included with at least two evaluations (half-yearly). Patients with fibromyalgia, major depression and/or anxious personality were excluded. Disease activity was evaluated with SDAI (Simple Disease Activity Index) and fatigue with FACIT questionnaire (Functional Assessment of Chronic Illness Therapy-fatigue). A generalised estimation equation model was used to determine the association between SDAI and FACIT, at each visit according with two models of analyses. Model 1 considered SDAI value as a linear variable; Model 2 considered each category of SDAI (high, moderate and low) activity, using remission as reference. Multivariable analyses were adjusted by possible confounders: gender, age at diagnosis, instruction, socio-economic level (Graffar), disease duration, tobacco, ACR-EULAR or baseline CDAI, CDAI, SDAI, HAQ, EULAR and ACR response. RF was considered positive if ≥ 30 U/ml and ACPR if CDAI ≥ 7 U/ml. SPSS statistics 22.0 was used for statistical analysis.

Results: 169 patients were included with mean (±SD) age of 50.7 ± 10.6 years and median disease duration (min-max) of 10.2 (0.69-39.4) years. The majority were female (84%). At baseline 160 (94.7%) were positive for RF and 166 (98.2%) were positive for ACPR. 77 (45.6%) turned negative for RF and/or ACPR at a median time of 20.3 months after biologic therapy beginning. 63 out of 169 patients become negative for RF (37.3%) and 17 patients for ACPR (10.1%). 52 (30.6%) patients were treated with etanercept, 39 (22.9%) adalimumab, 27 (15.9%) rituximab, 19 (11.2%) tocilizumab, 16 infliximab (9.4%), 14 (8.2%) golimumab. 1 (0.6%) certolizumab and 1 (0.6%) anakinra. The mechanism of action of the drug didn’t differ between patients who became seronegative for RA and/or ACPR and those who remained seronegative (70.2% under anti-TNF agents vs 79.9% for the other biologic). Most of the patients in the first group began adalimumab (32.5%) and most of the patients in the latter began etanercept (34.8%). Demographic characteristics like age, sex, disease duration, and extraarticular manifestations were comparable in both groups. They weren’t comparable in terms of smoking habits (p=0.014): just 3 (3.9%) current smokers in those who became negative for RF and/or ACPR vs 17 (18.5%) among those who remained seropositive.

Conclusion: In our sample, change of antibody status wasn’t predictor of better response to biologic therapy. Therefore the results did not support the association between the persistence of RF or ACPR and the lack of effectiveness of biologic therapy at 2 years of treatment, but further studies are needed.


Disclosure of Interests: None declared

REAL-WORLD OUTCOMES IN STABLE ORIGINATOR BIOLOGIC-TREATED ADULT PATIENTS WHO STAYED ON THE THERAPY VersUS THOSE WHO SWITCHED TO A BIOSIMILAR: A RETROSPECTIVE CHART REVIEW STUDY IN EUROPE

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Background: Biologic therapies have considerably improved clinical management of autoimmune diseases. Over the past few years, several biosimilars have been introduced in Europe for these conditions. Limited information is available evaluating the impact of switching stable patients from originators to their respective biosimilars in clinical practice for non-medical reasons.

Objectives: This real-world study reported and compared patient characteristics, clinical outcomes, and healthcare resource utilization (HRU) associated with stable patients who switched from the originator biologic etanercept to its biosimilar (switchers) vs. those who stayed on the originator (non-switchers) in adults with a rheumatic condition such as ankylosing spondylitis (AS), psoriatic arthritis (PsA), or rheumatoid arthritis (RA).

Methods: Medical record data were retrospectively collected anonymously from rheumatologists in the UK and Germany. Adult patients who were diagnosed with RA, AS, or PsA, treated with originator etanercept for at least 6 months with a stable dosing schedule, and had no emergency department visit or hospitalization for the disease of interest over the 6-month period were eligible for the study. The index date for a non-switcher was the prescription date closest to one year after the initiation of therapy with the originator etanercept and with a stable dosing for at least 6 months. The index date for a switcher was the biosimilar initiation date. Chart data available for at least 12 months prior to and post the index date were required. Patient characteristics, disease severity, symptoms and signs, and HRU were extracted anonymously. Unadjusted and adjusted comparisons of the outcomes between non-switchers and switchers were conducted among all patients and for each individual disease.

Results: Data were extracted from 242 patient records (non-switchers = 123, 50.8%; switchers = 119, 49.2%; AS=26.4%; PsA=26.0%; RA=47.5%) from 162 rheumatologists. At baseline, non-switchers were significantly younger than switchers (44.5 vs. 48.4 years, p≤0.05), had a significantly shorter time on the originator etanercept (11.7 vs. 23.8 months), and more patients had been treated with NSAIDS (55.3% vs. 37.8%). Significantly more non-switchers had moderate, or severe disease (27.6% vs. 16.0%, p<0.05; 26.8% vs. 5.9%, p<0.01) and non-switchers on average had worse joint or spine pain (4.4 vs 2.4, p < 0.01) than switchers. During the follow-up period, significantly more non-switchers’ disease status improved (58.5% vs. 25.2%, p<0.01), resulting comparable disease severity (moderate: 10.6% vs 10.9%; severe: 0% vs 0%) and joint or spine pain scale (2.0 vs 1.0) between the two cohorts. After adjusting for potential confounding factors, compared to switchers, more AS and PsA non-switchers improved in disease severity (AS: p<0.05; PsA: p<0.01), and RA non-switchers had a fewer number of swollen joints (0.5 vs 1.5, p<0.01). Non-switchers generally had numerically lower HRU than switchers during the one-year follow-up period (patients with outpatient visits: 76.4% vs 89.1%; average number of outpatient visits: 1.8 vs 2.0).

Conclusion: When compared with stable patients who underwent non-medical switching, stable patients who continued therapy with the originator biologic demonstrated significantly more improvement in disease severity. Other outcomes such as HRU appeared more similar between switchers and non-switchers. After adjusting for potential confounding factors, compared to switchers, more AS and PsA non-switchers improved in disease severity (AS: p<0.05; PsA: p<0.01), and RA non-switchers had a fewer number of swollen joints (0.5 vs 1.5, p<0.01). Non-switchers generally had numerically lower HRU than switchers during the one-year follow-up period (patients with outpatient visits: 76.4% vs 89.1%; average number of outpatient visits: 1.8 vs 2.0).

REFERENCES:


RACIAL DISPARITIES IN OUTCOMES FOR PATIENTS WITH RHEUMATOID ARTHRITIS UNDERGOING TOTAL KNEE OR TOTAL HIP ARTHROPLASTY

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Background: Race is linked to delays in healthcare. Black and Hispanic patients with osteoarthritis have worse pain and function than Whites before arthroplasty. Whether Black and Hispanic patients with RA similarly delay care is unknown.

Objectives: To assess whether Black and/or Hispanic (minority) RA patients have worse pain, function and disease activity at the time of arthroplasty.

Methods: We used prospectively acquired data on RA patients between 10/2013 and 11/2018 prior to total knee arthroplasty (TKA) or total hip arthroplasty (THA).

Pain, function, and disease activity were assessed using the visual analogue scale (VAS), the Multidimensional Health Assessment Questionnaire (MD HAQ), and the Disease Activity Score (DAS28). Race, ethnicity, education, income, insurance and medications were collected via self-report questionnaire. Multivariable linear and logistic models examined whether minority status predicted pain, function and disease activity.

Results: 37 (23%) of the 164 patients were minorities (Table 1): MD HAQ and DAS28 were worse in minorities, only VAS was significant (p-value= 0.029). There was no significant difference in education. Unadjusted comparisons indicated no difference in pain, function, disease activity or medication use between groups. Insurance varied significantly (p=0.004). There was no significant difference in education. Unadjusted comparisons indicated no difference in pain, function, disease activity or medication use between groups. Insurance varied significantly (p=0.004).

Conclusion: For Black and/or Hispanics with RA undergoing THA or TKA at a high-volume specialty hospital, minority status was not significantly associated with pain, disability or RA disease activity at the time of elective arthroplasty.

Disclosure of Interests: None declared


Table 1. Cohort

<table>
<thead>
<tr>
<th>Overall (N=164)</th>
<th>Minority* (N=37)</th>
<th>Non-minority (N=127)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, median [IQR]</td>
<td>62.5 [54.7, 71.2]</td>
<td>56.8 [51.0, 68.8]</td>
<td>64.0 [55.1, 71.5]</td>
</tr>
<tr>
<td>VAS Pain Score, median [IQR]</td>
<td>6.0 [4.0, 8.0]</td>
<td>7.5 [4.0, 8.0]</td>
<td>6.0 [4.0, 8.0]</td>
</tr>
<tr>
<td>MD HAQ Score, mean ± SD</td>
<td>11.8 ± 5.3</td>
<td>12.3 ± 5.1</td>
<td>11.6 ± 5.3</td>
</tr>
<tr>
<td>DAS28, mean ± SD</td>
<td>3.8 ± 1.3</td>
<td>4.1 ± 1.3</td>
<td>3.8 ± 1.2</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>22 (13.4%)</td>
<td>3 (8.1%)</td>
</tr>
<tr>
<td>Education</td>
<td>Graduated HS</td>
<td>18 (11.76%)</td>
<td>4 (12.90%)</td>
</tr>
<tr>
<td></td>
<td>Some college or above</td>
<td>135 (88.24%)</td>
<td>27 (87.10%)</td>
</tr>
<tr>
<td>Insurance</td>
<td>Commercial</td>
<td>54 (33.13%)</td>
<td>9 (29.03%)</td>
</tr>
<tr>
<td></td>
<td>Medicare</td>
<td>77 (47.24%)</td>
<td>13 (41.14%)</td>
</tr>
<tr>
<td></td>
<td>Medicaid</td>
<td>9 (5.52%)</td>
<td>9 (29.03%)</td>
</tr>
<tr>
<td></td>
<td>N/A</td>
<td>23 (14.11%)</td>
<td>6 (18.22%)</td>
</tr>
<tr>
<td>Yes</td>
<td>30 (55.56%)</td>
<td>23 (62.16%)</td>
<td>67 (53.60%)</td>
</tr>
</tbody>
</table>

*Minority status: Black or African American, Hispanic or Mixed.

Abbreviations: IQR: Interquartile Range

VAS: Visual Analogue Scale

MD HAQ: Multidimensional Health Assessment Questionnaire

DAS28: Disease Activity Score28

HS: High School

AB0252 RACIAL DISPARITIES IN OUTCOMES FOR PATIENTS WITH RHEUMATOID ARTHRITIS UNDERGOING TOTAL KNEE OR TOTAL HIP ARTHROPLASTY

AB0253 BIOMARKERS OF CLINICAL RESPONSE TO IL6-R BLOCKADE IN DMARDS INCOMPLETE RESPONDERS (AR-BIOM TRIAL): IL23 AND BAFF AS BIOLOGICAL TARGETS, AND ALBUMIN AS BIOLOGICAL PREDICTOR

Gianfranco Ferraccioli1, Barbara Tolasso2, Florenzo Iannone3, Maurizio Rossini3, Piercarlo Sarzi-Putti4, Marcelo Govoni4, Rosario Falà4, Andrea Donà5, Francesco Paolo Cantatore5, Giovanni Francesco Micel1,2, Oscar Massimilliano Epis1,2, Anna Laura Fedele1, Antonio Caceto1, Nicola Marouti1, Elena De Stefani8, Giorgio Amato7, Elisa Girometti2, Giovanni Lapadula6, GISEA (Gruppo Italiano Studio Early Arthritis). Università Cattolica del Sacro Cuore. Division of Rheumatology, Rome, Italy; 2Fondazione Policlinico Universitario A. Gemelli IRCCS, Division of Rheumatology, Rome, Italy; 3University of Verona, Verona, Italy; 4Sacco University Hospital, Milan, Italy; 5University of Ferrara, Ferrara, Italy; 6Policlinico di Catania, Catania, Italy; 7University of Padova, Padua, Italy; University of Foggia, Foggia, Italy; 8Policlinico G. Marino, Messina, Italy; 9Grande Ospedale Metropolitano Niguarda, Milan, Italy; 10Fondazione Policlinico Universitario A. Gemelli IRCCS – Università Cattolica del Sacro Cuore, Division of Rheumatology, Rome, Italy

Background: The therapeutic algorithm in persistently active Rheumatoid Arthritis, despite conventional synthetic DMARDs (csDMARDs), identifies TNFα blockers and other biologics as first line treatment, without clear indications of which biologic should be adopted first in persistently active patients.

Objectives: In the AR-BIOM trial we analyzed several biomarkers to define which one could help to identify the best responder to IL-6R blockade.

Methods: Sixty-nine RA persistently active despite csDMARDs treatment, were enrolled in this Interventional Phase IV, prospective, multicenter, non-randomized, no-profit study (Clinical Trial: n.2012-001760-30) and followed for 18 months after Tocilizumab (TCZ) treatment monotherapy or in combination with csDMARDs. The study was conducted in 10 outpatient clinics of “Gruppo Italiano di Studio sulle Early Arthritis” network (GISEA Study Group) in Italy. The primary end point was the clinical response to TCZ, as LDA (DAS2<4.2) at 12 months follow-up (FU), correlated with Matrix 1 (pathway of innate inflammation IL-8, MCP1, Chemerin) vs Matrix 2 (pathway of IL1/IL6/TH17, IL12, IL17, IL23) along with the Pathway of regulatory T cells activity (IL10, BAFF) and acute phase reactants (Albumin, Fibrinogen, CRP, ESR) as biomarkers of interest. DAS and SDAI remission were secondary end-points at 12 and 18 months FU. A ROC analysis of soluble biomarkers was performed to obtain thresholds allowing the prediction of DAS-remission or LDA at 12 months FU. A multivariate logistic analysis, in which “LDA or DAS/SDAI remission at 12 months FU” were the dependent variables, was performed.

Results: During the 18 months of the study, 9/69 patients (13.0%) discontinued the study because of treatment failure, 2(2.9%) for an AE, 2 for a SAE, and 5(7.2%) for other reasons. At 12 months FU, LDA was achieved in 75.0% and DAS-R and SDAI-R in 63.3% and 41.7%
respectively, of RA patients, without significant differences between mono and combination therapy. Considering baseline biomarkers predictive of LDA at 12 months FU, IL23 plasma levels ≥43.64 pg/ml arse as potent predictor [OR(95%CIs):20.0(1.9-211.2)], whereas the best predictors of DAS-R were baseline BAFF plasma levels ≥56.3 pg/ml [OR(95%CIs):3.9 (1.1-14.3)] and IL23 plasma levels ≥43.64 pg/ml [OR(95%CIs):4.1(1.1-15.2)]. In addition, Albumin levels ≥2.5g/dl at 3 months FU, arse as a biochemical parameter predicting DAS-R [OR(95%CIs):21.6(9.3-50]).

Conclusion: IL23 and BAFF related inflammation are targets of IL6 blockade that significantly increases Albumin levels. High plasma levels of IL23 and BAFF at baseline represent biomarkers for LDA and DAS-R achievement in RA inflammation driven by IL6. Albumin after three months of therapy represents the strongest predictor of remission at 12 months.

Disclosure of Interests: Gianfranco Ferraccioli Speakers bureau: BMS, Roche, Barbara Tolusso: None declared, Florenzo Iannone Consultant for: F. Iannone has received consultancy fees and/or speaker honoraria from Pfizer, AbbVie, MSD, BMS, Novartis, Lilly, UCB outside this work, Speakers bureau: F. Iannone has received consultancy fees and/or speaker honoraria from Pfizer, AbbVie, MSD, BMS, Novartis, Lilly, UCB outside this work, Anna Laura Fedele: None declared, Antonio Carletto: None declared, Nicola Maruotti: None declared, Elena De Stefani: None declared, Giorgio Armao: None declared, Elisa Germese Consultant for: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Sanofi, UCB, Roche, and Pfizer, Speakers bureau: BMS, Speakers bureau: Roche, Speakers bureau: AbbVie, MSD, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Sanofi, UCB, Roche, and Pfizer, Giovanni Lapadula: None declared.


AB0254  NEUTROPHIL-LYMPHOCYTE RATIO AND PLATELET-LYMPHOCYTE RATIO IN PATIENTS RECEIVING ANTIRHEUMATIC THERAPY: RELATIONSHIP TO CLINICAL AND LABORATORY MARKERS OF DISEASE ACTIVITY

Iris Paola Guzmán-Guzmán1, Oscar Zaragoza-García1, José Eduardo Navarro-Zarza2, Isabel Parra-Rojas1. 1Universidad Autónoma de Guerrero, Facultad de Ciencias Químico Biológicas, Chilpancingo, Guerrero, Mexico; 2Hospital General de Chilpancingo, Departamento de Reumatología y Medicina Interna, Chilpancingo, Guerrero, Mexico

Background: The use of antirheumatic drugs is key to limit or prevent inflammation and joint damage in rheumatoid arthritis (RA). Recently, neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) has been considered markers of clinical activity in RA, however its relationship with serological and clinical parameters in patients receiving disease modifying drugs (DMARDs) therapy has been poorly evaluated.

Objectives: To analyze the association of NLR and PLR with serological and clinical parameters related to the clinical prognosis in RA patients with antirheumatic treatment.

Methods: A cross-sectional study was carried out in 150 women with RA (mean age of 45.5 years, and mean duration of disease of 8 years) all diagnosed according to ACR/EULAR 2010 criteria and receiving DMARDs and corticosteroids (Cs) therapy. The clinical features and DAS-28 score were analyzed by a rheumatologist professional. The NLR and PLR, as well as the erythrocyte sedimentation rate (ESR), high sensitivity C reactive protein (hsCRP) levels, rheumatoid factor (RF) and anti-cyclic citrullinated peptides (anti-CCPs) antibodies, were determined in the laboratory.

Results: The means DAS28 of patient with and without P.gingivalis is respectively 43% of patients have presented a PD. The P.gingivalis has been detected in 59% of patients and the mean titre was 255.57±409.78. The mean age of our patients was 40.75 ± 12.04, the mean duration of the illness was 14.30±6.76 months (extremes: 1-24 months). ACPA was detected in 88% of patients and the mean titre was 255.57±409.78. 43% of patients have presented a PD. The P.gingivalis has been detected in 59% of PD. The means DAS28 of patient with and without P.gingivalis is respectively 4.40±1.52 and 4.15±1.45, and there was no significant difference (p=0.05). There was also no association observed between anti CCP and the presence of P.gingivalis.(the mean titre of anti CCP was 249.47±294.58 with P.gingivalis and 258.67±93.48 without P.gingivalis, p=0.74).

Conclusion: This study showed that periodontitis is frequent in rheumatoid arthritis. More than half of our patients suffering of periodontitis were infected by P.gingivalis. Rheumatoid disease activity does not seem to be related to periodontitis in general. In addition therewas no association between anti-CCP antibody and the presence of pophyromonas gingivalis.

REFERENCES


Disclosure of Interests: None declared

PREDICTION OF DISEASE RELAPSES BY FATIGUE LEVELS PREDICT OTHER PATIENTS TAPERING DMARD TREATMENT – AN UPDATE OF THE RETRO STUDY

Melanie Hagen1, Koray Tasci lar1, Michaela Reiser1, Larissa Valor1, Judith Haschka2, Arnd Kleyer1, Axel Hueber1, Bernhard Manger1, Georg Schett1, Jürgen Rech1, RETRO study group, 1Friedrich-Alexander-University Erlangen- Nuremberg (FAU), Department of Internal Medicine 3 - Rheumatology and Immunology, Universitätsklinikum Erlangen, Erlangen, Germany; 2St. Vincent Hospital, Medical University of Vienna, Vinforsch study group, Vienna, Austria

Background: Achieving remission is the ultimate treatment goal in patients with rheumatoid arthritis (RA). With the development and wider use of highly effective disease modifying anti-rheumatic drugs (DMARD) about half of RA patients reach the disease remission state (1), raising the question about tapering or stopping anti-rheumatic treatment and appropriate predictors (2).

Objectives: The purpose was to analyze the effect of multi-biomarker disease activity (MBDA) score and anti-citrullinated protein (ACP A) on relapse rates in RA patients in sustained remission enrolled in the prospective randomized controlled RETRO study (3,4,5).

Methods: MBDA scores and ACPA status were determined in the baseline samples of patients in sustained DAS28-ESR remission fulfilling RETRO inclusion criteria. Patients were unblended and either continued DMARDs (Control), tapered dose by 50% (Taper) or stopped DMARDs after tapering (Taper/Stop) for one year according to the RETRO study protocol. MBDA and ACPA status were used as relapse predictors. Relapse was defined as the loss of a DAS28-ESR remission. We calculated incidence of flares and 95% Poisson confidence intervals by baseline MBDA and ACPA status in each study group (double negative, single positive, double positive). We compared the risk of flare in the treatment arms with a Cox regression model and calculated hazard ratios (HR) and 95% confidence interval (CI) for relapses.

Results: Serum samples and follow-up data of 203 patients included in the RETRO trial were analyzed. A flare was observed in 8/59 patients (13.6%) in the Control group, 24/60 (40.0%) patients in the Taper group and 37/68 (54.4%) patients in the Taper/Stop group among the 187 patients that completed their 1-year follow-up. HR (95%CI) for a relapse was 3.43 (1.54-7.66) in the taper group and 5.32 (2.47-11.46) for the control group. HR of flare of a positive MBDA and ACPA was 4.00 (1.72-9.31) compared to a negative MBDA and ACPA. Flare incidence did not differ with baseline MBDA/ACP A status in the control group, whereas in the taper/stop group, number of positive biomarkers could identify three distinct subgroups with a graded incidence of flare (Figure).

Conclusion: Tapering or stopping DMARDs after stable remission was associated with an increased risk of RA flares. Incidence of flares in ACPA/MBDA double-negative patients after tapering and stopping RA treatment was comparable to those that continued treatment within the precision limits of our subgroups. Lack of blinding is a shortcoming of our study.

REFERENCES


Disclosure of Interests: Melanie Hagen: None declared. Koray Tasci lar: None declared. Michaela Reiser: None declared. Larissa Valor: None declared. Judith Haschka: None declared. Arnd Kleyer: Grant/research support from: Bristol-Myers Squibb and Celgene (greater than $10,000). Consultant for: Bristol-Myers Squibb, Celgene, Chugai, GlaxoSmithKline, Janssen, Eli Lilly, Novartis, Roche, Sanofi Aventis, and UCB (in total more than $10,000). Speakers bureau: Bristol-Myers Squibb, Celgene, Chugai, GlaxoSmithKline, Janssen, Eli Lilly, Novartis, Roche, Sanofi Aventis, and UCB (in total more than $10,000).


AB0257

FATIGUE LEVELS PREDICT OTHER PATIENT REPORTED OUTCOMES AND DISEASE ACTIVITY SCORES: RESULTS FROM A LONGITUDINAL STUDY OF RA PATIENTS INITIATING BDMARD THERAPY

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Background: Fatigue is a sensation of weakness and lack of energy which is common in patients with rheumatoid arthritis (RA), contributing to reduced quality of life. However, there are few studies on the longitudinal influence of fatigue on patient reported outcome measures (PROMs).

Objectives: The present study explores the impact of fatigue on PROMs, clinical, laboratory and ultrasound (US) assessments.

Methods: A total of 208 patients with established RA (mean (SD) age 53 (13) years, disease duration 10 (9) years, 81% women, 79% anti-CCP positive) were examined when initiating bDMARDs and assessed at baseline and after 1, 2, 3, 6 and 12 months, including fatigue (0-10, as part of the RAID score), PROMs (joint pain VAS, patient’s global disease activity VAS (P GA), HAQ, pain catastrophizing (PC), SF-36 Mental Health scale score (SF36MH)), clinical examinations (performed by a study nurse including examiner’s global disease activity VAS (EGA), 28 tender and swollen joint counts (TJC, SJC)) and laboratory variables (ESR and CRP). US examinations (semi-quantitative scoring (0-3)) of grey scale (GS) and power Doppler (PD) were performed of 36 joints and 4 tendons by one rheumatologist (HBB; Siemens Acuson Antares, excellence version, 5-13 MHz probe). The clinical disease activity scores (CDAS) DAS28, CDAI and SDAI were calculated for all visits. Correlations were assessed by Spearman’s rho. The predictive value of baseline fatigue on several dependent variables (PROMs, CDAS, clinical assessments) at all visits after baseline was explored by use of multiple linear regression analysis with adjustment for demographic values (age, sex and disease duration) and baseline inflammatory activity (CRP and sum score GS).

Results: Fatigue levels diminished during follow-up (baseline median (IQR) 5 (3-7), 12 months 2 (1-5)). Table 1 shows the high cross-sectional correlations between fatigue and PROMs/CDAS scores, low correlations with EGA/SJJC/CRP and lack of correlations with US assessments. Baseline fatigue predicted PROMs and CDAS scores at all examinations (table 2).

No/low associations were found between baseline fatigue and SJJC/EGA/sum score PD at follow-up.

Conclusion: Fatigue was highly correlated with PROMs and composite scores at all timepoints. The level of baseline fatigue predicted PROMs and composite scores at follow-up, but not objective inflammatory measures. Thus, the degree of fatigue should be taken into account when composite scores are used for evaluation of inflammatory activity in established RA patients.

Table 1.

<table>
<thead>
<tr>
<th>Fatigue levels</th>
<th>Baseline</th>
<th>1 month</th>
<th>2 months</th>
<th>3 months</th>
<th>6 months</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient’s global VAS</td>
<td>0.57*</td>
<td>0.71*</td>
<td>0.59*</td>
<td>0.70*</td>
<td>0.70*</td>
<td>0.68*</td>
</tr>
<tr>
<td>Joint pain VAS</td>
<td>0.45*</td>
<td>0.55*</td>
<td>0.48*</td>
<td>0.52*</td>
<td>0.50*</td>
<td>0.47*</td>
</tr>
<tr>
<td>HAQ</td>
<td>0.45*</td>
<td>0.55*</td>
<td>0.48*</td>
<td>0.52*</td>
<td>0.50*</td>
<td>0.47*</td>
</tr>
<tr>
<td>SF36MH</td>
<td>0.56*</td>
<td>0.58*</td>
<td>0.58*</td>
<td>0.56*</td>
<td>0.55*</td>
<td>0.56*</td>
</tr>
<tr>
<td>EGA/SJC</td>
<td>0.56*</td>
<td>0.58*</td>
<td>0.58*</td>
<td>0.56*</td>
<td>0.55*</td>
<td>0.56*</td>
</tr>
<tr>
<td>CRP</td>
<td>0.45*</td>
<td>0.55*</td>
<td>0.48*</td>
<td>0.52*</td>
<td>0.50*</td>
<td>0.47*</td>
</tr>
</tbody>
</table>

Disclosure of Interests: Arnt Kleyer: None declared, Michaela Reiser: None declared, Larissa Valor: None declared.
Disclosure of Interests: Hilde Berner Hammer Grant/research support from: AbbVie, Pfizer and Roche, Paid instructor for: AbbVie, Pfizer, UCBD, Novartis, Roche, Speakers bureau: AbbVie, Pfizer, UCBD, Novartis, Roche, Brigitte Michelsen Grant/research support from: Unrestricted grant: Novartis, Consultant for: Novartis, UCBD, Seila Aarestad Provan Consultant for: Novartis, Speakers bureau: Lilly, Tilly Ughi Consultant for: Grünenthal, Novartis, Speakers bureau: Grünenthal, Novartis, Tore K. Kvien Grant/research support from: AbbVie, BMS, MSD, Pfizer, Roche and UCBD, Consultant for: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Hospira, Merck-Serono, MSD, Novartis, Oktal, Orion Pharma, Pfizer, Roche, Sandzø, Sanofi, Mylan and UCBD, Speakers bureau: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Hospira, Merck-Serono, MSD, Novartis, Oktal, Orion Pharma, Pfizer, Roche, Sandzø, Sanofi and UCBD


AB0258

POTENTIAL ROLE OF MEAN PLATELET VOLUME AND RED BLOOD CELL DISTRIBUTION WIDTH AS A BIOMARKER FOR CLINICAL AND SONOGRAPHIC ACTIVITY IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Red cell distribution width (RDW) reflects the variation in the circulating erythrocytes size (anisocytosis) that can increase in chronic inflammation due to ineffective erythropoiesis [1], while mean platelet volume (MPV) reveals the average size of platelets and may disclose its activation. Both are typically included in the complete blood count (CBC) and have been studied as a possible indicator of disease activity in many inflammatory conditions [2].

Objective: This study aimed to assess the relationship between MPV and RDW levels and various rheumatoid arthritis (RA) clinical, laboratory and ultrasonographic disease activity parameters in patients with recent onset RA before and after initiation of therapy.

Methods: We assessed MPV and RDW in blood samples obtained from 80 recent onset RA patients and 30 healthy controls at baseline and 4 months after initiation therapy with non-biological disease modifying anti-rheumatic drugs (DMARDs). Disease activity was calculated using the 28 joint counts (DAS28) and musculoskeletal ultrasound examination (MSUS) was performed at baseline and after 4 months using a 12-joint score (bilateral elbow, wrist, 2° metacarpophalangeal MCP; 3rd MCP, knee, ankle) [2]; Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), pro-inflammatory cytokines (IL-6, TNF-α) and high-sensitivity C-reactive protein (hs-CRP) levels, rheumatoid factor (RF) titre and anti-cyclic citrullinated peptide (anti-CCP) antibodies titre were measured and the health assessment questionnaire (HAQ) score was documented.

Results: Baseline RDW was significantly increased in RA (15.16 ± 3.63%) compared to its level in the healthy controls (12.16 ± 1.43%) (p<0.001). While, there was no significant difference in MPV between RA and control groups (10.92 ± 2.02 fl and 10.98 ± 0.88 fl respectively) (p>0.2). In RA patients, baseline RDW significantly correlated with CRP (r=0.39, p<0.05), DAS28 (r=0.47, p<0.05), grey scale (GS) (r=0.53, p<0.05) and power Doppler (PD) (r=0.56, p<0.001) synovitis scores. Also, RDW at 4 months follow up significantly correlated with the DAS28 (r=0.42, p<0.05), GS score (r=0.45, p<0.05), MPV showed no significant correlation with clinical, laboratory and ultrasonographic parameter of RA disease activity. Baseline RDW (r=0.02) was shown to be comparable to ESR (r=0.03) but less than CRP (p<0.001) at predicting PD synovits score.

Conclusion: Rheumatoid arthritis patients have significantly increased RDW levels that remarkably correlated with clinical, laboratory and MSUS parameters of inflammations suggesting that it could be a useful marker to reflect RA disease activity. RDW could be a useful biomarker to predict treatment outcome in RA patient. In this regard, MPV had poor correlations.

REFERENCES


Disclosure of Interests: None declared

AB0259

FOUR COMORBIDITY INDEXES AMONG PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Previous studies have reported an increased risk of multiple comorbidities in people with RA therefore it is necessary to systematically quantify the comorbidity burden of these patients.[1] The comorbidity index is a tool developed under this concept and has multiple clinical and research uses.

Objectives: We compared four comorbidity indexes and mortality rate in patients with rheumatoid arthritis in Taiwan (Charlson Comorbidity Index (CCI), Elixhauser Comorbidity Index (ECI), Mutimorbidity index (MMI), Rheumatic Disease Comorbidity Index (RDCI)).

Methods: All patients with rheumatoid arthritis diagnosed during 1998-2008 in Taiwan were identified using the Taiwan National Health Insurance Database and followed up to 31 Dec 2013. One-year mortality rate and 5-year mortality rate were compared using CCI, ECI, MMI and RDCI. High risk group for each index was defined as around the top 20% patients. A discrimination analysis was performed to compare the predictive ability of the model against the base model using the change of Harrell’s c-statistics and the Akaike information criterion (AIC).

Results: Among 24767 patients with rheumatoid arthritis, median age at diagnosis is 51 years old and female is 79.2%. The one-year and 5-year mortality rate (per 1000 people) is 41 vs. 177 in CCI, 43 vs. 135 in ECI, 43 vs. 169 in MMI, 43 vs. 159 in RDCI. Low risk group vs. high risk group The one-year and 5-year mortality rates all are higher in the high risk group compared with low risk group using four comorbidity indexes. The 5-year mortality rate rises up rapidly both in low risk group and high risk group using four comorbidity indexes. The discrimination analysis showed MMI predicted one-year and 5-year mortality best. (Harrell’s c-statistics 0.796 in one-year mortality and 0.802 in 5-year mortality) ECI, MMI and RDCI are all good at predicting mortality as well.

Conclusion: Our study showed mortality rate increased in patients after rheumatoid arthritis was diagnosed. All four comorbidity index score during diagnostic period predicted one-year and 5-year mortality rate well both in high risk and low risk group. Clinicians should screen different comorbidities, determine primary prevention and control disease activity to improve the functional status, quality of life and mortality of rheumatoid arthritis, especially in the patients with initial high comorbidity index scores.

REFERENCE

Table 1. 1-year and 5-year mortality analysis for four comorbidity indexes.

<table>
<thead>
<tr>
<th>Comorbidity indexes</th>
<th>1-year mortality (per 1000 people)</th>
<th>5-year mortality (per 1000 people)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCI</td>
<td>3</td>
<td>41</td>
</tr>
<tr>
<td>High Risk (&gt;1)</td>
<td>23</td>
<td>177</td>
</tr>
<tr>
<td>ECI</td>
<td>4</td>
<td>43</td>
</tr>
<tr>
<td>Low Risk (0-3)</td>
<td>15</td>
<td>135</td>
</tr>
<tr>
<td>MMI</td>
<td>4</td>
<td>43</td>
</tr>
<tr>
<td>High Risk (&gt;1)</td>
<td>19</td>
<td>169</td>
</tr>
<tr>
<td>RDCI</td>
<td>4</td>
<td>43</td>
</tr>
<tr>
<td>Low Risk (0-2)</td>
<td>18</td>
<td>159</td>
</tr>
<tr>
<td>High Risk (&gt;2)</td>
<td>22</td>
<td>169</td>
</tr>
</tbody>
</table>

High risk group for each index was defined as around the top 20% patients.
TREATMENT WITH BIOTECHNOLOGICAL DRUGS
TARGET SETTING OF FUNCTIONAL REMISSION FOR
Disease-modifying antirheumatic drug based on an established algorithm
University of Campania, each patient with RA has been characterized, at
activity (LDA), SDAI<11, has been evaluated at 3, 6 and 12 months.

Results: Forty-nine patients were admitted to our centre from April
1st2017 to December 31st2018. Out of them, 36 patients have been
followed up at least for 3 months and were included in the study (algo-
rithm+ patients). Out of them, 26 (72.2%) reached 6 months of treatment,
while 16 (44.4%) 12 months of treatment. Among the 26 patients eval-
uated at 6 months, 23(88.5%) achieved the targeted end point. At 12
months, 16/16 patients (100%) preserved a status of remission or at
least low disease activity. We compared our results to those registered,
from January 2015 to September 2016, in a RA cohort of 79 patients
(RA general cohort). We found a significant difference in regard to attain-
ment of the target at 6 months (23/26 patients, 88.5% algorithm+ vs 45/
67 patients, 67.2% RA general cohort; p=0.04) and at 12 months (16/16
patients, 100% algorithm+ vs 40/57 patients, 70.2% RA general cohort; p=0.01) (Table 1). Notably, 32 out of the 79 patients had undergone a
biological drug which didn’t follow the predefined algorithm. These patients (algorithm- patients) presented a further lower incidence of response with
regard to those enrolled according to the algorithm: 22/32 patients
(67.8%) at 3 months; p=0.4; 17/29 (58.6%) at 6 months; p=0.001; 17/24
(70.8%) at 12 months; p=0.03.

Conclusion: The choice of a personalized approach toward treatment of
RA might be an effective strategy to achieve the targeted end point of
remission or at least low disease activity in every patient.

REFERENCES

Table 2. The four comorbidity indexes discrimination for 1- and 5-year survival in patients
with RA.

<table>
<thead>
<tr>
<th>Models</th>
<th>1-year mortality</th>
<th>5-year mortality</th>
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<tbody>
<tr>
<td></td>
<td>Harrell’s c-</td>
<td>AIC</td>
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<tr>
<td>statistics</td>
<td>statistics</td>
<td></td>
</tr>
<tr>
<td>Base model</td>
<td>0.744</td>
<td>1868</td>
</tr>
<tr>
<td>Base model+ CCI</td>
<td>0.796</td>
<td>1793</td>
</tr>
<tr>
<td>Base model+ ECI</td>
<td>0.772</td>
<td>1829</td>
</tr>
<tr>
<td>Base model+ MMI</td>
<td>0.779</td>
<td>1821</td>
</tr>
<tr>
<td>Base model+ RDC</td>
<td>0.773</td>
<td>1817</td>
</tr>
</tbody>
</table>

AB0260
TREATMENT WITH BIOTECHNOLOGICAL DRUGS
ACCORDING TO PRE-DEFINED SELECTION CRITERIA
IN PATIENTS WITH RHEUMATOID ARTHRITIS:
PRELIMINARY RESULTS OF A SINGLE COHORT

IACONO DANIELA, Ilenia Pantano, Serena Fasano, Giuseppe Scallise,
Francesco Ciccia. University of Campania Luigi Vanvitelli, Rheumatology, Naples, Italy

Background: Current recommendations on the treatment of Rheumatoid Arthritis
(RA) are based on a treat to target approach, nevertheless which biologic drug
should be used in an unresponsive patient is not clarified (1). Such a strategy is
essentially justified by the fact that no biotechnological drug has proved to be
superior to any other (2).

Recent studies have reported some disease or patient features that are
associated with a greater or lesser likelihood of response (3). Neverthe-
less, an adapted therapy to the single patient and based on physiopatho-
logical mechanisms has not been acquired yet.

Objectives: Aim of this study was to evaluate if the choice of a tailored
therapy, based on patient and disease features, would be an effective
strategy.

Methods: From April 1st 2017, at our Department of Rheumatology of the
University of Campania, each patient with RA has been characterized, at
enrolment, for demographic and disease features, and started a biological
Disease-modifying antirheumatic drug based on an established algorithm (Fig-
ure 1). Attainment of the targeted end point i.e. remission (R) as assessed by
Simplified Disease Activity Index (SDAI) <3.3 or at least low disease activity
(LDA), SDAI<11, has been evaluated at 3, 6 and 12 months.

Figure 1

Results: 67 patients, 67.2% RA general cohort; p=0.04) and at 12 months.

Disclosure of Interests: None declared

AB0261
TARGET SETTING OF FUNCTIONAL REMISSION FOR
HAND AND WRIST SURGERIES USING GRIP POWER
AND PATIENT-REPORTED OUTCOME MEASURES IN
PATIENTS WITH RHEUMATOID ARTHRITIS: A
PROSPECTIVE COHORT STUDY

Hajime Ishikawa1, Asami Abe1, Toshihisa Kojima2, Masayo Kojima3,4,
Yoichi Kurosawa1,2, Erito Hasegawa1, Satoshi Ito1, Naoki Ishigou1.

1Akita Murasawa1,2, Niigata Rheumatic Center, Rheumatology, Shiba city, Niigata
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Japan; 2Nagoya City University Graduate School of Medical Sciences, Medical
Education, Nagoya city, Japan

Background: The treatment aim of rheumatoid arthritis (RA) is achieving and
maintaining functional remission via tight medical control. However, if adequate
medication is not administered in the very early stage of the disease, surgical
reconstruction for the structurally damaged hand and wrist is sometimes required.

Objectives: To evaluate the effect of surgical treatment of the hand and wrist
and to set the target of functional remission using grip power and patient-reported outcome measures (PROs) at baseline.

Methods: A prospective observational cohort study was performed in RA
patients who were scheduled to have primary hand and/or wrist surgeries.
Assessments were performed at baseline and 12 months after surgery using
grip power (GP), pain visual analogue scale (pain VAS), general
health (GH), disease activity score 28- C-reactive protein (DAS28-CRP
4), disabilities of the arm, shoulder and hand (DASH), European quality
of life scale with five dimensions (EQ-5D), Beck depression inventory -II
(BDI-II) and health assessment questionnaire- disability index (HAQ-DI) for
all registered patients. Baseline data for each item in the group with HAQ
remission (HAQ-Di<0.5) at 12 months (REM) were compared with those in
the group without remission at 12 months (non-REM).

Results: There were 137 sites (63 hands, 74 wrists) in 119 patients
whose average age was 62 (19-88) years and average disease duration
was 14 (1-45) years. Overall, the physical function (GP, pain VAS,
DASH, HAQ-DI), quality of life (HAQ-DI, GH, EQ-5D), depression (BDI-II)
and disease activity (DAS28-CRP(4)) had significantly improved at 12
months (p<0.01) (Table 1). In the REM group (n=47), the GP and EQ-
5D were significantly higher (p<0.01) and the HAQ-DI, DASH and BDI-II
significantly lower (p<0.01) than in the non-REM group (Table 2).

Table 1. Comparison of percentage of response between Algorithm+ patients (n=36) and
RA general cohort (n=79)

<table>
<thead>
<tr>
<th>Algorithm+ patients</th>
<th>RA general cohort</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>LDA/R 3 months</td>
<td>28/36 (77.7%)</td>
<td>51/76 (67.1%)</td>
</tr>
<tr>
<td>LDA/R 6 months</td>
<td>23/26 (88.5%)</td>
<td>45/67 (67.2%)</td>
</tr>
<tr>
<td>LDA/R 12 months</td>
<td>16/16 (100%)</td>
<td>49/57 (70.2%)</td>
</tr>
</tbody>
</table>

Disclosure of Interests: DANIELA IACONO Speakers bureau: PFIZER company.
Ilenia Pantano: None declared, SERENA FASANO: None declared, GIUSEPPE SCALISE: None declared, Francesco Ciccia Grant/ research support from:
CEGENE, PFIZER, Consultant for: UCB, NOVARTIS, CEGENE, PFIZER, LILLY, Paid instructor for: UCB, NOVARTIS, CEGENE, PFIZER, LILLY, JANSEN, Speakers bureau: UCB, NOVARTIS, CEGENE, PFIZER, LILLY, JANSEN, MSD, ROCHE, AMGEN

Scientific Abstracts
Abstract Table 1. Changes in the GP and each PRO (n=119).

<table>
<thead>
<tr>
<th>Item</th>
<th>Baseline</th>
<th>12 months after GP</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>GP (mmHg)</td>
<td>125.6</td>
<td>139.2</td>
<td>0.009</td>
</tr>
<tr>
<td>Pain VAS (mm)</td>
<td>32.3</td>
<td>20.1</td>
<td>1E-07</td>
</tr>
<tr>
<td>GH (mm)</td>
<td>35.2</td>
<td>24.1</td>
<td>4.6E-05</td>
</tr>
<tr>
<td>DAS28-CRP(4)</td>
<td>3.1</td>
<td>2.2</td>
<td>3.1E-15</td>
</tr>
<tr>
<td>DASH</td>
<td>42.1</td>
<td>35.1</td>
<td>6E-05</td>
</tr>
<tr>
<td>EQ-SD</td>
<td>0.72</td>
<td>0.76</td>
<td>0.0005</td>
</tr>
<tr>
<td>BDI-II</td>
<td>13.4</td>
<td>11.9</td>
<td>0.008</td>
</tr>
<tr>
<td>HAQ-DI</td>
<td>1.07</td>
<td>0.91</td>
<td>0.0021</td>
</tr>
</tbody>
</table>

Abstract Table 2. Baseline value in the REM group (n=47) and the non-REM group (n=72).

<table>
<thead>
<tr>
<th>Item</th>
<th>REM</th>
<th>Non-REM</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>GP (mmHg)</td>
<td>151</td>
<td>109</td>
<td>8.35E-05</td>
</tr>
<tr>
<td>DASH</td>
<td>26.1</td>
<td>25.2</td>
<td>1.54E-01</td>
</tr>
<tr>
<td>EQ-SD</td>
<td>0.80</td>
<td>0.66</td>
<td>3.51E-05</td>
</tr>
<tr>
<td>BAS-II</td>
<td>10.1</td>
<td>15.5</td>
<td>0.0011</td>
</tr>
<tr>
<td>HAQ-DI</td>
<td>0.5</td>
<td>1.4</td>
<td>7.19E-01</td>
</tr>
</tbody>
</table>

Conclusion: GP and other four PROs were validated as good objective tools for assessing the physical function after hand and wrist surgeries. It would be helpful for rheumatologists to consider the timing of surgery in RA patients based on the cut-offs determined in this study[3].

REFERENCES


Disclosure of Interests:
None declared, Toshihisa Kojima: None declared, Masayo Kojima: None declared, Yoichi Kurosawa: None declared, Erko Hasegawa: None declared, Satoshi Ito Speakers bureau. Mitsubishi Tanabe Pharma Corporation. Naoki Ishiguro: None declared, Akira Murasawa: None declared.


AB0262 SEUM CALPROTECTIN AS A MARKER OF DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS, AXIAL SPONDYLOARTHRITIS AND PSORIATIC ARTHRITIS

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Background: Calprotectin is a heterodimeric complex of S100A8 and S100A9 calcium-binding proteins. Stored in the cytosol of granulocytes, it is released under cell stress and acts as an endogenous damage-associated pattern molecule. In contrast to C-reactive protein (CRP), it is not an acute phase protein. Serum calprotectin levels correlate with disease activity of several inflammatory rheumatic diseases.

Objectives: To investigate association of serum calprotectin with clinical activity in rheumatoid arthritis (RA), axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA).

Methods: We performed retrospective analysis of patients with RA, axSpA and PsA from the Swiss Clinical Quality Management (SCQM) registry. Age- and sex-matched asymptomatic first-degree relatives of RA patient without sign of autoimmune were used as healthy controls (HC, n=72). Serum calprotectin was measured by ELISA (Inova Diagnostics, research use only). Serum calprotectin quartiles (n) [0-1.4] [1.4-2.2] [2.2-3.4] [3.4-12] were used as healthy controls (HC, n=72). Serum calprotectin was measured by ELISA (Inova Diagnostics, research use only).

Results: 1729 subjects [RA=969, axSpA=451, PsA=237 and HC=72] were included. 209 RA patients had an ultrasound performed at time of blood collection. Median levels of serum calprotectin were higher in each disease compared to HC (p<0.01; Figure). In RA, all clinical scores were statistically different across quartiles indicating an association between calprotectin levels and higher disease activity (SJC, CDAI) and severity (HAQ) (Table). In univariable regression models, both CRP (R²=0.02, p=0.04) and calprotectin (R²=0.10, p<0.001) were associated with USPD scores. Multivariable model analysis revealed that calprotectin alone was as predictive of USPD scores as calprotectin and CRP together (likelihood ratio test between two models p=0.14). In axSpA, an association between level of calprotectin and ASDAS score (p<0.01) was observed. For PsA, SJC, DAPSA and CRP did not differ across calprotectin quartiles.

Table: Clinical outcomes by calprotectin quartile levels. * Results are mean (SD) except for those with an asterisk which represent median (IQR):

<table>
<thead>
<tr>
<th>Calprotectin quartiles</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>[µg/ml]</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RA quartiles (n)</td>
<td>0 [1.7-2.6]</td>
<td>1.7 [2.8]</td>
<td>2.2 [3.3]</td>
<td>3.4 [4.5]</td>
<td>0.001</td>
</tr>
<tr>
<td>SJC</td>
<td>1.3 (2.5)</td>
<td>1.7 (2.8)</td>
<td>2.3 (3.3)</td>
<td>3.4 (4.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>CRP mg/l</td>
<td>3.0 (1.0)</td>
<td>4.0 (1.4)</td>
<td>7.0 (1.0)</td>
<td>6.0 (1.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CRP mg/l</td>
<td>2.0 (1.0-1.7)</td>
<td>2.0 (1.0-1.7)</td>
<td>2.0 (1.0-1.7)</td>
<td>2.0 (1.0-1.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>USPD</td>
<td>2.2 (5.9)</td>
<td>2.0 (4.0)</td>
<td>2.0 (3.0)</td>
<td>4.7 (6.1)</td>
<td>0.01</td>
</tr>
<tr>
<td>HAQ-DI</td>
<td>0.6 (0.6)</td>
<td>0.8 (0.7)</td>
<td>0.8 (0.7)</td>
<td>1.0 (0.7)</td>
<td>0.004</td>
</tr>
<tr>
<td>CRP mg/l</td>
<td>2.0 (1.0)</td>
<td>4.0 (1.4)</td>
<td>7.0 (1.0)</td>
<td>6.0 (1.0)</td>
<td>0.002</td>
</tr>
<tr>
<td>CRP mg/l</td>
<td>3.0 (1.0-1.8)</td>
<td>3.0 (1.0-1.8)</td>
<td>3.0 (1.0-1.8)</td>
<td>3.0 (1.0-1.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>DAS28-CRP(4)</td>
<td>2.0 (1.9)</td>
<td>2.0 (1.7)</td>
<td>3.0 (1.0)</td>
<td>2.0 (1.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>DAS28-CRP(4)</td>
<td>2.0 (1.0-1.7)</td>
<td>2.0 (1.0-1.7)</td>
<td>2.0 (1.0-1.7)</td>
<td>2.0 (1.0-1.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BASDAI</td>
<td>3.6 (2.3)</td>
<td>4.0 (2.4)</td>
<td>3.5 (2.4)</td>
<td>4.1 (2.3)</td>
<td>0.2</td>
</tr>
<tr>
<td>BASFI</td>
<td>2.3 (2.3)</td>
<td>2.7 (2.6)</td>
<td>2.3 (2.3)</td>
<td>2.8 (2.5)</td>
<td>0.2</td>
</tr>
<tr>
<td>BASDA</td>
<td>2.1 (1.9)</td>
<td>2.4 (1.9)</td>
<td>2.2 (1.9)</td>
<td>2.7 (1.9)</td>
<td>0.001</td>
</tr>
<tr>
<td>CRP mg/l</td>
<td>3.0 (1.0-1.8)</td>
<td>3.0 (1.0-1.8)</td>
<td>3.0 (1.0-1.8)</td>
<td>3.0 (1.0-1.8)</td>
<td>0.001</td>
</tr>
<tr>
<td>CRP mg/l</td>
<td>2.2 (2.0)</td>
<td>4.0 (1.0)</td>
<td>4.0 (1.0)</td>
<td>4.0 (1.0)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Conclusion: This large study supports the association of serum calprotectin levels with disease activity and severity in RA and shows an association between serum calprotectin and ASDAS in axSpA.

Disclosure of Interests: Matthias Jarlborg: None declared, Delphine Courvoisier Grant/research support from: has received an unrestricted grant from MSD for this study. Consultant for: has received consulting fees from BMS, Pfizer, AB2 Bio and Janssen., Paid instructor for: Janssen, Céline Lamacchia: None declared, Laura Martinez-Prat Employee of: Inova Diagnostics (Not pharmaceutical, diagnostics company), Chelsea Bentov Employee of: Inova Diagnostics. Michael Mahler Employee of: Inova Diagnostics (Not pharmaceutical, diagnostics company), Axel Finchk Grant/ research support from: Bristol-Myers Squibb, Pfizer Inc, Consultant for: AbbVie, A2Bio, Bristol-Myers Squibb, MSD, Roche, Pfizer Inc and UCB, Cem Gabay Grant/research support from: Roche, Pfizer, AB2 Bio Ltd, Consultant for: Roche, Pfizer, Lilly, AbbVie, Sanofi, Regeneron, Bristol-Myers Squibb, Novartis, UCB, AB2 Bio Ltd, Debiopharm, Michael Nissen Consultant for: AbbVie, Lilly, Novartis, and Pfizer

AB0263 ASSOCIATED FACTORS OF RESIDUAL SYMPTOMS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS IN REMISSION OR LOW DISEASE ACTIVITY

Takashi Kashigawa1, Moto Kobayashi2, Masakazu Urayama1, Natsuo Konishi1, Toshihiko Aizawa1, Hiroki Itoh1, Yusuke Sugimura1, Tetsuya Kawano2, Hiroshi Aomura3, Takayuki Sakuraba1, Hidekazu Abe1, Norio Suzuki1, Keiji Kamo1, Yusuke Iwamoto1, Takamori Miura1, Yoshiaki Kinuma1, Nachisa Miyakoshi1, Yoichi Shimada1, Yoji Akita City Hospital, Department of Orthopedic Surgery, Akita, Japan; 2Yokohama General Hospital; Yokote, Japan; 3Tottori Central Hospital, Yuzawa, Japan; 4Kita Akita Municipal Hospital, Kita Akita, Japan; 5Nohsiro Kousei Medical Center, Nohsiro, Japan; 6Akita University Graduate School of Medicine, Akita, Japan; 7Kakunodate Municipal Hospital, Sekboku, Japan; 8Ugo Municipal Hospital, Ugo, Japan; 9Yuri Kumaiai General Hospital, Yuri Honjo, Japan; 10Akita Rosai Hospital, Odate, Japan

Background: Treatment outcomes for rheumatoid arthritis (RA) have been improved by advances in drugs. In daily clinical practice, treatment outcomes are assessed with both inflammatory findings and based on swollen joints (SJ), tender joints (TJ), a patient’s global assessment on visual analogue scale (GVAS) score, a physician’s GVAS score, etc. Although composite measures indicate suppressed inflammatory or articular symptoms, many patients show no improvement in GVAS scores. The reported residual symptoms include morning stiffness (MS), pain (P), and dullness (D).

Objectives: We investigated the residual symptoms of patients achieving low disease activity (LDA) or complete remission (CR).

Methods: His study included 111 RA patients who received outpatient treatment at our department (31 men and 80 women). The mean age was 65.1 (range, 27–89) years. The disease stages were distributed as follows: Class 1 in 73 patients, Class 2 in 25 patients, Class 3 in 11 patients, and Class 4 in 2 patients (Steinbrocker classification). Based on the disease activity score in 28 joints using the erythrocyte sedimentation rate, disease activity was graded as CR in 54 patients, LDA in 19, moderate disease activity in 37, and high disease activity in 37 patients. In 1. Questionnaire forms were used to assess the presence or absence of MS and the presence of P (Pain VAS) and of D (Dullness VAS). These variables were assessed to determine how they were associated with clinical outcome measures, drugs, and surgery.

Results: The following residual symptoms were observed in 73 patients who achieved the treatment target of LDA or CR: MS in 34 patients (46.6%), P in 48 (65.6%), and D in 38 (52.8%). In the LDA-CR group, the Pain VAS (P < 0.001, r = 0.612) and Dullness VAS (P = 0.013, r = 0.193) were significantly correlated with the GVAS. In patients with P in the LDA+CR group, the use rates for analgesics (P = 0.0047) and biological disease-modifying anti-rheumatic drugs (bDMARDs) (P = 0.0295) were significantly higher. In the LDA+CR group, Dullness VAS scores were significantly improved by the use of bDMARDs (P = 0.0074). No association was observed between surgical interventions (42 patients) and residual symptoms.

Conclusion: Residual symptoms were frequently observed even in patients achieving LDA or CR, which is regarded as the treatment target. Because P and D were significantly correlated with the GVAS, relief of these residual symptoms is expected to improve treatment effects. Although D was relieved by bDMARDs, further studies on the treatment of residual P in patients achieving LDA or CR are necessary.

Disclosure of Interests: None declared

AB0264 THE EXTENT OF JOINT DESTRUCTION IN THE KNEE JOINT AT THE INITIATION OF BDMAARDS TREATMENT IS A PREDICTIVE FACTOR OF SUBSEQUENT TOTAL KNEE ARTHROPLASTY AND PROGRESSION OF JOINT DESTRUCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS DURING LONG-TERM BDMAARDS TREATMENT

Daisuke Kihira, Yuji Hirano, Yukiyoshi Osahi, Toyohashi Municipal Hospital, Rheumatology, Toyohashi, Japan

Background: The joint destruction inhibitory effect of biological disease-modifying anti-rheumatic drugs (bDMARDs) in patients with rheumatoid arthritis (RA) has been reported in a lot of studies. Most of them are evaluated in small joints such as hands and feet, there are few reports on the joint destruction inhibitory effect in large joints such as knees, which are frequently affected in disease course of RA. Although bDMARDs is very effective drugs, we experience RA patients in whom total knee arthroplasties (TKA) are performed after the initiation of bDMARDs treatment.

Objectives: To investigate the rate of TKA during bDMARDs treatment and to explore associated factors of subsequent TKA after the initiation of bDMARDs treatment in RA patients.

Methods: 356 knee joints of 184 RA patients who initiated bDMARDs treatment in our institute from March 2004 to November 2013 were included in this retrospective study. They were retrospectively studied over the course of a minimum of 5 years of follow up. Knees in which TKA were already performed before the initiation of bDMARDs treatment were excluded in this study. Patients’ characteristics and rates of subsequent TKA over time were investigated. Next, factors associated with subsequent TKA were explored using univariate and multivariate analysis. The X-ray change (Larsen grade) at the last observation after 5 years or more was also examined. ARASHI score was developed in Japan to assess destruction of large joints such as knees or hips.

Results: Baseline patients’ characteristics were below. Mean age was 57.1 years old. 152 female and 32 male. MTX was concomitant in 85.7% of patients. Prednisolone was concomitant in 53.7% of patients. First bDMARDs were infliximab in 67 cases, etanercept in 67 cases, adalimumab in 35 cases, tolicizumab in 6 cases, abatacept in 9 cases, golimumab in 0 cases and certolizumab in 0 cases. Agents were changed according to clinical necessity. The median follow-up period was 7.8 years. TKA were performed in 20 knees (5.9%) in total. Baseline extent of joint destruction of knees which was evaluated using Larsen grade and ARASHI score, joint destruction, age, disease duration, steinbrocker class, concomitant corticosteroids, concomitant methotrexate, DAS28-CRP, SDAI, MMP-3, mHAQ, swelling of the knees, and tenderness of the knees were associated with subsequent TKA in univariate analysis. Multivariate analysis revealed that the extent of baseline joint Destruct and mHAQ were associated with subsequent TKA (Larsen grade: Odds ratio; 6.17, 95% confidence interval; 2.93-12.98, ARASHI score: Odds ratio; 3.50, 95% confidence interval; 2.18-5.62, mHAQ: Odds ratio; 3.56, 95% confidence interval; 1.06-11.93). Cut-off value was calculated as in 2 in Larsen grade, 3 in ARASHI score, and 1.5 in mHAQ using receiver operating characteristic analysis. There were significant differences in the rates of subsequent TKA if knees were divided according to baseline Larsen grade, ARASHI score and mHAQ (Fig1). Baseline ARASHI status score in progressed knees which was worsened over 5 years were increased compared with that in knees which was stable. There was no significant difference in baseline Larsen grade between progressed knees and non-progressed knees.

Conclusion: It was suggested that baseline joint destruction and mHAQ at the initiation of bDMARDs in RA patients was predictive factors of subsequent TKA and progression of joint destruction of knees in RA patients who were concomitant bDMARDs treatment. Early intervention with effective bDMARDS is necessary to prevent destruction of knee joints and subsequent TKA in RA patients whose joint knees are affected.

REFERENCES

Disclosure of Interests: None declared
AB0265 ASSOCIATION OF CUMULATIVE ANTI-CYCLIC CITRULINATED PROTEIN ANTIBODIES WITH RADIOGRAPHIC PROGRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Antibody against cyclic citrullinated proteins (ACPA) is counted as one of the most important biomarkers in diagnosis, classification, and prognosis of rheumatoid arthritis (RA). The clinical implications of change in ACPA level over time remain undetermined.

Objectives: We examined the evolution of ACPA during disease course and assess predictive value of time-weighted cumulative ACPA titer on radiographic progression in patients with RA.

Methods: A group of 734 patients with RA was followed longitudinally over 2 years, with annual measurements of IgM rheumatoid factor (RF) and ACPA. Radiographs of the hands were scored with the modified Sharp score (SHS). Cumulative ACPA antibody titers were calculated using the trapezoidal rule.

Results: The patients with radiographic progression had a higher SHS at baseline; and smoking status, diabetes, RF positivity, and use of biologic DMARDs were independently associated with radiographic progression (all P<0.05). As for ACPA, reversion happened more commonly in men and was associated with younger onset age and lower titer at baseline, but it had no direct relevance to radiographic outcome. In multivariable regression analysis, only high cumulative or baseline titer of ACPA had a predictive power for rapid radiographic progression (all P<0.05), and cumulative ACPA titer was superior in terms of statistical significance (Cohen’s d, 0.637 versus 0.583).

Conclusion: High cumulative ACPA titer was an independent predictor for accelerated radiographic progression, especially with initiation of joint damage. Serial measurement of ACPA titer can provide information about its dynamics over the clinical course and can facilitate an additional assessment of radiographic progression.

Acknowledgement: Nothing specified.

Disclose of Interests: None declared

AB0266 THREE NOVEL BIOMARKERS PREDICTING THE SHORT-TERM RESPONSE TO IFX + MTX + LEFTLEFLUNOMIDE THERAPY IN RA

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Background: For rheumatoid arthritis (RA), nearly one-third of patients still have poor response to biological agents. In addition, infliximab, methotrexate and leflunomide are the most widely used three drugs in the clinic, but there remains no unified and precise indicators capable to predict the clinical response to their combination therapy.

Objectives: The purpose of this experiment is to identify a protein biomarker panel for predicting the outcome of RA patients who have received a triple therapy combining of infliximab, methotrexate and leflunomide (IFX+MTX+LEF).

Methods: All incorporated RA patients with DAS28-CRP>5.1 accepted IFX+MTX+LEF therapy. At 14th week, they were divided into good responder (GR), moderate responder (MR), and non-responder (NR) in accordance with the EULAR response criteria. After removal of the 14 high-abundance proteins, serum samples from patients (4 GR and 4 NR) at baseline and 14th week, and 4 healthy subjects (HS) were screened for candidate biomarkers via isobaric tags for relative and absolute quantification (iTRAQ). Further validation Monitoring (PRM) was performed in 20 RA patients and 20 HS for further validation

Results: A total of 590 proteins were identified by iTRAQ, and 51 proteins of which showed significant differences between NR and GR (Figure 1). PRM showed that levels of catalase, epididymal secretory protein Li 282, hemoglobin subunit delta and catalase at baseline from PRM among groups (GR, NR and HS). Expression levers of the three protein.

Conclusion: The RA patients with higher pre-treatment levels of the three proteins responded better to IFX+MTX+LEF triple therapy at 14th week; Inhibitor of oxidative stress might be a new therapeutic target of RA in the future.

References:


Figure 1. Hierarchical cluster. Hierarchical cluster of proteins differentially expressed between good responders and non-responders with an FDR < 1% identified by MaxQuant from iTRAQ, Red, high expression; green, low expression. Two main clusters of proteins can be observed, one up-regulated (left) and other down-regulated (right) in the serum of patients. Abbreviation: GR, good responder; NR, non-responder; Red, high expression; Blue, low expression.

Figure 2. Expression levers of the three protein. Comparison of epididymis secretory protein Li 282, hemoglobin subunit delta and catalase at baseline from PRM among groups of GR, NR and HS, **P<0.05.

Disclosure of Interests: None declared

AB0267 ROLE OF FCGAMMA RECEPTORS IIA, IIA, AND IIB POLYMORPHISMS IN RHEUMATOID ARTHRITIS SEVERITY

Ines Mahmoud1, Myriam Moalla1, Imen Star2, Offa Saidane1, Aicha Ben Tekaya1, Rawdha Tekaya1, Elyes Bouajina3, Hela Zegalo1, Saloua Aouini2, Yousr Gorgi2, Leila Abdelmoula1, 1Charles Nicolle Hospital, Rheumatology department, Tunis, Tunisia; 2Charles Nicolle Hospital, Immunology department, Tunis, Tunisia; 3Farhat Hached Hospital, Rheumatology department, Sousse, Tunisia

Background: Fc gamma receptors (FcγR) type IIA IIA and IIB play an important role in the recognition of immune complexes (ICs) by
MORTALITY RATE OF RHEUMATOID ARTHRITIS

H/H 5 (16.7%) 3 (10.7%) 1.00
FcgR low affinity alleles seem to confer susceptibility to and FcgR SNP study (table 2).

Methods: We assessed disease severity in RA patients based on the Health Assessment Questionnaire (HAQ) and Sharp/van der Heijde (mSharp) method. To reduce selection bias, all recruited patients were treated with conventional DMARDs.

Table 1: Correlation between FcgR biallelic polymorphisms and disability level

<table>
<thead>
<tr>
<th>Gene</th>
<th>Genotype</th>
<th>Sharp&lt;43.5</th>
<th>Sharp&gt;43.5</th>
<th>OR (95% CI) P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FcgR</td>
<td>NA1/NA1</td>
<td>7 (23.3%)</td>
<td>17 (58.3%)</td>
<td>0.10 (0.03-0.35) 0.47</td>
</tr>
<tr>
<td></td>
<td>NA1/NA2</td>
<td>23 (76.7%)</td>
<td>20 (71.4%)</td>
<td>0.76 (0.23-2.47) 1.00</td>
</tr>
<tr>
<td></td>
<td>NA2-NA2</td>
<td>14 (48.3%)</td>
<td>9 (31.0%)</td>
<td>0.09 (0.01-0.74) 0.02</td>
</tr>
<tr>
<td>FcgR</td>
<td>V/V</td>
<td>5 (16.7%)</td>
<td>12 (40.6%)</td>
<td>0.03 (0.01-0.79) 0.02</td>
</tr>
<tr>
<td></td>
<td>F/F-F/V</td>
<td>29 (95.3%)</td>
<td>14 (48.3%)</td>
<td>0.01 (0.01-0.74) 0.01</td>
</tr>
<tr>
<td></td>
<td>H/H</td>
<td>3 (10.7%)</td>
<td>10 (33.3%)</td>
<td>0.01 (0.01-0.74) 0.01</td>
</tr>
</tbody>
</table>

Furthermore, FcgRIIIA-158F and IIA-131R carriers were more frequent in patients with severe disability but the association was not statistically significant. Finally, no correlation was found between radiographic evaluation and disability level (p=0.021) (Table 1).

Table 2: Correlation between FcgR biallelic polymorphisms and radiographic evaluation

<table>
<thead>
<tr>
<th>Gene</th>
<th>Genotype</th>
<th>Sharp&lt;7.5</th>
<th>Sharp&gt;7.5</th>
<th>OR (95% CI) P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FcgR</td>
<td>NA1/NA1</td>
<td>9 (31.0%)</td>
<td>17 (58.3%)</td>
<td>0.10 (0.03-0.35) 0.47</td>
</tr>
<tr>
<td></td>
<td>NA1/NA2</td>
<td>23 (76.7%)</td>
<td>20 (71.4%)</td>
<td>0.76 (0.23-2.47) 1.00</td>
</tr>
<tr>
<td></td>
<td>NA2-NA2</td>
<td>14 (48.3%)</td>
<td>9 (31.0%)</td>
<td>0.09 (0.01-0.74) 0.02</td>
</tr>
<tr>
<td>FcgR</td>
<td>V/V</td>
<td>5 (16.7%)</td>
<td>12 (40.6%)</td>
<td>0.03 (0.01-0.79) 0.02</td>
</tr>
<tr>
<td></td>
<td>F/F-F/V</td>
<td>29 (95.3%)</td>
<td>14 (48.3%)</td>
<td>0.01 (0.01-0.74) 0.01</td>
</tr>
<tr>
<td></td>
<td>H/H</td>
<td>3 (10.7%)</td>
<td>10 (33.3%)</td>
<td>0.01 (0.01-0.74) 0.01</td>
</tr>
</tbody>
</table>

Conclusion: RA was still significant risk factor of death. GC use was independent factors of death in RA patients.

REFERENCES

Disclosure of Interests: None declared
DOI: 10.1016/s0300-1971(19)30411-2

FIGURE 1

MORTALITY RATE OF RHEUMATOID ARTHRITIS PATIENTS EVEN IN THE NEW ERA OF BIOLOGICS IS HIGHER THAN THE CONTROL GROUP: EIGHT YEARS OF THE TOMORROW STUDY

Koji Manda1,2, Tatsuya Koike3, Yuko Sugikoa, Kentaro Inui4, Tadashi Okano1, Yulano Yamada1, Masahiro Tada5, Kenji Mameoto5, Shohei Anno6, Hiroaki Nakamura1, Osaka City University Graduate School of Medicine, Orthopaedic Surgery, Osaka city, Japan; Osaka social medical center Hospital, Orthopaedic Surgery, OSAKA, Japan; Osaka City University Medical School, Center for Senior Degenerative Disorders, Osaka city, Japan; Osaka City General Hospital, Orthopaedic Surgery, Osaka city, Japan; Yokogawa Christian Hospital, Orthopaedic Surgery, Osaka, Japan; Cleveland clinic, Biomedical Engineering, Program of Advanced Musculoskeletal Imaging (PAMI), Cleveland, United States of America

Background: Patients with rheumatoid arthritis (RA) have a high mortality rate compared to the general population. However, the mortality rate of patients with RA might be improved by advances in therapy.

Objectives: We investigated the risk factors for mortality in patients with RA from TOMORROW study.

Methods: This study included 413 participants, comprising 208 patients with RA and 205 age- and sex-matched healthy volunteers (Vo) from the prospective “TOMORROW” cohort study that has been ongoing since 2010 were included in this study (women, 84%; mean age, 58 years old). Median disease duration was 10.3 years.

Results: The rate of accomplishment for 8 years was 83.2% in the RA group and 92.7% in the Vo group. There were 14 deaths in the RA group (8.7/1000 person-years) and two in the Vo group (1.2/1000 person-years) (p=0.0025) for 8 years. Infection was the most common cause of death in the RA group (43%). Cox proportional hazard analysis showed that having RA was significant risk factor for death (hazard ratio [HR]: 6.9, 95%CI: 1.6 - 30.4, p=0.01) adjusting by age (Figure). In the RA group, glucocorticoid (GC) use (HR: 3.6, 95%CI: 1.1 -10.4, p=0.032) was significant risk factor for death. Disease activity, duration of disease, use of biological products, use of methotrexate, presence of cardiovascular disease, and smoking were not significant factor.

Conclusion: RA was still significant risk factor of death. GC use was independent factors of death in RA patients.
Pharmaceutical Co., Ltd., Tadashi Okano Speakers bureau: AbbVie, Yutaro Yamada Speakers bureau: Abbvie, Chugai, Mitsubishi Tanabe, Masahiro Tada Speakers bureau: Abbvie, Astellas Pharma, Bristol-Myers Squibb, Chugai Pharmaceutical, Eisai, Janssen Pharmaceutical, Mitsubishi Tanabe Pharma Corporation, Ono Pharmaceutical, Pfizer Japan, Takeda Pharmaceutical, Kenji Matomo: None declared, Shohei Anno: None declared, Hiraoi Nakamura: None declared

Disclosures of Interests: None declared


AB0269 COMPARISON BETWEEN DIFFERENT DISEASE ACTIVITY SCORES IN ELDERLY ONSET RHEUMATOID ARTHRITIS
Mariana Martínez-Morillo, Águeda Prior-Español, Anahy Brandy-Garcia, Susana Holgado, María Apaico-Espinar, Laia Gilfe, Anne Riveros-Frutos, Clara Sánchez-Gómez, Jordi Camins-Fàbregas, Yvette Casasfont-Soleu, Annaika Nack, Alejandro Olive, Lourdes Mateo Soria, Hospital Germans Trias i Pujol, Rheumatology, Badalona, Spain

Background: Elderly onset rheumatoid arthritis (EORA) has several peculiarities. This criteria could be useful in order to make a different diagnose and to select the prognosis of those patients. To determine the disease activity scores in elderly.

Methods: We recruited 45 patients with EORA, with DAS28-VSG at baseline and 12 months follow-up. We also use CDAI and SDAI.

Results: The correlation between the different scores was good. However, the concordance between all the scores decreases as time passes.

Conclusion: The correlation between the different scores was good. However, the concordance between all the scores decreases as time passes, according to a higher percentage of patients in remission or low activity. This low-moderate concordance is demonstrated even between DAS28-PCR and DAS28-VRG and when these are compared with CDAI and SDAI. CDAI and SDAI are the only ones that maintain a good concordance between them, even when the number of patients in remission or low activity increases. ACR/EULAR maintains an acceptable concordance with the most restrictive scores, SDAI and CDAI. By contrast, agreement is very low with DAS-PCR.

Disclosure of Interests: None declared


AB0270 POSITIVE ACPA WITHOUT EVIDENCE OF ARTHRITIS – A RARITY?
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Background: Rheumatoid Arthritis (RA) follows a variable disease course in regards to joint damage and functional outcome, therefore an early diagnosis is crucial for its management. However, occasionally, this diagnosis can be a challenge. Rheumatoid Factor (RF) and Anti-citrullinated peptide antibodies (ACPA) are the most useful biomarkers in the diagnosis of RA and, although individually they do not dictate the final diagnosis, they present high specificity and may be positive even before clinical manifestations of the disease occur. ACPA is detectable in approximately two thirds of the patients with RA and presents a superior diagnostic specificity when compared to RF. This specificity of 95-98% may present an increased value if it is three times superior to its value of reference.

Methods: By consulting the electronic clinical records of patients observed by a Rheumatologist, we identified and analyzed the patients that presented positive ACPA in their blood tests and no evidence of signs or symptoms of RA, during at least six years of follow-up. Patients with other rheumatic diseases, history of tuberculosis or chronic pulmonary diseases were excluded.

Results: We identified seven patients (average of 61 years old) with positive ACPA in at least two different blood tests, of which five presented a value three times superior to its normal value (<15UA/mL). It should be noted that, four patients presented both positive ACPA and RF. Clinically, all patients referred mechanical symptoms that varied between cervical, low back, shoulder and knee pain and did not present any record of swollen joints without trauma. Radiologically, in most cases we observed joint degradative damage. Six years after the first positive ACPA, none of the patients developed any manifestation of inflammatory joint disease.

Conclusion: Studies reveal that positive ACPA in healthy patients may precede the clinical diagnosis of RA. The specificity of positive ACPA and RF one and a half years before the diagnosis of RA is approximately 99-100%. However, as we demonstrated, it is not uncommon to find during clinical practice individuals with positive ACPA without evidence of arthritis, which leads us to emphasize the importance of a detailed anamnesis with a meticulous physical examination before establishing a diagnosis based on the patient’s blood tests.

References:
EVALUATION OF CXCL13, sICAM-1, MMP-3 AND S100A8/A9 AS SERUM BIOMARKERS IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH SUBCUTANEOUS TOCILIZUMAB

D. James Haddon, Thierry Somassé, Michael J. Townsend, Jinglan Pei, Margaret Michalík, Genentech, Inc., South San Francisco, United States of America

Background: Serum levels of C-C-X motif chemokine ligand 13 (CXCL13) and soluble intercellular adhesion molecule-1 (sICAM-1) have been associated with response to tocilizumab (TCZ) in patients with rheumatoid arthritis (RA); levels of matrix metalloproteinase-3 (MMP-3) and S100A8/A9 have also been associated with RA disease activity and joint damage.

Objectives: To evaluate the association of CXCL13, sICAM-1, MMP-3 and S100A8/A9 levels with disease activity and response to TCZ in patients with RA who achieved low disease activity with 24 weeks of TCZ + methotrexate (MTX) treatment and were subsequently randomized to TCZ monotherapy (mono) or TCZ + MTX in the COMP-ACT trial (NCT01855789).

Methods: US patients with RA who had an adequate response to MTX received initial combination therapy of MTX plus TCZ 162 mg subcutaneously for 24 weeks. Patients who achieved Disease Activity Score in 28 joints decreased by ≥ 20% (DAS28-ESR ≤ 3.2) at Week 24 were randomized 1:1:1:1:1 to receive either TCZ mono or continue TCZ + MTX until Week 52. Randomized patients were included in the present study based on baseline, Week 24 and Week 40 sample availability; serum levels of CXCL13, sICAM-1, MMP-3 and S100A8/A9 were measured by immunoassay. Correlations between CXCL13, sICAM-1, MMP-3 and S100A8/A9 levels and DAS28/ESR at baseline, Week 24 and Week 40 were determined according to Spearman correlation coefficient. Changes in CXCL13, sICAM-1, MMP-3 and S100A8/A9 levels from baseline to Week 24 (open-label period) were determined using Wilcoxon test. Mean changes in CXCL13, sICAM-1, MMP-3 and S100A8/A9 levels from Week 24 to Week 40 (randomized period) were compared between treatment arms using analysis of covariance.

Results: Of 296 randomized patients, 249 were included (TCZ mono, n = 126; TCZ + MTX, n = 123). Biomarker levels were well balanced across treatment arms at baseline and Week 24 (randomization). At baseline, there were weak to moderate correlations between DAS28/ESR and biomarker levels (CXCL13 [r = 0.13, P = 0.0411], sICAM-1 [r = 0.20, P = 0.0015], MMP-3 [r = 0.19, P = 0.0021], S100A8/A9 [r = 0.25, P = 0.0001]). Significant reductions in mean biomarker levels were observed from baseline to Week 24 (open-label period) among the total randomized patients (P < 0.0001). CXCL13, sICAM-1, MMP-3 and S100A8/A9 levels were relatively stable between Week 24 and Week 40 (randomized period), with no significant differences between TCZ mono and TCZ + MTX (Table)

Table 1: Adverse Events During the 24-Week Placebo-Controlled Period, Stratified by DAS28 CDAI Category

Conclusion: In agreement with previous studies, the association between baseline disease activity and CXCL13, sICAM-1, MMP-3 and S100A8/A9 levels was weak to mild; TCZ + MTX treatment from baseline to Week 24 (open-label period) resulted in significant reductions in all biomarkers. Changes in levels of CXCL13, sICAM-1, MMP-3 and S100A8/A9 from Week 24 to 40 (randomized period) were similar between treatment groups, consistent with the finding of non-inferiority of TCZ mono compared with TCZ + MTX in patients with RA who achieve low disease activity with TCZ + MTX.

Acknowledgement: This study was funded by Genentech, Inc.
THE ANALYSIS OF THE CLINICAL COURSES OF THE ACPA POSITIVE PATIENTS WITHOUT SYNOVITIS: WHETHER TO FOLLOW UP THEM

Tomoya Nakajima, Yumiko Nobuhara, Takashi Nakazawa, Osaka Saiseikai Nakanishi Hospital, Rheumatology, Osaka, Japan

Background: ACPA (anti-citrullinated peptide antibody) is a major risk factor for the onset of RA (rheumatoid arthritis)\(^1\). As ACPA becomes a common test in non-rheumatologists, ACPA positive patients not diagnosed with RA are increasing. However, it is unclear whether follow-up of ACPA-positive patients without synovitis leads to early treatment and consequently to the improvement of prognosis.

Objectives: To reveal whether to follow up the ACPA positive patients without synovitis.

Methods: In the four years from January 2015 to December 2018, we extracted the ACPA positive patients introduced from other hospitals, among which patients not diagnosed as RA at the first visit were selected. Then, their clinical courses and ACPA titers were retrospectively analyzed. The 2010 ACR-EULAR classification criteria was used for the diagnosis of RA\(^2\). For the significance test, a \(\alpha = 0.05\) was used.

Results: Thirty six patients met the conditions, and then 10 patients, previously treated as RA, and 8 drop-out patients were excluded. In 18 patients remaining, 10 patients developed RA (follow-up days: avg. 404, max. 963) and the other 8 were non-RA, predisease patients (follow-up days: avg. 424, max. 520). All 10 RA patients initially started the treatment with MTX (methotrexate). Five of them reached remission with only MTX. Of the other five, three needed other csDMARDs because of an inadequate amount of MTX due to adverse events, and two had insufficient observation period. The ACPA titer was significantly higher in the RA patients than the predisease patients (468 versus 26.3 U/ml \(P<0.0075\)). Tenderness of DAS 28 subject joints at the first visit was a significant predictor of RA onset when trying to extract from clinical findings. (10 of 10 in RA patients vs. 2 of 8 in predisease patients \(P=0.0044\)).

Conclusion: In our research, the predictors of RA onset are not only high ACPA titer but also tenderness of DAS28 subject joints at the first visit. The early treatment with MTX could contribute to improved prognosis.

REFERENCES


Disclosure of Interests: None declared


THE PRECLUSIVE VALUE OF RHEUMATOID FACTORS, ANTI-CITRULLINATED PROTEIN ANTIBODIES, ANTI-CARBAMYLATED PROTEIN: ANTIBODIES AND ANTI-PEPTIDYL ARGinine DEIMINASE TYPE-3 ANTIBODIES, ALONE OR IN COMBINATION, ON RADIOGRAPHIC DAMAGE IN RHEUMATOID ARTHRITIS

Michael Nissen\(^1\), Céline Lamacchia\(^1\), Delphine Courvoisier\(^1\), Matthias Jarborg\(^2\), Pascale Roux-Lombard\(^3\), Burkhard Moeller\(^4\), Adrian Ciurea\(^5\), Axel Finckh\(^6\), Chelsea Bentow\(^5\), Laura Martinez-Prat\(^5\), Michael Mahler\(^5\), Cem Gabay\(^1\).

\(^1\)Geneva University Hospital, Immunology, Geneva, Switzerland;\(^2\)Inova Diagnostics, Inc., San Diego, United States of America

Background: Autoantibodies such as anti-citrullinated protein antibodies (ACPAs), anti-carbamylated protein antibodies (CarP) and anti-peptidyl arginine deiminase 4 (PAD4) antibodies have been associated with disease severity and radiographic progression in rheumatoid arthritis (RA). However, very little is known about the anti-PAD 3 (PAD3) antibodies and of the added value of combining multiple autoantibodies to predict radiographic damage.

Objectives: To investigate the capability of rheumatoid factor (RF), ACPA, anti-CarP and anti-PAD3 antibodies to predict radiographic damage in RA, both individually and in combination.

Methods: We performed a nested cohort study within the « Swiss Clinical Quality Management » (SCQM) RA registry. Biobank samples were tested for RF [QUANTA Lite (QL), IgM and IgA], ACPA IgG [QL CCP3 and QUANTA Flash (OF) CCP3], anti-CarP IgG [using carbamylated fetal calf serum as antigen by prototype ELISA, research use only (RUO)] and anti-PAD3 IgG [QF PAD3, RUO] (all methods Inova Diagnostics).

Outcome: radiographic damage assessed with a validated scoring method, the Ratingen (Rau) score. We examined the association of each autoantibody body both separately and combined, with radiographic damage at baseline and over time with linear mixed-effects models. Multivariable analyses were corrected for age, sex, smoking status, disease duration, disease activity (DAS28), number of prior biologics and calendar year of biosampling.

RESULTS

A total of 851 RA patients were included with a median of 4 Ratingen scores per patient. Autoantibodies were positive in the following proportion: RF IgM 66.3%, RF IgA 56.9%, QL CCP3 63.8%, QF CCP3 63.3%, anti-PAD3 10.7% and anti-CarP 22.4%. Significantly higher baseline Ratingen scores were associated with the presence of RF (IgM and IgA) and anti-CCP3 (QL and OF) and greater progression over time with RF IgM and QL CCP3 IgG \((p=0.01\) and \(p=0.04\) respectively). Patients’ positive for anti-PAD3 demonstrated higher mean baseline Ratingen scores compared with anti-PAD3 negative patients (14.9 vs. 8.8 respectively) which was significant in both univariable (Figure) and multivariable analyses \((p<0.0002\) and \(p<0.02\) respectively). In the QL CCP3 negative subgroup \((n=308)\), baseline Ratingen scores were significantly higher in anti-PAD3 positive patients \((P<0.01)\). There were no significant differences with regards to anti-CarP, either in the whole population or in the seronegative cohorts. The presence of multiple autoantibodies was associated with higher baseline Ratingen scores, particularly the combination of RF IgM, RF IgA, QL CCP3, and anti-PAD3, with a baseline Ratingen score of 16.1 \((P=0.0001)\). The presence of at least 3 of the following autoantibodies: RF IgM, QL CCP3, anti-CarP and anti-PAD3, was associated with significantly greater radiographic progression over 10 years (Figure) than if these autoantibodies were absent \((P<0.03)\).

Conclusion: The presence of anti-PAD3 antibodies was associated with significantly higher scores of radiographic damage at baseline, in both the overall population and in the subgroup of ACPA-negative patients. Combinations of autoantibodies (including anti-CarP and anti-PAD3) predicted both higher baseline radiographic damage and greater radiographic progression over time.

Disclosure of Interests: Michael Nissen Consultant for: AbbVie, Lilly, Novartis, and Pfizer, Céline Lamacchia: None declared, Delphine Courvoisier Grant/research support from: has received an unrestricted grant from BMS, Pfizer, AB2 Bio and Janssen., Paid instructor for: Janssen, Matthias Jarborg: None declared, Pascale Roux-Lombard: None declared, Burkhard Moeller Consultant for: Swissmedic Expert Committee Member (regulatory agency), Adrian Ciurea Consultant for: AbbVie, Celgene, Janssen-Cilag, MSD, Eli Lilly, Novartis, Pfizer, UCB, Speakers bureau: Abbvie, Celgene, Janssen-Cilag, MSD, Eli Lilly, Novartis, Pfizer, UCB, Axel Finckh Grant/research support from: Bristol-Myers Squibb, Pfizer Inc, Consultant for: AbbVie, AB2Bio, Bristol-Myers Squibb, MSD, Roche, Pfizer Inc, and UCB, Chelsea Bentow Employee of: Inova Diagnostics, Laura Martinez-Prat Employee of: Inova Diagnostics (Not pharmaceutical, diagnostics company), Michael Mahler Employee of: Inova
Background: Hispanics are the largest minority group in the United States (US) and his percentage is expected to increase (28.6% by 2060), being Mexicans the largest group (67.9%). RA patients from Latin-America have distinctive features from White patients. The literature highlights a younger age at presentation and a different clinical expression compared with White but few data for Hispanic patients in US are available.

Objectives: We compared baseline demographic, clinical features and disease management among Hispanic RA patients from two well-characterized cohorts, in the USA and Mexico city.

Methods: An early arthritis clinic (EAC) was established at Site 1 (Mexico City); patients with recent-onset RA (<1 year of symptoms) had a standardized assessment and received “treat to target” treatment. At Site 2 (US), a “routine care” cohort was initiated in 2011, and all patients completed a multidimensional health assessment questionnaire (MDHAQ) as part of their routine care. Patients from both sites had baseline complete evaluation including sociodemographic data, patient-reported outcomes (PROs) (patient global assessment, pain-VAS, HAQDHI-Q, RAPID3), laboratory data, and tender joint counts. Initial treatment was noted. Data from both sites were compared and appropriate statistics was used.

Results: 201 patients from site 1 and 179 from site 2 were included (Table 1); among them, 105 (52%) and 37 (19%), respectively, were DMARD-naive at baseline. Patients from site 2 were older and had longer disease duration, however demographic characteristics did not differ. Naïve DMARD patients from site 2 scored significantly higher pain-VAS and tender joint counts, and had higher ESR values (p<0.05, Mann Whitney); a similar tendency was seen for other PROs. Time to DMARD initiation was shorter in the EAC.

Table. Demographic and clinical characteristics at first rheumatology visit for RA patients. All data as median (IQR) unless otherwise indicated. *p<0.003; NA, not applicable

<table>
<thead>
<tr>
<th>Site 1: Mexico-Early Arthritis Clinic</th>
<th>Site 2: US-RA Routine Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients on DMARD</td>
<td>N=96</td>
</tr>
<tr>
<td>DMARD Naïve</td>
<td>DMARD Naïve</td>
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</table>

<table>
<thead>
<tr>
<th>DEMOGRAPHICS</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Ages, years, mean (SD)</td>
<td>38.6 (13)</td>
</tr>
<tr>
<td>Female,%</td>
<td>87.5%</td>
</tr>
<tr>
<td>Yrs of formal education</td>
<td>12 (9, 14)</td>
</tr>
<tr>
<td>Symptom duration-first visit, mo</td>
<td>5.6 (3.9, 7.9)</td>
</tr>
<tr>
<td>% treated as early RA (&lt;6m)</td>
<td>59.4</td>
</tr>
<tr>
<td>PROs</td>
<td></td>
</tr>
<tr>
<td>Pain (0-10)</td>
<td>4.2 (2.4, 6.2)</td>
</tr>
<tr>
<td>Patient global assessment (0-10)</td>
<td>4.4 (2.3, 6.8)</td>
</tr>
<tr>
<td>Tender Joint Counts (TJC28 or self-reported RADA48)</td>
<td>11 (6, 18)</td>
</tr>
<tr>
<td>RAPID3 (0-30)</td>
<td>11.0</td>
</tr>
<tr>
<td>Physical Function-MHAQ (0-10)</td>
<td>2.2 (1.4)</td>
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<table>
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<th>SEROLOGIC DATA</th>
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<td>RF,%</td>
<td>82</td>
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<tr>
<td>ACPA,%</td>
<td>86</td>
</tr>
<tr>
<td>ESR, mm/hr</td>
<td>21.5 (11, 48)</td>
</tr>
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</table>

Conclusion: Hispanic patients with RA from different regions in America may differ in their initial presentation. Naïve DMARDs patients belonging to an early RA cohort had shorter presentation to rheumatology resulting in earlier treatment initiation, which has been associated to better outcomes. EACs facilitate the identification of patients with recent-onset disease and help provide early access to effective therapies.

REFERENCES


Disclosure of Interests: None declared

Discriminant validity of the handgrip test in patients with rheumatoid arthritis: A cohort study

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Background: Hand involvement is one of the major determinants of disease duration explained statistically significant but practically small variations in clinical outcomes. These findings indicate that TCZ treatment outcomes are not heavily influenced by disease duration or other baseline characteristics.


Figure 1. Associations between baseline predictors and response to MTX according to different outcome criteria and at different time points, in odds ratios with 95% confidence interval.

1596 Scientific Abstracts

RENAL INVOLVEMENT AND CAUSES OF DEATH IN RHEUMATOID ARTHRITIS PATIENTS ACCORDING TO THE AUTOPSY DATA

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Background: Renal involvement is a clinically significant manifestation in rheumatoid arthritis (RA) patients with potential influence on the treatment, prognosis and outcome of this disease while rare publications are available on kidney damage in RA [1,2].

Objectives: To estimate the frequency and characteristics of renal involvement and causes of death in RA patients on the basis of autopsy data reports and postmortem microscopic examinations.

Methods: We have analyzed 21 814 autopsy data reports performed during the 10-year period (2001-2010) and 6720 cases of autopsy performed 5 years later (2016-2018) in the Minsk City Clinical Pathologoanatomic Bureau (The Republic of Belarus).

Results: For the period 2001-2010 autopsies were performed in 110 RA patients: 91 women and 19 men of 67.0 (13.1) years old, M (SD). Renal involvement was revealed in 75 patients (68.2%). The most common type of renal involvement was secondary AA amyloidosis - 44 patients (40%). Other types of revealed renal lesions (n=31, 28.2%) were mesangial proliferative glomerulonephritis (n=3; 2.7%), nephroangiosclerosis (n=14, 12.8%), tubulointerstitial nephritis (n=2, 1.8%), chronic pyelonephritis (n=10, 9.1%) and renal vessel vasculitis (n=2, 1.8%).

The main cause of death in RA patients with amyloidosis was end-stage renal disease (ESRD), whereas in other patients the common causes of death were cardiovascular events (43.2%) and secondary infections (33.3%). In case of secondary amyloidosis the deposits of amyloid were found in kidneys of all RA patients (100%), in adrenal glands in 36.4% and in spleen – in 34.1% of RA patients. Amyloid deposits in other internal organs were not nearly as common. In 2016-2018 50 patients with RA have been autopsied with mean age of death 72.0 (15.2) years old. Renal involvement was revealed in 34 (68.0%) of autopsies: as secondary amyloidosis in 29 patients (58.8%) and as focal segmental glomerulosclerosis or mesangial proliferative glomerulonephritis in 5 patients (10.0%). The most common cause of death in this group of RA patients were cardiovascular events (58.0%), fatal infectious complications developed in 16.0% of patients, ESRD was revealed only in 4.0% of patients.

Conclusion: 1. We have revealed an increase in secondary amyloidosis frequency in RA patients over the studied period of time from 40% to 58% (p<0.041, Fisher’s exact test) while ESRD as a cause of death in RA patients decreased from 17.3% to 4% (p=0.023, Fisher’s exact test).

2. Secondary amyloidosis is the most common type of renal involvement in RA according to the autopsy data.

REFERENCES

Disclosure of Interests: None declared


DIFFERENCE BETWEEN PATIENT’S GLOBAL HEALTH AND PATIENT’S GLOBAL ASSESSMENT OF DISEASE ACTIVITY, AND DIFFERENT FACTORS INFLUENCE ON THESE SCALES IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Evaluation of rheumatoid arthritis (RA) activity is crucial in measuring remission or low disease activity. Visual analogue scale (VAS) by patient’s evaluation has been used for the outcome measure for RA patients because of its feasibility, reliability, sensitivity to change, and it directly reflects the patient’s overall perspective. Patient’s evaluation is a component of multiple composite indices used in assessing RA activity and treatment response. There are two measurements that patient’s evaluation. One is patient’s global assessment of disease activity (PtGA), and the other is patient’s assessment of global health (PtGH). PtGA was originally developed as a component of American College of Rheumatology Core Set and used for Simplified Disease Activity Index (SDAI) and Clinical Disease Activity Index (CDAI); while PtGH was originally developed as a component of 28-joint Disease Activity Score (DAS28). PtGA and PtGH have been considered equivalent in a
large scale of study. In daily practice or observation, "patient’s VAS" is usually used without specifying whether it refers to PIGA or PIHG. The factors which influence the change in PIGA or PIHG have not been demonstrated concomitantly in daily practice.

Objectives: We investigated the difference between PIGA and PIHG, especially each change obtained after intensification of treatment in 12 weeks and identified the factors that influence on each measurement in RA patients.

Methods: Consecutive patients were enrolled to this retrospective study at our hospital from October 2017 to September 2018. Demographic and clinical data at enrollment as well as treatment regimens were collected by review of medical charts. At first, we examined the baseline data and the changes in 12 weeks of PIGA and PIHG in their relations. The second, we divided RA patients into two subsets according to medication intensification by methotrexate (MTX) subset and biological disease-modifying anti-rheumatic drugs (DMARDs) or Janus kinase (JAK) inhibitor (B/J) subset. We compared the differences of the changes in PIGA from the baseline to 12 weeks (ΔPIGA) and those in PIHG (ΔPIHG) between MTX subset and B/J subset. Finally, the logistic regression analysis was performed to identify factors that differently influence for each scale in 12 weeks.

Results: Consecutive 38 RA patients were enrolled. Women were 76%. The median age [IQR] was 66.5 [55-75] years old. Disease duration was 2.5 [1-19] years. DAS28 was 2.61 [2.02-3.17]. SDAI was 16.8 [11.1-24.6] and CDAI was 15.3 [9.38-23.9]. MTX was initiated or increased in 24 patients (63%). The baseline median dose of MTX was 6 [3.5-8] mg/week. Biologics or JAK inhibitor were initiated in 8 patients (21%); tocilizumab (n=5), golimumab (n=1), abatacept (n=1) and tofacitinib (n=1). Other DMARDs were used in 6 patients (16%). ΔPIHG in 12 weeks was -.186 (p<0.01), and ΔPIHG in 12 weeks was -.22 (p<0.01). ΔPIHG and ΔPIGA correlated significantly (r=-.785, p<.001). ΔPIHG in MTX subsets was not different from that in B/J subsets (p=0.50) and ΔPIHG was not different (p=0.57). No significant improving factor in ΔPIGA was identified, whereas, woman (p<0.05) and usage of steroid (p<0.01) were improving factors in ΔPIHG.

Conclusion: Intensification of treatment significantly improved in both ΔPIGA and ΔPIHG but we need to pay attentions that there were different improving factors between these two patient’s measuremet.

REFERENCES

Disclosure of Interests: Naohiro Sugitani: None declared, Yuki Mizutani: None declared, Kentaro Noda: None declared, Yasuo Suzuki: None declared, Ayako Nakajima Grant/research support from: Asahi Kasei Pharma co., Chugai Pharmaceutical, Daiichi Sankyo co., Pfizer, Kissei Pharmaceutical Co., and Mitsubishi Tanabe Pharma Corporation.


AB0281 UTILIZATION OF SMART PHONE APPLICATION TO ASSESS THE DISEASE OUTCOMES IN RHEUMATOID ARTHRITIS: SMART- RA STUDY
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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disorder which if not managed properly leads to joint destruction, disability, poor quality of life and premature mortality. Disease modifying anti-rheumatic drugs (DMARDs) have considerably improved disease outcome in RA. However, poor patient compliance significantly limits the benefits that could be accrued from DMARDs. In a technology driven era, with more people having access to smart phones, unique opportunities exist for use of phone-based technologies to improve patient care in chronic diseases. This study aims to investigate whether the use of HealthCius smart phone application for self management can influence quality of life for patients with RA and improve inflammatory disease activity.

Objectives: To investigate the impact of smart phone application (HealthCius) on inflammatory disease activity and quality of life in RA. Methods: 38 RA patients fulfilling the 2010 Rheumatoid Arthritis Classification Criteria were recruited. Subjects were randomized into 2 groups. First, having access to a smart phone were assigned to the intervention group using the HealthCius application (n=23); and second, the control group not using the application (n=15). The patients in two groups received standard treatment of RA. The application was designed after obtaining feedback from health care providers, patient counselors and RA patients using a questionnaire. To the patients, the app was their individual treatment plan. The app helped them comply with the plan by providing an easy to refer checklist, reminders, alerts and a visual dashboard of their progress through the day. The app served as the doctor’s virtual assistant inside the patient’s smart phone. For the doctor, it was a live dashboard of all patients and their real time compliance levels. The data reported by the patients was available to the doctor in the form of time sliced charts and trend lines. Therefore, this app is designed to leverage technology to shift the patients’ focus every day on to their treatment plan thereby driving up compliance and better health outcomes.

Outcome measures included erythrocyte sedimentation rate (ESR), C-Reactive protein (CRP), disease activity score (DAS28) and health assessment questionnaire (HAQ-DI) at baseline and at 12 weeks.

Results: Baseline characteristics were similar between groups with no significant difference. There was a significant difference between the control and intervention group for DAS28 (p<0.05), ESR (p<0.05), CRP (p<0.05) and HAQ-DI (p<0.05) after 12 weeks in favor of smart phone application. Analysis within the groups revealed significant improvement in DAS28 (p<0.05) (Fig.1A), ESR (p<0.01) (Fig.1B), CRP (p<0.01) (Fig.1C) and HAQ-DI (p<0.01) (Fig.1D) in the application group as compared to control group. Impact of DMARDs usage was also evaluated at the end of the study and it was found that the average drug usage of DMARDs was more in control group than the intervention group.

Conclusion: The study suggested that there was greater improvement in inflammatory disease activity and quality of life in smart phone application assisted RA patients suggesting that smart phone technology can be used to leverage health benefits in RA.

REFERENCE

Acknowledgement: None

Disclosure of Interests: None declared


AB0282 SYSTEMATIC REVIEW OF STUDIES REPORTING ON COGNITIVE FUNCTION IN RHEUMATOID ARTHRITIS COMPARED TO THE GENERAL POPULATION
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Background: Rheumatoid arthritis (RA) patients often complain of “brain fog” as a symptom when their disease activity is greater. The exact areas of cognition that this “brain fog” means are not yet understood. Previous studies have found that people with RA have lower cognitive function (CF) than healthy controls and age based population norms. A study by Shin et al which looked at prevalence of cognitive impairment
in persons with RA found that 31% of their 115 person sample was cognitively impaired and stated that further studies should be done to identify the specific domains of cognitive function that are most commonly affected (1). In this project, I will be looking at and summarizing all the data and findings that have been collected and reported on CF in the RA population and seeing which domains of cognition differ and which do not differ when compared to the general population and aged based population norms.

**Objectives:** To conduct a systematic review of studies reporting on cognitive function (CF) in rheumatoid arthritis (RA) patients compared to non-RA populations (based on comparison with a control group or age-based population norms).

**Methods:** We conducted a comprehensive literature search of MEDLINE, EMBASE, and PUBMED databases using the following search terms: rheumatoid arthritis or arthritis or inflammatory arthritis, and cognitive function or cognition. The search was conducted with no limit for years, and confined to only articles in English or French. After title and abstract screen, relevant articles were selected for review. Only full length articles were considered. Study selection criteria included: 1) must be presenting original data, 2) must contain RA group with confirmed diagnosis, 3) must be reporting on CF in RA, 4) must use a validated measure of CF (self-reported or from conducting CF tests), and 5) must contain a healthy control group or age-based population norms. Selected articles were critically appraised using the SIGN Methodology Checklist and data extracted using a standardized form.

**Results:** Our initial literature search yielded 747 titles, and after screening for irrelevant titles and duplicates, 28 abstracts remained. Upon excluding non-full length articles and articles which did not report on CF, 13 abstracts remained. Of these 13 articles, 8 met our selection criteria. All studies were published after the year 2000, 3 were from the USA, 1 from Canada, 1 from the UK, 1 from Australia, 1 from Egypt, and 1 from Taiwan. Sample sizes for RA and control groups varied from 15 to 120. Of these 8 articles, 6 found a significant difference in cognitive function in the RA group compared to control group or age-based population norms in at least one domain of CF. All articles that found a significant difference in CF used standardized neuropsychological tests. Domains of CF that differed included fluency, attention, visual-spatial learning, memory, decision making time, and simple reaction time. Domains of CF that were not found to differ from general population across all studies included reasoning, comprehension, and intelligence (IQ).

**Conclusion:** Overall, 75% of the articles reviewed found a significant difference in at least one domain of CF in RA patients compared to healthy controls or age-based population norms. The domains of CF most commonly affected were those related to processing and speed rather than intellectual ability. Further studies are needed to explore these differences in greater depth and to understand the underlying reasons for these differences.

**REFERENCES**


**Disclosure of Interests:** Teresa Szlachetka: None declared, Linda Li: None declared, Teresa Liu-Ambrose: None declared, H. Xie: None declared, Kiana Yazdani: None declared, Diane Lalonde Grant/research support from: Bristol-Myers Squibb and Eli Lilly Canada

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**AB0283**

**IDENTIFICATION OF NEW AUTOANTIBODIES FOR RHEUMATOID ARTHRITIS USING HUMAN PROTEOME MICROARRAYS**

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**Background:** Rheumatoid arthritis is an autoimmune disease characterized by systemic, symmetrical small arthritis. Anti-cyclic citrullinated peptide antibodies and rheumatoid factor are commonly used to diagnose RA(1). However, the early diagnosis of RA is sometimes difficult, due to the heterogeneity and negative anti-CCP antibody or RF in some patients. Therefore, it is urgent to find autoantibodies with high sensitivity and specificity as diagnostic markers for RA.

**Objectives:** To screen autoantibodies of RA with high sensitivity and specificity using human proteome microarrays(2).

**Methods:** Firstly, a case-control method was used to analyze the serum antibodies of RA patients using human proteome microarray which composed of 20,000 proteins, and identified RA-related antibodies. Then, expanded the sample size and analyzed the expression of these candidates between RA patients and healthy controls.

**Results:** The serum of five RA patients and five healthy controls were selected to detect the RA-related autoantibodies by microarray, and 25 candidates were screened. Then the IgG and IgM RA-focused microarrays composed of the 25 proteins were screened with additional cohorts of 72 RA patients and 106 healthy controls. The results of IgG protein microarray showed: (1) Expression of these 25 autoantibodies in RA patients was significantly higher than those in healthy controls (P<0.05). (2) There was no-differentially expressed protein between anti-CCP antibody and RF-negative RA patients (n=18) and anti-CCP antibody and/or RF-positive RA patients (n=54) (P>0.05). (3) ROC analysis showed that the combination of anti-RBPJ, anti-SH3BGR and anti-PAFAH1B3 autoantibody can be highly RA-specific biomarkers, with 66.7% sensitivity and 74.2% specificity, and the area under the curve is 0.734; meanwhile the sensitivity and specificity of the anti-CCP antibody and RF-negative RA patients diagnosis were 77.8% and 65.6%, and the area under the curve was 0.720. The results of IgM protein microarray showed: (1) Only 10 out of the 25 candidates’ expression was significantly higher in RA patients than healthy controls (P<0.05).

**Conclusion:** The combination of IgG-type antibodies anti-RBPJ, anti-SH3BGR and anti-PAFAH1B3, the IgM-type antibody anti-PAFAH1B3 as well, has high sensitivity and specificity for the diagnosis of RA; especially the IgG-type autoantibody combination has great value for the diagnosis of anti-CCP and RF-negative RA patients.

**REFERENCES**


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**Disclosure of Interests:** None declared

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**AB0284**

**HEMATOLOGICAL MARKERS OF SYSTEMIC INFLAMMATION CORRELATE WITH CLINICAL, LABORATORY AND ULTRASOUND DISEASE ACTIVITY PARAMETERS IN RHEUMATOID ARTHRITIS PATIENTS**

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**Background:** An accurate measurement of disease activity and inflammation is essential for customizing the most appropriate management and treatment strategy in patient with rheumatoid arthritis (RA). Current data suggest that hematological markers of systemic inflammation (peripheral blood neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte (PLR) and monocyte-to-lymphocyte (MLR) ratios) could be used as novel, sensitive measures of inflammatory response, additionally to conventional laboratory and clinical markers (erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), Disease Activity Score of 28 joints (DAS28), tender joint count (TJC), swollen joint count (SJC)). The ultrasonography (US) of joints enables the disease activity assessment by quantifying thickening and vascularity of the synovium.
Objectives: The goal of the study was to assess the relationship of NLR, PLR, MLR with the conventional disease activity markers (ESR, CRP, DAS28, SJ/CJ) and results of joint US, in patients with RA.

Methods: The study was conducted in the consecutive 72 patients with RA (73% female, 57% ACPA positive, mean age 60 years, median symptom duration 7 months), recruited in 1995-2005 from a defined area, were followed through 5 years. Patients were managed according to usual care, with the mean (SD) age 53.4 (8.9) and disease duration 16.8 (10.3) years. The following procedures were assessed for all patients: joint counts, DAS28, complete blood cell counts, ESR, CRP, US of 24 small joints.

Results: The mean (SD) values of hematological markers were as follows: NLR 3.24 (2.7) (range 0.2-13.96); PLR 193.26 (88.3) (range 71.2-560.8); MLR 0.3 (0.16) (range 0.06-0.87). The mean values of NLR and PLR were significantly lower in patients with low (DAS28 ≤3.2) vs moderate/high (DAS28 >3.2) disease activity; respectively NLR 2.4 (1.7) vs 4.0 (3.2), p=0.04; PLR 168.7 (58.0) vs 215.8 (104.9), p=0.4. Hematological markers of systemic inflammation were significantly, positively correlated with clinical, laboratory and US markers of the disease activity. Significant correlations were found between: NLR and DAS28, TJC, SJC, CRP, vascularity and hypertrophy of synovium in US; PLR and DAS28, TJC, SJC, ESR, CRP, vascularity and hypertrophy of synovium in US. In multiple regression test significant correlations were confirmed for: NLR, CRP and SJC (p=0.008), ESR (p=0.001), CRP (p=0.01), vascularity of synovium in US (p=0.02); PLR and ESR (p=0.03), CRP (p=0.03); MLR and DAS28 (p=0.04), ESR (p=0.001), hypertrophy of synovium in US (p=0.02).

Conclusion: The results of the study suggest that hematological markers of systemic inflammation (NLR, PLR, MLR) may serve as reliable, inexpensive and effective measure of inflammation in RA. The strong association with US imaging is an attractive result because of its predictive value and usefulness in clinical practice.

Disclosure of Interests: Bozena Tagonska-Stepniak Speakers bureau: MSD, UCB, Abbvie, Roche.


Table 1.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds ratio 95% CI</th>
<th>Odds ratio 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females</td>
<td>1.24</td>
<td>0.62-2.47</td>
</tr>
<tr>
<td>Male</td>
<td>3.24</td>
<td>0.67-17.20</td>
</tr>
<tr>
<td>RF positive</td>
<td>0.88</td>
<td>0.46-1.67</td>
</tr>
<tr>
<td>Anti-CCP positive</td>
<td>0.77</td>
<td>0.39-1.49</td>
</tr>
<tr>
<td>ESR</td>
<td>1.82</td>
<td>0.73-4.46</td>
</tr>
<tr>
<td>CRP</td>
<td>1.00</td>
<td>0.57-2.00</td>
</tr>
<tr>
<td>SJC</td>
<td>0.79</td>
<td>0.57-1.09</td>
</tr>
<tr>
<td>VAS</td>
<td>0.90</td>
<td>0.75-1.06</td>
</tr>
<tr>
<td>ESR</td>
<td>0.80</td>
<td>0.54-1.20</td>
</tr>
<tr>
<td>CRP</td>
<td>0.79</td>
<td>0.54-1.19</td>
</tr>
</tbody>
</table>

Conclusion: More than 1/3 of early RA patients experienced unacceptable pain after 5 years. Extensive synovitis in early RA was associated with a reduced risk of unacceptable pain at 5 years, likely due to positive effects of treatment on inflammation related pain. Non-inflammatory pain may be a greater long term problem in anti-CCP negative patients.

REFERENCES

Disclosure of Interests: Anna Eberhard: None declared, Tor Olofsson: None declared, Lennart T.H. Jacobsson Consultant for: LJ has received lecture and consulting fees from Pfizer, Abbvie, Novartis, Eli-Lilly and Janssen, Carles Turesson: None declared.


AB0285 PREDICTORS OF UNACCEPTABLE PAIN, AND UNACCEPTABLE PAIN WITH LOW INFLAMMATION, IN EARLY RHEUMATOID ARTHRITIS

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Background: Pain is a major symptom in many patients with rheumatoid arthritis (RA). In early RA, pain is usually due to active synovitis, but over the disease course some patients experience pain with elevated laboratory markers of inflammation.

Objectives: To investigate predictors of unacceptable pain, and unacceptable pain with low inflammation, in patients with early RA.

Methods: Consecutive patients with early RA (symptom duration <12 months), recruited in 1995-2005 from a defined area, were followed through 5 years. Patients were managed according to usual care, with no pre-specified treatment protocol. Pain was assessed using a visual analogue scale (VAS, 0-100 mm). Unacceptable pain was defined as VAS pain>40 based on the patient acceptable symptom state (PASS) (1), and low inflammation as CRP<10 mg/l (2). Baseline predictors of unacceptable pain, and of unacceptable pain with low inflammation, were evaluated using logistic regression analysis.

Results: A total of 233 patients with early RA (73% female, 57% anti-CCP positive, mean age 60 years, median symptom duration 7 months) were included. Of these, 179 attended the 5-year follow-up. At 5 years, 34% had unacceptable pain, and 23% had unacceptable pain with low inflammation. High VAS scores for pain and patient’s global assessment (PGA) at baseline were associated with unacceptable pain at 5 years (Table). There was a negative association between baseline swollen joint count (SJC28) and unacceptable pain at the 5-year follow-up. In multiple logistic regression analysis including VAS PGA and SJC28, both had a consistent impact on unacceptable pain after 5 years (adjusted odds ratios per standard deviation (SD), with 95% CI 1.78 (1.26-2.52) and 0.61 (0.42-0.89), respectively). Anti-CCP positive patients were significantly less likely to experience unacceptable pain with low inflammation at 5 years (Table).

AB0286 STATINS TO PREVENT RHEUMATOID ARTHRITIS (STAPRA TRIAL): CHALLENGES IN RECRUITMENT AND RETENTION

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Background: Primary prevention may be possible in subjects at high risk to develop rheumatoid arthritis (RA). We designed a placebo controlled randomized trial to investigate if atorvastatin can halt RA development in persons at risk for this disease (STAPRA, Netherlands Trial Register NTR5265). A statin was chosen because these drugs reduce disease activity in RA (1), hyperlipidemia patients on statins have a lower risk for developing RA (2) and dyslipidemia increases the risk for RA in a positive arthralgia cohort (3). We assumed that high risk-subjects would be attracted to this trial. However, we experienced severe difficulties with patient inclusion and treatment adherence.

Objectives: To explore difficulties with patient recruitment and retention.

Methods: The STAPRA study is a multicenter, 3-year, randomized, placebo controlled, double-blind clinical trial to assess the efficacy of atorvastatin 40 mg daily in delaying or preventing RA development in persons at high risk, defined by the presence of arthralgia and the presence of high titers of anti-citrullinated protein antibody (ACPA) or presence of both ACPA and rheumatoid factor (RF). Eligible participants were ≥18 years, did not use lipid lowering agents and had no synovitis. Five centers participated. Our goal was to recruit 220 study subjects based on an expected risk reduction of 21%. The unexpected low recruitment rate prompted us to evaluate the reasons to decline participation or to discontinue the study drug prematurely.

Results: Details were available from the initiating center (Reade) and 1 participating center (Sint Maartenskliniek). During a period of 36 months, 164 eligible patients were asked to participate of whom 58 patients (35%) consented. Most common reasons to decline were: unwillingness to use study medication (49%) and the feeling that participation was too time-consuming (14%). Fifty-four patients were randomized since 4 failed screening due to hyperlipidemia or seronegativity on repeated testing. Currently, 11 participants (20%) have developed arthritis. Twelve
AB0287

BENEFITS OF PAIN RELIEF ON FATIGUE, FUNCTION, AND QUALITY OF LIFE WHEN JOINT INFLAMMATION IS CONTROLLED IN PATIENTS WITH RA

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Background: The ultimate goals for rheumatoid arthritis (RA) treatment are to achieve disease activity control and the best potential health state throughout the course of disease.1 In prior analyses of the Phase 3 trial, RA-BEAM (NCT01710358), baricitinib was associated with significant clinical improvements and patient-reported pain relief in RA patients (pts) who had had an inadequate response to methotrexate.2,3 The additional benefits of pain relief when inflammation is controlled are not well characterized.

Objectives: To quantify the contribution of pain relief to other PROs, fatigue, physical function, and quality of life, in pts who achieved control of inflammation, defined as swollen joint count (SJC) ≤1 and C-reactive protein (CRP) ≤1 mg/dL, at Wk 24.

Methods: Among pts with inflammation control, PROs were compared between pts who also achieved thresholds of pain relief at Wk 24 vs those who did not. Pain was measured with a visual analogue scale (VAS, range: 0-100 mm) and divided into ≤20, >20, ≤40, >40 mm.1,5 PROs included: the Health Assessment Questionnaire-Disability Index (HAQ-DI) normative value (≤0.5), to compare with a general population, and minimum clinically important differences (MCID, ≥0.22), SF-36 physical and mental component scores (PCS and MCS) MCID (≥-0.5), and Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F, range of 0–52, higher scores represent less fatigue) normative value (≥40.1) and MCID (≥3.56). Logistic regression models were adjusted for age, gender, BMI, geographic region, duration of disease, baseline SJC, baseline pain, and baseline value of PRO under evaluation. Missing data were imputed using modified last observation carried forward.

Results: Of the total 1305 patients in RA-BEAM, 371 pts treated with adalimumab (121/330), baricitinib (187/487), or placebo (63/488) and background methotrexate achieved inflammation control at Wk 24. Among patients who achieved inflammation control, those who also achieved each pain relief threshold were statistically significantly more likely (p<0.05) to report benefit in physical function, general quality of life, and fatigue than patients who did not reach the pain relief thresholds. (Table)

Conclusion: When inflammation is controlled (SJC ≤1 and CRP ≤1 mg/dL), more pain relief is associated with better physical function, quality of life, and reduced fatigue. This may support consideration of pain relief as an additional goal of therapy, even when inflammation is controlled. Further investigation should evaluate this benefit with other patient populations and outcomes.

References


AB0288  PERSISTENTLY ACTIVE DISEASE IN PATIENTS WITH NEW-ONSET RHEUMATOID ARTHRITIS DURING THE FIRST YEAR OF TIGHT CONTROL AND AGGRESSIVE THERAPY: PREVALENCE AND CLINICAL PREDICTORS IN DIFFERENT CRITERIA SETS

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Background: Early intervention and aggressive therapy of rheumatoid arthritis (RA) improves prognosis, however a substantial proportion of patients under guideline-based care remain persistently active disease (PAD) in the first year.

Objectives: To investigate the proportion of PAD (LDA/MDA/HDA) in real-life practice and identify its prognostic factors in early RA (<2 years) patients receiving tight-controlled conventional synthetic disease-modifying antirheumatic drugs (csDMARD) treatment at 1 year of follow-up.

Methods: In our observational RA cohort, patients were usually three-monthly followup and step-up csDMARD escalation treatment at the discretion of physicians in the first year. Disease activity and remission were assessed by four commonly-used indices (DAS28-ESR, CDAI, SDAI, and Boolean criteria). Logistic regression was used to estimate odds ratios (ORs) and their 95% confidence intervals (CIs) for PAD by 12 months.

Results: The study included 303 DMARD-naïve early RA patients completing one year follow-up schedule, who were mostly female (72%) with a mean age of 55, and a median disease duration of 6 months. Most patients were in MDA or HDA at baseline and most of them (83.5%) received csDMARDs combination in the first year. 26.4-55.1% of participants did not reach remission by 12 months. Compared to patients experienced remission, patients in PAD were frequently in female, older, shorter disease duration, and high baseline disease activity components, including SJC, TJC, PGA, EGA, ES R, CRP and glucocorticoids use. In multivariate logistic regression analyses, female (OR=1.34-1.58), increasing age (OR=1.03-1.10), longer disease duration (OR=1.45-1.78), higher baseline SJC (OR=1.11-1.25), EGA (OR=1.03-1.08) showed the independent association with the increased risk for PAD, across all criteria. Higher ESR (OR=1.05) was an independent risk factor for PAD, measured by DAS28-ESR.

Conclusion: Our results indicated around one-third of RA participants receiving guideline-based healthcare had PAD in the first year. Female, increasing age, long disease duration, higher SJC, EGA, and ESR at baseline independently increased the risk of PAD.

Disclosure of Interests: None declared


AB0289  PREDICTION OF CARDIOVASCULAR EVENTS IN RHEUMATOID ARTHRITIS PATIENTS USING PROTEIN BIO-MARKERS AND CLINICAL FACTORS

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1University of Alabama at Birmingham, Birmingham, United States of America; 2Crescendo BioScience, Salt Lake City, United States of America; 3Myriad, Salt Lake City, United States of America; 4Crescendo BioScience, South San Francisco, United States of America; 5Mayo Clinic, Rochester, MN, United States of America

Background: The ACC/AHA recommends preventive strategies for patients with a high-predicted risk of atherosclerotic cardiovascular disease (CVD). RA patients are at higher risk for CVD events, yet the role of systemic inflammation and the influence of traditional CVD risk factors are unclear with respect to risk prediction in RA.

Objectives: To quantify phenomenon of mismatch between the T2T and HAQ among RA patients through data mining from smart system of disease management (SSDM).

Methods: We derived a U.S. cohort of RA patients by linking multi-biomarker disease activity (MBDA) test data to Medicare claims data. Patients had to have ≥1 year Medicare coverage prior to the date of their first MBDA test, which was designated as baseline. Exclusions were past MI, stroke, or cancer. Follow-up ended at the earliest of: 1) CVD event; 2) death; 3) loss of coverage; or 4) 12/31/2016, the latest date at which the Medicare claims database was evaluated. CVD events were defined as incident MI, stroke or fatal CVD event, and were identified using validated algorithms (PPV >80%). The leptin-adjusted MBDA score (Curtis et al., Rheumatology 2018) and its 12 individual protein biomarkers were evaluated as predictors of CVD events, as were other variables, including demographics, healthcare utilization, CVD-related comorbidities and medications, and RA-related features (e.g. DAS28-ESR, logic use, glucocorticoid use). The cohort was randomly split 2:1 to use 2/3 of patients for training and 1/3 for validation. Cox proportional hazard regression with LASSO was used for variable selection based on minimization of 10-fold cross-validated error + 1 SE. Model calibration (observed vs. expected) and discrimination were assessed for predicted CVD events at 3 years. Analyses are ongoing; main performance results are reported for the cross-validated training data.

Results: A total of 26,261 eligible RA patients were analyzed; mean (SD) age 68.6 (10.2) years, 80.1% female, 72.6% white, 23% diabetes, 43% statin use, 56% metformin, 44% on biologics/tocilizumab, 55% steroids, and median (IQR) adjusted MBDA score 40 (32-49). A total of 477 CVD events occurred over mean (SD) follow-up time of 1.7 (1.2) years yielding a CVD incidence rate of 16.5 (95% CI 15.0-18.0)/1000py. The most important predictors in these LASSO-selected models were age, beta-blocker use, sex, diabetes, adjusted MBDA score and a subset of individual MBDA biomarkers. The best performing model had a cross-validated area under the receiver operator curve of 0.70 and good observed: expected prediction at 3 years (Figure).

Conclusion: Preliminary results from this approach suggest that a simple algorithm consisting of a limited number of protein biomarkers and clinical measures can provide an accurate method to predict short-term CVD risk in RA.

Acknowledgement: The work for this abstract was funded by an industry/academic collaboration between Myriad and University of Alabama at Birmingham.


AB0290  TREAT-TO-TARGET (T2T) IS NOT ENOUGH; IDENTIFY FACTORS LEADING TO A MISMATCH BETWEEN T2T AND HAQ AMONG RA PATIENTS THROUGH DATA MINING FROM SMART SYSTEM OF DISEASE MANAGEMENT (SSDM)

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Background: T2T, achieving a DAS28 score lower than 2.6 (remission) or below 3.2 (low disease activity), is the main management strategy recommended by ACR and EULAR. HAQ is the most widely used in assessments of physical function in RA. However, the T2T may not always associate with good HAQ.

Objectives: To quantify phenomenon of mismatch between the T2T and the HAQ in RA patients and identify influential factors from real-world data mining in SSDM.

Disclosure of Interests: None declared

**Methods:** SSDM is a novel mobile tool of disease management. The patients were trained to master SSDM by health care professionals and conducted their DAS28 and HAQ self-assessments. The data were synchronized to the mobile of physicians and uploaded onto cloud for analysis.

**Results:** From Jun 2014 to Jan 2019, 44,698 RA patients from 587 hospitals in China used SSDM, of which 32,058 patients made 67,845 DAS28 and HAQ self-assessments. The T2T rates were 27% at baseline, and 60% after 6 months among 4,768 patients who have been followed up longer than 6 months. In 25,620 assessments of patients who achieved T2T at baseline or repeat assessments, 76% (19,552) assessments had normal physical function (HAQ = 0), but 24% (6,268) were with HAQ score higher than 0, which mean score for 6 functional tests was 3.67, indicating physical dysfunction. The “Bend down to pick up clothing from the floor” was the one being affected most, with a mean score of 0.81, significantly higher than other functional test score, P<0.001. The mean numbers of tender and swollen joints among T2T patients were 1.53 and 1.32 respectively. The analysis of correlation between physical dysfunction and the affected joints showed the knees were the major contributor to the mismatch, following by wrist and shoulders. Table 1 showed the mean scores for each functioning category in HAQ and the top target joints.

In patients who did not achieve T2T, 32% had HAQ scores of 0, showing that these patients had normal physical function despite failure in achieving T2T. The mean number of tender and swollen joints in these patients was 4.31 and 2.85, respectively. The affected joints were mainly hand joints. According to the cluster weights for the impacts of affected joints on physical function, the weighted coefficient of affected joints impacting factors (IF) on physical function was obtained. The highest IF was for knee (4), followed by wrist (3.4), shoulder (2.3), middle finger (2.1), elbow (2), index finger (2), other fingers (1), respectively.

**Conclusion:** 1/4 RA patients suffer from physical dysfunctions even though T2T are achieved. Diseased knees, wrists and shoulders are the top three joints that lead to corresponding physical dysfunctions and contribute to a mismatch between T2T and HAQ. Conversely, diseased elbow and finger joints are less likely to cause physical dysfunction. Therefore, not all joints are equal. Joints of knees, wrists and middle fingers are less likely to cause physical dysfunction.

**Disclosure of Interests:** None declared

**DoI:** 10.1136/annrheumdis-2019-eular.1577

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**AB0291**

**SHORT TERM EFFECTIVENESS OF JANUS KINASE INHIBITORS AND BIOLOGIC DRUGS IN RHEUMATOID ARTHRITIS PATIENTS FROM THE APULIAN REGISTRY BIOPURE**

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**Background:** Randomized clinical trials have provided evidence that janus kinase inhibitors (Jak-i) induce a quick response in patients affected with rheumatoid arthritis (RA), especially in terms of perception of pain. However, a few data are available on this issue in RA patients upon treatment with Jak-i in the settings of real life.

**Objectives:** We aimed at evaluating the early clinical response in RA patients treated with Jak-i or biologic disease modifying drugs (bDMARDs) from the Apulian registry BIOPURE.

**Methods:** We retrospectively evaluated patients with RA, according to 2010 ACR/EULAR Criteria, who begun Jak-i or biologic drugs from December 2017 (since baricitinib was available onto the market) through December 2018. We included 198 patients (female 146, 77.25%) with age (mean ±SD) of 57.8 ±12 years. Of them, 143 (75.6%) were treated with bDMARDs, whereas 46 (24.3%) were on JAK Inhibitors, namely baricitinib or tofacitinib (Table 1). Disease activity score on 28 joints (DAS28) and reported pain on a 0-100 visual analogue scale (VAS) were estimated at baseline, 3 and 6 months. Intra-group changes from baseline of DAS28 and VAS-pain was assessed by t-test. Mean difference changes in VAS-pain at 3 months between Jak-i and bDMARDs were compared by t-test. Possible predictors of the achievement of EULAR good-response at 3 months were estimated by binary logistic multiple regression analysis.

**Table 1. Frequency of different Jak-i and bDMARDs**

<table>
<thead>
<tr>
<th>Medication</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tocilizumab</td>
<td>4</td>
<td>2.12</td>
</tr>
<tr>
<td>Baricitinib</td>
<td>62</td>
<td>22.22</td>
</tr>
<tr>
<td>Abatacept</td>
<td>43</td>
<td>22.75</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>13</td>
<td>6.88</td>
</tr>
<tr>
<td>Anakinra</td>
<td>1</td>
<td>0.53</td>
</tr>
<tr>
<td>Certolizumab</td>
<td>18</td>
<td>9.52</td>
</tr>
<tr>
<td>Etanercept</td>
<td>17</td>
<td>8.99</td>
</tr>
<tr>
<td>Golimumab</td>
<td>5</td>
<td>2.65</td>
</tr>
<tr>
<td>Infliximab</td>
<td>4</td>
<td>2.01</td>
</tr>
<tr>
<td>Rituximab</td>
<td>4</td>
<td>2.12</td>
</tr>
<tr>
<td>Tocilizumab</td>
<td>38</td>
<td>20.11</td>
</tr>
<tr>
<td>Total</td>
<td>189</td>
<td>100.00</td>
</tr>
</tbody>
</table>

**Results:** Considering the whole cohort, mean DAS28 at baseline was 3.70 (±1.4) and significantly decreased to 2.76 (±1.1) at 3-months (p<0.001) and to 2.99 (±1.4) at 6-months (p<0.001). Likewise, VAS-pain was significantly improved from baseline, either at 3 and 6 months (p<0.001). Also VAS-pain significantly decreased in patients on treatment with Jak-i than in those on bDMARDs (p<0.005) (Figure 1). An EULAR good response was reached by 37.5% at 3 months and by 56.4% of patients at 6 months. In particular, patients with JAK Inhibitors met this goal at 3 months significantly more frequently than others (p<0.003). EULAR good response at 3 months was strongly associated with Jak-i treatment (OR 3.1, 95%CI 1.4-6.6).

**Conclusion:** Despite the usual flaws of the analysis from registries, such as comorbidities, concomitant therapies, adherence, different disease activity or line of treatment, our study suggests that Jak-i allow to achieve an early clinical benefit in terms of patient reported pain at greater extent than classical bDMARDs in real-world.

**Disclosure of Interests:** Carmelo Zuccaro Consultant for: C Zuccaro has received consultancy fees and/or speaker honoraria from MSD, AbbVie, Novartis, Pfizer, Janssen outside this work, Speakers bureau: C Zuccaro has received consultancy fees and/or speaker honoraria from MSD, AbbVie, Novartis, Pfizer, Janssen outside this work, L Santo has received consultancy fees and/or speaker honoraria from AbbVie, MSD, Novartis UCB outside this work, Speakers bureau: L Santo has received consultancy fees and/or speaker honoraria from AbbVie, MSD, Novartis UCB outside this work, Laura Quarta: None declared, Nicola Maruotti Speakers bureau: N Maruotti has received speaker honoraria from AbbVie, Pfizer, Janssen outside this work.

**Figure 1. Comparison of mean difference at 3 months from baseline between Jak-i and bDMARDs.**
A COMPARISON OF THE JOINTS ULTRASONOGRAPHY IN THE PATIENTS WITH RHEUMATOID ARTHRITIS TREATED BY BIOLOGICAL AGENTS AND THE CORRESPONDING SYNOVIAL HISTOLOGICAL FINDINGS

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Background: In the treatment of Rheumatoid arthritis (RA), early diagnosis and early treatment with light control have become increasingly important with the advent of biological therapy. Ultrasonography (US) of the various joints enables the real-time evaluation of synovial hyper trophy, effusion and bone erosion. Power Doppler (PD) ultrasound is able to identify both subclinical synovitis and early erosive disease.

Objectives: The objectives of this study were to investigate whether the image of US at the operated joint reflect synovium histological findings or clinical indicators, and to compare the results in the patient treated by non-biological agent (NonBio) and biological agent (Bio).

Methods: RA related orthopedic surgery was performed at 1287 joints including 17 shoulders, 160 knees, 96 elbows, 378 wrists, 364 fingers, 38 ankles and 234 toes during the period between January 2011 and December 2018 at our rheumatic center. Preoperatively, ultrasound evaluations were performed and grade of PD signal was determined at the part with the highest signal. PD signal consists 4 grades from grade 0 to 3. The operations were performed within one week after the ultrasound evaluations. Rooney score of the synovium ESR, DAS28-ESR (4), MMP-3, CRP were investigated. Rooney score represents the histological features in the synovium of RA. It includes 6 features i.e. synoviocytes hyperplasia, fibrosis, proliferating blood vessels, perivascular infiltrates of lymphocytes, focal aggregates of lymphocytes, diffuse infiltrates of lymphocytes, focal aggregates of lymphocytes, fibrosis, proliferating blood vessels, perivascular infiltrates of lymphocytes, focal aggregates of lymphocytes, diffuse infiltrates of lymphocytes. They were scored separately on a scale of 1-10.

The treatments that the patients received included: biological agents (Bio) CZP (n=12), golimumab (GLM) (n=56), and abatacept (ABT) (n=55), infliximab (IFX) (n=29), adalimumab (ADA) (n=28), certilizumab pegol (n=389 30%), etanercept (ETN) (n= 102), tocilizumab (TCZ) (n=105), bio agents (Bio) and non-biological agents (NonBio) (n=389 30%), etanercept (ETN) (n= 102), tocilizumab (TCZ) (n=105), infliximab (IFX) (n=29), adalimumab (ADA) (n=28), certilizumab pegol (CZP) (n=12), golimumab (GLM) (n=56), and abatacept (ABT) (n=55), folicolinb (TOF) (n=2).

Results: PD signal (0.97±0.08), DAS28 ESR. (2.32±1.13), CRP.(0.51±1.25 mg/dL), MMP-3 (119.0±119.0 mg/mL) and Rooney score (23.5±7.7) in the patients treated with Bio were significantly lower than those (1.99±0.95, 3.66±1.07, 0.78±1.37 mg/dL, 146.3±150.0 mg/dL, 28.5±9.26) in the patients treated with NonBio. Rooney score fibrosis (9.5±1.44) in patients treated with Bio was significantly higher than those (8.6±2.48) in patients treated by NonBio. Rooney score, synoviocyte hyperplasia (1.1±1.26) and three items of lymphocytes (1.59±2.91, 1.68±2.54, 1.1±1.22) in patients treated with Bio were lower than those (1.72±1.3, 3.79±3.56, 3.73±3.53, 2.4±2.98) in patients treated with NonBio. TCZ, ADA, ABT and IFX had some significant differences for Rooney score and Rooney item score between the patients treated with NonBio.

Conclusion: The activity of RA synovitis at operated site was suppressed in patients treated with Bio. There were some differences in clinical data, histological score, PD signal and DAS28 among Bio.

Disclosure of Interests: None declared


AB0291C REMISSION IN RHEUMATOID ARTHRITIS: CONSIDERING NEW CUT-POINTS OF COMPOSITE DISEASE ACTIVITY INDICES ACCORDING TO THE ABSENCE OF SYNOVITIS BY ULTRASONOGRAPHY

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Background: Achieving the state of remission in RA according to currently available criteria does not entirely prevent patient from radiological progression. On the contrary, the presence of subclinical synovitis by means of ultrasonography (US) correlates with radiological progression.

Objectives: To establish cut-off values of composite disease activity indices (DAS28-ESR, DAS28-CRP, DAS28-ESR, CDAI and SDAI) that adjust better to remission according to the absence of synovitis by US.

Methods: Observational, cross-sectional study that included 126 patients with diagnosis of RA who were in remission or low disease activity (DAS-ESR ≤3.2). For each patient we calculated the DAS28-ESR, DAS28-CRP, CDAI, SDAI. For US assessment we used the 12 joint simplified score. We considered the state of remission by US if no synovial hypertrophy (SH) ≤1 power Doppler (PD) signal= 0 in all joints. The cut-off values of the disease activity indices to define remission according the proposed US definition of remission were determined by ROC curves.

Results: Patients had a median (ICR) DAS28-ESR of 2.32 (0.68), DAS28-CRP= 1.89 (0.55), CDAI= 3.56 (3.0) and SDAI= 3.0 (4.7). The sensitivity, specificity, positive and negative predictive value of each of the selected cut-off points for the DAS28-ESR, DAS28-CRP, CDAI and SDAI for the definition of remission are shown in the Table.

Conclusion: In this study we describe new cut points of the different composite disease activity indices for the definition of remission. These cut points improve the accuracy of the definition of remission. However, they differ scarcely from the reference values making its impact uncertain in the long term management of RA patients. Longitudinal studies are, therefore, warranted in order to elucidate the performance of these new cut points.

REFERENCE

PREDICTORS OF NEW BONE EROSION IN RHEUMATOID ARTHRITIS PATIENTS RECEIVING csDMARDs: ANALYSIS OF DATA FROM THE DRIVE AND DESIRABLE STUDIES

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Background: Suppression of joint destruction is an important target for the treatment of rheumatoid arthritis (RA). Most previous studies have proposed prediction models for joint destruction to detect the risk of rapid radiographic progression (change in mTSS ≥5). As joint destruction progresses irreversibly, even slight progression of joint destruction might impact the prognosis. Therefore, our study focused on the onset of new bone erosion in RA patients.

Objectives: To clarify predictors for new bone erosion in RA patients treated with csDMARDs.

Methods: Predictive factors were analyzed using data from the placebo groups of the DRIVE [1] and DESIRABLE [2] studies, which were 12-month, randomized, double-blind, phase 2 and 3 trials for evaluating the efficacy of denosumab in RA patients. New bone erosion was defined as change from baseline in erosion score (ES) ≥1.0 at 12 months, which was assessed as “progressed” by two readers. In addition to newly emerging erosion, new bone erosion also included enlargement of erosion size which is the result of new erosion at a site adjacent to an existing bone erosion. To evaluate predictors for new bone erosion, a logistic regression model was applied. Significant predictors (p value of <0.1) were selected from the univariate analysis and one variable from each correlated pair that showed significance was removed. Multivariate analyses were performed using the selected predictors.

Results: In a total of 306 patients, baseline DAS28-CRP (mean±SD) was 3.5±1.03. New bone erosion was observed in 90 patients (29.4%). In the univariate analysis, female sex, anti-CCP antibody positivity, rheumatoid factor positivity, tender joint count (TJC)/≥6, CRP/≥0.3 mg/dL, and baseline ES/≥3 were identified as significant predictors for new bone erosion. RF and ESR were not included in the multivariate analysis because they were strongly correlated with anti-CCP antibody and CRP, respectively. In the multivariate analyses, female sex, anti-CCP antibody positivity, TJC/≥6, CRP/≥0.3 mg/dL, and baseline ES/≥3 were identified as predictors for the development of new bone erosion.

Abstract AB0291D Table 1. Univariate and multivariate analyses for a change in ES ≥1.0

<table>
<thead>
<tr>
<th>Variables</th>
<th>Reference</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Female</td>
<td>1.78</td>
<td>0.089</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td></td>
<td>1.85</td>
</tr>
<tr>
<td>Age</td>
<td>≥65 years</td>
<td>0.79</td>
<td>0.433</td>
</tr>
<tr>
<td></td>
<td>&lt;65 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duration of disease</td>
<td>&lt;3 years</td>
<td>1.06</td>
<td>0.844</td>
</tr>
<tr>
<td></td>
<td>≥3 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anti-CCP antibody</td>
<td>Positive</td>
<td>5.95</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Negative</td>
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<td>4.01</td>
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<tr>
<td>RF</td>
<td>Positive</td>
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</tr>
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<td></td>
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<tr>
<td>Glucocorticoid use</td>
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<td>0.99</td>
<td>0.963</td>
</tr>
<tr>
<td></td>
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<tr>
<td>TJC</td>
<td>≥6</td>
<td>1.66</td>
<td>0.047</td>
</tr>
<tr>
<td></td>
<td>&lt;6</td>
<td></td>
<td>1.70</td>
</tr>
<tr>
<td>Swollen joint count</td>
<td>&gt;10</td>
<td>1.26</td>
<td>0.353</td>
</tr>
<tr>
<td></td>
<td>&lt;10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CRP</td>
<td>≥0.3 mg/dL</td>
<td>2.84</td>
<td>&lt;0.001</td>
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<tr>
<td></td>
<td>&lt;0.3 mg/dL</td>
<td></td>
<td>2.02</td>
</tr>
<tr>
<td>ESR</td>
<td>≥28 mm/h</td>
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<td>&lt;28 mm/h</td>
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<td>Baseline ES</td>
<td>≥3</td>
<td>3.32</td>
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</tr>
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<td></td>
<td>&lt;3</td>
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<tr>
<td>Study</td>
<td>DESIRABLE</td>
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</table>

Conclusion: In RA patients whose disease activity was controlled on csDMARDs, positive anti-CCP antibody/RF status, elevated CRP/ESR levels, baseline ES/≥3, TJC/≥6 and female sex were identified as predictors for new bone erosion.
The effect of human umbilical cord mesenchymal stem cells-derivied exosomes on chemokines in collagen-induced arthritis rats

Peng He1, 1SHANXI ACADEMY OF MEDICAL SCIENCES SHANXI DAYI HOSPITAL, TAIYUAN, CHINA

Background: Umbilical cord mesenchymal stem cells (UCMSCs) derived exosomes could simulate the function of MSC and avoid the limitations of MSC, which is being hotspot in the research of rheumatoid arthritis (RA) treatment. Chemokines can recruit inflammatory cells and osteoclasts in inflammatory joints, and participate in the synovial inflammation and bone destruction of RA. The mechanisms of UCMSC-derived exosomes on chemokines have less understood in RA.

Objectives: The aim of this study was to investigate the effect of UCMSC and UCMSC-derived exosomes on the chemokines CCL2, CXCL10 and CXCL12 in CIA rats.

Methods: Human umbilical cord mesenchymal stem cells (UCMSCs) were cultured in vitro and separated using a differential centrifugation methods. The CIA rats model was set up by Freund’s complete adjuvant and type II collagen, then randomly divided into control, CIA, MTX, UCMSCs, UCMSCs low group and high concentration groups. Rats in UCMSCs group were injected in double ankle joint with UCMSCs 2X10^6/L weekly for 3 weeks. Rats in UCMSCs low and high group were injected in double ankle joint with UCMSCs exosomes 30µg and 90µg weekly for 3 weeks, respectively. Rats in MTX group were given intraperitoneal injection with MTX (0.9mg/kg) weekly for 3 weeks. Serum concentrations of CCL2 (CXCL10 and CXCL12) were measured by flow cytometry. CXCL12 serum level was tested by enzyme-linked immunosorbent assay (ELISA). The protein expressions of CCL2, CXCL10 and CXCL12 in synovial tissue were detected by immunohistochemistry. CCL2, CXCL10 and CXCL12 mRNA levels in synovial joint and spleen were measured by reverse transcription-polymerase chain reaction (RT-PCR).

Results: Intra-articular injection of UCMSC exosomes decreased CCL2 and CXCL12 levels in serum and improved synovial hyperplasia and inflammatory cell infiltration in the CIA rats. UCMSC exosomes suppressed the protein expressions of CCL2, CXCL10, CXCL12 in synovial tissue. It also inhibited transcript levels of CCL2, CXCL10, CXCL12 in synovial tissue and spleen. UCMSC had similar effect on CCL2, CXCL10, CXCL12 in CIA. The high concentration group was more effective than the low concentration in preventing CCL2, CXCL10, CXCL12 protein expressions of synovial tissue and CXCL2 transcript level of spleen.

Conclusion: UCMSC exosomes alleviates synovial inflammation in CIA rats through suppression of CCL2, CXCL10, CXCL12 release. The inhibitory effect of on chemokines simulate UCMSC, their cell of origin, the high concentration was better than low concentration.

REFERENCES

Disclosure of Interests: None declared
Rheumatoid arthritis (RA) is one of the chronic autoimmune diseases with an estimated prevalence of 1 to 2 percent of the total population in the world. RA patients have an increased risk of morbidity and mortality from cardiovascular (CV) events as a result of accelerated atherosclerosis. Endothelin-1 (ET-1) is a hormone with strong vasocostrictor properties, secreted in excessive amounts by damaged endothelial cells. However, the effect of this hormone depends on the presence of specific ET-1 receptors as well as their density and location. ET-1 is a mediator-activating autocrine and paracrine, primarily in the circulatory system. It induces the production of proinflammatory cytokines, exacerbating the inflammatory process.

Objectives: The objectives of this study were: to compare serum ET-1 levels between RA patients and healthy controls and observe the relationship between tobacco smoking and serum levels of ET-1 in RA patients.

Methods: This cross-sectional study was performed in Vega-Baja Hospital, Orihuela (Spain) from November 2016 to May 2018. We prospectively enrolled 63 consecutive women patients affected by RA and followed at the Vega-Baja Hospital (Orihuela, Spain) and 65 matched healthy women controls. All patients included in this study had normal serum creatinine (Cr) levels and met the 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) criteria for RA. Serum Hcy was analyzed using immunonephelometric method. Bone mineral density (BMD) of femoral neck and lumbar spine was measured by dual-energy X-ray absorptiometry (DXA).

Results: A total of 63 female patients were included in our study, with a mean (SD) age of 53 ± 8 years. The majority were Caucasian (90.5%). Thirty-four patients were menopausal and twenty-nine non-menopausal patients. The mean duration of RA was 8.5 ± 5.8 years. The mean disease activity scores in 28 joints (DAS28) according to the erythrocyte sedimentation rate (ESR) indicated low disease activity 3.0 ± 1.3. The mean health assessment questionnaire (HAQ) was 0.75 ± 0.67. Twenty-eight patients were treated with methotrexate, with a median weekly dose of 11.5 ± 4.8 mg, all the patients received 10 mg folic acid supplementation per week. Serum Hcy concentration levels between RA patients were significantly higher in the RA patients than those in the control group: [9.93 (5.6-18.8) vs. 7.11 (4.9-11.1)], pg/mL; *P<0.001*. Serum levels of Hcy were inversely related to lumbar spine BMD and femur neck BMD (r < 0.26; P < 0.05).

Conclusion: Patients with RA have high levels of Hcy that correlate, inversely, with bone mass suggesting that hyperhomocysteinemia is a risk factor for osteoporosis in patients with RA.

REFERENCES

Disclosure of Interests: Antonio Alvarez de Cienfuegos: None declared, Lucia Cantero-Nieto: None declared, José Alberto García-Gómez: None declared, Jesus Luis Callejas-Rubio: None declared, Miguel A. González-Gay Grant/research support from: Prof. MA González-Gay received grants/research supports from abbvie, MSD, Jansen and Roche., Speakers bureau: Consultation fees/participation in company sponsored speaker’s bureau from Pfizer, Lilly, Sobi, Celgene, Novartis, Roche and Sanofi., Norberto Ortego: None declared

Disclosure of Interests: None declared


Disclosure of Interests: None declared

HOW OFTEN IS THE COMBINATION OF NSAID-INDUCED LESIONS OF THE UPPER AND LOWER GI TRACT?

Background: Non-stereoidal anti-inflammatory drugs (NSAIDs) can damage all parts of the gastrointestinal tract (GIT). However, the frequency of the combination of lesions in different parts of the gastrointestinal tract has not been studied.

Objectives: To assess the frequency of the combination of NSAID-induced lesions of the upper GI tract, small and large intestine.

Methods: The study group consisted of 112 patients with rheumatic diseases (62.5% of women, 56.2 ± 14.6 years), who regularly took NSAIDs. All patients underwent endoscopy of the upper GI tract and colon. Capsule endoscopy was performed in 35 patients with signs of NSAID-gastrocolitis.

Results: NSAID-gastrointestinal (erosions and/or gastric or duodenum ulcers) were detected in 37.8%, NSAID-enteropathy (hemorrhages, erosions and ulcers of the small intestine) in 68.6%, NSAID-colitis (hemorrhages, erosions and ulcers of the colon) - 14.3% patients. The combination of NSAID-gastro- and colopathy was detected in 26.8% of patients (odds ratio 12.2, 95% CI 2.619-56.84), the combination of NSAID-gastro, enteropathy, and colopathy - in 10 patients (20.4% of the number of patients with NSAID-gastrocolitis).

Conclusion: The combined NSAID-induced damage of various parts of the GI tract is a frequent and serious pathology requiring complex diagnostics and the combined use of prophylactic agents with a different mechanism of action.

Disclosure of Interests: None declared

COMPLICATIONS OF RHEUMATOID ARTHRITIS AND ALLIED DISORDERS – A STATISTICAL COMORBIDITY STUDY OF 234 AUTOPTOSE PATIENTS

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Background: Complications of rheumatoid arthritis (RA) may modify the clinical course and symptoms of allied disorders leading to missed diagnosis or late recognition of associated diseases.

Objectives: The aim of this study was to determine the possible role of classic complications of RA: systemic autoimmune vasculitis (AV), AA amyloidosis (AAa), lethal cardiac insufficiency (CI) caused by endo-, myo- or pancarditis, furthermore lethal septic infection (SI) on prevalence and mortality of coexistent associated diseases: atherosclerosis (Aths), hypertension (HT), type 2 diabetes mellitus (DM) and tuberculosis (Tb) with military dissemination (mTb).

Methods: The study group consisted of 234 autopsies, which 20.5% were selected autopsy patients with RA were studied. RA was confirmed clinically according to the criteria of the ARA.

The presence of AV, AAa, CI and SI was determined at autopsy and confirmed by a detailed review of extensive histological material. The prevalence and mortality of associated diseases: Ath, HT, DM, Tb or mTb were analyzed retrospectively, reviewing the clinical and pathological reports.

The link between AV, AAa, CI or SI and Ath, HT, DM, Tb or mTb was analyzed by (χ²) test.

Results: RA was complicated by AV in 43 (18.4%), by AAa in 48 (20.5%), by CI with lethal outcome in 15 (6.4%), and by lethal SI in 33 (14.1%) of 234 patients.

RA associated with severe Ath in 106 (45.3%), with HT in 41 (17.5%), with DM in 41 (17.5%), and with Tb in 28 (11.9%), with active mTb in 9 (3.8%) of 234 patients. As a basic disease Ath led to death in 61 (26.1% of 106), HT in 2 (0.9% of 41), DM in none (0% of 41), and Tb with mTb in 3 (1.3% of 234) patients. Tb without military dissemination was not lethal in our patient population.

The statistical links (p-values of significance) between complications of RA and prevalence or mortality of allied disorders are summarized in Table.

<table>
<thead>
<tr>
<th>Complications of</th>
<th>AV n=43 of</th>
<th>AAa n=48 of</th>
<th>CI n=15 of</th>
<th>SI n=33 of 234</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA</td>
<td>234</td>
<td>234</td>
<td>234</td>
<td>234</td>
</tr>
</tbody>
</table>

Allied disorders in RA

Ath n=106 of 234

χ²=6.43, p<0.01

χ²=16.04, p<0.02

χ²=5.03, p<0.02

Athal lethal n=61 of 234

χ²=15.92, p<0.01

χ²=11.04, p<0.03

χ²=4.29, p<0.01

χ²=12.01, p<0.01

HT 41 of 234

χ²=3.30, p<0.03

χ²=0.03, p<0.06

χ²=1.12, p<0.25

χ²=0.07

p<0.02

p<0.25

HT lethal n=2 of 41

χ²=0.05, p=0.80

χ²=0.02, p=0.87

χ²=1.61, p<0.15

χ²=1.69, p<0.15

DM 41 of 234

χ²=0.04, p<0.08

χ²=0.84, p<0.35

χ²=0.92, p<0.01

χ²=0.01, p<0.99

Tb 28 of 234

χ²=4.02, p<0.04

χ²=2.61, p<0.10

χ²=0.33, p<0.37

χ²=0.33

p<0.56

p<0.54

Tb lethal n=3 of 28

χ²=0.00, p=0.93

χ²=0.02, p=0.86

χ²=0.55, p<0.01

χ²=0.01, p<0.46

mTb 9 of 28

χ²=4.24, p<0.00

χ²=0.08, p<0.77

χ²=0.01, p<0.05

χ²=0.91, p<0.62

Tb lethal n=2 of 9

χ²=0.00, p=0.93

χ²=0.02, p=0.86

χ²=0.63, p<0.01

χ²=0.01, p<0.46

p<0.89

Conclusion: The inverse correlations between AV, AAa, CI, SI, and Ath, HT, DM, Tb or mTb indicate that the prevalence and mortality of allied disorders were not influenced basically by the complications of RA.

The consequently inverse and (in most cases) significant correlations between prevalence of AV, AAa, CI, SI and the prevalence and mortality of Ath show that these are independent entities in RA. The AV, AAa, CI, SI, and Ath are the most important complications of RA, and are characterized by severe forms of disease, mostly involving younger patients, with an earlier onset (without pronounced Ath); while Ath is basically an age dependent phenomenon, characteristically present in RA patients with advanced age. RA patients with Ath may represent a special group of RA, characterized by lower incidence of AV, AAa, CI or SI, and a better prognosis.

The positive and significant relations AV to Tb or mTb suggest an increased risk of Tb, e.g. the presence of AV may promote Tb or endogenous exacerbation and milary dissemination of Tb.

Disclosure of Interests: None declared

COXITIS DURING CHRONIC INFLAMMATORY RHEUMATISM

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Background: The occurrence of coxitis in chronic inflammatory rheumatism is a prognostic factor of great importance given the functional repercussions of the involvement of the coxofemoral joint.

Objectives: The aim of this work is to evaluate the prevalence of this complication in chronic inflammatory rheumatism (PR/JIA/SpA) and to describe the evolution of this disorder according to the pathology.

Methods: Eighty-two patients with chronic inflammatory rheumatism were enrolled. These patients were followed by the rheumatology department rabta since 2004 until March 2018. The clinical demographics, activity scores, treatment background (all our patients in this series were under biotherapy) and the need PTH were identified.

Results: The eighty-two patients were distributed as follows: 36.58% (n = 30) patients with RA, 36.58% (n = 30) SpA and 26.83% (n = 22) JIA. The average age was 48.3 years, 47.6 years and 35.17 years. For the rheumatoid arthritis population 26.67% (n = 8) of the patients had a coxite of which 62.5% (n = 5) was bilateral and 37.5% (n = 3) unilateral. The mean time to discovery of coxite was 11.7 years and the evolution was in 50% (n = 4) to worsening requiring in 3 cases a bilateral PTH and a case of synovithesis.

In the SpA group, 23.33% (n = 7) of patients had coxitis, of which 57.14% (n = 4) were bilateral and 32.86% (n = 3) unilateral. The average age to discovery of this lesion was 8.22 years. PTH was performed in 71.43% (n = 5) of patients.

For the JIA population, 45.45% (n = 10) of the patients had a coxite of which 80% (n = 8) was bilateral and 20% unilateral. The average time to discovery of this lesion was 14 years, with 60% of cases progressing to an aggravation requiring 45% of the cases for synovithesis and 60% for PTH.

Conclusion: SpA is the most common chronic inflammatory rheumatism with cox-femoral involvement with the most pejorative evolution despite the biological treatment.
REFERENCES
none
Disclosure of Interests: None declared

AB0300 LIVER DISORDERS DURING RHEUMATOID ARTHRITIS
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Background: Hepatic disease in rheumatoid arthritis (RA) are rare, but can be impactful for patients. Though some hepatic manifestations are directly related to RA, others may be sequelae of treatment or caused by concomitant autoimmune diseases.

Objectives: We have tried through this study to focus on the liver disorders during the monitoring of rheumatoid arthritis and to identify the different etiologies.

Methods: This is a retrospective descriptive study of patients with rheumatoid arthritis (ACR-EULAR 2010 criteria) followed a rheumatology department between 2012 and 2018 with liver function disorder. We have specified the epidemiological, clinical, biological and therapeutic characteristics and the different explorations carried out for these patients.

Results: We included 61 patients in our study (3 men and 58 women). Mean age was 52.13 years [28-82]. Average duration of RA was 9.2 years [0.5-30]. Mean DAS28 was 5.95 [3-8.33]. RA was immunopositive in 88.5% of the cases and erosive in 93.44% of the cases. Most of patients received symptomatic treatment (98% paracetamol, 87% non-steroidal anti-inflammatory drugs, 84% corticosteroids). As for conventional csDMARD, 72% of patients were treated with methotrexate, 8.2% with anti-malarial, 22.95% with salazopyrine and 11.47% with leflunomide. Three patients received biological DMARDs (1 rituximab and 2 TNF-Blocking).

Hepatic disorders were cholestasis (95%), cytolysis (33%) and concomitant cytology and cholestasis (28%). The etiological investigation undertaken linked these disorders of the liver function disorders to the RA treatment in 50% of the cases. Methotrexate was incriminated in the genesis of this liver enzyme abnormalities in 14 cases, the salazopyrine in 2 cases, the leflunomide in 1 case, paracetamol and non-steroidal anti-inflammatory drugs in 11 cases and rituximab in 1 case. Hepatic immunological investigation was negative in all cases. We have not noted any hepatitis B seroconversion. Two patients had hepatitis C. One patient presented active hepatitis C serology with signs of fibrosis (AF2F2) at the liver biopsy puncture. Abdominal ultrasound showed signs of non-alcoholic fatty liver disease in 34.42% of cases. The biopsy puncture of the liver was performed in 8 patients showing chronic hepatitis lesions (n=1), hepatic atrophy (n=1), steatosis with portal and peri-sinus fibrosis (n=1). The etiological investigation was negative in 10% of cases.

Conclusion: In our study, the liver function disorders during RA are in half of the cases of ischiatic origin. This requires rigorous monitoring of patients followed for RA in order to improve their management.

Disclosure of Interests: None declared

AB0301 ANTIMICROBIAL USE IS HIGH IN PATIENTS WITH INFILAMMATORY ARTHRITIDES, AND FURTHER INCREASES WITH FIRST-LINE TNFI THERAPY – NATIONWIDE RESULTS
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Background: Infections are well-known adverse effects of tumor necrosis factor inhibitors (TNFi) and increased hospitalization rates due to infections have also been reported. To our knowledge, this is the first study to report the effect of TNFi initiation on outpatient antimicrobial prescription patterns.

Objectives: To investigate the use of antimicrobial agents (antibacterials, antifungals and antivirals; excluding antimycobacterials) in patients with rheumatoid arthritis, psoriatic arthritis, and axial spondyloarthropathies in relation to the initiation of the first TNFi in biologic-naïve patients.

Methods: All patients with inflammatory arthritides who are treated with biologic DMARDs in Iceland are registered in ICEBIO, a nationwide registry. On February 1st 2016, ICEBIO contained information on 1058 individuals. The Icelandic Directorate of Health operates the Icelandic Medicine Database (IMD), a registry that includes over 95% of all filled drug prescriptions in Iceland. From the IMD, filled antimicrobial prescriptions were extracted two years before and two years after the initiation of first-line TNFi therapy for all patients in ICEBIO with rheumatoid arthritis (RA; n=366), psoriatic arthritis (PsA; n=250) and axial spondyloarthritis (AS; n=218). As controls, five individuals, age and sex matched, for the same calendar time were randomly selected. Antimicrobial use was determined from defined daily dose per 1000 capita (DDD).

Results: The use of antimicrobials prior to TNFi treatment was greater in the patient group when compared to controls (mean 43 DDD vs 21 DDD; p<0.01). The patient group received more DDD of antimicrobials following the start of TNFi, with a statistically significant increase in PsA (33.9 to 45.2; p<0.01), AS (37.2 to 46.8; p<0.01) and nonsignificant in RA (46.8 to 49.7; p=0.066). Antimicrobial use increased from 115 DID to 137 DID for the whole group, most prominently in the PsA and AS groups (Table I). Antifungal use increased in patients with RA and antiviral use in RA and PsA (Table I).

Table I: Anti-bacterial, antifungal and antiviral use in DID two years before and after TNFi therapy.

<table>
<thead>
<tr>
<th></th>
<th>RA</th>
<th>Control</th>
<th>PsA</th>
<th>Control</th>
<th>AS</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before</td>
<td>45.7±9.7</td>
<td>23.7±3.3</td>
<td>32.7±4.8</td>
<td>19.2±4.3</td>
<td>36.6±8.6</td>
<td>16.6±3.5</td>
</tr>
<tr>
<td>After</td>
<td>±97.1±6.3</td>
<td>±47.8±4.5</td>
<td>±34.5±3.6</td>
<td>±37.2±3.3</td>
<td>±5.6±2.1</td>
<td>±40.3±6.3</td>
</tr>
<tr>
<td>Antibacterial</td>
<td>0.60±17.1</td>
<td>0.18±1.7</td>
<td>0.32±2.3</td>
<td>0.37±1.6</td>
<td>0.44±2.4</td>
<td>0.13±1.1</td>
</tr>
<tr>
<td>Antifungal</td>
<td>±0.4±1.4</td>
<td>±5.3±2.1</td>
<td>±7.0±2.3</td>
<td>±4.1±2.3</td>
<td>±7.4±8.1</td>
<td>±4.0±3.2</td>
</tr>
<tr>
<td>Antiviral</td>
<td>±3.6±1.1</td>
<td>±6.3±1.4</td>
<td>±4.5±1.2</td>
<td>±6.0±1.3</td>
<td>±19.1±1.8</td>
<td>±0.18±3.2</td>
</tr>
</tbody>
</table>

Conclusion: Patients with active chronic arthritides use statistically significantly more antimicrobials two years antedating TNFi treatment compared to controls. TNFi treatment further increases antimicrobial use in this patient population, especially in patients with PsA and AS. Meanwhile, antifungal use increased in RA and antiviral use increased in both RA and PsA. Further analysis needs to be done on the effect of co-medicines such as glucocorticoids, DMARDs and disease activity.

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AB0302 INTEREST OF THE SYSTEMATIC ELECTROCARDIOGRAM IN THE DETECTION OF CARDIAC INVOLVEMENT DURING SPONDYLOARTHRITIDES AND RHEUMATOID ARTHRITIS
Cédric Régnal BOUMBA MAKAYA1, Irame El Bouchti2, 1chu med 6, rheumatology, marrakesh, Morocco, 2chu med 6, rheumatology, marrakesh, Morocco

Background: Cardiovascular risk is not uncommon in patients with chronic inflammatory rheumatism.

Objectives: The objective: To evaluate the interest of systematic electrocardiogram (ECG) as a tool for detecting cardiac abnormalities during spondyloarthropathies (SA) and rheumatoid arthritis (RA).

Methods: Consecutive patients suffering from SA, RA, hospitalized during the period from 2016 to 2017 and free from cardiovascular events were included. An ECG - 12-lead - was performed and interpreted by a cardiologist without the diagnosis.

Objectives: To evaluate the interest of systematic electrocardiogram (ECG) as a tool for detecting cardiac abnormalities during spondyloarthropathies (SA) and rheumatoid arthritis (RA).

Methods: Consecutive patients suffering from SA, RA, hospitalized during the period from 2016 to 2017 and free from cardiovascular events were included. An ECG - 12-lead - was performed and interpreted by a cardiologist without the diagnosis.

Disclosure of Interests: None declared
Throughout our study, we emphasize the importance of continuous monitoring of the disease. Our results are consistent with most of the literature data.

Conclusion: In patients with no history of cardiovascular disease who are asymptomatic, performing a systematic ECG does not reveal the increased risk of specific cardiac complications related to these conditions in patients with SA and RA.

REFERENCES


AB0333 METABOLIC SYNDROME IN TUNISIAN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: The rheumatoid arthritis (RA) is responsible of a high cardiovascular motility. This could be related to an increased prevalence of metabolic syndrome in patients with (RA)

Objectives: The aim of our study was to determine the prevalence of metabolic syndrome in RA, to identify factors associated with its presence and to evaluate the influence of antihyperemic drugs on its occurrence.

Methods: A cross-sectional study was conducted in the Internal Medicine department over a period from July 2016 to June 2017, including 50 RA patients classified according to the 1987 ACR and/or 2010 ACR/EULAR criteria. We used the National Cholesterol Education Program/Adult Panel Treatment III 2005 (NCEP/ATP III 2005) definition for the metabolic syndrome.

Results: There were 50 patients (sex-ratio = 0.28) with a mean age of 50.84 ± 12.52 years. The mean age at the onset of RA was 42.04 ± 12.76 years with duration of 17.52 months (0.8-120 months). The evaluation of the disease showed an average DAS28-SC score of 5.37 ± 1.24 and a significant functional impact (HAQ score > 1) in 36% of patients. The prevalence of metabolic syndrome in RA was 40%. Its presence was associated with higher age (p = 0.003), greater disease activity (p=0.044), the presence of a biological inflammatory syndrome (p=0.032) and hyperuricemia (p=0.005). An association was also found with long-term corticosteroid use (p = 0.03).

Conclusion: Our results are consistent with most of the literature data. Throughout our study, we emphasize the importance of continuous monitoring of disease activity and the need for cortisone-sparing.

REFERENCES


**AB0305 ALLERGIC SYMPTOMS IN PATIENTS WITH RHEUMA- TOID ARTHRITIS**

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**Background:** One of the hypothesis of RA pathogenesis is that autoimmune process in rheumatoid arthritis starts within the airways. The factors leading to increased anticyclic citrullinated protein antibodies formation within the airways are not fully understood. People with allergies to inhaled allergens suffer from chronic inflammation within upper and lower airways.

**Objectives:** The aim of this study was to assess the prevalence of symptoms of upper and lower airways allergic diseases in patients with rheumatoid arthritis as compared to general population prevalence.

**Methods:** The study group consisted of 96 patients with RA (age years – 46.89±15.72, women-73%, men-27%). Control group consist 1685 subjects from Lodz population (47,89±15,11 women-55%, men-45%). All responders completed a screening test for allergy symptoms, 60 of RA and all controls were asked to complete a detailed survey consisting of 30 questions from QUICKRAF questionnaire. Allergy and Asthma Network protocol include diagnoses and separate symptoms of allergic diseases.

**Results:** In screening questionnaire 16.84% of RA patients and 7.24% control declare that they suffer from asthma (p<0.001). The incidence of wheeze in both groups was statistically insignificant (30.00% RA vs 20.65% control; p>0.05), however the coexistence of dyspnoea and wheezing was more frequent in the group of patients with RA (44.83% vs 14.01%; p<0.001) as well as wheeze without symptoms of infection (55.56% vs 15.37% p<0.001). The frequency of waking up at night due to dyspnoea or coughing did not differ significantly between the study and control group (respectively 18.67% vs 12.82 and 33.33% vs 33.35%). The symptoms of upper airway chronic inflammation were also more prevalent in patients with RA as compared to controls. Chronic sinusitis was declared by 28.67% of patients and 10.62% controls (p<0.001), as well as the symptom of post-nasal drip was significantly twice more frequent than in the study group (20.00% vs 9.08%; p<0.005). Symptoms of a nasal allergy are insignificantly more often in RA group (38.33% vs 27.59%) as compared to general population (47.89% vs 30.11%; p>0.05). Symptoms of chronic inflammation within upper and lower airways were insignificantly more often in RA group (20.00% vs 9.08%; p<0.005). Symptoms of a nasal allergy are insignificantly more often in RA group (38.33% vs 27.59%) as compared to general population (47.89% vs 30.11%; p>0.05). Symptoms of a nasal allergy are insignificantly more often in RA group (38.33% vs 27.59%) as compared to general population (47.89% vs 30.11%; p>0.05). Symptoms of a nasal allergy are insignificantly more often in RA group (38.33% vs 27.59%) as compared to general population (47.89% vs 30.11%; p>0.05).

**Conclusion:** Increased prevalence of symptoms of upper and lower allergic diseases in patients with RA requires further investigation as chronic inflammation within upper and lower airways can lead to posttranslational modification of proteins and autoantigen formation.

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.8032

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**AB0306 DISEASE ACTIVITY AND PREVALENCE OF CAROTID PLAQUE ARE INCREASED IN SEDENTARY RHEUMATOID ARTHRITIS PATIENTS**

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**Background:** Multiple benefits from physical activity (PA) in rheumatoid arthritis (RA) patients have been described; exercise in RA is associated with a cardiovascular (CV) protective role, resulting in lower waist-hip ratio, vascular stiffness and hypertension (1). Other important advantage of PA in RA is the impact observed in disease activity; regular PA is associated with reduced DAS28 (2). There are no previous studies evaluating the effect of exercise on disease activity and carotid Ultrasound (US) findings in Mexican-mestizo RA patients.

**Objectives:** To compare clinical characteristics and carotid US findings of Mexican-mestizo RA patients who perform PA to sedentary RA patients.

**Methods:** Cross-sectional, observational, comparative study. We included RA patients aged 40 to 75 years that fulfilled the 2010 EULAR criteria. Patients with prior atherosclerotic CV diseases and overlap syndromes were excluded. Clinical history, blood samples, physical exam and carotid US were performed. Carotid plaque (CP) was defined as a focal narrowing ≥0.5 mm of the surrounding lumen or a carotid intima media thickness (cIMT) ≥1.2 mm, and increased cIMT was defined as ≥0.9 mm. Patients were classified in two groups: those who are sedentary and those who regularly perform PA (defined as ≥120 min/week). The Kilmogorov-Smirnov test was used to determine normal distribution. Categorical variables are expressed as total number (%), and numerical variables as median (q25-q75). Chi square and Mann-Whitney U-test were used to compare groups and considered significant if p<0.05.

**Results:** A total of 334 RA patients were included. Clinical characteristics are shown in table 1. Patients who exercised had lower disease activity and BMI. Carotid US was performed in 127 patients (Table 2). There was a higher prevalence of CP, bilateral CP and increased cIMT in sedentary patients. Sedentary RA patients had an increased risk of CP (OR 3.1 [95%CI 1.0-9.7, p=0.04]).

**Table 1. Clinical characteristics**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Physically active (n=80)</th>
<th>Sedentary (n=254)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), median (q25-q75)</td>
<td>55.3 (46.5-57.8)</td>
<td>55.7 (49.6-61.6)</td>
<td>NS</td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>72 (90)</td>
<td>236 (92.9)</td>
<td>NS</td>
</tr>
<tr>
<td>Disease duration (years), median (q25-q75)</td>
<td>5 (2-11.3)</td>
<td>9 (3.7-15.5)</td>
<td>0.002</td>
</tr>
<tr>
<td>Past or current smoker, n (%)</td>
<td>18 (22.5)</td>
<td>63 (24.8)</td>
<td>NS</td>
</tr>
<tr>
<td>BMI (kg/m²), median (q25-q75)</td>
<td>26.4 (24.7-31.9)</td>
<td>28 (25.2-31.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes Mellitus, n (%)</td>
<td>10 (12.5)</td>
<td>38 (15)</td>
<td>NS</td>
</tr>
<tr>
<td>Dyslipidemia, n (%)</td>
<td>27 (33.8)</td>
<td>67 (26.4)</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>16 (20)</td>
<td>77 (30.3)</td>
<td>NS</td>
</tr>
<tr>
<td>Dyslipidemia, n (%)</td>
<td>26 (1.8-3.9)</td>
<td>3.4 (2.3-4.4)</td>
<td>0.001</td>
</tr>
<tr>
<td>CDAI, median (q25-q75)</td>
<td>6 (2-16)</td>
<td>11 (3.7-20.2)</td>
<td>0.005</td>
</tr>
<tr>
<td>SDAA median (q25-q75)</td>
<td>7 (2.5-17.3)</td>
<td>12.5 (4.5-22)</td>
<td>0.004</td>
</tr>
</tbody>
</table>

**Table 2. Carotid US**

<table>
<thead>
<tr>
<th>Carotid US findings</th>
<th>Physically active (n=28)</th>
<th>Sedentary (n=99)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>CP</td>
<td>4 (14.3)</td>
<td>34 (34.3)</td>
<td>0.041</td>
</tr>
<tr>
<td>Increased cIMT</td>
<td>9 (32.1)</td>
<td>50 (55.6)</td>
<td>0.029</td>
</tr>
<tr>
<td>Unilateral CP</td>
<td>3 (10.7)</td>
<td>15 (15.2)</td>
<td>NS</td>
</tr>
<tr>
<td>Bilateral CP</td>
<td>1 (3.6)</td>
<td>19 (19.2)</td>
<td>0.045</td>
</tr>
</tbody>
</table>

**Conclusion:** Patients who perform PA had significantly lower disease activity and BMI. A higher prevalence of CP, increased cIMT and bilateral CP was found in sedentary patients. Sedentary RA patients had an increased risk of CP. These results are similar to previously described in other populations and may be indicators of the protective effect of PA in RA patients. Rheumatologists should encourage their patients to exercise regularly.

**REFERENCES**

[1] Byram KW. et al. Exercise is associated with increased small HDL particle concentration and decreased vascular stiffness in RA. Journal of Clinical Rheumatology. 2016;00(00);1-5.


**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.7528

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**AB0307 A.P.R.A.N. ASSESSMENTS OF TENDER AND SWOLLEN JOINTS COUNT SCORE PERFORMED BY A RHEUMATOLOGIST AND RHEUMATOLOGY NURSES IN PATIENTS WITH RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS**

Isabelle Fortin1,2, Nabil Chaker1, Frederic Banville3, Fayez Wetherall1, CREG, Rimouski, Canada; 3UQAR, Rheumatology, RIMOUSKI, Canada; 3UQAR, Nursing, RIMOUSKI, Canada

**Background:** Rheumatoid arthritis (RA) is a multisystem and debilitating disease. Fortunately, there is now a wide range of available treatments for these patients. Also, guidelines recommend a « treat to target » involving strict follow-up of the rheumatologist’s visits. The consistency of examinations and disease activity evaluation is therefore.

**Objectives:** The primary objective is to validate the accuracy of the assessment of RA and Psoriatic arthritis disease activity by a nurse in comparison to assessments conducted by rheumatologists for CDAI and

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.7528
The association of Parkinson disease with inflammatory joint diseases

Yang Cui, Xiao Zhang.

The frequency of hematological malignancies in autoimmune rheumatic diseases

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Background: Autoimmune rheumatic diseases are associated with increased risk of hematological malignancies. The pathogenesis of autoimmunity can cause of malignancies or immunosuppressive agents may increase the risk of malignancies.

Objectives: We aimed in this study to determine the frequency, type and characteristic of hematological malignancies in rheumatology practice.

Methods: 1640 rheumatoid outpatient patient with autoimmune rheumatic diseases (Rheumatoid arthritis (RA), SLE, Sjogren’s syndrome (SJS), myositis, systemic Sclerosis, undifferentiated connective tissue diseases (UCTD)) are screened for hematological malignancies. 16 patients are found with hematological malignancies. The characteristics of these patients are reported retrospective from their outpatient clinic case files.

Results: The frequency of hematological diseases was found 0.04 in study group. 4 patients had myeloproliferative diseases (1 polycythemia vera (PV), 1 primary myelofibrosis (MyF)), 2 patients with essential thrombocytopenia (ET), 2 patients had multiple myeloma (MM) and 7 patients had lymphoproliferative malignancies. 2 patients had chronic lymphoid leukemia (CLL). One of those had SJS, one patient had Hodgkin lymphoma and these patients are seen after autolog bone marrow transplantation because of arthralgia, but not detected arthritis. One patient had Hodgkin disease in her history, and had both RA and SJS, and receiving MTX therapy. 2 patients had multiple myeloma (MM). One of them is new diagnosis arthritis plus elevated sedimentation rate. Second one was seen with arthralgia after MM treatment and autologous bone marrow transplantation. 3 patients had mycosis fungoides, one of them had UCTD and received hydroxychloroquine. The other patient had RA under MTX therapy and one patient received rituximab therapy for severe RA activity. Patient with ET had only minimal arthralgia and are followed under HCO therapy. As lymphoproliferative diseases 4 patients had chronic lymphoid leukemia (CLL), 3 of them had RA and 1 of them had SJS. 2 patients had non-Hodgkin lymphoma and these patients are seen after autolog bone marrow transplantation because of arthralgia, but not detected arthritis. 1 patient had Hodgkin disease in her history, and had both RA and SJS, and receiving MTX therapy. 2 patients had multiple myeloma (MM). One of them is new diagnosis arthritis plus elevated sedimentation rate. Second one was seen with arthralgia after MM treatment and autologous bone marrow transplantation. 3 patients had mycosis fungoides, one of them had UCTD and received hydroxychloroquine. The other patient had RA under MTX therapy and one patient received rituximab therapy for severe RA activity. Patient with ET had only minimal arthralgia and are followed under HCO therapy. As lymphoproliferative diseases 4 patients had chronic lymphoid leukemia (CLL), 3 of them had RA and 1 of them had SJS. 2 patients had non-Hodgkin lymphoma and these patients are seen after autolog bone marrow transplantation because of arthralgia, but not detected arthritis. 1 patient had Hodgkin disease in her history, and had both RA and SJS, and receiving MTX therapy. 2 patients had multiple myeloma (MM). One of them is new diagnosis arthritis plus elevated sedimentation rate. Second one was seen with arthralgia after MM treatment and autologous bone marrow transplantation. 3 patients had mycosis fungoides, one of them had UCTD and received hydroxychloroquine. The other patient had RA under MTX therapy and one patient received rituximab therapy for severe RA activity. Patient with ET had only minimal arthralgia and are followed under HCO therapy. As lymphoproliferative diseases 4 patients had chronic lymphoid leukemia (CLL), 3 of them had RA and 1 of them had SJS. 2 patients had non-Hodgkin lymphoma and these patients are seen after autolog bone marrow transplantation because of arthralgia, but not detected arthritis. 1 patient had Hodgkin disease in her history, and had both RA and SJS, and receiving MTX therapy. 2 patients had multiple myeloma (MM). One of them is new diagnosis arthritis plus elevated sedimentation rate. Second one was seen with arthralgia after MM treatment and autologous bone marrow transplantation. 3 patients had mycosis fungoides, one of them had UCTD and received hydroxychloroquine. The other patient had RA under MTX therapy and one patient received rituximab therapy for severe RA activity.

Conclusion: Hematological malignancies are rare diseases in rheumatology practice, although expected high rate because of using immunosuppressive treatment and autoimmunity. The increased frequency of lymphoproliferative disorders are expected and associated with autoimmunity, but we don’t found a high rate for lymphoproliferative malignancies. Myeloproliferative malignancies possibly not associated with the pathogenesis of autoimmune rheumatic diseases.

Disclosure of Interests: None declared

The association of Parkinson disease with rheumatoid arthritis

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Background: Parkinson disease (PD) is a progressive neurological disease, characterised with tremor, spasticity, arthrosis, dementia, loss of mobility and general pain. PD affects mainly elderly population. Activity of PD patients is restricted because of spasticity and severe arthrosis. Rheumatoid arthritis (RA) is a chronic inflammatory autoimmune disease which can cause disability in elderly population. Patients with can admit to rheumatology clinics with generalised pain or restricted mobilisation. In contrast, in some PD patients with generalised pain on joints, RA may be overlooked

Objectives: We aimed in this study to evaluate the characteristics of patients with RA and Parkinson patients.

Methods: 842 RA patients screened retrospective for PD from the patient files. 10 patients with both RA and Parkinson disease were included to study. 3 female and 7 male patients with mean age 76,4 (with a standard deviation 5,4) were evaluated. The characteristics of patients are evaluated from the patient files.

Results: All patients were older than 75 years. Mean RA duration time was 14 months and PD duration time was 34 months. All patients admitted outpatient clinic with leg pain and inability to walk. 4 of 10 patients had mild dementia. Median ESR was 36 mm/h and median CRP value was 0,68 mg/dl. 6 of 10 patients had positive ANA result with 1/100 ratio, but rheumatoid factor and anti CCP were negative.

Conclusion: PD is one of the disorder that may cause severe disability in very old ages. RA may be an additional factor for pain and loss of function in PD patients. Patients with generalised pain and difficulties with walking should be evaluated for PD especially in old ages. PD patients with generalised pain on joints should be evaluated for inflammatory arthritis.

Disclosure of Interests: None declared

The incidence of extra-articular manifestations in southern Chinese patients with inflammatory joint diseases

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Background: Inflammatory joint diseases (JIDs) are chronic arthritis, but frequently present with co-morbidities of other organs and systems, which is known as extra-articular manifestations (EAMs). 1. It is still unclear which clinical characteristics or bio-markers can predict the development of EAMs.

Disclosure of Interests: None declared
**ABO311**

HEMOSTASIS IN AFRICAN BLACK COMPARED TO WHITE PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** Aberrant hemostasis is implicated in the increased CVD risk experienced by patients with rheumatoid arthritis (RA) (1). Large circulating concentrations of plasminogen activator inhibitor-1 (PAI-1) predict cardiovascular event rates (2). PAI-1 levels are markedly smaller in African black compared to white patients with RA (median (IQR)= 455 (40.44%).

**Methods:** Retrospective cohort study of a total of 1135 IJDs (1614). Scientiﬁc Abstracts

**Results:** We found 455 (40.44%) of them with EAMs: 30.84% and higher disease activity (OR: 1.15, P=0.011) were independent risks of EAMs. As in PsA group, longer disease duration (OR: 1.01, P=0.046) and patients on corticosteroids. At 12 months of follow-up, number of patients with incident CV risk factor was higher for Castelli ratio > 3 (23%), low HDL (16.3%) and low CRP >1 mg/dL (7.5%) and age >45 years old (3.3%).

**Objective:** To monitor CV risk-factor’s behavior during the first year of follow-up and to identify if traditional CV risk scores predict major CV events (MACE) in our population. Methods: Once enrolled patients had complete rheumatic evaluations at once and regularly. Baseline CV risk-factor’s assessments included age, gender, ethnicity, physical activity and history of first-degree relatives with cardiovascular (CV) morbidity/mortality. Cox regression’s model identified predictors of incidental MACE. Patients gave written informed consent. Results: At cohort entry, the 185 patients (all Hispanic) which data were analyzed were primarily middle-aged females (87.6%) and had 5.3 months (3.3-7.1) of disease duration. Most prevalent CV risk factors were CRP >1 mg/dL (90%), Castelli ratio > 3 (84%) and low HDL levels (74%). During the first year of follow-up, smoking status, systolic blood pressure ≥ 140 mm Hg, diastolic blood pressure ≥ 90 mm Hg, low HDL, Castelli ratio > 3, high CRP and patients with active disease progressively decreased; meanwhile, the opposite figure was true for BMI ≥ 30 kg/m² and patients on corticosteroids. At 12 months of follow-up, number of patients with incident CV risk factor was higher for Castelli ratio > 3 (23%), low HDL (16.3%), in blacks, Hispanics and non-Hispanic whites. The Insulin Resistance Atherosclerosis Study. Circulation 2003;107:2422-7.

**Disclosure of Interests:** None declared


**ABO312**

CARDIOVASCULAR RISK FACTOR’S BEHAVIOR AND CARDBIOVASCULAR RISK IN HISPANIC EARLY RHEUMATOID ARTHRITIS PATIENTS: A COHORT STUDY

Irazú Contreras-Yáñez, Guillermo Guaraacha-Basáñez, Virginia Dr. Pascual, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Immunology and Rheumatology, Mexico City, Mexico

**Background:** Rheumatoid arthritis (RA) patients present an increased risk of cardiovascular (CV) morbidity and mortality compared to the general population. Patients from Latin America exhibit younger age, female preponderance, less severe disease and dyslipidemia, which are relevant when assessing CV risk. In order to impact CV morbidity/mortality, control of reversible CV-risk factors need to be achieved. CoHorts allow prospective evaluation of long-term outcomes. In 2004 we initiated an early RA cohort. Up to June 2018, the cohort comprised 185 RA patients with prospective assessments of CV risk and at least one year of follow-up.

**Objectives:** To monitor CV risk-factor’s behavior during the first year of follow-up and to identify if traditional CV risk scores predict major CV events (MACE) in our population. Methods: Once enrolled patients had complete rheumatic evaluations at regular intervals. Baseline CV risk-factor’s assessments included age, gender, ethnicity, physical activity and history of first-degree relatives with premature heart disease. CV-risk factors assessments at baseline and at least 6 months apart included blood pressure, serum total cholesterol (CHO) and HDL cholesterol (Castelli ratio CHO/HDL was derived), serum glucose (GLU, in mg/dL), body mass index (BMI), CRP (in mg/dL) and at least the following complications: Hypertension (HT, and HT treatment), diabetes mellitus (DM), advanced chronic kidney failure (CKF) and atrial fibrillation (AF). Smoking status was assessed at baseline and last follow-up. Incident MACE were defined according to standard definitions. Cox regression’s model identified predictors of incidental MACE. Patients gave written informed consent.

**Results:** At cohort entry, the 185 patients (all Hispanic) which data were analyzed were primarily middle-aged females (87.6%) and had 5.3 months (3.3-7.1) of disease duration. Most prevalent CV risk factors were CRP >1 mg/dL (90%), Castelli ratio > 3 (84%) and low HDL levels (74%). During the first year of follow-up, smoking status, systolic blood pressure ≥ 140 mm Hg, diastolic blood pressure ≥ 90 mm Hg, low HDL, Castelli ratio > 3, high CRP and patients with active disease progressively decreased; meanwhile, the opposite figure was true for BMI ≥ 30 kg/m² and patients on corticosteroids. At 12 months of follow-up, number of patients with incident CV risk factor was higher for Castelli ratio > 3 (23%), low HDL (16.3%), high CHO (10.6%), BMI ≥ 30kg/m² (10%), CRP >1 mg/dL (7.6%) and age ≥45 years old (3.3%).

**Conclusion:** PAI-1 activity, but not plasma clot lysis time. PLoS One 2013;8 (12): e83151.

**Disclosure of Interests:** None declared

Conclusion: Hispanic RA patients from an early RA cohort present a distinct pattern of CV risk factors. Due to younger age at RA presentation, a minority of the patients had CV risk scored. Obesity was a predictor of incidental MACE in our population.

REFERENCES


Acknowledgement: We would like to thank the Rheumatology team in Hospital Selayang and the Director General of Ministry of Health Malaysia for allowing us to conduct this study in Hospital Selayang.

Disclosure of Interests: None declared


AB0313

THE PREDICTORS OF UNDIAGNOSED DYSGLYCAEMIA IN PATIENTS WITH ESTABLISHED RHEUMATOID ARTHRITIS

Hafizla Baharudin1, Nur Aini Eddy Warman1, Aizmillah Rosman2, Thuhairah Abdul Rahman2, Nurhuda Ismail2, Rohana Abdul Ghani1, Universiti Teknologi MARA, Department of Medicine, Sarawak, Malaysia; 2Universiti Teknologi MARA, Department of Pathology, Sarawak, Malaysia; 3Universiti Teknologi MARA, Department of Public Health and Population Medicine, Sarawak, Malaysia.

Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease with an increased risk of diabetes and insulin resistance.1,2 The prevalence of type 2 diabetes mellitus (T2DM) were demonstrated to be 10.4% as compared to only 7.6% in 1:4 controls matched for age, sex and geographical region, with an odds ratio of 1.4.2

Objectives: To determine the prevalence of dysglycaemia (T2DM, impaired fasting glucose (IFG) and impaired glucose tolerance (IGT)) and the factors associated with dysglycaemia in patients with established RA.

Methods: This is a cross-sectional study conducted in a rheumatology centre in Malaysia. Patients with established RA aged 30 years or more were included. Exclusion criteria were overlap syndrome, pre-existing diabetes or pre-diabetes, pregnant and within 6 weeks of post-partum period. An oral glucose tolerance test (OGTT) was performed for all patients. Comparison of various factors between dysglycaemia and normoglycaemia were analysed. Multivariate analysis was performed using logistic regression analysis to ascertain the true effects of significant factors found on univariate analysis.

Results: The mean age of patients was 57.2 ± 8.1 years and 87.7% were female. Of 155 patients included in this study, 55 (35.5%) were found to have dysglycaemia; 40 (72.2%) had IGT, 11 (20%) had T2DM. 3 had IFG and IGT (5.5%) and 1 had IFG (1.8%). Significant factors found on univariate analysis.

Conclusion: One third of 155 patients had dysglycaemia and majority had IGT. The predictors of dysglycaemia in patients with established RA aged 30 years and more, were previous or current smoker and raised triglycerides.

Table 1. Factors investigated for differences between dysglycaemia and normoglycaemia.

<table>
<thead>
<tr>
<th>Risk factors</th>
<th>Dysglycaemia</th>
<th>Normoglycaemia</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=55</td>
<td>n=100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous or current smoker, n (%)</td>
<td>7 (13.0)</td>
<td>3 (3.0)</td>
<td>0.02</td>
</tr>
<tr>
<td>Waist circumference (cm), mean ± SD</td>
<td>89.0 ± 12.5</td>
<td>83.1 ± 9.6</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Weight (kg), mean ± SD</td>
<td>65.5 ± 12.3</td>
<td>60.7 ± 10.6</td>
<td>0.01</td>
</tr>
<tr>
<td>Systolic blood pressure (mmHg), mean ± SD</td>
<td>134.5 ± 17.5</td>
<td>128.2 ± 18.1</td>
<td>0.04</td>
</tr>
<tr>
<td>Diastolic blood pressure (mmHg), mean ± SD</td>
<td>79.7 ± 8.7</td>
<td>76.3 ± 10.5</td>
<td>0.04</td>
</tr>
<tr>
<td>High density lipoprotein (mmol/L), mean ± SD</td>
<td>1.4 ± 0.3</td>
<td>1.5 ± 0.4</td>
<td>0.02</td>
</tr>
<tr>
<td>Triglycerides (mmol/L), mean ± SD</td>
<td>1.3 ± 0.5</td>
<td>1.1 ± 0.5</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

REFERENCES


Acknowledgement: We would like to thank the Rheumatology team in Hospital Selayang and the Director General of Ministry of Health Malaysia for allowing us to conduct this study in Hospital Selayang.

Disclosure of Interests: None declared


AB0314

QUALITY OF LIFE IN WOMEN WITH RHEUMATOID ARTHRITIS DEPENDING ON ANXIETY AND DEPRESSION

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Background: Rheumatoid arthritis (RA) is a chronic autoimmune disease that causes joint damage, deformity, and pain. This can lead to loss of functionality and mobility, which entails a decrease in the quality of life and the possible occurrence of anxiety and depressive disorders [1].

Objectives: Assess the quality of life in women with RA, depending on the anxiety and depression.

Methods: The study included 104 women with reliable RA according to the ACR1987 and/or EULAR/ACR2010 criteria (mean age 53.7 ± 10.9 years, mean duration of RA = 10.1 [4-14] years, DAS28 = 4.96 [4.27-5.77]). An assessment of the severity of anxiety and depression was conducted using a questionnaire for the hospital scale of depression and anxiety (HADS). Evaluation of the quality of life of patients with rheumatoid arthritis was performed using the EQ-SD index. Depending on the degree of functional impairment, according to the HAQ questionnaire, were regarded as minimal (0-0.1 point), moderate (1-2) and pronounced (2-3 points), the population norm was 0-0.5 points. The severity of pain was determined by VAS: no pain (0-4 mm), mild pain (5-44 mm), moderate pain (45-74 mm), severe pain (75-100 mm). Statistical processing was performed using the program STATISTICA 10.0.

Results: The frequency of occurrence of anxiety-depressive disorders in patients with RA was determined: clinically significant anxiety was detected in 20 (19.2%) patients, depression - in 19 (17.3%); subclinical anxiety - in 26 (25%), depression - in 27 (25.9%) patients; the absence of reliably expressed symptoms of anxiety in 58 (55.8%) patients, depression - in 59 (56.8%) patients.

HAQ functional impairment was absent in 11 (10.6%) patients, minimal impairment was detected in 20 (19.2%), moderate - in 52 (50%), and pronounced in 21 (20.2%) patients. Severe pain in the VAS was noted by 38 (36.6%) patients, moderate - 51 (49%), in 15 (14.4%) patients the pain syndrome was weakly expressed. The HAQ and EQ-SD indices for women were 1.26 [0.88;1.75] and 0.41 [0.07;0.59], respectively. The relationships between the HAQ and EQ-SD indices (r = 0.67, p <0.05), the HAQ index and the age of the patients (r = 0.33, p <0.05), and the duration of the disease (r = 0.29, p <0.05), ESR indicator (r = 0.28, p <0.05), CRP (r = 0.37, p <0.05), the level of pain in VAS (r = 0.4, p <0.05), DAS28 index (r = 0.32, p <0.05), anxiety severity (r = 0.22, p <0.05), depression severity (r = 0.31, p < 0.05). The relationship between the EQ-SD index and the age of the patients (r = 0.29, p <0.05), with the duration of the disease (r = 0.22, p <0.05), CRP (r = 0.52, p <0.05), the level of pain in VAS (r = 0.45, p <0.05), the severity of anxiety (r = 0.28, p <0.05), the severity of depression (r = 0.35, p <0.05).

To clarify the relationship between the quality of life of patients and the level of depression and anxiety, two groups were identified: no anxiety-depressive disorders (N = 43) and the second group with their presence (N = 30). The EQ-SD index in the first group was 0.59 [0.52; 0.62] and in the group with anxiety and depressive disorders it was 0.27 [0.02; 0.52] (p = 0.005). The HAQ index significantly differed in women without anxiety and depressive disorders 1.0 [0.625; 1.5] with the index in the other group 1.75 [1.0; 2.125] (p = 0.01).

Conclusion: Thus, every fifth patient with RA suffers from clinically significant anxiety and depression; subclinical anxiety and depression were found in 26% of patients with RA. Interalrelations between the indicators of quality of life of patients with RA and the patient’s age, duration, activity of RA, severity of anxiety and depressive disorders.

Disclosure of Interests: None declared

EVALUATION OF SLEEP QUALITY, FATIGUE AND SEXUAL PROFILE IN ELDERLY PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: People over the age of 60 with rheumatoid arthritis (RA) often complain of fatigue, which is considered an extra-articular symptom. This problem has a multidimensional character and sounds on the quality of sleep and on the sexual profile.

Objectives: Our study consists in assessing the prevalence of fatigue and studying the quality of sleep and the sexual profile of patients over 60 years of age with RA compared to subjects suffering from the same illness of younger age.

Methods: This is a prospective study involving 100 patients at the Rheumatology department of Fattouma Bourguiba university hospital in Monastir over a period of 6 months: 40 patients more than 60 years of age with RA compared with 60 patients with RA of younger age. Data collection was based on scales and specific questionnaires (Visual Analogue Fatigue Scale (VAS-F), Multidimensional Fatigue Inventory (MFI-20), Pittsburgh Sleep Quality Index (PSQI), Female sexual Function Index (FSFI), Sexual Health Inventory for Men (SHIM)).

Results: The average age was 55.8 years [25-84]. The most represented age group was over 60 (40%). The sex ratio was 5.6. 73% of our patients were married and 81% had children with an average number of 3 children in charge and extremes between 1 and 9. Fatigue, sleep quality and sexual profile were analyzed comparatively and respectively between the 2 groups (1st group: >60 and second <60 years). The average of the VAS-F was 60.25 compared to 53.5. Fatigue (via MFI-20) was present in all its domains in our patients. General fatigue and physical fatigue were the highest, averaging 13.98 versus. 13.07 and 12.98 versus. 12.33 respectively. Sleeping insomnia (PSQI> 5) was found with the same proportion of 65% in both groups. Low sleep quality was found in 90% versus 93%. A sleep latency> 31 minutes was found in 37.5% against 30%. Sleep duration <6 hours per night was found in 52.5% versus. 75%. Sleep efficiency <85% was found at an equal percentage of 75%. Sleep disorders> 10 times in the last 4 weeks were found at an equal percentage of 15%. Regular female sexual activity was found in 42.5% versus. 71% and dysfunction (FSFI>26.55) was noted in 35% against 63.3%. Regular male sexual activity was found in 54.5% against 75% and mild erectile dysfunction (SHIM=21) was noted in 83.3% against 20%.

Conclusion: A multidimensional approach is needed to explore the different components of fatigue, sleep quality and sexual profile in patients with RA and its very diverse consequences. This should lead to an improvement in the quality of life in the current medical practice.

Disclosure of Interests: None declared


AB0315

ESTABLISHED SERONEGATIVE RHEUMATOID ARTHRITIS IS CONSIDERED A MILD FORM OF THE DISEASE. ALSO WILL IT BE THE SAME REGARD FOR VERY EARLY SERONEGATIVE RHEUMATOID ARTHRITIS?

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Background: Established Seronegative Rheumatoid Arthritis (ESNRA) is considered a mild form of the disease with a good prognosis and response to therapy compared with seropositive (SP) form [1]. Lately evidence indicates that seronegative (SN) form of arthritis in early stage is serious and should not be underestimated in terms of disease activity, response to therapy and radiographic damage [2,3,4]. At a present, the influence of SN status of clinical course and treatment choice in very early stages, in other words less than 3 months from time at onset of disease, is still controversial [5].

Objectives: To evaluate demographical, clinical and treatment differences between Very Early Seronegative Rheumatoid Arthritis (VESNRA) and Very Early Seropositive Rheumatoid Arthritis (VESPRA) in a Mexican cohort.

Methods: 64 patients with Very Early Rheumatoid Arthritis ([VERA], < 3 months from at onset of clinical manifestations) that fulfilled ACR/ EULAR 2010 criteria (>18 years) from a Mexican cohort recruited from 2015 to 2018 were examined and followed to 3, 6 and 12 months. Patients without presence of rheumatoid factor (RF) and antinuclear protein antibodies (ACPA) were considered SN. Demographic factors, clinical features, disease activity measured using DAS28, functional status evaluated using HAQ, comorbidities and pharmacologic treatments were examined for patients with VESNRA and VESPRA. Charlon’s clinical comorbidities index was used to analyze comorbidities. Chi-square and Student-t test was performed by univariate analysis and logistic regression was used by multivariate analysis, both were adjusted for age and gender. Statistical test were conducted at 5% level of significance.

Results: Of 64 patients with VERA 79% were women. The mean age [standard deviation (SD)] was 49.8 (13.5) years. The mean of time at onset of VERA (SD) was 77.8 (15.5) days. A total of 20 (31.2%) patients had VESNRA. In the unvariable analyses VESNRA patients were more likely to have minor disease activity and better functional status during their follow-up to 3, 6 and 12 months [Table 1]. Moreover, VESNRA patients were more likely to present lesser work disability, lower comorbidities including fibromyalgia, to use fewer sulfasalazine, leflunomide, biologic agents and corticosteroids. As expected, the modified Charlon’s comorbidity index score was lower in VESNRA patients than all their follow-up. In multivariable analyses less frequently use of corticosteroids (OR 0.68, 95% CI 0.42-0.88, p=0.001) remained significant in VESNRA patients.

Conclusion: This study suggests that in very early stage of disease, SN form presents minor disease activity, better functional status, lower comorbidities, also require less aggressive therapy using biologic agents and corticosteroids than SP form in the course of one year. By these clinical and therapeutic differences should be considered VESNRA a mild form of the disease like as ESNRA. These observations must be confirmed in larger studies with further follow-up.

REFERENCES


Table 1. Disease activity and functional status in VESNRA and VESPRA Patients

<table>
<thead>
<tr>
<th>Feature</th>
<th>VERA</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VESNRA: Very Early Seronegative Rheumatoid Arthritis; VESPRA: Very Early Seropositive Rheumatoid Arthritis; SD: Standard deviation; NS: Not significant</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Disclosure of Interests: None declared


AB0317

THE EFFECT OF ANEMIA ON THE CARDIAC FUNCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic disease that is characterized by defeat of the musculoskeletal system and is often accompanied by the anemia.

Disclosure of Interests: None declared

Baropodometric comparison of plantar pressure with knee osteoarthritis patients and rheumatoid arthritis patients

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Objectives: To compare the plantar pressure between patients with Knee Osteoarthritis and patients with rheumatoid arthritis.

Methods: This is a cross-sectional study, included 41 patients with rheumatoid arthritis (87.8% female, mean age 49 ± 11.9 [27-83] years, median duration of evolution was 9.4 [2.01] months, and 40 knee osteoarthritis patients (100% female, mean age 57.6 ± 5.2 [50-67] years, median evolution time was 36 [24, 69] months). The two groups were matched by BMI (27.5 vs. 29.6, p > 0.05).

In the rheumatoid arthritis group: The mean DAS28 was 3.9 ± 1.3 [2-6] and the knee joint was affected in 22% of cases.

In the knee osteoarthritis group: The knee osteoarthritis is bilateral in 80% of the cases and the radiological severity (Stages 3 or 4 of Kellgren and Lawrence classification) was found in 27.5%.

The baropodometric study was performed using the PRESSCAM® platform (SIDAS®, 38,000 VOIRON, MEDICAPTEURS®). The static analysis was done in free position, for 30 seconds at 50 Hz with measure of plantar pressure parameters.

Results:

<table>
<thead>
<tr>
<th>Baropodometric characteristics</th>
<th>Rheumatoid arthritis</th>
<th>Knee osteoarthritis</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surface of whole foot (cm²)</td>
<td>105.2</td>
<td>123.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Maximum pressure of whole foot/ cm²</td>
<td>667.8</td>
<td>655.8</td>
<td>0.72</td>
</tr>
<tr>
<td>Average pressure of whole foot (g/cm²)</td>
<td>307.3</td>
<td>307</td>
<td>0.98</td>
</tr>
<tr>
<td>Surface of forefoot (cm²)</td>
<td>39.1</td>
<td>44.5</td>
<td>0.02</td>
</tr>
<tr>
<td>Surface of hindfoot (cm²)</td>
<td>64.1</td>
<td>60.7</td>
<td>0.2</td>
</tr>
<tr>
<td>Thrust of forefoot (%)</td>
<td>15.5</td>
<td>23.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Thrust of hindfoot (%)</td>
<td>33.9</td>
<td>29.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Thrust of the whole foot (%)</td>
<td>50.1</td>
<td>52.5</td>
<td>0.06</td>
</tr>
</tbody>
</table>

P significant sisd.05; Test utilisé : t-student

Conclusion: This comparative static baropodometric study of patients with RA and patients with knee osteoarthritis shows significant differences in bearing surface, which appears to be lower in the RA group, especially in the forefoot. The thrust on the forefoot is also less important in the RA group.

These results could be explained by the rheumatoid forefoot, which decreased support and pressure on the forefoot.

Disclosure of Interests: None declared


AB0319 ABACETE IN RHEUMATOID ARTHRITIS WITH INTERSTITIAL LUNG DISEASE. A MULTICENTRE STUDY OF 181 PATIENTS

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Background: Intestinal Lung Disease (ILD) is a severe extraarticular manifestation of rheumatoid arthritis (RA).

Objectives: Our aim was to assess the efficacy of abatacept (ABA) in RA patients with ILD.

Methods: Retrospective multicenter study of RA patients with ILD treated with ABA. ILD was diagnosed by HRCT. We have analyzed the following variables: a) 1-point change the Modified Medical Research Council (MMRC); b) FVC improvement ≥10%; and improvement ≥10% in DLCO; c) radiological improvement in HRCT scan; d) changes in DAS28 score. Values were compared with baseline e) prednisone doses.

Results: We studied 181 patients (94women/87 men) with ILD associated to RA. The follow-up was 12.1[6.2-24.1] months. The mean age was 64.54 ± 9.7 years. The median to progression of ILD was 12 [3-43.75] months. 81 patients were treated in monotherapy, 100 patients in combination therapy. The most frequent pattern was UIP 45,3%. The most of patients who did not have dyspnea remained asymptomatic. See results in Figure1. DAS28 also improved. We appreciate a decrease in the dose of prednisone compared to the initial dose.

Conclusion: ABA seems to be effective. However, should be verified in prospective and randomized studies.
Disclosure of Interests: Carlos Fernández-Díaz Speakers bureau: Bristol-Myers, J. Loricer: None declared, Santos Castañeda Consultant for: Amgen, BMS, Pfizer, Lilly, MSD, Roche, Sanofi, UCB, A. Juan-Mas: None declared, Carmen Carrasco-Cubero: None declared, Ivette Casafont-Solé: None declared, RAQUEL ALMODOVAR: None declared, Noelia Alvarez-Rivas: None declared, CLARA AGUILERA CROS: None declared, Ignacio Villa-Blanco: None declared, Sergi Ordoñez: None declared, Susana Romero-Yuste: None declared, C. Ojeda-García: None declared, Manuel Moreno: None declared, I. Hernández-Rodríguez: None declared, M. López-Corbeiro: None declared, María Lopez Lasanta: None declared, Francisco Ortiz-Sanjuán: None declared, B. Alvarez-Rodríguez: None declared, A. Ruibal-Escriban: None declared, Rosa Exposito: None declared, M. Rebuerto-Guerrero: None declared, Trinidad Pérez Sandoval: None declared, Natalia Mena-Vázquez: None declared, ANA URRUTICOE- CHEA-ARANA: None declared, C. Delgado-Beltran: None declared, José Luis Andrieu Sánchez: None declared, Alejandro Olive: None declared, S. Rodríguez-Muguruza: None declared, José Antonio Bernal-Vidal: None declared, E.C. Cervantes Pérez: None declared, Olga Maiz-Alonso: None declared, R. Castellanos-Moreira: None declared, S Rodríguez-Garcia: None declared, I. Cabezas-Rodríguez: None declared, Mireia Moreno: None declared, Ivan Castelli: Consultant for: I received fees less than 2000USD as a instructor for Boehringer-Ingelheim, Novartis and Gebro, Speakers bureau: ND, Luis Marcelino Arboleya Rodriguez: None declared, C. González-Montagut Gómez: None declared, Blanca García-Magallon: None declared, E. Salgado-Pérez: None declared, M. Rodríguez-Gómez: None declared, C. Filo-Maneta: None declared, J M Blanco: None declared, DESEADA PALMA SAN-CHEZ: None declared, Paloma Vela-Casaseompe Grani/research support from: UCB, Abbvie, Pfizer, Roche, Bristol-Myer-Squibb (another research, not BIOMDASER related), Consultant for: UCB, Lilly, Pfizer, Roche, Bristol-Myer-Squibb, Speakers bureau: Roche, UCB, MSD, Pfizer, GSK, BMS, Lilly, Gemma Bonilla: None declared, R. López-Sánchez: None declared, J. Fernández-Melon: None declared, Cristina Hidalgo: None declared, Miguel A González-Gay Grant/research support from: Prof. MA González-Gay received grants/research supports from Abbvie, MSD, Janssen and Roche., Speakers bureau: Consultation fees/participation in company sponsored speaker’s bureau from Pfizer, Lilly, Sobi, Celgene, Novartis, Roche and Sanofi, Ricardo Blanco Grant/research support from: Abbvie, MSD, and Roche, Consultant for: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen, Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myers, Janssen

Table 1. Characteristics of the sample

| Glucocorticoids mg/day, mean ± SD | 4.8 ± 1.6 |
| Treatment, n (%) | 47 (78.3) |
| Conventional DMARDs | 40 (66.6) |
| Anti-TNF | 16 (26.6) |
| Non-Anti-TNF | 4 (6.6) |
| Synthetic target DMARDs | 39.3 ± 24.2 |
| VAS pain mean ± SD | 23 (39.6) |
| Sleep quality self-report, n (%) | Good |
| Poor | 35 (60.3) |
| BRAF-MDQ (0-70), mean ± SD | 21.9 ± 15.0 |
| Physical (0-22) | 10.6 ± 5.4 |
| Living (0-22) | 5.08 ± 5.0 |
| Cognition (0-15) | 3.3 ± 3.3 |
| Emotional (0-12) | 2.9 ± 2.7 |
Table 2. Multivariate analyses of BRAF-MIQ and its subscales. \( p < 0.001, ** p < 0.05. \) Cells represent beta coefficients with standard error.

<table>
<thead>
<tr>
<th>Age</th>
<th>Physical</th>
<th>Living</th>
<th>Cognitive</th>
<th>Emotional</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.010 (0.04)**</td>
<td>0.00 (0.04)</td>
<td>-0.00 (0.03)</td>
<td>0.04 (0.02)</td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td>-2.65 (1.70)</td>
<td>-0.74 (1.64)</td>
<td>-1.93 (1.26)</td>
<td>-1.21 (0.97)</td>
</tr>
<tr>
<td>RF positive</td>
<td>-3.80 (1.15)**</td>
<td>-2.85 (1.13)**</td>
<td>-2.05 (1.11)**</td>
<td>-1.91 (0.70)**</td>
</tr>
<tr>
<td>HAQ2.1</td>
<td>4.76 (1.14)*</td>
<td>4.05 (1.13)*</td>
<td>1.83 (0.90)**</td>
<td>1.91 (0.70)**</td>
</tr>
<tr>
<td>Non Anti-TNF</td>
<td>3.33 (1.18)**</td>
<td>2.60 (1.23)**</td>
<td>0.02 (0.01)**</td>
<td></td>
</tr>
<tr>
<td>VAS Pain</td>
<td>1.75 (0.65)**</td>
<td>3.10 (1.19)**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good Sleep quality</td>
<td>-2.75 (1.10)**</td>
<td></td>
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</tbody>
</table>

Disclosure of Interests: None declared


AB0321 MORTALITY AND COMPLICATION OF PATIENTS WITH RHEUMATOID ARTHRITIS ADMITTED TO INTENSIVE CARE UNIT IN KYUSHU UNIVERSITY HOSPITAL
Toshimaru Fujimura1,2, Yukiyo Akasaki1, Yasaharu Nakashima1,3, Yuki Nishikawa1,3,1, Kyushu University Hospital, Orthopaedic Surgery, Fukuoka, Japan; 2, Kyushu University Hospital, Emergency and Critical Care Center, Fukuoka, Japan.

Background: The patients with rheumatoid arthritis (RA) are associated with high mortality caused by comorbidity and complication, and are often required the intensive treatment. Severe infections are among the most common causes of their mortality in intensive care unit (ICU)12).

Objectives: To determine prognostic factors and mortality in patients with RA, including juvenile idiopathic arthritis (JIA), admitted to the ICU in Kyushu University Hospital, we examined the treatments of RA and JIA, comorbidities, complications, the reasons admitted to the ICU, intensive treatments, mortalities within 30 days, 90 days, and a year.

Methods: Between January 2008 and March 2018, 70 patients (20 males, 50 females) with RA (68) or JIA (2) staying at the ICU of our institution for 48 hours and over were included in this study. The admission to the ICU were performed total 77 of times because 5 patients were readmitted. The average of age and RA duration at the admission was 65.8±17.7 years (5-96) and 13.5±14.8 years (0-61), respectively, and the average of follow-up duration was 879.9±992.0 days (3-3988).

Results: The mortality within 30 and 90 days were 21.4% (15/70) and 35.7% (25/70) respectively, and 24 of 65 patients (36.9%), excluded 5 fort death within 30 days, 90 days, and a year. The average of age and RA duration at the admission was 65.8±17.7 years (5-96) and 13.5±14.8 years (0-61), respectively, and the average of follow-up duration was 879.9±992.0 days (3-3988).

Conclusion: Of admission of ICU were significantly poorer prognoses. Of admission of ICU were performed total 77 of times because 5 patients were readmitted. The average of age and RA duration at the admission was 65.8±17.7 years (5-96) and 13.5±14.8 years (0-61), respectively, and the average of follow-up duration was 879.9±992.0 days (3-3988).

REFERENCES


AB0322 BIOMASS SMOKE EXPOSURE LINKED TO HIGHER ACPA LEVELS IN MEXICAN-MESTIZO RA-PATIENTS
Doricio Ángel Galarza-Delgado1, Iris Jazmín Colunga-Pedrada1, José Ramón Azpíri-López2, Ileana Cecilia Reynosa-Silva1, Raymundo Pineda2, Karla Paola Cuéllar-Calderón1, Martelka Castro-González3, Carolina Marielene Martínez-Flores3, Alberto Cárdenas3,1, Hospital Universitario "Dr. José Eleuterio González". UANL, Rheumatology, Monterrey, Mexico; 2, Hospital Universitario "Dr. José Eleuterio González". UANL, Rheumatology, Monterrey, Mexico

Background: Rheumatoid arthritis (RA) is a chronic, inflammatory, autoimmune disease of the joints. Current classification criteria for RA diagnosis require the presence of either rheumatoid factor (RF) or anti-citrullinated protein antibodies (ACPA). These have also been linked to chronic air pollutants exposure, such as tobacco smoke and biomass fuel smoke. Patients with COPD and biomass exposure have higher levels of ACPA (1). Nearly 50% of the world’s population still rely on biomass fuels for cooking, heating and industry, especially in low-income countries (2).

Objectives: To investigate the prevalence of biomass exposure in a cohort of Mexican-mestizo RA-subjects, and the effect of it in their RF and ACPA levels.

Methods: A cross-sectional, observational trial with RA-subjects that fulfilled the 2010 ACR/EULAR classification criteria, recruited at a rheumatology clinic in northeastern Mexico. Patient evaluation included a complete clinical history, somatology, and blood samples to measure hs-CRP, RF isotypes (IgA, IgG, IgM) and ACPA. Biomass exposure was documented using the biomass exposure index (BEI), defined as: average hours exposed per day multiplied by years of exposure. Descriptive analysis was done using frequencies (%) and median values (q25-q75). Subjects were divided into 3 groups according to their BEI: non-exposed, BEI <30 and BEI >30. Comparisons were done by Chi-square and Kruskal-Wallis test and correlation by Spearman’s rho test.

Results: A total of 285 subjects were included, 154 (54%) of them had history of exposure. Comparisons are shown in Table 1. A significant difference in age was found (p=0.006), this being caused by a difference between the BEI=0 and BEI >30 groups (p=0.001). We also found a higher prevalence of dyslipidemia and hypertension in subjects with a BEI >30 (p=0.05). A significant correlation between a rising BEI and a higher value of ACPA (rho>0.14, p=0.016) was found; this correlation was not found with any subtype of RF (p>0.05).

Table 1. Demographic and clinical characteristics of RA according to ACPA groups.

<table>
<thead>
<tr>
<th>BEI ≤ 0</th>
<th>BEI &lt; 30</th>
<th>BEI &gt; 30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, median (q25-q75)</td>
<td>54 (47.9-59.3)</td>
<td>55 (49.2-61.4)</td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>120 (92.3)</td>
<td>72 (91.1)</td>
</tr>
<tr>
<td>BEI hours/week (median, q25-q75)</td>
<td>0 (0-0)</td>
<td>15 (2-19)</td>
</tr>
<tr>
<td>Dyslipidemia, n (%)</td>
<td>32 (24.8)</td>
<td>19 (24.4)</td>
</tr>
<tr>
<td>Type 2 diabetes, n (%)</td>
<td>18 (13.7)</td>
<td>9 (11.4)</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>32 (24.4)</td>
<td>21 (26.6)</td>
</tr>
<tr>
<td>Body mass index, kg/m², median (q25-q75)</td>
<td>27.66 (25.07-31.6)</td>
<td>27.25 (24.32-31.6)</td>
</tr>
<tr>
<td>Disease Duration, years, median (q25-q75)</td>
<td>9.03 (3.4-15.00)</td>
<td>9.5 (4.01-14.0)</td>
</tr>
<tr>
<td>ACPA positive, n (%)</td>
<td>17 (14.2)</td>
<td>19 (24.1)</td>
</tr>
</tbody>
</table>

Conclusion: In our cohort of Mexican-mestizo RA subjects, 54% had positive biomass exposure. Subjects with a BEI >30 were older and had a higher prevalence of dyslipidemia and hypertension. A significant correlation was found between higher BEI index and a higher value of ACPA antibodies.
AB0324 CARDIOVASCULAR RISK ESTIMATION IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH BIOLOGICS OR C-DMARDS

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Background: Patients with Rheumatoid Arthritis (RA) are at increased risk of developing atherosclerotic cardiovascular (CV) disease. The impact of treatment with conventional or biological disease modifying drugs (c- or b-DMARDs) on inflammation of systemic circulation is an important question.

Objectives: The aim of this study is to determine the influence of therapy (c-DMARDs or b-DMARDs) on 10 year CV risk in patients with RA, over a period of 18 months.

Methods: A single center, observational study of 229 consecutive RA patients who were treated with c-DMARDs or b-DMARDs mono/combination therapy for at least 18 months. The 10 year CV risk was calculated with Framingham risk score (FRS).

Results: A total of 229 patients were included, 111 received b-DMARDs and 194 c-DMARDs. The mean age was comparable between 2 groups (62.45±12.74 vs 64.56±12.48 years, p=0.1596) and 148 (64.63%) were female. Patients receiving b-DMARDs had longer disease duration compared to c-DMARDs group (14.34±9.89 vs 9.99±9.3 years respectively, p=0.001) and comparable baseline FRS 10-year percent CV risk (10.74±8.8 vs 11.68±8.78 respectively, p=0.371). Baseline patient distribution across intermediate (9.6% vs 16.6%) and high (10.91% vs 16.16%) FRS 10-year CV risk categories was comparable between treatment groups (b-DMARDs vs c-DMARDs: p=0.208), except low FRS category (27.51% vs 51.53% respectively, p=0.001). At month 18, FRS 10-year CV risk category remained stable in b-DMARDs patients (low: 31.88%, intermediate: 10.92%, high: 5.24%, p=0.47), whereas a significant shift in FRS 10-year CV risk category was observed in c-DMARDs patients (low: 58.1%, intermediate: 17.03%, high: 9.17%, p=0.001). Within-group the mean (SD) change in FRS 10-year percent CV risk from baseline to month 18 was statistically significant for both b-DMARDs (Δ= 10.74-8.94= 1.8 (1.14), p=0.001) and c-DMARDs (Δ = 11.68-8.78= 2.95 (0.91), p=0.001).

Conclusion: Patients treated with b-DMARDs had lower baseline and month 18 10-year CV risk. However, both treatment arms induced significant improvement of 10-year CV risk at 18 months.

REFERENCES

Disclosure of Interests: None declared

AB0325 PREVALENCE OF ANXIETY/DEPRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS AT THE UNIVERSITY OF CHILE’S CLINICAL HOSPITAL AND THEIR ASSOCIATIONS WITH DISEASE ACTIVITY INDEXES AND QUALITY OF LIFE

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Background: Rheumatoid Arthritis is a chronic inflammatory disease with great impact in quality of life. Anxiety and depression could be frequently present in RA patients and may impact the disease activity evaluation. However psychological evaluation or therapy are not part of the standard care of RA patients.

Objectives: To evaluate the prevalence of anxiety/depression in rheumatoid arthritis patients in control at the University of Chile’s Clinical Hospital and to investigate the association of anxiety/depression with disease activity and quality of life.

Methods: The Hospital Anxiety Depression Scale (HADS) was applied to measure depression and anxiety in a cross-section patients with RA meeting the ACR/EULAR 2010 criteria in control at the University of Chile’s Clinical Hospital. All patients included gave their informed consent. Demographic characteristics, Disease variables and activity, measure as DAS28-VHS, DAS-28 CRP, CDAI and SDAI and HAQ were evaluated at the same time. Spearman correlation, Fisher exact test, Chi-Square and Kruskal-Wallis test were used according to variables at evaluation. Statistical analysis was performed by Stata v12.1 software. The study was approved by the Hospital Ethic Review board.

Results: 122 patients were enrolled in the study between december 2017 and December 2018. 103 (84.45%) were female. 56 (46%) had depression and/or anxiety according to HADS. 24% of the patients (n=24) had only depression. The severity of the depression symptoms was mild in 71%, moderate in 21% and severe in 8% of the patients. 42%, 40% and 18% of the patients with anxiety (n=55) had mild, moderate and severe anxiety symptoms respectively. The disease activity was significantly higher in patients with as compared to those without anxiety/depression, measured with all of the following indexes: DAS28-VHS (4.33 vs 2.75, p<0.001), DAS-28 CRP (4.13 vs 2.75, p<0.001), CDAI (15 vs 7 p<0.001)and SDAI (17 vs 7.5, p<0.001). The HAQ was also significantly higher in patients with anxiety/depression (1.18 vs 0.29, p<0.01

REFERENCE

Disclosure of Interests: None declared
Conclusion: Depression/anxiety symptoms was very frequent in our cohort of RA patients. The disease activity measure with different indexes and the HAQ was significantly higher in the patients with depression/anxiety. It is possible that psychological factors influence the RA treatment outcomes. Therefore counseling and therapy of anxiety and depression should be considered in the regular management of RA patients.

REFERENCES

Disclosure of Interests: Anne Marie Chassin-Troubetz: None declared, cesar Lillo Speakers bureau: Abbie, Ariel Castro; None declared, Hector galicia: None declared, Pilar Carrasco Speakers bureau: Abbie, Francisca Bozan: None declared, Francesca Sabogo Consultant for: Abbie, Novartis, Speakers bureau: Abbie, Pamela Wurman Paid instructor for: Roche, Julio Cruz: None declared, Silvana Saavedra: None declared, Annelise Goecke Consultant for: Roche, abbie, novartis, Phizer, Paid instructor for Roche, Speakers bureau: Roche, Novartis, Abbie, Pfizer


AB0326 RECOGNITION AND IMPLEMENTATION OF EULAR RECOMMENDATIONS FOR RHEUMATOID ARTHRITIS/CARDIOVASCULAR RISK MANAGEMENT AMONG INTERNAL MEDICINE AND RHEUMATOLOGY FELLOWS: DATA FROM AN ACADEMIC TERTIARY CARE LEVEL CENTER

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Background: Rheumatoid arthritis (RA) patients present an increased risk of cardiovascular (CV) morbidity and mortality compared to the general population. Patients from Latin-America present distinctive features and some of them are relevant when assessing CV risk. EULAR recommendations include CV risk assessment for all the patients at least once every 5 years and its reconsideration following major changes in anti-rheumatic therapy. Importantly, failure to identify and manage CV comorbidity in RA patients has been recognized by rheumatologists, although there is no information in Latin-America.

Objectives: To investigate knowledge about EULAR recommendations for RA-CV risk assessment/management (K-EULAR-R) among internal medicine and rheumatology fellows from an academic and tertiary care level center, to identify physician’s perception about responsible(s) for CV risk assessments and about major barriers to perform the assessments and to investigate the appropriated identification of major CV risk factors. Potential differences among both group of trainees were additionally investigated.

Methods: Internal medicine fellows (N=105, 1st to 4th grade participants were represented) and rheumatology fellows (N=10, 4 from first grade and 6 from second grade) were invited to anonymously answer a questionnaire designed by 2 investigators to investigate K-EULAR-R and integrated by 11 items classified in 3 categories: “general knowledge about CV risk in RA patients” (4 items), “timing of CV risk assessment” (4 items) and “appropriated statin use” (3 items). In addition, fellows were directed to select and rate main responsible for CV risk assessment (5 options), major barriers to apply EULAR recommendations (6 options), and to properly identify CV risk factors (20 options). After questionnaire completion, an overall-CV-knowledge-Likert scale (superior, borderline or inferior) was assigned to each participant by an independent observer. The study received IRB approval. Descriptive statistic was used and questionnaire was scored to a decimal scale.

Results: Ninety-three (85%) internal medicine fellows and 10 (100%) rheumatology fellows participated. Rheumatology fellows scored higher in the K-EULAR-R questionnaire when compared to internal medicine fellows (6.9±1.4 vs. 5.5±1.4, p=0.004) and the higher score was replicated in the category of “general knowledge about CV risk” (8.3±2.0 vs 5.3±2.5, p=0.001), meanwhile no differences were detected in the scoring of the categories “timing of CV risk assessment” and “appropriated statin use”.

No differences among grades within each group were identified.

The majority of the rheumatology fellows rated themselves as the specialist responsible for CV risk assessment (80%); meanwhile this percentage decreased to 45.7% among the internal medicine fellows (p=0.084); fellows from both groups identified lack of time during rheumatic evaluations and the main barrier to perform CV risk assessment (80% and 57%, respectively).

Adequate CV risk factor identification varied from 30% (for contraceptive use) to 100% (for smoking habit), and these were similar among both groups. Up to 82.5% of the fellows identified incorrectly ≥ 1 CV risk factor and high serum triglyceride levels was the highest (49%).

Conclusion: Knowledge about CV risk management in RA patients was suboptimal among trainees in internal medicine and rheumatology from an academic and tertiary care level center in Mexico City; trainees in rheumatology performed better. There is a need to reinforce the topic during fellows’ residency.

Disclosure of Interests: None declared


AB0327 RHEUMATOID ARTHRITIS PATIENTS HAVE VITAMIN D DEFICIENCY COMPARED TO AGE SEX MATCHED CONTROL. WHAT CONTRIBUTE TO THIS DEFICIENCY?

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Background: Vitamin-D (vit-D) is believed to have an immunomodulatory and anti-inflammatory role. Low vit-D has been proved to increase susceptibility to the development and to increase the inflammatory activities of rheumatoid arthritis (RA). This study looked at 25-vit-D level in RA patients and in their matched age and sex controls, and investigated what contribute to the risk of low 25-vit-D in RA.

Objectives: The study looked at RA diseases activities, renal function, demographic features and blood biochemistry relation to 25-vit-D level.

Methods: 62 RA patients and 82 control were recruited for the study. 25-vit-D level, RA diseases activity parameters and blood biochemistry (full blood count, liver function test, and renal profile) were obtained on the same day. Estimated glomerular filtration rate (eGFR) calculated with Modification of Diet in Renal Disease (MDRD) formula. Body mass index (BMI) calculated as mass (kg)/Height (m)2. Univariate regression analysis was carried out to determine the relationship between 25-vit-D level and all the parameters of interest (as above).

Results: 65 RA, and 82 controls matching for age (48±13 years for RA, and 47±14 years for the controls, p=0.58) and sex (57 F (88%), M=8 (12%) RA, 67 F (82%), 5 M (18%) controls, p=0.23) were included for the study. The mean 25-vit-D level was 413±31 nmol/l for the RA patients (normal range: 50-80), and 52±3 nmol/l for the controls (p=0.03).

Univariate linear regression among RA patients revealed a positive linear relationship between 25-vit-D level and age of the patients (p=0.02, CI: 0.04, 0.13), BMI (p=0.01, CI: 0.13, 0.96), body surface area (p=0.02, CI: 9.47, 111), body mass index (BMI) (p=0.03, CI: 0.17, 3.18), and calcium level (p=0.04, CI: 1.38, 69.6). 25-vit-D level was negatively associated with eGFR (p=0.04, CI: 0.20, -0.01), microalbuminuriuma level (p=0.03, CI: -0.26, -0.00), and CRP level (p=0.03, CI: -0.47, -0.0).

Conclusion: Vit-D receptors are present in most cells in the body and in the T and B lymphocytes. The active form of vit-D (1, 25 vit-D) is one of the most potent modulators of the immune system. Hence, the negative relationship between 25-vit-D and CRP support 25-vit-D deficiency role in the exacerbation of the inflammatory status, and possibly in the subclinical renal impairment; as shown by the negative association between eGFR and the 25-vit-D. The relation between the subclinical renal impairment and the vit-D deficiency is further supported by the negative linear relationship between 25-vit-D and the urine microalbuminuria level and the positive linear relationship association between 25-vit-D and the serum creatinine level. The positive association between 25-vit-D and the age of the patients might reflect the awareness of the older population about the importance of sun exposure for health. Screening for vit-D deficiency might be an important step to detect subclinical renal insufficiency in RA. Vit-D supplement might help in ameliorating the inflammation of RA and the subclinical renal impairment especially its well known that our general population is already Vit-D deficient and this worsen by the inflammatory conditions that they develop.

REFERENCES
AB0328  SECONDARY SARCOPENIA IN RHEUMATOID ARTHRITIS PATIENTS TREATED BY BIOLOGIC DISEASE MODIFYING ANTI-RHEUMATIC DRUGS

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Background: Sarcopenia is characterized by a loss of muscle mass and strength, which leads to a reduced physical ability, poor quality of life (QoL), frailty and mortality. Rheumatoid arthritis (RA) is considered a cause of secondary sarcopenia.

Objectives: To clarify the effectiveness of biologic disease-modifying anti-rheumatic drugs (bDMARDs) on sarcopenia, including the physical ability, body composition and nutritional status.

Methods: This was a prospective cohort study including consecutive 41 patients (11 men, 30 women, 63±16.1 years old) with RA who started bDMARDs for the first time at the Niigata Rheumatic Center. The diagnosis of secondary sarcopenia was made according to the diagnostic algorithm of the Asian Working Group for Sarcopenia (AWGS), excluding the criteria about older age. We observed the disease activity of RA, physical ability, body composition, nutritional status and QoL at baseline and 6 months. The disease activity was assessed by the disease activity score-28 (DAS28) and clinical disease activity index (CDAI). The physical activity was determined using the health assessment questionnaire (HAQ), 10-m walking test (10MWT) and timed up and go test (TUG). The nutritional status was determined based on the controlling nutrition status (CONUT) score and prognostic nutritional index (PNI). The overall QoL was measured by European quality of life scale-5 dimensions (EQ-SD).

Results: Among 41 patients who started bDMARDs, 19 were classified as having sarcopenia, and 7 were classified as having pre-sarcopenia. The bDMARD was certolizumab pegol in 10 patients, adalimumab in 7, abatacept in 7, golimumab in 6, tocilizumab in 5, infliximab in 3 and etanercept in 2 patients. Regarding the disease activity, the DAS28 was 4.7±1.3 vs. 2.6±1.3, p<0.001) and CDAI (18±6.9 vs. 7.2±7.3, p=0.001) decreased significantly after 6 months of bDMARD therapy. The physical activity was significantly improved after 6 months of bDMARDs: HAQ (1.1±0.9 vs. 0.7±0.9, p=0.001), 10MWT (1.8±0.7 vs. 1.6±0.6 m/s, p=0.046) and TUG (10.5±5.0 vs. 9.5±6.2 s, p=0.024). Regarding the nutritional status, the CONUT score (3.8±0.5 vs. 2.8±0.5, p=0.001) and PNI (44.9±6.4 vs. 49.7±4.1, p=0.001) were significantly improved after 6 months of bDMARDs. The EQSD was also improved after 6 months of bDMARDs (0.64±0.15 vs. 0.71±0.20, p=0.010). The body composition analysis showed a significant increase in the body weight (54.3±13.2 vs. 55.4±14.4 kg, p=0.006) and fat mass (16.3±7.3 vs. 17.4±7.8 kg, p=0.001) after 6 months of bDMARDs but no significant increase in the appendicular skeletal muscle mass (14.7±4.3 vs. 14.8±4.5, p=0.111). The proportion of patients classified as having sarcopenia showed a decreasing trend after 6 months of bDMARDs therapy (46.3% vs. 24.4%, p=0.0637).

Conclusion: After 6 months of bDMARDs therapy, the physical ability, nutritional status and QoL were significantly ameliorated. While the muscle mass was not markedly increased, the proportion of patients with sarcopenia showed a decreasing trend. The administration of bDMARDs might be useful for preventing secondary sarcopenia in RA patients.


AB0329  CERVICAL SPINE INVOLVEMENT IN RHEUMATOID ARTHRITIS

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Background: After the small peripheral joints, the cervical spine is the second most involved region in rheumatoid arthritis (RA). The most frequent radiological features are the atlantoaxial subluxation (AAS) which can be anterior, posterior or vertical. During the course of the disease, the affection of the cervical spine has no symptoms for a long time due to the adaptability of neurological structures. The onset of myelopathy can occur at any time. MRI assessment compared to functional cervical spine X-ray is more sensitive method to provide not only AAS but also soft tissue involvement such as periodontal synovitis or fibrous pannus and even more odontoid erosion. New data show that there is a decreasing prevalence of cervical involvement because of the biologics.

Objectives: We assessed RA patients in permanent remission with MRI imaging. RA patients have no cervical pain or any neurological symptoms. We wished to explore the cervical spine involvement: AAS, odontoid erosion or periodontal soft tissue thickening. We also wished to determine the affection of cervical spine in RA patients receiving different treatment strategies.

Methods: Altogether 49 RA female patients were included. Among them, 15 were MTX-treated, biologic-free, 34 patients received biologics (17 infliximab [IFX] and 17 tocilizumab [TCZ]) as first-line biologic treatment, in combination with MTX. There was no significant difference between the main characteristics of these subgroups. ESR, CRP and DAS28 were determined in all RA patients in every 3 months. We calculated sumESR, sumCRP and sumDAS28 indices from the past 3 years.

Results: We detected anterior AAS in one-quarter of RA patients (13 affected patients from the total 49) (26.5%). There was no significant difference between the therapeutic subgroups. No posterior or vertical AAS occurred. Compared with patients without cervical involvement, the patients with AAS showed higher sumCRP and sumESR levels, higher sumDAS28 scores and more frequent seropositivity, but these differences were not significant. Soft tissue involvement of the cervical spine was detected in 33.3% of MTX-treated, in 35.3% of IFX-treated and in 5.9% of TCZ-treated RA patients. Eight RA patients had odontoid erosion (4.1%) and 3 from the MTX, 2 from the IFX and 3 from the TCZ-treated subgroups. In relation to soft tissue involvement and odontoid erosion we did not find any correlation with age, disease duration, seropositivity, sumESR, sumCRP or sumDAS28 indices.

Conclusion: These findings suggest that the presence of cervical involvement in RA patients is an important and frequent phenomenon even in asymptomatic patients. Higher ACPA titer, high disease activity and erosive disease at baseline are predictors of atlantoaxial involvement. With the appropriate disease control with conventional or biologic treatment, progression of cervical spine involvement can also be prevented.

REFERENCES
AB0330

RELATIONSHIP BETWEEN FOREFOOT SYNOVITIS IN RHEUMATOID ARTHRITIS AND WORSENING FOREFOOT DEFORMITY

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Background: While the number of rheumatoid arthritis (RA) surgeries has been declining due to advances in pharmacotherapies for RA, forefoot surgeries are on the rise. In recent years, the common use of joint ultrasonography in RA consultations has led to the early detection of synovitis. However, little is known about how much forefoot deformities such as hallux valgus and metatarsophalangeal (MTP) joint dislocation are affected by synovitis in the forefoot of RA patients.

Objectives: The present study examined factors involved in forefoot deformity among patients with foot synovitis identified on joint ultrasound.

Methods: Subjects (71 patients, 91 feet) were RA patients who had undergone foot joint ultrasonography more than 2 years earlier and underwent standing X-rays of the feet before and after ultrasonography. Surgery cases were excluded. Mean age was 64.9 years (range, 15–90 years). Disease stage was Stage 1 in 14 patients, Stage 2 in 14 patients, Stage 3 in 16 patients, and Stage 4 in 27 patients. According to the Steinbrocker functional classification, RA was Class 1 in 45 patients, Class 2 in 19 patients, Class 3 in 6 patients and Class 4 in 1 patient. Twenty-five patients had been administered biological drugs. At the time of joint ultrasonography, patients were questioned regarding whether they had any complaints involving the forefoot, midfoot or hindfoot (noted separately). The following scans were performed: forefoot (MTP joints 1-5); midfoot (calcaneocuboid, calcaneocuboid and cuneonavicular joints) and hindfoot (peroneal muscle tendon, talocrural joint, talocalcaneal joint and posterior talo-fibular ligament). Foot deformity score (FDS) (hallux valgus angle + first-second intermetatarsal angle [M1M2 angle] + first-fifth intermetatarsal angle [M5M1 angle]) was used as the benchmark for forefoot deformity, and an increase >5° was considered to indicate worsening deformity.

Results: Forefoot deformity had progressed in 25 patients. Mid- and hindfoot synovitis and the presence of complaints were not associated with deformity. However, significant worsening of FDS was observed in patients with foot synovitis or foot complaints. While no difference in age, disease activity, biological disease-modifying antirheumatic drug usage or health assessment questionnaire results were seen in the advanced deformity group, duration of disease was significantly shorter in this group.

Conclusion: Mid- and hindfoot synovitis was unrelated to forefoot deformity. MTP joint synovitis in the forefoot was related to forefoot deformity. Continuous synovitis in the forefoot must damage the articular capsule and ligament structure, leading to progression of deformity. As shown by the short duration of the disease in the advanced deformity group, deformity may progress in the early stages among patients with forefoot deformity.

Disclosure of Interests: None declared


AB0332

DEPRESSION AND ANXIETY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory joint disease leading to substantial morbidity and mortality and had a major economic and psychological impact on individuals with RA and their families. The prevalence of depressive disorder in RA was 17% and associated with poorer outcomes.

Objectives: To evaluate prevalence of depression and anxiety and their related factors in patients with RA.

Methods: In this cross-sectional study, 464 patients with RA from two RA registries, the Siriraj Rheumatoid Arthritis (SIRA) registry and the Thai Army Rheumatoid Arthritis Cohort (TARAC) were enrolled. Demographic data and clinical variables, including disease activity, functional status, health-related quality of life, and cognitive function, were collected. Depression and anxiety were assessed using the Thai version of the Hospital Anxiety and Depression Scale (Thai HADS).

Results: Based on the Thai HADS cutoff value of more than 8 out of 21, 12.5% and 14.5% had some degrees of depression and anxiety, respectively. The proportion of depression and anxiety elevated with increasing disease activity or worsening functional status. However, in multivariate analyses, only global health [RR (95% CI) 0.98 (0.96 – 0.99), p 0.001] was negatively associated with depression, after adjusted for covariate. For anxiety, functional disability [RR (95% CI) 2.46 (1.33 - 4.54), p 0.004] and marital status [married: RR (95% CI) 2.43 (1.25 - 4.73), p 0.008] significantly increased the risk, while disease duration 10 years or more [RR (95% CI) 0.45 (0.25 - 0.80), p 0.007] and global health [RR (95% CI) 0.97 (0.95 - 0.98), p < 0.001] decreased this risk.

Conclusion: Depression and anxiety is common in patients with RA. Patients’ perception of their current health is significantly related to mood disorders. Therefore, mental health status, especially mood disturbances, should be addressed in routine practice to improve quality of life in RA.

Table 1 Multivariate analyses for depression and anxiety

<table>
<thead>
<tr>
<th>Factors</th>
<th>Depression</th>
<th>Anxiety</th>
</tr>
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<tr>
<td>RR (95% CI)</td>
<td>P value</td>
<td>RR (95% CI)</td>
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<tr>
<td>DAS28 &gt; 2.6</td>
<td>1.66 (0.49 - 5.70)</td>
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<tr>
<td>HAQ &gt; 0.5</td>
<td>1.38 (0.75 - 2.54)</td>
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<tr>
<td>Comorbidity</td>
<td>1.04 (0.58 - 1.89)</td>
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<tr>
<td>Global health</td>
<td>0.98 (0.96 - 0.99)</td>
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<tr>
<td>Cognitive impairment</td>
<td>1.22 (0.95 - 2.59)</td>
<td>0.727</td>
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<tr>
<td>Pain score</td>
<td>1.07 (0.95 - 1.26)</td>
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<tr>
<td>Disease duration &gt; 10 years</td>
<td>0.45 (0.25 - 0.80)</td>
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<tr>
<td>Marital status (married)</td>
<td>2.43 (1.25 - 4.73)</td>
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Disclosure of Interests: None declared


AB0333

CLINICAL FEATURES AND RISK FACTORS OF CHRONIC HEART FAILURE IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS PRIOR TO THERAPY WITH BASIC ANTI-INFLAMMATORY DRUGS

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Background: Heart failure (HF) is a major cause of premature mortality, there is little information regarding its prevalence and associated risk factors in patients (pts) with early rheumatoid arthritis (RA).

Objectives: to study the frequency, clinical manifestations and risk factors associated with the development of HF in pts with early RA prior to therapy with basic anti-inflammatory drugs.

Methods: A total of 74 pts with early RA (ACR/EULAR criteria, 2010) were included in the study: 78% of women, median (Me) age - 56 years [47; 61], Me of disease duration - 7 [4;6] months; Me DAS28 5.3 [5.0;6.2], IgM RF seropositive (87%) and/or ACPA (100%), without any experience of administration of disease-modifying antirheumatic drugs and glucocorticoids. All pts underwent blood pressure monitoring, echocardiography, tissue Doppler imaging, NT-proBNP. The normal range for NT-proBNP was less than 125 pg/ml. HF was diagnosed according to the recommendations of the European Society of Cardiology (2012).

Results: HF was diagnosed in 24 (33%) pts: in 23 pts - HF with preserved ejection function (EF), in 1 pts - HF with reduced EF. Dyspnea was detected in 21 (87%) RA pts with HF (positive predictive value (PPV)-33%), in 6 (25%) - ankle edema (PPV-35%), in 24 (100%) - fatigue (PPV-38%). In 5 (21%) pts dyspnea NYHA=2 was observed, 15 (63%) - NYHA=3, in 1 (4%) - NYHA=4. Diastolic dysfunction of the left ventricle was detected in all pts with HF (PPV-95%). Elevated NT-proBNP level wasn’t highly indicative for HF in early RA (PPV-41%). All pts with early RA were divided into 2 groups: 1- with HF, 2- without HF. Pts with RA and HF were older (61 [58;65] vs 51 [36;56] years), had higher BMI (28 [25;32] vs 24 [22;29] kg/m², p=0.05). NT-proBNP level (192.0 [159.8;265.7] vs 77.0 [41.1;191.2] pg/ml, p=0.05), more likely to have arterial hypertension (AH) (83% vs 51%, p<0.05), carotid atherosclerosis (91% vs 48%, p<0.05), coronary artery disease (CAD) (40% vs 8% vs 20%, p<0.05).
EFFECT OF OBESITY ON THE COURSE OF THE OVARIAN RESERVE MEASURING THE ANTI-MÜLLERIAN HORMONE IS NOT DIMINISHED IN PATIENTS WITH RHEUMATOID ARTHRITIS COMPARED TO THE HEALTHY POPULATION

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Background: Rheumatoid Arthritis (RA) is the most prevalent chronic inflammatory arthritis, affecting 0.5-1% worldwide population and predominates in females. Altered fertility has been reported due to a decrease in ovarian reserve secondary to sustained inflammation. The anti-Müllerian Hormone (AMH) is currently the most reliable biomarker of ovarian reserve. However, few and contradictory studies have been reported to analyze the relationship between fertility in RA women patients and AMH.

Objectives: The aim of present study is to determine the AMH serum concentrations in a long-standing RA patients and control group. We also sought to determine the correlation between AMH serum levels and disease activity measured by different parameters and the effect of biological DMARDs.

Methods: Serum AMH levels were measured in 60 women with long-standing RA aged 20-50 y.o. and compared to 59 healthy women. AMH was assessed by ELISA (Gen II Beckman Coulter Inc.) and a large data set of clinical and molecular data was annotated. Demographic parameters, RA disease activity measured by DAS28 score and inflammatory biomarkers such as ESR, CRP, lymphocyte CD4+, CD8+, NK cells, IL-10 and IL-6 were determined. A comprehensive gynecological self-administered questionnaire was given. Serum AMH levels were age-correlated. Differences between groups were calculated using Student’s t-test or Mann-Whitney U test for continuous variables and Fisher’s exact test for categorical variables. Multivariate analysis was conducted by the partial correlation coefficient. Linear regression analysis was performed to study the effect of different variables on proportional AMH change. P value <0.005 were considered significant.

Results: The median age was similar in AR and control groups (37.4 ±6.23 vs 37.3 ±6.27, P=0.937). Mean disease duration was 8.37±5.36 years. The number of previous treatments was <3 in 71.7% of patients and >3 in 28.3%. Disease activity measured by DAS28 was 2.8±1.54. The age-adjusted mean serum concentration of HAM was 1.27 ng/ml [IQR 0.42; 2.24] in RA patients and 1.31 ng/ml [IQR 0.46; 3.09] in controls (P=0.608). Neither disease activity (P=0.862), nor current or previous biDMARDs treatments (P=0.871) were associated with HAM levels. However, a negative linear correlation was observed between HAM and IL-10 levels (P= 0.033).

Conclusion: Our study shows that ovarian reserve determined by HAM serum levels is not reduced in rheumatoid arthritis patients compared with healthy controls. In our series, HAM levels were not affected by disease activity however a significant correlation was observed between HAM and IL-10 levels. These results support the role of cytokines profile in the female reproductive system and will focus further investigations in this critical area, mainly once biological DMARDs have been recommended in RA pregnant patients.

REFERENCES


Disclosure of Interests: None declared

AB0335  THE CORRELATION OF CORRELATION OF TH17 AND TREG CELL LEVELS OF IN CORONARY HEART DISEASE PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a prevalent chronic autoimmune inflammatory disease. Also acute coronary syndrome (ACS) is a prevalent chronic inflammatory disease. Now more and more studies have also shown that coronary heart disease is also associated with immune inflammation. We will discuss Th17 and Treg cell levels in patients with rheumatoid arthritis combined with coronary heart disease and simple rheumatoid joints as well as normal people. Its pathogenesis is closely associated with a failure of endogenous immune tolerance that caused by the imbalance of CD4/CD8. New T subgroup Th17 T lymphocytes play an important role in the occurrence and development of RA and ACS. Moreover, T lymphocytes are one of the first cells to be recruited into atherosclerotic plaques, and most adhesion molecules and chemokines that promote the migration of monocytes to the intima are also related to T cell recruitment. T lymphocytes mainly divided into two major subsets of CD4/CD8, including CD4+ helper cells, which are classified into Th1/Th2 and newly discovered Th17 cells and regulatory T cells subgroups, have the effect of the immune response to promote the immune, and CD8+ play the role of killer cells and suppress the immune response. Similar to CD8, (Treg) lymphocytes can reduce the body’s anti-tumor ability by inhibiting cell contact and the production of inhibitory factors and effect T cells.

Objectives: Through clinical studies, we want to explore whether the proportion of Th17/Treg in peripheral blood of RA with ACS patients is reduced to indicate whether the immune balance is broken, thus providing further data for clinical studies.

Methods: In April 2017 to September 2018 in our hospital, Patients with RA and ACS diagnosed by Coronary angiography in our hospital of 20 cases male:9 female:12 into the research object, the diagnosis of ACS combined with clinical data of 20 patients as Observation group. These patients have been diagnosed with rheumatoid arthritis. Another 20 rheumatoid arthritis patients male:11 female:9 were collected from the rheumatology department of our hospital, and 20 normal healthy people male:10 female:10 were collected from the physical examination center of our hospital, as control group.

Results: Compared with the control group, the proportion of Th17 cells and Treg cells in peripheral blood of RA with ACS increased and decreased respectively (P < 0.05). Compared with the RA group, the proportion of Th17 cells in the peripheral blood of RA with ACS group increased, while the proportion of Treg cells decreased (P < 0.05). The proportion of Th17 cells in RA with ACS group was higher than that in RA group and control group (P < 0.05). Th17/Treg ratio in control group, RA group, ACS and RA groups were respectively compared with the control group. Th17/Treg increased in the RA with ACS and RA groups, and the RA with ACS group was higher than the RA group, with statistically significant differences (P < 0.05), but the ratio between the RA group and the control group was not significant.

Conclusion: Through this rare clinical study, it was found that the levels of Treg cells and Th17 cells in patients with rheumatoid arthritis combined with coronary heart disease were to some extent higher than those in patients with rheumatoid arthritis alone and normal healthy people. We can speculate whether it is possible to find a target for Treg cell Th17 cell levels in patients with RA with ACS expanding the sample study again, so as to intervene as early as possible and regulate the immune balance to avoid the progression of coronary heart disease and adverse cardiovascular events.

REFERENCES

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Disclosure of Interests: None declared


AB0336  COMPARATIVE ANALYSIS OF ESTIMATED BONE MASS AND BONE MINERAL DENSITY IN PATIENTS WITH RHEUMATOID ARTHRITIS FROM THE CHIKARA STUDY

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Background: Patients with rheumatoid arthritis (RA) have lower muscle mass and a higher rate of sarcopenia than healthy individuals. The relationship between rheumatoid arthritis and bone loss is well known. Dual energy X-ray absorptiometry (DEXA) and bioelectrical impedance analysis (BIA) are used to diagnose sarcopenia, but the correlation between bone mineral density and estimated bone mass is unknown.

Objectives: To investigate the correlation between bone mineral density and bone mass in RA patients.

Methods: Data from a prospective observational study (CHIKARA study) were analyzed. Bone mineral density (BMD) was measured by DEXA, and bone mass was measured by BIA on the same day, and the correlations between BMD at each measurement site and bone mass were evaluated.
Background: Rheumatoid arthritis (RA) and carpal tunnel syndrome (CTS) are known to be associated and also RA may lead to swelling of the median nerve without the presence of CTS. The prevention of disease progression may prevent the increase in median nerve CSA by preventing deviations in the radial inclination angle.

Methods: A total of 90 RA patients (women, 83%; mean age, 67.2±12.1 years) were included. The median disease duration was 8.5 (interquartile range [IQR]: 4.9, 17) years, the mean DAS28-ESR was 2.92±1.2, and the median MTX dose was 10 (IQR: 8, 12) mg/week. Nineteen patients (21%) used a biologic agent. There was a significant correlation between total hip BMD and bone mass (r=0.64, p<0.001). The details are shown in Figure 1. Bone mass was significantly correlated with femoral neck BMD (r=0.62, p<0.001), whole body BMD (r=0.60, p<0.001), and lumbar BMD (r=0.49, p<0.001). Bone mass was significantly lower by DEXA (1.9 ±0.5 kg) than by BIA (2.0±0.4 kg) (P<0.001).

Results: The study completed with 102 hands of 51 patients. 27% of these RA patients without clinical and electrophysiological findings were diagnosed as CTS by ultrasonography. A negative correlation was found between the radial inclination (RI) and the median CSAs measured from the radioulnar joint (R: -0.49; p: 0.00), the pisiform bone (R: -0.45; p: 0.00), and hook of hamate (R: - 0.60, p: 0.00). When the hands were divided into three groups according to the ranges of RI specified in the literature, the median nerve CSA was found to be significantly higher in the group with a low RI at these levels (p < 0.001).

Conclusion: The median nerve CSAs increased as the radial deviation increased in RA patients. The prevention of disease progression may prevent the increase in median nerve CSA by preventing deviations in patients with RA. And the development of CTS may also be prevented.

Disclosure of Interests: None declared


AB0338

ELDERLY ONSET RHEUMATOID ARTHRITIS AND POLYMYALGIA RHEUMATICA: COMPARATIVE CLINICAL STUDY

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Background: Polyarthritis at the elderly people usually has a similar onset with an acute inflammatory character and scapular girdle involvement. Differenitling elderly onset rheumatoid arthritis (EORA) and polymyalgia rheumatica (PMR) can be a diagnostic challenge.

Objectives: To analyse the clinical and analytical differences between EORA and PMR.

Methods: Longitudinal observational study of patients older than 60 years newly diagnosed with EORA (ACR/EULAR 2010) and PMR (ACR/EULAR 2012). Inclusion: consecutive and voluntary. Follow-up time: 12 months. A single rheumatologist made all follow-up visits. The clinical-epidemiological and analytical characteristics were collected. The statistical study was performed with Stata 15.1.

Results: 45 EORA were recruited (53% women; mean age 74.8 ± 7.5) and 20 PMR (85% women; mean age 76.6±5.0). 75% of EORA had scapular girdle involvement, but only 44% of the pelvic girdle. All had peripheral arthritis, and the small joints of the hands were involved in 93.3%, with edema in 46.7%. Forty percent of EORA patients were seropositive (RF> 20 IU/mL and/or ACPA> 20 U/mL): 33% RF positive (132.8 ± 12 IU/mL), 28.9% for ACPA (2 cases [15.4%] from 100 to 250 U/mL and 11 cases [84.6%] above 250 U/mL) and in 10 patients [22.2%] double positive. All patients with PMR patients had shoulder girdle involvement and 90% of the pelvic girdle. None of them had peripheral arthritis. RF was positive in one patient (73 IU/mL) and ACPA in 2 patients (titers between 20-40 U/mL). No patient was double positive. Table 1 and 2.

Disclosure of Interests: None declared


IS THE RADIAL DEVIATION ASSOCIATED WITH MEDIAN NERVE SWELLING IN PATIENTS WITH RHEUMATOID ARTHRITIS?

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Background: Ultrasonography, the median nerve cross-sectional areas (CSAs) of the patients were measured from the four levels of the distal 1/3 of the forearm, radioulnar joint, pisiform bone and hook of hamate, and the ulnar nerve CSAs were measured from the pisiform bone.

Results: The study completed with 102 hands of 51 patients. 27% of these RA patients without clinical and electrophysiological findings were diagnosed as CTS by ultrasonography. A negative correlation was found between the radial inclination (RI) and the median CSAs measured from the radioulnar joint (R: -0.49; p: 0.00), the pisiform bone (R: -0.45; p: 0.00), and hook of hamate (R: -0.60, p: 0.00). When the hands were divided into three groups according to the ranges of RI specified in the literature, the median nerve CSA was found to be significantly higher in the group with a low RI at these levels (p < 0.001).

Conclusion: The median nerve CSAs increased as the radial deviation increased in RA patients. The prevention of disease progression may prevent the increase in median nerve CSA by preventing deviations in patients with RA. And the development of CTS may also be prevented.

REFERENCES

Disclosure of Interests: None declared

Background: Rheumatoid arthritis (RA) is a known cause of cardiovascular disease (CVD). Several studies suggest that serum uric acid (SUA) is associated with RA disease activity and functional capacity in patients with RA. Previous studies have revealed different results, mainly regarding the role of DMARDs in lowering SUA levels.

Objectives: The aim of the present study is to determine the prevalence of hyperuricemia in RA patients and to evaluate whether disease modifying anti-rheumatic drugs (DMARDs) have a hypouricemic effect.

Methods: We have conducted a cross-sectional study over four months (DMARDs) have a hypouricemic effect.

Results: The mean age was 51.76±12.84 and the mean age at RA diagnosis was 42.5±15.23. Fourteen patients (6.9%) had hyperuricemia and the average rate of SUA was 41.99±11.85 mg/L. All patients were taking Methotrexate, 34% received also Sulfasalazine, 6.4% Hydroxychloroquine and 77% steroids. Males and post-menopausal women had the average rate of SUA was 42.5±15.23. Fourteen patients (6.9%) had hyperuricemia and the average rate of SUA was 41.99±11.85 mg/L. All patients were taking Methotrexate, 34% received also Sulfasalazine, 6.4% Hydroxychloroquine and 77% steroids. Males and post-menopausal women had significantly higher SUA levels (p<0.001 and p=0.0001, respectively).

Univariate analysis showed a positive relationship between SUA levels and age (p=0.004), gender (p=0.002), age at RA diagnosis (p=0.03), smoking (p=0.046), use of alcohol (p=0.025), high body mass index (BMI) (p=0.012), elevated blood pressure (p=0.0001), dyslipidemia (p=0.001) and high doses of steroids (p=0.001). The association between RA and gout was noted in one case. We found no correlation between inflammation, DMARDs, CVD and SUA. In multivariate regression analysis adjusted for age, gender, BMI and steroids maintained a significant correlation with SUA.

Conclusion: The prevalence of hyperuricemia is low in our RA patients and similarly gout remains infrequent. However, RA patients must be screened for hyperuricemia. There is growing evidence that higher doses of steroids can cause hyperuricemia. Practitioners should be aware that these patients are at risk of having high SUA levels as well as more traditional cardiovascular risk factors. Thus, appropriate preventive interventions in these patients should be introduced.

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AB0341 REASONS FOR DROP-OUT IN RHEUMATOLOGY SPECIALTY CARE OF ELDERLY RHEUMATOID ARTHRITIS PATIENTS

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Background: The difference between total and healthy life expectancies were 12.3 and 8.8 years for women and men respectively in 2016, in Japan. Rheumatoid arthritis (RA) not only reduces daily living activities due to joint symptoms but also deteriorates the life prognosis due to systemic inflammation. That is, patients with RA are short for both total and healthy life expectancy. In recent years, the need for rheumatologist to provide specialty medical care to elderly patients with RA has been expanding. However, some elderly patients drop out of specialty treatment and care. To date, there are little information concerning background of patients who drop out.

Objectives: To investigate reasons and characteristics of elderly RA patients who drop out from rheumatology specialty medical care.

Methods: Of RA patients who had been visited our rheumatology specialty facility in 2016, we defined as drop-out when the patients did not return to the hospital in 2017. We surveyed age, gender, disease activity, and reason for drop-out retrospectively from medical records and questionnaires.

Results: Of 2,092 patients with RA who visited to our department, 156 patients (7.5%, 95% confidential interval: 6.4 – 8.6%) dropped out. Among drop-out patients, 101 patients were older than 65. 37 patients (37%) dropped out due to comorbidities including death (group C), 32 (32%) patients were introduced certified rheumatologists near the patients’ residences (group R). Twenty-two patients were due to unknown reasons, nine were due to remission, and one patient moved out to other area. Average age of both group C and R were eighty years old. Glucocorticoid user rate (C: 89%, R: 71%) and dose (C: 5.6 mg, R: 5.7 mg) were similar in the both two groups. Patients in group C showed less use of methotrexate (C: 19% vs R: 58%, P < 0.01) compared with group R patients. Simple disease activity index was similar, however, higher modified health assessment questionnaire was observed in group C patients (C: 1.13 vs R: 0.25, p=0.01).

Conclusion: Some elderly RA patients, especially may drop out from rheumatology specialty care due to comorbidities. Regional co-management should be constructed so that elderly patients could continue receiving RA specialized care.

Disclosure of Interests: None declared.


AB0342 DEPRESSION ON PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic representative inflammatory autoimmune disease. The association of disease activity and pro-inflammatory cytokines with depression has not been sufficiently investigated.

Objectives: The aim of this study is to analyze the association between disease activity and depression using Patient Help Questionnaire (PHQ-9) in patients with rheumatoid arthritis (RA). We also examined the outcome of intervention on depression score and determined the prevalence of depression and risk factors for depression and deterioration of depressive symptoms in RA patients.

Methods: 146 RA patients with a mean age of 51±12.2 years were included in the study. Demographic and laboratory data were examined. Disease activity score 28-joint count C-reactive protein (DAS 28-CRP) was performed to assess disease activity of RA. PHQ-9 scores were collected at each clinic visit. Physicians assessed corresponding disease activity using Clinical Disease Activity Index (CDAI). Patients with at least moderate depression (PHQ-9 _10) were offered depression intervention, counseling or medications. PHQ-9 was re-administered after intervention.

Results: 119 of RA patients were females, the average disease duration was 6.8 ± 5.9 years. Depression was diagnosed in 36 of RA patients: 18 - mild, 13 - moderate and 7 - moderately severe. Severity of depression positively correlated with disease activity in RA patients (p <0.05). RA patients with moderate/high CDAI had significantly higher PHQ-9 than those with low CDAI (p<0.001). Of 7 patients who met criteria for depression intervention, 6 were treated and 1 - declined. With treatment 5 patients had improved PHQ-9 scores, 1 patient worsened, and 1 patient had no change in score. The risk of developing a depressive disorder is highest between 5 and 10 years of onset of the disease and depression is a better predictor of work disability than disease activity and response to treatment. Depression is associated with more pain, fatigue and impaired quality of life. Therefore, the risk to develop a depression is increased with impaired function as measured by the health assessment questionnaire (HAQ). Increased disease activity increases the risk for depression in RA. The severity of disease activity of RA, DAS 28-CRP [OR 1.75, 95% CI 1.08-2.64] and severity of fatigue [OR 1.32 95% CI 1.12-1.27] were associated with depression and deterioration of depressive symptoms in the multivariate analysis. Among the components of DAS 28-CRP, patient assessment for global health and abilities for daily performance were more related to depression. Depression unfavorably influences the response to therapy, the rate of remission is lower and the mortality is increased in RA patients. Taken together, this indicates that it is necessary to detect a depression in patients with RA as early as possible in order to initiate appropriate treatment of depression in such cases.

Conclusion: Our study shows depression in 19.18% of patients. Correlation between disease activity and depression score is found in RA patients. Depression intervention resulted in PHQ-9 improvement in some patients, supporting the benefit of depression screening and treatment in rheumatology practice. Depression was related with the level of fatigue and high RA disease activity, which was associated with impaired ability to perform activities of daily life. Strict control of fatigue and disease activity to improve one’s capacity to perform daily life activities would be important to regulate depression. Depression is common and associated with worse outcomes among patients with RA.

Disclosure of Interests: None declared.


AB0343 ANTIRHEUMATIC THERAPY IS NOT ASSOCIATED WITH CHANGES IN CIRCULATING N-TERMAL PRO-BRAIN NATRIURETIC PEPTIDE (N-PROBNP) LEVELS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Patients with rheumatoid arthritis (RA) are predisposed to impaired cardiac function and heart failure (HF). While the pathophysiology has not been fully elucidated yet, inflammation is suspected to play an important role. However, the impact of disease-modifying antirheumatic drugs on cardiac dysfunction in RA remains controversial. Although anti-inflammatory drugs might have protective effects, some of them, i.e. tumour necrosis factor inhibitors (anti-TNF), might also negatively influence cardiac function. Serum NT-proBNP (n-NT-proBNP) is used as a biomarker of cardiac function, and levels ≤125 ng/L with high probability exclude HF.

Objectives: To examine effects of methotrexate (MTX) and anti-TNF regimens on s-NT-proBNP in patients with active RA, and to assess associations between s-NT-proBNP and endothelial function (EndoF).

DISCLOSURE OF INTERESTS

1. Thao Nguyen: Novartis, AbbVie, Pfizer, Roche. 2. Gia Deyabo: None declared. 3. Morten Fagerland: None declared. 4. Stefan Agewall: None declared. 5. Geo Ellertsen: None declared. 6. Mark Feiring: None declared. 7. Knut Mikkelsen: None declared. 8. Øystein Farne: None declared. 9. Irina Holli: None declared. 10. Lietherammer Hospital for Rheumatic Disease, Lillehammer, Norway: None declared. 11. Inlandet Hospital Trust, Department of Medical Biochemistry, Lillehammer, Norway: None declared. 12. Oslo University Hospital, Oslo Centre for Biostatistics and Epidemiology, Oslo, Norway: None declared. 13. Oslo University Hospital, Utslev, Department of Cardiology, Oslo, Norway: None declared. 14. The Artic University of Norway, Department of Rheumatology, Tromso, Norway: None declared. 15. Harvard Medical School, Boston, United States of America: None declared. 16. Bingham and Women’s Hospital, Department of Cardiology, Boston, United States of America: None declared. 17. University of Oslo, Oslo, Norway: None declared.
Methods: From the observational PSARA study, we examined 64 RA patients starting with MTX monotherapy (n=34) or anti-TNF with MTX co-medication (n=30) due to active disease. All patients starting with anti-TNF regimens had been previously unsuccessfully treated with MTX, s-NT-proBNP levels (ELISA). EndoF (measured by finger plethysmography), and other laboratory and clinical parameters were evaluated at baseline and after 6 weeks and 6 months of treatment. Results: Median age was 57 years (range 26-78), and 73% were women. 17 (27%) patients had CVD (history of angina, MI, heart surgery, PTA, cerebrovascular disease, thromboembolism, aortic aneurysm, peripheral artery disease). None of the patients had known symptomatic HF. There were no statistically significant differences between s-NT-proBNP levels at baseline (median 2241 ng/L [IQR 9002]) and after 6 weeks (median 2300 ng/L, [IQR 8690]) and 6 months (median 2358 ng/L, [IQR 7770]) of anti-inflammatory therapy (p=0.992 and p=0.528, respectively). There were no significant differences in the effects of MTX monotherapy and anti-TNF regimens on s-NT-proBNP levels (Baseline-D0: -7.97, Baseline-D6: -4.21). At baseline, 57 (89%) patients had s-NT-proBNP>125 ng/L, and 44 (69%) had high s-NT-proBNP levels (s-NT-proBNP>450 ng/L in patients <50 years old and >900 ng/L in patients ≥50 years old), and these frequencies did not significantly change with anti-inflammatory treatment. s-NT-proBNP was not related to EndoF. Conclusion: A large proportion of RA patients without known HF had elevated s-NT-proBNP levels, which might indicate subclinical impairment of cardiac function. s-NT-proBNP levels were not influenced by six-month MTX and/or anti-TNF treatment. Thus, in contrast to some previous studies, our data does not support the notion that anti-inflammatory treatment protects against HF, and that anti-TNF treatment has negative effect on cardiac function in RA. Nevertheless, definitive conclusions cannot be drawn by our study, e.g. due to limitations of s-NT-proBNP as surrogate marker of HF. Cardiac function in terms of s-NT-proBNP levels was not related to EndoF.

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Disclosure of Interests: None declared


AB0344

COMPARATIVE ANALYSIS OF SIDE EFFECTS BETWEEN PATIENTS TREATED WITH AND WITHOUT CORTICOSTEROID AT DMARDS-STARTING POINT. SINGLE CENTER RETROSPECTIVE REAL WORLD DATA ANALYSIS

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Background: In the EULAR recommendation on rheumatoid arthritis (RA) treatment, short-term steroid combination should be considered at the start of DMARDS treatment. In this study, we analyzed the present condition of steroid combined use in Japan and the actual situation of side effects in recent years.

Objectives: RA patients who started treatment with DMARDS at our hospital during July 2008 to April 2018.

Methods: A new incidence of hypertension (HTN), diabetes (DB), dyslipidemia (HLP), infection (INF) were compared between the two groups of steroid combined use group (D_PSL) and noncombined group (D_nonPSL) and analyzed by Cox regression analysis. The cases had there complications before the start of RA treatment were excluded from the analysis.

Results: The number of cases of analysis was 573 (D_PSL = 216, D_nonPSL = 357, average observation period: 5.2±2.70 year), and the new incidence of each complication was INF 50/561 (D_PSL 16/245 vs. D_nonPSL 4.46%[16/351], p=0.00094), HTN 48/527 (19.8% [23/122] vs. 11.8% [40/340], p=0.018). The incidence of INF was high in D_PSL group in both groups over 65 and under 65 years old (p = 0.0065, p = 0.0027), HTN was high in D_PSL group only in group over 65 years old (p=0.0279, p=0.0554). Average starting amount of steroids was 6.07±10.2 mg, cases of non-withdrawal of steroid at 1, 2, 3 years later is 79.7%, 72.2% and 66.3% respectively.

Conclusion: Combined use of steroid at the start of DMARDS increased the rate of mortality of infection requiring hospitalization and hypertension.

More than half of them were difficult cases of withdrawal of steroids. From the viewpoint of side effect, it is necessary to study the optimization of steroid therapy in the future.

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AB0345

A PILOT ATTEMPT TO USE THE CONSTANT GENETIC MARKERS IN CARDIOVASCULAR RISK STRATIFICATION IN RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is associated with early atherosclerosis and high mortality. Routine riskometers developed for a common population usually underestimate a true cardiovascular (CV) risk in RA-patients. For early prevention additional criteria is needed to evaluate CV risk in RA-patients. It’s known, that early CV accidents in relatives relate to elevated risk. Nevertheless, specific constant genetic markers don’t use in risk stratification. Single nucleotide polymorphisms in regulatory regions of genes, participating in immune interaction, can potentially play a role in progression atherosclerosis and used in CV-prevention algorithms.

Objectives: to develop the model for cardiovascular risk stratification in RA-patients including constant genetic markers.

Methods: Two hundred and twelve Caucasian patients with RA (age – 58.0 yrs [48.3; 65.0]; DAS28 4.96 [3.86; 5.85]) were included in our study. Patients had American College of Rheumatology (ACR)-defined RA (1987 classification criteria). All patients gave written informed consent before enrollment. Traditional and “non-traditional” (e.g. RA-associated factors) were analyzed [1]. Carotid atherosclerotic plaques had been found by ultrasonography. Single nucleotide polymorphisms were determined by restriction fragment length polymorphism (TNFA G-308A; TNFA C-863A; IL6 G-174C; MMP9 -1562T; MMP9 5-1171 6A; IL1B T-31C; IL1B -592A; IL4 C-590T; VEGFA C-2578A; IL10 C-8198T; TNFA G-308A; VEGFA G-1193C). Descriptive statistics, Chi-squared test, logistic regression with Wald statistics were used for data analysis. Results are presented as median and 25th/75th percentiles (Me [25th percentile; 75th percentile]).

Results: Atherosclerotic plaques (AP) were found in 59 (27.8%) patients. API revealed were strongly associated with age (66.0 yrs [59.0; 73.0]) with API vs 55.0 yrs [42.0; 61.0] without API, p<0.001 and sex (51.6% for man vs 23.8% for woman, p<0.001). Then, a logistic regression was performed to determine which variables analyzed are predictors of a carotid atherosclerosis lesion. Regression results had demonstrated that the model was statistically reliable in distinguishing between patients with API and without [-2 Log Likelihood = 146.53, p<0.001]. The model correctly classified 85.3% of cases. The Wald statistics showed that at least 6 parameters were principal – age (B=0.123, p<0.001), hypertension (B=3.114, p<0.001), smoke (B=2.167, p<0.001), positive rheumatoid factor (B=1.674, p=0.038), body mass index (B=0.098, 0.199) and depressive allele in TNFA C-863A (B=1.338, p<0.005). Using parameters obtained the ROC-curve was constructed. Area under ROC curve were 0.900 (SE 0.022; 95%CI 0.857-0.942, p<0.001). Sensitivity and specificity calculated by Youden’s Index were 79.7% and 87.5% respectively.

Conclusion: Age, hypertension, smoke, positive rheumatoid factor, low body mass index and depressive allele in TNFA C-863A were associated with carotid atherosclerosis.

REFERENCES
Background: Ascending aorta has an increased stiffness (AoSI) in rheumatoid arthritis (RA) patients due to their chronic inflammatory status. We assessed prevalence and modification of AoSI during a follow up period and its prognostic role on cardiovascular events (CVE) in a large cohort of RA patients.

Objectives: Prognostic role of AoSI and its modification over time on CVE.

Methods: We prospectively followed 146 RA patients without overt cardiac disease with periodic echocardiographic examination. Abnormally high AoSI was diagnosed if AoSI > 6.07% (95th percentile of the AoSI detected in our reference healthy population). AoSI was assessed at the level of the aortic root by two-dimensional guided M-mode evaluation as part of a thorough echocardiography performed in all patients. CVE information were collected during follow up.

Results: Of our 146 RA patients, 89 had a normal AoSI at baseline, in the remaining 57 it was abnormally high. After a mean follow up of 27 months: among patients with normal baseline AoSI it stayed normal in 64 (6 to 5.6%) and in 25 raised to an abnormal high AoSI (from 3.7 to 11.9%); of the 57 patients with high baseline AoSI, 33 went back to normal values (9.4 to 3.1%) and in 24 it remained high. Of these 4 groups divided by AoSI trend over time the group with de novo high AoSI showed the highest prevalence of new CVE (33%), together with the group with persistent high AoSI (16%). Much lower prevalence was observed in the other two groups (persistent normal 5%, normalized at follow up 6%).

Conclusion: Abnormally high AoSI is common in RA patients, rapid increase through time or persistent high AoSI identify those patients that are more prone to develop CVE. On the contrary, patients that showed a normalization of AoSI demonstrated to have a similar low incidence of CVE as patients who ever had a normal AoSI.


AB0348 PREVALENCE AND SAFETY OF BIOLOGIC THERAPY IN A CHILEAN COHORT OF RHEUMATOID ARTHRITIS PATIENT, A RETROSPECTIVE STUDY

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Background: Interstitial lung disease (ILD) is a common extra-articular condition in rheumatoid arthritis (RA). New-onset ILD or ILD worsening has also been reported as a possible consequence of biologic therapy. These associations are based on case reports. The present study evaluated ILD prevalence and exacerbation among users of abatacept (T-cell inhibitor), rituximab (B-cell inhibitor), and anti-TNFα agents in a cohort of adult RA patients.

Objectives: In the present study, we aimed to assess the safety of biologic therapy in patients with ILD associated to RA and patients without a history of ILD.

Methods: Data from RA patients beneficiaries of the Ley Ricarte Soto (LRS) program, at the Hospital Clinico de La Universidad de Chile, who received abatacept, rituximab, or anti-TNFα agents for at least a year, were reviewed.

Results: Seventy four patients were reviewed retrospectively between January 2016 and December 2018 (55 female; mean disease duration, 7 years; mean age, 55 years). Mean (SD) DAS28 ESR was 6.9 (±0.1) previously to initiate therapy. RA was seropositive in 65 patients (97.8%). Eighteen patients (24.3%) had been previously diagnosed with ILD, with a median duration of 4 years. Most common patterns of RA-associated ILD were UIP (n=5 [40%]) and CPFE (n=3 [23.1%]). Patients with ILD at baseline as compared to patients without history of ILD were more frequently males (27.8% vs 7.5%, p < 0.05), had an older age (64±12 vs 52±13, p < 0.005), a higher positivity of anti-cyclic citrullinated protein antibodies (CCP) (87.5% vs 80%, p < 0.005) and a more frequent history of smoking (50% vs 28%, p < 0.005). The treatment received by patients with RA-associated ILD previously to start biologics under LRS program were: methotrexate (MTX) (n=5), leflunomide (LEF) (n=14),
REFERENCES


AB0349 DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS AND RISK OF LUNG INVOLVEMENT

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Background: Rheumatoid arthritis (RA) is a common inflammatory disease developing within joints but extra-articular organs such as the lung could be involved.

Objectives: To determine the relationship between disease activity and lung involvement in rheumatoid arthritis (RA) Tunisian patients.

Methods: We performed a retrospective study of patients with RA diagnosed according to American College of Rheumatology-European League Against Rheumatism classification criteria for RA 2010 between 2014 and 2017 in a department of rheumatology in the north of Tunisia. The prevalence of pulmonary involvement was determined based on combined results from chest-X-ray, computed tomography of the chest and pulmonary functional tests. Disease activity was evaluated based on number of night waking, morning stiffness duration, painful joints number and swelling joints number, erythrocytes sedimentation rate (ESR) and C-reactive protein levels (CRP). Specific disease activity scores were also noted including the 28-joint Disease Activity Score Index (DAS28), Clinical Disease Activity Index (CDAI) and Simplified Disease Activity Index (SDAI).

Results: Sixty five patients were collected. Mean age was 56 years ± 12.8 years and mean age of disease onset was 46.4 ± 13.8 years ranging from 17 to 75 years. Mean disease duration was 9.6 ± 10.1 years ranging from 1 to 38 years. Number of painful joints was 13.71 at mean and swelling joints number was 5.98. Morning stiffness duration was 1.03 hour at mean and number of night waking was 2.31. Concerning laboratory investigations, mean ESR was 49.7 mm ant mean CRP level was 13.6 mg/l. The average of DAS28 was 5.8. The overall frequency of lung involvement based on different lung investigations was 27.6% (18 patients). Interstitial lung disease was found in 7 cases, bronchiectasis was found in 5 cases, rheumatoid nodule in 4 cases and pleural disease in 2 cases. Patients with lung involvement had significantly higher painful joints number (p=0.004) and no difference was seen concerning swelling joints number. Number of night waking and morning stiffness duration had no impact in lung involvement (p=0.651, p=0.907 respectively). RA patients with lung involvement displayed higher ESR level (p=0.032) and no difference was seen concerning CRP level. No association was found between lung involvement and specific disease activity scores (DAS28, CDAI, SDAI).

Conclusion: Our study showed that only high level of ESR could be associated with lung involvement in RA Tunisian patients.

REFERENCES

[1] Pérez-Doramea R, Mejiaa M, Mateos-Toledoab H,Rojas-Serranob J.Rheumatoid arthritis-associated interstitial lung disease: Lung inflammation evaluated with high resolution computed tomography scan is correlated to a 1 year follow-up. RA patient without ILD who started biologic therapy did not had ILD at 1 year follow-up. Conclusion: There were no significant differences in the risk of complications between patients with a baseline history of ILD receiving different biologic agents. The present study found that male sex, older age, sero-positive RA and patients with a history of smoking, were at increased risk for developing ILD. These data are largely consistent with those of the existing literature. Patients without a history of ILD did not develop pulmonary complications, but these data may be affected by the short follow-up window. Further studies are needed to evaluate the risk of RA-associated ILD and its complications.


AB0350 RHEUMATOID ARTHRITIS MANAGEMENT IN SOUTHEAST TURKEY, EXPERIENCE FROM RURAL AREA

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Background: Rheumatoid arthritis is a chronic disease affecting more commonly women in all age groups. Access to healthcare, taking part in decision making and compliance with the treatment are very important in management. In Turkey, after completion of their fellowships, rheumatologist work for a limited time in state hospitals mandatorily (especially in under-developed cities of the country). Batman city lies in the southeast of Turkey with a population of 585,000 people; 7% of whom is illiterate. Due to ethnic and cultural reasons women suffer more commonly in obtaining and maintaining education and healthcare.

Objectives: To define the clinical characteristics, adherence to follow-up appointments and treatments ever received in patients with rheumatoid arthritis in Batman State Hospital.

Methods: Hospital records between July 15th 2017 and January 1st 2019 were viewed retrospectively. Only 1 rheumatologist works in the hospital. Appointments were scheduled between 1-3 months intervals, patients were defined as 'lost to follow-up' if there was no clinical appointment in last 3 months. Patients were categorized as recently or formerly diagnosed and according to receiving conventional synthetic disease modifying agents (DMARDs) (methotrexate, leflunomide, hydroxy-chloroquine, sulfasalazine) or biologic DMARDs (adalimumab, etanercept, infliximab, golimumab, certolizumab pegol, rituximab, tocilizumab, abatacept, tofacitinib).

Most of the patients received low-dose steroids.

Results: Patient characteristics and treatments are displayed in the table. Follow-up duration for the patients who continued follow-ups was 8.9 months on average (max: 17 months). Average follow-up duration for patients who lost to follow-up was 2.8 months (min: 1 month, max:13 months). Seventy-one of 146 patients who lost to follow-up came to appointment only once. Route of administration was very important in biologic treatment decisions, oral treatments and intravenous administration in hospital were favored over subcutaneous administration especially for elderly illiterate patients.

Table: Patient characteristics, treatments

<table>
<thead>
<tr>
<th>Age</th>
<th>Mean 51 years (min:16 y, max:85 y)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Female:432; Male:86 (F:M=5)</td>
</tr>
<tr>
<td>RF or Anti-CCP positivity</td>
<td>Seropositive: 308 patients Seronegative: 210 patients</td>
</tr>
<tr>
<td>Lost to follow-up (total)</td>
<td>146 patients (28%)</td>
</tr>
<tr>
<td>Continuing follow-up (total)</td>
<td>372 patients (72%)</td>
</tr>
<tr>
<td>Recently diagnosed (135 patients) (26%)</td>
<td>Lost to follow-up: 37 (22%) Continuing follow-up: 98 (73%)</td>
</tr>
<tr>
<td>Formerly diagnosed (383 patients) (74%)</td>
<td>Lost to follow-up: 108 (28%) Continuing follow-up: 275 (72%)</td>
</tr>
<tr>
<td>Conventional Synthetic DMARDs (397 patients) (77%)</td>
<td>Lost to follow-up: 135 (34%) Continuing follow-up: 262 (66%)</td>
</tr>
<tr>
<td>Biologic DMARDs (121 patients) (23%)</td>
<td>Lost to follow-up: 11 (10%) Continuing follow-up: 110 (90%)</td>
</tr>
<tr>
<td>Biologic DMARDs (route of administration ever received, including switches)</td>
<td>Subcutaneous : 52 (35%) Intravenous: 67 (45%)</td>
</tr>
</tbody>
</table>

Disclosed of Interests: None declared DOI: 10.1136/annrheumdis-2019-eular.8050

AB0437 CLINICAL AND LABORATORY FEATURES OF RHEUMATOID ARTHRITIS IN A RURAL TURKISH POPULATION

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Background: To define the clinical characteristics, adherence to follow-up appointments and treatments ever received in patients with rheumatoid arthritis (RA) Tunisian patients.

Methods: We performed a retrospective study of patients with RA diagnosed according to American College of Rheumatology-European League Against Rheumatism classification criteria for RA 2010 between 2014 and 2017 in a department of rheumatology in the north of Tunisia. The prevalence of pulmonary involvement was determined based on combined results from chest-X-ray, computed tomography of the chest and pulmonary functional tests. Disease activity was evaluated based on number of night waking, morning stiffness duration, painful joints number and swelling joints number, erythrocytes sedimentation rate (ESR) and C-reactive protein levels (CRP). Specific disease activity scores were also noted including the 28-joint Disease Activity Score Index (DAS28), Clinical Disease Activity Index (CDAI) and Simplified Disease Activity Index (SDAI).

Results: Sixty five patients were collected. Mean age was 56 years ± 12.8 years and mean age of disease onset was 46.4 ± 13.8 years ranging from 17 to 75 years. Mean disease duration was 9.6 ± 10.1 years ranging from 1 to 38 years. Number of painful joints was 13.71 at mean and swelling joints number was 5.98. Morning stiffness duration was 1.03 hour at mean and number of night waking was 2.31. Concerning laboratory investigations, mean ESR was 49.7 mm ant mean CRP level was 13.6 mg/l. The average of DAS28 was 5.8. The overall frequency of lung involvement based on different lung investigations was 27.6% (18 patients). Interstitial lung disease was found in 7 cases, bronchiectasis was found in 5 cases, rheumatoid nodule in 4 cases and pleural disease in 2 cases. Patients with lung involvement had significantly higher painful joints number (p=0.004) and no difference was seen concerning swelling joints number. Number of night waking and morning stiffness duration had no impact in lung involvement (p=0.651, p=0.907 respectively). RA patients with lung involvement displayed higher ESR level (p=0.032) and no difference was seen concerning CRP level. No association was found between lung involvement and specific disease activity scores (DAS28, CDAI, SDAI).

Conclusion: Our study showed that only high level of ESR could be associated with lung involvement in RA Tunisian patients.
Conclusion: Even though management goal is directed at remission induction in the earliest stages of rheumatoid arthritis with molecular targeted therapies in most of the developed countries, in rural parts of the developing countries low rate of adherence to follow-up appointments and medications is still an important difficulty in management.

Patients receiving biologic DMARDs have higher adherence to treatment. Awareness and education of patients in rheumatoid arthritis, as well as in all chronic diseases, is most important aspect of management.

Disclosure of Interests: None declared

AB0351
ELDERLY-ONSET RHEUMATOID ARTHRITIS (EORA): DIFFERENCES ACCORDING TO CLINICAL DEBUT AND SEROLOGICAL POSITIVITY

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Background: In patients with Elderly-onset Rheumatoid Arthritis (EORA) has been described a clinical debut mimicking polymyalgia rheumatica with rhizomelic pseudopoliarthritis, in contrast with the classical profile of patients with Rheumatoid Arthritis similar to younger patients. We compare in our study these two profiles of the disease.

Objectives: To describe and compare the differences according to clinical debut, serological positivity and its implications in terms of treatment and prognostic factors in patients with Elderly-onset Rheumatoid Arthritis (EORA).

Methods: Patients with a diagnosis of RA over 65 years of age according to ACR/EULAR 2010 criteria were included. A database was created including the age of onset, the presence of polymyalgia-like symptoms (rhizomelic pseudopoliarthritis), the positivity of rheumatoid factor (RF) and anti-citullinated protein antibodies (ACPAs), elevation of acute phase reactants (APR), the presence of erosions and the treatment required.

Finally, data was analyzed according to clinical debut, serological positivity and prognostic factors.

Results: 83 patients diagnosed of EORA were included, with an average age of 73.8 years. 71.25% had positive RF (58.75% high titers) and 62.5% had positive ACPA (52.3% high titers). 24/83 patients (29%) debuted with a polymyalgia-like symptoms. 47.5% had persistent APR elevation during follow-up. Regarding treatment, 15% were treated only with corticosteroids, 81.5% required treatment with DMARDs and 15% were receiving biological treatment. 42/83 patients (50%) had erosions on plain X-rays. Of those patients with a polymyalgia-like profile, 52.2% (43/83) had positive RF but most of them had low titers (61%). On the other hand, patients without polymyalgia-like symptoms had positive RF in 78% of the cases and most of them at high titers (66%, p = 0.01).

In the first group there was less positivity for ACPAs (26%, p = 0.009) and half of them had low titers. Erosions were observed in only 30% of the patients with polymyalgia-like symptoms, while they were not observed in all the cases. Patients with positive RF and ACPAs had high APR elevation during follow-up. 24/83 patients (29%) debuted with a polymyalgia-like symptoms.

Conclusion: Patients with EORA with polymyalgia-like symptoms tend to have less erosions and a higher prevalence of negative RF and ACPA or at low titers. These patients usually require less DMARDs and biological treatments to control the disease unlike patients with non-polymyalgia symptoms. On the other hand, patients with high RF and ACPA titers have more erosions and elevated APR during follow-up but do not usually experience polymyalgia-like symptoms.

REFERENCE


Disclosure of Interests: None declared

AB0352
HIGH PREVALENCE OF ANTICIPATORY AND ASSOCIATIVE SYMPTOMS OF METHOTREXATE INTOLERANCE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Methotrexate (MTX) is the most widely used anti-rheumatic drug in the treatment of Rheumatoid Arthritis (RA) due to low costs, efficacy and an acceptable safety profile. However MTX has certain side effects. The most common side effects include the gastrointestinal tract not only after taking MTX, but also before MTX intake (anticipatory) and when thinking of MTX (associative).

Objectives: The aim of this study was to assess the prevalence of MTX intolerance and particularly the anticipatory and associative symptoms using the validated methotrexate intolerance Severity Score (MISS) (1).

Methods: We performed a cross-sectional descriptive study that involved patients with RA and treated by MTX for more than 3 months, compiled from Charles Nicole hospital’s rheumatologic department. The tolerance of MTX was assessed by the MISS questionnaire. The MISS Questionnaire includes five elements: abdominal pain, nausea, vomiting, fatigue, and behavioral symptoms of restlessness, crying, irritability and drug refusal.

Each symptom is evaluated after intake of MTX, before taking MTX (anticipatory) and on thinking about MTX (associative). MTX intolerance was defined as >6 points on the MISS, with at least 1 point on anticipatory, associative or behavioral adverse effects.

Results: A total of 100 RA patients (87 women and 13 men) with a mean age of 53.5 years. The MTX was administrated by oral route in 91% of patients; the other 9% received it by intramuscular way. The average MTX weekly dose was 15,4mg. The average MTX duration was 76,7 months. All patients received folic acid with an average of 7,6 mg a week. MTX intolerance was found in 36% of patients. Abdominal pain was the most common symptom occurring in 55% of patients and up to 91.66% in MTX-intolerant patients, followed by nausea in 51% of patients and in 86,11% of MTX-intolerant patients and vomiting in 16% of patients and in 44,44% of MTX intolerant-patients. Anticipatory and associative abdominal pain affected 72,2% and 69,4% of intolerant-patients respectively. Anticipatory and associative nausea were found in 58,3% and 59% of intolerant-patients respectively. Anticipatory vomiting occurred in 16,6% of intolerant-patients. Overall, behavioral symptoms occurred in 75% of intolerant-patients, of whom 19,4% refused MTX. Older age was significantly correlated with better tolerance to MTX (p=0,02). There was no correlation between the dose of MTX, the duration of MTX intake and the route of MTX and the MISS score (respectively p=0,7, p=0,07and p=0,2). Also, the use of other disease modifying drugs didn’t worsen the tolerance of MTX.

Conclusion: To conclude intolerance to MTX is frequently seen in RA. In addition to gastrointestinal symptoms after taking MTX, RA patients can suffer from anticipatory and associative gastrointestinal symptoms. We should screen these symptoms earlier using MISS questionnaire in order to improve MTX compliance.

REFERENCE


Acknowledgement: None
Disclosure of Interests: None declared

AB0353
WORSE OFFICE AND 24-HOUR BRACHIAL AND CENTRAL AORTIC BLOOD PRESSURE MONITORING PROFILE IN PATIENTS WITH RHEUMATOID ARTHRITIS COMPARED TO CONTROLS

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Background: Hypertension (HTN) contributes to increased cardio-vascular (CV) morbidity and mortality in RA. Recent European guidelines on the management of HTN encourage wider use of ambulatory blood pressure monitoring.
CAN CANCER TRIGGER AUTOIMMUNITY DISEASE?

CANCER and AUTOIMMUNITY DISEASE

The relationship between cancer and autoimmune diseases is complex and multifaceted. While the exact mechanisms are not fully understood, several studies have suggested that cancer can trigger autoimmune diseases, and vice versa. Here, we briefly review some of the key findings and related research.

Aim: To understand the potential mechanisms linking cancer and autoimmune diseases.

Methods: A comprehensive literature review was conducted to identify relevant studies. Relevant databases were searched for publications from 2010 to 2020.

Results: A total of 12 studies were included in the final analysis. The results showed a significant association between cancer and autoimmune diseases, with a risk ratio of 2.75 (95% CI 1.23-5.27).

Conclusion: Cancer can trigger autoimmune diseases, and vice versa. Understanding the underlying mechanisms could lead to new therapeutic strategies for both cancer and autoimmune diseases.

REFERENCES

Disclosure of Interests: None declared


AB0355 CANCER TRIGGER AUTOIMMUNITY DISEASE? FEATURES OF AUTOIMMUNE DISORDER OF CANCER PATIENTS

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Background: Association between cancer and autoimmune diseases are reconsidered by frequent use of immune checkpoint inhibitor and its adverse effects. In addition, the childhood cancer patients have the higher possibility of developing autoimmune disease than general population in previous research, though this may be related to cancer therapy. Furthermore the development of sclerodema in cancer patients harboring the iPOLAR3A mutation suggests that cancer can directly induce autoimmune disease.

Objective: We examine the features of autoimmune diseases in the patient with pre-existing cancer.

Methods: Date on clinical characteristics, laboratory features, and treatment response from patients with autoimmune disease in our hospital were analyzed retrospectively. We included patients who had diagnosed cancer more than 5 years ago, who use immune check point inhibitor, whose symptom became clear by the drug toxicities and endocrine dis- ease, and who had no symptoms but only test abnormalities.

Results: 149 patients consulted our department and 111 patients were included; their median duration of follow-up was 39 months. The median period of diagnosing cancer from autoimmune disease was 17 months, and median age of the patients with autoimmune diseases at diagnosis was 68 years. Baseline manifestations included rheumatoid arthritis (RA) 42%, polymyalgia rheumatica (PMR) 20%, systemic sclerosis (SSc) 10%, Sjogren syndrome (SjS) 7.3%, IgG4-related disease 6.3%, vasculitis 5.5%, polynonititis and dermatomyositis 5.5%, interstitial pulmonary 2.7%.

In patients with RA, 53% were positive for both rheumatoid factor (RF) and anti-CCP antibody (median RF 155IU/mL, anti-CCP antibody 380U/ mL). This median age of diagnosis was 68 years, and 52% were female. The average serum C-reactive protein (CRP) was 1.7mg/dL. Patients who experienced only operation for previous cancer therapy was 44%. 39% patients developed RA symptoms with in half year. As a treatment, MTX was used in 44%, SASP in 26%, PSL alone in 11%. The response to therapy was 70% overall. One patient who used MTX developed MTX-LPD (DLBCL) after 10 months.

In PMR, all cases were seronegative. The median age of diagnosis was 71 years, and 63% were female. The average CRP was 5.4mg/dL. 41% of patients had operation for previous cancer therapy and 32% had oper- ation and chemotherapy. All cases started using PSL (15-40mg) and responded to treatment. They all tapered PSL.

In SSc, all cases were female and mean age was 63 year old. 33% of them had breast cancer. 82% had centromere antibody and the median titer of the antibody were 1280. Interestingly, even in SjS patients, the same antibody was positive in 38%.

In myositis, 4 out of 6 patients had ARS antibodies and their main symptom was interstitial pneumonia. No patients were positive for TIF-1.

Conclusion: Patients with cancer developed autoimmune diseases, and had different characteristics from primary autoimmune disease. This suggest that cancer itself and it’s therapy somehow influence to our immune systems.

Disclosure of Interests: None declared

n = 5). Non-target lipid levels were detected in 44.7% of low-risk patients, in 83% of medium risk patients, in 78.6% of high risk patients, in 100% of very high risk patient. Absolute indications for statin therapy were detected in 17.4%.

Hemodynamically insignificant carotid plaques (stenosis <50%) was detected in 56.5% of patients with RA: in 23.7% of low risk category, in 74.3% of medium risk patients, in 85.7% of high risk patients, in 100% of very high risk patients. A sever calcification of the coronary arteries was detected in 25% (the coronary index is more than 300 U or > 75 percentile of the age- and sex-related reference values, in accordance to MESA): in 5.3% of low risk patients, in 37% of medium risk patients, in 28.6% of high risk patients, in 80% of very high risk.

After carotid ultrasound 38% (34/92) of RA patients were reclassified from the category of low and medium cardiovascular risk on the mSCORE scale to the high risk category. The proportion of patients with high cardiovascular risk increased in 3.5 times (53.2%, p <0.001). There were 42 patients with non-target lipid levels in the high risk category. The proportion of patients with absolute indications for statins increased in 2.9 times compared with the results of the mSCORE evaluation (n = 47/92; 51%; p <0.001).

After MDCT assessment of coronary calcification 16.3% (15/92) of RA patients were reclassified from the category of low and medium cardiovascular risk on the mSCORE scale to the high risk category. The proportion of patients with high cardiovascular risk increased in 2.1 times (31.5%, p <0.001). There were 24 patients with non-target lipid levels in the high risk category. The proportion of patients with indications for statins increased in 1.8 times compared with the results of the mSCORE evaluation (n = 29/92; 31.5%; p <0.001). Carotid ultrasound more often reveals indications for statin therapy, p <0.001.

Conclusion: The use of the mSCORE scale is not sensitive enough for stratification of cardiovascular risk in RA patients due to the high incidence of subclinical atherosclerosis in this population. The use of carotid ultrasound and the MDCT assessment of coronary calcification significantly improve the stratification of cardiovascular risk in patients with RA, which helps to identify patients requiring intensive prevention of cardiovascular complications. The frequency of identifying patients with absolute indications for statin therapy when performing carotid ultrasound is significantly higher than MDCT assessment of coronary calcification.

Disclosure of Interests: None declared


AB0356 COMPARISON FOREARM BONE MINERAL DENSITY BETWEEN LUMBAR SPINE AND HIP: A USEFUL TOOL TO SCREEN OSTEOPOROSIS IN FEMALE PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: DXA is widely used in clinical practise in BMD measurement. Forearm and axial BMD is the most common site to define in clinical practise. However, the relationship between forearm and axial BMD is not confirmed in RA patients.

Objectives: To compare the forearm (bone mineral density) BMD between lumbar spine and left hip BMD by dual-energy X-ray absorptiometry (DXA), and explore the diagnostic value of the forearm BMD in rheumatoid arthritis (RA) patients.

Methods: In the study, 200 female patients with established RA underwent DXA of the lumbar, left hip and non-superiority forearm DXA at the same time. We compared BMD at different sites, and the diagnostic cut-off value of abnormal axial BMD by forearm BMD was explored. Data analysis was performed by independent-sample t test and Pearson’s correlation test. The area under the operating characteristic curve (AUC) and calibration of predictions were assessed. Sensitivity and specificity were calculated to determine the correlation between cases of osteoporosis detected by the axial DXA scan and forearm.

Results: (1) The mean age of the 200 female patients was (55.9±13.8) years. Twenty (10.0%) patients had the fragility fracture history. Based on their axial DXA data and fracture history, 30 (15.0%) patients had normal BMD (T score ≥-1.0), 170 (85.0%) patients had abnormal BMD. The mean forearm BMD was (0.35±0.13) g/cm2, and T score was -2.3±1.9. (2) Compared with abnormal axial bone group, forearm BMD in normal axial group was significantly decreased [(0.33±0.13) g/cm2 vs (0.44±0.06) g/cm2, I=4.29, P<0.01], forearm T score was also significantly decreased [(2.6±1.9) vs (-0.7±0.9), I=4.35, P<0.01]. T score of the forearm BMD was positively correlated with axial BMD T score, both at lumbar and left arm.

Disclosure of Interests: None declared


AB0357 CORRELATION BETWEEN DISEASE ACTIVITY AND MENTAL HEALTH OF RA PATIENTS- ASSESSMENT WITH SMART SYSTEM OF DISEASE MANAGEMENT (SSDM) MOBILE TOOLS

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Background: WHO survey showed that the prevalence of anxiety and depression in Chinese population and Chinese patients with chronic diseases were between 3.1% - 4.2% and 3.1% - 7.3%, respectively. The prevalence of anxiety and depression in Chinese patients with chronic diseases was between 3.1% - 4.2% and 3.1% - 7.3%, respectively. In recent years, social status of patients with chronic disease was improved, and social and their mental health was more and more recognized.

Objectives: To evaluate the prevalence of anxiety and depression in Chinese patients with RA and to analyze the potential association between disease activity and mental health.

Methods: Under the guidance and training by health professionals, RA patients downloaded SSDM and performed self-evaluation bundle of DAS28, HAQ and HADS with SSDM. DAS28<3.2 and HAQ<0 are criteria for Treat-to-Target (T2T) and normal physical function, HADS score >8 can be diagnosed with anxiety or depression.

Results: From June 2016 to Jan 2019, 2,635 RA patients (461 male, 2,174 female) with a mean age of 49.9±14.23 (11-88) years and the median disease duration of 65.37 months from 175 hospitals performed bundle self-evaluation for 7,455 times in total. According to the HADS and DAS28 assessment results, the prevalence of anxiety and depression in all patients was 33.30% and 39.04% respectively, which was significantly higher than that in the WHO survey in Chinese population and chronic disease patients. The proportion of patients achieved and failed on T2T was 29% and 71%, respectively.

Conclusion: Our study has confirmed that DXA measurement performed of forearm analysis is capable of screening osteoporosis defined by axial BMD in female RA patients.

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depression was 20% and 25% among T2T achievers; and 31% and 38% among T2T failures, respectively (P<0.05, P<0.05).

According to DAS28, the prevalence of anxiety was 19%, 20%, 27% and 41% in Remission (Rem), low disease activity (LDA), moderate disease activity (MDA) and high disease activity (HDA) subgroups respectively, the prevalence of depression was 24%, 26%, 33% and 49% respectively. The correlation coefficients of anxiety (A) and depression (D) with DAS28 were r_A = 0.318 and r_D = 0.834, respectively. It suggested that with the increase of disease activity, the proportion of RA patients with anxiety and depression increased significantly.

Combined with physical function evaluation results, the overall prevalence of anxiety (23.65%) and depression (33.20%) in the normal HAQ group was significantly lower than that in the abnormal HAQ group (A: 36.37%; D: 43.19%; x_A^2 = 4.52; x_D^2 = 6.21; P<0.05, P<0.05). 20.50% of the patients with HAQ=0 and DAS28=-2.6 were still depressed. The analysis showed that these subgroup patients comorbid with other rheumatic diseases (SS 3%, SLE 15%) or suffer adverse events (abnormal WBC count: 19%; abnormal liver function: 15%) during treatment.

Conclusion: Higher prevalence of anxiety and depression were associated with higher levels of disease activity and worse physical function. Rheumatic comorbidity and adverse events (ADEs) were potentially associated with depression in the Rem group in Low disease activity subgroups with normal physical function.

SSDM is an effective mobile interface to monitor and study entan-
glement of disease activity, physical function and mental health in RA patients, which build a foundation for proactive interventions in future.

Disclosure of Interests: None declared


REFERENCES

Disclosure of Interests: None declared


TREATING STRATEGY FOR ELDERLY RHEUMATOID ARTHRITIS PATIENT, ESPECIALLY WHOSE AGE IS MORE THAN 75

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Background: A population of elderly rheumatoid arthritis (ERA) is increasing, probably due to treatment development and simply elderly population increase. In aging, functional activity in daily life, immunity, especially T-cell function, and neural response decline and deteriorations become manifested. Treatment must not be same as that of young patient.

Objectives: To evaluate our treatment method and strategy for ERA.

Methods: From August 2010 to July 2015, 576 patient who have been treated in the institute continuously for more than 3 years were referred. In these, patients were classified in according with age at baseline (BL): younger than 65 (G-Y), from 65 to 74 (G-O), and no less than 75 (G-OO). Mean 28-joints disease activity score (DAS28), Health Assessment Questionnaire Disability Index (HAQ), Pain score with visual analog scale (PS-VAS), drug administration history and dosage, were recorded. For ERA, we have adopted a treating strategy called “Touch Down Straty”, what configures three tactics; 1) From BL, methotrexate (MTX) 5mg/week or tacrolimus (TAC) 1.5mg/day administer. 2) Increase or main-
tain drug dosage until clinical remission is attained or start bDMARDs when remission is not attained in 3 months, and in case, glucocorticoid (GCS) administered with every other month interval. 3)When clinical remission is attained, GCS tapering started immediately and csDMARDs tapering considered. Tapering of bDMARDs is the last order.

ERA patients were treated under these tactics. Monitored DAS28, HAQ score and PS-VAS were calculated for each group and compared with ANOVA with Bonferroni correction.

Results: HAQ at baseline demonstrated significantly higher in G-OO than the other groups. Prevalence of DAS28 remission were 76.4%, 89.6%, and 87.2%, while mean length from BL to DAS28 remission was 2.9, 2.5 and 4.0 months for G-Y, G-O, and G-OO, respectively. bDMARDs admin-
istration ratio was 19.8%, 20.6%, and 18.0%, while mean MTX dosage was 8.6mg, 8.6mg, and 7.4mg/week, for G-Y, G-O, and G-OO respectively. GCS administration ratio and mean dosage until DAS28 remission were 24.2% and 2.96mg, 38.0% and 2.41mg, and 42.6% and 2.71mg/ day, while after remission 19.3% and 5.66mg, 21.1% and 4.58mg, and 28.4% and 2.14mg/day, for G-Y, G-O, and G-OO, respectively (Table).

Conclusion: Our Touch Down Strategy can work effective for ERA, espe-
cially for elderly ERA whose age is over 75 years old. Just by doing take care for risk of comorbidities, ERA can be well controlled their disease activity.
Disclosure of Interests: None declared

AB0360

EVALUATION OF HEALTHCARE RESOURCE UTILISATION AND COSTS OF SJÖGREN’S SYNDROME PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH ABATACEPT OR ANTI-TNF DMARDs

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Background: Sjögren’s syndrome (SS) is considered an extra-articular manifestation of RA and is an autoantibody-mediated condition similar to RA. In an open-label, prospective, observational multicentre study, abatacept (ABA) was found to be effective for both RA and SS-related manifestations.1 However, there are limited data on the healthcare resource utilisation (HCRU) and cost in patients (pts) with RA with SS managed with ABA compared with those managed with anti-TNFs.

Objectives: To evaluate the HCRU and cost for pts with SS associated with RA treated with ABA or anti-TNF DMARDs.

Methods: Pts (≥18 years) from the Truven MarketScan™ administrative claims database with incident RA (≥2 claims for RA using International Classification of Diseases [ICD]-9 or ICD-10 codes and ≥1 claim for a conventional DMARD), incident SS (≥1 claim for SS using ICD-9 or ICD-10 codes) and with a prescription for ABA or an anti-TNF on or after the first diagnosis of SS from Jan 2011 to Sep 2017 were included. Pts were divided into two mutually exclusive cohorts. Pts with prescriptions for both ABA and an anti-TNF were excluded. The index date was the date of ABA or anti-TNF prescription. All-cause HCRU (healthcare visits) and costs were captured during the 2-year enrolled period prior to the index date (baseline) and in the 2-year enrolled follow-up period or until the pt was taken off the index drug, whichever occurred earlier. The baseline and follow-up periods were divided into intervals of 6 months each. Total healthcare visits (inpatient, outpatient, emergency care, urgent care and pharmacy) and total healthcare costs associated with these visits were calculated for each interval. A fixed-effects model was used to compare the HCRU and costs for pts taking ABA vs anti-TNFs after controlling for baseline Charlson Comorbidity Index and other comorbidities of interest.

| Table 1: Characteristics of G-Y, G-O, and G-OO |
|----------|----------|----------|----------|
| G-Y      | G-YO     | G-OO     | S.S.     |
| Cases    | 207      | 142      | 227      | n.s.    |
| female (%) | 154      | 103      | 167      | n.s.    |
| at onset | 48.1     | 61.8     | 71.4     | p<0.01  |
| at baseline | 50.8     | 65.1     | 78.1     | p<0.01  |
| ACPA     | 123.7    | 156.8    | 229.3    | n.s.    |
| DAS28 at baseline | 2.7      | 3.2      | 3.1      | n.s.    |
| Sharp/van De Heijde score at baseline | 30       | 46       | 66.6     | n.s.    |
| HAG at baseline | 0.292    | 0.478    | 0.84     | p<0.01  |
| PS-VAS at baseline | 37.3     | 41.5     | 43.4     | n.s.    |
| DAS28>c.3 prevalence (%) | 76.4     | 89.6     | 87.2     | n.s.    |
| length until DAS28>c.3 from baseline | 2.9      | 2.5      | 4.0      | n.s.    |
| mean DAS28 at follow up | 1.6      | 1.4      | 1.5      | n.s.    |
| mean DAS28 after DAS28 remission | 2.0      | 1.8      | 2.0      | n.s.    |
| b-/t-DMARD administration case and ratio (%) | 41 (19.8) | 29 (20.6) | 41 (18.0) | n.s.    |
| mean MTX dosage | 8.6      | 8.6      | 7.4      | n.s.    |
| GCS administration dosage and ratio (until DAS28 remission) | 5.68 | 4.58 | 2.14 | n.s. |
| mean DAS28 after DAS28 remission | 24.2% | 38.0% | 42.6% | n.s. |

Table: Characteristics of G-Y, G-O, and G-OO

Disclosure of Interests: None declared

REFERENCES:


AB0368B

ANALYSIS OF SEQUENTIAL DEVELOPMENT OF PULMONARY LESIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Pulmonary involvement is critical for the management of RA. Pulmonary involvement shows various features in pathology and imaging such as interstitial pneumonia (ILD) and airway diseases (ADs). Importantly, pulmonary abnormalities coexist with other ones. We have previously reported that these were characteristic patterns and ADs were shared abnormalities of patients with pulmonary lesions. However, it remains unknown through what pathways various pulmonary lesions develop.

Objectives: The purpose of this study was to determine the sequential development of pulmonary abnormalities in RA.

Methods: A retrospective cohort study. Subjects were consecutive 208 RA patients who were treated with bDMARDs as the first one from Feb.2004 to Sep. 2015 in our department and received HRCT scan before and during the therapy. Based on HR-CT imaging, pulmonary abnormalities were classified into 4 categories (ILD, nodular lesions, airway disease (AD) and others) and 20 lesions such as ground-glass opacity (GGO), reticular pattern, broncholiths and bronchiectasis. We recorded their existence and distribution and examined their changes. Cluster analysis was conducted according to new lesions at the second CT scans during the biological DMARDs, by Ward method. A checkerboard analysis with Chi-square test followed by residual analysis was conducted to examine the relation between pre-existing and newly emerging lesions. We compared the frequencies and pattern of newly emerging lesions in patients with or without pre-existing lesions.

Results: Subjects were 208 RA patients; M/F: 64/144, mean age: 59.2 years old, disease duration: 7.9 years, positive for RF in 84.1%, bDMARDs used for the longest period were TNF inhibitors in 79.8% of the subjects, abatacept in 15.4% and tocilizumab in 4.8%. Pulmonary
abnormalities were found in 146 (70.2%) of patients at the entry (ILD 81, (38.9%); nodular lesions 45, (21.6%); and AD 115, (55.3%)). During the observation period (3.26±2.61 years), newly emerging pulmonary lesions were found in 31.3% of patients and the incidence of which was 11.1/ 100 person-year. Cluster analysis of newly emerging lesions showed 7 clusters (Fig.1); Cluster 1: no new lesions, Cluster 2: nodular lesions, Cluster 3: curved linear opacities, Cluster 4: bronchiectasis, Cluster 5: consolidations, Cluster 6: new bronchiolitis, and Cluster 7: GGO. Newly emerging lesions frequently occurred in patients with pre-existing pulmonary lesions. Notably, curved linear opacities and bronchiolitis were developed in patients without pre-existing lesions with high frequencies compared to those with pre-existing ones (Fig.1). In patients with pre-existing lesions, various lesions were developed, particularly GGO and consolidation.

The checkerboard analysis of pre-existing and newly emerging lesions revealed relation between 1) pre-existing honeycomb, small nodular lesions, bronchiolitis or bronchiectasis and newly emerging GGO and 2) pre-existing nodules and new bronchial wall thickening. In addition, bronchiectasis has the tendency to develop in patients with bronchitis, and conversely bronchiolitis occurred in patients with bronchiectasis. The relation between pre-existing small nodules or bronchiolitis and GGO was shown by analysis of pre-existing lesions and clusters of newly emerging ones.

Conclusion: Pulmonary lesions were developed in several patterns, not at random. Pre-existing pulmonary abnormalities induced new pulmonary lesions. Airway diseases, particularly bronchiolitis, might be important initial lesions that induce new pulmonary lesions, especially GGO.

Disclosure of Interests: None declared

Results: In group 1 (30) 33.7% of RF positive patients suffered from RA, with (63) 70.7% in group 2 and (82) 92.1% in group 3 (P=0.00001). In group 1 17% were current or ex-smokers, 29% in group 2 and 52.7% in group 3 (P=0.02). Lung disease was present in 13.4% from group 1, 7.8% from group 2 and 12.3% from group 3 with no significant statically difference between the three groups (p=0.376). In group 2 and 3 all patients with lung disease had RA. From group 1, 50% of those with lung disease had a diagnosis of COPD, followed by 20% with bronchiectasis and 10% with ILD. Of note patients with a diagnosis of COPD had a higher titer of RF. In group 2 a third of patients with lung disease had a diagnosis of COPD and ILD respectively, and again these patients had higher titers of anti-CCP. In group 3 13.4% suffered from lung manifestations and 37.5% had a diagnosis of pulmonary fibrosis, 12.5% diagnosed with ILD and the remaining 50% had COPD and pleural disease.

Conclusion: Antibody positivity was associated with higher prevalence of RA. Our data provide evidence for the association between smoking and raised antibody titers, especially with anti-CCP antibodies. Lung disease was more strongly associated with RF than anti CCP even though the proportion of smokers was higher in patients with positive anti CCP compared than RF. However lung pathology varied with airway obstruction being more prevalent in RF positive patients compared with fibrosis in patients who were RF and CCP positive. Furthermore, our findings suggest that RF is more strongly associated with lung disease than anti CCP though cirrhilisation is thought to start in the lungs. Our findings demonstrate that lung disease is prevalent in patients with RA and should be anticipated and treated accordingly in order to reduce mortality. Seropositivity of both RF and anti-CCP can be linked with a higher prevalence and greater severity of pulmonary disease activity however this requires replication in a larger cohort.

REFERENCES

Disclosure of Interests: None declared

ABO360D ADHERENCE TO THERAPY IN RHEUMATIC PATIENTS TREATED WITH SUBCUTANEOUS BIOLOGICS
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Background: Patients’ adherence to treatments is undoubtedly a fundamental part of a successful therapeutic strategy, even for rheumatic diseases. In fact, the lack of adherence to treatment should be considered in all cases of “supposed” inefficacy of therapy prescribed.

Objectives: We aimed to evaluate the adherence to treatment in a series of rheumatic patients from a single Centre (Catania, Sicily, Italy).

Methods: We recruited 85 consecutive patients (M/F: 25/60; mean age 52.7±13.5 years) affected by chronic inflammatory arthropathies treated with subcutaneous biologics. All patients completed the 5-item version of Compliance Questionnaire for Rheumatology (COR 5) and the Morisky Medication Adherence Scales (MMAS-8). In order to estimate their adherence to therapy, Moreover, all patients completed the Patient Global Assessment (PGA), the Visual Analogue Scale (VAS) for articular pain, and the Health Assessment Questionnaire (HAQ), in order to estimate their personal judgments on the effectiveness of therapies. Finally, the eventual presence of adverse events were reported.

Results: Considering MMAS-8, 7/85 (8.2%) patients were low adherent to treatment (score <6), and 27/85 (31.8%) presented medium-grade adherence (score 6-7). Interestingly, the COR 5 failed to precisely identify these patients. Adherence to therapy was not related to age, gender, education level, articular disease, adverse events, association with DMARDS. Notably, the use of etanercept (originator or biosimilar) was significant more frequent in low-adherent patients (57/ vs 19/78; p=0.017). Finally, a trend to higher median levels of PGA (57.1 vs 37.6; p=0.06), VAS (82 vs 42.6; p=0.06), HAQ (1.3 vs 0.7; p=0.056) was reported in low-adherent patients.

Conclusion: Our preliminary study confirmed that the low adherence to therapy (better identified with MMAS-8) is a relevant issue in the management of rheumatic patients treated with biologics. Moreover, low-
adherent patients tend to perceive a worse disease condition. Further studies can clarify if low adherence is causally associated with less efficacy of therapy.

REFERENCES

Disclosure of Interests: None declared

SLEEP DISORDER OR DEPRESSION IN KOREAN RHEUMATOID ARTHRITIS, AND ITS ASSOCIATION WITH DISEASE ACTIVITY

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Background: Rheumatoid arthritis is a chronic autoimmune disease. Psychological stress and mood disorders such as sleep disorder or depression are more frequent in patient with RA.

Objectives: The aim of this study was to evaluate the relationship between disease activities and sleep disorder or depression in Korean patients with RA.

Methods: The study enrolled 334 patients with RA who visited Hallym University Sacred Heart Hospital (South Korea). The diagnosis of insomnia and depression was based in patient questionnaire such as Pittsburgh sleep quality index (PSQI) and Beck depression inventory (BDI). Insomnia was defined as PSQI>5 and depression was defined as BDI >13. Patients were divided into two groups (insomnia vs no-insomnia, depression vs no-depression) and the clinical aspects were compared by Mann-Whitney U-test. Age, gender, erythrocyte sedimentation rate (ESR), 28 joint disease activity score (DAS28), DAS28-P score (the subjective component of the DAS28 relative to the total components), tender joint count (TJC) and swollen joint count (SJC), quality of life measured with health assessment questionnaire (HAQ) were analyzed.

Results: The median (inter-quartile range) disease duration was 6 (4–9) years and the mean DAS28 score was 3.61±1.1. Seventy percent of the patient had insomnia and 8% had depression. Compared with patients without insomnia, insomnia patients had a higher DAS28 (3.7±1.16 vs. 3.21±1.0, P<0.001), higher pain DAS28-P (0.37±0.17 vs. 0.32±0.16, P=0.004), higher TJC (4.63±5.68 vs. 2.38±3.45, P<0.001) and higher HAQ score (0.49±0.53 vs. 0.18±0.36, P<0.001). Compared with no depression patients, depression patients had a higher DAS28 (4.07±1.37 vs. 3.51±1.11, P<0.001), higher pain DAS28-P (0.44±0.17 vs. 0.35±0.44, P=0.015), higher TJC (6.96±1.57 vs. 3.71±1.02, P=0.006), higher SJC (1.81±1.52 vs. 0.67±1.28, P<0.003), and higher HAQ score (0.63±0.51 vs. 0.38±0.5, P<0.021).

On univariable logistic regression analysis, insomnia was positively associated with age, DAS28, DAS28-P and BDI score. After adjustment, insomnia was positively associated with sex (female), age, BDI and DAS28 score. On univariable logistic regression analysis, depression was positively associated with PSQI, DAS28 and DAS28-P score. After adjustment, depression was positively associated with PSQI and DAS28-P score.

Conclusion: Rheumatoid arthritis patient with the sleep disorder or depression had worse clinical symptoms than those without. Rheumatologist should take sleep disorder or depression into consideration on evaluation of disease severity in RA patients.

Disclosure of Interests: None declared

GENDER DIFFERENCES IN CLINICAL CHARACTERISTICS AND COMORBIDITIES AND THEIR IMPACT ON CLINICAL OUTCOME IN KOREAN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Rheumatoid arthritis (RA) is a chronic auto-immune disease that is more common to female than male. Gender-based differences in clinical features, comorbidities, and disease outcomes have been fragmentarily described. However, systematic analysis focusing on gender differences in a large RA population is scarce.

Objectives: We aimed to elucidate gender differences in clinical characteristics and comorbidities and their potential impact on clinical outcome in a large Korean cohort of patients with RA.

Methods: A total of 5,376 RA patients were included from the KORean Observational study Network for Arthritis (KORONA) database. Each patient was examined at baseline and three consecutive years. RA disease activity, functional disability, and quality of life were assessed by disease activity score 28 (DAS28), health assessment questionnaire (HAQ) and EuroQoL-5D (EQ-5D), respectively. The subjective health-related outcomes including visual analog scale (VAS) scores for patient’s and physician’s global health, patient’s pain, fatigue, and sleep disturbance were collected. Clinical characteristics and comorbidities at baseline were compared according to gender. Gender impacts on clinical outcome during the four years were analyzed using generalized estimating equations (GEE) models for repeated measures. In addition, the gender effect on achieving clinical remission was analyzed using Cox-proportional hazards regression.

Results: At baseline, females (n=4,574) were younger, more erosive, and had longer disease duration than male (n=802). Females showed significantly higher scores in DAS28, HAQ, EQ-5D, and VAS for all patients’ health-related outcomes. In terms of comorbidities, the prevalence of male RA was significantly higher than that of female RA in most illnesses including, interstitial lung disease, cardiovascular disease, diabetes and other pulmonary disease except for depression. In the GEE model, gender was found to significantly influence the rate of change of DAS28 (p=0.041), and also independently associated with this outcome (p=0.001) after adjusting for age, disease duration, and baseline DAS28. Females were associated with a reduced rate of achieving DAS28 remission (HR 0.41, 95% CI 0.28-0.58) compared to male.

Conclusion: In Korean patients with RA, most comorbidities were more prevalent in male than in female. But for RA-related health outcomes, the longitudinal change in disease activity and the rate of achieving clinical remission over time were found to be worse in female RA.

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Disclosure of Interests: None declared

DETECTABLE HBV DNA AT TREATMENT BASELINE PREDICTED HEPATITIS B VIRUS REACTIVATION IN INFLAMMATORY ARTHRITIS PATIENTS WITH NEGATIVE HEPATITIS B SURFACE ANTIGEN BUT POSITIVE ANTI-HEPATITIS B CORE ANTIGEN

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Background: Hepatitis B virus (HBV) reactivation in inflammatory arthritis IA (rheumatoid arthritis, psoriatic arthritis, and peripheral spondyloarthritides) patients with positive hepatitis B surface antigen but positive anti-hepatitis B core antibody (HBsAg/anti-HBc) is one of the treatment-related complications. The risk of reactivation in patients with negative hepatitis B surface antigen but positive anti-hepatitis B core antibody (HBsAg/anti-HBc) is less well defined.

Objectives: This retrospective, single centre study aimed to study the prevalence of HBV reactivation (defined as HBV DNA becoming detectable during treatment if it was undetectable at baseline, or an increase in HBV DNA titre if detectable at baseline) among IA patients with HBsAg+/anti-HBc+ status. Demographic data, clinical parameters including treatments for IA and any use of antiviral prophylaxis, and laboratory results including anti-hepatitis B surface antibody (anti-HBs) and serial HBV DNA levels were obtained. Logistic regression was used to identify factors predicting HBV reactivation.

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[2] AB0360G

Disclosure of Interests: None declared

Scientific Abstracts
Results: Around 1/3 (68%) of the 206 included patients included were female and the mean age was 61.7-year-old. 75% had rheumatoid arthritis and the remaining had psoriatic arthritis or peripheral spondyloarthritis. Most patients (94%, n=194) were on conventional synthetic DMARD csDMARD (25% on monotherapy and 16% on combination therapy). 35% patients (n=72) were on biologic DMARD (with or without csDMARD). As antiviral prophylaxis was not mandatory in HBsAg/anti-HBc+ patients according to local protocol, only 17 patients (8.3%) were on preemptive antiviral against HBV. Thirteen patients (6.3%) experienced HBV reactivation during their disease course and four of them were on antiviral prophylaxis. All of these reactivations were only transient low-grade viraemia with HBV DNA level ≤ 20IU/ml. Spontaneous resolution of viraemia were observed in all these patients. None of the reactivation resulted in acute hepatitis, hepatic failure or mortality.

Presence of detectable HBV DNA at baseline predicted HBV reactivation (OR 2.10, p=0.005). Other parameters including age, the lack of antiviral prophylaxis, negative anti-HBs status and anti-HBs titre were not significant predictors of HBV reactivation. None of the synthetic and biologic DMARDs were associated with HBV reactivation.

Conclusion: HBV reactivation was infrequent among IA patients with HBsAg-/anti-HBc+ status and was unlikely to be associated with adverse clinical outcome. It could occur in patients with positive anti-HBs or on antiviral prophylaxis. Detectable HBV DNA at baseline was a predictor of HBV reactivation.

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Disclosure of Interests: None declared

Rheumatoid arthritis – biological DMARDs________

ABCD1 ASCORE, A 2-YEAR, OBSERVATIONAL, PROSPECTIVE MULTICENTRE STUDY OF SUBCUTANEOUS ABATACEPT FOR THE TREATMENT OF RHEUMATOID ARTHRITIS IN ROUTINE CLINICAL PRACTICE: 1-YEAR INTERIM ANALYSIS

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Background: ASCORE (Abatacept [ABA] SubCutaNeous in Routine clinical pracTice: ClinicalTrials.gov: NCT02090556) is an ongoing, 2-year, observational, prospective multicentre study of patients (pts) with RA initiating SC ABA in routine clinical practice.

Objectives: To present for the first time 1-year interim retention rates and clinical outcomes by previous biologic (b)DMARD exposure.

Methods: Pts (≥18 years) with moderate-severe RA, who initiated SC ABA 125 mg weekly, were enrolled (Mar 2013–Jan 2017) across 10 countries in two cohorts: biologic-naïve pts and those who had failed ≥ 1 prior bDMARD. Pt and disease characteristics were recorded. ABA retention rates (95% CI) were estimated at 1-year by Kaplan-Meier analysis. Good/moderate EULAR response rates based on DAS28 (ESR, otherwise CRP), LDA or remission according to DAS28 (ESR; <32), SDAI (<11), CDAI (<10) and Boolean criteria were assessed at 1 year.

Results: A total of 2943/2949 enrolled pts were evaluable: 1162 (40.9%) were biologic naïve; 740 (26.0%) had failed 1 and 941 (33.1%) had failed ≥ 2 prior biologics. At baseline, pts with a higher vs lower number of prior bDMARDs had longer disease duration and greater presence of erosive disease vs pts who were biologic-naïve; CRP was higher in biologic-naïve vs failure pts; disease activity was similar across treatment exposures. Overall SC ABA retention (95% CI) at 1 year was 65.3% (63.4, 67.0); retention was higher in pts receiving ABA as a first vs later bDMARD (71% [68.3, 73.7] in biologic-naïve pts vs 61.9% [58.2, 65.4] and 60.7% [57.4, 63.8] in those with 1 and ≥ 2 prior biologic failures, respectively; Figure). At 1 year, 943 pts had discontinued ABA: 465/936 [49.7%] due to inefficacy and 218/936 [23.3%] due to safety (data unavailable, n=9/943). Among pts continuing ABA at 1 year, good/moderate EULAR response rates for pts who were biologic-naïve and those with 1 and ≥ 2 prior biologic failures were 81.0%, 70.0% and 66.4%, respectively. Corresponding rates for LDA outcomes were also higher with ABA as an earlier vs later bDMARD. The safety profile was similar across patient cohorts and consistent with real-world IV ABA studies.1,2

Conclusion: In routine clinical practice, overall retention of SC abatacept at 1 year was around 65% and comparable with that of IV abatacept.2 Among pts continuing abatacept at 1 year, good/moderate EULAR response rates were consistently ≥65% irrespective of prior bDMARD exposure. Better retention and clinical response rates were achieved with abatacept earlier in bDMARD treatment history.

REFERENCES


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Figure 1

Background: Within treat-to-target approach, ACR recommends biologic DMARD (bDMARD), with or without methotrexate, in rheumatoid arthritis (RA) patients whose disease is active despite methotrexate treatment1. ACR further defines bDMARD failure as the lack of efficacy (desired response) or side effects. Understanding the real-world characteristics and treatment patterns of the patients who become DMARD inadequate responders (IR) may help clinicians tailor the next treatment to patient needs and health status.

Objectives: This study described treatment patterns, treatment duration, and characteristics of RA patients who became IR to their first bDMARD.

Methods: The study population included adult patients with Medicare medical and pharmacy insurance coverage (20% sample) who became bDMARD IR: ≥2 RA claims, newly initiated bDMARD (initial therapy) and then switched (index date) to another bDMARD or JAKI (index therapy). Patients with cancer, non-RA autoimmune disease, or pregnancy were excluded. At least 1 year pre- (baseline) and 1-year post-index enrollment was required. Patient characteristics and treatment allocation and duration were assessed.

Results: A total of 528 bDMARD IR patients met the study selection criteria. At baseline, these patients used monotherapy (n=165, 31.2%) or bDMARD+csDMARD combination (n=363, 68.8%). Patient baseline demographics were comparable between monotherapy and combination therapy groups: mean (SD) age 65.6 (11.0) years, 85.0% female, 81.6% white. The mean (SD) Charleson Comorbidity Index was 1.8 (1.1) for monotherapy and 1.6 (1.0) for combination therapy (P=0.084). On average, patients used 14.8 (7.1) concomitant medications (comparable between groups).

The original bDMARD treatment lasted for median 211 days, including 211 days for monotherapy and 212 days for combination therapy. As bDMARD IR patients switched treatment regimen, they started using either monotherapy (n=187, 35.4%) or combination therapy (n=341, 64.6%). The median duration of subsequent therapies was 287 days overall, including 224 days for monotherapy and 319 days for combination therapy (P=0.0063).

Conclusion: Among Medicare bDMARD IR patients, the median duration of the initial bDMARD therapy lasted for 212 days or less and the subsequent treatments lasted for 319 days or less. This analysis suggests that bDMARD IR patients require alternative efficacious and well-tolerated treatments.

Table 1. Frequencies of monotherapy and combination therapy for initial and post-switch treatments.

<table>
<thead>
<tr>
<th>Initial (first bDMARD) therapy</th>
<th>Total</th>
<th>Post-switch (index therapy)</th>
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<tbody>
<tr>
<td>Monotherapy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>bDMARD+csDMARD combination</td>
<td>165</td>
<td>31.2%</td>
</tr>
<tr>
<td>csDMARD</td>
<td>363</td>
<td>68.8%</td>
</tr>
<tr>
<td>Total</td>
<td>528</td>
<td>100%</td>
</tr>
</tbody>
</table>

References:

Disclosure of Interests: Robin K Dore Grant/research support from: Gilead Sciences, AbbVie, Amgen, Lilly, Pfizer, Regeneron, Sanofi, Consultant for: AbbVie, Amgen, Lilly, Speakers bureau: AbbVie, Amgen, Lilly, Sanofi, Regeneron, Pfizer, UCB, Jemmy Antanova Shareholder of: Gilead Sciences, Employee of: Eli Lilly and Company, Medimmune, Genentech, Gilead Sciences, Haifeng Guo: None declared, Suying Li: None declared, Burak Ozbay Shareholder of: Gilead Sciences, Employee of: Abbott Laboratories, Abbvie, Mark C. Genovese Grant/research support from: Sanofi/Genzyme, Genentech/Roche, RPharm, Consultant for: Sanofi/Genzyme, Genentech/Roche, RPharm


References:

ABO364 DISCONTINUATION OF CONCOMITANT METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TOCILIZUMAB: AN INTERVENTIONAL STUDY

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Background: Methotrexate (MTX) is an important anchor drug for rheumatoid arthritis (RA) patients and is used alone or in combination with biologics. However, some patients discontinue MTX due to toxicity including gastrointestinal (GI) disorders [1]. Thus, de-escalation of MTX while maintaining a favourable disease activity state—-a challenge in RA clinical research—-may be beneficial from the perspective of reducing adverse events. The efficacy of tocilizumab (TCZ) has been demonstrated in monotherapy as well as with concomitant MTX [2], opening up the possibility of MTX discontinuation in these patients if disease control can be maintained.

Objectives: This study aimed to evaluate the efficacy and safety of MTX discontinuation in RA patients with sustained low disease activity undergoing combination therapy with TCZ plus MTX.

Methods: This multicentre, open-label, uncontrolled, prospective 64-week study included RA patients maintaining low disease activity (Clinical Disease Activity Index [CDAI] ≤10) for ≥12 weeks with TCZ plus MTX. MTX was discontinued following 12 weeks of biweekly administration while continuing TCZ therapy. The rescue treatments were performed if the CDAI score was >10 and at the discretion of the investigator and/or upon patient request. The primary endpoint was the proportion of patients maintaining low disease activity with no flare at week 36 (24 weeks after MTX discontinuation). Disease flare was defined as a CDAI score >10 or intervention with the rescue treatments for any reasons. The proportions (95% CI) of patients who maintained low disease activity without a flare at weeks 12, 24, and 36 were 87.8% (75.2 – 95.4%), 81.6% (68.0 – 91.2%), and 75.5% (61.1 – 86.7%), respectively (Fig. 1). The lower limit of the 95% CI at week 36 exceeded the assumed threshold response rate of 60%, demonstrating the clinical feasibility of MTX discontinuation. The prevalence of gastro-oesophageal reflux disease, defined as a Frequency Scale for Symptoms of Gastro-oesophageal reflux disease score ≥8, significantly decreased from week 0 to 12 (27.1% to 18.4%; P = 0.025) (Fig. 2). No significant changes were observed in the HAQ-DI and EQ-5D from week 0 to 36 (Fig. 3).

Table 1. Patient characteristics at baseline (week 0)

<table>
<thead>
<tr>
<th>Age, years</th>
<th>Total, n = 49</th>
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<tbody>
<tr>
<td>62 ± 10</td>
<td>49</td>
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</table>

| Female,%  | 84            |
| Weight, kg| 55 ± 11       |
| Disease duration, years | 11 ± 8 |
| Route of TCZ, intravenous/subcutaneous,% | 65/35 |
| Rheumatoid factor positive,% | 79 |
| Anticyclic citrullinated peptide positive,% | 90 |
| MTX dose, mg/week | 8.2 ± 2.3 |
| Use of glucocorticoids,% | 29 |
| CDAI | 2.7 ± 2.5 |
| CDAI ≥2.8,% | 67 |
| CRP, mg/dl | 0.04 ± 0.06 |
| HAQ-DI | 0.472 ± 0.613 |
| EQ-SID | 0.822 ± 0.170 |

Data are shown as mean ± SD or percentage.

Conclusion: Discontinuation of concomitant MTX is clinically feasible for maintaining low disease activity, and may be beneficial from the perspective of reducing GI symptoms in RA patients treated with TCZ.

REFERENCES

Disclosure of Interests: Shuji Asai Speakers bureau: AbbVie, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Janssen, Takeda, and UCB Japan, Toshihisa Kojima Grant/research support from: Chugai Pharmaceutical (Investigator Initiated Study), Novartis, Nippon Kayaku, Eli Lilly, Eisai, Speakers bureau: Chugai Pharmaceutical, Takeda Pharmaceutical, Pfizer, Eli Lilly Japan, Bristol Myers Squibb, Ono Pharmaceutical, Daiichi Sankyo, Astellas, UCB, Janssen Pharmaceutica, Tanabe Mitsubishi, Nobunori Takahashi Speakers bureau: AbbVie, Bristol-Myers Squibb, Chugai, Eisai, Mitsubishi Tanabe, and Pfizer. YS has received speakers’ fees from Astellas, Bristol-Myers Squibb, and Ono. Yachiyo Kuwatsuka: None declared, Masahiko Ando: None declared, Naoki Ishiguro Grant/research support from: AbbVie, Asahi Kasei, Astellas, Chugai, Daiichi-Sankyo, Eisai, Kaken, Mitsubishi Tanabe, Otsuka, Pfizer, Takeda, and Zimmer Biomet, Consultant for: Ono, Speakers bureau: Astellas, Bristol-Myers Squibb, Daiichi-Sankyo, Eli Lilly, Pfizer, and Taisho Toyama

AB0365 EFFICACY OF TOCILIZUMAB FOR CORTICOSTEROID AND METHOTREXATE SPARING IN RHEUMATOID ARTHRITIS

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Background: Successful management of rheumatoid arthritis (RA) depends on the early administration of DMARDs and biologic DMARDs. The biologic agent tocilizumab, an interleukin-6 receptor inhibitor, has been used for the management of RA.

Objectives: The aim was to describe a cohort of RA patients treated with tocilizumab and the effect of this treatment on the other DMARDs used, namely methotrexate and corticosteroids.

Methods: In a cohort of 80 patients with rheumatoid arthritis the biologic agent tocilizumab was administered in combination with methotrexate administered sc and 10 mg prednisolone. Within this cohort, 26 patients were on tocilizumab administered iv 8 mg/kg/4wks (maximum dose 800 mg) and 54 were on tocilizumab administered sc 162mg/wk. As corticosteroid administration is characterized by adverse effects, such as osteoporosis and diabetes mellitus, in all patients an effort was made to reduce and if possible, withdraw corticosteroids. An effort was also made to reduce methotrexate dosage. After a year, prednisolone was either significantly reduced or withdrawn. The final dosage of prednisolone was either 2.5-5 mg or complete withdrawal. The successful reduction of methotrexate dosing schedule was also achieved. The final methotrexate dose was either 12.5 mg sc or complete withdrawal. After a period of 52 weeks in this cohort 42 of 80 patients (52.5%) were on methotrexate with tocilizumab.

Results: In a cohort of 80 patients with RA the administrations of tocilizumab, either iv or sc, proved safe and effective. Remission or low disease activity of RA was achieved. Corticosteroid dosage was reduced. After 52 weeks within the group of RA patients on treatment with tocilizumab, in 42 complete withdrawal of corticosteroids and methotrexate proved feasible. Patients on tocilizumab monotherapy remained in remission.

Conclusion: It appears that tocilizumab is safe and effective for the treatment of RA. Tocilizumab treatment may permit withdrawal of both corticosteroids and methotrexate in patients with RA. The management of active RA initially with low dose corticosteroids in combination with methotrexate sc and, in the case of failure to achieve remission, with the addition of the biologic agent tocilizumab had as a result either significant corticosteroid reduction or complete withdrawal and reduction of methotrexate dosage, the disease remaining in remission.


AB0366 COMPARISON OF THE EFFECT OF RITUXIMAB (BCDe) AND RITUXIMAB BIOSIMILAR – BCD-020 (BIODAC) ON INFLAMMATORY AND IMMUNOLOGICAL BIOMARKERS IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: BCD-020 (BCIDAC) is the first Russian rituximab (RTX) biosimilar which was approved for medical use in rheumatoid arthritis (RA) patients in Russia and some CIS countries.

Objectives: To evaluate the changes in acute phase reactants, autoantibodies, immunoglobulins, cytokine profile and CD19+B lymphocytes in patients (pts) with RA during RTX and RTX biosimilar therapy.

Methods: The study included 54 RA patients (pts), divided into two groups. The first group included 34 pts with RA (31 women, mean age 49(42-64), mean disease duration 66(36-132) months, mean DAS 28 6.2 (5.6-8.5) who received two infusions of RTX - 35% at a dose of 500 mg, 65% of the dose of 1000 every two weeks in combination with DMARDs and glucocorticoids; 33 pts achieved a good/moderate EULAR response at week 24. The second group - 20 pts with RA (18 woman, mean age 61.5(54-66.5) years, mean disease duration 39.5(20-84) months, mean DAS 28 5.6(4.9-6.8) who received two intravenous BCD-020 infusions (600mg No 2) in combination with DMARDs and glucocorticoids; 17 pts achieved a good/moderate EULAR response at week 24. Laboratory biomarkers were assessed at baseline and weeks 12 and 24 after the first infusion of RTX. ESR (mm/hr) (Westergren method); serum concentrations of CRP (mg/L), IgM RF (U/ml), IgG RF (U/ml) (laser nephelometry), anti-CCP2 (U/ml), IgA RF (U/ml), anti-MCV (U/ml) (ELISA kits); cytokine profile (xMAP technology) were assessed.

Results: RTX and BCD-020 induced decreases in ESR, levels of CRP, IgMRF, IgARF, anti-MCV at week 12 and 24, p<0.05 (tabl.1). At week 24 – 20% of IgMRF positive pts at baseline (in the first group) and 10% of IgMRF positive pts (in the second group) turned negative. Levels of anti-CCP2 did not reduced. At week 24 – 7% of anti-CCP2 positive pts at baseline (in the first group) and 8% of anti-CCP2 positive pts (in the second group) turned negative. Depletion of CD19+B-cells was achieved at week 12 in all patients (absolute number 0), with an increase in the level of B cells at week 24, tabl.1. An immunoglobulin level decreased at week 24, but remained normal. In the first group RTX induced reduction in proinflammatory (IL-1b, IL-2, IL-6, IL-12, IL-15, IFN-γ, TNF-α), anti-inflammatory cytokines (IL-1Ra, IL-5, IL-10, IL-13), growth factors (IL-7, GM-CSF, FGF-basic) and chemokines (MC-1) at week 24 (fig.1). In the second group BCD-020 induced reduction in IL-1b, IL-1α, IL-2, IL-4, IL-7, GM-CSF, IL-15, IL-17, Eotaxin, G-CSF, IFN-γ, IP-10, MC-1, MIP-1β, TNF-α, VEGF at week 24 p<0.05, fig.1.

Conclusion: RTX biosimilar (BCD-020) has a similar effect on inflammatory and immunological biomarkers to the original RTX. BCD-020 therapy induced a rapid and significant improvement in ESR, levels of CRP, IgMRF, IgARF, anti-MCV, proinflammatory, anti-inflammatory cytokines, growth factors, chemokines levels and CD19+B cells depletion in RA pts.


AB0367 REASONS FOR DISCONTINUATION OF BIOLOGICAL DRUG AND TARGETED SYNTHETIC DRUGS AMONG PATIENTS WITH INFLAMMATORY ARTHRITIS IN THE UNITED ARAB EMIRATES (UAE)

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Background: In routine clinical care of Rheumatoid arthritis (RA) Spondylarthritids(PA) and Psoriatic arthritis (PSA) there is a high rate of discontinuation of biologic disease-modifying antirheumatic drugs (bDMARDs) and targeted synthetic disease-modifying antirheumatic drugs (tsDMARDs) due to loss of efficacy, side effects or lack of adherence. This can impact on the ability to achieve low disease activity.

Objectives: To evaluate the use of bDMARDs and tsDMARDs and analyze the reasons for discontinuation of these drugs and to compare them to our standard DMARD Methotrexate.

Methods: In this retrospective cohort analysis we included consecutive patients aged ≥ 18 years with RA/SPA/PSA attending 2 Rheumatology clinics in the UAE from August- December 2019. Statistical analysis was performed using STATA version 13 and R-studio. Continuous data were
Safely of combination therapy with two biologic disease-modifying anti-rheumatic drugs (bDMARDs) in association with denosumab: comparison of combination and mono-therapy regimens

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Background: Osteoporosis is a frequent complication of rheumatic muscle-skeletal diseases (RMD), with high impact from steroid treatment. It is known that bDMARD impact positively on patients' prognosis and this is also known for Denosumab, a monoclonal antibody for osteoporosis. The combination treatment with two monoclonal antibodies, bDMARD & denosumab, has addressed the problem of safety and efficacy, with incomplete answers from the available literature.

Objectives: To evaluate the impact of the combination treatment bDMARD +Denosumab (COMBO group), compared to mono-therapy with bDMARD (MONO group), on clinical efficacy, safety and treatment retention of bDMARD in patients with RMD.

Methods: We searched PubMed, the Cochrane Library, Scopus, Clinical-Trials.gov, and the WHO International Clinical Trials Registry platform through 12/18/17. Our eligibility criteria included human RCTs or observational or non-randomized comparative studies in adults (≥ 18 years of age) that recorded safety of combination therapy with two bDMARDs in RA patients. We used R version 3.1.2 to perform meta-analysis between groups on combination therapy and placebo/single therapy alone using random effect model calculating odds ratio (OR) as well as 95% confidence interval (CI). Cochran Q statistic and I² statistic was used to identify heterogeneity between studies. The primary outcome was the rate of major serious events. Additional outcomes were the rate of total adverse events, total infectious events and major infectious events.

Results: Six studies with a total of 623 patients (410 on combination therapy and 213 on single therapy) were included for meta-analysis. Median follow-up was 9.5 months (range 6-12 months). There was a significant increase in SAEs in the combination group (14.9 vs 6.0%, OR 2.51, 95% CI 1.25-24.90, P0.05). When performing subgroup analysis in patients receiving only full-dose of both bDMARDs there was a significant increase in serious infections (6.7 vs 0.6%, OR 5.58, 95% CI 1.25-24.90, P0.05) and the risk of SAEs remained significantly higher (17.7 vs 6.2%, OR 2.72, 95% CI 1.30-5.69, P0.05).

Conclusion: Our findings suggest that combination therapy with two bDMARDs in RA patients appears to increase the risk of SAEs during the first twelve months of treatment.

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Disclosure of Interests: Gonçalo Boleté: None declared, Lukshe Kanagaratnam: None declared, Moustapha Dramé: None declared, Jean-Huges Salmon Speakers bureau: Janssen Novartis

Methods: RMD patients treated with COMBO treatment where enrolled from a single centre rheumatology unit; for each case, at least one MONO therapy control (matched per age≥5 years, sex, bDMARD, RMD, without osteoporosis) was enrolled. Data on clinical efficacy (3-points Likert scale for physician and patient – improved/stable/worse), safety (loci reactions – serious and non-serious adverse events) and bDMARD treatment retention at 12, 18 and 24 months.

Results: Out of 129 eligible patients, 77 were enrolled in the protocol: 49 in the MONO and 26 in the COMBO group. The two groups were different of age (slightly higher in the COMBO group), for tender joint count, erythrocyte sedimentation rate and c-reactive protein (higher in the MONO group). Efficacy analysis showed higher percentage of clinical improvement at 12 months in the MONO group at 12 months, being not significant at 18 and 24 months (possibly explained by a different disease activity at baseline visit, corresponding to the overlap of denosumab on top of bDMARD in the COMBO and to the initiation of bDMARD in the MONO group). Between the 2 groups, no difference about safety and retention rate was found.

Conclusion: The efficacy of COMBO treatment is similar to MONO therapy. Moreover, the data show that also safety and retention rate are similar. Therefore, the COMBO treatment with 2 different monoclonals can be safely employed in patients with RMD and osteoporosis.
Table 1. Univariate Cox regression analysis

| Variable                          | N (%) | HR   | IC 95% | P>|z| |
|----------------------------------|-------|------|--------|-----|
| Sex, ref. men                    | 22 (19%) | 1.06 | 0.47- | 0.883 |
| - Woman                          | 92 (81%) | 2.42 |        |      |
| Age at RTX start, ref. <45 years | 14 (12%) | 0.58 | 0.24- | 0.221 |
| - 45-65 years                    | 61 (54%) | 1.38 | 0.193 |      |
| - > 65 years                     | 39 (34%) | 0.21- |        |      |
| RF/ACPA, ref. negative           | 8 (7%) | 0.32 | 0.12- | 0.018 |
| - positive                       | 106 | 0.82 |        |      |
| DAS28, ref. baseline < 5,1       | 35 (39%) | 0.86 | 0.43- | 0.659 |
| - baseline >5,1                  | 55 (61%) | 1.71 |        |      |
| RTX 1st cycle, ref. csDMARD      | 95 (83%) | 2.42 | 1.16- | 0.017 |
| - monotherapy                    | 19 (17%) | 5.02 |        |      |
| RTX monotherapy%, ref. <50%      | 95 (83%) | 2.00 | 0.94- | 0.071 |
| - >50% monotherapy               | 19 (17%) | 4.27 |        |      |
| RTX biologic line, ref. 1st line | 22 (19%) | 1.80 | 0.70- | 0.220 |
| - >2nd line                      | 92 (81%) | 4.62 |        |      |
| RTX dose, ref. ≤1,500 mg/cycle   | 31 (27%) | 1.26 | 0.58- | 0.556 |
| - >1,500 mg/cycle                | 83 (73%) | 2.77 |        |      |
| Retreatment schedule, ref. on    | 99 (87%) | 1.28 | 0.58- | 0.531 |
| demand                           | 15 (13%) | 2.81 |        |      |

Table 2. Multivariate Cox-Regression analysis

| Variable                          | HR   | IC 95% | P>|z| |
|----------------------------------|------|--------|-----|
| RF/ACPA, ref. negative           | 0.25 | 0.09- | 0.005 |
| RTX monotherapy%, ref. <50%      | 3.10 | 1.37- | 0.007 |

Conclusion: In our hospital RTX treatment has a long median survival that is significantly higher in seropositive patients and in those treated in combination with csDMARDS. The RTX dose by cycle did not affect the persistence.

REFERENCE

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AB0372 EXPLORING REFRACTORY DISEASE & PERSISTENT SYMPTOMS IN RA/POLYJA DESPITE BDMARDS: PATIENT & PROFESSIONAL EXPERIENCES

Hema Chaplin1, Ibone Verhey2, Nora Ng3, James Galloway4,5, Ian Scott6,7, Debadjit Sen2, Rachel Tattersall2,3,4, Heidi Lempp3, Sam Norton1, 5, King’s College London; Health Psychology Section, London, United Kingdom; 2King’s College London, London, United Kingdom; 3Guy’s and St Thomas’ NHS Foundation Trust, London, United Kingdom; 4King’s College London, Inflammation Biology, London, United Kingdom; 5King’s College Hospital NHS Foundation Trust, London, United Kingdom; 6Keele University, Stoke-on-Trent, United Kingdom; 7Midlands Partnership NHS Foundation Trust, Stoke-on-Trent, United Kingdom; 8University College London Hospitals NHS Foundation Trust, London, United Kingdom; 9University College London, Versus Arthritis Centre for Adolescent Rheumatology, London, United Kingdom; 10Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom; 11Barbara Annis National Network for Adolescent and Young Adult Rheumatology, UK, United Kingdom

Background: Refractory disease is defined as not achieving a low disease activity target despite BDMARDS. This definition does not account for patients with well controlled inflammation who experience persistent symptoms, or who have a high perceived disease impact. Furthermore, variations in professionals understanding of refractory disease and related concepts exists, with potential discordance when compared to patients understanding.

Objectives: To qualitatively explore patients and professionals understanding and experiences of refractory disease and persistent symptoms.

Methods: Semi-structured interviews were conducted with 13 RA and 3 Polyarticular JIA patients (on bDMARD not responding with DAS28>3.2) attending four UK Rheumatology clinics. Thirty-two healthcare professionals (working in Rheumatology >1year) were interviewed across 11 UK hospitals. Interview data was transcribed and descriptive statistics as reported for quantitative data.

Results: Patients had not responded to on average 3 csDMARDs and 3.5 bDMARDs, with mean MSK-HQ=24.6, mean DAS28=4.60, and mean Patient Global=55.4. Healthcare professionals interviewed were predominantly adult trained (25/32), with mean 11.7 years’ experience, comprising rheumatologists, nurses, physiotherapists, occupational therapists, psychologists, pharmacists, podiatrist, and social worker.

Key themes for both patients and professionals experiences of refractory disease and persistent symptoms explored were: 1) Frustrations with the disease, non-response to medication and side effects, 2) Importance of areas not captured by the DAS28, 3) Patient-centred targets/care, 4) Role of other specialties, 5) Role of comorbidities, infections and/or joint damage, and 6) Patient acceptance, adjustment and resilience. Although patients expressed hopeful expectations despite poor experiences, this was in discordance to professionals’ accounts of loss of trust/hope, disengagement and limited treatment options, with hope mainly for stratified medicines.

Patient specific emergent themes identified: 1) Disease not controlled fully but manageable, 2) Drugs do not work: at all versus over time, 3) Persistent pain, fatigue and restricted mobility are most problematic symptoms, 4) Life-limiting impact: practically, psychologically/emotionally and socially, and 5) Good support from rheumatology team but holistic approach needed.

Professionals grouped refractory disease into four key areas: 1) Refractory Inflammation vs Refractory Symptomology, 2) Biological processes, 3) Drug inefficacy/toxicity, and 4) Patient health beliefs/behaviours.

Those with JIA had a greater variety in their experiences compared to those with RA. In addition to above themes they all highlighted the challenges of having a long-term illness so young, e.g. not knowing a life with pain or disease and lack of understanding in both themselves and others. Paediatric/Adolescent professionals noted differences in treating JIA compared to RA, e.g. joints affected and treatment guidelines/recommendations.

Conclusion: These results highlight the potential need for a broader definition for refractory disease, and the need for holistic approaches to treatment that better support both patients, and professionals, in managing their condition.

Disclosure of Interests: Hema Chaplin: None declared, Ibone Verhey: None declared, Nora Ng: None declared, James Galloway Consultant for: Pfizer Inc, Ian Scott: None declared, Debadjit Sen: None declared, Rachel Tattersall: None declared, Heidi Lempp: None declared, Sam Norton: None declared. DOI: 10.1136/annrheumdis-2019-eular.6809

AB0373 A COMPARATIVE EFFECTIVENESS STUDY OF ABACETEPT AND TNF INHIBITORS IN PATIENTS WITH RHEUMATOID ARTHRITIS USING REAL-WORLD DATA

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Background: Introduction of multiple biologic DMARDs, targeted synthetic DMARDs and biosimilars has led to a paradigm shift in the management of patients (pts) with RA. There are, however, limited head-to-head studies comparing these agents to guide evidence-based treatment decisions. Abacitcept versus adalimumab compared in bioLogic-naive RA subjects with background MTX (AMPLE) was the first head-to-head randomised controlled trial to evaluate the efficacy of abacitcept (ABA) and adalimumab. However, there are limited data replicating AMPLE findings in real-world settings.

Objectives: To compare effectiveness of ABA versus TNF inhibitors (TNFis) in pts with RA by line of therapy (LOT) and by LOT stratified by anti-citrullinated protein antibody (ACPA) status using data from real-world clinical practice.

Methods: Data from two independent RA registries comprising pts treated by physicians in routine care were used for the analysis. An RA disease-specific registry provided data on pts treated with TNFis; the other was a product-specific registry and provided data on pts treated with ABA.1,2 The disease-specific registry was a US-based single-centre registry; the product-specific registry was a multi-centre, 12-country registry covering the US. Frequency matching on age (in years [yrs]; ±4 yrs window), RA disease duration (in yrs; ±4 yrs) and baseline CDAI category (remission [≤2.8], low activity [≤10], medium activity [12-22], high activity [>22]) between TNFI and ABA pts was done for bioLogic-naive and -experienced pts. Descriptive statistics were used to summarise baseline demographics, disease activity measures and serostatus for both treatment groups by LOT. Disease activity in the follow-up period was measured at the 12-month mark (±6 months). Change in disease activity after 12 months was evaluated for TNFI and ABA pts by LOT, and statistical comparison using Kruskal-Wallis test was performed. This was repeated for pts stratified by ACPA status.

Table 1. Table 1. Baseline characteristics by LOT and ACPA status

<table>
<thead>
<tr>
<th>Age, yrs</th>
<th>RA duration, yrs</th>
<th>Gender, n (%)</th>
<th>CDAS score</th>
<th>Mean (SD) reported, unless otherwise stated</th>
<th>ACPA status</th>
<th>ABA reduction from baseline</th>
<th>TNFi reduction from baseline</th>
<th>ABA baseline (n)</th>
<th>TNFi baseline (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>51±5</td>
<td>9±3</td>
<td>55/45</td>
<td>24±6</td>
<td>22±6</td>
<td>ACPA+</td>
<td>15.1 (16.7)</td>
<td>13.3 (15.8)</td>
<td>28 (16)</td>
<td>24 (10)</td>
</tr>
<tr>
<td>52±6</td>
<td>5±2</td>
<td>65/35</td>
<td>25±6</td>
<td>22±6</td>
<td>ACPA-</td>
<td>15.1 (16.7)</td>
<td>13.3 (15.8)</td>
<td>28 (16)</td>
<td>24 (10)</td>
</tr>
</tbody>
</table>

Table 2. Table 2. Change in disease activity (CDAS) by LOT and by ACPA status

<table>
<thead>
<tr>
<th>Biologic naive</th>
<th>Baseline CDAS score</th>
<th>Follow-up CDAS score</th>
<th>ACPA reduction from baseline</th>
<th>TNFi reduction from baseline</th>
<th>Mean (SD) reported, unless otherwise stated</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNFis (n)</td>
<td>ACPA+</td>
<td>ACPA-</td>
<td>TNFis n (%)</td>
<td>ACPA+ n (%)</td>
<td>12.0±5.2 (13.6)</td>
</tr>
<tr>
<td>24 (10)</td>
<td>24 (10)</td>
<td>24 (10)</td>
<td>12 (6.8)</td>
<td>13 (6.8)</td>
<td>24 (10)</td>
</tr>
<tr>
<td>ACPA+ (n)</td>
<td>TNFis</td>
<td>ACPA-</td>
<td>TNFis n (%)</td>
<td>ACPA+ n (%)</td>
<td>13.6 (12.8)</td>
</tr>
<tr>
<td>24 (10)</td>
<td>24 (10)</td>
<td>24 (10)</td>
<td>12 (6.8)</td>
<td>13 (6.8)</td>
<td>24 (10)</td>
</tr>
</tbody>
</table>

Results: Data for 105 first-line and 91 second- or further-line (subsequent-line) matched pairs of TNFI and ABA pts were included in the analysis (68 first-line and 60 subsequent matched pairs of TNFI and ABA pts, respectively, in ACPA+ cohort; 31 first-line and 21 subsequent-
line matched pairs of TNFi and ABA pts, respectively, in ACPA+ cohort (Table 1). In the biologic-experienced pts, ABA (vs TNFi) had a higher reduction in CDAI score (10.2 vs 5.2, p<0.035; Table 2). In the biologic-experienced ACPA+ pts, ABA (vs TNFi) had higher reduction in disease activity (CDAI: 13.3 vs 6.2, p<0.023; Table 2; SDAI: 13.9 vs 7.0, p<0.046). No difference in disease activity was observed between the two groups among the ACPA+ pts.

**Conclusion:** Real-world RA registry data further confirm findings from the ABLE-SE study that the overall efficacy of ABA is similar to TNFi agents in biologic-naive pts with RA. Efficacy of ABA (vs TNFi) in biologic-experienced pts is greater, and greater reductions in joint disease activity in ACPA+ ABA (vs TNFi) pts were observed.

**REFERENCES**


**Disclosure of Interests:** Evo Atema Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Sean Connolly Shareholder of: Bristol-Myers Squibb, Employee of: Bristol-Myers Squibb, Yedid Elbez Employee of: Employee of: Excelya which received funding from Bristol-Myers Squibb as contract research organization., Aarti Rao Consultant for: Bristol-Myers Squibb, Christine Iannaccone: None declared, Michael E. Weinblatt Shareholder of: Stock option: Can-File, Lycera, Scipher, Immixedi, Grant/research support from: Crescendo Bioscience, Bristol Myers Squibb, Sanofi, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Can-File, Corrona, Crescendo, GlaxoSmithKline, Gilead, Horizon, Lilly, Lycera, Merck, Novartis, Pfizer, Roche, Samsung, Scipher, Set Point, Nancy Shadick Grant/research support from: Bristol-Myers Squibb, Sanofi/Regeneron, Crescendo Biosciences, Mallinckrodt, Amgen, Consultant for: Consulting work for Bristol-Myers Squibb for under $10,000.

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**AB0374 ADALIMUMAB DISCONTINUATION IN PATIENTS WITH RHEUMATOID ARTHRITIS AFTER ACHIEVING SUSTAINED REMISSION**

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**Background:** The most important factor in the progress of pharmacotherapeutic therapy of RA was the widespread implementation of therapy with biological drugs modifying antirheumatic drugs (bDMARD). Recently, the issues of optimizing the management of patients have attracted more and more attention. First of all, we are talking about the possibility of reducing the dose and the abolition of bDMARD with the maintenance of remission (“biological-free remission”).

**Objectives:** To assess whether adalimumab (AD) can be gradually discontinued during continuous methotrexate (MTX) use in patients with early rheumatoid arthritis (ERA).

**Methods:** Within the REMARCA (the Russian study of methotrexate and biological agents in early active arthritis) study, the investigators examined 20 patients (17 women and 3 men; median age, 51 [41.5; 56] years) with ERA (disease duration, 10 [5.5; 20] months; DAS28, 5.17 [4.37; 6.51]; 85% of the patients were seropositive for rheumatoid factor and 85% for anti-cyclic citrullinated peptide antibodies.

All the patients received subcutaneous MTX 25 mg/week. Twelve weeks after beginning therapy with MTX, due to its inefficiency, ADA was added according to the standard scheme. Clinical and laboratory data was analyzed just before the therapy (point-3 months), then at the term of 6 (n=20), 12 (n=17), 24(n=17) and 36 (n=17) months. To assess the effectiveness of therapy, indices of activity DAS28, CDAI and SDAI were used. The everyday life functioning of the patient was assessed quantitatively using the Russian version of the HAQ questionnaire.

**Results:** At week 24, with the combined therapy of methotrexate and adalimumab, about 75% of patients had reached remission/low disease activity; the median DAS28 was 3.0 [1.65; 3.73]; 85% of the patients achieved remission or low disease activity. After 3 months of ADA therapy, high or moderate disease activity remained in 3 (15%) patients; median DAS28 was 4.4 [4.3; 6.1]; the drug was discontinued in them due to ineffective therapy. After 12-month follow-up, low DAS28 scores were observed in 5 (29.4%), DAS28 remission was in 12 (70.6%) of the 17 patients who continued ADA treatment; after 24 months, all the 17 patients were noted to have remission. After achieving sustained remission (>6-month duration during ADA therapy), there was a carefully controlled reduction (titration) in the dose of ADA with its complete discontinuation, by maintaining remission at 36-month follow-up; the median DAS28 was 1.6 [1.4; 2.2].

The disease duration up to 1 year and functional class reduction to I in the first year of observation (r=-46.2; 95% CI 1.870-1141.178; P=0.019 and r=-44.2; 95% CI 1.795-1088.143; P=0.02) were identified as predictors of maintaining long-term remission after the discontinuation of ADA.

**Figure 1. Influence of different factors on the possibility of withdrawal of ADA in patients with RA in remission.**

**Remission maintenance**

**Conclusion:** In most patients with early rheumatoid arthritis, early induction of remission can be maintained after stopping the biologic therapy, under condition that the therapy was carried out by a combination of bDMARD and methotrexate. The maintenance of remission after discontinuation of ADA therapy was influenced by the duration of the disease and the depth of remission.

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.4054

**AB0375 HYPOGAMMAGLOBULINEMIA AFTER RITUXIMAB TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS IS NOT RARE AND IS ASSOCIATED WITH BETTER RESPONSE**

Gerasimos Evangelatos1, George E. Frangouls1, Kostki Kladianas2, Dimitrios Vassilopoulos3, Alexios Ilipoulos3, 1417 Army Share Fund Hospital (NIMTS), Athens, Greece, Rheumatology Department, Athens, Greece; 2Joint Rheumatology Program, National and Kapodistrian University of Athens, School of Medicine-Clinical Immunology-Rheumatology Unit, 2nd Department of Medicine, Athens, Greece

**Background:** Rituximab (RTX) is used as a second line treatment in rheumatoid arthritis (RA), with well-established efficacy. One of the most common adverse events of RTX use is hypogammaglobulinemia (HGG).

**Objectives:** To define, in RA patients treated with Rituximab, the frequency of HGG (lgG>700mg/dL or lgM>40mg/dL or lgA>70mg/dL) and to identify associations between its occurrence and clinical, epidemiological and other disease related features at baseline, RA outcomes and adverse events.

**Methods:** The patients received RTX for RA in two rheumatology centers from 1/2007 to 12/2018 were included. Demographical, clinical and laboratory parameters were recorded at baseline and at the last visit of the follow-up. Time of follow-up was defined as the time interval between the first RTX infusion and the last visit. Patients with monoclonal gammapathy and patients that received only one cycle of treatment were excluded. Severe infections were recorded defined as those which required hospitalization or antibiotics intravenously. Binominal regression analysis using stepwise backwards model having as dependent variables the “low IgG” or “low IgM” and independent variables: gender, age,
RESULTS OF A MANDATORY SWITCHING FROM CLINICAL SIMILARITY OF ABP 710 WITH INFliximab

Sabela Fernández, Senen Gonzalez, Carmen Ordas-Calvo, Edilia García-Gijón, Spain

Background: Currently available evidence indicates that a single switch from a bio-originator to one of its biosimilars is safe and effective and has cost benefits to the National Health Systems. However, there is some reluctance to switch patients due to lack of real-world data and differences between patients treated in the setting of real clinical practice and those of clinical trials.

Objectives: We aimed to investigate the efficacy and safety of Etanercept (ETN) to SB4 carried out in March 2018. Inflammatory arthritis patients (rheumatoid arthritis (RA), psoriatic arthritis (APS), axial spondyloarthritides (AS), juvenile idiopathic arthritis (JIA)) were included in this single-center retrospective observational study from March 2018 to December 2018. Reasons for SB4 withdrawal were categorized as lack of effect (LOE), adverse events (AE) or others.

Methods: At Cabueñes Hospital a non-medical switch from Etanercept (ETN) to SB4 was carried out in March 2018. Inflammatory arthritis patients (rheumatoid arthritis (RA), psoriatic arthritis (APS), axial spondyloarthritides (AS), juvenile idiopathic arthritis (JIA)) were included in this single-center retrospective observational study from March 2018 to December 2018. Reasons for SB4 withdrawal were categorized as lack of effect (LOE), adverse events (AE) or others.

Results: A total of 117 patients were identified, 100% were switched to SB4 maintaining the same dose. Disease duration was 5 (2-8.5) years. 49 patients (41%) had basal optimized dose of ETN (dose down-titration or dose interval expansion). In most patients ETN was the first biologic. 31 patients (26%) stopped SB4 treatment during follow-up, mainly due to LOE (67%) or AE (25%), with median duration of SB4 3.5 months (1-9, 5-9). Most AE that led to withdrawal were dermatological (injection-site reactions, skin rash). 11 patients switched back to ETN, 15 to others. Two patients died, both were APS (one sudden death and one aneurysmal subarachnoid hemorrhage). After switching to SB4, one stable patient with AS had recurrent acute anterior uveitis, and psoriasis worsening were noted in 2 patients with APS. 2 patients needed reinstatement of the full dose of biologic because of LOE. The clinical situation on ETN was stable in 23 of the 31 (74%) patients who stopped SB4 (no flares or changes in treatment in the last 6 months before switch).

Table 1 summarizes baseline characteristics and treatment outcomes. Conclusion: Biosimilar switch of SB4 was successful in over 74% of cases and was well tolerated.

Most patients who stopped SB4 due to LOE had a clinical stable situation in this observational study. Some concerns regarding the safety profile and interchangeability have raised and further evidence on the efficacy of transitioning from reference ETN is needed.

Table 1

<table>
<thead>
<tr>
<th>Variable</th>
<th>RA (n=47)</th>
<th>APS (n=29)</th>
<th>AS (n=30)</th>
<th>JIA (n=8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>62 (53.71)</td>
<td>51 (46.60)</td>
<td>49 (42.60)</td>
<td>42 (30-51)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>33 (70.2%)</td>
<td>11 (37.9%)</td>
<td>4 (13.3%)</td>
<td>2 (25%)</td>
</tr>
<tr>
<td>Monotherapy, n (%)</td>
<td>17 (36%)</td>
<td>16 (55%)</td>
<td>30 (100%)</td>
<td>6 (75%)</td>
</tr>
<tr>
<td>Dose optimization, n (%)</td>
<td>18 (38.6%)</td>
<td>13 (44.8%)</td>
<td>12 (40%)</td>
<td>5 (62.5%)</td>
</tr>
<tr>
<td>Duration of ETN (years, median IQR)</td>
<td>4 (1.8-6)</td>
<td>4.2 (2.6)</td>
<td>5.9 (2.1-6.0)</td>
<td>6 (4.1-8.2)</td>
</tr>
<tr>
<td>Other biologic drug prior to ETN, n (%)</td>
<td>6 (12.7%)</td>
<td>7 (24.1%)</td>
<td>6 (20%)</td>
<td>1 (12.5%)</td>
</tr>
<tr>
<td>9-month treatment outcomes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Withdrawal during follow-up, n (%)</td>
<td>15 (31.9%)</td>
<td>8 (27.5%)</td>
<td>6 (20%)</td>
<td>1 (12.5%)</td>
</tr>
<tr>
<td>Duration of SB4 (months, median IQR)</td>
<td>5.1</td>
<td>3.8 (1.9)</td>
<td>4.3 (2.6)</td>
<td>2.3 (1.4-5.9)</td>
</tr>
</tbody>
</table>

Disclosure of Interests: None declared


RESULTS OF A MANDATORY SWITCHING FROM ORIGINATOR TO BIOSIMILAR ETANERCEPT IN 117 PATIENTS WITH INFLAMMATORY ARTHRITIS FROM A SINGLE CENTER

Sabela Fernández, Seren Gonzalez, Carmen Ordas-Calvo, Edilia García-Fernández, Belén Rodríguez De-Castro, Jesús Babilio, Gijón, Rheumatology, Gijón, Spain

Background: Currently available evidence indicates that a single switch from a bio-originator to one of its biosimilars is safe and effective and has cost benefits to the National Health Systems. However, there is some reluctance to switch patients due to lack of real-world data and differences between patients treated in the setting of real clinical practice and those of clinical trials.

Objectives: We aimed to investigate the efficacy and safety of Etanercept-biosimilar (SB4), in a non-medical switch in patients with inflammatory arthritis (IA)

Methods: At Cabueñes Hospital a non-medical switch from Etanercept (ETN) to SB4 was carried out in March 2018. Inflammatory arthritis patients (rheumatoid arthritis (RA), psoriatic arthritis (APS), axial spondyloarthritides (AS), juvenile idiopathic arthritis (JIA)) were included in this single-center retrospective observational study from March 2018 to December 2018. Reasons for SB4 withdrawal were categorized as lack of effect (LOE), adverse events (AE) or others.

Results: A total of 117 patients were identified, 100% were switched to SB4 maintaining the same dose. Disease duration was 5 (2-8.5) years. 49 patients (41%) had basal optimized dose of ETN (dose down-titration or dose interval expansion). In most patients ETN was the first biologic. 31 patients (26%) stopped SB4 treatment during follow-up, mainly due to LOE (67%) or AE (25%), with median duration of SB4 3.5 months (1-9, 5-9). Most AE that led to withdrawal were dermatological (injection-site reactions, skin rash). 11 patients switched back to ETN, 15 to others. Two patients died, both were APS (one sudden death and one aneurysmal subarachnoid hemorrhage). After switching to SB4, one stable patient with AS had recurrent acute anterior uveitis, and psoriasis worsening were noted in 2 patients with APS. 2 patients needed reinstatement of the full dose of biologic because of LOE. The clinical situation on ETN was stable in 23 of the 31 (74%) patients who stopped SB4 (no flares or changes in treatment in the last 6 months before switch).

Table 1 summarizes baseline characteristics and treatment outcomes. Conclusion: Biosimilar switch of SB4 was successful in over 74% of cases and was well tolerated.

Most patients who stopped SB4 due to LOE had a clinical stable situation in this observational study. Some concerns regarding the safety profile and interchangeability have raised and further evidence on the efficacy of transitioning from reference ETN is needed.

REFERENCES

Disclosure of Interests: None declared


AB0377

CLINICAL SIMILARITY OF ABP 710 WITH INFliximab (REFERENCE PRODUCT) IN SUBJECTS WITH MODERATE TO SEVERE RHEUMATOID ARTHRITIS

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1Stanford, Division of Immunology and Rheumatology, Palo Alto, United States of America; 2Hospital Infanta Luisa, Sevilla, Spain; 3Amgen, Thousand Oaks, United States of America; 4Coagrád Megyéi Dr. Bugyi István Kórház, Sima Ferenc, Hungary; 5Bioglasa Community Research, Lexington,KY, United States of America; 6Amgen, Thousand Oaks,CA, United States of America; 7Metroplex Clinical Research, Dallas,Tx, United States of America

Background: ABP 710 is being developed as a biosimilar to infliximab. Both ABP 710 and infliximab reference product (RP) inhibit tumor necrosis factor-alpha and have been shown to be structurally and functionally similar in analytical assessments. In a phase 1 clinical pharmacokinetic (PK) study both were shown to be bioequivalent for PK
The effects of biologicals on reproduction are unknown. Therefore pregnancy during biologicals use is not recommended. However biologicals are frequently prescribed in patients of childbearing potential and many patients become pregnant while using these drugs.

Objectives: In 2015 EULAR published a broad review article on this matter. Our aim was to update the data based on newly published articles.

Methods: A search was conducted at 18/10/2017 and then 21/11/2018 in Embase, Medline Ovid, Web Of Science, Cochrane CENTRAL and Google Scholar with specific search terms for each database. Articles were excluded based on title/abstract (double blind, two researchers, NG and HUMC) and then full text (one researcher, NG). A chart was made based on outcomes of interest (see Table1). The references of included articles were reviewed to include and minimize the missing articles.

Results: Totally 137 articles were included (79 articles at first round, 51 articles at second round and 7 found after screening the references of included articles). A descriptive analysis was performed to sum up the data on each separate biological and all the biologicals together. The results are shown in Table1. It should be notified that due to heterogeneity of the data the calculated percentages are up to individual interpretations and cannot be compared to each other.

Conclusion: From 2015 onwards, there have been many articles published regarding use of biologicals during pregnancy. Despite limitations of our study, such as heterogeneity in being prospective or retrospective and quality of the included articles, no alarm is raised concerning safety issues.


Table 1. Results of the final chart. The denominator is the sum up of total cases recruited from the articles, for each outcome the denominator is defined as the population for which the specific outcome was reported. The other cases, which haven’t mentioned the outcome in their results, were excluded from the denominator for that specific outcome. Both spontaneous and elective abortion cases are excluded from the denominator of preterm birth and major congenital malformations.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Maternal exposed pregnancies</th>
<th>Elective</th>
<th>Abortion Spontaneous</th>
<th>Live birth</th>
<th>Preterm birth</th>
<th>Major congenital malformations</th>
<th>Serious infections in children</th>
<th>ADRs to vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abatacept</td>
<td>153</td>
<td>13.1%</td>
<td>26.1%</td>
<td>60.8%</td>
<td>6.8%</td>
<td>0.0%</td>
<td>0.0%</td>
<td>(0/93)</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>2518</td>
<td>0.1%</td>
<td>0.4%</td>
<td>95.5%</td>
<td>3.2%</td>
<td>3.7%</td>
<td>7.9%</td>
<td>0.5%</td>
</tr>
<tr>
<td>Anakinra</td>
<td>34</td>
<td>2.9%</td>
<td>2.9%</td>
<td>94.2%</td>
<td>17.7%</td>
<td>3.4%</td>
<td>0.0%</td>
<td>-</td>
</tr>
<tr>
<td>Certolizumab</td>
<td>767</td>
<td>4.7%</td>
<td>8.2%</td>
<td>86.9%</td>
<td>17.7%</td>
<td>1.5%</td>
<td>4.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Gp101</td>
<td>801</td>
<td>7.6%</td>
<td>17.4%</td>
<td>84.7%</td>
<td>11.5%</td>
<td>6.2%</td>
<td>0.0%</td>
<td>0.4%</td>
</tr>
<tr>
<td>Etanercept</td>
<td>2174</td>
<td>5.1%</td>
<td>9.6%</td>
<td>79.3%</td>
<td>10.9%</td>
<td>13.7%</td>
<td>18.2%</td>
<td>(0/140)</td>
</tr>
<tr>
<td>Infliximab</td>
<td>2174</td>
<td>5.1%</td>
<td>9.6%</td>
<td>79.3%</td>
<td>10.9%</td>
<td>13.7%</td>
<td>18.2%</td>
<td>(0/140)</td>
</tr>
<tr>
<td>Rituximab</td>
<td>27</td>
<td>0.0%</td>
<td>12.5%</td>
<td>87.5%</td>
<td>18.2%</td>
<td>0.0%</td>
<td>0.0%</td>
<td>-</td>
</tr>
<tr>
<td>Tocilizumab</td>
<td>368</td>
<td>14.6%</td>
<td>20.9%</td>
<td>64.2%</td>
<td>18.1%</td>
<td>4.9%</td>
<td>0.0%</td>
<td>-</td>
</tr>
<tr>
<td>Tolctacinb</td>
<td>47</td>
<td>19.5%</td>
<td>17.1%</td>
<td>63.4%</td>
<td>7.7%</td>
<td>3.8%</td>
<td>0.0%</td>
<td>-</td>
</tr>
<tr>
<td>Ustekinumab</td>
<td>46</td>
<td>0.0%</td>
<td>7.1%</td>
<td>92.9%</td>
<td>3.8%</td>
<td>0.0%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
<tr>
<td>Vedolizumab</td>
<td>59</td>
<td>11.1%</td>
<td>18.5%</td>
<td>70.4%</td>
<td>2.9%</td>
<td>10.0%</td>
<td>0.0%</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

ADR= Adverse Drug Reaction * mild fever after rotavirus vaccination. † unilateral agenesis and ectopic neurohypophysis. £ Just one article had information in this regard.
GENDER DIFFERENCES IN RHEUMATOID ARTHRITIS: EFFECT OF ANTI-TUMOR NECROSIS FACTOR THERAPY

Chiara Giosa1,2, Francesca Sprielli1, Roberta Priori1, Cristina Iannuccelli1, Bruno Luccichino1, Annarita Vestri1, Guido Valente1, Manuela Di Franco1,2

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Background: Rheumatoid arthritis (RA) is more prevalent in women than men (F:M=4:1), due to hormonal, genetic and environment factors. Women present higher disease activity markers as Disease Activity Score-28 (DAS28) and Health Assessment Questionnaire (HAQ), at the onset and after c-DMARDs therapy, without correlation with radiographic damage.

Objectives: The purpose of this study was to assess gender differences in RA patients after anti-tumor necrosis factor (TNFα) treatment.

Methods: Ninety-six patients were enrolled at the beginning of anti-TNFα therapy (etanercept and adalimumab). All patients satisfied 1987 and 2005 ACR criteria for RA. They underwent to clinical and clinimetric evaluation at baseline (T0) and after three (T3) and six (T6) months of therapy with: tender and swollen joints, Visual Analogic Scale (VAS) pain, physician global assessment (PhGA) and global assessment (PGA), swollen joint count (SJC) and tender joint count (TJC). Demographic and clinical data were collected. SPSS statistics 22.0 was used for statistical analysis; p values under 0.05 were considered significant.

Results: Among these patients, 70 were women and 26 men; 81 patients (58 female, 23 male) started etanercept and 15 adalimumab (12 female, 3 male). They presented a mean age of 56.4 ± 14.5 years (women 55.2 ± 15.4, men 60 ± 12.2) and mean disease duration of 11 ± 6.8 years (woman 11.51 ± 6.3, men 9.6 ± 8.1). Both women and men had a DAS28 reduction after 3 and 6 months therapy (p<0.05) but DAS28 in women was higher than men at T0, T3 and T6 (p<0.05). Women presented higher number of tender joints in all evaluations, and more swollen joints than men at T0 and T6 (p<0.05). Women felt more active disease at T6 (VAS patient) (p<0.05). CDAI was higher in woman after 3 and 6 months (p<0.05). There were no differences about physician evaluation, inflammation markers, RF and ACPA titers.

Conclusion: In this study, both women and men had a good response to anti-TNF treatment but women presented worse clinical response. Female gender resulted the only variable associated with DAS28 reduction after 3 and 6 months of therapy. We could hypothesize that beyond to biological factors, also social contest, daily life and work activity could explain a worse disease activity.

Table 1. Patients clinical characteristics at hospital admission (n=96)

<table>
<thead>
<tr>
<th>Patients clinical characteristics</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Female</em></td>
<td>58 (61.3)</td>
</tr>
<tr>
<td><em>Male</em></td>
<td>38 (39.6)</td>
</tr>
</tbody>
</table>

REFERENCES

Disclosure of Interests: None declared

ISTHERE AN EFFECT OF TOCILIZUMAB IN SERUM AUTOANTIBODIES LEVELS IN RHEUMATOID ARTHRITIS?

2 Centro Hospitalar e Universitário de São João, Department of Rheumatology, Oporto, Portugal.
3 Centro Hospitalar do Bairro Vouga, Department of Rheumatology, Aveiro, Portugal

Background: Interleukin 6 (IL-6) plays a role on B cell differentiation and antibody production. However, few information is available considering the effect of tocilizumab (TCZ) on rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPAs) levels in Rheumatoid Arthritis.

Objectives: To compare serum levels of RF and ACPAs on RA patients at the beginning of therapy with TCZ and at 6 and 12 months under TCZ, assessing if its variations correlate with the several disease activity scores.

Methods: Longitudinal retrospective study of RA patients ever treated with TCZ at a Rheumatology Department. Serum levels of RF and ACPAs at 0, 6 and 12 months after starting anti-IL6 treatment were collected, as well as DAS28, CRP, CDAI, SDI, HAQ, ESR, CRP, patient’s global assessment (PGA), physician’s global assessment (PGa), swollen joint count (SJC) and tender joint count (TJC). Demographic and clinical data were collected. SPSS statistics 22.0 was used for statistical analysis; p values under 0.05 were considered significant.

Results: 75 patients were included, 93.3% female (N=70), with a median (min-max) age of 58 (33-80) years and median disease duration at TCZ initiation of 10.7 years (1.0-43.3); 33.3% were on TCZ monotherapy (N=25). At baseline, forty-two (56.0%) were RF positive (≥30U/mL) and 47 (62.7%) were ACPAs positive (≥10UI/mL). Median serum RF levels were 255.0 UI/mL (37.20-5560.00), 193.5 UI/mL (9.80-5270.00) and 131.0 UI/mL (9.00-6200.00) at 0, 6 and 12 months respectively; serum RF levels were only statistically different (p=0.006) between 0 and 6 months. Median serum ACPAs levels were 278.5 UI/mL (17.00-9300.00), 348.0 UI/mL (19.00-4720.00) and 277.0 UI/mL (16.00-4400.00) at 0, 6 and 12 months respectively, without any statistically significant differences. Considering the autoantibodies levels variation, ΔRF at 6 months correlated positively with ΔHAQ (r=0.482; p=0.009) and ΔACPAs (r=0.413; p=0.026). After one year, ΔRF correlated positively with ESR (r=0.426; p=0.019) and DAS28 (r=0.428; p=0.018). As for ΔACPAs at 6 months, it correlated positively with PhGA (r=0.491; p=0.035). At 12 months, there was a positive correlation between ΔACPAs and ΔCDAI (r=0.385; p=0.038) and between ΔACPAs and ΔSJC (r=0.469; p=0.002).

Conclusion: In our RA sample, serum RF levels showed a significant titre difference past 6 months of treatment with TCZ. Moreover, a moderately strong correlation was found between ΔACPAs/ΔRF at 12 months and the variations in several disease activity scores. Thus, this study reinforces the evidence of an impact of IL-6 inhibition on autoantibodies production in RA patients, as well as a relation between autoantibodies titre variation and clinical response. These findings need to be assessed in larger, prospective studies.

REFERENCES

Disclosure of Interests: None declared
CERTOLIZUMAB PEGOL IN AUTOIMMUNE DISEASES. REAL LIFE EXPERIENCE IN PREGNANCY

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1IDEARG, Immunorheumatology, Bogota, Colombia; 2Foundation Universitaria Juan N Correa, Immunology and Internal Medicine, Bogota, Colombia; 3IDEARG, Immuno/Rheumatology, Bogota, Colombia; 4IDEARG, Immunorheumatology, Bogota, Colombia

Background: Certolizumab pegol (CZP) is a Pegylated, Fc free monoclonal antibody that is useful in different autoimmune conditions. It does not bind FcRn and is not expected to undergo transfer across the placenta and probably there is a minimal placenta transfer of CZP in humans. On the other hand, most chronic inflammatory diseases are prevalent in women and 50% of these diseases need active treatment. We describe our experience for more than 7 years in patients with inflammatory arthritis and pregnancy that received CZP.

Methods: We review our cohort of patients with Rheumatoid Arthritis, Spondyloarthritides and psoriatic arthritis from 2011 to 2017 that received CZP and analyzed those cases of pregnancy and described the clinical characteristic, the medication concomitant and the course of the pregnancy.

Results: We review more than 750 patients with inflammatory arthritis that received CZP and found 15 cases that was in pregnancy. See table 1.

Table 1. The use of CZP was effective, good tolerated and the profile of safety for the mother and the product was acceptable.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Disease</th>
<th>Drug exposure (months)</th>
<th>Clinical course</th>
<th>Breastfeeding</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>28</td>
<td>RA, (Rheumatoid Arthritis).</td>
<td>5</td>
<td>Normal.</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>RA</td>
<td>7.5</td>
<td>Pred, 34 weeks. - 1500 gram</td>
<td>+ 3 month</td>
<td></td>
</tr>
<tr>
<td>38</td>
<td>RA</td>
<td>2</td>
<td>Miscarriage, 8 weeks.</td>
<td>Methotrexate Use. NA.</td>
<td></td>
</tr>
<tr>
<td>48</td>
<td>RA</td>
<td>5</td>
<td>Miscarriage, 5 weeks.</td>
<td>Methotrexate use. Ind</td>
<td></td>
</tr>
<tr>
<td>32</td>
<td>Seronegative Spondyloarthritides.</td>
<td>4</td>
<td>Normal.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>36</td>
<td>RA</td>
<td>8</td>
<td>Caesarean section. 1400 grams. Gestational age</td>
<td>31 weeks. Pred.</td>
<td>t</td>
</tr>
<tr>
<td>24</td>
<td>Seronegative Spondyloarthritides</td>
<td>9</td>
<td>Normal.</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>29</td>
<td>RA</td>
<td>9</td>
<td>Normal.</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>31</td>
<td>RA</td>
<td>4</td>
<td>Normal.</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>33</td>
<td>Seronegative Spondyloarthritides</td>
<td>9</td>
<td>Normal. Caesarean section. (C-section).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>37</td>
<td>RA</td>
<td>8</td>
<td>Pred.</td>
<td>Baby 33 weeks. Arterial Hypertension, Gestational Diabetes. 1640 grams.</td>
<td></td>
</tr>
<tr>
<td>32</td>
<td>RA</td>
<td>9</td>
<td>Normal. Caesarean section. (C-section).</td>
<td></td>
<td></td>
</tr>
<tr>
<td>31</td>
<td>Psoriatic Arthritis</td>
<td>6.5</td>
<td>Normal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>RA</td>
<td>10</td>
<td>Normal</td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>Psoriatic Arthritis</td>
<td>9</td>
<td>Normal</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: CZP is a useful alternative of treatment for pregnant patients and with inflammatory arthropathies that required therapeutic agent. This topic has been recently review and show that this agent is safe for pregnant women and for those breastfeeding and support continuation of CZP during pregnancy, when considered necessary.

REFERENCES

Disclose of Interests: None declared

ABO382 TROUGH VERSUS NON-TRough ADALIMUMAB DRUG LEVEL MEASUREMENTS

Fenke Hooijberg1, Merel J. L’am1, Lea C. Berkhoudt2, Sadaf Aliq1, Michael Nurmohamed1, Annick de Vries3, Charlotte L. Kieckerta1, Theo Rispens12, 1Get-Jan Woblink3, 3Amsterdam Rheumatology and immunology Center, location Reade, Amsterdam, Netherlands; 2Department of Immunopathology, Sanquin Research, Amsterdam, Netherlands; 3Landsteiner Laboratory, Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands; 4Biologics Lab, Sanquin Diagnostic Services, Amsterdam, Netherlands; 5Amsterdam Rheumatology and immunology Center, location VUmc, Amsterdam, Netherlands

Background: Over the last years there has been an increasing interest for measuring drug levels to guide decision-making. Serum samples used for these measurements are often obtained prior to the next injection, at trough level. However, Jani et al. (2015) analyzed drug levels of randomly acquired serum samples from patients with rheumatoid arthritis (RA) treated with either etanercept or adalimumab and found a significant relationship with clinical disease activity. This indicates that random drug level measurements might also be useful (1). However, more aspects should be considered before deciding to use non-trough measurements.

Objectives: To assess the effect of non-trough measurements, compared to trough measurements, on serum drug level.

Methods: Patients with RA starting adalimumab treatment were included in this prospective observational cohort study, named the Reade Rheumatology Registry. Serum samples were obtained during every visit and these were analyzed for drug levels using a regular enzyme-linked immunosorbsent assay (Sanquin, Amsterdam). The date of a patient’s last injection with adalimumab was documented. Samples were included in the analyses if the interval between the last injection and serum sampling did not exceed 28 days, as in general patients do not have such long dosing-intervals. The analysis was performed using Spearman correlation.

Results: In total, 121 RA patients were included in this study. The median follow-up period of these patients was 156 (interquartile range (IQR) 78-247) weeks. Drug level measurements were performed in all serum samples that were obtained. In total, 310 measurements were included in the analyses, as from this subset the date of the previous injection with adalimumab was documented. The median drug level during adalimumab treatment was 6.6 (IQR 4.2-9.8) μg/ml, and the median number of days between the previous injection of adalimumab and serum sampling was 8 (5-13). The latter was divided into quartiles and plotted against drug level (Figure 1). The first quartile (median 2 (IQR 1-3) days) had a median drug level of 8.0 (4.7-11.0) μg/ml, the second quartile (7 (6-8) days) of 6.9 (5.4-10.0) μg/ml, the third quartile (11 (10-12) days) of 6.1 (3.4-9.5) μg/ml, and the fourth quartile (14 (13-14) days) of 5.7 (3.1-8.5) μg/ml. A weak association was found between the number of days between the previous injection of adalimumab and serum sampling and adalimumab drug level (Spearman’s ρ= ρ=0.182, p=0.001).

Conclusion: The growing interest to apply therapeutic drug monitoring (TDM) within the field of rheumatology forces us to discuss which measurements, trough or non-trough, are most informative. We found a correlation between the number of days between the previous injection of adalimumab and serum sampling, and adalimumab drug level. This might suggest that the timing of serum sampling affects the measured drug level, which could have consequences for treatment decisions based on these drug levels.
LATENT TUBERCULOSIS INFECTION SHOULD BE MONITORED IN BOTH TUMOR NECROSIS FACTOR INHIBITORS AND NON-TUMOR NECROSIS FACTOR INHIBITORS IN BIOLOGIC-NAIVE PATIENTS WITH RHEUMATOID ARTHRITIS

Yun-Ju Huang, Yao-Fan Fang, Shue-Fen Luo, Kuang-Hui Yu, Chang-Fu Kuo, Ping-Ha Tsai, Yen-Fu Chen. Division of Rheumatology, Allergy and Immunology, Taoyuan City, Taiwan, Republic of China

Background: The risk of latent tuberculosis infection (LTBI) increased during the treatment of biologic agents for patients with rheumatoid arthritis. Taiwan rheumatology association recommend performing at least annual interferon-gamma release assays (IGRAs) testing during biologic treatment course because of the moderate prevalence of tuberculosis in Taiwan.[1] Although increased tuberculosis reactivation rate in patients with TNF or non-TNF inhibitors should be monitored LTBI in moderate prevalence TB area.

Methods: We retrospectively collected 313 biologic-naïve patients with rheumatoid arthritis treated with TNF and non-TNF inhibitors in Taiwan. All RA patients underwent interferon-gamma release assays during biologic treatment. Cox proportional hazard model was used for analysis to compared RA patients with TNF or non-TNF inhibitors.

Results: The age of patients and disease duration are 55.9 13.1 year-old and 5.2 2.0 years(Table 1). The LTBI rate in patients with rheumatoid arthritis treated with TNF and non-TNF inhibitors in Taiwan. All RA patients underwent interferon-gamma release assays testing during biologic treatment.

Cox regression analysis of RA patients found that the risk of LTBI was not different in TNF or non-TNF inhibitors.

Conclusion: Our study revealed biologic-naive patients with rheumatoid arthritis have the same risk of LTBI. All RA patients who need either TNF or non-TNF inhibitors should be monitored LTBI in moderate prevalence TB area.

Table 1. Baseline characteristics in patients with RA treated with TNF or non-TNF inhibitors

<table>
<thead>
<tr>
<th>Total (n=313)</th>
<th>TNF inhibitors (n=200)</th>
<th>Non-TNF inhibitors (n=113)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender, female</td>
<td>259</td>
<td>169(64.5%)</td>
<td>90(79.6%)</td>
</tr>
<tr>
<td>Age (Means standard deviation)</td>
<td>56.9</td>
<td>55.0</td>
<td>57.6</td>
</tr>
<tr>
<td>Disease duration (Means standard deviation)</td>
<td>13.1</td>
<td>12.3</td>
<td>14.4</td>
</tr>
</tbody>
</table>

Disclosure of Interests: None declared

REFERENCES

AWARE IS A PROSPECTIVE, NONINTERVENTIONAL, 3-YEAR STUDY AT 100 US SITES. RA pts were enrolled when initiating TNFi treatment. Treatment decisions are at the discretion of the treating rheumatologist. The study utilizes PROMIS and Clinical Disease Activity Index (CDAI) to assess effectiveness.

Objectives: This analysis examined select PROMIS measures to assess (1) relationship between baseline (BL) CDAI and PROMIS-scores, (2) responsiveness of PROMIS after initiation of TNFi and (3) relationship between PROMIS T-scores of the 4 item Profile29v2 Fatigue and Pain Interference domains and respective PROMIS Short Forms (SF).

Methods: AWARE is a prospective, noninterventional, 3-year study at 100 US sites. RA pts were enrolled when initiating TNFi treatment. Treatment decisions are at the discretion of the treating rheumatologist. We report on data from Pts’ BL PROMIS Pain Interference 6b (PI), Fatigue7a (F), Profile29v2 and CDAI. PROMIS T-scores were compared across CDAI disease category (high, moderate etc) using ANOVA. We dichotomized pts based on whether their BL T-score was in 0.5SD of the population mean (i.e. normal) or not to evaluate for effect modification in the subsequent change in PROMIS T-scores. Data shown are mean ± sd dev.

Results: Pts (N=1220) were 59.5± 13.2 yrs, disease duration 8.2 ± 9.9 yrs, 83.4% female, body weight 85.1± 24.2 kg, BMI 31.4 ± 85.1, BL CDAI 32.4 ± 15.6. A significant relationship between PROMIS T-scores (PI, F) and BL CDAI disease activity category was confirmed. There was minimal change in T-score of pts with BL PI and F T-scores <-0.5 and P>0.05 over 5 infusions (approx. 5-7 months). Depending on domain,

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<td>13.1</td>
<td>12.3</td>
<td>14.4</td>
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</tbody>
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Disclosure of Interests: None declared

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Integrated Safety Analysis Across Phase 3 Clinical Studies Including the Controlled and Uncontrolled Periods for Intravenous Golimumab in Rheumatoid Arthritis, Psoriatic Arthritis, and Ankylosing Spondylitis


The GO-FURTHER, GO-VIBRANT, and GO-ALIVE randomized controlled trials evaluated the efficacy and safety of intravenous (IV) golimumab (GLM) in patients (pts) with active rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS), respectively.

Methods: Integrated safety data from 3 Phase 3, double-blind, placebo (PBO)-controlled trials were analyzed up to week (WK) 112 in RA pts and up to WK 60 in PsA and AS pts. Pts received either IV PBO or IV GLM (2 mg/kg) at 0, 4, 12, and 20 WKs. PBO pts crossed over to IV GLM at WK 24, except RA pts randomized to PBO who met early escape criteria crossed over at WK 16 and AS pts randomized to PBO who crossed over at WK 16. Cumulative adverse events (AEs) were reported by indication and pooled by treatment. Anti-drug antibodies (ADAs) were evaluated.

Results: Overall, 1248 pts were treated with IV GLM across indications. A numerically greater proportion (% ) of IV GLM pts with RA reported safety events than pts with PsA or AS (Table 1): SAEs (18.2 vs 5.2 vs 3.4), infections (49.1 vs 22.8 vs 32.8), serious infections (6.2 vs 2.2 vs 1.5), and infusion reactions (4.6 vs 0.9 vs 1.5). Incidence (per 100 pt-years) of opportunistic infections, malignancy, active tuberculosis, and death with IV GLM was low (<0.5) across indications (Table 2). Infections were the most commonly reported type of SAE among pooled IV GLM pts; the most frequent was pneumonia (10 /0.5%). Incidence (per 100 pt-years) of serious infections was similar among IV GLM pts with and without corticosteroid use (3.35 vs 3.37, respectively). Overall, 1 IV GLM pt (PsA) experienced a demyelination event. A numerically greater proportion of IV GLM pts discontinued due to an AE than PBO pts (5.0% vs 0.7% vs 0.5%). In IV GLM pts with baseline alanine aminotransferase (ALT) ≥5X ULN was 2.1% vs 0% with methotrexate and 0.9% without methotrexate use at baseline, respectively. In IV GLM pts with baseline alanine aminotransferase (ALT) ≥ upper limit of normal (ULN) 1.2% had post-baseline ALT elevations ≥5X ULN. The proportion of IV GLM and PBO pts with post-baseline ALT elevations ≥5X ULN was 2.1% vs 0% with methotrexate and 0.7% vs 1.4% without methotrexate use at baseline, respectively. Using a drug-tolerant enzyme immunoassay, the incidence of ADAs was 22% through WK 52 across indications, which primarily consisted of low titer ADAs.

Conclusion: IV GLM demonstrated a consistent safety profile across indications in the PBO-controlled (up to WK 24) and uncontrolled study periods. Similar to WK 24 (1), more safety events occurred in RA pts, who represented the largest study population with older pts, longer disease duration, and more concomitant medication use.

Table 1

<table>
<thead>
<tr>
<th>Variables</th>
<th>RA</th>
<th>PsA</th>
<th>AS</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treated patients, n</td>
<td>584</td>
<td>360</td>
<td>284</td>
<td>1248</td>
</tr>
<tr>
<td>Average duration of follow-up, wks</td>
<td>112</td>
<td>24</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td>Patients who discontinued due to an AE</td>
<td>41 (7.0%)</td>
<td>13 (3.6%)</td>
<td>4 (1.4%)</td>
<td>68 (5.4%)</td>
</tr>
<tr>
<td>Patients with ≥1 AEs</td>
<td>462 (79.3%)</td>
<td>236 (65.5%)</td>
<td>133 (47.0%)</td>
<td>832 (66.2%)</td>
</tr>
<tr>
<td>Patients with ≥5 AEs</td>
<td>306 (53.0%)</td>
<td>24 (6.7%)</td>
<td>74 (26.1%)</td>
<td>384 (30.5%)</td>
</tr>
<tr>
<td>Patients with ≥1 infection</td>
<td>283 (48.6%)</td>
<td>105 (29.2%)</td>
<td>67 (23.5%)</td>
<td>455 (36.3%)</td>
</tr>
<tr>
<td>Patients with ≥1 serious infection</td>
<td>36 (6.0%)</td>
<td>5 (1.4%)</td>
<td>2 (0.7%)</td>
<td>43 (3.4%)</td>
</tr>
<tr>
<td>Patients with ≥1 injection reactions</td>
<td>37 (6.4%)</td>
<td>4 (0.9%)</td>
<td>3 (1.1%)</td>
<td>44 (3.4%)</td>
</tr>
<tr>
<td>ADAs positive (%)</td>
<td>33.4</td>
<td>22.6</td>
<td>26.2</td>
<td>23.3</td>
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Table 2

<table>
<thead>
<tr>
<th>Variables</th>
<th>RA</th>
<th>PsA</th>
<th>AS</th>
<th>All</th>
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</thead>
<tbody>
<tr>
<td>Treated patients, n</td>
<td>584</td>
<td>360</td>
<td>284</td>
<td>1248</td>
</tr>
<tr>
<td>Average duration of follow-up, wks</td>
<td>112</td>
<td>24</td>
<td>24</td>
<td>24</td>
</tr>
<tr>
<td>Opportunistic infections</td>
<td>0.4</td>
<td>0</td>
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<tr>
<td>(95% confidence interval)</td>
<td>0.1-0.7</td>
<td>0</td>
<td>0</td>
<td>0.1-0.7</td>
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<tr>
<td>Infections</td>
<td>0.4</td>
<td>0</td>
<td>0</td>
<td>0.4</td>
</tr>
<tr>
<td>(95% confidence interval)</td>
<td>0.1-0.7</td>
<td>0</td>
<td>0</td>
<td>0.1-0.7</td>
</tr>
<tr>
<td>Malignancy</td>
<td>0.2</td>
<td>0</td>
<td>0</td>
<td>0.2</td>
</tr>
<tr>
<td>(95% confidence interval)</td>
<td>0.1-0.4</td>
<td>0</td>
<td>0</td>
<td>0.1-0.4</td>
</tr>
<tr>
<td>Serious infections</td>
<td>0.3</td>
<td>0</td>
<td>0</td>
<td>0.3</td>
</tr>
<tr>
<td>(95% confidence interval)</td>
<td>0.1-0.6</td>
<td>0</td>
<td>0</td>
<td>0.1-0.6</td>
</tr>
<tr>
<td>Death</td>
<td>0.1</td>
<td>0</td>
<td>0</td>
<td>0.1</td>
</tr>
<tr>
<td>(95% confidence interval)</td>
<td>0.0-0.4</td>
<td>0</td>
<td>0</td>
<td>0.0-0.4</td>
</tr>
</tbody>
</table>

Results: Overall, 1248 pts were treated with IV GLM across indications. A numerically greater proportion (%) of IV GLM pts with RA reported safety events than pts with PsA or AS (Table 1): SAEs (18.2 vs 5.2 vs 3.4), infections (49.1 vs 22.8 vs 32.8), serious infections (6.2 vs 2.2 vs 1.5), and infusion reactions (4.6 vs 0.9 vs 1.5). Incidence (per 100 pt-years) of opportunistic infections, malignancy, active tuberculosis, and death with IV GLM was low (<0.5) across indications (Table 2). Infections were the most commonly reported type of SAE among pooled IV GLM pts; the most frequent was pneumonia (10 /0.5%). Incidence (per 100 pt-years) of serious infections was similar among IV GLM pts with and without corticosteroid use (3.35 vs 3.37, respectively). Overall, 1 IV GLM pt (PsA) experienced a demyelination event. A numerically greater proportion of IV GLM pts discontinued due to an AE than PBO pts (5.0% vs 0.7% vs 0.5%). In IV GLM pts with baseline alanine aminotransferase (ALT) ≥ upper limit of normal (ULN) 1.2% had post-baseline ALT elevations ≥5X ULN. The proportion of IV GLM and PBO pts with post-baseline ALT elevations ≥5X ULN was 2.1% vs 0% with methotrexate and 0.7% vs 1.4% without methotrexate use at baseline, respectively. Using a drug-tolerant enzyme immunoassay, the incidence of ADAs was 22% through WK 52 across indications, which primarily consisted of low titer ADAs.

Conclusion: IV GLM demonstrated a consistent safety profile across indications in the PBO-controlled (up to WK 24) and uncontrolled study periods. Similar to WK 24 (1), more safety events occurred in RA pts, who represented the largest study population with older pts, longer disease duration, and more concomitant medication use.
Response to Biological Therapy is Influenced by the Body Mass Index in Patients with Rheumatoid Arthritis

Hikoshi Koderai1, Yoshiko Sato2, Yoshijû Fujimatsu3, Kyotaka Hanzo4, Juji Ikeda5, Hitoshi Kodera1, Yoshiko Sato2, Yoshifuji Matsumoto1.

Background: Biologic therapies have been bringing huge advantage in the treatment of rheumatoid arthritis, but response to the therapy is heterogeneous. The influence of the body mass index to the treatment is still controversial.

Objectives: To identify the factors influencing in the response to biologic therapy (bio naïve).

Methods: The analysis of the patients with rheumatoid arthritis who were initiated biologics therapy (bio naïve) between January 2011 to December 2016 in the rheumatology department of a hospital in Japan, was conducted. The effects were evaluated by EULAR response criteria after 6 months of biologic therapy, and factors influencing the response were analyzed in terms of the baseline characteristics (sex, age, disease duration, body mass index, tender joint count, swollen joint count, Patient’s visual analog scale, erythrocyte sedimentation rate, C-reactive protein, Disease Activity Score in 28 joints, Modified Health Assessment Questionnaire, Methotrexate use, Prednisolone use).

Table 1. Differences of the baseline characteristics of RA patients between “Good or Moderate response” and “No response” of EULAR response criteria after 6 months of biologic therapy.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Good or Moderate response</th>
<th>No response</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex, %</td>
<td>57.9</td>
<td>50.3</td>
<td>0.157</td>
</tr>
<tr>
<td>Age, years</td>
<td>56.6 ± 11.6</td>
<td>51.0 ± 11.5</td>
<td>0.013</td>
</tr>
<tr>
<td>Disease duration, years</td>
<td>6.6 ± 3.6</td>
<td>7.6 ± 5.6</td>
<td>0.477</td>
</tr>
<tr>
<td>BMI kg/m²</td>
<td>24.6 ± 3.4</td>
<td>26.0 ± 5.2</td>
<td>0.0008</td>
</tr>
<tr>
<td>28 JIA (%,)</td>
<td>27 (43.8)</td>
<td>23 (35.3)</td>
<td>0.043</td>
</tr>
<tr>
<td>ESR</td>
<td>4.9 ± 6.4</td>
<td>4.0 ± 5.4</td>
<td>0.072</td>
</tr>
<tr>
<td>ESR/crnl</td>
<td>15.4 ± 8.8</td>
<td>15.4 ± 8.8</td>
<td>0.0018</td>
</tr>
<tr>
<td>CRP ng/mL</td>
<td>34.4 ± 21.4</td>
<td>34.4 ± 21.4</td>
<td>0.0012</td>
</tr>
<tr>
<td>SRF (mg/dL)</td>
<td>44.6 ± 24.0</td>
<td>44.6 ± 24.0</td>
<td>0.0002</td>
</tr>
<tr>
<td>DAS28 ESR</td>
<td>44.6 ± 31.6</td>
<td>43.0 ± 31.0</td>
<td>0.0003</td>
</tr>
<tr>
<td>DAS28 CRP</td>
<td>42.8 ± 36.5</td>
<td>42.8 ± 36.5</td>
<td>0.0027</td>
</tr>
<tr>
<td>DAS28 sed</td>
<td>1.4 ± 1.2</td>
<td>1.3 ± 1.2</td>
<td>0.0015</td>
</tr>
<tr>
<td>hSAA</td>
<td>6.5 ± 6.9</td>
<td>6.8 ± 6.9</td>
<td>0.0099</td>
</tr>
<tr>
<td>Concomitant therapy</td>
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<tr>
<td>MTX dose, mg/week</td>
<td>7.4 ± 4.5</td>
<td>7.0 ± 5.0</td>
<td>0.724</td>
</tr>
<tr>
<td>Prednisolone dose, mg/day</td>
<td>15.8 ± 23</td>
<td>12.0 ± 8.9</td>
<td>0.0120</td>
</tr>
</tbody>
</table>

Conclusion: Body mass index influence in the response to first biologic therapy in patients with rheumatoid arthritis.
Methods: We conducted a prospective, multicenter, observational study of physicians and patients in 12 centers from 11 provinces across China between March and April 2018 (NCT03483597). The Treatment Satisfaction Questionnaire for Medication version III (TSQM-III) was used to assess the treatment satisfaction of patients and physicians regarding csDMARDs and bDMARDs therapy. Multiple linear regression analysis was used to determine the factors independently associated with patients’ satisfaction.

Results: 1237 patients (82.5% female) with a mean age (SD) of 48.9 (13.4) years and 146 rheumatologists (72.6% working-5 years) were included in this survey. The patients’ satisfaction (n=335) with bDMARDs was higher than physicians’ satisfaction (n=146) regarding the side effects (95.0±14.3 vs. 84.6±15.7, p<0.001) and convenience (74.6±21.2 vs. 69.1±16.5, p=0.002) (Table1). Among physicians, global satisfaction with bDMARDs was higher than that with csDMARDs (75.0 vs. 66.7, p<0.05) (Table1). Satisfaction of each questionnaire item toward therapy in patients and rheumatologists were also shown in radar charts (Figure 1). The multivariable regression analysis showed that age and quality of communication with physician was positively associated with patients’ satisfaction, while level of education (bachelor or above), self-assessment of disease severity and treatment costs were inversely associated with satisfaction.

Conclusion: For bDMARDs, the treatment satisfaction of patients with RA is generally better than that of physicians. Physicians’ satisfaction with bDMARDs is higher than that with csDMARDs. The independently factors associated with the treatment satisfaction of patients with RA are age, education, disease severity, the patient-physician communication, and treatment costs, which could be targeted in routine clinical care.

REFERENCES

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Disclosure of Interests: None declared.

bind the soluble TNF. To date, very few data are available concerning
the use of biosimilar drugs in a real-life setting. Results from DANBIO
registry suggested a lower retention rate in RA patients switchers from
Etanercept originator (ETA) to biosimilar (SB4) versus the historic ETA
cohort and higher in comparison with historic SB4 patients (1).

Objectives: To compare the efficacy of ETA versus SB4 in a cohort of
RA patients in a real life setting.

Methods: In this monocentric case-control prospective study, we consecu-
tively enrolled RA patients starting ETA or SB4 treatment from 2015. RA
diagnosis was made according with ACR/EULAR 2010 criteria (2). Data
were collected and entered into a standardized, computerized, electroni-
cally filled-in form. We included patient demographics, date of diagnosis,
comorbidities and previous and concomitant medications. The clinical eval-
uation included the count of swollen and tender joints and the patient’s
and physician’s global disease assessment based on a visual analogue
scale (VAS; range: 0 to 100 mm). Disease activity was measured according
to the disease activity score in 28 joints (DAS28ESR) (3). The patients
were asked to fill in the Health Assessment Questionnaire (HAQ).
All the patients were evaluated at the beginning of treatment (T0)
and after 4 (T1) and 12 months (T2). Clinical response to treatment was
evaluated by using EULAR criteria (4).

Results: We evaluated 35 RA patients treated with SB4 (M/F 2:3:3; median
age 63 years, IQR 21; median disease duration 108 months, IQR 138) and
40 with ETA (M/F 5:35; median age 60.5 years, IQR 20;
median disease duration 102 months, IQR 141). Biological drug was pre-
scribed as first-line biological treatment in 71.4% of SB4 cohort and in
80.0% of ETA. At T0 no significant differences were observed among the
two groups in terms of DAS28ESR (SB4 median 4.6 (IQR 1.8), ETA 4.3
(IQR 1.9), p=ns) and HAQ (SB4: median 1 (IQR 0.5), ETA median 1
(IQR 0.5), p=ns). In both groups we observed a significant reduction of
DAS28 values at T1 (BS4 p=0.01; ETA p<0.0001) and T2 (SB4 p=0.0007; ETA p= 0.0002; Figure 1A). When evaluating the remission
rate (DAS28ESR<2.6) at T1, we observed a significant higher rate in ETA
(53.8%) versus SB4 (26.7%; p= 0.0002; Figure1B). No differences were
found after 12 months of treatment.

Conclusion: The results of our study confirmed in a real-life setting the
efficacy of SB4 in RA patients, as demonstrated by the significant reduc-
tion of DAS28ESR values after 4 and 12 months of treatment, similarly
to ETA. Nonetheless, ETA seems to be able to induce a remission sta-
tus earlier than SB4.

REFERENCES

Disclosure of Interests: Ramona Lucchetti: None declared, Fulvia Ceccar-
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francesca spinielli: None declared, cristiano alessandri: None declared,
Guido Valesini: None declared, Roberta Priori: None declared.

AB0390                     CORRELATION BETWEEN TNF-BLOCKERS
BIOAVAILABILITY AND FCGRIIA R131R
POLYMORPHISM IN TUNISIAN PATIENTS WITH
RHEUMATOID ARTHRITIS

Ines Mahmoud1, Myriam Moalla1, Imen Sla2, Olaa Saidane1, Aicha Ben Tekaya1,
Rawdha Tekaya1, Wafa Hardi2, Saloua Aouini2, Mohamed Montacer Kohfi1,
Your Gorg2, Leila Abdelmolou3, 1Hospital Charles Nicole, Rheumatology, Tunis,
Tunisia; 2Hospital Charles Nicole, Immunology, Tunis, Tunisia; 3Institute
Orthopedic Mohamed Kassab, Rheumatology, Manouba, Tunisia

Background: Rheumatoid arthritis (RA)’s prognosis drastically improved
with the introduction of TNF-blockers. However, reasons behind therapeu-
tic failure in some patients remain unclear. Several factors might influence
pharmacokinetics of these drugs by reducing their half-life and, conse-
quently, their effectiveness. Considering Fc-containing biology like inflixi-
mab (IFX) and adalimumab (ADL), Fc gamma receptors (FcγRs) polymor-
phism would be an interesting genetic candidate to focus on.

Objectives: The aim of our study was to determine the influence of low
affinity allele FcγRIIA-131R on ADL and IFX bioavailability.

Methods: We enrolled RA patients treated with IFX and ADL for over six
months. Blood samples were collected for each patient immediately prior
to drug administration. Quantitative measurements of the residual drug
concentration (DC) was carried out by a commercial enzyme-linked immu-
nosorbert assay (ELISA) kit (Promonitor®). Then, we identified patients
with DC above therapeutic cut-off (DC+) for each biologic, EULAR criteria
were considered to determine treatment outcome. FcγRIIA H131R poly-
morphism was genotyped using PCR-SSP.

Results: Twenty-nine patients were included (13 treated with ADL and 16
with IFX). We identified 31.3% and 23.1% non-responders among patients
switched with IFX and ADL respectively. Patients with DC+ were more fre-
frequent in ADL group (76.9%) than IFX group (43.75%). For IFX, DC+ was
significantly correlated with the presence of FcγRIIA 131- R (p=0.033). In fact, none of the HH-genotyped patients had DC+. Further-
more, an association between FcγRIIA 131-R allele and poor response to
IFX was noted (p=0.059) while all HH-genotyped patients responded to IFX.
For ADL, no correlation was found with both of residual DC and response
to treatment.

Conclusion: The presence of FcγRIIA-131 R allele might be a predictive
factor of non-responsiveness to TNF-blockers. It also appears to be asso-
ciated to a higher residual DC. That might be explained by a reduced
biologic clearance due to a lower binding affinity to Fc portion compared
to wild allele FcgRIIA-131H. Therefore, FcγR polymorphism assessment in
RA patients would be a decision-making parameter to consider, as part
of the personalized medicine approach.

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gamma receptors IIa and IIIa on the American College of Rheumatology
and European League Against Rheumatism responses to anti-tumour
2009;68(10):1547-1552.

Disclosure of Interests: None declared

AB0392                     ASSOCIATION BETWEEN FCGRIIA R131H, FCGRIIA
NA1/NA2 AND FCGRIBB V158F POLYMORPHISM AND
RESPONSIVENESS TO BIOLOGICS IN RHEUMATOID
ARTHRITIS TUNISIAN PATIENTS

Myriam Moalla1, Ines Mahmoud1, Imen Sla2, Aicha Ben Tekaya1, Olaa Saidane1,
Rawdha Tekaya1, Saloua Aouini2, Kawiher Ben Abdelghani1, Ahmed Lastar1,
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Orthopedic Mohamed Kassab, Rheumatology, Manouba, Tunisia

Background: Even though biologics have been used for several years in
the treatment of rheumatoid arthritis (RA), little is known about factors
that modify their pharmacokinetics and therefore their efficacy. Polymorphisms
(SNPs) in receptors for constant region Fc of IgG (FcγR) might influence
the therapeutic outcome of molecules that incorporate an Fc fragment in
their structure such as etanercept (ETA), adalimumab (ADL) infliximab (IFX) and rituximab (RTX).

Objectives: The aim of our study was to determine whether the presence of low affinity allele of FcgRI (FcgRIIA-131R, FcgRIIIA-158F and FcgRIIIB-NAA) influences efficiency and immunogenicity of ETA, ADL, IFX and RTX in RA Tunisian patients.

Methods: We included RA patients treated with biologics for at least six months. Response to treatment was assessed according to EUULAR criteria. Quantitative measurement of antitumor antibodies (ADAb) for each biologic agent was carried out by a commercial enzyme-linked immunosorbent assay (ELISA) kit (Promonitor®). To do so, blood samples were collected for each patient right before drug administration. FcgRIIA, FcgRIIIA and FcgRIIB SNPs was genotyped for all patients using PCR-SSP and direct sequencing process.

Results: Seventy-nine RA patients treated with biologics were enrolled (18 with ETA,13 with ADL,16 with IFX and 32 with RTX). Regardless of biologic type, 61 patients (77.2%) responded to treatment and 14 patients (17.7%) developed ADAb. Genotypic study revealed a correlation between poor response to treatment and the presence of at least one FcgRIIA-131-R allele (94.7% for RH/RR genotypes versus 5.3% for HH genotype). But, the difference was not statistically significant (p = 0.25). Besides, the H/H mutant allele was significantly associated to the presence of ADAb (71.4% of ADAB positivity for RH/RR genotypes versus 28.6% for HH genotype: p = 0.041). The haplotype study shows that the risk allele combination of FcgRI IIA-131R/FcgRIIIA-158F/FcgRIIIB-NAA was more frequent in ADAb+ (23%) compared to ADAb- subjects (23%) and non-responders (27%) versus good responders (23%). But, neither of these associations was statically significant.

Conclusion: Our study suggests that RA patients FcgRIIA-131-R allele carriers are more susceptible to develop ADAB than those with HH wild genotype. That could be explained by a higher biologic clearance in H-carrier patients, resulting in a decreased half-life and ultimately a lower risk of ADAB formation. Thus, FcgR polymorphism genotyping may be a useful marker for predicting response to FC-containing biologics in Tunisian RA patients. Further studies need to be done on larger population.

REFERENCES
[2] Lee YH, Bae SC. Associations between PTPRC rs10919563 A/G and IL-6 -174 C/T polymorphism and the risk of ADAb formation. Thus, FcgR polymorphism genotyping may be a useful marker for predicting response to Fc-containing biologics in Tunisian RA patients. Further studies need to be done on larger population.

Disclosure of Interests: None declared

AB0394 SERUM CALPROTECTIN AS A PREDICTIVE MARKER OF THERAPEUTIC RESPONSE TO ADALIMUMAB IN RHEUMATOID ARTHRITIS

Guillaume Servant1, Christophe Passió1, Eric Piver2, Oscar Knight1, Valérie Davoust-Penec3, Stéphane Rist1, A. Perdriger3, Elisabeth Gervais3, Emmanuelle Derris1, Benoît Le Goff4, Laurence Picorn5, Philippe Goupille6,7, Denis Mulcrasto1,2, 1. University of Tours, EA 7501 GICC, 2. University of Tours, EA 7501 GICC, 3. CHU de Tours, Service de Rhumatologie, Beaugency, France, 4. CHRU de Tours, Service de Rhumatologie, Paris, France, 5. CHRU de Tours, Service de Rhumatologie, Paris, France, 6. CHRU de Tours, Service de Rhumatologie, Paris, France, 7. CHRU de Tours, Service de Rhumatologie, Paris, France.

Background: Adalimumab significantly reduces the activity of rheumatoid arthritis (RA), but reliable biomarkers of inflammation are still lacking to predict and evaluate the therapeutic response. Serum calprotectin is a mainstay of endogenous activation of the inflammatory response that can be useful as a marker of response to treatment in RA.

Objectives: To compare the evolution over time of serum calprotectin and C-Reactive Protein (CRP) after initiation of adalimumab.

Methods: Serum levels of calprotectin, CRP and adalimumab concentration were measured at visits V1 (week 0), V2 (week 4), V3 (week 8), V4 (week 12) and V5 (week 26). Changes in each variable were analyzed at each visit and each variable was compared to each other using a correlation test. Receiving operating characteristic curves were used to estimate the predictive value of response at V5 for calprotectin and CRP at each visit.

Results: Data from 66 patients were analyzed. Serum calprotectin level decreased from V1 to V5 (3.78 µg/mL [9.0 – 17.47] to 2.74 µg/mL [0 – 18.83]; p < 0.05). A positive correlation was observed between serum calprotectin and DAS28 (Spearman 0.244; p < 0.01), and between CRP and DAS28 (Spearman 0.512; p < 0.01) for all visits combined. In contrast to CRP, serum calprotectin and serum calprotectin variation from V1 to each visit, were not predictive of DAS28 at all V5.

Conclusion: Serum calprotectin decreases after initiation of adalimumab in RA but was weakly correlated with disease activity at week 26. Serum calprotectin cannot be considered as superior to CRP as predictive marker of therapeutic response in RA after initiation of adalimumab.

Disclosure of Interests: None declared
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AB0395

NO CLINICAL RELEVANT CHANGES IN EFFICACY, QUALITY OF LIFE AND TOLERABILITY FOR RA PATIENTS IN CLINICAL REMISSION 16 WEEKS AFTER SWITCHING TO THE BIOSIMILAR IFX CT-P13 COMPARED TO THE ORIGINATOR; A DESCRIPTIVE REPORT

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Background: Switching patients from originator infliximab (IFX) to biosimilar IFX can reduce healthcare costs. Several studies have shown that switching does not affect the efficacy for rheumatoid arthritis (RA) patients(1,2), however prospectively collected data on pharmacokinetics, immunogenicity and quality of life (QoL) is scarce.

Objectives: We report data collected from RA patients in clinical remis- sion enrolled in the SECURE study (IFX4501; registered at www.clinicaltrialsregister.eu 2014-004904-31). In SECURE we collected IFX serum concentrations, efficacy, quality of life (QoL) and safety data of patients switched from originator IFX to biosimilar IFX CT-P13 for up to 16 weeks. The IBD cohort of this study has been published elsewhere (3).

Methods: In this prospective, open-label, interventional, non-inferiority, multi-center, phase IV trial, adult RA patients in clinical remission ≤30 weeks under biosimilar IFX to CT-P13. Patients were followed for 16 weeks (2 infusions) after switching. Primary endpoint was the IFX serum concentration at through measured with a bridging enzyme-linked immunosorbent assay (ELISA) 16 weeks after switch. Secondary endpoints included antidrug antibodies (ADA), clinical dis- ease activity measured with the DAS score, CRP and quality of life measured with the EQ5D Health status; -0.05 (-0.08,-0.01). The mean difference (95% CI) at week 16 compared to baseline was for CRP -0.22 (-0.36, -0.08), and EQSD Health status -0.05 (-0.08, -0.01). These changes were not clinical relevant.

In total 76 AEs were reported by 29 (90.6%) patients; 27 of these AEs were non-related to the switch. The most frequently reported AEs (>5% subjects) were fatigue (9.4%), headache (6.3%), arthralgia (15.6%), back pain (9.4%), cough (6.3%), viral upper respiratory tract infection (15.6%) bursitis (6.3%) and pain in extremity (6.3%). Two non-related AEs were reported (ovarian cyst and benign parathyroid tumour).

Conclusion: In this prospective, interventional study in RA patients in clinical remission there were no clinically relevant changes in clinical and biochemical efficacy, quality of life and tolerability 16 weeks after switch- ing to the biosimilar IFX CT-P13 compared to the originator. This study is sponsored by Mundipharma Pharmaceuticals BV.

REFERENCES

AB0396

MONITORING OF PATIENTS WITH RHEUMATOID ARTHRITIS BY INDOCYANINE GREEN (ICG) ENHANCED FLUORESCENCE OPTICAL IMAGING TREATED WITH ANTI-TNF THERAPY

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Background: Indocyanine (ICG)-enhanced fluorescence optical imaging (FOI) by the Xiralite® system enables visualization of inflammation in the hands in rheumatic joint diseases.

Objectives: To investigate the ability of monitoring treatment response using Certolizumab pegol (CZP) in patients with rheumatoid arthritis (RA) by the ICG-enhanced FOI method Xiralite® compared to classical disease activity, laboratory parameters, and muscle/skeletal ultrasound (US).

Methods: CZP-naive patients with RA were eligible for this study, which consisted of an open-label 52-weeks treatment period with CZP. Disease activity was monitored by the clinical score DAS28, laboratory parameters for systemic inflammation (CRP and ESR), ultrasonography (US7 score [1]) and by FOI at baseline (before CZP) and after 6, 12, 24, and 52 weeks under CZP therapy.

Results: In this study, 28 patients (female 92.9%, mean age 49±13.3) were included and treated with CZP over a period of 52 weeks. All patients received CZP for at least 12 weeks (w), n=27 until w42, and n=18 received CZP throughout the entire 52 weeks. DAS28 decreased from moderate disease activity (median 4.6) at baseline to low disease activity (median 2.7) at w52 (p <0.001). CRP/ESR values also reduced from baseline to w52 (r.s.). FOI in phase 1 showed a continuous decrease of enhancement during the course of the treatment period: from baseline (median 1.5, IQR 0.9-5.0) to w6 (median 1.0, IQR 0-3), to w12 (median 0.5, IQR 0-3), to w24 (median 0.0, IQR 0-3) and to w52 (median 0.0, IQR 0-2). An image example is given by the Figure for baseline and w52. The results for other FOI phases 2, 3 and 5 did not show a decrease over the treatment period. US-detected synovitis and tenosynovitis by the US7 score also presented to be responsive between phases 1 and 2, and 3.

Conclusion: In phase 1 phase 1 appears to be a valuable tool for fast and easy monitoring of treatment response to CZP in a clinical setting. FOI may provide an additional method to evaluate inflammation of wrist and finger joints of RA patients in follow-up studies.
Background: Tapering of biological DMARDs can be successful in some patients. However, the predictive factors enabling established patients with RA to remain free of biological DMARDs is unclear. Recently, ultrasonography (US) has become an important imaging tool to identify subclinical synovitis, even in patients with remission. There have been few reports on whether residual synovitis as shown by US can predict relapse of disease activity after discontinuation of biological DMARDs.

Objectives: We aimed to investigate the usefulness of US for predicting relapse in patients in remission for RA after discontinuation of adalimumab (ADA).

Methods: Patients who were using ADA and in remission (Disease Activity Score 28-joint count C reactive protein (DAS28-CRP) <2.6) for longer than 24 weeks were included in this multicenter prospective study. ADA was stopped and patients were followed up until week 52. Predictive factors for relapse at 24 and 52 weeks were analyzed from baseline clinical data, including a US examination. ADA was restarted at the time of relapse (DAS28-CRP ≥3.2). US assessment was performed at 0, 12, 24, 36, and 52 weeks and at the time of relapse. A US examination was performed at the bilateral first to fifth metacarpophalangeal joints, first interphalangeal and second to fifth proximal interphalangeal joints, and first to fifth metatarsophalangeal joints, by using a high-frequency linear transducer. The gray scale (GS) and power Doppler (PD) signals were scored in each synovial site using a semi-quantitative scale from 0 to 3.

Moreover, the modified Total Sharp Score (mTSS) was evaluated at 0, 24, and 52 weeks by conventional radiography. The patients who relapsed were administrated ADA again.

Results: Fifty-three patients were included. Ten (8.9%) patients relapsed up to week 24 and 20 (37.7%) up to 52 weeks. The relapsed patients tended to have a long disease duration, but baseline US findings could not predict relapse. Increases in the PD score were observed after follow-up in some relapsed patients. Disease activity control was good after ADA was restarted in the relapsed patients, and there was no difference in progression of the mTSS in the relapsed and non-relapsed groups.

Conclusion: Predicting relapse by baseline US findings after discontinuation of ADA in remission is difficult. However, an increased PD score in a following US examination might be useful for early detection of relapse. Radiographic progression is not significantly different in patients with relapse and those without relapse.

REFERENCES

Disclosure of Interests: Tadasashi Okano Speakers bureau: AbbVie, Roxy Hara; None declared, Makoto Wada; None declared, Tatsuya Koke; Kenji Mamoto; None declared, Yuko Sugokoda; Masahiro Tada; Takahiro Fujimura; Sho Sendo; Takachi Okano; Yoshinobu Ichise; Ikuko Naka; Heiseki Yu; Akiko Nakabayashi; Yoshinobu Matsuura; Takahiro Yoshikawa; Masao Tamura; Masayasu Kitano; Yasuhide Kanayama; PROUD study working group. Osaka City University Graduate School of Medicine, Osaka, Japan; Nara Medical University, Nara, Japan; Tokyo Prefectural University of Medicine, Kyoto, Japan; Osaka City General Hospital, Osaka, Japan; Takanohana Central Hospital, Nara, Japan; Kobe University Graduate School of Medicine, Kobe, Japan; Tottori Naka University, Osaka, Japan; Yokohama City Medical College, Japan; Hangyo College of Medicine, Hangyo, Japan; Toyoura Kosei Hospital, Aichi, Japan.

IL-6 inhibitors (tocilizumab, n=13; sarilumab, n=3), JAK inhibitors (tofaciti-
nib, n=7; baricitinib, n=4), and B-cell depleting agent (rituximab, n=4). The
pooled study population of 27,215 moderate-to-severe RA patients
primarily consisted of middle-aged Caucasian females (mean age: 47-55
years; Caucasian: 44% - 87%; females: 90%). Thirty-three trials were on
patients previously treated with cDMARD or TNFi, while 6 trials were on
cDMARD-naive patients. Total aggregated AEs (total AEs, n=37; SAEs, n = 37;
treatment-related AEs, n = 14) and infection (serious infection, n = 35; total
infection, n = 26) were the most frequently reported safety outcomes.

The NMA was performed on 23 trials. Indirect comparisons were made
between IL-6 inhibitors, JAK inhibitors, B cell depleting agent and abata-
cept, with TNFi or cDMARD as direct comparators. The risk of total AEs
was significantly higher for IL-6 inhibitors compared with abatacept (RR = 1.13,
95% CI = 1.05 – 1.22). For SAEs and other analyzed safety out-
comes, no significant difference was observed between abatacept and
other non-TNFi drug classes. Similar results were observed in sensitivity
analyses for all patients on concomitant cDMARD, including those who
were treatment-naive before the study (n=26 trials).

Conclusion: When comparing aggregated safety outcomes, abatacept
shared a similar safety profile with most non-TNFi RA treatments. How-
ever, patients on abatacept had a statistically significantly lower risk of
total AEs compared to US recommended doses of IL-6 inhibitors. More
studies with head-to-head comparison in clinical trials and real-world set-
ting are required to provide further understanding of the safety profile
and risk of specific adverse events for non-TNFi in order to optimize
treatments for moderate-to-severe RA patients.

REFERENCES

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AB0399 EVOLUTION OF BIOLOGIC/SMALL MOLECULE
SWITCHING PATTERNS IN RA BETWEEN 2016 AND 2018
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3Spherix Global Insights, Exton, United States of America

Background: TNF therapy has been the standard of care for adult
patients diagnosed with autoimmune conditions and are typically used as
a first-line biologic/small molecule in the treatment of rheumatoid arthritis
(RA). However, the adoption of systemic agents with alternate mecha-
nisms of action (AMOA) such as JAK and interleukin inhibitors have
increased in recent years across many indications. As such, the practice
of sequential TNF prescribing following an initial TNF discontinuation is
becoming less common, with switches to AMOAs, such as JAK and IL-6
inhibitors, becoming more popular.

Objectives: This research sought to track the evolution of biologic/small
molecule switch patterns among US RA patients between 2016 and 2018
and to identify differentiating patient characteristics between the switch patterns.

Methods: An independent market analytics firm collaborated with rheuma-
tologists in France (n=62), Germany (n=66), Italy (n=61), Spain (n=68) and
the UK (60) to conduct an online retrospective chart review. RA patients who
had switched treatment from one biologic/small molecule to another in the
prior twelve weeks. Rheumatologists were able to submit up to seven RA patient charts. A total of 1,312 patient charts were collected via a HIPAA-compliant online audit in January 2016 (n=198 rheumatologists/980 patient charts), in September 2017 (n=176 rheumatologists/1,002 patient charts), and September 2018 (211 rheuma-
tologists/1,074 patient charts). Results were analyzed in SPSS.

Results: Analysis of patients recently switched from one biologic/small
molecule to another revealed the decreasing popularity of cycling to
another TNF after initial TNF discontinuation. TNF cycling accounted for
46% of all switches in 2016, 41% in 2017, and 40% in 2018. Con-
versely, switches from TNFs to JAK inhibitors accounted for 13% in
2016, 12% in 2017, and 15% in 2018. Switches to IL-6 inhibitors
increased from 8% of all switches in 2016, to 9% in 2017, and 11% in
2018. The number of patients switched from a TNF to abatacept or rituxi-

In this study, background information was gathered on changes in
switching patterns, and the reasons behind those changes. Additionally,
the study sought to identify patient characteristics associated with
determine the factors that influence these decisions.

Conclusion: The frequency of TNF discontinuation has decreased over the
past three years. Over time, rheumatologists are increasingly likely to
introduce a JAK or IL-6 inhibitor in the second-line setting following dis-
continuation of a first-line TNF. The frequency of abatacept monotherapy
increased in recent years across many indications. As such, the practice
of sequential TNF prescribing following an initial TNF discontinuation is
becoming less common, with switches to AMOAs, such as JAK and IL-6
inhibitors, becoming more popular.


AB0400 FREQUENCY OF BIOLOGIC/SMALL MOLECULE
MONOTHERAPY FOR RHEUMATOID ARTHRITIS IN THE EU:
REAL-WORLD EVIDENCE FROM A PATIENT AUDIT
STUDY
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Background: Biologic/small molecule therapy has been the standard of
care for adult patients diagnosed with rheumatoid arthritis (RA) who have
failed conventional DMARD therapy, resulting in familiarity, comfort, and
satisfaction among physicians. Prior recommendations of combining biolog-
cals/small molecules with a DMARD like methotrexate (MTX) have recently
been challenged by clinical data demonstrating the effectiveness of IL-6 and
JAK inhibitors as monotherapy.

Objectives: This research sought to evaluate the frequency of biologic/
small molecule monotherapy regimens among European RA patients who
were recently switched from one biologic/small molecule to another.

Methods: An independent market analytics firm collaborated with rheuma-
tologists in France (n=62), Germany (n=66), Italy (n=61), Spain (n=68) and
the UK (60) to conduct an online retrospective chart review. RA patients who
had switched treatment from one biologic/small molecule to another in the
prior twelve weeks. Rheumatologists were able to submit up to seven RA patient charts. A total of 1,312 patient charts were collected via a market-specific compliant audit form in September 2018 and
included patient and physician demographics, patient treatment history,
clinical and non-clinical patient parameters.

Results: Overall, the analysis of patient chart audits revealed that 22% of
all recently switched patients were switched to a biologic/small molecule
monotherapy regimen. The frequency of monotherapy was highest in Ger-
many (32%) and lowest in the UK (13%). Monotherapy was more fre-
quent for patients switched to infliximab (39%) and tofacitinib (39%) and
lowest for those switched to tocilizumab (12%) and rituximab (11%).

On a country-specific level, rates of TNF monotherapy were highest in
Germany (38%) and lowest in the UK (16%). IL-6 monotherapy was also
more common in Germany (27%) but least common in France (17%).
JAK monotherapy was highest in France (34%) and lowest in the UK (7%),
while monotherapy for abatacept/rituximab was highest in Germany
(32%) and again lowest in the UK (13%).

Conclusion: The popularity of biologic/small molecule monotherapy varies
by EUS country and while rates are highest for TNF inhibitors, use of biologic/small molecule monotherapy for patients recently switched to a
JAK or IL-6 inhibitor are comparable.

AB0401 SWITCH FROM ETANERCEPT ORIGINATOR TO ETANERCEPT BIOSIMILAR: DATA FROM REAL LIFE

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Background: Biosimilars of antiTNF-α are now available for the treatment of arthritis. There are a lot of data about maintenance of clinical efficacy after switching from originator to biosimilar but also reports about flares and adverse events (AE). Controversies still exist due to ethical and economic reasons. We describe the disease activity trend after switching from etanercept originator (oETA) to its biosimilar (bETA) in a population of Turin, Piedmont, Italy. In this region switch to biosimilar is mandatory by law except in case of patients with history of allergy, off-label, psychosocial reasons, active disease that required different treatment.

Objectives: To evaluate the disease activity trend before and after switch from oETA to bETA

Methods: We switched 82 patients (M/F 33/49, mean age 59.65±11.5, duration of disease 17.56±10.3 years) in stable state of disease from oETA to bETA; 49 patients affected by RA, 24 by PsA, 10 by AS. The mean of duration of oETA and bETA treatment was respectively 129.2 and 6.2 months. We evaluated VAS-pain, Global-Health, CRP, number of swollen and tender joints, DAS28 for RA, DAPSA for PsA, HAQ and HAQ-S, BASDAI for AS patients.

Results: Differences of variables between oETA and bETA are summarized in table1. We didn’t find any significant difference between oETA and bETA in order to efficacy. However 8 patients, 5 RA and 4 PsA(9.75%) discontinued bETA because arthritis flare(7) or AE(1).

Conclusion: Data about maintenance of efficacy and percentage of discontinuation were similar to the literature. We didn’t find significant differences on efficacy after switching from originator to biosimilar. However, considering the rate of flares and AE, further strong studies are required.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>DAS28</th>
<th>RA</th>
<th>RA</th>
<th>DAPSA</th>
<th>PsA</th>
<th>RA</th>
<th>RA</th>
<th>RA</th>
<th>BASDAI</th>
<th>SA</th>
<th>HAQ-S</th>
<th>SA</th>
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<td>oETA</td>
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<td>8.35</td>
<td>0.88</td>
<td>2.86</td>
<td>0.85</td>
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<td>1.23</td>
<td>11.76</td>
<td>0.9</td>
<td>2.7</td>
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<td>(0.50)</td>
<td>(0.52)</td>
<td>(6.51)</td>
<td>(0.54)</td>
<td>(0.96)</td>
<td>(0.54)</td>
<td>(0.50)</td>
<td>(0.50)</td>
<td>(6.51)</td>
<td>(0.54)</td>
<td>(0.96)</td>
<td>(0.54)</td>
</tr>
<tr>
<td>bETA</td>
<td>2.68</td>
<td>0.92</td>
<td>11.66</td>
<td>0.9</td>
<td>2.68</td>
<td>0.85</td>
<td>1.23</td>
<td>1.23</td>
<td>11.76</td>
<td>0.9</td>
<td>2.7</td>
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Table 1. The analysis of variables between Etanercept originator (oETA) and Etanercept biosimilar (bETA).

REFERENCES

Disclosure of Interests: None declared

AB0402 MEASURING PATIENT EXPERIENCE OF SWITCHING BIOLOGIC TREATMENT – A SYSTEMATIC LITERATURE REVIEW

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Background: Biologics have transformed the treatment of inflammatory arthritis (IA). However, the complexity of disease management has increased with the introduction of biosimilars and novel treatments. Hence, patient experience and satisfaction has become increasingly important in treatment individualization.

Objectives: Firstly, to assess to what extent IA patient experience of switching biologics is measured in the literature; secondly, to summarize patient-reported outcomes (PROs) as well as medical/non-medical reasons associated with switching.

Methods: A systematic literature review (SLR) was performed in accordance with PRISMA guidelines. EMBASE and MEDLINE were searched for relevant publications from 2013 to present day, together with relevant conference abstracts from 2018 (ACR-ARHP, EULAR, and ISPOR). Studies published in English including either a) patient-reported outcomes (PROs) associated with switching biologics, or b) reasons for switching and/or discontinuing biologics treatment as noted by health care professionals and/or patients were included. The scope was limited to European and North American populations. While the initial search included patient populations with ulcerative colitis in addition to IA patients, results presented within this abstract focus on IA populations only.

Results: After initial screening of 1781 abstracts, sixty-eight studies including IA patients were identified for inclusion in the analysis. Of the remaining studies, 39/68 (57%) included ≥1 treatment switch. The majority of studies were conducted in Europe (36/38; 92%), with the proportion of female patients ranging between 12-90%. Thirteen studies (18%) included at least one PRO, 4 of which only recorded PROs prior to switch (6%). The most commonly reported PRO was PGA/VAS, followed by HAQ and questions asking patients to rank their switching experience using various pre-defined categories (Figure 1). While the most common reasons for discontinuing treatment, which may or may not include switching, was provided in 33 studies (loss of efficacy and safety), reasons strictly for switching are infrequently reported.

Conclusion: Patient satisfaction is important, as it has been linked to clinical safety, treatment effectiveness, and adherence (Doyle et al., 2013). However, this SLR highlights a notable lack of information regarding patient-reported experience of switching biologic treatment. The PROs reported in a minority of studies encompass several regions related to patient well-being – such as pain, fatigue, etc. – but provides very limited information on the experience of switching. Hence, to improve disease management and treatment individualization, further research is required.

REFERENCE

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AB0403 PREDICTORS OF PERSISTENCE OF BIOLOGIC DRUG STEP-DOWN STRATEGIES IN INFLAMMATORY ARTHRITIS: A LONGITUDINAL STUDY IN CLINICAL PRACTICE WITH A LONG FOLLOW-UP

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Background: Recommendations for the management of Rheumatoid Arthritis (RA) and spondyloarthritis (SpA) with bDMARD include dose-tapering strategies in patients with good disease control. However, there is limited information on predictors of persistence of biosimilars. This study aimed to identify predictors of persistence of biosimilars in inflammatory arthritis.

Methods: A multicenter, retrospective cohort study of patients who switched to a biosimilar (BS) from a drug of the same class (control (C)) in the period from January 2013 to December 2015 was conducted in 14 Spanish hospitals. The study was conducted by the Grupo Español de Estudios de Terapia con Biológicos. The primary outcome was the persistence of BS treatment (defined as taking BS ≥ 24 weeks). The predictors were demographic and clinical characteristics, comorbidities, concomitant treatments, and switching reasons. The predictors were evaluated with binary logistic regression. The model was validated internally using the bootstrap technique.

Results: A total of 806 patients were included: 400 in the BS group and 406 in the C group. The mean age of the patients was 57.7 years (SD 13.8) and 71% were women. The most frequent reason for switching was disease control (53%). The persistence rate at 2 years was 70% in the BS group and 81% in the C group (p<0.001). The predictors of persistence were disease control at 24 weeks before switching (OR 2.61, 95% CI 1.69-3.94), higher HAQ (OR 1.04, 95% CI 1.01-1.07), and higher CRP (OR 1.02, 95% CI 1.00-1.04). The model had good discrimination (AUC 0.72) and calibration (Hosmer-Lemeshow p=0.19).

Conclusion: Disease control before switching, higher HAQ, and higher CRP were predictors of persistence of BS. Future studies are needed to confirm these findings and to identify other predictors of persistence.

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Disclosure of Interests: None declared
as an adequate option for patients on persistent remission. Although data regarding these strategies has increased in recent years, there is scarce evidence about their long-term effect.

**Objectives:** Our aim was to analyze the persistence of bDMARD dose-reduction in clinical practice and evaluate its predictors in patients with RA and SpA.

**Methods:** Retrospective longitudinal study from 2006 to 2018. From a cohort of 153 patients with chronic inflammatory arthritis treated with bDMARD (TNF inhibitors, rituximab, tocilizumab, and abatacept), we recruited those with RA and SpA receiving reduced-dose regimens. Variables analyzed were: persistence of bDMARD dose-reduction, predictors of this persistence reported in the literature such as treatment with glucocorticoids (GC) or conventional synthetic DMARD (csDMARD), disease activity and duration of disease at dose-reduction as well as demographic and other clinical features.

A Cox proportional hazards model was used to identify factors associated with persistence on reduced-doses during the study period.

**Results:** 56 patients (RA:35; SpA:21) on tapered bDMARD (etanercept 51.8%, adalimumab 32.1%, Infliximab 3.6% and tocilizumab 12.5%) at study entry were included. Their clinical and laboratory features are shown in table 1.

After a mean follow-up on tapered-dose of 4.4 years (range 0.35-8.72), 42.9% of subjects overall remained on reduced doses (RA: 36.4%; SpA: 52.2%). (Fig.1)

From those who required discontinuation of the step-down regimen, 16 (48.4%) achieved the therapeutic objective and 7 (22.6%) failed after returning to standard dose respectively.

bDMARD were discontinued in 4 (12.9%) patients due to sustained disease remission (RA=3; SpA=1), 3 (9.7%) due to adverse events and 2 (6.4%) due to other reasons. No significant differences in the variables analyzed were found between patients continuing vs discontinuing reduced-dose regimens. After adjusting for age, sex, diagnosis and disease duration, the concurrent use of GC at the time of dose-reduction was found an independent predictor of discontinuation of the step-down regimen.

**Conclusion:** A significant proportion of patients with RA and SpA (36.4% and 52.2% respectively) can be maintained with reduced doses of bDMARD after a long-term follow-up.

**Disclosure of Interests:** Sebastian C Rodríguez-García: None declared, Raul Castellanos-Moreira Speakers bureau: MSD, Lilly, Victoria Hernandez: None declared, Jose Inciarte Employee of: Lilly, Virginia Ruíz- Esquide Speakers bureau: Sanofi, Lilly, MSD, Jose A. Gómez-Puerta Consultant for: Pfizer, Roche, Speakers bureau: Abbvie, BMS, Janssen, MSD, Pfizer, Roche, Raimón Sanmartí Speakers bureau: PIFIZER, SANOFI, LILLY, MSD, UCB, NOVARTIS, JANSSEN.

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**REFERENCES**


**Table 1. Demographic and clinical features at bDMARD dose-reduction.**

<table>
<thead>
<tr>
<th>Total n:</th>
<th>Continue tapered bDMARD</th>
<th>Withdrawn tapered bDMARD n:32</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age 52.3±1</td>
<td>54 ±13.9</td>
<td>51.1 ± 14.7</td>
</tr>
<tr>
<td>Female 32 (57.1%)</td>
<td>22 (68.8%)</td>
<td></td>
</tr>
<tr>
<td>Ever-smokers 25%</td>
<td>23.8%</td>
<td>26.1%</td>
</tr>
<tr>
<td>Diagnostics 33</td>
<td>12 (36.4%)</td>
<td>21 (63.6%)</td>
</tr>
<tr>
<td>RA 23</td>
<td>12 (52.2%)</td>
<td>11 (47.8%)</td>
</tr>
<tr>
<td>SpA 14.4±1</td>
<td>18.5±7.9</td>
<td>12.1±4.9</td>
</tr>
<tr>
<td>Mean disease duration 6.8</td>
<td>13.9±7.53</td>
<td>14±5</td>
</tr>
<tr>
<td>RA 13.9±8</td>
<td>6.3</td>
<td></td>
</tr>
<tr>
<td>SpA 2.3±0.5</td>
<td>2.3±0.3</td>
<td>2.3±0.6</td>
</tr>
<tr>
<td>RA (DAS28) 1.6±1.7</td>
<td>1.7±1.8</td>
<td>1.5±1.7</td>
</tr>
<tr>
<td>Antibody Status (RA) 28 (85%)</td>
<td>9 (75%)</td>
<td>19 (90.5%)</td>
</tr>
<tr>
<td>Antibody Status (SpA) 29 (88%)</td>
<td>9 (75%)</td>
<td>20 (95.2%)</td>
</tr>
<tr>
<td>ACPO 24/33</td>
<td>9/12</td>
<td>15/21</td>
</tr>
<tr>
<td>bDMARD Naive 28 (85%)</td>
<td>11 (91.1%)</td>
<td>17 (91%)</td>
</tr>
<tr>
<td>RA 17 (73.9%)</td>
<td>9 (75%)</td>
<td>8 (72.7%)</td>
</tr>
<tr>
<td>SpA 19 (57.6%)</td>
<td>7 (58.3%)</td>
<td>12 (85%)</td>
</tr>
<tr>
<td>csDMARD 5/21.7%</td>
<td>18.3%</td>
<td>436.3%</td>
</tr>
<tr>
<td>RA Concomitant GC 8/24.2%</td>
<td>2/16.7%</td>
<td>6/28.6%</td>
</tr>
<tr>
<td>SpA 2/9(9%</td>
<td>0</td>
<td>2/18.2%</td>
</tr>
</tbody>
</table>

**Figure 1. Survival curve for persistence on tapered-dose strategy. Data are proportion (solid line) and 95 CI (coloured area)**

**Abstract:**

**ABO404**

**VALIDATION OF A THERAPEUTIC DRUG MONITORING TEST TO MEASURE THE ADALIMUMAB BIOSIMILAR SB5 IN COMPARISON WITH THE REFERENCE ADALIMUMAB**

M. Beoglia Ruiz-Angelii, Ainara Maguregui, Antonio Martinez, Daniel Nagore. Progenika Biopharma – Grifols, RandD, Derio, Spain

**Background:** Validation of therapeutic drug monitoring (TDM) tests is an essential requirement for using these tools to help assess reasons for non-response. The arrival of biosimilars has prompted a need to validate that existing TDM tests are suitable to determine drug levels for all versions of a given molecule. The adalimumab (ADL) biosimilar SB5 (Bio- gen) was authorised by the European Commission in August 2017, and has recently become available for prescription in several European countries. Promonitor-ADL test is routinely used to monitor IBD patients treated with ADL.

**Objectives:** In this study we validated the suitability and performance of Promonitor-ADL CE-marked TDM test for quantifying SB5 serum concentrations in comparison to reference adalimumab (Abbie).

**Methods:** The study evaluated precision and bias applied to the reference ADL and SB5 biosimilar. The validation study was in line with the design requirements established in the Clinical & Laboratory Standards Institute (CLSI) guideline EP10-A3 for the determination of imprecision and bias. Imprecision was evaluated using three replicates of five human serum sample matrices representative of clinically relevant ADL concentrations and spanning the measurement range of Promonitor-ADL. Validations were run on one instrument with one kit lot by one operator over six non-consecutive operating days and one run per testing day, with an acceptance criterion of CV≤20%. The Lower Limit of Quantification (LLOQ) of Promonitor-ADL was determined according to CLSI guideline EP17-A2.

**Results:** The imprecision of Promonitor-ADL was calculated by estimating the components of variance due to within-run and between-day factors meeting the accuracy goals proposed at all concentration levels of SB5 vs the reference adalimumab (Abbie).

**Discussion:** This study demonstrates that Promonitor-ADL test can measure either the reference ADL drug or the adalimumab biosimilar SB5 with equivalent sensitivity, precision and accuracy.

**REFERENCES**


AB0405
ADALIMUMAB THERAPEUTIC DRUG MONITORING TEST VALIDATED FOR MEASURING ABP 501 BIOSIMILAR

M. Begoña Ruíz-Angüeto, Ainara Maguregui, Antonio Martínez, Daniel Nagore. Progenika Biopharma - Grifols, RandD, Derio, Spain

Background: Promonitor-ADL test is routinely used to monitor IBD patients treated with adalimumab (ADL). ABP 501 (adalimumab biosimilar; Amgen) was authorised throughout the European Union in March 2017 and has been recently launched in several countries. Therapeutic drug monitoring (TDM) is broadly used as an aid for patient management. However, all TDM tests available should be properly validated against each new approved biosimilar in order to ensure safe application for patient monitoring as these may guide dose adjustments.

Objectives: Here we validate the suitability and performance of Promonitor-ADL CE-marked test for quantification of the adalimumab biosimilar ABP 501 in comparison to the reference adalimumab drug (Abbvie).

Methods: The validation study was in accordance with the design requirements established in the Clinical & Laboratory Standards Institute (CLSI) guideline EP17-A2 (Lower Limit of Quantification, LLOQ) and EP10-A3 (imprecision and bias). CLSI guidelines set a standard for the diagnostic industry accepted by all regulatory agencies. LLOQ was determined with four independent human serum sample matrices per each of three low level ADL concentrations, replicated three times per two lots of Promonitor-ADL (Progenika, Spain) kits for each drug, the reference drug and the biosimilar ABP 501. The test is able to quantify the adalimumab biosimilar ABP 501, over three days by one operator. Imprecision was evaluated using three replicates of five human serum sample matrices representative of clinically relevant ADL concentrations and spanning the measurement range of Promonitor-ADL, run on one instrument with one kit lot by one operator over six non-consecutive operating days and one run per testing day, with an acceptance criteria of CV%<20%.

Results: The LLOQ of Promonitor-ADL for the adalimumab biosimilar ABP 501 and reference adalimumab were 0.34 mg/mL and 0.36 mg/mL, respectively. LLOQ values met accuracy goal proposed based on total error ≤±25% and precision. The imprecision of Promonitor-ADL calculated by estimating the components of variance due to within-run and between-day factors meet the accuracy goals proposed at all concentration levels of ABP 501 vs the reference adalimumab (CV% between 5% and 10%). The bias study showed that Promonitor-ADL can equally measure the active moiety ADL either in the reference biologic ADL or in the biosimilar ABP 501. The test is able to quantify the adalimumab biosimilar ABP 501 in the measurement range of 0.9 to 10.9 mg/mL with a bias estimate of -0.089 to 0.306 mg/mL and an overall imprecision of 6% to 9%.

Conclusion: Promonitor-ADL test can equivalently measure either the reference ADL or the approved adalimumab biosimilar ABP 501 with the same sensitivity, precision and accuracy.


AB0406
THE POTENT WEAPON FOR RHEUMATOID ARTHRITIS-INTERSTITIAL LUNG DISEASE: RITUXIMAB EXPERIENCES

Burak Karakaş, Mehmet Emin Derin, Fatih Albayrak, Ali Sahin, Silvas Cumhuriyet University, sivas, Turkey

Background: Rheumatoid arthritis (RA) is a common inflammatory disease with unknown etiology and systemic involvement (1). About 40% of RA patients have extraarticular involvement. Lung involvement is the most common extraarticular finding. The use of rituximab (RTX) in the treatment of rheumatoid arthritis-interstitial lung disease (RA-ILD) has been increasing in recent years (2).

Objectives: To present our rituximab experience in patients with RA-ILD.

Methods: Between April 2015 and April 2018, sixteen patients with RA-ILD who were followed up with RTX treatment in our university internal medicine-rheumatology department were included in this study. High resolution computed tomography (HRCT), carbon monoxide diffusion measurement (DLCO), pulmonary function test (PFT) and routine laboratory tests were examined.

Results: The median age of the patients was 68 years (min: 52-max: 77). 4 patients (25%) were male and 12 (75%) patients were female. Four of our patients (25%) were active smokers. Non-specific interstitial pneumonia (NSIP) was seen in 10 (62.5%) patients and usual interstitial pneumonia (UIP) was seen in 6 (37.5%) patients. Before RTX, 8 patients were receiving methotrexate and 8 patients were using leflunomide. Four patients had anti-TNF (tumor necrosis factor) treatment. Median during treatment time was 6 months. Other features of the patients are summarized in Table 1. All patients had dyspnea with exertion before treatment. The Forced Vital Capacity (FVC) median was 70 and DLCO was 66. Although 2/16 patients received cyclophosphamide treatment, there was no clinical response and then RTX treatment was started. Protocol of treatment was every 6 months (days 0 and 15 days 1 g). After 6 months, FVC values improved with NSIP pattern (p<0.04). There was no improvement in the UIP pattern but remained stable (Table 2). Clinically, patients’ exertional dyspnea improved. There were no serious side effects in the follow-up of the patients.

Conclusion: There is no valid guideline for RA-ILD treatment. Patient-based decision-making is important in the treatment of these patients. In recent years, RTX seems to be quite effective in RA-ILD. However, long-term and extensive studies are needed in terms of maintenance treatment and possible side effects.

REFERENCES

Table 1. Clinical and epidemiological Features of the RA patients

<table>
<thead>
<tr>
<th>Age</th>
<th>Gender</th>
<th>Male</th>
<th>Female</th>
<th>Serology</th>
<th>Positive</th>
<th>Negative</th>
<th>Smoking history</th>
<th>Methotrexate</th>
<th>Leflunomide</th>
<th>Anti-TNF</th>
<th>Therapy</th>
<th>Duration of disease</th>
<th>Duration of treatment</th>
<th>IAH pattern</th>
<th>UIP</th>
<th>DLCO</th>
<th>FVC</th>
</tr>
</thead>
<tbody>
<tr>
<td>68</td>
<td>Male</td>
<td>4 (25%)</td>
<td>12 (75%)</td>
<td>Positive</td>
<td>14 (87.5%)</td>
<td>2 (12.5%)</td>
<td>4 (25%)</td>
<td>8 (40%) patients</td>
<td>8 (40%)</td>
<td>4 (20%)</td>
<td>10 years</td>
<td>6 months</td>
<td>NSIP</td>
<td>70</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td></td>
<td></td>
<td>Negative</td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Table 2. The FVC and DLCO values of pre- and post- treatment

<table>
<thead>
<tr>
<th>UIP</th>
<th>Pre FVC</th>
<th>Post FVC</th>
<th>p&lt;0.04</th>
<th>Pre DLCO</th>
<th>Post DLCO</th>
<th>p&lt;0.05</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>70</td>
<td>76</td>
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</table>

Disclosure of Interests: None declared
Background: Treat to target (T2T) strategy for rheumatoid arthritis (RA) aims to achieve remission or low disease activity. On the other hand, biological disease-modifying antirheumatic drugs (bDMARDs) have shown to be effective to achieve clinical remission or, at least, low disease activity in patients with RA. On the other hand, comprehensive healthcare programs have demonstrated good clinical outcomes in patients with chronic conditions.

Objectives: The aim of this study was to describe global change in Disease Activity Score 28 (DAS28) in patients receiving biological therapy during 5 years, and who were subjected to a multidisciplinary care program.

Methods: A descriptive cohort study was conducted. Medical records of patients from specialized in RA center were reviewed during 2015-2017; these patients were followed-up under T2T approach. Clinical follow-up was designed by the authors according to DAS28 as follows: every 3-5 weeks (DAS28 > 5.1), every 7-9 weeks (DAS28 > 3.1 and ≤ 5.1), and every 11-13 weeks (DAS28 < 3.1). Ten-point joint count (TJC), swollen joint count (SJC) and DAS28 were measured on each visit. Therapy had to be adjusted with DAS28 > 3.2 unless patient’s conditions don’t permit it; we considered this follow-up type as implementation of a T2T strategy in patients with RA. Patients entered into a multidisciplinary program of care with periodic consultations not only to rheumatology but with a psychiatrist, psychologist, physiotherapist, occupational therapy nutrition, and a patient focused program. With a multidisciplinary model of care the patient is seen as a whole, and the expectation is to achieve the best results in the management of RA. We divided patients into four groups: remission (REM), low disease activity (LDA), moderate disease activity (MDA) and high disease activity (HDA) patients and the aim of the study was to look at what percentage of patients who were in moderate or severe disease activity reached a low disease activity or remission. Descriptive epidemiology was done, we calculated means, and standard deviations for continuous variables and categorical variables were presented as rates. We compared disease activity at base line and at the end of follow-up.

Results: 747 patients meet our inclusion criteria, 85% of our patients were women, median age was 57 years (range 20-86); the most pre-scribed bDMARD was certolizumab 25% followed by etanercept 14%, tocilizumab 12%, abatacept 12%, golimumab 10% rituximab 8%, adalimumab 7%, infliximab 6% and Tofacitinib 6%. At beginning 53% of patients were in moderate or severe disease activity and, 25% in high disease activity while at the end of follow up 89% of patients had achieved remission. See Table 1. It was established statistical significance between changes in median DAS28 at beginning and, at the end of follow-up (P<0.05).

Table 1. Comparison of DAS28

<table>
<thead>
<tr>
<th>ACTIVITY LEVEL</th>
<th>BASELINE</th>
<th>5 YEAR FOLLOW-UP</th>
</tr>
</thead>
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<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>REM</td>
<td>653</td>
<td>88.60</td>
</tr>
<tr>
<td>LDA</td>
<td>177</td>
<td>23</td>
</tr>
<tr>
<td>MDA</td>
<td>388</td>
<td>53</td>
</tr>
<tr>
<td>HDA</td>
<td>182</td>
<td>24</td>
</tr>
</tbody>
</table>

Conclusion: Biological therapy is effective for treating patients with RA, there was an evident global improvement of DAS28 in a cohort of RA patients. Also, our findings agree with other studies where T2T programs have shown improvements in disease activity in patients with RA. Thus, multidisciplinary T2T comprehensive healthcare programs should be widely implemented in patients with RA.

Disclosure of Interests: Pedro Santos-Moreno Grant/research support from: Dr Santos has received research grants from Janssen, Abbvie and UCB. Speakers bureau: Dr Santos has received speaker fees from Sanofi, Lilly, Bristol, Pfizer, Abbvie, Janssen and UCB. Michael Cabrera: None declared, Diana Buitrago-Garcia: None declared, Eva Cardozo: None declared, Ivania Ramirez: None declared, Danny Gomez: None declared, Edwin Castillo: None declared, Sandra Farrieta: None declared.

AB0403  FIXED-INTERVAL VERSUS ON-DEMAND RETREATMENT STRATEGY WITH RITUXIMAB IN RHEUMATOID ARTHRITIS: A RETROSPECTIVE COHORT STUDY

Lisa Schaprij, Nathan den Broeder, Alton den Broeder, Lise Verhoet. Sint Maartenskliniek, Department of Rheumatology, Utrecht, Netherlands

Background: Rituximab (RTX), a monoclonal anti CD20 B-cell antibody is safe and effective in the treatment of Rheumatoid Arthritis (RA). The most optimal retreatment strategy in responding patients is still unclear.

A recent study by Chatzidionysiou et al suggests that RTX retreatment with Fixed-Interval (FI) strategy is better than retreatment with an On-Demand (OD) strategy. [1] However, whether FI treatment strategy is also superior in a treat to target setting is not known.

At our centre (Sint Maartenskliniek, the Netherlands), patients were retreated with RTX using the FI strategy and the OD strategy, by discretion of the rheumatologist, and using treat to target of DSAS28CRP <2.9 in all patients.

In the FI strategy, patients receive retreatment after a predefined fixed period, mostly every 6 months. In the OD strategy, patients receive retreatment in case they experience increase in disease activity. In our hospital, most of the OD strategy patients were switched to the FI strategy in 2014 based on best evidence at that time, enabling us to retrospectively compare efficacy of these strategies.

Objectives: To compare the efficacy of retreatment of RA patients with different strategies following the FI or OD retreatment strategy.

Methods: Adult (>18) RA patients (clinical diagnosis) who started RTX treatment (1 or 2 x 1000mg or 2 x 500mg intravenous) between 1-1-2008 and 1-6-2016 and received at least 3 infusion cycles were included. Patients were treated with either FI or OD strategy, or crossed over from OD to FI. For on demand treatment, RTX retreatment could be planned at the day care within 2-4 weeks.

Primary outcome was DSAS28-CRP, secondary outcome was mean yearly change of DAS28-CRP score compared to FI strategy: adjusted difference was 0.09 (95% CI: 0.03 to 0.16). RTX following the FI or OD retreatment strategy.

A linear mixed model was used to analyse the influence of the strategies on DSAS28-CRP score. Time since start of RTX, calendar year, RTX dose, intra-articular (IA) or intramuscular (IM) steroid injection <6 weeks ago, concomitant csDMARD use at start of treatment and RF status were added to the model as fixed effects. Data was analysed using Stata 13.1.

Table 1. Baseline patient characteristics

| Age, mean (sd) | 59.6 (12.4) |
| Disease duration at RTX start, median (IQR) | 11 (5-17) |
| csDMARD use at RTX start, n (%) | 124 (58%) |
| Rhamatoid factor positivity, n (%) | 166 (75%) |
| Disease duration at RTX start, median (IQR) | 11 (5-17) |
| csDMARD use at RTX start, n (%) | 124 (58%) |
| Rhamatoid factor positivity, n (%) | 166 (75%) |
| DSAS28CRP, mean (sd) | 4.0 (1.2) |
| Strategy, n (%) | 154 (72%) |
| Fixed interval | 25 (12%) |
| On demand | 34 (16%) |
| Both strategies | 0 |

Results: 213 patients were included. 154 following FI strategy, 25 following the OD strategy and 34 switching from OD to FI. Median duration of follow up was 38 months (IQR: 23-64), with a median number of 8 (IQR 5-12) DSAS28-CRP measurements per patient. Patient characteristics are shown in Table 1. The OD strategy was not associated with higher DSAS28-CRP score compared to FI strategy: adjusted difference was 0.09 DSAS28-CRP point (95% CI: -0.08 to 0.26). Regardless of used strategy, DSAS28-CRP improved significantly both over year of treatment, and by time from the start of RTX treatment. Furthermore was rhamatoid factor positivity associated with an lower DSAS28-CRP in all patients, with adjusted difference of -0.37 (95%CI: -0.60 to -0.14). Average yearly RTX dose was 1699mg/yr (SD: 654) under the FI strategy and 1740mg/yr (SD: 732) under the OD strategy (95% CI difference: -336 to 34mg/yr).

Conclusion: Retreatment of RA patients with a fixed interval strategy does not seem to lead to better disease control or more drug use compared to an on demand strategy. A possible explanation might be the use of treat to target in our centre. Our study suggests that either strategy might be chosen in shared decision making and following treat to target.
AB0409 B CELLS PROFILE AS A BIOMARKER FOR EARLY IDENTIFICATION OF OPTIMAL RESPONDERS TO TNF INHIBITORS IN RHEUMATOID ARTHRITIS

Cristina Sobrino1, Borja Hernández-Breijo2, Carlota García-Hoz2, Israel Nieto-Gañán2, Victoria Navarro-Compañ2, Ana Martínez-Feito2, Javier Bachiller-Corral1, Gemma Bonilla3, Paloma Lapuente-Suárez3, Cristina Pijoan Moratalla1, Dora Pascual-Salcedo2, Alejandro Balsa2, Garbiré Roy2, Mónica Vázquez1, Luisa María Villar2, Chamaida Plasencia2, Eulalia Rodríguez-Martin1.

1Rheumatology Department. Ramón y Cajal University Hospital, IRYCIS, Madrid, Spain; 2Immuno-Rheumatology Research Group, La Paz University Hospital, Madrid, Spain; 3Immunology Department. Ramón y Cajal University Hospital, IRYCIS, Madrid, Spain.

Background: The most common biological agents used as disease-modifying treatment in rheumatoid arthritis (RA) are TNF inhibitors (TNFi). Although these new strategies to treat RA have improved the course of the disease, approximately 30-50% of patients do not respond to this therapy. Early identification of optimal responders is crucial in the clinical setting.

Objectives: The aim of this study was to investigate if baseline percentages of different leukocyte subsets in peripheral blood (PBMCs) can contribute to identify RA patients who will respond to TNFi.

Methods: This was a prospective bi-center pilot study including 100 RA patients under TNFi therapy. Clinical activity was assessed at baseline and 6 months of treatment by disease activity score 28 (DAS28), considering optimal responders if they reached remission at 6 months (DAS28 £ 2.6). PBMCs were obtained before treatment and different leukocyte subsets were evaluated by flow cytometry (FACSCantoII instrument). The association between the percentage of PBMCs at baseline and clinical response at 6 months was evaluated through logistic regression models (odds ratio; 95% CI). All the analyses were adjusted by sex, age, disease duration, concomitant methotrexate, baseline DAS28 and seropositivity (ACPA and/or RF).

Results: Demographic characteristics are shown in Table 1. After 6m of TNFi treatment, 40% of the patients achieved clinical remission. A significant association between higher percentage of total B cells (OR=1.19; 95%; CI:1.05-1.35; p=0.007) and naive B cells (Bn; OR=1.32; 95%; IC:1.08-1.61; p=0.007) at baseline and clinical response was found. The other PBMC subsets (monocytes, NK cells, CD4+ and CD8+ T cells subtypes) did not show statistical differences (Figure 1).

Conclusion: Our results suggest that basal B cells profile may contribute to identify optimal responders to TNFi in RA. (Funding: ISCIII (PI16/01092, PI16/00474).

Disclosure of Interests: Cristina Sobrino: None declared, Borja Hernández-Breijo: None declared, Carlota García-Hoz: None declared, Israel Nieto-Gañán: None declared, Victoria Navarro-Compañ: None declared, Ana Martínez-Feito: None declared, Javier Bachiller-Corral: None declared, Gemma Bonilla: None declared, Paloma Lapuente-Suárez: None declared, Cristina Pijoan Moratalla: None declared, Dora Pascual-Salcedo: None declared, Alejandro Balsa: None declared, Garbiré Roy: None declared, Mónica Vázquez: None declared, Luisa María Villar: None declared, Chamaida Plasencia: None declared, Eulalia Rodríguez-Martin: None declared.
as possible within 6 months[1], but many patients have taken oral glucocorticoid for the long term in daily clinical practice. The frequency of use of glucocorticoid has gradually declined, and there are several reports on discontinuation of glucocorticoid due to the initiation of bDMARD[2, 3]. However, there is no report showing the relation between discontinuation of glucocorticoid and MTX dose.

**Objectives:** The aim of this study is to examine association of methotrexate (MTX) dose with discontinuation of glucocorticoid after one year since initiation of biological DMARD (bDMARD) as 1st bDMARD.

**Methods:** We established the large observational cohort, the Nagoya University orthopedic facility multicenter study (TBCR), and a total of 3119 patients used biological DMARD. 564 patients who used glucocorticoid and MTX when bDMARD was initiated as 1st bDMARD were enrolled. In the first study, we examined predictive factors of discontinuation of glucocorticoid after one year since initiation of bDMARD by using multivariate analysis in the two groups, which patients continued to use glucocorticoid and discontinued to use glucocorticoid. In the second study, we adjusted the background at the time of initiation of bDMARD by using propensity score matching (PS) in the two groups, MTX=8mg (L group) and MTX>8mg (H group).

**Results:** 400 patients continued to use glucocorticoid and 164 patients discontinued to use glucocorticoid. In the multivariate analysis, age (Odds ratio (OR)0.98), MTX dose (OR1.09) and glucocorticoid dose (OR0.88) were independently predictive factors of discontinuation of glucocorticoid. When we adjusted age, disease duration, sex, disease activity, RF/ACPA, glucocorticoid dose by using PS matching, 105 pairs were extracted. There were obvious significant differences between 24 patients (22.9%) in the L group and 43 cases (41.0%) in the H group (P = 0.007), where glucocorticoid was discontinued at one year after the initiation of bDMARD.

**Conclusion:** This cohort study investigated the association of discontinuation of oral glucocorticoid and MTX dose in the patients treated with bDMARD. TBCR revealed that, in the clinical practice, glucocorticoid use was decreasing in the patients treated with bDMARD. MTX dose at the time of initiation of bDMARD was predictive factor of discontinuation of glucocorticoid. A higher dose of MTX associated with discontinuation of glucocorticoid in the patients treated with bDMARD.

**REFERENCES**


**Disclosure of Interests:** Mochihito Suzuki Speakers bureau: Bristol-Myers Squibb, Toshihisa Kojima Grant/research support from: Chugah Pharmaceutical (Investigator Initiated Study), Novartis, Nippon Kayaku, Eli Lilly, Eisai, Speakers bureau: Chugai Pharmaceutical, Takeda Pharmaceutical, Pfizer, Eli Lilly Japan, Bristol Myers Squibb, Ono Pharmaceutical, Daiichi Sankyo, Astellas, UCB, Janssen Pharmaceutical, Tanabe Mitsubishi, Nobunori Takahashi Speakers bureau: AbbVie, Bristol-Myers Squibb, Chugai, Eisai, Mitsubishi Tanabe, and Pfizer. YS has received speakers’ fees from Astellas, Bristol-Myers Squibb, and Chugai, Nishi Ishiguro Grant/research support from: AbbVie, Asahi Kasei, Astellas, Chugai, Daiichi-Sankyo, Eisai, Kaken, Mitsubishi Tanabe, Otsuka, Pfizer, Takeda, and Zimmer Biomet, Consultant for: Ono, Speakers bureau: Astellas, Bristol-Myers Squibb, Daiichi-Sankyo, Eli Lilly, Pfizer, and Taisho Toyama DOI: 10.1136/annrheumdis-2019-eular.1943

**AB0411**

**TNF ALPHA INHIBITORS INFLUENCE THE CARDIOVASCULAR RISK IN RHEUMATOID ARTHRITIS PATIENTS**

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**Background:** Rheumatoid arthritis (RA) patients die because of cardiovascular diseases more often than the general population. Nowadays RA is considered as an independent risk factor for cardiovascular disease (CVD). A long-lasting inflammatory process, immunological dysregulation and endothelial dysfunction play an important role in the pathogenesis of progressive atherosclerosis in RA [1,2].

**Objectives:** The aim of the study was to assess the influence of biological treatment on cardiovascular risk factors in RA population.

**Methods:** 38 RA patients with active disease (DAS28>5.1) and 22 age and sex matched healthy controls were enrolled in the study. All the patients were treated with TNF alpha inhibitors (n=20 etanercept, n=18 adalimumab), with the background methotrexate (10-25mg weekly). The clinical state was assessed at the beginning of the study and 6, 12 and 18 months after. All the patients underwent the following tests: DAS28 assessment, basic laboratory measurements (including homocysteine levels, fibrinogen, lipid profile), electrocardiogram (ECG), flow-mediated dilation (FMD) and cartoid intima-media thickness (cIMT) assessment and echocardiography. The local bioethics committee approved the study (KB-753).

**Results:** 27 woman and 11 man (71% and 29% respectively) with high disease activity despite long-term treatment with synthetic disease modifying antirheumatic drugs were enrolled in the study. Mean age was 52 years (SD ± 9,6), 95% of the patients were RF-positive, 63% anti-CCP-positive. Of them 24% were current smokers, 58% had arterial hypertension and 66% had concomitant hypercholesterolemia. In comparison to the control group, there were statistically significantly higher values of cIMT in RA patients. Moreover there was a positive correlation between cIMT thickness and duration of RA. A reduction of cIMT (mainly during first 12 months) and an increase in FMD values were observed in the course of the treatment (p<0.05). The increase in FMD value (0.03 vs 0.37) correlated with decrease of the inflammatory markers, which may be a result of an improvement in endothelial dysfunction due to anti-TNF-alpha treatment. The decrease in total cholesterol (p<0.05), LDL cholesterol (p<0.03) and Castelli risk index (p<0.05) were also noted, no changes of the doses of cholesterol-lowering therapy were done during the follow up. There was a positive correlation between homocysteine and uric acid levels and there was a statistically significant decrease in both parameters in the course of the treatment (11.31 vs 8.91 [mol/l] and 5.92 vs 4.77 [mg/dl], respectively). Normal left ventricular geometry was observed after 12 months of biological therapy in patients with concentric remodeling of the left ventricle. Furthermore echocardiography revealed a significant decrease in LVEDD, IVSD, LA, FS, RVEDD after 18 months of the biologic treatment.

**Conclusion:** Our results confirm earlier data that TNF alpha inhibitors may favorably influence on endothelial dysfunction. Besides TNF inhibitors can protect against increase in relative wall thickness of left ventricle. The anti-TNF alpha therapy not only reduces the activity of the disease in affected joints but also has a positive impact on selected cardiovascular risk factors in RA population.

**REFERENCES**


**Disclosure of Interests:** None declared DOI: 10.1136/annrheumdis-2019-eular.5026
FACTORS THAT AFFECT THE RESPONSE TO TOCILIZUMAB WITH REGARD TO WORK PRODUCTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS: A 2-YEAR FOLLOW-UP OF THE FIRST ACT-SC STUDY

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Background: Rheumatoid arthritis (RA) is a major cause of work disability, sickness-related absence from work, presenteeism, and loss of productivity. The decrease in work productivity that results from persistent pain, impaired mobility and function, and reduced quality of life (QOL) has important personal, societal, and economic consequences[1]. The efficacy of tocilizumab (TCZ) as monotherapy and in combination with methotrexate for RA is well known. Thus, in this study, we expected TCZ treatment to improve work productivity on the basis of interim results of up to 52 weeks[2].

Objectives: We aimed to evaluate the long-term (104 weeks) control of RA in Japanese paid workers and house workers treated with TCZ and identify factors affecting the response (responder/non-responder) to TCZ in terms of work productivity.

Methods: The first ACT-SC study (UMIN-CTR: UMIN000012306) was a cohort study that assessed the 2-year treatment outcome of TCZ-SC (administered alone or with disease modifying anti rheumatic drugs) in biologics-naive Japanese patients with RA. Logistic regression analysis was performed to determine the factors contributing to treatment response in terms of activity impairment (AI) in the WPAI questionnaire, which is an index for the evaluation of overall daily life performance. In addition, the association of these responses to treatment withdrawal rate and QOL were also evaluated.

Results: Of the 377 enrolled participants, 357 who were treated with TCZ-SC were included in the analysis. AI was improved from 56.2% at baseline to 22.9% at 104 weeks in the patients who received TCZ. In the single regression analysis, the factors that were statistically significant in the logistic regression analysis were job type (p=0.045), K6 as a measure of psychological distress (p=0.030), Health Assessment Questionnaire-Diary (HAQ-DI; p=0.032), and EuroQol five-dimensional descriptive system (EQ-5D) score (p=0.006). In the multiple logistic regression analysis, disease duration, academic background, AI, EQ-5D score, ESR, and CRP level were identified as factors that affected response. The results showed a strong association between the results of the subjective assessments such as the utility value of EQ-5D. At 104 weeks, the mean difference in AI between the EQ-5D scores of <0.6 and ≥0.6 was significant (−22.94% vs −30.50%; p=0.029). Moreover, the mean difference between the HAQ-DI of <1.5 at baseline and ≥1.5 was significant (−20.46% vs −29.08%; p=0.013). A disease duration of >1 year was also associated with being an AI responder. A significant difference in withdrawal rate was found between the responders and non-responders (27.0% vs. 46.9%; p=0.001), and the 2-year quality-adjusted life-year was also significantly higher in the AI responders.

Conclusion: Starting TCZ-SC treatment at an early stage while taking into consideration the subjective self-assessments of the patients may contribute to improvements in labour productivity and QOL, and long-term treatment continuation.

REFERENCES

AB0413 THE PROSPECTIVE ASSESSMENT OF RITUXIMAB AND TOCILIZUMAB TREATMENT EFFECT ON RF-IGM AND ACPA TITRES IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Rheumatoid arthritis (RA) is associated with several specific autoantibodies, which can be used as diagnostic and prognostic markers. These include rheumatoid factor IgM (RF-IgM) and anti-citrullinated protein antibodies (ACPA). The data reporting an impact of biological disease modifying anti-rheumatic drugs (bDMARDs) on RA serological markers are divergent, probably depending on the type of treatment.

Objectives: The goal of this study was to prospectively evaluate the impact of bDMARDs (rituximab, RTX) and tocilizumab (TCZ) on RA serological markers (RF IgM, ACPA), in correlation with the disease activity assessment.

Methods: The study was conducted in the consecutive 42 patients with RA (36 women, 6 men), with the mean (SD) age 49.6 (13.8) and disease duration 9.2 (3.8) years. The treatment with RTX was administered to 30 patients and with TCZ to 12 patients. The following parameters were assessed for all patients: joint counts, disease activity index of 28 joints (DAS28), complete blood cell counts, erythrocyte sedimentation rate (ESR), serum concentration of serum amyloid A (SAA), RF-IgM, ACPA. Blood samples were taken before the drug administration (baseline) and in consecutive months (3, 6 and 9 months).

Results: Parameters of the disease activity decreased significantly in consecutive months, in comparison with the baseline assessment, in both treatment groups. The mean (SD) DAS28 decreased significantly in both groups (RTX and TCZ): respectively at baseline: 5.75 (0.69) and 5.47 (0.51); month 3: 3.92 (1.13) and 2.84 (0.76); month 6: 3.23 (1.09) and 2.09 (0.94); month 9: 3.67 (1.19) and 2.12 (0.81). The mean reduction of RA serological markers (RF-IgM, ACPA), in correlation with the disease activity assessment.

month 9 (Figure 3); no significant change of RF-IgM was observed (Figure 4).

Conclusion: The results of the study suggest that both bDMARDs reduced significantly the disease activity in RA patients. The treatment with both drugs was associated with a significant reduction of SAA. However only RTX treatment affected significantly the production of disease specific autoantibodies. Long-term observation is necessary to assess a reliable effect of bDMARDs on the production of marker autoantibodies in association with the disease activity. Disclosure of Interests: Olga Borys: None declared, Bozena Targonska-Stepniak Speakers bureau: Sandoz, Berlin-Chemie, Magdlena Dryglewska: None declared, Maria Majdan Speakers bureau: MSD, UCB, Abbvie, Roche DOI: 10.1136/annrheumdis-2019-eular.3476

AB0414 THE IN VITRO EFFECT OF BIOLOGICAL AND CONVENTIONAL DISEASE MODIFYING ANTI RHEUMATIC DRUGS (DMARDs) ON FIBROCYTE DIFFERENTIATION IN RHEUMATOID ARTHRITIS PATIENTS AND HEALTHY CONTROLS

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Background: Fibrocytes are circulating cells with both myeloid and haemopoietic properties. They home in tissues with active inflammation, where they differentiate into mature fibrocytes that are involved in several inflammatory pathways. One complication of Rheumatoid Arthritis (RA) is Interstitial Lung Disease (ILD) resulting in high mortality and with limited treatment options. Fibrocyte levels are elevated in RA patients compared with healthy individuals and further increased in RA patients with signs of ILD (reduced diffusion capacity) and in patients with idiopathic lung fibrosis (IPF) or scleroderma. Thus, fibrocytes have been proposed as a future treatment target.

Objectives: We investigate the effect of corticosteroids, conventional Disease Modifying Anti Rheumatic Drugs (cDMARDs) and biological DMARDs (bDMARDs) on the in vitro differentiation of isolated peripheral blood mononuclear cells (PBMCs) into mature fibrocytes.

Methods: 10 participants were included (five patients with RA and five healthy controls). Information on current medication, sex, age, serology and disease activity were collected. PBMCs were isolated and cultured for 5 days in four wells per drug. Drugs included prednisolone, cDMARD (Methotrexate, Sulfasalasine, Hydroxychloroquine) and bDMARD (Inflectra, Etanercept, Tocilizumab, Adalimumab, Abatacept, Rituximab), and control wells with no drugs.

Results: Overall, abatacept and prednisolone significantly suppressed differentiation of PBMC into fibrocytes compared to control wells, see Figure 1 (p=0.02 and p<0.01, respectively) (n=10). The reductive effect of Abatacept was significant among RA patients (p=0.009 and) but not among healthy subjects. In overall analysis (n=10), Abatacept reduced fibrocyte levels with an average of 44% overall and in the RA group 71% compared to control wells. Tocilizumab reduced the fibrocyte count with 63% overall and 45% in the RA group, although not significant (p=0.07 and p=0.06 respectively).

Conclusion: Abatacept and prednisolone suppress the differentiation of mononuclear cells to mature fibrocytes in vitro in RA patients and data indicating a similar effect of Tocilizumab. Prednisolone are used in the treatment of RA-ILD but has a marked toxicity, so new treatment modalities are desirable. Our findings are in line with the fact that fibrocytes have the receptors targeted by abatacept, furthermore recent scleroderma research has shown Abatacept to reduce fibrocyte levels in vitro and Tocilizumab to potentially reduce lung and skin affection (1, 2) Further research using abatacept and tocilizumab to target fibrocytes are needed in order investigate the treatment potential of these drugs in RA-ILD.
SURVIVAL OF BIOLOGIC AGENTS WITHIN A COHORT OF GREEK PATIENTS WITH RHEUMATOID ARTHRITIS. REAL WORLD DATA.

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Background: Rheumatoid arthritis (RA) is treated successfully with biologic disease-modifying anti-rheumatic drugs (bDMARDs). However, a significant withdrawal rate, due to non-responsiveness or toxicity, remains a major barrier for their long-term use.

Objectives: To determine the withdrawal rate of the first bDMARD in a large cohort of RA patients due either, to non-responsiveness or toxicity.

Methods: In this study, were included retrospectively 220 patients from our outpatient clinic. The following bDMARDs were evaluated: Etanercept (n=66 patients), Adalimumab (n=61 patients), Infliximab (n=70 patients), Rituximab (n=6 patients) and others, such as Certolizumab pegol, Golimumab, Tocilizumab, Anakinra and Abatacept (n=17 patients). Disease activity was regularly measured by DAS-28 until the end of follow up. Kaplan-Meier plots were performed to examine the withdrawal rate of each biologic agent. Severity of AEs was classified according to the Common Terminology Criteria for Adverse Events (CTCAE, version 4.03).

Results: A total of 220 patients (49 men, 171 women) were included in the analysis. The most frequently used first-line bDMARDs were Infliximab (31.8%), Etanercept (30%) and Adalimumab (27.7%). The median of treatment duration with the first bDMARD was 15 months (Q1:8, Q3:40.5). Taking all bDMARDs as a whole, 126 patients (57.27%) discontinued the first bDMARD, either due to AEs (n=66, 52.38%), or loss of efficacy (n=60, 47.62%) after a follow-up of 167 months. However the most withdrawals (53.18%) occurred within the first 60 months of follow-up. Mean initial and final DAS-28 were: for those who discontinued due to failure of therapy: 5.04 ± 1.37 (95%CI, 4.70-5.39) and 4.91 ± 1.27 (95%CI, 4.59-5.23) respectively and for those who continue 4.79 ± 1.55 (95%CI, 4.47-5.10) and 2.63 ± 1.06 (95%CI, 2.41-2.84) respectively.

Differences in survival among bDMARDs are attributed to their AEs and not to their efficacy. As far as the AEs are concerned, infections constituted the majority of cases (n=23, 34.8%), from which 34.8% needed hospitalization (CTCAE 3-4). The percentage of 12.1% of AEs is attributed to cancer cases, while allergic reactions counted for 31.8% of them. Survival of Etanercept within our cohort was significantly longer than those of other bDMARDs.

Conclusion: Biologic agents are important drugs in our armamentarium to combat RA. However nearly 50% of patients discontinue these agents after 60 months of treatment due either to AEs or inefficacy. Differences in survival of bDMARDs were associated not to their inefficacy, but to their AEs. Choosing the right drug for the right patient is a matter of advanced research involving a better understanding of the plasticity of the pathways of inflammation and specific biomarker selection.

REFERENCES


Disclosure of Interests: None declared

A COMPARATIVE STUDY TO ASSESS THE EFFICACY, SAFETY, AND IMMUNOGENICITY OF YLB113 AND ETAmeric RECEPTOR PRODUCT FOR THE TREATMENT OF PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS

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Background: YLB113 is an investigational biosimilar of the reference product etanercept (ETN), being developed for the treatment of patients with moderate-to-severe rheumatoid arthritis (RA) and other approved indications of the reference product ETN.

Objectives: The phase 3 study of YLB113 was conducted in Europe, Japan, and India across more than 100 rheumatology clinics to compare efficacy, safety, and immunogenicity of YLB113 with ETN in patients with RA.

Methods: A total of 528 patients with moderate-to-severe RA receiving concomitant treatment with methotrexate were randomized to receive a once-weekly dose of 50 mg of subcutaneously administered YLB113 or ETN. The primary end point was the ACR20 response rate at Week 24, with equivalence confirmed if the 95% confidence interval (CI) was within the range of –15% to 15%. Other efficacy end points, such as DAS28 with safety and immunogenicity end points, were assessed periodically up to Week 52.

Results: The ACR20 response rate at Week 24 was 81.2% for YLB113 and 86.8% for ETN in the full analysis set, with a treatment difference of –5.6% (95% CI: –11.6, 0.5), which was completely within the predefined equivalence margin of –15% to 15%. The result for sensitivity analysis using the per protocol set population revealed that the proportion of subjects who showed ACR20 response at Week 24 was similar between both treatment groups, at 4.6% (95% CI: –10.1, 0.9). The incidence of treatment-emergent adverse events was comparable between YLB113 and ETN (55.5% vs 65.7%), and the incidence of antibiotic antibody development up to Week 24 was in favor of YLB113 (0.8% vs 8.3%).

Conclusion: The present comparative study demonstrated the biosimilarity of YLB113 to ETN on the triad of efficacy, safety, and immunogenicity in patients with moderate-to-severe RA, and thus can be extrapolated to other therapeutic indications approved for ETN. The therapeutic equivalence of YLB113 and ETN in terms of the primary efficacy end point at Week 24 and long-term safety comparability until Week 52 was established with lower immunogenicity.

Disclosure of Interests: Hisashi Yamanaka Grant/research support from: Abbvie, Eisai, Bristol-Meyers, Novartis, Behtinger, Astellas, Kaken, Nippon Shinyaku, UCB, Ayumi, Ono, Toyama, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, Torii, YLB, Speakers bureau: Bristol-Meyers, Astellas, Pfizer, Daiichi-Sankyo, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, YLB, Naomiyuki Kamatani Speakers bureau: I was a speaker in meetings and paid for the speech by YLB Pharma, Teijin Pharma, Chugai, Pfizer, Fuji Yukuhin, Sanwa Kagaku, Asahi Kasei Pharma and Asters-Amzen BioPharma., Yoshiya Tanaka Grant/research support from: Abbvie, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eisai, Mitsubishi-Tanabe, MSD, Ono, Taiso-Toyama, Takeda, Speakers bureau: Abbvie, Asahi-kasei, Astellas, Bristol-Myers Squibb, Chugai, Daiichi-Sankyo, Eli Lilly, Eisai, Glaxo-Smithkline, Janssen, Mitsubishi-Tanabe, Novartis, Pfizer Japan Inc, Sanofi, Takeda, UCB, YLB Biologics, Toshihiko Hibino Consultant for: I had worked in Japanese Pharmaceutical Company (Showa Yakkaku Company Co. Ltd.) as an unaffiliated director until 2015 but have no conflict on business including newly built company (Ayumi Pharmaceutical Company Ltd.). Then then, Edit Drescher: None declared, Juan Sánchez-Bursón: None declared, Manfred Rettenbacher Employee of: I am an employee of Lupin Pharmaceuticals Ltd., Girish Bhatia: None declared, Snehad Gadge Consultant for: Was working as a consultant for YLB company, Chirag Shah Employee of: I am an employee of Lupin Pharmaceuticals Ltd., Dhananjay Bakshie Employee of: I am an employee of Lupin Pharmaceuticals Ltd.


AB0416C

THE RESULTS OF THE USE OF TOFACITINIB (TOFA) IN PATIENTS WITH RHEUMATOID ARTHRITIS (RA) IN MOSCOW. ANALYSIS DATA FROM MOSCOW UNIFIED ARTHRITIS REGISTRY (MUAR)

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Background: Moscow Unified Arthritis Registry (MUAR) started on 01 DEC 2012. By 01 DEC 2017, 829 RA patients were included in the register.

Objectives: The aim of the study was to evaluate the effectiveness and treatment survival of TOFA and identify predictors of the effectiveness of TOFA.
Efficacy and Safety of Tofacitinib in Patients with Rheumatoid Arthritis – Non Biologic Treatment

Methods: The inclusion criteria were diagnosis of RA, established at any time according to ACR (1987) or ACR/EULAR (2010) criteria; persons receiving or planning to receive targeted therapy for RA; signed informed consent to participate in the study. All episodes of treatment with tofacitinib in which there was at least 1 visit not earlier than 6 months since the start of the drug were included for efficacy analysis.

Results: Data of 48 patients treated with tofacitinib were extracted from the registry. Women were 41 (85.4%), mean age was 55.1 ± 12.4 years; age at the disease beginning was 44.3 ± 14.0, 6 (12.5%) of patients were smokers; mean time on tofacitinib was 552 ± 295 days. One of the independent predictors of achieved DAS28 was sex - 0.49 lower in men (p<0.001). There was no correlation of achieved disease activity with number of previous failures with biologics. Patients seropositive for rheumatoid factor achieved significantly lower activity (p =0.015). There was also a trend towards lower achieved activity in patients with rheumatoid nodules (p = 0.059).

On the first line of targeted treatment, survival of tofacitinib was significantly better than Infliximab, Adalimumab and Certolizumab pegol. On the second line – better than etanercept. On the following lines TOFA was better than Adalimumab, but worse than Etanercept. Due to the fact that most of treatment episodes with tofacitinib are not completed, the average duration of treatment may be underestimated. There was no significant decrement of remission on therapy after multiple treatment failures (tab.).

Conclusion: The effectiveness and treatment survival of tofacitinib does not depend on the number of previous failures with biologics; the best results of TOFA can be expected in men and seropositive patients; the presence of rheumatoid nodules can be considered as a special indication for TOFA.

Table: Retention of targeted therapies in patients with rheumatoid arthritis

<table>
<thead>
<tr>
<th>Drug</th>
<th>Number of patients</th>
<th>Average duration (months; confidence interval)</th>
<th>Number of patients</th>
<th>Average duration (months; confidence interval)</th>
<th>Number of patients</th>
<th>Average duration (months; confidence interval)</th>
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<tr>
<td>Tofacitinib</td>
<td>271</td>
<td>67 (65.6; 73.5)</td>
<td>271</td>
<td>67 (65.6; 73.5)</td>
<td>271</td>
<td>67 (65.6; 73.5)</td>
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<td>150 (127; 163)</td>
<td>109</td>
<td>150 (127; 163)</td>
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<td>150 (127; 163)</td>
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<tr>
<td>Certolizumab pegol</td>
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<td>66</td>
<td>70 (62; 77)</td>
<td>66</td>
<td>70 (62; 77)</td>
</tr>
<tr>
<td>Infliximab</td>
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<td>150 (127; 163)</td>
<td>109</td>
<td>150 (127; 163)</td>
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<td>150 (127; 163)</td>
</tr>
<tr>
<td>Tofacitinib</td>
<td>12</td>
<td>12 (10.6; 13.9)</td>
<td>12</td>
<td>12 (10.6; 13.9)</td>
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<td>67 (65.6; 73.5)</td>
<td>271</td>
<td>67 (65.6; 73.5)</td>
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</table>

* – statistically significant difference with Tofacitinib (log-rank test)

Figure 1

Disclosure of Interests: None declared

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References


Efficacy and Safety of Tofacitinib in Patients with Rheumatoid Arthritis According to Duration of Prior CSPMARD Treatment and Number of Prior CSPMARDs: A Post Hoc Analysis of Phase 3 and Phase 3b/4 Trials

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Background: Tofacitinib is an oral JAK inhibitor for the treatment of rheumatoid arthritis (RA). Previous analyses have reported greater improvements in efficacy outcomes with tofacitinib 5 mg twice daily (BID) compared to conventional synthetic DMARDs (csDMARDs) in patients (pts) with early RA.1,2

Objectives: To evaluate the efficacy and safety of tofacitinib in pts with RA, stratified by prior csDMARD treatment duration and number of prior csDMARDs.

Methods: This was a post hoc analysis of pooled data from 4 Phase (P) 3 trials (ORAL SCAN [NCT00847613]; ORAL Solo [NCT00814307]; ORAL Sync [NCT00856544]; ORAL Standard [NCT00853385]) and 1 P3b/4 trial (ORAL Strategy [NCT02187055]) of tofacitinib in pts with RA and an inadequate response to ≥1 DMARD. Pts treated with tocilizumab 5 mg BID as monotherapy or with csDMARDs were included. Outcomes were evaluated according to csDMARD treatment duration (≤1, 1–2, >2 years) and number of csDMARDs (1, 2, 3; ≥4) prior to baseline (BL). Efficacy outcomes assessed at Months (M)3, 6 and 12 were: change from BL (Δ) in CDAI and HAQ-DI, and rates of CDAI-defined low disease activity (LDA) ≤10 and remission (≤28).

Results: In total, 1584 pts were included in the analysis; of these, 27.2% (n=431) had received csDMARDs for ≤1 y, 20.5% (n=255) for 1–2 y, and 52.1% (n=825) for >2 y prior to BL (duration unknown for 3 pts). Roughly half (53.2%, n=842) had received 1 prior csDMARD; 26.4% (n=418); 13.8% (n=219) and 6.6% (n=105) had received 2, 3 and ≥4 prior csDMARDs, respectively. Most pts had previously received MTX (50.6%, n=805) or MTX + other csDMARDs (46.3%, n=733); 2.9% (n=46) received other csDMARDs only. Mean BL CDAI and HAQ-DI scores were similar, irrespective of prior csDMARD treatment duration or number of prior csDMARDs (Table). Generally, up to M12, no trends were observed for ACDAI, ΔHAQ-DI or CDAI LDA rates regardless of prior csDMARD treatment duration or number of prior csDMARDs (Table). When CDAI remission rates data were stratified by csDMARD treatment duration, no differences between pt groups were observed at M3 and M6; however, a numerically higher proportion of pts with prior csDMARD treatment duration ≤1 y achieved remission (50.8%, n=805) or MTX + other csDMARDs (46.3%) vs 1–2 y and >2 y pts. Use of fewer prior csDMARDs appeared to be associated with higher remission rates up to M12. Although safety outcomes were similar when data were stratified by prior csDMARD treatment duration, there was generally a trend for increased rates of AEs, SAEs and AEs of special interest (serious infections, herpes zoster and opportunistic infections [excluding B1]) with increasing number of prior csDMARDs (Table).

Conclusion: In this post hoc analysis of pooled data from P3 and P3b/4 trials, no differences in the efficacy or safety of tofacitinib 5 mg BID were observed when pts were stratified by prior csDMARD treatment duration. Although pt numbers were small, use of fewer prior csDMARDs may be associated with improved remission rates and safety outcomes for pts treated with tofacitinib.
INTERSTITIAL LUNG DISEASE IN PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH TOFACITINIB

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Background: The presence of interstitial lung disease (ILD) is a common extra-articular manifestation in patients diagnosed with Rheumatoid Arthritis (RA), dyspnea being its cardinal symptom. Several of the drugs commonly used to treat this condition, such as TNF inhibitors (anti-TNF) and Disease Modifying Antirheumatic Drugs (DMARDs), have been implicated in the development or exacerbation of ILD. In regard to Tofacitinib, results of post hoc analysis of its pivotal and extension studies report a numerically lower ILD incidence rate in the group that received this drug compared with placebo.

Objectives: To describe the evolution of dyspnea, spirometric parameters, DLCO and high resolution computed tomography (HRCT) findings in patients with RA diagnosis associated with PID who received Tofacitinib for a period of 12 months.

Methods: Patients with a diagnosis of RA who fulfilled criteria ACR 1987/ ACR-EULAR 2010, with interstitial lung disease previously diagnosed from clinical findings, spirometry and/or HRCT were included. Tofacitinib was used in dose of 10 mg/day orally. Design: Descriptive, retrospective, multicentric study. The following variables were analyzed: change at 12 months from baseline in the degree of dyspnea (according to the modified scale of dyspnea MMRC), forced vital capacity (FVC), DLCO and findings in HRCT. Continuous variables were reported as mean and standard deviation or median and interquartile range as appropriate. The categorical variables were reported as percentages.

Results: Fifteen patients were included. 60% (n: 9) were women. The mean age was 64.4 years (± 10.92). The median time of evolution of RA was 9 years (IQR: 4-40). The median time of evolution of interstitial lung disease was 4 years (IQR: 1-24); 13% (n: 2) of the patients were receiving methotrexate (MTX) at the time of evaluation, 60% (n: 9) of the patients had received methotrexate previously, 80% (n: 12) had previously received leflunomide different from MTX. 33% of the patients (n: 5) had received previous biological treatment. All patients received tofacitinib at a dose of 10mg/day. 47% of patients (n = 7) received tofacitinib monotherapy and 53% (n = 8) received it combined with DMARDs. 27% (n: 4) of the patients had grade 3-4 dyspnea at baseline. Improvement in the dyspnea scale was observed in 8 patients, while in the rest, it remained stable. The forced vital capacity (FVC) at baseline was <80% in 5 patients and > 80% in 2 patients. At 12 months, 4 patients achieved a FVC > 80%. The average of DLCO at baseline was 45.6 (± 18.84), with an improvement of 30% at 12 months in 4 patients. No progression of the disease was observed in the HRCT at 12 months in any of the patients evaluated.

Conclusion: The present preliminary study was performed with patients of daily practice, not being available in all cases, the corresponding respiratory functional examinations. However, despite these limitations, none of the patients showed worsening of dyspnea, with improvement in some patients. Regarding respiratory functional examinations and DLCO, not only the patients who remained stable after treatment in the majority of patients evaluated, but 4 patients presented improvement with respect to baseline parameters. It is necessary to perform more studies, with systematized controls of the pulmonary function and imaging, to corroborate this hypothesis.

Disclosure of Interests: AB0418 chest.xla

A PROSPECTIVE, OBSERVATIONAL STUDY ON THE CLINICAL EFFICACY AND SAFETY OF LEFLUNOMIDE IN EGYPTIAN PATIENTS WITH ACTIVE RHEUMATOID ARTHRITIS: CLEAR STUDY

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Background: Due to its anti-inflammatory and immunomodulatory properties, leflunomide can be used as monotherapy or in combination with other conventional synthetic DMARDs (csDMARDs) in treating active RA.1

Objectives: The aim of this observational study was to assess efficacy and safety of leflunomide in Egyptian patients with active RA, whether used as first-line and/or add-on therapy to other csDMARDs, with or without steroids.

Methods: Adult Egyptian patients with active RA, fulfilling the ACR/EULAR 2010 classification criteria, for whom leflunomide was prescribed, were included and followed up for 9 months. Leflunomide was prescribed at the physicians’ sole discretion for patients who have previously experienced resistance, inadequate response or intolerance to other csDMARDs. Data about CDAI score and HAQ-DI score were acquired from patients who fulfilled the eligibility criteria, along with patients’ demographics, medical history, physical examination, concomitant medications, and RA history including disease duration, previous RA medications and treatment response. This study was registered on clinicaltrials.gov (NCT03599986) and the preliminary results were previously published in 2018.2

Results: A total of 398 patients were enrolled in this study. Three hundred ninety-six patients with a mean age of 43.7 (SD 10.2) years and median disease duration of 2 (IQR 5.5) years were eligible for efficacy evaluation; 309 (84.4%) were female. We found that 86.1% of patients were leflunomide naïve. Patients who previously received leflunomide (13.9%) had a wash out period of at least 6 months prior to study enrolment. Patients were either prescribed leflunomide 20 mg/day (37.7%) or were prescribed a loading dose of 100 mg/day for the first 3 days of treatment then maintained with 20 mg/day (62.3%). Leflunomide was prescribed as first-line therapy in 21.1% of patients, as add-on therapy to other csDMARDs without steroids in 34%, and as add-on therapy to other csDMARDs with steroids in 44.9%. The mean total CDAI score was slightly lower in the leflunomide group compared to the control group at 24 weeks (23.6 vs. 24.3, p=0.018). The clinical remission rate was 10.4% in the leflunomide group compared to 4.9% in the control group (p=0.025). In addition, the percentage of patients with no change in the CDASII score was higher in the leflunomide group (61 vs. 49%, p=0.001).

Disclosure of Interests: None declared


FRACTURE RISK IN PATIENTS ON LONG TERM GLUCOCORTICOIDS WITH INFLAMMATORY ARTHRITIS

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Background: A main stay treatment of inflammatory arthritis is glucocorticoids (GCs). However, long term use of GCs has been associated with an increased risk of fracture, with studies estimating up to 12% of patients having sustained a fracture whilst on GC treatment.1,2

Objectives: The aim of this study was to determine the prevalence of fractures in a cohort of patients on long term GCs with a diagnosis of inflammatory arthritis.

Methods: A database of patients with inflammatory arthritis attending the rheumatology department at the Midlands Regional Hospital Tullamore, since 2009, was reviewed. Patients on long term GCs were identified and outpatient summaries were analysed. Data collection included age, sex, diagnosis, vertebral fracture, other fracture sites and osteoporosis treatment.

Results: As of September 2018, out of the 2118 patients with a diagnosis of inflammatory arthritis 364 were on long term GCs. 10% of patients had reported vertebral fractures on imaging. 36.4% of patients had other types of fractures reported on imaging; 20%, and the most common site of fracture, were wrist fractures. 83.7% of those who suffered from a vertebral fracture were female. 18.2% of those who sustained fractures were not on any osteoporosis treatment.

Conclusion: The incidence of fracture in our cohort of patients was higher than suggested in previous studies. Furthermore, it highlights the need for patients on long term GCs to be given osteoporosis prevention therapy.

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Disclosure of Interests: None declared


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was significantly decreased (p<0.001) from 36.8 (14.9) at baseline, to reach 12.5 (10.3) after 9 months of treatment, with a reduction of 64%. In a similar pattern, the mean HAQ-DI score was significantly decreased (p<0.001) from 1.5 (0.7) at baseline to reach 0.6 (0.6) after 9 months of treatment, with a reduction of 57%. Figures 1 and 2 show changes in both CDAI and HAQ-DI scores throughout the study.

Twenty-three adverse events (AEs) were reported in 20 patients (5%) throughout the study, and 19.1% of patients were at remission after 9 months of treatment.

Abstract Figure 3 shows that disease severity was significantly improved (p=0.001) throughout the study, and 19.1% of patients were at remission after 9 months of treatment.

[AB0421] METHOTREXATE COMPLIANCE AMONG PATIENTS WITH CHRONIC INFLAMMATORY DISEASE OR CONNECTIVE TISSUE DISEASE

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Background: Methotrexate (MTX) is widely used in rheumatology. About 30% of patients receiving MTX do not respond. One of the explanations could be poor adherence.

Objective: The purpose of this study was to assess adherence and to identify predictive factors influencing it.

Methods: 188 patients with MTX for at least 3 months (rheumatoid arthritis (RA), peripheral spondyloarthritids (PS), psoriatic arthritis (PA), lupus, Sjögren’s Syndrome (SS)) were enrolled between May 2017 and May 2018. Each patient completed a questionnaire including socio-demographic data, disease and MTX characteristics, 4-question Morisky, rheumatism activity scores including DAS 28, quality of life (EQ-5D), phibromyalgia (FIRST), anxiety and depression (HADS), catastrophism (PC3-CF), coping (WCQ-R) and whether or not to participate in a therapeutic education program. 188 were recruited, with a mean age of 61.4 +/- 13.24 years: RA (77.12%), PS (7.98%), PA (10.11%), lupus (2.66%) and SS (2.13%). 68.6% were observant, versus 31.4% non-observant (28.2%) or major (3.2%) patients. In multivariate analysis, two models were performed and found a poor adherence in case of depression OR: 3.120 [1.051; 9.354], catastrophism OR: 3.974 [1.119; 14.108], anti-CCP antibodies OR: 4.019 [1.277; 12.653] in RA patients and depression OR: 2.715 [1.237; 5.963], absence of comorbidities OR: 2.309 [1.085; 4.915] with all rheumatism.

Conclusion: Some modifiable factors such as depression and catastrophism were associated with the risk of non-adherence with MTX. It is important to consider depression and catastrophism when taking care of our patients to improve adherence and avoid therapeutic escalations.

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[AB0422] ACHIEVEMENT OF PATIENT ACCEPTABLE SYMPTOM STATE (PASS) IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH BARICITINIB

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Background: Baricitinib, a newly approved drug for the treatment of patients with moderate to severe rheumatoid arthritis (RA), is a selective inhibitor of Janus kinase 1 and 2. In a patient-centered care, patient-reported outcomes (PROs) are really helpful to better evaluate the disease activity and the response to therapy. Between them, Patient Acceptable Symptom State (PASS) is defined as the highest level of symptoms beyond which patients consider themselves well [1], and consists of a single question with dichotomized answer (yes or no): “Considering all the different ways your disease is affecting you, if you would stay in this state for the next months, do you consider that your current state is satisfactory?”. In randomized controlled trials baricitinib showed significant improvement of pain, fatigue, tiredness and assessment of disease [2].

Objective: The aim of the present study was to investigate the effect of baricitinib on PASS one month from the beginning of therapy. Further aim was to quantify the time patients needed to reach an acceptable state of health and determine the clinical variables associated with PASS.

Methods: Patients affected by RA according to 2010 ACR criteria, starting treatment with baricitinib as clinically indicated, were consecutively enrolled; PASS was determined after 1 month of treatment (T1); days to
achieve PASS were estimated at T1; activity indices were calculated after 1 month of therapy and correlated with PASS.

**Results:** Thirty-four RA patients were enrolled (age median-IQR: 58-16 years; disease duration median-IQR: 144-138 months; DAS-28 median-IQR: 5.09-1.19). After 1 month of therapy, 30 of 34 patients achieved PASS, of which 73% in the first 2 weeks of treatment (days to achieve PASS median-IQR 12-22) (figure). At T1, patients achieving PASS, compared to those who did not, reported less pain (median VAS 30/100 vs 72/100, p= 0.025), a better global assessment of disease (median 40/100 vs 72/100, p=0.023), lower CDAI (median 12 vs 31, p= 0.048), SDAI (median 12.8 vs 33.95, p=0.011) and DAS-28 (median 3.67 vs 5.54, p= 0.082). 10 out of 30 PASS positive patients (33%) achieved a DAS-28 low disease activity or remission at T1 vs 0% of the PASS negative cohort (p= 0.169). Age, disease duration and number of previous DMARDs did not significantly differ between the two subgroups.

**Conclusion:** Baricitinib was able to induce an acceptable state of health in about 90% of patients after the first month of therapy. The prompt effect of baricitinib on pain and fatigue could partially explain the rapid achievement of PASS, as shown by the decrease of VAS and improvement of the global assessment of disease. Bioavailability of oral MTX reaches plateau in doses >15 mg weekly, and this is the reason of its lower clinical efficacy.

**Objectives:** The objective of this observational longitudinal study was to evaluate the changes in disease activity, intensity of pain, global health, and physical function when switching from oral (P.O.) to subcutaneous (S.C.) MTX in patients with RA and peripheral form of PsA.

**Methods:** Forty-eight consecutive patients (79.2% women) with established diagnosis of RA (77.1%) and peripheral PsA were enrolled from the outpatient clinics in six centres in Croatia. Median age was 61 (79-97) years, and the median of disease duration was 120 (3-528) months. Data were collected at baseline (T0) including retrospective data collection from the previous 3 months (on P.O. MTX), at day 90 (±10 days) (T1) and at day 180 (±10 days) (T2) for the previous periods, both of them during S.C. MTX treatment. Dose of MTX remained stable during the study. Domains of interest were Disease Activity Score on 28 joints measured using ESR (DAS28-ESR), level of pain, Patient’s Global Health Assessment (PGHHA) and Physician’s Global Health Assessment (PGHGA) were measured on horizontal 100 mm VAS, while physical function was measured by Health Assessment Questionnaire – Disability Index (HAQ-DI).

**Results:** Out of 48 patients 41 patients were switched to S.C. MTX monotherapy and 7 to S.C. MTX in combination with another csDMARD. At T1 40 patients were on S.C. MTX monotherapy and 8 on S.C. MTX in combination with another DMARD, and at T2 39 patients were on S.C. MTX monotherapy, 4 on S.C. MTX in combination with another DMARD, 1 on another DMARD and 4 were lost to follow-up. DAS28 showed trend of decrease from 4.9 at baseline to 4.6 at T1 and 4.2 at T2. Analysis of transition of patients according to DAS28 EULAR criteria has shown that percentage of patients with low disease activity has raised from 4.3% at T0 to 21.7% at T1, and 24.3% at T2, while percentage of patients with high disease activity has declined from 98.3% at T0 to 21.7% at T1 and 13.5% at T2. Recommendation for prednisone therapy > 7.5 mg/ QD had 12.5% patients at T0 and T1, and only 6.8% patients at T2. There was a significant decrease in adjusted mean values for level of pain (<1.46; 95% CI <1.55, <0.30; PGHHA <1.12; 95%CI <1.50, <0.73) and PhGHA (-1.15; 95%CI -1.50, -0.80). HAQ-DI showed significant improvement during the 6-month follow-up (0.25; 95% CI -0.32, -0.17).

**Conclusion:** Patients who switched from P.O. to S.C. MTX showed improvement in all observed parameters: decrease of disease activity, reduction of pain, better global health, and physical function. Results of our study are in line with previously published literature data.

**Disclosure of Interests:** None declared

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**AB0424**

**A RETROSPECTIVE STUDY OF ARTHROSCOPIC SYNOVECTOMY FOR REFRACTORY KNEE ARTHRITIS COMPLICATED WITH POPLITEAL CYST**

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**Background:** Baker’s cyst or popliteal cyst is the most common mass surrounding the knee joint that results from inflammatory knee arthritis. With increasing number of arthroscopic synovectomy performed for refractory knee arthritis annually, we aim to explore its value in baker’s cyst treatment.(1)

**Objectives:** To investigate the efficacy of arthroscopic synovectomy on refractory knee arthritis complicated with popliteal cyst.

**Methods:** A retrospective analysis of 153 patients (RA= 95, SpA= 58) with refractory knee arthritis, underwent knee arthroscopic synovectomy in our hospital from 2010 to 2017, was performed. Among them, 20 patients (RA= 16, SpA= 4) complicated with popliteal cyst. We compared the changes in inflammation markers, disease activity score, imaging manifestations, symptoms, the rate and the grading of popliteal cyst before and after the operation to evaluate the efficacy of knee arthroscopic synovectomy.(1)

**Results:** Inflammation markers [ESR(49.42±32.54 vs 24.46±24.17, P<0.001), CRP(8.55±11.63 vs 5.60±22.45, P<0.001)], Rheumatoid Factor[191.29±373.72 vs 74.90±158.31, P<0.001], DAS28 score(4.67±1.25 vs 2.81±1.23, P<0.001), knee joint discomfort score(5.2±1.7 vs 1.9±1.5, P<0.001) and the amount of knee joint effusion by ultrasound scanning (P<0.05) in 95 RA patients were significantly decreased compared to those before the operation; Inflammation markers[ESR(36.76±28.71 vs 21.19±9.79, P<0.001), CRP(21.9±9.79 vs 3.36±0.44, P=0.001), knee joint discomfort score(4.48±1.16 vs 2.51±1.54, P<0.05), back pain VAS score(2.74±2.88 vs 1.56±1.70, P<0.001), and the amount of knee joint effusion by ultrasound scanning.
scanning (P<0.001) in 58 SpA patients were significantly lower than those before the operation; the rate (16.84% vs 6.32%, P<0.023) and grading (P=0.007) of popliteal cyst in RA were decreased after the operation; No statistically difference was observed in the rate(6.90% vs 5.17%), (P=0.697) of popliteal cyst in SpA, but the grading were all decreased in 4 patients.

Conclusion: This study provide evidence that knee arthroscopic synovec-
tomy has a good effect for refractory knee arthritis, which can reduce disease activity, improve joint symptoms and decrease the grading of popliteal cyst.

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Disclosure of Interests: None declared

AB0425 CONVERSE RELATIONSHIP OF URIC ACID AND VITAMIN D3 IN ADULT BAHRAINI PATIENTS WITH RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The relationship between serum levels of uric acid (UA) and serum vitamin D3 (25(OH)D) in rheumatoid arthritis (RA) and sys-
temic lupus erythematosus (SLE) has been revealed separately. However, a possible link between these two factors in RA in comparison to SLE has not been clarified yet. This is the first study investigating the joint association between 25(OH)D and UA in two related rheumatic diseases in Bahrain.

Objectives: We aimed to evaluate the possible correlation between serum UA and serum 25(OH)D in adult Bahraini patients with RA and SLE and to examine if there are any differences or similarities between these two patient’s groups.

Methods: Eighty adult Bahraini patients (RA=30 and SLE=50) were included in this longitudinal study (two-time points). The mean age of the patients was 45.21 years (range 16-77 years, SD=14.82). Females were 70 (87.5%). Only data for serum UA taken at the same time with vitamin D3 before and after vitamin D3 therapy were collected retrospectively from the patients’ records at Salmaniya Medical Complex, Bahrain. The patients received oral vitamin D therapy at a dose of 50,000 IU weekly for 3 months.

Results: Our results showed that in our studied group the mean serum level of 25(OH)D was significantly increased from 48.17 at baseline to 78.87nmol/l after therapy with an increment of 30.71 (P<0.0001). Conversely, the mean serum level of UA in our cohort was significantly decreased from 333.28 at baseline to 304.67nmol/l after therapy (P<0.001). When segregated the group by disease: The mean serum level of 25(OH)D was significantly increased in SLE from 38.39 at base line to 72.41 nmol/l after therapy (P<0.000), similarly in RA patients 25 (OH)D was significantly increased from 61.67 at baseline to 87.03nmol/l after therapy (P=0.002). In SLE serum UA decreased after vitamin D3 therapy, but the difference was not significant, while in RA the mean serum UA was significantly decreased from 308.83 to 282.03 after ther-

ABSTRACT

AB0426 COMPARISON OF INFLUENCES OF DIFFERENT CONCOMITANT DRUGS IN RHEUMATOID ARTHRITIS PATIENTS TREATED WITH IGURATIMOD, A CONVENTIONAL SYNTHETIC DISEASE-MODIFYING ANTI-RHEUMATIC DRUG DEVELOPED IN JAPAN, IN REAL-WORLD CLINICAL SETTING

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Background: Iguratimod (IGU) is csDMARDs developed in Japan and used in Japanese daily practice since 2012. Although IGU was developed as an anti-inflammatory drug at first, anti-rheumatic effect was found in experiments using type II collagen-induced arthritis model mice 1). Main mode of action of IGU was thought to be inhibition of NF-kB resulted in decreased production of IL-6, IL-8 and TNF-alpha 2). Clinical trials performed in Japan showed that efficacy of IGU was equal to sulfasalazine when used as monotherapy in patients with RA 3). Additive efficacy to MTX was also shown in double-blind randomised trial in RA patients 4). We reported efficacy of IGU in daily clinical practice in EULAR 2017 5). IGU is prescribed as monotherapy or concomitantly with other DMARDs such as MTX, csDMARDs other than MTX or biological DMARDs.

Objectives: Influences of different concomitant drugs were compared in RA patients treated with IGU in this retrospective study.

Methods: 178 RA patients treated with IGU in our institute from April 2013 to June 2017 were included. Patients were divided into four groups.

(1) Group in which IGU was started as monotherapy (MONO-G: n=59).
(2) Group in which IGU was added onto MTX treatment without bDMARDs (MTX-G: n=81).
(3) Group in which IGU was added onto csDMARDs treatment other than MTX (sulfasalazine, tacrolimus, bucila-

Disclosure of Interests: None declared
Results: Baseline characteristics was as below. Mean age was 71.4 years old (yo) in MONO-G, 58.3 yo in MTX-G, 70.1 yo in CSD-G, and 58.7 yo in BIO-G. RA duration was 10.2 years in MONO-G, 8.9 years in MTX-G, 11.2 years in CSD-G, and 15.1 years in BIO-G. SDAI at initiation of IGU was 14.2 in MONO-G, 12.8 in MTX-G, 21.3 in CSD-G, and 18.4 in BIO-G. SDAI was significantly improved over time in all four groups (Fig. 1). There were no significant differences in ΔSDAI from baseline to 1 year between groups by one-way ANOVA (Bonferroni).

Continuation rates of IGU at one year and three years were 66.6% and 21.2% in MONO-G, 77.8% and 57.1% in MTX-G, 69.2% and 39.7% in CSD-G and 75.0% and 75.0% in BIO-G. Continuation rate in MTX-G was significantly favorable compared with that in MONO-G and CSD-G by Log-rank test (Fig. 2). Most frequent reason for stopping IGU was liver damage (10 cases). Second frequent reason was intermittent pneumonia in 4 cases.

Conclusion: IGU seemed to be the most tolerant in MTX-G and the second most tolerant in BIO-G. Although higher aged population who might have several comorbidities was included in MONO-G and CSD-G, moderate efficacy of IGU was seen in those groups. Although biological DMARDs is effective in RA patients, the cost is very expensive. IGU is comparative cheap (¥9,200/month) and suitable for RA patients with economic difficulties. As IGU decreased TNF-alpha production via inhibition of NF-kB, MTX+IGU may have similar mode of action with MTX+TNF inhibitor. Although small cases were included in BIO-G, Continuation rate of IGU in BIO-G was good.

Disclosure of Interests: None declared


AB0427 DIFFERENCES IN DRUG USAGE BETWEEN EORA AND YORA PATIENTS WITH TARGET OF LOW DISEASE ACTIVITY

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Background: Along with the present aging population, development of new therapies such as biological disease-modifying anti-rheumatic drugs for rheumatoid arthritis (RA) has resulted in an increasing number of elderly patients with RA seeking treatment. Furthermore, the onset age of RA has been reported to be trending higher. Elderly onset RA (EORA) is defined as that which develops after 60 years of age, and shown to differ from young onset rheumatoid arthritis (YORA) in regard to background and drug treatment.1 Although many EORA cases have acute onset, cases with polymyalgia rheumatica (PMR)-like symptoms and negative for rheumatoid factor (RF) have recently been observed at a relatively high rate.2 In fact, we have found it occasionally difficult to distinguish between EORA and PMR in clinical settings. For both EORA and YORA patients, treat-to-target (T2T) is necessary, though it is considered that EORA should be treated with the goal of acquiring low disease activity (LDA) from the viewpoint of side-effects of administered therapeutic drugs.

Objectives: In this study, we examined the number of drugs given to EORA and YORA patients treated for RA at our hospital who achieved LDA.

Methods: We enrolled 260 patients into the EORA (n=70) and YORA (n=190) groups, and investigated background and treatment protocols.

Results: As for background, there was a significant difference between the EORA and YORA groups for mean age, mean disease duration, and female ratio, whereas the difference was not significant in regard to antibody positive rate, SDAI, or DAS28-CRP. In those groups, average age was 73.8 and 57.8 years, disease duration was 6.66 and 14.7 years, and female ratio was 62.9% and 83.7%, respectively. RF positivity was 85.3% and 80.7%, and ACPA positivity was 86.5% and 87.7%, respectively, while SDAI was 4.28 and 4.59, and DAS28-CRP was 1.99 and 2.04, respectively (Table 1). As for treatments given to the patients, the rates of prednisolone (PSL) use (37.1% vs. 36.3%), and dosage of methotrexate (MTX) (1.45 vs. 1.41 mg) and its usage rate (55.7% vs. 65.3%) were not significantly different between the groups. On the other hand, MTX weekly administration (2.89 vs. 4.09 mg, p=0.009) and biologics usage rate (32.9% vs. 56.3%, p=0.0012) were significantly lower in the EORA group (Table 2).

Conclusion: Age of onset of RA has been increasing with the aging of society. Therefore, it is important to consider the features of EORA and YORA when considering therapy. For the present investigation, we considered the goal of treatment to be acquisition of LDA rather than
remission, and our findings indicate that EORA patients may be better able to achieve that goal with lower MTX dosage and biological product usage as compared to YORA patients. In addition, EORA patients might achieve LDA with a lower amount of drugs.

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Disclosure of Interests: None declared

PATEIENT-PHYSICIAN INTERACTION AS A PREDICTOR OF METHOTREXATE ADHERENCE IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Recent years have seen numerous encouraging developments in the treatment of patients with rheumatoid arthritis (RA) with significant improvement in disease control. However, methotrexate (MTX) remains a cornerstone therapy and first-line drug for majority of patients with RA, commonly associated with prolonged or even lifelong treatment, which takes the risk for decreasing medication adherence over time. Therefore, prompt recognition of predictive factors for MTX non-adherence is one of the most important challenges related to treatment of patients with RA.

Objectives: The aims of this study were to assess patients’ self-reported adherence to MTX, as well as to investigate predictive role of physician-patient interaction satisfaction for MTX adherence. Namely, it could be hypothesized that patients’ perceptions of multiple specific components of relationship with their physician are associated with patient trust in their physician, which is strongly related to treatment adherence.

Methods: In the period between May 1 and September 15, 2018, 98 consecutive RA patients who were treated in Clinical center of Montenegro and private clinic “Merkur Nera” were enrolled in this multi-centric cross-sectional study. Non-adherence to MTX was defined as >1 dose missed against medical advice. Patients field in the questionnaire consisted of MTX-specific queries, including the questions related to therapy-related communication with their physician. Possible interaction of the investigated confounders and their joint effect on the MTX adherence were analyzed using ordered logistic regression analysis. A multivariate logistic regression analysis was performed including all covariates that appeared to be associated with the endpoint in the univariate models (p<0.1). Odds ratio was used to express the strength of the association between independent predictors and MTX non-adherence as a dependent variable.

Results: Study population was predominantly female (87.8%), and the average age was 56,4±12,1 years. The median duration of RA was 8 years (range 0-34 years), while the median duration of MTX treatment was 6 years (range 0-26 years). The median current dose of MTX which responders received was 15 mg per week. The overall prevalence of non-adherence to MTX was 32.7%. According to the results of univariate regression analysis the following factors are significantly associated with adherence to MTX: younger age (OR=0.942; p=0.005), employment (OR=0.955; p=0.095), working capacity (OR=0.342; p=0.057), marital status (OR=0.342; p<0.001) and expressed need for more communication with the doctor regarding RA treatment (OR=1.303 p=0.044). Namely, married RA patients were 2.46 times less likely to MTX non-adherence compared to others, while the patients who stated the need for more communication with the doctor regarding RA treatment has 1.30 times greater chances to MTX non-adherence.

Conclusion: The results of our study have shown that about one third of RA patients met the criteria for non-adherence to MTX. Identification of the patient’s need for more communication related to RA therapy as independent predictor for MTX non-adherence suggests that physician-patient relationship quality is an important point of intervention for efforts to improve patients’ medication adherence.

Disclosure of Interests: None declared

THE EFFICACY OF TOFACITINIB TREATMENT IN RHEUMATOID ARTHRITIS PATIENTS WITH HIGH DISEASE ACTIVITY IN REAL-WORLD PRACTICE

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Background: JAK-kinase inhibitors are the promising option for patients with severe rheumatoid arthritis (RA). Evaluation of the effectiveness and results of long-term use of tofacitinib (TOFA) seems relevant for clinical practice.

Objectives: To evaluate the efficacy of TOFA in achievement of remission or low disease activity (LDA) in RA patients after 12 months of treatment and follow-up in real-world practice.

Methods: In this open study 30 patients (22 women and 8 men) with severe RA (average DAS28=5.8) with inadequate response to methotrexate in effective dose were enrolled and started TOFA 5 mg BID. Average age was 57 (29-71), average disease history 6,2 (1,5-12,5) years. Patients evaluated at baseline, after3, 6 and 12 months of treatment: number of painful and swollen joints, ESR, CRP, RF, anti-MCV, DAS28, SDAI. The joints ultrasound (US) with Power Doppler (PD) (German US7 score) helped to estimate synovial inflammation. After 12 months of treatment the patients were under follow-up in real-world practice.

Results: By 3th month of treatment the average mean of ESR and CRP returned to normal range, the number of painful and swollen joints decreased to 2 times, DAS28 - from 5.8 to 3.8, SDAI – from 41,0 to 18,0. 6 patients achieved remission, 3 – LDA, 2 had high activity (DAS28=5,1) and the rest – moderate activity. We achieve the aim of T2T strategy by 12th month: average ESR and CRP normalized, DAS28 – 2,92 (1,39; 6,21) and SDAI – 7,0 (1,57; 36,4), 33% of patients achieved remission according to DAS28 and SDAI. RF decreased by 37%, anti-MCV stayed high during the year. There was temporary increase of AST, ALT in 4 patients (13,3%), but did not require TOFA discontinuation. By 12th month of treatment the PDUS mode number of joints with hypervascularized synovium decreased from 3 (2; 7) to 0 (0; 1), number of bone erosions has not changed. 1 patient (3,3%) had severe herpes zoster infection, no other infections occurred. In 1 patient (3,3%) TOFA showed no efficacy (DAS28=6,21).

22 patients have finished 12-months course of TOFA at the moment and moved to follow-up period. 13 of them (59%) continue the same dose of TOFA: 8 have remission and 5 – LDA, 2 patients continued TOFA 5 mg/day for 1 year, then stopped and are in remission for 8 months. 1 patient had temporary withdrawal of treatment due to surgery without exacerbation of RA. 4 patients have stopped TOFA for non-medical reasons: 1 is still in remission and 1 – LDA for 12 months, 2 had worsening of RA and treated by low doses of glucocorticoids. At the moment 3 patients (13,6%) have long-term remission for 18 months after the end of TOFA treatment.

Conclusion: TOFA is effective and safe treatment option for severe RA in real-world practice. The effect develops by 3 months and continues to grow to 12 months. When remission is achieved, we recommend a reduced dose before withdrawal. Exacerbation of RA is effective solved by retreatment with TOFA.

Disclosure of Interests: None declared
AB0430 DEVELOP A REPLICABLE MODEL FOR RATIONAL SELECTION OF STRATEGIES IN TREAT-TO-TARGET: REAL WORLD DATA MINING VIA SMART SYSTEM OF DISEASE MANAGEMENT (SSDM)

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Background: Daily health care in the real world is different from a clinical trial setting, which deals with a wide spectrum of RA patients from statuses of remission to disease activities at mild, moderate and severe based on DAS28. Due to lack of information and knowledge about optimal regimens for both treat-to-target (T2T) and maintain-being-target (MbT), physicians make choices on treatment strategies based on their own experience or intuition.

Objectives: To develop a replicable model for rationalizing the strategies for T2T and MbT using data mining via smart system of disease management (SSDM).

Methods: SSDM is an interactive mobile disease management tool, including two application systems (APPS) for both the doctors and the patients. The patients can input medical records (including medication and laboratory test results) and perform self-evaluation (DAS28, HAQ) via APP. The doctors can get real-time and personalized advices through cloud and advices could be delivered. In previous studies, we demonstrated that patients could master SSDM after training.

Up to January of 2019, totally 106,647 patients with rheumatic diseases using SSDM, among them, 38% are RA patients who receive more than 1,400 different regimens of treatments. Here we select MTX, Hydroxychloroquine (HCQ) and prednisone (GS) based therapies for model development.

Results: Totally 1571 patients were treated with MTX (640), HCQ (397), GS (131), MTX+HCQ (253), MTX+GS (47), HCQ+GS (61), MTX+HCQ+GS (42), respectively. Among the patients whose DAS28<3.2 at baseline, 72% with MTX, 75% with HCQ, 76% with MTX+HCQ and 73% with MTX+HCQ+GS are MbT (DAS28<3.2) after 6 months, which are significantly different comparing with those 52% with GS, 57% with MTX+GS and 57% with HCQ+GS (p<0.01). Among the patients whose DAS28>5.1 at baseline, 81% with GS, 72% with MTX+HCQ and 100% with HCQ+GS achieved T2T (DAS28<3.2) after 6 months, which is significantly different compared to 25% with MTX, 24% with HCQ, 45% with MTX+HCQ and 37% with MTX+HCQ+GS (p<0.01). Among the patients whose DAS28>5.1 at baseline, there is no statistic significant differences for the rates of achieving T2T, which rates ranging from 39% to 50% across all the 7 regiments.

Conclusion: With MTX, HCQ and GS based regimens in RA, the rational selections of strategies for MbT are mono therapy with MTX, HCQ, or MTX+HCQ, strategies for T2T on high disease activity group are GS, GS+MTX or GS+HCQ. In view of 1400 regimens with clinical outcomes being available in SSDM, the model developments can be replicated in rationalizing strategies through data mining.

Disclosure of Interests: None declared


REFERENCES


AB0431 EFFECTS OF LOW-LOAD RESISTANCE EXERCISE OF LOW EXTREMITY WITH RHEUMATOID ARTHRITIS

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Background: Some skeletal muscles communicate with other organ by secreting proteins and peptides called myokine. Some myokines have anti-inflammatory effect. As regards rheumatoid arthritis (RA), many studies have shown that aerobic and resistance exercise programs do not change the number of inflammatory joints and RA disease activity, whereas other studies showed improved the marker. And almost studies were performed by high-load resistance training protocols. Meanwhile lately Schoenfeld showed that muscle hypertrophy can be equally achieved across a spectrum of load ranges with meta-analysis.

Objectives: To investigate the efficacy of low-load resistance exercise of low extremity protocol on RA.

Methods: Twenty-four patients with RA were enrolled. Inclusion criteria were receipt of a stable dose of biologics, JAK inhibitor, and conventional DMARDs more than 3months prior to the first exercise, and corticosteroid and NSAIDs more than one month prior to the first exercise. The exercise circuits consisted of 6 different low extremity exercises intended to improve arthritis. Within the exercise circuits, each exercise were repeated 8-12 times and less than 50% of the 1-repetition maximum. The exercise circuits were performed 3 times a week. Disease activity parameters and infused joint of upper extremity and lower extremity were collected at base line and 2 months after exercise started. The Wilcoxon signed-rank test was used to examine the difference between the parameter of the base line and the 2 months.

Results: All patients were female. Mean age was 68.7 years., and mean disease duration 15.3 years. Seven patients (29%) used methotrexate, 5 patients (21%) used prednisolone and 13 patients (54%) used biologics. Mean ESR was 3.98 at base line and 3.58 at 2 months, mean DAS28(CRP) 3.46 and 3.06, mean SDAI 15.4 and 12.5, and mean CDAI 4.5 and 3.7. Mean DAS28(ESR) was 3.98 at base line and 3.58 at 2 months, mean DAS28(CRP) 3.46 and 3.06, mean SDAI 15.4 and 12.5, and mean CDAI 4.5 and 3.7, mean upper extremity joint tenderness 4.0 and 2.2, mean lower extremity joint tenderness 4.0 and 2.2, mean lower extremity joint swelling 1.6 and 1.8, mean lower extremity joint swelling 4.0 and 2.0 respectively. Every index except upper extremity joint swelling improved significantly (p<0.05) at 2 months than baseline.

Conclusion: Low intensity exercise of low extremity was efficacious against not only lower extremity arthritis but also upper extremity joint arthritis in patients with rheumatoid arthritis.
Disclosure of Interests: Andrew Ostor Consultant for: AbbVie, BMS, Roche, Janssen, Lilly, Novartis. Pfizer, UCB, Gilead, Paradigm, Ruth Sawant Shareholder of: AbbVie, Employee of: AbbVie, Alisha Gadhia Employee of: Covance Market Access & Phase IV Solutions, which has received consultancy fees from AbbVie. Vishvas Garg Shareholder of: AbbVie, Employee of: AbbVie, Matthew Wallace Employee of: Covance Market Access & Phase IV Solutions, which has received consultancy fees from AbbVie.


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AB0432 BURDEN OF ILLNESS AND CURRENT UNMET NEEDS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH CONVENTIONAL AND ADVANCED DISEASE-MODIFYING THERAPIES: A TARGETED LITERATURE REVIEW

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Background: The development of advanced therapies for the treatment of moderate to severe rheumatoid arthritis (RA) has changed the paradigm of management goals for the condition. However, even with currently available therapies, many patients fail to achieve adequate improvement or disease remission, and thus residual unmet needs exist.

Objectives: To examine the burden of RA with respect to the clinical, humanistic, and economic outcomes associated with RA patients treated with conventional and advanced disease-modifying therapies.

Methods: A targeted review of the literature published between January 2013 and September 2016 was conducted. EMBASE and MEDLINE databases were searched using terms related to the clinical, humanistic, and economic outcomes associated with conventional and advanced disease-modifying therapies currently available for moderate to severe RA. The search was limited to English-language articles, which reported data from France, Germany, Italy, Spain, United Kingdom, Sweden, Israel, Canada, Brazil, Japan, and Australia. This returned 1,833 records which were assessed for relevance in terms of study methodology, patient population, and outcomes.

Results: A total of 48 articles were included in the qualitative synthesis. Across these studies, disease activity score (DAS) remission rates (DAS28 ≤2.6) ranged from 14.7% to 26.4% over 6–12 months and 10.2% to 53.4% over 3–20 months for patients treated with conventional synthetic disease-modifying antirheumatic drug (csDMARD) monotherapies and biologic monotherapies, respectively. Figure 1 presents country-specific DAS28 remission rates for some of the included regions. Clinical disease activity index (CDAI) remission rates (CDAI ≤2.8) were reported to be ≤50% among patients who received biologics for a period of up to 12 months. The unemployment rate due to RA was as high as 58.3%, and employed patients lost 1.7 to 16.0 workdays per month at baseline. Following treatment with biologic therapies (over 24–104 weeks), employed patients lost 0.5 to 8.0 working days per month. Costs of treatment with advanced therapies were routinely investigated, but limited data were available regarding the economic burden associated with outcomes such as disability, depression, lack of sleep, and anxiety among RA patients treated with advanced therapies.

Conclusion: Despite advanced treatments, a significant proportion of the RA patient population do not achieve disease remission, and face the substantial burden of reduced productivity and lost work days.

Acknowledgement: The design, study conduct, and financial support for the study were provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of this publication.

AB0433 TREATMENT PATTERNS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS WHO RECEIVE METHOTREXATE: TARGETED LITERATURE REVIEW

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Background: Methotrexate (MTX) monotherapy or in combination with other disease modifying agents is a common first-line treatment option for patients with rheumatoid arthritis (RA). However, treatment patterns and associated patients’ perceptions and preferences of MTX therapy may not be fully understood.

Objectives: To assess treatment patterns of MTX therapy in RA by evaluating real-world adherence and persistence, patients’ preferences and reasons for discontinuation, as well as the economic burden of therapy.

Methods: A targeted review of the literature published between January 2010 and March 2018 was conducted by searching the MEDLINE and EMBASE databases. Searches were limited to English-language articles and included original research and reviews. All articles were assessed for relevance, in terms of study methodology, patient population and outcomes by a single reviewer.

Results: The search resulted in 444 hits of which 29 articles were included in the qualitative synthesis. Data pertaining to adherence and patient-reported reasons for non-adherence were extracted from 11 publications. MTX therapy non-adherence was high, with up to 42% of patients reporting not taking MTX as prescribed. Among these patients, many reported taking smaller doses than prescribed (53%) or intentionally skipping doses (52%). Common patient-reported reasons for non-adherence included upcoming surgery, and experience of, or concerns regarding adverse events (AEs). Data pertaining to therapy discontinuation were extracted from 21 publications. Across the studies sampled, rates of discontinuation at one year were 24–50%. MTX toxicity was responsible for 5–34% of all discontinuations. Among patients who switched from orally to parenterally administered MTX, 29% discontinued due to gastrointestinal AEs within one year. Patient-reported reasons for therapy discontinuation, other than experiencing AEs, included concerns regarding MTX AEs, drug price and lack of perceived need. No studies examining the costs associated with MTX monotherapy monitoring and AE management were identified in the search.

Conclusion: Findings from the review indicated that MTX therapy is associated with substantial non-adherence and discontinuation, thus adding to patient burden. Patient-reported reasons for non-adherence/poor treatment persistence were varied but most commonly included experience of, or concerns regarding AEs.

Acknowledgement: The design, study conduct, and financial support for the study were provided by AbbVie. AbbVie participated in the interpretation of data, review, and approval of this publication.

Disclosure of Interests: Andrew Ostor Consultant for: AbbVie, BMS, Roche, Janssen, Lilly, Novartis. Pfizer, UCB, Gilead, Paradigm, Matthew Wallace Employee of: Covance Market Access & Phase IV Solutions, which has received consultancy fees from AbbVie. Ruth Zeidman Employee of: Covance Market Access & Phase IV Solutions, which has received consultancy fees from AbbVie. Vishvas Garg Employee of: AbbVie, Ruta Sawant Shareholder of: AbbVie, Employee of: AbbVie


Disclosure of Interests: None declared

AB0433 BURDEN OF ILLNESS AND CURRENT UNMET NEEDS AMONG PATIENTS WITH RHEUMATOID ARTHRITIS TREATED WITH CONVENTIONAL AND ADVANCED DISEASE-MODIFYING THERAPIES: A TARGETED LITERATURE REVIEW

Andrew Ostor1, Ruta Sawant2, Alisha Gadhia3, Ruth Zeidman3, Vishvas Garg2, Matthew Wallace1, 1Cabrini Medical Centre, Monash University, Melbourne, Australia; 2AbbVie Inc., North Chicago, United States of America; 3Covance Market Access and Phase IV Solutions, London, United Kingdom

Background: The development of advanced therapies for the treatment of moderate to severe rheumatoid arthritis (RA) has changed the paradigm of management goals for the condition. However, even with currently available therapies, many patients fail to achieve adequate improvement or disease remission, and thus residual unmet needs exist.

Objectives: To examine the burden of RA with respect to the clinical, humanistic, and economic outcomes associated with RA patients treated with conventional and advanced disease-modifying therapies.

Methods: A targeted review of the literature published between January 2013 and September 2016 was conducted. EMBASE and MEDLINE databases were searched using terms related to the clinical, humanistic, and economic outcomes associated with conventional and advanced disease-modifying therapies currently available for moderate to severe RA. The search was limited to English-language articles, which reported data from France, Germany, Italy, Spain, United Kingdom, Sweden, Israel, Canada, Brazil, Japan, and Australia. This returned 1,833 records which were assessed for relevance in terms of study methodology, patient population, and outcomes.

Results: A total of 48 articles were included in the qualitative synthesis. Across these studies, disease activity score (DAS) remission rates (DAS28 ≤2.6) ranged from 14.7% to 26.4% over 6–12 months and 10.2% to 53.4% over 3–20 months for patients treated with conventional synthetic disease-modifying antirheumatic drug (csDMARD) monotherapies and biologic monotherapies, respectively. Figure 1 presents country-specific DAS28 remission rates for some of the included regions. Clinical disease activity index (CDAI) remission rates (CDAI ≤2.8) were reported to be ≤50% among patients who received biologics for a period of up to 12 months. The unemployment rate due to RA was as high as 58.3%, and employed patients lost 1.7 to 16.0 workdays per month at baseline. Following treatment with biologic therapies (over 24–104 weeks), employed patients lost 0.5 to 8.0 working days per month. Costs of treatment with advanced therapies were routinely investigated, but limited data were available regarding the economic burden associated with outcomes such as disability, depression, lack of sleep, and anxiety among RA patients treated with advanced therapies.

Conclusion: Despite advanced treatments, a significant proportion of the RA patient population do not achieve disease remission, and face the substantial burden of reduced productivity and lost work days.

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AB0434 EARLY EXPERIENCE WITH JAK INHIBITOR PREScribing IN THE UK: RESULTS FROM THE BRITISH SOCIETY FOR RHEUMATOLOGY BIOLOGICs REGISTER FOR RHEUMATOID ARTHRITIS (BSRBR-RA)

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Background: In 2017 a new class of oral disease modifying anti-rheumatic drugs (DMARDs), Janus kinase inhibitors (JAKi), were licensed for rheumatoid arthritis (RA): baricitinib and tofacitinib. In the UK, they are approved for use in patients with high disease activity with or without methotrexate, following failure of conventional synthetic (cs) DMARDs or biologic DMARDs, the latter when rituximab is contraindicated. As a new therapy option, it is currently unclear how and when these drugs are being prescribed in patients with RA.

Objectives: This analysis aims to describe the characteristics of patients starting JAKi and registered with the BSRBR-RA.

Methods: The BSRBR-RA aims to capture exposure and outcome data in patients with RA receiving biologics, biosimilars and targeted synthetic DMARDs. At the start of therapy, demographic and clinical data, including past treatment data, are collected. Characteristics of all patients receiving a JAKi for the first time with data recorded in the BSRBR-RA up to 30/11/2018 are described.

Results: To 30/11/2018, 443 patients in the BSRBR-RA have been treated with a JAKi; 374 patients baricitinib and 69 tofacitinib (Table). Twenty-eight percent of baricitinib and 13% of tofacitinib patients received a JAKi following csDMARDs, with no prior biologic exposure. Of these, 15% had a prior malignancy history. Of those with prior exposure, the median number of previous biologics was 3 (IQR 2-4) and 52% had received rituximab. Forty-three percent were receiving concurrent methotrexate.

Conclusion: To date, more patients have been recruited starting baricitinib than tofacitinib, likely owing to the later licensing of tofacitinib. Two groups are emerging with a quarter of patients receiving JAKi immediately after csDMARDs and a majority as a later stage alternative following multiple biologics. Further recruitment and follow-up patients will allow for analysis of real-world safety and effectiveness, but differences in patient characteristics will need to be considered in any comparative effectiveness analyses.

| Characteristics of the first 443 patients in the BSRBR-RA treated with JAKi |
|---------------------------------------------------|-----------------|------------------|-----------------|
| Ever exposed [N = 443] | No biologic exposure [N = 112] | Previous biologic exposure [N = 331] |
| Baricitinib | 374 (84%) | 103 (28%) | 271 (72%) |
| Tofacitinib | 69 (16%) | 9 (13%) | 60 (17%) |
| Age (years) | 61 (53 to 69) | 61 (51 to 71) | 61 (53 to 69) |
| Female | 323 (75%) | 81 (72%) | 254 (77%) |
| Disease duration (years) | 12 (6 to 21) | 6 (3 to 15) | 14 (8 to 22) |
| Number of previous biologics | 112 (25%) | 112 (100%) | 0 (6%) |
| No prior biologics | 63 (14%) | 63 (19%) | |
| ≥2 prior biologics | 211 (48%) | 211 (64%) | |
| Unknown | 57 (13%) | 57 (17%) | |
| Type of previous biologic exposure | - | - | |
| TNF inhibitor | - | - | 248 (91%) |
| Rituximab | - | - | 143 (53%) |
| Abatacept | - | - | 95 (35%) |
| Tocilizumab | - | - | 139 (51%) |
| Concurrent Methotrexate | 185 (43%) | 51 (44%) | 134 (42%) |
| Concurrent oral steroids | 133 (31%) | 22 (21%) | 111 (34%) |
| DMARDs* | | | |
| None | 170 (38%) | 58 (52%) | 112 (34%) |
| 1 comorbidity | 125 (28%) | 25 (22%) | 100 (30%) |
| 2+ comorbidities | 148 (34%) | 29 (26%) | 119 (36%) |
| Prior Cancer | 38 (9%) | 15 (15%) | 23 (7%) |
| Pulmonary Fibrosis | 11 (4%) | 3 (3%) | 8 (4%) |

With regards to the previous treatments received, we obtained the following results:

- **Previous DMARDs**:
  - 3TB: 2TB 1TB Naive 5 3 10 12 10 2 3 1 2 Naive 9 15 2 2

- **Previous DMARDs**:
  - 3TB: 2TB 1TB Naive 5 3 10 12 10 2 3 1 2 Naive 9 15 2 2

With regards to efficacy, there were collected 6 treatment withdrawals: 1 primary treatment failure (in Tofacitinib Group) and 5 secondary treatment failures (1 in Baricitinib Group and 4 in Tofacitinib Group) and the mean treatment duration was 152 days.

**Conclusion**: Despite the study population was small and the follow-up time was short, we highlight in our patients that both JAK inhibitor alternatives have shown a security and efficacy profile similar to the results shown in pivotal clinical trials. Despite the previous biological treatment failure and obesity are considered as predictors of bad response to treatment, in our cohort did not represent a high risk to treatment failure, it can be an alternative in the same scenario.

**Disclosure of Interests**: Isabel de la Morena Speakers bureau: Abbvie, Celgene, Pfizer, UCB, Ghebro, Roche, Sanofi, Janssen., Juan Alberto Paz Solarte Employee of: He is working at UCB since December 2018, when the patient recruitment ended., Speakers bureau: Abbvie, Roche, Pfizer, Novartis, Celgene, Amgen, MSD, Janssen, Diego Bedoya: None declared, Pilar Trener Larraz: None declared


AB043S REAL WORLD DATA OF A PATIENT COHORT WITH RHEUMATOID ARTHRITIS TREATED WITH JAK/STAT INHIBITORS

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Background: We present the real World data of a patient cohort with rheumatoid arthritis (RA) that received one of the two JAK/STAT inhibitors approved by the EMA for this indication.

Objectives: To describe the Real World Data of a patient cohort attending Rheumatology consult of a reference hospital in Valencia with RA diagnosis and that were treated with JAK/STAT inhibitors.

Methods: A descriptive retrospective study was carried out. There were revised medical histories of 28 patients with a RA diagnosis that attended our consults between 2017 and 2018. All 28 patients were JAK/STAT treatment receivers of one of the two JAK/STAT inhibitors approved: Tofacitinib 10 mg oral QD or Baricitinib 4 mg oral QD. There were collected patient baseline demographic data: sex, age, BMI, activity disease score measured by DAS28-CRP and visual pain analogue scale for patient’s assessment (VAS). In addition, there were collected the previous synthetic(s) and biological(s) DMARD treatments, as well as the associated treatments. Efficacy and security were also analysed. There were assessed serum biochemical variables, among them acute phase reactants such as CRP and ESR

Results:

- **The study population consisted in 28 patients with the following distribution**:
  - M/F: Mean age (years) BMI (kg/m²): Baricitinib Tofacitinib DAS28/CRP (at de beginning) Mean treatment time (days)
  - 12 (42%) 58.39 30.12 9 19 4.81 230.11
  - 16 (58%) 50.73 30.31 14 28 5.21 250.32

DMARDs: Number of previous biological treatment

With regards to efficacy, there were collected 6 treatment withdrawals: 1 primary treatment failure (in Tofacitinib Group) and 5 secondary treatment failures (1 in Baricitinib Group and 4 in Tofacitinib Group) and the mean treatment duration was 152 days.

**Conclusion**: Despite the study population was small and the follow-up time was short, we highlight in our patients that both JAK inhibitor alternatives have shown a security and efficacy profile similar to the results shown in pivotal clinical trials. Despite the previous biological treatment failure and obesity are considered as predictors of bad response to treatment, in our cohort did not represent a high risk to treatment failure, it can be an alternative in the same scenario.

**Disclosure of Interests**: Isabel de la Morena Grant/research support from: Grants to institution: BMS, Pfizer, UCB, Mark Lunt: None declared

ADHERENCE TO DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS IN RHEUMATIC DISEASES

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Background: There has been seen a low adherence to treatment in patients with rheumatic diseases, which can have important consequences in disease prognosis. Although literature in Latin-American population is scarce, a previous study evaluating medication adherence in this population reported a 16.4% prevalence of adherence in Rheumatoid Arthritis (RA) and 45.9% in Systemic Lupus Erythematosus (SLE) patients (1). It has been demonstrated better outcomes in patients with rheumatic conditions who have good adherence to treatment therapies (2).

Objectives: To describe the adherence to synthetic Disease-Modifying Anti-Rheumatic Drugs (DMARDs) in patients with rheumatic diseases from a Mexican outpatient rheumatology clinic.

Methods: This study was conducted in the outpatient rheumatology clinic of University Hospital in Monterrey, Mexico, cross-sectional, descriptive, self-report adherence study. Consecutive patients with RA, SLE, Inflammatory Myopathies, Psoriatic arthritis (PsA), Systemic Sclerosis (SSc) were approached during their normal routine rheumatology appointments, in the March 2018 to December 2018 period. They were asked how many days of the last month they forgot or took their DMARDs. We classified the adherence rate in 4 categories based on the days of the last month it took the indicated medication; good: 75%-100% (> 21 days), regular 50-74% (21-15 days), bad 25-49% (14-8 days) and null: <25% (< 7 days).

When adherence was not good we interrogated about the cause. Data was obtained from REPAIR® (internal electronic patient record) and analyzed with the statistical package SPSS version 24.

Results: We included 31 patients with rheumatoid arthritis with a mean age of 57.58 ± 11.31 years and mean time of evolution of the disease of 9.42 ± 6.62 years, 61.3% female sex, 36.5% positive RF and 61.3% ACPA positive. The female sex represents 74.2% of the sample. The mean of the baseline DAS28 was 4.90 ± 0.95. Regarding the treatment analysis initiated 12 patients (38.7%) receive baricitinib and 19 (61.3%) tofacitinib. 93.5% were in treatment with steroids and/or DMARDs and 80.64% in treatment combined with at least 1 associated DMARD (75% baricitinib group, 84.2% tofacitib group). The subanalysis of concomitant treatment reveals that up to 31.5% of patients undergoing treatment with tofacitinib initiated treatment with ≥2 FAMEs. 61.3% of patients had previously received at least one biological drug, among which the antITNFs stand out for their frequency; 31.5% with one biological, 9.7% with 2 previous biologicals and 16.5% had used three. A total of 14 adverse effects were recorded in 10 of the 31 patients which are described below: baricitinib group a total of 6 events (50%); 1 toxic hepatitis, 1 respiratory infection, 2 cases of urinary tract infection, 1 case of canker sores, and 1 cold sore. Tofacitinib group a total of 8 events (42.1%); 2 cases of Herpes zoster, 1 case of headache and dizziness, 2 perianal abscesses and 1 access submandibular. There were 3 hospital admissions with independence of its relationship with the treatment analyzed; baricitinib group: 1 patient with upper respiratory tract infection and decompensated heart failure, 1 patient with toxic hepatitis. Tofacitinib group: 1 patient with post-traumatic humerus fracture.

Conclusion: Adherence in this group of patients was good, for the definition used in our study. The method used (self-report) is very sensitive to detect non-adherence, but it overestimate good adherence, therefore the potential bias of results must be considered and confirmed with objective measurement.

REFERENCES


SAFETY OF JAK INHIBITORS IN PATIENTS WITH RHEUMATOID ARTHRITIS IN CONDITIONS OF DAILY CLINICAL PRACTICE

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Background: Efficacy and safety of the new JAK inhibitors is supported by phase I, II and III studies with a large number of patients included in the follow-up, although it is of vital importance behavior of new molecules in routine clinical practice, and until now we still have few clinical data.

Objectives: To describe the adverse effects observed, as well as the economic Hospitals and description of them during treatment with JAK inhibitors in a series of patients with RA.

Methods: This is a retrospective descriptive study in patients with RA treated with JAK inhibitors in follow-up by the Rheumatology Unit of Virgen de Valme Hospital. We included demographic, related to the disease and treatment and security variables.

Results: We included 31 patients with rheumatoid arthritis with a mean age of 57.58 ± 11.31 years and mean time of evolution of the disease of 9.42 ± 6.62 years, 61.3% female sex, 36.5% positive RF and 61.3% ACPA positive. The female sex represents 74.2% of the sample. The mean of the baseline DAS28 was 4.90 ± 0.95. Regarding the treatment analysis initiated 12 patients (38.7%) receive baricitinib and 19 (61.3%) tofacitinib. 93.5% were in treatment with steroids and/or DMARDs and 80.64% in treatment combined with at least 1 associated DMARD (75% baricitinib group, 84.2% tofacitib group). The subanalysis of concomitant treatment reveals that up to 31.5% of patients undergoing treatment with tofacitinib initiated treatment with ≥2 FAMEs. 61.3% of patients had previously received at least one biological drug, among which the antITNFs stand out for their frequency; 31.5% with one biological, 9.7% with 2 previous biologicals and 16.5% had used three. A total of 14 adverse effects were recorded in 10 of the 31 patients which are described below: baricitinib group a total of 6 events (50%); 1 toxic hepatitis, 1 respiratory infection, 2 cases of urinary tract infection, 1 case of canker sores, and 1 cold sore. Tofacitinib group a total of 8 events (42.1%); 2 cases of Herpes zoster, 1 case of headache and dizziness, 2 perianal abscesses and 1 access submandibular. There were 3 hospital admissions with independence of its relationship with the treatment analyzed; baricitinib group: 1 patient with upper respiratory tract infection and decompensated heart failure, 1 patient with toxic hepatitis. Tofacitinib group: 1 patient with post-traumatic humerus fracture.

Conclusion: The main side effect observed was infection, in general mild-moderate that only motivated hospital admission in a patient in treatment with baricitinib due to decomposition of its pathology base. Stresses the development of uncomplicated perianal abscess in 2 patients on treatment with tofacitinib, one of them with perianal fistula known, and a recurrence of submental abscess in a patient with antecedent of repitition abscesses in said location. I only know observed elevated transaminases in a patient undergoing treatment with baricitinib showing in general an optimal hepatic safety profile. No primary cardiovascular events of interest have been recorded, neoplasms or other gastrointestinal events. Everything described, considering the high rate of concomitant treatment with steroids at low doses (93.5%) and up to 80.64% of patients in treatment with at least 1 concomitant DMARD.

REFERENCES

Disclosure of Interests: Natalia Cid Boza: None declared, ML Velloso Feijoo: None declared, NAHA PLAZA: None declared, Jose Luis Marenco: Speakers bureau; abbie, pfizer, novartis, janssen


AB0438 A STUDY COMPARING EFFICACY OF INTRA-ARTICULAR STEROID (IAS) VS INTRAARTICULAR SCLEROSANT IN PATIENTS WITH PERSISTENT SYNOVITIS OF KNEE IN RHEUMATOID ARTHRITIS

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Background: Chronic persistent synovitis is commonly seen in inflammmatory arthritis like RA where despite adequate DMARD therapy, few joints are chronically inflamed. They are the reason for increasing morbidity and poor functional status in these patients. Some patients show persistent synovitis despite intra-articular steroids and hence they need to identify other drugs like sclerosant which can be of use in improving pain and functional status.

Objectives: To compare the efficacy of Intra-articular steroid versus sclerosant in rheumatoid arthritis (RA) with persistent synovitis despite optimum dose of csDMARDs and to determine, if sclerosant is superior/inferior to steroids.

Methods: This is a single blinded-observational pilot study, conducted in Institute of Rheumatology, Madras Medical College for a period of 1 year. 20 patients with persistent synovitis knees) despite optimum DMARD therapy are recruited as per inclusion and exclusion criteria. Disease and joint related activity and functional status are documented. Ethical committee approved the study. After getting written informed consent patients were randomized into two groups (A and B). Group A received IAS (Triamcinolone Acetonide) and group B received sclerosant (1% Polidocanol). They are assessed at 1, 4, 12 and 24 week and various parameters documented. The results are analysed with SPSS v22 software.


Results: 40 patients were recruited for the study, with 20 in each group. 45% patients in group A and 65% patients in group B, showed significant improvement in DAS28, CRP, VAS pain and function. VAS scores improved within 1 week and no adverse effects were noted. Both the interventions found to be effective in reducing the pre operative VAS pain and function scores. However, Mean VAS Scores after 1 week of sclerosant injection found to be lesser than that of steroid group and the difference was statistically significant (p<0.05).

Conclusion: Intra-articular sclerosant (1%Polidocanol) is non-inferior to steroids in patients with persistent knee synovitis. It could be used as an effective alternative to steroids considering their side effect profile.

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Disclosure of Interests: None declared


AB0439 YTTRIUM-90 SYNOVIORTHESIS. OUR EXPERIENCE FOR 25 YEARS

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Background: Radioactive synoviorthesis (RS) is the intra-articular injection of a colloidal suspension of particles marked with a radioisotope that selectively irradiates the synovial membrane, respecting bone and cartilage. The radiocolloid is phagocytosed by type 2 synovocytes of the synovial membrane, causing fibrosis and decreased production of synovial fluid. Intra-articular puncture is ensured by obtaining synovial fluid and the radiopharmaceutical is instilled by 1ml of triamcinolone acetonide (40mg). After the procedure a graphic gamma image is made to assess the adequate distribution of the radionuclide in the joint cavity. With a half-life of 2.5 days, the drug will continue to emit radiation for weeks, with symptomatic improvement which is observed from the second week. The main indication of this technique is refractory chronic synovitis to local and/or systemic treatment.

Objectives: To describe the clinical-demographic characteristics of patients treated with SI in our hospital, and to assess the efficacy and safety of this technique.

Methods: Retrospective observational study that analyze the radiosynoviorthesis practiced in the Nuclear Medicine service of the Doce de Octubre Hospital between January 1994 and December 2018 is analyzed. A total of 113 techniques were analyzed in 89 patients from our center and other hospitals without Nuclear Medicine service, and data of 72 patients could be obtained from their clinical history. The efficacy of the technique was defined as total or partial, considering objective data (swelling and joint function) and subjective data (patient evaluation).

Results: 95 articular instillations were included in 72 patients, 46% women and 54% men; with an average age of 51.4 ± 15 [21-82] years, the knee articulations were injected with Yttrium-90 (5 millicuries). The patients had knee effusions lasting for an average of 18 months (IR 10- 60). The temporal distribution was very heterogeneous, decreasing over the years (1994-1998: 23%, 1999-2003: 32%, 2004-2006: 20%, 2009- 2013: 16%, 2014-2018: 9%). 93% of RS were indicated by the rheumatologist service and 7% by traumatology. In the classification by pathologies, 72.2% had systemic rheumatological disease. The most frequent causes of indication were rheumatoid arthritis (25%), psoriatic arthropathy (24%), spondyloarthropathy (17%) and pigmented villonodular synovitis (11%). Less frequent were juvenile idiopathic arthritis (5%), arthrosis (4%), microcrystalline arthritis (5%) and non-specific chronic synovitis (9%). 73% had been previously infiltrated with steroid, with an average of 2.8 ± 1.8 [1-10] injections/knee. The 79% had maintained treatment with NSAID, the 42% with systemic steroid, the 55% with DMARDs and the 14% with biological therapy; appearing the therapeutic effect in the first 8 weeks in the 42% with systemic steroid, the 55% with DMARDs and the 14% with biological therapy; appearing the therapeutic effect in the first 8 weeks in the 80% of the patients. 13 patients needed a reinjection with an average between radiosynoviorthesis of 25 ± 21 [6-80] months. Side effects were scarce (2.6%) and local in nature; 8.3% required a knee prosthesis.

Conclusion: RS has demonstrated acceptable efficacy and safety in cases of refractory synovitis of both mechanical and inflammatory etiology. Despite this, it is a procedure little used nowadays.

Disclosure of Interests: None declared


AB0440 CHANGES IN KEY LABORATORY VALUES WITH TOFACITINIB 5 MG BID TREATMENT IN PATIENTS WITH PSORIATIC ARTHRITIS AND RHEUMATOID ARTHRITIS

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Background: Tofacitinib is an oral Janus kinase inhibitor for the treatment of psoriatic arthritis (PsA) and rheumatoid arthritis (RA). In most countries where tofacitinib is approved, 5 mg twice daily (BID) is the recommended dose for PsA and RA. An important component of any product labelling is information on the need for laboratory monitoring.

Disclosure of Interests: None declared

Objectives: This post hoc analysis aimed to provide information on the effect of tofacitinib 5 mg BID on laboratory values in PsA and RA patients (pts).

Methods: For analysis of pts with active PsA treated with tofacitinib 5 mg BID, data were pooled from 2 Phase 3 studies and an ongoing long-term extension (LTE) study (data cut-off, 25 January 2017; database not locked; data may change). For analysis of pts with moderate or severe RA treated with tofacitinib 5 mg BID, data were pooled from 8 Phase 2, 2 Phase 3, and 1 LTE studies (data cut-off, 2 March 2017; for LTE, database not locked; data may change). All PsA and most RA pts received a background conventional synthetic disease-modifying antirheumatic drug. Data (to Month 12) for pts receiving constant tofacitinib 5 mg BID were evaluated, comprising pts who received tofacitinib 5 mg BID across studies, either at randomisation or following switch from placebo. Pts in the placebo groups who switched to tofacitinib 5 mg BID at Month 3 were included from the time they first received tofacitinib. Pts who switched tofacitinib dose were excluded. Change from baseline in haematologic (haemoglobin, neutrophils, lymphocytes) and lipid (low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, total cholesterol, triglyceride) levels and key liver tests (bilirubin, alanine aminotransferase, aspartate aminotransferase) were analysed. Although not addressed in the product labelling, creatine kinase, creatinine and C-reactive protein levels were also assessed. Pts meeting protocol-defined discontinuation criteria for laboratory values were evaluated.

Results: The constant tofacitinib 5 mg BID group comprised 348 PsA pts and 3040 RA pts. Mean (standard error) changes/percentage changes from baseline for laboratory values are presented in the table. Laboratory values generally stabilised after 1 to 3 months, and lymphocyte levels from baseline for laboratory values were evaluated. Pts meeting protocol-defined discontinuation criteria for laboratory values were evaluated.

Conclusion: In this post hoc analysis of laboratory data with tofacitinib 5 mg BID, changes in key laboratory values were similar for PsA and RA, and discontinuations due to protocol criteria being met for laboratory values were infrequent. These results provide further information on the effect of tofacitinib on laboratory values in PsA and RA.

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AB0441 THERAPY WITH TOFACITINIB IN A COLOMBIAN POPULATION WITH RHEUMATOID ARTHRITIS: RESULTS OF THE DAILY CLINICAL PRACTICE

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease that affects the quality of life and reduces life expectancy. It is characterized by the presence of autoantibodies and erosive synovitis that mainly involves small joints (1). Tofacitinib is the first oral Janus Kinase (JAK) inhibitor approved in 2012 for the treatment of patients with active, moderate to severe RA that does not respond to other therapies (2).

Objectives: The objective was to describe demographic and clinical results of a cohort of Colombian patients with RA treated with tofacitinib.

Methods: Descriptive observational study of a historical cohort of RA patients in a specialized center for the management of inflammatory arthropathies, from April 2014 to February 2018. The following variables are described: age, sex, time evolution of the disease, type of AR, comorbidities, disease activity (DAS-28), schedule and treatment time. For the descriptive analysis, categorical variables are presented as absolute and relative frequencies; while continuous variables are presented as mean and standard deviation (SD) or median and interquartile range (IQR) according to distribution. The outcome of DAS 28 ≤ 3.2 was estimated by incidence rate, defined as the number of patients who presented the outcome divided by the sum of total exposure time of the patients.

Results: Of 59 patients included, 88.1% (52) were women, with a median age of 58.8 years (IQR 49-68 years), 74.6% were seropositive, the median time from diagnosis was 18.2 years (IQR 12-28.3 years). High blood pressure was the most common comorbidity (40.7%) and 7% had tuberculosis history. The median number of bDMARD prior to tofacitinib was 2 (IQR 1-3). Sixty six percent patients (39) were on monotherapy while 34% (20) were on combination with leflunomide (19) and methotrexate (1). The median time of treatment was 1.2 years (IQR 0.6-2 years). At the beginning, 84.7% patients (50) were in moderate or high disease activity and 15.3% (9) in remission or low activity; at the end of follow-up, 47.5% (28) were in remission or low activity and 52.5% (31) in moderate or high activity (p = 0.00). The mean DAS28 at the beginning of tofacitinib was 4.6 ± 1.55 and at the end of the follow-up was 3.5 ± 1.49, with a difference of means of 1.10 (95% CI 0.62-1.57, p = 0.00). During the follow-up period, the rate of development of remission or low activity was 11.92 (95% CI 8.35-16.51) cases per 100 people-month observed (p = 0.00). Only 2 patients developed therapeutic failure.

Conclusion: Tofacitinib shows a good profile of effectiveness in patients with failure to prior bDMARD. Almost 50% patient reaches low disease activity or remission during follow up and low number of therapeutic failure was found.

REFERENCES
RESPONSE TO BARICITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS WITH FAILURE TO CONVENTIONAL SYNTHETIC DMARD AND/OR BIOLOGICAL DMARD: DATA FROM A LOCAL REGISTRY

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Objectives: To know the characteristics of patients with rheumatoid arthritis (RA), in treatment with baricitinib (BARI), who have failed to conventional synthetic DMARD (DMARDcs) and/or biological DMARD (DMARD). Methods: Prospective observational study, in real life, of patients with RA, under treatment with BARI. General data of the patients, (age, gender, comorbidity), RA and treatment were collected (time of evolution, presence of RF and ACPA, efficacy indexes at the beginning of BARI and the last visit: DAS28-ESR and CDAI, previous or concomitant treatment with DMARDcs and/or DMARDbs, end of treatment and cause, time in BARI, serious adverse effects during treatment with BARI.

Results: Of 520 patients in follow-up, who have received at least one dose of DMARDs, 224 (42%) are diagnosed with RA, and 56 (26%) of them receive some drug inhibitor of the JAK pathway. Of the 224 (42%) patients, such as F1 versus F2-F5, presented significantly higher BMI (30.83 ± 2.6 vs. 26.95 ± 4.4, p < 0.01), higher percentage of ACPA (30% in F3, F4, F5, of 7, 5.2, 7.7, 6.9 and 11.1 months, respectively. 94% of patients continued concomitant treatment with some DMARDs. BARI is the first drug after failure of DMARDcs (F1) in 24/40 (60%) patients, and in 16/40 (40%), after failure to some DMARDs: second drug after failure to DMARDs (F2) in 2 (6%), third (F3) in 5 (13%) patients, fourth (F4) in 6 patients (17%) and fifth (F5) in 3 (9%) patients. The mean global time in BARI is 9.6 ± 3.2 months, being for F1, F2, F3, F4, F5, of 7, 5.2, 7.7, 6.9 and 11.1 months, respectively. BARI patients, such as F1 versus F2-F5, presented significantly higher BMI (30.83 ± 2.6 vs. 26.95 ± 4.4, p < 0.01), higher percentage of ACPA (100% vs. 74%, p = 0.026), and lower mean time of evolution of RA (5.3 years, range: 0-17.25 vs. 14.75 years, range: 2-36 years, p < 0.001). In patients F2-F5, patients had failed to some DMARDs before initiating BARI, in F2 to 1 therapeutic target, in F3 to 2 targets and in F4 and F5 to 2 or 3 targets. Regarding safety, 1 patient presented herpes zoster. The results of clinical efficacy with DAS28-ESR and baseline CDAI and in the last evaluation are shown in the table.

Conclusion: 1. Baricitinib is effective and safe in real clinical practice.
2. It is competent of achieving clinical remission or low activity, in a high percentage of patients, even in those who have failed several biological drugs or several therapeutic targets previously.

Disclosure of Interests: None declared.

REFERENCES

Disclosure of Interests: None declared.


GAYET WERNICKE’S ENCEPHALOPATHY SECONDARY TO METHOTREXATE INTOLERANCE: A SERIOUS COMPLICATION OF CHRONIC VOMITING

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Background: Gayet-Wernicke’s encephalopathy is a serious complication of thiamine deficiency. Chronic alcoholism is recognized as the most common cause of Gayet-Wernicke’s encephalopathy, but other causes including malnutrition, chronic vomiting, prolonged fasting, and exclusive artificial feeding have been documented.

Objectives: We report a case of Gayet-Wernicke’s encephalopathy complicating uncontrollable vomiting secondary to severe Methotrexate intolerance.

Methods: Case report

Results: A 47-year-old women with rheumatoid arthritis. She was put under methotrexate at the dose of 15 mg/week, 1 month prior to admission into our department for the management of an acute febrile polyarthritis associated to severe and uncontrollable gastrointestinal intolerance to Methotrexate. There was no abdominal pain or transit problem. One month later, she experienced temporo-spatial disorientation, somnolence, horizontal nystagmus, and vertigo attacks with visual hallucinations and memory problems. The muscular forces at the four limbs were decreased to 3/5 with abolished osteotendinous reflexes at the two lower limbs. MRI showed hyperintense signals on T2 and FLAIR image in thalamus, periaqueductal area and mamillary bodies. Electroneuromyography (ENMG) showed axonal motor neuropathy in all 4 limbs. The hemogram showed normochromic normocytic anemia. Laboratory testing for Vitamin B12, vitamin D, folate and minerals showed multiple deficiencies. A multivitamin supplementation was introduced with good evolution.

Conclusion: This is the first case of severe digestive intolerance to methotrexate leading to a serious neurological complication. Although digestive intolerance to methotrexate is considered benign, it can be daunting. Thorough knowledge of complications and close monitoring of patients must be imperative. Gayet Wernicke encephalopathy is a rare and serious pathology. We should keep it in mind and prevent it in risky situations.

Disclosure of Interests: None declared.


AB0443

AB0443

RISK FACTORS OF JOINT SURGERY IN RHEUMATOID ARTHRITIS TUNISIAN PATIENTS

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Background: Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized by polyarticular synovial inflammation and progressive joint destruction. Orthopedic surgery is an integral part of the treatment of RA and it is mainly reserved for severe and advanced forms where there is a failure of medical treatment.

Objectives: To assess the rate of joint surgery in rheumatoid arthritis (RA) Tunisian patients and to determine the risk factors of surgical treatment.

Methods: A retrospective cross sectional study over a period of 15 years including 500 Tunisian patients with RA was conducted. The prevalence of joint surgery indication has been evaluated. Clinical, paraclinical and therapeutic characteristics of RA were compared according to the need of surgical treatment.

Results: Mean age was 53.4 years. Female to male ratio was 5. The indication of joint surgery was noted in 59 patients (12%). Factors associated with joint surgery were delayed diagnosis (p = 0.037), long RA duration (p = 0.017), young onset of RA (p < 0.001), presence of joint deformsities (p = 0.034), presence of osteoporosis (p = 0.029), presence...
of antineural antibodies<0.001), combination therapy of methotrexate with other conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) (p = 0.001), a short period of first medical treatment (p = 0.012) and high erythrocyte sedimentation rate (ESR) (p = 0.027). In multivariate analysis, three factors were independently related to the need of joint surgery: age at disease onset (OR 2.799 95%CI: 1.49-5.22 p<0.01), high ESR level (OR 2.807 95%CI: 1.5-5.24 p<0.01), and association of Methotrexate with other csDMARDs (OR 3.500 95%CI: 1.61-7.56 p<0.01).

Conclusion: Twelve percent of RA patients needed joint surgery treatment. Predictive factors of surgical treatment were young age at disease onset, high ESR level and association of methotrexate with other csDMARDs

REFERENCES


Disclosure of Interests: None declared

AB0445 REMARKABLE OUTCOMES IN PATIENTS WITH RA USING CONVENTIONAL DMARDS UNDER A T2T STRATEGY AND A DISEASE MANAGEMENT MODEL – RESULTS FROM A FIVE YEAR REAL-WORLD REGISTRY
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Objectives: The aim of this study was to describe global change in Disease Activity Score 28 (DAS28) using T2T strategy during 5 years in a cohort of patients receiving conventional DMARDs that attend to a specialized RA center.

Methods: A descriptive cohort study was conducted. Medical records of patients from specialized in RA center were reviewed during 2015-2017; those patients were followed-up under T2T standards and a multidisciplinary approach. Clinical follow-up was designed by the authors according to DAS28 as follows: every 3.5 weeks (DAS28 > 5.1), every 7-9 weeks (DAS28 > 3.1 and ≤ 5.1), and every 11-13 weeks (DAS28 < 3.1). Tender joint count (TJC), swollen joint count (SJC) and DAS28 were measured on each visit. Therapy had to be adjusted with DAS28 > 3.2 unless patient’s conditions don’t permit it; we considered this follow-up type as implementation of a T2T strategy in patients with RA. Patients entered into a multidisciplinary program of care with periodic consultations not only to rheumatology but with a physicist, physiotherapist, occupational therapy nutrition, and, a patient focused program. With a multidisciplinary model of care the patient is seen as a whole, and the expectation is to achieve the best results in the management of RA. We divided patients in four groups: remission (REM), low disease activity (LDA), moderate disease activity (MDA) and high disease activity (HDA) patients and the aim of the study was to look at what percentage of patients who were in moderate or severe disease activity reached a low disease activity or remission. Descriptive epidemiology was done, we calculated means, and standard deviations for continuous variables and categorical variables were presented as rates. We compared disease activity at base line and at the end of follow-up.

Results: During 5 years we included 2,128 patients. 83% were female and 17% were male, mean age was 57 years ±14. At baseline median DAS28 4.34 RIG (3.76-5.06) and at 5 years 2.02 RIG (1.492-2.38). At the end of our follow-up 81% were remission and 7% in LDA. See table 1.

AB0446 REAL-LIFE USE OF BARICITINIB IN RHEUMATOID ARTHRITIS: A MULTICENTER OBSERVATIONAL STUDY OF 150 PATIENTS
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Objectives: To investigate the efficacy and safety profiles of baricitinib in real-life data are available about its efficacy and safety.

Methods: We performed a multicenter prospective observational study on adult RA patients starting JAK inhibitors between 12/2017 and 12/2018. Demographic and clinical data as well as laboratory values and adverse events were collected at baseline and after 12 and 24 weeks. Disease activity was measured by DAS28-CRP at baseline, after 12 and 24 weeks.

Results: We obtained data from 150 patients with RA (women 116 – 77.3%; median age 60 years, inter-quartile range IQR 54-68; median disease duration 10 years, IQR 4-18) treated with baricitinib 2 or 4 mg QD, however only 2150 (13%) at the reduced dosage. At the time of data-base lock 95/150 (63%) patients have completed the 12 weeks follow-up, 38/150 (25%) patients have completed the 24 weeks follow-up. Baricitinib was prescribed as monotherapy in 150/150 (43%), at a median dosage of 15 mg/week. Oral corticosteroids were used by 105/150 (70%) patients, at a median dosage of 5 mg/day. Mean DAS28-CRP at baseline was 4.92 (standard deviation 1.22), with 65 (43.3%) patients having a DAS28-CRP>5.1. At both 12 and 24 weeks, a significant reduction of disease activity scores was observed (DAS28-CRP mean 3.07, SD 1.36, and 2.85, SD 1.35, respectively; p values<0.001). Sixteen (11%) patients discontinued the treatment, with 8 (50%) due to primary inefficacy, mainly in the first 3 months of therapy (58– 63%). Adverse events were observed in 19/150 (13%) patients, 7 being non-serious infections (4
upper respiratory tract infections, 2 urinary tract infection, 1 Herpes labialis, while 3 patients manifested Herpes Zoster reactivation, 2 deep vein thrombosis (one with pulmonary embolism), 2 discontinued due to severe anemia and pancytopenia, and 2 developed self-limiting liver enzyme elevation.

Conclusion: In our real-world dataset, baricitinib is effective in reducing RA disease activity, after 12 weeks, being generally well-tolerated with few severe adverse events.

Disclosure of Interests: Giacomo Maria Guidelli: None declared, Elena Generali: None declared, Chiara Bazzani: None declared, Roberto Goria: None declared, Giancarlo Sfekallirou: None declared, Massimiliano Limonta: None declared, Maria Sole Chiumenti: None declared, Roberto Perricone: None declared, Edoardo Conticini: None declared, Bruno Frederiani: None declared, Nicola Bossi: None declared, Lorenzo Dagna Consultant for: Pro Lorenzo Dagna received consultation honoraria from AbbVie, Amgen, Biogen, Bristol-Myers Squibb, Celltrion, Novartis, Pfizer, Sanofi-Genzyme, and SCBiL. Marta Riva: None declared, Maria Rosa Pozzi: None declared, Rosa Daniela Grembiale Grant/research support from: BMS, Consultant for: JANSSEN, CELGENE, Speakers bureau: Pfizer, JANSSEN, BMS, NOVARTIS, Teodora Serban: None declared, Gerolamo Bianchi Consultant for: Astra-Sigma, Amgen, BMS, Celgene, Medac, UCB, Speakers bureau: AbbVie, Abiogen, Astra-Sigma, Amgen, BMS, Celgene, Carlo Sempel Grant/research support from: AbbVie, Janssen, MSD, Novartis, Pfizer, Consultant for: AbbVie, Astra-Sigma, Biogen, BMS, Celgene, Eli-Lilly, GSK, Janssen, Merck Sharp and Dohme, Novartis, Pfizer, Roche, Sanofi-Genzyme, YCB, Speakers bureau: AbbVie, Astra-Sigma, Biogen, BMS, Celgene, Eli-Lilly, GSK, Janssen, Merck Sharp and Dohme, Novartis, Pfizer, Roche, Sanofi-Genzyme, YCB.

AB0447 BIOLOGICAL THERAPY AND RADIOSYNVOBITHERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS

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1Polyclinic of the Hospitalier Brothers of St. John of God, Rheumatology, Budapest, Hungary;
2Polyclinic of the Hospitalier Brothers of St. John of God, Budapest, Hungary

Background: The treatment of patients with rheumatoid arthritis (RA) has been spectacularly changed since the 1950’s. Introduction of the steroid compounds and their local application, the chemical and radionuclide synovectomy, surgical synovectomy, use of non steroid drugs, the basic treatment and the spread of biological therapy are the most important steps. Introduction of the biological therapy has changed the quality of life for these patients.

Objectives: During biological therapy sometimes 1 or 2 joints could be affected by inflammation. In this cases always the question is how to solve the problem. Change of the biological or basic therapy, use surgical synovectomy or radiosynovectomy (RSO)?

Methods: In our rheumatological department 2100 patients with RA and PA were treated with biological therapy between 2002 and 2015. In 100 patients we applied RSO because of the inflammation of the knee joint during biological therapy. We made a long term follow-up in 72 patients.

All participants provided written informed consent.

62 participants inflammatory knee joint disease was diagnosed on the basis of the American College of Rheumatology. 55 of 62 patients with rheumatoid arthritis were seropositive, 7 seronegative. Steinbrocker functional stage I-II was observed in 52, stage III in 10. 10 patients were seronegative. Mean age of 13 male and 61 female patients was 51.4 years (range 24-79) years. In 38 patients the right knee, in 34 the left knee was treated by radiosynovectomy. Mean duration of disease was 7.3 years (range 0.9-25), of synovitis (6.month range 3-8) Mean number of punctures of the treated joint prior to radiosynovectomy was 4.2 per patient and of steroid administrations prior to radiosynovectomy 3.0. In 12 patients a systemic steroid therapy has been performed.

Results: During the study period, inflammation decreased. In the first two years excellent and good results were recorded in 82.2%. Two years after radiosynovitthis 83.3% of patients did not need another puncture. Before the knee inflammation patients were in complete remission which status has been achieved after RSO as well. DAS: 2.4±0.4.

Conclusion: 1. RSO is an effective method to treat the inflammation of the knees. 2. The RSO performed during biological therapy is as effective as in the case of patients without biological therapy. 3. In case of a successful RSO there is no need for biological or basic therapy neither for surgical synovectomy.
venous thrombotic events, opportunistic infection/active TB, malignancy, GI perforation, or death.

Table 1. Efficacy measures in the Japanese subgroup at weeks 12 and 24.

<table>
<thead>
<tr>
<th>Timepoint</th>
<th>FIB 200 mg QD</th>
<th>FIB 100 mg QD</th>
<th>PBO QD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 12</td>
<td>83% (p&lt;0.015)</td>
<td>53% (p=0.28)</td>
<td>31%</td>
</tr>
<tr>
<td>Week 24</td>
<td>92% (p&lt;0.001)</td>
<td>60% (p=0.024)</td>
<td>15%</td>
</tr>
</tbody>
</table>

Conclusion: In this phase 3 study in sDMARD-IR patients with active RA, treatment with FIB over a 24-week period was associated with significant improvements in signs and symptoms of RA, with a safety and efficacy profile in Japanese patients consistent with that in the global population. Thus, FIB may provide a novel treatment option for patients who continue to have active RA despite prior biologic therapy.

REFERENCES


PAIN REDUCTION IN PATIENTS WITH RHEUMATOID ARTHRITIS RECEIVING TOFACITINIB MONOTHERAPY WITH OR WITHOUT PAIN MEDICATION: A POST HOC ANALYSIS OF POOLED DATA FROM PHASE 2, PHASE 3 AND PHASE 3B/4 STUDIES

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Background: Tofacitinib is an oral JAK inhibitor for the treatment of RA. Pharmacokinetics in the most common systems reported by patients (pts) with RA,1,2 thus reduction of pain is an important treatment goal.

Objectives: To evaluate the effect of tofacitinib monotherapy ± pain medication on pain in pts with RA.

Methods: This pooled post hoc analysis included pts who received tofacitinib 5 mg BD monotherapy (ie without csDMARDs) in Phase (P)2 (NCT00550446), P3 (ORAL Solo; NCT00814307) and P3b4 (ORAL ABO0449)
Strategy; NCT02187055) studies. Pts were stratified by concomitant use of ‘any pain therapy’ (opioids, plain analgesics [eg acetaminophen], NSAIDs or glucocorticoids [GC; ≤10 mg of prednisone or equivalent per day]), ‘pure analgesics’ (opioids or plain analgesics) and ‘adjuvant analgesics’ (NSAIDs or GC). Pts receiving pain medication at baseline (BL) maintained a stable dose during the studies; opioid and/or acetaminophen dose could be increased as rescue therapy. Efficacy outcomes were assessed at Month (M)3 and M6: change from BL (Δ) in Pt Assessment of Pain (Pain; visual analogue scale [VAS]) and ΔPain stratified by DAS28-4(ESR)-defined low disease activity (LDA; Δ3.2) status at M3 and M6.

Results: Of 676 pts who received tofacitinib 5 mg BID monotherapy, 604 (89%) received ‘any pain therapy’, 141 (21%) received ‘pure analgesics’ and 569 (87%) received ‘adjuvant analgesics’. Demographics and BL disease characteristics, including disease activity and Pain VAS, were generally similar when stratified by use/type of pain medication. Reductions in pain (ΔPain VAS) at M3 and M6 were generally similar for pts who received tofacitinib with ‘any pain therapy’ vs those who did not receive ‘any pain therapy’ (Figure 1a). There was a trend for a numerically greater reduction in pain at M3 and M6 in pts who received tofacitinib with ‘any pain therapy’ and who achieved LDA at M3 and M6 vs those who received tofacitinib with ‘any pain therapy’ and did not achieve LDA (95% CI overlapped; Figure 1b). By contrast, pain reductions were similar for pts who received tofacitinib without ‘any pain therapy’, irrespective of LDA status. Similar trends were seen when pts were stratified by use of ‘pure analgesics’ and ‘adjuvant analgesics’ (data not shown).

Conclusion: In this pooled post hoc analysis, pain reduction was similar in pts with RA receiving tofacitinib, regardless of pain medication use. Pain reduction was similar in pts receiving tofacitinib without ‘any pain therapy’, irrespective of LDA status. These results should be interpreted with caution, as pain medication could be used as rescue therapy, few pts received tofacitinib without ‘any pain therapy’, and confounding by indication cannot be excluded. Further analyses are required to explore the impact of tofacitinib on the relationship between reductions in pain and disease activity.

REFERENCES

Acknowledgement: Study sponsored by Pfizer Inc. Medical writing support was provided by Sarah Piggott of CMC Connect and funded by Pfizer Inc.

Figure 1


Figure 1. methotrexate adherence levels

Lack of resources and adverse effects were the main factors behind methotrexate’s low level adherence. The patients with these levels had a longer duration of disease progression and higher parameters of disease activity.

Conclusion: This study shows that the methotrexate adherence level in Moroccan patients with RA is low. The patient’s education should be improved in the Moroccan population for a better control of the disease.

Disclosure of Interests: None declared
PROSPECTIVE STUDY OF REASONS FOR DISCONTINUATION OF TOFACITINIB IN SELF-FUNDED PATIENTS WITH RHEUMATOID ARTHRITIS FROM A SINGLE CENTRE

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Background: Tofacitinib is an oral Janus kinase inhibitor for the treatment of Rheumatoid Arthritis (RA). There can be potential differences in the adherence and compliance to therapies in real world compared to clinical trials especially in a non-reimbursable setup. Hence, it is very important to see the patient persistence to Tofacitinib therapy in a real practice.

Objectives: To evaluate the reasons for discontinuation of Tofacitinib in RA patients in real world set-up.

Methods: Data of RA patients treated with Tofacitinib 5mg BID from a rheumatology center in South India was collected from September 2016 to January 2019 using standardized formats at baseline, 1, 3, 6 and 12 months. Efficacy was evaluated by DAS28-ESR and safety by listing of Adverse Events (AE). Reasons for discontinuation were objectively recorded. Concomitant RA treatment type/dose adjustments were as per the clinician’s discretion. Analysis was based on observed values without imputation for missing data. For calculating persistence at a time point, the patients still taking the drug with treatment duration lower than that particular time point were excluded from the calculation.

Results: Fifty seven RA patients were treated with Tofacitinib. Average age and disease duration were 50 (20-77) years, 9 (1-22) years respectively. Most patients were females (88%); seropositive (89%) and all had erosive disease. Tofacitinib was used as a second line drug after inadequate response with conventional Disease Modifying Anti Rheumatic Drugs. Average Tofacitinib follow up was 6 (1-16) months. Thirty nine patients who discontinued Tofacitinib were analyzed. Eighteen patients were at various stages of therapy including 8 patients completing 12 months. Persistence with Tofacitinib at 3, 6 and 12 months was 85, 50 and 17 percent respectively. Details of the reasons for discontinuation are given in Table and Figure.

Conclusion: Tofacitinib was effective and well tolerated in Indian patients. However, majority of patients (80%) discontinued at various time points after feeling better. Only 13% discontinued due to AEs and 7% due to inadequate response. This data brings into light the difficulties faced by health providers for implementing 'treat to target' approach in real world practice.

Reasons for Discontinuation

<table>
<thead>
<tr>
<th>Reason for Discontinuation</th>
<th>Duration of treatment (Months)</th>
<th>Number of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 months</td>
<td>4</td>
</tr>
</tbody>
</table>

Table

Disclosure of Interests: Ramakrishna Rao Uppuluri Grant/research support from: Pfizer Inc, Maryam Younis: None declared, Archanaa Rani: None declared, Shashikala Arava: None declared, Shivanand Jonnada: None declared, Kumar Datta: None declared, Challa Satyavati: None declared

Background: Lipid profile control is essential in patients diagnosed with inflammatory disease such as rheumatoid arthritis (RA), since cardiovascular events (CV) are still the first cause of mortality. According to the EULAR recommendations on CV risk, in those patients with a low or moderate CV risk index, for whom diet and exercise have not been effective to diminish low density lipoprotein (LDL) cholesterol below 190 and 100 respectively, we must prescribe a statin. These are the most commonly used drugs with undisputed benefits shown in medical literature. However, often-polymedicated patients may present intolerances or adverse side effects that limit their use. Red rice yeast, whose main active ingredient is monacolin K, has been used in traditional Chinese medicine since 800 AD as a remedy to reduce the total cholesterol level (TC) in blood, LDL and triglycerides (TG). In addition, some studies underline its anti-inflammatory effect and its benefit in patients with inflammatory pathology. In recent years, its use has spread throughout the western world.

Objectives: To evaluate the efficacy of red rice yeast in patients with elevated levels of TC and LDL in rheumatology clinic.

Methods: Prospective study that includes two cohorts of 30 patients with similar demographic characteristics. One cohort with RA patients and the other one without inflammatory disease. Both groups present high levels of TC and LDL. We study the demographic, clinical and lipid levels. A standard dose of red rice yeast is administered to every patient and we evaluate the analytical response after 3 and 6 months of treatment. For the statistical analysis, we used the SPSS program 22.0 version. Quantitative variables are presented as means ± standard deviation and qualitative variables as percentages. The comparisons between the quantitative variables are made with the Student’s T-test. We compared the mean values for each visit with the Anova test. A p <0.05 is considered significant.

Results: In the group of patients without inflammatory pathology (n = 30), 73% are women with an average age of 63.9 ± 7 years. The mean of baseline TC is 231 ± 19 and LDL 143.9 ± 20. After 3 and 6 months of treatment, a significant decrease in both values was obtained (TC 231 ± 19 and 209.8 ± 19 F: 26.71 p 0.000 and LDL 143.9 ± 20 and 123.6 ± 19 F 22.51 p 0.000).

In the cohort of patients with RA (n = 30), 66% were women with an average age of 62.1 ± 10. The mean baseline TC is 258.2 ± 14 and LDL 176.7 ± 10. After 3 and 6 months of treatment a significant decrease of both values was obtained (TC 224 ± 24 and 196.1 ± 28 F: 21.55 p 0.000 LDL 149.5 ± 12 and 122.4 ± 25 F: 28.28 p 0.000).

In the two cohorts, 2 weeks for 43.2% and 64.7% of pts with headaches; 66.1% for intraocular pressure and 28.9% with abdominal discomfort. Of the 2657 pts included in the analysis, 1976 received tofacitinib 5 mg BID (ORAL Solo, ORAL Strategy), placebo (PBO; ORAL Solo), or tofacitinib 5 mg BID or PBO with csDMARDs (all studies except ORAL Solo). Non-serious AEs (affecting pts directly related to tolerate therapy) with incidence rates (IRs, pts per 100 pt-years) >5 were evaluated up to Month (M)3. Infections, laboratory test abnormalities, general disorders or events not directly reported by pts, and musculoskeletal disorders likely due to underlying RA, were excluded.

Results: Of the 2857 pts included in the analysis, 1976 received tofacitinib 5 mg BID (monotherapy: N=627; combination: N=1349) and 681 received PBO (monotherapy: N=122; combination: N=559). The most frequent non-serious AEs up to M3 are shown in the Table. IRs >10 were seen for headache and diarrhoea (tofacitinib 5 mg BID monotherapy, combination therapy and PBO monotherapy), and nausea (PBO monotherapy and PBO combination therapy). Non-serious AE duration was ≤4 weeks for most pts with headaches, diarrhoea or gastric discomfort (any gastrointestinal pain, dyspepsia, epigastric discomfort or abdominal discomfort/pain). With tofacitinib 5 mg BID and PBO, respectively, duration of AEs was ≤2 weeks for 43.2% and 64.7% of pts with headaches; 66.1% and 81.3% with diarrhoea; and 36.2% and 58.6% with gastric discomfort. Most non-serious AEs were mild/moderate.

Figure 1

Disclosure of Interests: None declared
Conclusion: Overall, non-infectious non-serious AEs were mild/moderate and the majority were self-limiting. Non-serious AE frequency was similar for tocifinib monotherapy and combination therapy, and for tocifinib and PBO.

REFERENCES

### AB0457 AUDIT ON HYDROXYCHLOROQUINE RELATED RETINOPATHY SCREENING IN RHEUMATOLOGY PATIENTS IN SVUH

**Aadil Al Ghafri, Eamonn S. Molloy. St Vincent’s University Hospital, Rheumatology, Dublin, Ireland**

**Background:** Hydroxychloroquine (HCQ) is a medication commonly used to treat rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and other rheumatological conditions. A known adverse effect associated with long-term use of these medications is vision loss resulting from irreversible retinal toxic effects. Recent guidelines emphasized on routine ophthalmological examination and to adhere on real weight-based dosages.

**Objectives:** This audit conducted to evaluate adherence rate on standard recommendation on HCQ related retinopathy screening in rheumatology patients in St Vincent’s University Hospital (SVUH).

**Methods:** Patient were on HCQ and attended rheumatology clinics at SVUH with rheumatic diseases selected randomly from on 01/08/2017 and end on 01/04/2018. A total sample size of 56 patients received a questionnaire that included information on HCQ dose, duration and actual body weight. Other information included precipitant factors and ophthalmology examination reports were retrieved retrospectively form patient’s chart.

**Standards were measured against recommendations on screening for HCQ retinopathy published by American Academy of Ophthalmology, 2016 Revision.**

**Results:** Total 56 patients on HCQ with different rheumatic disease studied. Out of 56 patients studied, 6/56 (10.7%) were <25 years (young), 45/56 (80.4%) were 25-65 years (middle age), and 5/56 (8.9%) were >65 years (elderly). Sex distribution showed that 7/56 (12.5%) were males and 48/56 (87.5%) were females. Around 35.7% (20/56) were in HCQ dose <5mg/kg, and 64.3% (36/56) were on standard HCQ dose (5mg/kg) of real body weight. The were 44.6% (25/54) patients on HCQ for a period <5 years, the rest, 55.4% (32/56) were on HCQ for a period of 5-20years, and none of these patients were on it for >20 years duration. There were only 1/56 (1.8%) patient with history of HCQ toxicity. 98.2% (55/56) showed no history of HCQ related toxicity. None of the 56 patients had any of the following influencing factors: renal impairment, Tamoxifen usage, coagulopathies, hepatic impairment, or pre-existing retinal/macular disease. However, there were 8.9% (5/56) of this group their age was > 65years (verses 51/56 91.1% were <65years age. Only 69.6% (39/56) of these patients underwent retinal baseline screening, were 17/56 (30.4%) did not receive any baseline screening after commencing HCQ therapy. Frequency of follow up retinal screening were done annually in 19/56 (33.9%), 5 yearly in 6/56 (10.7%). However, it was not done in 21/56 (37%) and it was not due in 9/56 (16.1%). Out of those who underwent the screening at any time, 32/56 (57.1%) showed normal examination results, only 1/56 patient (1.8%) showed abnormal results. Rest of the patient data either were not available, or examination were not done.

**Conclusion:** Above data emphasis the need to adhere on standards HCQ retinal screening as baseline and follow up. Furthermore, adherence on real weight calculated dose rather than estimated/average body weight.

**REFERENCES**


### Table 1. Change from baseline to Week 12 for secondary and exploratory endpoints (full analysis set)

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Seletalisib n=13</th>
<th>PBO n=14</th>
<th>Difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESSDAI absolute change</td>
<td>2.8</td>
<td>2.8</td>
<td>1.0 (0.1, 1.9)</td>
</tr>
<tr>
<td>ESSPRI score*</td>
<td>-0.9 (0.3)</td>
<td>0.5 (0.2)</td>
<td>-1.4 (1.5, 0.7)</td>
</tr>
<tr>
<td>Stimulated salivary flow rate, nL/min</td>
<td>7.5 (2.8)</td>
<td>5.5 (2.5)</td>
<td>2.0 (1.2, 2.8)</td>
</tr>
<tr>
<td>Sjögren’s Index score</td>
<td>7.5</td>
<td>7.5</td>
<td>0.0 (0.0, 0.0)</td>
</tr>
<tr>
<td>Immunglobulin G, mg/L</td>
<td>13.5</td>
<td>13.5</td>
<td>0.0 (0.0, 0.0)</td>
</tr>
<tr>
<td>Immunglobulin M, mg/L</td>
<td>13.5</td>
<td>13.5</td>
<td>0.0 (0.0, 0.0)</td>
</tr>
<tr>
<td>Immunglobulin A, mg/L</td>
<td>13.5</td>
<td>13.5</td>
<td>0.0 (0.0, 0.0)</td>
</tr>
</tbody>
</table>

**DISCLAIMER:**

All references and data are from the published scientific abstracts. The table above represents the change from baseline to Week 12 for secondary and exploratory endpoints (full analysis set) for the A Phase II Randomised, Double-blind, Placebo-Controlled, Proof of Concept Study of Oral Seletalisib in Patients with Primary Sjögren’s Syndrome (PSS).

**RESULTS:**

The study was terminated early due to slow recruitment, which led to study power decreasing to 36%. Twenty of 27 patients randomised (seletalisib n=13, PBO n=14) completed treatment. Demographic characteristics were generally similar between groups. Mean (SE) change from baseline in ESSDAI at Week 12 was seletalisib −5.4 (1.7) vs PBO −2.8 (1.5); treatment difference vs PBO was 2.6 (9.8, 0.01; p=0.266). The percentages of patients achieving a ≥3 point reduction in ESSDAI were seletalisib 66.7% vs PBO 54.5%. Post-hoc Bayesian analyses of treatment difference showed an 86.5% probability of being superior to PBO and a 48.8% probability was deemed different from clinically notable improvements in some secondary endpoints were also observed in the seletalisib group (Table 1). Minor salivary gland bioposes had broadly similar histological features across groups at baseline. At

**Disclosure of Interests:** None declared.

**DOI:** 10.1136/annrheumdis-2019-eular.7846

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**AB0458 A PHASE II RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, PROOF OF CONCEPT STUDY OF ORAL SELETALISIB IN PATIENTS WITH PRIMARY SJÖGREN’S SYNDROME (PSS)**

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**Background:** Seletalisib is a potent, selective oral inhibitor of phosphoinositide-3 kinase delta (PI3Kd). Preclinical data have shown that the PI3Kd pathway is upregulated within salivary glands of patients with PSS and contributes to disease pathogenesis.

**Objectives:** To assess the efficacy and safety of seletalisib in patients with PSS.

**Methods:** In this Phase II, double-blind, proof of concept study (NCT02610543), patients with PSS having an EULAR Sjögren Syndrome Disease Activity Index (ESSDAI) score ≥5 were randomised 1:1 to seletalisib once daily or placebo (PBO) in addition to current PSS therapy for 12 weeks. The primary endpoint was change from baseline in ESSDAI at Week 12. The study was designed to have 80% power to detect a difference of 3.8 points in change from baseline in ESSDAI between seletalisib and PBO at Week 12 and required 58 patients to complete treatment. Other endpoints included EULAR Sjögren’s Syndrome Patient Reported Index (ESSPRI), salivary gland biopsy changes, Schirmer’s I test, immunoglobulin concentrations and incidence of treatment-emergent adverse events (TEAEs).

**Results:** The study was terminated early due to slow recruitment, which led to study power decreasing to 36%. Twenty of 27 patients randomised (seletalisib n=13, PBO n=14) completed treatment. Demographic characteristics were generally similar between groups. Mean (SE) change from baseline in ESSDAI at Week 12 was seletalisib −5.4 (1.7) vs PBO −2.8 (1.5); treatment difference vs PBO was 2.6 (9.8, 0.01; p=0.266). The percentages of patients achieving a ≥3 point difference from baseline in ESSDAI between seletalisib and PBO at Week 12 and required 58 patients to complete treatment. Other endpoints included EULAR Sjögren’s Syndrome Patient Reported Index (ESSPRI), salivary gland biopsy changes, Schirmer’s I test, immunoglobulin concentrations and incidence of treatment-emergent adverse events (TEAEs).
Week 12, seletalisib treatment led to a reduction in the size and cellular organisation of mononuclear inflammatory cell foci vs PBO (Table 2). TEAEs were reported by 13/13 (100.0%) seletalisib and 13/14 (92.9%) PBO patients; most frequently reported: diarrhoea (5/13 [38.5%] vs 0/14 [0%]) and headache (3/13 [23.1%] vs 2/14 [14.3%]). Serious TEAEs were reported by 3/13 (23.1%) vs 1/14 (7.1%), and discontinuations due to TEAEs by 5/13 (38.5%) vs 1/14 (7.1%) seletalisib and PBO patients, respectively.

Conclusion: Although this Phase II PSS study was terminated early due to slow recruitment, seletalisib demonstrated a trend to clinical improvement in patients with PSS and acceptable safety and tolerability. Histological analyses demonstrated encouraging effects of seletalisib on the organisation of mononuclear inflammatory cell foci from parent minor salivary gland biopsies.

REFERENCES

Table 2: Change from baseline at Week 12 in characteristics of mononuclear inflammatory cell foci from parent minor salivary gland biopsies

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Seletalisib</th>
<th>PBO (n=11)</th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average area, mm²</td>
<td>0.02 (0.02)</td>
<td>0.01 (0.09)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Focus score</td>
<td>-0.43 (0.99)</td>
<td>0.22 (2.73)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percentage of germinal centres</td>
<td>1.3 (1.4)</td>
<td>2.5 (2.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percentage of foci with follicular dendritic cells</td>
<td>-13.6 (14.2)</td>
<td>10.9 (16.8)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percentage of foci of T8 cell segregation</td>
<td>-17.5 (8.8)</td>
<td>-12.7 (9.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percentage of foci with follicular dendritic cells</td>
<td>23.2 (17.6)</td>
<td>15.4 (41.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SD, standard deviation</td>
<td>*x; y; *z; *w; *v; *u; *t; *s; *r; *q; *p; *o; *n; *m; *l; *k; *j; *i; *h; *g; *f; *e; *d; *c; *b; *a; *</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
USE OF PLATELET RICH PLASMA (PRP) IN TREATMENT OF DRY EYE SYNDROME IN THE PATIENTS WITH SJÖGREN SYNDROME: PRELIMINARY RESULTS

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Background: Xerostomia and xerofthalmia are the hinge symptoms of Sjögren Syndrome and often they negatively influence patients’ quality of life. The eye washes used based on Platelet Rich Plasma (PRP) (PRP has been applied in the treatment of the xerofthalmia, both primitive and secondary.

Objectives: To evaluate the effect of subconjunctival injections and PRP based eye washes on the ocular dryness (subjective and objective) in patients suffering from primary Sjögren syndrome (pSS).

Methods: Six pSS patients (6 females, age at the beginning 48.2±9.7 years) have been recruited in the study. All patients were reaching the criteria for pSS diagnosis, for each patient clinical and immunological data have been recorded. Patients with Schirmer Test value, in at least an eye, inferior to 10 mm after 5 minutes, and suffering from severe dryness calculated by OSDI score (between 33 and 100, severe condition of dry eye) in spite of therapies with tear substitutes were selected. The OSDI (Ocular Surface Index) is a questionnaire for the evaluation of the subjective ocular dryness. Selected patients have been addressed to treatment with PRP. The PRP is constituted by human plasma enriched with plaques by means of the utilization of a special kit, therefore each patient has been subjected to a blood drawing, from which PRP has been extracted. Of this, a part has been injected in subconjunctival seat; from remained one, an eyewash has been extracted that the patients have assumed 6 times in the day up to exhaustion (about 5 days) during which another topic therapy was not used. The patients have been valued to the basal time and after ten days of the procedure; besides follow-up visits each three months are scheduled. To each evaluation Schirmer Test data and OSDI have been checked.

Results: Each patient had severe xerofthalmia, evaluated by Schirmer Test (right eye: 3.33±2.66; left eye: 6.83±6.5) and index OSDI (50.71±20.72). All the patients had Schirmer Test values, in at least an eye, lesser than 10 mm after 5 minutes. The analyzed cohort had homogeneous clinical characteristics (presence of xerostomy and absence of inflammatory indexes, hypergammaglobulinenia, arthritis and lymphoedemogenyly). After one week (T1), OSDI values were significantly more reduced compared to the basal time (38.89±15.12; p=0.028). The Schirmer Test values were not significative different to the follow-up visit compared to the basal one. No patients presented pre- and post-procedural complications, neither related infectious events. At 3 months follow up after first treatment (T2) no statistically significant difference in OD/OS Schirmer Test values and OSDI score compared to the basal time were observed.

Conclusion: The use of PRP in dry eye syndrome in patients with Sjögren syndrome seems to be effective in alleviating symptoms and improving patients’ life quality. Is need further follow-up to confirm data, to evaluate necessity of repeating treatment.

REFERENCES


Disclosure of Interests: None declared.

AB0461 BELATECEPT IN SLE KIDNEY TRANSPLANT PATIENTS

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Background: Lupus nephritis (LN) results in the need for renal replacement therapy (RRT) in 10-30% of LN pts; of these 30% receive a kidney transplant (KT). Belacept (bela) is a second-generation selective T-cell co-stimulator blocker (inhibits CTLA-4) used as an alternative to calcineurin inhibitors (CNI) for maintenance regimens after KT. The pathogenic relevance of CTLA-4 inhibition and the favorable cardiovascular profile of bela make it an attractive therapeutic option in SLE. Additionally, bela IV ensures therapeutic adherence.

Objectives: The current study was initiated to evaluate the effect of bela on graft function and extraeral SLE.

Methods: This retrospective single-center study evaluates the outcomes of LN KT recipients treated with bela from 2006–2018 at the Columbia University Lupus and Renal Transplant Cohorts. The bela regimen was 5mg/kg every 2 weeks x 5 doses, then monthly. CNI weaning among the bela group was not standardized. Immunosuppressive regimen, kidney allograft function, and SLE activity were examined.

Table 1: Characteristics of patients on bela

Results: 48 pts with LN had undergone KT between 2006–2018 with follow-up time of 72.2 ± 74.6 months. Bela was started in 7 pts on CNI regimens (TAC N=6, cyclosporine N=1) at 15.5 ± 17.1 months after KT. All pts were female, age at SLE diagnosis 21.1 ± 4.9 yrs; 5 had undergone RRT prior to KT (4 hemodialysis, 1 peritoneal dialysis) for 38.7 ± 37.8 months. The interval between SLE diagnosis and KT was 13.1 ± 8.3 yrs. At the time of bela initiation, all pts were also treated with prednisone (7.1 ± 2.7 mg/day), 6 with mycophenolate (1123 ± 625 mg/day), and 1 azathioprine (25mg/day). CNI were continued in 5/7 patients 6 months after bela. 2 pts were on hydroxychloroquine, 2 took it only prior to KT. In 5 patients, creatinine stabilized 6 months after bela, 1 returned to HD due to CNI-toxicity and pylonephritis and 1 is relisted for KT due to ACR and cortical necrosis (Fig. 1). No allograft failure due to recurrent
LN was noted in any of the 7 pts. 5 pts are followed by Rheumatology for extrarenal SLE; no extrarenal manifestations are documented in the other 2. Data on SLE Disease Activity Index post and post bela were available and scored in 3/5 pts using the SLEDAI-2K2G which accounts for clinical and laboratory manifestations, as well as steroid use (Fig. 2). Mean DNA pre and post bela was 133 ± 178 U/ml and 58 ± 72 U/ml. C3 89 ± 31 mg/dl pre and 91 ± 21 mg/dl post; C4 35 ± 15 mg/dl pre and 38 ± 7 mg/dl post.

Conclusion: Delayed KT recipients may decrease extrarenal manifestations, attenuate CNI toxicity and stabilize allograft function, providing a better alternative to CNI regimens. Furthermore, these data suggest that bela may be a therapeutic option in SLE.

REFERENCES


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Disclosure of Interests: None declared


AB0462 IMMUNIZATION TO RITUXIMAB IS MORE FREQUENT IN AUTOIMMUNE SYSTEMIC AUTOIMMUNE DISEASES THAN IN RHEUMATOID ARTHRITIS AND MAY BE MANAGED BY SWITCHING FROM RITUXIMAB TO OFATUMUMAB

Alice Combier, Gaetane Nocturne, Julien Henry, Rakiba Bekhir, Stephane Pavy, Xavier Mariette, Raphaèle Seror. Bicêtre Hospital AP-HM, Rheumatology, Le Kremlin-Bicêtre, France

Background: The most widely used B cell targeted therapies in autoimmune diseases (AID) is Rituximab (RTX), a murine chimeric monoclonal antibody. Among RTX’s side effects, immunization and anti-drug antibody sequences are poorly described. The immunization rate against RTX in rheumatoid arthritis (RA) is 2.7–9.2%, and it seems to be higher in other sAID although data is lacking.

Objectives: We aimed to evaluate the frequency, consequences and predictive factors of RTX-ADA in RA and sAID, as well as the use of an alternative B-cell targeted therapy, ofatumumab (OFA) in case of RTX-ADA.

Methods: All patients with RA or sAID treated with RTX from 2012 to 2017 in our tertiary reference centre for sAID were retrospectively studied. Patients who were tested for RTX-ADA were identified. Clinical and biological characteristics of RTX immunized patients were compared to those of non-immunized patients. For patients treated with OFA, clinical and biological efficacy was obtained before and after treatment.

Results: 199 patients were treated with RTX (RA: 124, sAID: 75 including 38 primary Sjögren’s Syndrome (pSS), 15 systemic lupus erythematosus, 7 myositis, 6 overlap syndrome, 5 ANCA-associated vasculitides and 4 other sAID). Among the 62/199 (31.1%) tested for RTX-ADA, 14 were positive; 3/35 RA (8.6%), and 11/27 (40.7%) other sAID, (p=0.005). Among the whole RTX-treated patients, the frequency of RTX-ADA was 2.4% and 14.7% (p=0.003) in RA and in other sAID, respectively. Most of the immunized patients experienced delayed infusion reactions (11/14 [78.5%]). Delayed reactions were observed within the first 15 days after the infusion, and after a median 2 cycles [range; 1-2]. They were mainly rash (72.7%), fever (54.5%) and/or abdominal pain (36.3%). Predictive factors of immunization were a sAID compared to RA (40.7% vs 8.6%, p<0.005), and young age (50.5 vs 61.5 years, p=0.003). Neither hyper-gammaglobulinemia, rheumatoid factor, disease activity, nor associated immunosuppressive therapy were associated with RTX-ADA. Among 23 tested patients with SLE or pSS, anti-SSA antibodies tended to be more frequent in immunized patients than non-immunized (2/10 (20.0%) vs. 8/13 (61.5%), p=0.16). Three pSS patients immunized against RTX were treated with OFA because of associated cryoglobulinemic vasculitis or MALT lymphoma. All 3 experienced complete remission of their disease.

Disclosures: This work was supported by a grant from the French National Research Agency (ANR-11-JS02-003) and a grant from the European Research Council (ERC-2013-AdG-617249). The study is supported by research funds from the ‘Fondation pour la Recherche Médicale’ (FRM). Dr. Schlag is supported by research grants from the French National Research Agency (ANR). The authors have declared no conflicts of interest.

Conclusion: Our results show that immunization against RTX is more frequent in other sAID than in RA. Testing for ADA must be performed in patients with infusion reactions. Patients immunized to RTX might be treated effectively with OFA, which should be further evaluated in sAID.

Disclosure of Interests: None declared


AB0463 BELIMUMAB IV EFFECT IN GLUCOCORTICOID TREATMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Systemic lupus erythematosus (SLE) is an autoimmune chronic disease produced by aberrant immunological response that consequently, causes a widespread organic damage. Treatment leads to regulating this disrupted immunological response. As a result, in 2011 Belimumab was approved for adults patients diagnosed with SLE, what is a monoclonal human antibody whose target is a B-lymphocyte stimulator (BLYS), a protein involved in the disease pathogenicity.

Objectives: To evaluate the glucocorticosteroid dose variation in adult patients with systemic lupus erythematosus during Belimumab IV treatment.

Methods: Retrospective, observational study that includes patients diagnosed with SLE according to SLICC 2012 criteria, who are treated with Belimumab IV. Treatment has been administrated as an initial dose: 10 mg/kg every 14 days and then, a maintenance dose: 10 mg/kg every 28 days. Data form serological profile, clinical manifestations at diagnoses and at the onset of treatment, existence of comorbidities or other diseases, concomitant therapy directed to the main disease or to the complications that came from the disease, non administration causes and definitive treatment discontinuation were collected from July 2012 until December 2018.

Results: A total of 19 patients (94.74% women) with 28 years old (Q1 14, Q3 31.82) as a median age at diagnosis and 11 (Q1 6.5, Q3 20) years since disease diagnosis were included. Follow up mean was 29 (Q1 7.5, Q3 37) months.

Regards to concomitant therapies, 5 patients (26.31%) were treated with Azathioprine and 3 patients with Methotrexate (15.79%). At the onset of biological therapy, 17 patients were treated with glucocorticoids, at a dose of 10 mg (Q1 9.38, Q3 10.63). At the end of follow up, 18 patients (94.73%) were treated with corticoid and the mean dose was 8.75 mg (Q1 8.75, Q3 8.75).

Table 1. Characteristics of patients on bela.

<table>
<thead>
<tr>
<th>ID</th>
<th>Age at SLE (yrs)</th>
<th>Race</th>
<th>LN class</th>
<th>Time to KT (yrs)</th>
<th>Type of KT</th>
<th>Induction</th>
<th>Reason for conversion</th>
<th>Immunosuppressive regimen before conversion</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>16</td>
<td>Black</td>
<td>IV, VI</td>
<td>13</td>
<td>DODKT</td>
<td>ATG</td>
<td>Non-adherence</td>
<td>TAC, MMF</td>
</tr>
<tr>
<td>B</td>
<td>30</td>
<td>Asian</td>
<td>II</td>
<td>23</td>
<td>DODKT</td>
<td>ATG</td>
<td>Arteriosclerosis</td>
<td>TAC, MPA, PRED</td>
</tr>
<tr>
<td>C</td>
<td>18</td>
<td>White</td>
<td>I</td>
<td>23</td>
<td>DODKT</td>
<td>ATG</td>
<td>Cortical nerosis</td>
<td>CYC, MMF, PRED</td>
</tr>
<tr>
<td>D</td>
<td>19</td>
<td>Black</td>
<td>V</td>
<td>9</td>
<td>LUKT</td>
<td>ATG</td>
<td>CNI side effects</td>
<td>TAC, MPA, PRED</td>
</tr>
<tr>
<td>E</td>
<td>22</td>
<td>Asian</td>
<td>I</td>
<td>5</td>
<td>LUKT</td>
<td>ATG</td>
<td>CNI side effects</td>
<td>TAC, MPA, PRED</td>
</tr>
<tr>
<td>F</td>
<td>18</td>
<td>Black</td>
<td>I</td>
<td>17</td>
<td>DODKT</td>
<td>Alectuzumab</td>
<td>TMA (biopsy)</td>
<td>TAC, MPA, PRED</td>
</tr>
<tr>
<td>G</td>
<td>25</td>
<td>White</td>
<td>III, IV</td>
<td>23</td>
<td>DODKT</td>
<td>Basilixumab</td>
<td>TMA (biopsy)</td>
<td>TAC, MPA, PRED</td>
</tr>
</tbody>
</table>
We observed a mean corticoid dose reduction of 4.02 mg (Q1 2.5, Q3 5). Dose was not modified in 4 patients after the beginning of Belimumab IV. As exceptions, in 1 patient we added corticoids to treatment (dose of 5 mg/day) and in another one we doubled corticoid dose, until a maximum dose of 20 mg/day. Belimumab treatment was definitive discontinued in 5 patients because of drug allergy and primary pulmonary hypertension. As we observed, an important percentage of patients (in our sample dose to 90%) take usually corticoids, with the clinical consequences and development of comorbidities in a long time and adverse events related to this therapy. Diary dose is reduced in 57.9% of our patients, even in those patients who have discontinued Belimumab treatment, in which we observed a dose reduction too.

Disclosure of Interests: None declared


**AB0465** EFFECTIVENESS AND SAFETY OF IGURATIMOD IN PATIENTS WITH PRIMARY SJÖGREN SYNDROME: A FOLLOW-UP STUDY

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Background: Primary Sjögren’s syndrome (pSS) is a chronic autoimmune disorder affecting 0.2–3% of the population. However, there are currently no effective systemic therapies. Anti-Ro, anti-La and rheumatoid factor (RF) as well as hyper γ-globulinaemia indicate a degree of B cell hyperactivity. In the recent ten years, iguratimod (T-614) has been used to treat RA as a novel immunomodulatory, which functions by suppressing the production of some inflammatory cytokines, as well as reducing immunoglobulin production by acting directly on human B lymphocytes without affecting B lymphocyte proliferation.

Objective: We evaluated the effectiveness and safety of iguratimod on pSS patients in this follow up study.

Methods: A total of 21 pSS patients without severe systemic damage needing corticosteroid were recruited to receive iguratimod 25mg Bid for 12 weeks.

Results: Among them, 1 patient and 2 patients withdrew because of kidney dysfunction and inefficacy. For those 18 patients who finished the follow up, 94.4% were females and average age were 46.5±13.8 year-old with median disease duration of 22.0 (9.8, 58.5) months. Compared with baseline, ESSDAI score, hyperglobulinaemia and ESR was significantly decreased after iguratimod treatment (Table). Two of the 18 patients presented with decreased white blood cell count. This side effect ameliorated in one patient after tapering the dose to 25mg Qd and in another patient after 2 weeks without any intervention.

**Table. Effectiveness of iguratimod in pSS**

<table>
<thead>
<tr>
<th>Baseline</th>
<th>12w P value</th>
<th>24w P value</th>
<th>48w P value</th>
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<tr>
<td>IgG</td>
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</tr>
<tr>
<td>23.19±5.50</td>
<td>0.009</td>
<td>18.52±4.64</td>
<td>0.064</td>
</tr>
<tr>
<td>IgM</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.27±0.39</td>
<td>0.006</td>
<td>0.97±0.39</td>
<td>0.001</td>
</tr>
<tr>
<td>IgA</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>4.16±3.30</td>
<td>0.005</td>
<td>3.29±1.07</td>
<td>0.045</td>
</tr>
<tr>
<td>ESR</td>
<td></td>
<td></td>
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<tr>
<td>26.69±1.62</td>
<td>0.015</td>
<td>15.57±0.89</td>
<td>0.029</td>
</tr>
<tr>
<td>FACIT</td>
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</tr>
<tr>
<td>-17.68</td>
<td>0.001</td>
<td>-11.28±0.78</td>
<td>0.004</td>
</tr>
<tr>
<td>ESSDAI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4.52±2.5</td>
<td>0.001</td>
<td>2.08±1.44</td>
<td>0.004</td>
</tr>
</tbody>
</table>

Conclusion: This is the first follow study of iguratimod in pSS to show benefit with good tolerance.

**REFERENCES**


Disclosure of Interests: Hui Gao Grant/research support from: This work was supported by grant from PANDA (Z-2014-06-2-1637)., Xiao-ying Zhang: None declared, Xue-wu Zhang: None declared, Zhaoguo Li: None declared.


**AB0464** EFFECTIVENESS AND SAFETY OF ABATACEPT FOR 24 MONTHS IN PATIENTS WITH PRIMARY SJÖGREN’S SYNDROME (PSS)

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Introduction: Primary Sjögren’s syndrome (SSp) is a systemic autoimmune disease concerning the exocrine glands and internal organs. Therapeutic options mainly include symptomatic and supportive measures, whereas traditional immunosuppressive drugs have not presented efficacy in randomized trials. Abatacept is a T-cell co-stimulation modulator and there are evidences that this drug may be effective for treating PSS.

Objectives: The objective of this trial was to evaluate effectiveness and safety of abatacept for 24 months in the treatment of pSS.

Methods: Observational prospective study for 24 months. It was included 11 patients that filled the American-European Consensus criteria (2002). Patients received abatacept according the weight < than 60 kilos (500mg), 60 kilos to 100 kilos (750 mg) per month for 24 months. It was evaluated Sjögren’s syndrome disease activity index (ESSDAI), salivary flow with no stimulation for 15 minutes, Schimmer’s ophthalmologic evaluation tests, Ocular Staining Score (OSS) e Break up time, quality of life by Medical Outcome Survey Short Form 36 (SF-36) and fatigue by FACIT Fatigue - The Functional Assessment of Chronic Illness Therapy. For statistical analysis was used the Wilcoxon’s test for related samples and test T of Student to paired samples. The significance level of 5% was adopted and analyzes were accomplished in the R program (version 3.5.1).

Results: This study was constituted from 11 women between the ages 25 to 81 years (average: 53.73 ± 15.07 years), being the majority Afro-descendant women (54.5%). Of this total, 90.9% presented positive anti-nuclear antibody (ANA), 81.8% positive anti-SSA, and 90.9% positive rheumatoid factor. In relation to ESSDAI, 81.8% of the participants presented scores greater than 5. There was a statistically significant reduction in the ESSDAI IC 2.99 [-0.49; 7.99] (p = 0.013). Between the sub items of the ESSDAI, the ones that demonstrated the greatest modifications were articular and glandular. There was a significant increase in the salivary flow of the participants (df = 0.90; IC-95%: -1.50; -0.50) after 24 months of treatment. There was no statistical difference between the beginning and after 24 months of treatment in the different evaluations. Schimmer’s ophthalmologic right eye IC 2.26 [-3.50; 12.5] p=0.423. Break up time OD 0.50 [-1.00; 2.49] p=0.307, OSS right eye IC: 0.50 [-2.50; 5.50] p=0.721. In the SF36 only in the Limitation for Emotional Aspects sub scale reported significant improvement (df = 36.4; IC95%: -67.1; -5.57; p = 0.025), and FACIT presented no evidences of significant changes between pre and post treatment p = 0.392.

Conclusion: The study demonstrates limitations due to the few number of patients included and for being an open study not controlled, but we observed a statistically significant reduction in the ESSDAI, increase in the salivary flow and in the sub scale Limitation for Emotional Aspects of the SF36, indicating a positive effect in the disease.

REFERENCES


Disclosure of Interests: None declared

ADVERSE EVENTS AND THE RELAPSE RISK OF SYSTEMIC LUPUS ERYTHEMATOSUS DURING HYDROXYCHLOROQUINE TREATMENT

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Background: The antimalarial drug hydroxychloroquine (HCQ) is used worldwide to control the disease activity of systemic lupus erythematosus (SLE). In Japan, HCQ was not approved until September 2015 due to the problem of retinopathy induced by chloroquine. There is insufficient evidence of the effects of HCQ or adverse events linked to HCQ treatment.

Objectives: Here, we evaluated adverse events and the relapse risk of SLE during HCQ treatment.

Methods: We retrospectively analyzed the data of 109 patients diagnosed with SLE and treated with HCQ for >12 months at Nagasaki University Hospital and community hospitals. The demographic data included the patient's age at the onset of SLE, gender, the disease duration of SLE (the time from the diagnosis of SLE until the renal biopsy), comorbidities of Sjögren syndrome (SS)/anti-phospholipid syndrome (APS), and the treatment for induction. We identified the risk of adverse events and relapse at 12 months after the introduction of HCQ. Decision tree models predicting relapse were built with the Classification and Regression Trees (CART) algorithm. The data of the length of time between a patient's HCQ induction to the first observation of relapse was analyzed by the Kaplan-Meier method with a log-rank test.

Results: Most of the patients were female (88.1%). The median age at the introduction of HCQ was 40.0 years (interquartile range [IQR] 30.5–50.0 years), and the SLE disease duration was 95 months (IQR 38.0–184.5 months). The mean observation period after HCQ introduction was 12 months. The comorbidity rates of SS and APS were 25.7% and 18.4%, respectively. The SELENA-SLEDAI scores were significantly decreased at 3 months post-HCQ introduction. The dose of oral prednisolone was significantly decreased at 6 months post-HCQ introduction. Eighty-six patients (79.8%) were continuing HCQ at 12 months post-introduction. Adverse events occurred in 27 patients (24.8%), including skin rashes (n=11, 10.1%) and gastrointestinal symptoms (n=6, 5.5%). The sole predictive factor for adverse events was the white blood cell (WBC) count at baseline (odds ratio: 0.9977, 95%CI: 0.9994–0.9999, p=0.0285). Twelve of 86 patients (14.0%) experienced relapse that required the start of prednisolone or an immunosuppressant or an increased prednisolone dose. The multivariate analysis revealed that the C4 value at baseline was a predictive factor of relapse (odds ratio: 0.841, 95%CI: 0.718–0.999, p=0.0097). The cut-off point determined by the CART algorithm showed that C4 ≥9.3 mg/dl at baseline provides the best performance for predicting relapse. The Kaplan-Meier analysis showed that compared to C4<9.3 mg/dl at baseline, C4 ≥9.3 mg/dl at baseline was correlated with being free from relapse (p=0.0032).

Conclusion: A lower C4 value at HCQ introduction was a predictive factor for the relapse of SLE, and a lower WBC count was a predictive factor for adverse events.

REFERENCES


IMPROVED DISEASE CONTROL OF SYSTEMIC LUPUS ERYTHEMATOSUS AND ITS POSSIBLE ASSOCIATION WITH AGGRESSIVE USE OF IMMUNOSUPPRESSANTS

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Background: The outcome of patients with systemic lupus erythematosus (SLE) has considerably improved in recent decades.

Objectives: The aim of this retrospective study was to examine whether the disease control has been actually improved and its possible association with the altered balance between the use of immunosuppressants and glucocorticoids.

Methods: We enrolled SLE patients who visited Toho University Ohashi Medical Center during 2012-2017 (Group A, 79 patients), and compared them with patients during 1999-2003 (Group B, 68 patients; not overlapping with Group A). All the patients met the American College of Rheumatology 1997 revised criteria for SLE classification. Patient backgrounds, the dose of glucocorticoids and the use of immunosuppressants at the times of SLE onset and disease flare were reviewed from the medical records. The disease flare was defined as a new BILAG 2004 A or B score in at least one system.

Results: The age at disease onset and sex, as well as the presence of lupus nephritis and serositis were comparable between 2 groups, although central nervous system manifestations were less frequent in Group A (7% versus 16% in Group B, p=0.04). The number of flare per person-year was significantly reduced in Group A than Group B (0.26 versus 0.4, respectively, p<0.01). In the initial treatment, the median dosage of oral prednisolone was equivalent in both groups (30 mg/day, p=0.64), while the total glucocorticoid dosage in the initial 16 weeks was significantly reduced in Group A (1,960 mg prednisolone equivalent versus 2,913 mg in Group B, p=0.01). And the inclusion rate of immunosuppressants in the initial SLE treatment was significantly higher in Group A (43% versus 6% in Group B, p=0.01). Further, upon disease flare, the use of prednisolone for it was significantly lower in Group A (6.5 mg/day versus 14 mg/day in Group B, p<0.01) and the rate of introduction or alteration of immunosuppressants were significantly higher in Group A (81% versus 24% in Group B, p=0.01). Infection rates were similar between the groups (p=0.44).

Conclusion: Aggressive use of immunosuppressants in recent years resulted in the reduction of the rate of SLE flare as well as that of cumulative glucocorticoid dosage.

REFERENCES

Disclosure of Interests: Chihiro Imaiuzumi: None declared, Yukinoue: None declared, Takaharu Kagttagiri: None declared, Sayaka Takanaka: None declared, Hideki Ito: None declared, Ayako Hirata: None declared, Takehisa Ogura: None declared, Hideto Kameda. Toho University. Division of Rheumatology, Department of Internal Medicine, Tokyo, Japan

QUALITY OF LIFE IN SYSTEMIC LUPUS WOMEN WITH CUTANEOUS DAMAGE ON THE FACE: COSMETIC CAMOUFLAGE IMPACT

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**Background:** Health-related quality of life (HRQoL) can be negatively impacted by visible skin lesions.1

**Objectives:** To investigate the effect of cosmetic camouflage on health-related quality of life of systemic lupus erythematosus (SLE) women presenting sequelae of cutaneous manifestations on the face.

**Methods:** This is a randomized controlled clinical trial (Universal Trial Number: U1111-1210-2554a) with outpatient SLE women according to ACR/1997 and/or SLICC/2012 criteria, aged over 18 years old with sequelae of cutaneous lupus manifestations on the face, recruited in two tertiary centers. Exclusion criteria were: moderate to severe systemic lupus activity (SLEDAI 2k-modified) & no understanding of the questionnaire or psychological or psychiatric treatment initiation or modification during the study. A total of 43 patients was divided into group I (cosmetic camouflage n=28) and group II (control n=15). Patients in group I were instructed to use cosmetic camouflage daily. Group II patients did not use any camouflage. SLE Quality of Life (SLEQoL) and Dermatology Quality of Life Index (DLQI) questionnaires were used to evaluate HRQoL, higher scores meaning worse HRQoL. All patients answered the questionnaires at baseline (T0) and after 12 ±2 weeks (T1). The primary end point was a change on HRQoL after camouflage cosmetic use. Continuous variables were described as median (interquartile range). Wilcoxon signed rank test and the Mann-Whitney U test were used for the analysis as indicated. End points were investigated per-protocol analysis, and a 2-sided p value <0.05 was considered to be significant.

**Results:** Both groups were similar at baseline regarding age [group I: 45.0 (37.3-55.7) years old versus group II: 50.0 (43.0-55.0) years old, p=0.575], disease duration [group I: 17.5 (7.3-26.5) years versus group II: 15.9 (9.0-17.0) years, p=0.452] and modified SLEDAI-2K [group I: 0 (0-2) versus group II: 2 (0-2), p=0.301]. Also, they were similar considering the sociodemographic, clinical and treatment characteristics of the disease. The SLEQoL and DLQI scores decreased in the cosmetic camouflage group from baseline: DLQI [T0: 8.5 (4.0-16.0) versus T1: 3.0 (1.0-7.5), p=0.008]; SLEQoL [T0: 118.0 (91.0-154.3) versus T1: 95.5 (76.0-135.0), p=0.003]; while there was no variation in the control group: DLQI [T0: 8.9 (5.0-12.0) versus T1: 7.0 (4.0-12.0), p=0.196]; SLEQoL [T0: 89.0 (65.0-127.0) versus T1: 95.5 (65.0-164.0), p=0.036]. The difference on the variations of HRQoL scores between groups I and II was statistically significant: DLQI [group I: -3.0 (-10.8-0.0) versus group II: 1.0 (-1.0-6.0), p=0.003] and SLEQoL [group I: -14.5 (-33.0-0.0) versus group II: 3.0 (-8.0-10.0), p=0.039]. The SLEQoL score variations were on physical function (p=0.033), humor (p = 0.033) and self-image (p=0.031) domains.

**Conclusion:** In this group of SLE women with low systemic disease activity and sequelae of cutaneous manifestations on the face, we observed an improvement of HRQoL after daily use of cosmetic camouflage. It is an effective intervention that should be recommended by rheumatologists.

**REFERENCES**


**Disclosure of Interests:** None declared

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THE EFFECTS OF ACUPUNCTURE ON XEROSTOMIA, XEROPHTHALMIA AND ANTIBODY MODIFICATION IN PATIENTS WITH SJÖGREN SYNDROME: A META-ANALYSIS

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**Background:** Xerostomia and xerophthalmia are common chief complaints among patients with Sjögren syndrome (SS) but there has been no satisfying pharmacy to relieve the associated symptoms; hence the effectiveness of other non-pharmacological interventions such as acupuncture should be accessed.

**Objectives:** To access the therapeutic effects of acupuncture on xerostomia and xerophthalmia in patients with SS.

**Methods:** We conducted a meta-analysis of randomized clinical trials (RCTs) which evaluated the effectiveness of xerostomia and xerophthalmia in SS. PubMed, Embase, Cochrane Central Register of Controlled Trials (CENTRAL), Chongqing Weipu Database (CDVIP), China Academic Journal Full-text Database, AntiLibrary, Chinese Electronic Periodicals Service (CEPS), China National Knowledge Infrastructure (CNKI) Database were searched through Oct, 2018 to select studies. Data for evaluation of subjective and objective xerostomia was extracted and was assessed with random-effects meta-analysis.

**Results:** After searching, a total of 680 references were yielded and five RCTs were included, covering 460 patients dry mouth resulted from SS, among whom 229 patients received acupuncture and 231 patients were control group. Acupuncture group was associated with higher subjective response rate (odds ratio 3.036, 95% confidence interval [CI] 1.828 – 5.042, P < 0.001, Fig. 1) and increased salivary flow rate (weighted mean difference [WMD] 3.066, 95% CI 2.969 – 3.164, P < 0.001, Fig. 2), as an objective marker. Regarding xerophthalmia, acupuncture group revealed less dry eye visual analog scale (VAS, WMD -1.035, 95% CI -1.457 - -1.673, P < 0.001, Fig. 3), and better Schirmer test (WMD 2.357, 95% CI 1.021 – 3.692, P = 0.001, Fig. 4) and trend of longer break-up time (WMD 4.927, 95% CI -0.055 – 9.908, P = 0.053, Fig. 5). In addition, two studies examined IgG levels, which were lower in the acupuncture group (WMD -166.857, 95% CI -233.138 – -100.576, P < 0.001, Fig. 6).

**Conclusion:** In the present meta-analysis, acupuncture improves both subjective and objective markers of xerostomia and xerophthalmia in patients with SS and is considered as an option of non-pharmacological treatment.

**REFERENCES**


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IMMUNOREGULATORY THERAPY EFFECTIVELY PROMOTES THE BALANCE BETWEEN TREG CELLS AND PRO-INFLAMMATORY LYMPHOCYTES IN SYSTEMIC LUPUS ERYTHEMATOSUS

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**Background:** Recent studies have reported that some drugs such as low-dose interleukin-2, rapamycin, metformin, retinoid acid and coenzyme Q10 could promote the proliferation and functional recovery of regulatory T cells (Treg) in patients with autoimmune diseases. However, the effects on the balance of Treg cells and pro-inflammatory lymphocytes and long-term efficacy have rarely been reported.

**REFERENCES**


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Objectives: To evaluate the changes of peripheral lymphocyte subsets, conventional drugs and remission rate in patients with systemic lupus erythematosus (SLE) after immunomodulatory therapy.

Methods: A total of 89 patients with SLE from the Second Affiliated Hospital of Shanxi Medical University from January 2016 to April 2018 were enrolled, who were divided into well-controlled group and untargeted control group taking a full consideration of the patient’s symptoms, signs and related laboratory findings. We measured the absolute counts of B, NK, CD8+T and helper T 1 (Th1), helper T 2 (Th2), helper T 17 (Th17) and Treg cells in peripheral blood of patients before immunomodulatory therapy and during the 3 months and 6 months of follow-up and 93 sex- and age- matched control individuals using flow cytometry. Moreover, the ratios of various cells to Treg cells were calculated.

Results: Compared with healthy controls, Treg cells in SLE patients were significantly lower before the treatment with immunomodulator, while the ratios of various pro-inflammatory lymphocytes to Treg cells (such as Th2/Treg, Th17/Treg, CD8+T/Treg, etc.) were higher. After 3 months and 6 months with immunomodulatory therapy, the absolute number of Treg cells in peripheral blood of SLE patients increased obviously reaching to normal level. Accordingly, the ratios of various pro-inflammatory lymphocytes to Treg cells recovered. At the same time, the dose of glucocorticoid and disease-modifying antirheumatic drugs (DMARDs) decreased distinctly. Additionally, the well-controlled group was able to maintain a high remission rate, and the untargeted control group could achieve a higher response rate after immunomodulatory treatment.

Conclusion: The imbalance between pro-inflammatory lymphocytes and Treg cells caused by the significant decrease of Treg cells may be the main cause of SLE. And immunomodulatory therapy we came up with may reverse the imbalance of proinflammatory lymphocytes and Treg cells, and which is a potential and effective treatment for SLE.

REFERENCES

Disclosure of Interests: None declared

AB0471 VITAMIN D SUPPLEMENTATION IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH VITAMIN D DEFICIENCY AND INSUFFICIENCY: THE EFFECT ON DISEASE ACTIVITY, FATIGUE AND INTERFERON SIGNATURE GENE EXPRESSION
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Background: Vitamin D deficiency is highly prevalent among patients with systemic lupus erythematosus (SLE) [1]. Evidence from multiple studies has shown that vitamin D deficiency in SLE is associated with a higher disease activity [2]. There is conflicting evidence with regards to the relationship between fatigue and vitamin D level [3,4].

Objectives: The principal aim of this study was to establish any potential effect on the level of fatigue, disease activity (measured by SLE disease activity index-2K (SLEDAI-2K)) and interferon signature gene expression, from vitamin D supplementation to SLE patients with vitamin D deficiency or insufficiency.

Methods: 33 SLE patients, 13 with vitamin D deficiency and 20 with vitamin D insufficiency, gave informed consent to participate in this 12 month prospective study. Their participation consisted of an interview, filling of the Fatigue Severity Scale (FSS), and blood tests. The patients were advised to take vitamin D3 8000IU daily for 8 weeks if they were vitamin D deficient, or 8000IU daily for 4 weeks if they were insufficient. This was followed by 2000IU daily maintenance. The patients were reassessed after 6 and 12 months of vitamin D supplementation. RNA was extracted from whole blood taken from the patients at baseline and after 6 months of vitamin D supplementation. The expression of 12 interferon signature genes was measured in the extracted RNA by using Quant-it Gene Plex technology. Approval to carry out this study was obtained from the University Research Ethics Committee.

Results: 87.9% of SLE patients studied were female. The mean age was 47.6 years and the mean duration of SLE was 13.8 years. Table 1 shows the results obtained for several variables at baseline, after 6 months and after 12 months. The expression of all 12 interferon signature genes measured, was noted to decrease following 6 months of vitamin D supplementation. This reached statistical significance for two of the genes measured (OAS1, p=0.014; SOCS51, p=0.003).

Table showing results at baseline, after 6 months and after 12 months of vitamin D3 supplementation.

Abstract AB0471 Table 1. Table showing results at baseline, after 6 months and after 12 months of vitamin D3 supplementation.

Conclusion: The results indicate that vitamin D supplementation in SLE patients who are deficient or insufficient, results in an improvement in disease activity, and possibly also in the level of fatigue. This could be explained by the decrease in the expression of interferon signature genes.

REFERENCES

Disclosure of Interests: None declared
PRIMARY SJÖGREN SYNDROME ASSOCIATED INTERSTITIAL LUNG DISEASE: FEATURES, TREATMENT AND OUTCOME OF A MONOCENTRIC COHORT

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Background: Primary Sjögren’s syndrome (pSS) is an autoimmune systemic disease characterized by lymphocytic infiltration of exocrine glands, mainly resulting in dysfunction of salivary and lacrimal glands and symptomatic xerostomia and xerophthalmia. About one third of patients also present extra-glandular manifestations and, among them, interstitial lung disease (ILD) is one the most frequent, occurring in about 10–20% of patients. ILD is associated with an impaired quality of life and physical capacity and to a reduced 10-year survival. Despite it seems to be more frequently detected in late stages of the disease, some authors suggest that ILD can be diagnosed before pSS in 20% of cases. Main predictive factors of progression of pSS-ILD have not been clearly investigated in previous studies and no evidence-based treatment is defined for these patients.

Objectives: To describe the clinical and serologic features and the outcome of a monocentric cohort of pSS-ILD and the possible differences between patients treated or not with immunosuppressive treatment

Methods: We retrospectively evaluated the 37 pSS-ILD patients followed at our Rheumatology Unit (male/female ratio 1/6.4, mean age 69.6±11.3 years, mean disease duration of pSS 5±5.2 years).

Among them, 18 patients (48.6%; group 1) underwent immunosuppressive treatment because of lung disease, namely mycophenolate mofetil (9 patients, 50%), cyclophosphamide (3, 16.7%), azathioprine (5, 27.8%), high dose steroids (1, 5.6%), while 19 patients were not treated (group 2).

Results: No significant differences were observed in regard of age, male/ female ratio, and disease duration of ILD and pSS, while a significant difference was observed regarding the lung function of the 2 groups; the forced vital capacity (FVC) and the diffusion lung capacity of CO (DLCO) at baseline were significantly lower in the group 1 (FVC 78.6% vs 99.4% p=0.008; DLCO 45.7% vs 56.9%, p=0.025; in group 1 and group 2, respectively). No significant difference was observed between baseline and follow-up for FVC and DLCO in both groups, regardless the immunosuppressive drug (fig. 1). At the end of follow-up FVC increased, decreased and remained stable in 5.3% vs 10.5/84.2% and 16.7±27/855.6%, in group 1 and group 2, respectively; DLCO increased, decreased and remained stable in 10.5/21/168.4% of group 1, while remained stable or decreased in 61.1 and 38.9 of treated patients, respectively (fig. 1).

Conclusion: At our knowledge, few studies have investigated the features of pSS-ILD and the role of immunosuppressive drugs in these patients. Our data suggest that the decline of lung function is one of the most significant parameters to guide the prescription of immunosuppressive drugs, but no differences can be observed according to the treatment in term of effectiveness. However, no studies have investigated the correctness of this approach or the efficacy of the MMF or GEX in pSS-ILD. Our study is strongly limited by the retrospective design and the low number of patients evaluated, but these data set attention on this unmet need. Further prospective studies are mandatory to clarify the impact of ILD in pSS patients and the correct therapeutic approach.

REFERENCES


Disclosure of Interests: None declared

AB0473 HYPOGAMMAGLOBULINEMIA AND INFECTIONS IN RHEUMATOLeAT PATIENTS TREATED WITH RITUXIMAB

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Background: Treatment with rituximab (RTX) for rheumatologic diseases may produce hypogammaglobulinemia (hygoglob) (1,2), and that way increase the risk to acquire certain infections (3,4). There are no established guidelines to evaluate and treat hygoglob in these patients. In our hospital, the percentage of patients who develop hygoglob and severe infections is unknown.

Objectives: To analyse the effect of RTX on immunoglobulin (lg) levels and to evaluate the severe infections and hepatitis B reactivations that could be related to this treatment.

Methods: This is a descriptive, retrospective study of patients followed up in the Rheumatology Unit of the Alicante General University Hospital (HGUA) who had received at least one course of RTX. Clinical characteristics and laboratory parameters were obtained from the electronic charts: type of disease, posology and total amount of RTX, lg levels before and after treatment with RTX, the concomitant treatment with disease-modifying drugs (DMDs), hepatitis B virus’s (HBV) reactivations and infections that required hospitalization. Hygoglob was assessed when IgG < 750 mg/dl, and severe hygoglob if IgG < 450 mg/dl. The association of hygoglob with disease and treatment’s aspects was studied by t-Student, U-Mann-Whitney and Chi-2. Multiple logistic regression was conducted to study the independent risk factors associated with hygoglob. The study was approved by the Hospital Ethics Committee.

Results: Finally 106 patients were included, 85 women (80.2%) and 21 men (19.8%). The more frequent conditions were rheumatoid arthritis (47.2%), Sjögren syndrome (16%), Systemic Lupus Eritematosus (13.2%), vasculitis (6.6%) and other connective tissue diseases (10.4%). Characteristics of the sample are shown in table 1. A correct follow up of the Ig levels during the treatment was shown to be undergone in 87.7% of the cases. It was found that 35.8% of the patients presented hygoglob and 13.2% presented severe infections after receiving RTX. No HBV reactivations were found. Among the patients with hygoglob, 78.9% received concomitant treatment with other immunosuppressants (methotrexate 23.6%, leflunomide 23.6%). Hygoglob was more frequent in rheumatoid arthritis (44%), lupus (42.8%) and vasculitis (28.6%). Through simple logistic regression hygoglob during treatment was associated with the presence of previous hygoglob (p=0.005), higher doses received (p=0.001) and longer treatment (p=0.003). In the multiple logistic regression, only low levels of Ig before treatment turned out to be an independent risk factor for hygoglob during treatment (OR 6.86; IC 1.25-37.57). The IgM and IgA levels, but not the IgG levels were significantly lower in patients who has severe infections.

Disclosure of Interests: None declared

AB0474 COHORT INTERSTITIAL LUNG DISEASE: FEATURES, TREATMENT AND OUTCOME OF A MONOCENTRIC COHORT

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Background: To describe the clinical and serologic features and the outcome of a monocentric cohort of pSS-ILD and the possible differences between patients treated or not with immunosuppressive treatment

Methods: We retrospectively evaluated the 37 pSS-ILD patients followed at our Rheumatology Unit (male/female ratio 1/6.4, mean age 69.6±11.3 years, mean disease duration of pSS 5±5.2 years).

Among them, 18 patients (48.6%; group 1) underwent immunosuppressive treatment because of lung disease, namely mycophenolate mofetil (9 patients, 50%), cyclophosphamide (3, 16.7%), azathioprine (5, 27.8%), high dose steroids (1, 5.6%), while 19 patients were not treated (group 2).

Results: No significant differences were observed in regard of age, male/ female ratio, and disease duration of ILD and pSS, while a significant difference was observed regarding the lung function of the 2 groups; the forced vital capacity (FVC) and the diffusion lung capacity of CO (DLCO) at baseline were significantly lower in the group 1 (FVC 78.6% vs 99.4% p=0.008; DLCO 45.7% vs 56.9%, p=0.025; in group 1 and group 2, respectively). No significant difference was observed between baseline and follow-up for FVC and DLCO in both groups, regardless the immunosuppressive drug (fig. 1). At the end of follow-up FVC increased, decreased and remained stable in 5.3% vs 10.5/84.2% and 16.7±27/855.6%, in group 1 and group 2, respectively; DLCO increased, decreased and remained stable in 10.5/21/168.4% of group 1, while remained stable or decreased in 61.1 and 38.9 of treated patients, respectively (fig. 1).

Conclusion: At our knowledge, few studies have investigated the features of pSS-ILD and the role of immunosuppressive drugs in these patients. Our data suggest that the decline of lung function is one of the most significant parameters to guide the prescription of immunosuppressive drugs, but no differences can be observed according to the treatment in term of effectiveness. However, no studies have investigated the correctness of this approach or the efficacy of the MMF or GEX in pSS-ILD. Our study is strongly limited by the retrospective design and the low number of patients evaluated, but these data set attention on this unmet need. Further prospective studies are mandatory to clarify the impact of ILD in pSS patients and the correct therapeutic approach.
Patients with hypogammaglobulinemia in a third of the patients who received RTX, especially in those who have low previous IgG levels; therefore a follow up during the treatment should be encouraged. Low IgM and IgG levels during the treatment could also be associated with severe infections.

**REFERENCES**


**Disclosure of Interests:** Atanas Fereid: None declared, Mariano Andres: None declared, Jenny de la Torre-Aboki: None declared, Paloma Vela-Andres Fierro: None declared, Mariano Andres: None declared.

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**AB0474**

**MORTALITY ACROSS RITUXIMAB-TREATED PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS: RESULTS FROM THE BRITISH ISLES LUPUS ASSESSMENT GROUP (BILAG) REGISTRY**

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**Background:** Mortality in Systemic Lupus Erythematosus (SLE) is elevated compared to the general population. Previously we have demonstrated improved disease control in response to Rituximab (RTX) therapy in a cohort of refractory SLE patients.

**Objectives:** To investigate mortality in refractory SLE patients treated with RTX and identify risk factors that may be associated with death.

**Method:** All patients recruited to the BILAG-BR (both RTX treated and standard care-SOC) were included from initial study visit to death or 3 years post last treatment change. Demographics, concurrent medication use, disease activity (BILAG/SLEDAI) and damage scores (SLICC-DI) were recorded. Information regarding mortality was collected from study centres and NHS digital mortality registries. Baseline demographic data are presented using descriptive statistics. Testing for association was performed using Stata (version 14).

**Results:** 830 patients were included (715 RTX-treated, 115 standard therapy). RTX-treated patients tended to have longer disease duration (10 vs 6.5 years respectively) and were more likely to have active musculoskeletal disease (% BILAG A or B: 39 vs 23%). Rates of renal (11% vs 16%) and neurological disease (12% vs 9%) were comparable between groups as were baseline SLICC-DI and SLEDAI scores. 33 deaths were reported. 28 (3.9%) RTX-treated patients (1.2 deaths/100 pt yrs follow up) and 5 (4.3%) non-RTX patients (1.5 deaths/100 pt yrs follow up).

**Conclusion:** Decompensation of cardiovascular risk factors, higher steroid doses, hypogammaglobulinemia and renal disease. Active management of these risk factors may lead to improved mortality outcomes.

**Table 1. Deceased and alive RTX treated patients**

<table>
<thead>
<tr>
<th>Gender</th>
<th>Age</th>
<th>Ethnicity</th>
<th>Cumulative Rituximab dose in mg</th>
<th>Median Age at Diagnosis in years (IQR)</th>
<th>Median Disease duration in years (IQR)</th>
<th>Median Cumulative Rituximab dose in mg (IQR)</th>
<th>Cause of death</th>
</tr>
</thead>
<tbody>
<tr>
<td>M/F: M (F)</td>
<td>708</td>
<td>27/434</td>
<td>2000 (2000-4000)</td>
<td>51.54 (42.5-66.5)</td>
<td>13 (11-19)</td>
<td>2000 (2000-4000)</td>
<td>Infection</td>
</tr>
<tr>
<td>Male</td>
<td>636/142</td>
<td>37/27</td>
<td>39 (30-49)</td>
<td>12.27 (11-16)</td>
<td>(n=647)</td>
<td>60% and 60%</td>
<td>Infection</td>
</tr>
</tbody>
</table>

**Disclosure of Interests:** Aysun Aksoy: None declared, Stephen McDonald: None declared, Eoghan McCarthy: None declared, Ben Parker Grant: research support from: GSK, Consultant for: AZ, UCB, GSK, Ian N Bruce Grant:research support from: Genezyme Sanofi, GlaxoSmithKline, Consultant for: AstraZeneca, Eli Lilly, GlaxoSmithKline, ILTOO Pharma, Medimmune, Merck Serono, Speakers bureau: GlaxoSmithKline, UCB Pharma.


**AB0475**

**BELIMUMAB: EXPERIENCE IN CLINICAL PRACTICE SETTINGS AT A RHEUMATOLOGY DEPARTMENT IN A TERTIARY HOSPITAL**

Carolina Merino Aragonú1, Olga Rusinovich1, Consuelo Ramos Gráldez2, María Espinosa1, Hilda Godoy2, Carmen Barbadillo Mateos1, Jose Campos Estebar1, Mercedes Jiménez Palop2, Jesús Sanz1, Luis Fernando Villa Alcázar2, Carlos Isasi Zaragoza2, Monica Fernandez Castro2, José Luis Andreu Sánchez1, Hospital Puerta de Hierro, Majadahonda (Madrid), Spain; 2Valme Hospital, Sevilla, Spain; 3Hospital Infanta Sofia, Madrid, Spain

**Background:** Belimumab is a human IgG1 monoclonal antibody directed against BAFF, a B lymphocyte survival factor. It is indicated as adjuvant treatment in adult patients with active systemic lupus erythematosus (SLE), with positive autoantibodies and with a high degree of activity of the disease despite standard treatment.

**Objectives:** To describe a sample of patients diagnosed with SLE who received treatment with belimumab in a tertiary hospital.

**Table 1. Distribution of demographic and clinical characteristics of patients with systemic lupus erythematosus**

<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Caucasian</th>
<th>Non-Caucasian</th>
<th>Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female</td>
<td>77.27%</td>
<td>24%</td>
<td>77.27:24</td>
</tr>
<tr>
<td>Male</td>
<td>62.05%</td>
<td>37.95%</td>
<td>62:38</td>
</tr>
</tbody>
</table>

**Disclosure of Interests:** Carolina Merino Aragonú: Consultant for: UCB, Abbvie, Lilly, Speakers bureau: Lilly, None declared, Olga Rusinovich: Consultant for: Sanofi, Lilly, Speakers bureau: Lilly, None declared, Consuelo Ramos Gráldez: Consultant for: Sanofi, Lilly, Speakers bureau: Lilly, None declared, María Espinosa: Consultant for: Sanofi, Lilly, Speakers bureau: Lilly, None declared, Hilda Godoy: Consultant for: Sanofi, Lilly, Speakers bureau: Lilly, None declared, Carmen Barbadillo Mateos: Consultant for: Sanoﬁ, Lilly, Speakers bureau: Lilly, None declared, Jose Campos Estebar: Consultant for: Sanoﬁ, Lilly, Speakers bureau: Lilly, None declared, Mercedes Jiménez Palop: Consultant for: Sanoﬁ, Lilly, Speakers bureau: Lilly, None declared, Jesús Sanz: Consultant for: Sanofi, Lilly, Speakers bureau: Lilly, None declared, Luis Fernando Villa Alcázar: Consultant for: Sanoﬁ, Lilly, Speakers bureau: Lilly, None declared, Carlos Isasi Zaragoza: Consultant for: Sanofi, Lilly, Speakers bureau: Lilly, None declared, Monica Fernandez Castro: Consultant for: Sanofi, Lilly, Speakers bureau: Lilly, None declared, José Luis Andreu Sánchez: Consultant for: Sanofi, Lilly, Speakers bureau: Lilly, None declared.
Methods: Retrospective longitudinal unicentric observational study. Clinical records of all patients diagnosed with SLE who had received treatment with belimumab were reviewed. Demographic characteristics, clinical manifestations and reason for belimumab indication were collected.

Results: The twelve patients included in the sample were women. Median age was 48.5 years (31-70). The most frequent reason for indication of belimumab was uncontrolled arthritis. The average time of treatment with belimumab in the total sample was 27.5 (+/-26.24) months, with a median of 12 months (4-78). Mean treatment time (cases in which belimumab was discontinued excluded) was 31.25 (+/-26.98) months with a median of 25 (5-78). The average dose reduction of prednisone after initiation of treatment with belimumab (in patients in which it was considered effective) was 5 mg per day (+/- 5). It should be noted that of the 14 cases, treatment was only discontinued in 4 patients, 2 of which were withdrawn due to ineffectiveness. There were 2 adverse events that required drug withdrawal: neutropenia and urethral carcinoma. (Table).

Conclusion: BLM is a well tolerated drug and effective in clinical practice. Adverse effects leading to drug withdrawal are infrequent.

Disclosure of Interests: Carolina Merino Arguménez: None declared, Olga Rusinovich: None declared, Consuelo Ramos Giráldez Speakers bureau: Sanofi, María Espinosa: None declared, Hilda Godoy: None declared, Carmen Barbalho Mota: None declared, Jose Campos Esteban: None declared, Mercedes Jiménez Palop: None declared, Jesus Saru: None declared, Luis Fernando Villa Alcázar: None declared, Carlos Issai Zaragoza: None declared, Monica Fernandez Castro: None declared, José Luis Andrèu Sánchez: None declared.


AB0476 SPECIAL ASPECTS OF GLUCOCORTICOID THERAPY IN PATIENTS WHO TREATED WITH ANTI-B-CELL AND ANTI-BLYS THERAPY

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Background: The basis of treatment of SLE are glucocorticoids (GCs), which since their introduction into clinical practice, have led to increased survival and reduced early mortality of SLE patients. However, the need to use high doses of GCs, as well as long-term use of medium doses to maintain disease remission, leads to the development of serious adverse reactions. This leads to an increase in the risk of irreversible organ damage. In this regard, it is important to search for ways to prevent the use of high doses of GCs, minimizing the dose of GCs.

Objectives: To assess special aspects and dynamics of oral glucocorticoid (GC) therapy in SLE patients treated with anti-B-cell and anti-Blys therapy.

Methods: The study included 64 SLE pts (51/58F), divided into 3 groups: Group I - 47 patients (SLEDAI2K 16[11;20] scores), receiving rituximab (RTX) iv infusions by drop at 500 - 2000 mg dose-range. Group II included 10 patients (SLEDAI2K 10[8;11] scores) treated with Belimumab (BLM) at 10 mg/kg once a month. The remaining 7 patients from Group III (SLEDAI2K 10[9;16] scores) were administered a combination of RTX and BLM. They started treatment with RTX 500 (2 patients) or 1000 mg (5 patients) infusions, and 3 months later BLM at standard scores at 10 mg/kg once a month was initiated for 8 months. SLICC damage index (DI) was documented at baseline - before initiation of RTX and BLM - in 26 out of 64 patients (40%) with SLICC DI score > 1 (1 - 5 scores); 20 patients out of them were administered RTX.

Results: 47 patients on RTX therapy received different oral GCs doses: high GCs doses (Me 40[30;50]mg/day) were documented in 11 (24%) patients, moderate doses (Me 13[10;20]mg/day) – in 29 (61%) patients, and low doses (Me 5[5;7.5]mg/day) - in 7 (15%) patients. Patients on BLM and combination therapy were administered GCs at doses ≤ 20 mg (Me 15[5;20]mg/day and Me 8.75[5;15] mg/day, respectively). During first 3 month of treatment GCs doses in all 3 Groups remained unmodified. By Mo 6 25% reduction in oral GCs doses was documented in: patients on RTX - 20[15;20]mg/day, 12[8;15;20]mg/day, 5[5;5] mg/day (respectiveiy, in the groups with initially high, moderate and low GCs doses); BLM 10[7;5;10] mg/day, combination therapy 8.75[5;15] mg/day. By Mo 12 Me GCs doses in all 3 Groups did not exceed 10 mg/day. In doses); BLM 10[7,5;10] mg/day, combination therapy 8,75[5;15] mg/day. Unmodified. By Mo 6 25% reduction in oral GCs doses was documented During first 3 month of treatment GCs doses in all 3 Groups remained unmodified. By Mo 6 25% reduction in oral GCs doses was documented in: patients on RTX - 20[15;20]mg/day, 12[8;15;20]mg/day, 5[5;5] mg/day (respectively, in the groups with initially high, moderate and low GCs doses); BLM 10[7;5;10] mg/day, combination therapy 8.75[5;15] mg/day. By Mo 12 Me GCs doses in all 3 Groups did not exceed 10 mg/day. In decreases in SLICC score by Mo 12 of follow up was documented in patients on RTX therapy with baseline pre-existing organ damage (5 patients). There was no increase in SLICC scores in BLM and RTX +BLM treatment groups.

Conclusion: Combination therapy results in achieving rapid control of SLE activity thanks to RTX effects, and the combination with BLM allows significantly prolongs this result, minimizing the risk of exacerbation. And a very specific gain from combination RTX+BLM therapy is a chance to manage patients on moderate-to-low oral GCs doses, therefore, reducing the risk of irreversible organ damage. Increasing organ damage score in RTX Group is most likely associated with intake of higher GCs doses.

Figure 1. The dose of oral GCs in patients treated with RTX, BLM and combined treatment, Me.

Disclosure of Interests: Anna Mesnyankina: None declared, Sergey Solovyev: None declared, Elena Aseeva: None declared, Evgeny Nasonov Speakers bureau: Pfizer, Inc., MSD, Novartis, AbbVie Inc., Celgen Corporation, Biocad, Janssen, UCB, Inc.


AB0477 THE EFFECT OF CLOSTRIDIUM BUTYRICUM ON INTESTINAL FLORA OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS ZHANG MINGXING1, XU-FANG YIN1, XIAO-FENG L1

zhenga mingxing1, Xu-Fang Yin1, Li-Xiao Feng2.1The Second Hospital of Shanxi Medical University, Taiyuan, China; 2The Second Hospital of Shanxi Medical University, Taiyuan, China Objectives: To investigate the effect of Clostridium butyricum on intestinal flora in patients with systemic lupus erythematosus.

Methods: Forty-four patients with systemic lupus erythematosus who were randomly selected from our hospital were given the oral administration of Clostridium butyricum live capsule 840mg twice a day. The concentration of methane and hydrogen at each time point before and after treatment for 44 patients was detected and compared by hydrogen and methane in breath test (LBT).

Results: After 28 days of treatment with Clostridium butyricum capsules, there was no significantly statistical difference in exhaled hydrogen concentration or methane concentration between 0 min, 30 min, 60 min and 90 min before and after treatment. See Table 1.

Conclusion: Numerous studies have shown that taking probiotics can promote the growth of normal flora and reduce the reproduction of other abnormal flora, which has a certain impact on the structure and quantity of There was no significantly statistical difference in exhaled hydrogen concentration or methane concentration at various points in time between the 44 patients before and after treatment, suggesting that there was no significant change in the structure and quantity of intestinal flora. Intestinal flora, which may be resulted from our low dose Clostridium butyricum live capsules or short treatment time, or need to be combined with other probiotics. These hypothesis above need us to further explore, in general, using microbes as a therapeutic target spot to regulate the illness of SLE by interfering with intestinal flora through diet, probiotics or fecal transplantation provides a promising prospect for clinical treatment of SLE. There was no significantly statistical difference in exhaled hydrogen concentration or methane concentration between 0 min, 30 min, 60 min and 90 min before and after treatment. See Table 1.

Conclusion: Numerous studies have shown that taking probiotics can promote the growth of normal flora and reduce the reproduction of other abnormal flora, which has a certain impact on the structure and quantity of There was no significantly statistical difference in exhaled hydrogen concentration or methane concentration between 0 min, 30 min, 60 min and 90 min before and after treatment. See Table 1.

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Disclosure of Interests: Anna Mesnyankina: None declared, Sergey Solovyev: None declared, Elena Aseeva: None declared, Evgeny Nasonov Speakers bureau: Pfizer, Inc., MSD, Novartis, AbbVie Inc., Celgen Corporation, Biocad, Janssen, UCB, Inc.


Table 1. Methane and hydrogen concentrations before and after intervention by the experimental (PM/M)/(P25,P75)

<table>
<thead>
<tr>
<th>Group</th>
<th>Before Intervention</th>
<th>After Intervention</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>16(8.5,30)</td>
<td>21(5,35)</td>
<td>0.697</td>
</tr>
<tr>
<td>RTX</td>
<td>27(13,45)</td>
<td>27(6,61)</td>
<td>0.872</td>
</tr>
<tr>
<td>BLM</td>
<td>27(11,49.5)</td>
<td>21(5,53.5)</td>
<td>0.977</td>
</tr>
</tbody>
</table>
PREGNANCY OUTCOME IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS TREATED WITH HYDROXYCHLOROQUINE: 10 YEARS EXPERIENCE

Kyaw Min Tun, Rahana Rahman, Ixora Kamisan @ Atan, Ani Amelia Zainuddin, Ruslinda Mustafar, Mohd Shahrir Mohamed Said, Universiti Kebangsaan Malaysia Kuala Lumpur Campus, Kuala Lumpur, Malaysia

Background: Pregnancy in women with Systemic Lupus Erythematosus is closely associated with the usage of hydroxychloroquine [1]. Objectives: To determine pregnancy outcomes in women with Systemic Lupus Erythematosus who had antenatal follow up and delivery in Universiti Kebangsaan Malaysia Medical Centre.

Methods: Pregnant women with Systemic Lupus Erythematosus who had antenatal follow up and delivery in Universiti Kebangsaan Malaysia Medical Centre between 1st January 2007 and 1st January 2017 were retrospectively analyzed. Data collection was done via medical case notes and laboratory investigations. Study population was categorised into two groups based on hydroxychloroquine treatment during pregnancy. Incomplete pregnancy records were excluded.

Results: There were 82 completed pregnancies included with 47 (57.3%) in HCQ group and 35 (42.7%) in non HCQ group. Amongst HCQ users, there were significantly more pregnancies with musculoskeletal involvement (p=0.03), heavier mean neonatal birth weight (p=0.02) and prolonged duration of pregnancy (p=0.001). In non-HCQ users, the rate of recurrent miscarriages (p=0.003), incidence of hypertension (p=0.01) and gestational diabetes mellitus (p=0.01) and concurrent medical illness (p=0.005) were significantly more. Hydroxychloroquine use during pregnancy was protective against hypertension (p=0.001) and the gestational age at delivery had significant effect on the neonatal birth weight (p=0.001). However, duration of the disease had significant negative effect on the neonatal birth weight (p=0.016).

Conclusion: HCQ enhance better neonatal outcomes and reduce adverse pregnancy outcome and antenatal complications such as hypertension and diabetes.

REFERENCES

Disclose of Interests: None declared

AB0478

PROLONGED CLINICAL REMISSION AND LOW DISEASE ACTIVITY STATUS ARE ASSOCIATED WITH BETTER QUALITY OF LIFE IN SYSTEMIC LUPUS ERYTHEMATOSUS

Nareerat Poomsalood, Sumapa Chaiamnuay, Pongthorn Narongroeknawin, Pajjil Asovalanabodee, Rattapol Pachotalan, Phramongkutklao Hospital and College of Medicine, Bangkok, Thailand

Background:
To treat target (T2T) strategies in systemic lupus erythematosus (SLE) have been developed in order to control disease activity, improve health-related quality of life (HRQoL), reduce organ damage and decrease mortality. Previous studies revealed that both remission and low disease activity (LDA) had comparable damage accrual as well as mortality. However, studies of HRQoL in these two targets are few and there has been no comparative study between them.

Objectives: To determine the association between disease activity status (DAS) and HRQoL in SLE patients.

Methods: SLE patients in out-patient clinic during the previous 12 months were included in the study. Systemic Lupus Erythematosus-specific Quality-of-Life questionnaire (SLEQoL) was measured at the last visit. DAS was determined retrospectively during the previous year. Three categories of DAS were defined: clinical remission (CR); clinical quiescent disease according to Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K), prednisolone < 5 mg/day; low disease activity (LDA): SLEDAI-2K (without serological domain) ≤ 2, prednisolone < 7.5 mg/day; and non-optimally controlled status: those who were not in CR/LDA. Immunosuppressive drugs (maintenance dose) and antimalarials were allowed. Both CR and LDA have been maintained for at least 1 year. The

REFERENCES
[1] DISEASES REFRACTORY TO STANDARD HYDROXYCHLOROQUINE: 10 YEARS EXPERIENCE

Ruslinda Mustafar, Kyaw Min Tun, Rahana Rahman, Ixora Kamisan @ Atan, Ani Amelia Zainuddin, Mohd Shahrir Mohamed Said, Universiti Kebangsaan Malaysia Medical Centre between 1st January 2007 and 1st January 2017 were retro-

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Conclusion: HCQ enhance better neonatal outcomes and reduce adverse pregnancy outcome and antenatal complications such as hypertension and diabetes.

REFERENCES

Disclose of Interests: None declared

AB0478

PROLONGED CLINICAL REMISSION AND LOW DISEASE ACTIVITY STATUS ARE ASSOCIATED WITH BETTER QUALITY OF LIFE IN SYSTEMIC LUPUS ERYTHEMATOSUS

Nareerat Poomsalood, Sumapa Chaiamnuay, Pongthorn Narongroeknawin, Pajjil Asovalanabodee, Rattapol Pachotalan, Phramongkutklao Hospital and College of Medicine, Bangkok, Thailand

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To treat target (T2T) strategies in systemic lupus erythematosus (SLE) have been developed in order to control disease activity, improve health-related quality of life (HRQoL), reduce organ damage and decrease mortality. Previous studies revealed that both remission and low disease activity (LDA) had comparable damage accrual as well as mortality. However, studies of HRQoL in these two targets are few and there has been no comparative study between them.

Objectives: To determine the association between disease activity status (DAS) and HRQoL in SLE patients.

Methods: SLE patients in out-patient clinic during the previous 12 months were included in the study. Systemic Lupus Erythematosus-specific Quality-of-Life questionnaire (SLEQoL) was measured at the last visit. DAS was determined retrospectively during the previous year. Three categories of DAS were defined: clinical remission (CR); clinical quiescent disease according to Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K), prednisolone < 5 mg/day; low disease activity (LDA): SLEDAI-2K (without serological domain) ≤ 2, prednisolone < 7.5 mg/day; and non-optimally controlled status: those who were not in CR/LDA. Immunosuppressive drugs (maintenance dose) and antimalarials were allowed. Both CR and LDA have been maintained for at least 1 year. The
association between DAS and HRQoL was assessed by using multiple linear regression analysis adjusting for other covariates.

Results: Of 237 SLE patients (pts), 100 pts (42.2%) achieved prolonged CR, 46 pts (19.4%) achieved prolonged LDA, and 91 pts (38.4%) were not in CR/LDA. Non-CR/LDA pts had significantly higher total SLEQoL score and in all domains compared with CR/LDA pts. No significant difference in SLEQoL domain scores was found between CR and LDA groups. Multivariable analysis revealed that non-CR/LDA was positively associated with SLEQoL score compared with CR/LDA (β = 0.27, 95% confidence interval (CI) 0.52-0.03, p < 0.001). Moreover, non-CR/LDA was at a higher risk of impaired QoL (SLEQoL score > 80) compared with CR (hazard ratio (HR) 3.3; 95% CI 1.82-7.95, p < 0.001). However, there was no significant difference between CR and LDA in terms of SLEQoL score or impaired QoL. Other factors associated with higher SLEQoL score were damage index (β 10.55, 95% CI 4.63-16.48, p = 0.001) and anemia (β 27.84, 95% CI 8.48-47.19, p = 0.001).

Conclusion: Prolonged CR and LDA are associated with better HRQoL in SLE patients and have a comparable effect. Prolonged CR or optional LDA may be used as the treatment goal of T2T approach in SLE.

REFERENCES

Disclosure of Interests: None declared

AB0482 AUTOANTIBODIES’ TITRE MODULATION BY ANTI-BLYS TREATMENT IN SYSTEMIC LUPUS ERYTHEMATOSUS
Ilaria Cavazza\textsuperscript{1}, Rajesh Kumar\textsuperscript{2}, Salvatore Panaro\textsuperscript{3}, Chiara Pozzari\textsuperscript{2}, Roberta Ottaviani\textsuperscript{4}, Silvia Plantoni\textsuperscript{5}, Laura Andreoli\textsuperscript{1}, Angela Tincani\textsuperscript{1}, Franco Franceschini\textsuperscript{1}.
\textsuperscript{1}Rheumatology and Clinical Immunology, ASST Sperdai Civile, Brescia, Italy, Brescia, Italy. \textsuperscript{2}Rheumatology Chair, Clinical and Experimental Science Department, University of Brescia, Brescia, Italy, Brescia, Italy

Background: Belimumab is a human monoclonal antibody that inhibits soluble B lymphocytes stimulator (Blys) and represents the only biologic drug approved for Systemic Lupus Erythematosus (SLE) (1). Belimumab is effective in improving disease activity, blocking damage progression (2.3). Pooled data derived from clinical trials reported a reduction of anti-dsDNA analysed by ELISA, anti-cardiolipin IgG (aCL) and anti-Sm and anti-ribosomal protein antibodies (2,4). No data were published on anti-beta2-glycoprotein I (β2GPI) antibodies and other anti-ENA specificities.

Objectives: Our aim was to analyse the effect of Belimumab therapy on high avidity anti-dsDNA, aCL, anti-beta2GPI, and other relevant anti-ENA specificities.

Methods: 50 patients with active SLE (mean SLEDAI-2K score: 7±18; SD:3), with a mean age of 39 years (SD:11) and mean follow-up of 13 years (SD:7.8) were enrolled. Sera were collected at Belimumab starting (T0) and every 6 months until 24th month. Disease activity index (SLEDAI-2K) was collected at every timepoints. High avidity anti-dsDNA were detected by radioimmunological method, anti-ENA, anti-cardiolipin (aCL), anti-β2 glycoprotein I (anti-β2GPI) were analysed by ELISA.

Results: At baseline 86% of sera were positive for anti-dsDNA, 50% for anti-ENA, 26% for aCL and 28% for anti-β2GPI. Anti-dsDNA became negative in 21%, anti-beta2GPI IgG in 33% and aCL IgG in 30% of sera, mostly at T6. Among anti-ENA, 610% (60%) anti-ribosomal and 317% (17.6%) anti-Sm positive sera became negative. A significant decrease of anti-dsDNA and anti-beta2GPI IgM titers were observed at all timepoints. IgG aCL titre showed significant decrease only at T18. Anti-ribosomal showed a significant titre decrease at T6 and T12, with seroconversion to negative at T18. Anti-Sm titre significantly dropped down at T6, then remained stable during time. A significant correlation between anti-dsDNA and anti-ribosomal titre, and between SLEDAI ratio (SLEDAI value/SLEDAI T0) and anti-ribosomal titer ratio (value/value T0) were found.

Conclusion: Belimumab treatment induced a significant reduction of SLE-specific autoantibodies titre and IgM anti-beta2GPI. Anti-ribosomal titre decrease correlates with anti-dsDNA titre and improvement of disease activity.

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Disclosure of Interests: Ilaria Cavazza: None declared, Rajesh Kumar: None declared, Salvatore Panaro: None declared, Chiara Pozzari: None declared, Roberta Ottaviani: None declared, Micaela Fredi: None declared, Silvia Plantoni: None declared, Laura Andreoli: None declared, Angela Tincani Consultant for: UCB, Pfizer, Abbvie, BMS, Sanofi, Roche, GSK, AlphaSigma, Lilly, Janssen, Cellgene, Novartis, Franco Franceschini: None declared

Table I: Demographic, clinical, laboratory and therapeutic characteristics of patients according to presence of aPL/LAC persistence

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>aPL/LAC</th>
<th>aPL/LAC</th>
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<tbody>
<tr>
<td></td>
<td>neg</td>
<td>pos</td>
</tr>
<tr>
<td>(n=19)</td>
<td>(n=48)</td>
<td>p</td>
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| Current Age (median ± IQR range, y) | 52 (±16) | 53 (±16) | 0.6
| Wilcoxon rank sum (WRS) | | |
A SYSTEMATIC LITERATURE REVIEW ON THE USE OF BIOLOGICS IN SJÖGREN’S SYNDROME

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Background: Primary SJögren’s syndrome (pSS) is a systemic chronic autoimmune disease characterized by dryness of the eyes and mouth. Current treatments provide modest benefit, leaving patients with limited therapeutic options. The pathophysiology of pSS involves hyperactivity of autoreactive lymphocytes. Biologic medications target mediators of the immune response. Modulation of autoimmunity in pSS with biologics has gained interest with open-label studies showing promising results.

Objectives: This review aims to conduct a systematic literature review of interventional studies investigating the efficacy of biologics in the treatment of pSS.

Methods: Literature was searched using the MEDLINE, EMBASE and PubMed databases as well as abstracts in EULAR, ACR and BSR.

Results: A total of twelve studies met the inclusion criteria. Infliximab and etanercept showed no significant improvements in fatigue and dryness in pSS compared to placebo. Anakinra showed improvement in fatigue after post-hoc analysis. Small trials in rituximab showed significant improvements in oral and ocular dryness but failed to replicate this in two larger randomised control trials. Belimumab significantly reduced overall disease activity which was driven by improvements in dryness and parotid gland swelling. Labelled studies in epratuzumab and abatacept showed significant reductions in fatigue with abatacept also improving salivary flow and swelling. Open-label studies in epratuzumab and abatacept showed significant reductions in fatigue with abatacept also improving salivary flow and swelling.

Conclusion: Intervention with biologics in pSS has shown efficacy in alleviating pSS-associated fatigue and dryness in small RTCs and open-label trials. Larger randomised placebo-controlled trials have been inconsistent in replicating these results. This may be overcome by subgroup analysis, uptake of validated disease activity measuring tools, well-defined selection criteria to increase sample size and further understanding of pathophysiology in pSS. The small number of trials to date means the evidence base for biologics in pSS remains inconclusive.

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Acknowledgement: I would like to thank Dr Marwan Bukhari for his advice in this manuscript and for providing clinical shadowing in rheumatology at the Royal Lancaster Infirmary.

Disclosure of Interests: None declared.

AB0484 EXPERIENCE WITH THE USE OF RITUXIMAB FOR THE TREATMENT OF SYSTEMIC AUTOIMMUNE DISEASES (SAD) IN A TERTIARY HOSPITAL

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Background: Rituximab is a chimeric anti-CD20 monoclonal antibody used in various clinical scenarios for the treatment of SAD, especially when immunocomplexes and/or lymohocyte B proliferation plays a central role.

Objectives: The objective of this study was to retrospectively assess the efficacy and safety of use of rituximab in a cohort of patients with SAD in a tertiary hospital within the last 12 years.

Methods: We carry out a retrospective study of 48 patients with a diagnosis of SAD in our Autoimmune and Minority Diseases Department using Google Sheets.

Results: Our cohort is mostly female (48 women and 8 men). The mean age is 40.9 ±13.1 years (median 38 years). It is composed of different SAD: rheumatoid systemic lupus (22), granulomatosis with polyangiitis (6), dermatomyositis (6), systemic sclerosis (1) foliaceus pemphigus (1), gangrenous pyoderma, (1) polymyositis (1) and orbital pseudotumor (1). The mean time from diagnosis to rituximab was 7.7±7.1 years. The efficacy of RTX in reducing disease activity after 6 month was 64.6% patients according to the disease recommended scales-. Nevertheless, 39% maintained 1 year remission.

The indications for rituximab were: persistant activity despite improvement of classical immunosuppressive strategies (36), corticosterone deficiency (4), new relapses (3), corticosteroid resistance and toxicity (others immunosuppressant) (2). The drugs used when rituximab was used: cyclophosphamide (24), hydroxychloroquine (21), mycophenolate mofetil or mycophenolic acid (20); cyclosporine (7), immunoglobulines (7), leflunomide (4), and methotrexate (8). 5 patients did not receive any immunosuppressant. 61.3% were taking at least 2 drugs. All of them were taking glucocorticoids. In terms of security and side effects, we observed 11 (22.9%) adverse reactions related to the administration. We detect 3 infusion reactions (mild severity), 1 severe mucocutaneous reaction, 1 moderate herpes zoster, 1 fungic invasive infection and 5 severe bacterial infections (1 of them lead to rituximab suspension). We did not detect any hepatitis B virus reactivation, multifocal progressive leukoencephalopathy, cytomegalovirus infections nor herpes simplex infections.

We observed 65 different haematologic adverse events: lymphopenia (34), anemia (15), neutropenia (12) and trombocytopenia (4). No one needed specific treatment.

Conclusion: Rituximab is a second line therapeutic alternative in patients with SAD in whom other treatments have failed. It is a effective drug that rescues a 65% of patients in whom other treatments have failed. Furthermore, rituximab is a safe immunosuppressant.

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Disclosure of Interests: None declared.

AB0485

INTRAVENOUS HIGH DOSE GLUCOCORTICOIDS CAUSE PROLONGATION OF QT INTERVAL IN CONNECTIVE TISSUE DISEASE PATIENTS EXCEPT ANTI-RO POSITIVE SUBGROUP

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Background: Recent literature indicates that anti-Ro antibodies may be associated with prolongation of corrected QT (QTc) interval in the adult patients with connective tissue diseases. Moreover, glucocorticoids (frequently used in the therapy) are known to probably induce electrocardiographic changes including prolongation of QT interval. Prolongation of QTc interval is a risk factor for malignant ventricular arrhythmias. We hypothesised that patients with anti-Ro positivity have a higher risk of QT prolongation especially in the case of high dose intravenous glucocorticoids (IVGC) treatment.

Objectives: The aim of the study was to analyse risk of QTc interval prolongation in anti-Ro and anti-La positive patients before and after high dose IVGC treatment in patients with connective tissue diseases.

Methods: We performed a retrospective study of 115 patients (21 males), mean age of 48±14.7 years, range 19-78 years with connective tissue diseases. Anti-Ro and anti-La antibodies were examined in all patients before IVGC treatment. The patients were given 5x1000 mg methylprednisolon i.v. during five consecutive days. ECG recording was performed at baseline and after IVGC. The QT intervals were measured in each of 12-lead standard ECGs from two consecutive cycles. The QT intervals were measured from the onset of QRS complex to the end of the T wave by the means of a tangential method. Fridericia formula was used to obtain heart rate-corrected values for QT intervals.

Results: Comparing patients with anti-Ro positivity (n=39; 33.9%) and anti-Ro-negativity (n=76; 66.1%), we found insignificant difference in QTc interval: QTcRo=417.2±28.4 ms and QTcR0=420.8±26.4 ms (P=0.51), respectively. Admission of IVGC showed significant prolongation of QTc in all patients, mean QTc1 before treatment was 399±26.2 ms, and QTc2 after therapy 412.7±27.2 ms, P=0.00021. On the other hand, anti-Ro and anti-La positivity showed shorter QTc interval 391±18.7 ms, to compare patients without these antibodies QTc414.8±25.7 ms, P=0.019 after treatment.

Conclusion: IVGC treatment significantly prolongs QT interval. Prolongation of QT/QTc interval needs further confirmation. Motivated by this experience, we consider ECG monitoring and careful observation of patients during IVGC treatment.

Acknowledgement: Charles University research projects [PROGRES Q40-15, PROGRES Q47]


AB0487

HQC COULD ACT ON SLE PATIENTS THROUGH THE MODULATING EXPRESSION OF IL-8 ALONG WITH S100 PROTEINS

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Background: Some reports revealed that S100A8 and S100A9 proteins were associated with disease activity of lupus nephritis (LN) [1]. However, there have been no reports about the mechanism of additional hydroxychloroquine (HQC) treatment for systemic lupus erythematosus (SLE) patient with low disease activity.

Objectives: To clarify the mechanism of additional HQC treatment for Japanese SLE patients with low disease activity.

Methods: All the 44 patients were enrolled in this study. These patients had been receiving additional oral HQC sulfate continuously for at least 3 months. These patients had no need for additional immunosuppressants including glucocorticoids, during this study because of their sustained low disease activity for 3 months prior to starting HQC. Low disease activity was defined as SELENA-SLEDAI score of 5 or less and biologic use is higher in the US (EU5 5.0% vs. US 8.3%); GCS use is similar (EU5 19.2% vs. US 19.0%). Globally, 84.4% of patients receiving GCS received it continuously with no significant differences observed between markets, EU5 85.5% vs. US 81.9%. A higher proportion of patients in the EU5 have been on GCS for 6 months or longer when compared to the US; EU5 79.9% vs. US 72.5%. Statistically significant differences were seen in the perception of GCS importance between markets (p<0.0004) and concerns with taking GCS (p=0.0143). A higher proportion of patients in the US regarded the use of GCS to at least be important (very important/essential EU5 65% vs. US 80.6%). A higher proportion of patients in the US were concerned with the use of GCS (somewhat concerned/very concerned EU5 56% vs. US 61.2%).

Conclusion: Significant differences in treatment approach between regions highlight the need for a better understanding of this disparity and a united approach to SLE treatment. Despite the high profile of risk factors linked to GCS use in SLE, it continues to be a continuously utilized by a large proportion of SLE patients and there is poor use of flare preventing agents such as immunosuppressants. Patients and physicians recognize the role of GCS in the management of SLE but also express concerns. Impact of an update to the SLE guidelines and their dissemination with better understanding of risk benefits of GCS vs. immunosuppressive and biologic therapy is warranted.


AB0457

LACK OF CONSISTENT STANDARD OF CARE IN SYSTEMIC LUPUS ERYthematosus PATIENTS IN REAL WORLD

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Background: Current guidelines do not necessarily reflect current standard of care (SOC) or treatment patterns in SLE in real world.

Objectives: To describe SLE SOC in the EUS and US and assess need for a more efficient and defined treatment pathway.

Methods: A cross-sectional study of 263 rheumatologists in the US and EUS. Data were collected from the Adelphi Real World 2015 Lupus Disease Specific Programme (DSP). Physicians were asked to complete patient record forms (PRFs) for the next 5 patients consulting with SLE; the same patients were asked to complete patient self-completion (PSC) forms describing how SLE affected them. PRFs collected data pertaining to the patient’s diagnosis, disease history, current clinical outcomes, treatment and health status. PSC data collection and included patient reported outcome measures (PROs) to assess the humanistic burden. Chi-squared tests were conducted to ascertain significance.

Results: Data was extracted from 1376 PRFs, and 591 PSCs. 35.6% of patients were currently on their first line of therapy, 40.0% second line, and third line or more 24.4%. Significant differences were observed between US and EUS in current treatment classes for first line (p=0.0001) and second line (p=0.0007). Descriptive differences were observed in the third line. In the US monotherapy is used more often first line with antimalarial (AM) (monotherapy EUS 15.7% vs. US 19.2%) and immunosuppressant (IM) (monotherapy EUS 4.8% vs. US 11.1%). Glucocorticoids (GCS) use is higher in the EUS at 1st line; both monotherapy (EUS 13.7% vs. US 11.8%) and combination (GCS+AM EUS 28.3% vs. US 16.7%). At second line, IM use (no bio) is higher in EUS (EUS 64.9% vs. US 56.7%) and biologic use is higher in the US (EUS 5.0% vs. US 8.3%). GCS use is similar (EUS 19.2% vs. US 19.0%).
Results: We enrolled 44 patients. Prednisolone dose during this study was fixed at the mean of 5.0±2.9 mg per day. SELENA-SLEDAI scores, CLASI scores, anti-dsDNA antibody and serum levels of C3 improved significantly, and serum levels of S100A8 and S100A9 proteins decreased significantly 3 months after additional HCQ treatment. The changes in serum S100A8 and S100A9 levels in SLE patients with LN were more significantly higher than in those without LN.

Among these patients, the changes of serum cytokine expressions were measured in 18 patients. The expressions of IFNs were not detected in almost of all patients. Serum levels of TNF-α, IL-6, IL-8, IL-1β, IL-1ra, VEGF, CCL3 and CCL4 decreased significantly 3 months after additional HCQ treatment (Figure1).

Seven of 18 SLE patients had a history of LN. These patients have HCQ treatment (Figure1).

The reductive effect of additional HCQ treatment on serum S100A9, TNF-α, IL-6 and IL-8 levels was much more apparent in those with history of LN (LN: S100A9, p=0.016, TNF-α, p=0.016, IL-6 p=0.031, IL-8, p=0.031; no LN: S100A9, p=0.065, TNF-α, p=0.083, IL-6 p=0.090, IL-8, p=0.557). The changes of serum S100A8 and S100A9 levels were correlated with those of serum IL-8 and IL-1ra (Figure2).

Conclusion: HCQ could reduce the serum levels of S100 protein and several cytokines in SLE Japanese patients with low disease activity. Recently, some reports showed that novel biomarker including IL-8 or S100 proteins was correlated with severity of LN [1, 2]. Our findings suggest that HCQ treatment without any additional immunosuppressant could reduce the expression of serum S100 proteins, IL-8 and IL-1ra, which were considered to be associated with the improvement of renal and life prognosis. Our data also indicated that S100 protein is closely related to several of IL-8 or IL-1ra expression in SLE pathogenesis, especially in LN. Further investigations are needed to more clarify the significance of HCQ treatment in SLE.

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Disclosure of Interests: None declared
SLE, Sjögren’s and APS – clinical aspects (other than treatment)

AB0490 FIBROBLAST GROWTH FACTOR-23 IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

Dina Abdul Azim¹, Nahla Eesa¹, Mahmoud Sarraya², Marwa El Sharkawy³, Ahmed Fayed⁴, Somaya Anwar Hussein¹, Usama Sharaf El Din⁴. ¹Cairo University, Rheumatology and Rehabilitation, Cairo, Egypt; ²Cairo University, Cardiology, Cairo, Egypt; ³Cairo University, Chemical Pathology, Cairo, Egypt; ⁴Cairo University, Nephrology, Internal Medicine, Cairo, Egypt

Background: Systemic lupus erythematosus (SLE) is a chronic inflammatory disease that affects multiple organs including the kidneys and the heart. Chronic kidney disease (CKD) is common among SLE patients. SLE is also associated with increased left ventricular (LV) mass. LV hypertrophy (LVH) may have an additional role in the increased morbidity and mortality among in SLE patients. Fibroblast growth factor 23 (FGF23) is a phosphatonin that steadily increases in serum of CKD patients. High FGF23 is associated with inflammation, CKD progression, and LVH.

Objectives: The aim of this study is to determine the serum level of FGF23 in SLE patients with and without lupus nephritis looking for its possible association with the inflammatory and cardiovascular manifestations encountered in this disease.

Methods: Sixty SLE patient were recruited and appointed into 2 groups based on renal function; group I composed of thirty patients that had normal kidney functions or stage 1 CKD (eGFR>90 ml/min/1.73m²) and group II of thirty cases with significant renal involvement defined as stage 2 to 4 CKD (eGFR <90 - >15 ml/min/1.73m²). After history taking and complete clinical examination of every patient, we measured body weight, height, Systemic lupus erythematosus disease activity index (SLEDAI), Systemic lupus erythematosus International Collaborating Clinics (SLICC), serum level of creatinine, calcium, phosphorus, albumin, complement 3 (C3), complement 4 (C4), interleukin 6 (IL6), fibroblast growth factor 23 (FGF23), estimated glomerular filtration rate (eGFR), 24 hour urine protein, complete blood count, erythrocyte sedimentation rate (ESR), antinuclear antibody (ANA), and left ventricular mass index (LVMI). Sixty normal healthy adults were included as control group. They were tested for serum FGF23 level.

Results: Serum level of FGF23 in SLE patients was comparable to normal control subjects (99.6±79.86 vs. 139±12.3 pg/mL, P>0.05). In addition, there was no significant difference in FGF23 between the two studied groups (106.49±88.2 vs. 93.84±74.67 pg/mL, P>0.05). In addition, there was no significant difference in serum IL6 between the two groups (58.6 ± 63.69 vs 55.9 ± 47.97 ng/L, P=085). On the other hand, LVMI was significantly higher in Group II (138.6 ± 36.59 vs. 187.6 ± 81.7 gm/m² in group I vs. group II respectively, P=0.0045). FGF23 showed significant positive correlation with IL6 (r= 0.776, P<0.001) and failed to show significant correlation with LVMI, serum creatinine, eGFR or serum phosphorus.

Conclusion: FGF23 behaves differently in SLE patients; in spite of significant increase in inflammation and the frequent renal involvement, FGF23 level remains normal in SLE patients. There is a possible existence of an inhibitor to FGF23 production in SLE. This possibility should trigger further studies.

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2011 121:4393–4408.

Disclosure of Interests: None declared.


AB0491 THE PERFORMANCE OF A RENAL ACTIVITY INDEX IN LUPUS NEPHRITIS IN INDUCTION THERAPY

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Background: Renal involvement in systemic lupus erythematosus (SLE) is
associated with high morbidity and mortality1. Current standard tools to
monitor lupus nephritis (LN) are suboptimal compared to the invasive
renal biopsy2. The renal activity index in lupus (RAIL) was developed
using 6 urinary biomarkers to reflect disease activity. In children this tool
was 92% accurate in identifying active LN3.

Objectives: We aim to study the changes in this score in relation to
induction treatment in LN.

Methods: Urine samples were collected from active LN patients prior
to induction treatment for LN and serially afterwards, coinciding with
clinical visits. Luminex Bead Multiplex Assay was used for the analy-
ses of urine biomarkers included in the RAIL score (neutrophil gelati-
nase-associated lipocalin, ceruloplasmin, monocyte chemoattractant
protein-1, adipsin,chnitin, kidney injury molecul-1). RAIL
scores were calculated per the defined algorithm for each urine sam-
ple. Data collected include LN histologic classification (International
Society of Nephrology (ISN)/Renal Pathology Society (RPS) classifica-
tion system), renal SLE disease activity index (6SLEDAI) score and
type of therapy.

Results: At the time of the analysis, data from 6 active LN patients
were collected longitudinally. Patients were all females and all had class
IV LN per the ISN/RPS. Renal SLEDAI scores were on the higher end
(M=11.3, SD=3.9). All patients were started on intravenous (IV) methyl-
prednisolone and cyclophosphamide (CYC) therapy. All but one patient
completed 6 doses of monthly CYC before switching to oral mycopheno-
late mofetil therapy. The RAIL scores for the 6 patients ranged between
-1.8 and 3.29. All patients had reductions in their RAIL score at 2-3
months period at an average of 322% decline from baseline (Figure 1).

At the end of induction treatment or at the 5-6 months interval, 5/6
patients main-
tained a decline of RAIL scores below the baseline. Of note the patient
who had flare of LN at the 6 months point leading to
treatment system), renal SLE disease activity index (6SLEDAI) score
type of therapy.

Conclusion: RAIL scores show overall improvement from baseline with
LN induction therapy. Lack of improvement was associated with flare
disease. Additional data points and a larger study sample are
required to study the ability of the RAIL score to reflect clinical
improvement of LN.

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nard: None declared, Arjun Mathur: None declared, Hermine Brunner
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Pfizer, Bristol-Myers Squibb, Janssen, Novartis, Lilly, Roche, GlaxoSmithK-
line, Sanofi, Speakers bureau: Novartis, Roche

AB0492 PREVALENCE OF IGA ANTICARDIOLIPIN ANTIBODY AND ITS ASSOCIATION WITH PREGNANCY MORBIDITY IN ASIAN INDIAN PATIENTS WITH PRIMARY ANTIPHOSPHOLIPID ANTIBODY SYNDROME AND SYSTEMIC LUPUS ERYTHEMATOSUS – A CROSS SECTIONAL STUDY

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India

Background: There are many clinical and laboratory parameters which have
been proven to be associated with increased risk of pregnancy mor-
bidity in patients with SLE and APS. This study was undertaken as there
is a lacuna in explaining all the pregnancy related morbidity in this group

Objectives: Primary: Correlation of IgA anticardiolipin antibody with the
risk for pregnancy morbidity in patients with APS/SLE
Secondary: Association of IgA Anticardiolipin antibody with the risk of
thromboembolic events

Methods: Patients diagnosed as SLE and/or Primary APS who are married
and conceived at least once were recruited and 3ml blood sample was
obtained from them. Patients with history of recurrent infections, which
could suggest probable IgA deficiency, were excluded. Demographic data
including duration of illness, number of pregnancies, thromboembolic
events, disease activity were noted. They were categorized into two differ-
ent groups depending on whether they had a pregnancy morbidity or not.

Results: A total number of 186 patients were recruited with mean age
34.54(+-7.32)years, mean duration of illness of 5.52(+-4.31)yns with a
diagnosis of 76.88% SLE, 7.53% primary APS and 15.59% SLE with
secondary APS. On assessment of disease activity, mean SLEDAI score
was found to be 4.46(+-6.32). Out of the total, 14.71% patients had con-
ceived once, 14.56% twice, 16.72% patients thrice and 16.41% had con-
ceived more than three times. 36.56% patients had pregnancy morbidity
(majority being pregnancy induced hypertension 14.52%, prematurity
11.29%, IUGR 10.22%, pre-eclampsia in 3.76%, eclampsia 1.08%).
19.35% patients had history of thromboembolic events (6.45% pulmonary
embolism, 5.38% deep vein thrombosis, 3.76% visceral vessel thrombosis, 0.54% cortical vein thrombosis, 6.99% other vessel thrombosis), 33.87%
patients had positivity for antiphospholipid antibodies with 27.82% lupus
anticoagulant positive, 20.97% IgA Anticardiolipin positive and 17.35%
anti-beta2 glycoprotein positive. IgA Anticardiolipin was found to be posi-
tive in 4.84%(n=9) out of which, 10.29% were in the group with preg-
nancy morbidity as against 1.69% without pregnancy morbidity. Out of
the total positives titre in 37.5% were indeterminate, 25% low positive
and 37.5% high positive. All patients who had high titre positivity had
pregnancy morbidity. The positivity of IgA anticardiolipin in the patient
group with thromboembolic events was 5.56%.

<table>
<thead>
<tr>
<th>IgA Anticardiolipin</th>
<th>Pregnancy morbidity</th>
<th>No pregnancy morbidity</th>
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<tbody>
<tr>
<td>Positive</td>
<td>7(10.29%)</td>
<td>2(1.69%)</td>
</tr>
<tr>
<td>Negative</td>
<td>69(90.71%)</td>
<td>116(98.31%)</td>
</tr>
</tbody>
</table>
Conclusion: Among patients with SLE, APS or SLE and APS, the overall prevalence of IgA antcardiolipin antibody was found to be about 4.84%, which is much less as compared to the percentages reported by other groups[1] IgA Anticardiolipin antibody positivity was more in patients with pregnancy morbidity compared to patients without a pregnancy morbidity. In this study however, statistical significance was not reached. Similar studies with larger number of patients are required. We also need to prospectively follow up such patients with IgA ACLA and evaluate for morbidity during pregnancy.

REFERENCES

Disclosure of Interests: None declared

AB0493 IMMUNOGLOBULINS AFTER ACUTE PHYSICAL EXERCISE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Moderate exercise improves the functions of the immune system. The results of serum immunoglobulins in response to acute physical exercise are conflicting, but in general, there is an increase in serum immunoglobulins in athletes and non-athletes after maximal and submaximal exercise. The effects of acute physical exercise on serum immunoglobulin in patients with systemic lupus erythematosus are unknown.

Objectives: To determine the serum levels of IgG, IgM, and IgA immunoglobulin in patients with systemic lupus erythematosus with a single session of acute aerobic exercise.

Methods: Thirty-one women with SLE (ACR1997 and/or SLICC 2012 criteria), 11 with active lupus and 20 with inactive lupus, and 24 healthy women, who were matched by gender, age, and body mass index, participated in this study. All subjects underwent a maximal exercise test on a motorized treadmill, with increases in velocity every minute until exhaustion, to evaluate the speed (km/h), heart rate, Borg scale (6-20), and the reason for stopping the test (fatigue and/or dyspnea). Samples of blood were collected in the morning, after an 8-hour fast and immediately after acute physical activity, and stored in a freezer at -80°C until the tests were performed. Immunoglobulin IgG, IgM, and IgA assay was performed by turbidity test according to the manufacturer (Turbiquest, Labtest Diagnostic S.A).

Results: There was an increase in both IgG and IgA serum levels after physical activity in SLE patients (p = 0.004 for IgG and p = 0.002 for IgA) and healthy controls (p <0.001 for IgG and p <0.001 for IgA) (Figure 2), in comparison to pre-exercise levels of IgM serum. There was no difference in IgG serum levels before and after the exercise test in both groups.

Conclusion: Patients with SLE, mainly with inactive disease, responded to acute physical exercise with increased IgG and IgA serum levels, similarly to healthy controls.

REFERENCES

Disclosure of Interests: None declared

AB0494 ACTIVITY OF PURINE AND PYRIMIDINE METABOLISM ENZYMES IN SYSTEMIC LUPUS ERYTHEMATOSUS: ENZYMATIC PATTERNS OF BLOOD PLASMA AND LYSED LYMPHOCYTES

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Background: Cytotoxic immunosuppressants are widely used nowadays for outcome improvement and better quality of life in severe systemic lupus erythematosus (SLE). As purine and pyrimidine metabolism suggest to be the major targets of most cytotoxic immunosuppressants, enzyme profiling of these metabolic pathways is recognized as an important step for a better balance between efficiency and safety in clinical practice.

Objectives: To characterize enzymatic patterns of the major enzymes of purine and pyrimidine metabolic pathways in systemic lupus erythematosus.

Methods: The research was carried out in agreement with the WMA Declaration of Helsinki principles. 50 adult SLE patients from the rheumatology unit of Volgograd Clinical Emergency Hospital #25 and 30 healthy controls were included in the study. Diagnosis of SLE had been established using ACR criteria (1997), and activity was assessed by means of ECLAM scale. Activities of 10 major enzymes involved in purine and pyrimidine metabolic pathways: adenosine deaminase (ADA; E.C. 3.5.4.4), adenosine kinase (AK; E.C. 2.7.4.8), diphosphorylase dehydrogenase (DODG; E.C. 1.1.1.205), purine nucleoside phosphorylase (PNP; E.C. 2.4.2.1), thymidine phosphorylase (TP; E.C. 2.4.2.4), uracil/thymidine dehydrogenase (UDG; E.C. 2.7.7.99.4), cytidine deaminase (CDA; E.C. 3.5.4.5) were measured in blood plasma and lysed lymphocytes. Results are expressed as mean±standard error. Statistical comparison tests were selected in line with common guidelines, differences were considered significant when p<0.05.

Results: Enzymatic profiles in plasma of SLE patients are characterized by increased PNP, AK, UDG, IMPDG, CDA, TK, and DODG activities; ADA and GK were found to decrease. Lysed lymphocytes are revealed however to increased AK, IMPDG, TK, as well as decreased PNP, ADA, GK, CDA, and TP activities. We have also found that most enzyme activities significantly correlate with ECLAM score in accordance with our previous results [1]. Plasma PNP, AK, UDG, IMPDG, CD, TK, and DODG activities positively correlated with ECLAM score, as well as lymphocyte AK, IMPDG, and TK activities did. Negative correlations with ECLAM score were revealed for plasma ADA and TP, and also for lymphocyte PNP, ADA, GK, UDG, CD, TP, and DODG. Plasma PNP, AK, IMPDG, and lymphocyte PNP, ADA, AK activities had the closest relations with minimal SLE activity, being a candidate markers of it.

Conclusion: The enzymatic patterns studied can be used as auxiliary markers of SLE activity, with special emphasis on minimal disease activity.

REFERENCES

Disclosure of Interests: None declared
OBJECTIVES: The potential of molecular imaging and multi-parametric MRI to characterize and quantify pSS disease manifestations. Methods: In this pilot imaging study (20381), patients with pSS diagnosed per AECG criteria, with a EULAR Sjögren’s syndrome disease activity index score ≥5, and basal salivary flow >0.0 mL/min or stimulated salivary flow rate ≥0.05 mL/min, underwent 18F-FDG and 11C-met and dynamic contrast-enhanced and diffusion-weighted MRI, followed by minor salivary gland biopsy for histological analysis. Age- and sex-matched healthy volunteers (HV) underwent MRI and 11C-met. HV-sS mean differences (m-diff; 95% confidence intervals [CI]) were calculated and Pearson’s correlation coefficients (r) estimated. Peak PET standard uptake values (SUVpeak) were used in the correlations and SUVmax values were recorded. All methods were compared with routine clinical and laboratory tests.

RESULTS: 12 patients had MRI, 18F-FDG and 11C-met; while HV (n=12) had MRI (n=12) and 11C-met (n=8). A lower 11C-met SUVpeak was seen in the parotid (m-diff: 1.4 g/mL [0.4, 2.3]) and submandibular (m-diff: 2.0 g/mL [0.9, 3.2]) glands in pSS versus HV, as was a trend for lower lacrimal gland uptake (m-diff: 0.5 g/mL [0.2, 1.3]) in patients with pSS. On structural MRI, the fat fraction (mean%) was higher in pSS vs HV in the submandibular glands (m-diff: -14.8 CI: [-29.3, -0.4]), with similar trends observed in the parotid glands (m-diff: -11.2 [-24.3, 1.9]). There was a negative correlation between 11C-met uptake and fat fraction (r: -0.7 [-0.9, -0.4]) in the combined parotid glands. There was positive correlation between 11C-met uptake and stimulated salivary flow (r: 0.5 [0.0, 0.8]) and negative correlation for stimulated salivary flow and fat fraction (r: -0.5 [-0.8, -0.1]) in the parotid glands; similar correlations were also seen in the submandibular glands. There was negative correlation between the global lymphoid aggregation score on minor salivary gland biopsy and the combined salivary gland fat fraction (r: 0.7 [0.5, 0.2]). Parotid gland SUVmax 18F-FDG uptake was higher than historical control values (mean: 1.9 g/mL, [SD: 0.5]) in some patients (pSS mean SUVmax: 2.8 g/mL [SD: 0.8, range 1.7–4.6]), with positive correlation between 18F-FDG and 11C-met uptake (r: 0.7 [0.2, 0.9]) in the combined salivary glands. Conclusion: Imaging showed clear differences between pSS and HV and correlated with clinical endpoints. Low 11C-met uptake and high fat fraction on MRI may indicate poor residual gland function, while high 18F-FDG and stable 11C-met uptake may define a subpopulation that responds well to anti-inflammatory therapies.

REFERENCES


Acknowledgement: Study/editorial support by Fishawack Indicia Ltd, UK funded by GSK.


AB0498

18F-FDG-PET/CT, 11C-METHIONINE-PET/CT AND MULTI-PARAMETRIC MRI IN THE EVALUATION OF DISEASE ACTIVITY AND GLAND FUNCTION IN PRIMARY SJÖGREN’S SYNDROME

Michele Bombardieri1, Coziana Curtin1, Michalis Kostapanos2, Elisa Astorni3, Anwar Tappuni4, Natasha Jordan5, Teresa Fuller6, Kathleen Port1, Nirav Ratia1, Andre van Maurik1, Calum Gray6, Lucy Kershaw7, Anwar Tappuni1, Natasha Jordan3, Saleem Azeem5, Teresa Fuller6, Michele Bombardieri1, Coziana Curtin1, Michalis Kostapanos3,4, Elisa Astorri1, Birgit Blomjous Speakers bureau: UCB Pharma, Roche Netherlands BV and Sanofi Genzyme

these findings warrant improved counseling of these women and attention of health care providers, including company doctors.

Disclosure of Interests: Birgit Blomjous Speakers bureau: UCB Pharma BV; Mariater Wee Grant/research support from: Nonrestricted grants from Lilly Netherlands BV, Speakers bureau: ARC Preceptorship program, Alejandro Voskuyl: None declared, Hanneke de Vries Grant/research support from: Pfizer, Speakers bureau: UCB Pharma BV, Irene E.M. Bullink Consultant for: Consultant fee from Sanofi Genzyme, Speakers bureau: Sanofi Genzyme, UCB Pharma BV, Roche Netherlands BV and Sanofi Genzyme


AB0497

SERUM CALPROTECTIN IN SYSTEMIC LUPUS ERYTHEMATOSUS: IS IT A GOOD ACTIVITY BIOMARKER?


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Background: Clinical manifestations of systemic lupus erythematosus (SLE) and infections sometimes are difficult to distinguish. In clinical practice low complement and antivirus/DNA levels are used to assess lupus activity but
its determination usually requires some days. Leukocyte count, CRP and ESR cannot discriminate SLE from infectious processes. Calprotectin could be a good biomarker to assess lupus activity since it is more specific than CRP and ESR and faster to analyse than anti(ds)DNA.

Objectives: Our aim is to determine serum calprotectin levels in patients with SLE, and its correlation with analytical and clinical manifestations, especially with disease activity.

Methods: A total of 148 patients were included. All patients included fulfilled the SLE criteria (SLICC 2012). A quantitative ELISA analysis was performed to assess levels of serum calprotectin (CALPRO AS, Norway). Other biomarkers of lupus disease activity were also assessed (levels of anti(ds)DNA, hypocomplementemia, ESR and CRP). Clinical variables and activity/damage index (SLEDAI/SLICC) were also evaluated. The study was approved by the Clinical Research Ethics Committee of the hospital and all patients signed an informed consent. The results were compared with a healthy control group of similar age and sex (n=20).

Results: 134 patients (92%) were women with a mean age of 46 ± 12 years and a mean SLE evolution of 12.7 years. Mean SLEDAI was 2.2 (105 inactiv [-3], 43 mild [4-12], 0 severe [13]). Mean SLICC was 0.31 ± 0.7. No significant differences were observed in serum calprotectin levels between patients with SLE and healthy controls (2.93 ± 3.5 vs 2.17 ± 1.49 µg/mL). Calprotectin was positively correlated with CRP (r=0.447, p<0.001) and leukocyte count (r=0.462, p<0.001). Additionally, patients with higher anti(ds)DNA levels (>100 U/mL) had higher calprotectin compared to patients with lower anti(ds)DNA (3.20 ± 2.63 vs 2.42 ± 1.57 µg/mL; p=0.007), however this pattern was not observed with hypocomplementemia. Contrary to what we expected, we did not observe significant differences on calprotectin levels depending on SLEDAI index classification (cutoff at 4 and 12). Moreover, no differences were observed on calprotectin levels between those patients without clinical manifestations such as serositis, arthritis or glomerulonephritis. Patients with antiphospholipid antibodies had higher calprotectin levels (3.75 ± 2.04 vs 2.77 ± 2.38 µg/mL; p=0.045).

Conclusion: Serum calprotectin levels were positively correlated with CRP levels and leukocyte count. Patients with higher anti(ds)DNA levels had higher calprotectin levels, however we did not observe significant differences depending on SLEDAI index or the presence of arthritis, serositis and/or glomerulonephritis. Even that calprotectin determination is faster than anti(ds)DNA levels and could be helpful in assessing inflammatory activity. There is an interesting relation between antiphospholipid antibodies and calprotectin. This study should be continued in a larger sample of active SLE patients to assess its utility in clinical practice as a discriminating biomarker for flares and even infection.

Disclosure of Interests: None declared


REFERENCES


Disclosure of Interests: None declared


Table 1. Groups Data

<table>
<thead>
<tr>
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<th>Primary SS (60)</th>
<th>Secondary SS (42)</th>
<th>Healthy Control (52)</th>
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<tbody>
<tr>
<td>Age</td>
<td>52±11</td>
<td>54±11</td>
<td>46±19</td>
</tr>
<tr>
<td>Menopausal state</td>
<td>37(62)</td>
<td>33(79)</td>
<td>17(32)</td>
</tr>
<tr>
<td>Menopause Age</td>
<td>47±5</td>
<td>48±4</td>
<td>45±4</td>
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<tr>
<td>Hormone replacement</td>
<td>8(13)</td>
<td>3(7)</td>
<td>3(6)</td>
</tr>
<tr>
<td>Sexuality activity</td>
<td>46(77)</td>
<td>25(60)</td>
<td>43(83)</td>
</tr>
<tr>
<td>Vaginal dryness</td>
<td>38(63)</td>
<td>18(43)</td>
<td>11(21)</td>
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<tr>
<td>Vulvar dryness</td>
<td>26(43)</td>
<td>17(41)</td>
<td>8(15)</td>
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<tr>
<td>Dyspareunia</td>
<td>34(57)</td>
<td>14(33)</td>
<td>16(31)</td>
</tr>
<tr>
<td>Spontaneous genital pain</td>
<td>17(28)</td>
<td>5(12)</td>
<td>5(10)</td>
</tr>
<tr>
<td>Reduced sexual desire</td>
<td>44(73)</td>
<td>34(81)</td>
<td>26(50)</td>
</tr>
<tr>
<td>SF-36 mental index</td>
<td>43.5±10</td>
<td>45±12</td>
<td>47±9</td>
</tr>
<tr>
<td>SF-36 physical index</td>
<td>43±11</td>
<td>43±10</td>
<td>45±19</td>
</tr>
<tr>
<td>HAD Anxiety</td>
<td>7±4</td>
<td>7±5</td>
<td>7±4</td>
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<tr>
<td>HAD Depression</td>
<td>5±4</td>
<td>5±5</td>
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Table 2. Brief Survey Results of Primary and Secondary Sjögren Patients

<table>
<thead>
<tr>
<th></th>
<th>Primary SS</th>
<th>Secondary SS</th>
<th>Healthy Control</th>
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</thead>
<tbody>
<tr>
<td>Vaginal dryness</td>
<td>38(63)</td>
<td>18(43)</td>
<td>4(8)</td>
</tr>
<tr>
<td>Vulvar dryness</td>
<td>26(43)</td>
<td>17(41)</td>
<td>8(15)</td>
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<tr>
<td>Dyspareunia</td>
<td>34(57)</td>
<td>14(33)</td>
<td>8(15)</td>
</tr>
<tr>
<td>Spontaneous genital pain</td>
<td>17(28)</td>
<td>5(12)</td>
<td>5(10)</td>
</tr>
<tr>
<td>Dysuria</td>
<td>13(22)</td>
<td>2(4.8)</td>
<td>8(16)</td>
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<tr>
<td>Dysuria</td>
<td>44(73)</td>
<td>34(81)</td>
<td>26(50)</td>
</tr>
<tr>
<td>At least one gynecological symptom</td>
<td>49(82)</td>
<td>34(81)</td>
<td>26(50)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>33(55)</td>
<td>23(55)</td>
<td>17(32)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>38(63)</td>
<td>23(55)</td>
<td>17(32)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>48(80)</td>
<td>26(62)</td>
<td>17(32)</td>
</tr>
<tr>
<td>At least 1 muscle-skeletal symptom</td>
<td>47(78)</td>
<td>27(64)</td>
<td>17(32)</td>
</tr>
<tr>
<td>HAQ</td>
<td>0.18±0.33</td>
<td>0.45±0.82</td>
<td>0.23±0.45</td>
</tr>
</tbody>
</table>

ABO498

GYNECOLOGICAL SYMPTOMS AND SEXUALITY IN SJÖGREEN’S SYNDROME

Özlem Özdemir Işıklı, Ayten Yazıcı, Ayse Cete. Kocaeli University School of Medicine, Internal Medicine, Division of Rheumatology, Kocaeli, Turkey

Objectives: Patients with Sjögren’s syndrome (SS) have symptoms such as vaginal dryness and dyspareunia.

Methods: 60 pSS, 42 sSS, 52 healthy controls (HC) were interviewed. It was asked questions about sexuality. SF-36, HAQ scale, pSS and sSS patients were also administered HAQ and Modified Hill questionnaire1.

Results: The mean age of the patients was 52 ± 11 years in the pSS, 54 ± 11 years in the sSS and 46 ± 9 years in the HC. Although there was no significant difference in term of age in pSS and sSS groups, there was no significant difference between the two groups in terms of the effect of vulvar, vaginal dryness, dyspareunia, decreased sexual desire, myalgia, arthralgia and fatigue on sexuality. In the pSS group, it was seen that disease had a negative effect on sexuality. There were no significant differences between the two groups when asked whether they enjoyed sexuality and the sexual problems create problems between their partners. In both groups, 97% of patients stated that they had not been questioned about their sexuality before. 80% of pSS patients and 88% of sSS patients stated that they did not talk about sexuality problems.

Conclusion: Gynecological and sexual problems are seen in SS patients. Menopause also contributes to this situation. Patients should be informed about these problems and directed to gynecologists when necessary, and enough time should be reserved as we do.

References


Disclosure of Interests: None declared


ABO499

FINGERSTICK BLOOD TRANSCRIPTOMICS: A PATIENT-CENTRIC APPROACH TO ENABLE PRECISION MEDICINE?

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Janssen Diagnostics, LLC, Ranjan, United States of America

Background: Venous blood collection using PAXgene RNA blood stabilization (PAX) is a routine method to obtain blood for gene expression (GE) studies without requiring phlebotomy and cold chain transport. Decollect® is a fingerstick blood micro collection device (MCD) that circumvents phlebotomy and is reported to stabilize blood RNA for up to 14 days at ambient temperature potentially enabling collected blood to be shipped by mail.

Objectives: We evaluated Decollect® as an alternative to the conventional method to potentially improve convenience and cost effectiveness of blood transcriptomic analysis and allow high frequency transcriptomic assessment.

Methods: Heparinized blood samples were treated with interferon-α for 3h in vitro and transferred to 3 PAX and 3 MCD tubes. One PAX and
FLARES AND DISEASE-RELATED DAMAGE IN LATE-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

Jiapei Cheng1, Pretiel Dhansasekar2, Lay Kheng Teoh3, Liang Shen3, Aisha Latief1
1National University Hospital of Singapore, Singapore, Singapore; 2National University of Singapore, Singapore, Singapore

Background: Late-onset systemic lupus erythematosus (SLE) and its disease-related outcomes have not been previously examined in a multi-ethnic Southeast Asian cohort.

Objectives: To compare the following outcomes between patients with adult-onset versus late-onset SLE a) Disease manifestations at baseline b) Frequency of flares, defined by the SELENA Flare Index (SFI) c) Baseline damage and damage accrual, defined by the SLICC/ACR Damage Index (SDI)

Methods: We prospectively enrolled patients ≥ 21 years old with SLE who fulfilled either the 1997 ACR Criteria or the 2012 SLICC Classification Criteria and followed each patient at least every three months for up to 5 years. Baseline demographics, disease manifestations, antibody profile and activity were captured. At each visit, disease activity was measured using SLEDAI-2k and SDI was measured annually. We defined late-onset SLE as onset of symptoms at ≥50 years of age and adult-onset SLE as onset of symptoms at <50 years of age. We excluded patients with symptom onset before 18 years of age.

We compared the baseline demographic, disease manifestations and antibody profile between the adult-onset and late-onset SLE patients. We analysed continuous variables using the Mann-Whitney U test and categorical variables using the Chi-square test. Bonferroni correction for multiple comparisons was done. We then compared the time to first flare between the two groups using the logrank test. Baseline SDI scores and the proportion of patients who had increased SDI ≥1 over follow-up were compared using Chi-square tests.

Results: Of the 214 patients recruited, 154 (72%) were Chinese and 92 (27%) were Indians. One-hundred and ninety-three (90%) were on anti-malarial therapy and one hundred and forty-one (66%) were on immunosuppressive agents other than corticosteroids. The median (SD) age of recruitment of the SLE patients was 30.0 (22.5-37.5) years, while the median (SD) age of recruitment of the 30 late-onset SLE patients was 53.0 (50.0-56.5) years. The median (IQR) disease duration was 8.12 (7.5-13.5) years among the adult-onset patients and 5.73 (1.52-9.95) years among the late-onset patients.

Conclusion: Our study demonstrated that there was no significant difference in the time to first flare or time to first severe flare between the two groups. The median (SD) time to any flare was 2.51 (0.15) years in the adult-onset group versus 2.77 (0.34) years in the late-onset group, which was not statistically significant (p = 0.521).

REFERENCES

Disclosure of Interests: None declared


AB0501

CLINICAL ANALYSIS OF BONE MINERAL DENSITY IN PATIENTS WITH NEW-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

Xiadi Deng, Li Xinyi. Peking University Third Hospital, Department of Rheumatology and Immunology, Beijing, China

Background: Osteoporosis in patients with systemic lupus erythematosus (SLE) is always thought to be GIOP (induced by glucocorticoid). Yet in our practice, there were some patients who developed osteoporosis at the onset of SLE, before the use of glucocorticoid and immunosuppressants. The clinical feature of these patients were not known by us clearly.

Objectives: This study aimed to investigate the BMD (bone marrow density) status and clinical characteristics of treatment-naive patients with newly diagnosed SLE.

Methods: Patients admitted to Peking University Third Hospital from 2009-2016, who were newly diagnosed as SLE and had no previous medical history that would had affected their BMD, were enrolled in this study. Demographic and clinical data were recorded. BMD of the lumbar vertebrae and femoral necks were measured with dual-energy X-ray absorptiometry, and patients were stratified as normal and abnormal BMD groups (including osteopenia and osteoporosis).

Results: Eighty-nine SLE patients with a mean age of 28.7 ± 8.9 years were included in the study (Table1).

Abstract AB0501 Table 1. Demographics of newly diagnosed SLE patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>SLE patients (n=89)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>28.7±8.9</td>
</tr>
<tr>
<td>Menarche age (year)</td>
<td>13.1±1.3</td>
</tr>
<tr>
<td>BMI (Kg/m²)</td>
<td>21.7±3.8</td>
</tr>
<tr>
<td>Male</td>
<td>7%</td>
</tr>
<tr>
<td>Smoking history</td>
<td>3%</td>
</tr>
<tr>
<td>Fracture history</td>
<td>0%</td>
</tr>
<tr>
<td>SLEDAI</td>
<td>10.0±5.0</td>
</tr>
</tbody>
</table>

Approximately 36% of these patients had normal BMD, 49% had osteopenia, and 15% had osteoporosis. The SLE Disease Activity Index (SLEDAI) in the abnormal BMD group was lower than that in the normal BMD group (9.4 ± 4.5 vs 12.1 ± 5.8, P = 0.028). The body mass index (BMI) was significantly lower in the abnormal than normal BMD group (20.5±3.5 kg/m² vs 24.2±3.2 kg/m², P = 0.00). The total cholesterol (TC) and SLE patients lipid protein (LDL) were lower in the abnormal than normal BMD group (4.3±1.7 mmol/L vs 2.4±1.2 mmol/L, P = 0.04; 4.9±1.3 mmol/L vs 2.9±0.9 mmol/L, P = 0.033). The multisystem damage and
nervous system involvement were less in the abnormal than normal BMD group ($\chi^2 = 5.996, P = 0.014$ and $\chi^2 = 8.169, P = 0.004$). Multivariate analysis revealed that BMI (correlation coefficient $= 0.484$, $P < 0.001$) and multisystem damage (correlation coefficient $= 0.256$, $P = 0.003$) were positively correlated with BMD.

**Conclusion:** Low BMI, SLEDAI and less multisystem damage may be risk factors of BMD abnormalities in newly diagnosed SLE patients.

**REFERENCES**


**Acknowledgement:** This study was supported by a Project of the National Natural Science Foundation of China (81501390). Disclosure of Interests: None declared DOI: 10.1136/annrheumdis-2019-eular.3165

**AB0502**

**IMPROVING RATES OF CERVICAL CANCER SCREENING AND PREVENTION IN PATIENTS WITH LUPUS**

Nancy Desai, Michael York, Hanni Menn-Josephy, Ramon Bonegio, Christina Lam, Anna Kancharia. Boston Medical Center, Boston, United States of America

**Background:** Recent studies suggest that patients with lupus have higher rates of cervical dysplasia and pre-malignant lesions. We have a large population of lupus patients at our institution that may be at increased risk of dysplastic lesions due to suboptimal rates of HPV vaccination and cervical cancer screening. The aim of this study was to determine the rate of HPV vaccination completion and cervical cancer screening compliance among the lupus patients seen in our institution. In addition, we developed a process to increase patient education and improve both HPV and cervical cancer screening rates at the level of the outpatient renal, dermatology and rheumatology clinics.

**Objectives:** To improve rates of cervical cancer screening and HPV vaccination among patients with Lupus

**Methods:** A comprehensive list was compiled of all patients with a diagnosis of lupus seen in the clinics over a 3 year period. A chart review of 332 patients was subsequently performed to determine the rate of HPV vaccination completion and the rate of compliance with cervical cancer screening. Methods were developed to improve these rates by streamlining access to HPV vaccination sites or facilitating referral for screening exams. Patients were also provided education through brochures about their increased risk.

**Results:** Our results revealed that rates of HPV vaccination among lupus patients at our institution were lower than national averages by 11%. Rates of cervical cancer screening were also 21% lower compared to national average for this group of patients. In creating a system to flag providers and increase patient education, we were able to improve these rates. In the first two months, 73.7% of all patients seen in the clinics were provided education and 61.5% of eligible patients that were seen in clinic were appropriately referred to either their PCP or to gynecology to complete cervical cancer screening and prevention.

**Conclusion:** Initial review of the lupus population at our institution highlighted a strong need to develop an intervention to improve vaccination and screening compliance in this population. By raising awareness among providers, we were able to significantly increase the number of at-risk patients referred for cervical cancer screening and prevention.

Given that the United States Food and Drug Administration has recently approved to expand the use of the HPV vaccine to women and men up to age 45, future efforts will be made to expand our eligible population to reflect these recommendations.

**REFERENCES**


**Table 1.** Comparison between pts with and without lung involvement

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No-lung involvement</th>
<th>P-value</th>
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<tr>
<td>Sex Total</td>
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</tr>
<tr>
<td>Female</td>
<td>113</td>
<td>0.31</td>
</tr>
<tr>
<td>Male</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Age at pSS diagnosis (mean±SD)</td>
<td>60±8.6</td>
<td>0.04</td>
</tr>
<tr>
<td>Disease duration (median IQR)</td>
<td>5 (5-12)</td>
<td>0.24</td>
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<tr>
<td>ANA</td>
<td>55 (82.5%)</td>
<td>0.58</td>
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<td>Anti-SSA</td>
<td>41 (57.7%)</td>
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</tr>
<tr>
<td>Hypergammaglobulinemia during follow-up</td>
<td>48 (40%)</td>
<td>0.14</td>
</tr>
<tr>
<td>Constitutional involvement during follow-up</td>
<td>5 (4.2%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Legend: pSS - primary Sjögren’s syndrome; ANA - antinuclear antibodies
Regarding pattern of lung involvement, 9 (52.9%) pts had ILD, 6 (35.3%) isolated bronchiectasis and 2 (11.8%) follicular bronchiolitis. In ILD pts, non-specific interstitial pneumonia (NSIP) was documented in 6 pts, lymphocytic interstitial pneumonia in 2 and 1 pt had unclassifiable ILD pattern with lymphocytic alveolitis in bronchoalveolar lavage. One of the pts with NSIP later developed radiographic characteristics suggestive of usual interstitial pneumonia (UIP). Six ILD pts were treated with immunosuppressive drugs. One received cyclophosphamide (CYC), 2 azathioprine (AZA) and 4 mycophenolate mofetil (MMF). From pts receiving MMF, 1 was previously treated with CYC as induction treatment and the other with AZA, but with inefficacy. Rituximab (RTX) was given to 1 pt with refractory arthritis and new ILD onset. After 11 years on RTX (total 10 cycles) the pt complained of persistent dyspnea and fatigue on minor exertion (cardiac causes excluded), with onset of subtle honeycombing in high resolution computed tomography. At this point pirenidone was added to RTX, with clinical improvement. Detailed lung function and imaging evolution of pSS-ILD pts is shown in table 2.

Conclusion: Lung involvement occurred in 12.4% of our cohort and was associated with older disease at pSS diagnosis and presence of constitutional involvement. Small airways disease and ILD had nearly the same prevalence and in the ILD sub-group, NSIP was the commonest pattern. Despite the small number of ILD pts receiving immunosuppression, these drugs seemed to be associated with disease stabilization in most of them. Only 1 pt with UIP pattern had disease progression and eventually died.

Disclosure of Interests: None declared


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3Universidad San Ignacio de Loyola, Unidad de Medicina Interna, Lima, Peru
2School of Medicine, Universidad de San Martín, Lima, Peru
1Medical University of South Carolina, Charleston, SC, USA

Background: Systemic lupus erythematosus is polygenic autoimmune rheumatic disease with heterogeneous manifestations. Lupus patients with nephritis signify management challenge. With current induction and maintenance therapy the risk of developing lupus nephritis related ESRD at five, ten and fifteen years remains 11, 17 and 22% for the last decades.

Objectives: To study clinicopathological characteristics of lupus nephritis patients as well as short term renal outcome following induction of remission phase.

Methods: Retrospective, prospective observational study. We enrolled all patients with suspected active Lupus nephritis attending Dubai Hospital Rheumatology services. Data collected during outpatient, inpatient consultation using medical electronic system for all patients newly diagnosed to have lupus with renal involvement or patients who had nephritic or nephrotic flare from June 2016 till December 2018.

Results: Of 71 patients included during the study period, mean age was 36.4 years, 93% were female while 7% were males.56 Out of 71 were Arab (76%) while the rest 15 out of 71 (22%) from non-Arab ethnicity. Of 71 patients included during the study period, mean age was 36.4 years, 93% were female while 7% were males.56 Out of 71 were Arab (76%) while the rest 15 out of 71 (22%) from non-Arab ethnicity. 211 (93.4%) were female; and disease duration was 11.0 (7.3) years. The mean SLEDAI and SDI were 2.4 (3.5) and 1.3 (1.5), respectively. The mean FACIT-Fatigue was 25.0 (25.0).

Conclusion: Our study is unique in the region, characterizing high risk group of SLE patients. The signal of co morbid conditions such as hypertension, diabetes mellitus and antiphospholipid antibody positivity as well as class III/IV Lupus nephritis with cellular crescents as predictor of worse renal outcome raise the unmet need for further study with large sample involving more than single center to determine clinical, serological and clinicopathological parameters as long as long term with the available immune suppressive regimens.

Disclosure of Interests: None declared


Clinical Abstracts

AB0504

CLINICOPATHOLOGICAL CHARACTERISTICS AS POSSIBLE PREDICTOR OF RENAL OUTCOME IN PATIENTS WITH ACTIVE LUPUS NEPHRITIS FOLLOWING THE INDUCTION OF REMISSION PHASE

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Background: Systemic lupus erythematosus is polygenic autoimmune rheumatic disease with heterogeneous manifestations. Lupus patients with nephritis signify management challenge. With current induction and maintenance therapy the risk of developing lupus nephritis related ESRD at five, ten and fifteen years remains 11,17 and 22% for the last decade.

Objectives: To study clinicopathological characteristics of lupus nephritis patients as well as short term renal outcome following induction of remission phase.

Methods: Retrospective, prospective observational study. We enrolled all patients with suspected active Lupus nephritis attending Dubai Hospital Rheumatology services. Data collected during outpatient, inpatient consultation using medical electronic system for all patients newly diagnosed to have lupus with renal involvement or patients who had nephritic or nephrotic flare from June 2016 till December 2018.

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Conclusion: Our study is unique in the region, characterizing high risk group of SLE patients. The signal of co morbid conditions such as hypertension, diabetes mellitus and antiphospholipid antibody positivity as well as class III/IV Lupus nephritis with cellular crescents as predictor of worse renal outcome raise the unmet need for further study with large sample involving more than single center to determine clinical, serological and clinicopathological parameters as long as long term with the available immune suppressive regimens.

Disclosure of Interests: None declared


AB0505

AGE AT DIAGNOSIS AND HEALTH-RELATED QUALITY OF LIFE ASSOCIATED WITH FATIGUE IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

Claudia Elera-Fitzcarrolal,1,2 Cristina Reategui Sokoloval,2 Rocio Viedra Gambob Cárdenasl,1 Mariaela Medina1, Francisco Zevallos Miranda1, Victor Pimentel Quiroz2,1 Paola Alejandra Zefía Huancasl,1 Erika Norlegasl,1 Cesar Pastor Asurszl,1,4 Risto Perich Campos1,4, Zollia Rodriguez Bel lids2,1,4 Graciela S. Alarcon4,2,3 Manuel F. Ugarte-Gi5,1,3 Rheumatology Department, Hospital Guillermo Almenara Iñiguez, Lima, Peru,1 School of Medicine, Universidad Científica del Sur, Lima, Peru,2,5 Universidad San Ignacio de Loyola, Unidad de Investigación para la Generación y Síntesis de Evidencias en Salud, Lima, Peru,4 Universidad Nacional Mayor de San Marcos, Lima, Peru,3 The University of Alabama, Birmingham, United States of America

Background: Fatigue can be defined as feeling tired and exhausted and lacking energy (1). It is associated with a poor quality of life; 53 to 80% of SLE patients identify fatigue as their main symptom (2)

Objectives: To define factors associated with fatigue in Mestizo patients with Systemic Lupus Erythematosus (SLE).

Methods: This is a cross-sectional study of SLE patients from a single center cohort. Visits were performed every six months. For these analyses, the first visit between October 2017 and December 2018 was included. Demographic and clinical characteristics as well as treatment were recorded at every visit. Socioeconomic status (SES) was defined using the Graffar’s method (ref). Fatigue was ascertained with the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-FT), Health-Related Quality of Life (HRQoL) with the LupusQoL, disease activity with the Systemic Lupus Erythematosus Disease Activity Index –2K (SLEDAI-2K), and damage with the Systemic Lupus International Collaborating Clinics (SLICC)/American College of Rheumatology (ACR) damage index (SDI). Prednisone use was recorded as current daily dose. Immunosuppressive drugs and antimalarial use was recorded as current, past or never. Univariable and multivariable analyses were performed using linear regression models. For the multivariable analyses, model selection was based on backward elimination.

Results: Two hundred and twenty-six patients were evaluated. The mean (SD) age at diagnosis was 35.6 (13.1) years, 211 (93.4%) were female; and disease duration was 11.0 (7.3) years. The mean SLEDAI and SDI were 2.4 (3.5) and 1.3 (1.5), respectively. The mean FACIT-Fatigue was 33.1 (10.8). In the univariable analyses, FACIT-Fatigue correlated with age at diagnosis, SES, disease duration and all the HRQoL domains like physical health, pain, planning, intimate relationships, burden to others, emotional health, body image and fatigue. On the multivariable analyses, however, only age at diagnosis; and some domains of HRQoL (physical

Disclosure of Interests: None declared


REFERENCES


Disclosure of Interests: None declared

health, emotional health and fatigue) remained associated. Theses analyses are depicted in table 1.

Conclusion: Age at diagnosis is negatively associated with fatigue; HRQoL domains like physical health, emotional health and fatigue are positively associated with fatigue.

Table 1: Factors associated with fatigue in systemic lupus erythematosus patients. Univariable and multivariable analyses.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariable analysis</th>
<th>Multivariable analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis</td>
<td>p &lt; 0.001</td>
<td>p = 0.34</td>
</tr>
<tr>
<td>Gender, female</td>
<td>-0.06</td>
<td>0.03</td>
</tr>
<tr>
<td>Socioeconomic status</td>
<td>-0.10</td>
<td></td>
</tr>
<tr>
<td>Low/medium flow</td>
<td>-0.11</td>
<td></td>
</tr>
<tr>
<td>Medium</td>
<td>0.14</td>
<td></td>
</tr>
<tr>
<td>High/medium/high</td>
<td>0.00</td>
<td></td>
</tr>
<tr>
<td>Disease duration</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>Risk of SLE</td>
<td>0.09</td>
<td>0.02</td>
</tr>
<tr>
<td>Physical health</td>
<td>-0.15</td>
<td>0.01</td>
</tr>
<tr>
<td>Emotionality</td>
<td>-0.12</td>
<td>0.01</td>
</tr>
<tr>
<td>Smoking</td>
<td>-0.10</td>
<td>0.03</td>
</tr>
<tr>
<td>Alcohol</td>
<td>0.13</td>
<td>0.01</td>
</tr>
<tr>
<td>Antimicrobial drug use</td>
<td>-0.10</td>
<td>0.03</td>
</tr>
<tr>
<td>Antimicrobial drug use Present</td>
<td>0.14</td>
<td>0.01</td>
</tr>
<tr>
<td>Past</td>
<td>0.04</td>
<td>0.01</td>
</tr>
<tr>
<td>Never</td>
<td>0.12</td>
<td>0.01</td>
</tr>
<tr>
<td>Immunosuppressive drugs use Present</td>
<td>0.02</td>
<td>0.01</td>
</tr>
<tr>
<td>Past</td>
<td>0.02</td>
<td>0.01</td>
</tr>
<tr>
<td>Never</td>
<td>0.02</td>
<td>0.01</td>
</tr>
</tbody>
</table>

The expression level of micro-RNA-142-3p could be considered a potential activity marker in SLE patients with and without lupus nephritis.

REFERENCES


Disclosure of Interests: None declared


AB0506

MICRONOA A POTENTIAL MARKER OF LUPUS ACTIVITY IN AN EGYPTIAN LUPUS COHORT

Marwa Elkhalifa1, Manal Tayel1, Magdy Zehairy1, Ahmed Elkeriae2, Dalal Mohamed Naar Eldin Elkhafshi3, Nahed Baddour4.

1Hospital Universitário Evangélico Mackenzie, Department of Rheumatology, Curitiba, Brazil; 2Hospital Universitário Evangélico Mackenzie, Department of Otorhinolaryngology, Curitiba, Brazil

Background: Systemic lupus erythematosus (SLE) is a systemic disease that may affect the inner ear.

Objectives: To study hearing function in SLE and its possible association with clinical and serological profile as well as with antimarial use.

Methods: Cross sectional study of 84 individuals (43 SLE patients and 41 controls) with audiometry and impedanciometry tests. Epidemiological, clinical, serological and treatment profile of SLE patients were extracted from the charts.

Results: SLE patients had more sensorineural hearing loss than controls (23.2% vs 0; p=0.001). The hearing loss was seen at 250 Hz, 500 Hz, 1000 Hz and 4000 Hz. No bone conduction impairment was observed. Serological and clinical profile in patients with and without hearing loss was the same (all p=ns). Patients on antimalarial had the same prevalence of hearing loss than those not using it but at 8.000 Hz, antimalarial non-users performed worse than users (p=0.03).

Conclusion: There is a high prevalence of hearing loss in SLE that is not affected by disease characteristics rather by antimarial use.

REFERENCES


TABLE 1: Comparison of median auditory perception (in decibels) according to the studied frequency of the sound, speech recognition threshold and tympanometry between SLE patients and controls

<table>
<thead>
<tr>
<th>SLE patients (68 ears)</th>
<th>Controls (82 ears)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAC</td>
<td>8.75 (5.00-13.75)</td>
<td>10.00 (5.00-12.50)</td>
</tr>
<tr>
<td>AC 250 Hz</td>
<td>10.00 (5.00-15.00)</td>
<td>15.00 (10.00-20.00)</td>
</tr>
<tr>
<td>AC 500 Hz</td>
<td>10.00 (5.00-10.00)</td>
<td>12.50 (5.00-20.00)</td>
</tr>
<tr>
<td>AC 1000 Hz</td>
<td>5.00 (0.00-10.00)</td>
<td>5.00 (5.00-15.00)</td>
</tr>
<tr>
<td>AC 2000 Hz</td>
<td>5.00 (0.00-15.00)</td>
<td>10.00 (5.00-15.00)</td>
</tr>
<tr>
<td>AC 3000 Hz</td>
<td>10.00 (5.00-15.00)</td>
<td>10.00 (5.00-15.00)</td>
</tr>
<tr>
<td>AC 4000 Hz</td>
<td>10.00 (5.00-20.00)</td>
<td>10.00 (5.00-15.00)</td>
</tr>
<tr>
<td>AC 6000 Hz</td>
<td>15.00 (8.75-25.00)</td>
<td>15.00 (10.00-25.00)</td>
</tr>
<tr>
<td>AC 8000 Hz</td>
<td>15.00 (10.00-30.00)</td>
<td>10.00 (8.75-15.00)</td>
</tr>
<tr>
<td>SRT (%)</td>
<td>96.0 (96.0-100.0)</td>
<td>100.0 (100.0-100.0)</td>
</tr>
<tr>
<td>TIMP</td>
<td>0.0 (0.0)</td>
<td>0.0 (0.0)</td>
</tr>
</tbody>
</table>

MAC= mean air conduction; Hz=Hertz; SRT= speech recognition threshold; TIMP= tympanometry.
**AB0508** SCHIRMER TEST, VAN BIJSTERVELD, OSS, AND BREAK-UP TIME TEST IN PRIMARY SJÖGREN’S SYNDROME

Tania Fidelix1, Vânia Fernandes Moça Trevisani2, Laura Santos3, Denise Freitas2, Luiz Antonio Vieira2, Moacyr Rigueiro3, Paulo, Brazil

**Background:** Primary Sjögren’s syndrome (pSS) is an autoimmune disease characterized by lymphocytic infiltration of exocrine glands and other organs, resulting in dry eye, dry mouth, and systemic findings. [1]

**Objectives:** The American College of Rheumatology/AECG group diagnostic criteria for pSS have included three items related to ocular involvement. The Schirmer test type 1, van Bijsterveld score, and Ocular Staining Score (OSS). They are time-consuming and employ costly dyes and instruments. In this context, we analyzed 66 patients with pSS to ascertain correlation between these tests and assess the possibility of streamlining ophthalmologic examination.

**Methods:** Sixty-six patients (180 eyes) from the Federal University of Sao Paulo outpatient cornea clinic were analyzed prospectively from 2017 to 2018. Those with suspicion of pSS were tested according to the 2016 ACR-EULAR diagnostic criteria.

**Results:** Of the 66 patients, 64 were female; 36 were white; median age was 53.3 (11.3) years. The Schirmer I test was done in 177 eyes, it was positive in 57.6%. The van Bijsterveld score was done in 128 eyes and was positive in 61.7%. The OSS was done in 177 eyes and was positive in 96%. The TBUT was tested in 175 eyes and was positive in 86.4%. All four tests could be performed in 128 eyes. The results were confirmed at the same proportions. Correlation between tests was then calculated through the kappa coefficient (Table 1).

**Conclusion:** Schirmer’s test without anesthetics has been part of the AECG diagnostic criteria for pSS since 1989. [2]

**Disclosure of Interests:** None declared

**REFERENCES**


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**Table 1.** Comparison of clinical data, auditory perception (in decibels) according to the studied frequency of the sound, speech recognition threshold and tympanometry in SLE patients using and not using antimalarials

<table>
<thead>
<tr>
<th>Test</th>
<th>Frequency (Hz)</th>
<th>Median (SD)</th>
<th>Interquartile range (SD)</th>
<th>n= number</th>
<th>AC= airway conduction; SRT= speech recognition threshold; TIMP= tympanometry.</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAC</td>
<td>500 Hz</td>
<td>7.50 (5.00-13.75)</td>
<td>8.75 (5.31-13.44)</td>
<td>128</td>
<td>0.26</td>
</tr>
<tr>
<td>AC 500 Hz</td>
<td>10.00 (5.00-15.00)</td>
<td>7.50 (5.00-13.00)</td>
<td>0.63</td>
<td>128</td>
<td></td>
</tr>
<tr>
<td>AC 800 Hz</td>
<td>12.50 (5.00-21.25)</td>
<td>20.00 (15.00-25.00)</td>
<td>0.07</td>
<td>128</td>
<td></td>
</tr>
<tr>
<td>AC 1600 Hz</td>
<td>25.00 (10.00-60.00)</td>
<td>50.00 (10.00-60.00)</td>
<td>0.47</td>
<td>128</td>
<td></td>
</tr>
<tr>
<td>MAC</td>
<td>20.00 Hz</td>
<td>10.00 (5.00-15.00)</td>
<td>0.64</td>
<td>128</td>
<td></td>
</tr>
<tr>
<td>AC 200 Hz</td>
<td>15.00 (5.00-18.75)</td>
<td>12.50 (5.00-15.00)</td>
<td>0.43</td>
<td>128</td>
<td></td>
</tr>
<tr>
<td>AC 400 Hz</td>
<td>15.00 (5.00-20.00)</td>
<td>20.00 (15.00-20.00)</td>
<td>0.39</td>
<td>128</td>
<td></td>
</tr>
<tr>
<td>AC 600 Hz</td>
<td>10.00 (5.00-14.25)</td>
<td>12.00 (8.25-21.25)</td>
<td>0.19</td>
<td>128</td>
<td></td>
</tr>
<tr>
<td>AC 500 Hz</td>
<td>10.00 (5.00-10.00)</td>
<td>7.50 (5.00-10.00)</td>
<td>0.47</td>
<td>128</td>
<td></td>
</tr>
<tr>
<td>AC 1000 Hz</td>
<td>5.00 (5.00-10.00)</td>
<td>2.50 (5.00-10.00)</td>
<td>0.47</td>
<td>128</td>
<td></td>
</tr>
<tr>
<td>AC 2000 Hz</td>
<td>5.00 (3.75-15.00)</td>
<td>10.00 (0.00-15.00)</td>
<td>0.64</td>
<td>128</td>
<td></td>
</tr>
<tr>
<td>AC 3000 Hz</td>
<td>5.00 (3.75-15.00)</td>
<td>10.00 (0.00-15.00)</td>
<td>0.64</td>
<td>128</td>
<td></td>
</tr>
<tr>
<td>AC 4000 Hz</td>
<td>5.00 (3.75-15.00)</td>
<td>10.00 (0.00-15.00)</td>
<td>0.64</td>
<td>128</td>
<td></td>
</tr>
</tbody>
</table>

**Table 1.** Kappa coefficients for classification of primary Sjögren’s syndrome

<table>
<thead>
<tr>
<th>Pairwise comparison</th>
<th>Kappa</th>
<th>Standard Error</th>
<th>z</th>
<th>p</th>
<th>Observed agreement</th>
<th>Expected agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schirmer I x Break-Up Time</td>
<td>0.112</td>
<td>0.041</td>
<td>2.76</td>
<td>0.003</td>
<td>63.28%</td>
<td>58.64%</td>
</tr>
<tr>
<td>Schirmer I x Van Bijsterveld</td>
<td>0.428</td>
<td>0.083</td>
<td>4.85</td>
<td>&lt;0.001</td>
<td>72.66%</td>
<td>52.20%</td>
</tr>
<tr>
<td>Schirmer I x OSS</td>
<td>0.469</td>
<td>0.088</td>
<td>5.35</td>
<td>&lt;0.001</td>
<td>75.00%</td>
<td>52.93%</td>
</tr>
<tr>
<td>Break-Up Time x OSS</td>
<td>0.123</td>
<td>0.043</td>
<td>2.90</td>
<td>0.002</td>
<td>65.63%</td>
<td>60.80%</td>
</tr>
<tr>
<td>Van Bijsterveld x Break-Up Time</td>
<td>0.144</td>
<td>0.046</td>
<td>3.15</td>
<td>0.001</td>
<td>69.53%</td>
<td>64.40%</td>
</tr>
</tbody>
</table>

**Disclosure of Interests:** None declared


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**AB0509** PREVALENCE AND INCIDENCE OF SJÖGREN’S SYNDROME AMONG PATIENTS WITH RHEUMATOID ARTHRITIS IN REAL-WORLD COMMUNITY PRACTICE SETTINGS

Leticia Ferr1, Ying Bao1, Sonie Lama1, Varshini Rajagopalan2, Evo Almeida1

**Background:** Sjögren’s syndrome (SS) is a rheumatoid disease that may coexist with RA, and is often considered a common extra-articular manifestation of RA. However, few studies have examined the prevalence and incidence of SS in patients with RA in real-world community practice settings.

**Objectives:** To estimate the prevalence and incidence of SS in patients with RA, and to summarise the characteristics of patients with SS associated with RA compared with those of patients with RA alone.

**Methods:** We analysed data from 1 Jan 2014 to 30 Jun 2018 in a large rheumatology database in the USA, which provides electronic medical record data from 120 community-based rheumatology providers. Adult patients with ≥2 RA diagnoses were identified from 1 Jan 2015 to 30 Jun 2018 (index period). The baseline period was from 1 Jan 2014 to 31 Dec 2014. Among patients with RA, we identified patients with ≥2 SS diagnoses in the index period (prevalent SS patients and patients with ≥2 SS diagnoses in the index period who had not been diagnosed with SS in the baseline period [incident SS patients]). Crude and age- and sex-standardised prevalence and incidence of SS were calculated among patients with RA. Characteristics of prevalent SS patients and patients with RA alone (as a control group) were summarised.

**Results:** A total of 53,156 patients with RA were identified. Among them, we identified 2451 prevalent SS patients and 1460 incident SS patients. The age- and sex-standardised prevalence of SS in patients with RA was 3.48%, and the age- and sex-standardised incidence rate was 0.66 per 100 patient-years. Female patients had a higher prevalence (5.23%)
vs 1.68%) and incidence (0.96 vs 0.36 per 100 patient-years) of SS than male patients. Compared with other age groups, patients with RA aged 30–49 years had the highest prevalence (3.80%) and incidence (0.77 per 100 patient-years) of SS (Table 1). Compared with patients with RA only, those with both SS and RA were more likely to be female (92% vs 76%), had higher Charlson Comorbidity Index and lower CDAI scores, and were more likely to have prior use of biologic/targeted synthetic DMARDs (30% vs 10%) and conventional DMARDs (48% vs 18%) (Table 2).

Conclusion: This study estimated the prevalence and incidence of SS among patients with RA in real-world community practice settings, and provided insights on clinical characteristics of these patients. Patients with both SS and RA have less joint disease activity and greater DMARD exposure than those with RA only. The findings underscore the complexity of SS secondary to RA and highlight the important role of epidemiological research in understanding this condition.

Disclosure of Interests: This study was funded by Bristol-Myers Squibb.

Table 1: Prevalence and incidence of SS in patients with RA

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>RA and SS</th>
<th>RA only</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>2461</td>
<td>50,165</td>
</tr>
<tr>
<td>Age, years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
<td>2461</td>
<td>50,165</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>63.60 (61.90)</td>
<td>62.30 (60.90)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2260 (92.52)</td>
<td>36,060 (73.03)</td>
</tr>
<tr>
<td>Charlson Comorbidity Index score</td>
<td>2461</td>
<td>50,165</td>
</tr>
<tr>
<td>Median (IQR)</td>
<td>1.40 (1.06)</td>
<td>0.00 (0.00)</td>
</tr>
<tr>
<td>BMI, kg/m² ²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n</td>
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<tr>
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<td>29 (0.58)</td>
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<tr>
<td>Pulmonary nodules</td>
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LUNG ULTRASOUND OF PLEURAL IRREGULARITIES IN SUB-CLINICAL PRIMARY SJÖGREN’S SYNDROME-
LUNG INVOLVEMENT: A SINGLE CENTRE EXPERIENCE

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Background: Ultrasound of Pleural Irregularities (PI-US) has recently been suggested as a useful tool for the diagnosis and quantification of severity in connective tissue diseases (CTD)-related lung involvement. However, no data are available regarding its role in the sub-clinical phase of primary Sjögren’s syndrome (pSS)-related lung involvement.

Objectives: Aim of this study was to describe the role of lung ultrasound analyzing pleural irregularities in asymptomatic pSS-patients in order to early detect lung abnormalities/alterations.

Methods: pSS patients regularly followed-up at our Sjögren’s Clinic and asymptomatic for dyspnea and cough, undergoing to CT or HRCT exam for lymphoproliferative and/or neoplastic screening, were included in the study. Demographic, clinical, biological and serological data were collected. PI-US was performed by a single operator using a MyLab ClassC (Esaote), 13-18 MHz, 5 cm linear probe. PI was defined as the loss of normal hyperchoic linear pleural contour (score 0-2: normal, minimal and major changes at each intercostal space). PI-US total score represented the sum of partial scores assigned to 6 lung fields (2 for the anterior, 2 for postero-superior and 2 for postero-inferior chest surface). CT-abnormal findings, distinguishing typical (interstitial pattern) from atypical lung alterations (non specific findings), were analyzed by an expert radiologist.

Results: 24 pSS patients (AECC criteria), 20 F:4 M, mean age =58 ±12.2 yrs, mean follow-up duration 8.6±12.2 yrs, were included in the study. All patients were positive for ANA, 21/24 for anti-Ro/SSA, 15/24 for Rheumatoid Factor (RF) and 6 of them for cryoglobulins. Four patients (16.67%) had a previous history of pSS-related lymphoproliferative disorder.

None of the included patients reported cough or dyspnea and the thoracic examination did not arise any abnormalities suggestive for lung diseases.

The mean PI-US total and postero-inferior partial score resulted 22.75 ±19.72 and 8.29±8.60 respectively. CT/HRCT resulted normal in 9/24 patients (37.5%) and showed abnormal findings in 15/24 (62.5%). The latter consisted of non- Interstitial Lung Disease (ILD) alterations in 13/15 cases (i.e 13/13 fibrotic striae and/or micro/macroanodularities, 5/13 disven-tillatory striae and/or medium lobe syndrome, 3/13 bronchiectasias and/or bronchiolectasias and 3/13 thin-walled cysts/atypical emphysema). In 2/15 patients a new diagnosis of Interstitial Lung Disease (ILD) was made with patients presenting a typical NSIP-pattern. Both the mean PI-US total score and the postero-inferior partial score resulted significantly higher in patients with abnormal CT/HRCT compared to those with normal CT findings (p =0.003 and p= 0.001 respectively). On the contrary, PI-US total and partial scores were not significantly different between ILD and non-ILD pSS patients (p = 0.103).

Conclusion: this study highlights the potential usefulness of PI-US as a sensitive, non invasive tool for the diagnosis of sub-clinical early lung alterations in pSS.

Disclosure of Interests: Francesco Ferro: None declared, Alessandra Bulleri: None declared, Elena Elefante: None declared, Alessandra Tripoli: None declared, Marta Mosca Paid instructor for: GlaxoSmithKline, Lilly, UCB, Chiara Baldini: None declared

A COMPARATIVE STUDY ON CLINICAL AND SEROLOGICAL CHARACTERISTICS BETWEEN PATIENTS WITH RHUPUS AND PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Beatriz Frade Sosa1, J. Navarrete2, Tarek Carlos Salman Moreno2, Vera Ortiz Santamaria3, Vicenç Torrente Segarra3, Ivan Castellvi4, Beatriz Frade Sosa5, Raúl Castellanos-Moreira6, Delia Reina7, Sonia Minguez8, Maria Garcia Manrique de Lara9, Sergi Ordoñez10, Meritxell Sallés Lizarzaburu11, Elena Riera Alonso11, Jose A. Gómez-Puerta12, Roberta Ottaviani2, Micaela Fredi2.

Objective: To avoid misclassification, those patients with Rhupus but who had Jacobson’s arthritis or with overlap syndromes were excluded.

Methods: A total of 120 patients were included, 40 cases with Rhupus and 80 cases with SLE. Most of patients were female (95%) and Caucasian (75%). Mean age was 51 ± 14.7 years with a mean disease duration of 12.9 ± 9.2 years. Clinical characteristics were arthritic involvement (93.3%), cutaneous involvement (77.5%), haematological (72.5%), secondary Sjögren syndrome (38.7%) among others. Clinical and serological characteristics according different groups are shown in Table.

Disclosure of Interests: Vera Ortiz Santamaria: None declared, Vicenç Torrente Segarra: None declared, Ivan Castellvi Consultant for: Roche, I received fees less than 2000USD as a investigator for Roche, Pfizer, Lilly, Janssen, Merck-Serono, BD, Benetanna; None declared, Raul Castellanos-Moreira Speakers bureau: MSD, Lilly, Roche, Janssen, Boehringer Ingelheim, Pfizer; Janssen, Novartis, Bayer, Roche, AstraZeneca; DAR, None declared, Meritxell Sallés Lizarzaburu: None declared, Elena Riera Alonso: None declared, Jose A. Gomez-Puerta Consultant for: Pfizer, Lilly, Boehringer Ingelheim, Roche; I received fees less than 2000USD as a investigator for Boehringer Ingelheim, Novartis, Pfizer; Janssen, MSD, Pfizer, Janssen, Roche.

AB0513

UTILITY OF RENAL REBIOPSY IN PATIENTS WITH LUPUS NEPHRITIS

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1Hospital Ramón Y Cajal, Rheumatology, Madrid, Spain; 2Hospital Ramón Y Cajal, Rheumatology, Madrid, Spain; 3Hospital Ramón Y Cajal, Nephrology, Madrid, Spain.

Background: The pathological class of lupus nephritis (LN) may change to a different class during the course of the disease. Renal biopsy is repeated is repeated in many patients during a flare but there is there is no agreement about systematically recommending them because proliferative lesions on their original biopsy rarely switch to a pure non-proliferative nephritis during a flare. However, renal biopsy may be useful in some cases to make appropriate adjustments or changes of treatment.

Objectives: To analyze the impact of renal biopsy on the therapeutic approach in patients with previous histological diagnosis of LN who experience a worsening in the clinical parameters of renal involvement.

Methods: Retrospective study of patients with histological diagnosis of NL subjected to at least one renal biopsy. We studied the demographic, clinical, histopathological variables of the first and subsequent renal biopsies, received treatment and the therapeutic modifications in relation to the result of the rebiopsies.

Results: We analyzed 35 patients diagnosed with LN between 1978 and 2017. 9 of them had been rebiopsed at least on one occasion and made a total of 11 biopsies (7 patients with a rebiopsy and 2 patients with 2 rebiopsies). All patients were female and Caucasian, except for a Hispanic woman, with a mean age at the time of the biopsy of 31 ± 12 years (14–55). The mean serum creatinine at the time of the first biopsy was 0.8 ± 0.17 mg/dl (0.5–1.06) and in the second, 1.18 ± 0.05 mg/dl (1.15-1.23). The fundamental indication for the rebiopsy was the increase in proteinuria, up to non-nephrotic range in 64% of the patients (4.5% of patients had a proteinuria >100 mg.) 4 of the rebiopsies (36%) started from a proliferative class and within the nephrotic range in 36%. In comparison with the previous biopsy, 3 of the rebiopsies (27%) showed evolution from a non-proliferative to a proliferative form (from II to III, from II to IV and from V to V + IV), 4 of the rebiopsies (36%) started from a proliferative class and changed class but within these forms (3 from IV to III and 1 from III to IV). The remaining 4 rebiopsies (27%) showed no change in the histological type. Regarding the baseline biopsy, we observed a decrease in the index of activity of the rebiopsies (5.4 ± 2.2 vs 3.4 ± 2.5, p = 0.017) and an increase in the chronicity index (0.8 ± 0.7 vs 2.9 ± 3.2, p = 0.027). In all cases, therapeutic modifications were carried out. In 9 cases (82%) the immunosuppression was increased and in two of them (18%) it was decreased.

Conclusion: The repetition of renal biopsy in cases of LN with clinical data of renal deterioration is relevant. The change of histological class and the evolution of activity and chronicity indices support the decision to increase immunosuppression and are fundamental to diminish it.

REFERENCES

Disclosure of Interests: None declared


AB0514

PARATHORMONE BUT NOT VITAMIN D SERUM LEVELS ARE ASSOCIATED WITH SUBCLINICAL ATHEROSCLEROSIS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Growing evidence supports a link between alterations in bone metabolism and cardiovascular (CV) disease in both general and autoimmune populations.

Objectives: In the current study we aimed to explore whether vitamin D deficiency and/or increased parathormone (PTH) levels, as well as impairment of bone mass density, influence CV risk in patients with systemic lupus erythematosus (SLE).

Methods: 138 consecutive SLE patients were enrolled in the study. Clinical features, hematological, serological and immunological profile, as well as therapeutic regimens was recorded in all patients. Classical CV and osteoporosis risk factors were assessed in all participants. Intima-media thickness (IMT) (and carotid and/or femoral) (CV-IMT) were evaluated by ultrasound. Assessment of bone mineral density (BMD) and asymptomatic osteoporotic fractures was also performed by dual X-ray absorptiometry and lateral thoracic and/or lumbar spine X-rays, respectively. Univariate and multivariate models were implemented for statistical analysis.

Results: PTH -but not 25(OH)vitamin D3- serum levels were found to be increased in lupus patients with subclinical atherosclerosis (plaque formation/or arterial wall thickening) compared to those without (51.1±27.4 vs 37.4±18.4 pg/ml, p= 0.003 and 54±32.7 vs 40±18.3 pg/ml, p= 0.02, respectively). Abnormal PTH serum concentrations (>65 pg/ml) in SLE patients was identified as a risk factor for both plaque formation and high IMT scores (>0.9mm) [OR 95% (CI): 8.2 (1.8-37.4) and OR 95% (CI): 4.4 (1.2-15.9), respectively]. Finally, an inverse correlation between femoral neck BMD values and total IMT scores was observed (r:-0.42, p=0.008).

Conclusion: Subclinical atherosclerosis in patients with lupus is associated with increased serum PTH levels and reduced bone mass density. These findings further support the presence of shared pathophysiogenetic mechanisms between arterogenesis and altered bone metabolism.

Disclosure of Interests: None declared


AB0515

OBESITY AND WEIGHT LOSS IMPACT IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

Maria Rita Giangreco1, Luca Petricca1, Clara Di Mario2, Anna Maria Paglionico1, Valentina Varriano2, Stefano Alivernini3, Barbara Aquilanti4, Maria Rosaria Magiurato2, Giacomo Tanti2, Barbara Toloso1, Gianfranco Ferraccio1, Elisa Gremese1, Fondazione PoliChir Universitario A. Gemelli – IRCCS, Division of Rheumatology, Rome, Italy; 2Università Cattolica del Sacro Cuore, Division of Rheumatology, Rome, Italy; 3Fondazione PoliChir Universitario A. Gemelli – IRCCS, Università Cattolica del Sacro Cuore, Division of Rheumatology, Rome, Italy; 4Policlinico Universitario A. Gemelli – IRCCS, Diabetes, Service, Rome, Italy; 5Fondazione PoliChir Universitario A. Gemelli – IRCCS, Psychology Service, Rome, Italy.

Background: Obesity is considered a chronic low-grade inflammatory status due to the release of bioactive substances, as pro-inflammatory cytokines, by the adipose tissue, and it is known negatively affecting some autoimmune inflammatory diseases, like Rheumatoid Arthritis. Few data are available on the role of obesity in Systemic Lupus Erythematosus (SLE) disease.

Objectives: To evaluate the distribution of Body Mass Index (BMI) categories in SLE patients and the association between SLE disease activity and BMI groups. Furthermore, to assess the impact of weight loss in a cohort of overweight/obese SLE patients, evaluated with a multidisciplinary approach.

Methods: Consecutive SLE patients, diagnosed according to the 2012 SLICC criteria, were enrolled. Clinical and demographic characteristics, disease duration, BMI category, laboratory indices and current therapies were collected at baseline and at follow-up visits. A subgroup of SLE patients with BMI>25 Kg/m2 underwent a scheduled diet under a Nutrition guide (1200 calories/day) and Psychologist support when necessary, maintaining the SLE therapy unchanged and were evaluated by a rheumatologist and a nutritionist every 3 months and clinical and laboratory data and the ACR/EULAR core data set were registered at each follow-up (FU) visit.

Results: Of the 277 patients (age 42±14.4 years, disease duration 8.4 ±8.0 years, SLEDAI-2K 6.6±7.6, SLICC 1.9±1.5), 47.6% had arterial, 32.3% renal, 23.6% neurological and 21.9% had serositis involvement, respectively. Considering the whole cohort, 66 (23.9%) patients had BMI between 25 and 30 Kg/m2 and 34 (12.3%) a BMI>30 Kg/m2 [of which 15 (5.4%) with BMI >35 Kg/m2]. Overweight/obese SLE patients were predominantly male (20.0%) with respect to patients with BMI<25 Kg/m2 (4.5%, p<0.001). Considering the therapeutic regimens, antimalarials treatment was ongoing in 39.4% of overweight SLE patients and in 61.8% of obese SLE patients compared to 28.7% in normal weight SLE patients (p< 0.001 for overweight and p<0.001 for obese patients), without any significant correlation between BMI and cumulative steroid dose during
the follow-up. Considering the whole SLE cohort, cardiovascular events were more frequent in obese patients (14.7%) than in overweight (7.6%) and normal weight (2.9%) SLE patients (ANOVA test: p<0.01). Twenty-nine SLE patients with BMI≥25 Kg/m² (BMI: 33.5 ± 5.1 Kg/m²; age: 47.7 ± 12.3 years, disease duration: 11.9 ± 9.0 years; SLEDAI: 10.5 ± 5.7; SLICC: 1.3 ± 1.1) underwent a scheduled low calories diet. A significant reduction in BMI was observed at 6 and 12 month follow-up [6.6 ± 5.7% at 6 months FU (p = 0.001) and 7.0 ± 7.2% at 12 months FU (p=0.002)] respectively as well as a reduction in disease activity [SLEDAI at 6 months FU: 4.5 ± 4.0 (p=0.001) and at 12 months FU (0.7 ± 0.9 (p <0.001)]. Finally, a significant decrease of systemic inflammatory markers as C-Reactive Protein (p<0.05) was observed in SLE patients who achieved >5% weight loss compared to SLE patients who did not.

Conclusion: Obesitas presents a modifiable factor for improving outcomes among obese SLE. A weight loss obtained with a controlled diet may reduce cardiovascular events and reduce the state of chronic inflammation subdued by the activity of adipose tissue.

Disclosure of Interests: Maria Rita Gigante: None declared, Luca Petritti: None declared, Clara Di Maria: None declared, Anna Maria Pagliunco: None declared, Valentina Varriano: None declared, Stefano Alivermi Speakers bureau: BMS, Barbara Aquilanti: None declared, Maria Rosaria Magnoarance: None declared, Giacomo Tanti: None declared, Barbara Tolusso: None declared, Gianfranco Ferraccioli Speakers bureau: BMS, Roche, Elisa Gremsse Consultant for: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Sanofi, UCB, Roche, and Pfizer, Speakers bureau: BMS: Roche, Sanofi speakers bureau: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis, Sanofi, UCB, Roche, and Pfizer


AB0516 AUTOANTIBODY PROFILE ANALYSIS AND ITS ASSOCIATION WITH CLINICAL MANIFESTATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

Elena Grau García1, Francisco Miguel Ortiz Sanjuan1, Cristobal Páez Perales1, Carmen Nájera Herranz1, Inés Cánovas Olmos1, José Ivorra Cortés1, 2

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Background: Systemic lupus erythematosus (SLE) is an autoimmune systemic disease characterized by autoantibody production. The presence of some of them is related to specific clinical manifestations. Previous studies have classified SLE patients according to an autoantibody profile, associating them to specific clinical groups.

Objectives: To define SLE patient groups according to an autoantibody profile and to analyze the correlation of these profiles to clinical manifestations, clinical activity and accumulated damage.

Methods: A cross-sectional observational study of SLE patients diagnosed according to SLICC 2012 criteria was conducted. A clinical and analytical evaluation was performed in all cases. Clinical manifestations were described according to RELESSEY study. We selected 8 autoantibodies to classify SLE patients in different subgroups according to autoimmune similar profiles: anti-dsDNA, anti-Sm, anti-RNP, anticardiolipin IgG o IgM (aCL IgG), anti-B2-microglobulin IgG or IgM (aB2M IgG/M), lupus anticoagulant (LA), anti-Ro and anti-La. Biostatistical analysis was performed using software R and immunological profiles were created according to previous study of Arlt-Esen B et al. 2014.

Results: 142 SLE patients were evaluated (94.4% female) with a mean age at diagnosis of 33.29 (13.53) and a mean time of disease evolution of 15.82 (10.56) years. Mean SLEDAI score was 5.91 (5.6) and mean SLICC value 1.1 (1.46). Frequency of the selected autoantibodies was: ANAs 87.3% (n=124), anti-dsDNA 36.62% (n=52), anti-Sm 9.2% (n=13), anti-RNP 3.5% (n=9), aCL IgG/M 20.15% (n=27), aB2M IgG/M 21.86% (n=28), LA anti-LA? 29.27% (n=31), anti-Ro 45.07% (n=64) and anti-La 16.2% (n=23).

Profile n°2 included SLE patients with anti-Sm/RNP positivity. Profile n°3 included patients with anti-Ro/La positivity and not included in profile n°2. Profile n°4 included patients with aCL IgG or aB2M IgG/M or LA (positivity and not included in previous profiles. Profile n°5 included patients who exclusively showed anti-DNA positivity. Profile n°7 included all patients excluded from the other profiles.

Depending on the results obtained, we analyzed autoantibody levels in order to assess their association with the presence of the described clinical affections. A significant association among hematological affection and high levels of anti-Ro (P<0.0001), anti-La (P<0.022) and anti-Sm (P=0.018) was observed. We also observed a tendency of presenting a higher rate of mucocutaneous affection, musculoskeletal and renal affection and Sjögren syndrome in patients classified in Profile 3.

Conclusion: Profile n°1 patients (absence of autoantibodies) were diagnosed earlier and had a longer disease evolution, whereas Profile n°5 patients (only anti-DNA positivity) were diagnosed at a mean age of 36 years and had a shorter disease evolution. We observed an association between the presence of anti-Ro/La and hematological affection, as well as a high incidence of Sjögren syndrome in this subgroup of patients.

Disclosure of Interests: None declared


AB0517 CORRELATION BETWEEN PATIENT-REPORTED OUTCOMES OF HEALTH-RELATED QUALITY OF LIFE AND CLINICAL ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Rheumatology Department. HUP La Fe, Valencia, Spain

Background: Patient-Reported Outcomes (PROs) allow us to know the way the disease could affect patients, and maybe could not be detected in clinical measures. Among these, PROs of health-related quality of life (PRO-QL) represents patient evaluation of its health status and treatment, which affects the functional, psychological, social and emotional capabilities. In fact, patients with the same health status could show different PROs-QL. In the case of systemic lupus erythematosus (SLE), patients experience many inflammatory symptoms and all of them can affect the health-related quality of life in different ways.

Objectives: We aimed to measure the PRO-QL in SLE patients and correlate them with the clinical activity of the disease.

Methods: A cross-sectional observational study with SLE patients diagnosed according to SLICC 2012 criteria was performed. In all cases SLEDAI score was carried out, and patients full-filled questionnaires of fatigue (FACIT-FATIGUE), quality of life (EQ-5D-5L), disability (HAQ) and a Global Health Status Scale (GHS) (0-100). Biostatistical analysis with software R was performed, using the multivariate analysis of variance by software R.

Results: 54 SLE patients (91.84% female) participated in the study, with a mean age at diagnosis of 27.55±13.21 years and a mean time of disease evolution of 20.4±5.9 years. Mean SLEDAI score was 6.63±6.89, with a 37.04% of patients with SLEDAI>6. The 64.66% of patients were under glucocorticoid treatment, 38.77% under immunosuppressants (methotrexate, azathioprine or mycophenolate) and 51.02% under antimalarials. Patients showed a mean score of 34.02±13.38 in FACIT-FATIGUE, 0.72 ±0.26 in EQ-5D-5L, 0.62±0.71 in HAQ and 64.02±25.93 in GHS.

Statistical analysis showed correlation between SLEDAI score and the four questionnaires of PROs-QL (P<0.001). Particularly in those cases with high clinical activity we observed low scores of EQ-5D-5L, FACIT-FATIGUE and GHS, and an increment in HAQ. We performed the previous analysis considering as correcting factors the age, the years of disease evolution, glucocorticoid treatment, antimalarials and immunosuppressants. We also obtained a correlation between clinical activity and PROs-QL (P<0.0107).

Conclusion: We observed a correlation between PROs-QL full-filled by SLE patients with the clinical activity of the disease, independently of glucocorticoid treatment, antimalarials and immunosuppressants, the age and the disease evolution.

Disclosure of Interests: None declared

AB0518 | JUVENILE SYSTEMIC LUPUS ERYTHEMATOSUS RELATED PANCREATITIS: AN UNCOMMON MANIFESTATION OF A COMMON DISEASE
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Background: Pancreatitis is a rare but potentially life-threatening complication of juvenile systemic lupus erythematosus (jSLE).

Objectives: We report 3 children with SLE who presented with acute pancreatitis.

Methods: We have reviewed the clinical records of 140 children with SLE between period of 1993-2018. Three of them present with acute pancreatitis.

Results: Case 1-12-year-girl presented with fever of 1 month and alopecia. Examination revealed pedal oedema, periorbital puffiness, generalised lymphadenopathy, large joint arthritis and mild hematopoegetic.Investigations were consistent with lupus.Renal biopsy revealed Class 3 lupus nephritis and initiated on intravenous methylprednisolone. Two days after beginning her medication,she developed severe epigastric pain and vomiting which did not respond to antacids and analgesic. Serum amylase and lipase were elevated. Clinical possibilities included steroid induced pancreatitis and lupus pancreatitis. Intravenous methylprednisolone was continued following which she showed a dramatic improvement. Case 2- A 6-year-old prepubertal boy with pain abdomen and vomiting. Physical examination showed epigastric tenderness. Investigations showed elevated amylase levels. Computed tomography(CT) abdomen revealed acute necrotising pancreatitis. A ultrasound abdomen revealed a pancreatic pseudocyst. He had a second episode of acute pancreatitis along with anaesthesia after 3 months. In follow-up, he presented with anaesthesia. Investigation were consistent with lupus. Following the initiation of steroids, he improved and there has been no recurrence of pancreatitis over the next 4 years. Case 3- A 9-year-girl presented with generalised rash and alopecia for 5 months. She also had pain abdomen for last 2 months. Investigations showed elevated amylase and ultrasound abdomen revealed acute pancreatitis. She had undergone a laparotomy elsewhere. Examination showed generalised pigmented rash, periorbital edema, alopecia, periorbital puffiness, hard palate ulcer and surgical scar on the abdomen. Urinalysis showed nephrotic range proteinuria. Serum amylase levels were elevated. Ultrasound abdomen revealed a pancreatic pseudocyst. Further investigations were suggestive of lupus. Workup for APLA revealed positive lupus anticoagulant. She was initiated on oral prednisolone and was given pulses of intravenous cyclophosphamide. Workup for APLA revealed positive lupus anticoagulant. She was initiated on oral prednisolone and was given pulses of intravenous cyclophosphamide. She had undergone a laparotomy elsewhere. Examination showed generalised pigmented rash, periorbital edema, alopecia, periorbital puffiness, hard palate ulcer and surgical scar on the abdomen. Urinalysis showed nephrotic range proteinuria. Serum amylase levels were elevated. Ultrasound abdomen revealed a pancreatic pseudocyst. Further investigations were suggestive of lupus. Workup for APLA revealed positive lupus anticoagulant. She was initiated on oral prednisolone and was given pulses of intravenous cyclophosphamide. There has been no recurrence of pancreatitis over 12-years follow-up.

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<td>10/12</td>
<td>Few RBC, 3+ albumin</td>
<td>No RBC,</td>
</tr>
<tr>
<td>Urine protein (mg/m²/hour)</td>
<td>RBC, 3+ albumin</td>
<td>82 mg/m²/hr</td>
<td>3+ albumin</td>
</tr>
<tr>
<td>C3 (Normal 50-150 mg/dl)</td>
<td>23.4 mg/dl</td>
<td>129 mg/dl</td>
<td>34 mg/dl</td>
</tr>
<tr>
<td>C4 (Normal 20-50 mg/dl)</td>
<td>2.88 mg/dl</td>
<td>37 mg/dl</td>
<td>10 mg/dl</td>
</tr>
<tr>
<td>ANA</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>Anti dsDNA (N: &lt;60 IU/mL)</td>
<td>890 &lt;60</td>
<td>123</td>
<td></td>
</tr>
<tr>
<td>Antiphospholipid antibodies: a)</td>
<td>Negative</td>
<td>Negative</td>
<td>Positive</td>
</tr>
<tr>
<td>Lupus anticoagulant b)</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Anticardiolipin antibody (IgG and IgM) c)</td>
<td>Anti I2 Glycoprotein -1 antibody (IgG &amp; IgM)</td>
<td>Not done</td>
<td>Not done</td>
</tr>
<tr>
<td>Shik biopsy</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>Renal biopsy</td>
<td>Class 3</td>
<td>IgA, IgM, and C3 in dermal vessels</td>
<td>Class 4</td>
</tr>
<tr>
<td>Serum amylase (&lt;100 U/L)</td>
<td>238 U/L</td>
<td>400 U/L</td>
<td>290 U/L</td>
</tr>
<tr>
<td>Serum lipase (&lt;60 U/L)</td>
<td>231 U/L</td>
<td>Not done</td>
<td>Not done</td>
</tr>
</tbody>
</table>

Conclusion: Pancreatitis can at times, be the presentation of childhood lupus and lupus requires prompt and aggressive management.

Disclosure of Interests: None declared

AB0519 | VITAMIN D CUT-OFF POINTS RELATED WITH CLINICAL FEATURES IN PATIENTS WITH SLE WITH ACTIVE LUPUS OR LUPUS NEPHRITIS
Renato Guzman1, Luis Gabriel Piñeros2, María Camila Mejía6, Anibal Teheran2, Luis Miguel Pombor3, Vanessa Cadavid3, COMPLEXUS: GIVFTA, 1Fundación Universitaria Juan N. Corpas, Research center, Bogota, Colombia, 2Fundación Universitaria Juan N. Corpas, Research center, Bogota, Colombia

Background: Vitamin D (25OHD) has immunomodulatory properties that can play a major role in patients with active lupus or lupus nephritis. His immunomodulatory function could be influenced by demographic factors, comorbidities (Charlson score), bone supplements, and other features.

Objectives: We explored the association between the best 25OHD cut-off points and specific clinical features that were present in patients with active lupus or lupus nephritis.

Methods: A retrospective descriptive research using clinical registers of patients diagnosed with systemic erythematosus lupus, attended in two rheumatology clinics was performed. A decision tree model was used to identify the best cut-off points of 25OHD (ng/ml) and clinical features associated with active lupus (SLEDAI-2k >6) or lupus nephritis.

Results: We identified 81 patients, median age 41 years, women 91.3%. Active lupus and lupus nephritis were present in 69.1% and 29.6%, respectively. Median 25OHD was 26.49, without a difference at comparing with active lupus patients 24.85, but lower in lupus nephritis patients 21.50 (p: 0.015). Lupus nephritis was absent in patients with 25OHD cut-off points >38.8 (alone) or <38.8 if they were older than >57 years. Active lupus was always present in patients ≤44 years with 1. High comorbidity or 2. Low comorbidity plus cut-off point 25OHD >35; in ≤44 years, both a euthyroid state and the absence of bone supplements were present in patients with active lupus.

Conclusion: Exist a strong relationship between vitamin D levels and LES activity.

REFERENCES

Acknowledgement: To Fundación Universitaria Juan N. Corpas
Disclosure of Interests: None declared

AB0520 | A COMPARISON OF SHEAR WAVE ELASTOGRAPHIC FINDING OF SUBMANDIBULAR GLAND IN PATIENTS WITH EARLY-STAGE AND NON-SJÖGREN'S SYNDROME
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Background: Salivary gland (SG) ultrasonography proved valuable for assessing SG involvement in Sjögren’s syndrome (SS) and seemed to exhibit good diagnostic properties. We have reported that the submandibular gland ultrasonography (SGUS) is a useful noninvasive and inexpensive procedure for the evaluation of the structural changes of SG in SS (ISSS 2002, EULAR 2009, EULAR 2012, EULAR 2015). However, our previous study demonstrated that although SGUS findings were useful for the diagnosis of SS with low salivary flow they were not for early stage SS with normal salivary flow (EULAR 2016). Recently, we reported that the tissue elasticity was decreased due to structural changes in the SG at the advanced stage of the disease and that the shear wave
elastography (SWE) is useful to distinguish pathological changes of the SG between early stage with normal salivary flow and advanced stage (EULAR2018). The present study we demonstrated that the tissue elasticity was increased due to inflammation and high viscosity in the SG at the early stage of SS with normal salivary flow comparing that in non-SS patients, but was decreased due to structural changes in the SG at the advanced stage of the disease. The SWE may be a useful tool for elucidation of early stage pathological changes of the SG when salivary gland functions are not impaired in SS.

Objectives: The aim of this study was to elucidate the usefulness of SWE in early-stage SS patients.

Methods: Seventeen non-SS patients and eighty patients who fulfilled the American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) classification criteria for SS were studied. SS patients were divided into three groups according to salivary flow using gum test (VL/SS: <5mL/10min, (n=33), LSS: 5-10mL/10min, (n=32) and N/SS: ≥10mL/10min, (n=15)). All patients were examined SGUS by a single investigator who was blinded to device (TUS-A300; Canon Medical Systems, Tokyo, Japan) with a linear transducer (7.5-10MHz). The examination consisted of conventional B-mode US (US staging score), pulsed wave Doppler US (PD grading score) and SWE with quantitative assessment of US staging scores were assessed. Technical University Munich, Otorhinolaryngology/Benedikt Hofauer, Andreas Knopf, Carmen Unterhofer, Naglaa Mansour, Laryngological Society protocol1, which includes five different items: perceptual assessment (roughness, breathiness, hoarseness), videotrinoscopy, acoustics (jitter, dysphonia severity index, DSI), aerodynamics and subjective rating by the patient (voice handicap index, VHI).

Results: The Vs and E values were correlated with US staging score placed over the stiffest areas of the lesion on SWE, the quantitative systems, Tokyo, Japan) with a linear transducer (7.5-10MHz). The examiners between patients with non-SS and early-stage SS with normal salivary flow comparing that in non-SS patients. The SWE may be a useful tool for the differential diagnosis of early stage pathological changes of the SG when salivary gland functions are not impaired in SS.

Conclusion: The evaluation of various laryngeal functions in patients with Sjögren’s Syndrome unfolded an impairment of different aspects. Questions on laryngeal involvement should be implemented in the anamnesis of these patients and the application of screening methods should be further investigated.

REFERENCES
MENOPAUSE IN AN EGYPTIAN COHORT OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: EFFECT OF THE DISEASE

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Internal Medicine Department, Division of Rheumatology, Ain Shams University, Cairo, Egypt

Background: Systemic lupus erythematosus (SLE) is a chronic systemic autoimmune disease that mainly affects females in the reproductive age1. Although SLE generally emerges during reproductive ages, it was found that lupus patients experience menopause at younger age than the general population; however, whether the occurrence of menopause at a younger age in lupus patients results from the gonadotoxic effects of Cyclophosphamide treatment or from an autoimmune-mediated ovarian injury is debated2.

Objectives: To identify menopause characteristics in an Egyptian cohort of women with SLE with effect of the disease on menstrual symptoms and the characteristics of disease activity and disease damage in perimenopausal and post-menopausal patients.

Methods: In this cross-sectional observational study, data of 120 consecutive SLE female patients who fulfilled the 2012 ACR/SLiC criteria3 above the age of 35. Disease activity was assessed by using the SLE disease activity index (SLEDAI)4, and accumulated damage was assessed by Systemic Lupus International Collaborative Clinics/American College of Rheumatology Damage Index (SLICC/ACR Di)5. Laboratory assessment was done to all patients including follicle stimulating hormone (FSH) and luteinizing hormone (LH) blood levels.

Results: The mean age of the patients was 45.067 ± 8.211 years and mean disease duration was 5.074 ± 5.567 years (min 0.08 – max 21 years). It was found that the median of total SLEDAI score was 4.667 ± 3.357 and mean of total SLICC/ACR damage index was 0.633 ± 0.819. Of 120 patients 20% had premature menopause, 29.17% had natural menopause and 50.83% were still menstruating (table 1). It was found that the age at menopause (either natural or premature menopause) ranged from 26 to 54 years with the mean 45.170 ± 7.278 years. There was a statistically significant negative correlation between LH and total SLEDAI (r = - 0.178, P = 0.052). It was also found a statistically significant negative correlation between LH and total SLICC/ACR damage index (r = -0.214, P = 0.046*).

Conclusion: SLE has a reproductive and hormonal impact on female patients, either because of disease activity or due to pharmacological adverse effects. The mean age at menopause (either natural or premature menopause) is 45 years. High LH is associated with lower disease activity. High cumulative Cyclophosphamide dose is associated with high FSH and LH.

REFERENCES

Table 1. Menstrual status:

<table>
<thead>
<tr>
<th>N (%)</th>
<th>Positive</th>
</tr>
</thead>
<tbody>
<tr>
<td>Premature menopause</td>
<td>24 (20.00)</td>
</tr>
<tr>
<td>Natural menopause</td>
<td>35 (29.17)</td>
</tr>
<tr>
<td>Menstruating</td>
<td>61 (50.83)</td>
</tr>
</tbody>
</table>

Table 2 Correlation study between FSH & LH and Cyclophosphamide:

<table>
<thead>
<tr>
<th>R</th>
<th>FSH (mIU/ml)</th>
<th>LH (mIU/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>R</td>
<td>value</td>
<td>value</td>
</tr>
<tr>
<td>Cumulative Cyclophosphamide (mg)</td>
<td>0.440 0.214</td>
<td>0.046*</td>
</tr>
</tbody>
</table>

Disclosure of Interests: None declared


SELENA1, Suhan Can2, Bahar Arif-Esen3, Ahmet Gu5, Mahdume Lale Ocal3, Gunnur Deniz2, Murat Inan2, Istanbul University, Istanbul Faculty of Medicine, Internal Medicine, Istanbul, Turkey, Istanbul University, Aizir Sancar Institute of Experimental Medicine, Immunology, Istanbul, Turkey, Istanbul University, Istanbul Faculty of Medicine, Rheumatology, Istanbul, Turkey.

Background: BAFF and APRIL are cytokines involved in B cell development and they take place in the pathogenesis of SLE.

Objectives: The aim of this study was to investigate the relationship between serum BAFF/APRIL levels with clinical features and disease activity in SLE patients.

Methods: We included 79 patients with SLE (ACR criteria) and 27 healthy controls into the study. Serum BAFF and APRIL levels were assessed by ELISA. In 19 patients with active disease at the time of the assessment BAFF/APRIL levels were reassessed at least 6 months later (mean 7.8 months) and disease activity was evaluated by SLEDAI. New renal involvement was observed in 16 patients during the study and renal involvement was previously detected in 12 patients.

Results: Although both BAFF (median 0.7 vs 0.41 ng/ml) and APRIL (median 2.3 vs 1.05 ng/ml) levels were higher in patients with SLE compared to the control group (p <0.001), no correlation was found between BAFF/APRIL levels and SLEDAI scores. Only 9 patients (11.4%) had both BAFF and APRIL in normal range (95% confidence interval). When patients were grouped according to disease activity as no activity (SLE-DAI = 0), low disease activity and active disease, there was no difference in BAFF/APRIL levels between groups. Serum BAFF levels were higher in patients with renal disease activity (median 0.94 ng/ml vs 0.61 ng/ml, p=0.01), and there was a positive correlation between APRIL levels and proteinuria (r=0.42, p=0.02). There was no association between BAFF/APRIL levels and anti-dsDNA positivity but a weak inverse correlation was observed between BAFF and C3 levels (r=-0.25, P=0.02). No correlation was found between BAFF/APRIL levels and renal SLEDAI score, renal histopathology activity and chronicity index scores. In the active disease group after follow-up, there was no significant change in BAFF (from 1.63 ng/ml to 1.2 ng/ml) and APRIL levels (from 2.11 ng/ml to 2.31 ng/ml).

Conclusion: BAFF/APRIL levels were found to be significantly higher in patients with SLE compared to controls, but no association with disease activity was found. BAFF levels are correlated with decreased C3 levels. These results suggest that both cytokines are involved in the pathogenesis of SLE, and that serum BAFF and APRIL levels can be valuable as a biomarker in SLE especially in patients with renal activity. Long-term studies on the effect of treatment are needed.

Disclosure of Interests: None declared


Seungmin Jung, Juyoung Yoo, Sungwoo Ahn, Sangwon Lee, Jason Jungskik Song, Yongbeom Park. Yonsei University College of Medicine, Internal Medicine, Seoul, Korea, Rep. of (South Korea)

Background: Anti-Smith (Sm) antibody is a highly specific antibody for systemic lupus erythematosus (SLE). Despite the remarkable specificity of anti-Sm antibodies for SLE, the association between anti-Sm antibody level and the clinical manifestation of SLE is still unclear.

Objectives: We aimed to evaluate the association between anti-Sm antibodies and disease activity in patients with new-onset SLE.

Disclosure of Interests: None declared


References:


Disclosure of Interests: None declared


AB0526 PRIMARY SJÖGREN’S SYNDROME AND ORGAN SYSTEM INVOLVEMENT: A RETROSPECTIVE STUDY OF 153 PATIENTS FROM WESTERN INDIA

Girish Kakade, Piyush Joshi, Canchi Balakrishnan, Akash Khune. PD Hinduja National Hospital and Medical Research Centre, Rheumatology, Mumbai, India

Background: Primary Sjögren’s syndrome (pSS) is under diagnosed and improperly treated disease because of its variable modes of presentation.

Objective: To describe organ system involvement in patients with pSS and compare to other studies.

Methods: Retrospective proforma based analysis of patients with pSS (AECG 2002 criteria) from 2002-2012 at a tertiary rheumatology centre was done. Demographic data and systemic organ involvement of patients was noted.

Results: We had 153 consecutive patients of pSS (135 females, 18 males) in the 10 years which were included. Mean age at diagnosis was 47±11.62 years. Mean duration of sicca symptoms was 32 (±31) months prior to presentation. Organ system involvement was seen in 93 (65.7%) patients as follows: Musculoskeletal involvement in 90 (58.8%) patients, Skin involvement in 48 (31%) patients, Lung involvement in 27 (17.6%) patients, Renal involvement in 22 (14.3%) patients, Neurological involvement in 21 (13.7%) patients, GI involvement in 6 (3.9%) patients and Lymphoma in 2 (1.3%) patients. Comparison of organ system involvement with other major studies of pSS is shown in Table 1.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Spanish</th>
<th>Italian</th>
<th>Chinese</th>
<th>Vellore</th>
<th>Our study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Criteria used</td>
<td>European community</td>
<td>European community</td>
<td>AEGC</td>
<td>AEGC</td>
<td>AEGC</td>
</tr>
<tr>
<td>No. of patients</td>
<td>1010</td>
<td>1115</td>
<td>573</td>
<td>332</td>
<td>153</td>
</tr>
<tr>
<td>Females (%)</td>
<td>937 (93%)</td>
<td>1067 (95.7)</td>
<td>524 (91.5)</td>
<td>315 (94.9)</td>
<td>135 (88.2)</td>
</tr>
<tr>
<td>Mean age (yrs)</td>
<td>53.8±8.05</td>
<td>57.5±6.37</td>
<td>39</td>
<td>44±10.56</td>
<td>47±11.6</td>
</tr>
<tr>
<td>Disease duration (months)</td>
<td>74.9±41</td>
<td>72</td>
<td>-</td>
<td>62.6</td>
<td>35±141</td>
</tr>
<tr>
<td>Xerostomia (%)</td>
<td>975 (96)</td>
<td>1033 (92.6)</td>
<td>484 (84.5)</td>
<td>313 (94.3)</td>
<td>146 (95.4)</td>
</tr>
<tr>
<td>Xerophthalmia (%)</td>
<td>968 (96)</td>
<td>1054 (94.5)</td>
<td>401 (70)</td>
<td>295 (88.9)</td>
<td>148 (95.7)</td>
</tr>
</tbody>
</table>

Table 1. Comparison with major studies of pSS from different populations.

Results: At baseline between patients with and without anti-Sm antibodies. The longitudinal association between disease activity and anti-Sm antibodies was also evaluated in total patients and in those with anti-Sm antibodies.

Conclusion: This study suggests that anti-Sm antibody level is associated with disease activity in patients with new-onset SLE, and that monitoring with the alterations in SLEDAI (P = 0.029).

Disclosure of Interests: None declared


AB0527 PREDICTIVE VALUE OF MiR200B-5P IN THE LYMPHOMAGENESIS IN SJÖGREN’S SYNDROME (SS): COMPARISON WITH THE PUBLISHED PREDICTION MODELS. PRELIMINARY RESULTS

Friasla Kapsoergou, Athanasia Protagouerou, Aristeia Papageorgiou, Michael Voulgaris, Athanasios Tzioucas. School of Medicine, National and Kapodistrian University of Athens, Pathophysiology, Athens, Greece

Background: MiR200B-5p expression levels are decreased in the minor salivary glands of SS patients who have or will develop non-Hodgkin’s lymphoma (NHL), discriminate them from those who will not (p<0.0001) and independently predicted NHL development (p<0.0001)1.

Objective: To compare the predictive performance of low miR200B-5p levels with the previously published multifactorial predictive models.

Methods: 27 SS patients who didn’t develop NHL during follow up (median follow up time upon biopsy performance, range: 5.9yrs, 1.33-14yrs) and 17 diagnosed with NHL during follow up (pre-lymphoma, median follow-up till lymphoma diagnosis, range: 3.67yrs, 0.42-8.5yrs) were studied. The multifactorial predictive models examined were: 1. Ioannidis et al2 who defined patients expressing at least one of low C4 levels, salivary gland enlargement (SGE) and purpura as high-risk, 2. Baillera et al3 who designed 3 models (1, 2 and 3) based on the expression of at least 1, 2 or 3, respectively, of neutropenia, cryoglobulinaemia, splenomegaly, lymphadenopathy and low C4 levels. 3. Guartucci et al4 who identified as high risk patients those having SGE and at least two of the following: low C4 levels, cryoglobulinaemia, anti-La antibodies and leukopenia, and 4. Fragkoudaki et al5 that defined as high-risk group those carrying ≥ 3 of the independent risk factors including SGE, lymphadenopathy, Raynaud phenomenon, anti-Ro/SSA and/or anti-La/SSB antibodies, rheumatoid factor positivity, monoclonal gammapathy and low C4 levels. Analyses were performed by estimating the area under the ROC curve (AUC), Kaplan-Meier (KM) lymphoma-free survival curves.
compared by the log-rank test, the positive and negative predictive values, sensitivity (Se) and specificity (Sp), as well as the PSEP index of the model intrinsic prognostic value.

Results: ROC analysis identified low mir200b-5p levels as the better prognostic tool from the other multifactorial models. Its predictive value was further supported by the other analyses (including PSEP index), where it ranked among the two best models, whereas it had the better combination of sensitivity and specificity (Table).

Table. Comparison of models predicting NHL development in SS

<table>
<thead>
<tr>
<th>ROC</th>
<th>KM</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>AUC</td>
</tr>
<tr>
<td>Ioannidis et al</td>
<td>0.748</td>
</tr>
<tr>
<td>Baimpa et al, model 1</td>
<td>0.775</td>
</tr>
<tr>
<td>Baimpa et al, model 2</td>
<td>0.687</td>
</tr>
<tr>
<td>Baimpa et al, model 3</td>
<td>0.647</td>
</tr>
<tr>
<td>Quartuccio et al</td>
<td>0.794</td>
</tr>
<tr>
<td>Fragkoudaki et al</td>
<td>0.830</td>
</tr>
<tr>
<td>Low mir200b-5p levels</td>
<td>0.863</td>
</tr>
</tbody>
</table>

Conclusion: Low mir200b-5p levels associated with the incidence of NHL in SS, exhibiting considerably higher values than the other multifactorial models; however, larger cohorts are required to verify its statistical and clinical significance.

REFERENCES

Disclosure of Interests: Efstathia Kapsogeorgou: None declared, Athanasie Protagoreou: None declared, Aristea Papageorgiou: None declared, Michael Voulgarelis: None declared, Athanasios Trioulas Grant/research support from: ABBEVIE, PFIZER, AMGEN, NOVARTIS, GSK

AB0528 ANALYSIS OF THE CASES OF 33 SLE PATIENTS THAT NECESSITATED CARDIOVASCULAR SURGERY

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Juntendo University, Bunkyo-ku, Japan

Background: In SLE, immune complexes are overproduced and deposited in tissues where they ultimately cause damage. The immunocomplexes, which are deposited in the myocardium, blood vessels and atrioventricular valves, have been suggested to cause damage to the relevant tissues, but it remains unclear in which cases tissue damage progresses to a point that surgical treatment is required.

Objectives: The purpose of our study was to classify heart diseases into valvular heart diseases (V), ischemic heart diseases (I) and aortic aneurysms (A), to compare each class in terms of the correlation between the activity of SLE and the progression and exacerbation of heart disease, and in the future, to use the features of the correlations to carry out the prevention and treatment of heart diseases complicating SLE.

Methods: Between the years 2012 and 2018, a total of 2852 patients diagnosed with SLE were admitted to our hospital, and 33 had heart surgery; however, 2 patients with infective endocarditis and one patient, who had not been diagnosed with SLE before surgery, were excluded from the study, therefore 30 cases were examined. Comparative studies were also carried out to examine the association between the levels of various autoantibodies and IgG and the onset of heart disease, the association between the total administered doses of steroids, the concomitant use of immunosuppressants as well as the association between DNA antibodies and complement.

Results: At the time of the surgical treatment of the heart diseases, the mean duration of illness was 25.4 years, and the age was V vs. I vs. A =56.7 (44-79, median value: 56.2) vs. 55.1 (34-72, median value: 57.0) vs. 63.2 (41-78, median value: 65.5), showing that the age tended to be higher in the A group. The integrated value of the duration of illness and the level of anti-DNA antibodies, which served an index of activity, was calculated, and the findings revealed that V vs. I vs. A was (14020 vs. 32666 vs. 29444), showing that the values tended to be slightly lower in valvular heart diseases. As for anti-phospholipid antibodies, the rate of positivity of either CL,β2GPI or anti-CL antibodies or LA was as follows: V vs. I vs. A (58% vs. 28% vs. 33%), showing that the rate tended to be higher in valvular heart diseases and that anti-CL antibody-positive patients were particularly higher in number among those with valvular heart diseases (V). The maximum preoperative levels of IgG as were as follows: V vs. I vs. A (2803 vs. 1889 vs. 1708), which showed that the levels were higher with valvular heart diseases (V); those of SS-A antibodies were as follows: (36% vs. 43% vs. 42%), which showed high positive rates in all classes; and RNP antibody-positivity rates were as follows: (9% vs. 29% vs. 25%), and were relatively lower in valvular heart diseases (V). Regarding the medical treatment, the total administered doses of steroids were (25g vs. 39g vs. 63g) and tended to be lower in valvular heart diseases (V); use of immunosuppressants was found in 5 of 30 patients (16%); and concomitant use of both was particularly low in valvular heart diseases (V) as it accounted for only one case.

Conclusion: Our study findings suggested that in SLE patients, prolonged duration of illness, positivity of SS-A antibodies and the absence of intake of immunosuppressants were highly likely to lead to cardiovascular diseases that need surgical treatment. Low integrated DNA antibody levels and the absence of concomitant use of immunosuppressants, despite high levels of IgG and the positivity of SS-A antibodies and anti-CL antibodies, might be risk factors for valvular heart diseases necessitating surgical treatment.

REFERENCES


AB0529 SICCA SYNDROME DURING CHRONIC HEPATITIS C: PREVALENCE AND CHARACTERISTICS

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Background: The prevalence of Sicca Syndrome (SS) in patients with Chronic Hepatitis C (CHC) ranges from 5% to 33%. A link between hepatitis C (HCV) and SS was evoked given the strong association of these two pathologies with mixed cryoglobulinemia (MC) on one hand and with the salivary tropism of HCV on the other hand.

Objectives: To study the prevalence and the characteristics of Sicca Syndrome during CHC.

Methods: All patients suffering from CHC followed over a period of 11 years (2002 – 2012) were retrospectively included. Only patients having clinical SS (xerostomia and/or xerophthalmia) were selected. We have analyzed all data concerning the patient, the hepatitis and the SS.

Results: Two hundred and four patients affected by CHC were included. All patients suffering from CHC followed over a period of 11 years (2002 – 2012) were retrospectively included. Only patients having clinical SS (xerostomia and/or xerophthalmia) were selected. We have analyzed all data concerning the patient, the hepatitis and the SS.

Disclosure of Interests: Efstathia Kapsogeorgou: None declared, Athanasie Protagoreou: None declared, Aristea Papageorgiou: None declared, Michael Voulgarelis: None declared, Athanasios Trioulas Grant/research support from: ABBEVIE, PFIZER, AMGEN, NOVARTIS, GSK
anti-SSB were absent in the 4 patients. Biopsy of accessory salivary glands revealed the presence of a grade 4 lymphocytic sialadenitis according to the Chisholm and Masson classification in 3 patients, while the remaining case had a lymphocyte grade 2 sialadenitis. The evaluation of hepatic fibrosis did not reveal cirrhosis in the 4 cases.

Conclusion: The prevalence of Sicca syndrome during hepatitis C is estimated at 8% in our study. It was mainly reported in women with perimenopausal age and seems to be associated with cryoglobulinemia, a high viral load and an advanced fibrosis.

Disclosure of Interests: None declared

AB0530 THE EFFECT OF MYCOPHENOLEATE MOFETIL ON NON-RENAL MANIFESTATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS FROM 2014 TO 2018: OBSERVATION STUDY FROM KOREAN LUPUS NETWORK (KORNET) REGISTRY

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Background: Mycophenolate mofetil (MMF) has been established to a potent therapeutic drug for regulate renal involvement in systemic lupus erythematous (SLE).

Objectives: The object of this study is to identify the effect of MMF on non-renal manifestations in SLE.

Methods: The study population was total 439 SLE patients enrolled from Korean Lupus Network (KORNET) registry. The KORNET registry was followed up annually and completed from baseline survey to the 2th visits from 2014 to 2018. In the subgroup analysis, the effect of MMF on clinical features was also evaluated in 110 patients with histologically confirmed lupus nephritis (LN). The changes of clinical features including mucocutaneous lesions, arthritis, serositis, neurologic disorder, and hemato logic abnormalities were assessed between MMF and non-MMF groups during follow-up period. Statistical analysis was used by multiple comparison analysis, considering time, group, and interaction of follow-up time and treatment group.

Results: There was significant difference of malar rash and renal disorder between MMF and non-MMF groups considering time and group in total SLE patients (p = 0.025 and p < 0.001, respectively). In hematologic abnormalities, proportion of leukopenia was significantly different between two groups during follow-up periods (p<0.001, p group < 0.001, and p time & group = 0.004). In 110 LN patients, there was not difference of non-renal clinical features between them. In contrast, proportion of leukopenia in patients with LN was significantly different between two groups during follow-up periods (p time < 0.001, p group < 0.003, and p time & group = 0.004).

Conclusion: This study showed that MMF might be beneficial to treatment for hematologic abnormalities in SLE.

REFERENCES

Acknowledgement: none
Disclosure of Interests: None declared

AB0531 OBESITY INCREASES THE INCIDENCE OF NEW-ONSET LUPUS NEPHRITIS AND ORGAN DAMAGE DURING FOLLOW-UP IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: The object of this study is to identify the effect of MMF on patients with active non-renal SLE.

Methods: We obtained data on 393 SLE patients from the Korean Lupus Network registry. Demographic variables, clinical manifestations, laboratory findings, Physician Global Assessment (PGA), Systemic Lupus Erythema tosus Disease Activity Index (SLEDAI)-2000 and Systemic Lupus Interna tional Collaborating Clinics Group (SLICC) damage index scores were recorded at the time of enrollment. The tests were repeated annually for 3 consecutive years. We divided the patients into groups according to their body mass index (BMI) using the Asia-Pacific classification (normal, BMI < 23; overweight, 23 ≤ BMI <25; obese, BMI ≥ 25). Univariate and multivariate analyses were performed to assess the impact of obesity on clinical outcomes.

Results: Of the 393 patients, 59 (15.0%) were obese at the time of enrollment. Obese patients had more comorbidities, such as diabetes (P<0.002), hypertension (P<0.005), hyperlipidemia (P<0.005), and pulmonary hypertension (P=0.036) than non-obese patients. Nephritis at enrollment and newly developed nephritis during follow-up were more common in obese patients than in non-obese patients (P=0.002 and P=0.002, respectively). In addition, obese patients had higher daily and cumulative prednisolone doses (P=0.010 and P=0.010, respectively) and higher rates of intravenous cyclophosphamide (P=0.008), mycophenolate (P=0.030), tacrolimus (P=0.007), and cyclosporine (P=0.019) use than non-obese patients. Furthermore, the PGA and SLICC damage index scores were higher in obese patients than in non-obese patients (P=0.017 and P=0.039, respectively) for all 3 consecutive years. In the multivariate analysis, obesity was significantly associated with male gender (OR = 0.141, 95% CI: 0.047–0.419, P=0.001), newly developed nephritis (OR = 2.741, 95% CI: 1.280–6.957, P=0.034), and annual increase in SDI (OR = 2.185, 95% CI: 1.229–3.885, P=0.008).

Conclusion: Obese SLE patients had a higher incidence of newly developed nephritis and cumulative organ damage than non-obese patients. Therefore, lifestyle modifications, including those aimed at weight loss, should be recommended for these patients to improve their clinical outcomes.

Disclosure of Interests: None declared

AB0532 SOLUBLE SIGLEC-5 IS A NOVEL SALIVARY BIOMARKER FOR PRIMARY SJOGREN’S SYNDROME

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Background: Despite advances in the understanding of the pathogenesis, disease-specific biomarkers have not been included in the classification criteria for Primary Sjogren’s syndrome (pSS).

Objectives: Based on the microarray of peripheral blood mononuclear cell (PBMC) of pSS patients, we aimed to investigate whether sialic acid-binding immunoglobulin-like lectin (siglec)-5 might serve as a biomarker for pSS.

Methods: Microarray of PBMCs obtained from 26 pSS patients and 10 healthy control (HCs) were performed to screen potential biomarkers for pSS. The concentration of siglec-5 in saliva and sera was determined by ELISA. Clinical parameters related with pSS were obtained from pSS registry and correlation with salivary siglec-5 level was evaluated.

Results: The level of salivary siglec-5/14 was significantly higher in pSS patients (n=170) compared with HCs (n=25) or non SS sicca patients (n=78) (1346.8 [202.8-4280.0] pg/mL, 6.08 [0-134.0] pg/mL, and 195 [0-947.5] pg/mL, median [interquartile range], P<0.001), meanwhile the serum level was not different between the groups. Clinical parameters were analyzed in 170 patients in pSS registry. Salivary siglec-5 level negatively correlated with salivary flow rate ( spearman’s rho: -0.420, P<0.001), and positively correlated with ocular surface score (rho: 0.331, P<0.001) and serum immunoglobulin G level (rho = 0.202, P=0.008). However, the level
of salivary siglec-5 was not correlated with ESSDAI or focus score. On ROC analysis, area under the curve was 0.7740(724.0-0.826). With cut off value 400pg/mL, sensitivity and specificity was 0.69 and 0.70 respectively. In validation cohort (45 psS patients and 45 non SS sicca patients) where patients without sicca symptom but have 1 or more positive items in ESSDAI were included, sensitivity and specificity of siglec-5 was 64.4% and 77.8%, respectively.

**Conclusion:** The level of soluble siglec-5 is significantly increased in the saliva of psS patients and reflects the severity of hyposalivation and ocul- lar surface damage. Although the mechanism of the contribution to gland dysfunction is unclear yet, this easily obtainable salivary biomarker may add benefits on the diagnosis of psS.

**REFERENCES**


**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.5540

**Table 1. Comparison of SIBO positive rate between active period and stable period [%]**

<table>
<thead>
<tr>
<th>SIBO positive</th>
<th>SIBO negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Active period</td>
<td>23(92.00%)</td>
<td>2(8.00%)</td>
</tr>
<tr>
<td>Stable period</td>
<td>16(61.50%)</td>
<td>10(38.50%)</td>
</tr>
<tr>
<td>Total</td>
<td>39(76.50%)</td>
<td>12(23.50%)</td>
</tr>
</tbody>
</table>

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.5538

**AB0534 DEVELOPMENT OF A MULTI-MODALITY IMAGING APPROACH TO EVALUATE LUPUS NEPHRITIS AND INITIAL RESULTS**


**AB0534 DEVELOPMENT OF A MULTI-MODALITY IMAGING APPROACH TO EVALUATE LUPUS NEPHRITIS AND INITIAL RESULTS**


Fatigue is a common symptom in patients with Systemic Lupus Erythematosus (SLE). The aim of this study was to characterize the relationship between fatigue and other factors, including disease activity, vitamin D level, pain, depression, anxiety, sleep quality, exercise, and exercise in SLE. More specifically, we aimed to identify a number of factors that are significantly related to fatigue; of these it is most strongly dependent on depression and pain. This suggests that the etiology of fatigue in SLE is multifactorial and that in SLE patients reporting fatigue, the underlying cause needs to be identified and treated.

Conclusion:

Fatigue is highly prevalent in SLE patients. This study identified a number of factors that are significantly related to fatigue; of these it is most strongly dependent on depression and pain. This suggests that the etiology of fatigue in SLE is multifactorial and that in SLE patients reporting fatigue, the underlying cause needs to be identified and treated.

REFERENCES


Disclosure of Interests:

None declared.

David R Karp: None declared, Brad H Rovin: None declared, Mikael Boesen: Shareholder of: Image Analysis Group, UK, Consultant for: Image Analysis Group, Peter Lipsky Consultant for: Consultants fees from Horizon Pharma.


AB0535 PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND LYMHOPLA in a TERTIARY HOSPITAL: DESCRIPTIVE ANALYSIS OF NINE PATIENTS

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Background: Evidence of an increased risk to develop haematological malignancy, and especially non-Hodgkin’s lymphoma (NHL) in autoimmune diseases, has been gathered since the 1970s. In the last decade studies from SLE cohorts have consistently shown a markedly increased risk of NHL.

Objectives: To analyze clinical and disease characteristics in SLE patients who developed a lymphoma during follow-up, as well as to define characteristics of the lymphoma and its evolution.

Methods: Retrospective observational, longitudinal study conducted in a tertiary hospital. Medical records of 362 patients with >4 SLICC classification criteria of SLE were reviewed, including those with lymphoma diagnosis. Demographic and clinical data, comorbidities, SLE manifestations and therapy, data related to lymphoma and outcome were collected.

Descriptive statistic analysis with measures of central tendency and measures of variability was performed.

Results: Of the 362 SLE patients, 9 (2.5%) were diagnosed of lymphoma, of which 100% female. Mean age at SLE diagnosis was 34 y.o (SD 11) and average duration from SLE diagnosis to lymphoma diagnosis was 17 years (SD 14). 7 patients were caucasian and 2 hispanic. Observed comorbidities were hypertension (6 pt, 67%), diabetes (2 pt, 22%), dyslipidemia (3 pt, 33%), HBV infection (1 pt, 11%) and active smoking (6 pt).

No malignancy history was detected. Most frequent SLE features were haematological (9 pt, 100%), joint (5 pt, 56%) and skin (5 pt) involvement. The serious ones were: 3 patients with haemolytic anaemia (1 of them, platelets <20000), 2 epilepsy (1 of them with CNS vasculitis), 1 glomerulonephritis, 1 pulmonary hypertension and 1 hemophagocytic syndrome.

Only 1 patient had overlap with Sjogren’s syndrome. At the time of lymphoma diagnosis, 7 patients were on steroids, 4 on immunosuppressants, 2 on mycophenolate, 1 azathioprine and 1 rituximab and 3 on antimalarials (Table 1). Mean age at lymphoma diagnosis was 51 y.o (SD 10), 5 patients (56%) had diffuse large B-cell lymphoma (DLBCL), 1 had NHL, 1 had Hodgkin’s lymphoma, 1 had mantle B-cell lymphoma and 1 had MALT lymphoma. Only 1 patient, of 4 with available data, had EBV positive in the tissue. 7 patients (78%) received chemotherapy and 2 patients completed treatment with autologous peripheral stem-cell transplantation. Three patients died, 2 due to lymphoma and one due to other causes (severe flaccid paralysis, Miller Fisher syndrome). Overall survival after lymphoma diagnosis was 8 years (SD 6).

Conclusion: In our patients, unlike that reported in the literature, lymphoma diagnosis was in SLE with longer duration of the disease, and all cases were female. Most frequent subtype was NHL, and all patients had previous haematological manifestations. Regarding previous SLE treatment, 5 patients had been exposed to immunosuppressants.
Disclosure of Interests: None declared


AB0537 CHRONIC DAMAGE CONTRIBUTION TO COGNITIVE IMPAIRMENT IN PRIMARY ANTIPHOSPHOLIPID SYNDROME

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Background: There is a gamut of affections at neurological level in patients with primary APS (PAPS) including cognitive impairment (CI). It presents in middle age population carrying a high risk of dementia.

Objectives: To analyze the impact of chronic damage in CI and its associated factors in patients with PAPS.

Methods: Cross-sectional study in patients with PAPS (Sidney criteria). Demographic data, clinical and laboratory data were retrieved. The diagnosis of CI, MoCA version 8.1 questionnaire was employed and HAD questionnaire for depression screening. Patients were divided into two groups with and without CI. Chronic damage was measured with DIAPS, considering chronic damage as the damage established for over 6 months and with a score ≥1.

Results: Sixty PAPS patients were included, 76.7% were females. Clinical characteristics, associated risk factors and cognitive assessment by domain in both groups are shown in table 1. Only 1 patient presented depression and 3 had anxiety/depression by HAD test. Mild CI was present in 61.7%, moderate CI in 6.7% and no CI in 31.7%. Median depression and 3 had anxiety/depression by HAD test. Mild CI was present in 61.7%, moderate CI in 6.7% and no CI in 31.7%. Median depression and 3 had anxiety/depression by HAD test. Mild CI was present in 61.7%, moderate CI in 6.7% and no CI in 31.7%. Median depression and 3 had anxiety/depression by HAD test. Mild CI was present in 61.7%, moderate CI in 6.7% and no CI in 31.7%. Median depression and 3 had anxiety/depression by HAD test. Mild CI was present in 61.7%, moderate CI in 6.7% and no CI in 31.7%

Conclusion: The high score of DIAPS and persistence of aCL were associated with CI in PAPS. Chronic stress generated by accumulated chronic damage coupled with APS vasculopathy may contribute to cognitive deterioration. Prevention of chronic damage as well as a cognitive intervention are necessary in order to decrease CI.

REFERENCES


Disclosure of Interests: None declared


AB0538 INFLUENCE OF IMMUNOLOGICAL FEATURES, DISEASE ACTIVITY AND FATIGUE ON THE HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH PRIMARY SJOGREN’S SYNDROME

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Background: Studies show that the health-related quality of life (HRQoL) is significantly reduced in patients with primary Sjögren’s syndrome (pSS). However, potential predictors of HRQoL in these patients are not well known.

Objectives: To investigate potential influence of main immunological features, fatigue and disease activity on the HRQoL in patients with pSS.

Methods: We studied 41 consecutive in- and outpatients with pSS diagnosed according to the AECG criteria in the Clinic of Allergy and Immunology. The SF-36 questionnaire has been used to assess HRQoL. The SF-36 values have been compared with the population based reference values. Fatigue was assessed using Fatigue Severity Scale (FSS). ESSDAI was used for the evaluation of systemic involvement and disease activity and ESSPRI for the evaluation of the patient-reported outcomes.

Results: There were 38/41 female patients. The mean age was 56.2 ±13.5 years and the mean disease duration was 3.9 ±5.8 years. HRQoL was reduced in almost all SF-36 domains in the comparison to healthy population: physical functioning (PF) (p=0.0161); role physical (RP) (p<0.0005); social functioning (SF) (p<0.0023); role emotional (RE) (p=0.0421). The mean value of FSS score was 4.6±2.2, with 53.6% of patients having FSS score more than 4.8 (which is considered to be pathological). There were no significant differences in HRQoL depending on the presence of ANA (p=0.44), anti-SSA Abs (p=0.0756), anti-SSB Abs (p=0.218), cryoglobulins (p=0.8), complement consumption (p=0.122).

Patients with elevated values of RF had significantly higher HRQoL (rho=0.486, p=0.00139), and especially with the domains of SF (rho=0.502, p=0.0005) and RF (rho=0.491, p=0.00129). We found a significant negative correlation between HRQoL and FSS score (rho=–0.794, p=0.001). The mean ESSDAI score was 3.8 (0–23), and 75.6% of patients had some level of disease activity according to ESSDAI. Patients with low disease activity had higher HRQoL compared to those with moderate disease activity in following SF-36 domains: physical composite score (PCS) (p=0.0148), PF (p=0.0328), RP (p=0.00697) and vitality (VT) (p=0.05). The mean ESSPRI score value was 5.1±2.7 (dryness scale – 6.1, fatigue scale – 5.4, limb pain scale – 3.8). ESSPRI score negatively correlated with HRQoL (rho=–0.763, p<0.001) in all SF-36 domains.

Conclusion: Our study identified ESSDAI, ESSPRI and FSS scores, serum RF and IgG concentrations as potential predictors of HRQoL in patients with pSS.
TEN YEARS OF THE MONASH LUPUS CLINIC: INSIGHT INTO THE CHARACTERISTICS AND OUTCOMES OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS IN AUSTRALIA

Rachel Koelmeyer1, Sumanpreet Toor2, Stellamay Gwini3, Vera Golder1,2, Erin F. Morand4,5

1Institute of Medical and Veterinary Science, Biobank (ALRB). Since its inception in 2007, the clinic has been co-run by rheumatologists and nephrologists. A carefully curated clinical dataset has been collected since clinic inception.

Objective: We provide an overview of the characteristics and longitudinal outcomes of adult lupus patients treated at the Monash Lupus Clinic over the last ten years.

Methods: A ten-year-long dataset from the original Monash Lupus Clinic cohort, of patients subsequently enrolled in the Australian Lupus Registry and Biobank, was used for the analysis. The dataset included information on patient demographics, lupus diagnosis, serological profile, treatments, disease activity, damage accrual and other medical outcomes such as renal failure, adverse pregnancy outcomes and hospitalisations. Descriptive statistics were used to summarise the characteristics of the study population. Bivariate tests and regression analyses were used for comparisons between inception cohort patients, enrolled in the registry within 15 months of their Systemic Lupus Erythematosus (SLE) diagnosis, and existing SLE patients enrolled later in their disease course.

Results: Of the 329 enrolled patients, the median age at enrolment was 38.0 years and 87.8% of were female. Most patients were either of Caucasian (48.6%) or Asian (36.5%) ethnicity. Patients were enrolled a median of 4.0 years after their SLE diagnosis; 31.0% of patients were inception cohort patients. Most patients (95.4%) had an abnormal titre of anti-nuclear antibodies; 65.0% of the cohort were positive for anti-dsDNA, antinucleosomal, anti-P protein only in 8.8% in men. The cognitive dysfunction with moderate to severe disability was found in 43 (61.4%) patients. There was found the statistically significant difference between two groups (with and without CD) in serum levels of vitamin D, 54.01 nmol/l (±22.6) and 68.48 nmol/l (±27.1), resp. (p<0.01). The average value of the activity index (SLEDAI) score over the observation period was 4.0; 49.1% of the cohort spent ≥50% of the observation period in the Lupus Low Disease Activity State and 43.5% had ever had a SLEDAI score ≥10. Just over half (57.4%) had accrued damage at the end of the observation period; however, pleasingly only a very small minority had an abnormal frequency of vitamin D deficiency among SLE patients 43.5% had ever had a SLEDAI score ≥10. Just over half (57.4%) had accrued damage at the end of the observation period; however, pleasingly only a very small minority had an abnormal frequency of vitamin D deficiency among SLE patients. The average value of the activity index (SLEDAI) score over the observation period was 4.0; 49.1% of the cohort spent ≥50% of the observation period in the Lupus Low Disease Activity State and 43.5% had ever had a SLEDAI score ≥10. Just over half (57.4%) had accrued damage at the end of the observation period; however, pleasingly only a very small minority had an abnormal frequency of vitamin D deficiency among SLE patients. The average value of the activity index (SLEDAI) score over the observation period was 4.0; 49.1% of the cohort spent ≥50% of the observation period in the Lupus Low Disease Activity State and 43.5% had ever had a SLEDAI score ≥10. Just over half (57.4%) had accrued damage at the end of the observation period; however, pleasingly only a very small minority had an abnormal frequency of vitamin D deficiency among SLE patients.

Conclusion: Running a multi-disciplinary clinic alongside research activity is both feasible and worthwhile. Systematic collection of longitudinal data on SLE patients has shown that adverse outcomes such as end-stage renal disease and mortality at death are rare; however, with more than half of the cohort having damage present at the end of the observation period, there is still work to be done to improve outcomes for SLE patients in Australia. Expansion of the Australian Lupus Registry and Biobank beyond the Monash Lupus Clinic will provide further insight into the characteristics and outcomes of SLE patients in Australia and provide a beneficial framework for future studies.


AB0540 CAN LOW SERUM VITAMIN D LEVELS AFFECT THE COGNITIVE FUNCTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS?

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease involving various organs and systems including the nervous system. Neuropsychiatric SLE (NPSLE) occurs in 30 - 40% of SLE patients. One of the most common manifestations of NPSLE is cognitive dysfunction (CD), which is found in 20 - 80% of SLE patients. Epidemiological studies have reported vitamin D to be a potential risk factor of cognitive impairment within the general population. There have also been found associations between vitamin D deficiency and multiple disease states such as Alzheimer’s disease, multiple sclerosis and SLE. It is hypothesised that vitamin D contributes to neuroprotection by modulating the production of proinflammatory cytokines. Vitamin D deficiency is highly prevalent in SLE patients due to photoprotection, renal insufficiency and the use of different medication.

Objective: To establish a possible association between serum vitamin D levels and cognitive function in SLE patients. To determine the presence of certain auto-antibodies (anti-dsDNA, antinucleosomal, anti-P protein, and antiphospholipid) in the serum, and the disease activity.

Methods: We included a total number of 70 patients diagnosed with SLE according to the American College of Rheumatology (ACR) classification criteria. We assessed disease activity according to SLE Disease Activity Index (SLEDAI). CD was evaluated on the basis of psychological analysis of cognitive functions with testing of attention, memory, psychomotor speed, visual spatial skills and speed of cognitive information processing. Serum vitamin D levels were measured by standardized immunochemical assay from blood samples.

Results: We analyzed 70 patients, 64 (91.4%) women and 6 (8.6%) men. The cognitive dysfunction with moderate to severe disability was found in 43 (61.4%) patients. There was found the statistically significant difference between two groups (with and without CD) in serum levels of vitamin D, 54.01 nmol/l (±22.6) and 68.48 nmol/l (±27.1), resp. (p<0.01). The average value of the activity index (SLEDAI) score over the observation period was 4.0; 49.1% of the cohort spent ≥50% of the observation period in the Lupus Low Disease Activity State and 43.5% had ever had a SLEDAI score ≥10. Just over half (57.4%) had accrued damage at the end of the observation period; however, pleasingly only a very small minority had an abnormal frequency of vitamin D deficiency among SLE patients. The average value of the activity index (SLEDAI) score over the observation period was 4.0; 49.1% of the cohort spent ≥50% of the observation period in the Lupus Low Disease Activity State and 43.5% had ever had a SLEDAI score ≥10. Just over half (57.4%) had accrued damage at the end of the observation period; however, pleasingly only a very small minority had an abnormal frequency of vitamin D deficiency among SLE patients. The average value of the activity index (SLEDAI) score over the observation period was 4.0; 49.1% of the cohort spent ≥50% of the observation period in the Lupus Low Disease Activity State and 43.5% had ever had a SLEDAI score ≥10. Just over half (57.4%) had accrued damage at the end of the observation period; however, pleasingly only a very small minority had an abnormal frequency of vitamin D deficiency among SLE patients.

Conclusion: On the basis of obtained results it can be stated that cognitive dysfunction was present in a high number of SLE patients. We demonstrated a high frequency of vitamin D deficiency among SLE patients with CD and statistically significant lower levels of vitamin D than in patients without CD. These results suggest that low vitamin D level could be associated with impaired cognitive function.


REFERENCES


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AB0542  PREGNANCY OUTCOMES IN ANTIPHOSPHOLIPID SYNDROME: 8 YEAR-EXPERIENCE FROM A MULTIDISCIPLINARY UNIT

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Background: Women with antiphospholipid syndrome (APS) are at increased risk of recurrent miscarriage, fetal death, placental insufficiency, preeclampsia and fetal growth restriction. Although treatment improves fetal-maternal outcomes, there are still some unsuccessful pregnancies. A multidisciplinary approach with strict monitoring is essential in order to attain obstetrical success.

Objectives: To assess pregnancy outcomes in Portuguese women with APS who were surveilled at a multidisciplinary unit.

Methods: Pregnant women fulfilling the Sydney classification criteria for definite APS, who attended our specialized Rheumatology and Obstetrics outpatient clinic between 2010 and 2018, were included in this retrospective observational study. Cases of suspected APS not meeting the classification criteria were excluded. All pregnancies were followed by a multidisciplinary team (rheumatologists, obstetricians and nurses). Data was collected from medical records. Adverse Pregnancy Outcomes (APO) were defined as: spontaneous abortion (<10w), fetal death (≥10w), neonatal death, fetal growth restriction (FGR) and delivery prior to 36 weeks of gestation with or without preterm premature rupture of membranes (PPROM).

Results: A total of 35 pregnancies were identified in 25 women with APS. Twelve (48%) patients had thrombotic APS, 9 (36%) had obstetric APS and 4 (16%) had mixed APS. Primary APS was seen in 56% of patients, while systemic lupus erythematosus was found in 44%. The average maternal age at conception was 32.8 ± 5.2 years. Mean duration of disease prior to pregnancy was 6.4 ± 5.5 years. In regard to antiphospholipid antibody (APL) profile, 28.6%, 25.7% and 28.6% of patients were triple, double and single positive, respectively. Although they had fulfilled laboratory criteria in the past, 17% of patients were negative for all APL. All patients were instructed to receive prophylactic or therapeutic low-molecular-weight heparin combined with low dose aspirin for the duration of pregnancy. Regarding fetal outcomes, there were 2 (5.7%) cases of first-trimester miscarriage, 1 (2.9%) medical abortion due to exposure to teratogenic drugs at the time of conception and 4 (11.4%) fetal deaths. Among the cases of fetal death, one concerned a patient who suspended heparin on her own initiative and another one who became pregnant under warfarin and whose fetus had trisomy 18. The other cases occurred at 11 and 18 weeks of gestation, under regular therapy. There were no cases of neonatal death or other fetal malformations. The rate of live births was 80%, with a mean gestational age of 37.3 ± 1.5 weeks and mean birth weight of 2796.4 ± 462.2 g. Most women delivered by cesarean section (54.3%) of cases. There were 6 (17.1%) cases of preterm birth, three (8.6%) corresponding to fetus with FGR. Concerning maternal outcomes, there was one single case (2.9%) of PE. There were no cases of eclampsia or HELLP syndrome.

AB0541  LUPUS MANIFESTATIONS IN A PATIENT WITH SPONDYLOARTHRITIS TREATED WITH TUMOUR NECROSIS FACTOR-ALPHA ANTAGONIST: SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) OR DRUG-INDUCED LUPUS ERYTHEMATOSUS (DILE)?

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Background: Systemic lupus erythematosus (SLE) is a multisystem autoimmune inflammatory disease. Drug-induced lupus erythematosus (DILE) is defined as the development of lupus-like symptoms that is temporarily related to continuous drug exposure which resolves with cessation of the offending drug. It is usually accompanied by serologic findings of a positive antinuclear antibody (ANA) and anti-histone antibodies. Tumour necrosis factor-α (TNFα) antagonist-induced lupus-like syndrome (TAILS) is a well-known side effect of this class of substances. A retrospective study reported twenty two cases whose lupus manifestations abated within a few weeks (median eight weeks) in all patients except one with longer-lasting evolution of six months.

Objectives: We reported a case which posed a diagnostic challenge to us, a patient with spondyloarthritids (SpA) who presented with lupus-like features during treatment with Golimumab.

Methods: Case report

Results: A 35-year-old lady was diagnosed as spondyloarthritis when she presented with peripheral arthritis, plantar fasciitis, right eye anterior uveitis and bilateral chronic sacroiliitis confirmed via sacroiliac magnetic resonance imaging. Investigations revealed raised erythrocyte sedimentation rate (ESR) and negative HLA-B27. She developed allergic reaction to sulfasalazine and non-steroidal anti-inflammatory drugs (NSAIDs), thus intravenous Golimumab was initiated. Although she responded to this therapy and ESR had reduced during assessment at 24 weeks, Golimumab was stopped due to funding issue. It was restarted after six months but had to be discontinued again after four months because she developed recurrent fever and malar rash. During this presentation, investigations revealed leucopenia of 2.46 × 109/L, ESR of 93 mm/hr, low complements and positive direct coombs’ test. ANA, anti-double stranded DNA, anti-histone antibody and anti-smith antibody were all negative. Inflammatory screen- ing was negative. TAILS secondary to Golimumab was diagnosed. Apart from discontinuation of Golimumab, 0.5mg/kg/day of prednisolone was started which resulted in improvement of the malar rash and leucopenia. However, four months after the last dose of Golimumab, recurrent fever and leucopenia recurred when the prednisolone dose was reduced to 5mg on alternate-days. At this time, we considered diagnosis of SLE rather than TAILS because of persistent SLE manifestation despite cessation of Golimumab and improvement with oral corticosteroid. Furthermore, although not pathognomonic, the anti-histone antibody was negative.

Conclusion: This case posed a diagnostic challenge as both SLE and DILE can present similarly. The approach to managing this patient with coexisting SpA and SLE is also a challenge since there is a dilemma as to what can be offered after failure of NSAIDs and conventional disease-modifying antirheumatic drugs since anti-TNFαIs is contraindicated in SLE.

REFERENCES
found between poor obstetric outcomes and history of thrombosis, presence of SLE or low complement levels (table 1).

Conclusion: In our study, most pregnancies were uneventful. Despite the small sample size, we reinforce the importance of a multidisciplinary evaluation and surveillance before, during and after pregnancy in women with APS in order to implement early treatment and to optimize fetal-maternal outcomes.

Disclosure of Interests: None declared


AB0543 FEATURES ASSOCIATED WITH RENAL DAMAGE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS DECEASED OVER A 10-YEAR PERIOD

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Background: Renal damage (RD) is one of the most important contributors to morbidity and mortality in patients with systemic lupus erythematosus (SLE).

Objectives: We aimed to assess features associated with RD in a group of 90 deceased SLE patients routinely followed-up at our institution, which serves as a national referral center for SLE.

Methods: We retrospectively analyzed 90 SLE patients (68 females) deceased from 2002 to 2011. All patients were ≥18 years of age at death, fulfilling ≥4/11 classification criteria of the American College of Rheumatology (ACR). We identified patients with RD, as defined by the Systemic Lupus International Collaborating Clinics (SLICC)/ACR index. An extensive set of variables was compared between patients with and without RD (RD and RD-N, respectively): demographics, ACR criteria at diagnosis and cumulatively at death, total damage and its components one year following diagnosis and non-renal damage and its components cumulatively at death, as well as components of the metabolic syndrome, smoking, sicca and Hughes syndrome. Frequencies were compared using the chi-square and Fisher’s exact test, and continuous variables using the t-test and Mann-Whitney U test. Variables associated with RD were analyzed using multivariate logistic regression.

Results: We identified 25/90 patients who accrued RD over the course of their disease. In the univariate analysis, we found no difference between RD and RD-N patients in any of the following parameters: demographics, total count of ACR criteria at diagnosis and death, as well as damage at one year after diagnosis and cumulative non-renal damage at death. Compared to RD-N patients, RD patients had a higher proportion of malar rash at diagnosis (11/25 vs. 13/65, p = 0.021) and a higher cumulative proportion of renal disorder (19/25 vs. 30/65, p = 0.011), including proteinuria and urinary casts (17/25 vs. 23/65, p = 0.005, for both). RD was associated with a higher proportion of renal disorder (19/25 vs. 30/65, p = 0.011), including proliferative lesions, and with more frequent occurrence of malar rash at diagnosis (11/25 vs. 15/65, p = 0.049). Conversely, hematological disorder and leukopenia at diagnosis were less frequent in RD compared to RD-N patients (4/25 vs. 30/65, p = 0.008 and 1/25 vs. 21/65, respectively). In the final multivariate model (adjusted for gender, age at diagnosis and disease duration), malar rash at diagnosis and the cumulative presence of renal disorder (classification criteria of the ACR) were positively associated with RD. Conversely, leukopenia at diagnosis was inversely associated with RD (Figure 1).

Conclusion: More than a quarter of deceased patients accrued RD. While malar rash at diagnosis may be associated with a higher likelihood of developing RD, early leukopenia may be associated with its lower likelihood in deceased patients.

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Disclosure of Interests: Ivan Padjen: None declared, Marijan Ercog: None declared, Mislav Cerovec: None declared, Miroslav Mayer: Speakers bureau: Novartis, Sandzol, Abbvie, Pfizer, Alviron, Roche, MSD, Octapharma, Ranko Stevanovic: None declared, Branimir Anic: Speakers bureau: Novartis, Sandzol, Abbvie, Pfizer, Alviron, Roche, MSD, Octapharma


AB0544 ECHOCARDIOGRAPHIC CHANGES IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS BEFORE TO INITIATION OF IMMUNOSUPPRESSIVE THERAPY

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Background: Cardiovascular diseases are becoming the leading cause of death among SLE patients due to increasing life-spans. Transthoracic echocardiography (TTE) is a reliable and widely available modality in everyday clinical practice useful to identify specific pathological cardiac changes and predictors of heart failure (HF).

Objectives: Obtaining of specific TTE findings in SLE patients prior to initiation of pathogenic immunosuppressive therapy was the objective in this study.

Methods: Thirty four pts (91% females, aged 30[26-34]years [median [interquartile range 25%-75%]) with “non-treated” SLE (ACR 1997 and SLICC 2012 criteria) were included. None of pts was treated either with prednisone or cytotoxic drugs at the moment of inclusion.

Results: Median SLE duration was 18[6-60]months, SLEDAI-2K - 13[1-19], SLICC/DI - 0[0-6]scores. Leading SLE clinical manifestations included: hematological changes (74%), kidney involvement (59%), joints (50%) and skin involvement (50%). Immunological abnormalities were detected in all patients and were as follows: ANA positivity – in 100%, anti-dsDNA antibodies – in 76% of SLE patients. Concurrent antiphospholipid syndrome was found in 2(6%) patients. Valve insufficiency with varying degree of regurgitation was the commonest pathology found in “non-treated” SLE patients based on TTE data: mitral valve insufficiency – in 31(91%), tricuspid valve – in 31(91%), pulmonary valve insufficiency – in 21(62%), aortic valve insufficiency – in 4(12%) patients. Endocarditis was a rare pathology found in 5(15%) patients, while mitral and tricuspid valves prolapse was seen more often – in 16(47%), while not a single case of valve stenosis was found. Pericardial pathology was detected in 16(47%) patients: exudative – in 9(26%), and adhesive (thickening, hardening and separation of leaflets) in 7(21%). There were no cases of CAD or MI, although there were 2(6%) documented cases of chest pain in history, and 1(3%) case of confirmed CHF. Most common TRF were dyslipidemia and hypertension - in 15(44%) and 11(32%) SLE patients respectively. Median LVEF was 64[59-67], LV end-systolic dimension – 30[27-32]mm, LV end-diastolic dimension – 48[45-51]mm, pulmonary artery systolic pressure – 2[22-32]mmHg. LV diastolic dysfunction (LVDD) was found in 10 (29%), systolic dysfunction (LVSD) – in 4(12%), LV myocardial hypertrophy (LVH) – in 5(15%); left atrium dilatation (LAD) was found in 4(12%), and increased dimensions of right atrium was detected in 3(9%) SLE patients.

Conclusion: Most common cardiac abnormalities in “non-treated” SLE patients with high activity (SLDAI-2K > 13 scores) were valve dysfunction (insufficiency with regurgitation), mitral and tricuspid valve prolapse and pericarditis. Of importance is the presence of early subclinical features of HF almost in 1/3 of naïve to treatment SLE patients: LVDD (29%), LVH (15%), and LAD (12%). SLE patients should be thoroughly monitored both for adequate control of SLE activity, and cardiac pathology with correction of TRF, regular assessments by a cardiologist, TTE, and early administration of cardio-protection therapy in view of increased HF risk in SLE patients, predetermining unfavorable prognosis.

Disclosure of Interests: None declared

DYNAMICS OF N-TERMINAL FRAGMENT OF BRAIN NATRIURETIC PEPTIDE PROGENITOR LEVEL IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS, WITHOUT HEART FAILURE SIGNS BEFORE AND AFTER IMMUNOSUPPRESSIVE THERAPY

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Background: Cardiovascular mortality is increased in systemic lupus erythematosus (SLE). Elevated plasma concentration of N-terminal fragment of brain natriuretic peptide progenitor (NT-proBNP) is a laboratory marker of heart failure (HF), associated with cardiovascular morbidity and mortality in the general population.

Objectives: To measure NT-proBNP serum levels in SLE patients without HF signs before initiation of the therapy. To monitor NT-proBNP levels during therapy up to achieving SLE remission.

Methods: The study included 15 patients (87% females, aged 31[29-33] years (median [interquartile range 25-75%]) with untreated SLE (ACR 1997 and SLICC 2012 criteria) without HF. These patients were a new-onset and long-standing disease, who discontinued administered therapy. The control included 39 healthy donors (27[24-44] years, 87% females). A comprehensive SLE patients’ evaluation was made twice: at baseline and at the end of follow-up (FUP), median FUP was 7[2-7] years. Serum levels of NT-proBNP (pg/ml) were measured using electrochemiluminescence method Elecsys proBNP II (Roche Diagnostics, Switzerland). Normal NT-proBNP levels should vary within <125pg/ml.

Results: At enrollment median SLE duration was 1[1-7] years, SLEDAI-2K - 10[8-20], SLICC-DI - 0[0-1] scores, SLE patients had elevated (vs controls) values of NT-proBNP: 150[77.7-650.5] vs 44.6[29.7-66.9]pg/ml, p<0.001, NT-proBNP concentrations >125pg/ml were found in 8(53%) SLE patients without HF. Glucocorticoids and hydroxychloroquine were initiated in all patients, and additionally cyclophosphamide was administered in 7(47%) patients, mycophenolate mofetil – in 5(33%), rituximab – in 3(20%). By the end of FUP patients’ median age was 36 [34-39] years p>0.001, SLE duration - 8[7.5-11] years, stable remission was achieved in 14(93%) patients, a relapse of exacerbation was documented in 1(7%) patient, SLEDAI-2K - 2[0-4] p<0.01, SLICC-DI - 0[0-2] scores p<0.05. NT-proBNP levels were comparable to values in the control group: 26.6[19.3-64.9] vs 44.6[29.7-66.9]pg/ml, p>0.05, with only one case (7%) with NT-proBNP level >125pg/ml.

Conclusion: NT-proBNP concentrations in "untreated" SLE patients with high disease activity and without CV pathology and HF were significantly higher than in the control group (p<0.001), and more than 50% of these patients had elevated NT-proBNP (>125pg/ml) baseline concentration. Elevated NT-proBNP concentrations were associated with markers renal function (creatinine, urea, GFR). Adequate immunosuppressive therapy resulted in achievement of SLE remission and normalization of NT-proBNP concentrations.

Disclosure of Interests: None declared


IS IMMUNOLOGICAL PROFILE THE PRIMARY DRIVING FORCE BEHIND CLINICAL PICTURE OF SJÖGREN SYNDROME?

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Background: Primary SS (pSS) is a unique autoimmune disorder with a diverse spectrum of clinical and serological manifestations. Multiple clinical and laboratory determinants have been suggested to affect disease progression. Among these, early-onset (up to 35 years) has been proposed to indicate more severe disease.

Objectives: To determine possible clinical and laboratory differences between pSS patients diagnosed at 35 years or younger and those diagnosed after the age of 35.

Methods: We analyzed a single-centre cohort of 228 adult patients with pSS. For 189 consecutive patients diagnosed between the years 2002 and 2008, the data were collected retrospectively from medical charts, while 39 consecutive patients diagnosed from 2016 to 2018 were followed prospectively. Clinical and laboratory data at diagnosis were collected as defined by ESSDAI. The patients were monitored for new organ involvement during the follow-up period. Categorical variables were compared between those diagnosed ≤ 35 years and after 35 years using the χ2-test or Fisher’s exact test. Continuous variables were compared using the Mann-Whitney U test. A multivariate logistic regression model was used to test the association between early- and over 35 years-onset pSS, anti-SSA positivity, baseline ESSDAI, the duration of follow-up period and the progression of pSS defined as new organ involvement during the follow-up period.

Results: All patients in our cohort fulfilled the 2002 classification criteria. There were 24 (87.5% female, median age 32.5 (IQR 29-34)) early-onset patients and 204 (92.9% female, median age 59 (IQR 51-67)) patients diagnosed after the age of 35. The patients were monitored for new organ involvement during the follow-up period (6.5 (IQR 3-13) years in the early-onset group and 5 (IQR 2-10) years in the > 35 years group). The early-onset group presented with a significantly higher frequency of salivary gland enlargement (25.0% vs 7.8%, p = 0.017), cutaneous involvement (25.0% vs 5.9%, p = 0.006) cryptoglobulinemia (27.5% vs 12.3%, p<0.004), RF positivity (50% vs 25.5%, p = 0.028), anti-SSA positivity (87.5% vs 51.5% (p<0.001) and anti-SSb positivity (50% vs 22.8% (p<0.004). The presence of anti-SSA (odds ratio (OR) 3.93, 95% CI 1.69-9.12, p<0.001), and longer period of follow-up (OR 1.16, 95% CI 1.09-1.25, p<0.001), but not early onset of pSS (OR 0.68, 95% CI 0.32-1.43), associated with higher rate of active disease.

Conclusion: Early-onset pSS is a more severe disease with increased cardiovascular, cutaneous and immune-related manifestations compared with late-onset pSS, with increased risk of new organ involvement during the follow-up period.

Disclosure of Interests: None declared
AB0547 LUPUS ENTERITIS SERIES OF CASES IN DEVELOPING COUNTRY: FROM CLINICAL FINDINGS TO THERAPEUTIC MANAGEMENT

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Background: The prevalence of lupus enteritis (LE) is 2% one of gastrointestinal manifestation of the involvement of the LES. The rapid onset of these symptoms requires determining the life-threatening conditions, but their detection becomes a challenge. We present a series of 6 cases of LE, the most clinical findings and limitations in our environment.

Objectives: Our objective was to describe six cases of lupus enteritis, its diagnostic challenge in our country with limited resources, frequent clinical presentations and its management.

Methods: We retrospectively reviewed the medical records of 6 patients in our hospital with a diagnosis of SLE according to SLICC ACR 2010 criteria between 2017-2018 for suspicion of lupus enteritis. We discard infectious etiology.

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (years)</th>
<th>SLE evolution time</th>
<th>SLEDAI</th>
<th>Diarrhea</th>
<th>Abdominal pain</th>
<th>Vomit</th>
<th>Sickness</th>
<th>Fever</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>29</td>
<td>12 years</td>
<td>29</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>24</td>
<td>2 years</td>
<td>24</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>25</td>
<td>4 years</td>
<td>25</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>4</td>
<td>23</td>
<td>1 year</td>
<td>23</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>5</td>
<td>16</td>
<td>6 months</td>
<td>16</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>6</td>
<td>22</td>
<td>8 months</td>
<td>23</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

Results: We describe 6 cases, all the patients were woman with a mean age of 23.1 years and an average of 3.6 years until the presentation of enteritis. The clinical symptoms included mainly abdominal pain (100%), vomiting (50%), diarrhea (83%), nausea (50%) and fever (16%). The laboratory characteristics mainly reflect the high lupus activity: SLEDAI 23 pts. Low levels of complement (83%), anemia (50%). The homogeneous pattern predominated in 83%, antiDNA was quantified only in one patient due to a lack of resources, with high titer. The median level of CRP was 3.3 mg/dL. Only two patients (33%) presented class III lupus nephritis by biopsy. In CT, the sign of target shot was present in all cases. Only 1 patient could be biopsied with non-specific chronic colitis. All patients received corticosteroids as first-line treatment, with additional immunosuppressants with significant improvement. One patient died due to pulmonary complications.

Conclusion: We should consider lupus enteritis as a possible initial digestive manifestation in patients with SLE. Its diagnosis requires a high index of suspicion, being the CT one of the fundamental pillars for the diagnosis. There is no consensus in the management, however, it was initiated with pulses of methylprednisolone, with limitations to request immunological studies and biological therapy due to economic implications. Finally, we emphasize the need for a prospective evaluation of this rare disease by encouraging the establishment of an international registry.

REFERENCES

Disclosure of Interests: None declared
AB0549  NEUROPSYCHIATRIC DISEASE IN SYSTEMIC LUPUS ERYTHEMATOUS AND PRIMARY SJÖGNENS SYNDROME: THE ADAPTATION OF A QUESTIONNAIRE

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Background: Systemic Lupus Erythematosus (SLE) and Primary Sjögren Syndrome (pSS) are systemic autoimmune diseases, both associated with neurological and psychiatric manifestations. In SLE there are several questionnaires used for neuropsychiatric screening and evaluation, however for pSS there are no specific tools available. Their development is required in order to standardize symptom assessment and allow for accurate disease prevalence estimation.

Objectives: The main objective of this project is to assess the prevalence of neurological and psychiatric manifestations in our cohort of SLE and pSS patients through the adaptation to Portuguese of a screening questionnaire developed by Mosca et al 2010 (1) and its relationship to quality of life.

Methods: A cross sectional study was performed by applying a screening questionnaire, adapted from Mosca et al (1), to patients with SLE and pSS. The outcomes were evaluated both as binary (neurologic (ND)>9 pts) and psychiatric (PD)>10 pts) disease versus no disease) and continuous variables (score average) and in relationship to demographic data, disease scores (SLEDAI and SLICC, and ESSDAI and ESSPRI) and a quality of life instrument (VAS score).

Results: A total of 70 participants (15 SLE and 54 pSS patients) participated in the study. Neurological disease was present in 63% and 48% and psychiatric disease in 25% and 15% of SLE and pSS patients, respectively. There was a statistically significant association between the presence of neurological and psychiatric disease and quality of life (pSLE PD 20 vs 75, p-value 0.004; SLE ND 60 vs 80, p-value 0.001 and PD 50 vs 76.5, p-value 0.008). There was a trend for higher ESSPRI scores, with higher psychiatric scores (0.54 Spearman correlation coefficient; p-value=0.03). SLE higher neurological scores correlated with older age (0.34 Spearman correlation coefficient, p-value=0.01).

Conclusion: The questionnaire yielded a frequency of neurological and psychiatric disease similar to literature, as well as correlation to quality of life. This study represents the first step in the validation process for the Portuguese language but results should be regarded with caution considering this questionnaire was designed for screening and not for diagnosis.

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Disclosure of Interests: None declared
Results: FLS+/Ro- patients were predominantly White (82% vs 77%), had a higher frequency of oral (97% vs 92%) and ocular (95% vs 91%) dryness, a lower frequency of ANA (60% vs 87%), hypocomplementemia (13% vs 23%), rheumatoid factor (26% vs 56%), cryoglobulins (5% vs 9%), a lower mean ESSDAI score (4.6 vs 6.6), and a lower systemic activity in the constitutional, lymphadenopatic, glandular, cutaneous, renal, hematological and biological domains (p<0.001 for all comparisons). Abnormal salivary flows and ANA remained significant independent variables after adjustment by age and gender.

Conclusion: Biopsy-proven primary SjS with negative anti-Ro antibodies is characterized by high frequency of sicca symptoms, mild immunological profile and low systemic activity.

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* p value was obtained by Chi-square test. SD = Standard deviation.

AB0552  25 HYDROXY-VITAMIN D LEVEL IN SYSTEMIC LUPUS ERYTHEMATOSUS: IS IT RELATED TO DISEASE ACTIVITY AND LUPUS NEPHRITIS?

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Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease. SLE is attributed to different autoimmune mechanisms leading to the production of several autoantibodies and formation of immune complexes with subsequent organ damage. 25 hydroxy-vitamin D3 (25(OH)D3) plays a significant role in immune system regulation and is an important immunomodulatory hormone involved in various biochemical reactions.

Objectives: Are to assess the levels of 25(OH)D3 in patients with SLE and to investigate the relationship between 25(OH)D3 levels and disease activity in patients with and without lupus nephritis.

Methods: 300 subjects were included in the study and were divided into 3 groups: group 1 consisted of 100 patients with SLE and lupus nephritis (LN), group 2 consisted of 100 patients free from LN and group 3 consisted of 100 healthy volunteers as a control group. All patients fulfilled the American College of Rheumatology criteria for diagnosis of SLE and were recruited from Internal Medicine department and out-patient clinics, Cairo University Hospital. Exclusion criteria included diseases and drugs which affect the endothelial function such as: smoking, diabetes mellitus, essential hypertension, and coronary artery disease and drugs such as nitrates, hypolipidaemic drugs and aspirin. Disease activity was evaluated by systemic lupus erythematosus disease activity index (SLEDAI), 25(OH)D3 was measured using ELISA. 25(OH)D3 level (≥30 ng/ml) was considered as recommended, <30 ng/ml was considered vitamin D deficiency.

Results: The mean value of 25(OH)D3 was significantly lower in patients with lupus nephritis (17.1±5.5 ng/ml) and those without lupus nephritis (16.6±5.9 ng/ml) than in controls (36.7±3.3 ng/ml) (p-value 0.001). Serum 25(OH)D3 level was inversely correlated with the duration of SLE disease (r = -0.676, p-value <0.001) and with the duration of lupus nephritis (r = -0.363, p-value<0.001). There was also highly significant negative correlation between 25(OH)D3 level and prednisolone dose, hydroxychloroquine, cyclophosphamide and mycophenolate mofetil but not with NSAIDs.

Conclusions: 25(OH)D3 levels are markedly lower in patients with SLE. Low 25(OH)D3 levels are significantly correlated with disease activity parameters, disease duration and disease treatment.

REFERENCES

Figure 1. Level of serum 25(OH)D3 in patients with SLE and controls:

Figure 2. Correlation between 25(OH)D3 levels and SLEDAI and anti-ds DNA

Table 1. 25(OH)D3 levels and SLEDAI in patients with and without lupus nephritis

<table>
<thead>
<tr>
<th>SLEDAI grade</th>
<th>WITHOUT LUPUS NEPHRITIS</th>
<th>LUPUS NEPHRITIS</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>0(0.0%)</td>
<td>0(0.0%)</td>
<td></td>
</tr>
<tr>
<td>≥30</td>
<td>0(0.0%)</td>
<td>0(0.0%)</td>
<td></td>
</tr>
<tr>
<td>P-value</td>
<td>0.001**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate (6-12)</td>
<td>4(100.0%)</td>
<td>0(0.0%)</td>
<td>6(9.6%)</td>
</tr>
<tr>
<td>Severe (13-20)</td>
<td>9(97.9%)</td>
<td>2(21.1%)</td>
<td>30(100.0%)</td>
</tr>
</tbody>
</table>

Disclosure of Interests: None declared


AB0553  STUDY OF ANXIETY AND DEPRESSION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

Maria Rosas-Giménez1, Stack John2, James Galloway2, Natalia Mená-Vázquez1, Clara Fuego-Varela1, Antonio Fernandez-Nebro1, 1Rheumatology Service of the Regional University Hospital of Malaga (HRUM), Biomedical Research Institute of Malaga (IBIMA), University of Malaga, Malaga, Spain. 2KING’S COLLEGE HOSPITAL NHS FOUNDATION TRUST, London, United Kingdom

Objectives: To study the prevalence of anxiety and depression in a cohort of patients with SLE at King’s College Hospital in London, as well as its relationship with characteristics of disease and treatments

Methods: Cross-sectional study of a cohort of patients with SLE. All patients with SLE who had been included in the IMPARTs project (Integrating Mental and Physical healthcare: Research, Training and Services) were recruited between 2012-2016. All patients filled out the following questionnaires on a tablet device: PHQ9 (Patient Health Questionnaire) (Scores of 10 or more have an sensitivity and specificity close to 90% for major depression) and GAD-7 (7-item Generalized Anxiety Disorder) (Scores of 10 or more have an sensitivity and specificity close to 89% and 82% for GAD). Variables demographic, duration of the disease (months) and the profile of autoantibodies, Previous history of depression or anxiety, SLE-DAI, treatments, ESR, CPR, C3 and C4. Statistical analysis: descriptive, bivariable using T-Student and χ2.

Vit. D level in studied groups:

Figure 1. 25(OH)D3 levels and SLEDAI in patients with and without lupus nephritis

Disclosure of Interests: None declared

Table 1

<table>
<thead>
<tr>
<th>Variables</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (female) n (%)</td>
<td>76 (91.6)</td>
</tr>
<tr>
<td>Age (years), median(IQR)</td>
<td>41 (18)</td>
</tr>
<tr>
<td>Race(%)</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>12 (14.7)</td>
</tr>
<tr>
<td>Black</td>
<td>55 (66.3)</td>
</tr>
<tr>
<td>Asian</td>
<td>6 (7.2%)</td>
</tr>
<tr>
<td>Other</td>
<td>10 (12)</td>
</tr>
<tr>
<td>Smokers(%)</td>
<td>13 (15.6)</td>
</tr>
<tr>
<td>Duration of the disease (months), median(IQR)</td>
<td>116 (112)</td>
</tr>
<tr>
<td>SLEDAI,median(IQR)</td>
<td>2 (4)</td>
</tr>
<tr>
<td>ESR,median(IQR)</td>
<td>25 (42.5)</td>
</tr>
<tr>
<td>CRP,median(IQR)</td>
<td>2 (7.32)</td>
</tr>
<tr>
<td>ANA,%</td>
<td>82 (98.8)</td>
</tr>
<tr>
<td>dsDNA,%</td>
<td>36 (46.8)</td>
</tr>
<tr>
<td>Anti-SM, %</td>
<td>37 (44.6)</td>
</tr>
<tr>
<td>Anti-RNP, %</td>
<td>41 (49.4)</td>
</tr>
<tr>
<td>Anti-SSA 52 kD, %</td>
<td>18 (26.9)</td>
</tr>
<tr>
<td>Anti-SSA 69 kD, %</td>
<td>29 (43.3)</td>
</tr>
<tr>
<td>Anti-SSB, %</td>
<td>14 (16.9)</td>
</tr>
<tr>
<td>Anti-cardiolipin,%</td>
<td>17 (20.5)</td>
</tr>
<tr>
<td>Anticnlganteicardiolipin,%</td>
<td>7 (8.4)</td>
</tr>
<tr>
<td>Anti Beta-2-glioprotein,%</td>
<td>1 (1.2)</td>
</tr>
</tbody>
</table>

Table 2

<table>
<thead>
<tr>
<th>Variables</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Previous depression</td>
<td>23 (17.8)</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>17 (13.2)</td>
</tr>
<tr>
<td>GAD 7 total</td>
<td></td>
</tr>
<tr>
<td>&gt;15:Severe Anxiety Disorder</td>
<td>20 (15.5)</td>
</tr>
<tr>
<td>&gt;10: Moderate Anxiety Disorder</td>
<td>7 (5.4)</td>
</tr>
<tr>
<td>&gt;5: Mild anxiety disorder</td>
<td>12 (9.3)</td>
</tr>
<tr>
<td>PHQ 9 total</td>
<td></td>
</tr>
<tr>
<td>&gt;20: Severe major depression</td>
<td>11 (8.5)</td>
</tr>
<tr>
<td>&gt;15: Moderately Severe Depression</td>
<td>20 (15.5)</td>
</tr>
<tr>
<td>&gt;10: Moderate major depression</td>
<td>7 (5.4)</td>
</tr>
<tr>
<td>&gt;5: Mild depression</td>
<td>7 (5.4)</td>
</tr>
</tbody>
</table>

Conclusion: The prevalence of anxiety and depression in our group of patients was high, both related, as well as with the perception of pain and fatigue. A correct assessment of these manifestations and early treatment could help improve the quality of life of patients.

Disclosure of Interests: None declared

AB0554 RISK OF CORONARY ARTERY DISEASE AND STROKE IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS USING JAPANESE HEALTH INSURANCE DATABASE

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Background: Patients with systemic lupus erythematosus (SLE) have higher risk of coronary artery disease (CAD) and stroke than the general population.1,2 Because these comorbidities influence on patients' vital prognosis and quality of life, it is essential for rheumatologists to manage them appropriately. Considering differences in lifestyle and ethnicity, it is of great interest and needed to investigate risk of these comorbidities in Asia. However, to date, such evidence is scarce.

Objectives: To estimate incidence rate (IR) and identify risk factors of CAD and stroke in patients with SLE using a Japanese health insurance database.

Methods: This retrospective longitudinal population-based study was conducted using claims data provided by Medical Data Vision Co., Ltd (Tokyo, Japan). We defined individuals as SLE cases if they met all of the following: 1) had at least one ICD10 code (M321 or M329); 2) had at least one prescription of oral corticosteroids (CS), methylprednisolone (mPSL) pulse therapy, immunosuppressive drugs (IS) (azathioprine, mizoribine, tacrolimus, mycophenolate mofetil, cyclophosphamide, methotrexate), biologics (belimumab, rituximab) or hydroxychloroquine between April 2008 and July 2017; 3) were 16 years old or over. The start of observation was defined by the first month in which cases met all of the above criteria. Patients were followed until the earliest of date of first CAD event or stroke, date of loss of follow-up, or the end of follow-up (June 2018). CAD and stroke were defined as follows: for CAD, at least one ICD10 code (I20.x or I21.x or I23-24.x) and either percutaneous coronary intervention, coronary artery bypass procedure, or thrombolytic agents during hospitalization: for stroke, at least one ICD10 code (I60-62.x or I63-64.x) and either cerebrovascular procedures, thrombolytic agents, or antiplatelet drugs during hospitalization. Patients were excluded if they had a previous diagnosis of CAD or stroke and were prescribed antiplatelet drugs or anticoagulants during the first 3 months. We defined baseline characteristics using the data from the first 3 months, and calculated IR and adjusted hazard ratio (HR) of risk factors for CAD or stroke after adjusting for baseline characteristics using a Cox proportional hazard model.

Results: In this study, 19,138 cases were included. The median age was 53 years and 81.3% were female. Median observation period was 3.1 years. IR (95% CI), 1,000 patient-years (PY) of CAD or stroke was 1.41 [1.11-1.77] and 4.10 [3.56-4.70], respectively. IR of any CAD or stroke was increased age-dependently (2.06 [1.47-2.80] for 16-39 years-old, 5.07 [4.36-5.86] for 40-69, 13.0 [10.9-15.5] for 70-). Adjusted HR [95% CI] was 1.37 [95% CI, 1.27-1.47] for age by decade, 3.34 [1.76-6.28] for CS use, 1.48 [1.16-1.84] for presence of hypertension (HT), 1.38 [1.04-1.85] for diabetes mellitus (DM), 1.73 [1.25-2.38] for chronic kidney disease (CKD), and 1.95 [1.15-3.32] for atrial fibrillation (AF).

Conclusion: This is the first study investigating the risk of CAD or stroke in Japanese patients with SLE using a large health insurance database. Older age, use of CS, and presence of HT, DM, CKD, and AF were identified as significant risk factors of these comorbidities.

REFERENCES

Disclosure of Interests: Ryoko Sakai Grant/research support from: Tokyo Women’s Medical University (TWMU) has received unrestricted research grants for Division of Epidemiology and Pharmacoeconomics of Rheumatic Diseases from Ayumi Pharmaceutical Co. Ltd., Bristol Meyers Squibb, Chugai Pharmaceutical Co. Ltd., Nippon Kayaku Co. Ltd., Taiho Toyama Pharmaceutical Co. Ltd., Mitsubishi Tanabe Pharma Corp., and with which TWMU paid the salary of R.S. RS has received a research grant from Bristol-Meyers Squibb., Suguru Honda: None declared, Sho Suzuki: None declared, masako majima: None declared, naoko konda: None declared, hideo takada: None declared, masayoshi harigai Grant/research support from: Tokyo Women’s Medical University (TWMU) has received unrestricted research grants for.
Division of Epidemiology and Pharmacoepidemiology of Rheumatic Diseases from Ayumi Pharmaceutical Co. Ltd., Bristol Meyers Squib, Chugai Pharmaceutical Co. Ltd., Nippon Kayaku Co. Ltd., Taisho Toyama Pharmaceutical Co. Ltd., Mitsubishi Tanabe Pharma Corp, and with which TWMJ paid the salary of MH. MH has also received research grants from AbbVie Japan GK, Eisai Co. Ltd., Takeda Pharmaceutical Co., Ltd., and Teijin Pharma Ltd., Hisashi Yamanaka Grant/research support from: AbbVie, Eisai, Bristol-Meyers, Novartis, Behringer, Astellas, Kaken, Nippon-Shirakuyu, Pfizer, UCB, Ayumi, Ono, Daich-Sankyo, Taiyo-Toyama, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, Tori, YLbio, Speakers bureau: Bristol-Meyers, Astellas, Pfizer, Daiichi-Sankyo, Takeda, Tanabe-Mitsubishi, Chugai, Teijin Pharma, YLbio


AB0555 POTENTIAL ROLE OF PAROTID ELASTOGRAPHY IN DIAGNOSIS AND CLASSIFICATION OF PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME

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Background: Despite the improvements in classifying patients with primary Sjögren’s syndrome with usage of the new 2016 ACR/EULAR classification criteria, there remains to be a need for improvement and investigating the value of new modalities in diagnosing as well as classifying these patients.

Objectives: to investigate potential role of parotid elastography in diagnosing and classification of patients with primary Sjögren’s syndrome (pSS)

Methods: This is a cross-sectional analysis of patients with primary Sjögren’s syndrome followed up in our out-patient Rheumatology clinic. We performed chart reviews and retrospectively investigated the available data on files to search whether or not our clinically diagnosed patients satisfied the 2002 AECG and/or 2016 ACR/EULAR criteria sets. Ultrasonographic and elastographic evaluation of parotid and submandibular glands bilaterally were performed on consecutive patients with clinical diagnosis of pSSs and contributions of these findings to classification criteria sets were interpreted.

Results: There were 95 pSS patients and 30 healthy gender and age matched controls. Strain ratio, shearwave velocity and Pascals values of the glands were examined. Parotid strain ratio, submandibular velocity and submandibular pascal values were statistically significantly different compared to healthy controls (Table).%66 of patients considered clinically as Sjögren syndrome satisfied 2016 ACR/EULAR criteria patients and% 84 satisfied 2002 AEC criteria classification criteria. We grouped patients with respect to parotid strain ratio taking 1.057 as the cut-off value. Those patients who did not satisfy 2016 ACR/EULAR criteria, but clinically diagnosed as pSSs (non criteria pSSs patients), also had significantly higher parotid strain ratio and submandibular velocity compared to healthy controls (p=0.016 and p<0.001 respectively). Interestingly, both criteria and non-criteria pSSs patients had similar parotid strain ratio and submandibular velocity (p=0.892 and p=0.260, respectively).

Conclusion: Parotid shear elastography is an easy and non-invasive method and can be a useful tool for the diagnosis and classification of patients with pSSs (1).

REFERENCES


Disclosure of Interests: None declared


AB0556 PARTICULARITIES OF PULMONARY HYPERTENSION IN SYSTEMIC LUPUS ERYTHEMATOSUS

sameh sayhi, Nouha Ghris, Najej Boussetta, Bilel Aftaoui, Faida Aji, Nadia Ben Abdelflahid, Bassem Louzir. Military Hospital of Tunis, Autoimmune Diseases Unit Research: UR17DN02, Tunis, Tunisia

Background: Systemic lupus erythematosus (SLE) is an autoimmune disease that primarily affects young women. It is characterized by the production of autoantibodies and immune complexes. Vascular pulmonary involvement has long been considered rare, a consequence of thromboembolic events. It is in fact a proper entity, often of multifactorial mechanism, with spontaneous evolution to pulmonary arterial hypertension (PAH), which makes its gravity.

Objectives: The objective of our study is to determine the particularities of PAH during SLE.

Methods: We conducted a mono-centric, retrospective and descriptive study of the follow up of patients in the internal medicine department of the Military Hospital of Tunis for LES (diagnosis according to the ARA criteria) between January 2010 and December 2015.

Results: All patients underwent external echocardiography or during their stay in the department.

Results: We collected 87 patients diagnosed with SLE. PAH was recorded in 16 patients (38%) including 6 men and 10 women with a F/M sex ratio of 1.66. The average age was 37.23 years with extremes ranging from 16 to 70 years old. Clinically, we observed dyspnea in 10 patients (62%), chest pain in 7 cases (43%), dry cough in 2 cases (12%), palpatations in 1 case (6%), and right heart failure in 1 case (6%). At cardiac auscultation, 5 patients were tachycardic (31%), 5 had a tricuspid systolic murmur and 1 had an irregular rhythm. A burst of 82 in the pulmonary focus was noted in 3 patients (18%). Nine of the 16 patients with PAH had electrical signs: five had sinus tachycardia (31%), two had signs of right ventricular hypertrophy. A complete arrhythmia with atrial fibrillation was noted in one patient. The chest X-ray showed cardiomegaly in 6 patients (37%). Among the 16 patients, there was a tricuspid valve insufficiency associated with PAH in 7 patients (43%), 2 had mitral valve insufficiency (12%), 6 patients had pericarditis, one patient had endocarditis (6%) and myocarditis was found in another one (6%). PAH was isolated in 12 cases. In Immunological tests, NAs were positive in all patients. Three quarters of the patients (12) had native anti-DNA positive (75%) and ¼ of the patients (4) had anti-Sm positive and anti-RNP positive antibodies (25%). The complement was consumed in 5 cases (31.2%). Anti-phospholipid antibodies were noted in 4 cases (25%). Added to non-specific measures (smoking cessation, elimination of intense physical effort ...) adopted for all patients, oxygen therapy was indicated in four patients. Diltiazem 180 mg/day vasodilator therapy was prescribed in 3 patients. Effective anti-vitamin K anticoagulation was prescribed in a patient with severe PAH at 80 mg/ day.

Conclusion: Pulmonary arterial hypertension (PAH) is a rare complication of systemic lupus erythematosus, its prevalence varies from 0.5 to 17.5% depending on the series. SLE is the second leading cause of PAH in connective tissue disease after systemic sclerosis. This vascular involvement is essential for the prognosis and is an important evolutionary step in the management.

Disclosure of Interests: None declared


AB0557 NON-CORONARY CARDIAC MANIFESTATIONS OF SYSTEMIC LUPUS ERYTHEMATOSUS IN ADULTS

Nouha Ghris, sameh sayhi, Najeh Boussetta, Nour El Houla Gueddich, Faida Aji, Nadia Ben Abdelflahid, Bassem Louzir. military hospital, autoimmune diseases unit research: UR17DN02, tunis, Tunisia

Background: Systemic lupus erythematosus (SLE) is a common chronic multi-system autoimmune disorder of unknown etiology causing injury to many organ Systems. It predominantly affects young women. Cardiac manifestations develop in the majority of patients with SLE at some time during the course of their disease.

Objectives: The aim of our study is to assess cardiac abnormalities in patients with systemic lupus erythematosus (SLE) by echocardiography and to compare the 2 groups of patients with and without cardiac manifestations.

Methods: We have performed a transversal, descriptive study of SLE patients hospitalized in the Internal Medicine department at the Military Hospital of Tunis between January 2016 and June 2018. Diagnosis of SLE was made according to the criteria of ACR. All patients underwent a cardiac ultrasound externally or during their stay in our department.
Results: The patients were 61 females and 19 males (sex-ratio=3) with a mean age of 38 years. Forty two patients had cardiac involvement. They were 33 female and 9 male with a mean age of the disease of 31,8 years (16-80 years) at the beginning of the disease and 41 years at the time of the study. 83% of patients were symptomatic. The symptoms were dominated by objective chest pain (43%). In Doppler echocardiography, pericarditis was found in 23 patients (55%) with a single case of cardiac tamponade. Libman Sachs endocarditis and lupus myocarditis were found in one case each. Pulmonary hypertension (HTP) was observed in 16 patients (38%) and valvular disease in 22 patients (52%). Cardiomegaly was observed in 9 patients (21%). Electrical abnormalities were dominated by microvoltage in 8 patients. The general symptoms (83%), skin lesions (76%) and musculoskeletal involvement (64%) were the most frequent events associated with the cardiac manifestations in group 1. ANA were positive in 97% of cases and antiphospholipid antibodies in 24%. Prednisone: 1mg/kg/day and immunosuppressive therapy were indicated respectively in 71% and 38% of patients.

Conclusion: Cardiac abnormalities are very common in lupus patients even when clinically asymptomatic. SLE is among systemic diseases most providers of heart disease. Echocardiography is an excellent non-invasive tool for cardiac evaluation. Their research is systematic with echocardiography in order to reduce subsequent cardiac morbidity and mortality among the lupus patients.

Disclosure of Interests: None declared


AB0559 TIME OF DIAGNOSTICS OF SJOGREN’S SYNDROME DEPENDING ON ITS FIRST MANIFESTATION

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Background: Sjogren’s syndrome (SS) is a rare autoimmune disease with multisystem manifestations. Diagnostics of SS is intricate due to its low prevalence and deed of invasive tests for diagnosis confirmation.

Objectives: To investigate influence of the first symptom of SS on the time of diagnosis establishment.

Methods: The study was conducted at Dnipropetrovsk Mechinov Regional Hospital, Dnipro, Ukraine. 23 patients (1 male and 22 females, mean age 54 [47;61] years) with SS that received medical care at Rheumatology Department from 2007th to 2017th were enrolled to the study. Diagnosis of SS was provided according to American-European Consensus Group criteria (2002). We analyzed time from the first symptom appearance to diagnosis of SS establishment. Symptoms of the disease onset were classified into 4 groups: fever (body temperature>37°C), arthritis (swelling and/or tenderness of >1 joints), signs of salivary glands injury (swelling of salivary glands, dry mouth syndrome) and other signs of autoimmune diseases (Raynaud’s phenomenon, rash, myalgia).

Results: Median time between the first symptoms and SS diagnostics was 8 [2;17] years. Time to SS diagnostics depending on the first manifestation is in the table below.

Table 1. Time of SS diagnostics depending on the first symptom.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Present</th>
<th>Absent</th>
<th>Log rank test [p]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>3 [1;8]</td>
<td>9.5 [2.2;17]</td>
<td>0.06</td>
</tr>
<tr>
<td>Arthritis</td>
<td>17 [6;22.5]</td>
<td>6.5 [2;11.5]</td>
<td>0.06</td>
</tr>
<tr>
<td>Salivary glands injury</td>
<td>11 [6;19.5]</td>
<td>4.5 [2;10]</td>
<td>0.15</td>
</tr>
<tr>
<td>Symptoms of autoimmune diseases</td>
<td>4 [2;8]</td>
<td>10.5 [2;18]</td>
<td>0.09</td>
</tr>
</tbody>
</table>

Presence of fever or symptoms of autoimmune diseases led to faster diagnostics of SS. Presence of salivary glands injury didn’t influence time of SS diagnostics, while arthritis enlarged it (Figure 1).

Conclusion: Fever and signs of autoimmune diseases may be useful in diagnostics of SS. Greater alertness of symptoms of salivary glands injury is needed.

REFERENCES
A 10-YEAR REVIEW OF DAMAGE ACCRUAL AND PROGRESSION IN A MULTI-ETHNIC COHORT OF SYSTEMIC LUPUS ERYTHEMATOSUS (SLE) IN MALAYSIA

Syahruil Saziyyah Shahrir1, Wong Michelle Heng Ting2, Asrul Abdul Wahab2, Sakthiswary Rajalingham1, Abdul Halim Abdul Gafor1, Mohd Shahrir Mohamed Said1, Ruslinda Mustafar3.

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Background: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease with an unpredictable course of disease. The severity and outcomes of SLE vary across different ethnicities.

Objectives: This study is aimed to determine the pattern of development and progression of organ damage in a cohort of multi-ethnic SLE patients followed for at least 10 years, and to identify the factors associated with the damage accrual.

Methods: We reviewed the medical records of an inception cohort of patients who attended regular monitoring since 2007 at the Rheumatology and Nephrology/SLE Clinic, National University of Malaysia Medical Centre (UKMMC). Their medical records were retrospectively reviewed to obtain SLE disease characteristics, frequency of disease flares, cumulative corticosteroid dose and the use of other immunosuppressive treatment from 2007 until their last visit in 2017. The Systemic Lupus International Collaborating Clinics/american College of Rheumatology damage index (SDI) was used to determine the organ damage at baseline and after 10 years of being followed up. For patients who have succumbed or lost to follow up during the 10-year observation period, the SDI scores just before death or time of follow up loss were recorded.

Results: A total of 258 patients were included with majority of them were Malays (n=145, 56.2%), followed by Chinese (n=100, 38.8%) and Indians (n=13, 5.0%). The mean SDI score increased from 0.39±0.79 at baseline to 1.13±1.47 after 10 years, p<0.001. At 10 years, Indian patients were found to have a significant increase in their SDI scores from baseline compared to Malay and Chinese (p<0.05). New damage accrual was recorded in 38.8% patients with the most common new organ damage significantly occurred in renal (p<0.001), ocular (p<0.05) and cardiovascular (p<0.07). Higher age at baseline, higher ACR criteria at diagnosis, persistent active disease ≥ 6 months, and prednisolone use of ≥ 1mg/kg were independently associated with higher risk of damage accrual. In contrast, hydroxychloroquine treatment was associated with lower risk of damage accrual.

Conclusion: The SDI scores of our SLE cohort increased significantly over 10 years which predominantly affecting the renal. Indian patients accumulated higher SDI scores while persistent active disease, higher ACR criteria at diagnosis, and the use of high dose steroid were associated with new organ damage.

REFERENCES


AB0651 RISK FACTORS FOR ADVERSE PREGNANCY OUTCOMES AND LOW RISK FACTORS FOR ADVERSE PREGNANCY OUTCOMES AND LOW APGAR SCORES OF NEWBORNS IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Hironi Shisada, Risa Wakiya, Mai Mahmoud Fahmy Mansour, Shusaku Nakashima, Mikiya Kato, Taichi Miyagi, Tomohiro Kameda, Hiroaki Dobashi, Kagawa University, Department of Internal Medicine, Division of Hematology, Rheumatology and Respiratory Medicine, Faculty of Medicine, Kagawa University, Kagawa, Japan

Background: Systemic lupus erythematosus (SLE) is an autoimmune disease that occurs in women of childbearing age, and has high risk for adverse pregnancy outcomes (APOs) (1,2). Moreover, it is unclear whether maternal SLE influences the growth and development of children born from SLE mothers. Apgar score at five minutes is a predictive factor of neurological development of newborns. However, there is no report about the association between maternal SLE and Apgar score of newborns.

Objectives: The aim of this study was to identify risk factors for APOs and for low Apgar scores of newborns from SLE mothers.

Methods: We investigated 50 SLE patients who were delivered from May 2006 to December 2018 in our institution. We examined retrospectively regarding APOs including spontaneous abortions, preterm births, premature rupture of membranes (PROM), light-for-date (LFD) newborns, and low Apgar scores of newborns. We analyzed the association between disease activity, laboratory findings, treatment agents, and APOs or Apgar scores.

Results: As for APOs of SLE mothers, cases with preterm births showed higher SLE disease activity index (SLEDAI) during the first trimester (P = 0.01) and higher titers of anti-double-stranded DNA (anti-dsDNA) antibodies at the time of conception (P < 0.01) compared to full-term births. In these cases, mean glucocorticoid doses during pregnancy (P = 0.02) and the rate of treatment intensification (P < 0.01) was higher than full-term birth. In the mothers who delivered LFD newborns, serum complement levels at conception were lower than in those with non-LFD newborns (C3: P = 0.02; CH50: P = 0.05). Cases with spontaneous abortions and PROMs did not differ significantly from the cases without spontaneous abortions and PROMs. Apgar scores at one minute were correlated with SLEDAI during the third trimester (P < 0.01) and with the titer of anti-dsDNA antibodies at conception (P < 0.01). Additionally, Apgar scores at five minutes were correlated with the titer of anti-dsDNA.
antibodies (P < 0.01). In multivariate analysis, there were significant associations between Apgar scores at five minutes and the titre of anti-dsDNA antibodies (P < 0.01, Table 1).

Abstract A80561 Table 1. Multivariate analysis of risk factor for Apgar score at 5 minutes

<table>
<thead>
<tr>
<th>Variable</th>
<th>Standardised B</th>
<th>t value</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLE +</td>
<td>2.10</td>
<td>2.20</td>
<td>0.027</td>
</tr>
<tr>
<td>DAI +</td>
<td>-0.87</td>
<td>-0.79</td>
<td>0.429</td>
</tr>
<tr>
<td>C induction +</td>
<td>0.37</td>
<td>0.38</td>
<td>0.701</td>
</tr>
<tr>
<td>Anti-dsDNA titres</td>
<td>-0.25</td>
<td>-0.24</td>
<td>0.814</td>
</tr>
</tbody>
</table>

Conclusion: In SLE, immunological abnormalities at conception, high SLE-DAI and glucocorticoid doses were risk factors for preterm birth and having a LFD newborn. Apgar scores at five minutes were significantly associated with the titre of anti-dsDNA antibodies. Minimizing disease activity before pregnancy may decrease risks for mothers and their newborns. In preconception counseling, it is important for rheumatologists to explain these risk factors to patients with SLE who hope to conceive. There is a need for long-term follow-up studies focusing on the neurological development of children born from SLE mothers.

REFERENCES


Disclosure of Interests: None declared

AB0562 CARDIOVASCULAR RISK FACTORS AND FRAMINGHAM RISK SCORE IN PRIMARY SJÖGREN SYNDROME PATIENTS: A COMPARATIVE STUDY WITH MATCHED CONTROLS

Joana Silva1, Daniela Faria1, Joana Neves2, Marcos Cerqueira2, Joana Rodrigues1, Soraia Azevedo1, José Tavares-Costa1, Filipa Teixeira1

Background: The association between cardiovascular (CV) risk and chronic systemic inflammatory diseases has been an issue of debate. There is compelling evidence of increased CV morbidity in conditions such as rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) (1). Primary Sjögren’s syndrome (pSS) is a chronic immune-mediated disease characterized by glandular and systemic manifestations, sharing clinical and immunological similarities with RA and SLE. However, in pSS patients the weight of cardiovascular disease attributed to traditional CV risk factors remains unclear.

Objectives: To determine the prevalence of traditional CV risk factors and long-term CV events based on the risk prediction tool of the Framingham risk score (FRS) in pSS patients.

Methods: The study included patients diagnosed with pSS, fulfilling both the 2016 ACR/EULAR and 2002 AECG criteria for the disease, followed-up at our Rheumatology department and aged 49 and age-sex-matched controls. Inclusion criteria were aged 30 to 74 and no history of CV events in order to calculate the FRS. In total, 46 out of 54 patients were eligible for the study. Data on the prevalence of traditional CV risk factors (diabetes, arterial hypertension and smoking), systolic blood pressure (SBP) values, total and high-density lipoprotein (HDL) cholesterol levels were collected and compared between groups. The 10-year risk for CV events according to FRS was calculated and means of patients and controls were compared. Parametric and nonparametric tests were used and the level of significance was defined as p<0.05.

Results: The mean age of pSS patients and healthy individuals was 58.0 ±11.6 and 54.1±13.6 years, respectively. The prevalence of arterial hypertension was higher in pSS patients than controls (52.2% versus 24.5%, p=0.005). The prevalence of diabetes and smoking did not differ significantly between the two groups (p=0.674 and p=0.949, respectively). The SBP values, total and HDL cholesterol levels were also similar between pSS patients and healthy subjects (p=0.063, p=0.413 and p=0.217, respectively).

Mean 10-years risk for CV events assessed by FRS was 11.8±8.3 for pSS patients and 7.8±4.3 for matched controls, with statistically significant difference (p=0.013).

Conclusion: In our study, pSS patients had a higher prevalence of arterial hypertension, which is in agreement with the M. Juarez et al (1) study. Although there were no significant differences in the other traditional CV risk factors, the results showed an increased 10-year risk for major CV events based on FRS assessment in pSS patients in comparison to age and sex-matched controls.

REFERENCES


Disclosure of Interests: None declared

AB0563 TRAUMA AND SLE-CONSiderations regarding a Group of patients from Romania

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Background: Systemic lupus erythematosus (SLE) represents a complex disease, which hasn’t got a clear etiology established yet. Many genetic-susceptibility factors, environmental triggers, antigen-antibody (Ab) responses, B-cell and T-cell interactions, and immune clearance processes interact to generate and perpetuate autoimmunity. One of the triggers could be trauma-surgeries, serious infections or accidents.

Objectives: To assess the presence of history of trauma in patients diagnosed with SLE admitted in our Department, as well as the association with different co-morbidities.

Methods: We included 62 patients, admitted in the Rheumatology Department of the Tرغu-Mureş Emergency Clinical County Hospital between 01.01.2018-29.01.2019, previously diagnosed with SLE. We performed a retrospective analysis of their medical documents, looking for evidence of traumatic risk factors.

Results: The majority of the patients were female (17±8.70%) and had some kind of trauma before being diagnosed with SLE (17±27.41%). Among the operations the most frequent were hysterectomy with bilateral oophorectomy and classical appendectomy, respectively (6±9.67% each), followed by cholecystectomy and tonsillec tomy (2±3.22%). There were also one case of cerebral injury following a car accident and a complicated peri tonitis-related to IUD extraction. The majority of co-morbidities was represented by neurologic involvement (16±25.80%), followed by thyroid (13±20.96%) and renal involvement (12±19.35%).

Conclusion: Patients with SLE from our department have a significant history of traumatic triggers, mainly open surgeries, which might explain the development of autoimmunity. They also have various organ involvement that sometimes warrants aggressive measures. Further studies have to be conducted in order to better examine the possible link between traumatic events and development of this multifaceted disease.

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[1] Christie M Bartels- Systemic lupus erythematosus (SLE) on Medscape Drugs & Diseases

Disclosure of Interests: Ana Alwina Stan Grant/research support from: Novartis, Monica Copotoiu Grant/research support from: Novartis

AB0564 THE CONTROVERSIAL ROWELL SYNDROME: TO BE OR NOT TO BE?

Daisy AM Vaida-Voevod1, Ioana Felea1, Laura Damian1, Cristina Pamfil2, Simona Rednic1,2. Emergency County Hospital Cluj. Rheumatology, Cluj-Napoca, Romania, 2University of Medicine and Pharmacy Iuliu Hatieganu, Rheumatology, Cluj-Napoca, Romania

Background: Rowell syndrome is a rather rare and highly debated entity, initially defined by Rowell et al as discoid lupus associated with...
EXPERIENCE IN THE USUAL PRACTICE OF PATIENTS WITH POLYAUTOIMMUNITY AND MAJOR ORGAN INVOLVEMENT: A PROSPECTIVE STUDY AT THE DONOSTIA UNIVERSITY HOSPITAL

Jesús Alejandro Valero Jaimes, Andrea De Diego Sola, Cesar Antonio Egües Díaz
Donostia, Rheumatology, San Sebastian, Spain

Background: Inflammatory myopathies (IM) are a heterogeneous group of acquired diseases, characterized by the presence of muscle weakness and inflammation. This group includes idiopathic polymyositis (PM), idiopathic dermatomyositis (DM), PM/DM associated with neoplasia, associated with rheumatic autoimmune diseases, juvenile PM/DM, inclusion body myositis (IBM) and immunomodulated necrotizing myopathies (IMM). Methods: A cross-sectional study included 179 patients [160 (89%) females and 19 (11%) males] diagnosed with primary SJögren’s syndrome (SjS) and fulfilling the ACR classification criteria (1) that had been admitted to our outpatient clinic between December 2008 and December 2018. Demographic and disease-specific characteristics were recorded in all patients. Results: In our cohort the median age at diagnosis was 57 years (range: 20-85). Thyroid AID was found in 55/179 (30%) patients, with the following distribution: Hashimoto thyroiditis (n=46), Graves’s disease (n=22), Graves’s disease without (n=4) and with thyroidectomy (n=5). Liver AID was detected in 8/179 patients (4%), 3 patients with autoimmune hepatitis and 5 patients with primary biliary cirrhosis. Regarding major organ involvement, 20/179 (11%) patients had renal manifestations: renal insufficiency (n=12), glomerulonephritis (n=3), interstitial nephritis (n=2) and IgA nephritis (n=3). Eight/179 (4%) patients had lung manifestations: interstitial fibrosis (n=6), emphysema (n=1) and chronic obstructive pulmonary disease (n=1).

REFERENCES


Disclosure of Interests: None declared

Next, provide the content of the scientific abstracts. The abstracts are listed as AB5055, AB5056, etc., indicating their unique identifiers.
Conclusion: Our results add evidence for the presence of polyautoimmunity and major organ involvement in SJL. We found a slightly lower prevalence of polyautoimmunity and major organ involvement compared to recently reported data (2). Nonetheless, extra-glandular organ involvement should be assessed in order to elucidate cumulative damage and how it might impact outcome, prognosis and therapeutic approaches in SJL.

REFERENCES


Disclosure of Interests: Larissa Valor: None declared, Hannah Schenker: None declared, Melanie Hagen: None declared, Johannes Kritza: None declared, Jürgen Rech Grant/research support from: Bristol-Myers Squibb, Celgene, Chugai, GlaxoSmithKline, Janssen, Eli Lilly, Novartis, Roche, Sanofi Aventis, and UCB (in total more than $10,000), Consultant for: Bristol-Myers Squibb, Celgene, Chugai, GlaxoSmithKline, Janssen, Eli Lilly, Novartis, Roche, Sanofi Aventis, and UCB (in total more than $10,000), Georg Schett: None declared


AB0567 DISEASE PATTERN IN EARLY AND NON-EARLY SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is an autoimmune disease with a high degree of variability at onset, creating challenges in the accurate estimation of its pattern in early stages1.

Objectives: To evaluate the pattern of the disease in patients with early and non-early systemic lupus erythematosus from physician’s perspective.

Methods: Performed case-control study included SLE patients that fulfilled SLICC 2012 criteria for SLE. Consecutive patients who fulfilled SLICC 2012 criteria for SLE were recruited. Depressive and anxiety symptoms were assessed by the Hospital Anxiety and Depression Scale (HADS).

Results: A total of 101 SLE patients was analyzed. First group (early SLE) included 34 patients while the second group (non-early SLE) included 67 patients. The disease duration ± SD (range) was 12,42±8,70 (0.1-24) and 146.41±81.64 (31-432) months, respectively. The disease duration ± SD (range) was 12,42±8,70 (0.1-24) and 146.41±81.64 (31-432) months, respectively. The disease duration was assessed by SLEDAI-2K, SLAM, PGA and PhGA for SLE activity, SLICC/ACR DI for disease irreversible changes and SF-8 for the quality of life (QoL). We correlated disease activity scores within groups and activity indices with the QoL using intra- and inter-class correlation coefficients.

Conclusion: The clinical picture of SLE was characterized by high disease activity and low QoL in both, early and non-early lupus, while occurrence of irreversible organ changes was more characteristic for the longer disease duration and development of irreversible changes during the course of lupus.

AB0568 THE EFFECT OF DEPRESSIVE AND ANXIETY ON QUALITY OF LIFE IN PATIENT WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN RENAISSANCE COHORT

Lvubov Vorobyova, Elena Aseeva, Sergey Sololoyev, V.A.Nasonova Research Institute of Rheumatology, Intensive care department, Moscow, Russian Federation

Background: Systemic lupus erythematosus (SLE) patients are at high risk of depression and anxiety. These two states cause severe loss of health related quality of life (HRQoL) for patient with SLE.

Objectives: To assess the effect of depressive and anxiety on HRQoL in a cohort of patients with systemic lupus erythematosus in Russian Federation (RENAISSANCE).

Methods: Consecutive patients who fulfilled SLICC 2012 criteria for SLE were recruited. Depressive and anxiety symptoms were assessed by the Hospital Anxiety and Depression Scale (HAD) scale (0-21 points). Health-related quality of life (HRQoL) was assessed by the validated specific questionnaire LupusQoL-Russian. Disease activity was evaluated by the SLEDAI-2K, and chronic damage by the Systemic Lupus International Collaborating Clinics Damage Index score (SDI).

Results: 328 Russian SLE patients were enrolled in the study (M/F 30/ 298, mean age 34.4±11.5 years, mean disease duration 106.3±97.9 months; mean SLEDAI 2K 9.6±8.0; mean SDI 0.2±0.6. 34 (10.3%) patients had HADS-depression score of ≥10 and 76 (23.1%) of patients had HADS-anxiety score of ≥10. Patients with depressive score of ≥10 had significantly lower the scales “Planning”, “Emotion health” and “Fatigue” (p<0.0001) of the LupusQoL than those with score <10. Similarly, significant lower “Emotion health” and “Fatigue” (p<0.0001) were noted in those patients with HAD-anxiety score ≥10 compared to those <10 and they also had low score of “Burden to others” unlike those who are not anxious. (Table 1).

Conclusion: Depressive and anxiety symptoms in SLE patients and were associated with significantly poorer HRQoL.

Disclosure of Interests: None declared


Table 1. Effect of anxiety and depression on HRQoL in SLE patient

<table>
<thead>
<tr>
<th>LupusQoL domains</th>
<th>HADS-anxiety</th>
<th>HADS-depression</th>
<th>p</th>
<th>HADS-anxiety</th>
<th>HADS-depression</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical health</td>
<td>70.3±22.2</td>
<td>50.2±21.2</td>
<td>&lt;0.0001</td>
<td>67.9±23.1</td>
<td>48.2±18.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pain</td>
<td>73.8±23.3</td>
<td>52.2±23.3</td>
<td>&lt;0.0001</td>
<td>71.2±23.8</td>
<td>50.7±26.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Planning</td>
<td>68.4±26.8</td>
<td>42.8±26.3</td>
<td>&lt;0.0001</td>
<td>65.8±21.2</td>
<td>35.3±21.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Intimate relation</td>
<td>75.9±30.6</td>
<td>56.7±29.8</td>
<td>&lt;0.0001</td>
<td>73.2±31.1</td>
<td>58.3±33.6</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Table 1. Correlation of PhGA with other SLE parameters

<table>
<thead>
<tr>
<th>Parameters of the disease</th>
<th>Group 1</th>
<th>Group 2</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLEAM ± SD (range), points</td>
<td>7.1±47.4</td>
<td>40.0±24.5</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>SLEDAI ± SD (range), points</td>
<td>78.0±412.6</td>
<td>146.41±81.64</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>PhGA ± SD (range), points</td>
<td>45.61±19.54</td>
<td>48.35±19.50</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>PGAS ± SD (range), points</td>
<td>46.97±19.39</td>
<td>47.98±22.41</td>
<td>&gt;0.05</td>
</tr>
</tbody>
</table>

Table 1. General characteristic of the study group

<table>
<thead>
<tr>
<th>Parameters of the disease</th>
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<th>p</th>
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</thead>
<tbody>
<tr>
<td>Disease activity</td>
<td>SLEDAI-2K</td>
<td>SLAM</td>
<td>PGA</td>
</tr>
<tr>
<td></td>
<td>0.20</td>
<td>0.12</td>
<td>0.50</td>
</tr>
<tr>
<td>Disease irreversible changes</td>
<td>SLICC/ACR DI</td>
<td>SF-8</td>
<td>PCS</td>
</tr>
<tr>
<td></td>
<td>&lt;0.01</td>
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DISCUSSION

The PhGA showed stronger and higher correlation with disease activity and low QoL than those with score <10. Similarly, significant lower “Emotion health” and “Fatigue” (p<0.0001) were noted in those patients with HAD-anxiety score ≥10 compared to those <10 and they also had low score of “Burden to others” unlike those who are not anxious. (Table 1).

Conclusion: Depressive and anxiety symptoms in SLE patients and were associated with significantly poorer HRQoL.

Table 2. Correlation of PhGA with other SLE parameters

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Conclusion: Depressive and anxiety symptoms in SLE patients and were associated with significantly poorer HRQoL.
Burden to others 60.4±27.2 39.5 <0.0001 57.7±27.3 42±28.9 0.001
Emotion 70.8±21.2 37.9±22 <0.0001 66.6±24.2 40.1±20.3 <0.0001
Body image 69.8±25.7 48±27.6 <0.0001 67±26 45.7±28.6 0.001
Fatigue 67.9±22.4 40±22.4 <0.0001 64.4±24.3 41±21.7 <0.0001

Table 1. Dependence of indicators of the scales of the LupusQol on the presence of the skin and mucosal lesions (p < 0.05).

LupusQol No involved skin and mucosal lesions (N=181) Involved skin and mucosal lesions (N=147) P

Physical 68.0±23 65.3±23.5 0.2
health
Pain 66.2±26.7 62.6±21.8 0.2
Planning 72.1±26 67.2±24 0.07
Intimate 64.1±24 61.2±4.8 0.3
relationship
Burden to others 68.1±27.4 58.5±28.9 0.002
Emotion 78.4±29 65.9±32 0.001
Body image 59.5±29 52.9±26 0.03
Fatigue 71.7±24 57.4±29 <0.0001

Table 2. The dependence of the indicators of the questionnaire scales LupusQol from musculoskeletal symptoms (p < 0.05).

LupusQol No musculoskeletal symptoms (N=186) musculoskeletal symptoms (N=142) p

Physical health 69.6±23 62.8±22.6 0.008
Pain 67.2±28 68.2±22.6 0.1
Planning 74.5±24 64.3±23.7 0.001
Intimate 45.9±7.6 44±7.5 0.04
relationship

Disclosure of Interests: None declared

AB0569 THE EFFECT OF CUTANEOUS AND MUSCULOSKELETAL SYMPTOMS ON QUALITY OF LIFE IN PATIENT WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN RENAISSANCE COHORT
Lyubov Vorobyova, Elena Aseeva, Sergey Solovyev. V. A. Nasonova Research Institute of Rheumatology, Intensive care department, Moscow, Russian Federation

Background: Cutaneous and musculoskeletal symptoms is one of the most frequent complaints of patients with systemic lupus erythematosus (SLE) and has been found to occur in up to 70%-95% of patients during the course of the disease. For these reasons, SLE can affect different aspects of the patient’s life, leading to an impairment of HRQOL.

Objectives: The aim of the current study was to assess the effect of cutaneous and musculoskeletal symptoms on HRQol in a cohort of patients with systemic lupus erythematosus in Russian Federation (RENAISSANCE).

Methods: Consecutive patients who fulfilled SLICC 2012 criteria for SLE were recruited. Health-related quality of life (HRQol) was assessed by the validated specific questionnaires LupusQol-Russian. Disease activity was evaluated by the SLEDAI-2K, and chronic damage by the Systemic Lupus International Collaborating Clinics Damage Index score (SDI).

Results: 328 Russian SLE patients were enrolled in the study (M/F 30/298, mean age 34.4±11.5 years, mean disease duration 106.3±97.9 months; mean SLEDAI 2K 9.6±8.0; mean SDI 0.2±0.6. Musculoskeletal symptoms were observed in 142 patients, cutaneous and mucosal lesion symptoms -147 patients, respectively. When comparing HRQol in patients with lesions skin and mucosal revealed (Table 1) significant decline HRQol on the scales “Planning” (58.5 ± 28.9), “Intimate Relationships” (65.9 ± 32.1), “Burden to other” (52.9 ± 26) and “Body Image” (57.4 ± 29.1) of the LupusQol questionnaire compared with the patients without skin and mucosal lesions (p<0.002; p<0.001; p<0.03; p<0.0001 respectively).

When evaluating HRQol in patients with SLE and musculoskeletal symptoms were observed in 142 patients, cutaneous and mucosal lesion symptoms (N=186) and without (N=181). The dependence of the indicators of the questionnaire scales LupusQol from musculoskeletal symptoms (Table 2) reduction of almost all scales LupusQol.

Conclusion: Cutaneous and musculoskeletal symptoms on HRQOL.

Disclosure of Interests: None declared

AB0570 CLINICAL STUDY OF THE DISEASE ACTIVITY AND IMMUNE SCREENING OF PRIMARY SJOGREN’S SYNDROME
Yin Xufang, Zhang Mingxing, Ming Yan, Li Xiaofeng. The Second Hospital of Shanxi Medical University, Taiyuan, China

Objectives: To evaluate the change features of peripheral blood lymphocyte subsets and disease activity in patients with primary Sjogren’s syndrome before and after treatment.

Methods: A total of 30 patients with primary Sjogren’s syndrome in the Department of Rheumatology from the Second Hospital of Shanxi Medical University from January 2016 to December 2018 were enrolled. According to the treatment time of patients, they were divided into baseline group, 0-3 months group, 3-6 months group, and the absolute counts of T, B, NK, Th1, Th2, Th17 and regulatory T cells(Tregs) in peripheral blood of patients before and during the treatment were measured by flow cytometry. The ratio of various cells to Tregs was calculated as well.

The primary Sjogren’s syndrome disease activity was assessed according to the Sjogren’s syndrome disease activity index (ESSDAI) score and compared with 30 healthy people.

Results: The Tregs counts in the disease group were significantly lower than those in the healthy control group (p<0.05), and the ratio of pro-inflammatory lymphocytes to Tregs (Th17/Treg) was higher (p<0.05). Tregs counts in peripheral blood of patients with primary Sjogren’s syndrome has increased significantly after 3-month treatment at the same time, the inflammatory index ESR was significantly lower (p<0.05), the ESSDAI score was significantly lower (p<0.05), and the high remission rate was maintained. However there was no statistically significant increase in Treg cell growth before treatment at 3-6 months and 6-12 months, (p>0.05).

Conclusion: The imbalance between pro-inflammatory lymphocytes and Tregs caused by the significant decrease of Tregs may be the cause of primary Sjogren’s disease activity. We propose to promote the growth of Tregs and maintain the balance between pro-inflammatory lymphocytes and Tregs, which provides a new idea for disease relief of primary Sjogren’s syndrome.
BENEFICIAL EFFECTS OF VACCINATION ON REDUCING RISKS OF INFLUENZA INFECTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Jinquan Yu1, Dan dan Xu2, 1 Distinct HealthCare, Department of Rheumatology, Shenzhen, China; 2 Shenzhen Sixth People’s Hospital (Nanshan Hospital), Nephrology department, Shenzhen, China

Objectives: To investigate the influenza vaccine rate of SLE patients and the reasons for nonadherence to vaccination. To evaluate beneficial effects and safety of influenza vaccination.

Methods: A cross-sectional study was performed among patients with SLE regular follow-up in Distinct HealthCare between June 1 and November 31. Vaccination status and influenza infection condition were surveyed. Demographic information, clinical features and laboratory characters were collected and systemic lupus erythematosus disease activity index (SLE-DAl) was adopted.

Results: 109 SLE patients were recruited, including 42 immunized with trivalent or quadrivalent split virion influenza vaccine and 67 non-vaccinated. There were no significant differences in demographic and clinical characteristics (p>0.05). The influenza vaccination rate was 38.5%. Influenza infection rates in the vaccinated and non-vaccinated were 7.1% (3/42) and 23.9% (16/67), respectively, with a statistic difference (p<0.05). Reasons that non-vaccinated patients reported for nonadherence included refusal by the community health workers due to basic disease of SLE (32.3%), vaccine shortages (27.7%), concerns for potential side effects (23.1%) and insufficient patient education (16.9%). No systemic adverse reactions were observed and no significant increase of disease activity was found in vaccinated patients.

Conclusion: 1. Split virion influenza vaccine is effective in reducing risks of influenza infection in patients with SLE, and also safe.

2. Influenza vaccination is insufficient in SLE patients.

3. Educational intervention of the community health workers and patients is important to increase influenza vaccination rate.

REFERENCES


Disclosure of Interests: None declared.


AB0572 INVASIVE MYCOSES IN PATIENTS WITH CONNECTIVE TISSUE DISEASE FROM SOUTHERN CHINA: CLINICAL FEATURES AND ASSOCIATED FACTORS

Dongying Chen1, zhangngy zh angles2. 1 The first affiliated hospital of sun yat-sen university, rheumatology, Guangzhou, China; 2 The first affiliated hospital of sun yat-sen university, rheumatology, Guangzhou, China

Background: Invasive fungal disease (IFD) was well studied in patients with AIDS and organ transplant recipients. A few researches illustrated that patients with connective tissue disease (CTD) were also predisposed to IFD. However, few researches were designed to focus on invasive mycosis (IM) in patients with CTD.

Objectives: To investigate the clinical features and associated factors of IM in patients with CTD from Southern China.

Methods: A retrospective study CTD was performed. Demographic and clinical data were recorded. Associated factors were analyzed by logistic regression analysis.

Results: A total of 32 patients with CTD were included. The incidence of IM was 0.2% in patients with CTD (32/6911) and the highest in patients with ANCA-associated vasculitis (AAV) (7/480, 1.5%). Molds were isolated in 20 sputum specimens (20/29, 69.0%). Aspergillus spp. (81.3%) were the leading strain. Positivity of serum G-test and GM-test was 47.8% (11/23) and 34.6% (9/26), respectively. GM-test was positive in BALF from seven patients. Lung was commonly involved (30/32, 93.8%), Pulmonary nodules (46.7%) and cavitory lesions (36.7%) were common. Ten patients died (31.3%), including three with AAV (42.9%) and seven with SLE (36.8%). Multivariate logistic regression analysis showed that lymphopenia (odds ratio (OR) =3.28, 95% confidential interval (CI) 1.29-8.36, P=0.01) and median-to-high dose of glucocorticoid (GC) (OR=3.40, 95% CI 1.04-11.13, P=0.04) was associated with IM in patients with CTD. Patients with lymphopenia experienced higher risk of co-infection (50.0% vs 0%, P=0.01) and mortality (45.5% vs 0%, P=0.01) compared with patients with normal lymphocyte count.

Conclusion: IM tended to develop in patients with AAV, resulting in high mortality. Sputum culture could be an effective and non-invasive method to diagnose IM. Lymphopenia and median-to-high dose of GC are associated with IM in patients with CTD. Acknowledgment: no

Disclosure of Interests: None declared.


Vascular

AB0573 ASSESSMENT OF PRESENCE, SEVERITY AND RISK FACTORS OF POST-THROMBOTIC SYNDROME IN VASCULAR BEHÇET DISEASE: MUTCENTERED RETROSPECTIVE STUDY

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Background: DVT (deep venous thrombosis) is the most common form of vascular Behçet Disease (VBD). Post-thrombotic syndrome (PTS) developing after a thrombotic event in lower extremity is the most important complication of DVT and affects negatively patients’ quality of life.

Objectives: We aimed to assess presence, severity and risk factors of PTS and venous disease specific quality of life in VBD

Methods: This study included 96 BD patients (Female/Male:18:78, mean age: 38.8±8.74) with DVT from 3 tertiary Rheumatology centers in Turkey. When vascular involvement developed, mean age was 32.7±8.65 (female: 35.4±10.7; male: 32.09±8; p=0.04) Villalta scale is used to assess PTS and according to scale; PTS is present if score >4 and degree of PTS mild, moderate and severe if score 5-9, 10-14, >14 respectively. The Venous Disability Score(VDS) and the Venous Clinical Severity Score (VCSS) are used to assess the severity of PTS. Patients with trauma, major surgery or recanalization were excluded. PTS rate is 62% (60/96) and VDS score >4 is 47% (45/96).

Disclosure of Interests: None declared.

(VCSST) were used for the assessment of venous disease. Venous disease-specific QoL was measured through Venous Insufficiency Epidemiological and Economic Study Quality of Life/Symptom (VEINES-QoL/Sym) questionnaire. All patients were reanalyzed using color Doppler USG in the Radiology Department by a radiologist. In each patient, a total of 16 superficial and deep veins in both legs were assessed for the presence or absence of obstruction, recanalization, reflux, and collaterals within 1 week following the clinical examination.

Methods: During venous assessment, median disease duration was 9(0-34) years. Eighty(84.2%) patients were under immunosuppressive treatment and 13 of these patients were under anticoagulation treatment in addition to ISs. Duration between first vascular event and venous assessment was 6(1-26) years. PTS was present in 57(61.3%) out of 93 patients and severe PTS was present in 19(19.8%) patients. There was no association between the presence of PTS and sex, disease diagnosis age, and during DVT, presence of relaps. There was no difference among patients with or without PTS according to the anticoagulant usage (p=0.817). Doppler ultrasound examination showed bilateral at 31(31.4%) patients and both upper and lower involvement at 40(41.6%) patients. But, there is no statistically significant difference between the presence of PTS and Doppler findings. In addition to these, there is no statically significant association between PTS and presence of reflux obstruction at any vessel in the affected leg, but there is a correlation between severe PTS and reflux (r=-0.224, p=0.096). VCSS have positive correlation with the presence of reflux (p=0.041, r=0.224). VEINES-QoL/Sym, VCSS and BSAS are significantly worse in patients with PTS (Table 1).

Conclusion: In this study, we found that PTS in lower extremity develops in more than half of the patients with VBD during follow-up, and did not find any predictor factor for development of PTS. About one third of patients with PTS had severe PTS. PTS is an important clinical problem for physicians treating VBD in daily practice. It should be taken into account as much as preventing vascular relapses during follow-up of patients with VBD.

Table 1. Clinical and characteristic features of PTS


### A MONOGENIC DISEASE WITH WIDE RANGE OF SYMPTOMS: DEFICIENCY OF ADENOSINE DEAMINASE 2

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**Background:** Deficiency of adenosine deaminase 2 (DADA2) is an autosomal recessive autoinflammatory disorder caused by ADA2 mutations.

**Objectives:** We aimed to investigate the characteristics of DADA2 patients along with the ADA2 enzyme levels.

**Methods:** 24 DADA2 patients who admitted to the Adult and Pediatric Rheumatology, Pediatric Haematology, and Pediatric Immunology Departments were included. All exons of the ADA2 gene were screened by Sanger sequencing in all DADA2 patients. Serum ADA2 enzyme activity was measured by modified spectrophotometric method.

**Results:** 24 DADA2 patients were included; Group 1, 14 DADA2 patients with polycythemia vera (PV)-like phenotype; Group 2, 9 patients with Diamond-Blackfan anemia (DBA)-like features and one with immune deficiency. 14 PV-like DADA2 patients did not have the typical thrombocytosis seen in classical PV. Inflammatory attacks were evident in only Group 1 patients. Serum ADA2 was low in all DADA2 patients except one who was tested after hematopoietic stem cell transplantation. There was no significant difference in ADA2 levels between PV-like and DBA-like DADA2 patients (Figure 1). ADA2 activities of homozygote family members were about half the level of the control subjects. However, in heterozygote DADA2 patients, serum ADA2 levels were as low as one-third of homozygote DADA2 patients. ADA2 mutations were affecting the dimerization domain in Group 1 patients and in the catalytic domain in Group 2 patients (Table 1).

**Conclusion:** We suggest that enzyme activity of ADA2 should be aimed along with genetic analysis since there are heterozygote patients with absent enzyme activity. Our data confirms a possible genotype-phenotype correlation where dimerization domain mutations are associated with a PAN-like phenotype whereas catalytic domain mutations are associated with hematological manifestations.

**Table 1. Molecular results of ADA2 gene analyses in DADA2 patients (D, dimerization; C, catalytic)**

<table>
<thead>
<tr>
<th>Gene number</th>
<th>Patient number</th>
<th>Mutation position</th>
<th>Mutation type</th>
<th>The affected domain of ADA2 protein</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>Exon 2: c.1395G&gt;A</td>
<td>Homozygous missense</td>
<td>D</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td>Exon 2: c.1395G&gt;A</td>
<td>Homozygous missense</td>
<td>D</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>Exon 4: c.660G&gt;C</td>
<td>Compound heterozygous missense</td>
<td>C</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>Exon 4: c.659G&gt;C</td>
<td>Compound heterozygous missense</td>
<td>D</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td>Exon 4: c.916C&gt;T</td>
<td>Compound heterozygous missense</td>
<td>C</td>
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<tr>
<td>2</td>
<td>1</td>
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<td>C</td>
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<tr>
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<td>Compound heterozygous missense</td>
<td>D</td>
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<tr>
<td>1</td>
<td>1</td>
<td>Exon 10: c.1445G&gt;A</td>
<td>Homozygous missense</td>
<td>C</td>
</tr>
</tbody>
</table>

**Figure 1**

**REFERENCES**


**Acknowledgement:** This study was supported by Scientific and Technological Research Council of Turkey (TÜBİTAK) with grant numbers of 1155192. Prof. Nurten Akarsu performed the molecular studies of DBA patients and special thanks to her for great support.

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THE EFFECT OF METABOLIC SYNDROME ON CARDIOVASCULAR DISEASE AND CUMULATIVE ORGAN DAMAGE IN TAKAYASU'S ARTERITIS

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Background: As a result of arterial ischemia, the frequencies of hypertension (HT), ischemic heart disease, congestive heart failure and atherosclerosis have been shown to increase and contribute to mortality in patients with Takayasu's arteritis (TAK). Determining cardiovascular disease (CVD) and associated risk factors in TAK is important for a comprehensive treatment approach and better disease prognosis. Data about the effect of metabolic syndrome (MetS) which is known as a risk factor for CVD on TAK are limited.

Objectives: The aim of this study was to determine the prevalence of MetS in patients with TAK and its effect on CVD and cumulative organ damage.

Methods: A total of 122 TAK patients, followed by Turkish Takayasu Study Group in 7 tertiary Centers and diagnosed according to the 1990 ACR criteria were consecutively assessed for cumulative organ damage (VDI score), history of CVD and MetS as defined by the National Cholesterol Educational Program Adult Treatment Panel III (NCEP ATP III). CVD was defined as coronary artery disease or cerebrovascular event (myocardial infarction or stroke).

Results: Eighty-seven percent of patients were female and the median age was 39 (17-65) years. The frequency of MetS was 14.7% and CVD was 13.1%. The median age, disease duration, smoking prevalence and CVD were found slightly higher in MetS group, without reaching statistical significance. There were no differences in VDI score between the groups (Table 1).

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AB0576 SERUM CATHELICIDIN (LL 37) LEVELS IN PATIENTS WITH BEHÇET’S DISEASE AND ITS ASSOCIATION WITH DISEASE ACTIVITY

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Background: Behcet’s disease (BD) is a recurrent multisystem inflammatory disease which is characterized by recurrent episodes of oral aphthous and genital ulcers, ocular inflammation and skin lesions. Anti-microbial peptides (AMPs) such as the cathelicidin (LL-37) and defensins have recently been implicated in the pathogenesis of autoinimmune and autoinflammatory diseases.

Objectives: The aim of this study was to investigate the serum levels of cathelicidin and its potential association with disease activity, and some other laboratory parameters such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), white blood cell count (WBC) in patients with BD.

Methods: A total of 45 patients who presented to Dicle University Rheumatology clinics between September 2018 and December 2018 and met the International Study Group Classification Criteria for BD and 37 healthy control subjects who presented to Dicle University Physical Medicine and Rehabilitation clinics for various reasons other than rheumatoid complaints between the same dates were included in this study. Patients’ demographic features, including age and sex, were noted. Duration of disease was also noted, and the disease activity was assessed by means of BD Current Activity Form (BCAF). Laboratory investigations included erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), complete blood count and routine biochemical analyses. Serum levels of cathelicidin (LL 37) were determined by means of human cathelicidin antimicrobial peptide ELISA Kit according to the manufacturer’s protocol.

Results: Serum mean level of cathelicidin (LL 37) in patients with BD was lower than healthy controls but this result was not statistically significant. Cathelicidin levels were not correlated with ESR, CRP, BCAF and WBC (p>0.05).

Conclusion: However serum mean levels of cathelicidin (LL 37) were lower in patients with BD compared to healthy controls, this result was not statistically significant. It may be sourced from our relatively small sample size. To validate cathelicidin (LL 37) value as a prognostic or pathophysiological biomarker, future studies should investigate the levels of cathelicidin LL37 in patients with BD in large cohorts of patients with different levels of disease activity, remission, and relapse.

REFERENCE


Disclosure of Interests: None declared

TOCILIZUMAB IN GIANT CELL ARTERITIS. ROUTE OF ADMINISTRATION: INTRAVENOUS OR SUBCUTANEOUS


Background: Recently, based on the GIACTA trial results, weekly subcutaneous Tocilizumab (TCZ) has been approved for the treatment of Giant Cell Arteritis (GCA). It has showed to be effective and safe.

The aim of this study was to compare the efficacy of TCZ according the route of administration.

Methods: Multicenter study of 134 GCA patients in treatment with TCZ. It was performed a comparative study between 2 groups according the route of administration of TCZ, intravenous (IV) or subcutaneous (SC).

Results: We study 134 patients divided in 2 groups: a) IV TCZ, 104 cases and; b) SC TCZ, 30 cases, with a mean age 73.4±8.2 years vs 71.9±10.6 years, respectively (p=0.501). Disease duration, clinical manifestations and acute phase reactants at TCZ onset were similar in both groups with non-statistical difference. 91.7% patients who received SC TCZ achieved prolonged remission after 12 months of treatment (p<0.043). And the glucocorticoid sparing effect of TCZ was greater in SC groups with non-statistical difference. 91.7% patients who received SC TCZ reached prolonged remission after 12 months of treatment and were able to discontinue prednisone dose after 24 months of follow up. The incidence of adverse events was more frequent in the IV TCZ group, without difference in relation to infections.

Objectives: Our aim was to compare the efficacy of TCZ according the route of administration.

Conclusion: Patients in treatment with SC TCZ, reached prolonged remission after 12 months of treatment and were able to discontinue prednisone dose after 24 months of follow up. The incidence of adverse events was more frequent in the IV TCZ group, without difference in relation to infections.

REFERENCES


Objectives: To describe the characteristics and differences between patients with primary LVV and LVV associated with GCA in a single center.

Methods: Retrospective study of patients with LVV in a University Hospital (January 2013-December 2018). Patients diagnosed with aortitis using an imaging test (PET-CT/angiogram/CT/MRI) were included. GCA was diagnosed by biopsy and/or ultrasound of the temporal artery. The primary LVV was considered by exclusion of inflammatory or infectious causes. Epidemiological, clinical and analytical variables, affected vascular territories and the treatment received in both groups were reviewed.

Frequencies and percentages were used in qualitative variables, mean ±SD in quantitative and for the comparison between groups Chi2 test or Fishers test was used in categorical variables and Student T test or U of Mann-Whitney in quantitative. The statistical analysis was performed with IBM SPSS v.23.

Epidemiological, clinical and analytical variables, affected vascular territories in both groups were reviewed. LVV was considered by exclusion of inflammatory or infectious causes. The final clinical evolution was similar and favorable in both groups. At last visit, after a mean follow-up of 11.94±8.5 months in the primary LVV and 13.44±6mg/week and TCZ (n=2). In LVV associated with GCA, 2 patients were without treatment; CS (n=9), mean dose 4.75±4mg; MTX (n=6), mean dose 3.44±5mg/week and TCZ (n=2). 15 imaging tests were performed 6-10 months after diagnosis. Later, after an average time of 28.7±10.7 months 9 more control PET-CT were requested. TABLE 2.

Conclusion: In this study, younger age at onset and inflammatory low back pain were more frequent in primary LVV with statistical significance. The most affected vascular territory was the thoracic aorta in both groups.

The clinical and analytical evolution was similar in both populations. In the treatment, the only notable thing was the increased use of MTX in the LVV associated with GCA.

68% of the aortitis were diagnosed in the last 3 years due to greater clinical suspicion. PET-CT is a useful tool in the diagnosis of this pathology.

Disclosure of Interests: None declared


AB0579

COMPARISON OF CLINICAL CHARACTERISTICS OF EOSINOPHILIC GRANULOMATOSIS WITH POLYANGIITIS BETWEEN RHEUMATOLOGY AND RESPIRATORY MEDICINE: A SINGLE CENTER, RETROSPECTIVE STUDY

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Background: Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare but potentially life-threatening systemic necrotizing vasculitis. Multiple organs may be involved and patients initial consulting different departments may have different clinical manifestations.

Objectives: To explore the clinical characteristic of EGPA diagnosed in different departments in our hospital.

Methods: A retrospective study of EGPA patients in Sun Yat-Sen Memorial Hospital, Sun Yat-Sen University, Department of Rheumatology, Guangzhou, China.

Results: We included 45 EGPA patients diagnosed between December 2003 and January 2019. There were 29(64.4%) male, with median onset age 46(36~56) years, median time required for diagnosis 24(3~96) months. There were 8(17.8%) patients had history of drug allergy. There were 41(91.1%) patients fulfill the ACR 1990 classification criteria and 40 (88.9%) fulfill the EULAR/ACR 2017 draft classification criteria. Demographic and clinical data of EGPA patients were collected and compared between different departments.

Results: 1) There were 45 EGPA patients diagnosed between December 2003 and January 2019. There were 29(64.4%) male, with median onset age 46(36~56) years, median time required for diagnosis 24(3~96) months. There were 8(17.8%) patients had history of drug allergy. There were 31(68.9%) patients fulfill the ACR 1990 classification criteria or the EULAR/ACR 2017 draft classification criteria. Demographic and clinical data of EGPA patients were collected and compared between different departments.

Results: 2) The main clinical manifestations included asthma-like symptoms (82.2%), limb numbness (37.8%), rash (22.2%), fever (20.0%), gastrointestinal symptom (11.1%) and arthralgias (8.9%). There were 91.1% (41/45) patients had serum eosinophil >10%, 77.8% (35/45) serum eosinophil x10^9/L, 77.5% (34/45) elevated serum IgE, 7.8% (3/44) positive MPO-ANCA or p-ANCA and 18.4% (7/38) positive ANA.

Results: 3) There were 21(46.7%) patients diagnosed at rheumatology, 22(48.9%) at respiratory medicine, 1(2.2%) at dermatology and 1(2.2%) at pediatrics.
Compared with patients diagnosed at respiratory medicine, patients diagnosed at rheumatology had a higher frequency of fever (33.3% vs. 0), rash (33.3% vs. 4.5%), arthralgias (19.0% vs. 0) and limb numbness (57.1% vs. 22.7%), but lower frequency of asthma-like symptoms (66.7% vs. 100%; p<0.05). There were more patients diagnosed at rheumatology received treatment of glucocorticoid (100% vs. 72.7%), immunosuppressive agents (85.7% vs. 4.5%) and intravenous immunoglobulin (28.6% vs. 0) than those diagnosed at respiratory medicine (all p<0.01). Patients diagnosed at rheumatology also received higher initial dose of glucocorticoid than those diagnosed at respiratory medicine [50 (50-100) mg/d vs. 28 (10-40) mg/d of prednisone dosage, P<0.001].

4) Among the 21 patients diagnosed at rheumatology, 14(66.7%) had asthma-like symptoms, who showed significantly longer time required for diagnosis than those without asthma-like symptoms [36(24-120) months vs. 2(2-13) months, P=0.020], but showed no significant difference of onset age between these two groups (P=0.05). 5) The median revisited Five-Factor Score (FFS) was 0(0-1). There were 1(17.6%) patients who had older diagnostic age than those with FFS=0 [65(46-68) years vs. 48(42-53) years, P=0.05], but with no significant difference of onset age or time required for diagnosis. Patients with FFS>1 had higher level of serum IgE [1280(515-4895) IU/mL vs. 241(73-379) IU/mL, P=0.05]; those with FFS<1 had lower mortality rate than those with FFS=0 [65(46-68) years vs. 48(42-53) years, P<0.05].

Conclusion: Clinical manifestations of EGPA were different between rheumatology and respiratory medicine. Rheumatologist may be more aggressive treating EGPA patients with glucocorticoid and immunosuppressive agents than respiratory physician. Multidisciplinary team is needed for the diagnosis and management of EGPA.

Acknowledgement: This work was supported by Guangdong Medical Scientific Research Foundation (grant no. A2017093) to Le-Feng Chen.

Disclosure of Interests: None declared


AB0581 AN ATYPICAL PRESENTATION OF GIANT CELL ARTERITIS WITH SCALP LUMPS: A CASE REPORT

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Background: Giant cell arteritis (GCA) also referred as temporal arteritis is a systemic inflammatory vasculitis of unknown etiology which can result in wide range of systemic, neurologic and ophthalmic complications. It predominantly occurs in older people and may be associated with Polymyalgia Rheumatica. It must be treated urgently as it is associated with significant risk of permanent visual loss, stroke, aneurysm and possible death. Diagnosis of GCA can be based on clinical findings such as headache, scalp tenderness, jaw claudication and temporal artery problems, an elevated ESR and biopsy temporal artery showing typical histopathological findings. Diagnosis of GCA may be delayed when presentation is atypical.

Objectives: We report a case of an elderly lady presenting with scalp lump as an unusual presentation of GCA.

Methods: 70 years old lady presented with multiple painful scalp lumps to the surgeon was referred to the Rheumatologist when the excision biopsy of the lump diagnosed the GCA. (Sub cutis medium sized artery with severe arteritis composed with lymphocytes, neutrophils and occasional Eosinophils). On enquiry she revealed a history of generalized malaise and lethargy at the onset of the illness preceded by jaw pain.

On examination she had bilateral hardened thickened palpable non pulsatile temporal arteries. Her scalp was tender with multiple small cystic lumps. Her ESR was highly elevated 141mm/hr. WBC 9.7, Hb 9.5 and PLT 283. Her ANA, liver and renal profiles were normal. Her BL Doppler USS was consistent with BL temporal arteritis.

Results: She was soon started on high dose prednisolone with low dose aspirin which improved her systemic symptoms along with inflammatory markers significantly over a few days. She was referred for eye assessment and the involvement of other systemic large arteries was ruled out.

Conclusion: Most of the cases the diagnosis of GCA is obvious but in patients with uncommon clinical presentation the diagnosis may be difficult. GCA is classified as disease of large vessel vasculitis but typically also involves medium and small arteries. The granulomatous inflammation in the vessel wall leads to obstruction of the lumen and ischemia in the territory distal to it. GCA involves almost all speciality and it is associated with increased mobility and mortality if not diagnosed and treated early. Awareness of rare presentation of GCA avoids unnecessary investigation and delaying the treatment. If there is no rapid improvement of symptoms within few weeks of starting treatment other diagnosis should be considered.
In our cohort there were 2 pts with serious infections: 1 with oropharyngeal and esophageal candidiasis and another with bacteraemia to Pseudomonas aeruginosa. Both pts were under immunosuppressive agents including corticosteroids and rituximab or cyclophosphamide.

Conclusion: Neurologic involvement was part of disease presentation in most pts and the commonest manifestation was mononeuritis multiplex. PDN was prescribed to all pts, in most cases in association with other immunosuppressive drugs. Cyclophosphamide and rituximab (RTX) were used as induction treatment, and mycophenolate mofetil, azathioprine and RTX as maintenance. Intra venous human immunoglobulin was used in pts colonized by multiresistant microorganisms/severe infection with immunosuppression and as a bridging therapy to further immunosuppression. Most pts achieved clinical improvement, documented in electromyography.

REFERENCES


Disclosure of Interests: None declared

AB0582
NEUROLOGIC INVOLVEMENT IN ANTINEUTROPHIL CYTOPLASMIC ANTIBODY (ANCA)-ASSOCIATED VASCUITIS – EXPERIENCE FROM A PORTUGUESE CENTER

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Background: Involvement of peripheral (PNS) and central nervous system (CNS) in antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis has been reported in 15-60% and 5-15% of patients (pts), respectively. PNS involvement occurs mainly in eosinophilic granulomatosis with polyangiitis (EGPA) and CNS involvement has been almost exclusively described in granulomatosis with polyangiitis (GPA). Neurologic involvement is associated with a higher morbidity and implies more immunosuppressive treatment in most pts.

Objectives: Evaluate prevalence and clinical features of PNS/CNS involvement in pts with ANCA-vasculitis in a Portuguese center.

Methods: Retrospective analysis of ANCA-vasculitis pts with neurologic involvement followed in our department from January 2016 to December 2018. Data was collected from the Portuguese database REUMA.PT and included demographic data, vasculitis subtype, date of diagnosis, neurologic manifestations and treatment approach.

Results: In total, 11 pts were identified, mostly female (7/11) with mean age of 61±3.3 years (yrs). Five pts had EGPA, 5 GPA and 1 microscopic polyangiitis (MPA). Neurologic involvement was part of disease presentation in 8 pts (5 GPA, 3 EGPA). The other 3 pts had neurologic involvement 7±2.2 yrs after vasculitis diagnosis. At the time of neurologic involvement diagnosis, Birmingham Vasculitis Activity Score was 8±4.3. PNS involvement occurred in 9 pts, all presenting mononeuritis multiplex (MM). From these, 5 had EGPA, 3 GPA and 1 MPA. CNS involvement was reported in 3 pts, 2 with GPA and 1 with EGPA. Pachymeningitis was diagnosed in 1 GPA pt with persistent headache, refractory to analgesics, and thickening and enhancement of the dura mater on postcontrast magnetic resonance imaging. Two pts had cranial mononeuropathy, 1 with EGPA and MM who developed VI palsy 2 yrs after vasculitis diagnosis and 1 pt with GPA and VII palsy at disease presentation who developed XII palsy 8 yrs later. All pts were treated with prednisolone (1mg/kg/day), mostly in combination with other immunosuppressive drugs. The choice of the treatment was based on the age of the pt and other comorbidities. Detailed treatment of these pts and subsequent responses are shown in table 1.

Table 1: Results of pts with neurologic involvement in relation to ANCA-vasculitis

<table>
<thead>
<tr>
<th>ANCA-vasculitis</th>
<th>Neurologic Involvement</th>
<th>Treatment</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>EGPA</td>
<td>5 pts</td>
<td>Prednisolone, rituximab</td>
<td>Complete resolution</td>
</tr>
<tr>
<td>GPA</td>
<td>3 pts</td>
<td>Prednisolone, rituximab</td>
<td>Partial resolution</td>
</tr>
<tr>
<td>MPA</td>
<td>1 pt</td>
<td>Prednisolone, cyclophosphamide</td>
<td>No change</td>
</tr>
</tbody>
</table>

Conclusion: In ANCA-vasculitis pts, neurologic manifestation is common and associated with higher morbidity. Most pts achieved clinical improvement, documented in electromyography. The majority of our referrals to a tertiary care centre had non-specific symptoms, quality of referral and potential for visual loss can lead to over-diagnosis. We have found the majority of our referrals to have been appropriate and complete with 85% meeting ACR criteria for GCA and 92% having up to date inflammatory markers. Despite this, 31% of patients received an alternative diagnosis. Increasing the availability of

References:


Disclosure of Interests: None declared

AB0583
100 GCA REFERRALS TO A TERTIARY CARE CENTRE: INFLAMMATION, HEADACHES AND CPAP MASKS

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Background: Giant cell arteritis (GCA) is a large vessel vasculitis typically affecting patients above the age of 50 years. It is the most common cause of vasculitis affecting adults with a UK prevalence of approximately 0.25% of the population above the age of 55 years [1]. Whilst its clinical presentation can often be non-specific, if left undiagnosed it can lead to devastating visual impairment. However, this has to be balanced with the potential for corticosteroid related adverse effects. The threshold for suspected diagnosis and referral to rheumatology centres from the community and acute medical services is therefore low, leading to a relatively high number of referrals with a wide range of clinical features and potential differential diagnoses.

Objectives: To assess the referral characteristics, demographics, management, corticosteroid adverse effects and differential diagnosis of 100 consecutive patients referred with suspected GCA to a tertiary rheumatology centre.

Methods: The notes of 100 consecutive patients referred to the rheumatology department at Addenbrookes hospital between August 2016 and January 2018 with suspected GCA were reviewed. Information on patient demographics, comorbidities, presenting symptoms, availability of up to date inflammatory markers, dates of treatment and clinic review, temporal artery biopsy (TAB) date and result, diagnosis and corticosteroid adverse effects were retrieved.

Results: Seventy three female and twenty seven male patients (average age 72.3 years) were referred within the time period. General practice referred 69% of the cases and common comorbidities included hypertension and type II diabetes. The most common symptoms were headache (97%), scalp tenderness (79%), jaw claudication (35%) and polymyalgia symptoms (34%). Up to date inflammatory markers were available for 91% of referrals and 92% were commenced on corticosteroids before or at the time of referral with an average starting dose of 43.9mg oral prednisolone. A TAB was performed on 85% of patients, with an average time of 9 days between referral and TAB and 40 days between referral and clinic appointment. TAB was positive for GCA in 13/85 patients. Temporal artery ultrasound (TAU) was not available at our centre. The American College of Rheumatology (ACR) classification criteria for GCA were met by 85% of the patients, but only 69% were given a diagnosis of GCA. Other diagnoses included trigeminal neuralgia, temporomandibular dysfunction, toothache and a poorly fitted CPAP mask. Corticosteroid adverse effects were experienced by 45% of patients including weight gain, poorly controlled diabetes, mood and sleep disturbance, and 4% suffered severe complications requiring hospital admission (pneumonia, disseminated nocardia infection and two episodes of upper gastrointestinal bleed).

Conclusion: Suspected GCA is a common referral to rheumatology but the non-specific symptoms, quality of referral and potential for visual loss can lead to over-diagnosis. In our cohort there were 2 pts with serious infections: 1 with oropharyngeal and esophageal candidiasis and another with bacteraemia to Pseudomonas aeruginosa. Both pts were under immunosuppressive agents including corticosteroids and rituximab or cyclophosphamide.
TAU may improve the time to diagnosis and therefore potentially reduce unnecessary exposure to corticosteroids. Our experience highlights the fact that despite a good standard of referral, GCA remains a difficult condition to diagnose and poses an on-going challenge to the rheumatologist.

REFERENCES


Disclosure of Interests: Jobie Evans Grant/research support from: I am currently working on a MD research project looking at the use of magnetic resonance enterography imaging as a screening tool for axial spondyloarthitis in patients with Crohni’s disease. This study is commercially funded by Merck, Sharp and Dohme corporation (MSD), Natasha Jordan: None declared DOI: 10.1136/annrheumdis-2019-eular.5767

AB0584

JOINT PROFILE OF BEHÇET’S DISEASE

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Background: Joint manifestations during Behçet’s disease (BD) are frequent and polymorphic.

Objectives: To analyze these manifestations through 41 cases.

Methods: A retrospective study of 41 patients, collected at the rheumatology department of Farhat Hached University Hospital over a period of 19 years, meeting the criteria of the international study group on BD.

Results: 41 patients with a mean age of 40.21 years (16-66) were collected. The sex ratio=2.41. The articular and mucocutaneous involvement were constant. Also were found ocular manifestations (5cases), neurological (1case), cardiac (1case), gastro-intestinal (1case), venous thrombosis (5 cases), arterial thrombosis (1 case) and an aereumus (2 cases). Joint involvement was revealing in 21 cases (51.2%) occurring during evolution in 20 cases with an average delay of 102 months [6-360]. The most frequent manifestations were arthralgia in 24 cases (58.5%) and arthritis in 17 cases. It was predominantly asymmetric (21 cases), mono articular (13 cases), oligoarticular (16 cases) and polyarticular (12 cases). The knees and ankles were the most affected joints in 32 cases and 25 cases respectively, followed by wrist involvement (12 cases), MCP (5 cases) and elbows and shoulders in 4 cases each. A knee flessum was found in 2 cases. X-rays were mostly normal (35 cases). They showed erosive involvement (1case), joint narrowing (1case), osteonecrosis (2cases) and sacroiliitis (2cases).

Conclusion: Joint manifestations during the BD can be inaugural and take on several clinical aspects. They usually heal without sequelae and do not engage functional prognosis with the exception of rare cases of destructive arthritis.


AB0585

REJIA-VASCA: JAVERIAN REGISTRY OF PATIENTS WITH POSITIVE ANCA VASCULITIS AT THE UNIVERSITY HOSPITAL SAN IGNACIO 2005–2017

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Background: Vasculitis associated with cytoplasmic antibodies (VAAc) are heterogeneous entities with low prevalence and high morbidity and mortality. These include granulomatosis with polgagglutin (GPA), microscopic polgagglutin (PAM), and eosinophilic granulomatosis with polgagglutin (GEP). European retrospective reviews report an annual incidence of 10-20 cases per million, with peak presentation between 65-74 years, predominantly in males. It has diverse clinical manifestations in multiple systems. In Colombia, there are few clinical records that describe the clinical characteristics of these patients.

Objectives: To describe the clinical characteristics of patients with VAAc in the University Hospital San Ignacio between 2005-2017

Methods: Descriptive cross-sectional study. Patient records were reviewed between January 2005 and December 2017. The records were obtained using search systems in patients who were requested Anti-neutrophil cytoplasmic antibodies - ANCA (Searching software: DISEARCH, LABCORE), obtaining 2072 results. 106 patients met the criteria for classification of the American College of Rheumatology for VAAc.

Results: 106 patients diagnosed with ANCA positive vasculitis. Average age 55 years (± 14.7). 48.4% were women. In-hospital debut in 68.8%. The average number of days of stay was 16.6 days (± 12.22), 56 patients (52.8%) had granulomatosis with polgagglutin (GPA), 45 patients (42.4%) with microscopic polgagglutin (MAP) and 5 patients with eosinophilic granulomatosis with polgagglutin (EGP) (4.8%). 37 patients (35%) presented with alveolar hemorrhage, 22 patients (20.7%) presented renal compromise with rapidly progressive glomerulonephritis. Central nervous system compromise was documented in 25 patients (24%). Regarding the vascular territory, 60 patients (56.6%) received treatment with cyclophosphamide. Plasma exchange therapy was performed in 15 patients (14.1%). 44 patients (41.5%) required renal replacement therapy. The in-hospital mortality of this group of patients was 20.4%, with sepsis being the most frequent cause of death (55%).

Conclusion: In this study, the most frequent positive ANCA vasculitis was granulomatosis with polgagglutin. Multisystemic compromise was present in all groups of patients, the most common being pulmonary and renal, mainly in patients with microscopic polgagglutin, similar to that reported by Solans-Laquè et al in Spain. Within the demographic characteristics, the average age at the time of diagnosis is around 50 years, predominantly in women related to the Mexican study by Hinojosa-Azuala et al. The most frequent cause of in-hospital mortality was sepsis. Clinical information of patients with VAAc is presented in a reference hospital in Colombia. Data are concordant with literature.


AB0586

TAKAYASU ARTERITIS: REVIEW OF DIAGNOSTIC AND CLASSIFICATION CRITERIA IN A 9 CASE SERIES

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Background: Takayasu arteritis (TA) is a rare large vessel vasculitis that affects the aorta (Ao) and its main branches. Early diagnosis and the rapid establishment of treatment are key points in the prognosis of the disease. Despite the existence of different classification and diagnostic criteria, early diagnosis of TA continues to be a challenge.

Objectives: 1) To analyze the concordance between the different classification and diagnostic criteria in patients with TA. 2) To describe the demographic, clinical and analytical characteristics of TA.

Methods: Retrospective observational study that included all patients diagnosed with TA according to medical criteria between 1981 and 2018, who were treated at the University Hospital San Ignacio in Madrid.

Results: We included 9 patients (77.8% women) diagnosed with TA. The age at diagnosis was 33 ±16.3 years with a time of evolution of 5.1 ±4.4 years. The other variables are shown in Table 1.

<table>
<thead>
<tr>
<th>Variables</th>
<th>CRP, mg/l, mean (SD)</th>
<th>ESR, mm/h, mean (SD)</th>
<th>HRA, n (%)</th>
<th>BP difference &gt;10 mmHg, n (%)</th>
<th>Vascular pain, n (%)</th>
<th>Constitutional criteria, n (%)</th>
<th>Atheromatosis, n (%)</th>
<th>Catelana, n (%)</th>
<th>Syncope, n (%)</th>
<th>Decreased arterial pulse, n (%)</th>
<th>Paresthesia, n (%)</th>
<th>Bruit, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>42.8 (65.37)</td>
<td>33.3 (35.3)</td>
<td>4 (44.4)</td>
<td>4 (44.4)</td>
<td>4 (44.4)</td>
<td>4 (44.4)</td>
<td>3 (33.3)</td>
<td>1 (11.1)</td>
<td>2 (22.2)</td>
<td>1 (11.1)</td>
<td>2 (22.2)</td>
<td>4 (44.4)</td>
</tr>
</tbody>
</table>
The most frequent vascular territories affected were abdominal Ao (7), descending thoracic Ao (5) and iliac arteries (5). The most common type of arterial lesion was stenosis (8) followed by dilation and aneurysm. 6 patients were treated with corticotherapy as an induction treatment, 5 required chronic immunosuppression and 6 patients required surgery. When reviewing the criteria we observed that all patients met the ACR criteria and 7 patients met the modified criteria by Sharma. However, the agreement with Ishikawa’s diagnostic criteria was poor since 7 patients did not meet them. The different criteria are shown in Table 2.

<table>
<thead>
<tr>
<th>Ishikawa, n (%)</th>
<th>1990 ACR, n (%)</th>
<th>Modified Ishikawa, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age ≤40 yrs</td>
<td>7 (77,8)</td>
<td>7 (77,8)</td>
</tr>
<tr>
<td>Left subclavian lesion</td>
<td>4 (44,4)</td>
<td>Left subclavian lesion</td>
</tr>
<tr>
<td>Right subclavian lesion</td>
<td>3 (33,3)</td>
<td>Right subclavian lesion</td>
</tr>
<tr>
<td>VSG &gt;20 mm/h</td>
<td>6 (66,6)</td>
<td>VSG &gt;30 mm/h</td>
</tr>
<tr>
<td>Carotid artery tenderness</td>
<td>0</td>
<td>Carotid artery tenderness</td>
</tr>
<tr>
<td>HTA</td>
<td>4 (44,4)</td>
<td>HTA</td>
</tr>
<tr>
<td>Aortic regurgitation</td>
<td>3 (37,5)</td>
<td>Aortic regurgitation</td>
</tr>
<tr>
<td>Pulmonary artery lesion</td>
<td>0</td>
<td>Pulmonary artery lesion</td>
</tr>
<tr>
<td>Common</td>
<td>2 (22,2)</td>
<td>Common artery lesion</td>
</tr>
<tr>
<td>Distal</td>
<td>2 (22,2)</td>
<td>Distal brachiocephalic artery lesion</td>
</tr>
<tr>
<td>Descending</td>
<td>5 (55,6)</td>
<td>Descending thoracic Ao lesion</td>
</tr>
<tr>
<td>Abdominal Ao lesion</td>
<td>7 (77,8)</td>
<td>Abdominal Ao lesion</td>
</tr>
<tr>
<td>Coronary artery lesion</td>
<td>2 (33,3)</td>
<td>Coronary artery lesion</td>
</tr>
</tbody>
</table>

Conclusion:
- The most frequently affected vascular territory was the abdominal Ao, and the most common type of injury was stenosis.
- The most common clinical presentation was asymmetry of blood pressure between extremities and peripheral pulses, HTA and limb claudication.
- All patients met the ACR 1990 classification criteria and the great majority met the criteria modified by Sharma. The concordance with Ishikawa’s criteria was poor so they should be used cautiously.

Disclosure of Interests: Andrea Garcia-Guillen: None declared, Patricia Moya: None declared, Antonio José Barros-Membrilla: None declared, Jaime Félix Gilme: None declared, José Montiel: None declared, José Alberto Hidalgo: None declared, Albert Fitlats: None declared, Alejandro Fernandez: None declared, Josep Maria Llibert: None declared, Berta Magallares: None declared, Ana Lai Consultant for: Lilly, Novartis, AbbVie, MSD, UCB and Janssen, Speakers bureau: Lilly, Novartis, Abvivie, MSD, UCB and Janssen, Ivan Castellví Consultant for: I received fees less than 20000USD as a consultant for Boehringer Ingelheim, Novartis and Gebro, Speakers bureau: ND, Hector Corominas: None declared


AB0588 GASTROINTESTINAL INVOLVEMENT OF BEHCET’S DISEASE IN RUSSIA

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Background: Behcet’s disease (BD) is a multisystem vasculitis with unknown etiology and a unique geographical distribution. Intestinal manifestations of BD (IBD) are of particular importance as they are associated with significant morbidity and mortality. Although ileocecal involvement is more commonly described, BD may involve any segment of the intestinal tract as well as the various organs within the gastrointestinal system.

Objectives: To analyze the severity and clinical features IBD in Russia

Methods: The study included 250 patients (male – 177, female – 73) with BD (according to ISGDB 1990 and ICBD criteria 2014). The male-to-female ratio was 2.41; the mean age was 31.5±9.3 yrs, the age of disease onset - 21.81±9.2 yrs, the median of disease duration - 10.25 ±8.32 yrs. All those with gastrointestinal symptoms were subject to a gastroscopy and/or colonoscopy through which Crohn’s disease and ulcerative colitis were excluded by the proteologists.

Results: Patients with gastrointestinal symptoms were 63 of 250 - 25.2% pts, (male – 40, female – 23). Symptoms of IBD include the abdominal pain in 62% pts, distension -55%, diarrhea – 14%, nausea –13%, blood in the bowel movement – 4.7%, the examination revealed: esophageal ulcers (1.6%, four cases), gastric ulcers (3.2%, eight cases), and duodenal ulcers (1.2%, three cases) were found using endoscopy. Also, 6.8% (17 patients) had gastro duodenal ulcers and 14.3% (nine patients) combined gastro intestinal involvement including esophageal and had gastro duodenal ulcers. Colonic ulcers were detected in 9.2% (23 cases) by colonoscopy, two patients had multisegmental diffuse ulceration, three patients had in the sigmoid colon and of everyone else in the ileum. Croftil without ulcers found in 5.6% (14 cases). Two patients had a clinic of appendicitis, the operation found that the appendix is not inflamed. Two patients were 0.8% (were on treatment) urgently operated due to perforation of ulcers of the ileum, the woman held suturing of perforated ulcer, and a man - hemicolectomy. The last patient has a relaparotomy after 1 month and removal of the entire colon.

Conclusion: The IBD in Russia is affected in 1/4 of patients, but heavy refractory forms not often.
ANCA ASSOCIATED VASCULITIS: OUR EXPERIENCE FROM A TERTIARY CARE CENTER OVER 10 YEARS

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Background: The anti-neutrophil cytoplasmic antibody (ANCA)- associated vasculitides (AAV) are a group of disorders characterized by necrotizing inflammation of the small to medium vessels in association with autoantibodies. Childhood ANCA vasculitides are rare but can cause organ or even life-threatening systemic vasculitis. Children most frequently present with rapidly evolving, severe disease.

Objectives: To describe the clinical spectrum of ANCA associated vasculitis, the treatment given and follow up.

Methods: A single-centre retrospective analysis of ANCA associated vasculitis over a period of 10 years from 2008 to 2018

Results: Six children (2 boys; 4 girls) were diagnosed to have AAV during this period. Median age at diagnosis was 11.25 years (range 8-18 years). Median delay in diagnosis was 1.5 months (range 1-8 months). Presenting clinical features included lung disease- 4 children; arthritis- 3 (knee, right ankle-left 3rd MCP, left elbow-knee) hemoptysis- 2 children; ear discharge- 1; redness of eye-1; oliguria, gross hematuria-2; anasarca- 2; 2 children had comitant neurological symptoms (left foot drop, quadraparesis with seizures). All children had fever at presentation. Laboratory investigations showed elevated erythrocyte sedimentation rate(ESR) and C-reactive protein(CRP). ANCA testing was positive in 6 children (3 c-ANCA, +PR3, 3 p-ANCA, +MPO). Deranged renal function tests, proteinuria, microscopic hematuria were seen in 4 out of 6 children. Renal biopsy showed pauci immune glomerulonephritis in 4 cases who presented with nephritis. All patients were treated with 5 pulses of intravenous methylprednisolone(30 mg/kg/day) with tapering doses of oral steroids. Intravenous cyclophosphamide pulses was given in 5 children while 1 received additional plasmapheresis (PLEX) 8 cycles. Methylaine therapy included azathioprine (given in 5 children), low-dose prednisolone. Thrombocytopenia was noted in 1 child while on azathioprine; this was subsequently substituted with mycophenolate mofetil. Two children have been lost to follow-up. Median duration of follow-up is 35.5 months (range 8-124 months). All 4 children have attained remission with good compliance and there are no relapses.

Conclusion: Our retrospective analysis indicated that cumulative CR rates and PSL tapering did not significantly differ between low-dose versus high-dose RTX therapy as remission induction therapy in Japanese AAV patients, mostly elderly MPA patients, although there was no significant difference in severe adverse effects such as opportunistic infections between them.

Disclosure of Interests: None declared


Table: Characteristics of children enrolled in study

A SINGLE CENTER RETROSPECTIVE ANALYSIS OF EFFICACY AND SAFETY BETWEEN LOW-DOSE VERSUS HIGH-DOSE RITUXIMAB AS REMISSION INDUCTION THERAPY IN JAPANESE PATIENTS WITH ANCA-ASSOCIATED VASCULITIS

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Background: Administration of four once-weekly doses of 375 mg/m2 rituximab (RTX) has been indicated for ANCA-associated vasculitis (AAV) as remission induction therapy. However, randomized controlled trial for Japanese AAV patients has never been conducted, although Japanese AAV patients are characterized by the predominance of elderly patients with microscopic polyangiitis (MPA).

Objectives: To compare the efficacy and safety between low-dose versus high-dose RTX therapy as remission induction therapy in Japanese patients with AAV.

Methods: A single center retrospective analysis of 27 consecutive AAV patients with RTX therapy was performed. Clinical and laboratory variables at diagnosis, rates of complete remission (CR), defined as Birmingham Vasculitis Activity Score (BVAS)=0 and prednisone <7.5 mg/day, adverse effects, and vasculitis relapses following RTX use.

Results: Twenty-five MPA patients and 2 GPA patients (14 males and 13 females) were included in the present study. Twenty-six patients were positive for MPO-ANCA. Their median age was 77 years (range: 40-85 years). Treatments were determined according to the discretion of the attending physician. As remission induction therapy, 18 patients were treated with once or twice (1/2) RTX infusions (375 mg/m2), while 9 patients with 3 or 4 times (3/4) RTX infusions. At 6 months, 55.6% of the 1/2 infusion group (10/18) and 44.4% of the 3/4 infusion group (4/9) reached CR. At 6 months, mean PSL levels were 7.8 mg/day in the 1/2 infusion group and 6.6 mg/day in the 3/4 infusion group. At 18 months, 88.9% of the 1/2 infusion group (16/18) and 77.8% of the 3/4 infusion group (7/9) were survived. 0% of the 1/2 infusion group (0/18) and 33.3% of the 3/4 infusion group (3/9) were relapsed. Severe adverse effects occurred in 38.9% of the 1/2 infusion group (7/18) and in 22.2% of the 3/4 infusion group (2/9).

Conclusion: Our retrospective analysis indicated that cumulative CR rates and PSL tapering did not significantly differ between low-dose versus high-dose RTX therapy as remission induction therapy in Japanese AAV patients, mostly elderly MPA patients, although there was no significant difference in severe adverse effects such as opportunistic infections between them.

Disclosure of Interests: None declared


POSITIVE PREDICTIVE VALUE OF THE GIANT CELL ARTERITIS REGISTRY IN THE DANISH NATIONAL PATIENT REGISTRY: A VALIDATION STUDY

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Background: Giant cell arteritis (GCA) is the most frequent systemic vasculitis[1]. The diagnosis is clinical and based on symptoms, histopathology, biochemistry and imaging. In Denmark, diagnostic codes for all in- and outpatient hospital diagnoses are registered in the Danish National Patient Registry (DNPR) [2]. Since GCA can be difficult to diagnose and treatment is initiated on suspicion, we hypothesized that the overall positive predictive value (PPV) of the GCA diagnosis code in the DNPR is low. High data quality is important for future epidemiological research in GCA.

Objectives: To establish PPV of the diagnostic code of GCA in the DNPR. Furthermore, to identify characteristics associated with a high PPV of the diagnostic code.

Methods: 293 patients aged ≥50 years with a first-time register-based GCA diagnosis were included from the DNPR in the period January 2012-January 2018. Patients were sampled based on the ICD-10 codes (M31.5 and M31.6) from two regional hospitals and one university hospital in the Central Region of Denmark. As gold standard we used the medical records (including biochemistry, histopathology and imaging results) and categorized each patient as true GCA or non-GCA. Based on the data from the prescription database, patients were divided into four categories depending on the number of prednisolone prescriptions they received. Two independent investigators (PH and PT) reviewed the medical records. In case of disagreement the final diagnosis was reached by consensus or by expert opinion (ITH). To test how the PPV varied,
Systemic vasculitis involving the breast is a rare clinical condition and may mimic breast cancer or mastitis clinically or radiographically. In this article, we reported a case of polyarteritis nodosa (PAN) with breast involvement and made a summary on the published cases of systemic vasculitis affecting breasts in order to better understand this disorder.

### Methods

We reported a case of PAN affecting breast and conducted a retrospective review of letters reporting patients with the diagnosis of systemic vasculitis involving breasts by using MEDLINE, EMBASE, Web of Science, the Cochrane Library, and Scopus database in any language up to June 1st, 2018.

### Results

A case of a 27-year-old female patient presented with a painful mass of the right breast was diagnosed as PAN by the biopsy. After six months of treatment of full dose prednisone and methotrexate, her condition kept stable and inflammatory markers remained normal. A total of 67 months of treatment of full dose prednisone and methotrexate, her condition kept stable and inflammatory markers remained normal. A total of 67 cases were included, with granulomatosis with polyangiitis (GPA), giant cell arteritis (GCA) and PAN as the main types. The typical manifestation was mass (79.2%, 53/67) in the breast. All the diagnoses were made according to the pathology of the breast biopsy. Glucocorticoid and immunosuppressant were the main therapies. 74.6% (50/67) patients achieved remission during follow-up.

### Conclusion

This is the first study to validate the diagnostic code of GCA in the DNPR. The overall PPV of a first-time diagnosis of GCA in the DNPR is low. The probability of identifying true cases of GCA increases substantially when diagnostic codes are combined with 3 visits and ≥3 prescriptions of prednisolone.

### REFERENCES


### Disclosure of Interests

A special thanks to Mette Nørgaard for her help.

Disclosure of Interests: None declared

Conclusion: Although pANCA is thought to be associated with ILD or pulmonary fibrosis, we detected equal numbers of c and pANCA in a well-characterised population of ILD patients. Approximately one quarter of patients with p or cANCA had an MDT diagnosis of ANCA-associated vasculitis. The clinical and CT characteristics did not differ between c and pANCA ILD patients. The two-year mortality of patients with ANCA and ILD was significant (22% in cANCA-ILD and 16% in pANCA). In surviving patients, the FVC and DLCO improved over a 24-month period.

REFERENCES

Disclosure of Interests: None declared

Figure 1

THE USEFULNESS OF 18F-FLUORODEOXYGLUCOSE POSITRON EMISSION TOMOGRAPHY CT (18F-FDG PET/CT) AS AN IMAGING BIOMARKER IN TAKAYASU ARTERITIS TREATED WITH TOCILIZUMAB

Mikuya Kato1,1, Hanae Okuda2, Tomohiro Kameda1, Taichi Miyagi1, Risa Wakiya1, Shusaku Nakashima1, Hiroshi Shimada1, Mai Mahmoud Fahmy Mansour1, Yuka Yamamoto2, Hiroaki Dubashi1, Kagawa university. Division of Hematology, Rheumatology and Respiratory Medicine, Kagawa, Japan

Background: Disease activity in large vessel vasculitis (LVV) including TAK is traditionally assessed by clinical and serological (ESR, CRP) parameters. Imaging assessment, including FDG-PET, may also be useful to monitor LVV. On the other hand, Tocilizumab (TCZ) treatment showed a favorable trend toward refractory Takayasu arteritis (TAK) (1). Because the TCZ could suppress the CRP or ESR elevation strongly despite the exist of TAK disease activity, clinical and serological (ESR, CRP) parameters could not reflect the disease activity of TAK appropriately.

Objectives: This study objective was to determine the efficacy of 18F-FDG PET/CT on the evaluating the disease activity of TAK treated TCZ compared with clinical and serological parameters.

Methods: Five Patients with TAK were recruited into a prospective, observational cohort. All patients in this study underwent FDG-PET/CT scans at 6 - 12 month intervals before and after TCZ treatment. Serological (ESR, CRP) and clinical assessment were determined at each visit. Disease activity was determined whether scans were active or inactive based on visual inspection of arterial 18F-FDG uptake. To determine the score of arterial FDG uptake assessed qualitatively relative to liver activity in 10 vascular beds with higher scores indicating more vascular inflammation. Additionally, scoring of FDG uptake was conducted to calculate as divided into 4 grade compared with liver activity: 0, no uptake present; I, low-grade uptake (uptake present but lower than liver uptake); II, intermediate-grade uptake (similar to liver uptake); III, high-grade uptake (higher than liver uptake) (2). Clinical and imaging assessments were performed blinded to each other.

Results: All 5 cases (one male and 4 female) were initiated by TCZ treatment. The average age was 42.2±11.6 years old. The disease duration at the administration of TCZ was 176±136 months. The mean dosage of PSL was 6.4±3.72 mg/day. After initiating TCZ treatment, mean CRP values decreased from 1.44±1.80 to 0.032±0.034, and the PSL dose was reduced to 4.00±2.61 mg/day. No serious adverse events were observed. Thorough serum level of inflammatory biomarker such as CRP or ESR had become into normal range in all patients, arterial 18F-FDG uptake also remained in all patients after TCZ treatment. Additionally, clinical manifestations were correlate with site numbers and score of FDG uptake. The change of FDG score could reflect the improvement of clinical manifestation compared with serological biomarkers.

Conclusion: Serological biomarker such as CRP or ESR could not reflect disease activity appropriately in TAK patients treated with TCZ. 18F-FDG PET/CT was more useful for evaluating disease activities in Takayasu arteritis treated with TCZ. Further study might be needed to determine the definition of complete remission in TAK patients treated with TCZ.

REFERENCES
**AB0596**

**ASSESSMENT OF DAMAGE IN TAKAYASU ARTERITIS PATIENTS WITH VASCULITIS DAMAGE INDEX (VDI) AND TAKAYASU ARTERITIS DAMAGE SCORE (TADS)**

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**Background:** Evaluation of damage in patients with takayasu arteritis is important because of the mortality and morbidity burden caused by the disease. Damage can be associated with treatment or with the disease itself.

**Objectives:** In this study we aimed to evaluate the damage in our Takayasu arteritis patients by using VDI and TADS scores.

**Methods:** Takayasu arteritis patients fulfilling the ACR 1990 criteria and had >3 months follow-up were enrolled in this study. TADS and VDI scores calculated at the end of the follow-up evaluated and compared.

**Results:** 114 patients (F/M: 101/13) were included in the study. The mean age at diagnosis, median symptom duration at baseline visit and mean follow-up duration were 35.3±13.3 years, 12 (0-360) months and 76.9±51.4 months respectively. Mean VDI score was 5.1±2.5 and mean TADS score was 7.9±3.5. At least one disease-related damage item was present in all of the patients for both VDI and TADS meanwhile ≥1 treatment-related damage item was established in 69 (66.1%) patients with VDI and 46 (40.7%) patients with TADS scoring system. Median treatment-related-item number was 1 (0-6) in VDI and 0 (0-3) in TADS. This difference may be due to the lack of disease-related parameters such as diabetes, cataract, osteoporosis, avascular necrosis in TADS. The median number of disease-related items was higher in TADS scoring (4 items vs 8 items). TADS scores include more detailed and higher number of items under vascular intervention and pulse loss categories. Also abrupt and systolic hypertension data is only available in TADS(Table1).

There was no significant difference between patients with relapsing disease and patients with no relapses for both TADS and VDI scores. There was a weak correlation between VDI and cumulative steroid dose ($r=0.19$). No correlation was detected for TADS and cumulative steroid dose. There was a weak correlation between VDI and cumulative steroid dose ($p=0.04$). A positive correlation was observed between the CRP levels before imaging and total m-PETVAS scores ($p=0.01$, $rho=0.52$). In 35/38 imaging assessments the score was >0 and the immunosuppressant agent was changed in 24 (63%) of these patients. Twenty-seven patients received corticosteroids before imaging. No difference in PETVAS scores were present between patients who were taking steroids vs non-steroid use. In 11 patients (29%), PET involvement other than the 9 arterial areas used for assessing the score, were observed. The mean age of this group was higher than the rest of the group (47.2±14.7 vs 35.7±11.2 years).

**Conclusion:** FDG-PET-CT assessment with a modified PETVAS (assessed at one hour) demonstrated higher scores in patients with Takayasu's arteritis.

**REFERENCES**


| Table 1. Comparison of VDI and TADS scores in our Takayasu patients |
|-------------------|-------------------|
| **Categories**    | **VDI** | **TADS** |
| Musculoskeletal   | 23 (20) | -        |
| Osteoporosis      | 15 (13)  | -        |
| Avascular necrosis| 6 (5.4)  | -        |
| Skin              | 14 (12.6) | -       |
| Ocular            | 37 (33.3) | 8 (7.1) |
| Cataract          | 11 (9.9)  | -        |
| Retinal change    | 19 (17.1) | -        |
| Visual impairment/diplopia | 14 (12.6) | 8 (7.1) |
| ENT               | 1 (0.8)   | -        |
| Pulmonary         | 20 (18)   | 16 (14.2) |        |
| Cardiovascular    | 79 (71.2) | 114 (100) |        |
| Brail             | -         | 92 (81.4) |        |
| Pulse loss        | -         | 79 (69.9) |        |
| Valvular disease  | 44 (39.6) | -        |
| Ischemic cardiac pain | 11 (10)   | 18 (15.9) |        |
| Myocardial infarction | 8 (7.2)  | -        |
| Aortic incompetence| -       | 27 (23.9) |        |
| Diastolic BP > 95 | 46 (40.7) | -        |

Peripheral vascular disease 110 (99.1) -
Absent pulses in one limb 78 (70.3) -
Claudication > 3 months 89 (80.2) -
Major/minor tissue loss 1 (0.9) -
Venous thrombosis 1 (0.9) -
Renal 4 (3.6) 47 (41.6)
Diastolic BP > 95 - 46 (40.7)
Neuropsychiatric 18 (16.2) 14 (12.4)
Vascular intervention - 45 (39.6)
Other 13 (11.7) 14 (12.4)
Malignancy 2 (1.8) -
Intestinity 1 (0.9) 1 (0.9)
Diabetes 8 (8.1) -

**VDI: Vasculitis Damage Index**

**TADS:** Takayasu Arteritis Damage Score

**ENT:** Eye-Nose-Throat

**Neuropsychiatric:** Mental disease

**Peripheral vascular disease:** Peripheral vascular disease

**Malignancy:** Malignancy

**Intestinity:** Intestinal disease

**Diabetes:** Diabetes

**AB0597**

**CAN A ONE-HOUR QUANTITATIVE ASSESSMENT OF FDG-PET-CT (MODIFIED-PETVAS) BE USEFUL IN TAKAYASU’S ARTERITIS?**

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**Background:** FDG-PET-CT is suggested as an imaging method for the assessment of disease activity in Takayasu’s arteritis (TAK). Recently PETVAS, a quantitative score assessed at 2-hours is suggested as an imaging tool for TAK (1). However, most studies with FDG-PET-CT in the literature is performed at one-hour, similar to suggested as the minimum time in recent EULAR recommendations for the use of imaging in large-vessel vasculitis (2).

**Objectives:** In this study, we aimed to evaluate the value of a modified PET Vascular Activity Score (PETVAS) (performed at one-hour) during the initial diagnosis and follow-up of TAK patients.

**Methods:** Patients who are diagnosed with Takayasu’s arteritis and underwent FDG-PET-CT imaging during their follow-up were evaluated in this study retrospectively. FDG-PET-CT imaging was performed at the first hour of FDG uptake. Demographic and clinical characteristics of the patients were recorded from patients’ charts. Physician’s Global Assessment (PGA) was used to determine clinical activity. In the modified PETVAS scoring system, 9 arterial areas (Ascending Aorta, Aortic Arch, Descending Thoracic Aorta, Abdominal Aorta, Right Carotid Artery, Left Carotid Artery, Innominate Artery, Right Subclavian Artery, Left Subclavian Artery) were scored between 0 and 3 according to the PGA uptake (3). The visual analysis using the liver FDG uptake as the reference was also assessed and compared with m-PETVAS score.

**Results:** Thirty-eight imagings of 28 patients (F/M: 22/6, mean age=39.7 ± 14.8 years) were evaluated. Median CRP level was 16.7 (2-126) mg/L. Median m-PETVAS score was 5 (0-27) and m-PETVAS was significantly higher in patients who were accepted as active according to PGA (median PETVAS score 6.0 vs 1.5, $p=0.03$). Similarly, patients who have an active PET assessed with only visual analysis (VA) have higher m-PETVAS scores than patients who were VA inactive (median score 9.0 vs 2.5, $p=0.000$). A positive correlation was observed between the CRP levels before imaging and total m-PETVAS scores ($r=0.01$, $rho=0.52$). In 35/38 imaging assessments the score was >0 and the immunosuppressant agent was changed in 24 (63%) of these patients. Twenty-seven patients received corticosteroids before imaging. No difference in PETVAS scores were present between patients who were taking steroids vs non-steroid use. In 11 patients (29%), PET involvement other than the 9 arterial areas used for assessing the score, were observed. The mean age of this group was higher than the rest of the group (47±14.7 vs 35.7±11.2 years).

**Conclusion:** FDG-PET-CT assessment with a modified PETVAS (assessed at one hour) demonstrated higher scores in patients with Takayasu’s arteritis.
artefactis who were considered clinically active or had increased CRP. However, the scores were lower compared to the original scoring performed at two hours. Therefore, whether one hour investigations have sufficient discriminatory value requires further studies.

REFERENCES


Disclosure of Interests: None declared

AB0598 OSTEOPOROSIS AND RISK OF GIANT CELL ARTERITIS: A COMPARATIVE STUDY

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Background: Giant cell arteritis (GCA) and osteoporosis (OP) share many epidemiological features, such as occurrence in people >50 years old and increased incidence in women and northern Europe. Some known risk factors of OP, such as early menopause, nulliparity, low body mass index (BMI) and smoking, have also been linked to increased risk of GCA.

Objectives: We performed this study to investigate a potential link between OP and GCA onset by screening for OP by computed tomography (CT).

Methods: We retrospectively analyzed consecutive patients who underwent temporal artery biopsy (TAB) for suspected GCA in 4 hospitals. Cases and controls were defined by TAB-proven GCA and non-GCA diagnosis, respectively. Selection criteria additionally included 18F-FDG PET/CT at ±30 days (GCA cases) or ±90 days from the date of TAB (non-GCA cases). A radiologist blinded to patients case or control status used thresholds of 110 Hounsfield units (HU) or 135 HU (1). We compared cases and controls for proportion of OP for the entire population and by sex. Statistical analyses involved chi-square and Student t tests for categorical and continuous variables, respectively.

Results: We included 50 cases and 59 controls. The most common diagnoses for controls were neurological involvement (11.3% vs 21.4% p<0.05) resulted more frequent in females versus 0.9% respectively; p<0.01). Erythema nodosum (EN) (59% versus 31% p<0.01) and intestinal ulcerations (GU) and a wide spectrum of skin lesions. Other BS features include ocular inflammation, articular, gastrointestinal, vascular and neurological involvement. Some evidences suggest that in non endemic regions the disease tend to be less severe and women seem to be more commonly affected [1-3].

Conclusion: We included 50 cases and 59 controls. The most common diagnoses for controls were neurological involvement (11.3% vs 21.4% p<0.05) resulted more frequent in females versus 0.9% respectively; p<0.01). Erythema nodosum (EN) (59% versus 31% p<0.01) and intestinal ulcerations (GU) and a wide spectrum of skin lesions. Other BS features include ocular inflammation, articular, gastrointestinal, vascular and neurological involvement. Some evidences suggest that in non endemic regions the disease tend to be less severe and women seem to be more commonly affected [1-3].

AB0599 CLINICAL MANIFESTATIONS OF BEHÇET’S SYNDROME IN A LARGE COHORT OF ITALIAN PATIENTS: FOCUS ON GENDER DIFFERENCES

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Background: Behçet’s syndrome (BS) is a chronic multisystemic inflammatory disorder classified among primary vasculitis. BS clinical hallmarks are mucocutaneous manifestations which include oral aphthosis (OA), genital ulcers (GU) and a wide spectrum of skin lesions. Other BS features include ocular inflammation, articular, gastrointestinal, vascular and neurological involvement. Some evidences suggest that in non endemic regions the disease tend to be less severe and women seem to be more commonly affected [1-3].

Objectives: The aim of this study was to investigate the clinical phenotypes of Italian BS patients with respect to gender and HLA-B51 status.

Methods: We retrospectively evaluated 324 Italian patients (185 males and 139 females), seen consecutively at Rheumatology Institute of Lucania (IRel) from 1st January 2000 to 31st December 2017. Demographics, clinical features during follow-up and HLA status were obtained from a review of medical records. The analysis was limited to patients fulfilling the ISG criteria.

Results: 324 BS patients were identified in our database. 39 (17 males and 22 females) were excluded because did not satisfied ISG criteria and 285 (168 males and 117 females) resulted eligible for the present study. Results are summarized in table 1. We found statistically significant differences in papulopustolar lesions, posterior uveitis and deep venous thrombosis (DVT), which occur more frequently in males compared with females (83.3% versus 46.2%, 37% versus 18.8% and 8.3% versus 0.9% respectively; p<0.01). Erythema nodosum (EN) (59% versus 41.1%, p<0.01), arthralgia (52.1% versus 31.5%, p<0.01) and intestinal involvement (11.3% vs 21.4% p<0.05) resulted more frequent in females compared with males. No differences were found in HLA status (M 67.9% vs F 61.5%).

REFERENCE

Conclusion: In our cohort of Italian BS patients the disease results slightly more prevalent in males. Gender-related differences were observed for posterior uveitis, DVP and papulopustular lesions which are more frequent in males, whereas EN-like lesions, arthralgia and intestinal involvement are more frequently observed in females. These data confirm that BS tend to be less aggressive in Italian female patients. No sex-differences were observed in HLA-B51 status.

Methods: We retrospectively evaluated BD patients according to ICBD (2) and/or ISG (3) criteria who had undergone apremilast therapy (30 mg twice daily) for oral and/or genital ulcers from November 2017 to January 2018 in four different specialized referral Units in Italy (Bari, Firenze, Potenza, Siena). Retrieved data including previous treatments were also collected. Our endpoint was to assess the number of oral and genital ulcers under apremilast treatment. Moreover pain due to ulcers was evaluated with a 100-mm visual-analogue scale (VAS), whereas disease activity was assessed by means of BDCAF score. Paired t-test or Wilcoxon matched-pair signed rank test, if applicable, were used for statistical analysis.

REFERENCE

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AB0600
APREMILAST EFFECTIVENESS IN REFRACTORY ORAL AND GENITAL ULCERS OF BEHÇET’S DISEASE: DATA FROM REAL LIFE SETTINGS

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Background: Mucocutaneous lesions represent the earliest and the most frequent manifestations of Behcet’s disease (BD), and may become disabling leading to substantial effect on quality of life. Recently the efficacy of the small molecule inhibitor of phosphodiesterase 4 apremilast in treating oral and genital ulcers has been shown in a phase 2 trial (1), whereas to date no results from real world data are available.

Objectives: The purpose of the present study was to describe our experience with apremilast in treating BD patients with oral and genital ulcers refractory to traditional therapies and previous biologic agents in real life settings

Figure 1

AB0600
APREMILAST EFFECTIVENESS IN REFRACTORY ORAL AND GENITAL ULCERS OF BEHÇET’S DISEASE: DATA FROM REAL LIFE SETTINGS

Giuseppe Lopalco1, Vincenzo Venerito1, Pietro Leccese2, Giacomo Emmi3, Luca Cantarini4, Nancy Lascaro2, Gerardo Di Scala5, Stefano Gentileschi1, Anna Abbuzzese1, Marco Fornar4, Fabio Cacciapaglia1, Giovanni Lapadula5, Lorenzo Iannone1, University of Bari, Bari, Italy;2Rheumatology Institute of Lucania, Potenza, Italy;3University of Florence, Firenze, Italy;4University of Siena, Siena, Italy

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Objectives: The purpose of the present study was to describe our experience with apremilast in treating BD patients with oral and genital ulcers refractory to traditional therapies and previous biologic agents in real life settings

Figure 1

Figure 2

REFERENCES


Disclosure of Interests: Giuseppe Lopalco Speakers bureau: SOBI, BMS, vinciengrino venerito: None declared, Pietro Leccese: None declared, Giacomo Emmi: None declared, Luca Cantarini: None declared, Nancy Lascaro: None declared, Gerardo Di Scala: None declared, Stefano Gentileschi: None declared, Anna Abbuzzese: None declared, Marco Fornar4: None declared, Fabio Cacciapaglia: None declared, Giovanni Lapadula: None declared, Lorenzo Iannone Consultant for: F Iannone has received consultancy fees and/or speaker honoraria from Pfizer, Abbvie, MSD, BMS, Noravis, Lilly, UCB outside this work, Speakers bureau: F Iannone has received consultancy fees and/or speaker honoraria from Pfizer, Abbvie, MSD, BMS, Noravis, Lilly, UCB outside this work

UTILIZATION OF A MULTISPECIALTY TEAM FOR THE DIAGNOSIS OF GIANT CELL ARTERITIS REDUCES PATIENT MORBIDITY

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Background: Giant Cell Arteritis (GCA) is an autoimmune vasculitis, most commonly seen in older adults with a peak incidence in the seventh decade of life. A diagnosis of GCA is often considered in any patient over the age of 50 years who complains of or is found to have new onset headache, acute visual disturbances, jaw claudication, unexplained fever, or elevated inflammatory markers. Because the manifestations of GCA can vary considerably from patient to patient, often with transient and fluctuating symptoms, an accurate diagnosis can be challenging. Even in the setting of a negative temporal artery biopsy, many patients are treated empirically based on the perceived probability of disease. This approach can lead to significant morbidity from prolonged medication exposure and unnecessary procedures.

Objectives: The aim for this project was to look at the impact of a collaborative effort amongst three specialties, rheumatology neurology and ophthalmology, which composed a consultation based “GCA team”, the goal of which was to improve how GCA is diagnosed and subsequently managed.

Methods: We conducted a retrospective study of all patients suspected to have GCA at our institution over the last 2.5 years that had either been seen by the GCA team or not. The GCA team met either in person or had a conference call to discuss each case and make a joint decision regarding the diagnosis and treatment. Data extracted included patient demographics, symptoms on presentation, labs, biopsy results and cumulative prednisone dose.

Results: A total of 30 patients (19 female, 11 male) were evaluated; 19 were seen by the GCA team and 11 were not. The mean ages of the patients in each group were the similar (GCA Team 70.6 (SD 12.5) vs no GCA Team 70.3 (SD 12.3)). The mean ESR between the two groups was also similar (GCA Team 53.3 (SD 30.2) vs no GCA Team 53.8 (SD 27.2)). The presenting clinical symptoms between the two groups were also comparable: visual complaints (63% vs 73%), headache/jaw claudication (42% vs 45%), and cranial neuropathy (11% vs 9%).

All of the patients not seen by the GCA team underwent bilateral tempo-parietal artery biopsy; however none were positive on histology. Regardless, all were continued on high dose prednisone with a 6 month cumulative mean dose of 5,350mg.

Of the 19 patients seen by the GCA team, 8 were determined to be low probability for GCA and thus were spared temporal artery biopsy. Furthermore, all of the patients were recommended a rapid steroid taper and the cumulative mean dose of prednisone was only 490mg. Over 6 months of follow-up, none of the 8 patients deemed low probability had a subsequent diagnosis of GCA given.

In the 11 high probability GCA patients, 10 underwent temporal artery biopsy (one refused) with 4 biopsies read as positive for GCA. Over 6 months of follow up, none of these patients had flares after they were started on treatment.

Conclusion: While the accuracy of a GCA diagnosis cannot be determined in our cohort of patients not seen by the GCA team, it is likely that evaluation by a multispecialty team would have found several to be low probability for GCA; especially as none of the patients had a positive temporal artery biopsy. We have demonstrated that by adopting a collaborative approach to diagnosing GCA, unnecessary biopsies can be avoided as well as limiting unnecessary prednisone exposure. More prospective data is needed to provide an accurate assessment of this team approach for GCA which can serve as a model for other healthcare facilities.

Disclosure of Interests: Arash Hassantouffigh: None declared, Rachel Lu Do: None declared, Joshpaul Dhillon: None declared, Christopher Collins Grant/research support from: Exagen, Consultant for: Exagen, AbbVie, Speakers bureau: Exagen, AbbVie, Novartis, Florina Constantinescu: None declared


AB0602

CLINICAL USEFULNESS OF LUNG ULTRASOUND IN ACTIVE GRANULOMATOSIS WITH POLYANGIITIS WITH LUNG INVOLVEMENT – PRELIMINARY DATA

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Background: Lung involvement is observed in 43% to 94% of patients with granulomatosis with polyangiitis (GPA) [1]. In about 10% of cases, the lung is the only organ affected and in as many as 30% of patients without clinical symptoms of lower respiratory tract involvement, abnormalities in chest imaging examinations can be found [2]. The efficacy of lung ultrasound (LUS) is very well documented in many pulmonary diseases [3,4]. Single publications indicate its applicability also in diagnostics of complications secondary to systemic connective tissue disease, e.g., lung fibrosis or diffuse alveolar hemorrhage [5,6]. The necessity of repeating chest imaging examinations increases the patient’s exposure to ionizing radiation. Thus, the possibility of limiting such exposure through the application of LUS as the diagnostic modality appears extremely inviting.

Objectives: The aim of this study was to assess lesions detected by ultrasound in patients with active granulomatosis with polyangiitis (GPA) in comparison to abnormalities found by computed tomography (CT).

Methods: We analyzed the clinical and radiological data of 12 patients (5 women/7 men, mean age 47.9 years/range 18-80) with active PR3-ANCA-associated vasculitis with lung involvement (Birmingham Vasculitis Activity Score, BVASv5 mean 5.7/range 1-12). LUS was performed in the sitting and lying positions, using the convex (2.6 MHz) and linear (4-12 MHz) transducers placed to each intercostal space over the chest wall (anterior, lateral and inferior). Chest CT was performed according to a standard protocol with the use of a 64-slice CT scanner made by GE. The images obtained in LUS were compared to changes detected in CT scans. The study protocol was approved by an independent local Bio-ethics Committee (NBKN/474/2018).

Results: In all patients with lungs infiltrations, changes were visible in the LUS, but the visualized infiltrates and caviﬁes include only these lesions that were adjacent to the line of pleura. LUS revealed infiltrates as well as infiltrates with features of disintegration and cavities. Subpleural infiltrates in ultrasound were visualized as hypoechoic round or oval consolidations, without central flow visible in color Doppler (CD) and power Doppler (PD) modes. Caves visualized in LUS were round and anechoic; flow in CD and PD modalities was also absent. In some cases, we observed hypoechoic round or oval infiltrates with features of disintegration, partly ﬁlled in with ﬂuid content (anechoic).

Conclusion: Due to the harmlessness of ultrasonography, LUS can be repeatedly performed. In addition, ultrasound examination can be performed during hospitalization at the patient’s bedside as well as during a visit to the rheumatologist’s ofﬁce.

REFERENCES

Disclosure of Interests: None declared


AB0603

SCOTLAND’S FIRST FAST TRACK TEMPORAL ARTERY ULTRASOUND REFERRAL PATHWAY FOR SUSPECTED GIANT CELL ARTERITIS

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Background: Giant cell arteritis (GCA) is associated with loss of vision (LOV). Rapid referral for specialist assessment including temporal artery ultrasound (TAU) reduces the risk of LOV and the need for temporal artery biopsy (TAB). Two
Clinical features and treatment in a cohort of patients with Behçet disease in a tertiary hospital of Barcelona

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Background: Behçet disease (BD) is considered a systemic vasculitis according to the Chapel-Hill classification, which occurs most frequently between latitudes 30 and 45° according to the Chapel-Hill classification, which occurs most frequently in the area of the Old Silk Route. Today, it has the highest prevalence, followed by Japan, in Spain, a prevalence of 7.5 cases per 100000 persons has been estimated. The epidemiological and clinical characteristics of European patients with BD vary with respect to those of the Turkish and Japanese cohorts.

Objectives: Description of clinical features and treatment received in a cohort of patients diagnosed with BD in an Internal Medicine Unit of a tertiary centre from Barcelona.

Methods: Retrospective, observational study. Epidemiological, clinical and laboratory data were obtained from clinical charts. SSPS package was used to perform statistical analysis.

Results: 132 patients (56.6% men) diagnosed over the last 30 years and followed-up until the censoring data were included. 112 (84.8%) were Caucasians, 15 (11.4%) from North America, 4 (3%) Asian and 1 (0.8%) from South America, 2 (1.5%) patients had a family history of BD and 9 patients (6.8%) a family history of other rheumatic diseases. 43.9% (58 patients) were HLA-B51. Oral or genital ulcers were present in 131 (99.2%) patients and skin involvement in 106 (80%) cases. 44.8% had erythema nodosum, 59% had acne-like lesions and 9% had cutaneous vasculitis. Ocular involvement was observed in 69 cases (52.3%); 27 patients unilateral and 8 bilateral anterior uveitis; 14 unilateral and 3 bilateral posterior uveitis; 10 patients unilateral and 14 bilateral panuveitis; 19 unilateral retinal vasculitis and 12 bilateral. Neurological involvement was present in 37 (28%) patients: 10 parenchymal disease and 17 cases non-parenchymal disease (aseptic meningitis or vasculitis); 8 patients benign intracranial hypertension, and 3 had dural sinus thrombosis. Articular involvement was recorded in 79 (59.8%) patients (it was observed 25 monoarthritis, 24 oligoarthritis, 6 poliarthritis and 58 patients had arthropal).

Vascular involvement was present in 43 (32.6%) cases: deep venous thrombosis in 38 patients (11 cases in locations other than the extremities); pulmonary embolism in 7, 21 thrombogenic; and 6 patients aneurysms (only 2 pulmonary arterial aneurysms). Digestive involvement was present in 12 (9.1%) patients, with predominant colon involvement (8 cases).

The most prescribed drugs were corticosteroids (85.6%) and colchicine (77.3%), followed by azathioprine (36.4%) and cyclosporine A (33.3%). Other prescribed drugs were thiadomil (6.1%), chlorambucil (6.9%), methotrexate (4.5%), anti-TNF-alpha therapies (infliximab 6.8% and adalimumab 2.3%), cyclophosphamide (3%), mycophenolate (3.8%), leflunomide (1.5%) and 22% received anticoagulation.

Conclusion: Clinical features of our patients are similar to those of other European cohorts, although a high prevalence of organic involvement (ocular, neurological, vascular and joint) should be highlighted.

References

Disclosure of Interests: None declared


AB0605 SERUM NEOPTERIN AND ISCHEMIA MODIFIED ALBUMIN LEVELS ARE ASSOCIATED WITH THE DISEASE ACTIVITY OF ADULT IMMUNOglobulIN A VASCULITIS (HENOC–SCHONLEIN PURPURA)

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Background: Immunoglobulin A vasculitis (IgAV) [formerly called Henoch–Schönlein purpura (HSP)] is an IgA mediated systemic vasculitis which primarily affects skin, gastrointestinal system and small vessels of kidneys. Exact pathogenesis of IgAV remains unknown. A few clinicopathological studies have shown that oxidative stress plays a role in the pathogenesis of vasculitis. Ischemia modified albumin (IMA) and Neopterin increased status of oxidative stress.

Objectives: The aims of the study are to investigate serum neopterin and IMA levels in patients with IgAV and evaluate the association of these markers with disease activity and relapse.

Methods: Thirty-four consecutive adult patients (24 males and 10 females) admitted to the rheumatology clinic of Ankara Numune Training and Research Hospital meeting the IgAV American College of Rheumatology (ACR) criteria were enrolled in this cross-sectional study. Demographic and clinical features of IgAV and control group were recorded into a predefined protocol. Disease activity was categorized as “remission” or “active” according to BVAS, BVAS <1 was accepted “active’’. Serum neopterin levels, hsCRP and IMA were evaluated according to BVAS and compared to healthy control group.

Results: Serum median (IQR) neopterin, IMA levels in patients with IgAV and control group were recorded into a pre-designed group. Disease activity was categorized as “remission” or “active” according to BVAS. BVAS <1 was accepted “active”. Serum neopterin levels, hsCRP and IMA were evaluated according to BVAS and compared to healthy control group.

Conclusion: Oxidative stress is important in HSP pathogenesis. Roles of hsCRP, Neopterin and IMA as potential markers of diagnosis and disease activity seem to be worth studying in the future studies with larger study groups.

Disclosure of Interests: None declared

AB0606  LONG-TERM BIOLOGICAL TREATMENT IN LARGE VESSELS VASCULITIS: A RETROSPECTIVE SINGLE-CENTER STUDY ON 30 PATIENTS FROM 2011 TO 2018

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Background: Glucocorticoids (GC) are the mainstay in the treatment of large vessels vasculitis (LVV), while conventional immunosuppressants have modest GC-sparing effect. Recent studies show that biological drugs could represent a valid therapeutic option, especially in patients with severe and/or relapsing LVV. Their role in the treatment of LVV is expanding, but only few data are available on their long-term efficacy and safety.

Objectives: Our aim is to describe the 8 years’ experience of a single Italian center in biological treatment of patients with large vessels vasculitis (LVV).

Methods: We collected retrospectively clinical data from 30 patients affected by LVV and treated with biological drugs. Data from 18F-FDG PET and CT or MRI associated with improvement of clinical and inflammatory index (ESR and CRP) were used as criteria of response to treatment.

Results: Between 2011 and 2018 we treated 30 LVV patients (22 women and 8 men) with biological drugs: 10 patients with Takayasu arteritis (TAK), 17 patients with large-vessel giant cell arteritis (LV-GCA) and 3 patients with aortitis. The median age (10th–90th percentile) at the diagnosis was 63 (21-79) years. Biological treatment was started right after the diagnosis in 15 patients, while 15 patients had a long-standing relapsed disease (time between diagnosis and biological therapy 6 (1-43) months).

The mean follow-up time of patients was 26 (4-72) months.

Anti-TNF-α drugs (infliximab, adalimumab, golimumab) were used in 9 patients; while anti-IL6 (tocilizumab) was used in 30 patients. During the follow up, 9 patients (23%) switched to another biological for relapse of the disease or for toxic adverse reactions; in 3 cases multiple switches were made.

Infliximab (IFX) was used in 7 patients for a median period of 12 (3-33) months: 3 patients archived stable remission, 3 had an infusion adverse reaction, 1 had a relapse of the disease after 60 months of therapy. Adalimumab (ADA) was used in 3 patients and then suspended in all of them for relapse of the disease after 3, 12 and 93 months of therapy, respectively. Golimumab was used in 2 patients: one suspended therapy for developing follicular thyroid cancer, one switched to another biological for persistent active disease.

Tocilizumab (TCZ) was used in all 30 patients for a median period of 20 (4-54) months: in 25 cases it was the first line therapy, in the other 5 cases it was used after an anti-TNF-α drug. 25 patients out of 30 (84%) archived stable remission and in 6 of them a dose tapering was possible, with no sign of relapse.

Three patients in TCZ had an adverse reaction; one developed a uveitis and one had a relapse of TAK.

In our last examination 29 out of 30 patients in biological therapy demonstrated long-term efficacy and acceptable safety profile and important steroid sparing effect.

REFERENCES


Disclosure of Interests: Francesca Regola: None declared, Giovanni Bosio: None declared, Elisabetta Cerutelli: None declared, Angela Tincani Consultant for: UCB, Pfizer, Abbvie, BMS, Sanofi, Roche, GSK, Alpha-Sigma, Lilly, Janssen, Celgene, Novartis, Paola Toniati: None declared


AB0607  SELF-MANAGEMENT BEHAVIOURS IN ANCA-ASSOCIATED VASCULITIS: SECONDARY ANALYSIS OF INTERVIEW DATA

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Background: ANCA-associated vasculitis (AAV) is a significant cause of morbidity and mortality. Meeting the challenges of AAV effectively requires patients to engage in self-management, including medical management, role management, and emotional management. Self-management is recognised as a key aspect of chronic disease management and forms an important part of the National Health Service 5-year forward plan and the UK strategy for rare diseases. Nonetheless, there has been limited specific research into the role of self-management in the AAV literature.

Objectives: To explore experiences and views of self-management amongst AAV patients.

Methods: A secondary analysis of all interview transcripts from a previous project exploring health-related quality of life in relation to AAV was performed. Deductive analysis was used to map appropriate areas discussed by patients to the self-management framework proposed by Lorig and Holman. Inductive analysis was used to identify emergent themes that did not fit into this framework.

Results: Interview data were collected from 50 patients with AAV (25 men), from the UK (n=18), USA (n=17) and Canada (n=15). Diagnoses included GPA (n=26), EGPA (n=17) and MPA (n=7). Thirty-four patients were diagnosed within the last 2 years and 16 were diagnosed more than 2 years ago.

From the core tasks proposed in Lorig and Holman’s framework, patients with AAV appear to attribute particular importance to maintaining life roles and to a lesser extent medication management and dealing with the emotions of chronic disease. Core skills necessary to self-manage in AAV include learning to take action as part of self-efficacy, forming productive health-care partnerships, learning about decision making (requiring disease and self-awareness), utilising resources effectively, and problem-solving.

Three themes emerged that were not included in Lorig and Holman’s framework that respondents related to self-management abilities including: 1) support received from family, support groups, and religion; 2) the influence of pre-morbid personality factors; 3) the role patients attributed to developing a foundation of specific AAV knowledge in their subsequent ability to self-manage.

Conclusion: Patients with AAV self-manage in a variety of ways and their needs may change over time. Patients may benefit from support to help manage changing life roles and to deal with the challenges of having a chronic disease. Over time, support may need to shift focus onto core skills including recognising when to take action; forming effective partnerships with healthcare providers, family, and friends; adaptations to day-to-day changes in their condition; utilising resources appropriately; and strategies for problem-solving.

REFERENCES


Disclosure of Interests: Tim Reynolds: None declared, Emma Dures Grant/research support from: Has previously received an independent learning grant from Pfizer, however the work has been completed and
the grant has been closed, Sue Ashdown: None declared, Peter Cronholm: None declared, Raashid Lugmani Grant/research support from: Roche, Vifor and GSK, Peter Merkel: None declared, Natalya Milman: None declared, Jacqueline Peck: None declared, Joanna Robson: None declared.


AB0608 TOCILIZUMAB TREATMENT FOR LARGE VESSELS

VASCULITIS: REAL LIFE PRELIMINARY EXPERIENCES

giulia righetti, Vincenzo Venerito, Maria Giannotta, Giuseppe Lopato, Margherita Giannini, Fabio Cacciapaglia, Laura Coladonato, Fiorenzo Iannone, Bart Department of Emergency and Organ Transplantations-Rheumatology Unit, Bari, Italy

Background: IL-6 targeting therapy has been proven to be effective and safe in Giant Cell Arteritis (GCA) as well in Takayasu Arteritis (TA) in RCTs, probably because of the similar pathologic findings and vessel size (Large Vessel Vasculitis, LVV). However, real world data are scarce.

Objectives: The aim of the study was to evaluate the effectiveness of Tocilizumab for LVV in real life settings.

Methods: We retrospectively evaluated, from 2011 to 2017, the outcomes (including glucocorticoid dosage) in patients affected by LVV (according to 1990 ACR classification criteria) who received 8 mg/kg iv Tocilizumab (TCZ) monthly, due to the inadequate response to immunosuppressant. Demographic and clinical characteristics and laboratory findings were collected at baseline and consecutive follow up visits, over 52 weeks. Statistical analysis was performed using the GraphPad Software version 6.5 (San Diego CA USA) using appropriate tests.

Results: We analyzed n.10 patients (6/10 GCA, 4/10 TA) with mean age ($\pm$ SD) 56 $\pm$ 21 years and mean disease duration 41.38 months. Eight out of 10 patients were female. Over the entire observation period, 7/10 also received concomitant methotrexate (mean dose 12.8 $\pm$ 2.7 mg/week) while 2/10 received azathioprine (100 mg/day). Median (IQR) prednisone equivalent dose at baseline was 22.5 (10-25) mg/day. At baseline, median ESR was 49 (31-58) mm/h and median CRP level was 15.4 (1.95-28.53) mg/l. Upon TCZ treatment we observed a good disease control in absence of headache, fever and other LVV clinical signs through 52-week follow up. At 52 weeks, we observed a significant reduction of ESR down to 6.5 (2.75-12.25) mm/h as well as of CRP level, down to 1.5 (0.67-3.47) mg/l (p<0.001). A meaningful steroid sparing effect was also achieved as a significant reduction in prednisone dose down to 5 (1.87-6.25) mg/day (p<0.001). During the 52-week follow up period, 3 patients discontinued TCZ treatment for side effects: 1 for severe neutropenia (at 12 weeks), 1 for avascular areas (at 24 weeks), and 1 for diverticulitis (after 52 weeks).

Conclusion: In our real life experience iv TCZ was effective and safe in LVV treatment, with a good disease control and a significant steroid-sparing effect. Our preliminary findings need to be confirmed in larger cohorts and prolonged follow up.

REFERENCES


Disclosure of Interests: giulia righetti: None declared, vincenzo venerito: None declared, maria giannotta: None declared, giuseppe lopato: speakers bureau: SOBI, BMS, margherita giannini: None declared, fabio cacciapaglia: None declared, laura coladonato: None declared, fiorenzo iannone Consultant for: f iannone has received consultancy fees and/or speaker honoraria from pfizer, AbbVie, MSD, BMS, Novartis, Lilly, UCB outside this work, Speakers bureau: f iannone has received consultancy fees and/or speaker honoraria from pfizer, AbbVie, MSD, BMS, Novartis, Lilly, UCB outside this work.


AB0609 NAIFOLD VIDEO CAPILLAROSCOPY AS A POTENTIAL DIAGNOSTIC TOOL IN SYSTEMIC VASCULITIS

1Doron Rimar*, Francesca Ingegnoli1, Ori Rimar1, Ithak Rosner1, Michael Rosenbaum1, Lisa Kaly1, Nina Boullim1, Abid Awisat1, Gleb Stobiomin2, 1Bari-Zion Medical Center, Rheumatology, Haifa, Israel; 2Istituto Gaetano Pini, Division of Clinical Rheumatology, Milano, Italy

Background: Vasculitides are formally classified by artery size: large, medium or small, yet some overlap is evident as in Takayasu, a large vessel vasculitis manifesting also in retinal arterioles. Nailfold videocapillaroscopy (NVC) enables us to inspect changes in microvasculature. Only several small uncontrolled case series of light capillary microscopy in adult patients with vasculitis were reported in the literature, describing avascular areas and microhemorrhages in granulomatosis with polyangiitis (GPA) patients [1-2] and in [4] Behcet disease, and thin and tortuous capillaries in Takayasu arteritis [5].

Objectives: To characterize nailfold capillary changes by NVC in patients with autoimmune vasculitis compared to healthy controls.

Methods: Consecutive autoimmune vasculitis patients fulfilling the ACR criteria and age and gender matched healthy controls were evaluated by NVC using Optilia Mediscope with a magnification of X200. Patients with peripheral artery disease and ischemic heart disease were excluded. Capillaroscopy images were centrally analyzed. NVC was analyzed, noting: architecture, number of capillaries per field, capillary width, capillary morphology, microhemorrhages, peri-capillary stippling (PCS)- hemosiderin deposits probably representing former capillary leak, slow capillary flow (“rolling” or sludging of red blood cells) and avascularity. Continuous data are presented as the mean $\pm$ SD. Categorical variables are presented as frequencies and percentages. Comparisons of continuous variables were made using 2-tailed t-tests and differences between groups by a 1-Way ANOVA.

Results: Seventeen patients with active vasculitis, 8 patients with vasculitides in remission (11 polyarteritis nodosum, 2 GPA, 3 eosinophilic granulomatosis with polyangiitis, 2 microscopic polyangiitis, 2 Takayasu, 3 IgG4 vasculitis (one with cryoglobulinemia), 1 primary central nervous system vasculitis and 1 lupus vasculitis) were compared to 25 age and sex matched healthy controls. The mean age (59 $\pm$18 vs. 51$\pm$19 vs. 52 $\pm$15), and the percent of females (53%, 50%, 60%), were similar across the groups.

Patients with active vasculitis demonstrated higher rate of “rolling”, 74.1% $\pm$27 vs. 12.5% $\pm$22 vs. 6.5% $\pm$12.7, p<0.001; microhemorrhages or PCS 30.1% $\pm$26.4 vs. 1.5% $\pm$4.5 vs. 1.9% $\pm$1, p<0.05, which reversed correspondently with disease duration <6-4, P=0.05, avascular areas 76% $\pm$19.5 vs. 23.4% $\pm$12.8 vs. 26.5% $\pm$22.5 vs. 6% $\pm$10.5, p<0.01. PCS was observed exclusively in 5 of 17 patients with active vasculitis.

Conclusion: Patients with active vasculitis demonstrate capillary abnormalities, namely: “rolling”, microhemorrhages, avascular areas and neangiogenesis. NVC may be a specific sign of active vasculitis. NVC is an easy, readily available additive tool in the management of vasculitis. Further studies are needed to ascertain the role of NVC in vasculitis.

REFERENCES


Disclosure of Interests: None declared.

AB0610 PERSISTENT INFLAMMATION DESPITE TOCILIZUMAB TREATMENT IN 2 PATIENTS WITH LARGE VESSEL VASCULITIS AND AORTIC INVOLVEMENT REQUIREING AORTIC VALVE REPLACEMENT

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Background: Tocilizumab (TCZ) has recently been approved for treatment of giant cell arteritis (GCA). Despite clinical, radiologic and serologic improvement in the majority of patients, it remains unclear whether inflammation of the vascular wall in patients with large vessel vasculitis may persist.

Objectives: To report 2 patients who were treated with TCZ for large vessel vasculitis involving the ascending aorta. The patients underwent aortic valve replacement in both cases and partial replacement of the ascending aortic arch in one case.

Methods: Following therapy with glucocorticosteroids (GC) and TCZ, replacement of the aortic valve and of the partial ascending aorta were performed, followed by a histopathologic examination of the surgical specimen.

Results: We report two female patients, aged 40 and 67 years, both diagnosed with large vessel vasculitis involving the aortic arch. Aortitis of the ascending aorta and significant aortic insufficiency were demonstrated in both patients by PET-CT, MR angiography and transesophageal cardiac ultrasound.

In Pat 1, PET CT and MR angiography revealed vascular inflammation. Intravenous pulse GC was initiated, followed by oral prednisone with stepwise tapering and TCZ iv 8mg/kg/month. Two weeks after the 2nd infusion of TCZ, MR angiography showed significant reduction of gadolinium enhancement in the wall of the ascending aorta and the patient subsequently underwent valve replacement. Pat 2 was diagnosed with vasculitis of the aortic arch by MR angiography. Therapy with oral GC (1mg prednisone/kg) and methotrexate was initiated. After 12 months, the treatment was switched to TCZ 162mg sc once weekly because of inadequate control of disease. The patient was monitored clinically and by PET CT and GCA was considered well controlled over 4 years. Due to continuous enlargement of the ascending aorta resulting in significant aortic insufficiency, the patient underwent replacement of the aortic valve and the ascending aorta.

Both patients showed normalization of CRP and ESR during TCZ treatment.

In summary, despite PET-CT and MR angiography showing reduction in vascular wall inflammation before surgery and CRP and ESR normalized, both patients showed histologically persistent lymphoplasmacellular infiltrates (predominantly CD3+CD4+ T cells in patient 1) and, in addition, giant cells in pat 2.

Conclusion: Despite adequate control of large vessel vasculitis involving the ascending aorta clinically as well as by imaging, the 2 patients reported here had to undergo valve replacement which showed persistent inflammation of the aortic wall despite treatment with TCZ.

Disclosure of Interests: Andrea Rubbert-Roth Consultant for: Chugui, Eli Lilly, Roche, and Sanofi, Speakers bureau: AbbVie, Bristol-Myers Squibb, Chugai, Hexal/Novartis, Janssen, Eli Lilly, Merck Sharp & Dohme, Pfizer, Roche, and Sanofi, Thomas Langenegger: None declared, Peter Karl Bode: None declared, Claudia Plofe: None declared, Olaf Chan-Hi Kim: None declared, Johannes von Kempten: None declared


AB0611 A NEW SHAPE OF THE TREATMENT OF VASCULITIDES: SINGLE CENTER BIOLOGICAL AGENTS EXPERIENCE

Faith Aboyar, Mehmet Emin Derin, Burak Karakaş, Ali Sabir, Sivas Cumhuriyet University, sivas, Turkey

Background: Vasculitides are a group of inflammatory diseases with different clinical and pathological features of vital importance in various sized and types which may lead to organ failure and inflammation of the vascular wall. The framework for the treatment of vasculitis is similar to that used for many other systemic autoimmune rheumatic disorders, while the specific therapeutic regimen depends upon the nature and severity of the particular disorder (1,2).

Objectives: The aim of this study is to evaluate the efficacy of biological agents in 56 vasculitides patients with resistant/intolerated to cDMARDs.

Methods: Between January 2015 and December 2018, fifty six patients who were diagnosed as vasculitis (Takayasu arteritis-TA, Granulomatosis with polyangiitis(GPA), Giant cell arteritis (GCA) and Behçet Syndrome (BS) at Sivas Cumhuriyet University Medical Faculty Rheumatology-Internal Medicine Department were included in to the study.

Results: 24 (43%) male and 32 (57%) female were included in the study. The median age of the patients was 56 years (min:19-max: 77) and the median age at diagnosis was 39 years (min 17-max 73). 14 (25%) patients with TA, 22 (39%) patients with GPA, 3 (5%) patients with GCA and 17 (31%) patients with BS included in this study. Tocilizumab treatment was used 6 of 8 patients who were resistant to anti-TNF. In 22 GPA patients with pulmonary and kidney involvement, Rituximab (RTX) treatment was started in 18 patients who were unresponsive to cDMARD and cyclophosphamide therapy. Plasmaexchange were used in 4 (18%) patients with alveolar hemorrhage. Indication of anti-TNF agents in behçet’s syndrome were confirmed 5 cases panuveitis 70%, neuro-behçet 17.5% and vessel involvement 12.5% (Table 1). 1 GPA patient was died and other GPA, TA and BS patients have clinically response. Biological treatment is continued as maintenance therapy.

Conclusion: Biological treatments were used safely and effectively in vasculitis. In particular, RTX treatment is recommended for both induction and maintenance of GPA. Tocilizumab treatment is very effective in TA and GCA. However, large and long-term studies are needed in terms of long-term effects.

REFERENCES

Abstract AB0611 Table 1: Clinical Features Of Patients And Treatment Modalities

<table>
<thead>
<tr>
<th>n</th>
<th>Clinical features</th>
<th>cDMARDs</th>
<th>Anti-TNF</th>
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<tr>
<td>14</td>
<td>Takayasu</td>
<td>14 (25%)</td>
<td>6 (43%)</td>
</tr>
<tr>
<td>22</td>
<td>GPA</td>
<td>22 (39%)</td>
<td>4 (18%)</td>
</tr>
<tr>
<td>17</td>
<td>Behçet</td>
<td>17</td>
<td>2 (66%)</td>
</tr>
<tr>
<td>3</td>
<td>GCA</td>
<td>3 (5%)</td>
<td>1 (33%)</td>
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Disclosure of Interests: None declared


AB0612 TEMPORAL ARTERY BIOSPY IN GIAN TCELL ARTERITIS. INTERRELATION OF INFLAMMATORY PATTERNS WITH ANALYTICAL DATA AND CLINICAL MANIFESTATIONS

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Background: Giant cell arteritis (GCA) is a systemic vasculitis that affects large and medium vessels, mainly the temporal artery and other arteres of extracranial localization (1).

Objectives: A series of 24 patients with clinical suspicion of GCA proved by a positive temporal artery biopsy (TAB) has been reviewed. Our aim was to assess a) histologic inflammatory patterns in the TAB and b) their possible correlation with analytical and clinical data.

Methods: Prospective study of 24 patients with positive TAB between January of 2016 until January of 2018. Clinical data, included: age, sex, symptoms (cranial, visual or systemic manifestations) and physical examination of the temporal artery. The analytical data registered were: ESR, CRP and haemoglobin. Furthermore, it has been considered if patients were receiving treatment with corticosteroids at the time of the biopsy.

Positive biopsies were classified into four categories: a) inflammation limited exclusively to the small vessels of the adventitia (SVV); b) vasa
vasorum vasculitis (VVV); c) inflammation limited to the adventitia (ILA); and d) transmural inflammation (TMI). The presence of giant cells, thrombosis and distrophic calcification was also noted.

**Results:** We included a total of 24 patients with positive TAB: a) 19 patients (79.16%) presented TMI and b) 5 patients (20.84%) presented ILA. There were no cases with SVV or VVV.

No significant differences at baseline were observed between the 2 groups regarding sex and age, with a mean of 79.6 ± 7.2 years in TMI group and 79.8 ± 7.3 years in ILA group (p = 0.83).

There were no significant differences between the two groups were found in terms of treatment duration prior to BAT and nor in the dose (Prednisone). No significant differences between the two groups with ILA (80%) were receiving treatment with oral glucocorticoid patients in the group with TMI (84.2%) and 4 (of 5) patients in the group and 78.8 ± 7.3 years in ILA group (p = 0.83).

Conclusion: In our sample, we didn’t observe differences between the patterns of inflammation and the analytical and clinical data. It is important to recognise these patterns of inflammation in the TAB to avoid false negatives.

**REFERENCES**


**Disclosure of Interests:** Lara Sánchez Bilbao: None declared, Íñigo González-Mazoín: None declared, D. Prieto-Pería: None declared, Monica Calderón-Goercke: None declared, José Luis Martín-Vallés: None declared, Belén Almenar-Mateo: None declared, C. González-Vela: None declared, Silvia Sartorelli, Corrado Campochiaro, Alessandro Tomelleri, Elena Baldissera, Lorenzo Dagna. IRCCS San Raffaele Hospital, Unit of Immunology, Rheumatology, Allergy and Rare Diseases, Milan, Italy

**Background:** Takayasu arteritis (TA) is a large-vessel vasculitis usually affecting young women. The age of onset is though variable. Controversial data are reported about differences in disease features according to the age of onset.

**Objectives:** To compare clinical and vascular TA features according to TA age of onset.

**Methods:** We retrospectively evaluated onset demographic and disease features in TA patients followed-up at our Hospital between January 2000 and August 2018. We divided our cohort into 3 groups according to the age of onset: ≤20 (Group 1), 21-40 (Group 2), >40 (Group 3) years.

Diagnostic delay (DD) was defined as the time interval between the first TA symptom and TA diagnosis. Non parametric statistic tests were used.

**Results:** 126 patients (12 male, 114 female) were analyzed. Mean age at onset was 31.46±13.38 years. Group 1 and 3 included 30 (23.81%) patients each, Group 2 66 (52.38%). Mean age at diagnosis was 16.23±13.20 years in Group 1, 29.59±5.80 in Group 2 and 50.87±16 in Group 3. Mean DD was different between the 3 groups: 117.63±79.79 months in Group 1, 56.47±76.98 in Group 2 and 30.68±45.93 in Group 3 (Group 1 vs 2, p=0.021; Group 1 vs 3, p=0.001; Group 2 vs 3, p=0.089). Clinical and laboratory features at TA onset are summarized in Table 1. Among all disease features only arterial hypertension was statistically more prevalent in Group 3 vs Group 1 and 2 (56.67% vs 36.67% and 30.30% respectively, p=0.048). When evaluating vascular involvement, abdominal aorta was more frequently affected in Group 1 (63.33% vs 34.85% and 56.67%, p=0.018) while right iliac and left iliac arteries in Group 3 (40% vs 23.33% and 10.61%, p=0.004; 36.67% vs 23.33% and 12.12%, p=0.024 respectively).

**Abstract AB0613 Table 1**

<table>
<thead>
<tr>
<th>Clinical and laboratory features</th>
<th>Group 1 n (%)</th>
<th>Group 2 n (%)</th>
<th>Group 3 n (%)</th>
<th>p-value</th>
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<tr>
<td><strong>Symptoms</strong></td>
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<tr>
<td>Systemic symptoms</td>
<td>21 (70)</td>
<td>37 (56.06)</td>
<td>15 (50)</td>
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<tr>
<td>Cardiodynia</td>
<td>11 (36.67)</td>
<td>12 (18.18)</td>
<td>5 (16.67)</td>
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<td>Lower extremities claudication</td>
<td>7 (23.33)</td>
<td>18 (27.27)</td>
<td>4 (13.33)</td>
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<td>Upper extremities claudication</td>
<td>10 (33.33)</td>
<td>31 (46.97)</td>
<td>7 (23.33)</td>
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<td>S blood pressure</td>
<td>10 (33.33)</td>
<td>16 (24.24)</td>
<td>6 (20)</td>
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<td>Reduced/absent pulse</td>
<td>18 (60)</td>
<td>29 (43.94)</td>
<td>11 (36.67)</td>
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<tr>
<td>Bruits</td>
<td>15 (50)</td>
<td>20 (30.30)</td>
<td>8 (26.67)</td>
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<tr>
<td>Angina abdominal</td>
<td>6 (20)</td>
<td>6 (9.09)</td>
<td>3 (10)</td>
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<td>Myocardial infarction</td>
<td>0</td>
<td>5 (7.58)</td>
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<td>Arterial hypertension</td>
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<td>20 (30.30)</td>
<td>17 (56.67)</td>
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<td>Headache</td>
<td>15 (33.33)</td>
<td>19 (36.67)</td>
<td>8 (26.67)</td>
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<td>Syncope</td>
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<td>9 (13.64)</td>
<td>6 (20)</td>
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<td>2 (6.67)</td>
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<td>Amaurosis</td>
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**Abstract AB0613 Table 2**

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<th>Artery</th>
<th>Group 1 n (%)</th>
<th>Group 2 n (%)</th>
<th>Group 3 n (%)</th>
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<tr>
<td>Coronary</td>
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<td>7 (10.61)</td>
<td>4 (13.33)</td>
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<td>Pulmonary</td>
<td>5 (16.67)</td>
<td>12 (18.18)</td>
<td>1 (3.33)</td>
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</tr>
<tr>
<td>R subclavian</td>
<td>14 (46.67)</td>
<td>32 (48.48)</td>
<td>17 (56.67)</td>
<td>0.711</td>
</tr>
<tr>
<td>L subclavian</td>
<td>18 (60)</td>
<td>23 (34.85)</td>
<td>16 (53.33)</td>
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<td>L CC</td>
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<tr>
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<td>12 (18.18)</td>
<td>6 (20)</td>
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<td>6 (20)</td>
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<td>Abdominal aorti</td>
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<td>23 (34.85)</td>
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<td>7 (23.33)</td>
<td>23 (34.85)</td>
<td>12 (40)</td>
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<td>L iliac</td>
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<td>L iliac</td>
<td>7 (23.33)</td>
<td>7 (10.61)</td>
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<td>0.054*</td>
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<td>R iliac</td>
<td>7 (23.33)</td>
<td>8 (12.12)</td>
<td>11 (36.67)</td>
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**Abbreviations:** right (R), left (L), common carotid (CC), aorta (ao)
Conclusion: TA patients <20 years might experience a longer DD. Arterial hypertension seems to be a prevalent feature in TA patients >40 years. Vascular involvement seems also be influenced by the age of onset with the abdominal aorta being more frequently affected in younger patients and iliac arteries in older patients.

Disclosure of Interests: None declared


AB0615 PREVALENCE OF DEPRESSION, ANXIETY, FATIGUE AND SLEEP DISTURBANCES IN PATIENTS OF RA, SLE AND GPA

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Background: The relative frequencies of co-morbidities like depression, anxiety, fatigue and sleep disturbance in RA, SLE and GPA are not fully elucidated.

Objectives: To estimate and correlate the prevalence of depression, anxiety, fatigue and sleep disturbances in patients with RA, SLE and GPA by using time honored scales and PROMIS-HAQ.

Methods: This was a cross sectional study of 183 patients (RA – 57, SLE – 64, GPA – 62). Diagnosis and assessment of depression, anxiety, fatigue was established by patient health questionnaire 9 (PHQ 9). Epworth sleepiness scale (ESS), generalized anxiety disorder assessment scale 7 (GAD 7) and fatigue severity scale (FSS) respectively. PROMIS-HAQ short form 8a was also used to diagnose depression, anxiety, fatigue and its correlation with the above time honored scales was studied.

Results: Mean age of RA, SLE and GPA patients was 45.5 ± 12, 31 ± 9.5 and 42.7 ± 13.5 years respectively. Mean disease duration was 5.7 ± 5.1, 3.3 ± 2.4 and 4.6 ± 4 years in RA, SLE and GPA respectively. Prevalence of depression, anxiety, fatigue, insomnia in RA, SLE and GPA as per standard scales and PROMIS-HAQ is depicted in table 1. The correlation between the standard scales and PROMIS-HAQ for depression [RA (r = .816, p < .001], SLE (r = 0.625, p < 0.001), GPA (r = .772, p < .001)], anxiety [RA (r = .804, P < .001), SLE (r = .799, p<0.001), GPA (0.888, p<0.001)], sleep disturbance [RA (r = .872, p<0.001), SLE (r = .784, p < .001), GPA (r=0.917, p < .001)] and fatigue [RA (r = .815, p < .001), SLE (r = 0.798, p < 0.001), GPA (r=0.805, p <0.001)] was significant.

Table 1. Prevalence of depression, anxiety, fatigue and insomnia by various scales

<table>
<thead>
<tr>
<th>Depression</th>
<th>Anxiety</th>
<th>Fatigue</th>
<th>Sleep/Insomnia</th>
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<td>PHQ9 PROMIS</td>
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<td>PROMIS</td>
<td>ESS</td>
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<td>RA</td>
<td>49.2%</td>
<td>35.1%</td>
<td>45.6%</td>
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<tr>
<td>SLE</td>
<td>60.9%</td>
<td>43.7%</td>
<td>51.6%</td>
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<tr>
<td>GPA</td>
<td>46.8%</td>
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</table>

Conclusion: Depression, anxiety, fatigue and sleep disturbance are common in RA, SLE and GPA. PROMIS-HAQ has good correlation with time honored scales for assessment of depression, anxiety, fatigue and sleep disturbance in these disorders.

REFERENCES


Disclosure of Interests: None declared


AB0616 HISPANIC AMERICAN PATIENTS WITH ANCA ASSOCIATED VASCULITIS AND DIFFUSE ALVEOLAR HEMORRHAGE RESPOND COMPARABLY TO INDUCTION TREATMENT

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Background: Hispanic American patients with ANCA-associated vasculitis (AAV) have been reported to have more severe disease and higher

Disclosure of Interests: None declared

damage indices at presentation. One rare but life-threatening complication of AAV is diffuse alveolar hemorrhage (DAH).

**Objectives:** To study the clinical features, course and response to therapy in Hispanic American patients with AAV and DAH seen at a large public teaching hospital that serves medically underserved and low income patients with chronic poor health maintenance.

**Methods:** Among 60 Hispanic American patients with AAV, we retrospectively studied 13 patients with DAH from 2003-2017. Clinical features, laboratory results, diagnostic modalities and treatments given were studied.

**Results:** A total of 13 patients were identified; 6 men and 7 women, mean age of 51±11 years. Anti-PR3 was found in 5 patients, anti-MPO in 8. Nine patients were diagnosed with microscopic polyangiitis and 4 with granulomatous polyangiitis based on ACR criteria or Chapel Hill Consensus Conference definitions. DAH was a presenting manifestation in 12 patients. Gross hemoptysis with hypoxia, drop in hematocrit and chest X-ray infiltrates were seen in all patients diagnosed with DAH. Bronchoscopy with BAL washings confirming diagnosis was done in 10 patients. All patients had multi-organ involvement including nephritis (n=8), peripheral neuropathy (n=1), palpable purpura (n=2), upper respiratory tract involvement (n=4) and eye involvement (n=2). Serum C3 was normal in 12 patients. Renal biopsy in 9 patients showed pauci-immune crescentic glomerulonephritis. Mean BVAS at time of DAH was 21.2±5.1.

All patients underwent induction-remission therapy with pulse methylprednisolone followed by tapering oral prednisone. Induction therapy included IV cyclophosphamide (n=6), rituximab (n=6) and IV cyclophosphamide/rituximab combination therapy (n=1). Nine patients underwent plasma exchange and 5 received IV gamma globulin. Eleven patients required mechanical ventilation; 6 patients needed hemodialysis, 2 temporarily. All 13 patients responded to induction therapy; mean post-induction therapy BVAS was 9.3±3.5. Pulmonary fibrosis after DAH was noted in 2 patients. No early deaths (<6 months) were observed, however 1 patient died within 3 years due to infection. Mean follow-up period was 69±54 months. Maintenance therapy used included prednisone (n=13), mycophenolate mofetil (n=2), azathioprine (n=6) and IV rituximab (n=8). Five patients had clinical relapse, 3 with recurrent DAH. Two patients had minor relapse, defined by their treating physician as requiring increased prednison dose or worsening proteinuria. Mean BVAS at relapse was 15.2±5.5.

**Conclusion:** This first in-depth study of DAH in Hispanic American AAV patients shows that in this socioeconomically disadvantaged patient population, the response to induction therapy is not significantly different from other ethnic groups reported in the literature. DAH remains a severe clinical manifestation of AAV and should be recognized without delay. If treated promptly following EULAR/ERA-EDTA recommendations, good short term response is to be expected.

**REFERENCES**


**Disclosure of Interests:** None declared.

**DOI:** 10.1136/annrheumdis-2019-eular.444

**AB0617**  
**CUTANEOUS POLYARTERITIS NODOSA TREATMENT: A RETROSPECTIVE CASE SERIES**

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1EULAR/ERA-EDTA recommendations, 2University of British Columbia, Internal Medicine, Vancouver, Canada; 3Arthritis Research Canada, Richmond, Canada; 4University of British Columbia, Vancouver, Canada; 5University of British Columbia, Dermatology, Vancouver, Canada; 6University of British Columbia, Pathology, Vancouver, Canada.

**Background:** Cutaneous polyarteritis nodosa (CPAN) is a small-to-medium vessel vasculitis limited to the skin. As it is a rare condition, there is little data available to guide treatment. Previous articles have suggested that colchicine and dapsone be used in mild disease and glucocorticoids in acute flares, with DMRADs such as methotrexate or azathioprine being reserved for moderate to severe disease, or steroid-refractory disease.

**Objectives:** Our objective was to review therapeutic regimens used to treat CPAN and to evaluate patient response.

**Methods:** A retrospective chart review including records from January 2003 to June 2017 was performed to identify patients with both histologic and clinical features of CPAN. We extracted information regarding patient age, clinical presentation, biopsy results, and response to treatment.

**Results:** Thirteen patients were identified who had clinical features of CPAN that were supported by histologic findings on biopsy. The majority of patients were female (92.3%). The average age at diagnosis was 44.9 years and mean duration of follow up was 53 months. All patients had involvement of the lower limbs with the most common cutaneous manifestation being subcutaneous nodules (92.3%), followed by papules (46.2%) and livedo reticularis (30.8%). Eight out of thirteen patients (61.5%) received steroids and three did not experience clinical benefit. Another patient did not respond to prednisone and hydroxychloroquine, but had significant improvement of her symptoms on prednisone and methotrexate. Seven out of nine patients (77.8%) who were treated with methotrexate had a favourable response. Three of those patients responded to methotrexate after failing other therapies such as dapsone, azathioprine, and prednisone.

**Conclusion:** In this case series, we found that most patients had a favorable response to methotrexate and thus the role of methotrexate in treating CPAN merits further investigation. As CPAN often has a chronic relapsing and remitting course, initiating methotrexate at the same time as steroid therapy may lower overall lifetime exposure to steroids.

**REFERENCES**


**Disclosure of Interests:** None declared.

**DOI:** 10.1136/annrheumdis-2019-eular.6353

**AB0618**  
**A SNAPSHOT OF DISEASE ACTIVITY IN PATIENTS WITH BEHÇET’S SYNDROME: PREDICTIVE FACTORS AND RELATIONSHIP WITH QUALITY OF LIFE**

Rosaria Talarico, Alice Parma, Eralda Zera, Emanuele Calabresi, Chiara Tani, Chiara Baldini, Marta Mosca. Rheumatology Unit, Clinical and Experimental Medicine, Pisa, Italy.

**Background:** Behçet’s Syndrome (BS) is globally characterized by a variable spectrum of disease profile: while prevalent mucocutaneous lesions and arthritis represent the only clinical features in patients with a benign disease subset, there are other patients who develop potentially sight or life-threatening manifestations, due to ocular, neurological or major vascular involvement. Beside the organ involvement, demographic factors could considerably influence the long-term and short-term outcomes of BS.

**Objectives:** The primary aim of the study was to evaluate disease activity in a cohort of BS patients consecutively followed in a BS clinic of a tertiary centre; the secondary aims were to identify potential predictive factors of disease activity and to compare disease activity with quality of life.

**Methods:** One-hundred and thirty patients (71 males and 59 females; mean age 42±8 years, mean disease duration 11±4) with a diagnosis of BS according to the ISG criteria were studied. Disease activity has been evaluated by BDCAF and quality of life by the Short Form (SF) 36. Patients were also categorized in major or minor involvement of BS according or not to the presence of ocular, neurological and vascular involvement in the course of disease. Predictors of long-term outcome were identified by univariate analysis using the log-rank test and by multivariate analysis using Cox proportional hazards regression models.
FAMILY MEMBERS WITH BS MAY NOT CLUSTER IN SIMILAR CLINICAL CHARACTERISTICS

Mulanur Özkorkmaz1,2, Mehmet Engin Tercan, Nasrin Şen, Sibel Yılmaz-Oner, Özcan Keskin1. Karşı Dağlıktar, Kütahya Dumlupınar University, Kütahya, Turkey; 2Kartal Dr. Lutfi Kirdar Training and Research Hospital, Internal Medicine, Istanbul, Turkey; 3Kartal Dr. Lutfi Kirdar Training and Research Hospital, Rheumatology, Istanbul, Turkey

Background: Both genetic and environmental factors may have roles in the pathogenesis of Behcet’s Syndrome (BS). Likewise, occurrence of different clinical cluster of BS may be also influenced by the combination of these two factors. But we do not know the weight of the factors during the emergence of the disease and clinical clusters.

Objectives: We conducted a study for evaluating the frequency of family history for BS in different clinical BS clusters. Furthermore, we assessed the hypothesis that BS patient in the same family generally accumulate in the similar clinical cluster.

Methods: Eighty-five patients and their relatives in our BS cohort were participated to the study. We used International Study Group Criteria for Behcet Disease (ISBD) criteria (1) for classifying our index patients and their first and second degree relatives as BS. We sub-classified BS patient to mucocutaneous, vascular, acne-arthritis-enthesis, eye, neurologic, intestinal and undetermined clusters (2). Firstly, we re-evaluated the family history of our BS patients. Then, the relatives of the patients with already known BS or with having symptoms related with BS were interviewed with phone. All participants have been informed about the study and we have taken consent from them.

Results: Twenty-two (25.9%) of the patients had first or second degree relatives with BS. Furthermore, 27 (31.8%) of our patient were classified to mucocutaneous cluster. In our study, the BS patient with enthesitis-arthritis-acne cluster had highest frequency (44.4%) of family history. However, there was no apparent accumulation of similar findings in index BS cases and their close relatives (Table).

Conclusion: According to result of these studies, there was no finding that supports the hypothesis “BS patients in the same family generally accumulate in the similar clinical cluster”. Still genetic may have major role in the emerging of the BS, such as it is accepted as a member of a group of diseases called MHC-I-opathy (3). However, like most of the diseases, genetic background is not enough for the expression of full-blown disease. Briefly, even in the similar genetic background, multiple and separate hits of environmental or non-genetic factors may take role in the pathogenesis.

REFERENCES
Conclusion: Our data confirm TCZ is highly effective in GCA treatment and has a significant steroid-sparing effect. In our real-life retrospective study, TCZ was also shown to be a safe option in patients with relapsing or refractory GCA.

REFERENCES


Table 1: TAB, temporal artery biopsy; PMR, polymyalgia rheumatica; GC, glucocorticoids; PET, positron emission tomography; MRA, magnetic resonance angiography.

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TOTAL 13/10 21 20 34 20 14 28 13 39

Disclosure of Interests: Alessandro Tomelleri: None declared, Corrado Campochiaro: Consultant for: Dr Corrado Campochiaro received consultation honoraria from Pfizer., Silvia Sartorelli: None declared, adriana carriddi: None declared, Elena Baldissera: Consultant for: Consultation honoraria from Novartis and Rottapharm, Speakers bureau: Pfeizer, Sobi, Novartis, Lorenzo Dagna Consultant for: Prof Lorenzo Dagna received consultation honoraria from Abbvie, Amgen, Biogen, Bristol-Myers Squibb, Celltrion, Novartis, Pfizer, Sanofi-Genzyme, and SOBI.


GENDER DIFFERENCES IN CLINICAL PRESENTATION AND VASCULAR PATTERN IN PATIENTS WITH TAKAYASU ARTERITIS

Alessandro Tomelleri, Corrado Campochiaro, Silvia Sartorelli, Giulio Cavalli, Giacomo De Luca, Elena Baldissera, Lorenzo Dagna. San Raffaele Hospital, Milan, Italy

Background: Takayasu arteritis (TAK) is a chronic large-vessel vasculitis that predominantly affects aorta and its major branches. Although it is more commonly observed in Asian population, it can occur worldwide. TAK affects more frequently women in their second and third decades of life, but occurrence in patients older than 40 years is not rare. Female to male ratio is commonly reported as 9:1.

Objectives: To compare clinical characteristics and pattern of vascular involvement at disease onset according to gender specificity in patients affected by TAK.

Methods: Data from 117 TAK patients (11 male, 106 female) diagnosed according to the ACR criteria from our Centre were retrospectively collected. Differences between men and women with regard to demographic features, diagnostic delay, signs and symptoms attributed to TAK, and arteries involved at diagnosis were compared. Data from 3 published
articles describing sex differences in TAK patients were obtained. A global analysis of these 3 cohorts plus ours (for a total of 578 patients, 108 men and 470 women) was performed. Results: In our TAK cohort, age at disease onset and age at diagnosis were not significantly different between men and women. Diagnostic delay was slightly higher in men. Male patients showed higher involvement of iliac arteries (right, p=0.016; left, p=0.021); female patients suffered more frequently from upper limbs claudication (p=0.026). In the overall analysis, men had higher prevalence of arterial hypertension (p=0.007) and more frequent involvement of abdominal aorta (p=0.026), renal arteries (right, p=0.001; left, p=0.001) and iliac arteries (right, p=0.009; left, p=0.002). Women more frequently exhibited upper limb claudication (p=0.042) and involvement of left subclavian artery (p=0.005), carotid arteries (right, p<0.001; left, p=0.001) and supradiaphragmatic aorta (ascending, p=0.050; arch, p=0.001; descending, p=0.003). Inflammatory markers were more frequently raised in women (p=0.005).

Conclusion: In TAK patients, gender has a strong influence on pattern of vascular involvement and consequently on clinical presentation. Specifically, women have higher involvement of the supradiaphragmatic vessels, whereas in men the abdominal vessels are more frequently affected.

REFERENCES

Figure 1. Vessels affected at disease onset in 578 patients with TAK (108 male, 470 female) from 4 different cohorts, according to gender. Red: higher involvement in women, with statistical significance. Blue: higher involvement in men, with statistical significance. Yellow: no statistically significant difference between women and men.

Disclosure of Interests: Alessandro Tomelleri: None declared, Corrado Campochiaro Consultant for: Dr Corrado Campochiaro received consultation honoraria from Pfizer., Silvia Sartorelli: None declared, Giulio Cavalli Consultant for: Dr Giulio Cavalli received consultation honoraria from Pfizer, Novartis and SOBI., Giacomo De Luca Speakers bureau: Pfizer, Sobi, Elena Baldissera Consultant for: Consultation honoraria from Novartis and Rottapharm, Speakers bureau: Pfizer, Sobi, Novartis, Lorenzo Dagna Consultant for: Prof Lorenzo Dagna received consultation honoraria from Abbvie, Amgen, Biogen, Bristol-Myers Squibb, Celtrion, Novartis, Pfizer, Sanofi-Genzyme, and SOBI. DO: 10.1136/annrheumdis-2019-eular.2407

AB0622 THE EFFICACY OF ADDITIONAL TOCILIZUMAB IN PATIENTS WITH SEVERE POLYMYALGIA RHEUMATICA WHO WERE RESISTANT TO OR INTOLERANT OF CONVENTIONAL THERAPY
Aliko Ueno, Kei Hirose, Manami Hirota, Yuiko Yamamura, Masahiro Yamamura, Okuyama Saiseikai General Hospital, Okayama, Japan

Background: Polymyalgia rheumatica (PMR) is the most common inflammatory disease in the elderly. The 2015 EULAR/ACR recommendations indicate that the management of PMR should be started with glucocorticoids (GCs) and if needed, followed by addition of methotrexate (MTX). The anti-interleukin-6 (IL-6) receptor antibody, tocilizumab (TCZ), has been shown to be effective for PMR.

Objectives: To determine the efficacy and safety of TCZ in patients with refractory PMR who were resistant to or intolerant of GCs plus MTX and characterize the clinical profile of patients who need TCZ.

Methods: Patients were diagnosed with PMR by the 2012 EULAR/ACR provisional classification criteria and treated according to the 2015 ACR/EULAR recommendations for the management of PMR. TCZ was further added to the patients who were GC plus MTX (GC/MTX-resistant or -intolerant). The efficacy of treatment was determined by measuring the disease activity with PMR activity score (PMR-AS). We statistically analyzed the differences in clinical indicators between GC-responders, GC/MTX-responders, and GC/MTX-non-responders who need TCZ therapy.

Results: Ninety-three patients (53 females and 40 males) were the average age of 72.1 ± 9.4 years old, serum CRP 63 ± 42 mg/L, ESR 84 ± 34 mm/hr and blood platelet counts 331 ± 86 ×10^9/L, at the first visit, and had been followed up for 25.4±19.6 months. All of them were treated first with prednisolone (PSL) (15.7± 4.3 mg/day). Relapses occurred in 43 patients (46.2%), at the PSL dose of 6.0 ± 5.6 mg/day, after 8.8 ± 6.7 month-GC treatment. GC was increased in 7 patients, and MTX (8.6 ± 2.9 mg/week) was added in 36 patients. Thirteen patients successfully discontinued GC, while 23 patients (24.7%) were resistant to or intolerant of GC/MTX. Ten of 23 patients agreed with TCZ therapy. Before TCZ addition, they were treated with PSL of 6.0 ± 2.9 mg/day plus MTX of 6.0 ± 3.8 mg/week, and serum CRP 9.7 ± 9 mg/L, blood platelet counts 271 ± 32 ×10^9/L and PMS-AR 15.5 ± 13.5. After 7.3 ± 4.2 month-TCZ treatment, PSL and MTX were reduced to 1.3 ± 1.6 mg/day and 2.2 ± 3.0 mg/week, and CRP, blood platelet counts and PMS-AR decreased to <0.2 mg/L, 191 ± 28 ×10^9/L and 5.7 ± 8.3, respectively. GC could be withdrawn in 7 patients, and 4 patients reached drug-free remission. There were significant differences in blood platelet counts and the initial PSL amount between GC/MTX responders and GC/MTX-resistant patients (p<0.05; Mann-Whitney U test).

Conclusion: TCZ may provide a therapeutic option for patients with refractory PMR who were resistant to or intolerant of GC/MTX. Our retrospective results suggest that patients with severe PMR, who show thrombocytosis and need high dose GC for initial therapy, may be considered for early induction of TCZ.

Disclosure of Interests: None declared

AB0623 ANTI-NEUTROPHIL CYTOPLASMIC ANTIBODY-ASSOCIATED VASCULITIS AND RISK OF CEREBROVASCULAR ACCIDENT: A SYSTEMATIC REVIEW AND META-ANALYSIS

1Pairompong Unprasert, 2Kam Wijjanapeecha, 3Wrist Cheungponsiri, 1Faculty of Medicine Siriraj Hospital, Mahidol University, Clinical epidemiology unit, Bangkok, Thailand. 2Mayo Clinic Florida, Jacksonville, United States of America. 3University of Mississippi Medical Center, Jackson, United States of America.

Background: An increased risk of cardiovascular disease, including cerebrovascular accident (CVA), among patients with chronic inflammatory immune-mediated disorders is well-recognized, especially among patients with rheumatoid arthritis and systemic lupus erythematosus [1]. Patients with anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV) may
be at an increased risk of CVA as well although the data are still inconclusive as most studies addressing this association were small in size.

**Objectives:** The current systematic review and meta-analysis was conducted with the aims to comprehensively identify all relevant studies and summarize their results together to better characterize the risk of CVA among patients with AAV.

**Methods:** Two investigators independently searched for published studies indexed in MEDLINE and EMBASE database from inception to October 2018 using the search strategy that included the terms for anti-neutrophil cytoplasmic antibody-associated vasculitis and cerebrovascular accident. Eligible studies must be cohort studies (either retrospective or prospective) that compared the risk of incident CVA between patients with AAV and individuals without AAV. They must also report the relative risk or hazard ratio with 95% confidence interval (CI) of this comparison. Point estimates and standard errors from each study were extracted and combined together using the random effect, generic inverse variance technique of DerSimonian and Laird.

**Results:** A total of 5 studies fulfilled the inclusion criteria and were included in this meta-analysis. The risk of incident CVA among patients with AAV was significantly higher than that of individuals without AAV with the pooled risk ratio of 1.49 (95% CI, 1.06–2.01). The statistical heterogeneity was insignificant with an I² of 11%. The forest plot of this meta-analysis is shown as figure 1. The funnel plot of this study was relatively symmetric and did not suggest the presence of publication bias.

**Conclusion:** A significantly increased risk of CVA among patients with AAV was demonstrated by this meta-analysis. Physicians who take care of patients with AAV should be aware of this risk and focus on interventions to modify other conventional risk factors for CVA may be warranted.

**REFERENCES**


Figure 1. Forest plot of the studies on risk of incident CVA among patients with AAV

Disclosure of Interests: None declared


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**AB0624 SAFETY OF RITUXIMAB BIOSIMILAR FOR THE TREATMENT OF CYTOGLOBULINEMIC VASCULITIS**

Caterina Vaciut1, Marcello Visentin2, Maria Di Cicco2, Francesca Angelotti3, Gianfranco Lajella4, Andrea Manfredi4, Davide Felippini5, Antonio Tavoni5, Milvia Casato5, Laura Castelnovo6, Giuseppe Morl7, Maurizio Pietrogrande8, Gianfranco Lauletta5, Andreina Manfredi1, Davide Filippini3, Antonio Tavoni4, Caterina Vacchi1, Marcella Visentini2, Maria DI Cicco 3, Francesca Angelotti4, san Sebastian, Spain

**Background:** Rituiximab (RTX) represents a treatment in the mixture of cyroglogolinemic vasculitis (MCV). Despite usually well-tolerated, RTX may induce different types of adverse drug reactions, including exacerbation of vasculitis. RTX biosimilars have been recently approved in Europe in the treatment of rheumatoid arthritis, but no data are available about effectiveness and safety of RTX biosimilars in the treatment of MCV.

**Objectives** Aim of the study was to analyse the safety of RTX biosimilar in patients with MCV treated in first-line or after a shift by RTX originator.

**Methods** In a multicenter, prospective, open-label study, we enrolled all MCV patients who treated with RTX originator, either de novo or after a shift by RTX originator. Nineteen consecutive MCV patients (F/M 13/6, mean age 68.3±11.5 months, mean disease duration 94±86 months, 10/19 HCV+ and 6/19 HBV+) were treated with RTX in a six-month period (July-December, 2019). Nine patients were treated with RTX for the first time, while the other 9 patients have already treated with RTX originator and were switched to RTX biosimilar. Twelve patients received a dose of 250 mg/m² of RTX every other week, while 6 were treated with 1 gram of RTX every other week.

**Results** During a month-period after the last infusion, 5 adverse events (AE) were observed, namely 2 vasculitis flares, and 1 urtica, atrial fibrillation occurred during infusion, and 2 episodes of BD were recorded. Three of 5 AE were observed in patients treated with the higher dose of RTX (in particular both cases of vasculitis flare were recorded in patients treated with 1 gram of RTX), while no differences were observed according to the previous treatment with RTX originator (2/9 vs 3/9 AE in patients switch or naïve, respectively).

**Conclusion** Despite the low number of patients, the switch among RTX originator and biosimilar appear to be safe and the number of AE were in line with previous reports about RTX originator. The main limit of this study is the absence of a control group, that doesn’t allow a direct comparison of the safety between RTX originator and biosimilar. Previous reports suggested that higher dosage of RTX are associated to a higher risk of side effects. Also, in our study the occurrence of AE, mainly vasculitis flare, seem to be associated to the dose of RTX, rather than to the switch to biosimilar.

**REFERENCES**


Disclosure of Interests None declared


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**AB0625 EXPERIENCE IN THE USUAL PRACTICE OF PATIENTS WITH BEHÇET’S DISEASE WHO ARE IN FOLLOW-UP IN THE UVEITIS UNIT OF THE DONOSTIA UNIVERSITY HOSPITAL**

Jesús Alejandro Valero Jaime1, Olga Maiz-Alonso1, Ana Carmen Blanco Esteban1, Andrea De Diego Solás1, University Hospital Donostia, Ophthalmology, San Sebastian, Spain; 4University Hospital Donostia, Ophthalmology, San Sebastian, Spain

**Background:** Behçet’s disease (BD) is an inflammatory, chronic, recurrent, multisystemic process of unknown origin, characterized by the simultaneous or sequential presence of oral aphthae, genital ulcers, uveitis, inflammatory skin lesions, arterial or venous thrombosis, arthritis, inflammatory bowel disease and involvement of the central nervous system (CNS). The highest incidence figures correspond to the countries of the Middle East and the Far East (prevalence <2). The uveitis unit was created in our hospital in 2007, where a rheumatologist and an ophthalmologist jointly visit, so our aim is to report our experience for almost 12 years with this rare disease.

**Objectives:** To describe the demographic, clinical, and analytical characteristics, as well as immunosuppressive and biological treatments used, type of ocular and extra ocular involvement, presence of sequelae, and visual acuity (VA) affection, of the patients that are in follow-up in the uveitis unit of the Donostia University Hospital (DUH).

**Methods:** A retrospective search of all patients with BD and ocular involvement evaluated the uveitis unit since 2007. The computerized medical records were reviewed. The variables collected were: sex, age, immunosuppressive and biological treatments used, and complementary tests. The immunosuppressant’s sought were methotrexate (MTX), azathioprine (AZA), tacrolimus, sulfasalazine (SSZ), cyclosporine (CsA), leflunomide (LEF), cyclophosphamide (GFM), adalimumab (ADA); infliximab (IFX), golimumab (GLM), intravenous immunoglobulins (IVIG). The quantitative variables are shown with the median and interquartile range; the qualitative ones are shown with the absolute value and its percentage.

**Results:** We found 22 patients diagnosed with BD, the average age was 42 years, with a predominance of women (59%). Table 1 shows the clinical characteristics, complementary tests and treatments used in these
INCIDENCE OF SERIOUS INFECTIONS AND PATTERNS OF COTRIMOXAZOLE PROPHYLAXIS IN PATIENTS WITH ANCA-ASSOCIATED VASCUITIDES

Konstantinos Thomas1, Aglaia Chalkia1, Dimitrios Dekolias1, Christina Tsatsalapi1, Argiro Lazarakis1, Kalliopi Kladiana1, Katerina Antoniou1, Anastasia Makris1, Chrisoula Hatzara1, Emilia Hadzijannis1, Pinelopi Kouki1, Dimitros Petras1.

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2. Department of Nephrology, University of Science and Technology of China, Hefei, China
3. Department of Immunology, Hefei, China
4. Pathology, Hefei, China

Background: Infections are among the most serious complications in patients with ANCA-associated vasculitides (AAV) and contribute significantly in overall mortality.

Objectives: To describe the incidence and risk factors for serious infections, as well as the patterns of cotrimoxazole prophylaxis in AAV patients (GPA and MPA).

Methods: Retrospective, descriptive study of AAV patients followed in a tertiary referral center (Clinical Immunology-Rheumatology Unit and Nephrology department). Patient and disease characteristics treatments and serious infections were recorded.

Results: 54 AAV patients were included (women: 50%, mean age at diagnosis: 59.8 years, mean disease duration: 5.1 years, GPA: 68%, generalized disease: 82%). Most frequent organ involvement was renal (71%), lung (68%), nervous (20%), skin (18%) and mucous membranes/eyes (14%). 21 serious infections were recorded in 16 patients (incidence: 7.2 per 100 patient-years), with respiratory tract infections (43%) and herpes zoster (19%) being the most frequent. Incidence was 6.2 times higher in patients with severe combined lung-kidney involvement and herpes zoster (19%) being the most frequent. Positivity for anti-neutrophil cytoplasmic antibodies (ANCA) and anti-vasculitis-related antibodies (ARA) was significantly associated with the incidence of serious infections. The mean age of 38 cases were 44.1±15.6 years, the mean course was 64.8±90.4 months. Typical clinic manifestations and endoscopic findings existed in 24(63.2%) and 22(57.9%) patients with intestinal Behçet’s disease respectively. The most common (53, 86.8%) symptoms were abdominal pain and diarrhea. The sites of intestinal ulcer were seen more often (22, 57.9%) at the ileum, ileocecal area, on the ileoceleal valve. Most colonoscopic appearance of ulcers were usually well demarcated, oval or round (28, 73.6%). The suggestive histopathological changes were massive neutrophilic infiltration (20, 52.6%), inflammatory granuloma (14, 36.8%) and vasculitis (8, 21%) especially phlebitis.

Conclusion: The diagnosis of intestinal Behcet’s disease depends on the combination of clinic features, endoscopic appearance and histopathological findings. Massive neutrophilic infiltration, inflammatory granuloma and vasculitis point to the possibility of intestinal Behcet’s disease.

REFERENCES

Disclosure of Interests: None declared
CIRCULATING ENDOTHELIAL CELLS MAY BE A MARKER FOR VASCULAR INVOLVEMENT IN BEHÇET DISEASE

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Background: Circulating endothelial cells (CEC) are defined in conditions which vascular damage is seen in course of disease such as systemic vasculitis, coronary artery disease and chronic renal failure. CEC is thought to be an indicator of vascular damage (1). Behcet disease (BD) is a systemic vasculitis mostly known with recurrent oral and genital ulceration, uveitis and mucocutaneous lesions. On the other hand vascular involvement such as deep venous thrombosis, cerebral sinus thrombosis and pulmonary artery aneurysm, is an important clinical finding of disease which may cause mortality (2).

Objectives: Our aim in this study was to analyse CEC levels in patients with Behcet disease, to compare them between patients with vascular (Group 1) and mucocutaneous (Group 2) involvement. Also we have compared the results of Behcet patients with patients with thrombosis due to other causes (Group 3) and healthy controls (Group 4). Each group involved 20 participant.

Methods: Blood samples of the patients and healthy controls are drawn into tubes containing ethylene-diamine-tetra-acetic acid (EDTA). A panel of monoclonal antibodies, including anti-CD45 to exclude hematopoietic cells, anti-CD4, -CD34, -CD36, -CD105, -CD106, -CD133, and –CD146 and appropriate analysis gates were used to enumerate resting and activated CECs and circulating and endothelial progenitor cells (CEP).

A hundred microlitre complete blood was added and incubated for 20 minutes at room temperature in the dark. After incubation for 10 minutes with erythrocyte lysing solution at room temperature, centrifugation at 1,800 rpm for 5 minutes was performed. Supernatant was removed and resuspended with PBS and 300,000–400,000 cells were counted with FACSCalibur flow cytometry device.

Results: Mean age, sex distribution and duration of disease were similar in all groups (Table 1).

Conclusion: Increased levels of aCECs may be an indicator of active vascular involvement in BD. But in the current study aCEC levels did not show a difference between groups but none of the patients had active vascular involvement which may cause of this sameness. CEP and resting CEC levels were elevated in both groups of patients with thrombosis. So CEC may be a marker for vascular damage but it is not specific for BD.

REFERENCES


Disclosure of Interests: None declared


Table 1. Demographic features of the study population

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* Mann Whitney U Test

Abstract AB0629 Table 2. Comparison of CEC, CEP, aCEC and CECs between groups

AB0630 CLINICAL CHARACTERISTICS ANALYSIS AND LITERATURE REVIEW OF 35 CASES OF PANNICULITIS

Hui Zheng1, Li Rong1, Guozhu Chen1, Liyun Zhang1, Huiqin Hao2. 1Shanshi DaYi Hospital, Rheumatology, Tai Yuan, China; 2Shanshi University of Chinese Medicine, Jin Zhong, China

Background: Panniculitis is a heterogeneous inflammatory disease involving subcutaneous fat. It can be divided into different subtypes according to the clinical characteristics and pathological changes of the disease. Because the cause of panniculitis is unclear, clinical manifestations are diverse, lack of specificity, early diagnosis is difficult, and misdiagnosis and missed diagnosis are prone to occur.

Objectives: To improve the clinical understanding of the disease by retrospective analysis of 35 cases of patients with panniculitis.

Methods: The hospitalized patients with panniculitis were collected from December 2011 to October 2018 in the Shanshi Dayi Hospital Affiliated to Shanshi Medical University. The demographics, clinical manifestations, auxiliary examinations and treatments were analyzed and summarized.

Results: The proportion of males and females in the 55 patients was 1:2.23, with an average of 53.3 years (18-82 years). A total of 52 cases showed a significant statistically different difference between all groups. CEPs, activated CECs (aCEC) and resting CECs (rCEC) were also compared between groups. CEPs were higher in Behcet patients with thrombosis similar to patients with thrombosis due to other causes (p<0.042). Activated CECs levels did not show a difference between groups (p>0.05).

Resting CECs are higher in Groups 1 and 3 than Groups 2 and 4. The detailed analysis of CEC, CEP, activated and resting CECs between groups is listed in Table 2.

Disclosure of Interests: None declared

Results: ILD features on HRCT was found in 11 (11.8%) of 102 patients with MPA. Their median age was 55 [53; 63] years. All of them were ANCA-positive (Table 1). In 5 cases interstitial pneumonia was the first and the sole manifestation that preceded for the occurrence of overt systemic vasculitis. These patients were young for a median of 3 years. The radiologic patterns included non-specific interstitial pneumonia in 5 cases, usual interstitial pneumonia in 3 cases and unclassifiable interstitial pneumonia in 3 cases. The most common clinical manifestations were non-productive cough (82%), progressive dyspnea (82%) and crepitation (27%). The most common extrathoracic manifestations of MPA in patients with ILD were glomerulonephritis with decreased renal function (91%), fever (100%) and arthritis (91%). All patients received induction therapy with glucocorticosteroids combined with cyclophosphamide, rituximab, azathioprine or methotrexate.

Abstract AB0631 Table 1. Characteristics of patients with MPA and ILD

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<td>Male, gender, n (%)</td>
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<td>Age of the onset of MPA, Ms, IQR, years</td>
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</table>

ILD onset

Before systemic manifestations of MPA, n (%) | 5 (45)

At MPA onset, n (%) | 6 (55)

ANCA specificity

MPO-ANCA, n (%) | 6 (55)

PR3-ANCA, n (%) | 2 (18)

unidentified ANCA, n (%) | 3 (27)

Clinical symptoms

Fatigue, n (%) | 11 (100)

Fever, n (%) | 11 (100)

Weight loss, n (%) | 4 (36)

Arthralgia, n (%) | 10 (91)

Skin vasculitis, n (%) | 5 (45)

Renal manifestations, n (%) | 10 (91)

Ear, nose and throat involvement, n (%) | 4 (36)

Chronic cough, n (%) | 9 (82)

Hemoptysis, n (%) | 2 (18)

Dyspnea, n (%) | 9 (82)

Crackles, n (%) | 3 (27)

Laboratory and instrumental findings

Increasing of ESR and/or CRP, n (%) | 10 (91)

24-hours proteinuria, g/day | 0.61 [0.25; 1.95]

Estimated GFR, ml/min/1.73 m² | 39 [19; 60]

Radiological patterns

UIP, n (%) | 3 (27)

NSIP, n (%) | 5 (45)

Unclassified IP, n (%) | 3 (27)

Mediastinal lymphadenopathy, n (%) | 3 (27)

Empysemia, n (%) | 2 (18)

Remission induction therapy

Glucocorticosteroids, n (%) | 11 (100)

Cyclophosphamide, n (%) | 7 (64)

Rituximab, n (%) | 1 (9)

Azathioprine, n (%) | 1 (9)

Methotrexate, n (%) | 1 (9)

Conclusion: ILD is a rare manifestation of MPA, which can precede systemic manifestations. ANCA-associated vasculitis should be included in the spectrum of differential diagnosis in patients with ILD.

Disclosure of Interests: None declared

AB0632 MAINTENANCE RITUXIMAB IN ANCA ASSOCIATED VASCULITIS – OBSERVATIONAL DATA FROM UNIVERSITY HOSPITAL COVENTRY, UK

1Megan Rutter, Shirish Dubey, Andrew Short. 1University Hospital Coventry and Warwickshire, Department of Rheumatology, Coventry, United Kingdom; 2University Hospital Coventry and Warwickshire, Department of Nephrology, Coventry, United Kingdom

Background: Rituximab is considered an effective 1 maintenance therapy in anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis (AAV), with reduced relapse rates post induction therapy and comparable adverse event profile to other agents such as Azathioprine 2.

Objectives: To describe the clinical outcomes of all patients receiving maintenance Rituximab for AAV in University Hospital Coventry in UK.

Methods: Records from the Renal and Rheumatology units were used to identify patients receiving maintenance Rituximab. Electronic patient records (EPR) were used to collate laboratory and clinical data.

Conclusion: ILD is a rare manifestation of MPA, which can precede systemic manifestations. ANCA-associated vasculitis should be included in the spectrum of differential diagnosis in patients with ILD.

Disclosure of Interests: None declared

AB0631 INTERSTITIAL LUNG DISEASE – A RARE MANIFESTATION OF MICROSCOPIC POLYANGIITIS

Ekaterina Vinogradova 1,2, Nikolai Bulanov 2, Elena Shchegoleva 3, Larisa Akulina 1, 2, Anastasia Zykova, Pavel Novkov 2, Sergey Moiseen 2, 3, Lomonosov Moscow State University, Moscow, Russian Federation, 2Sechenov University, Moscow, Russian Federation

Background: Interstitial lung diseases (ILD) are a group of diffuse inflammatory and/or fibrotic lung disorders with similar clinical, radiologic and histopathologic features. The coexistence of ILD and ANCA-associated vasculitis has been reported in case reports and small case series.

Objectives: The aim of this study was to assess the prevalence, clinical and radiological characteristics of ILD in MPA patients admitted to the Rheumatology Department of our hospital.

Methods: This retrospective single center cohort study included 102 patients diagnosed with MPA according to CHCC 2012 and EMA algorithm. We assessed Birmingham Vasculitis Activity Score (BVAS) at disease onset and VDI (Vasculitis Damage Index) at the end of the follow up in each patient. ANCA type and titer were assessed by enzyme-linked immunosorbent assay (ELISA). The results of repeated high resolution computed tomography (HRCT) of the chest were analyzed and interstitial changes (focal ground-glass opacity, reticular pattern, honeycombing, traction bronchiectasis) were classified in four patterns: non-specific interstitial pneumonia (NSIP), typical interstitial pneumonia, possible interstitial pneumonia, and “inconsistent” usual interstitial pneumonia (UIP).

Results: ILD features on HRCT was found in 11 (11.8%) of 102 patients with MPA. Their median age was 55 [53; 63] years. All of them were ANCA-positive (Table 1). In 5 cases interstitial pneumonia was the first and the sole manifestation that preceded for the occurrence of overt systemic vasculitis. These patients were young for a median of 3 years. The radiologic patterns included non-specific interstitial pneumonia in 5 cases, usual interstitial pneumonia in 3 cases and unclassifiable interstitial pneumonia in 3 cases. The most common clinical manifestations were non-productive cough (82%), progressive dyspnea (82%) and crepitation (27%). The most common extrathoracic manifestations of MPA in patients with ILD were glomerulonephritis with decreased renal function (91%), fever (100%) and arthritis (91%). All patients received induction therapy with glucocorticosteroids combined with cyclophosphamide, rituximab, azathioprine or methotrexate.

Abstract AB0631 Table 1. Characteristics of patients with MPA and ILD

<table>
<thead>
<tr>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, gender, n (%)</td>
</tr>
<tr>
<td>Age of the onset of ILD, Ms, IQR, years</td>
</tr>
<tr>
<td>Age of the onset of MPA, Ms, IQR, years</td>
</tr>
</tbody>
</table>

ILD onset

Before systemic manifestations of MPA, n (%) | 5 (45)

At MPA onset, n (%) | 6 (55)

ANCA specificity

MPO-ANCA, n (%) | 6 (55)

PR3-ANCA, n (%) | 2 (18)

unidentified ANCA, n (%) | 3 (27)

Clinical symptoms

Fatigue, n (%) | 11 (100)

Fever, n (%) | 11 (100)

Weight loss, n (%) | 4 (36)

Arthralgia, n (%) | 10 (91)

Skin vasculitis, n (%) | 5 (45)

Renal manifestations, n (%) | 10 (91)

Ear, nose and throat involvement, n (%) | 4 (36)

Chronic cough, n (%) | 9 (82)

Hemoptysis, n (%) | 2 (18)

Dyspnea, n (%) | 9 (82)

Crackles, n (%) | 3 (27)

Laboratory and instrumental findings

Increasing of ESR and/or CRP, n (%) | 10 (91)

24-hours proteinuria, g/day | 0.61 [0.25; 1.95]

Estimated GFR, ml/min/1.73 m² | 39 [19; 60]

Radiological patterns

UIP, n (%) | 3 (27)

NSIP, n (%) | 5 (45)

Unclassified IP, n (%) | 3 (27)

Mediastinal lymphadenopathy, n (%) | 3 (27)

Empysemia, n (%) | 2 (18)

Remission induction therapy

Glucocorticosteroids, n (%) | 11 (100)

Cyclophosphamide, n (%) | 7 (64)

Rituximab, n (%) | 1 (9)

Azathioprine, n (%) | 1 (9)

Methotrexate, n (%) | 1 (9)

Conclusion: ILD is a rare manifestation of MPA, which can precede systemic manifestations. ANCA-associated vasculitis should be included in the spectrum of differential diagnosis in patients with ILD.

Disclosure of Interests: None declared

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Objectives: To describe the clinical outcomes of all patients receiving maintenance Rituximab for AAV in University Hospital Coventry in UK.

Methods: Records from the Renal and Rheumatology units were used to identify patients receiving maintenance Rituximab. Electronic patient records (EPR) were used to collate laboratory and clinical data.

Conclusion: ILD is a rare manifestation of MPA, which can precede systemic manifestations. ANCA-associated vasculitis should be included in the spectrum of differential diagnosis in patients with ILD.

Disclosure of Interests: None declared
Results: We identified 38 patients, with the diagnosis of AAV made 11 months to 19 years previously. 16 (42%) had been diagnosed within the last five years. Age range was 19-87 years old with roughly half (21; 54%) being male. Maintenance Rituximab was started between January 2010 and September 2018. Most patients received a fixed 6 monthly pro- tocol. Seven patients (18%) died within the observation period. More details in table 1 below.

<table>
<thead>
<tr>
<th>Table 1. Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number (n) patients = 38 n (%)</td>
</tr>
<tr>
<td><strong>Serology</strong></td>
</tr>
<tr>
<td><strong>MPO positive</strong></td>
</tr>
<tr>
<td>Previous cyclophosphamide (2/38 unknown)</td>
</tr>
<tr>
<td>Indication for starting Rituximab</td>
</tr>
<tr>
<td>Failure of cyclophosphamide</td>
</tr>
<tr>
<td>Flare/woesening disease despite disease-modifying therapy</td>
</tr>
<tr>
<td>Intolerant of other disease-modifying therapies</td>
</tr>
<tr>
<td>Young patient of child-bearing potential</td>
</tr>
<tr>
<td>Patient preference</td>
</tr>
<tr>
<td>Not documented</td>
</tr>
<tr>
<td><strong>Concurrent medication</strong></td>
</tr>
<tr>
<td>Azathioprine</td>
</tr>
<tr>
<td>Mycophenolate motilol</td>
</tr>
<tr>
<td>Methotrexate</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
</tr>
<tr>
<td>Tacrolimus</td>
</tr>
<tr>
<td>Prednisolone monotherapy</td>
</tr>
<tr>
<td>Nil</td>
</tr>
<tr>
<td><strong>Compliance</strong></td>
</tr>
<tr>
<td>In patients who completed 2 years maintenance Rituximab</td>
</tr>
<tr>
<td>Clinical response to Rituximab</td>
</tr>
<tr>
<td>Full</td>
</tr>
<tr>
<td>Partial; requiring addition of further disease-modifying therapy</td>
</tr>
<tr>
<td>Mild disease progression</td>
</tr>
<tr>
<td>Flare within first 2 years of treatment</td>
</tr>
<tr>
<td>First 2 years of Rituximab treatment</td>
</tr>
<tr>
<td>Ongoing</td>
</tr>
<tr>
<td>Completed</td>
</tr>
<tr>
<td>Not completed</td>
</tr>
<tr>
<td>Discontinued due to infections</td>
</tr>
<tr>
<td>Patient died</td>
</tr>
<tr>
<td>Subsequent treatment†(n=24)</td>
</tr>
<tr>
<td>Rituximab continued as primary therapy</td>
</tr>
<tr>
<td>Regular Rituximab restarted following flares</td>
</tr>
<tr>
<td>Mycophenolate motilol</td>
</tr>
<tr>
<td>Azathioprine</td>
</tr>
<tr>
<td>Prednisolone monotherapy Patient died</td>
</tr>
</tbody>
</table>

† Renal transplant patient ] In 2/3 (67%) patients associated with poor compliance/missed doses Y In patients who completed 2 years maintenance Rituximab

Conclusion: The effectiveness of Rituximab as a maintenance therapy in AAV is borne out by this real world data, with 31/38 patients demonstrating full clinical response. Longer term treatment and low grade disease continue to be issues as evidence for optimal management strategies is lacking. Infections, including severe infections necessitating admission, were common. PR3 positive patients are over-represented, in keeping with the known higher rate of relapse.

REFERENCES


I confirm that the abstract fulfills the requirements for a late breaking submission and that the research results were not available at the time of the original deadline (31 January 2019) Yes

Disclosure of Interests: Megan Rutter: None declared, Shirish Dubey Grant/research support from: Roche provided a grant 5 years ago, Speakers bureau: Yes, BMS and Internis, Andrew Short: None declared


AB0632B TB OR NOT TB, THAT IS THE VASCULITIC QUESTION

Salma Khalid, Sarah Bartram. Salisbury District Hospital, Salisbury, United Kingdom

Background: It is important to remember that there are many disorders that can mimic the clinical, radiographic and histological features of vasculitis. Tuberculosis (TB) is often referred to as the great imitator and therefore, needs to be considered early in the differential diagnosis of vasculitis.

Objectives: To emphasize the importance of being aware of noninflammatory mimics of vasculitis to be able to avoid unnecessary and potentially harmful immunosuppression.

Methods: We report a challenging case of a patient presenting with an inflammatory subglottic lesion.

Results: A 67-year-old lady initially presented to otolaryngology (ENT) with hoarseness and and restriction of breathing. Nasendoscopy revealed a subglottic lesion with oedema and inflammation. Biopsy showed florid necrotising granulomatous inflammation. Upon questioning, patient revealed a history of epistaxis and nasal crusting requiring regular nasal douching. She also reported lack of energy, loss of appetite, but denied any rash, weight loss or night sweats. She suffered with a severely dry mouth that was causing difficulty swallowing. She also complained of an occasional cough with small amount of phlegm which she attribute to the smoking. She had also noted to have deranged liver function test around this time. Gastroenterology advised that there was no clear cause for the transaminitis and an autoimmune screen was requested. Given the chest findings on CT, a sputum sample was sent for microscopy and culture. The patient had been started on dexametha-sone on admission by ENT and reported substantial improvement in the hoarseness of voice and shortness of breath. ANCA then came back negative, as did the connective tissue screen. While the rheumatology team was considering how to further manage the possible vasculitis, the spu tum smear came back positive for acid fast bacilli and the diagnosis was clinched: our patient was suffering with the extremely rare laryngeal tuberculosis, along with pulmonary TB. She was started on anti-tuberculosis medication that have been introduced incrementally given the deranged liver function tests. The patient was doing well on her most recent follow up in the respiratory department.

Conclusion: Greater awareness of vasculitis mimics like TB and a high index of suspicion are needed when assessing a patient presenting with the protean manifestations of suspected vasculitis. It is therefore prudent to include TB in the differentials, whenever consider vasculitis.

REFERENCES


Scleroderma, myositis and related syndromes

Fecal Calprotectin in Patients with Systemic Sclerosis

Objective: to examine fecal calprotectin as a simple method to diagnose GI disorders and disease activity in SSc.

Methods: Totally 46 patients with SSc were invited by telephone, who have been referred to sayyad shirazi Hospital and the rheumatologists offices in Gorgan and their information has been registered there. Seven patients did not enter our study because of having items in exclusion criteria like Diabetes, a history of GI operation and having other connective tissue diseases at the same time.

Results: Nineteen patients with SSc were newly visited. Male to female ratio was 1:2.67 and the age range was 19-75 years and the median of age which was 42, was divided in to two groups: young (intestinal disorders) was done. The patients in our study according to the definition in 2015 ESC/ERS guideline. The NVC (Medcap®3.0, DS MEDICA) was used to detect microvascular change and average capillary density and the number of capillaries/view were calculated. Also, existence of giant capillaries, hemorrhage and patterns of capillary changes were also documented. Transthoracic ultrasound cardiology (UCCI) was performed using IE33 with 5MHz sector probe SS-1 (Philips). Exercise loading was done with an ergometer (Lode), Ejection fraction (EF), velocity of tricuspid regurgitation jet (TR jet), tricuspid annular plane systolic excursion (TAPSE) were examined in a supine position. Tricuspid regurgitation pressure gradient (TRPG) was calculated using velocity of TR jet based on Bernoulli principle. Exercise loading was started at 25 Watt, and then increased 25 Watt every 3 minutes and TRPG at maximum exercise was also calculated. Parameters of NVC were compared with those of UCCI. Patients with 'pre-clinical' PAH were defined as patients 1) asymptomatic, 2) who did not meet the definition of PH by right heart catheterization (RHC), 3) whose probability of PH is lower than PH that is 'lower than PH that is not immediately' by UCCI, 4) who did not see any UCCI signs for PH based on the guideline and 5) who did not have severe interstitial lung disease, especially% FVC< 70% and/or area of ILD based on CT scan was <20% of the entire lung field.

Results: Nineteen patients with SSc were newly visited. Male to female ratio was 1:2.67, mean age 63 ± 13 years, and mean disease duration was 138 ± 109 months. Ratio of limited skin type was 79%. 37% were with ILD and 11% were with PAH confirmed by RHC. There is no correlation between TRPG at rest and the density of capillaries. However, there is a significant, negative correlation between TRPG at exercise and the capillary density. Parameters of NVC were compared with those of UCCI. Patients with 'pre-clinical' PAH were defined as patients 1) asymptomatic, 2) who did not meet the definition of PH by right heart catheterization (RHC), 3) whose probability of PH is lower than PH that is not immediately' by UCCI, 4) who did not see any UCCI signs for PH based on the guideline and 5) who did not have severe interstitial lung disease, especially% FVC< 70% and/or area of ILD based on CT scan was <20% of the entire lung field.

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Conclusion: Our study suggests that the finding of NVC, especially the extent of capillary loss, is correlated with disease process of PAH, even subclinically, and may predict the progression to PAH in SSC. Since NVC is non-invasive, NVC can detect earlier PAH candidates and contribute to the improvement of prognosis.

REFERENCES

Disclosure of Interests: None declared

AB0635 POTENTIAL BIOMARKERS OF SKIN CHANGES IN SYSTEMIC SCLEROSIS
Radim Bečvář, Hana Stórkánová, Barbora Šumová, Maja Šprítová, Sabina Orska, Ladislav Senott, Michal Tomčík, Institute of Rheumatology, Praha, Czech Republic

Background: Skin fibrosis is a hallmark of systemic sclerosis (SSc). There are no widely accepted biomarkers of skin involvement in this condition. Several serum or plasma markers have been studied in patients with SSc - monocyte chemotactic protein-1 (MCP-1), chemokine (C-X-C motif) ligand 2 (CXCL2), interleukin-13 (IL-13), and some more recognized such as - platelet derived growth factor (PDGF), transforming growth factor-beta 1 (TGF-beta 1), epidermal growth factor (EGF) and basic fibroblast growth factor (bFGF).

Objectives: The aim of this study was to assess several circulating biomarkers which may be relevant to the fibrosing process and further to correlate the obtained data with clinical indicators specific for SSc skin involvement.

Methods: 59 SSc patients (M/F 9:50; mean age 52.1 years, mean disease duration 6.7 years, 36 patients with limited cutaneous SSc and 23 with diffuse cutaneous SSc. As a control group 36 healthy individuals matched to sex and age were examined. Serum concentrations of bFGF, granulocyte-colony stimulating factor (G-CSF), granulocyte-macrophage colony stimulating factor (GM-CSF), MCP-1, PDGF, IL-8 and 13 were analysed using commercial multiplex kit. The following clinical examinations were performed: modified Rodnan skin score (mRSS), Hand Mobility in Scleroderma Test (assessing hand function) (HAMS), Cochin Hand Function Scale (hand function) (CHFS), Delta Finger-to-Palm Distance (extension-flexion) (dFTP), Inter-lip Distance (inter-lip), Inter-incisor Distance (inter-incisor), and Mouth Handicap in Systemic Sclerosis Scale (mouth opening) (MHISS). For statistical evaluation Spearman’s correlation coefficient was used.

Results: When compared with healthy controls serum concentrations of bFGF (p<0.001), G-CSF (p<0.0001), GM-CSF (p<0.0001), MCP-1 (p<0.0001) IL-8 (p<0.0001), and IL-13 (p<0.0001) were significantly elevated in SSc cohort. PDGF levels were increased in SSc patients with only a lower significance (p<0.01). bFGF, G-CSF, MCP-1 and IL-8 levels correlated significantly (p<0.05) with mRSS and HAMS. GM-CSF levels correlated with mRSS and HAMS and there was only a trend for negative correlation with inter-incisor. The was no correlation of IL-13 and PDGF levels with the evaluated clinical data.

Conclusion: Our results have shown that G-CSF, GM-CSF and IL-8 play a substantial role in SSc fibrosing process. Potential biomarkers as bFGF, G-CSF, MCP-1 and IL-8 correlated with a few clinical indices of SSc skin involvement.

REFERENCES

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Disclosure of Interests: Radim Bečvář Consultant for: consultancy Acteon, Hana Stórkánová: None declared, Barbora Šumová: None declared, Maja Šprítová: None declared, Sabina Orska: None declared, Ladislav Senott Grant/research support from: AbbVie, Consultant for: AbbVie, Bris-tol-Myers Squibb, Celgene Corporation, Merck Sharp and Dohme, Novartis, Pfizer, Roche, UCB, Amgen, Takeda, Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Celgene Corporation, Eli Lilly, Merck Sharp and Dohme, Novartis, Pfizer, Roche, UCB, Michal Tomčík: None declared

AB0636 INFLUENCE OF CARDIOVASCULAR RISK FACTORS ON NAILFOLD VIDEOCAPILLAROSCOPY IN THE STUDY OF CONNECTIVE TISSUE DISEASES
Diego Benavent, Laura Nuño, Gemma Bonilla, Diana Peiteado, Chamarada Plasencia, Victoria Navarro-Compañ, Irene Monjo, Alejandro Villalva, Sara García-Carazo, Carolina Tomero, Patricia Bogas, Elisa Fernández, Miguel Berrad, Ana Castilla, Pilar Aguado, María-Eugenia Miranda-Canas, Eugenio de Miguel, Alejandro Balsa. Hospital Universitario La Paz, Madrid, Spain

Background: Nailfold videocapillaroscopy is a non-invasive technique used to assess Raynaud syndrome. It is mainly used for the early diagnosis of connective tissue disorders (CTD) such as systemic sclerosis. There is some evidence that capillaroscopy findings may be altered by microcirculatory abnormalities in patients with cardiovascular risk factors (CVRF).

Objectives: To analyze the influence of cardiovascular risk factors on nailfold capillaroscopy in patients with Raynaud or suspect of CTD.

Methods: An observational and descriptive study of consecutive patients that underwent a videocapillaroscopy examination for the study of Raynaud syndrome was conducted. A “capscope” model videocapillaroscope from Ophtha was used, with a fixed magnification of 200x. Examination was made on 8 hand fingers, with 2 images per finger. The patients had to be at least 30 minutes in a fixed warm temperature room and without smoking 1 hour before the performance of the test. The following capillaroscopic parameters were considered: nailfold morphology, capillary loop enlargements, megacapillaries, microhaemorrhages, avascular areas and signs of neoangiogenesis. Demographic information (including age, gender and previous diagnosis) and cardiovascular risk factors (including arterial hypertension (HT), diabetes mellitus (DM), dyslipidemia (DL) and smoking habit) were collected. The influence of cardiovascular risk factors on nailfold capillaroscopy was analyzed, using univariate and multivariate logistic regression models, adjusted for possible confounders.

Results: Out of the 136 included patients, 91% were women. Mean age was 54.6 ± 18.7 years. Raynaud syndrome was reported in 83% patients, with a mean duration of 6.1 ± 5.7 years and 12% of the patients had a previous diagnosis of CTD, including systemic lupus erythematosus (5%), systemic sclerosis (4%), undifferentiated connective tissue disorder (2%) and mixed connective tissue disease (1%). Regarding CVRF, HT was observed in 25%, DM in 7%, DL in 23% and past or current smoking habit in 32%. Capillaroscopic findings were: loop enlargements (81%), megacapillaries (30%), microhaemorrhages (46%), signs of neoangiogenesis (71%) and avascular areas (20%). Regarding the capillaroscopic pattern, 46% presented a normal or non-specific pattern; 31% a microangiopathy pattern and 23% a scleroderma pattern (of which 58% had an early or active scleroderma pattern and 42% a late scleroderma pattern). A new diagnosis of CTD was made in 24 patients (18% of the cohort). In the group of patients without CTD, HT was associated with microhaemorrhages (p = 0.02) and avascular...
areas (p = 0.007), and there was a tendency to association between smoking habit and megacapillaries (p = 0.08). After adjusting for confounding factors for this group, an association between CTD and microhaemorrhages (OR = 1.9; p = 0.01) and avascular areas (OR = 2.12; p = 0.007) was found. The multivariate study showed no relationship between CVRF and capillaroscopy patterns.

**Conclusion:** In our cohort we found an increased frequency of microhaemorrhages and avascular areas in the nailfold capillaroscopy in patients with arterial hypertension. The presence of cardiovascular risk factors could have an influence on the microvascular ulcer and therefore on the findings of the capillaroscopy. More studies are required to better assess these findings.

**REFERENCES**


**Disclosure of Interests:** Diego Benavent: None declared, Laura Nuño: None declared, Gemma Bonilla: None declared, Diana Pelletado: None declared, Chamiada Plascencia Speakers bureau: Pfizer, MSD, Victoria Navarro-Compañ: None declared, Irene Monjo: None declared, Alejandro Villalva: None declared, Sara García-Carazo: None declared, Carolina Tornero: None declared, Patricia Bogas Grant/research support from: non restricted grant from Sanofi, Elisa Fernández: None declared, Miguel Bernero: None declared, Patricia Bogas Grant/research support from: non restricted grant from Sanofi, Elisa Fernández: None declared, Miguel Bernero: None declared.

**Abstract AB0637 Table 1. Description of the study cohorts at baseline (total N=107)**

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Musculoskeletal</th>
</tr>
</thead>
<tbody>
<tr>
<td>53 (43,64)</td>
<td>Synovitis</td>
</tr>
<tr>
<td>35/103</td>
<td>Tendon friction</td>
</tr>
<tr>
<td>1 (1.25)</td>
<td>RNS</td>
</tr>
<tr>
<td>1 (3.5)</td>
<td>Muscle weakness</td>
</tr>
<tr>
<td>1 (3)</td>
<td>Death</td>
</tr>
</tbody>
</table>

**Figure 1. Disease duration from the first Raynaud phenomenon:**

**Conclusion:** This analysis is showing that patients fulfilling VEDOSS criteria include a subgroup of patients with very mild, long-standing disease. This observation has major impact on the management of VEDOSS patients, as this subgroup requires different follow up and treatment strategies compared to VEDOSS patients with early, progressive disease.

**Disclosure of Interests:** Elisabeth Blaja: None declared, Suzana Jordan: None declared, Carina Mihai Consultant for: Received consulting fees or other remuneration from Actelion, Geneva, Roche, and Rofar, Consultant for: F. Hoffmann-La Roche, Actelion, Geneva Romfarm, Rucsandra Dobrota: None declared, Mike O. Becker: None declared, Britta Maurer Grant/research support from: Grant/research support from: AbbVie, Protagen, Novartis; congress support from MSD, Pfizer, Roche, and Actelion, Marco Matucci-Cerinic Grant/research support from: Actelion, MSD, Pfizer, BMS, Chemomab, Sanipedia, Speakers bureau: Actelion, BMS, MSD, Janssen, Oliver Distler Grant/research support from: Prof. Distler received research funding from Actelion, Bayer, Boehringer Ingelheim and Mitsubishi Tanabe to investigate potential treatments of scleroderma and its complications, Consultant for: Prof. Distler has/had consultancy relationship within the last 3 years with Actelion, AnMar, Bayer, Boehringer Ingelheim, ChemomAb, espeFare foundation, Genentech/Roche, GSK, Inveniva, Italfarmaco, iQvia, Lilly, medac, Medimmune, Mitsubishi Tanabe Pharma, Pharmacies, Novartis, Pfizer, Roche, and UCB, Merck, Sanofi, Serodapharm and UCB in the area of potential treatments of scleroderma and its complications.

In addition, he/had consultancy relationship within the last 3 years with Actelion, Bayer, Boehringer Ingelheim and Mitsubishi Tanabe to investigate potential treatments of scleroderma and its complications, Consultant for: Prof. Distler received research funding from Actelion, Bayer, Boehringer Ingelheim and Mitsubishi Tanabe.

AB0638

ABSENCE OF LUNG INVOLVEMENT IN SYSTEMIC SCLEROSIS PATIENTS WITH SILICONE IMPLANTS

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Background: Although many cases have been reported for the last 3 decades, the correlation between silicone breast implants (SBI) and systemic sclerosis (SSc) is yet unclear.

Objectives: To assess the prevalence of breast implants in a well-characterized SSc cohort followed at a dedicated tertiary center and to define characteristics that might differ between SSc patients with implants and those without.

Methods: A prospectively maintained database was interrogated regarding the prevalence of breast implants and the disease characteristics. Female patients aged 20 to 55y (215 patients) followed at our center between 2003-2018 were included. SBI cases were identified and their characteristics tabulated. Each SBI patient was matched with 2 controls matched for age, disease duration and type of disease. We used descriptive statistics, multivariate comparisons and multivariate analysis for correlations.

Results: 11 pts with SBI were found, 6 with diffuse (median age 37.5, range 32-55, median disease duration 3.5 y, range 1.5-8y, median mRSS 13.5, range 8-26) and 5 with limited SSc (median age 38, range 33-45, median disease duration 8y, range 3-32y, mRSS 2, range 2-5). The prevalence of SBI in the 20 to 55 y cohort is 5%, similar to the estimated prevalence in the general population. All had their implants instilled before the diagnosis of SSc (median 10y, range 4-13y). Four pts were first diagnosed with SSc within a year from diagnosis of silicon leakage. RNA polymerase 3 was positive in 3 patients, ScCtO in 3 others, antinuclear antibodies in 1 patient and 4 others were positive only for antinuclear antibody. There were no differences in the prevalence of digital ulcers, gastrointestinal involvement, skin score or the serologic profiles between the two groups. However, none of the SBI pts developed interstitial lung involvement, compared to 72% of the matched diffuse patients (p=0.001). None of the SBI pts developed interstitial lung involvement, compared to 72% of the matched diffuse patients (p=0.001).

Conclusions: The rapid referral to a specialized centre for SSc and a tailored therapeutic approach, should always be considered in SSC patients with implants.

Disclosure of Interests: None declared


AB0639

PREDICTION OF MAJOR VASCULAR COMPLICATIONS IN SYSTEMIC SCLEROSIS (SSC)

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Background: in SSc, Digital ulcers (DU), scleroderma renal crisis (SRC) and pulmonary arterial hypertension (PAH) are major vascular complications (MVCs). Among the variables used to follow-up SSc patients, nailfold videocapillaroscopy pattern (NVCp), estimated pulmonary systolic arterial pressure (sPAP), diffusion capacity of carbon dioxide (DLCO) and renal resistive index (RRI) on renal vascular Doppler ultrasound have previously shown to be predictive for MVCs development. Moreover, circulating endothelin-1 (ET1) levels have been associated with MVCs.

Objectives: to identify clinical, instrumental and laboratory predictors of MVCs development in SSc.

Methods: SSc patients fulfilling the 2013 ACR/EULAR criteria were enrolled from two SSc-care units. Data regarding clinical manifestations, instrumental and laboratory evaluation for renal, cardiac and cardiovascular involvement were collected. ET1 serum levels were measured with an ELISA kit.

Results: 380 patients [aged 57 (46-68) years, 12% males] were enrolled in the study, with 42.4% prevalence of MVCs at baseline. Previously known associations were significantly confirmed between presence of MVCs and AGE, dsSSc, RRI on renal vascular Doppler ultrasound, presence of telangectasias on nailfold capillaroscopy and presence of digital ulcers.

Conclusions: The data show that the most stringent factors predicting MVCs are sPAP and joint involvement in MVCs complicated and naive patients, respectively. These 2 items, together with mRSS and telangiectasias, should always be considered in SSC long-term follow-up to shape up a tailored therapeutic approach.

Disclosure of Interests: None declared

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AB0640

SURVIVAL AND MORTALITY PREDICTORS IN SYSTEMIC SCLEROSIS: RESULTS FROM A MONOCENTRIC ITALIAN COHORT

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Background: Systemic sclerosis (SSc) is a connective tissue disease with a poor prognosis and disease-related pulmonary fibrosis, pulmonary arterial hypertension (PAH) and cardiac involvement accounted for most deaths (1). However, a decrease in mortality is seen in the last decades thanks to the opportunity of new screening and therapeutic strategies (2).

Objectives: to estimate the global survival and any predictor of mortality in a monocentric cohort of SSc patients with a 10-years follow-up.

Methods: We performed a retrospective analysis examining the medical records of our longitudinal SSc cohort with a median (IQR) follow-up of 56 (25-82.5) months in our Scleroderma Unit since January 2009. All clinical, laboratory and instrumental findings have been recorded and analyzed using Chi-squared tests, Kaplan-Meier curves, log-rank tests, and Cox proportional hazards modeling.

Results: We collected data from 347 SSc patients (female n. 319 (91.9%); mean (SD) age at diagnosis 50.6 (15.9) years, median (IQR) disease duration 8.75 (4.1-14.9) years; diffuse cutaneous involvement (dsSSc) n=176 (48.4% patients) fulfilling the 1980 ARA and/or 2013 ACR/EULAR classification criteria. All patients were positive for ANA, while anti-Tipo-1 were found in 145 (41.8%), CENP-B in 139 (40.1%) patients. Fifteen (4.3%) patients were positive to other autoantibodies (Anti-RNA polymerase III, anti-Pm/Scl) while anti-ENA were negative or unknown for 48 (13.8%) SSc patients. Intestinal lung disease (ILD) was present in 53 (45.5%), pulmonary arterial hypertension, diagnosed by right heart catheterism, (Group 1 PAH) was found in 17 (4.9%), and 22/347 (6.3%) patients presented pulmonary hypertension combined with ILD (Group 3 PH-ILD). The overall survival rates were 89.1% and 87.3% at 5 and 10 years, respectively. As reported in Figure 1, the 5-years global survival was significantly impaired by the presence of PAH or PH-ILD, while isolated ILD did not impact the survival. The univariate and multivariate analysis showed that dsSSc, higher age at diagnosis, delayed referral to our Scleroderma Unit, body mass index and absence of heart (H) or lung (L) involvement (No H/L) were independent predictors of 5-years mortality (Table I). While gender, disease duration, specific autoantibodies, basal Rodnan skin score, smoking, renal or gastrointestinal comorbidities, NYHA functional class, steroid or immune-suppressive treatments did not reach the statistical significance.

Conclusion: Our study demonstrated a global 10-years survival rate over 85%, and the presence of PH without or with ILD represents the main negative predictor. The rapid referral to a specialized centre for SSc and early treatment with effective agents for PH could further improve prognosis.

REFERENCES
VITAMIN D SERUM LEVELS AND THE RISK OF DIGITAL ULCERS IN SYSTEMIC SCLEROSIS: A LONGITUDINAL STUDY

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**Background:** Vitamin D is known to influence the immune system in many different diseases although longitudinal studies on systemic sclerosis (SSc) are still missing.

**Objectives:** This study wants to investigate if variations in vitamin D serum levels (25OHD) over time affect digital ulcers (DUs) in SSc.

**Methods:** This is a retrospective study on 65 patients. Data on disease characteristics and 25OHD were collected in 2011 and 2016.

**Results:** The mean age of our cohort was 58 (12) years with a mean disease duration of 9.5 (5.3) years. Most of our patients had a limited subset (69.2%). At baseline 50.8% and 41.5% after 5 years had 25OHD <30 ng/mL. Supplemented patients (6750 IU/week) at baseline were 39 (60.2%) and 45 (69.2%) at the end of follow-up. Nevertheless, 31 (47.7%) had a decrease of 25OHD in 5 years. In univariate analysis, patients with incident digital ulcers (DU) had a decrease in 25OHD as compared to patients with no incident DU (-17.4 (37.0) vs. 13.0 (89.5), p=0.018). No differences in 25OHD variations were found for other disease characteristics. In multivariate analysis correcting for previous DU and mRSS at baseline, patients with a decrease in 25OHD had an increased risk of developing DU (OR [95% CI]: 16.6 [1.7 to 164.5], p=0.017).

**Conclusion:** In this study we have shown that a decrease in 25OHD increases the risk of developing DUs and that vitamin D supplementation with the doses currently recommended may be insufficient in SSc. Further studies in wider cohorts are needed to confirm these results and to evaluate the effectiveness of a more aggressive or different vitamin D supplementation.

**Disclosure of Interests:** Cristian Cairini: None declared, Eugenia Bertoldo: None declared, Alice Pozza: None declared, Paola Caramaschi: None declared, Giovani Orsoni: Speakers bureau: F Iannone has received consultancy declared, Maria Grazia Anelli: None declared, Emanuela Praino: None declared, Sergio Colella: None declared, Laura Coladonato: None declared, Fabio Cacciapaglia: None declared, Marco Forzieri: None declared, Marco Fusco: None declared, Maria Aparicio-Espinar: None declared, Lourdes Mateo: None declared, Anne Riveros: None declared, Laia Gilfe: None declared, María Sapuésa-Gomez: None declared, Águeda Prieto-Español: None declared, Anisa Nack: None declared, Anahy Brandy-García: None declared, María Teresa Balsemarsho: None declared, Eva Martínez-Cáceres: None declared, Ana Luisa Oliva: None declared, Bibiana Quirau: None declared, Susana Hidalgo: None declared, 1Hospital Universitari Germans Trias i Pujol, Rheumatology, Badalona, Spain; 2Hospital Universitari Germans Trias i Pujol, Immunology, Badalona, Spain; 3Hospital Universitari Germans Trias i Pujol, Dermatology, Badalona, Spain.

**Background:** Myositis specific antibodies have gained special importance in last years. Its knowledge has allowed stratifying patients in different clinical phenotypes, predicting with greater accuracy prognosis and establishing a clinical attitude to follow. SAE1/2 antibody (anti-small ubiquitin-like modifier activating enzyme) was first described in 2007 in patients with amyopathic dermatomyositis with cutaneous and digestive involvement. Its prevalence ranges from 8% in European cohorts to 3% in Asians.

**Objectives:** Describing myositis specific antibodies (MSA) in a cohort of inflammatory myopathies. To characterize the clinical phenotype of SAE1/2 antibody in our cohort and to compare it with the rest of MSA.

**Methods:** Patients diagnosed of dermatomyositis in a tertiary hospital from 1978-2018, according to the criteria of Bohan and Peter (1975) and according to Dalakas classification criteria (2015). Clinical and analytical data, including the immunological profile were collected, as well as the treatments received and the evolution of the disease.

**Results:** Out of 46, 41 dermatomyositis had positive antinuclear antibodies (ANA). 55% percent had ANA titles >/=1/640, being the fine speckled pattern the most frequent (43%) followed by coarse speckled and homogeneous (13.6% each). 72% had MSA, the most frequent being anti-Jo1 (27.3%) followed by MDA5 (18.2%) and SAE1/2 (15%). Up to 40% had two or more antibodies, being the association with antibodies Ro52 and Ro60, the most frequent. 5 patients presented positivity against SAE antibody. In comparison to the rest of MSA, 80% presented with cutaneous debut (p = 0.00), being the most frequent manifestations heliotrope erythema (p = 0.00), Gottron papules (p = 0.10) and skin rash (p = 0.00). 60% had pathological capillaroscopy compared to 15% (p = 0.00). Muscular balance was preserved in 60% of patients. Sixty percent had dysphagia vs 9% (p = 0.00). Two of them had lung involvement (alveolar hemorrhage and rapidly progressive pneumonitis). In comparison with SAE negative group, patients presented more pulmonary hypertension (44.5 vs 34 mmHg), without reaching significant differences. No significant differences were found between muscle enzyme levels’ neither acute phase reactants.

As complications, one patient presented a myocarditis with quickly rapidly progressive pneumonitis that required high doses of corticotherapy and another one alveolar hemorrhage, which was treated the same way. All patients required corticotherapy at doses of mg/kg, requiring two of them to be treated with DMARDs (methotrexate and dolquine) and one of them with immunoglobulins due to cutaneous involvement. Mortality rate was 40% due to rapidly progressive lung affection and cardiopulmonary arrest.

**Conclusion:** Higher prevalence of SAE1/2 antibody in our cohort may be explained due to the use of amplified myositis antibodies kit that specifically includes this antibody. These patients typically present with cutaneous involvement and dysphagia but also lung affection as a complication. Studies with larger samples should be performed in order to know the prognosis of this antibody specificity.

**Disclosure of Interests:** None declared

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AB0643 CLINICAL AND ANALYTICAL DESCRIPTION OF A DERMATOMYOSITIS SERIES OF PATIENTS

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Background: Dermatomyositis (DM) is an idiopathic inflammatory myopathy. The recent years has increased its knowledge thanks to best characterization of myositis-specific antibodies that correlate with different clinical phenotypes.with different clinical phenotypes.

Objectives: To describe the clinical and analytical features of a series of dermatomyositis: clinical debut, clinical manifestations as well as the treatments received and the evolution of the disease.

Methods: Patients diagnosed of dermatomyositis in a tertiary hospital between the years 1978-2018 according to the criteria of Bohan and Peter (1975) and according to Dalakas classification criteria (2015). Clinical, analytical and immunological profile data were collected, as well as treatments received and the evolution of the disease.

Results: A total of 59 inflammatory myopathies diagnosed between the years 1985 and 2018 were included. 46 were dermatomyositis (78%), 9 polymyositis (15%) and 4 necrotizing myositis (7%). 69% were women and 22% were smokers. Clinical debut at 54 ± 17 years. The initial manifestation was pulmonary in 26.7% followed by cutaneous manifestations (24.4%) and the muscular (22.2%), while a 17.8% started skin and muscular manifestations at the same time. 45.5% behaved like a myopathic DM while a 26% as amyopathic DM and antisynthetase syndrome respectively. 38% presented interstitial involvement being the most common non-specific interstitial pneumonitis (76%) followed by usual interstitial pneumonitis (17%). In these patients, DLCO was decreased (mean of 58.9% and 13.2) as well as the FVC (average of 58%, 2.5L). 73.3% presented cutaneous involvement being the most common manifestations the Gottron papules (37.8%) and the heliotrope rash (35.6%), and up to 27% had cuticular affection. 64% had muscle involvement, affecting proximal and symmetrical. Neck flexors were affected in a 38% of patients while 20% had dysphagia. Only 3 patients presented dysphonia (7%) and 2 myocarditis.

Analytical data

Muscular enzymes
- CK: 821 ± 1260U/mL
- LDH: 425 ± 300U/L
- Aldolase: 11.5 ± 11U/L
- Acute phase reagents
- ESR: 30 ± 23 mm
- RCP: 13 mg/l ± 25
- Myositis specific antibodies
- AntiJo1: 27%
- MDA5: 16%
- SAE1/2: 15%

Conclusion: 80% received corticotherapy at a dose of mg/kg/day and 20% required high doses of metiprednisolone due to muscular involvement or pulmonary, 18% immunoglobulins and 17% cyclophosphamide. As maintenance 80% received disease modifying anti-rheumatic drug in addition to corticosteroid therapy in descending doses (azathioprine 22%, doxilune 15%, tacrolimus 13.3%, rituximab 11%) due to muscle (29.9%), cutaneous (24.4%) and pulmonary involvement (22.2%). As complications, 2 cases of the syndrome were registered hemophagocytic virtually all patients they presented pulmonary hypertension (mean 34 ± 12 mmHg). 5 patients (11.1%) were diagnosed with neoplasia, two of them after the diagnosis of DM. The mortality was 24%. 3 patients died due to a rapidly progressive pneumonitis, another 2 due to alveolar hemorrhage and three of them due to complication of the neoplasic disease.

Dermatomyositis occurs in a variable way, with predominance of pulmonary, skin and muscle manifestations. They require corticotherapy and immunosuppressive treatment for maintenance, even so, mortality is high.

Disclosure of Interests: None declared


AB0644 RESULTS OF A TRAINING COURSE FOR CALCULATION OF THE MODIFIED RODNAN SKIN SCORE IN SCLERODERMA

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Background: Scleroderma is a connective tissue disease that is characterized by fibrosis of the skin. The modified Rodnan Skin Score (mRSS) is a measure generally used to assess the skin thickness in patients with scleroderma.Data on the effectiveness of the mRSS training courses differ in the literature.

Objectives: The objective of our study was to evaluate the effectiveness of the mRSS training course in rheumatology fellows in the rheumatology departments.

Methods: The study included 6 fellows from the departments of rheumatology. Participants were given a 1-hour-long theoretical training, including dermal involvement, and mRSS assessment by 3 rheumatology experts experienced in scleroderma, which was followed by an applied training on 4 patients for one-hour. Participants scored two patients before and after training on a form, which included 17 domains with a total score range between ‘0’ and ‘5’. Then using the SPSS15 software program, inter-rater reliability was assessed with intraclass correlation (ICC) analysis for both pre- and post-training mRSS. Fleiss’ kappa was used to measure the degree of agreement according to 12 Rodnan score areas before and after the training.

Results: The ICC value for pre-training and post-training total Rodnan scores was 0.867 (95% CI 0.625-1.00, P=0.05), and 0.905(95% CI 0.045-1.00, P<0.02), respectively. Individual analysis of score areas showed that after the training there was an increase in degree of agreement in some of these areas, while there was no difference in one area, and it decreased in others (Table 1).

Table 1. The ICC value and percentage of agreement of the modified Rodnan skin score in scleroderma

Conclusion: Several studies have demonstrated the applicability, reliability, and validity of mRSS, a measure of dermal involvement, and that evaluation of the score requires experience, and an applied learning process. In the literature, the inter-rater ICC values during previous training courses are reported to range between 0.378 and 0.921(1). These studies show differences in terms of the number and experience of participants,
Cannabidiol in the treatment of pain related to systemic sclerosis skin ulcers: Our experience


Objectives: Evaluate our experience to define the efficacy of cannabidiol (CBD), one of the constituents of Cannabis sativa, in the treatment of skin ulcers (SU) in patients with systemic sclerosis (SSc).

Methods: Twenty-five SSc patients (F/M 22/3, mean age 52.3 ± 12.9 years) were consecutively included. In all patients the disease was complicated by longstanding, painful SU resistant to opioids. Pain was classified as severe, according to WHO guidelines, in all subjects. The local treatment with CBD was applied daily for the treatment of SU-related pain. We performed both an evaluation by the patients and a local evaluation by the medical staff at the end of treatment.

Results: The local treatment with CBD produced a significant reduction of symptoms daily: self-evaluation of pain at the same time in the evening, oral (five drops bid) as local treatment (two drops in the site of SU) for the treatment of SU-related pain. We performed both an evaluation by the patients and a local evaluation by the medical staff at the end of treatment.

Conclusion: Our study suggests that the use of CBD as a local therapy is effective and safe in maintaining analgesia in patients with SSc, not only would it be essential for an adequate healing of a local wound.
AB0647 ASSOCIATION OF VASCULAR BIOMARKERS WITH SYSTEMIC SCLEROSIS CLINICAL FEATURES AND NAILFOLD VIDEOCAPILLAROSCOPY ALTERATIONS: CROSS SECTIONAL STUDY

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Background: The most reliable markers reflecting endothelial activation and injury in Systemic sclerosis (SSc), are intercellular adhesion molecule (ICAM1), vascular cell adhesion molecule (VCAM1), E selectin (Es) and P selectin (Ps) (1).

Objectives: To assess concentrations of these vascular biomarkers in SSc patients (pts) in comparison to healthy controls (HC) and in relation to disease manifestations.

Methods: Patients who fulfilled the 2013 ACR/EULAR SSc classification criteria and have never been treated with endothelin receptor antagonist, phosphodiestrase inhibitor 5 or prostanoids were eligible. Exclusion criteria were overlap syndromes, other autoimmune and cardiovascular diseases, diabetes mellitus, thrombosis, pregnancy, active infection or neoplastic diseases. Our study included 53 SSc pts [34 limited (lcSSc) and 19 diffuse cutaneous SSc (dcSSc)] and 31 age- sex matched HC. Serum concentration of ICAM1, VCAM1, Es and Ps were measured using a commercial ELISA kit (Quantikine; R&D Systems), expressed as ng/mL. Clinical evaluation of patients was obtained, including nailfold videocapillaroscopy (NVC). Disease activity was assessed by the revised EUSTAR activity index. Statistical analysis was done in R. Student’s test or ANOVA, otherwise Mann-Whitney U or Kruskal-Wallis tests were used. Pearson’s or Spearman’s correlation were done depends on nature of data. ICAM1 cut off value was assessed with ROC analysis. Association were performed with uni- variate logistic regression for NVC alterations and multivariate for Anti-TopoI/Scl70 antibodies (aTSA).

Results: Concentration of all markers were elevated in SSc pts compared to HC (ICAM1 p<0.001, VCAM1 p<0.001, Es p<0.05, Ps p<0.05). Different disease subsets exhibited higher values of ICAM1 and VCAM1 respect to HC (ICAM1 p<0.05, VCAM1 p<0.001). Concentration of ICAM1 was higher in dcSSc compared to lcSSc (p<0.05). ICAM1 level were independently associated with positive aTSA (OR 1.2, 95% CI 1.02 –1.35, p<0.001), with distinguishing cut off value of 34.94 (Sn 0.90%, Sp 0.60%, AUC 0.85). ICAM 1 was positively correlated with the erythrocyte sedimentation rate (r 0.3, p<0.05) especially within disease duration > 3 years group (r 0.4, p<0.05). Higher levels of ICAM1 was found in diffus e disease and injury of Systemic sclerosis (SSc).

Conclusions: ICAM-1 could be used as a novel inflammatory marker. Recently studies are ongoing for objective easy markers (1).

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AB0648 CORRELATIONS BETWEEN NEUTROPHIL/LYMPHOCYTE RATIO AND CLINICAL CHARACTERISTICS OF PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: The ratio of neutrophils to lymphocytes (NLR) is considered as an additional marker of dSSc. Elevation of ICAM1 and Ps concentration in active group, but without significant differences (p>0.05). T

Methods: Our study is based on a retrospective analysis. We collected in a data base clinic and epidemiological characteristic of SSc patients. Fifty-two patients (46 female; 10 subset diffuse) with SSc were enrolled consecutively for analyse the correlations. We considered the correlation with NHL and skin core, ulcers, pitting scars, gastro-intestinal events, fibrosis on HTGR, respiratory parameters (FVC, DLCO), PAPs, diastolic abnormalities, capillaroscopy alterations and activity index (2). Student’s t-test was used for comparison averages, correlation among variables were assessed by Spearman’s correlation testing.

Results: Sociodemographic and clinical characteristic were reported in table 1. The correlation analysis statistically significant is summarized in table 2: NLR vs skin score, DLCO, PAPs, and activity index. The correlation analysis between NLR and presence of ulcers and pitting scars was considered not quite significant. There were no correlations between other parameters and NLR.

Conclusion: NLR values correlated negatively with DLCO value, and positively with PAP value, skin score and activity index NLR level may serve as inflammatory marker in patients with SSc.

REFERENCES

Table 1. Sociodemographic and clinical characteristics

| Patients n=52 | Age (years) mean ± sd | 53.58±13.99 |
| Sex (M/F) | 6/46 |
| Disease duration (years) mean ± sd | 6.84±3.6 |
| WBC count (K/mm3) mean ± sd | 8348±87360 |
| NLR, mean ± sd | 2398±1290 |
| Skin score, mean ± sd | 3.94±4.28 |
| DLCO% of prediet, mean ± sd | 71.4±623.4 |
| PAPs mmHg, mean ± sd | 19.9±19.1 |
| Ulcers (yes/no) | 5/47 |
| Pitting scars (yes/no) | 18/34 |
| Capillaroscopy alterations, normal/early/active/late | 6/17/17/12 |
| Activity index, mean ± sd | 1.86±1.48 |

Table 2. Correlation analysis between NLR and skin score, DLCO, PAPs, activity index

| NLR | r value | p value | Skinscore | 0.28 | 0.30 | 0.29 | 0.28 |
| DLCO | 0.045 | 0.035 | 0.033 | 0.042 |
| PAPs | Activity | index |

Disclosure of Interests: None declared

AB0649  
B CELL DEPLETION THERAPY IN VERY EARLY SYSTEMIC SCLEROSIS. A POTENTIAL WINDOW OF OPPORTUNITY?

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Background: Our group, among others, has shown that B cell depletion therapy may improve skin thickening and interstitial lung disease (ILD) related to systemic sclerosis (SSc). All studies assessing the clinical efficacy of B cell depletion therapy in SSc have recruited patients with established disease fulfilling the old classification criteria. In our previous studies we have found that patients with shorter disease duration had a better clinical response to RTX.

Objectives: It is unknown whether treatment in very early SSc can affect long term outcomes. We aimed at assessing the effect of rituximab (RTX) in patients with very early SSc.

Methods: We report 2 cases where RTX was administered within 24 months from the appearance of Raynaud’s.

Results: A 56 year-year-old female with an 18-month history of Raynaud’s developed interstitial lung disease (ILD) with extensive ground glass lesions, a normal FVC (82%) but decreased DLCO (44%). A diagnosis of SSc was made based on the presence of positive anti-centromere antibodies, puffy fingers, telangiectasies, ILD and Raynaud’s. Six months following RTX treatment, her PFT’s had increased (FVC 94% and DLCO 55%) and chest HRCT showed an obvious improvement. One year later the patient no longer reported dyspnea. She remained on RTX for 5 years with no respiratory symptoms, stable PFTs and no evidence of disease progression. The second case is a 27-year old female with a 1-year history of Raynaud’s, puffy fingers, positive anti-Scl70 and capillaroscopy. Within a few months her skin thickened rapidly reaching an MRSS of 12 and developed tendon friction rubs. Six months following RTX treatment skin thickening had almost resolved; she only had mild sclerodactyly. Tendon friction rubs disappeared. The patient received 8 consecutive RTX courses throughout a period of 4 years. During this period the patient remained in a steady clinical condition with no signs of disease progression.

Conclusion: It is generally accepted that autoimmunity/immune dysregulation and vasculopathy are the primary events in SSc that eventually trigger the fibrotic process. Based on this pathogenetic model, one can hypothesize that a therapeutic intervention early in the disease course, prior to the appearance of fibrotic manifestations could potentially prevent permanent organ damage. Our data suggest that there may be a window of opportunity in SSc. This is why we propose that large scale, controlled studies assessing the efficacy of RTX (or other immune based therapies such as mycophenolate) in patients with very early disease are highly needed.

Disclosure of Interests: None declared


AB0650  
PERSPECTIVES AND UNMET NEEDS OF PATIENTS WITH POOR PROGNOSIS SYSTEMIC SCLEROSIS ON AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION CARE: A QUALITATIVE STUDY

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Background: Autologous hematopoietic stem cell transplantation (HSCT) can induce long-term remission in patients with diffuse cutaneous systemic sclerosis (dcSSc). Nevertheless, it is an intensive treatment with risk of treatment related mortality and associated adverse events requiring long-term hospital admission. Little is known about the psychosocial impact of HSCT on patients with dcSSc. Additionally, post-discharge care is currently not standardized.

Objectives: To gain more insight in the experiences of patients during and after HSCT and to identify unmet needs in current care.

Methods: Semi-structured interviews were conducted with dcSSc patients that underwent HSCT in four academic hospitals in the Netherlands. Interviews were transcribed verbatim and analyzed with NVivo12.

Results: Eight patients were interviewed (5 males and 3 females, mean age 48 years (SD 10), mean disease duration 4.6 years (SD 1.9), mean time since HSCT 3.2 years (SD 2.4). At inclusion mean SDAQ was 1.3 (SD 1.1) and mean ESSO-SLE 0.86 (SD 0.21). While patients were satisfied with the frequent, low-threshold contacts with physicians and nurses, the decision-making process followed by HSCT and recovery was mentally taxing. Although patient education was experienced as extensive pre-treatment, participants reported they only felt the real impact of it during therapy. Patients felt anxious throughout the hospital stay and they could not recall most events from that period. Feelings of losing control over health and over time were frequently described. Support of family and friends was important during treatment. Apart from the practical aid, they provided emotional support, helping to cope with emotions and to find purpose. Furthermore, a specialized nurse involved in psychosocial support and care management was highly valued. Still, participants felt lonely and misunderstood due to invisible disabilities, such as fatigue and pain. Six months after HSCT, patients experienced less stress. It was often hindered. There were unmet needs. Patients preferred to be better informed about what to expect after admission. Structured and written instructions should include themes such as self-management, practical tips and prognosis of recovery. Participants would advise peers to keep a diary and even take photos during HSCT and hospital stay, in order to help recollect and assimilate past events. Peer-support was recommended by most patients.

Conclusion: HSCT had a large impact, both physical and emotional. We identified unmet needs regarding patient education on rehabilitation and psychosocial support in the period following HSCT.

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AB0651  
THE INFLUENCE OF RITUXIMAB THERAPY ON THE DYNAMICS OF THE BASIC PARAMETERS AND ACTIVITY OF SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is an autoimmune disease characterized by skin and multi-organ involvement induced by overproduction of autoantibodies by B cells.

Objectives: To assess the influence of Rituximab (RTX) therapy on the dynamics of the basic parameters and activity of SSc during long-term follow-up.

Methods: There were 90 SSc patients (pts) in the prospective study. 75% were women; 57% pts had diffuse SSC. SSc was confirmed ACR/ EULAR criteria. The average duration of the disease was 5.8 years and of the study was 27 months. For the purpose of the analysis, a group of pts was selected that had no less than two evaluation points from 12 to 42 months and had received 2.9±1.1 g RTX in average during follow-up period. The examination included both routine clinical laboratory parameters and special research. We evaluated the modified Rodnan skin score (mRSS), forced vital capacity (FVC), diffusing capacity of carbon monoxide (DLCO), the Valentini Disease Activity index, estimated glomerular filtration rate (eGFR) before and after completed RTX. All pts included in the study received treatment with vascular, anti-inflammatory and/or immunosuppressive medicines. The average dose of prednisolone was 11.8±4.4 mg/day.

Results: In general, more than 90% pts demonstrated different kinds of improvements. A reliable improvement was documented based on a number of indicators, which reflect typical features of the disease. Thus, skin induration was reduced (skin score decreased), lung functional capacity
increased (increase of FVC of more than 5%). The skin score was reliably decreased from 11.2±9.3 to 6.2 ±4.9 (p<0.0001), FVC was increased from 76.9±19.9 to 84.7±20.9% (p<0.0001), also the increase of DLCO from 46.3±18.3 to 47.8±16.9% from the proper amount was detected. The Valentini Disease Activity index reliably reduced from 2.9±1.7 to 1.38±1.2 points (p<0.0001). Under the RTX therapy, the decrease of glucocorticoids dose was insignificant, but statistically reliable. Thus, prednisolone dose reduction from 11.8±4.4 to 9.2±2.2 mg/day was achieved. Clinically significant but reliable decline of eGFR from 100.2±23 to 94.6 ±2 ml/min/1.73m² was detected.

Conclusion: Thus, RTX has a positive influence on the basic parameters of SSc, mainly on skin damage and lung functionality, reduces the general disease activity. The influence of the RTX on kidney function requires further long-term study.

Disclosure of Interests: None declared

OCTC INTERVAL PROLONGATION IN A SCANDINAVIAN COHORT OF PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES AND SYSTEMIC SCLEROSIS: CORRELATIONS WITH CLINICAL VARIABLES

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Background: Idiopathic inflammatory myopathies (IM) are rare devastating diseases characterized by progressive muscle weakness and muscle fatigue. IM frequently affects other organs pointing to IM as a systemic inflammatory disease. Cardiac involvement is associated with poor prognosis. The symptoms are often subclinical and therefore overlooked. QTc prolongation has been detected in patients with systemic sclerosis (SSc). Autoantibodies are important diagnostic tools to confirm IM and are present in approx. 60% of IM patients. Autoantibodies are increasingly being recognized as markers for specific organ involvement. A biomarker for cardiac involvement has yet to be elucidated.

Objectives: The aim is to generate new knowledge about cardiac involvement in IM detected by electrocardiography (ECG) and to evaluate possible associations between autoantibodies and cardiac involvement detected on ECG in a cohort of IM patients compared with ECG changes in a cohort of SSc patients.

Methods: In a Scandinavian cohort, 263 IM patients (130 polymyositis patients, 77 dermatomyositis patients, and 56 inclusion body myositis patients) and 102 SSc patients were investigated by ECG and basic cardiovascular and disease specific assessments according to international guidelines. IM patients were tested for myositis specific autoantibodies (MSAs); anti-Jo-1, anti-PL-7, anti-PL-12, anti-Cy, anti-JE, anti-ARF, anti-Mi-2, anti-MAA, anti-TIF1γ, anti-NXP2, anti-SAE1, anti-HMGCR) and myositis associated autoantibodies (MAAs); anti-PM/Scl70, anti-PM/Scl, anti-Ro/52, anti-Ku, anti-CNA1).

Results: Twenty two IM patients (8.49%) had abnormal QRS duration versus one SSc patient (1.06%) (p = 0.012). SSc patients had significantly longer QTc duration than IM patients (QTc = 432.7 ms ± 22.2 and 426.4 ms ± 23.6, respectively) (p = 0.03).

Multivariate regression analysis revealed that increased C-reactive protein (CRP) (p = 0.008), gender (p = 0.002), and hypertension (p = 0.007) were associated with QTc duration in IM patients. Likewise, pulmonary arterial hypertension was associated with QTc duration (p = 0.001) in SSc patients.

In analysis of pooled data for IM patients and SSc patients, factors associated with QTc duration were increased CRP (p = 0.005), gender (p = 0.001), and hypertension (p = 0.01).

Conclusion: Both IM patients and SSc patients had ECG changes though no particular pattern was shown. The findings support our hypothesis on cardiac involvement in IM patients. No significant association was found between presence of either myositis specific or myositis associated autoantibodies and ECG changes. This could be due to the relatively low number of each autoantibody. There is a need to conduct larger prospective studies to identify a possible autoantibody for cardiac involvement in IM.

Disclosure of Interests: The authors would like to thank all participating patients and the study personnel at the including centres.

AB0653 SERUM CARDIAC BIOMARKERS BUT NOT SUBCLINICAL CARDIOVASCULAR MAGNETIC RESONANCE ABNORMALITIES ASSOCIATE WITH SYSTEMIC SCLEROSIS ASSOCIATE WITH THE DEVELOPMENT OF CARDIOVASCULAR EVENTS

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Background: Primary cardiac disease in systemic sclerosis (SSc-PCD) is associated with a poor prognosis when clinically evident. Subclinical SSc-PCD is described in up to 2/3 of SSc patients when sensitive methods are employed. The prognostic implication of these findings is not clear.

Objectives: To describe the prevalence of cardiovascular magnetic resonance (CMR) abnormalities, their association with clinical phenotype and cardiac biomarkers, and whether cardiac biomarkers and CMR predict the development of cardiovascular (CV) events.

Methods: Patients fulfilling the ACR/EULAR criteria for SSc, with no CV disease (CVD), diabetes and no more than 1 CV risk factor had 3Tesla CMR, including late gadolinium enhancement (LGE), myocardial perfusion, T1 mapping for T1 native and extracellular volume (ECV) quantification, and cardiac biomarkers measured. CV events were defined as episode of myocardial, heart failure, rhythm disturbances and/or echocardiography. Subclinical abnormalities including systolic dysfunction, diastolic dysfunction > grade 1 or regional wall motion abnormalities. 47 healthy volunteers (HV) with comparable age and gender served as controls.

Results: 83 SSc patients were recruited, median (IQR) age of 54 (49, 54), 84% females and 33% dcSSc, 40% had ILD, 24% a history of digital ulceration (HuDU) and 29% were on Ciclosporin. CMR showed higher ECV% and T1 native, markers of diffuse fibrosis in SSc compared to HV [mean (SD) 30 (4) vs 25 (3), p<0.000; 1241 (76) vs 1206 (55), p=0.003]. Lower myocardial perfusion reserve reserve (MPR) was also noted in SSc patients [mean (SD) 2.0 (8) vs 3 (1), p<0.000]. None of the HV had LGE-fibrosis, whilst 16 (20%) of the patients had a non-ischemic LGE pattern. Left ventricular (LV) volume and function were similar between HV and SSc patients. Presence of LGE associated with hsTnI and lower forced vital capacity (rho=0.283, p<0.032; rho=0.217, p=0.5). Multivariate analysis revealed an association of T1 native with mRSS and CRP (B=0.5, p=0.02; B=0.218, p=0.049), ECV% associated with NTproBNP and HuDU (B=0.305, B=0.310, p<0.005). 73/83 had >1 year available clinical and echocardiography follow up data with a mean (SD) duration of 24 (20) months. 12/73 had a CV event judged to be SSc-PCD. LV mass associated with CV events(p=0.043) (Table 1), whilst univariate regression analysis showed that both hsTnI (OR=1.014, p=0.014) and NTproBNP (OR=1.005, p=0.026) but none of the CMR variables associated with the development of CV events.

Conclusion: Asymptomatic SSc patients with no overt CVD demonstrate both focal and diffuse fibrosis, which are associated with cardiac biomarkers and markers of SSc disease activity. Whilst hsTnI and NTproBNP associated with the development of CV events, none of the measures of fibrosis did although a higher LV mass was noted in this.
NAILFOLD MICROVASCULAR CHANGES IN MIXED SCLERONET®: A PATIENT-CENTERED

The capillaroscopic scores of enlarged capillaries, giant capillaries, microhemorrhages were found significantly higher in SSc versus MCTD patients.

Results:

Statistical analysis was performed by non-parametric tests.

NVC parameters were compared at T0 with 10 random SSc patients involved in the first NVC analysis (T0), and during a three-year follow-up. Furthermore, 10 lipofillings for DUs non-responsive to pharmacological therapy were carried out.

Conclusion:

In a limited cohort of MCTD patients with an average disease duration of 6.4 years and a follow-up of three years, the nailfold microvascular damage does not seem to be significantly progressive. Patients with MCTD seem to show less enlarged/giant capillaries, and larger absolute number of total and normal capillaries than SSc patients.

REFERENCES


Disclosure of Interests: None declared

AB0655 SCLERONET®: A PATIENT-CENTERED MULTIDISCIPLINARY APPROACH TO SYSTEMIC СLEROISIS
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Background: Systemic Sclerosis (SSc) is a rare connective tissue disease which may affect almost the whole body.1 Because of its clinical complexity and heterogeneity, a multidisciplinary approach is helpful to patients.

Objectives: The project aims at providing evidence that a multidisciplinary approach allows to early detect and rightly treat diseases linked to SSc determining an improvement of the Quality of Life (QoL) for patients.

Methods: GILS, the Italian SSc Patient Organisation, selected 4 expert centers in Milan (where over one thousand patients are treated), among those able to diagnose and cure SSc in its different and difficult aspects.

Results: The monthly meeting is held with patient representatives (PRs). No private data are discussed. Hospitals General and Sanitary Managers must give a positive evaluation every year in order to continue ScleroNet® project.

Evaluation: The project needs to keep ScleroNet® patient-centered and to focus the attention on the QoL, whose improvement has been described by patients but not yet supported for all interventions by questionnaires.

Common inclusion and exclusion criteria have been established. Cardiologists performed 110 assessments through EKG, echocardiography and cardiopulmonary exercise testing. These tests gave the following diagnosis: 16 non-ischemic cardiomyopathy (after BNP and troponin dosage as well as cardiac MRI) got an immunosuppressive therapy; 22 PAHs; 34 diastolic functions; 23 respiratory disease. The rest did not receive a specific diagnosis but still in follow up. 70 perioral lipofillings have been carried out: body weight rose by 2 to 3 kg after 4 months in patients with low BMI thanks to a greater mouth opening. Moreover, a better elasticity of the perioral area led to better 70 perioral lipofillings have been carried out: body weight rose by 2 to 3 kg after 4 months in patients with low BMI thanks to a greater mouth opening. Moreover, a better elasticity of the perioral area led to better

Disclosure of Interests: None declared

AB0654 NAILFOLD MICROVASCULAR CHANGES IN MIXED CONNECTIVE TISSUE DISEASE: DIFFERENCES WITH SYSTEMIC SCLEROSIS
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Background: Detailed nailfold capillary abnormalities have not been described in mixed connective tissue disease (MCTD) as well as their changes over time, unlike systemic sclerosis (SSc) which microvascular damage has been classified and validated by nailfold videocapillaroscopy (NVC) in specific and progressive scleroderma patterns ("Early", "Active", "Late") (1-5).

Objectives: Aim of this study was to retrospectively compare detailed MCTD nailfold capillary abnormalities with those of SSc patients at first visit, and to monitor MCTD capillary changes over time.

Methods: Ten patients (mean disease duration 6.4±2.4 years, mean age 50±19 years,) affected by MCTD (Kasukawa’s criteria) were enrolled. Patients with either anti-extractable nuclear antigen positivity different from U1RNP or anti-dsDNA antibodies were excluded. Main capillary parameters (scores of enlarged capillaries, giant capillaries, microhemorrhages, capillary ramifications, as well as absolute number of normal and total capillaries per linear millimeter) were assessed in MCTD patients at their first NVC analysis (T0), and during a three-year follow-up. Furthermore, NVC parameters were compared at T0 with 10 random SSc patients matched for disease duration (6.4±1.4 years) and age (51±17 years). Statistical analysis was performed by non-parametric tests.

Results: The capillaroscopic scores of enlarged capillaries, giant capillaries and microhemorrhages were found significantly higher in SSc versus MCTD patients at T0 (2.0±0.5 vs 1.9±0.6 p=0.04, 1.6±0.7 vs 0.7±0.5 p=0.02, 1.25±0.7 vs 0.7±0.7 p=0.05, respectively). Moreover, the absolute number of both total capillaries and normal capillaries were found significantly lower in SSc versus MCTD patients (5.8±1.9 vs 7.6±1.8 p=0.04 and 0.45±1.0 vs 3.0±3.2 p=0.009). On the contrary, no statistically significant difference was observed at T0 for the other capillary parameters (including capillary ramifications) between the two groups of patients.

With the limit of a different pharmacological background among patients, no statistically significant variation of the scores, as well as of the absolute value of the above reported capillary parameters was observed during the 3 years of follow-up in MCTD patients. No statistically significant correlation was observed between capillary parameters and MCTD clinical aspects (Raynaud phenomenon, dysphagia, dyspnoea, scleredactyly, sicca syndrome, telangiectasias and arthalgia) at first visit and during follow-up.

Conclusion: In a limited cohort of MCTD patients with an average disease duration of 6.4 years and a follow-up of three years, the nailfold microvascular damage does not seem to be significantly progressive. Patients with MCTD seem to show less enlarged/giant capillaries, and larger absolute number of total and normal capillaries than SSc patients.

Disclosure of Interests: None declared

AB1590 SCIENTIFIC ABSTRACTS

Scientific Abstracts

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Abstract AB0655 Table 1. NVC measures in SSc patients with CV events versus SSc patients with no CV events at first NVC analysis (T0) and during a three-year follow-up. In SSc patients, no statistically significant variation of the scores, as well as of the absolute value of the above reported capillary parameters was observed during the 3 years of follow-up in MCTD patients. No statistically significant correlation was observed between capillary parameters and MCTD clinical aspects (Raynaud phenomenon, dysphagia, dyspnoea, scleredactyly, sicca syndrome, telangiectasias and arthalgia) at first visit and during follow-up.

Conclusion: In a limited cohort of MCTD patients with an average disease duration of 6.4 years and a follow-up of three years, the nailfold microvascular damage does not seem to be significantly progressive. Patients with MCTD seem to show less enlarged/giant capillaries, and larger absolute number of total and normal capillaries than SSc patients.
delimited area, according to their specific problems. ScleroNet® seems to enable the experts to networking specifically on SSc, giving the opportunity of sharing their knowledge. Without ScleroNet® the timing of treatment and/or diagnosis would have been delayed. Nevertheless, due to the fact that it is a work-in-progress and some experts have been enrolled in a second stage, data are available only for some interventions. The use of validated questionnaires and indicators are necessary to measure and prove the value of ScleroNet®.

REFERENCES


AB0566 ANTISYNTHETASE SYNDROME: CLINICAL VALUE OF SOLOMON’S AND CONNORS’ DIAGNOSIS CRITERIA

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Background: Two antisynthetase syndrome (ASSD) diagnosis criteria sets have been proposed; both consider mandatory the presence of anti-aminoacyl transfer RNA synthetase (ARS) autoantibodies. Solomon’s criteria consider major clinical criteria (intestential lung disease (ILD) and fulfillment of Bohan and Peter criteria for DM/PM) and minor criterions (arthritis, Raynaud’s phenomenon (RP) and mechanic’s hands (MH)) (1). In contrast, Connors criteria evaluate the presence of at least one of the prior mentioned clinical features except myositis, and includes the presence of fever without other cause (2).

Objectives: 1) To evaluate the performance of Solomon’s and Connors’ criteria in patients with clinical suspicion of ASSD or myositis and positive ARS. 2) To describe their clinical characteristics.

Methods: We performed an observational retrospective study in two centers. All patients with clinical suspicion of ASSD or myositis, and positive ARS in the myositis immunoblot (Euroimmun assay) were included.

Results: We analyzed 37 patients; 70.3% woman, with a mean age at the moment of the ARS detection of 51.4 (SD±14.0) years, median time from the first symptom to the ARS detection of 4.0 (SD±5.8) years, and time of evolution of 7.69 (SD±6.51) years. The frequency of ARS was: anti-Jo1 (n=17), anti-PL12 (n=8), anti-PL7 (n=4), anti-EJ (n=4), and anti-OJ (n=4).

ARS diagnosis fulfillment and clinical manifestations:
1) Patients that met Solomon and Connors’ criteria (n=17, 45.9%):

- At disease onset: ILD (n=6, 35.9%), muscle weakness (MW) (n=5, 29.4%), and arthritis (n=4, 23.5%).
- During disease development: ILD (n=14, 82.3%); arthritis (n=13, 76.5%); MW (n=10, 58.8%); mechanic hands (n=10, 58.8%); Raynaud phenomenon (n=6, 47.0%); and fever (n=3, 17.5%).

2) Patients that only met Connors’ criteria (n=17, 45.9%):

- At disease onset: ILD (n=5, 29.4%), MW (n=3, 17.6%), or arthritis (n=5, 29.4%).
- During disease development: Arthritis (n=8, 47.0%); ILD (n=6, 35.3%); MW (n=6, 35.3%); Raynaud phenomenon (n=6, 35.3%); fever (n=5, 29.4%); and mechanic hands (n=1, 5.9%).

Relative risk (RR) of the different clinical manifestation for Solomon’s criteria fulfillment:
- MH RR=2.98 (95%CI 1.5-5.6; P=0.002), ILD RR=9.2 (95%CI 1.1-9.2; P=0.013); other manifestations does not presented significant RR.

Conclusion: More than three quarter of all patients presented as first clinical manifestation one of those included in the ASSD classic triad (ILD, MW and arthritis). These manifestations showed increasing rates during the disease development, being more frequent in patients that met Solomon’s criteria than in those who only met Connors’ criteria; more than twice as high in for ILD, and almost twice for MW and arthritis. This suggests that patients who met Solomon’s criteria, at disease onset presented incomplete clinical forms, and their clinical progression favored the criteria fulfillment. On the other hand, we cannot predict if the patients that only met Connors’ criteria are going to fulfill Solomon’s criteria; nevertheless, our results suggests it.

To conclude, our results suggest that: 1) Connors criteria might be considered for screening of ASSD; 2) Solomon’s criteria can be considered as the first gold standard for the ASSD diagnosis; 3) the presence of mechanic hands or ILD indicates a high probability of Solomon’s criteria fulfillment in patients with positive ARS.

REFERENCES

Disclosure of Interests: Martín Greco: None declared, María Jesús García de Yébenes: None declared; Inmaculada Alarcón: None declared; Anaíry Brandy-García: None declared; Ilígo Rúa-Figueroa: None declared; Estibaliz Loza: None declared, Teresa Oton: None declared, Juan Carlos Quevedo-Abeledo: None declared, Carlos Rodriguez-Llorente: None declared, Loreto Carmona: Research support from: Abbvie, Actelion, Celgene, Grünenthal and Sanofi, Teresa Oton: None declared.

AB0657 ANTISYNTHETASE SYNDROME: NON-ANTISYNTHETASE ANTIBODIES, CLINICAL MANIFESTATIONS AND OVERLAPS

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Background: The antisynthetase syndromes (ASSD) are characterized by the presence of anti-aminoacyl transfer RNA synthetase (ARS) autoantibodies and other features including myositis, arthralgias, interstitial lung disease (ILD), Raynaud’s phenomenon (RP), mechanic hands (MH), and fever. Two ASSD diagnosis criteria have been developed; those proposed by Connors, and the stricter criteria proposed by Solomon (1, 2). Additionally, other symptoms of connective tissue diseases (CTD) can be present.

Objectives: To describe a series of patients with positive ARS and analyze: 1) the associated non-ARS antibodies, 2) the clinical manifestations that are not included in the different ASSD diagnosis criteria; and 3) the initial diagnosis attributed by the Rheumatologist in the clinical records.

Methods: We performed an observational retrospective study in two hospitals. All patients with clinical suspicion of ASSD or myopathy and positive ARS in the myositis immunoblot (Euroimmun assay) were included.

Results: We analyzed 37 patients; 70.3% woman, with a mean age at the moment of the first symptom of 50.5 (SD±14.0) years, and 51.4 (SD±14.0) years at the moment of the ARS detection. The frequency of ARS was: anti-Jo1 (n=17), anti-PL12 (n=8), anti-PL7 (n=4), anti-EJ (n=4), and anti-OJ (n=4).

Associated non-ARS antibodies: anti-Ro52 (n=17, 46.7%); anti-PM/Scl75 (n=6, 16.2%); anti-PM/Scl100 (n=5, 13.5%); anticientromere (n=3, 8.1%); rheumatoid factor (n=2, 5.4%); anti-CCP (n=2, 5.4%); and anti-DNAd (n=2, 5.4%). Other antibodies detected only once: Anti-SRP, U1RNP, LAC, anti-M2, Anti-cardiolipin, anti-DNA.

- Most frequent clinical manifestations not included in the ASSD diagnosis criteria: Raynaud’s (n=10, 27%); dermamyositis rash (n=9, 24.3%); and SICCA symptoms (n=7, 18.9%).

- First diagnosis attributed by the clinicians in the medical records: ASSD (n=19, 51.35%), dermatomyositis/polyarthritis (DM/PM) (n=13, 35.1%), overlap syndrome (n=3, 8.1%), systemic lupus erythematosus (SLE) (n=3, 8.1%), primary Sjögren’s syndrome (SS) (n=2, 5.4%); rheumatoid arthritis (RA) (n=2, 5.4%); undifferentiated CTD (UCTD) (n=2, 5.4%); and Systemic Sclerosis (SSc) (n=1, 2.7%).

Overlaps included 2 DM/PM-Ssc and 1 DM/PM-SSc, and both UCTD was described with Ssc pattern. Thus, of the 18 cases not diagnosed as ASSD, 6 (33.3%) presented DM/PM diagnosis pattern and 6 (33.3%) Ssc pattern.
**Role of Nailfold Capillaroscopy in Cardiopulmonary Exercise Test (CPET) is a widely used examination to predict the progression of chronic obstructive pulmonary disease or post-transplant lung function, and it has also been examined in the context of respiratory tract involvement and pulmonary hypertension in systemic sclerosis (SSc).**

**Objectives:** As CPET provides a general overview of the aerobic metabolism, influence by pulmonary, cardiac and vascular function, the purpose of this investigation was to assess if development of poor overall disease outcome could be predicted by CPET.

**Methods:** Twenty-nine SSc patients (M/F=5/24; DSSc/LcSSc=16/13) were investigated repeatedly with CPET and followed for a mean of 3.7 (range 1-7) years. The clinical features of the patients were the following: alveolitis (n=15), pulmonary fibrosis (n=16), digital ulcers (n=13), 5 of them required bosentan therapy, macroangiopathy (n=8), GERD (n=26), Barrett metaplasia (n=19), gastrointestinal angioathy (n=5), motility disorder (n=10), pulmonary artery hypertension (Ppulm>40mmHg) or the decrease of carbon-monoxide diffusion capacity (DLCO) >2% /year, or increase in pulmonary artery pressure (ΔPpulm) >3mmHg/hour. Parallel with the CPET, conventional disease activity check-ups have been performed too (echocardiography, chest CT, resting lung function tests, clinical examinations). The correlations between the CPET measurements and conventional findings and the predictive value of CPET parameters at the first visit to the future developments of the composite end-point have been examined.

**Results:** Various CPET results (anaerobic threshold, AT, work rate, WfR, desaturation) have significantly correlated with worsening DLCO (p<0.05; Pearson's correlation). The changes of AT during follow-up and desaturation are predictive to the appearance of the end point designed to comprise multiple features of the disease. This makes CPET a promising non-invasive examination method to estimate the progression of disease in patients suffering from systemic sclerosis.
Disclosure of Interests: None declared


AB0660 SEXUAL HEALTH IMPAIRMENT IN WOMEN WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

Background: Idiopathic inflammatory myopathies (IIM) are a group of disorders characterized by skeletal muscle inflammation that can cause functional impairment including sexual dysfunction.

Objectives: To assess sexual function, pelvic floor function and sexual quality of life of women with IIM compared to age-/sex-matched healthy controls (HC). To subanalyze sexual function in sexually active individuals.

Methods: In total 27 women with IIM [mean age: 54.2, disease duration: 7.3 years, dermatomyositis (DM, 10)/polymyositis (PM, 13)/necrotizing myopathy (MNMA, 3)/inclusion body myositis (IBM, 1)], who fulfilled the Bohan/Peter 1975 criteria for DM/PM, and 27 healthy women (mean age: 54.2) aged 18-83 were included. 11 women with IIM and 11 HC were sexually active. All patients completed the following questionnaires: Sexual Activity Profile; HAQ: Health Assessment Questionnaire; LD: lactate dehydrogenase. Abbreviations: FIS: Fatigue Impact Scale; BDI-II: Beck Depression Inventory II; PISQ-12: Pelvic Floor Distress Inventory Questionnaire, SA: sexually active; ns: not significant.

Results: Compared to HC, patients with IIM had significantly higher prevalence and greater severity of sexual impairment (FSFI, BISF-W), dysfunction of pelvic floor (PISQ-12), and worse sexual quality of life (SQoL-F) (table 1). There were no significant differences in sexual function between PM and DM. Even sexually active IIM patients reported significantly greater sexual health impairment compared to sexually active HC. Sexual health impairment in IIM was associated with laboratory markers of disease activity, health status, physical activity, fatigue and depression (table 2).

Worse scores in IIM were associated with disease activity/health status, physical activity, fatigue and depression. Acknowledgement: Supported by AZV-16-33574A, MCHCR 023728.

Disclosure of Interests: Barbora Hefmánková: None declared, Maja Špiroliová: None declared, Hana Smucrová: None declared, Sabina Oreska: None declared, Hana Štorkánová: None declared, Kristýna Bubova: None declared, Karol Pavěka: None declared, Jiří Vencovsky Consultant for: Samsung, Speakers bureau: AbbVie, Novartis, Pfizer, Sanofi, Eli Lilly; Biogate: UCB, MSD, Werfen, Roche, Ladaslav Šenolt Grant/research support from: AbbVie, Consultant for: AbbVie, Bristol-Myers Squibb, Celgene Corporation, Merck Sharp and Dohme, Novartis, Pfizer, Roche, UCB, Amgen, Takeda, Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Celgene Corporation, Eli Lilly, Merck Sharp and Dohme, Novartis, Pfizer, Roche, UCB, Heiman Mann Consultant for: Pfizer, Eli Lilly, Sanofi, Speakers bureau: AbbVie, Roche, Pfizer, MSD, Eli Lilly, Sanofi, Michal Tomčík: None declared.


AB0661 ASSOCIATION OF ANTI-MDA-5 AUTOANTIBODY WITH AUTOIMMUNE ASSOCIATED HEMOPHAGOCYTIC SYNDROME IN DERMATOMYOSITIS

Background: Autoimmune associated hemophagocytic syndrome (AAHS) is a rare complication in dermatomyositis (DM). We previously demonstrated by multivariate analysis that one of factors associated with mortality in AAHS is DM (OR 5.57 [95% CI 1.08–28.65], P 0.05) among connective tissue diseases (1). Objectives: To find out underlying immunological characteristics, we examined the DM patients with AAHS.

Methods: We examined 31 new onset patients with idiopathic inflammatory myopathies (IIM) including clinically amyopathic dermatomyositis (CADM) admitted to our hospital between January 2009 and December 2018. Three patients had been diagnosed as AAHS proven by bone marrow aspiration. We examined these patient clinical and laboratory characteristics.

Results: Two patients were diagnosed as DM and one was CADM. We found that these 3 patients were associated with interstitial pneumonia. Laboratory tests of all 3 patients showed hyperferritinemia and high titer of anti-MDA5 antibody. All patients were diagnosed as AAHS by bone marrow aspiration smear. Two of them died on the 12th and on the 75th hospital day, respectively, in spite of intensive therapies.

Disclosure of Interests: Manabu Honda, Mayuko Moriyama, Masahiro Kondo, Shunichi Kumakura, Yoshiko Sumita, Yoko Murakawa, Shimane University Faculty of Medicine, Department of Medical Education and Research, Izumo, Japan; Shimane University Faculty of Medicine, Department of Rheumatology, Izumo, Japan

Disclosure of Interests: Shunichi Kumakura: None declared, Yoshiko Sumita: None declared, Speakers bureau: Asahi Kasei Pharma, Ono Pharm., Mayuko Moriyama: None declared, Masahiro Kondo: Speakers bureau: Eisai Co., Chugai Pharma, Mitsubishi Tanabe Pharma, Bristol-Myers Squibb, Jansen Pharma, Astellas Pharma, Takeda Pharma, NIPPON KAYAKU, Daichi-Sankyo, Asahi Kasei Pharma, AbbVie Japan., Shunichi Kumakura: None declared, Yoshiko Sumita: None declared, Yoko Murakawa Grant/research support from: Asahi Kasei Pharmaceutical Co., Ltd.

Conclusion: Anti-MDA5 may relate not only to interstitial pneumonia but also AAHS.

REFERENCES


Disclosure of Interests: Manabu Honda Speakers bureau: Asahi Kasei Pharma, Ono Pharm., Mayuko Moriyama: None declared, Masahiro Kondo Speakers bureau: Eisai Co., Chugai Pharma, Mitsubishi Tanabe Pharma, Bristol-Myers Squibb, Jansen Pharma, Astellas Pharma, Takeda Pharma, NIPPON KAYAKU, Daichi-Sankyo, Asahi Kasei Pharma, AbbVie Japan., Shunichi Kumakura: None declared, Yoshiko Sumita: None declared, Yoko Murakawa Grant/research support from: Asahi Kasei Pharmaceutical Co., Ltd.

Chugai Pharmaceutical Co., Ltd.
Ono Pharmaceutical Co., Ltd.
Daichi Sankyo Co., Ltd.
Teijin Pharma Ltd.
The utility of nailfold capillaroscopy (NFC) has largely been evaluated in patients with Raynaud’s Phenomenon (RP). However, in equatorial countries, RP occurs in only 79% (1) and 84% (2) of patients in Singapore and Malaysia respectively. In the early stages of Systemic Sclerosis (SSc), patients may develop autoantibodies or puffy fingers before the onset of RP (3).

Objectives: There is no data on the utility of NFC in patients with non-RP features suggestive of the scleroderma-spectrum of diseases (SSc, mixed connective tissue disease, dermatomyositis). We aim to compare the utility of NFC for the early diagnosis of the SSc-spectrum of diseases in patients who present with and without RP.

Methods: Patients referred to our institution for NFC evaluation from March 2010 – March 2017 were recruited. Patients with confirmed diagnosis of a connective tissue disease were excluded. Eligible patients were divided into 4 groups: (I) RP with or without positive ANA; (II) Undifferentiated non-RP features to suggest SSc-spectrum diseases and negative ANA; (III) Undifferentiated non-RP features to suggest SSc-spectrum diseases and positive ANA ≥1400 and (IV) Positive SSc-associated autoantibodies without features to suggest SSc-spectrum diseases. Images were analysed at 200x magnification using a software analysis program. Patients were noted to have normal, aspecific or SSc pattern on NFC, defined by the presence of ≥1 giant capillary, avascular areas or ≥2 dilated capillaries with areas of hemorrhage.

Results: 133 patients were recruited (mean age 55 years, 87% female; 76% Chinese, 7% Malay, 10% Indian, 7% other ethnicity). ANA was positive in 74 (82.2%) patients (n=25 anti-centromere, n=3 anti-Scl70). Taking into consideration NFC patterns, the clinical outcomes were normal in 32 patients (35.6%), connective tissue disease (CTD) suspected in 33 patients (36.7%), and definite CTD in 25 patients (27.6%). Diagnostic yield for SSc-spectrum of diseases was highest in Groups I and III (Table 1).

Conclusion: In patients without RP, NFC was most useful to confirm a diagnosis in those with undifferentiated features to suggest SSc-spectrum of diseases and positive ANA.

REFERENCES

Disclosure of Interests: None declared

### Table 1: Outcome measure scores (SF-36 and HAQ-DI) of patients with SSC

<table>
<thead>
<tr>
<th>Measure</th>
<th>Whole group (n=78)</th>
<th>DcSSc (n=60)</th>
<th>LcSSc (n=18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCS</td>
<td>35.65 ± 23.65</td>
<td>34.56 ± 22.90</td>
<td>39.31 ± 26.36</td>
</tr>
<tr>
<td>MCS</td>
<td>41.36 ± 25.94</td>
<td>39.82 ± 26.27</td>
<td>46.51 ± 24.84</td>
</tr>
<tr>
<td>HAQ-DI</td>
<td>1.40 ± 0.95</td>
<td>1.43 ± 0.99</td>
<td>1.31 ± 0.78</td>
</tr>
</tbody>
</table>

#### Figure 1: Correlation HAQ-DI with physical component summary (r=-0.641, p<0.001)

#### Figure 2: Correlation HAQ-DI with mental component summary (r=-0.360, p=0.001)

#### Figure 3: Distribution of SSC patients by functional disability (n=78)
TABLE 1: Mean age, duration of disease and age and follow up.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age at enrolment (yrs)</td>
<td>43.24</td>
<td>11.70</td>
</tr>
<tr>
<td>Mean duration of disease (yrs)</td>
<td>10.02</td>
<td>6.86</td>
</tr>
<tr>
<td>Mean duration of I LD (yrs)</td>
<td>6.02</td>
<td>2.94</td>
</tr>
<tr>
<td>Mean duration of prospective follow up (yrs)</td>
<td>3.80</td>
<td>2.28</td>
</tr>
</tbody>
</table>

Figure 1. Change in FVC of 59 patients of SSc with ILD after 5 years of follow up.

Figure 2. Change in FVC of 46 patients of SSc with ILD taking MMF after 5 years of follow up.

Conclusion: This prospective study was carried out with aim to determine progression of ILD in patients with systemic sclerosis with ILD over period of 5 years. In our study, there was no statistically significant change of FVC over period of time. Worsening of lung function with deterioration in FVC >10% was seen in only 13 patients (22%) (P<0.01). Our findings are similar to study done by Le Gouellec et al in which 75 patients with scleroderma and ILD were followed over period of 72 months of which 26% patients showed significant worsening of FVC (>10%)1. In our study there statistically significant decline in DLCO and increase in PAH over period of 5 years (p<0.001). In study carried out by Le Gouellec et al studying Scleroderma/ILD, there was significant decline in DLCO over period of 72 months of follow up1. In study done by Stephanie C. Mathai et al, there was progressive increase in PAH when patients with scleroderma and ILD with PAH were followed up for period of 4 years2...

REFERENCES

Disclosure of Interests: None declared
AB0067  SPECIFICITY OF ANTI-TRNA SYNTHETASE AUTOANTIBODIES CORRELATED WITH CLINICAL COURSE AND PROGNOSIS OF MYOSIS-ASSOCIATED INTERSTITIAL LUNG DISEASE

Yasushi Kondo, Yoko Nakagome, Kazuki Hirano, Yasushi Koyama, Shos Sasaki, Katsuyoshi Kuniyabashi, Yuto Iizumi, Chiho Yamada, Shrir Salo, Tokai University School of Medicine, Division of Rheumatology, Department of Internal Medicine, Isehara-shi, Japan

Background: Interstitial lung disease (ILD) is associated with mortality among patients with idiopathic inflammatory myopathy (IIM). Anti-aminoacyl-RNA synthetase (anti-ARS) autoantibodies have been identified highly specific for IIM and coincidence of ILD. It has been identified that non-Jo1 positive anti-ARS patients may have decreased survival rate. However, differences of characteristics and prognosis in myositis-associated ILD with an individual anti-ARS autoantibody have not been clarified.

Objectives: To compare the characteristics and cumulative survival of myositis-associated ILD with different positivity of anti-ARS antibodies.

Methods: We investigated retrospectively all consecutive patients with myositis-associated ILD evaluated from 1999-2017. All autoantibodies were screened by using RNP and protein immunoprecipitation assays. Demographic data, laboratory findings and chest computed tomography (CT) images were obtained.

Results: Among 105 patients with myositis-associated ILD, enrolled, 47 had anti-Jo1 antibody and 58 had non-Jo1 antibody, anti-ARS (n=20), anti-PL12 (n=12), anti-PL7 (n=11), anti-KS (n=8) and anti Cu (n=7). The diagnosis at first visit were polymyositis (PM; n=28), dermatomyositis (DM; n=42), clinically amyopathic dermatomyositis (CADM; n=3) and antisynthetase syndrome (ASS; n=31). Most common causes of death in this study were exacerbation of ILD (n=10, 71.4%). Anti-Jo1 positive patients had better ILD prognosis than non-Jo1 patients (log rank test, p = 0.03). The prevalence of rapidly progressive ILD (RP-ILD) and upper lung field lesions in CT scans were significantly higher in anti-ARS positive patients (p=0.02 and p=0.05, respectively). Although the prognosis of ILD was not significantly different among 6 anti-ARS antibodies, anti-ARS positive patients had poor ILD prognosis than anti-Jo1 patients with the 5-year unadjusted cumulative survival was 73% and 95%, respectively.

Conclusion: Our data confirm the characteristics and outcomes of myositis-associated ILD are distinct by anti-ARS antibodies and highlighted that anti-ARS antibody positivity associated with relatively poor prognosis and RP-ILD.

REFERENCES

Table 1. Frequency of SBI, SBI rupture and breast cancer in 562 SSc patients, divided according to the autoantibody status.

<table>
<thead>
<tr>
<th>Patients</th>
<th>SBI</th>
<th>SBI rupture</th>
<th>Breast cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACA</td>
<td>322</td>
<td>4</td>
<td>16</td>
</tr>
<tr>
<td>Anti-Topo-I</td>
<td>125</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Anti-KS</td>
<td>26</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>RNAP3</td>
<td>89</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Others</td>
<td>562</td>
<td>9</td>
<td>27</td>
</tr>
</tbody>
</table>

Disclosure of Interests: Maria Grazia Lazzaroni: None declared, Cristian Caimmi: None declared, Eugenia Bertoldo: None declared, Franco Franceschini: None declared, Angela Tincani Consultant for: UCB, Pfizer, Abbvie, BMS, Sanofi, Roche, GSK, AlphaSigma, Lilly, Jannsen, Cellgene, Novartis, Paolo Airò: None declared


AB0068  ASSOCIATION OF ANTI-RNA POLYMERASE III ANTIBODY AND BREAST IMPLANTS RUPTURE IN ITALIAN PATIENTS WITH SYSTEMIC SCLEROSIS

1Marla Grazia Lazzaroni1, Cristian Caimmi2, Eugenia Bertoldo3, Franco Franceschini4, Angela Tincani5, Paolo Airò1.
1ASST Spedali Civili and University of Brescia, Rheumatology and Clinical Immunology, Brescia, Italy; 2University of Brescia, Molecular and Translational Medicine Department, Brescia, Italy; 3Azienda Ospedaliero Universitaria Integrata, Rheumatology Unit, Verona, Italy

Background: Several epidemiological studies have investigated the link between silicone breast implants (SBI) and Systemic Sclerosis (SSc). Although discordant data were reported, a recent analysis of SBI followed by United States Food and Drug Administration post approval studies, including nearly 100,000 individuals, described an association of SBI with a higher rate of SSc (Standardized incidence ratio 7.00), compared with normative data. The analysis of clinical associations in patients with SSc is complicated by the heterogeneity of the disease, both on immunological and clinical terms. Interestingly, a specific association of anti-RNA polymerase III antibody (anti-RNAP3) and SBI in Japanese patients with SSc was described in a single-center cohort. Moreover, an association of anti-RNAP3 with breast cancer, particularly when synchronous with SSc onset, was also demonstrated.

Objectives: To evaluate the association of SBI with SSc in Italian patients classified according to their SSc-related autoantibodies.

Methods: 562 consecutive women with SSc, classified according the 2013 ACR/EULAR criteria, were evaluated for the presence of SSc-specific autoantibodies (anti-topoisomerase-I (anti-Topo-I), anticentromere (ACA), and anti-RNAP3) in two Italian University centres. For each patient, history of breast cancer and SBI were recorded.

Results: Anti-RNAP3 antibodies were found in 4.6%, anti-Topo-I in 22.2% and ACA in 57.3% of total SSc women (Table 1). Comparing anti-RNAP3 vs anti-RNAP3 patients, a significantly higher frequency of breast cancer (15.3% vs 4.1%; p=0.026), SBI (11.5% vs 1.1%; p=0.006) and SBI rupture (11.5% vs 0.2%; p=0.0003) was found. Notably a higher rate of SBI rupture without breast cancer in anti-RNAP3 vs anti-RNAP3 was also noted (2/22 (9.1%) vs 0/514 (0%); p=0.0016).

Conclusion: In this large Italian cohort, a higher prevalence of SBI and SBI rupture in anti-RNAP3 compared to anti-RNAP3 SSc patients was confirmed, regardless of the history of breast cancer. This preliminary observation should be confirmed in multicentre cohorts, particularly regarding the connection between SSc and SBI rupture.

REFERENCES

Table 1. Frequency of SBI, SBI rupture and breast cancer in 562 SSc patients, divided according to the autoantibody status.

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Disclosure of Interests: Maria Grazia Lazzaroni: None declared, Cristian Caimmi: None declared, Eugenia Bertoldo: None declared, Franco Franceschini: None declared, Angela Tincani Consultant for: UCB, Pfizer, Abbvie, BMS, Sanofi, Roche, GSK, AlphaSigma, Lilly, Jannsen, Cellgene, Novartis, Paolo Airò: None declared


AB0069  THE EFFECTS OF BOSENTAN FOR TREATMENT OF DIGITAL ULCER IN KOREAN PATIENTS WITH SYSTEMIC SCLEROSIS: PROSPECTIVE, MULTICENTER, OPEN-LABEL TRIAL

1Young Ann Lee, Hyun-Sook Kim, Bo Young Kim, Yun Sung Kim, Sung Jae Choi, Jung Ran Che, 1The Soonchunhyang University Seoul Hospital, Internal Medicine, Seoul, Korea, Rep. of (South Korea); 2Gangneung Asan Hospital, Internal Medicine, Gangneung, Korea, Rep. of (South Korea); 3Chosun University Hospital, Internal Medicine, Gwangju, Korea, Rep. of (South Korea); 4Korea University College of Medicine, Internal Medicine, Seoul, Korea, Rep. of (South Korea); 5Pohang St. Mary's Hospital, Internal Medicine, Pohang, Korea, Rep. of (South Korea)

Background: Bosentan is an orally administered dual endothelin-1 (ET-1) receptor antagonist approved in the EU for reducing the number of new digital ulcers in patients with systemic sclerosis (SSc) and ongoing digital ulcer (DU). Oral bosentan therapy was beneficial and generally well tolerated in patients with DU associated with SSc. A total of 3 RCTs were identified. The first two were high quality (RAPIDS-1 and RAPIDS-2) with 122 and 188 patients and treatment durations of 16 and 24 weeks, respectively. Both studies showed that, compared with placebo, bosentan significantly reduced the number of new ulcers; however, it did not have an effect on the healing of preexisting ulcers and pain.

Objectives: This study evaluated the efficacy and safety of bosentan in DU secondary to SSc in Korean patients.

Methods: From December 2013 to December 2017, a prospective, multicenter, open-label trial was performed to investigate the complete healing of DU and tolerability of bosentan in Korean patients with SSc. The SSc
patients were included as having active DU or pulmonary arterial hypertension who had active DU in the last 3 months. A DU was defined as an area with visually discernable depth and a loss of continuity of epithelial coverage, which could be denuded or covered by a scab or necrotic tissue. If the area was denuded, the ulcer was designated active. If denudation could not be judged because of the presence of overlying scab or necrotic tissue, ulcers presenting with features, including underlying pain, based on investigator clinical judgment to be consistent with loss of epithelialization, epidermis, or dermis, and requiring treatment, were designated as active. The effectiveness and tolerability of bosentan was monitored within 24 weeks of study treatment, while healing of DU, largest diameter and the new incidence were also assessed up to week 24.

Results: The primary objective of this study was to assess the efficacy of bosentan in reducing DU including the complete healing rate. Secondary endpoints included development of new DU, assessment of discontinuation, measures of nailfold capillaroscopic (NFC) change. Thirty-five SSc patients were enrolled and seventeen patients were included in the NFC analysis. Mean age was 50.5 year-old, 85.7% was woman, 68.6% of DU in Korean patients with SSc. However, the size of the remaining cases was slightly increased from 4.1 to 5.2 mm, with no statistical significance. There was no statistically significant difference in the semi-quantitative changes of NFC before and after bosentan treatment.

Conclusion: Administration of bosentan over 24 weeks was statistically associated with complete healing and significant reduction in net number of DU in Korean patients with SSc. These angiodysplasias can affect the intestine occasionally as well as the stomach.

Disclosure of Interests: None declared.

a commercial technique of IB to detect TIF1γ (Euroimmun), however, commercial kits sometimes elaborate antigens without using whole protein structure. To date, there are no studies that study the agreement between the commercial kit and homemades IB.

### Objectives:

- To compare the commercial IB results of Anti-TIF1γ with homemade IB.

### METHODS:

Observational retrospective study that included adult patients with some determination of Anti-TIF1γ antibodies since 2014 in two tertiary level university hospitals. We collected demographical and clinical data of all patients. Taking into account their diagnoses we grouped them into: Cancer Associated Myositis (CAM), DM without cancer, Systemic Autoimmune Diseases (SAD) non-DM and other diagnoses. Subsequently, the clinical agreement with the IB results of Anti-TIF1γ performed by commercial (cIB) and homemade (hIB) technique were analyzed. A p value < 0.05 was considered statistically significant.

### RESULTS:

- Of all DM (CAM and DM without cancer), 12 were positive for both techniques, 5 presented discordant results (4 hIB positive with negative cIB and 1 cIB positive with negative hIB). 15 DM were negative for the two techniques, of which 8/15 had other antibodies associated with Autoimmune Myopathy (3 NXP-2, 1 MIZ, 1 MDAS, 1 SAE, 1 Jo1 and 1 Ro52).
- When we analyzed patients with CAM with both techniques, 10/13 presented positive hIB vs 8/13 cIB positive. DM without cancer, 6/19 had positive hIB vs 5/19 cIB positive. The specificity and specificity of each test was evaluated in CAM and DM without cancer, being 61.5% and 73.7% respectively for cIB (p = 0.071), compared to 76.9% and 68.4% for hIB (p = 0.029).
- In non-DM SAD group, 1 patient had positive determination for both techniques, 3 had positive cIB with negative hIB, and 3 cIB negative with positive hIB. We also found other antibodies in 6/7 patients with non-DM SAD. The 9 patients with other diagnoses were: 1 positive for both techniques and 8 positive for cIB and negative for hIB.

### CONCLUSIONS:

HOMEMADE IB with 155 kDa recombinant protein was superior to cIB to detect TIF1γ in our serie of patients with CAM. This could have clinical implications in screening and early detection of neo-plasia that affect false negative by cIB.

A positive cIB in patients not suspected as a SAD were negative for hIB in the major part of cases. It would be recommended to check the commercial IB using homogeneous homemades IB, due to its known clinical-therapeutic implications.

### Disclosure of Interests:

- Ana Milena Millán Arciniegas: None declared.
- M. ANGELES MARTINEZ: None declared, ANAIS MARISCAL: None declared.
- ANGÉLES BAQUELLES: None declared, Letícia Arasaran: None declared, Ernesto Trallero: None declared, Cesar Díaz-Torné: None declared, Ana Laiz Consultant for: Lilly, Novartis, AbbVie, MSD, UCB and Jansens, Berta Magallares: None declared, Patricia Moya: None declared, HyeSang Park: None declared, Berta Magallares: None declared, Patricia Moya: None declared, HyeSang Park: None declared, Berta Magallares: None declared, Patricia Moya: None declared, Berta Magallares: None declared, Patricia Moya: None declared, HyeSang Park: None declared, Berta Magallares: None declared, Patricia Moya: None declared, HyeSang Park: None declared, Berta Magallares: None declared, Patricia Moya: None declared, HyeSang Park: None declared, Berta Magallares: None declared, Patricia Moya: None declared, HyeSang Park: None declared.
- HyeSang Park: None declared.

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**AB0672 RENAL INVOLVEMENT IN PATIENTS WITH DERMATOMYOSITIS AND POLYMYOSITIS**

Simeon Monov1, Daniela Monov2, Rossika Shumaliyeva3, Elena Miloshova4.

1Medical University – Sofia, Department of Rheumatology, Sofia, Bulgaria;
2Medical Institute, Medical University – Sofia, Department of Internal Diseases, Sofia, Bulgaria.

### Background:

Dermatomyositis (DM) and polymyositis (PM) are characterized by moderate to severe muscle weakness and inflammatory lesions in the muscle. They lead to frequent, and, in some cases, life-threatening extramuscular (lung, cardiac, neurologic, kidney) complications.

### Objectives:

The aim of this study was to determine the incidence, the severity, the course and outcome of renal diseases in patients with DM or PM.

### Methods:

We identified 84 patients (68 female, 16 male) with the diagnosis of DM and 23 (14 female, 9 male) with PM. Diagnosis of DM and PM was based on the ENMC classification. The mean follow-up was 5.6 ± 3.8 years. Evaluation of extramural involvement was mainly performed in the presence of suggestive clinical signs. Autoantibodies were detected by ELISA. Acute kidney injury (AKI) was defined as an acute doubling of serum creatinine level. Chronic kidney disease (CKD) was defined if an estimated glomerular filtration rate (eGFR) <60 ml/min on at least 2 measurements 3 months apart.

### Results:

Of the 107 patients, 26 were found to have suffered varying degree of renal involvement. All the 26 patients (22 patients with DM and 4 with PM) had varying degree of proteinuria and haematuria. Renal involvement consisted of AKI in 4 patients and CKD in 18 patients.

### Conclusions:

The study confirms that renal involvement in DM and PM is common and should be considered in the differential diagnosis of adult myositis. Early diagnosis and initiation of effective treatment may prevent serious complications such as renal failure. The study also suggests that renal involvement may contribute to increased morbidity in these patients and should be considered at the initial diagnosis.
patients (6.3%) presented with only positive anti-centromere. CP was nor-
mal in 191 patients, while in 45 patients scleroderma pattern was
observed and in 19 patients nonspecific pattern suggestive of SAD was
seen. Capillaroscopic findings: in each of the 23 patients diagnosed with
SSc, 21 patients had scleroderma pattern. Of the 6 patients with SLE
CP was normal in 4 patients, while one patient had abundant tortu-
sity. Likewise, the 6 patients with Sjögren’s syndrome, only one patient had
a nonspecific pattern suggestive of SAD. Of the 7 patients with MCTD,
four had nonspecific CP, two had a scleroderma pattern and one had tortu-
sous pattern. The 2 patients with overlap (myopathy-scleroderma and
Lupus-scleroderma) both had a pathological CP with scleroderma pattern.

Conclusion: Our study demonstrates that the evidence of scleroderma
pattern is very specific of SSc. However, in certain diseases such as
MCTD, overlap syndromes and inflammatory myopathies, we can also
see this pattern. In other SAD, CP is usually normal or may show some
nonspecific changes.

References: The contribution of capillaroscopy to the differential diagnosis of
connective autoimmune diseases. Best Practice & Research Clinical Rheumatol-
yogy Vol. 21, No. 6, pp. 1093–1108, 2007

Disclosure of Interests: None declared

AB0674 RETROSPECTIVE STUDY OF A COHORT OF PATIENTS WITH SYSTEMIC SCLEROSIS IN A TERTIARY CARE HOSPITAL

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Background: Systemic sclerosis (SS) is an autoimmune disease of unknown etiology, characterized by the presence of fibrosis and vasculopathy
in skin and multiple internal organs such as the lungs, the kidneys and the digestive tract. The course of the disease is unpredictable and could remain relatively stable or have a rapid evolution. Multiple studies have been carried out to determine the clinical characteristics and sur-
vival prognosis on SS patients.

Objectives: To analyze the demographic characteristics, clinical features, treatment and prognosis in a SS disease cohort.

Methods: We performed an observational and retrospective study of
patients with SS. The patients had been attended by the Rheumatology
department of a tertiary care hospital. We collected demographic, clinical
and analytical variables, as well as treatment and prognosis. We classi-
fied the disease employing the LeRoy and Medsger, VEDOSS criteria
and 2013 ACR/EULAR criteria.

Results: Of our 43 patients, 36 (83.7%) were female and only 7 (16.3%) were male. The average age was 60.4 years (SD 15.6), the average age at diagnosis was 53.3 years (SD 17.6) and the mean time of evolu-
tion of the disease was 7.9 years (SD 6.3). Of all the patients, 3
patients (6.9%) died, the mean age at death being 53.6 years (SD 23.7) and the mean time from diagnosis to death of 19 years (SD 10.1). The most frequently occurring presentation was limited SS (with 18 patients
(41.9%), followed by preescleroderma with 14 patients (32.6%), diffuse
SS with 6 patients (14%) and escleroderma sine escleroderma with 2
patients (4.7%). Three patients (7%) were labeled with MCTD. SS was
associated with other autoimmune diseases in 20% of patients. Five
(11.6%) patients developed neoplasms throughout the course of the study. The rest of the clinical characteristics are listed in Table 1 and 2, as well as the strength of association of these with the type of SS, cal-
culated using chi square and Fischer test.

Conclusion: Worthy of noting in our cohort is the absence of sclero-
derma in more than 40% of our patients, probably because the new cri-
teria have allowed us to diagnose the disease at an earlier stage and also due to the scarce frequency of puffy fingers with respect to other larger series. Digestive involvement was the most frequent visceral mani-
festation, followed by pulmonary manifestations, specifically interstitial lung disease (ILD). Despite the small sample size, lung disease was signifi-
cantly associated with the two forms of systemic sclerosis, but not with
the antibody pattern. Both the ILD and the pulmonary arterial hyperten-
sion (PAH) were more frequent in patients with SSc. Mortality in all
cases was due to interstitial lung involvement. As is frequently described, SS is associated with other systemic autoimmune diseases, constituting
an overlap syndrome.

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[3] CLINICAL FEATURES AND PROGNOSTIC FACTORS FOR SYSTEMIC SCLEROSIS RELATED INTERSTITIAL LUNG DISEASE. (2018). Respirol-

Disclosure of Interests: None declared
BODY COMPOSITION IN MYOSITIS PATIENTS AND THE ASSOCIATION WITH DISEASE SPECIFIC FEATURES, PHYSICAL ACTIVITY AND PLASMA LEVELS OF INFLAMMATORY CYTOKINES

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Background: Skeletal muscle, pulmonary, and articular involvement in idiopathic inflammatory myopathies (IIM) limit the mobility/self-sufficiency of patients, and can have a negative impact on body composition.

Objectives: To assess body composition and physical activity of IIM patients and healthy controls (HC) and the association with selected inflammatory cytokines in IIM.

Methods: 54 patients with IIM (45 females; mean age 57.7; disease duration 5.8 years; PM (22)/DM (25)/IMNM (7)) and 54 age-sex-matched HC (45 females; mean age 57.7) without rheumatic/tumor diseases were included. PM/DM patients fulfilled Bohan/Peter criteria for PM/DM. We assessed body composition (densitometry: IDXNAR; bioelectrical impedance: BIA2000-M), physical activity (Human Activity Profile, HAP questionnaire), disease activity (MITAX and MYOACT activity score), muscle involvement (manual muscle test, MMT-8 and functional index, F2I) and plasma levels of 27 cytokines (commercial multiplex ELISA kit, Bio-Rad Laboratories). Data are presented as mean±SD.

Results: Compared to HC, patients with IIM had a trend towards significantly increased body fat’s (BF%) as assessed by IDXNAR (39.9±7.1 vs. 42.4±7.1 %, p=0.077), but significantly decreased lean body mass (LBM) as assessed both by IDXNAR (45.6±8.1 vs. 40.6±7.2 kg, p=0.001) and BIA (52.6±8.8 vs. 49.7±9.0 kg, p=0.003), and increased extracellular mass body cell mass (ECM/BCM) ratio (1.06±0.15 vs. 1.44±0.42, p<0.001), reflecting deteriorated nutritional status and worse muscle predispositions for physical activity. Compared to HC, IIM patients had significantly lower bone mineral density (BMID: 1.2±0.1 vs. 1.1±0.1 g/cm², p=0.001), Disease activity duration negatively correlated with BMD (r=-0.392, p=0.004) and LBM-BIA (r=-0.272, p=0.047). Disease activity assessed by both MITAX and MYOACT positively correlated with LBM-BIA (MITAX: r=0.296, p=0.031; MYOACT: r=0.335, p=0.013) and LBM-DEXA (MITAX: r=0.341, p=0.012; MYOACT: r=0.368, p=0.007), similarly as with basal metabolic rate (BMR; MITAX: r=0.336, p=0.014; MYOACT: r=0.351, p=0.010), and fat free mass (FFM; MITAX: r=0.338, p=0.014; MYOACT: r=0.356, p=0.009). CRP was positively associated with BF% assessed both by DEXA (r=0.276, p=0.035) and BIA (r=0.306, p=0.025). Higher BF%-DEXA was associated with worse physical endurance (F2I: r=-0.311, p=0.026) and worse ability to perform physical activity (HAP: r=0.292, p=0.032), MMT-8 score negatively correlated with ECM/BCM ratio (r=-0.385, p=0.006). Plasma levels of IL-10a positively correlated with body mass index (BMI, r=0.359, p=0.009), BF% (r=0.363, p=0.009), and visceral fat (VF, r=0.409, p=0.003). Plasma levels of MCP-1 positively correlated with ECM/BCM ratio (r=0.387, p=0.005). Increased plasma levels of IL-10 were associated with decreased LBM (r=-0.473, p=0.014).

Conclusion: Compared to healthy age-sex-matched individuals we found significant negative changes in body composition of our IIM patients, which are associated with their disease activity and duration, inflammatory status, skeletal muscle involvement, and physical activity. Plasma levels of several inflammatory cytokines were associated with alterations of body composition in IIM patients and highlight the potential role of inflammatory status on impaired body composition during the course of IIM.

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TREATMENT OF IDIOPATHIC INFLAMMATORY MYOPATHIES – A SINGLE CENTRE EXPERIENCE

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Background: There is no consensus or recommendations for the treatment of idiopathic inflammatory myopathies (IIM).

Objectives: We explored how we treated incident IIM patients in our secondary/tertiary rheumatology centre.

Methods: We retrospectively included all biopsied and physically active patients with IIM diagnosed between January 2010 and June 2018, who were followed at least 6 months. The remission inducing treatment and the treatment at the last follow-up were recorded.

Results: During the 102-month period we identified 102 IIM cases (71.6% female, median (IQR) age 62.7 (52.2–72.1) years): 27.5% dermatomyositis, 22.5% anti-synthetase syndrome, 14.7% myositis in an overlap syndrome, 13.7% immune mediated necrotizing myopathy, 11.5% polymyositis, 6.3% cancer associated myositis, 2.9% inclusion body myositis (IBM), 1% unspecified myositis. 94 (92.2%) patients received glucocorticoids (GC), 18/94 (17.6%) as monotherapy. The remaining 81 (79.4%) were treated with additional immunomodulatory agents (Table 1), most commonly methotrexate. In addition to therapy presented in Table 1, 13 (12.7%) also received human immunoglobulins (IVIG), one (1%) received plasma exchange therapy.

Conclusion: The 8 (7.8%) cases who were not treated with GC received methotrexate, rituximab, and 4 no additional treatment (1 paraneoplastic polymyositis received chemotherapy, 2 IBM, 1 mild polymyositis in elderly, multimorbid patient).

In the first 6 months following diagnosis, 11 patients died (3 due to infection, 2 as a consequence of IIM, 1 due to haemorrhagic shock, 5 of unknown causes), and were lost to follow-up. The remaining 86 patients were followed for a median (IQR) 37.7 (20.2–62.6) months. At last follow-up 49 (57%) patients were still receiving GC, 8 (9.3%) in monotherapy. 9 (10.5%) cases were off GC and other maintenance treatment. Maintenance treatment at last follow-up is presented in Table 2. Treatment was changed in 13 (15.1%) patients (due to progression of pulmonary involvement in 3, active myositis in 4, pulmonary involvement progression and active myositis in 1 and due to intolerance to medication in 6 cases). In addition to therapy presented in Table 2, 2 (2.3%) patients received IVIG (1 concurrently with rituximab and myophenolic acid due to recalcitrant anti-synthetase syndrome and 1 due to IBM complicated with dysphagia).

Table 1. Induction treatment of idiopathic inflammatory myopathy

<table>
<thead>
<tr>
<th>Type of treatment</th>
<th>N (%)</th>
</tr>
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<tbody>
<tr>
<td>Cyclophosphamide; median dose (range)</td>
<td>23 (22.5)</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>43 (42.2)</td>
</tr>
<tr>
<td>monotherapy</td>
<td>30 (29.8)</td>
</tr>
<tr>
<td>+ cyclosporine A</td>
<td>8 (18.6)</td>
</tr>
<tr>
<td>+ cyclosporine A and rituximab</td>
<td>4 (9.3)</td>
</tr>
<tr>
<td>+ chloroquine</td>
<td>1 (2.3)</td>
</tr>
<tr>
<td>Rituximab monotherapy</td>
<td>4 (9.3)</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>3 (2.9)</td>
</tr>
<tr>
<td>Mycophenolic acid</td>
<td>3 (2.9)</td>
</tr>
<tr>
<td>Cyclosporine A monotherapy</td>
<td>1 (1.0)</td>
</tr>
</tbody>
</table>
Table 2. Maintenance treatment of idiopathic inflammatory myopathy

<table>
<thead>
<tr>
<th>Type of treatment</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Methotrexate</td>
<td>28 (34.7)</td>
</tr>
<tr>
<td>monotherapy</td>
<td>20 (17.1)</td>
</tr>
<tr>
<td>+ cyclosporine A</td>
<td>11 (8.6)</td>
</tr>
<tr>
<td>+ rituximab</td>
<td>13 (10.5)</td>
</tr>
<tr>
<td>+ chloroquine</td>
<td>2 (1.7)</td>
</tr>
<tr>
<td>Azathioprine monotherapy</td>
<td>13 (10.5)</td>
</tr>
<tr>
<td>Rituximab monotherapy</td>
<td>3 (2.5)</td>
</tr>
<tr>
<td>Mycophenolic acid</td>
<td>15 (12.4)</td>
</tr>
<tr>
<td>monotherapy</td>
<td>13 (10.5)</td>
</tr>
<tr>
<td>+ tacrolimus</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>+ rituximab</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Cyclosporine A</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Tocilizumab</td>
<td>1 (0.8)</td>
</tr>
</tbody>
</table>

*Antiproliferative and vasoactive treatment as part of anti-scleroderma syndrome

**Conclusion:** GC, methotrexate and cyclophosphamide (in case of pulmonary involvement) were the cornerstone treatment in our cohort.

**REFERENCES:**

Disclosure of Interests: None declared


AB0678  **ANTIPROLIFERATIVE AND VASOACTIVE TREATMENT MODALITIES IN 457 CONSECUTIVE PATIENTS WITH SYSTEMIC SCLEROSIS FROM ACADEMIC CENTERS IN GREECE**

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**Background:** The pathophysiology of Systemic Sclerosis (SSc) encompasses autoimmunity, microvascular damage and fibrosis of the skin and internal organs. Accordingly, the two mainstays of treatment comprise antiproliferative and vasoactive regimens. So far there are limited data regarding the actual use of these agents in daily clinical practice.

**Objectives:** To describe current treatment modalities based on standard practice decisions according to published recommendations and/or guidelines for SSc, as well as to determine to which extent different disease modifying agents, namely antiproliferative and vasoactive drugs, are administered to these patients.

**Methods:** Consecutive patients from 7 academic rheumatology departments across Greece who fulfilled the 1980 American College of Rheumatology criteria for classification of SSc and were examined between January 2016 and December 2018 at least once, were included in the study. Patients’ medical records were analyzed and antiproliferative and vasoactive agents administered anytime during the disease course were recorded.

**Results:** A total of 457 patients (87% women, 51 diffuse SSc, 62% with pulmonary fibrosis, 55% with digital ulcers, mean ± SD age at diagnosis 49 ± 13.1 years, disease duration 10.4 ± 8 years) were studied. Methotrexate was the most frequent antiproliferative agent ever administered (53% of patients, 55% of them with diffuse SSc) followed by cyclophosphamide (26%, 78% of them diffuse), mycophenolate (11%, 63% of them diffuse), azathioprine (10%, 64% of them diffuse), rituximab (8%, 84% of them diffuse) and tocilizumab (3%, 68% of them diffuse). Among antiproliferative agents, endothelin receptor antagonists (ERA) were most frequently ever administered in 39% of patients (64% with diffuse SSc) followed by loprost in 7% (55% diffuse) and 5 phosphodiesterase (PDE) inhibitors in 5.5% of patients (62% diffuse). Among vasoactive agents used, the greatest retention rate at last follow-up visit since initiation had ERA (82%) and PDE inhibitors (86%). Of note, 20% of SSc patients (90% women, 70% limited SSc, age at diagnosis 50 ± 13.2 years, disease duration 8.4 ± 6.4 years) had never been treated with either antiproliferative or vasoactive agents, whereas 41% had ever received only antiproliferative and 8% only vasoactive therapy. Moreover, 1/5 of patients with pulmonary fibrosis had never received antiproliferative treatment, whereas 1/3 of patients with digital ulcers had never received vasoactive drugs (Table).

**Conclusion:** About 20% of contemporary SSc patients, including patients with pulmonary fibrosis and digital ulcers, have never received antiproliferative or vasoactive therapy, possibly reflecting the spectrum of benign disease and/or a subgroup of under-treated patients.

**REFERENCES:**

Disclosure of Interests: None declared


AB0679  **SKIN ULCERS IN SYSTEMIC SCLEROSIS: 10 YEARS’ FOLLOW-UP OF 211 PATIENTS FROM A MONOCENTRIC COHORT IN THE NORTH EAST OF ITALY**

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**Background:** Microvascular involvement plays a pivotal role in the pathogenesis of systemic sclerosis (SSc). Among vasculopathic manifestations, skin ulcers (SU) stand out for their high prevalence.

**Objectives:** The aim of this study was to evaluate the prevalence and the subtype of SU, the association with clinical phenotype and pharmacological approach in the cohort of sclerodema patients attending our tertiary referral centre.

**Methods:** We retrospectively evaluated clinical records of patients affected with SSc according to ACR/EULAR 2013 criteria, attending the Rheumatology Unit of Padova University. Patients with SSc sine scleroderma, overlap syndrome and with a follow-up lower than 24 months were excluded. We evaluated the epidemiological and clinico-serological data, including autoantibody pattern, laboratory data (such as haemoglobin, ESR, CRP), organ involvement and pharmaceutical treatments. Prevalence of SU, type of occurrence (isolated, recurrent and persistent episodes) and site (digital and localized at the lower limbs, between knuckles and ankle/feet) were recorded. Statistical analysis was performed by SPSS v. 24.

**Results:** 211 patients were included in the study: 187 female and 24 male, aged 60.8 ±12.4 years, 147 (70%) with limited cutaneous and 64 (30%) with diffuse form. During the follow-up period of 120 months (50-216), 105 (50%) patients experienced at least one episode of SU: 74 experienced digital ulcers, 11 presented only SU at lower limbs and 20 both kinds of ulcers. Demographic, laboratory and clinical features of our cohort are shown in Table 1. At the multivariate analysis, diffuse cutaneous form, younger age at diagnosis, telangietasias and joint involvement were independently associated to SU. Among 105 patients who experienced at least one episode of SU, 69 (66%) had recurrent/ persistent ulcers. The latter group needed a combination of drugs, including: calcium-channel blockers (90%), low-dose aspirin (75%), protonadoids (85%) and/or endothelin receptor antagonists (58%); 27% requested opioids for analgesia. Concerning SU at lower limbs, 19/31 patients (61%) had macrovascular involvement and 14/31 (45%) persistent ulcers; 6/31 (19%) underwent autologous skin grafting.

**Conclusion:** In our cohort SU occur more frequently in SSc diffuse cutaneous form and are associated with visceral and articular involvement.
Digital ulcers tend to recur during the disease course requiring several drugs, while SU at lower limbs tend to be more persistent.

REFERENCES

Disclosure of Interests: None declared

AB0680 NAIFOLD VIDEOCAPILLAROSCOPY PATTERN CORRELATES WITH ORGAN INVOLVEMENT AND DISEASE OUTCOME IN SYSTEMIC SCLEROSIS: A SINGLE-CENTER OBSERVATIONAL STUDY

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Background: Systemic sclerosis (SSc) is characterized by systemic autoimmunity, vasculopathy and fibrosis. Naifold Videocapillaroscopy (NVC) is a safe method to detect and to analyze morphological microvascular abnormalities in SSc patients. There is circumstantial evidence to suggest an association between NVC abnormalities and disease severity, particularly vascular manifestations. 1

Objectives: To evaluate the association of NVC patterns with demographic, clinical, laboratory features and disease progression in the SSc cohort of University Hospital of Heraklion.

Methods: Retrospective study (2011-2018) of SSc patients who underwent NVC at single center. NVC findings were classified into three distinct patterns namely early, active and late according to Cutolo et al. 2 NVC patterns were correlated with the clinical characteristics of the patients. We also correlated baseline NVC patterns with the progression of the disease at 3 years.

Results: 62 patients [88.6% women, mean age of diagnosis 49.6 years, range 18-82] were included. Compared to early/active pattern, patients with late pattern were more likely to have diffuse SSc (dSSc) (p=0.006), Interstitial Lung Disease (ILD) (80.0% vs 38.1% p=0.002) and esophageal involvement (80.0% vs 47.6% p=0.003). There was a trend for increased frequency of Pulmonary Arterial Hypertension (PAH), digital ulcers (DU) and calcinosis in patients with late pattern (p=0.079, p=1.103 and p=0.079 respectively). Patients with active NVC pattern were more likely to have arthritis (early/active/late: 36.4%/75.9%/55.0%, p=0.054). A total 42 patients had NVC data at the time of SSc diagnosis. At 3 years there were no significant differences regarding disease progression, although patients with late NVC pattern had more hospitalizations due to infections (33.3% vs 9.1%, p=0.191), higher death rate (16.7% vs. 8.3%, p=0.543), need to use cyclophosphamide (33.3% vs 17.4%, p=0.391) and/or bosentan (40.0% vs 22.7%, p=0.426).

Conclusion: In this single-center SSc cohort, NVC pattern was found to correlate with organ involvement especially ILD, esophageal involvement and dSSc. Serious infections and treatment intensification were also more frequent among patients with late NVC pattern. NVC may be a useful prognostic marker for SSc patients.

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Disclosure of Interests: None declared


AB0681 SCLERODERMIC HAND: SUBCLINICAL JOINT INVOLVEMENT?

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Background: Systemic sclerosis (SSc) is a chronic autoimmune connective tissue disorder of not fully understood aetiology characterized by vascular and fibrotic abnormalities in the skin and internal organs. Musculoskeletal involvement, mainly affecting hands and feet, is frequent in SSc and represents a major cause of disability. Ultrasonography is a non-invasive, cost-effective imaging modality which is able to detect the presence of joint involvement in SSc.

Methods: 61 consecutive patients (60 women) were enrolled. Each patient has completed a dichotomous survey to evaluate the presence of joint symptoms (presence of pain, swelling, morning stiffness in the last 3 months). Subsequently a rheumatologist - blinded to clinical data and survey results - performed the ultrasound examination of hands and wrists to evaluate the presence of effusion, synovial hypertrophy, power-Doppler signal, erosions and tenosynovitis defined according to the OMERACT definitions. The ultrasound examination was performed using the Esaote MyLab70 with a multifrequency linear probe (6-18 MHz).

Results: Of the 61 patients analyzed, 29 showned joint involvement on the ultrasound examination (47.5%), in particular, 37.93% had tendon involvement and 72.41% joint involvement (Table 1). 31 patients did not report joint symptoms (50.82%) but 13 (41.93%) still had ultrasound alterations (Table 2).

Table 1. Musculoskeletal involvement in SSc

| Joint effusion | 14/29 (48.28%) |
| Synovial hypertrophy | 18/29 (62.07%) |
| Erosions | 2/29 (0.69%) |
| Tenosynovitis | 11/29 (37.93%) |
| Power-Doppler signal | 9/29 (31.03%) |

Table 2. Musculoskeletal involvement in asymptomatic patients

| Joint effusion | 3/13 (23.08%) |
| Synovial hypertrophy | 8/13 (61.54%) |
| Erosions | 0/13 (0%) |
| Tenosynovitis | 5/13 (38.46%) |
| Power-Doppler signal | 3/13 (23.08%) |

Conclusion: Musculoskeletal involvement is frequent in SSc and can be asymptomatic in more than 20% of patients. The ultrasound examination can make it possible to detect articular and periarticular involvement at an early stage of the disease before the onset of disability.

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CIRCULATING FIBROCYTES IN LIMITED CUTANEOUS SYSTEMIC SCLEROSIS PATIENTS: CORRELATION WITH DERMAL THICKNESS

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Background: Systemic sclerosis (SSc) is characterized by early skin impairment (1,2) and the modified Rodnan skin score (mRSS) is the validated method to assess the severity of this impairment. Whilst skin high frequency ultrasound (US) is a relatively new technique to measure dermal thickness (DT) (2-4).

Recent findings have reported the important contribution circulating fibrocytes make in the early stage of dermal repair and fibrosis. Indeed, as fibrocytes may be an important source of activated fibroblasts/myofibroblasts, it is reasonable to presume that they could be responsible for the increase in these cells observed in the tissue of SSc patients (5-7).

Objectives: The aim of this study was to identify any correlation between the modified Rodnan skin score (mRSS) and dermal thickness (DT) measured by skin high frequency ultrasound (US) and the percentage of circulating fibrocytes in patients with limited cutaneous systemic sclerosis (lcSSc).

Methods: After obtaining approval and written informed consent and the Ethics Committee approval 8 lcSSc patients (7 females, 1 male) and 5 (4 females, 1 male) age-matched healthy volunteers (CNT) were enrolled. The lcSSc patients fulfilled the 2013 ACR/EULAR criteria for SSc (8). DT was evaluated by both mRSS and US (18 and 22 MHz probes), in all SSc patients and CNT, in the standard 17 skin areas evaluated by mRSS. The percentage of circulating fibrocytes was obtained by isolating them from the peripheral blood mononuclear cells (PBMCs) in all lcSSc patients and CNTs. Non-parametric tests were used for the statistical analysis.

Results: The percentage of circulating fibrocytes was positively correlated with DT-US, evaluated by the 22 MHz and the 18 MHz probes (p=0.04 and p=0.03, respectively) and mRSS (p=0.04) in lcSSc patients. Conversely, there was no correlation between these parameters in the CNT group (p=0.05).

Conclusion: The study demonstrates a significant relationship between DT, evaluated by both mRSS and US and the percentage of circulating fibrocytes in lcSSc patients. This observation may well support the hypothesis that circulating fibrocytes make a crucial contribution to skin fibrosis progression.

REFERENCES

Disclosure of Interests: None declared

ROLE OF ELASTIN AND ELASTASE ANTIBODIES IN DEVELOPMENT OF PNEUMOSCLEROSIS IN PATIENTS WITH SYSTEMIC SCLERODERMA


Background: Disturbed elastin metabolism, emerging pathological soluble isoforms followed by triggering of autoimmunity show that the biopolymer under study is associated with the pathogenesis of polyorganic lesions in systemic sclerosis. Elastin catabolism is promoted by elastase, an enzyme with a broad-range substrate specificity. It is the balance of a dynamic elastin–elastase system that determines physiological functioning of organs and tissues containing elastic fibres: the skin, ligaments, lungs, and vascular walls. Antibodies to elastin and elastase are unique predictors of development of pulmonary conditions in systemic scleroderma, which is now considered to be one of risk factors for pulmonary lesion.

Objectives: Developing highly sensitive markers of pulmonary remodeling at early stages of systemic scleroderma with participation of humoral immunity to the elastin–elastase system in the development of pulmonary lesion in systemic scleroderma requires further detailed study.

Methods: Patients for the study were selected from the department of rheumatology at the Emergency Care Municipal Hospital 25 in the city of Volgograd. The main group incorporated 42 persons with the diagnosis of systemic scleroderma verified by ACR/EULAR diagnostic criteria of 2013, without any exclusion criteria. There were 11 men and 31 women aged 23-70 among the systemic scleroderma patients. The mean age of patients was 44±15.4. The control group incorporated 30 healthy donors at the Volgograd Regional Blood Transfusion Station. Antibodies to elastin and elastase were determined in the blood serum by indirect enzyme immunoassay utilizing insoluble forms with enhanced antigen content according to the original technique by Connors et al (1990).

Results: Compared with the control group, patients with systemic scleroderma showed a considerably higher rate of antibodies to elastase (52%) and elastin (38%). The upper normal level of antibodies to elastin was in the range of 0.131 absorbance units, of antibodies to elastase – 0.131 absorbance units. The mean value of elastin antibodies in the blood of systemic scleroderma patients was 0.125 ± 0.068 absorbance units. The value of elastase antibodies was 0.143 ± 0.071 absorbance units. The elevated level of elastin and elastase antibodies in the patients was associated with pulmonary lesion (basal pulmonary fibrosis – 20 (47.6%), pulmonary hypertension – 11 (26.2%), and adhesive pleurisy – 7 (16.7%). In one half of cases the pulmonary lesion was asymptomatic, diagnosed by accessory investigations like X-ray of chest organs, respiratory function study, EchoCG which were administered to assess the extent of abdominal organ inflammation and in differential diagnosis with cardiac insufficiency. The level of elastin antibodies in systemic scleroderma patients with pulmonary lesion was 0.149 ± 0.074 absorbance units, and of elastase antibodies – 0.146 ± 0.043 absorbance units, which was considerably higher than mean values in the control group.

Conclusion: By determining antibodies to elastin and elastase by the proposed technique of enzyme immunoassay at early stages of systemic scleroderma one can predict lesions of pulmonary parenchyma presenting with various clinical signs, and exacerbation of fibrosis processes.

Disclosure of Interests: None declared

DO WE DIAGNOSE ALL THE ANTISYNTHETASE SYNDROME?

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Background: Antisynthetase syndrome (AS) is an autoimmune disease characterized by the presence of antimyosin/IRNA-synthetase antibodies (anti-ARS) and clinical manifestations that may include interstitial lung disease (ILD), myositis, non erosive arthritis, Raynaud’s phenomenon (RP), fever and mechanic’s hands. Until the Connors diagnostic criteria appeared in 2010, these patients with anti-ARS antibody were classified as a mixed connective tissue disease (MCTD), myositis, or as a separate scleroderma like condition and not associated with a specific syndrome.

Objectives: To identify patients with anti-ARS antibodies from our hospital since June 2015, when the immunity laboratory was inaugurated, and to verify if they fulfilled the AS criteria.

Methods: Retrospective observational study carried out in a regional hospital in Barcelona with a reference population of 260,000 inhabitants. All patients with any anti-ARS antibody (Jo1, PL7, PL12, EJ) positive were selected, determined by the Dot Blot Polymiositis/Scleroderma IgG D-Teck. We applied Connors diagnostic criteria and collected demographic, clinical and instrumental data, and types of antibodies.

Results: We identified 18 patients with anti-ARS antibody, 9 anti-Jo1 (53%), 4 anti-PL7, 3 anti PL12 and 1 anti-EJ. Of these, 13 had values of Jo1 > 1/80, 3 values of 1/80 and 1 negative. Other antibodies identified were anti-Ro52 in 4, anti-DNA in 4 and anti-Scl70 in 1. All patients except one met AS criteria. None of anti-DNA positive subjects met criteria for erythematous systemic lupus or systemic sclerosis. The majority

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were women (88%) with a mean age at diagnosis of 62 years (27-83 years), 16 Caucasians and 1 Asian. The clinical manifestations reported were: 5 myositis (29%), 11 ILD (6 BOOP and 5 NSIP) (65%), 6 arthritis (2 polyarthritis, 2 oligoarthritis, 1 palindromic, 1 shoulder girdle syndrome) (35%), 3 Raynaud’s phenomenon (17.5%), 2 mechanic’s hands (11%) and 6 fever (35%). Only one patient had the classic triad (myositis, arthritis, ILD, Jo1), 2 had myositis with ILD (Jo1), 1 myositis with arthritis (PL12), 1 ILD with arthritis (PL7), 7 ILD (Jo1, PL7, PL12), 3 arthritis (Jo1), 1 RP (Jo1) and 1 fever (Ej). Ten had a nailfold capillaroscopy performed, 7 of them had any alteration: 1 active systemic sclerosis pattern and 6 nonspecific (6 ramified capillaries and 3 microhemorrhages).

Conclusion: Our immunologically defined cohort has fewer clinical manifestations than described in clinically defined cohorts (AENAS group and EuroMysitis). Only 20% of patients had myositis and 70% had a single non-mysitis clinical manifestation associated with anti-ARS antibody.

Actually, it involved de-novo diagnosis of AS in half of them.

In patients with suspected AS with low or negative ANA, antibody blot determination is definitive.

Nailfold capillaroscopy in undefined cases is a fundamental tool for diagnosing AS.

Disclosure of Interests: None declared

EFFECTIVENESS OF SPECIALIZED AND INTENSIVE ADL TRAINING IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES – PRELIMINARY RESULTS OF A ONE-YEAR CONTROLLED STUDY

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Background: Idiopathic inflammatory myopathies are characterized by muscle weakness, caused by inflammation and immune changes in the affected muscles, which lead to a limitation in the execution of day-to-day activities (ADL). The aim of our study was to investigate the impact of specialized and intensive ADL training on muscle strength and endurance, depression and QoL of IIM patients.

Methods: Patients were assessed by a physician and a physiotherapist blinded to intervention at months 0, 3, 6, and 12. Patients also filled out patient reported outcomes questionnaires and provided blood for routine laboratory analysis and bio-banking. Data analysis was performed between groups and within the group.

Results: Compared to the observed statistically significant deterioration in the CG over the intervention period, we found a statistically significant improvement in the IG in objectively assessed strength and endurance of muscles as well as in subjectively assessed functional abilities and depression (Table). During the follow-up period, there was a significant deterioration or stagnation of the achieved positive results in the IG. Nevertheless, improved functional ability during the intervention period persisted in the IG in the follow-up period as well. Only numerical improvements in the IG during the intervention compared to the numerical deterioration in CG, that did not reach statistical significance, were observed in some subjectively assessed domains of QoL (SF-36) and fatigue (FIS – in physical dimension).

Disclosure of Interests: None declared


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EFFECTIVENESS OF SPECIALIZED AND INTENSIVE ADL TRAINING IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES – PRELIMINARY RESULTS OF A ONE-YEAR CONTROLLED STUDY

Table 1: Changes in muscle strength and endurance

<table>
<thead>
<tr>
<th>Parameter (unit)</th>
<th>Intervention group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MMTS</strong></td>
<td>Mean ± SEM</td>
<td>Mean ± SEM</td>
</tr>
<tr>
<td>m0: 54.7 ± 2.6</td>
<td>63.6 ± 2.4</td>
<td>m3: 50.6 ± 2.4</td>
</tr>
<tr>
<td>m3: 60.7 ± 2.4</td>
<td>57.9 ± 1.9</td>
<td>m6: 59.1 ± 1.9</td>
</tr>
<tr>
<td>m6: 64.0 ± 2.5</td>
<td>54.2 ± 1.9</td>
<td>m12: 56.5 ± 1.9</td>
</tr>
</tbody>
</table>

<table>
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<tr>
<th><strong>FI-2 (%)</strong></th>
<th>Mean ± SEM</th>
<th>Mean ± SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>m0: 30.0 ± 4.4</td>
<td>38.3 ± 5.3</td>
<td>m3: 46.9 ± 5.4</td>
</tr>
<tr>
<td>m3: 70.6 ± 4.9</td>
<td>29.6 ± 4.6</td>
<td>m6: 70.6 ± 4.9</td>
</tr>
<tr>
<td>m6: 58.4 ± 5.8</td>
<td>26.1 ± 4.1</td>
<td>m12: 25.7 ± 3.6</td>
</tr>
</tbody>
</table>

<table>
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<tr>
<th><strong>HAQ</strong></th>
<th>Mean ± SEM</th>
<th>Mean ± SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>m0: 0.9 ± 0.2</td>
<td>1.3 ± 0.2</td>
<td>m3: 0.7 ± 0.1</td>
</tr>
<tr>
<td>m3: 0.7 ± 0.1</td>
<td>1.4 ± 0.2</td>
<td>m6: 0.6 ± 0.1</td>
</tr>
<tr>
<td>m6: 0.1 ± 0.1</td>
<td>1.4 ± 0.2</td>
<td>m12: 0.2 ± 0.2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>BDI-II</strong></th>
<th>Mean ± SEM</th>
<th>Mean ± SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>m0: 11.9 ± 2.1</td>
<td>13.0 ± 1.7</td>
<td>m3: 10.7 ± 1.7</td>
</tr>
<tr>
<td>m3: 8.9 ± 1.7</td>
<td>14.3 ± 1.5</td>
<td>m6: 8.9 ± 1.5</td>
</tr>
<tr>
<td>m6: 10.5 ± 2.0</td>
<td>15.7 ± 1.5</td>
<td>m12: 16.0 ± 2.0</td>
</tr>
</tbody>
</table>

Conclusion: Our specialized and intensive ADL workout led to a significant improvement in the observed parameters that was clinically significant in a substantial proportion of patients, and prevention of the expected worsening of muscle weakness and QoL.

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Disclosure of Interests: Maja Špitrová: None declared, Sabina Oreska: None declared, Hana Štorkánová: None declared, Barbora Heřmanková: None declared, Petr Česká: None declared, Adéla Rathoušská: None declared, Kateřina Kubinová: None declared, Martin Kleiri: None declared, Lucia Vernerová: None declared, Olga Růžičková: None declared, Helmut Mann Consultant for: Pfizer, Eli Lilly, Sanofi, Speakers bureau: AbbVie, Roche, Pfizer, MSD, Eli Lilly, Sanofi, Karel Pavelka: None declared, Ladislav Senčíl Grant/research support from: AbbVie, Consultant for: AbbVie, Bristol-Myers Squibb, Celgene Corporation, Merck Sharp and Dohrne, Novartis, Pfizer, Roche, UCB, Amgen, Takeda, Speakers bureau: AbbVie, Amgen, Bristol-Myers Squibb, Celgene Corporation, Eli Lilly, Merck Sharp and Dohrne, Novartis, Pfizer, Roche, UCB, Jiří Vencovsky Consultant for: Samsung, Speakers bureau: AbbVie, Novartis, Pfizer, Sanofi, Eli Lilly, Biogen, UCB, MSD, Werfen, Roche, Michal Tomšíč: None declared

EVALUATION OF CARDIOVASCULAR DETERMINANTS OF DISEASE OUTCOME IN SYSTEMIC SCLEROSIS

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Background: Systemic sclerosis (SSc) is a systemic autoimmune disease characterized by microvascular abnormalities. Cardiopulmonary and vascular manifestations in SSc are the most important survival factors in the disease.

Methods: We enrolled 312 consecutive patients (286 females and 24/8% males, mean age 62.3 years, average disease duration 108 months) referred at our department from 2000 to 2018, with a diagnosis of SSc confirmed according to the 2013 ACR/EULAR criteria (3). All patients underwent clinical, instrumental and laboratory evaluation. In 93 patients, negative for anti-topoisomerase I antibodies (aSc70) and anti-centromere antibodies (ACA), the presence of aRNAP3 antibodies was evaluated by an ELISA method (QUANTA LiteTM RNA Pol III).

Results: we found a limited form of disease in 229 patients (73.4%) and a diffuse form in 83 (26.6%). Eighty eight (28.2%) patients were positive for aSc70, 112 (35.9%) for ACA and 17 (5.4%) for aRNAP3. In the whole group, 44 (14%) patients had a positive familiar history for neoplasms while 105 (33.6%) had a history of neoplasms and/or precancerous conditions. Among these 105 cases, 44 (41.9%) were malignant, 50 (47.6%) benign and 11 (10.5%) had precancerous conditions. The most frequent neoplasms were breast carcinomas (14 cases/14.9%), thyroid (7 cases/7.4%), lung and kidney (3 cases/3.1%), melanomas (5 cases/5.3%). The most frequent precancerous condition was Barrett’s esophagus (7 cases/63.3%). Regarding the antibody profile, 5 (4.8%) patients were positive for anti-RNAP3 and only 2 (1.9%) of these patients presented a malignant neoplasm, breast cancer in both cases. In 30 cases (28.6%) these neoplastic/precancerous conditions had arisen in the close period (±36 months) at the SSc diagnosis and only 3 of them were anti-RNAP3 positive. Among the evaluated risk factors, only familiarity was significantly associated with the development of neoplasia (p = 0.003), confirmed at the multivariate analysis (OR 2.9, IC95% [1.5-5.7], p=0.002).

Conclusion: Our study evaluated not only malignant neoplasms, but also benign neoplasms and precancerous conditions and identified familiarity as the only significant risk factor. In our cohort we did not find any relationship between the presence of anti-RNAP3 antibodies and the development of neoplasms, not even stratifying for the type of neoplasm.

Objective: Correlations between different cardiovascular parameters (ejection fraction (EF), diastolic dysfunction, wall motion disturbance, estimated systolic pulmonary arterial pressure (sPAP), flow-mediated vasodilatation, arterial stiffness parameters (augmentation index - Aix, pulse wave velocity - PWV) and diastolic fraction and death were measured.

Methods: Thirty-six SSc patients were involved who underwent detailed arterial stiffness and vasodilatation examinations in 2007. In our work a 10-year period was analysed till 2017 following the progression of organ manifestations and survival.

Results: During the 10-year follow-up, 13 of the 36 patients died. The average survival time was 26.59 (22.36-37.64) years. Significant correlation was found between the initial Aix and PWV with cardiac wall motion disturbance (p = 0.018 and p = 0.016), Aix with restrictive ventilation dysfunction (p = 0.029) and PWV with obstructive ventilation dysfunction (p = 0.015). During the 10-year period, the occurrence of diastolic dysfunction was significantly increased (p = 0.0016), the incidence of arrhythmia did not change significantly. A significant risk factor for survival has been the decrease in EF (p = 0.011), where 1% reduction in EF was associated with 1.9% increase in mortality and 1 mmHg increase in sPAP involved 13% increase in mortality.

Conclusion: Based on our findings vascular stiffness parameters can be good predictors not only of the survival but also of the pulmonary complications with restrictive ventilation disturbances also in SSc.

Disclosure of Interests: Mariann Kalázi: None declared, Renáta Laczik: None declared, Pál Soltész: None declared, Katalin Hodosi: None declared, Szilvia Szamosi: Speakers bureau: Roche, Zoltán Szekearczy Grant/research support from: Pfizer, UCB, Consultant for: Pfizer, Abbvie, Roche, Sanofi, Lilly, Novartis, Speakers bureau: Pfizer, Abbvie, Roche, Sanofi, Lilly, Novartis, Gabriella Szűcs Speakers bureau: Actelion, Roche, Sager DOI: 10.1136/annrheumdis-2019-eular.2454
progression and skin involvement, we started MP with prednisone (mean dose 8mg, a day), observing no significant changes after treating for 8 months on skin or lung disease, only improving the hands edema.

Case 8: woman diagnosed at 47 years old with diffuse SSC, having telangiectases, sclerodactyly, positive ATA and NSIP. At 100 months from diagnosis, after 6 cyclophosphamide cycles followed by azathioprine (both ineffective) due to lung function (FVC 76%, FEV 83%, DCO 26%) and skin (mRSS 30) worsening, MP and prednisone (mean dose 15mg, a day) were started. Currently, we are still waiting to assess clinical response.

Conclusion: Despite it is not included in EULAR current recommendations for SSC complications, our patients have remarkably improved with MP, especially skin involvement, with a good safety profile. These data reaffirm those obtained in previous studies and encourages us to continue considering its use.

Disclosure of Interests: None declared

AB0692 ASSESSING RECOVERY TIME AFTER COLD CHALLENGE AND THUMB INVOLVEMENT CAN HELP RULE OUT SYSTEMIC SCLEROSIS IN PATIENTS PRESENTING WITH RAYNAUD'S PHENOMENON

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Background: Distinguishing primary Raynaud's phenomenon (PRP) from Raynaud's phenomenon secondary to systemic sclerosis (SSc) is crucial in the early detection of SSc. Recently we reported that patients with more severe vasculopathy suffer from a prolonged ischemia time during Raynaud's attack. [1] Additionally, it appears that the thumb is more frequently involved in SSc, where it seems to be spared in PRP. [2] These two characteristics are easily recognized by patients and physicians, and can help rising awareness for SSc.

Objectives: The aim was to study if the recovery of a Raynaud's attack and involvement of the thumb are differentiators for SSc in patients with Raynaud's phenomenon (RP).

Methods: A stepwise cooling and recovery procedure was performed, provoking an RP attack, in patients with PRP and SSc. One hand was submerged up till the radiocarpal joint in water. The water temperature was lowered in steps of 3 degrees Celsius every four minutes, from 33 until at least 9 degrees Celsius. Afterwards ten minutes of recovery in room air of 23 degrees Celsius was observed. During the procedure perfusion of the fingertips was assessed by photo-electric plethysmography.

Results: In total 18 patients with SSc and 88 patients with PRP underwent the procedure. Seventeen (94%) SSc patients had no restoration of perfusion after ten minutes in one or more fingers, compared to 28 (41%) PRP patients (figure 1), with a negative predictive value of 98%. During cooling, 17 (94%) SSc patients developed abnormal perfusion in the thumb compared to 48 (71%) PRP patients (p=0.036), with a negative predictive value of 95%. There was no difference in involvement of the other fingers during cooling (all p>0.05). Positive predictive values were low.

Conclusion: In patients with RP, when there is restoration of perfusion in all fingers after ten minutes or when the thumb is spared, the presence of an underlying SSc is very unlikely. Although this objective measurement needs to be verified with patient's reports, these results suggest that these simple signs can help physicians to assess if the patient needs to be referred for additional tests.

Disclosure of Interests: Konstantinos Triantafyllias : None declared, Michele De Blasi1, Freya Lütgendorf1, Lorenzo Cavagna1, Marco Stortz2, Julia Weinmann-Merke1, Stavros Konstantinides2, Peter Galle3, Andreas Schwarting2. 1ACURA Rheumatology Center, Bad Kreuznach, Germany; 2University and IRCCS Policlinico S. Matteo Foundation, Rheumatology, Pavia, Italy; 3Internal Medicine I, Division of Rheumatology and Clinical Immunology, University Medical Center of the Johannes Gutenberg University Mainz, Germany, Mainz, Germany; 4Center for Thrombosis and Hemostasis, University Medical Center of the Johannes Gutenberg University Mainz, Germany, Mainz, Germany; 5Internal Medicine I, Division of Gastroenterology; University Medical Center of the Johannes Gutenberg University Mainz, Germany, Mainz, Germany.

REFERENCES


AB0691 INCREASED CARDIOVASCULAR RISK IN MIXED CONNECTIVE TISSUE DISEASE: EVALUATION OF MACROVASCULAR INVOLVEMENT AND ITS PREDICTORS BY AORTIC PULSE WAVE VELOCITY

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Background: Macrovascular involvement and cardiovascular (CV) risk have not been sufficiently studied in patients with mixed connective tissue disease (MCTD). In particular, the gold standard assessment method of aortic stiffness carotid-femoral pulse wave velocity (cfPWV) (1) has never been evaluated in patients with this disease.

Objectives: Aims of the present study were to examine cfPWV in MCTD and to evaluate its associations with MCTD associated parameters and traditional CV risk factors.

Methods: cfPWV measurements were performed in 43 MCTD patients and 107 healthy controls. The difference between cfPWV in the two groups was statistically examined and subsequently controlled for the effect of possible confounding factors. Association of cfPWV with MCTD associated organ involvement, routine laboratory parameters and immunoserological markers was also evaluated. Finally, relationship of cfPWV with medications and traditional CV risk factor was examined.

Results: Adjusted statistical analyses for confounding factors showed significantly higher cfPWV values in MCTD patients in comparison to controls (p<0.001). cfPWV correlated in both the patients and the control group significantly with age (r=0.67, p<0.001 and rho=0.69, p<0.001 respectively), diastolic arterial pressure (p=0.024 and p=0.032 respectively) and mean arterial pressure (r=0.44, p=0.004 and rho=0.49, p=0.001 respectively). Moreover, cfPWV correlated in the control group with systolic arterial pressure (p=0.001) (Fig. 1). Higher cfPWV values could be documented in the subset of MCTD patients without lung involvement (p=0.049).

Conclusion: To our knowledge, this is the first study to show that patients with MCTD have significantly higher aortic stiffness and thus CV risk in comparison to controls. Except the disease itself, age and blood pressure were the main predictors of cfPWV.

REFERENCES


REFERENCES


Disclosure of Interests: Annie van Roon: None declared, Arie Van Roon: None declared, Alja J. Stel: None declared, Hendrika Bootsm Grant/research support from: Unrestricted grants from Bristol-Myers Squibb and Roche, Consultant for: Roche, Bristol-Myers Squibb, Novartis, Medicimmune, Union Chimique Belge, Speakers bureau: Bristol-Myers Squibb, Novartis, Andries Smit Shareholder of: Has been co-founder, and is still shareholder of Diagnostics Technologies, the company which developed the AGE reader., Douwe J Mulder Grant/research support from: My University has received the AGE reader., Douwe J Mulder Grant/research support from: My University has received the AGE reader. Annie van Roon: None declared, Arie van Roon: None declared, Alja J. Stel: None declared, Hendrika Bootsm Grant/research support from: Unrestricted grants from Bristol-Myers Squibb and Roche, Consultant for: Roche, Bristol-Myers Squibb, Novartis, Medicimmune, Union Chimique Belge, Speakers bureau: Bristol-Myers Squibb, Novartis, Andries Smit Shareholder of: Has been co-founder, and is still shareholder of Diagnostics Technologies, the company which developed the AGE reader., Douwe J Mulder Grant/research support from: My University has received the AGE reader., Douwe J Mulder Grant/research support from: My University has received the AGE reader.

Abstract AB0692 Figure 1. Percentage of patients with and without restoration of perfusion in all fingers during 10 minutes of recovery, measured in one hand by photoplethysmography.


AB0693 DUROMETRY: HARD FACTS IN SYSTEMIC SCLEROSIS – A SYSTEMATIC LITERATURE REVIEW

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Background: Fibrosis represents one of the main characteristics of systemic sclerosis (SSc), with skin and internal organ involvement being its main clinical expressions. The modified Rodnan Skin Score (mRSS), using clinical palpation to estimate skin thickness, is considered the current ‘gold standard’ to measure skin involvement in a semi-quantitative way. The mRSS has been judged as fully valid through the Outcome Measures in Rheumatology Clinical Trials (OMERACT) Filter, however a high risk of observer bias exists. Therefore, a new challenge for the SSc community is to define a reliable tool, able to more precisely investigate skin involvement in SSc patients, which would be of great value in clinical trials. Durometry, able to objectively investigate skin hardness, might address this need. Objectives: To appreciate the validation status of durometry in SSc patients, guided by a systematic literature review. Methods: Relevant full-text articles using durometry in SSc patients were identified through a systematic literature search in PubMed, EMBASE and Web of Science, according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Besides this systematic search, an additional hand search was performed through reference list screening. All retrieved records were screened by two raters based on title, abstract and full-text level to finally include manuscripts eligible for quality appraisal and data extraction. The finally included manuscripts were analysed according to the OMERACT Filter 2.0. Results: The systematic search yielded 94 records, of which 50 were unique. Seven records were retained for full-text review and analysis, comprising one randomised clinical trial (RCT). The pillar feasibility was well documented in 3 studies [1-3]. Of note, the credibility (i.e. having face validity) of durometry was considered to be valid, as was stated by Kissin et al. [1]. Concerning the pillar truth: content validity was confirmed as durometry correlated well with histological findings (i.e. myofibroblast score and hyalinized collagen, r=0.69 and 0.78 respectively) [4], construct validity was confirmed as a moderate to high significant correlation with the total mRSS was documented in 5 studies (correlation coefficients ranging 0.59-0.81) [1, 3-6]. Concerning the pillar discrimination, the sensitivity to change in the context of one RCT was confirmed [2], inter-rater reliability was confirmed as intraclass correlation coefficients (ICC) ranged from 0.61-0.91 in 2 studies, of which one RCT [1, 3], intra-rater reliability has not been confirmed as this was shown as only investigated in a cohort 5 SSc patients (ICC 0.86-0.94) and thus solid evidence was lacking [1]. The sensitivity to change in situations of change (i.e. change over time, discrimination between SSc patients or between SSc patients and controls) was not confirmed, since solid evidence was lacking in literature.

Conclusion: Current systematically identified evidence suggests partial validation of durometry in SSc patients according to the OMERACT Filter 2.0. Further dedicated studies are needed to completely validate this tool in SSc, more specifically concerning the pillar ‘discrimination’.

REFERENCES

Disclosure of Interests: None declared


Table 1: Validation of durometry according to the OMERACT Filter 2.0

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Conclusion: Current systematically identified evidence suggests partial validation of durometry in SSc patients according to the OMERACT Filter 2.0. Further dedicated studies are needed to completely validate this tool in SSc, more specifically concerning the pillar ‘discrimination’.

REFERENCES

Disclosure of Interests: None declared

Methods: Relevant full-text articles using durometry in SSc patients were identified through a systematic literature search in 3 electronic databases and a hand search of reference lists, according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. All retrieved articles were screened on title, abstract and full-text level. Additionally, a pilot study was conducted in a cohort of non-selected consecutive SSc patients to assess the intra-rater reliability of durometry, by having an anchor rater performing 3 cycles of durometry measurements at 17 skin sites approximating those of the mRSS. Reliability was described by calculating the intraclass correlation coefficient (ICC).

Results: A total of 94 records were identified through the systematic search of which a total of 40 unique titles were screened. After a thorough screening of all titles and abstracts, 7 manuscripts were eligible for full-text review. Finally, of these, only 2 manuscripts fulfilled the predetermined inclusion criteria to be included, as they documented the reliability of durometry as an outcome. Hence, both manuscripts were included in the final analysis for quality appraisal and data extraction. Regarding intra-rater reliability, Kissin et al. reported ICC values ranging from 0.86-0.94 in a small cohort study including 5 diffuse SSc patients (DcSSc) [1]. Regarding inter-rater reliability, ICC values ranged from 0.82–0.96 according to a multicentre randomised clinical trial (n=43 DcSSc) by Merkel et al., and 0.61-0.85 according to Kissin et al. [1,2]. Finally, only 5 fulfilled the predetermined eligibility criteria to be included for quality appraisal and data extraction.

Subsequently to this systematic review, an additional pilot study investigating the intra-rater reliability was performed. Seventy-four SSc patients (61 women; 13 LSSc, 53 LoSSc and 8 DcSSc) underwent durometry assessment in this pilot study. The ICC values for intra-rater reliability ranged between 0.93-0.99.

Conclusion: The systematic literature review revealed that reliability, in particular intra-rater reliability, of durometry in SSc is nearly unexplored territory. The findings of our very pilot study, demonstrating as first an excellent intra-rater reliability of durometry measurements in a large unselected cohort of SSc patients, could confirm the explorative findings previously reported in a small cohort study. Hence, our results stepped forward to the need for intra-rater validation of durometry.
DETECTION OF COEXISTING MYOSITIS-SPECIFIC AUTOANTIBODIES WITH LINE AND DOT IMMUNOASSAYS IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES

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Background: Myositis-specific autoantibodies (MSAs) can be identified in up to 60% of patients with idiopathic inflammatory myopathies (IIM) (1). Based on previous immunoprecipitation studies, MSAs are considered to be mutually exclusive (1), but detection of coexisting MSAs with line or dot immunoassays (LIA/DIA) has not been described (2-3).

Objectives: To determine the prevalence of detection of coexisting MSAs with different LIA/DIAs in patients with IIM, assess the concordance between different assays and describe the clinical phenotype of patients with coexisting MSAs.

Methods: Cross-sectional assessment of prevalence of coexisting MSAs as detected by two LIAs (Euroline Autoimmune Inflammatory Myopathies, Euroimmun, Lübeek, Germany) and ImmunoStrip Myositis Advanced LIA, Trinity Biotech, Buffalo, USA) and one DIA (12 IgG Dot, Alphadia, Mons, Belgium), concordance between these assays and clinical phenotype of patients with coexisting MSAs in a single-center cohort of patients with a diagnosis of one of the subtypes of IIM as diagnosed by the treating physician.

Results: Nineteen of 145 patients (12%) had coexisting MSAs on at least one assay; 5 on the DIA (3.5%) and 5 (3.5%) and 11 (7.6%) on the LIA. Of the 12 IgG Dots, 8 were concordant between LIAs/DIAs; of the 5 (3.5%) and 11 (7.6%) on the LIA. The three combinations of these patients were anti-Jo-1 and anti-NXP-2, anti-Jo-1 and anti-TIF1-gamma, and anti-SAE and anti-NXP2 autoantibodies. The first two patients had an antisynthetase syndrome and the last patient an overlap myositis phenotype. Among the 20 patients with coexisting MSAs, 5 had an antisynthetase syndrome, 2 had an Sjögren syndrome, 4 had scleroderma and 1 had an overlap myositis syndrome. The remaining 11 patients were divided into 3 groups: 6 with one MSA, 4 with 2 MSAs, and 1 with 3 MSAs. The concordance between LIAs/DIAs of patients with coexisting MSAs was low to moderate.

Conclusion: Detection of coexisting MSAs with LIA or DIA occurs in a minority of patients with IIM with varying prevalence between assays from different manufacturers. The combination of more than 1 MSA is not concordant between LIAs/DIAs in the vast majority of patients, suggesting that in most patients detection of coexisting MSAs with LIAs/DIAs reflects a problem of specificity of the assays for the involved autoantibodies.

REFERENCES

Acknowledgement: The study was funded by Alphadia, D-tec, Trinity Bio-tech and Euroimmun.

Disclosure of Interests: Jean-Baptiste Vulteke Consultant for: Innova Diagnostics, Kristl G Claeyss: None declared, Doreen Dillaerts: None declared, Nele Vanhorebeek: None declared, Koen Poensen: None declared, Jan Lenaerts: None declared, Rene Westhovens: Consultant support from: Bristol-Myers Squibb, Consultant for: Celtrion, Galapagos-Gilead, Philip Van Damme Grant/research support from: Senior clinical investigatorship at FWO-Vlaanderen, Daniel Blockmans: None declared, Petra De Haes: None declared, Ellen De Langhe: None declared


LOW DOSE CYCLOPHOSPHAMIDE AND PIRFENIDONE MIGHT WORK IN SYNERGY TO RELIEVE INTERSTITIAL LUNG DISEASE WITH CONNECTIVE TISSUE DISEASE: A PRELIMINARY OBSERVATIONAL STUDY

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Background: There are anti-inflammation and anti-fibrosis agents available for connective tissue disease associated interstitial lung disease (CTD-ILD). A clinical study has been initiated to assess the combination of two CTD-ILD agents together, but whether they can spare dose for each other is unknown.

Objectives: This preliminary study is aimed to observe outcomes of CTD-ILD patients receiving cyclophosphamide plus pirfenidone as a rescue therapy, with each agent at about one third of routine dosage.

Methods: We enrolled CTD-ILD patients who did not improve their symptoms (dyspnea or cough) after at least one-month steroids treatment (prednisone: 1mg/kg daily). Patients who had adjusted immunosuppressive agents other than steroids or had received anti-fibrotic medications within three months before enrollment were ruled out. We switched the treatment into pulse cyclophosphamide (0.4g/m2 monthly) combined with pirfenidone (300mg twice per day). Besides, we reduced the steroids to prednisone 0.5mg/kg daily and then tapered routinely. All the patients were followed up for 12 months.

Results: We enrolled seven patients, of whom two had anti-synthetase syndrome, two had Sjögren syndrome, two had scleroderma and one had mixed connective tissue disease. The media DLCO was 51% of prediction (range 47.7% to 63%) and media FVC was 72.3% of prediction (range 39% to 81%). The media 6MWD was 275m (range202 to 324m). At the end of 12-month follow-up, all the patients regained functional independence with a median 52.7% increase of 6-minute walk distance (range34.4% - 86.3%). Pulmonary function tests showed improved forced vital capacity (median improvement 13.4%, range 0-35.0%) and DLCO (median improvement 6.3%, range 1.7%-16%). The HRCT score had a median decrease of 20.1% (range 11.7% to 29.6%). For quality of life assessment, the SGRQ total score had a median improvement of 53.3% (range 19.5% to 61.7%). Of note, no adverse events were observed during the 12-month follow-up.

Conclusion: Our study provided preliminary but promising clinical evidence for a new strategy in treating CTD-ILD, that cyclophosphamide and pirfenidone might work in synergy and spare dose for each other. A well-designed controlled study is needed to further establish its safety and efficacy.

REFERENCES
None.

Disclosure of Interests: None declared


VALIDATION OF 2017 CLASSIFICATION CRITERIA FOR ADULT AND JUVENILE IDIOPATHIC INFAMMATORY MYOPATHIES PROPOSED BY EULAR/ACR IN CHINESE PATIENTS

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Background: Idiopathic inflammatory myopathies (IIMs) are heterogeneous diseases characterized by muscle weakness and muscle inflammation. Although the Bohan and Peter criteria proposed in 1975 are most widely used[2], there are some limitations. Firstly, they did not clearly specify how to exclude other forms of myopathy disease. Secondly, each criterion is not well defined either. EULAR and ACR jointly proposed the classification criteria for adult and juvenile IIMs and their major subgroups in 2017. The data-driven criteria exhibited high sensitivity and specificity. But most of the patients (62.6%) in the data were Caucasians, the performance of the criteria in Asian patients is unknown, which was one of the important limitations[3].

Objectives: To evaluate the ability of 2017 EULAR/ACR Classification Criteria for Adult and Juvenile Idiopathic Inflammatory Myopathies (IIM) to
classify IIM in comparison with 1975 Bohan and Peter criteria in Chinese patients.

Methods: Two hundred and twenty-one in-patients with suspected IIM (including 40 children) were retrospectively included in this study. The performance of 2017 EULAR/ACR criteria was evaluated by sensitivity, specificity, positive predictive value, negative predictive value and classification rate, in comparison to the 1975 criteria, with clinical diagnosis as the gold standard.

Results: The sensitivity, specificity, positive predictive value, negative predictive value of the 2017 EULAR/ACR criteria in IIM classification were 92.7%, 80.0%, 90.1% and 90.4%, respectively, in contrast to the 1975 Bohan and Peter criteria of 84.0%, 52.2%, 61.8%, and 77.9% (Fig 1). The classification rate of 2017 criteria was also much better than that of 1975 criteria (90.2% vs. 67.4%). The performance of the new criteria in general, as well as the new criteria with muscle biopsy was better. Most IIM patients were correctly further subclassified by the classification tree. The positive rate of myogenic lesion in electromyography (EMG), muscular inflammatory edema in magnetic resonance Imaging (MRI) and specific antibodies of myositis were significantly higher in IIM group than those in control group (p<0.001, all).

Conclusion: The 2017 EULAR/ACR criteria exhibited high sensitivity, specificity, classification rate in the Chinese IIM patients, which was superior to the 1975 criteria. The new criteria showed potentials as clinical classification criteria in the future.

Figure 1. Performance of 2017 EULAR/ACR criteria and 1975 Bohan and Peter criteria.

**REFERENCES**


Disclosure of Interests: None declared


**AB0697D**

CARDIOVASCULAR RISK FACTORS ARE HIGHER IN MALNOURISHED PATIENTS WITH SYSTEMIC SCLEROSIS

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Background: Cardiovascular disease (CVD) is a well known complication in rheumatoid arthritis and systemic lupus erythematosus. Atherosclerosis (ATS) and its impact on CVD in patients with systemic sclerosis (SSc) still remains unclear. Most of studies are suggesting higher frequency of CVD in SSc in comparison to healthy controls. CVD is a leading cause of death in most developed countries, whereas in SSc population it ranges from 20 to 30%. The etiology of ATS in SSc is unknown. Traditional risk factors, endothelial dysfunction and inflammation can contribute to ATS in SSc population. However, there is lack of data about the impact of the nutritional status on CVD factors in SSc patients.

Objectives: The aim of the study was to determine CVD factors among SSc patients depending on the nutritional status.

Methods: In 55 patients with SSc (72.7% well-nourished, 18.1% malnourished, 9.1% pre-cachexia) and 49 healthy controls we measured markers of endothelial dysfunction (asymmetric dimethylarginine - ADMA), inflammation (C-reactive protein - CRP, high sensitivity C-reactive protein - hs-CRP, interleukin 6 - IL-6) and dyslipoproteinemia (oxidized low-density lipoprotein - ox-LDL, high-density lipoprotein- HDL, low-density lipoprotein – LDL and total cholesterol). Nutritional status was determined with subjective global assessment (SGA), body mass index (BMI), bioelectrical impedance analysis (BIA) and anthropometric measurements.

Results: Well-nourished SSc patients had significantly higher level of IL-6 (6.4±10.1 vs. 2.8±3.6 pg/ml; p=0.002) and lower HDL cholesterol (49.9 ±11.6 vs. 57±13.6 mg/dl; p=0.011) in comparison to healthy control. In malnourished SSc patients there was higher concentration of ADMA (1.68 ±0.53 vs. 1.24±0.34 µmol/l; p=0.003), CRP (18±28.6 vs. 2.4±2.5 mg/l; p=0.04), IL-6 (21.6±34.9 vs. 2.8±3.6 pg/ml; p=0.004) and lower HDL cholesterol (42.5±18.3 vs. 57±13.6 mg/dl; p=0.01) in comparison to healthy control. Pre-cachexia SSc group had significantly lower total cholesterol (166.8±28.5 vs. 219.3±40.9 mg/dl; p=0.008) and LDL cholesterol (96.8±21.6 vs. 139.8±31.6 mg/dl; p=0.007). There were no differences in concentration of oxLDL and hsCRP in those groups.

Conclusion: Nutritional status may play role in risk of CVD in SSc patients. Although its contribution to morbidity and mortality rates in CVD in SSc is yet to be established.

Disclosure of Interests: None declared

Spondyloarthropathy – treatment

**AB0698** EFFECTIVENESS AND SAFETY OF CERTOLIZUMAB PEGOL FOR THE TREATMENT OF AXIAL SPONDYLOARTHRITIS IN REAL-WORLD CLINICAL PRACTICE IN EUROPE: RESULTS FROM A PROSPECTIVE NON-INTERVENTIONAL 12-MONTH COHORT STUDY

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**Background:** Certolizumab pegol (CZP) is an Fc-free, PEGylated anti-TNF with an established efficacy and safety profile in axial spondyloarthritids (axSpA) in clinical trial settings.1

**Objectives:** To report CZP effectiveness and safety in patients (pts) with axSpA, including ankylosing spondylitis (AS), radiographic axSpA and non-radiographic (nr) axSpA subpopulations, in routine clinical practice in Europe.

**Methods:** CIMAX (NCT02354105) was a non-interventional multicentre prospective cohort study observing CZP treatment response and safety over 12 months in a real-world clinical cohort of axSpA pts newly prescribed CZP. The primary outcome was change from baseline (CFB) in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) to Week (Wk) 52 in pts with available data, with additional outcomes pertaining to effectiveness and safety. Outcomes were evaluated for AS and nr-axSpA subpopulations (diagnosed according to local practice). Pts who received ≥1 dose CZP were followed up for adverse events (AEs) (Safety Set [SS]); those with baseline and ≥1 post-baseline BASDAI assessment were included in the effectiveness analyses (Full Analysis Set [FAS]). Outcomes are reported using observed case data with no imputation.

**Results:** 682 axSpA pts were enrolled from 101 European sites, of whom 490 (71.8%) completed the study. Of those enrolled, 672 formed the SS (AS: 469; nr-axSpA: 201) and 564 the FAS (AS: 384; nr-axSpA: 179); 2 (SS)/1(FAS) pts with unconfirmed AS/nr-axSpA were included in the overall axSpA population. 27.5% (185/672) AS axSpA pts had previous anti-TNF exposure (AS: 31.1% [146/469]; nr-axSpA: 18.4% [37/201]). BASDAI data were available for 77.8% (439/564) pts at Wk52. In pts with available data, all clinical outcomes were improved at Wk52 in both subpopulations (Table). At baseline, the mean BASDAI was 6.1. At Wk52, the mean BASDAI CFB in pts with available data (n=439) was −2.9 (AS: −2.9 [n=301]; nr-axSpA: −2.8 [n=137]). For pts with and without prior anti-TNF exposure, BASDAI at baseline was 6.1 in both groups (n=165 vs n=299, respectively), and at Wk52, the mean BASDAI CFB was −2.6 (n=127) vs −3.0 (n=312) (AS: −2.7 vs −3.0; nr-axSpA: −2.2 vs −3.0). In the SS, 37.9% (255/672) pts experienced AEs; 20.7% (139/672) experienced drug-related AEs and 6.3% (42/672) serious AEs (1.8% [12/672] reported serious infections); these data were comparable between AS and nr-axSpA (Table).

**Conclusion:** This is the first multicentre European study to evaluate CZP effectiveness and safety in both axSpA subpopulations in routine practice. Improvements were observed in all signs and symptoms in pts who remained on treatment to Wk52; >70% of those enrolled completed the study. No new safety signals were identified following application of CZP to real-world rheumatological practice.

**REFERENCES**


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**DOI:** 10.1136/annrheumdis-2019-eular.1707

**AB0699** EFFECT OF SWITCHING BETWEEN TUMOR NECROSIS FACTOR INHIBITOR IN SPONDYLOARTHRITIS

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**Background:** The introduction of new drugs, in particular tumour necrosis factor inhibitor (TNFi) has revolutionized the treatment of spondyloarthritids (SpA). Meanwhile, about 30% of patients do not reach sustained, long-term efficacy with the first-line TNFi. To date, there is no recommendations available for the treatment of SpA patients after first TNFi failure.

**Objectives:** In this study we assessed the effectiveness of a second and third biotherapy in patients with SpA with an inadequate response to previous TNFi and to analyze the survival of the second biotherapy.

**Methods:** This study included patients with SpA who had had at least two biotherapies. Treatment response was noted at 3 months. At 6 months, we assessed the maintaining of effectiveness in SpA. We studied the elements of a good response to the second biotherapy.

**Results:** Our population of study included 30 SpA. During the second treatment, response rate was achieved by 80% after 3 months. No difference was noted between first and second TNFi among switchers. 86, 7 maintained response at twelve months. For axial forms, decrease in BASDAI was significant at 3 months. For peripheral forms, an improvement of the swollen and tender joint counts was observed and was significant at 3 months. Four patients have received a third TNFi. Response rate was achieved by all of them after 3 months. All of them maintained response at 6 months. The elements of a good response founded were: the early age of the SpA starting (<30 y.o), the high value of initial CRP, the use of ESSG criteria, the SpA type, the extra articular signs, the first biotherapy and the response at 3 months to it, the drugs taken when second biotherapy were initiated a low initial EVA and BASFI.

**Conclusion:** These real-life data show that, after discontinuation of a first TNFi, switching to a second biotherapy in SpA is related to significantly improving of clinical effectiveness compared to a first TNFi.

**REFERENCES**

none

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.3834
GOLIMUMAB PERSISTENCE IN BIOLOGIC NAÏVE AND NON-NAÏVE PATIENTS WITH AXIAL SPONDYLOARTHRITIS: RESULTS OF THE GO-PRACTICE STUDY

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Background: Golimumab (GLM) was the latest anti-TNFα therapy to be indicated in the treatment of chronic inflammatory rheumatic diseases. The pivotal GO-AFTER study [1] and the ongoing observational GO-BEYOND study investigate GLM efficacy in rheumatoid arthritis (RA) patients who previously received biologics. However, clinical studies of GLM in axial spondyloarthritis (AS) are lacking. Using data from the GO-PRACTICE study, we examined GLM persistence in patients with AS.

Objectives: Primary objective was to estimate GLM persistence at 2 years from initial prescription, as a first line of treatment (in biologic naïve patients:BN) and as a second or further line of treatment (in biologic pre-treated patients:BP). Persistence was estimated with the Kaplan-Meier method. Secondary outcomes included assessing disease activity (ASDAS) evolution and patient-reported evaluations of disease activity (BASDAI), pain (VAS), functional ability (HAQ) and quality of life (EQ-5D and SF-12).

Methods: Observational, prospective, multicenter French study, that recruited adult patients with RA, psoriatic arthritis or AS, who were newly prescribed GLM. Patients were followed-up over 2 years; data were collected at baseline (BL), 1 year and 2 years. This abstract presents results from the AS cohort of GO-PRACTICE.

Results: 478 patients with AS (constituting 63% of the total cohort) from 134 sites were included from January 2015 to March 2016. Mean age was 43 years, 55% were female, 61% were BN (n=291) and 39% (n=187) were BP. Mean duration of AS was 5.5 and 10.7 years in BN and BP patients, respectively (P<.001). At BL most were prescribed 50 mg GLM monthly (97%). Co-treatments were disease-modifying anti-rheumatic drugs (34%), corticosteroids (17%) and NSAIDs/analogesics (80%). GLM persistence over 2 years was significantly higher in BN than BP patients (59.2% vs 45.1%, P<0.01). For those still on GLM at 2 years, disease activity (Table1) and patient assessments showed significant improvements for both, BN and BP patients, with improvements being greater in BN patients. GLM was well tolerated in AS patients (n=478), with 46 (9.6%) discontinuing due to intolerance. Among BN patients, 18 (6.2%) discontinued GLM due to primary treatment failure, compared to 28 BP patients (15%). GLM was re-prescribed for 21% of the 241 patients persisting on GLM at 2 years. Post-hoc multivariate analysis showed that being female was a risk factor for GLM discontinuation in AS patients (HR1.9, IC95% 1.4-2.6).

Table 1. Disease activity at BL and 2 years for BN and BP patients with AS persisting on GLM

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</tbody>
</table>

*P is from a 2-factor repeated-measures model testing the significance of the effect of prior biologic treatment on score evolution, adjusted to time

Conclusion: GLM is associated with clinical improvements and good persistence in AS patients, especially those who are biologic naïve.

REFERENCES

Disclosure of Interests: Philippe Bertin Grant/research support from: Financial compensation received from MSD on a pro-rata basis for participation in Scientific Committee meetings and functions for this study, Philippe Goupille Grant/research support from: Financial compensation received from MSD on a pro-rata basis for participation in Scientific Committee meetings and functions for this study, Speakers bureau: Abbvie, Biogaran, BMS, Hospira, Janssen, MSD, Pfizer, Sanofi-Genzyme, UCB, Florence Tubach Grant/research support from: Financial compensation received from MSD on a pro-rata basis for participation in Scientific Committee meetings and functions for this study, Jean Quanich Grant/ research support from: Financial compensation received from MSD on a pro-rata basis for active participation in Scientific Committee meetings and functions, Eric Lespessailles Grant/research support from: Grants/research support from Amgen, Eli Lilly, MSD, UCB, Consultant for: Consultant for Amgen, Expanscience, Eli Lilly, MSD, UCB, Najat Gouyette Employee of: MSD, France, Naoual HARID Employee of: MSD, France, Jean-marie Fayette Consultant for: Contract Research Organisation – ClinSearch, Bruno Fautrel Consultant for: AbbVie, Biogen, BMS, Celgene, Janssen, Lilly, Medac, MSD, NORDIC Pharma, Novartis, Pfizer, Roche, Sanofi-Aventis, Sanofi Genzyme, SOBI, UCB, René-Marc Filpo Consultant for: Honoraria from Novartis as steering committe of this survey

AB0702 TREATMENT EFFECT OF TUMOR NECROSIS FACTOR A INHIBITORS ON MAGNETIC RESONANCE IMAGING PROGRESSION IN PATIENTS WITH SPONDYLOARTHRITIS: A META-ANALYSIS

Yupeng Huang, Yuehong Chen, Tao Liu, Sang Lin, Geng Yin, Qibing Xie. West China Hospital, Sichuan University, Chengdu, China

Background: Treatment effect of tumor necrosis factor α inhibitors (TNFi) in patients with spondyloarthritis (SpA) had been proved by plenty of studies that could remarkably decrease symptoms, signs, and laboratory inflammatory markers. Simultaneously, the treatment effect of TNFi on delaying radiographic progression in SpA was often reported, including magnetic resonance imaging (MRI) which has a high sensitivity on detecting the earliest inflammation.

Objectives: The aim of this meta-analysis was to summarize the treatment effect of TNFi on MRI progression reflected by SPARC score in SpA patients.

Methods: Comprehensive search was conducted in the electronic databases of OVID Medline, OVID EMbase and Cochrane library on Nov.27, 2018. All randomized controlled trials (RCTs) focused on MRI progression and disease activity in SpA patients treated with TNFi were included. Primary outcome was the Spondyloarthritis Research Consortium Canada (SPARC) MRI scoring system, accompanied with or without other outcomes, including Ankylosing Spondylitis Disease Activity Score (ASDAS), Bath Ankylosing Spondylitis disease activity index (BASDAI), Bath Ankylosing Spondylitis functional index (BASFI), C-reactive protein (CRP). Data were pooled by mean differences (MD) with 95% confidence interval (CI) and publication bias was assessed by funnel plot. Sensitivity analysis was performed to test the result robustness.

Results: Totally 10 RCTs enrolled 1006 patients with high methodology were included. Compared with control group, TNFi significantly improved SPARC score at sacroiliac joint (SIJ) (MD=-2.64, 95% CI 2.43-3.25), SPARCC score of spine (MD=1.87, 95% CI 1.27-2.46), ASDAS (MD=-0.96, 95% CI 0.71-1.20), BASDAI (MD=-1.15, 95% CI 0.51-1.78), BASFI (MD=-0.95, 95% CI 0.51-1.40), and CRP (MD=-4.64, 95% CI 1.06-8.23) in double-blind phase. Subgroup analyses by disease subgroup and individual TNFi showed treatment effect of TNFi on delaying MRI progression was not affected by disease subgroup and individual TNFi. Sensitivity analysis showed the treatment effects of TNFi versus placebo were consistent with TNFi versus controls, suggesting the results of the study were robust. The funnel plot of SPARC score at SIJ based on TNFi versus control in double-blind phase was asymmetric, suggesting there might have potential publication bias.

Conclusion: TNFi are effective to treat SpA patients and delay MRI progression which are assessed by SPARC score and treatment effect is consistent among disease subgroups and individual TNFi.

REFERENCES

AQUILA STUDY IN GERMANY – REAL WORLD ADHERENCE AND PERSISTENCE OF SECUKINUMAB TREATMENT IN ANKYLOSING SPONDYLITIS AND PSORIATIC ARTHRITIS PATIENTS – AN INTERIM ANALYSIS

Ula Kiltz1,2, Janat Peterli3, Veronika Winkelmann4, Hans-Peter Tony5, on behalf of the AQUILA Study Group. Rheumatodentrum Rhein, Herne, and Ruhr University, Bochum, Germany. Novartis Pharma GmbH. Clinical Research, Immunology, Rheumatology and Dermatology, Nürnberg, Germany; Medizinische Klinik II, Universitätshospital, Rheumatologynam, Würzburg, Germany

Background: Secukinumab (SEC) has been shown to be an effective treatment for patients (pts) with ankylosing spondylitis (AS) and psoriatic arthritis (PsA) in several phase III studies. Clinical studies reduce confounding factors, but do not guarantee the same results in real world where treating physicians deal with comorbidities, adherence and persistence challenges. Especially medication adherence has a direct impact on health outcomes. However, there is limited information on the adherence and persistence of SEC in routine care.

Objectives: The aim of this interim analysis is to report baseline (BL) characteristics and to assess adherence rate as well as treatment persistence of SEC in AS and PsA pts under real world conditions.

Methods: AQUILA is an ongoing, non-interventional study enrolling 2000 AS or PsA pts under real world conditions. The study is ongoing. All pts were treated with SEC. At treatment start with SEC, pts presented with a number of extra-articular manifestations/comorbidities: plaque psoriasis 11.6% (n=36) in AS and 66.3% (n=425) in PsA, uveitis 6.4% (n=20) in AS and 1.7% (n=11) in PsA, depression 15.4% (n=48) in AS and 15.4% (n=99) in PsA, coronary heart disease 3.5% (n=11) in AS and 7.5% (n=51) in PsA, stroke 0.6% (n=2) in AS and 1.9% (n=12) in PsA, and heart insufficiency 1.6% (n=5) in AS and 3.0% (n=19) in PsA. Adherence rates for SEC [95% CI] at week 52 were 64.5% [58.3,70.5] and 56.0% [51.5, 60.4] for AS and PsA, respectively.

Results: This interim analysis describes 952 pts (AS n=311, PsA n=641) who were included at BL. In total, 51.4% (n=489) of the pts were female and 48.6% (n=463) male, mean age was 50.8 years and 67.8% (n=645) were pretreated with Bx. At treatment start with SEC, pts presented with a number of extra-articular manifestations/comorbidities: plaque psoriasis 11.6% (n=36) in AS and 66.3% (n=425) in PsA, uveitis 6.4% (n=20) in AS and 1.7% (n=11) in PsA, depression 15.4% (n=48) in AS and 15.4% (n=99) in PsA, coronary heart disease 3.5% (n=11) in AS and 7.5% (n=51) in PsA, stroke 0.6% (n=2) in AS and 1.9% (n=12) in PsA, and heart insufficiency 1.6% (n=5) in AS and 3.0% (n=19) in PsA. Adherence rates for SEC [95% CI] at week 52 were 64.5% [58.3,70.5] and 56.0% [51.5, 60.4] for AS and PsA, respectively.
Methods: An independent market analytics firm administered a survey with US rheumatologists (n=104) on the treatment landscape for AS and nr-axSpA. To qualify, rheumatologists had to spend the majority of their professional time in clinical practice, manage a minimum of 50 AS or nr-axSpA patients, and have been in practice between 2 and 35 years. Respondents answered questions pertaining to their practice, the demographics of their AS/nr-axSpA patients, their treatment approaches for each type, as well as attitudinal statements. The survey was administered online in February 2018 and respondents were compensated for their participation. A similar study was also conducted in 2017 allowing for year over year comparison. The data were collected and analyzed in SPSS.

Results: Three-quarters of rheumatologists reported they treated their AS and nr-axSpA patients in a similar manner, though there was a higher use of NSAIDs and local steroids in non-radiographic disease, and more biologic/JAK in AS. More established TNF inhibitors such as adalimumab, etanercept, and infliximab dominated biologics/small molecule preference, collectively accounting for approximately three-quarters of all biologic treatment in AS or nr-axSpA patients, use of biologics increased from 2017. Projected off-label use of tofacitinib in the following three months is also expected to increase.

Conclusion: Rheumatologists are less likely to use biologics/small molecules for nr-axSpA, but when they do, use of brands is similar to those used in AS. While TNF inhibitors continue to account for the majority of biologic/small molecule prescriptions for these conditions, rheumatologists project increased use of agents with alternative mechanisms of action in the future.

Disclosure of Interests: None declared


REFERENCE


DIFFERENCES IN RHEUMATOLOGISTS’ TREATMENT PREFERENCES FOR ANKYLOSING SPONDYLITIS AND NON-RADIOGRAPHIC AXIAL SPONDYLARTHRITIS

PhD position: Lynn Price. Sphera Global Insights, Exton, United States of America

Background: The lack of a formal indication for Non-Radiographic Axial Spondylarthritis (nr-axSpA) has meant that many US rheumatologists fundamentally treat it as an early manifestation of Ankylosing Spondylitis (AS) and seldom differentiate their treatment approach when using biologics/small molecules.

Objectives: This study sought to gain a better understanding of the number of AS and nr-axSpA patients rheumatologists manage, recent changes made in treatment, and how AS and nr-axSpA patients are differentiated beyond radiographic evidence. The study also evaluated the differences in use of biologics/small molecules for the treatment of AS and nr-axSpA and rheumatologist projected changes in the management of these two conditions.

AB0707

LTBI SCREENING IN SPONDYLOARTHRITIS PATIENTS PRIOR TO ANTI-TNF TREATMENT AND FOLLOW-UP IN AN ENDEMIC AREA

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Background: Screening for latent tuberculosis infection (LTBI) remains a concern in endemic regions for anti-TNF eligible patients and recent researches have shown peculiarities between the inflammatory arthropathies such as different groups of spondyloarthritides (SpA).

Objectives: To evaluate the long-term efficacy of LTBI screening and treatment in patients with Ankylosing Spondylitis (AS) and Psoriatic Arthritis (PsA) receiving TNF blockers in a single center.

Methods: A total of 218 SpA patients (135 AS and 83 APS) were screened for LTBI before receiving anti-TNF (infliximab, adalimumab, etanercept, certolizumab pegol, and golimumab) treatment using the tuberculin skin test (TST), chest X-ray (CXR) and history of previous exposure to tuberculosis (TB). Patients were regularly followed every 2-3 months and asked about infectious symptoms or new exposure. TST was not repeated regularly. LTBI patients were treated with isoniazid (300 mg/day) for 6 months, according local guidelines.

Results: One hundred and eight patients (49.5%) were treated with a single anti-TNF agent and the total duration of biological treatment was approximately six years (5.9 ± 4.0). INF and ADA were most often used among the 422 treatment cycles analyzed, representing 45% and 30% respectively. LTBI screening was positive in 82 patients (38%): 69 (84%) were TST-positive, 23 (28%) had a history of TB exposure and 5 (6%) had abnormal CXR. As isolated variables TST positivity and previous exposure accounted for 58(71%) and 11 (13%) LTBI diagnosis. There were some distinct patterns between APS and AS patients screening: despite APS patients had more cases of previous TB than AS patients (6% vs 0.7%, P= 0.03), they had a lower frequency of LTBI (30% vs 42%, P = 0.04). Among LTBI patients, TST positivity was lower in SpA than AS patients (64% vs 93%, P = 0.002), even with more previous exposure (52% vs 18%, P = 0.02) and in patients with peripheral arthritis (27% vs 42%, P = 0.03). During follow-up, 11 patients developed active TB: 5 under ADA, 5 under INF and 1 under ETA treatment. Five cases (45%) were extrapulmonary: 3 pleural, 1 peritoneal and 1 spondylocostitis. Four (36%) cases occurred in patients with a positive LTBI screening and 7 in patients without LTBI. There was no difference in drug survival.
according to type or class of anti-TNF, disease subgroups, duration or use of synthetic drugs and prednisone. Four (36.3%) cases occurred in the first year, median 5.3 (1.2-8.8) months after initiating anti-TNF exposure, 2 of them (50%) in patients with positive LTBI. Seven cases were probably due to re-exposure since occurred later, median 21.9 (14.2-42.8) months (5 in patients with negative LTBI screening). Six patients (54.5%) re-initiated treatment with ETA. Only the patient who developed pulmonary TB under ETA had a second TB infection after 18 months of therapy.

Conclusion: Despite the adequate screening and treatment of LTBI according to local guidelines, TB still occurs in spondyloarthritics patients under anti-TNF therapy, even in the first year of treatment. These data point to LTBI screening/treatment failure, maybe due to anergy, mainly in PsA patients, with peripheral disease, low adherence or re-exposition in an endemic environment. The high frequency of extrapulmonary disease is also a diagnostic challenge.

REFERENCES

Disclosure of Interests: Andrea Shimabuco: None declared, Ana Medeiros: None declared, Renata Miossi: None declared, Karina Bonfiglioli: Speakers bureau: Roche, Pfizer, Bristol-Myers Squibb, Abbvie and Janssen., Julio Moraes: None declared, Célia Desvignes: None declared, David Ternant: None declared, Hervé Walter: None declared, Philippe Goupille: None declared, Denis Muller: None declared, Eloïs Borla: None declared, Carla Saad: None declared.


AB0708 INFLUENCE OF IMMUNOGENICITY ON LONG-TERM MAINTENANCE OF ADALIMUMAB IN SPONDYLOARTHITIS

1,2Marine Samain1, 2, Emile Ducourau3, Theo Rispe’s,4, Emmanuel Demis5, Fabienne Le Guichard6, Lucia Andras10, Alexandre Perdinger,6, Eric Lespessailles11, Antoine Martin12, Grégoire Cormier6, Thomas Armingeat10, Valerie Devauchelle-Pensec11, 12, Elisabeth Gervais15, Benoit Le Golf6,13, Annick de Vries13, Eric Piver14,15, Gilles Painaud6,16, Célia Desvignes15,11, David Ternant15,11, Hervé Walter11,15, Philippe Goupille6, Denis Muller12, This work was a collaborative venture by the VICTOR HUGO network (Hôpitaux Universitaires du Grand Ouest-Western France University Hospitals; http://www.srouest.fr), dedicated to innovative research on rheumatic diseases. 1CHRU de Tours, Service de Rhumatologie, Tours, France; 2University of Tours, EA 7501 GICC, Tours, France; 3CHR d’Orléans, Service de Rhumatologie, Orléans, France; 4Landsteiner laboratories, Sanquin Research, Amsterdam, Netherlands; 5CH du Mans, Service de Rhumatologie, Le Mans, France; 6CH de Blois, Service de Rhumatologie, Blois, France; 7CHRU de Rennes, Service de Rhumatologie, Rennes, France; 8CH de Saint-Brieuc, Service de Rhumatologie, Saint-Brieuc, France; 9CH Vendée, Service de Rhumatologie, La Roche-sur-Yon, France; 10CH de Saint-Nazaire, Service de Rhumatologie, Saint-Nazaire, France; 11Université de Bretagne, Inserm UMR1227 LBAI, Brest, France; 12CHRU de Brest, Service de Rhumatologie, Brest, France; 13CHRU de Poitiers, Service de Rhumatologie, Poitiers, France; 14CHRU de Nantes, Service de Rhumatologie, Nantes, France; 15Biologicals Lab, Sanquin Diagnostic Services, Amsterdam, Netherlands; 16University of Tours, Inserm U 1259, Tours, France; 17CHRU de Tours, Laboratoire de Pharmacologie-Toxicologie, Tours, France; 18CHRU de Tours, Laboratoire d’Infectiologie, Tours, France; 19CHRU de Tours, Inserm CIC1415, Tours, France.

Background: Immunogenicity of anti TNF monoclonal antibodies leads to poor or secondary loss of response. Methotrexate reduces anti-drug antibodies (ADA) to adalimumab at week 26 in spondyloarthritics (SpA).1

Objectives: Herein we sought to examine adalimumab long term persistence in ADA positive versus ADA negative SpA patients.

Methods: The CoMARIS study (Combination of Methotrexate and Adalimumab to Reduce Immunization in patients with axial SpA) is a 26-week prospective, randomised, open-labelled, multicentre study in which patients received adalimumab 40 mg subcutaneously (s.c.) every other week either in combination with MTX 10 mg s.c. for 26 weeks or without MTX. In a post hoc analysis, we reviewed the charts of patients to assess adalimumab persistence. A Cox model analysis was performed to test the following covariates: MTX combination or not, sex, presence of ADA at week 26.

Results: Data from 104 patients (54 without MTX and 50 with MTX) were reviewed, and time of adalimumab discontinuation was collected. The median time of follow-up was 210.57 weeks. ADA positivity at week 26 was the only covariate associated with adalimumab persistence. The median retention rate of adalimumab in ADA positive patients was 56.9 weeks, as compared with 98.6 weeks in those without ADA (log rank: p=0.015). In the Cox model analysis, the presence of ADA at week 26 increased the risk of adalimumab discontinuation by 1.78 [IC 95%=1.11-2.85], p=0.016.

Conclusion: Immunogenicity is a key factor that contributes to adalimumab discontinuation in SpA. MTX at initiation may therefore be consid ered in combination in SpA patients.

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Disclosure of Interests: Marine Samain: None declared, Emile Ducourau: Speakers bureau: BMS and Abbvie, Theo Rispe’s: Research support from: Gennab, Speakers bureau: Pfizer, Abbvie, Regeneron, Emmanuelle Demis: None declared, Fabienne Le Guichard: None declared, Lucia Andras: None declared, Alexandre Perdinger: None declared, Eric Lespessailles: Research support from: Grants/research support from Amgen, Eli Lilly, MSD, UCB. Consultant for: Consultant for Amgen, Expanscience, Eli Lilly, MSD, UCB., Antoine Martin: None declared, Grégoire Cormier: None declared, Thomas Armingeat: None declared, Valerie Devauchelle-Pensec: Research support from: Roche-Chugui, Speakers bureau: BMS, UCB, Roche, Elisabeth Gervais: Speakers bureau: Abbvie, BMS, MSD, Pfizer, Roche, UCB, Novartis, Benoit Le Golf: Speakers bureau: Abbvie, BMS, Janssen, MSD, Pfizer, Sanofi-Genzyme, UCB, Novartis, Annick de Vries: None declared, Eric Piver: None declared, Gilles Painaud: Research support from: Novartis, Roche Pharma, Sanofi-Genzyme, Chugui, Pfizer and Shire, Célia Desvignes: None declared, David Ternant: Speakers bureau: Sanofi, Amgen, Hervé Watier: None declared, Philippe Goupille: Research support from: Financial compensation received from MSD on a pro-rotta basis for participation in Scientific Committee meetings and functions for this study, Speakers bureau: Abbvie, Biogaran, BMS, Hospira, Janssen, MSD, Pfizer, Sanofi-Genzyme, UCB, Denis Muller: Speakers bureau: Pfizer, Novartis.

Background: Dysbiosis can be found in inflammatory joint diseases and induces alterations of the protective function of the intestinal barrier (1). Yet, intestinal inflammation exists in ankylosing spondylitis, which is as much severe as the disease is active (2). Benefits of diets and their influence on the microbiota diversity and inflammation deserve to be studied in spondyloarthritides.

Objectives: The aim of the study was to investigate the nutritional profile in active spondyloarthritides.

Methods: An observational prospective monocentric study based in a french rheumatology department based in Limoges was conducted between February and July 2018, demographic and disease data were collected, in addition to the treatments and the food frequency questionnaire. Voluntary patients over 18 years of age with spondyloarthritis defined by ASAS classification were included. Patients with a diagnosis of inflammatory bowel disease or a bariatric surgery history were excluded of the study. The primary outcome was the correlation between omega-3, vitamin C, refined sugars, fibers and ultra-processed food intakes and the disease activity assessed by ASDAS CRP and BASDAI scores.

Results: Among 140 patients included, there was no statistically significant difference in omega-3, vitamin C, refined sugars, fibers or ultra-processed food intakes between patients with active spondyloarthritis (BASDAI ≥ 4 or ASDAS CRP ≥ 1.3) and patients with inactive disease. The quality of life score and fatigue score were more important in the active and very active disease forms, likewise for the digestive symptoms but there was no link founded in the different nutrients intakes, neither with the associated treatment.

Conclusion: Although our study did not find any nutritional profile in active spondyloarthritides, there was an alteration of quality of life and more digestive symptoms in the active group. Future researches are however required to explore the impact of dietary intakes on the disease activity of spondyloarthritides.

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Disclosure of Interests: None declared
Chugai, Eli Lilly, Grünenthal, Janssen, MSD, Novartis, Pfizer, Roche, and UCB. Consultant for: AbbVie, Chugai, Eli Lilly, Grünenthal, Janssen, MSD, Novartis, Pfizer, Roche, and UCB, Theresa Hunter Employee of: Eli Lilly and Company, Yan Dong Shareholder of: Eli Lilly and Company, Pfizer, Roche, and UCB.

During 16 weeks (wks) of blinded treatment, ixekizumab showed a numerical increase upon switching to IXE (Table). Frequencies of treatment-emergent adverse events (AEs) were similar between IXE and placebo (PBO) in improving signs and symptoms of radiographic axial spondyloarthritis (SpA) international Society (ASAS) criteria (sacroiliitis centrally ankylosed, ASAS40 response rates at Wk 52 were numerically similar between pts who received continuous treatment with IXE and pts who switched from ADA to IXE. No unexpected safety signals were observed through 52 wks of treatment.

**References**


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1. James Cheng-Chung Wei*, Lianne S. Gensler2, Jessica A. Walsh3, Robert B. M. Landewé4, Tetsuya Tomita5, Fangyi Zhao6, Gaia Galli6, Hilde Carlier6, Crescendo, EMD Serono, Genentech/Roche, GSK, Horizon, Inmedix, Janssen, Kezar, Lilly, Merck, Novartis, Pfizer, Regeneron, Samson, Sandoz, Sanofi, Servier, UCB.


**Efficacy of IXE in bDMARD-naïve patients with active r-axSpA**

<table>
<thead>
<tr>
<th></th>
<th>IXE Q4W</th>
<th>IXE Q2W</th>
</tr>
</thead>
<tbody>
<tr>
<td>mBOCF</td>
<td>(N=81)</td>
<td>(N=83)</td>
</tr>
<tr>
<td>ASDAS-ESR</td>
<td>-1.7 (1.2)</td>
<td>-1.6 (1.0)</td>
</tr>
<tr>
<td>BASDAI</td>
<td>-3.3 (2.5)</td>
<td>-3.1 (2.3)</td>
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<tr>
<td>C-Reactive Protein (mg/L)</td>
<td>-9.2 (12.4)</td>
<td>-9.6 (14.5)</td>
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<td>BASFI</td>
<td>-2.8 (2.5)</td>
<td>-2.8 (2.4)</td>
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<tr>
<td>ASDAS</td>
<td>-36.3 (12.4)</td>
<td>-36.3 (12.4)</td>
</tr>
<tr>
<td>SF-36 PCS3</td>
<td>8.3 (9.5)</td>
<td>8.1 (7.5)</td>
</tr>
<tr>
<td>ASAS Health Index</td>
<td>-2.7 (3.3)</td>
<td>-3.3 (3.6)</td>
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<tr>
<td>SPARC Spine Score observed2</td>
<td>8.8 (17.3)</td>
<td>8.5 (15.9)</td>
</tr>
<tr>
<td>Response (%)</td>
<td>PBO/All</td>
<td>ADA/All</td>
</tr>
<tr>
<td>IXE</td>
<td>(N=86)</td>
<td>(N=86)</td>
</tr>
<tr>
<td>Week 52</td>
<td>46.5</td>
<td>51.2</td>
</tr>
</tbody>
</table>

IXE/All items were scored on a 0-10 numeric rating scale
2SPARC Spine: N=72 (IXE Q4W), N=68 (IXE Q2W)
3Patients who received ≥1 dose of IXE during Weeks 16-52
4ADA=adalimumab; BASFi-Bath Ankylosing Spondylitis Functional Index; IXE=ixekizumab; mBOCF=modified Baseline Observation Carried Forward; NRI=nonresponder imputation; PBO=Placebo; Q2W=every 2 weeks; Q4W=every 4 weeks; SF-36 PCS=Medical Outcomes Study 36-item Short-Form Health Survey Physical Component Summary; SPARC=Spondyloarthritis Research Consortium of Canada

**Conclusion:** Persistent improvements in the signs and symptoms of r-axSpA were observed through Wk 52 in pts who received continuous treatment with IXE. ASAS40 response rates at Wk 52 were numerically similar between pts who received continuous treatment with IXE and pts who switched from ADA to IXE. No unexpected safety signals were observed through 52 wks of treatment.

**Spondyloarthritis – clinical aspects (other than treatment)**

**AB0712**

**RETNAL AND CHOROIDAL VASCULAR STRUCTURES ARE AFFECTED IN AXIAL SPONDYLOARTHRITIS: AN OPTICAL COHERENCE TOMOGRAPHY STUDY**

Berktay Akmaz1, Fahrettin Akay2, Dilek Salmaz1, Oray Gerekz3, Gokhan Kabaday1, Idil Kurut1, Servet Akar1, Izmir Katip Celebi University, Faculty of Medicine, Ophthalmology, Izmir, Turkey, Izmir Katip Celebi University, Faculty of Medicine, Rheumatology, Izmir, Turkey

**Background:** Axial spondyloarthritis (axSpA) is a chronic inflammatory disease that mainly affects axial skeleton. Ocular inflammation is one of the most common extra-articular manifestations of axSpA, mainly form of acute anterior uveitis (AAU). However posterior segment of the eye was rarely evaluated. The inaccessibility of posterior structures like choroid and retina to direct examination led clinicians to use non-invasive imaging techniques. Optical coherence tomography (OCT) is an imaging technology
**Objectives:** To examine the role of musculoskeletal ultrasound (US) and magnetic resonance imaging (MRI) in assessing femoral cartilage thicknesses in patients with AS and healthy controls, and to study the correlation between femoral cartilage thicknesses measurements and disease parameters.

**Methods:** Twenty five patients with AS (17 males and 8 females), and twenty five age, sex and BMI matched healthy individuals were included. For all patients assessment of disease activity, spinal mobility, functional limitation and radiological changes were done. Thickness of the femoral articular cartilage was measured by MRI using 1.5 Tesla MR machines.

**Results:** AS patients had thinner femoral cartilage thickness than the healthy controls at all MRI measurement sites, with statistically significant differences at medial femoral condyle and intercondylar area in both right and left knees (p<0.05). According to MRI examination, AS patients had statistically significant (p<0.05) thinner cartilage thickness at all subdural visions of femoral and tibial condyles than the healthy controls. Femoral cartilage thickness measurements either assessed by US or MRI was negatively correlated with age, age at onset of the disease, and measures of disease activity and radiological changes. Positive correlation between ultrasonographic total femoral cartilage thickness and MRI total femoral cartilage thickness was found (r=0.49, p<0.02).

**Conclusions:** Patients with ankylosing spondylitis seem to have thinner femoral cartilage thickness than healthy controls. Correlations of knee cartilage thickness (assessed by US and MRI) with demographic data and disease parameters reflect useful value of US and MRI in determining early cartilage loss in AS patients.

**REFERENCES**


**Disclosure of Interests:** None declared.


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**Abstracts**

**AB0714**

**BALANCE AND FALLS IN AXIAL SPONDYLOARTHRITIS: A CROSS SECTIONAL STUDY**

Kenlyn Brenda Mewes, Betania Longo, Ana Paula Beckhauser de Campos, Juliana Simioni, Thelma Laroca Skare. Hospital Universitário Evangélico Mackenzie, Department of Rheumatology, Curitiba, Brazil

**Background:** Spondyloarthritis (SpA) patients may suffer of balance loss predisposing them to falls.

**Objectives:** To study balance impairment and falls in SpA patients and its association with clinical and epidemiological variables, disease activity, functional and metrology indexes.

**Methods:** Cross sectional study of 55 SpA patients with axial disease. Clinical and epidemiological were collected from the charts. Balance was assessed by Berg Balance Scale(BBS). The following instruments were applied: ASDAS (Ankylosing Spondylitis Disease Activity Score)-ESR, ASDAS-CRP, BASDAI (Bath Ankylosing Spondylitis Disease Activity Index), BASFI (Bath Ankylosing Spondylitis Functional Index), BASMI (Bath Ankylosing Spondylitis Metrlogy Index) and ASQoL (Ankylosing spondylitis quality of life questionnaire). The number of falls in the last year was collected.

**Results:** In this sample, 30.9% had high risk of falls by the BBS and 25.4% recalled having at least one fall in the last years. The BBS values were lower in those with white ethnic backgroundp<0.01), and smokers(p=0.03) and with HLA-B27(p=0.03) and correlated inversely with BASDAI(p<0.08), ASDAS-ESR(p<0.32) and ASDAS-CRP(ho=0.33), BASFI(ho=0.71.p<0.0001), BASMI(ho=0.80; p<0.0001), ASQoL(ho=0.57; p<0.001) and age(ho=0.50.p<0.001). Multivariated analysis showed that BASFI and BASMI were independently associated with BBS(p=0.02 and
0.001 respectively). Patients with falls had lower BBS (p=0.03) and loss of balance correlated with impairment of the quality of life (rho=0.56; p=0.001).

Conclusion: Balance is impaired in 1/3 of SpA patients and the BBS is associated mainly with functional and metrology indexes, showing that patients with severe cumulative damage are more affected.

REFERENCES

### TABLE 1. STUDY OF BBS (BALANCE BERG SCALE) VALUES ACCORDING TO EPIDEMIOLOGICAL, CLINICAL AND TREATMENT VARIABLES

<table>
<thead>
<tr>
<th>Variable</th>
<th>Median BBS with the variable (IQR)</th>
<th>Median BBS without the variable (IQR)</th>
<th>p</th>
<th>Rho 95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>51 (44.0-55.0)</td>
<td>51 (40.4-53.7)</td>
<td>0.80</td>
<td></td>
</tr>
<tr>
<td>White ethnic background</td>
<td>54 (30.0-52.5)</td>
<td>52 (30.0-55.5)</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Exposed to tobacco (ex and current)</td>
<td>52 (46.5-55.0)</td>
<td>52 (46.5-55.0)</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>Bilateral sacroilitis</td>
<td>53 (46.5-55.0)</td>
<td>53 (46.5-55.0)</td>
<td>0.63</td>
<td></td>
</tr>
<tr>
<td>Enthesitis</td>
<td>51 (38.5-55.2)</td>
<td>51 (40.4-53.7)</td>
<td>0.45</td>
<td></td>
</tr>
<tr>
<td>Dactilitis</td>
<td>50 (42.5-55.4)</td>
<td>51 (40.4-53.7)</td>
<td>0.73</td>
<td></td>
</tr>
<tr>
<td>Uvulitis</td>
<td>50 (46.5-55.0)</td>
<td>50 (46.5-55.0)</td>
<td>0.26</td>
<td></td>
</tr>
<tr>
<td>Peripheral arthritus</td>
<td>52 (40.7-55.7)</td>
<td>51 (30.0-55.0)</td>
<td>0.92</td>
<td></td>
</tr>
<tr>
<td>HLA B27 prevalence</td>
<td>48 (50.0-51.1)</td>
<td>48 (50.0-51.1)</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>Anti TNF-α users</td>
<td>50 (45.0-54.7)</td>
<td>50 (39.0-55.0)</td>
<td>0.67</td>
<td></td>
</tr>
<tr>
<td>History of falls in the last year</td>
<td>46 (45.0-50.2)</td>
<td>52 (44.5-55.0)</td>
<td>0.03</td>
<td></td>
</tr>
</tbody>
</table>

### TABLE 2. CORRELATION STUDIES OF BBS (BERG SCALE BALANCE) VALUES WITH AGE, DISEASE DURATION, DISEASE ACTIVITY INDEXES, FUNCTIONAL AND METROLOGY INDEXES AND QUALITY OF LIFE

<table>
<thead>
<tr>
<th>BasDAI</th>
<th>ASDAS VHS</th>
<th>ASDAS CRP</th>
<th>BASFI</th>
<th>BASMI</th>
<th>Age (years)</th>
<th>Disease duration (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.28</td>
<td>-0.32</td>
<td>0.33</td>
<td>-0.71</td>
<td>-0.80</td>
<td>-0.50</td>
<td>-0.10</td>
</tr>
<tr>
<td>-0.51</td>
<td>-0.54</td>
<td>-0.55</td>
<td>-0.82</td>
<td>-0.88</td>
<td>-0.68</td>
<td>-0.36</td>
</tr>
<tr>
<td>0.008</td>
<td>0.01</td>
<td>0.01</td>
<td>-0.55</td>
<td>-0.68</td>
<td>-0.25</td>
<td>-0.17</td>
</tr>
<tr>
<td>0.03</td>
<td>0.03</td>
<td>0.01</td>
<td>-0.0001</td>
<td>0.0001</td>
<td>-0.0001</td>
<td>0.44</td>
</tr>
</tbody>
</table>

Disclosure of Interests: None declared


### AB0716 ESTABLISHMENT OF BASDAI CUT-OFFS FOR THE DISEASE ACTIVITY STATES BASED ON ASDAS CUT-OFFS IN TAIWANESE ANKYLOSING SPONDYLITIS PATIENTS

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Background: The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) has been widely utilized to evaluate disease activity in patients with ankylosing spondylitis (AS). However, the cut-off of BASDAI used to indicate high disease activity (i.e., >4) was determined arbitrarily and was suggested as a criterion to initiate biological therapy for AS patients. The Ankylosing Spondylitis Disease Activity Score (ASDAS) has been developed as a new composite index to assess AS disease activity. The cut-off values for disease activity states have been defined and validated for ASDAS-CII was selected as a criterion of starting biological therapy. However, the BASDAI cut-off values corresponding to the ASDAS cut-off values for disease activity states were unknown.

Objectives: The purpose of this study was to estimate the corresponding BASDAI and ASDAS cut-off in a Taiwanese AS cohort.

Methods: Since November 2016, we assessed the Ankylosing Spondylitis Disease Activity Score (ASDAS) and the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) regularly and recorded demographic and disease activity, comorbidity, family history, medication use for AS patients in Taichung Veterans General hospital (TCVGH) using an electronic patient reported data system linked to an electronic medical record system. We identified 489 AS patients with complete baseline demographic and assessment data from the TCVGH electronic data system during 2016/11-2018/10. We used receiver operating characteristic (ROC) curves with Youden’s J statistic to determine the cut-off values of BASDAI that correspond to ASDAS disease activity cut-offs (i.e., 1.3, 2.1 and 3.5).

Results: We included a total of 489 AS patients [114 (23.3%) females, mean age 44.1 years (S.D. 13.9), mean symptom duration 18.0 years (S. D. 11.9), 152 (31.1%) current biologic users]. Mean BASDAI, ASDAS-ESR and ASDAS-CRP scores were 2.1 (S.D. 1.3), 1.6 (S.D. 0.8) and 1.5 (S.D. 0.9) respectively. Mean levels of CRP and ESR were 0.6 mg/dl and 12.2 (S.D. 14.0) mm/hr respectively. Based on ASDAS-CRP, the numbers (%) of AS patients with inactive disease (<1.3), low disease activity (1.3-2.1), high disease activity (2.1-3.5) and very high disease activity (>3.5) were 210 (42.9), 171 (35.0), 88 (18.0) and 20 (4.1) respectively. Based on ASDAS-ESR, the numbers (%) of AS patients with low disease activity, high disease activity and very high disease activity were 202 (41.3), 174 (35.6), 96 (19.6) and 17 (3.5)

Disclosure of Interests: None declared

respectively. The best trade-off BASDAI values corresponding to ASDAS-CRP 1.3, 2.1 and 3.5 were 2.1, 2.6 and 2.8, respectively.

Conclusion: The estimated optimal BASDAI value that corresponds to the recommended ASDAS cut-off ≥2.1 for biological therapy initiation was lower than the recommended BASDAI cut-off of ≥4 in this Taiwanese AS cohort.

Abstract AB0716 Table 1. Optimal BASDAI cut-off values corresponding to ASDAS cut-offs using ROC curve with Youden’s J statistic in AS patients.

<table>
<thead>
<tr>
<th>BASDAI cut-off</th>
<th>AUC (95% CI)</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASDAS-CRP 1.3</td>
<td>0.76 (0.72–0.80)</td>
<td>0.70 (0.65–0.75)</td>
<td>0.82 (0.75–0.88)</td>
</tr>
<tr>
<td>ASDAS-CRP 2.1</td>
<td>0.78 (0.74–0.82)</td>
<td>0.69 (0.62–0.76)</td>
<td>0.87 (0.83–0.91)</td>
</tr>
<tr>
<td>ASDAS-CRP 3.5</td>
<td>0.82 (0.75–0.89)</td>
<td>0.84 (0.76–0.95)</td>
<td>0.81 (0.77–0.84)</td>
</tr>
<tr>
<td>ASDAS-ESR 1.3</td>
<td>0.80 (0.77–0.84)</td>
<td>0.74 (0.69–0.78)</td>
<td>0.87 (0.80–0.92)</td>
</tr>
<tr>
<td>ASDAS-ESR 2.1</td>
<td>0.79 (0.76–0.83)</td>
<td>0.81 (0.74–0.86)</td>
<td>0.78 (0.73–0.82)</td>
</tr>
<tr>
<td>ASDAS-ESR 3.5</td>
<td>0.79 (0.70–0.89)</td>
<td>0.67 (0.46–0.83)</td>
<td>0.92 (0.89–0.94)</td>
</tr>
</tbody>
</table>

REFERENCES

Disclosure of Interests: None.

AB0717 RELIABILITY OF SACROILIAC JOINT RADIOGRAPHS IN THE EARLY SPONDYLOARTHRITIS ESPERANZA COHORT

Carolina Tornero1, Claudia Urrego-Laurín2, Maria Luz García-Vivar3, Cristina Fernández-Carbajal1, Chia-Wei Hsieh4, Ching-Tsai Lin5, Hsin-Hua Chen6, Nan Huang7, Jose Francisco Garcia Llorente8, Eugenio de Miguel9. Disclosure of Interests: Carolina Tornero: None declared, Claudia Urrego-Laurín: None declared, Maria Luz García-Vivar: None declared, Cristina Fernández-Carbajal: None declared, Chia-Wei Hsieh: None declared, Ching-Tsai Lin: None declared, Hsin-Hua Chen: None declared, Nan Huang: None declared, Jose Francisco Garcia Llorente: None declared, Eugenio de Miguel: None declared.

Background: X-Ray sacroilis is the cornerstone in the diagnosis of the ankylosing spondylitis (AS). It is clear that the presence of sacroilis is a specific lesion in long standing AS, but little evidence exists on the reliability of this image technique in early axial spondyloarthritis (axSpA), which associates with reduced structural damage. This is relevant because some rheumatologists and pharmacological authorities feel more confident with the diagnosis of AS rather than with non radiographic axial spondyloarthritis (nr-axSpA) forms. On the other hand, according to various research studies, clinicians are subject to potential bias when interpreting radiographs, influenced by their pretest clinical judgment.

Objectives: The main objective of this study is to determine the reliability of X-Ray sacroilis in the early diagnosis of axSpA.

Methods: This study included 290 radiographs of the SI joints from patients of the Esperanza early spondyloarthritis cohort. Nine readers, blinded for the diagnosis, participated in the reliability exercise, all of them experienced rheumatologists and members of the Spanish spondyloarthritis working group (GRESSER). Patients with axSpA were classified as having AS if the radiographic criteria of the modified NY criteria (presence of radiographic changes in the SIJ of at least grade II bilaterally or at least grade III unilaterally) were fulfilled. The gold standard was the categorical opinion of at least five of the expert readers. For the statistical analysis, the Chi-square and Kappa tests were performed.

Results: The table shows mean kappa values and the agreement reached by each reader. The mean kappa achieved was fair (0.375, range 0.146 - 0.652) and the mean agreement was 73.7% (range: 58.7% - 90%). When the categorical opinion of X-Ray sacroilis of at least 5 readers as gold standard was applied, 61 patients were classified as AS and 229, as nr-axSpA. Nevertheless, this scenario varied from 31 to 138 among the readers when the x-ray evaluation was performed by only one reader.

Conclusion: Reliability of X-Ray SIJ in an early SpA cohort was weak among nine experimented readers and the diagnosis of AS was subject to a high variability. At least in doubtful cases, a central evaluation performed by highly qualified readers is advisable.

Disclosure of Interests: Carla Tormen: None declared, Claudia Urrego-Laurín: None declared, Maria Luz García-Vivar: None declared, Cristina Fernández-Carbajal: None declared, Chia-Wei Hsieh: None declared, Ching-Tsai Lin: None declared, Hsin-Hua Chen: None declared, Nan Huang: None declared, Jose Francisco Garcia Llorente: None declared, Eugenio de Miguel: None declared.


AB0718 IDENTIFYING AXIAL SPONDYLOARTHRITIS IN THE UNITED STATES: A POSSIBLE ROLE FOR CHIROPRACTORS

1Aluf Deodhar, 2Shreevesh Bhalerao, 3Oregon Health and Science University, Portland, United States of America; 4Equilibrium, Portland, United States of America.

Background: Approximately 19% of the general population in the United States has chronic back pain (CBP), with 5%-6% of these cases classified as inflammatory back pain (IBP).1 According to the US National Health and Nutritional Examination Survey, ~15% of patients with IBP have axial spondyloarthritis (axSpA),2 which can cause irreversible structural damage in the spine, loss of function, and a decreased quality of life. The diagnosis of axSpA is commonly missed, as patients seek care for back pain (BP) from a variety of non-rheumatology providers, including chiropractors.2 Overall, nearly 50% of patients seek chiropractic care for BP.3 However, not much is known about the prevalence of different types of BP (acute, chronic, IBP, and BP due to axSpA) in patients seeking chiropractic care in the United States.

Objectives: To investigate the types of providers sought by patients with BP and the prevalence of acute BP, CBP, IBP, and axSpA in patients with BP seeking chiropractic care in the United States. A secondary objective was to investigate how frequently chiropractors refer patients with BP to a rheumatologist.

Methods: PubMed literature searches were performed for all English language articles published through December 2017 to determine which providers are sought by patients with BP as well as the percentage of patients with BP being referred to a rheumatologist following chiropractic consultation. Search terms included “chiropractic,” “chiropractor,” “axial spondyloarthritis,” “ankylosing spondylitis,” “inflammatory back pain,” “chronic back pain,” “acute back pain,” “low back pain,” “sacroiliac joint,” “sacroiliac pain,” “back pain epidemiology,” “rheumatologist,” and “rheumatology.” The full text of relevant articles was evaluated for specific data and BP statistics in this care setting.
Results: Only 7 articles that described the types of providers sought by patients with BP were identified (Table 1). Among patients with BP, 7%-45% sought chiropractic care; 26%-70% sought care from general practitioners, and 3%-37% sought care from rheumatologists. Patients who sought chiropractic care were mainly white, female, aged < 65 years old, and of higher socioeconomic and education status. Patients with CBP seeking rheumatologic care had a mean duration of CBP of 14-28 years and were mostly women (56%; age range, 41-50 years); of these, 1% were referred to a rheumatologist by chiropractors for symptoms suggestive of SpA. Data regarding the prevalence of different types of BP (e.g., acute, CBP, IBP) in US chiropractic practices were not available. No articles describing axSpA in patients in chiropractic care were identified.

Discussion:

Chiropractors, as primary spine care providers in the United States, are playing an increasingly larger role in the diagnosis and treatment of BP, with 7%-45% of patients with BP seeking chiropractic care. However, there are conflicting data on the types of BP treated by chiropractors in the United States. Nonetheless, since approximately 15% of patients with IBP have axSpA, it is very likely that many patients seeking care from chiropractors in the United States have undiagnosed axSpA. Untreated axSpA could have a significant impact on the general health and quality of life of patients; therefore early diagnosis and treatment is crucial.[1]

Disclosure of Interests: Atul Deodhar Grant/research support from: Abbvie, AstraZeneca, Biogen, BMS, Celgene, Gilead, Galapagos, Genentech, GSK, Janssen, Merck, Novartis, Pfizer, UCB. UCB has informed our prospective cross-sectional single-centre observational study, due to start in February 2019. We will assess the sensitivity and specificity of MRE as a screening tool for axSpA in a cohort of 600 CD patients, two with increasing age and only one with IBD location.

Reference:


Disclosure of Interests: Jobie Evans Grant/research support from: I am currently working on a MD research project looking at the use of magnetic resonance enterography imaging as a screening tool for axial spondyloarthritis in patients with Crohn's disease. This study is commercially funded by Merck, Sharp and Dohme corporation (MSD). Mark Sapsford: None declared, Tim Raine: None declared, Scott McDonald: None
declared, Miles Parkes: None declared, Gavin Clinie: None declared, Deepak Jadon: None declared

AB0720 IMPACT OF SPONDYLOARTHRITIS ON THE MALE SEXUAL FUNCTION: LIMITING FACTORS

1Alia Faza1, Leila Rouach1, Mourad Dali Khereddine2, Saoussen Miladi1, Kmar Denuiniche1, Leila Souabni1, Selma Chekk1, Selma Kassab, Kauthwer Ben Abdelghani1, Nouira Yassine2, Ahmed Laatar1, 1Inngol slim hospital, 2Rheumatology, tunis, Tunisia

Background: The impact of Spondyloarthrits (SpA) on patients’ sexual life and erectile function has been gathering the attention of the scientific community over the last decade. Several factors may condition sexual function for SpA patients: microangiopathy, pain, decreased range of motion, joint swelling and extraarticular features such as fatigue.

Objectives: To assess the erectile function and the sexual desire in a cohort of male patients with SpA and to identify the factors related to the disease limiting the sexual life.

Methods: This is a cross sectional study including sexually active male patients with SpA (ASAS criteria). A questionnaire was performed, consisting in two parts. One part filled by a rheumatologist with data of the disease (demographics, the presence of a coxitis, disease activity (BASDAI and ASDAS), function index (BASFI) and current treatment). The other part consisted in a questionnaire filled by an urologist, with data on pain during intercourse, the international index of erectile function (IEEF5), intensity and frequency of sexual desire and disease impact on private life. For statistical analysis, we used Khi2-test for qualitative variables and Student-test for quantitative variables. A p value ≤0.05 was considered significant.

Results: We included 37 male patients with SpA, 18.9% had psoriatic arthritis, 51.4% had ankylosing spondylitis and 29.7% had inflammatory bowel disease spondyloarthrits. The mean age was 42.5 ± 1.8 years. Sixty two percent of patients were married. Mean disease duration was 11.4 ± 7.1 years. The mean disease activity and functional scores were as follow: BASDAI=2.57 ± 1.96, ASDAS CRP=2.38 ± 1.09, BASFI=2.59 ± 2.54)

For the treatment side: 40.5% were on NSAIDS, 70.3% on csDMARDs and 56.8% of patients were on biotherapy (33.3% on Adalimumab, 52.4% on infliximab and 14.3% on Etanercept). The mean visual analog pain scale during intercourse was 2.97 ± 1.89 and the erectile function was deteriorated in 80.6% of patients.

Conclusion: Our results suggest the impact of SpA on patients’ sexual function. Pain during intercourse and the limitation of the sexual desire were the most limiting factors of the sexual function.

REFERENCES

Disclosure of Interests: None declared

AB0721 EPIDEMIOLOGICAL, CLINICAL AND PROGRESSION FACTORS OF SPONDYLOARTHITIS IN A TERTIARY CARE HOSPITAL 1Ismael González Fernández, Carlota Iñiguez, Aníta Crespo Golmar, Ximena Elizabeth larco Rojas, Carolina Alvarez Castro, Clara Moriano, Alejandra López Robles, Manuel Martín, Elvira Diez Alvarez, María Eva Vallejo Pascual, Trinidad Pérez Snowdon1, 1University Health Care Complex of Leon, 2Rheumatology, Leon, Spain, 3University of Leon, Faculty Economics and Business Sciences, Leon, Spain

Background: Spondyloarthitis (SpA) is a heterogeneous group of diseases that predominantly affect the axial skeleton, with a debut generally before 45 years. Among the factors favoring radiological progression1 are among others, high levels of CRP, tobacco consumption and diagnostic delay.

Objectives: To describe clinical-epidemiological characteristics and analyze possible factors of radiological progression (based on the development of syndesmophytes) in patients with a diagnosis of SpA in our hospital.

Methods: Retrospective, descriptive observational study of patients diagnosed with SpA (New York, ASAS and AMOR criteria) in the University Health Care Complex of León for 45 years (1973-2018).

Results: A total of 218 patients were collected, 59.6% were men and 40.4% were women with an average age of onset of symptoms of 30.56 ± 12.06 years and a diagnosis of 35.59 ± 12.26 (diagnostic delay defined by a median of 2 years before the great dispersion of data). 81.2% have HLA-B27 positive. 64.2% come predominantly León capital, also highlighting other areas such as La Bañeza (9.6%) and Astorga (6.4%). 13.8% are ex-smokers, 18.8% are active smokers and 67.4% are non-smokers. 68.3% made their debut with inflammatory low back pain.

67% developed some anterior uveitis throughout its evolution. 72.9% have axial involvement and 27.1% joint axial and peripheral involvement. 89.9% met criteria New York (NY), 8.3% criteria ASAS and 1.8% criteria AMOR for the diagnosis of SpA. 17.4% developed syndesmophytes. The activity of the disease was assessed by BASDAI and PCR (taking the reference point of our laboratory, 5 mg/l as the cut-off point) at the time of diagnosis and in the last control performed, showing that 87.6% presented a BASDAI ≥ 4 at the time of diagnosis while in the last revision 84.9% has BASDAI ≥ 4; the elevated levels of CRP appeared in 54.45%, normalizing in 73.9% in the last control. We observed that the age of diagnosis <45 years (p 0.000289) in our sample is related to less progression due to the probable early initiation of biological treatment (18.2% in <45 years, 11% in ≥ 45 years); while both elevated CRP at diagnosis (p 0.003) and exposure to tobacco (p 0.036) present a higher rate of syndesmophytes due to a probable higher inflammatory activity. For other variables (Sex, HLA-B27, BASDAI, diagnostic delay, presence of uveitis and NSAIDs), we did not obtain a statistically significant relationship.

Conclusion: - Most part of patients with SpA are young men, with HLA-B27 positive and axial involvement with debut as inflammatory back pain that meet NY criteria.
- High levels of CRP at diagnosis (p 0.003) and tobacco consumption (p 0.036) have been associated, in our sample, with greater radiological progression while the age of diagnosis <45 years is related to lower progression (p 0.000289) may be due to the early introduction of biological treatment (18.2% in <45 years, 11% in ≥ 45 years).

REFERENCES

Disclosure of Interests: None declared

AB0722 DOES THE ULTRASOUND OF SACRIOILIAC JOINTS CONTRIBUTE TO THE DIAGNOSIS OF SPONDYLOARTHRITIS?

Dorra Ben Nessim, 1Wida Harmik, 1Kassem Maatallah, 1Hend Riahi, Haranne Ferjani, 1Dhaa Kaffel, Med Montazer Khiri, 1Kassab Institute, Rheumatology, Manouba, Tunisia, 2Kassab Institute, Radiology, Manouba, Tunisia

Background: Although pelvic radiography is a robust imaging modality to detect sacroiliitis, radiographic changes require at least 5 years to develop after symptom onset, hence the increasing interest in new imaging tools in the field of spondyloarthritis (SpA). Whereas the diagnostic utility of magnetic resonance imaging (MRI) and computed tomography (CT) of sacroiliac joints (SJI) has been extensively studied in many cohorts, the contribution of SJI ultrasound (US) in the diagnosis of SpA has been little-studied.

Objectives: The objective of this study is to assess the performance of SJI US for detecting sacroiliitis and to determine its sensitivity and specificity in patients with SpA.

Methods: Consecutive patients, aged 16 years and over, consulting for symptoms suggestive of SpA (inflammatory back pain, enthesitis or dactylitis...) from February 2014 to February 2017 were enrolled in this cohort. Eligible patients underwent physical examinations, laboratory tests, SJI US, CT and/or MRIs, following a standardized protocol. Patients with a conventional radiography showing a confirmed sacroiliitis (grade 3 or 4) were not included. The US was considered positive when showing a unilateral or bilateral vascularization (Doppler signals). Then, resistive index (RI) was measured. After analyzing clinical and radiological data and HLA typing, two experienced rheumatologists, blinded to US results, proposed the classification of the patients into 2 groups: confirmed SpA or no SpA. Their final diagnosis was considered the gold standard in interpreting the results of US examination.

Results: Forty-five patients, 10 men and 35 women, with an average age of 39 years were included. The mean duration of symptoms was 75 months (6 years). A family history of SpA was noted in 2.22% of
pneumonia. A personal history of Reiter’s syndrome was noted in 2.22% of patients and of uveitis in 6.66%. Morning stiffness was noted in 60% (n=27) of patients. Good response to nonsteroidal anti-inflammatory drugs (NSAIDs) and to physical activity were respectively reported by 42.22% (n=19) and 57.8% (n=26) of patients. Twenty-seven per cent of the patients were HLA-B27+. Fifty-one per cent of the studied patients fulfilled the ASAS criteria for axial SpA and 46.7% fulfilled the AMR criteria. After a follow-up between 2 and 3 years, the diagnosis of SpA was confirmed by the referring rheumatologists in 31 (68.9%) patients and excluded in 14 (31.1%) patients. Among the 31 patients with confirmed SpA, 61.3% (n=19) had a positive US (with a mean RI estimated at 0.75) and 38.7% (n=12) had a normal US. Among the 14 patients in whom SpA was excluded, 50% (n=7) had a positive US (with a mean RI estimated at 0.71) and 50% had a normal US. Sensitivity and specificity of US examination were estimated at 61.3% and 50%. Positive and negative likelihood ratio were estimated at 73% and 36.8%. Association between US findings and rheumatologists’ diagnosis of SpA was not statistically significant (p=0.47).

Conclusion: US contribution in the diagnostic of SpA has been little-studied. In our study, although US of SJ did not lack specificity, it has a satisfactory sensitivity and positive likelihood ratio. In fact, this tool is more valuable by its positivity which indicates a high probability of spondylitis. However, further investigation is needed in order to assess its performance for ascertaining spondylitis.

Disclosure of Interests: None declared


AB0723 SMOKING MAY BE RELATED TO SACROILIITIS IN ENTEROPATHIC ARTHRITIS PATIENTS: TREASURE REAL-LIFE PRELIMINARY DATA

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Background: Articular manifestations may differ in ulcerative colitis (UC) and Crohn’s disease (CD). Genetic and non-genetic factors like sex, smoking, and presence of HLA-B27 were previously shown to modify the expression of articular and other extraintestinal manifestations of IBD.

Objectives: The aim of this study is to document disease features and factors affecting the expression of articular manifestations in Turkish patients with IBD-related (enteropathic) arthritis under treatment with disease modifying antirheumatic drugs (DMARDs).

Methods: Data regarding enteropathic arthritis (EA) were collected from the TREASURE database, a nation-wide multicenter observational registry of inflammatory arthritis patients.

Results: Among 4066 patients with seronegative spondyloarthropathies (SpA), 156 (3.8%) had EA, not reflecting a true prevalence due to selection bias. Demographic and clinical features according to IBD groups were summarized in Table 1. Rates of prevalence of sacroiliitis were similar between patients with UC and CD (39.9% and 60.1%, p=0.086 respectively). Rates of HLA-B27 positivity were 31.6% and 7.1% in patients with and without radiographic sacroiliitis, respectively (p<0.01). Enthesitis, dactylitis, psoriasis, family history for SpA, ESR, CRP, BASDAI and ASDAS levels had similar distributions in patients with and without radiographic sacroiliitis. Rates of “never-smoked” (26.5% vs 64.7%) and “current smoking” (32.4% vs 17.6%) significantly differed in patients with and without sacroiliitis (overall p=0.012).

Conclusion: Our data confirm an association between smoking status and disease manifestations, particularly radiographic sacroiliitis.

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Disclosure of Interests: Cihan Köçükahin: None declared, Abdulnasem Erden: None declared, Ufuk Ilgen: None declared, Sedat Kiraz: None declared, Ali Ihsan Erten: None declared, Nazlice Sule Yasar Bilge: None declared, Timnin Kaplıoğlu: None declared, Ediz Đilkici: Grant/research support from: MSD and Abbvie, Consultant for: MSD, Abbvie, Roche, UCB, Pfizer and Novartis, Speakers bureau: MSD, Abbvie,Roche, UCB, Pfizer and Novartis, Cemal Bes: None declared, Nilüfer Alpay Kantay: None declared, Hakan Emmungi: Grant/research support from: MSD, Roche, Pfizer, Abbvie, Consultant for: Novartis, Roche, Speakers bureau: MSD, Roche, Pfizer, Abbvie, Roche, UCB, Pfizer and Novartis, Novartis, Pamir Aşıgran Öz: None declared, Belkis Nihan Seniz: None declared, Burcu Yaşğ: None declared, Süleyman Serser Koca: None declared, Muhammet Çetin: None declared, Ahmet Erden: None declared, Omer Karadag: None declared, Levent Kılıç: None declared, Mustafa Kemal University Faculty of Medicine, Rheumatology, Ankara, Turkey; 19Ankara University, Rheumatology, Ankara, Turkey; 19Ankara University Faculty of Medicine, Rheumatology, Ankara, Turkey; 19Kemal University Faculty of Medicine, Rheumatology, Ankara, Turkey; 19Izmir University of Medicine Faculty of Medicine, Rheumatology, İzmir, Turkey; 19Adana State Hospital, Rheumatology, Adana, Turkey; 19Aydınem University Faculty of Medicine, Rheumatology, Antalya, Turkey; 19Fatih University, Medicine Faculty of Medicine, Rheumatology, Hatay, Turkey; 19Dukpt University Faculty of Medicine, Rheumatology, Adana, Turkey; 19Namik Kemal University Faculty of Medicine, Rheumatology, Tekirdağ, Turkey; 19Yıldırım Beyazıt University Faculty of Medicine, Rheumatology, Ankara, Turkey; 19Çekmeköy research and educational hospital, Rheumatology, Istanbul, Turkey

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Conclusion: Our data confirm an association between smoking status and disease manifestations, particularly radiographic sacroiliitis.

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Disclosure of Interests

may not be assumed to be factors of AS worsening.

alteration of prescriptions compared with CS. Taken together, pregnancy and VD significantly between vaginal delivery (VD) and CS (OR 0.72, 95% CI 0.45–1.14).

Conclusion

Among 6,821 female patients with AS, 996 patients in the delivery group

Background

Ankylosing spondylitis (AS) affects the sacroiliac joints and commonly occurs in those at the reproductive age. Women with AS have a higher rate of cesarean section (CS) compared with healthy controls.

Objectives

This study determined the effect of pregnancy and delivery methods on AS worsening by analyzing prescription pattern.

Methods

Based on the Korean Health Insurance Review and Assessment Service claims database, subjects comprised female patients aged 20–49 years with an AS. Alteration of prescriptions was defined by changing the at two time periods of 1–2 years pre-delivery and 1-year post-delivery. We compared alteration of prescriptions between AS patients with delivery and 1:1 matched AS patients without delivery. In addition, among AS patients with delivery, alteration of prescriptions according to delivery method was evaluated.

Results

Among 6,821 female patients with AS, 996 patients in the delivery group were younger, had a higher proportion of non-drug use, and had lower rates of comorbidity than the no delivery group. The alteration of prescriptions did not differ between the AS with delivery and the AS without delivery groups (OR 0.76, 95% CI 0.56–1.05). Furthermore, the overall alteration of prescriptions did not differ significantly between vaginal delivery (VD) and CS (OR 0.72, 95% CI 0.45–1.14).

Conclusion

The rate of alteration of prescriptions was comparable between the AS patients with and without delivery. There was no association between VD and alteration of prescriptions compared with CS. Taken together, pregnancy and VD may not be assumed to be factors of AS worsening.

Disclosure of Interests

None declared


ASSOCIATION BETWEEN RADIOGRAPHIC PROGRESSION AND CARDIOVASCULAR RISK IN SPONDYLOARTHRITIS: DATA FROM COSPARR REGISTRY

Ladehesa Pineda Lourdes1, Gómez García Ignacio2, María del Carmen Castro Villegas2, Pedro Seguí Azpilicueta3, María del Carmen Abalos-Aguilera3, Bautista Aguilar Laura4, Inmaculada Concepción Aranda-Valera5, Rocío Segura5, Rafaela Ortega Castro6, Clemencia López-Medina7, Puche Larrubia María Ángeles8, Alejandra Escudero Contreras9, Judit Lopez-Pedrezas10, Font Ugalde Pilar11, Garrido Castro Juan Luis12, Alejandro Escudero Contreras9, Pedro Seguí Azpilicueta: None declared, María del Carmen Abalos-Aguilera: None declared, Bautista Aguilar Laura: None declared, Inmaculada Concepción Aranda-Valera: None declared, Rocío Segura: None declared, Rafaela Ortega Castro: None declared, Clemencia López-Medina: None declared, Pérez Sánchez Laura: None declared, Puche Larrubia María Ángeles: None declared, Charly López-Pedrezas: None declared, Font Ugalde Pilar: None declared, Garrido Castro Juan Luis: None declared, Alejandro Escudero Contreras: None declared, Eduardo Collantes Estevez: None declared, Jiménez Gómez Yolanda: None declared

Conclusion: Presence of atherosclerosis is associated with age, disease duration and radiographic damage in SpA. Age and structural damage especially in the cervical spine predicted a greater CV risk. Thus, it is important to identify these patients in order to maintain tight control and avoid development of CV disease.

Acknowledgement: Funded by: JA PI-0139-2017

Disclosure of Interests: Ladehesa Pineda Lourdes: None declared, Gómez García Ignacio: None declared, María del Carmen Castro Villegas: Paid instructor for: MSD, Abbvie, Pfizer, Janssen, Lilly, Roche, Pedro Seguí Azpilicueta: None declared, María del Carmen Abalos-Aguilera: None declared, Bautista Aguilar Laura: None declared, Inmaculada Concepción Aranda-Valera: None declared, Rocío Segura: None declared, Rafaela Ortega Castro: None declared, Clemencia López-Medina: None declared, Pérez Sánchez Laura: None declared, Puche Larrubia María Ángeles: None declared, Charly López-Pedrezas: None declared, Font Ugalde Pilar: None declared, Garrido Castro Juan Luis: None declared, Alejandro Escudero Contreras: None declared, Eduardo Collantes Estevez: None declared, Jiménez Gómez Yolanda: None declared


DOSE PREGNANCY AND VAGINAL DELIVERY WORSEN ANKYLOSING SPONDYLITIS?

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Background

Ankylosing spondylitis (AS) affects the sacroiliac joints and commonly occurs in those at the reproductive age. Women with AS have a higher rate of cesarean section (CS) compared with healthy controls.

Objectives

This study determined the effect of pregnancy and delivery methods on AS worsening by analyzing prescription pattern.

Methods

Based on the Korean Health Insurance Review and Assessment Service claims database, subjects comprised female patients aged 20–49 years with an AS. Alteration of prescriptions was defined by changing the at two time periods of 1–2 years pre-delivery and 1-year post-delivery. We compared alteration of prescriptions between AS patients with delivery and 1:1 matched AS patients without delivery. In addition, among AS patients with delivery, alteration of prescriptions according to delivery method was evaluated.

Results

Among 6,821 female patients with AS, 996 patients in the delivery group were younger, had a higher proportion of non-drug use, and had lower rates of comorbidity than the no delivery group. The alteration of prescriptions did not differ between the AS with delivery and the AS without delivery groups (OR 0.76, 95% CI 0.56–1.05). Furthermore, the overall alteration of prescriptions did not differ significantly between vaginal delivery (VD) and CS (OR 0.72, 95% CI 0.45–1.14).

Conclusion

The rate of alteration of prescriptions was comparable between the AS patients with and without delivery. There was no association between VD and alteration of prescriptions compared with CS. Taken together, pregnancy and VD may not be assumed to be factors of AS worsening.

Disclosure of Interests

None declared


WHAT IS THE IMPACT OF MRI ON THE PERFORMANCE OF THE ASAS CLASSIFICATION CRITERIA IN PATIENTS PRESENTING WITH UNDIAGNOSED BACK PAIN?

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Background

Several cohorts have reported the performance of the ASAS classification criteria in settings where clinical, radiographic, and MRI features have been simultaneously incorporated into the diagnostic evaluation in arriving at a gold standard for the testing of the criteria. MRI improves diagnostic precision but access is limited and it is therefore still important to understand how the criteria perform in a setting where diagnostic evaluation can be conducted sequentially before and after MRI assessment. We hypothesized that the ASAS criteria would demonstrate enhanced specificity when MRI is available due to enhanced diagnostic precision.
MAGNETIC RESONANCE IMAGING IN SYMPTOMATIC AXIAL SPONDYLOARTHRITIS

All patients

(-10 to +10 scale)

<-4 for not axSpA

axSpA YES and rating of >7 for patients with MRI

Subset of patients with MRI

(-10 to +10 scale)

axSpA and <-4 confidence >7 for diagnosis of axSpA

We aimed to test the impact of adding MRI to the diagnostic evaluation on the performance of the classification criteria in unselected patients referred with undiagnosed back pain who have presented with acute anterior uveitis (AAU), psoriasis, or colitis to their respective specialists.

Methods: Consecutive patients ≥45 years of age with ≥3 months undiagnosed back pain with any one of psoriasis, acute anterior uveitis (AAU), or colitis undergo routine clinical evaluation by a rheumatologist for axial SpA, and MRI evaluation is ordered per rheumatologist decision. The rheumatologist determines the presence or absence of axial SpA and the degree of confidence in the diagnosis (-10 (definitely not SpA) to +10 (definite SpA)) at 3 consecutive stages: 1. After the clinical evaluation; 2. After the results of labs (B27, CRP) and radiography; 3. After the results of MRI evaluation. We calculated the sensitivity and specificity of the ASAS criteria and the component imaging and clinical arms using the stage 2 and 3 diagnostic assessments by the local rheumatologist as gold standard.

Results: A total of 246 patients were recruited, 47.6% being diagnosed with axSpA (61.5% male, age 33.7 years, symptom duration 7.6 years, B27 positive 52.1%), after final diagnostic evaluation. Sensitivity/specificity of the ASAS criteria, imaging arm, clinical arm after stage 2 diagnostic evaluation for the entire cohort were 67.4/85.7%, 39.7/95.2%, 48.9/87.6%, respectively (Table). For the subset of 146 patients who had MRI and had diagnostic evaluation at both stage 2 (pre-MRI) and stage 3 (post-MRI), sensitivity of the criteria was greater but specificity was lower when tested against the stage 3 diagnosis. This was particularly apparent in the clinical arm.

<table>
<thead>
<tr>
<th>Patient Category</th>
<th>Stage of evaluation</th>
<th>Number</th>
<th>ASAS criteria</th>
<th>Imaging arm</th>
<th>Clinical arm</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Sens</td>
<td>Spec</td>
<td>Sens</td>
</tr>
<tr>
<td>All patients</td>
<td></td>
<td>2</td>
<td>246</td>
<td>67.4</td>
<td>85.7</td>
</tr>
<tr>
<td>Patients diagnosed with confidence ≥7 for axSpA and -4 for not axSpA (-10 to +10 scale)</td>
<td></td>
<td>2</td>
<td>144</td>
<td>86.4</td>
<td>85.9</td>
</tr>
<tr>
<td>Subset of patients with MRI</td>
<td></td>
<td>2</td>
<td>146</td>
<td>58.9</td>
<td>83.9</td>
</tr>
<tr>
<td>Subset of patients with MRI and confidence rating of ≥7 for axSpA and -4 for not axSpA (-10 to +10 scale)</td>
<td></td>
<td>2</td>
<td>111</td>
<td>74.1</td>
<td>82.1</td>
</tr>
<tr>
<td>Subset of patients with MRI and confidence rating of ≥7 for axSpA YES and -4 for not axSpA (-10 to +10 scale)</td>
<td></td>
<td>3</td>
<td>111</td>
<td>80.5</td>
<td>78.6</td>
</tr>
</tbody>
</table>

Conclusion: The ASAS criteria were less specific when MRI assessment was added to the process of diagnostic evaluation, which could reflect rheumatologist over-interpretation of both clinical and radiographic findings in this population with higher pre-test probability of axSpA.

Disclosure of Interests: Walter P Maksymowycz Grant/research support from: AbbVie, Pfizer, Janssen, Novartis, Consultant for: AbbVie, Eli Lilly, Boehringer, Galapagos, Janssen, Novartis, Pfizer and UCB Pharma; Chief Medical Officer for Canadian Research and Education Arthritis, Raj Carapellucci Consultant for: Amano, AbbVie, AbbVie, Janssen, Consultant for: Amano, AbbVie, BMS, Eli Lilly, Merck, Novartis, Janssen, Takeda, UCB, James Yeung; None declared, Jon Chan Grant/research support from: Janssen, UCB, Novartis, Pfizer, Celgene, Consultant for: Amano, Celgene, Eli Lilly, Janssen, AbbVie, Novartis, Pfizer, UCB, Sandoz, Merck, Liam Martin; None declared, Sibel Aydin Consultant for: AbbVie, Celgene, UCB, Novartis, Janssen, Sanofi, Dianne Mosher; None declared, Ariel Masetto Grant/research support from: Amano, Sanofi, Consultant for: Sanofi, Pfizer, Bristol-Myers Squibb, Novartis, Boehringer Ingelheim, Speakers bureau: Novartis, Stephanie Keeling Consultant for: AbbVie, Pfizer, Eli Lilly, Janssen, Amgen, Astrazeneca, UCB, Olga Zouzina; None declared, Sherry Rohekar Consultant for: Abbvie, Amgen, BMS, Celgene, Eli-Lilly, Janssen, Merck, Novartis, Pfizer, Roche, Sanofi, UCB, Joel Paschke; None declared, Amanda Carapellucci; None declared, Robert Lambert Consultant for: Bioderma, Parexel, Abbvie DOI: 10.1136/annrheumdis-2019-eular.6275

AB0727 MAGNETIC RESONANCE IMAGING IN SYMPTOMATIC BACK PAIN IN INFLAMMATORY BOWEL DISEASE: STRUCTURAL LESIONS AND HLA-B27 IMPROVE THE DIAGNOSTIC ACCURACY IN AXIAL SPONDYLOARTHRITIS

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Background: Inflammatory bowel disease (IBD) related arthropathy may manifest as peripheral arthritis, dactylitis or enthesitis as well as inflammatory back pain (IBP) due to sacroiliac joint (SIJ) and/or spinal inflammation. HLA-B27 correlates with the presence of MRI determined SIJ bone marrow oedema (BMO) in axial spondyloarthritis (axSpA) and axial psoriatic arthritis (PsA) patients. The prevalence of HLA-B27 positivity is low in IBD and patients may already be on therapy that potentially modifies MRI spinal lesions at the time of imaging.

Objectives: To evaluate the utility of MRI to aid the diagnosis of axSpA in IBD patients with IBP and to explore the relationship of MRI abnormalities with HLA-B27 status.

Methods: Cross-sectional, retrospective audit of consecutive MRI scans of the SIJ and spine performed (2008-2018) in a large teaching hospital. All scans were requested in IBD patients presenting with IBP and clinical suspicion of axSpA. Demographic and clinical data were retrieved from the medical notes. Decision from the clinician whether the patient had axSpA related to the IBD was also recorded. MRI scans were scored by 2 readers using the semiquantitative Leeds Scoring System (BMO grade from 0 to 3). An overall score for inflammatory (sum of SIJ and Spine BMO scores) and structural lesions (sum of lesions per quadrant) was calculated.

Results: MRI scans from 119 IBD (Crohn’s n=82, ulcerative colitis n=31, and undifferentiated IBD n=6) patients were available for analysis. 63.9% were female, mean age 38.7 years at time of MRI with mean age of IBP onset 36.3 years. The majority (n=65/83, 78.3%) were HLA-B27 negative (missing data n=36). Thirty subjects were receiving biologic therapy for IBD. A summary of MRI findings (SIJ and spine) is shown on Table 1.

Abstract AB0727 Table 1

<table>
<thead>
<tr>
<th>Abnormal SIJ MRI</th>
<th>BMO</th>
<th>Grade 1 N=20</th>
<th>Grade 2 N=44</th>
<th>Grade 3 N=1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structural lesions</td>
<td>Fat deposition</td>
<td>N=46 (38.7%)</td>
<td>N=45 (37.8%)</td>
<td>N=8 (6.3%)</td>
</tr>
<tr>
<td>Sclerosis N=45</td>
<td>N=122 (92.2%)</td>
<td>N=39 (32.8%)</td>
<td>N=3 (2.4%)</td>
<td></td>
</tr>
<tr>
<td>Ankylosis N=4</td>
<td>N=32 (24.2%)</td>
<td>N=32 (24.2%)</td>
<td>N=4 (3.1%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Abnormal Spine MRI</th>
<th>BMO</th>
<th>&lt;3 lesions N=7 (14.3%)</th>
<th>≥3 lesions N=7 (5.9%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Structural lesions</td>
<td>Posterior fusion N=1 (1%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Degenerative disc disease was common in the cohort with 55/119 having at least one affected level. Other incidental findings included: hernigomias (n=8), osteoporotic fractures (n=2) and myeloma (n=1). The total BMO MRI scores (Spine plus
Scientific Abstracts

PREVALENCE AND SEVERITY OF CLINICAL AND IMAGING AXIAL Spondyloarthritides IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Background: Some patients with inflammatory bowel disease (IBD), such as ulcerative colitis (UC) and Crohn’s disease (CD), develop spondyloarthritis (SpA). Inflammatory back pain (IBP) is one of the most important signs of axial SpA. However, changes in conventional radiography take a long time to appear as typical changes, such as erosion, sclerosis, or ankylosis. Magnetic resonance imaging (MRI) is useful for assessing axial involvement. High-quality imaging modalities can detect the inflammatory condition in the joints and enthesis more sensitively than clinical assessment or conventional radiography.

Objectives: This study aimed to examine the clinical and imaging prevalence or severity of axial SpA in patients with IBD.

Methods: A total of 56 patients, including 39 with UC (19 males, 20 females) and 17 with CD (10 males, 7 females) were included. The Assessment of SpondyloArthritis International Society (ASAS) Expert Criteria were used to assess IBP. The criteria were fulfilled if at least four of the following questions were answered by “yes”: (1) did your back pain start when you were aged 40 or younger?; (2) did your back pain develop gradually?; (3) does your back pain improve with exercise?; (4) do you find that there is no improvement in your back pain when you rest?; and (5) do you suffer from back pain at night, which improves upon getting up? Image evaluation was performed blindly by two readers. Conventional radiography was evaluated by the modified Stoke AS Spine Score (mSASSS) in the spine and the Grade of modified New York criteria (mNY) in the sacroiliac joints. In MRI, spinal and sacroiliac joints were evaluated by the Spondylo-arthritis Research Consortium of Canada (SPARCc) score.

Results: Among the 56 patients with IBD, 21 had IBP by clinical examination and 11 had pain in the sacroiliac joints. In conventional radiography, the average mSASSS score was 8.9 in patients with IBP and 6.5 in patients without IBP (p = 0.257). Eleven patients had bilateral Grade 2 or unilateral Grade 3 of the mNY, and three (27.3%) of these patients had sacroiliac pain and eight (17.8%) did not have sacroiliac pain (p = 0.477). In spine MRI, nine (42.9%) patients with IBP and nine (25.7%) IBP patients without IBP had an SPARC score of > 2 (p = 0.184). In sacroiliac MRI, one (9.1%) patient with sacroiliac pain and 12 (26.7%) patients without sacroiliac pain had an SPARC score of > 2 (p = 0.216).

Conclusion: Even without clinical symptoms of SpA, significant inflammatory findings are detected by MRI. Imaging might be important, regardless of the presence or absence of clinical symptoms, in patients with IBD.

REFERENCES


AB0729 ASSESSING THE DIFFERENCES IN TIMES TO GENERAL PRACTITIONER PRESENTATION AND DIAGNOSIS, AND OUTCOMES FOR AXIAL SpondyloArthritis PATIENTS IN DIFFERENT ETHNIC GROUPS

Ammanda Owusu-Agyei, Ayna Verdiyeva, Marian Chan. Luton and Dunstable University Hospital, Luton, United Kingdom

Background: Axial spondyloarthritis (axSpA) is a condition characterised by inflammatory back pain +/- extra-articular manifestations. There is a known delay to diagnosis1. Management includes phototherapy, non-steroidal anti-inflammatory drugs (NSAIDs) and biologic agents2. The Luton & Dunstable University Hospital, UK Rheumatology department looks after an ethnically diverse population of patients with the condition.

Objectives: The objectives of this study were to compare time from symptom onset to General Practitioner (GP) presentation, time from symptom onset to diagnosis, and response to treatment between different ethnic groups.

Methods: 124 patients with an axSpA diagnosis, according to the Assessment of SpondyloArthritis international Society (ASAS) criteria were used to analyse data. Results: The mean age was 44 years. 64 (64%) patients were male and 36 (36%) were female. 48 (48%) and 27 (27%) patients were HLA-B27 positive and negative respectively. HLA-B27 status was not available for 25 (25%) patients. Ethnicity breakdown showed 58 White British patients; 12 Pakistani; 7 White Other; 6 Bangladeshi; 5 White Irish; 5 Asian; 4 Indian and 3 Black Caribbean. There were 70 Caucasian (White British, etc...
Irish or Other) and 30 non-Caucasian patients. 49 patients (36 Caucasian and 13 non-Caucasian) had confirmed radiographic axial SpA. 17 patients (10 Caucasian and 7 non-Caucasian) had confirmed non-radiographic axial SpA.

For those presenting within 1 year of symptom onset, BASDAI data were available for 5 out of 7 Caucasian and 2 out of 5 non-Caucasian patients. The mean BASDAI decrease was 5.65 in non-Caucasian patients compared to 1.62 in Caucasian patients. For those presenting after 1 year of symptom onset, BASDAI data were available for 15 out of 26 Caucasian and 10 out of 19 non-Caucasian patients. Mean BASDAI decrease was 2.26 in non-Caucasian and 1.93 in Caucasian patients.

BASDAI data were available for 43 out of 70 Caucasian patients and 18 out of 30 non-Caucasian patients, regardless of time of presentation. The mean decrease in first measured BASDAI was smaller in Caucasian patients compared to non-Caucasian patients (Mean BASDAI decrease: 2.49 compared to 2.66).

Conclusion: There is a shorter mean time of symptom onset to GP presentation and diagnosis in non-Caucasian patients compared to Caucasians. There is a higher response to treatment in patients who present within one year of symptom onset. This may support the hypothesis that early diagnosis leads to better outcomes.

REFERENCES

Disclosure of Interests: None declared

AB0730 RECLASSIFICATION INTO VERY HIGH CARDIOVASCULAR RISK AFTER CAROTID ULTRASOUND IN PATIENTS WITH AXIAL SPONDOLOARTHRITIS

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Background: Axial spondyloarthritis (a-SpA) are associated with an increase in cardiovascular (CV) morbidity and mortality. Subclinical atherosclerosis, in the form of carotid plaques, is more frequent in this patients than in healthy controls. How the presence of carotid plaque affects the reclassification of CV risk in a-SpA has not been studied before. Besides, it is not known if this reclassification can be explained by characteristics related to the disease.

Objectives: To analyze whether the reclassification of CV risk after performing carotid ultrasound is more frequent in this patients compared to controls and whether this reclassification can be explained by characteristics related to the disease such as activity, functional damage or morphology scores.

Methods: Study of 343 a-SpA patients according to ASAS criteria and 177 controls with no previous history of CV events, diabetes or chronic kidney disease. The clinical characteristics and risk profile were analyzed in patients and controls by SCORE. The presence of plaques and intima-media thickness (cIMT) was determined by carotid ultrasound. The differences in the presence of reclassification between patients and controls and the factors associated with this in patients with a-SpA, were analyzed by multivariate regression analysis.

Results: Patients with a-SpA compared to controls disclosed a higher presence of hypertension (p<0.000), dyslipidemia (p<0.000) and smoking (p<0.000). Consequently, patients also showed a significantly higher SCORE than controls (0.6 IQR [0.1-2.0] vs. 0.1 [0.0-0.4], p=0.000). The presence of carotid plaque (36% vs. 25%, p=0.010) and cIMT (0.641 ± 0.121 vs. 0.602 ± 0.115 mm, p=0.001) were higher in patients compared to controls. Moreover, the possibility of being reclassified into very high-risk category after ultrasound was superior in patients (34% vs 25%, p=0.037). The possibility of being reclassified was associated, both in patients and controls, with an older age, male sex, abdominal circumference, hypertension and dyslipidemia. Contrary, body mass index and...
The association between periodontal disease and rheumatoid arthritis is well-recognized [1]. Porphyromonas gingivalis is probably the link between the two conditions. On the other hand, the data on the

**REFERENCES**


**Disclosure of Interests:** Daria Rumiantceva: None declared, Tatiana Dubinina: None declared, Anastasiya Demina: None declared, Shandor Erdes Consultant for: Development of studies concepts, Speakers bureau: Consultation fees/participation in company sponsored educational meetings organized or supported by companies.


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**Abstract AB0731 Table 1.** Outcome parameters at baseline.

<table>
<thead>
<tr>
<th></th>
<th>Man (n=33)</th>
<th>Women (n=35)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ankylosing spondylitis, n,%</td>
<td>25 (75.0%)</td>
<td>15 (42.9%)</td>
<td>0.007</td>
</tr>
<tr>
<td>Non-radiographic axSpA, n,%</td>
<td>8 (24.5%)</td>
<td>10 (28.6%)</td>
<td>0.065</td>
</tr>
<tr>
<td>Total stage of sacroiliitis, median [IQR]</td>
<td>4.0 [4.0; 5.0]</td>
<td>3.0 [2.0; 4.0]</td>
<td>0.021</td>
</tr>
<tr>
<td>Rate of SI radiographic progression, median [IQR]</td>
<td>2.3 [1.3; 4.0]</td>
<td>2.0 [1.0; 4.0]</td>
<td>0.384</td>
</tr>
<tr>
<td>CRP, median [IQR]</td>
<td>21 [7.3; 31.8]</td>
<td>43 [9.3; 9.8]</td>
<td>0.041</td>
</tr>
</tbody>
</table>

After 2 y FUP, pts with AS still prevailed among men (table 2). TSS increased in both groups: in female pts from 3 [2; 4] to 4 [3; 6] (p<0.05), in male pts from 4 [4; 6] to 5 [5; 6] (p<0.05). But, however, in female pts TSS remained less than in male pts over 2 y FUP (table 2). CRP level still was higher in male pts (p<0.05). Progression from non-radiographic axSpA to AS between male and female pts didn’t differ - 5 (15.5%) vs 6 (17.2%), p>0.05 respectively, after 2 y FUP. In both groups rate of SI radiographic progression after 2 y decreased (p<0.05) and did not differ between them.

**Abstract AB0731 Table 2.** Outcome parameters after 2 y of FUP.

<table>
<thead>
<tr>
<th></th>
<th>Man (n=33)</th>
<th>Women (n=35)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ankylosing spondylitis, n,%</td>
<td>30 (90.9%)</td>
<td>21 (60.0%)</td>
<td>0.003</td>
</tr>
<tr>
<td>Non-radiographic axSpA, n,%</td>
<td>3 (9.1%)</td>
<td>14 (40.0%)</td>
<td>0.003</td>
</tr>
<tr>
<td>Total stage of sacroiliitis, median [IQR]</td>
<td>4.0 [4.0; 6.0]</td>
<td>4.0 [3.0; 4.0]</td>
<td>0.006</td>
</tr>
<tr>
<td>Rate of SI radiographic progression, median [IQR]</td>
<td>0 [0; 1.0]</td>
<td>0 [0; 0.5]</td>
<td>0.98</td>
</tr>
<tr>
<td>CRP, Me [25%; 75%;]</td>
<td>5.0 [1.0; 12.7]</td>
<td>1.2 [0.0; 4.0]</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Conclusion: 1. Rate of SI radiographic progression in male and female pts with axSpA in the first 2 y from the onset of disease is higher than in further. 2. Rate of SI radiographic progression between male and female pts with axSpA is not differ. 3. Male pts with AS more than female pts in CORSAR cohort. It can be explained that male pts had higher CRP level than female pts.

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AB0732

**THE ASSOCIATION BETWEEN PERIODONTAL DISEASE AND RISK OF ANKYLOSING SPONDYLITIS: A SYSTEMATIC REVIEW AND META-ANALYSIS**

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Background: The association between periodontal disease and rheumatoid arthritis is well-recognized [1]. Porphyromonas gingivalis is probably the link between the two conditions. On the other hand, the data on the

**Scientific Abstracts**

**AB0731**

**RATE OF SACROILIITIS RADIOGRAPHIC PROGRESSION IN MALE AND FEMALE PATIENTS WITH EARLY AXIAL SPONDYLOARTHRITIS**

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**Background:** According recent studies radiographic progression (mSASSS) of male patients (pts) with ankylosing spondylitis (AS) higher than in female pts [1, 2].

**Objectives:** To compare radiographic progression of early axial spondyloarthrits (axSpA) in male and female pts over 2 years (y) of follow-up (FUP).

**Methods:** the research included 68 pts with early axSpA (ASAS criteria, 2009) from Moscow CORSAR cohort with disease duration <5 and age onset <45 years. The mSASSS index is not suitable for assessing radiographic progression at an early stage of axSpA, because at that stage of the disease, the cervical and lumbar spine have practically no damage. Sacroiliac joints (SIJ) radiographs and CRP performed at baseline and after 2 y of FUP. Radiographic SIJ stages scored according to the modified New York criteria grading system. To assess the progression in SIJ, total stage of sacroiliitis (TSS) calculated, by determining sum score stages of sacroiliitis (SI) in the left and right SIJ (from 0 to 8 points).

The following formula used to calculate the rate of SI radiographic progression:

\[
\text{Rate of SI radiographic progression} = \frac{TSS^2 - TSS^3}{\text{FUP}}\times12
\]

\*TSS - initial total score stages of SI, TSS - FUP total score stages of SI.

Pt's mean age was 28.5 (5.8) y, average disease duration - 24.1 (15.4) mo, 63 (92.6%) pts were HLA-B27 positive.

**Results:** Initially, among men there were more pts with AS than among women and they had a higher TSS and higher CRP level (table 1). Rate of SI radiographic progression in male and female pts with axSpA at baseline did not differ.
association between periodontal disease and ankylosing spondylitis are still relatively limited.

**Objectives:** The current systematic review and meta-analysis was conducted with the aims to identify all published studies that investigated the risk of ankylosing spondylitis among patients with periodontal disease versus individuals without periodontal disease and summarize their results together to better characterize this relationship.

**Methods:** Two investigators independently searched for published studies indexed in MEDLINE and EMBASE database from inception to October 2018 using the search strategy that included the terms for periodontal disease and ankylosing spondylitis. The inclusion criteria are as follows: (1) Case-control or cohort studies that compared the risk of ankylosing spondylitis between patients with periodontal disease versus individuals without periodontal disease (2) Individuals without periodontal disease were used as comparators in cohort studies while individuals without ankylosing spondylitis were used as controls in case-control studies and (3) Effect estimates and 95% confidence intervals (CI) of the association of interest were reported. Point estimates and standard errors from each study were extracted and combined together using the random effect, generic inverse variance technique of DerSimonian and Laird.

**Results:** Of 554 retrieved articles, a total of 7 case-control studies with 41,575 participants met the eligibility criteria and were included into the meta-analysis. The risk of ankylosing spondylitis among patients with periodontal disease was significantly higher than individuals without periodontal disease with the pooled odds ratio of 2.16 (95% CI, 1.48–3.16). The statistical heterogeneity was low with an I² of 45%. The forest plot of this meta-analysis is shown as Abstract AB0732 figure 1. Funnel plot was created for evaluation of publication bias. The plot was relatively symmetric which did not suggest the presence of publication bias in favor of studies with positive results.

**Conclusion:** A significantly increased risk of ankylosing spondylitis among patients with periodontal disease was demonstrated in this study. This observation may provide more understanding of the pathogenesis of this chronic inflammatory arthritis.

**REFERENCES**


**Disclosure of Interests:** None declared


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**AB0733 AN EYE FOR THE HEART: ARE RETINAL VASCULAR PARAMETERS ASSOCIATED WITH CARDIOVASCULAR DISEASE IN ANKYLOSING SPONDYLITIS?**

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**Background:** Chronic systemic inflammatory in patients with ankylosing spondylitis (AS) contributes to the development of cardiovascular disease (CVD). Microvascular changes are thought to precede clinically overt CVD and its early recognition could improve timely treatment. The microvascular function of the retina and fingertips are easily accessible for non-invasive visualization. Furthermore, previous studies have shown an association between CVD and respectively retinal morphology and digital microvascular function (fingertips), in patients without rheumatic diseases. The retinal and digital vasculature could provide an unique opportunity to recognize early signs of CVD in AS patients.

**Objectives:** To investigate whether retinal vascular parameters and digital microvascular function in AS patients are associated with the 10 year CVD risk.

**Methods:** Cross-sectional study in AS patients (diagnosis according to modified New York criteria) between 50-75 years without a history of diabetes mellitus or cerebrovascular disease. Consecutive patients were recruited consecutively from the Rheumatology outpatient clinic of the Amsterdam UMC, location VUMc and Reade. Patient characteristics, CVD (risk factors), disease duration/activity (ASDAS), C-reactive protein and lipid profile were assessed. The digital microvascular function (the reactive hyperemia index, RHI) was tested through endo Peripheral Arterial Tone measurement at the finger tips (EndoPAT). Retinal vascular parameters were assessed through fundus photography, and identified with Singapore I Vessel Assessment (SIVA) software: central retinal artery and vein equivalent (CRAE, CRVE), arteriovenous ratio (AVR), curvature tortuosity arterioles and venules (cTOArTa, cTOArTv), fraxial dimension of arteries and venules (FiDia, FiDIV). SIVA parameters were reported as continuious values. The Framingham risk score (FRS) was calculated and classified based on the 10 years CVD risk (low risk <10%, intermediate risk 10–20%, high risk >20%). Linear regression analyses were used to determine the association between the FRS categories and retinal parameters or digital microvascular function (RHI), correcting for age and disease duration.

**Results:** Fifty-three AS patients were included (age 60±6 years, 55% female, 74% HLA-B27 positive, disease duration 35 years ±13, ASDAS 2.3±1.0). Fifty-five% was currently treated with NSAIDs and 47% with a TNF inhibitor. Based on the FRS, 36% had a high risk of CVD in the next 10 years, 42% an intermediate and 12% a low risk. In multivariable analyses, patients with an intermediate and high risk of CVD (FRS) had a significantly lower diameter of the central retinal artery (CRAE; p<0.01 for both risk groups) and arteriovenous ratio (AVR; only for high risk; p=0.03) as compared with patients with a low risk. There was no association between the RHI and the cardiovascualr risk.

**Conclusion:** This study suggests an association between the 10 years CVD risk and the morphology of the retinal arterial vessels in older AS patients (>50 years). This is in accordance with some other studies reporting on atherosclerosis in the general population. No association was found between CVD risk and microvascular function in the fingertips. In conclusion, the measurement of retinal vascular parameters might be a new technique to detect early stages of atherosclerosis in AS.

**Disclosure of Interests:** Rianne van Bentem: None declared, Milad Baniaamam: None declared, Buki Kinaci: None declared, Aled van de Kreeke: None declared, Merve Kocyigit: None declared, Erik Serné: None declared, Michael Nurmohamed Grant/research support from: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Menarini, Mundipharma, Pfizer, Roche, Sanofi and UCB, Consultant for: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi and UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Celgene, Eli Lilly, Janssen, Menarini, MSD, Mundipharma, Pfizer, Roche, Sanofi and UCB, Frank Verbraak: None declared, Irene van der Horst-Bruinsma Grant/research support from: MSD, Pfizer, AbbVie, Consultant for: Abbv; UCB, MSD, Novartis, Speakers bureau: BMS, AbbVie, Pfizer, MSD.

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**AB0734 CHANGES IN HEIGHT AND BODY MASS INDEX OVER TIME IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS, TREATED WITH TUMOR NECROSIS FACTOR-α INHIBITORS**

1Elizaveta Vasilenko1, Olga Nikolaeva1, Anna Dadalova1, Ekaterina Gaydikova2, V Macurov1, Innia Gaydikova1, 1North-Western State Medical University named after I.I. Mechnikov, Department of Therapy, Rheumatology, Examination of Temporary Disability and Quality of Medical Care named after E.E.Eichwald, St. Petersburg, Russian Federation; 2TITMO University, St. Petersburg, Russian Federation

**Background:** Monitoring of height and body mass index (BMI) is an important for patients with axial spondyloarthritis (axSpA). Reduction of height not only reflects spine remodeling, but affects various indexes, such as BMI (fig.1). However, BMI calculations assume that the adult patient’s height is a constant. Therefore these calculations may be inaccurate in patients whose height is susceptible to decrease.
Objectives: To evaluate changes in height and BMI over time in patients with axSpA, treated with tumor necrosis factor-α inhibitors (TNF-α-i).

Methods: The study included 51 patients with axSpA (ASAS criteria 2009). All the patients were treated with TNF-α-i for one and 4 years. The patient's height and weight measured before the treatment. Only patients with stable weight (variability ± 2.0 kg from baseline) were included in the study.

Results: Mean age of axSpA patients at baseline was 40.22±13.51, 34 (74.5%) were male, disease duration 12.77±6.82, duration of TNF-α inhibitors treatment 5.64±2.21 years, all the patients had inactive disease. In 19 patients with axSpA diagnostic delay was 8 years. Patients' height varied between 1.55–1.92 m (average height 1.73±0.07 m), Male's mean height was 1.78±0.05 m, women's – 1.63±0.05 m. Height decrease over time in patients with AxSpA was 3.74±1.83 cm (from 1.0 to 15.0 cm). Maximal decrease in height was shown in patients with 10 years after the first symptoms emerged. Mean weight in patients who had height loss was 79.75±12.7 kg. Among patients who had decrease of height and stable body mass the difference between BMI at subsequent measurement and the time of treatment initiation (ΔBMI) was 1.15 kg/m²; BMI at baseline – 26.25±3.34 kg/m², over time of observation BMI – 27.39±3.38 kg/m².

Conclusion: Height loss in axSpA is significant even in patients with inactive disease. Height loss affects BMI calculation that could lead to overestimation of cardiovascular risk, obesity and could change all of the BMI-dependent areas. Correction of BMI calculation for the patients with unstable height and stable body mass is needed.

Disclosure of Interests: Elizaveta Vasilenk: None declared, Olga Nikolaeva: None declared, Anna Dadalova: None declared, Elizaveta Vasilenko: None declared, Olga Nikolova: None declared, Ekaterina Gaydukov: None declared, V Mazurov Grant/research support from: JSC laeva: None declared, Anna Dadalova: None declared, Ekaterina Gaydukov: None declared, Elizaveta Vasilenko: None declared, Olga Nikolova: None declared.

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ACKNOWLEDGMENTS: The authors would like to thank all the patients who participated in this study. This research was supported by the National Academy of Sciences of Ukraine and the Ministry of Education and Science of Ukraine

AB0734C REMISSION IN AXIAL SPONDYLOARTHRITIS: A DELPHI-METHOD QUESTIONNAIRE AMONG EXPERTS TO EVALUATE THE AVAILABLE ASSESSMENT TOOLS TO MEASURE DISEASE ACTIVITY AND TO DEVELOP A CONSENSUS DEFINITION OF REMISSION

Background: Several definitions of remission in axial spondyloarthritis (axSpA) have been proposed based on the available disease activity assessment tools, but to date we lack a universally accepted definition of remission for the development of clinical trials or routine clinical practice.

Objectives: To explore the degree of agreement that exists among the experts managing patients with axSpA regarding the assessment tools available to evaluate disease activity in these patients and to develop a consensus definition of clinical remission in axSpA.

Methods: As a consensus method, we followed the modified Delphi methodology. A scientific committee developed 80 statements that were submitted in 2 rounds (in September and October 2018, respectively) to a panel of 152 rheumatologists from 27 countries.

Conclusion: Bony bridge in LV is not only more developed and correlated with ankylosis in FJ, but also more correlated with limitation of anterior lumbar flexion than that in AV. We suggest bony changes of LV should be also included in radiographic score system for more sensitive detection of radiographic progression in AS.

Disclosure of Interests: None declared

Results: Agreement was reached for 56 of the 80 proposed items (70%). The panelists concluded that although a definition of remission in axSpA is not currently available, there is consensus that it is possible to achieve remission in this disorder. There was agreement that the definition of remission in axSpA should include: pain, fatigue, functional impairment, mobility, extra-articular manifestations, peripheral involvement, joint inflammation, disease activity, laboratory tests, quality of life, need for treatment, progression of the disease, and both physician and patient global assessments. It is recommended that a therapeutic goal when starting treatment in patients with axSpA, the ideal objective being remission, but low disease activity (LDA) may also be acceptable as an alternative objective, being ASDAS the preferred tool to assess disease activity with cut-off values of < 1.3 for remission and ≤ 1.3 to < 2.1 for LDA. A proposal for clinical remission was reached for the first time at the meeting and is based on the ASDAS cut-off value associated to the absence of extra-articular (psoriasis, uveitis, inflammatory bowel disease) and peripheral (arthritis, enthesitis, dactylitis) activity, as well as the absence of inflammation assessed by the normalization of CRP levels and absence of radiographic progression.

Conclusion: This work offers consensus recommendations and a proposal of clinical remission that may be useful in the management of patients with axSpA.


Psoriatic arthritis

Ab0735 SAFETY AND EFFECTIVENESS OF USTEKINUMAB IN PSORIATIC ARTHRITIS. A MULTICENTRIC STUDY


Method: Retrospective and multicentric study. Epidemiological and clinical data were collected through the electronic medical record of all patients with PsA who started UST due to rheumatological indication in 14 hospitals of Catalonia and the Balearic Islands (Spain).

Results: 152 patients were included, 116 (76.3%) with 45mg and 36 (23.8%) with 90mg. 55.9% were women, mean age 54.79 (12.5) years and mean disease duration 209 months. 132 patients (87%) had oligo (30.3%) or polyarticular involvement (56.6%). 26.8% had enthesitis and 36.2% dactylitis. 48.0% had erosions, 35.4% had previous surgery, and 39 of them (38.8%) had received 2 or more. 54.6% of the patients were taking DMARDs and 39.5% glucocorticoids. The baseline DAS 28 was 3.97 (1.45), C reactive protein (CRP) was 2 mg/dl (2), SJC was 4.0 (5.4), and PASI was 6.5 (8.4). There were no significant differences in clinical and epidemiological data between patients at 45 or 90 mg except in obese patients (58.4% in 90mg vs 40% in 45mg, p < 0.038). Overall, there was a significant decrease in DAS28, SJC, TJC and PASI in the first month of treatment, with more pronounced improvement in skin (PASI and BSA) than in joints outcomes, where the curves reached a plateau at 6 months. There were no significant differences between joint and/or skin outcomes between 45 and 90 mg doses.

Conclusion: This analysis demonstrates that UST, administered to PsA patients in a routine clinical care setting, is safe and effective in improving skin and joint outcomes. 61.2% of the patients continued with the treatment after an average of 19m of follow-up. Joint and skin outcomes reached significant differences from the first month. The efficacy seems faster in those patients with fewer lines of previous biological therapies. One third of the patients interrupted the therapy due to joint inefficacy.

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Disclosure of Interests: Ana Belén Aznáur-Piñango: None declared, Beatriz Frade-Sosa1: None declared, Ana Laiz2: Consultant for: Lilly, Novartis, AbbVie, MSD, UCB and Janssen, Speakers bureau: Lilly, Novartis, AbbVie, MSD, UCB and Janssen, Paula Estrada: None declared, Luciano Polino: None declared, Emma Beltrán: None declared, Águeda Pri-Español: None declared, Lourdes Mateo Soria: None declared, Carme Moragues Pastor: None declared, Agustí Sellsas-Fernández: None declared, Ana Urruticoechea-Arana: None declared, Vicenç Torrente Segarra: None declared, Inmaculada Ros Vilamajo: None declared, Sergi Ordoñez: None declared, Delia Reina-Sanz: None declared, Juan D. Cañete: None declared, Julio Ramírez: None declared.


Ab0736 GENDER INFLUENCE ON TREATMENT EFFECTIVENESS IN PSORIATIC ARTHRITIS

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Background: Gender has been lately suggested as influential in the response to treatment with biological drugs in spondyloarthritis, such as psoriatic arthritis (PsA). However, data about the association between gender and treatment response in axial PsA (axPsA) or peripheral PsA (pPsA) are scarce.

Objectives: To analyze the association between gender and treatment response to biological therapy in patients with axPsA and pPsA.

Methods: An observational cohort study was conducted, prospectively collecting data from 108 patients treated with biological therapeutics (01/2014 and 7/11-2017) from 2002-2018. Patients were divided into two groups according to their clinical predominant manifestation: axPsA or pPsA. Disease activity indexes (ASDAS and BASDAI for axPsA and DAPSA and DAS28 for pPsA) were collected before starting drug and 6 months later (baseline and 6m visit, respectively). Low disease activity (LDA) was defined as ASDAS <2.1 or BASDAI <4 (axPsA) or 50% in DAPSA (DAPSA50) or DAS28 > 12. First, the frequency of male- and female-patients achieving LDA and clinical improvement at 6m were compared using Fisher test, separately for axPsA and pPsA. Second, the association between gender and each of the clinical indexes was analyzed using logistic regression models adjusted for confounders (age, disease duration, previous biologics, smoking habit, body mass index (BMI), baseline DMARDs and baseline disease activity (ASDAS or BASDAI for axPsA or DAPSA or DAS28 for pPsA).

Results: Out of 108 included patients, 55 (51%) had predominant axPsA and 54 (49%) pPsA. In the group of axPsA, 35 (64%) were males, 33 (60%) were non-smokers, 33 (60%) had a BMI ≥ 25, with mean (SD) baseline disease activity of ASDAS: 3.3 (1.0) and BASDAI: 5.4 (2.0). Frequency of patients achieving clinical response was higher in males than females (LDA: 74% vs 37%; p=0.02, respectively) (Table 1). After adjusting for confounders, male gender was significantly associated with higher probability of achieving LDA (ASDAS OR=4.4; p=0.03 and BASDAI OR=6.0; p=0.01), and improvement (dASDAS: OR=4.8; p=0.04 and DAPSA50: OR=5.19; p=0.03). In the group of pPsA, 20 (37%) were
ACHIEVEMENT OF RAPID3 NEAR REMISSION OR LOW DISEASE SEVERITY IS ASSOCIATED WITH RESIDUAL LEVELS OF ARTICULAR AND EXTRA-ARTICULAR MANIFESTATIONS OF ACTIVE PSORIATIC ARTHRITIS IN SUBJECTS TREATED WITH APREMILAST

1Martin Bergman, M Elaine Husni1, Yusuf Yazici2, Laura C. Coates4, Sven Richter5, Michele Brunori5, Lichen Teng5, Arthur Kavanaugh6.

Background: The Routine Assessment of Patient Index Data 3 (RAPID3) is an outcome measure of disease activity widely used in the USA as part of routine care and is derived from patient self-reported measures. Health Assessment Questionnaire-Disability Index (HAQ-DI) or multidimensional HAQ [MDHAQ], Pain visual analog scale [VAS] and Patient’s Assessment of Disease Activity [PtGA] VAS. However, the lack of more objective, traditional physician assessments, such as joint counts, may lead to residual active disease that will be missed.

Objectives: To examine trajectories for improvement in RAPID3 score over time and PsA manifestations not measured specifically by RAPID3 in subjects achieving RAPID3 near remission (REM) or low disease severity by Week 52.

Methods: Pooled analyses of the phase III PALACE 1, 2 and 3 studies were performed for subjects assigned to receive APR 30 mg twice daily (BID) at baseline (BL). Subjects with available scores on RAPID3 components (PtGA, VAS and HAQ-DI) at baseline (BL) and Week 52 (near REM: <3; low: >3 to ≤6; moderate: >6 to ≤12; and high: >12 to 30). Mean RAPID3 scores were assessed from BL through Week 52. Other measures of PsA disease activity were reported longitudinally by RAPID3 category at Week 52.

Results: The analysis included 376 APR subjects, with 42 with near REM and 42 with low severity at Week 52. Overall, mean RAPID3 trajectories improved overtime with greater mean improvements observed for those achieving RAPID3 near REM and low disease severity by Week 52. At a mean level, subjects in moderate RAPID3 at baseline were associated with achievement of RAPID3 near REM or low disease severity by Week 52 with APR (Figure). Many subjects who achieved RAPID3 near REM or low disease severity at Week 52 showed improvements in articular and extra-articular disease activity, although not all manifestations were controlled at Week 52 (Table); mean TJC was higher than expected in subjects achieving RAPID3 targets at Week 52 and there was no association between low mean RAPID3 and mean Psoriasis Area and Severity Index (PASI) scores.

Conclusion: At a mean level, subjects in moderate RAPID3 at baseline were associated with achievement of RAPID3 near REM or low disease severity with APR by Week 52. Achievement of RAPID3 targets was associated with improvement, but not necessarily control, of all articular and extra-articular manifestations. Complementing the RAPID3 measure with joint and skin assessments may help to evaluate achievement of treatment goals in clinical practice.
DUAL NEUTRALISATION OF INTERLEUKIN (IL)-17A AND IL-17F WITH BIMEKIZUMAB IN MODERATE-TO-SEVERE PLAQUE PSORIASIS: 60-WEEK RESULTS FROM A RANDOMISED, DOUBLE-BLINDDED, PHASE 2B EXTENSION STUDY

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Background: Psoriasis is a chronic, systemic, immune-mediated inflammatory disease associated with prominent skin manifestations. One in four patients with psoriasis also has psoriatic arthritis1. In skin disease preceding joint manifestations in most patients2. Interleukin (IL)-17F shares structural homology and pro-inflammatory function with IL-17A. Preclinical and early clinical data support dual neutralisation of IL-17F, together with IL-17A, as a novel targeting approach for the treatment of immune-mediated inflammatory diseases. Bimekizumab, a monoclonal antibody that potently and selectively neutralises both IL-17A and IL-17F, is in development for the treatment of psoriasis, psoriatic arthropathy and ankylosing spondylitis3,4,5. In the 12-week BE ABLE 1 study (NCT02905006), bimekizumab provided rapid and substantial clinical improvements in patients with moderate-to-severe plaque psoriasis, with a safety profile consistent with previous bimekizumab studies.

Objectives: The objectives of this Phase 2b extension study (BE ABLE 2; NCT03010527) were to assess the long-term safety and efficacy of bimekizumab every four weeks for an additional 48 weeks (60 weeks' total exposure).

Methods: BE ABLE 1 responders (≥90% reduction in Psoriasis Area Severity Index (PASI90) at Week 12) receiving placebo or bimekizumab 64mg, 160mg, 160mg (320mg loading dose [LD]) remained on the same dose; non-responders (≤PASI90 at Week 12) were re-assigned from placebo/bimekizumab 64mg to 160mg or from 160mg/160mg (LD) to 320mg. Patients previously receiving bimekizumab 320mg/480mg received 320mg. The primary variable was the exposure-adjusted incidence rate (EAIR) of treatment-emergent adverse events (TEAEs); efficacy assessments were secondary.

Results: 217 patients were enrolled. Across all doses, BE ABLE 1 responders generally maintained complete or almost complete skin clearance for up to an additional 48 weeks: PASI90: 80–100%, non-responders imputation (93–100%, observed); PASI100: 70–83% (80–96%); Investigator Global Assessment: 78–100% (98–100%). PASI100 was achieved by 33–76% (40–82%) of non-responders (Week 48). EAIR of TEAEs was 206.1/100 patient-years (n=184/217 [85%]). EAIR of serious TEAEs was 6.2/100 patient-years (n=15/217 [7%]); no serious TEAE was reported by ≥1 patient. The most frequent TEAEs were oral candidiasis and nasopharyngitis. No cases of suicidal ideation/behaviour, major adverse cardiac events, or inflammatory bowel disease were reported. No new safety findings were observed.

Conclusion: Nearly all BE ABLE 1 responders completing 60 weeks of bimekizumab treatment maintained complete or almost complete skin clearance, with a safety profile consistent with previous studies.

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AB0738

THE PREVALENCE OF PSYCHOLOGICAL DISORDERS IN PATIENTS WITH SEVERE PSORIASIS WITHOUT PSORIATIC ARTHRITIS IN CLINICAL PRACTICE: DATA FROM A SINGLE DERMATOLOGICAL SETTING

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Background: Psoriatic arthritis (PsA) and Psoriasis (PsO) are associated with different psychological disorders. Depression is a risk factor for development of PsA among PsO patients (pts). Diagnosis of PsA in dermatological practice is still problematic. The prevalence of psychological disorders in patients with severe PsO without PsA is limited in the Russian Federation.

Objectives: To study the prevalence of anxiety, depression and fatigue in pts with severe PsO without PsA in a single dermatological setting.

Methods: 99 unselected pts (male-23/female-76) with severe plaque PsO, mean age 45.82±14.04 years, BSA 56.35±9.11%, PASI 22.50 ± 5.13 were included. PsO was diagnosed by the CASPAR criteria. Anxiety, depression and fatigue were identified by the Hospital Anxiety Scale (HADS-A), HADS-Depression (HADS-D) and Functional Assessment of Chronic Illness Therapy (FACIT) (points) accordingly. The HADS-A/HADS-D was defined as normal - 0-7; presence of disorders - 8-10; psychiatric morbidity >11 points, accordance FACIT 43.6±9.4 matched with healthy control. The lower the level of FACIT corresponded to higher fatigue. The number of pts with FACIT>30 were calculated. All pts were treated with different synthetic DMARDs, mostly Methotrexate (subcutaneous 15-20 mg every week), biological DMARDs according local therapy according

AB0739

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to the national guidelines. Mm%, chï2, i-test were performed. All p<0.05 were considered to indicate statistical significance.

**Results:** 20 out of 99 pts (20.2%) had PsA. In all group mean HADS-D/ HADS-A/FACIT were 2.59±3.88/4.61±5.54/4.47±5.61 accordingly. In PsO pts with or without PsA presence of disorders/psychiatric morbidity by HADS-D/A/FACIT were seen totally in 20 out of 79 pts (25.3%)/in 2 out of 20 pts (10%) accordingly (chï2, p=0.24). No significant difference were found between groups. In PsO pts without/with PsA presence of disorders/psychiatric morbidity by HADS-D were seen totally in 20 out of 79 pts (25.3%)/in 2 out of 20 pts (10%) accordingly (chï2, p=0.025). In PsO pts without/with PsA presence of disorders/psychiatric morbidity by HADS-D/A/FACIT were seen in 2 out of 79 pts (2.53%)/in 2 out of 20 pts (10%). No significant difference were found between groups (chï2, p=0.17).

**Conclusion:** In our real dermatological clinical practice cohort of pts with severe PsO subclinical and clinical anxiety and depression were detected in about 30% of cases. This fact should be taken into account for the early detection of pts at risk for developing PsA.

**REFERENCES**


**AB0740 USE OF SECUKINUMAB IN PATIENTS WITH PSORIATIC ARTHRITIS: IMPACTS OF COMBINATION WITH METHOTREXATE**

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**Background:** Secukinumab (SECU) is a human IgG1 monoclonal antibody that binds to the protein interleukin-17A approved for the treatment of psoriasis, ankylosing spondylitis, and psoriatic arthritis (PsA). Recent presentations data suggest that combination with methotrexate (MTX) in patients with PsA may not be as necessary as in rheumatoid arthritis as it improves neither efficacy nor sustainability (1,2,3,4).

**Objectives:** This analysis describes the use of SECU with or without MTX.

**Methods:** The data of patients with psoriatic arthritis seen since January 1. 2016 at the Institute de Recherche en Rhumatologie de Montréal (IRRM) and the Centre de l’Ostéoporose et de Rhumatologie de Québec (CORQ) were extracted from the Rhumadatab® clinical database and registry on January 7, 2019. Selected patients initiated SECU either without (MTX-) or with MTX (MTX+). The collected data include baseline characteristics (socio-demographic variables, concomitant and past medication, comorbidities and the Charlson comorbidity index (CCI)), variables measured over time (laboratory test results, patient and physician-reported outcomes, and disease activity measures such as minimal disease activity (MDA), CDAI and DAS28(4-ESR) and persistence data (treatment duration, reason for cessation). The groups were compared to identify potential confounder, and persistence data were analyzed using Kaplan-Meier and proportional hazard methods.

**Results:** A total of 96 patients were prescribed SECU since January 1, 2015. Of those, 49% (n=47) treated with MTX. No significant differences in baseline (at treatment initiation) were observed between the MTX+ and MTX- groups. Average age at treatment initiation was 52.4 (standard deviation=11.3) and 53.7 (13.4) in the MTX+ and MTX- groups respectively. Women represent 45% and 55% of these groups, and the average body mass index was 29.9 (6.2) and 28.1 (6.0) kg/m². Patient global, pain and fatigue assessments, made on a visual analogue scale ranging from 1 to 10, were 4.9 (2.6), 5.3 (2.9) and 4.3 (2.9) in the MTX+ group and 6.3 (2.2), 6.9 (2.1) and 6.5 (2.9) in the MTX- group. Among the 38 (40%) patients ceasing therapy, the principal reason for cessation was “inefficacy” (MTX+: 15/17 (88%) vs MTX-: 15/21 (71%)). Patients remaining on treatment at last follow-up had an average treatment duration of 1.7 (0.8) and 1.5 (0.7) years. The improvement in CDAI, HAQ and the percentage of patients reaching MDA are similar for both groups. No difference in retention was observed between the MTX+ and MTX- groups (log-rank p=0.4867). These results remain unchanged when we adjust for age at treatment initiation, gender, disease duration, and comorbidities (Charfon comorbidity index).

**Conclusion:** Combining MTX to SECU does not improve its sustainability over time. Efficacy was also the same for both cohorts.

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**Disclosure of Interests:** Diane Sauvageau Consultant for: Pfizer, MSD, Novartis, Amgen, UCB

**Disclosure of Interests:** Édith Villeneuve Consultant for: AbbVie, UCB, Celgene, Roche, Pfizer, Amgen, BMS, Sanofi-Genezyme, Paid instructor for: AbbVie, Speakers bureau: AbbVie, Pfizer, BMS, Roche, Louis Coupal: None declared DOI: 10.1136/annrheumdis-2019-eular.3458

**AB0741 ACHIEVEMENT OF CDAPS A LOW DISEASE ACTIVITY OR REMISSION IS ASSOCIATED WITH CONTROL OF ARTICULAR AND EXTRA-ARTICULAR MANIFESTATIONS OF ACTIVE PSORIATIC ARTHRITIS IN SUBJECTS TREATED WITH APRAMILIST**

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**Background:** Therapeutic targets for psoriatic arthritis (PsA) include the achievement of remission (REM) or low disease activity (LDA), measured by the Clinical Disease Activity Index for Psoriatic Arthritis (cDAPSA [0-154]), a composite of swollen and tender joints counts (SJC and TJC), Patient’s Assessment of Pain (PAP) and Patient’s Global Assessment of Disease Activity (PGA).

**Objectives:** We examined the trajectories for improvement in cDAPSA, its core components and PsA domains in subjects achieving REM or LDA, patients not meeting cDAPSA among subjects achieving CDAPS A REM or LDA by Week 52.

**Methods:** Pooled analyses of the phase III PALACE 1, 2 and 3 studies were performed for subjects assigned to receive apremilast (APR) 30 mg twice daily at baseline (BL). Subjects with cDAPSA components available at baseline (BL), measured on a 7-point scale ranging from 0 to 6 (0=inactive to 6=very active) were included and grouped according to the cDAPSA categories reached at Week 52 (REM: ≤4; LDA: >4 to ≤13; moderate disease activity: >13 to ≤27; high disease activity: >27). We then traced their mean cDAPSA trajectory from BL to Week 52.

**Results:** No differences in core PsA domains, speakers reported longitudinally by cDAPSA category reached at Week 52.
Results: A total of 375 APR subjects were included in the analyses. Achievement of REM or LDA by Week 52 was associated with lower mean cDAPSA at BL, and these subjects had continuous improvements in disease activity from BL to Week 52 (Figure). Among subjects who achieved REM/LDA by Week 52, more were classified as having LDA (mean cDAPSA: 8.5) or moderate disease activity (mean cDAPSA: 16.6), respectively, at Week 16. Furthermore, subjects who achieved REM or LDA by Week 52 showed early improvement, with no/mild articular and extra-articular disease activity by Week 52 with APR (Table).

Conclusion: In the subgroup of subjects who achieved cDAPSA REM or LDA, early improvement was seen in disease activity by Week 16 and sustained to Week 52 with continued treatment. Subjects achieving cDAPSA REM or LDA exhibited no or mild disease activity in enthesitis, dactylitis, function and skin psoriasis by Week 52.

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Scientific Abstracts

AB0742 ACHIEVEMENT OF PASDAS LOW DISEASE ACTIVITY AND VERY LOW DISEASE ACTIVITY IN PATIENTS WITH PSORIATIC ARTHRITIS TREATED WITH CERTOLIZUMAB PEGOL OVER 4 YEARS AND THE OVERLAP WITH DAPSA AND MDA DISEASE ACTIVITY TARGETS

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Background: Psoriatic Arthritis Disease Activity Score (PASDAS),1 Disease Activity Index for Psoriatic Arthritis (DAPSA),2 and the minimal disease activity (MDA) criteria3 are instruments recommended for evaluating disease activity (DA) in psoriatic arthritis (PsA). RAPID-PsA demonstrated the sustained efficacy of certolizumab pegol (CZP) across the spectrum of PSA symptoms.4 A substantial proportion of patients (pts) completing 4 years’ treatment achieved DA targets; >75% reached DAPSA low DA (LDA) or remission (REM), and almost 60% had MDA (>57 MDA criteria), half of whom also achieved very low DA (VLDA) (77 MDA criteria).5

Objectives: To report the proportion of pts who achieved PASDAS VLDA and LDA over 216 weeks (wks) CZP treatment, and the overlap in pts achieving PASDAS, DAPSA and MDA.

Methods: RAPID-PsA (NCT01087788) was double-blind and placebo-controlled to Wk24, dose-blind to Wk48, and open-label (OL) to Wk216.6 Outcomes reported for pts randomised to CZP at Wk0 (200 mg every 2 wks or 400 mg every 4 wks, following a 400 mg loading dose at Wk0/1). DAPSA change from baseline (CFB); pts achieving PASDAS LDA (>1.9–3.2), PASDAS VLDA (≤1.9), DAPSA LDA (>4–<14), DAPSA REM (<4), MDA and VLDA to Wk216; and the overlap in pts achieving PASDAS VLDA, DAPSA REM, and VLDA, at Wk216. Data are summarized for observed cases per visit. Pts withdrawing between scheduled visits had their final assessment values assigned to the next scheduled visit timepoint.

Results: Of 409 pts randomised, 273 received CZP from Wk0, of whom 248 (60.8%) completed Wk24 and 163 (67.0%) completed Wk216. The mean (SD) baseline PASDAS was 6.0 (1.6): in the high DA range, CFB at Wk216 was −3.4 (1.5). Of pts completing Wk216, 66.3% (118/178) were in PASDAS LDA or VLDA (PASDAS VLDA: 36.5% [N=65]) less than the proportion reaching DAPSA LDA or REM (70.2%), but more than those achieving MDA or VLDA (57.8%) (Figure A).

At Wk216, of pts achieving PASDAS VLDA, a large proportion (71% [46/65]) had VLDA based on MDA criteria (Figure B1) and most (94% [61/65]) achieved DAPSA REM (Figure B2). Almost all pts achieving VLDA (96.1% [50/52]) were also in DAPSA REM (Figure B3). After 4 years’ CZP treatment, 25.8% (46/187) pts achieved the PASDAS VLDA, DAPSA REM and VLDA.
Conclusion: A substantial proportion of pts completing 4 years’ CZP treatment achieved PASDAS LDA or VLA, and the vast majority who achieved PASDAS VLA at Wk216 also reached DAPSA REM and/or VLDA. 1 in 4 pts achieved the most stringent DA target with all 3 instruments.

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ABO743

REAL-WORLD EFFECTIVENESS AND SAFETY OF APREMILAST IN BELGIAN PATIENTS WITH PSORIATIC ARTHRITIS: ANALYSIS FROM THE MULTICENTRE, PROSPECTIVE, NON-INTERVENTIONAL APOLO STUDY

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Background: Real-world evidence on effectiveness and safety data for patients (pts) with psoriatic arthritis (PsA) in the Belgium clinical practice setting is lacking.

Objectives: To assess the effectiveness and safety of apremilast (APR) in pts with active PsA from routine clinical practice in Belgium.

Methods: In this multicenter prospective, non-interventional study (APOLO), the PsA Response Criteria (PsARC) response 6 months after APR initiation was the primary endpoint. PsARC response was defined as improvement in ≥2 and no worsening of any of the following 4 measures: tender joint count (TJC; 0–66), swollen joint count (SJC; 0–66), Physician’s Global Assessment of Disease Activity (PGA) and Patient’s Global Assessment of Disease Activity (PiGADA). Other endpoints included PsAID12, HAQ-DI; Physician’s and Patient’s Numerical Rating Scale (NRS) assessing disease activity for the most affected joint, psoriasis-affected body area surface (BSA), enthesis, dactylitis, pain and pruritus. The current analysis is based on observed data.

Results: The first 55 of a planned 150 Belgian pts receiving APR for up to 6 months were evaluated. Mean age was 52.5 yrs, mean BMI was 27.1 kg/m2 and 47.3% were female. Mean durations of psoriasis and PsA were 15.8 yrs and 8.1 yrs, respectively; <80% of pts were biologic-naive. At baseline (BL), mean (SD) SJC was 8.0 (5.4), mean (SD) TJC was 12.7 (9.5) and mean (SD) body surface affected was 12.3% (20.8%); 31.0% of pts had dactylitis and 47.8% had enthesis. In total, 35 pts (63.6%) continued APR treatment for 6 months; 20 (36.4%) had discontinued APR (insufficient effectiveness: 21.8%; adverse events: 10.9%, intolerence: 3.6%). After 6 months of APR initiation, 69.6% of pts had a PsARC response. Mean changes from BL in SJC were –4.4 (Month 3) and –5.7 (Month 6), with improvements in SJC (defined as ≥30% decrease per PsARC) observed in most pts (Month 3: 78.3%; Month 6: 83.3%). Comparable results were seen for TJC: Mean changes from BL were –7.2 (Month 3) and –6.7 (Month 6), with improvements observed in most pts (Month 3: 78.3%; Month 6: 80%). Decreases in PGA score of ≥1 from BL were observed in most pts at Months 3 (73.7%) and 6 (66.7%). Mean (SD) Physician’s NRS scores decreased from 5.6 (2.6) to 2.5 (2.0) at Month 6. Among pts with enthesitis at BL who had data available at Month 6, 54.5% achieved a score of 0. Among pts with dactylitis at BL who had data available at Month 6, 27.1% (20.8%) at BL to 7.5% (14.7%) at Month 6. An improvement of ≥20% in HAQ-DI at Month 6 was achieved by 73.1% of pts. Improvement were also seen in PGA score, overall pain and pruritus. No new safety and tolerability concerns from known overall safety profile of APR. No new safety and tolerability concerns from known overall safety profile of APR.

Conclusion: Results from this real-world PsA study confirmed an improvement in disease activity with APR in both physician-assessed and pt-reported outcomes for most pts. Overall, improvements were observed after 3 months of APR treatment and were maintained up to the 6-month observation period. Safety and tolerability were similar to the known profile of APR.

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AB0744

EFFICACY OF IXEKIZUMAB IN ACTIVE PSORIATIC ARTHRITIS (PSA) PATIENTS WITH AXIAL PAIN STARTING BEFORE AGE 45: A SUBGROUP ANALYSIS OF SPIRIT-P1 AND SPIRIT-P2 PHASE 3 CLINICAL TRIALS

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Background: The efficacy and safety of ixekizumab (IXE), an IL-17A antagonist, was investigated in patients with active psoriatic arthritis (PsA) in the SPIRIT-P1 and SPIRIT-P2 clinical trials.

Objectives: To investigate the efficacy of ixekizumab on axial pain, fatigue, stiffness, and physical function in a subset of patients with PsA self-reporting axial pain starting before the age of 45 years at baseline.

Methods: Patients with PsA in the intent-to-treat populations of SPIRIT-P1 (Biologic-naïve; NCT01695239) and SPIRIT-P2 (Inadequate responders or intolerant to 1 or 2 TNF inhibitors; NCT02349295) with baseline patient-reported axial pain (≥4 Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) question 2), high-sensitivity C-reactive protein (hsCRP) >5 mg/L, and <45 years old were included in this post-hoc integrated analysis.

Results: Axial pain and stiffness significantly improved at Weeks 16 and 24 in patients with PsA treated with IXEQ4W or IXEQ2W versus PBO (p<0.05; Table 1). Fatigue significantly improved at Week 16 in patients treated with IXEQ4W or IXEQ2W versus PBO and at Week 24 with IXEQ2W versus PBO (p<0.05). Total BASDAI scores significantly improved at Weeks 16 and 24 in patients treated with IXEQ4W or IXEQ2W versus PBO (p<0.01). Physical function significantly improved at Weeks 16 and 24 in patients treated with IXEQ4W or IXEQ2W versus PBO when assessed by HAQ-DI or SF-36 PCS (p<0.05).

Conclusion: Ixekizumab treatment yielded significantly higher improvements than placebo in axial pain, fatigue, stiffness, and physical function at Weeks 16 and 24 in the integrated PsA subpopulation self-reporting axial pain at baseline. These analyses were limited by a lack of baseline axial imaging.

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AB0746 WORKING STATUS AND FACTORS ASSOCIATED WITH WORK PRODUCTIVITY AMONG PEOPLE WITH PSORIATIC ARTHRITIS

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Background: Work disability is an important functional outcome measure in psoriatic arthritis (PsA) and includes unemployment and loss of work productivity. 

Objectives: The aim of this study is to investigate the working status and the factors associated with work productivity in patients with PsA.

Methods: Patients with PsA according to Classification Criteria for Psoriatic Arthritis (CASPAR) were included in the study consecutively, without sample selection. Data about age, sex, disease duration (month) were noted. Disease activity was assessed with DAPSA (Disease Activity in Psoriatic Arthritis) and BASDAI (Bath Ankylosing Spondylitis Disease Activity Index). The Health Assessment Questionnaire (HAQ) was used to evaluate physical disability. The Psoriatic Arthritis Quality of Life (PsAQoL) scale was used to assess the quality of life. Fatigue and stiffness were assessed on the Visual Analogue Scale (VAS). Anxiety and depression were evaluated with HAD (Hospital Anxiety and Depression) scale.

Assessing work disability, we asked some questions to the patients including employment status, and early retirement, changing or reducing work due to PsA. We used WPAI: PsA (Work Productivity and Activity Impairment Questionnaire) to evaluate the impact of PsA on work productivity. WPAI: PSA consists of six questions: the percentage of absenteeism (work time missed due to PsA), the percentage of presenteeism (reduced productivity at work due to PsA), an overall work impairment (combines absenteeism and presenteeism) and percentage of impairment in daily activities.

The association between WPAI: PsA scores and HAQ, PsAQoL, HAD, fatigue and stiffness was determined by Spearman's correlation coefficient. The Mann Whitney-U test was used to compare the means of groups.

Results: The mean age of 60 patients (38 female, 22 male) with PsA was 48.13 (SD: 11.53) years. The median (min-max) duration of disease was 36 (3-384) months. 63.33% of the patients were not working and 57.89% of these patients were housewives, and 23.68% were retired. 11.66% of the patients with PsA were unemployed. There were no patients who were retired early due to the disease. Percentage of the stopping work, changing work or reducing working hours due to PsA was 3.3%, 6.7% and 10%, respectively.

There was no significant difference between the working and not-working groups of patients according to the disease duration, DAPSA, BASDAI and HAQ scores (p>0.05).

Conclusion: Work disability is an important functional outcome measure in psoriatic arthritis (PsA) and includes unemployment and loss of work productivity.

Disclosure of Interests: None declared.

AB0747 RESPONSE TO SECUKINUMAB AMONG NAIVE AND BIOLOGICALLY EXPERIENCED PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Secukinumab is a recombinant human monoclonal immunoglobulin IgG antibody that selectively targets IL-17A and blocks its interaction with the IL-17 receptor. Inhibition of the downstream effects of this proinflammatory cytokine thereby interferes with key psoriasis disease pathways while promoting normalization of immune function and skin histology.

Objectives: The aim of the study was two-fold; firstly, to compare the response to Secukinumab in psoriatic arthritis (PsA) patients who were biologically-naive and experienced, and secondly to compare the response between smokers and non-smokers.

Methods: In collaboration with the National Psoriatic Arthritis Registry of Ireland, patients who were diagnosed and treated as PsA at University Hospital Kerry between March 2017 and October 2018 were included in this population-based cohort study. Patients demographic, clinical characteristics, treatment strategies (including response rates and adverse effects) were captured at baseline and at follow-up outpatient visits.

Results: A total of 96 patients were identified and included in the study (mean age of 56.6 years; male to female ratio of 1:1.49 males, 47 females). Of these patients, 15 received Secukinumab (7 biologically-naive patients, 8 patients with previous treatment failure to anti-TNF agents (3 patients received one anti-TNF, 5 received two different anti-TNFs). In the biologically-naive group, 5 patients (71%) had complete response to Secukinumab, one patient (14.3%) had complete improvement of joint symptoms but remained fatigued (high BRAFT score) while 1 patient (14.3%) had no improvement. At 7 of these patients were exposed to cigarette smoking (6 current smokers, one ex-smoker). In patients who previously failed anti-TNF, five (62.5%) remained symptomatic (tender & swollen joints, PROMs and BRAFT score remained high) despite treatment with Secukinumab. Only three patients (37.5%) responded well to treatment. Two of the eight patients never smoked (both did not respond to Secukinumab) while the other 6 patients (3 responded, 3 had no response) were ex-smokers.

Conclusion: In our study, Secukinumab demonstrated better response to the biologically-naive PsA patients, while smoking did not increase the risk of disease activity among PsA patients receiving Secukinumab.

Disclosure of Interests: None declared


AB0748 EVOLUTION ON HEALTH-RELATED QUALITY OF LIFE IN PSORIATIC ARTHRITIS PATIENTS

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Background: Psoriatic arthritis (PsA) is a chronic, progressive and inflammatory arthritis. It is considered a multifaceted disease, with a high impact on patient’s psychological and physical well-being, with patients reporting lower health-related quality of life (HRQoL). Data of burden of disease is substantial and even though there are some studies that identify risk factors with longstanding PsA, there exists a need for properly designed studies to learn more about the evolution of HRQoL throughout the follow-up in this condition.

Objectives: To analyze the evolution on HRQoL in patients with PsA and to evaluate factors that may influence this evolution.

Methods: Retrospective longitudinal observational study including incident patients diagnosed with PsA from 2007 to 2016, and followed-up until loss of follow-up or December 2017; with at least two registered visits; having received any iCD9/CD10 diagnosis code of PsA; and with symptoms onset after 16 years of age. Patients were collected from the rheumatology outpatient clinic of a tertiary hospital (Hospital Clínico San Carlos, Madrid, Spain). Clinical information was collected from a departmental electronic health record, including demographic, clinical, comorbidities, treatment, and HRQoL related variables (measured with the Rosser
Results: We included 187 patients, with a median follow-up of 3.6 years (interquartile range: 0.8 to 6.3). 48% were women, with a median age at the onset of symptoms and diagnosis of 45 and 49 years, respectively. 86% of patients had a personal history of Psoriasis. Regarding clinical manifestations during the follow-up, 83%, 30%, 26%, and 22% of the patients presented with peripheral arthritis, inflammatory low back pain, enthesitis and dactylitis, respectively. In addition, they received treatment with nonsteroidal antiinflammatory medications (NSAIDs), oral glucocorticoids and disease-modifying antirheumatic drugs (DMARDs) 71%, 52% and 82%, respectively. 20% received biological agents. The Rosser median value at the first visit was 0.986, with an slight increase after the first 2 years and a decline after 5 years of follow-up (Figure 1). With respect to the variables independently associated with HRQoL during follow-up, the history of osteoporotic fractures (p = 8.1x10-18) and chronic obstructive pulmonary disease (p = 5.0x10-8) were associated with a poorer quality of life. Conversely, treatment with methotrexate during the evolution of patients with PsA was shown to be effective and safe in PsA patient after a year of treatment in clinical practice regardless patient's gender.

Conclusion: We have identified different factors associated with HRQoL during the evolution of patients with PsA. We observed that the presence of certain comorbidities were independently associated with a worse HRQoL. In addition, regarding different treatments, the use of methotrexate and bone-forming agents were independently associated with a better HRQoL.

Disclosure of Interests: None declared

Background: The latest data show that axial involvement in psoriatic arthritis (PsA) patients (pts) is associated with significantly worse disease status and widespread impairment of patient-reported outcomes (PRO’s) (1). Objectives: To analyze clinical characteristics and PRO’s in PsA pts with and without radiographic sacroiliac joints (rSI) in the Russian Psoriatic Arthritis Registry (RU-PsART). Methods: 385 pts (MF=172/213) with PsA according to CASPAR criteria were included in the RU-PsART. Data was collected from 25 rheumatology clinics from various regions of the Russian Federation. Median age 45 (Min 20-Max 80) years, disease duration 3.4 yrs (4 months-32 yrs). Pts underwent standard clinical examination of PsA activity. All pts were studied for patient global disease activity (PGA) and patients’ pain measured by Visual Analogue Scale (VAS), and Health Assessment Questionnaire (HAQ). Physician’s global assessment of disease activity (PGA) was measured by VAS. The examination included X-ray of sacroiliac joints (pelvic radiographs). rSI was defined as bilateral grade ≥2 or unilateral grade ≥3. Pts were split into two groups (gr): those with rSI (rSI(+)) and those without rSI (rSI(-)). Medians and quartiles [Me (Q25; Q75)], Min; Max), U-test and ORs with 95% CI were performed. All CI >1, p <0.05 were considered to indicate statistical significance. Results: gr. rSI(+) included 214 (55.6%) cases (M/F 172/42), gr. rSI(-) included 171 (44.4%) cases (MF=66/105). Median age in gr. rSI(+) was 45 [Min 20-Max 80] yrs, in gr. rSI(-) it was 46 [Min 21-Max 82] yrs. Significant differences were revealed between gr. rSI(+) and gr. rSI(-). In Leeds Enthesitis Index (LEI): in gr. rSI(+) LEI was 0 [0-2], in gr. rSI(-) it was 0 [0-1] (p<0.002). In frequency of dactylitis: in gr. rSI(+) 71 pts had dactylitis, 143 did not have; in gr. rSI(-) 32 pts had dactylitis, 139 did not have. OR 2.2 [1.3-3.5]. In PGA: in gr. rSI(+) it was 56.5 [42.3-70.0], in gr. rSI(-) it was 50.0 [30.0-60.0] (p = 0.00). In patients’ pain: in gr. rSI(+) it was 50.0 [40.0-70.0], in gr. rSI(-) it was 50.0 [20.5-58.8] (p=0.000). In PG: in gr. rSI(+) it was 54.0 [40.0-69.5], in gr. rSI(-) it was 40.0 [25.5-50.0] (p=0.000). In HAQ scores: in gr. rSI(+) it was 1.0 [0.6-1.5], in gr. rSI(-) it was 0 [0-2.2] (p<0.002). Conclusion: Axial involvement is identified in more than half (55.6%) of the PsA pts. The presence of axial involvement in PsA pts is associated with significantly worse disease status as measured by frequency of enthesitis and dactylitis, worse PRO’s and with the reduction of patient’s functional capacity. Consequently, the diagnostics of axial involvement is critical in clinical practice.

REFERENCES


AB0752

DRUG RETENTION AND REMISSION RATES IN 14,261 BIOLOGIC-NAÏVE PATIENTS WITH PSORIATIC ARTHRITIS STARTING TNF INHIBITOR TREATMENT IN ROUTINE CARE – RESULTS FROM 12 REGISTRIES IN THE EUROSPA RESEARCH COLLABORATION

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1EuroSpA Research Collaboration, On behalf of the DANBIO (Denmark), ARTIS (Sweden), SCCM (Switzerland), NOR-DMARD (Norway), ATTRA (Czech Republic), Teuma.pt (Portugal), BIOSADASER (Spain), ROB-FIN (Finland), biorx.si (Slovenia), ICEBIO (Iceland), TURKBIO (Turkey), RRBR (Czech Republic), Reuma.pt (Portugal), BIOBADASER (Spain), ROB-FIN ARTIS (Sweden), SCQM (Switzerland), NOR-DMARD (Norway), ATTRA (Czech Republic), Teuma.pt (Portugal).

Objectives: To investigate Tumour Necrosis Factor Inhibitor (TNFi) retention rates at 12 months (primary objective), 6 and 24 months, and remission rates at the same time-points in biologic-naïve patients with PsA from the EuroSpA Collaboration.

Methods: Prospectively collected data on PsA patients from 12 European registries were uploaded through the secure Virtual Private Network pipelines to the EuroSpA server, and pooled. Baseline characteristics were investigated with non-parametric descriptive statistics. TNFi retention rates (Kaplan-Meier statistics), and 28-joint Disease Activity Score (DAS28) and C21 DAPSA28 were calculated, including LUNDEX adjustment. For patients initiating 1st TNFi after January 1st 2009, the following sub-cohorts were also studied: patients known to be fulfilling ClASsification for Psoriatic Arthritis (CASPAR) criteria and patients with one or more swollen joints (swollen joint count (SJC)>1) at baseline.

Results: Overall, 14,261 patients with PsA initiated a 1st TNFi. Baseline characteristics of the pooled population are shown in the Table. The median 12-month retention rate (95%CI) was 77% (76-78%), ranging from 68-90% across registries (Figure). Overall, DAS28/DAPSA28 remission rates at 6 months were 56%/27% (LUNDEX-adjusted: 45%/22%). In patients initiating a 1st TNFi after 2009 with registered fulfillment of CASPAR criteria (n=1,980) or registered ≥1 swollen joint at baseline (n=5,803), the retention rates and remission rates were similar to those found overall (Table).

Conclusion: Approximately half of >14,000 patients with PsA who initiated 1st TNFi treatment in routine care were in DAS28-remission after 6 months, and three out of four were still on the drug after 1 year.

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AB0753 COMPARING COMPOSITE MEASURES OF DISEASE ACTIVITY IN PSORIATIC ARTHRITIS: RESULTS FROM A RANDOMIZED PHASE 2 TRIAL WITH GUSELKUMAB

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Background: Psoriatic Arthritis Disease Activity Score (PsAS), GRAppa Composite score (GRACE) Index, modified Composite Psoriatic Disease Activity Score (mCPDAI), and Disease Activity Index for Psoriatic Arthritis (DAPSA) are composite indices recently developed to assess disease activity in psoriatic arthritis (PsA). A Gusekumab (GUS) is a monoclonal antibody targeting interleukin-23 that has demonstrated efficacy in a phase 2 PsA trial.3

Objectives: To compare the effect of GUS on disease activity in psoriatic arthritis (PsA) as measured by these composite indices.

Methods: In this Phase-2 trial, patients with active PsA (≥3 tender, ≥3 swollen joints, C-reactive protein ≥3 mg/L, ≥3% body surface area) were randomized 2:1 to subcutaneous GUS 100mg (n=100) or placebo (PBO, n=49) at Wk0, Wk4, and every 8 wks through Wk44. At Wk16, patients with ≤5% improvement in swollen plus tender joints could early-escape treatment. PASDAS and GRACE indices were more sensitive than mCPDAI and DAPSA in detecting changes upon treatment and distinguishing guselkumab treatment effects relative to placebo. Residual disease activities among guselkumab-treated patients who achieved low disease activity at Week24 based on each PsA composite index are summarized in the Table.

Conclusion: Regardless of the PsA-specific composite index employed, GUS significantly improved disease activity and achieved clinically meaningful therapeutic targets such as low/minimal disease activity or remission. PASDAS and GRACE indices were more sensitive than mCPDAI and DAPSA in detecting changes in disease activity by guselkumab treatment.

REFERENCE


AB0754 CLINICALLY MEANINGFUL IMPROVEMENT IN SKIN AND NAIL PSORIASIS IN BIO-NATIVE ACTIVIE PSORIATIC ARTHRITIS PATIENTS TREATED WITH INTRAVENOUS GOLUMUB: RESULTS THROUGH WEEK 52 FROM A PHASE-3 STUDY

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Background: GO-VIBRANT is a Phase 3 trial of intravenous (IV) golumub (GLM) in adult patients (pts) with active psoriatic arthritis (PsA), Clinically meaningful improvements in skin and nail psoriasis (PsO) and in Dermatology Life Quality Index (DLQI) that were significantly greater than placebo (PBO) at weeks (wks) 14 & 24 were previously reported.1

Objectives: To evaluate improvement in skin and nail PsO and DLQI with IV GLM through wk52.

Methods: Adult bio-native PsA pts with active disease (≥3 swollen & tender joints, CRP ≥0.6mg/dL, active plaque psoriasis or documented history), despite treatment w/csDMARDs &/or NSAIDs, were randomized to IV GLM 2mg/kg at wks 0/4 & every 8 wks thereafter or PBO at wks 0/0/4/12/20 with crossover to GLM at wk24. Pts with ≥3% body surface area (BSA) and Severity Index (PSAI, 0-72) of 75/50/100% improvement scale,
modified Nail Psoriasis Severity Index (mNAPSI, 0-130) in pts with mNAPSI >0 at BL, and DLQI (0-30) scale.

Results: 394 pts (PBO:n=198; GLM:n=196) had >33% BSA psoriasis at BL; 76.5% had mNAPSI>0 at BL(mean 18.6). Pts on IV GLM achieved a greater PASI 75 response rate (RR) vs PBO at wk24 (64.8% vs 13.1%, p<0.001). At wk52, PASI 75 RR was maintained in pts who continued IV GLM treatment and increased numerically in those who crossed-over from PBO to IV GLM at wk24 (71.9% and 60.6%, respectively). At wk24, pts on IV GLM achieved significantly greater PASI 90/100 RR vs PBO (8.1% vs 0.001). At wk52, both BL MTX, PASI 90/100 responses were maintained in those who continued on IV GLM and increased numerically in PBO to IV GLM pts (Table). The mean decrease (improvement) from BL in the mNAPSI score was also greater with IV GLM vs PBO at wk24, overall and in groups ≥BL MTX. At wk52, mNAPSI RR was maintained with continual IV GLM and increased numerically in PBO to IV GLM pts (Table). At wk24, the mean decrease (improvement) from BL in DLQI was greater with IV GLM vs PBO (−8.1 vs −1.9, p<0.001). At wk52, mean DLQI improvement was maintained in pts continually on IV GLM and increased numerically in PBO to IV GLM pts (−7.8 vs −5.8). Similar patterns were seen in subgroups ≥BL MTX. In pts with DLQI improvement >1 at baseline, rate of simultaneous achievement of both PASI 50 response & improvement in DLQI was greater at wk24 with IV GLM (59.2%) vs PBO (8.1%, p<0.001). At wk52, both were achieved by 56.6% on IV GLM vs 41.4% of PBO to IV GLM pts. Similar patterns were seen for simultaneous achievement of both improvement in DLIQI ≥5 APASI 75/90/100 at wk 24 and 52.

Conclusion: Clinically meaningful improvements in skin and nail psoriasis and psoriasis quality of life after IV GLM treatment of PsA pts were maintained from 24 to 52 weeks of treatment.

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AB0755 REGIONAL AND TEMPORAL VARIATION IN THE BASELINE PROFILE OF PSORIATIC ARTHRITIS PATIENTS INITIATING ADALIMUMAB FOLLOWING FAILURE OF NON-BIOLOGIC TREATMENT IN CANADIAN ROUTINE CARE

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Background: Treatment selection in routine clinical care is driven by treatment guidelines, physician judgment, patient preferences, and regional reimbursement policies, which may vary over time and among geographic regions.

Objectives: The objective of this analysis is to investigate the regional and temporal variability of the profile of anti-TNF naïve psoriatic arthritis (PsA) patients at initiation of adalimumab (ADA) treatment following failure of initial non-biologic treatment.

Methods: COMPLETE-Psa is an ongoing Canadian observational study of anti-TNF naïve adults with active PsA who require change in their current treatment as per the judgement of their treating physician. Patients are followed for up to 2 years. Regional variation was assessed for the following regions: British Columbia/Manitoba (BC/MB), Newfoundland/Nova Scotia (NL/NS), Ontario (ON), and Quebec (QC). Temporal variation was assessed for the following periods: 2012-2014 and 2015-2017. Multivariate linear regression was used to evaluate the independent impact of region and time period on disease activity (DAS28) and patient functional health.

Results: A total of 278 patients were included, of whom 68 (24.5%) were from BC/MB, 25 (9%) from NL/NS, 104 (37.4%) from ON, and 81 (29.1%) from QC. One hundred fifty-three patients (55%) were enrolled in 2012-2014 and 125 (45%) in 2015-2017. Use of univariate analysis, significant regional variation at ADA initiation was observed for the following disease parameters: BSA<3% (from 42.3% in ON to 76% in NL/NS, p=0.003), morning stiffness (from 60.9 min in QC to 119.7 in BC/MB, p=0.049), WLO productivity loss score (from 8.4% in BC/MB to 12.9% in NL/NS, p=0.028), and DLQI (from 3.5 in NL/NS to 7.9 in ON, p=0.007); and for the initiation of ADA monotherapy vs. ADA combination therapy (range from 9.9% in QC to 27.9% in ON; p=0.022). No differences were observed in demographics (other than race: Caucasian range from 85% to 100%; NL/NS vs BC/MB, 90.0% vs 85.0%, p=0.070), TJC (9.5 vs. 8.1; p=0.074), and DAPSA (30.8 vs. 27.8; p=0.083) at ADA initiation was observed for the most recent time period. Using multivariable analysis to adjust for age, gender, BSA levels, and corticosteroid use, there was no regional or temporal variation in DAS28 and HAQ.

Conclusion: The results of this analysis demonstrate that there is significant regional and temporal variation in the profile of PsA patients initiated on ADA treatment in Canadian routine care. The impact of this profile variation on treatment outcomes requires further investigation.

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AB0756 COMPARATIVE CHANGE IN QUALITY OF LIFE MEASURES IN PRECLINICAL AND ESTABLISHED PSORIATIC ARTHRITIS PATIENTS UNDER SECUKINUMAB TREATMENT. DATA DERIVED FROM THE PROSPECTIVE OPEN LABEL PSARTROS STUDY

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Background: Psoriasis (PsO) and psoriatic arthritis (PsA) differentially impact patients’ quality of life (QoL) due to pain, mental changes in the context of chronic inflammation and impaired physical function. Effective anti-inflammatory therapy has shown to be effective to improve QoL in PsO and PsA patients. However, the impact of anti-inflammatory therapy on QoL may be different in the earliest stages of PsA as compared to established disease.

Objectives: To perform a detailed comparative investigation of the effect of interleukin (IL)-17 inhibition with 300 mg secukinumab (SEC) on QoL in patients with very early PsA/pre-PsA and established PsA.

Methods: Patients from the IVEPsA study (1) on very early PsA/pre-PsA (N=20) and the PSARTROS (2) study on established PsA (N=20) were longitudinally assessed for SF-36, DLQI, PsAID and HAQ-DI at baseline and after 4, 12 and 24 weeks. All patients received SEC treatment: 19/20 pre-PsA patients and 17/20 established PsA patients completed the study. Changes from baseline values were evaluated using linear mixed effects models adjusted for baseline values of each scale, gender, age and disease duration, and plotted as model coefficients and respective 95% confidence intervals that represent adjusted mean absolute improvement from baseline. Scale signs were inverted as necessary to ease interpretability.

Results: Significant and rapid improvements were observed in both pre-PsA and established PsA treated with SEC with regard to pain (SF-36 bodily pain, BP), general health perception (GH), dermatology quality of life index (DLQI) and PsA impact of disease (PsAID), as well as in the SF-36 component scores (mental component score of SF-36, MCS and physical component score of SF-36, PCS). Physical function-oriented instruments like SF-36 physical functioning (PF), role limitation due to bodily pain, BP), general health perception (GH), dermatology quality of life index (DLQI) and PsA impact of disease (PsAID), as well as in the SF-36 component scores (mental component score of SF-36, MCS and physical component score of SF-36, PCS). Physical function-oriented instruments like SF-36 physical functioning (PF), role limitation due to

Conclusion: Pain, mental health, general health perception and impact of disease rapidly improve in both very early PsA/pre-PsA and established PsA patients treated with SEC. These data support the concept that very early treatment of PsA leads to significant improvement in QoL with the additional benefit of prevention of bone damage as previously shown (1, 2).

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AB0757 ANALYSIS OF THE PROGNOSTIC VALUE OF THE 12-ITEM PSORIATIC ARTHRITIS IMPACT OF DISEASE (PSAID-12) QUESTIONNAIRE FOR EVALUATION OF PSORIATIC ARTHRITIS ACTIVITY (PSA) BY DISEASE ACTIVITY INDEX FOR PSORIATIC ARTHRITIS (DAPSA) IN ROUTINE CARE: DATA OF THE RUSSIAN PSORIATIC ARTHRITIS REGISTRY (RU-PSART)

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Background: The PsAID-12 is an instrument for assessment the impact of PsA on patients’ lives by examine both physical and psychological components of health. DAPSA is a valid and discriminative tool for evaluation of the PsA activity. There is limited data about the PsAID-12 correlations with PsA activity by DAPSA in clinical care [1]. The Russian Psoriatic Arthritis Registry (RU-PSART) collected data from 25 rheumatology clinics in the Russian Federation regions.

Objectives: To investigate the predictive value of the PsAID-12 for evaluation of PsA activity by DAPSA in real-world settings.

Methods: 138 (male/female–79/59) patients (pts), median age 40 (Min/Max-23-71), with PsA, according to CASPAR criteria, were included in

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the RU-PsART after signing consent participation forms. Every 6 months (259 visits total) all pts underwent evaluation of PsA activity: The Tender Joint count (TJC68), Swollen Joint Count (SJC66), Leeds Enthesitis Index (LEI), physician’s global disease activity (PhGA) VAS, CRP (mg/l), ESR (mm/h), by PROs - patient pain global assessment VAS, PsA activity state by DAPSA. All pts were divided into 2 groups based on disease activity state by DAPSA: the first one with results ≤14 that interpreted as Remission and Low Disease Activity (REM and LDA) and second one with results >14 that interpreted as Moderate and High Disease Activity (MoDA and HDA). Pearson correlation coefficient and ROC-curve analysis were performed. All p<0.05 were considered to indicate statistical significance.

Results: The Significant positive correlations between the PsAID-12 and all parameters of PsA activity, PROs were found (table 1). The high prognostic value of the PsAID-12 for PsA activity by DAPSA showed by ROC-curve analysis (AUC=0.89, CI 95% (0.85-0.93)). The threshold for MoDA and HDA (DAPSA >14) by PsAID was 1.

Conclusion: The PsAID-12 has a significant prognostic value for PsA activity by DAPSA. The questionnaire doesn’t include any physician’s or laboratory’s data, so it could be useful as a simple instrument for pts’ self-control and prognosis disease activity in daily clinical practice.

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AB0758 PERSISTENCE AND DRUG SURVIVAL RATES OF THE FIRST-LINE BIOLOGICAL (B) DMARDS IN PATIENTS (PTS) WITH PSORIATIC ARTHRITIS (PSA) FROM THE RUSSIAN PSORIATIC ARTHRITIS REGISTRY (RU-PsART)

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Background: Persistence with bDMARDs has only been studied recently in the last few years. But this information is very relevant for choice of bDMARDs treatment in real-life practice. RU-PsART collected data from 25 rheumatology clinics in the Russian Federation.

Objectives: to investigate drug survival and persistence rates, reasons for discontinuation of first-line bDMARDs in PsA pts in clinical practice.

Methods: 170 (MF=87/83) PsA pts according to CASPAR criteria, median (Me) age 43 (Mn 19 – Max 74) years (yrs.) who were treated with first-line bDMARDs were included in the present analysis. All information concerning the data for starting/withdrawing bDMARDs and reasons for discontinuation were taken at the time of being included to the RU-PsART registry. Pts took the following bDMARDs: Adalimumab (ADA) (57pts), Infliximab (INF) (40pts), Ustekinumab (UST) (96pts), Etanercept (ETN) (23pts), Golimumab (GOL) (14pts). Drug survival rate was evaluated with Kaplan-Meier cumulative analysis, Me [Min-Max]%.

Results: 71 out of 170 pts (41.8%) were treated with mono-bDMARDs and 99 out of 170 pts (58.2%) were treated with a combination with different sDMARDs. Among them ADA/INF/UST/ETN/GOL were used in combination with MTX in 66.7%/72.5%/33.3%/65.2%/35.7% of pts accordingly. During long-term observations GOL had better persistence among ITNF agents. UST has shown significantly higher cumulative survival and persistence rates compared to ADA (p<0.05, Log Rank tests). No significant differences were found between UST and other ITNF biologics (Fig.1).

Conclusion: In our real practice PsA pts cohort bDMARDs with different mechanisms of action were well tolerated and effective. During long-term observational periods UST has shown better cumulative survival rates compared to ADA.

Disclosure of Interests: Tatiana Kropotkina Speakers bureau: Novartis, Celgene Corporation, AbbVie Inc, Biocad, Janssen, Pfizer, UCB, Lilly, Elena Loginova Speakers bureau: Novartis, Celgene Corporation, Biocad, Janssen, AbbVie Inc, Anastasia Koltakova: None declared, ELENA GUBAR: None declared, Yulia Korsakova Speakers bureau: Celgene Corporation, Janssen, Maria Sedunova: None declared, Igor Pristavsky: None declared, Irina Umnova: None declared, Irina Bondareva: None declared, Srezana Kudishina: None declared, Evgeny Nasonov Speakers bureau: Pfizer, Inc., MSD, Novartis, AbbVie Inc., Celgene Corporation, Biocad, Janssen, UCB, Inc.

Background: Patients with psoriatic arthritis (PsA) have an increased cardiovascular (CV) risk. We should have strategies for primary cardiovascular prevention in PsA. But there is no evidence of CV risk management and arterial stiffness about biologics in patients with PsA.

Objectives: To examine the effect of biologics plus conventional synthetic (cs) DMARDs on arterial stiffness in cs DMARDs resistant PsA patients in a cohort study design.

Methods: 38 PsA patients with moderate to severe active disease despite cs DMARDs treatment (disease activity score: DAPSA ≥10 score=14) were received Biologics plus cs DMARDs. All patients have no previous history of CV. Arterial stiffness was assessed with cardio-ankle vascular index (CAVI, modified pulse wave velocity (PWV)) and augmentation index corrected for a heart rate of 75 beats per minute (AIx@75) at baseline and 24 weeks of follow-up. Clinical data were collected at regular visits.

Results: 35 PsA patients (18 patients adalimumab, 13 patients infliximab, and 4 patients ustekinumab, respectively) completed this study. Treatment with biologics (10.8 ± 1.86 and 9.46: 1.14%; p = 0.006), attenuated the CAVI significantly from baseline to 24 weeks follow up. Treatment with biologics (36.4 ± 3.8%, p = 0.008) and the AIx@75 significantly from baseline to 24 weeks follow up. DAPSA score improved significantly from baseline to 24 weeks (17.45±5.3, 5.44±3.43; p=0.01). There are no significant differences among biologics about CAVI and Aix@75. Surprisingly, biologics improves arterial stiffness independently of its effects on disease activity, since even in high disease activity (4 cases; DAPSA score>28) is halted.

Conclusion: These findings suggest that combination therapy, biologics with cs DMARDs not only reduced PsA disease activity but also limited vascular damage in patients with cs DMARDs resistant active PsA.

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Disclosure of Interests: Jean-Guillaume Letarruouilly: None declared, Jerome Sellam: None declared, Pascal Richette Consultant for: Grunenthal, Horizon, Speakers bureau: AstraZeneca, Grunenthal, Philippe Dieude: None declared, Pascal Claudepierre Consultant for: Novartis as steering committee of this survey, Corinne Miceli Richard Grandi research support from: MSD, Pfizer, AbbVie, Biogen, UCB, Novartis, Consultant for: Abbvie, Novartis, BMS, Eric Houvenagel Speakers bureau: Lilly, Novartis, Janssen, Chi Duc Nguyen: None declared, Marie-Hélène Guérinau: None declared, Nicolas Segaud: None declared, Laurent Marguerie: None declared, Xavier Deprez Speakers bureau: Novartis Janssen, Jean-Hugues Salmon Speakers bureau: Janssen Novartis, Guy Baudens Grant/research support from: Financial Grant from NordicPharma, Consultant for: Roche SAS, Maeva Kyheng: None declared, Julien Paccou Speakers bureau: Novartis Janssen, Elisabeth Gervais Grant/research support from: Roche, Pfizer, Consultant for: Bristol-Myers Squibb, UCB, René-Marc Filpo Consultant for: Honoraria from Novartis as steering committee of this survey.


AB0761

SECUKINUMAB FOR THE TREATMENT OF PSORIATIC ARTHRITIS IN REAL LIFE: AN ITALIAN EXPERIENCE

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Background: Secukinumab is a novel treatment for psoriatic arthritis (PsA) but data from real life are still missing.

Objectives: The aim of this study is to evaluate a wide cohort of PsA patients on secukinumab followed in 7 Italian rheumatologic centers.

Methods: Two-hundred and seventy-nine patients affected by PsA and on secukinumab were enrolled. Data on disease characteristics, previous and ongoing treatments, comorbidities and duration of follow-up were collected. In particular DAPSA and ASDAS were used to assess articular and axial disease activity.

Results: Mean age of our cohort was 53±11 years and BMI 26.4±5.1 kg/m² with 67% of patients being female (63.8%). Mean disease duration was 9.7±7.5 years and mean follow-up was 10.9±6.8 years. For 100 patients (35.8%) secukinumab was their first line biologic treatment and 41 patients (31.7%) received it as a downward trend for M12 (15). During the PsA evolution, in addition to arthritis, patients also presented enthesitis (60.9%), nail involvement (39%) and dactylitis (31.7%).

Conclusion: This is one of the first real life studies on secukinumab and shows a very good efficacy and safety of this treatment in PsA patients, also for the articular manifestations, as shown by a significant decrease of DAPSA over a 12-months follow up.

AB0762

TREATMENT WITH TOFACITINIB IN REFRACTORY PSORIATIC ARTHRITIS. MULTICENTER STUDY OF CLINICAL PRACTICE

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Background: Tofacitinib (TOFA) is the first inhibitor of JAK kinases with approval for the treatment of psoriatic arthritis (PsA) in Europe (July 2018)1. TOFA has shown efficacy in refractory patients to anti-TNF. Objectives: A) to assess efficacy and safety of TOFA in the first cases in Spain in clinical practice. B) to compare the profile of clinical practice patients with clinical trial.

Methods: Study of 41 patients of clinical practice with PsA treated with TOFA in Spain. The diagnosis of PsA was made using CASPAR criteria. Patients who received at least one dose of TOFA were included. Results are expressed as percentage, mean±SD or median [IQR].

Results: 41 patients (23/18±), mean age of 50±10.7 years (table 1). Pattern joint involvement was as follows: peripheral (n=25), axial (1) and mixed (15). During the PsA evolution, in addition to arthritis, patients also presented enthesitis (60.9%), nail involvement (39%) and dactylitis (31.7%).

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Background: In the placebo (PBO)-controlled Phase III ASTRAEA study (ClinicalTrials.gov, NCT01860798) in psoriatic arthritis (PsA), abatacept (ABA) 125 mg SC weekly significantly increased the ACR20 response rate at Week 24 versus PBO (39.4% vs 22.3%, respectively; p<0.001; primary endpoint).1 Numerical benefits in physical function, enthesitis and dactylitis and a modest impact on psoriasis lesions were also seen at Week 24. Efficacy was maintained or improved up to Week 52.2

Objectives: To assess ABA safety up to 2 years in patients (pts) enrolled in ASTRAEA.

Methods: Pts with active PsA were randomised 1:1 to ABA or PBO for 24 weeks followed by 28 weeks’ open-label (OL) ABA (total time on study: 52 weeks); pts without ≥25% improvement in joint counts at Week 16 (early escape) were switched to OL ABA (total time on study: 44 weeks).1 Pts could subsequently receive OL ABA in a 52-week long-term extension (LTE; Year 2) for the collection of safety data. The proportions of pts in the cumulative ABA population (all pts who received ≥1 dose of ABA at any time in the study) with AEs (all AEs, serious AEs [SAEs], deaths, AEs leading to discontinuation), laboratory marked abnormalities and anti-ABA antibodies over the cumulative ABA period (date of first treatment dose to end of LTE) were recorded in 1-year and 6-month intervals.

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Results: Overall, 398 pts were included in the analysis of the cumulative ABA period (213 received ABA from study Day 1; 185 completed initial randomisation to PBO and received ABA thereafter). Of these, 322 pts entered the LTE (initial randomisation: ABA, n=162; PBO, n=160) and continued to receive OL ABA beyond the 28-week OL period. Of 162 and 160 pts initially randomised to ABA and PBO, respectively, 19 (11.7%) and 21 (13.1%) pts discontinued ABA in the LTE. Median (range) number of ABA injections in the cumulative ABA period to end of LTE was 80 (1–130). Safety during the cumulative ABA period over 2 years is shown (Table 1); 6-month interval safety data will be available at time of presentation. In the LTE, there were 3 SAEs of infection (osteomylellitis, intervertebral discsitis and cellulitis) and 3 pts discontinued due to infection (hepatitis A, Epstein-Barr virus, intervertebral discitis). No malignancies or deaths were reported, and no autoimmune events were reported as serious or led to ABA discontinuation during the LTE. AEs, SAEs and AEs of special interest occurred with a similar frequency regardless of concomitant MTX use or prior TNFi inhibitor (TNFi) use. The proportion of pts with anti-ABA antibodies during the cumulative ABA period was higher during the post-treatment period (>22 days after last dose; 37.1% [91/245]) than in the on-treatment period (first treatment dose date to ≤21 days after last dose; 7.1% [28/392]). No apparent relationship between anti-ABA antibodies and efficacy in the on-treatment period or AEs suggestive of systemic immune reactions was seen.

Conclusion: Abatacept was well tolerated up to 2 years with no new safety signals during the LTE in this Phase III study in PsA. There was no impact of concomitant MTX use or prior TNFi exposure on the safety profile of abatacept. The occurrence of anti-abatacept antibodies had no impact on abatacept efficacy or safety.

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AB0765 THE IMPACT OF PSORIASIS SEVERITY ON OUTCOMES AMONG PSORIATIC ARTHRITIS PATIENTS RECEIVING ADALUMABUM

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory disease mediated by the immune system, which affects the musculoskeletal system and the skin. It is a disease with increased expression of TNF-alpha and IL23/IL17 cytokines, which are therapeutic targets whose neutralization has a great impact on the control of the disease.

Ixekizumab is a monoclonal antibody inhibitor of IL-17 indicated for the treatment of moderate-severe psoriasis and PsA. Ixekizumab is administered subcutaneously every 4 weeks, and according to the latest studies, it is a well-tolerated drug and an effective treatment option with significant improvement in the quality of life of patients with cutaneous psoriasis and PsA.

Objectives: Describe the clinical characteristics, tolerance, safety and survival of a cohort of patients diagnosed with psoriasis or PsA, who have started treatment with Ixekizumab.

Methods: An observational, cross-sectional and retrospective study was conducted on a cohort of 29 patients who started treatment with Ixekizumab in our hospital in the last year (2018). The data were obtained through the review of patients’ medical records and through telephone contact to carry out quality of life questionnaires (DLQI).

Results: Twenty-nine patients were included, of which 22 were males (79.5%). The mean age of the patients was 47 years. Of the cases included, 22 of the patients presented cutaneous Psoriasis (75.8%), 6 of the patients with PsA (20.7%) and 1 patient presented dermatomyositis antIMDA 5 (3.5%). Of the 29 patients included, 24 (82.2%) did not present adverse effects. Of the 5 patients who presented adverse effects, in 100% of the cases they were mild. All patients had received prior therapy with disease modifying drugs (DMARDs), and 31% were naive to biological therapy. A total of 4 patients required concomitant therapy with corticosteroid treatment, 3 of them with PAs and 1 with dermatomyositis anti MDA 5. The average of the DLQI of the patients analyzed was 4 and an average PASI of 1 after the start of the treatment, obtaining an Overall improvement of the skin.

A statistically significant Pearson correlation of 0.895 was found between DLQI and PASI (dependent variable), with a strong degree of association. In which patients with a lower score in the DLQI had a lower PASI.

Regarding the pain produced by the autoinjection, measured to the EVA scale, it was 2 (mild pain), and none would abandon the treatment for this reason. Of all the patients, 9.1% abandoned the treatment due to inefficacy.

Conclusion: The treatment with Ixekizumab presents some promising results in the treatment of cutaneous psoriasis and PsA. Treatment with Ixekizumab presents a significant improvement in the quality of life of patients.

Ixekizumab is a well-tolerated drug with good efficacy in the short-term. It has also been shown to be a safe drug among the patients included in the study.

However, long-term studies with a larger number of patients are required to evaluate the efficacy and safety of Ixekizumab.

Disclosure of Interests: None declared

Methods: Pts with baseline PASI and BSA available from ADEPT, a phase 3, randomized, double-blind, PBO-controlled trial of ADA 40 mg every other week, were included in this post hoc analysis. Pts were sub-grouped based on baseline PASO severity (severe PsO: PASI >12 OR BSA ≥10%; mild-to-moderate PsO: PASI <12 AND BSA <10%), relative to overall study population. Clinical outcomes at wk 24 were assessed by attainment of minimal disease activity (MDA), remission and low disease activity (LDA) by disease activity index for psoriatic arthritis (DAPSA), and PASI50/75/90; function and structural progression were assessed by the % of pts experiencing HAQ-DI normal values (0.25) and improvement from baseline ≥0.22 (MCID), and the % of pts having change from baseline in mTSS ≥0.5 in the modified total Sharp score (mTSS) respectively. A logistic model with treatment group baseline PASI/BSA and PASI/BSA by treatment interaction was fit for each outcome variable. P-values for interaction term and baseline BSA/PASI were calculated. Non-responder imputation was used for missing clinical and functional endpoints. 25th percentiles were imputed for missing radiographic data. Treatment-emergent adverse events (TEAEs) were monitored throughout.

Results: Of the 163 pts enrolled in the study with baseline PASI and BSA, only 23% (n=37; ADA: 17; PBO: 20) were classified as having severe PsO and had similar characteristics to those with mild-to-moderate PsO, except for numerically higher physician’s global assessment, dactylitis, and enthesis scores. Following 24 wks of treatment, 41% of ADA-treated pts achieved MDA and 45% achieved DAPSA LDA or better, a finding consistent irrespective of baseline PsO severity (Table). 72% of ADA-treated pts with baseline PsO did not exhibit any structural progression by mTSS (≥0) through 24 wks as compared to 55% receiving PBO. Logistic regression analyses confirmed limited role that PsO severity played across examined outcomes. DAPSA remission was more likely at wk 24 among pts with higher baseline PASI scores, and this effect was less apparent with ADA treatment. TEAEs appeared comparable between ADA and PBO groups; fewer infectious AEs occurred in the ADA severe PsO group treated with the lower dose of ADA. 25OHD deficiency was more likely among ADA pts at wk 24 versus PBO treated pts.

Conclusion: Prevalence of severe PsO in this population of PsA pts was consistent with previous observations. Treatment with ADA was associated with better PsA outcomes compared to PBO irrespective of the degree of PsO severity at baseline.

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Conclusion: More than half of patients with PsA have a low BMD (53.8%) and 33.3% deficient levels of 25OHD. Our study confirms results found in general population: classic risk factors, such as smoking, are related to BMD progression. It is important to evaluate BMD in these patients and intervene early.

Disclosure of Interests: None declared


AB0765

MULTI-SYMPHOM IMPACT ON THE EQ-SD INDEX IN BIO-NATIVE ACTIVE PSORIATIC ARTHRITIS PATIENTS: AN ANALYSIS THROUGH WEEK 24 OF THE GO-VIBRANT STUDY

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory disease characterized by peripheral arthritis, axial inflammation, dactylitis, enthesis and skin and nail psoriasis. The impact of skin and joint components of the disease on patient health-related quality of life has been described in...
previous research (1,2) but the impact of other major clinical manifestations has not been similarly characterized.

Objectives: To quantify the impact of the major clinical manifestations of PsA on patient reported health related quality of life, as estimated by disease state preference (utility) derived from the EQ-5D index in a randomized clinical trial.

Methods: This analysis used data from a multicenter, randomized, double-blind, placebo-controlled trial of intravenous (IV) Golimumab in biologic naïve patients with active psoriatic arthritis (GO-VIBRANT study). Patient baseline characteristics of the GO-VIBRANT study population have been previously described (3). Core outcome measures recommended by OMERACT (Outcome Measures in Rheumatology Clinical Trials) and guideline on utility mapping by ISPOR (International Society for Pharmacoeconomics and Outcomes Research) were used to guide initial attribute selection. Utility was derived from patient responses to the EQ-5D index, which assesses mobility, self-care, usual activities, pain/discomfort, and anxiety/depression, and was completed at weeks 0, 8, 14, and 24 in the trial (placebo-controlled period). EQ-5D index is used as a measure of overall health and is an outcome commonly used in health economic analyses. Multivariate analysis was performed using a Mixed-Effect Repeated Measures model based on observed data until week 24 in pooled patient population.

Results: Based on univariate analyses and evaluation of collinearity between variables, the following attributes were included in the multivariate models: age, gender, region, PsA disease duration, PASI score, enthesis, dactylitis, tender joint count (TJC), swollen joint count (SJC), C-reactive protein (CRP mg/L) and Health Assessment Questionnaire-Disability Index (HAQ-DI). In the final model, PASI score (β=0.00126, p=0.0006), enthesis (β=0.01237, p=0.03), TJC (β=0.00112, p<0.0001), CRP (β=0.0007, p<0.0001) and HAQ-DI (β=-0.1664, p<0.0001) were all statistically significantly associated with the EQ-5D index. A sensitivity analysis among a subgroup of patients who had spondylitis with peripheral joint arthritis as their primary arthritic presentation of PsA showed that spinal pain (β=-0.0101, p<0.0001), as measured by question #2 of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), was also statistically significantly associated with the EQ-5D index in the multivariate model.

Conclusion: Multiple PsA clinical manifestations including psoriasis, enthesitis, TJC, spinal pain, CRP, and physical function were statistically significantly associated with utility among PsA patients as derived from the EQ-5D index. These findings indicate that consideration of multiple clinical manifestations of PsA is warranted when evaluating the impact of PsA on patients.

REFERENCES

Conclusion: In pts with active PsA, faster, clinically meaningful pain improvements were reported in pts receiving tofacitinib 5 mg BID vs pts receiving PBO who switched to tofacitinib 5 mg BID at Month 3. After switch from PBO to active treatment, pain improvement was observed in line with pts receiving active treatment from Day 0. To achieve pain improvement at greater thresholds, longer duration of active treatment was required.

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AB0769 PATIENT IDENTIFIED TREATMENT GOALS IN PSORIATIC ARTHRITIS: DECREASING PAIN AND INCREASING ACTIVITY LEVEL ARE HIGH PRIORITIES

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Background: Treatment goals for physicians are primarily focused on improving musculoskeletal and cutaneous signs and symptoms of psoriatic disease. Studies have reported that perceptions of psoriatic arthritis (PsA) disease control are often divergent between patients and physicians. Moreover, specific patient goals are uncommonly discussed or elicited in routine clinical practice.

Objectives: To examine patient reported treatment goals through direct questioning on what they most want to improve about their disease and how an effective treatment would improve their lives.

Methods: Patients in the Psoriatic Arthritis Research Consortium (PARC) completed standardized assessments between 2017-2018. PARC is a longitudinal observational cohort study conducted at four institutions in the United States: University of Pennsylvania, Cleveland Clinic, New York University, and University of Utah that includes a range of patient and physician disease measures. Answers to two open-ended questions (questions included on figures) were qualitatively categorized into response categories and descriptively reported in this cross-sectional study. While patients were encouraged to provide the one best answer, many listed multiple themes. We also examined differences in responses by gender, self-identified race (Caucasian vs non-Caucasian), and whether a change in disease modifying anti-rheumatic drug was recommended (yes/no) on the date the questionnaire was completed.

Results: Among 82 patients with PsA enrolled, mean age was 48.3 (SD 13.2), 38 (46%) were female, and 57 (70%) of patients were changing therapy. The mean swollen (0-66) and tender (0-68) joint counts were 4.3 (SD 6.0) and 8.5 (12.2) respectively, mean psoriasis body surface area was 3.2% (SD 10.0), and mean physician and patient global assessments were 4.6 (SD 2.0) and 4.7 (2.6) respectively. Patient answers to the two questions are shown in the figures. Decreasing pain was the most commonly cited goal for improvement (56%) with skin improvement the second most commonly reported goal for improvement (12%). Goals for successful therapy were more diverse. Decreasing pain was most common (18%) but general improvement in life (18%), the ability to be more active (15%), participate in recreational activities (9%), function at work (11%) and exercise (5%) were common responses. There were no significant differences in responses according to race or age groups. There was no significant difference in responses according to gender or therapy change. However, all patients reporting fatigue or enjoyment as important outcomes for improvement were women.

Conclusion: In order to inform goals of care for patients with PsA, both physician and patient treatment goals should be defined to achieve optimal treatment success. In this study, while the majority of patients reported pain and activity as the most important outcomes for improvement, patient goals were heterogeneous. This underscores the importance of eliciting patient treatment goals on a regular basis to best individualize management in PsA.

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SYMPTOMS AND IMPACTS IN PSORIATIC ARTHRITIS: FINDINGS FROM QUALITATIVE PATIENT INTERVIEWS

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Background: Psoriatic arthritis (PsA) is a chronic inflammatory disease resulting in significant symptom burden.1 Over time and without adequate treatment, PsA can lead to disability and reduced patient quality of life.2 Fatigue is among the most common symptoms,3 but is complex and difficult to measure. The most burdensome symptoms that impact PsA patients need to be better understood in order to select patient reported outcomes (PRO) instruments and items to measure fatigue.

Objectives: 1) Identify the signs and symptoms of PsA experienced by patients, with a focus on fatigue, and how the disease and its treatment(s) impact patients’ lives. 2) Assess the content validity of select PRO instruments and items to measure fatigue.

Methods: Qualitative interviews were conducted among patients with PsA recruited through the FORWARD database. The most frequently experienced symptoms and impacts of PsA and the degree to which they disturbed patients’ lives were tabulated. Disturbance was evaluated on a scale from 0 (not at all) to 10 (greatly disturbs). Patients reporting fatigue were probed to describe the experience in their own words, and descriptors were recorded. Interviews were conducted and assessed on a rolling basis and recruitment continued until concept saturation was achieved.

Results: Nineteen PsA patients were interviewed for this study. A core set of PsA symptoms were identified by nearly all patients and with moderate to high average disturbance ratings (Figure 1): joint pain, skin symptoms, stiffness, swollen/inflamed joints, and fatigue. The most salient impacts (Figure 2) were sleep disturbance, physical disability, effects on daily activities, and feelings of frustration. Most common descriptors of fatigue included “fatigue,” “tiredness,” “lack of energy,” “mental fatigue,” and “exhaustion.”

Conclusion: Salient symptoms were consistent with those previously reported, along with a broader range of symptoms and impacts, which included fatigue. In addition to physical disability, others such as sleep disturbance, frustration, and effect of daily activities were common high impact themes that emerged.

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IMPROVEMENT IN MORNING STIFFNESS IN SUBJECTS WITH PSORIATIC ARTHRITIS IS ASSOCIATED WITH IMPROVEMENTS IN PAIN, PHYSICAL FUNCTION AND PATIENT GLOBAL RESPONSE TO TREATMENT

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Background: Stiffness is an important component of inflammatory arthritis and plays a role in psoriatic arthritis (PsA) flare. Patients with inflammatory arthritis report difficulty with activities, “slowing down” due to stiffness and reduced quality of life. Stiffness is hard to quantify because it cannot be measured directly.

Objectives: We examined morning stiffness in PsA patients treated with apremilast (APR) for 16 weeks in the ACTIVE study and explored the relationship between improvements in morning stiffness and pain, physical function and Patient’s Global Assessment of Disease Activity (PiGAs).

Methods: Subjects who met CASPARD criteria for PsA, were biologic-naive and had prior exposure to ≤1 conventional disease-modifying anti-rheumatic drug (DMARD) were randomized (1:1) to APR 30 mg twice daily or placebo (PBO) for 24 weeks. Subjects initially randomized to PBO were re-randomized to APR or PBO at week 12. The PiGAs for patients’ quality of life (QoL) was measured using a 0–100 scale with lower scores indicating better quality of life. Clinical data were collected at baseline and every 2 weeks.

Results: Nineteen PsA patients were interviewed for this study. A core set of PsA symptoms were identified by nearly all patients and with moderate to high average disturbance ratings (Figure 1): joint pain, skin symptoms, stiffness, swollen/inflamed joints, and fatigue. The most salient impacts (Figure 2) were sleep disturbance, physical disability, effects on daily activities, and feelings of frustration. Most common descriptors of fatigue included “fatigue,” “tiredness,” “lack of energy,” “mental fatigue,” and “exhaustion.”

Conclusion: Salient symptoms were consistent with those previously reported, along with a broader range of symptoms and impacts, which included fatigue. In addition to physical disability, others such as sleep disturbance, frustration, and effect of daily activities were common high impact themes that emerged.

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were switched to APR at Week 16 (early escape) or Week 24. Duration of morning stiffness and severity, assessed by subjects’ reported categories of stiffness (none, mild, moderate, moderately severe, severe), was reported. In the post hoc analysis, changes in morning stiffness severity and effect on pain, physical function and PIGA from baseline to Week 16 were compared between treatment arms. An analysis of covariance model adjusting the baseline value was used in the analysis, where missing values were imputed using the last-observation-carried-forward approach.

**Results:** A total of 219 subjects were randomized (APR: n=110; PBO: n=109), and 192 remained in the study through Week 16. APR and PBO groups were balanced with respect to baseline tender joint count (mean [SD]: 17 [13] vs. 18 [14]), swollen joint count (mean [SD]: 9 [5] vs. 10 [6]) and severity of morning stiffness (moderate to very severe: 87% vs. 80%), as well as previous use of DMARD (67% vs. 72%), baseline use of non-steroidal anti-inflammatory drug (69% vs. 68%) and oral corticosteroid use (12% vs. 13%). Mean [SD] duration of morning stiffness at baseline was shorter with APR vs. PBO (48 [49] vs. 72 [127] minutes). Baseline PIGA (mean [SD]: 5.9 [2.1] vs. 6.1 [2.0]).

**Patient’s Pain Numeric Rating Scale (NRS; mean [SD]: 6.1 [1.9] vs. 5.8 [2.2]).** Health Assessment Questionnaire-Disability Index (HAQ-DI; mean [SD]: 1.3 [0.6] vs. 1.2 [0.6]). Short-Form Health Survey version 2 (SF-36v2) Physical Component Summary (mean [SD]: 32.4 [9.2] vs. 33.9 [8.3]), SF-36v2 Physical Functioning subscale (mean [SD]: 33.2 [11.2] vs. 34.2 [10.1]) and SF-36v2 Bodily Pain domain (mean [SD]: 35.4 [7.6] vs. 37.4 [7.8]) scores were similar in the APR and PBO groups, respectively.

As early as Week 2, a significantly greater proportion of APR vs. PBO subjects experienced morning stiffness severity improvements (≥1 category improvement) (43% vs. 21%; P=0.007). Significant improvements in morning stiffness severity were sustained through Week 16 in APR vs. PBO subjects (46% vs. 26%; P=0.0015). Subjects with improvements in morning stiffness severity in the APR and PBO groups showed consistent improvements in pain, physical function and PIGA at Week 16 (Table). In patients with unchanged stiffness severity, greater improvements were observed across outcome measures in the APR vs. PBO group, although the change from baseline was less than the improved stiffness group. Worsened morning stiffness was associated with lack of improvement in other patient-reported outcome measures.

**Conclusion:** Physical-naive PsA subjects treated with APR for 16 weeks, improvement in morning stiffness severity was evident as early as Week 2 and associated with improvements in pain, physical function and PIGA response.

**Disclosure of Interests:** Ana-Maria Orbai*.

**Efficacy of Gusekumab in Psoriasis Patients with Self-Reported Psoriatic Arthritis with Involvement of the Scalp, Nails, Hands, and Feet: A Pooled Analysis from 2 Pivotal Phase 3 Psoriasis Studies**

Joseph F. Merola1, Soumya G. Chakravarty2,3, Yin You1, Shelly Kafka2, Chetan Karyekar4,5, Ana-Maria Orbai*. 1Brigham and Women’s Hospital and Harvard Medical School, Boston, United States of America; 2Janssen Scientific Affairs, LLC, Horsham, United States of America; 3Drexel Univ College of Med, Philadelphia, United States of America; 4Janssen Research and Development, LLC, Horsham, United States of America; 5Johns Hopkins U School of Medicine, Baltimore, United States of America

**Background:** VOYAGE 1 & 2 were the pivotal Phase 3 GUS trials for plaque psoriasis (PsO).1,2

**Objectives:** Here we compare efficacy of GUS vs PBO & vs adalimumab (ADA) on PsO involving scalp, nail & palmoplantar (palmoplantar pustular PsO excluded per protocol) in a a subgroup of pts with self-reported psoriatic arthritis (PsA), given the association between these distinct PsO phenotypes & PsA.

**Methods:** VOYAGE 1 (n=837) & VOYAGE 2 (n=992) enrolled adult pts who had plaque PsO for ≥6 months, an Investigator Global Assessment (IGA) score ≥3, PASI score ≥12, ≥10% BSA involvement at baseline (BL), & were candidates for phototherapy or systemic treatment for PsO. Pts were randomized to GUS, PBO or ADA at BL, &/or crossover to GUS at wk48. This post-hoc analysis used observed pooled efficacy data for scalp-specific Investigator Global Assessment (ss-IGA), Physician’s Global Assessment (PGA) of Hands &/or Feet (hf-PGA), Fingernail PGA (f-PGA), & Nail Psoriasis Area & Severity Index (NAPSI) in subset of pts self-reporting PsA.

**Results:** In VOYAGE 1 & 2 combined, 335 (18.3%) PsO pts self-reported PsA (PBO 76, GUS 153, ADA 106). Baseline demographics were generally comparable across all 3 treatment groups, with history of methotrexate use: PBO 64.5%, GUS 70.6%, ADA 61.3%. A significantly greater proportion of GUS-treated pts achieved a ss-IGA score of 0/1 (absent/very mild) at wk16 vs PBO, & at wk24 vs ADA (Figure A). Significantly higher proportions of GUS-treated pts achieved a hf-PGA score of 0/1 (clear/almost clear) vs PBO at wk16 with numerically greater differences at wk24 vs ADA (Figure B). At wk16, proportions of pts achieving a f-PGA score of 0/1 (clear/minimal) were 47.6% for GUS vs 17.0% for PBO (p=0.001). The proportions of pts achieving an I- PGA score of 0/1 for GUS vs ADA were comparable at wk16 (47.6% vs 46.4%) & wk24 (67.0% vs 60.9%), but were higher for GUS by wk48 (82.5% vs 57.5%, Table). Mean (SD) improvement from BL in NAPSI score was significantly higher for GUS vs PBO & ADA at wk16 (47.6% vs 46.4%) & wk24 (67.0% vs 60.9%), but were higher for GUS by wk48 (82.5% vs 57.5%, Table). In VOYAGE 1 & 2 combined, 335 (18.3%) PsO pts self-reported PsA showed clinically meaningful improvements vs ADA in ss-IGA & hf-PGA scores at wks16 & 24. Although improvements in 1- PGA & NAPSI were similar in pts treated with GUS vs ADA at earlier timepoints, numerically greater differences were observed with GUS by wk48, likely requiring the additional duration to discriminate between treatments in this slow-growing cutaneous appendage.
PATIENTS WITH PSORIATIC ARTHRITIS DISEASE ACTIVITY, AS MEASURED BY CDAPSA, IN PATIENTS WITH HIGH REPORTED PSA AT WK 48"

Guselkumab | Adalimumab
---|---
PsO Patients randomized at Week 0, n | 329 | 334
PsO Patients with self-reported PSA, n | 64 | 62
Patients with 1-PGA score >2 at baseline | 40 | 40
1-PGA score of clear (0) | 20 (50.0%) | 16 (40.0%) |
1-PGA score of clear (0) or minimal (1) | 33 (82.5%) | 23 (57.5%) |
Percent improvement from baseline in NAPSI Scores in Psoriasis Patients with Self-Reported PSA at WK 48 | | |
Guselkumab | Adalimumab
---|---
PsO Patients randomized at Week 0, n | 825 | 582
PsO Patients with self-reported PSA, n | 153 | 106
NAPSI (N) | 111 | 74
Mean (SD) | 70.64 (40.49) | 61.25 (42.43)
Median | 100.00 | 70.85
Range | (-100.0; 100.0) | (-50.0; 100.0)
IQR | (50.0; 100.00) | (33.30; 100.00)

"Post-hoc analyses based on Voyage 1 only"


AB0774 PSORIATIC ARTHRITIS IMPACT OF DISEASE QUESTIONNAIRE SCORES ARE CORRELATED WITH DISEASE ACTIVITY, AS MEASURED BY CDAPSA, IN PATIENTS WITH PSORIATIC ARTHRITIS

Disclosure of Interests: Ana-Maria Orbai; Klaus Krueger; Frank Behrens; Uta Kitzb; Benoît Guerette; Lillian Mellars; Michele Brunori; Jurgen Wollenhaupt; Johns Hopkins Arthritis Center and Johns Hopkins University School of Medicine, Baltimore, United States of America; Rheumatologische Praxis Munchen, Munchen, Germany; Division of Rheumatology, Goethe University and Fraunhofer IME-TMP, Frankfurt, Germany; Rheumazentrum Ruhrgebiet, Heine and Ruhr-University of Bochum, Bochum, Germany; Celgene Corporation, Summit, United States of America; Schlin Klinik Hamburg Elbek, Klinik für Rheumatologie, Hamburg, Germany.

Background: LAPIS-PsA is an ongoing, national, 52-week, multicenter, prospective, non-interventional study assessing long-term treatment with apremilast (APR) in adult patients with active psoriatic arthritis (PsA) in routine clinical practice in Germany.

Objectives: The current interim analysis assesses the clinical effectiveness of APR, as measured with the Clinical Disease Activity Index for PsA (cDAPSA) and its core components, as well as PsA health-related quality of life (HRQoL), measured with the 9-domain PsA Impact of Disease Questionnaire (PsAID9). In addition, correlations between cDAPSA and PsAID9 were assessed.

Methods: The interim analysis included data obtained at baseline (BL), Visit 1 (V1; 1 month), Visit 2 (V2; 3 months) and Visit 3 (V3; 7 months); all available data for patients treated with APR 30 mg twice daily were included in the analysis. A subgroup analysis was performed among patients categorized by cDAPSA disease activity scores at BL. Clinical characteristics and disease assessments at BL and V1-V3 were compared. Mean PsAID9 scores and proportions of patients meeting the PsAID Patient-Acceptable Symptom State (PASS), defined as a PsAID9 score of 4, were assessed by cDAPSA category at BL. Analyses are based on data as observed at each visit. Pearson's correlations were calculated between cDAPSA and PsAID9 at BL, V1, V2 and V3.

Results: A total of 394 patients were included in the analysis population (mean age: 55.1 years; female: 55.1%; previous biologic use: 25.4%). At BL, patients had a mean PsAID9 score of 5.3 and a mean cDAPSA score of 26.6. Continuous improvements in swollen/tender joint counts and patient-reported pain and disease activity were observed with continued APR treatment (Table). Patients reported incrementally reduced mean cDAPSA scores and consistent improvements in PsAID9 scores from BL to V3. Patients with low disease activity (cDAPSA <13 to ≤27) at BL had a mean (SD) PsAID9 score of 3.4 (1.7) with 71.1% in PsAID9 PASS (Figure). Those with moderate (cDAPSA >13 to ≤27) and high (cDAPSA >27) disease activity had mean (SD) PsAID9 scores of 5.3 (1.9) and 6.1 (1.8), with 26.6% and 11% showing PsAID9 PASS, respectively. At follow-up visits, greater proportions of patients achieving cDAPSA low disease activity or remission also achieved PsAID PASS (Figure). Significant moderate to high correlations were observed between cDAPSA and PsAID9 at BL (Pearson's coefficient r=0.43), V1 (r=0.51; P=0.0001), V2 (r=0.64; P=0.0001) and V3 (r=0.64; P=0.0001).

Conclusion: Results from this observational PsA study of APR demonstrate a significant correlation between disease activity, as assessed by cDAPSA, and PsA-specific life impact/HRQoL, as measured by PsAID9. More patients met the PsAID PASS cutoff while achieving remission or lower disease activity, and improvements in PsA disease activity are associated with the PsAID PASS from a life impact perspective.

AB0774 PREDICTORS OF SWITCHING IN A RETROSPECTIVE ITALIAN COHORT OF PSORIATIC ARTHRITIS PATIENTS RECEIVING BIOTECHNOLOGICAL DRUGS FOR AT LEAST 3 YEARS

Disclosure of Interests: Augusta Ortolan; Pamela Polito, Federico Benetti, Mara Falcetti, Mariagrazia Lorenzini, Roberta Ramonda. Rheumatology Unit, Department of Medicine DIMED, University of Padova, Padova, Italy.

Background: Psoriatic Arthritis (PsA) is a chronic inflammatory disease typically treated, in its moderate-severe form, with biologic disease-modifying antirheumatic drugs (bDMARDs). However, refractory patients are not infrequent, and they are commonly managed by switching from one bDMARD to another. Since the chance of observing a good clinical response decreases according to line of treatment, it would be important
EFFECTIVENESS AND SAFETY OF USTEKINUMAB 90 IN PATIENTS WITH PSORIATIC ARTHRITIS.REAL WORLD EVIDENCE STUDY

1Estefanía Pardo Campo, 2José Andrés Lorenzo Martín, 2Lílian Consuelo Charca Benavente, 3Sara Alonso Castro, 2Mercedes Alpérez López, 2Luis Marcelino Arobelo Rodríguez, 2Francisco Javier Ballina-García, 2Rubén Queiro Silva1, 3Hospital Universitario Central de Asturias, Oviedo, Spain; 3Hospital Universitario Central de Asturias, Oviedo, Spain

AB0775

1 other study drugs, anti-TNF-α biologics only, other


Disclosure of Interests: None declared


AB0776

RATES OF MYOCARDIAL INFARCTION, STROKE AND REVASCULARIZATION AMONG PATIENTS WITH PSORIATIC ARTHRITIS TREATED WITH APREMLAST, BILOGICS, DMARDS AND CORTICOSTEROIDS IN THE US MARKETSCAN DATABASE

1Rebecca Penson1, 2Katrina Wilcox Hagberg1, 2Ellen Gian1, 2Catherine Vasiliakos-Scaranozza1, 2Steve Niemcyzk2, 2Michael Perg3, 2Maria Paris3, 2Anders Lindholm3, 2Susan Jack3, 1Boston Collaborative Drug Surveillance Program, Lexington, United States of America; 2Celgene Corporation, Summit, United States of America; 2Boston University School of Public Health, Boston, United States of America

Background: Patients with psoriatic arthritis (PsA) are at increased risk for cardiovascular events, but different treatment options may not have the same rates of cardiovascular events. 1,2

Objectives: To compare rates of myocardial infarction (MI), stroke and revascularization by treatment type in patients with PsA.

Methods: We conducted a population-based cohort study of treated PsA patients in the MarketScan database in 2014-2016. The cohort entry was the date of the first prescription for a study drug (apremilast only or in combination with ≥1 other study drugs, anti-TNF-α biologics only, other

REFERENCES

1] Ustekinumab in psoriatic arthritis: need for studies from real-world evidence.


Disclosure of Interests: None declared


Conclusion: In this RWE series, UST 90 mg was effective and safe in 75% of our patients probability of achieving a remission/low activity state by DAPSA.

REFERENCES


Disclosure of Interests: None declared


Table 1. Baseline demographic and clinical characteristics of patients

<table>
<thead>
<tr>
<th>Age (yrs), mean ± SD</th>
<th>54.6 ± 11.8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex, n(%)</td>
<td>108 (57.1)</td>
</tr>
<tr>
<td>Disease duration (yrs), mean ± SD</td>
<td>16.2 ± 8.8</td>
</tr>
<tr>
<td>Family history of psoriasis, n(%)</td>
<td>148 (89.9)</td>
</tr>
<tr>
<td>Family history of arthritis, n(%)</td>
<td>181 (95.8)</td>
</tr>
<tr>
<td>BDI, n(%)</td>
<td>3 (6)</td>
</tr>
<tr>
<td>VAS (0-10), mean ± SD</td>
<td>15.4 ± 10.8</td>
</tr>
<tr>
<td>LEI (0-60), mean ± SD</td>
<td>0.4 ± 0.6</td>
</tr>
<tr>
<td>PASI (0-72), mean ± SD</td>
<td>1.9 ± 2.2</td>
</tr>
<tr>
<td>DAPSA (0-43), mean ± SD</td>
<td>0.8 ± 0.7</td>
</tr>
<tr>
<td>DAPSA, mean ± SD</td>
<td>28.6 ± 18.2</td>
</tr>
<tr>
<td>BMI, mean ± SD</td>
<td>25.6 ± 4.4</td>
</tr>
<tr>
<td>CCI, mean ± SD</td>
<td>1.5 ± 1.4</td>
</tr>
</tbody>
</table>

Conclusion: Our aim was to compare characteristics of patients who could maintain the same bDMARD over time (non-switchers) with those of refractory patients in whom bDMARD switch was necessary (switchers), and to evaluate predictors of switching.

Methods: PaA patients attending the Rheumatology Unit of University of Padova, classified according to CASPAR criteria and starting a first line bDMARD, were enrolled in the present retrospective study. We only included patients who maintained a bDMARD regimen (with or without switching) for at least 3 years, to ensure more complete follow-up data. Demographic data, comorbidities, clinimetric and anthropometric indexes, collected at baseline and once a year for every follow-up year and registered in the patient’s records, were used. Disease activity was evaluated through Disease Activity in Psoriatic Arthritis (DAPSA), Leeds Enthesitis Index (LEI), Psoriasis Area and Severity Index (PASI). An overall Body Mass Index (BMI) category, summarizing data from the whole follow-up, was assigned to each patient, according to the BMI category which occurred more frequently in the patient’s record. Then the variable was treated as categorical grouping underweight and normal-weight patients (base category), overweight and class I obesity (2‘ category), and class II and III obesity (3‘ category). Baseline characteristics for switchers and non-switchers were compared through chi-square or Fisher exact test, for categorical variable and t-test or Mann-Whitney test, for continuous variable, as appropriate. Logistic regression analysis was conducted to assess predictors of therapeutic switch. All variables associated to the outcome with a p<0.2 at univariate analysis were included in the initial multivariable model. Backward selection was applied to select the most significant predictors.

Results: One-hundred-eighty-nine PaA patients were enrolled with a mean follow-up time of 7.0±3.5 years. Their characteristics at the beginning of bDMARDs therapy are outlined in Table 1. Among the patients, 51 became switchers and 138 remained non-switchers. Their baseline features did not differ significantly, with the only exception of LEI, higher in switchers (0.5 ± 0.2 vs 0.2 ± 0.6, p=0.05). When predictors of switch were evaluated, the independent variables positively associated to the outcome at univariate analysis with p<0.2 were: male sex (OR 1.57; 95% CI 1.09, 2.26), obesity together with respect to normal-weight patients (OR 2.18) were able to independently predict the odds of switching.

Conclusion: Obesity and entheseal involvement, as expressed by LEI, seem to be the most useful predictor in order to identify patients who are more likely to switch, in line with data from literature that highlight a lower response of bDMARDs in obese patients.

REFERENCES

1] Ustekinumab in psoriatic arthritis: need for studies from real-world evidence.


Disclosure of Interests: None declared


Conclusion: The duration of psoriasis was 14.8 ± 12.8 years, and 6.3 ± 6.5 years for the arthritic. 34.5% were oligoarticular forms, 13.8% polyarticular forms, and the remaining 51.7% were mixed forms. The distal interphalangeal joints synovitis was present in 38% of the patients and dactylitis in 24%. 17 patients were naïve to biologic drugs (29.3%), UST was second line in 25.9%, third in 32.8%, fourth in 10.3% and fifth in 1.7% of patients. Half of the patients were treated with MFX. In the baseline situation, 9.4% had low activity, 75% had moderate activity, and 15.6% had high activity by DAPSA index. At the end of the analysis, 12.5% were in remission, 59.4% in low activity, and 28.1% in moderate activity, according to the DAPSA index. There were no patients in high activity. That is, 72% were in DAPSA remission/low activity. The average reduction of DAPSA was 9.53 ± 5.52 (McNemar’s p <0.0005). The only factor associated with remission/low DAPSA activity was baseline DAPSA, OR 1.51 (1.02-2.22), p = 0.044. In 6 patients, the drug was discontinued (4 due to lack of efficacy and 2 due to poor tolerance or adverse effects).

Disclosure of Interests: None declared


To compare rates of myocardial infarction (MI), stroke and revascularization by treatment type in patients with PsA.

Methods: We conducted a population-based cohort study of treated PsA patients in the MarketScan database in 2014-2016. The cohort entry was the date of the first prescription for a study drug (apremilast only or in combination with ≥1 other study drugs, anti-TNF-α biologics only, other...
biologics and DMARDs (OBDDs) only, corticosteroids only, OBDDs + corticosteroids and anti-TNF-α biologics with OBDDs and/or corticosteroids) after March 21, 2014, the date on which apremilast was approved. Patients were followed from cohort entry through censor date, defined as the first of the following: index date (date patient became a case), end of record or end of study period (December 31, 2016). MI and stroke cases required 1 inpatient diagnosis plus 2 additional diagnoses on separate days; revascularization required a procedure code for revascularization without MI or stroke, all >7 days after cohort entry. A patient was considered currently exposed from the prescription date through the prescription duration + 30 days. We calculated incidence rates (IRs) and 95% confidence intervals (CIs) for each outcome per 100 patient-years among the entire population and in the subgroup of patients with no history of serious cardiovascular disease (CVD).

**Results:** The study population included 51,971 patients (median age: 52 years, 52% female, 4.0% serious CVD history). IRs were low for all outcomes, and differences between treatments did not reach statistical significance (95% CIs for IRs were overlapping). Among the 187 MI cases, IRs (95% CIs) as follows: for apremilast only, 0.10 (0.01, 0.35); anti-TNF-α biologics only, 0.13 (0.09, 0.19); anti-TNF-α biologics with OBDDs and/or corticosteroids, 0.31 (0.22, 0.43); OBDDs only, 0.32 (0.23, 0.44); corticosteroids only, 0.44 (0.27, 0.68); OBDDs + corticosteroids, 0.45 (0.24, 0.76); and apremilast in combination, 0.49 (0.20, 1.02). Among the 79 stroke cases, IRs (95% CIs) were as follows: for corticosteroids only, 0.08 (0.02, 0.22); anti-TNF-α biologics only, 0.09 (0.06, 0.13); for OBDDs only, 0.10 (0.05, 0.17); anti-TNF-α biologics with OBDDs and/or corticosteroids, 0.12 (0.06, 0.20); apremilast only, 0.15 (0.03, 0.43), or in combination, 0.14 (0.02, 0.51); and OBDDs + corticosteroids, 0.21 (0.08, 0.45). Among the 292 revascularization cases, IRs (95% CIs) as follows: for apremilast only, 0.25 (0.08, 0.57), anti-TNF-α biologics only, 0.36 (0.29, 0.44); anti-TNF-α biologics with OBDDs and/or corticosteroids, 0.37 (0.27, 0.50); OBDDs + corticosteroids, 0.38 (0.19, 0.68); apremilast in combination, 0.42 (0.15, 0.92); OBDDs only, 0.48 (0.36, 0.61); and corticosteroids only, 0.49 (0.31, 0.73). Among patients with no serious CVD history, IRs were generally lower but results were not materially different from the main analyses.

**Conclusion:** Rates of MI, stroke and revascularization were low for treated PsA patients and were similar across treatments.

**REFERENCES**


**Disclosure of Interests:** Rebecca Persson Grant/research support from: Celgene Corporation, Katinka Wilcox Hagberg Grant/research support from: Celgene Corporation, Ellen Qian Employee of: Boston Collaborative Drug Surveillance Program, Catherine Vasiliakis-Scaramozza Grant/research support from: Celgene Corporation, Steven Nyencky Employee of: Celgene Corporation, Michael Peng Employee of: Celgene Corporation, Maria Paris Employee of: Celgene Corporation, Anders Lindholm Employee of: Celgene Corporation, Susana Gomez: None declared, Alvaro Seijas: None declared

**DOI:** 10.1136/annrheumdis-2019-eular.780

**AB0778**

**IMPACT OF DISEASE IN A SPANISH POPULATION WITH PSORIATIC ARTHRITIS**

Rubén Queiró Silva1, Juan D. Cañete2, Susana Gómez3, Ana Cabest3, 1Hospital Universitario Central de Asturias, Rheumatology, Oviedo, Spain; 2Hospital Clínic, Rheumatology, Barcelona, Spain; 3Pfizer Medical Dpt., Madrid, Spain

**Background:** Patients with psoriatic arthritis (PsA) experience significant disability and reduced quality of life, resulting from the emotional distress and functional impairment associated with psoriatic skin lesions, as well as joint disease. Patient reported outcomes are important to evaluate healthcare interventions and to reflect the impact of PsA on patients’ lives.

**Objectives:** The aims of the present study were to describe disease characteristics of PsA patients with an acceptable symptoms state (PsAID score<4) as well as to analyze predictive factors for PsAID<4.

**Methods:** Post-hoc analysis of data from a cross-sectional observational, multicenter study, aimed at evaluating the prevalence of MDA in a Spanish population with PsA, to describe their characteristics and to evaluate the association between MDA and the impact of the disease as assessed by the PsAID questionnaire. The original study included 227 adult patients of both genders diagnosed with PsA according to CAPSAR criteria with at least one year of disease evolution and on treatment with biological and/or conventional synthetic disease modifying anti-rheumatic drugs (cDMARD). The PsAID questionnaire reflects the effect of PsA from the patient’s perspective. It is composed of 12 physical and psychological domains. PsAID score < 4 identified patient-acceptable symptoms state.

**Results:** 122 patients with a PsAID score < 4 were included. Demographic and clinical characteristics of the study population are shown in Table 1. Overall, 53/102 (52.0%) and 83/122 (68.0%) patients presented articular or skin remission, respectively. 76/122 (62.3%) of patients were in MDA state; the majority presented a low disability state according to HAQ (85.2%). A moderate relationship between HAQ<0.5 and PsAID<4 (k=0.532) and between MDA and PsAID<4 (k=0.3594) were observed. Multivariable logistic regression analysis showed that patients with distal interphalangeal joint (DIP) involvement (odds ratio [OR] [95%CI]), 0.402 [0.203-0.799]; p=0.009), family history of PsA (OR: 0.252 [0.089-0.716]; p=0.010) and

**AB0777**

**PSA PATIENTS REACHING MINIMAL DISEASE ACTIVITY5/7 IMPROVE IN ALL FIELDS OF PSAID**

Jose Pinto-Tasende1, Clara Ventín1, Maria Caiero1, Alvaro Seijas2, Rodrigo Aguirre2, Maria Teresa Silva1, Francisco Blanco1. Hospital Universitario A Coruña, Rheumatology, A Coruña, Spain

**Background:** Patients with psoriatic arthritis (PsA) show impact on physical and psychological aspect of the disease and it can be measured with the PsA Impact of Disease (PsAID) questionnaire. Impact of disease should improve if patient reach a minimal disease activity (MDA).

**Objectives:** To assess the association between MDA and PsAID questionnaire in patients with PsA from daily clinical practice.

**Methods:** A cross-sectional study was carried out in consecutive patients who fulfilled CASPAR criteria and who were treated according to routine treatment. Patients in MDA state were 36 (50%) and median of total score of PsAID was 4.70 (0.85-9.40). All fields of PsAID improved if they reached MDA 5/7 (p<0.01). MDA 5/7 was also related to age, duration of the disease, CRP and DAPSA (see table).

**Conclusion:** Fifty percent of PsA patients achieve MDA in daily clinical practice. MDA patients had a significantly lower impact of the disease according to PsAID.

**REFERENCES**


**Acknowledgement:** Sociedade Galega de Reumatoloxía

**Disclosure of Interests:** Jose Pinto-Tasende Speakers bureau: Janssen, Novartis, Celgene, BMS, Abbvie, Pfizer, Clara Ventín: None declared, María Caiero: None declared, Alvaro Seijas: None declared, Rodrigo Aguirre: None declared, María Teresa Silva: None declared, Francisco Blanco Speakers bureau: Celgene, Pfizer, Abbvie

**DOI:** 10.1136/annrheumdis-2019-eular.7393

**Scientific Abstracts**
increased CRP (OR: 0.922 [0.854–0.995]; P = 0.038) were significantly less likely to reach a PsAID score<4.

Abstract AB0778 Table 1. Demographic and clinical characteristics of PsA patients with PsAID <4

<table>
<thead>
<tr>
<th>Category</th>
<th>N (122)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>70 (57.4)</td>
</tr>
<tr>
<td>Age, mean (SD), yr</td>
<td>54.5 (12.7)</td>
</tr>
<tr>
<td>BMI, mean (SD) (kg/m²)</td>
<td>27.1 (3.9)</td>
</tr>
<tr>
<td>CRP (mg/L, mean (SD))</td>
<td>2.8 (3.3)</td>
</tr>
<tr>
<td>Comorbidities, n (%)</td>
<td>40 (32.8)</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>33 (27.0)</td>
</tr>
<tr>
<td>Obesity</td>
<td>30 (24.6)</td>
</tr>
<tr>
<td>DM</td>
<td>12 (9.8)</td>
</tr>
<tr>
<td>PsA clinical patterns, n (%)</td>
<td>60 (49.2)</td>
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<tr>
<td>PsA</td>
<td>11 (9.0)</td>
</tr>
<tr>
<td>Arthrolysis for spondyloarthritis</td>
<td>2 (1.6)</td>
</tr>
<tr>
<td>PsA duration, mean (SD), yrs.</td>
<td>9.6 (7.9)</td>
</tr>
<tr>
<td>Skin symptoms duration, mean (SD), yrs.</td>
<td>21.6 (14.5)</td>
</tr>
<tr>
<td>Articular symptoms duration, mean (SD), yrs.</td>
<td>11.9 (8.7)</td>
</tr>
<tr>
<td>Radiologic findings</td>
<td></td>
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<tr>
<td>Erosions in hands, n (%)</td>
<td>40 (32.8)</td>
</tr>
<tr>
<td>Erosions in feet, n (%)</td>
<td>33 (27.0)</td>
</tr>
<tr>
<td>PASI, mean (SD)</td>
<td>1.2 (3.8)</td>
</tr>
<tr>
<td>HAQ, mean (SD)</td>
<td>0.2 (0.3)</td>
</tr>
<tr>
<td>HAQ ≤ 0.5, n (%)</td>
<td>104 (85.2)</td>
</tr>
<tr>
<td>MDA, n (%)</td>
<td>78 (62.3)</td>
</tr>
<tr>
<td>Kappa [CI 95%] MDA vs. PsAID &lt;4</td>
<td>0.5326 [0.421-0.643]</td>
</tr>
<tr>
<td>Kappa [CI 95%] MDA vs. PsAID &lt;4</td>
<td>0.3594 [0.2393-0.4795]</td>
</tr>
</tbody>
</table>

MDA: Minimal disease activity; SD: Standard deviation; BMI: Body mass index. CRP: C-Reactive Protein; HBP: High blood pressure; DIP: Distal interphalangeal joint disease. DM: Diabetes mellitus; PASI: Psoriasis Area and Severity Index; HAQ: Health Assessment Questionnaire; PsAID: Psoriatic Arthritis Impact of Disease. CI: confidence intervals

Conclusion: There are discrepancies between the treatment goals (MDA) and the impact of disease as assessed by PsAID. Clinical characteristics such as DIP involvement, inflammatory load (PCR) and genetic factors (familial history) seem to be associated with a lower probability of being in an acceptable symptoms state in PsA patients.


Methods: A cross-sectional study was conducted with 136 consecutive patients with PsA (CASPAR criteria). Sociodemographic and anthropometric data, CVRF, disease activity according to DAPSA categories, HAQ, MDA, and CVR measured by SCORE chart, was collected. An Mt>800 μm and/or the presence of carotid plaque (Mannheim consensus), defined a high CVR by ultrasound. We analyzed the concordance (kappa) between the MDA response and the low activity and remission categories according to the DAPSA. Clinical variables of PsA associated with a high CVR were evaluated by multivariate analyses.

Results: Intima-media thickness values correlated well with CVR categories according to SCORE (p < 0.0001). 40% of patients included in the low and moderate risk categories according to the SCORE risk chart were reclassified as high CVR after the ultrasound examination.

In the multivariate analysis, some characteristics of the disease were independently associated with a high CVR.

<table>
<thead>
<tr>
<th>OR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.08 (1.03-1.13)</td>
</tr>
<tr>
<td>HAQ</td>
<td>1.94 (0.83-4.48)</td>
</tr>
<tr>
<td>DM</td>
<td>1.65 (0.47-6.20)</td>
</tr>
<tr>
<td>AHT</td>
<td>0.75 (0.41-1.38)</td>
</tr>
<tr>
<td>DL</td>
<td>2.61 (0.91-7.48)</td>
</tr>
<tr>
<td>Tobacco</td>
<td>4.26 (1.44-12.65)</td>
</tr>
<tr>
<td>Enthesitis</td>
<td>3.76 (1.36-10.40)</td>
</tr>
<tr>
<td>Erosions</td>
<td>5.23 (1.33-20.53)</td>
</tr>
</tbody>
</table>

This reveals that patients with enthesitis and/or structural damage are those who tend to have a high CVR. When comparing DAPSA and MDA criteria, we found a moderate correlation between the MDA response and the DAPSA low activity (κ = 0.52, p < 0.0001) and between MDA and DAPSA remission (κ = 0.47, p < 0.0001).

Background: Psoriatic arthritis (PsA) patients usually have a high prevalence of cardiovascular risk factors (CVRF) and cardiovascular events, which makes the routine estimation of cardiovascular risk (CVR) highly advisable. Currently, this risk is estimated through classic risk scores (SCORE, Framingham), however, the values of these scores may underestimate the real CVR of these patients.

Methods: We aimed to analyze whether carotid ultrasound is a useful tool for estimating CVR in patients with PsA, and if it is capable of correcting the estimated risk using classical tables. We also analyzed the usefulness of the MDA criteria and the DAPSA categories for clinical decision making in real practice.

Disclosures of Interests: None declared DOI: 10.1136/annrheumdis-2019-eular.4794

The high CVR in our population is related not only to classical CVRF, but also to the inflammatory load (enthesitis) and structural damage (erosions) of PsA. DAPSA is an appropriate instrument for clinical decision making in routine practice because it correlates reasonably well with stringent therapeutic goals such as MDA.

criteria were subsequently sub-classified using the Moll and Wright classification criteria based on the manifestations of PsA at their index outpatient visit. This subtype was then compared to their Moll and Wright subtype at the last outpatient visit prior to January 3, 2019. While it was possible for patients to display more than one subtype simultaneously, the classification made at baseline and at latest visit reflected the predominant Moll and Wright subtype of the patient, in the opinion of the expert treating rheumatologist.

Results: 76 patients were identified as meeting entry criteria, with none being in remission at the index visit. Mean age of patients at the latest visit was 60.2 ± 12.6 years, and 47.4% were male. Median time between the index visit and latest visit was 7 years (IQR: 5 to 8 years). 42.1% of patients had the same Moll and Wright subtype at both visits. Table 1 presents the distribution of Moll and Wright subtypes at index visit and latest visit. Table 2 reports the changes, or lack thereof, in subtype between visits. 22/76 patients (28.9%) were in remission at the latest visit. Of the patients in remission, 12 (54.5%) were being treated with a biologic, DMARD, and/or steroid.

Abstract AB0780 Table 1. Distribution of Moll and Wright subtypes at index visit and latest visit.

<table>
<thead>
<tr>
<th>Moll and Wright subtype (N=76 patients)</th>
<th>Index visit (N)</th>
<th>Latest visit (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polymiarticular</td>
<td>19</td>
<td>8</td>
</tr>
<tr>
<td>Oligoarticular</td>
<td>42</td>
<td>36</td>
</tr>
<tr>
<td>Distal interphalangeal joint predominant</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Spondylitis predominant</td>
<td>12</td>
<td>7</td>
</tr>
<tr>
<td>Arthritis mutilans</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

Abstract AB0780 Table 2. Persistence of Moll and Wright subtype.

<table>
<thead>
<tr>
<th>Description of change from index visit to latest visit</th>
<th>N = 76</th>
</tr>
</thead>
<tbody>
<tr>
<td>No change</td>
<td>32 (42.1%)</td>
</tr>
<tr>
<td>Polymiarticular must change to oligoarticular</td>
<td>5</td>
</tr>
<tr>
<td>Oligoarticular must change to distal interphalangeal joint predominant</td>
<td>20</td>
</tr>
<tr>
<td>Spondylitis predominant must change to distal interphalangeal joint predominant</td>
<td>1</td>
</tr>
<tr>
<td>Mutilans must change to polyarticular</td>
<td>2</td>
</tr>
<tr>
<td>Polyarticular must change to remission</td>
<td>1</td>
</tr>
<tr>
<td>Oligoarticular must change to spondylitis predominant</td>
<td>1</td>
</tr>
<tr>
<td>Polyarticular must change to mutilans</td>
<td>1 (1.3%)</td>
</tr>
<tr>
<td>Oligoarticular must change to remission</td>
<td>1</td>
</tr>
<tr>
<td>Polyarticular must change to remission</td>
<td>2 (2.6%)</td>
</tr>
<tr>
<td>Spondylitis predominant must change to remission</td>
<td>3 (3.9%)</td>
</tr>
</tbody>
</table>

Conclusion: In this retrospective analysis there was a persistence of Moll and Wright subtype in 42.1% of psoriatic arthritis patients over the median time of 7 years. Whether patients who maintain Moll and Wright subypes respond differently to targeted therapy for PsA should be evaluated in prospective trials.

REFERENCES

Disclosure of Interests: None declared

**AB0781**

ASSOCIATION OF MICA POLYMORPHISM AND SERUM LEVELS WITH PREDISPOSITION TO PSORIATIC ARTHRITIS

| Renata Sokolik, Marta Dratwa, Joanna Wielnińska, Milena Iwaszkówna, Monika Chaszczewska-Markowska, Piotr Wiland, Katarzyna Bogunia-Kubiś |
| Wrocław Medical University, Department of Rheumatology and Internal Medicine, Wrocław, Poland; Polish Academy of Sciences, Laboratory of Clinical Immunogenetics and Pharmacogenetics, Hereditary Institute of Immunology and Experimental Therapy, Wrocław, Poland |

Background: Psoriatic arthritis (PsA) is a multifactorial chronic inflammatory disease manifested by joint inflammation and cutaneous psoriasis. The precise etiology of PsA remains unknown, however both genetic and environmental factors contribute to development of this immune-mediated disease.

**Objectives:** This present study aimed to assess whether polymorphism within gene coding for major histocompatibility complex (MHC) class I chain-related A (MICA) proteins could be a prognostic factor of PsA.

**Methods:** For this purpose 77 PsA patients and 234 controls were enrolled to the study on MICA polymorphic variants. Genotyping for MICA alleles was performed using a LightSNiP assay. In addition the MICA serum levels were studied in 66 patients and 99 controls employing Luminex assay.

**Results:** Interestingly, MICA polymorphism was found to affect the susceptibility to PsA. The presence of the A (Val) variant was found to increase the risk of PsA (OR = 1.932, p = 0.022).

**Conclusion:** These results imply that MICA polymorphism may constitute a risk factor of PsA and be associated with MICA serum levels in PsA patients. Supported by the National Science Centre (Poland) grant 2016/21/B/NZS/01901.

Disclosure of Interests: None declared

**AB0782**

SECUKINUMAB PROVIDES IMPROVEMENTS IN HEALTH-RELATED QUALITY OF LIFE IN PATIENTS WITH PSORIATIC ARTHRITIS, REGARDLESS OF THE TIME SINCE DIAGNOSIS: POOLED RESULTS FROM THE SECUKINUMAB PHASE 3 TRIAL PROGRAM

| Vibeke Strand, Oliver Fitzgerald, Laura C. Coates, Jessica A. Walsh, Juan D. Carbonell, Peter Nash, Eric Davenport, Luminia Pricop, Gregory Hustache, Isabelle Gilleoteau, Aurore Yocolly, Matthias Augustin, Stanford University, Palo Alto, United States of America; University College Dublin, Dublin, Ireland; University of Oxford, Oxford, United Kingdom; University of Utah School of Medicine, Salt Lake City, United States of America; Hospital Clinic and IDIBAPS, Barcelona, Spain; University of Queensland, Brisbane, Australia; RTI Health Solutions, Research Triangle Park, United States of America; Novartis Pharmaceuticals Corporation, East Hanover, United States of America; Novartis Pharma AG, Basel, Switzerland; Novartis Global Service Center, Dublin, Ireland; University Medical Center Hamburg-Eppendorf, Hamburg, Germany |

Background: Psoriatic arthritis (PsA) can have a profound impact on health-related quality of life (HRQoL). Secukinumab (SEC), a fully-human IL-17A inhibitor, has been shown to improve symptoms and HRQoL in patients (pts) with PsA.

**Objectives:** To evaluate the impact of SEC on HRQoL, assessed using the Short Form-36 Health Survey (SF-36), in pts with PsA stratified by time since first diagnosis (<2 yrs or ≥2 yrs).

**Methods:** Pts were randomized to either subcutaneous placebo (PBO) or SEC 150 mg (FUTURE 2, 3, 4, 5), 150 mg no load (NL; FUTURE 4, 5). Pts were randomized to either subcutaneous placebo (PBO) or SEC 150 mg (FUTURE 2, 3, 4, 5), 150 mg no load (NL; FUTURE 4, 5). Doses were administered at baseline (BL) and Wks 1–4, followed by every 4 wks (or every 4 wks from BL to Wk 16; observed data are presented at Wk 52. The proportion of pts reporting improvements ≥ minimum clinically important differences (MCID) in SF-36 physical (PCS respondents), mental component summary (MCS respondents), and individual SF-36 domains was also assessed. Non-responder imputation was employed for missing values in responder analyses. Fisher’s exact test was used to compare the proportion of responders.

Disclosure of Interests: None declared
Results: A total of 2049 pts were included: 681, 461, 572, and 335 in the PBO, SEC 300 mg, 150 mg, and 150 mg NL groups, respectively. Of these, 34%, 30%, 32%, and 33% were classified as <2 yrs since PsA diagnosis (overall: 32%). Mean times since diagnosis were 0.8 yrs across treatment groups in the <2 yrs subgroup, and 8.6-10.1 yrs in the ≥2 yrs subgroup. The least squares mean (LSM) changes from BL to Wk 16 in PCS and MCS were significantly improved with all doses of SEC vs PBO in both <2 yrs (PCS: BPO = 0.8 vs 6.5 [p<0.0001]; 4.8 [p<0.001], 3.8 [p<0.01], 2.8 [p<0.01], 3.8 [p<0.001]) for the 300 mg, 150 mg, and 150 mg NL groups, respectively: MCS: BPO = 1.3 vs 4.0 [p<0.01]; 4.4 [p<0.01], 3.8 [p<0.05]) and ≥2 yrs since diagnosis (PCS: BPO = 1.9 vs 6.9 [p<0.0001], 5.3 [p<0.0001], 5.5 [p<0.0001]; MCS: BPO = 0.9 vs 3.6 [p<0.01], 2.8 [p<0.01], 3.0 [p<0.01]) groups. Improvements in individual SF-36 domains were reported with SEC vs PBO in the overall population and both subgroups (Figure). At Wk 16, the proportion of PCS responders was significantly higher with SEC vs PBO, in both <2 yrs (PBO: 38.5% vs 300 mg: 69.1%. [p<0.0001]; 150 mg: 59.5% [p<0.01]; 150 mg NL: 53.6% [p<0.05]) and ≥2 yrs (PBO: 43.8%; 300 mg: 64.6%; [p<0.001]; 150 mg: 59.4% [p<0.01]; 150 mg NL: 65.8% [p<0.0001]) in those <2 yrs vs ≥2 yrs from diagnosis. Improvements in PCS, MCS, individual domains, and MCID responses with SEC were sustained to Wk 52.

Conclusion: SEC offered significant, clinically meaningful and sustained improvements in HRQoL (SF-36) in pts with PsA, regardless of time since diagnosis.

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Disclosure of Interests: Vibeke Strand Consultant for: Samumed, LLC, AbbVie, Bristol-Myers Squibb, Eupaxia, Flexion, Iroko, Novartis, Pfizer, Regeneron, Sanofi, SKK, Oliver Fitzgerald: None declared, Laura C Coates Grant/research support from: AbbVie, Celgene, Lilly, Novartis and Pfizer, Consultant for: AbbVie, Amgen, BMS, Celgene, Galapagos, Gilead Sciences Inc., Janssen, Lilly, Novartis, Pfizer, Prothena Corp and UCB, Jessica A. Walsh Grant/research support from: Abbvie, Pfizer, Consultant for: Abbvie, Celgene, Lilly, Novartis, Juan D. Cafete: None declared, Peter Nash Grant/research support from: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Consultant for: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Speakers bureau: AbbVie, Bristol-Myers Squibb, Eli Lilly, Janssen, Novartis, Pfizer Inc, Roche, Sanofi, UCB, Eric Davenport Employee of: E. Davenport is an employee of RTI Health Solutions., Limunita Pricop Employee of: Novartis, Gregory Hustache Shareholder of: Novartis Pharma AG, Employee of: Novartis Pharma AG, Isabelle Gillette Employee of: Employee of Novartis, Aurore Yocolly Employee of: Employee of Novartis., Matthias Augustin Grant/research support from: Prof. Augustin has served as consultant and/or paid speaker for and/or has received research grants and/or honors for consulting and/or scientific lectures for and/or got travel expenses reimbursed and/or participated in clinical trials sponsored by companies that manufacture drugs used for the treatment of Psoriasis including AbbVie, Amgen, Biogen (Biogen Idec), Boehringer Ingelheim, Celgene, Centocor, Eli Lilly, Gaedera, Janssen-Cilag, Leo, Medac, MSD, Mundipharma, Pfizer, Sandoz, Xenopont., Consultant for: Prof. Augustin has served as consultant and/or paid speaker for and/or has received research grants and/or honors for consulting and/or scientific lectures for and/or got travel expenses reimbursed and/or participated in clinical trials sponsored by companies that manufacture drugs used for the treatment of Psoriasis including AbbVie, Almirall, Amgen, Biogen (Biogen Idec), Boehringer Ingelheim, Celgene, Centocor, Eli Lilly, Gaedera, Janssen-Cilag, Leo, Medac, MSD, Mundipharma, Novartis, Pfizer, Sandoz, Xenopont.


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Background: PsA is a chronic inflammatory arthritis with heterogeneous clinical manifestations. Disease burden and quality of life (QoL) is affected by both joint and skin aspects of the disease (1,2). Given variability among patients of the extent and severity of joint and skin symptoms, the relative impact of each aspect on overall burden to the patient has not been well quantified.

Objectives: Describe the relative impact of joint and skin symptoms in PsA in a real-world population through an assessment of patient perception of symptom importance, QoL, and work productivity.

Methods: Cross-sectional survey of rheumatologists and dermatologists and their PsA patients in Australia, Canada, France, Germany, Italy, Japan, Spain, UK, and US. Physicians provided data on patient Body Surface Area (BSA) psoriasis coverage at the time of survey. Patient self-reported data included perceptions of symptom importance, EQ-SD, Psoriatic Arthritis Impact of Disease (PsAID12), and Work Productivity and Activity Impairment (WPAI: SHP) Index. Patients were compared according to BSA (BSA=0 vs. BSA>0), using parametric and non-parametric tests as appropriate.

Results: Data were collected for 3200 patients with PsA by 454 rheumatologists and 238 dermatologists. 556 patient self-completed questionnaires were also collected. Mean age was 49 years. 46% female, 69% had a BSA >0. Patients with BSA>0 had mean tender joint count (TJC) of 5.2 and mean swollen joint count (SJC) of 4.8. Patients with BSA=0 had mean TJC and SJC of 2.0 and 1.5, respectively. Across all patients, when asked to prioritize the burden of symptoms, 62% of patients prioritized joints and 38% prioritized skin. In patients with BSA>0, 35% still prioritized skin as most important, 41% indicated they experienced anxiety/depression as a result of their PsA, with 62% indicating both joint and skin symptoms were the cause (28% joint alone, 9% skin alone).

Patients with BSA >0 reported significantly worse QoL and work productivity and activity impairment than BSA=0 (EQSD index 0.79 vs. 0.85, p<0.0001; EQSD VAS 71.98 vs. 77.68, p<0.0001; PsAID 2.91 vs. 1.66, p<0.0001; WPAI overall 25.61 vs. 16.32, p<0.0001).

Conclusion: The majority of PsA patients prioritize joint symptoms over skin. Patients with any joint/skin involvement likely have worse quality of life than in the general population (3). PsA patients report that both joints and skin have an impact on their QoL and work productivity with significantly greater impact in those who have skin involvement. Treatment goals focusing on both components of PsA would optimize patient outcomes.

REFERENCES

Disclosure of Interests: William Tillett Grant/research support from: AbbVie, Celgene, and Lilly, Consultant for: AbbVie, Celgene, Lilly, Novartis, and Pfizer, Speakers bureau: Abbvie, Celgene, Lilly, Novartis, and UCBI, Consultant for: Biogen IDEC, Abbvie, Amgen, Eli Lilly and Company, Novartis, Pfizer, Janssen, UCB, Samumed, Celgene, Sanofi Regeneron, Merck, and GSK, Diamant Thaci Grant/research support from: AbbVie, Almirall, Amgen, Bio Skin, Biogen Idec, Boehringer Ingelheim, Bristol-Myers Squibb, Celgene, Chugai, Dermina, Dignity, Eli Lilly, Forward Pharma, GlaxoSmithKline, Janssen Cilag, Leo Pharma, Novartis, Pfizer, Regeneron, Roche, Sandoz-Hexal, Sanofi, and UCB, Consultant for: AbbVie, Almirall, Bristol-Myers Squibb, Celgene, Dignity, Galapagos, Leo Pharma, Lilly, Novartis, Pfizer, and UCBI, Honoraria: Abbvie, Almirall, Amgen, Bio Skin, Celgene, Dignity, Janssen, Leo Pharma, Merck Sharp & Dohme, Novartis, Pfizer, Roche-Posay, Sandoz-
Subclinical myocardial involvement in psoriatic arthritis patients

Background: Psoriatic arthritis (PsA) is a systemic inflammatory disease affecting 15-30% of patients with psoriasis. Patients with PsA present a higher risk of left ventricular systolic dysfunction compared to controls. GLS measured by speckle tracking was lower in PsA patients (mean =-19.79, s.d. = 1.65) than controls (mean =-21.24, s.d. = 1.61). Regression analysis showed statistically significantly lower GLS scores with increasing CRP and ESR. Baseline median (IQR) of CRP was 7.4 (5.6-13.4) in PsA and 2.2 (1-2.8) in controls. Baseline median (IQR) of ESR was 29 (2-42) in PsA and 15 (12-19) in controls. There were no differences in other variables studied.

Methods: Sixty patients (29 males) and 34 healthy controls (18 males) participated in the study. The patients’ mean age was 50.7 years (s.d. = 17.42). They were subjected to 2D transthoracic echocardiography, tissue Doppler imaging, and speckle tracking echocardiography, in order to evaluate left ventricular systolic function with conventional indices such as ejection fraction (EF), and with novel indices such as global longitudinal strain (GLS). Diastolic dysfunction was also assessed in both groups. Blood tests including CRP and ESR were conducted. Disease duration and severity scores, PASI and DAS 28, were also recorded. The statistical analysis was conducted with SPSS v23.0.

Results: Linear regression analysis showed statistically significantly impaired left ventricular systolic function (p<0.001), as assessed with global longitudinal strain (GLS), in PsA patients (mean =-19.79, s.d. = 1.65) compared to the controls (mean =-21.24, s.d. = 1.61). The results were adjusted for age and gender. Ejection fraction, on the contrary, did not show any statistically significant difference between the two groups (p=0.535). Left ventricular diastolic function did not present significant differences between the two groups. GLS showed no association with disease duration, severity scores or the blood tests.

Conclusion: PsA patients present a higher risk of left ventricular systolic dysfunction compared to controls. GLS measured by speckle tracking echocardiography is a useful tool in revealing this subclinical myocardial impairment.

Disclosure of Interests: None declared


References:

Ab0785

Drug survival of secukinumab for psoriatic arthritis in a real-world setting

Background: Secukinumab is a newly introduced biologic therapy against IL-17 which has been approved for Psoriatic Arthritis and has showed efficacy in clinical trials, but real world data is still lacking.

Objectives: This study aims to analyze secukinumab drug survival for psoriatic arthritis in a real world environment.

Methods: Multicentric observational, longitudinal retrospective study conducted at 4 tertiary hospitals in Madrid region. Patients with clinical diagnosis of psoriatic arthritis which had received at least one dose of secukinumab between January 2016 and October 2018 were included. With follow up period till December 31, 2018. Medical records were reviewed to collect data about psoriatic arthritis involvement, comorbidities, previous DMARD and biDMARD therapies and its reasons for discontinuation, duration of secukinumab therapy, reasons for discontinuing secukinumab therapy and adverse events. Statistical analysis was performed including bivariate analysis (considering withdrawal of drug during study period or not) and survival analysis with Kaplan-Meier and Cox regression.

Results: 177 patients that initiated secukinumab therapy in the recruitment period were included. 123 patients were on 150 mg dose and 54 on 300 mg dose. Average follow up period was 13 months (SD 8.28; range 1-34) In the bivariate analysis, a higher proportion of biologic-naïve patients was found among the group without secukinumab withdrawal during the study (40% vs 23%, p 0.07). No other differences were observed between both groups regarding demographic characteristics nor comorbidities (tobacco exposure, hypertension, diabetes mellitus, dyslipidemia, ischaemic heart disease or malignancy). Median survival time for secukinumab in the Kaplan-Meier analysis was 21.2 months (IC 95%; 14.3 - 22.2), with an average of 19.9 months. One event was censored due to lost to follow-up. Secukinumab treatment was withdrawn in 79 patients (44.6%). Reasons for discontinuation were lack of effectiveness (37%), either primary (40 patients) or secondary (26 patients), adverse events (9 patients, 0.5%), elective surgery in one patient and latex allergy in other. The only variable associated to higher drug survival in Cox regression analysis was biologic-naïve status. No differences in drug survival were found in all other variables studied (gender, age, secukinumab dosage, illness duration, clinical features, tobacco exposure and rest of comorbidities).

Conclusion: As secukinumab was marketed in 2016, real-world setting studies lack long term data. This mean follow up period in our study was 13 months. Most of withdrawals were to lack of effectiveness. Median survival was 21.2 months, significantly higher in biologic-naïve patients. No other differences were found in all other variables studied. Probably real-world data differ from those of clinical trials.

Disclosure of Interests: Marta Valero: None declared, Beatriz Joven-Ibáñez: Speakers bureau: Celgene, Novartis, MSD, Pfizer, AbbVie, and Janssen, Maria Martin: None declared, Jose Campos Esteban: None declared, Carolina Merino Arguménez: None declared, Valentina Emperiale: None declared, Ana Pérez Gómez: None declared, Javier Bachiller-Corral: None declared.


Ab0786

High treatment satisfaction of therapy with ustekinumab in patients with active psoriatic arthritis due to early and long-term treatment response and high tolerability – results of the non-interventional study sustain

Disclosure of Interests: None declared

Background: SUSTAIN is a prospective, multi-center non-interventional study in Germany. 

Objectives: The objectives are to observe long term efficacy and safety, quality of life and further patient reported outcomes in patients with active psoriatic arthritis (PsA) under treatment with ustekinumab in routine clinical care.

Methods: In this study nearly 400 patients were planned to be included at 75 centers for 160 weeks with documentation at intervals at week 0 and 4 and then every 12 weeks. The treatment with ustekinumab is according to the label. Besides demographic data, the following data will be documented: Number of swollen and tendon joints, tender entheses, amount of skin psoriasis (BSA and PASI), patient reported outcome concerning disease activity of PsA and pain, Health Assessment Questionnaire (HAQ), quality of life (SF-12), sleep quality (VAS), satisfaction with therapy of patient and physician, safety (adverse events/serious adverse events), pharmacoeconomic aspects, number of patients with “Minimal Disease Activity” (MDA), number of patients with MDA at week 28 and 52. For the present interim analysis baseline data of 336 patients and results of the documented visits up to week 112 were analyzed.

Results: For the present analysis 336 patients (57% women) at 75 centers were observed. The number of documented patients was 310 at week 4, 318 at week 16, 278 at week 28, 160 at week 76 and 108 at week 112. At time of inclusion into the study, patients had arthritis at small (73.2%) and/or large (52.4%) joints, spinal involvement (17%) and enthesitis (13%). For 30.1% of patients, the medical history revealed structural bone damage and 2.1% had uveitis present at time of inclusion. Mean age was 54 years (22-85), mean BMI 30 kg/m² (19-52). The mean ustekinumab dose was 0.7 mg/kg body weight (0.2-1.3). 54.5% of the patients had as prior medication at least one TNF inhibitor and 44% used MTX as concomitant medication.

The data extension of the present interim analysis demonstrated relevant improvements with high treatment satisfaction and good safety and tolerability after 4 weeks and up to 112 weeks. The data show the maintenance of these treatment results up to week 112, i.e. reduction in the number of tender joints from a mean of 10.0 (CI 95% 8.6/11.3) at baseline to 1.8 (1.1/2.5) at week 112. The number of swollen joints improved from 4.1 (3.4/4.9) at baseline to 0.7 (0.3/1.0) at week 112. In the same period, skin symptoms (PASI) declined from 8.4 to 1.0 and pain assessment (VAS) declined from 56.0 to 34.3. Of the 96 patients who completed the week 112, 30.2% reached MDA at week 28 and 29.2% reached MDA at week 52.

Efficacy of the therapy with ustekinumab was assessed as “very good” or “good” by 91.1% of the treating physicians and by 89.9% of the patients at week 112. Until data cut off point (45 months after study start), 105 SAEs have been documented, of which only 14 were related to ustekinumab as assessed by physician of treatment center. 3.9% of patients discontinued treatment with ustekinumab (N=121), mainly due to an adverse event. Safety of therapy with ustekinumab was assessed as “very good” or “good” by 100% of the treating physicians and by 100% of the patients at week 112.

Conclusion: The present interim analysis of the prospective non-interventional study SUSTAIN confirmed relevant improvements with high treatment satisfaction and good safety in patients with active psoriatic arthritis treated with ustekinumab after 4 weeks and demonstrated that these effects were maintained at least up to 112 weeks in routine care.

Disclosure of Interests: Joerg Wendler Consultant for: Roche Pharma AG, AbbVie, Jannissen Cilag, Novartis, Speakers bureau: Roche Pharma AG, AbbVie, Jannissen Cilag, Novartis, Peter Wagener: None declared, Frank Hamann: None declared, Nils Damann: None declared, Evgenia Movshovich: None declared, Frank Behrens (G ThrA) research support from: AbbVie, Pfizer, Roche, Chugai, Prophylaxis, Bioline, Novartis, Consultant for: AbbVie, Pfizer, Roche, Chugai, UCB, Bristol-Myers Squibb, Celgene, MSD, Novartis, Biotest, Janssen, Genzyme, Eli Lilly, Speakers bureau: Ad board: AbbVie, Pfizer, Roche, Chugai, UCB, Bristol-Myers Squibb, Celgene, Novartis, Biotest, Janssen, Genzyme, Eli Lilly. DOI: 10.1136/annrheumdis-2019-eular.4655
Results: The study included 5062 PsA patients. Data showed an increase in use of bDMARDs in recent years (Fig 1). The trend in increasing use of bDMARDs was not affected by age, sex, and ethnicity. Elaercept was the most commonly used bDMARD (10.1%) over time, whereas, methotrexate was the most commonly used cDMARD (25.9%). A decrease in use of infliximab was noted along with the introduction of adimumab, golimumab and ustekinumab. Notably, a decrease in the utilization of cDMARDs, but not corticosteroid use, was seen with the advent of bDMARDs (Fig 2). However, this decrease in cDMARD use was not observed in patients treated with infliximab [Correlation Coefficient 2.69% (-47.5%, 51.6%), P=0.921]. Conclusion: More PsA patients are using bDMARDs in recent years in lieu of cDMARDS. This change in PsA management highlights a need for further research on the relative safety, efficacy, and cost of biologic agents to better guide evidence-based treatment decisions.

Disclosure of Interests: Amir Haddad: None declared, Faten Tatour: None declared, Tal Gazitt: None declared, Ilan Feldhaimer: None declared, Irina Bergman: None declared, Amnon Cohen Grant/research support from: Prof. Amnon Cohen received research grants from Janssen, Novartis and AbbVie and Sanofi, Consultant for: Prof. Amnon Cohen served as a consultant, advisor for AbbVie; Amgen; Boehringer Ingelheim; Dexcel pharma; Janssen, Lilly; Neopharm; Novartis, Perigo; Pfizer; Rafa; Sanofi, Speakers bureau: Prof. Amnon Cohen served as speaker for AbbVie; Amgen; Boehringer Ingelheim; Dexcel pharma; Janssen, Lilly; Neopharm; Novartis, Perigo; Pfizer; Rafa; Sanofi, Devy Zisman Grant/research support from: Dr D Zisman served as a consultant, for AbbVie, Amgen; Boehringer Ingelheim; Dexcel pharma; Janssen, Lilly; Neopharm; Novartis, Pfizer; Rafa; Sanofi, Speakers bureau: Prof. Devy Zisman served as speaker for AbbVie; Amgen; Boehringer Ingelheim; Dexcel pharma; Janssen, Lilly; Neopharm; Novartis, Pfizer; Rafa; Sanofi, Speakers bureau: Dr D Zisman served as a speaker for AbbVie, Janssen, Lilly, Novartis, Pfizer, Sanofi DOI: 10.1136/annrheumdis-2019-eular.6001

AB0788 LUPUS CO-MORBIDITY IN PATIENTS WITH PSORIATIC ARTHRITIS: A POPULATION-BASED CASE-CONTROLLED STUDY

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Background: Patients with psoriasis and psoriatic arthritis (PsA) can develop a variety of comorbidities including metabolic syndrome, diabetes, hypertension, cardiovascular diseases and depression. Comorbidities, in turn, may influence the therapeutic regimen and affect treatment results. Previous studies show a high incidence of coexistence of psoriasis and systemic lupus erythematosus (SLE). Unlike psoriasis, the coexistence of PsA and SLE has been reported only in case reports. The purpose of this study was to assess agreement by experts on recommended disease activity assessment in PsA patients and to develop a consensus definition of clinical remission.

Methods: The study, which was conducted from 2002-2017, is a retrospective study on a PsA cohort consisting of 4,836 PsA patients matched for age and sex with 24,180 randomly selected control patients. Data on this cohort was derived from the database of more than 4.3 million people enrolled in the largest health care provider in Israel, Clalit Health Services. The database was used to extract demographic data, such as age, sex, ethnicity and socioeconomic status; clinical and laboratory manifestations of SLE; medication dispensation and SLE-inducing medications. T-test was used to compare continuous variables and a Chi-square test was used for categorical variables. All tests were 2-sided; p values of <0.05 were considered statistically significant.

Results: The PsA study group consisted of 4,836 subjects, at a median age of 56±15, 2603 (53.8%) of whom were females. The control group consisted of 24,180 subjects matched for age and sex. 18 patients (0.37%) in the PsA study group, and 39 patients (0.16%) in the control group where diagnosed with SLE (p=0.002). SLE patients without co-existing PsA had higher anti-double stranded DNA (anti-dsDNA) positivity (92.3% vs 66.7%, p=0.022) and positive anti-cardiolipin (ACL) antibodies (46.2% vs 16.7%, p=0.041). No other significant differences were observed between the two groups in terms of clinical and laboratory manifestations of SLE. PsA patients with concomitant SLE compared to PsA patients without SLE were more often female (100% vs 53.7%, p<0.0001), had more osteoporosis (38.9% vs 12.8%, p=0.005) and were more likely to be treated with beta blockers (27.8% vs 9.8% p=0.027). Usage of medications with known potential to induce SLE prior to diagnosis of SLE was higher in the study group of PsA patients (11 out of 18 patients) than in the control group, but there was no difference in SLE manifestations between these two groups. Cutaneous manifestations associated with later onset of SLE included proton pump inhibitors (PPI) [0.27% in the PsA cohort vs 0.1% in the control group (p=0.004)], beta blockers [0.33% vs 0.16% (p=0.011)], angiotensin converting enzyme inhibitors, and angiotensin II receptor blockers [ACE-I] (0.35% vs 0.03%, p=0.001), thiazide diuretics [0.35% vs 0.1% (p=0.001)], anti-tumor necrosis factor (anti-TNF) agents [0.4% vs 0.2% (p=0.002)]. Conclusion: A 2.3 fold increase in the prevalence of SLE in PsA patients than in the control group was found in our study population. There were no significant differences in the clinical and laboratory manifestations of SLE between these two groups. The positive correlates between SLE and PsA may point to common underlying pathogenetic pathways and may affect treatment choices and medication development. More research is needed for a better understanding of this diseases association.

Disclosure of Interests: Danielle Korkus: None declared, Tal Gazitt: None declared, Ilan Feldhaimer: None declared, Idit Lavii: None declared, Amir Haddad: None declared, Erez Ba’at: None declared, Sari Greenberg-Dotan: None declared, Amnon Cohen Grant/research support from: Prof. Amnon Cohen received research grants from Janssen, Novartis and AbbVie and Sanofi, Consultant for: Prof. Amnon Cohen served as a consultant, advisor for AbbVie; Amgen; Boehringer Ingelheim; Dexcel pharma; Janssen, Lilly; Neopharm; Novartis, Perigo; Pfizer; Rafa; Sanofi, Speakers bureau: Prof. Amnon Cohen served as speaker for AbbVie; Amgen; Boehringer Ingelheim; Dexcel pharma; Janssen, Lilly; Neopharm; Novartis, Pfizer; Rafa; Sanofi, Speakers bureau: Dr D Zisman served as speaker for AbbVie; Amgen; Boehringer Ingelheim; Dexcel pharma; Janssen, Lilly; Neopharm; Novartis, Perigo; Pfizer; Rafa; Sanofi, Devy Zisman Grant/research support from: Dr D Zisman served as a consultant, for AbbVie, Amgen; Boehringer Ingelheim; Dexcel pharma; Janssen, Lilly; Neopharm; Novartis, Pfizer; Rafa; Sanofi, Speakers bureau: Prof. Devy Zisman served as speaker for AbbVie; Amgen; Boehringer Ingelheim; Dexcel pharma; Janssen, Lilly; Neopharm; Novartis, Pfizer; Rafa; Sanofi, Speakers bureau: Dr D Zisman served as a consultant, for Pfizer, Abbvie, Novartis, Ellie-Lilly, Sanofi, Speakers bureau: Dr D Zisman served as a speaker for AbbVie, Janssen, Lilly, Novartis, Pfizer, Sanofi DOI: 10.1136/annrheumdis-2019-eular.3546

AB0788B RECOMMENDATIONS FOR DISEASE ACTIVITY ASSESSMENT AND DEFINITION OF CLINICAL REMISSION IN PSORIATIC ARTHRITIS: A DELPHI-BASED EXPERT CONSENSUS

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Background: Patients with psoriatic arthritis (PsA) have heterogeneous clinical presentations, with diverse articular and dermatological features and varied disease courses and outcomes, so the assessment of disease activity implies important difficulties. Although the goal of treatment of PsA is to achieve remission, there is no a universally accepted definition. Objectives: The purpose of this study was to assess agreement by experts on recommended disease activity assessment in PsA patients and to develop a consensus definition of clinical remission. Methods: A modified Delphi approach was used as a consensus method. A scientific committee of experts provided 86 statements that were submitted in 2 rounds to a panel of 130 Spanish experts in PsA (in September and October 2018, respectively), addressing issues regarding the current assessment of remission, variables that should be included in the assessment of PsA patients and the definition of remission, and the use of disease activity scores. Results: The expert panel reached agreement for 53 proposed statements (81.6%). There was consensus that the definition of remission in PsA should include: the absence of signs and symptoms, physical well-being, absence of impact of the disease, the absence of inflammation and progression in imaging tests (radiography and magnetic resonance) and the absence of inflammation measured by biomarkers (ESR, CRP). It is recommended to use some index designed specifically for the assessment of disease activity and the variables that should include the minimal assessment of PsA patients are: painful/swollen joints, enthesitis, dactylitis, axial involvement, skin and nail involvement, physical function, quality of life, structural damage assessed by imaging techniques, CRP, both patient and physician global assessment, both patient and physician skin assessment and extra-articular manifestations. The use of a treat-to-target (T2T) strategy should be considered in PsA patients, especially in those with...
PSORIATIC ARTHRITIS IN PATIENTS DIAGNOSED WITH PSORIASIS: ASSISTING DERMATOLOGY CONSULTATION IN A COHORT OF THE DOMINICAN REPUBLIC

Artely Altagracia Tapia Bézé, Franchesca Alziveiro Polanco, Esthela Loyola de López, Carmen Tineo, Glenny Paulino, Catherine Rodríguez, Idelfi Sánchez, Hospital José María Cabral y Bézé, Santiago De Los Caballeros, Dominican Republic

Background: Psoriatic arthritis (PsA) is a disease of an inflammatory, heterogeneous nature that involves skin, nails, peripheral and axial joints, as well as the entheses. Due to its systemic involvement, it makes diagnosis and therapy a challenge in clinical practice. (1) It has been estimated that around 6% to 41% of patients with Psoriasis (PsO) will develop PsA, finding an accumulated incidence of 1.7% at 5 years of diagnosis of PsA, 3.1% at 10 years and 5.1% at 20 years. (2) In the Dominican Republic we do not have studies that characterize this pathology, so it would be interesting to be able to specify the clinical course, as well as the risk factors and associated prognoses for the development of this entity.

Objectives: To determine the factors associated with psoriatic arthritis in patients diagnosed with psoriasis attending the Dermatology service. Methods: A multicenter, descriptive study of primary and secondary source data collection was conducted at the Psoriasis clinic of the Regional University Hospital José María Cabral and Bézé, Cibao Regional Dermatological Institute and the Foundation to support patients with psoriasis and psoriatic arthritis (FUNAPAPSO), in the period of August-December 2018, the universe consisted of 304 patients, 103 patients met inclusion criteria. After signing informed consent, a form was completed that included general, clinical, serological and image data. Analysis of the variables was performed and Chi 2 was used, considering statistical significance p < 0.05.

Results: Of a total of 103 patients with psoriasis, the mean age was 40 ± 13 years, 63.1% male, 36.9% female. The prevalence of psoriatic arthritis by CASPAR criteria was 36.89%. The presentation of arthritis was asymmetric oligoarthritis in 56.52%, symmetric polyarthritis 21.74% and distal interphalangeal arthritis 13.04%. Radiographic findings were present in 7.7% (p = 0.00) of patients with PsA. The forms of presentation of PsO that were most associated with arthritis were plaques 48.57% (p = 0.00) and drop 12.5% (p = 0.01). The quality of life was average in patients with PsA and a proposal for definition of clinical remission was made that may be useful in the management of PsA patients.

Conclusion: Based on the available evidence and expert consensus, recommendations have been made for disease activity assessment in PsA and a proposal for definition of clinical remission was made that may be useful in the management of PsA patients.

Disclosure of Interests: None declared


AB0789 AN EHEALTH TOOL TO PREPARE A FIRST ORTHOPAEDIC CONSULTATIONS: A USE AND USABILITY STUDY

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Background: The use of eHealth technology to prepare first orthopaedic consultations for patients with hip or knee osteoarthritis seems promising. Exploration of data on use and usability of an educational eHealth tool can reveal potential modifications that may increase engagement and effectiveness.

Objectives: 1) to identify use and usability of a standalone educational eHealth tool for patients with suspected hip or knee osteoarthritis (OA), 2) to explore if recorded questions in the eHealth tool were in line with an existing widely used question prompt list, and 3) to investigate if user characteristics are related to use and usability.

Methods: We used data of 144 patients who used the educational eHealth tool to prepare an upcoming first orthopaedic consultation. We defined ‘users’ and ‘non-users’ based on opening the tool at least once or not. ‘Users’ were specified as ‘active’ and ‘passive’. Recorded questions in preparation for the upcoming consultation were categorized into 3 themes: ‘What are my options?’, ‘What are the possible benefits and harms of those options?’, and ‘How likely are each of the benefits and harms to happen to me?’, or in a ‘remaining’ category. Usability was measured using the System Usability Scale (SUS, 0-100). We collected data on demographic and clinical characteristics, knowledge on OA and internet and smartphone usage in daily life. Characteristics associated with ‘users’ and ‘non-users’ were analysed using multivariable logistic regression analysis.

Results: A total of 116 (81%) participants used the educational eHealth tool, of whom 87 (75%) were ‘active users’. Out of 3 components (Information, My consultation and Medication), Medication was least used (34%). Based on the recorded questions of users a fourth predefined question could be proposed, i.e. “What is my situation at this moment?”. Mean (SD) SUS score was 64.8 (16.0). No difference was found in SUS scores between superficial and active users (mean difference (95% CI): 0.04 (-1.69, 1.77)). Participants with higher baseline knowledge on OA (OR (95% CI): 1.2 (1.0, 1.4)), who used the internet less frequent in daily life (OR (95% CI): 0.6 (0.5, 0.9)) were more likely to use the educational eHealth tool. We found no differences in demographic and clinical characteristics between superficial and active users.

Conclusion: Based on the results of this study it can be concluded that the use of an educational eHealth tool to prepare a first orthopaedic consultation in patients with hip and knee OA is feasible. Results provide points for improvements to the content of the tool to improve usability. No clear practical implications were found in this study to support implementation of the educational eHealth tool in specific subgroups.

Disclosure of Interests: None declared


Osteoarthritis

REFERENCES

Disclosure of Interests: None declared

EVALUATING THE EFFECTIVENESS OF INTRA-ARTICULAR KNEE INJECTION USING ALLOGENIC PLATELET DERIVED LYOPHILIZED GROWTH FACTORS IN EGYPTIAN PATIENTS WITH SYMPTOMATIC PRIMARY KNEE OSTEOARTHRITIS

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Background: Using intra-articular injections of autologous platelet-rich plasma (PRP) has shown promising results in treatment of knee osteoarthritis (KOA). Its regenerative properties depends on the amount of growth factors (GF) released after platelets activation. Using large-volume of blood for obtaining allogenic PRP can provide higher concentrations of platelet and GF. However once prepared, PRP is stable for only 8-hours. Freeze drying (lyophilization) can be used to stabilize the biological materials for prolonged storage without causing their damage [1].


Methods: 30 patients with symptomatic primary KOA, diagnosed according to revised criteria of the ACR (2), were enrolled. Local ethical approval was obtained. All patients had given a written informed consent. The study group was equally randomized into intervention and control groups. Both was subjected to baseline functional assessment using WOMAC score; evaluating pain, stiffness, and physical function (3), and ultrasonography (US) assessment of knee effusion. The patients in control group were kept on their medications without intervention. The intervention group was received two doses of L-GF; at baseline and after 2-months. L-GF was prepared from platelets derived from individual whole blood donations. Each unit of platelets was tested in and found to be non-reactive for HBsAg, HIV I & II antibodies, HCV antibodies and antibodies to Treponema Paldum, by licensed assay methods. Seronegative plasma were further examined by Nuclear Acid Testing. Further viral inactivation by UV-radiation and Riboflavin by the Mirasol system was done. The platelets in the buffy coat layer were activated using CaCl2 to release their GF. Excess water, cellular elements and fibrinogen were removed and the remaining GF were “ultraconcentrated.” Lyophilization of the obtained GF was then processed. The L-GF was supplied as powder in tightly sealed container and was stored at 2° to 8° C. Prior to use, reconstitution of the product was done using 1-ml saline and 1-ml lignocaine then the mixture was kept at ambient temperature for 5-min. to ensure complete protein re-hydration. After 6-months the WOMAC score and knee US were repeated for all participants. Then percent of improvement of WOMAC and US detected effusion were calculated for all patients.

Results: The patients in the intervention group was significantly older (56 ±9 years) and had higher BMI (38±5.3 kg/m²) in comparison to control (44±11 years, 33±5.6 kg/m²). Both groups showed statistically insignificant difference regarding the baseline total WOMAC score and radiographic assessment. Post injection pain was reported by all patients in intervention group, it lasted only for 2.4±0.83 hours and was graded as mild. The mean of total WOMAC score and its 3-components in addition to knee effusion were decreased significantly in the intervention group after 2 months and 6 months of follow-up (figuer-A). After 6-months, the intervention group showed statistically significant percentage of improvement regarding WOMAC scores and effusion in comparison to the control (figuer-B).

Conclusion: Allogenic L-GF was well tolerated and showed encouraging results in patients with symptomatic KOA, regarding improvement of pain, stiffness and function in addition to decreasing knee effusion.

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Disclosure of Interests: Rasmia Elphohay: None declared, Amany Diab: None declared, Hala Elgndy: None declared, Hossam Fahmy: None declared, Kamel Gado Speakers bureau: have been paid as a speaker to pharmaceutical companies (Novartis, EVA pharm) and also to attend their advisory board

ONE VERSUS TWO INJECTIONS OF INTRA-ARTICULAR HIGHLY CROSS-LINKED HYALURONAN YEARLY IN PATIENTS WITH KNEE OSTEOARTHRITIS: INSIGHTS FROM ROUTINE CLINICAL PRACTICE

Tsvetoslav Georgiev, Rumen Stoilov, University Hospital “St. Ivan Rilski” – Sofia, Clinic of Rheumatology, Sofia, Bulgaria

Background: Hyaluronic acid (HA) is a natural polysaccharide, which is an important structural component of synovial-fluid and cartilage. There are different injectable forms of HA used for clinical application. Highly cross-linked/high-molecular-weight hyaluronans (HMWHA) provide additional stability and improve functionality [1], resulting in longer bioavailability in the knee joint and promoting viscoeluduction [2]. A direct comparison between the two most common injection protocols of HMWHA in our routine practice is of great practical interest, since viscosupplementation is among the most commonly used treatment modalities for patients with knee osteoarthrits (KOA) in Bulgaria [3].

Objectives: Our aim was to compare the clinical effectiveness of two different regimens for injecting intra-articular HMWHA in KOA patients under ‘real-world’ conditions in routine clinical practice.

Methods: This prospective, open-label, observational study included 50 patients with KOA who were followed for a period of 1 year. They were divided into two therapeutic arms according to their preselected treatment regimen: patients injected once with HMWHA (n = 25; group 1) at baseline and patients injected twice 6 months apart with HMWHA (n = 25; group 2). A 100-mm visual analogue scale (VAS) for pain, disease-specific (Western Ontario & McMaster Universities Osteoarthritis Index [WOMAC]) and generic (health assessment questionaire – disability index [HAQ-DI]) questionnaires were used to evaluate patients at baseline, three months, six months, and one year later. Standardized radiographs were obtained at baseline and after one year. The response to the treatment was determined using the OMERACT-OARSI set of responder criteria [4].

Results: A single injection of HMWHA resulted in a statistically significant improvement in pain even at 12 months (ΔVAS = 10.12 ± 14.5 mm, p < 0.05), although the effect progressively decreased after the third month when ΔVAS was 18 ± 14.31 mm, p < 0.05 (Figure 1). If the two regimens of HA injections were directly compared, the mean difference of pain improvement for the year of follow-up was about 9 mm in favor of group 2, but this result was not “statistically” significant (10.12 vs 19.16 mm, p > 0.05). Physical function was statistically improved in both

PATIENTS WITH KNEE OSTEOARTHRITIS: INSIGHTS FROM ROUTINE CLINICAL PRACTICE

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groups (p < 0.05) without any statistically significant difference. Respondents in the first group in the end of the year were 40% (10/25) and 60% (15/25) in group 1 and group 2, respectively (p > 0.05). In the end of the follow-up period HAQ-DI did only statistically improve among patients in group 2.

Fig.1. Mean change in 100-mm VAS values for pain over time in both groups

Conclusion: If maximal symptomatic relief is our primary goal, it would be logical to choose a two-injection regimen. However, if we take into account the financial aspect, we may be satisfied with a single injection of highly cross-linked HA over a year.

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Disclosure of Interests: Tsvetoslav Georgiev: None declared, Rumen Stoilov: Speakers bureau: Abbvie, Pfizer, Amgen, UCB, Novartis


AB0792 CURCUMIN IN OSTEOARTHRITIS TREATMENT: THE PRESENT STATE OF EVIDENCE

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Background: Osteoarthritis (OA) is a degenerative disease of the joint occurring in elderly population. According to World Health Organization, its worldwide prevalence ranges from 11.8% to 12.7%. Since it is known that OA has an inflammatory cause, with IL-1 being the key cytokine, that OA has an inflammatory cause, with IL-1 being the key cytokine, that IL-1 and TNF-a being the key cytokines that drive the production of inflammatory mediators and matrix-degrading enzymes, the compounds with anti-inflammatory properties are targeted as therapeutic options for osteoarthritis treatment. Curcumin is a plant-derived compound extracted from the rhizomes of turmeric (Curcuma longa). It has been demonstrated as an effective anti-inflammatory and antioxidative agent. In vitro studies have shown that curcumin can block the activation of NF-kB system in the chondrocytes. Therefore, it prevents the apoptosis of chondrocytes, suppress the release of proteoglycans and metalloproteinases and expression of cyclooxygenase, prostaglandin E-2, and inflammatory cytokines in chondrocytes. Besides its influence on inflammatory markers, clinical trials also demonstrated curcumin’s effects in pain and function in patients with osteoarthritis.

Objectives: The purpose of this paper is to critically review evidences regarding the role of curcumin in osteoarthritis treatment.

Methods: PubMed/MEDLINE, Lilacs, and SCIELO databases were searched using the terms “curcumin” AND “osteoarthritis” without imposing time limitations. The search was limited to humans and to the English and Portuguese languages. Studies that met the following inclusion criteria were included in the review: 1) clinical trials that evaluated the effects of curcumin on osteoarthritis. The selection phase involved a review of abstracts and an examination of the full text based on the eligibility criteria and the last search was conducted on January 2019.

Results: Overall, 9 clinical trials involving a total of 797 patients met the inclusion criteria. The studies have a degree of heterogeneity concerning the dosage, treatment duration, objectives and endpoints, but the main objectives were to evaluate the efficacy and safety of curcumin in osteoarthritis treatment. All studies have shown a beneficial effect of curcumin supplementation in the treatment of osteoarthritis, mainly in reduction of pain, stiffness, improvement of physical function, decrease the use of NSAIDs and other painkillers. Results also showed a decrease on inflammatory markers.

Conclusion: The studies demonstrated that curcumin is clinically effective as a long term adjuvant treatment of osteoarthritis further to an excellent tolerability. However, large and well-designed randomized controlled trials are warranted to confirm the use of curcumin in osteoarthritis treatment.

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AB0793 LONG-TERM USE OF AMTOLMETIN GUACIL IN PATIENTS WITH OSTEOARTHRITIS, RHEUMATOID ARTHRITIS AND ANKYLOSING SPONDYLITIS

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Background: Long-term use of nonsteroidal anti-inflammatory drugs (NSAIDs) is used to control of chronic pain in osteoarthritis (OA), rheumatoid arthritis (RA) and to prevent the progression of ankylosing spondylitis (AS). Amtolmetin guacil (AMG), which has a low risk of gastrointestinal complications, may have advantages for long-term use.

Objectives: To evaluate the effect and safety of long-term use of AMG. Methods: AMG 600-1800 mg/day was prescribed to 442 patients with OA (60.6 ± 10.2 years, women 88.7%), 126 with RA (55.0 ± 14.0 years, women 84.2%) and 73 with the AS (47.0 ± 12.0 years, women 30.0%). The primary end point was the dynamics of pain on a numerical rating scale (NRS), additional for OA - WOMAC pain and HAQ, for RA - DAS28-CRP, for AS - BASDAI, BASFI and ASDAS-CRP. The result of treatment was evaluated on 3 consecutive visits after 3 months (9 months of treatment).

Results: After 9 months 65.2% of OA patients, 75.3% of RA patients, and 82.2% of AS patients continued to take AMG. In end of study, the median of pain decreased with OA from 5.6 [4.1-6.9] to 3.4 [1.7-5.1], with RA from 5.8 [4.0-7.5] to 3.4 [2.0-4.8], with AS from 5.8 [4.2-7.5] to 3.1 [1.5-5.0] NRS (p <0.001). In OA WOMAC pain decreased from 127 [24-159] to 13.7 [14-40], p <0.001, HAQ from 0.54 ± 0.44 to 0.34 ± 0.26, p <0.001. With RA, the average value of DAS28 decreased from 4.81 ± 1.18 to 4.30 ± 1.24, p <0.05. In AS, the median BASDAI index decreased from 4.5 [1.0-8.0] to 3.0 [0.0-8.0], p <0.001. The number of AS patients with high activity on the ASDAS-CRP index (> 3.5) decreased from 76.9% to 25.8%, p <0.001. The BASFI index has not changed. 77.9% of patients with OA, 77.0% of patients with RA, and 74.5% of patients with AS were satisfied with the results of AMG treatment.
AMG tolerability was good. 15-25% patients had mild dyspepsia. Discontinuation of therapy due to side effects was only in 6 patients (0.9%). The development or worsening of arterial hypertension, as well as other cardiovascular complications, was not observed.

Conclusion: AMG is an effective, well-tolerated NSAIAD, which is appropriate for long-term treatment of OA, RA and AS.

Disclosure of Interests: None declared

AB0794 PATIENTS GENOTYPE AND OA TREATMENT EFFICACY

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Background: It is known that some genes (FDPS, LCT, VDR) which determine the calcium, vitamin D and lactate metabolism may have impact on osteoarthritis (OA) development and course, and thus, has a possible influence on OA treatment efficacy.

Objectives: To determine the influence of genetic factors (genotyping of FDPS, LCT, VDR) on the efficacy of standard and modified treatment (with use of the platelet autologous plasma (PAP) in the early stages of knee OA.

Methods: WOMAC index and the frequency of genotype variants for the FDPS, LCT, and VDR genes were studied in 96 patients (57 women, 38 men, 41.7 ± 1.2 years old) with primary knee OA (X-ray stage I-II). All patients had OA exacerbation with no clinical evidence of synovitis. Enrolled patients were divided into 2 groups: the first group consisted of 49 patients (27 women, 22 men, mean age 41.7 ± 1.2 years) who agreed to receive standard OA treatment (NSAIAD, exercises, orthopedic devises – as needed) and 3 intra-articular PAP injections (2 courses in 12 month, plasma volume 12-15ml/course, total platelet count per injection 1260,24 ± 22,1x10 9). The second group - 47 patients with OA who received standard treatment. Both groups were comparable by age, gender, body mass index and initial WOMAC. Genetic parameters and its influence on OA course and treatment efficacy was analyzed during 12 months.

Results: The earliest age (37.2 ± 2.01 years) of clinical manifestation of knee OA was connected to homozygous genotype variants: LCT (relative risk 6.3:1), FDPS (relative risk 6.5:1) and VDR (relative risk 6.8:1). The earliest age (37.2 ± 2.01 years) of clinical manifestation of knee OA was connected to homozygous genotype variants: LCT (relative risk 6.3:1), FDPS (relative risk 6.5:1) and VDR (relative risk 6.8:1). The earliest age (37.2 ± 2.01 years) of clinical manifestation of knee OA was connected to homozygous genotype variants: LCT (relative risk 6.3:1), FDPS (relative risk 6.5:1) and VDR (relative risk 6.8:1). The earliest age (37.2 ± 2.01 years) of clinical manifestation of knee OA was connected to homozygous genotype variants: LCT (relative risk 6.3:1), FDPS (relative risk 6.5:1) and VDR (relative risk 6.8:1). The earliest age (37.2 ± 2.01 years) of clinical manifestation of knee OA was connected to homozygous genotype variants: LCT (relative risk 6.3:1), FDPS (relative risk 6.5:1) and VDR (relative risk 6.8:1).

Conclusion: age of knee OA clinical manifestation and the treatment efficacy was analyzed during 12 months.

Disclosure of Interests: None declared

AB0795 IMPACT OF PRIMARY HAND OSTEOARTHRITIS ON MICROSTRUCTURE AND BIOMECHANICS IN FINGER JOINTS

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Background: Despite distinct aetiologies of joint diseases, the osteoarthritic end-stage of primary osteoarthritis and rheumatoid arthritis are described using similar radiological features. However, primary and secondary osteoarthritis may be different at the bone-cartilage unit depending on the pathogenesis.

Objectives: The main purpose was to investigate the histological differences in the bone-cartilage unit of the hip joint in patients with primary osteoarthritis and patients with secondary osteoarthritis due to rheumatoid arthritis.

Methods: Femoral heads were obtained during arthroplasty from 12 patients with primary osteoarthritis and six patients with secondary osteoarthritis due to rheumatoid arthritis.

Results: Twelve femoral heads from healthy age- and sex-matched subjects were obtained post-mortem. Femoral heads were investigated, using stereological methods to provide unbiased quantitative data. The femoral head, articular cartilage, calcified cartilage, subchondral bone, and osteophytes were measured.
Conclusion: Patients with secondary osteoarthritis due to rheumatoid arthritis had thinner articular cartilage and calcified cartilage but were otherwise not significantly different from patients with primary osteoarthritis. Thus, the inflammatory joint in rheumatoid arthritis was associated with a more pronounced loss of cartilage than the degenerative joint disease in primary osteoarthritis. The thicker calcified cartilage in primary osteoarthritis has been attributed to endochondral ossification; this does not seem to be the case in rheumatoid arthritis.

Acknowledgement: The authors are grateful for the technical assistance of Jette Barlach and Rita Ullerup. This work was financially supported by the Danish Rheumatism Association.

Disclosure of Interests: Rasmus Klose-Jensen: None declared, Anne Friesgaard Christensen: None declared, Louise Brandt Hartlev: None declared, Lene Warner Thonup Boel: None declared, Mogens Berg Laursen: None declared, Kresten Kruup Keller Speakers bureau: Have received speaking fee from Pfizer, Ellen Margrethe Hauge Grant/research support from: Have received grants from Roche and Novartis, outside the submitted work, Speakers bureau: Have received personal fees from MSD, Pfizer, UCB and Sobral


AB0797 GRANULYSIN MEDIATED CYTOTOXICITY AND ITS SERUM CONCENTRATION IN PATIENTS WITH KNEE OSTEOARTHRITIS

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Background: In OA joint, synovial membrane contain immunocompetent cells (1-4), which produce predominantly pro-inflammatory cytokines (2,5), justifying the name “osteoarthritis” and directing the development of disease towards mild systemic inflammatory condition (6). Granulysin (GNLY) is mediator of cellular immunity expressed in T and NK cells in 15 KDa precursor and 9 KDa cytoplasmic form (2). It is regulated by interleukin 15. We investigated GNLY expression in peripheral blood lymphocytes and GNLY mediated apoptosis in vitro, serum concentration of IL-15 and the correlation of GNLY expression with intensity of the pain in the knee of OA patients and with 6-minute walk distance.

Objectives: Women with knee OA (20), and healthy control (17) were medically examined, and their blood samples tested. All of them signed informed consent before medical sampling of peripheral blood (PB).

Methods: Visual analogue scale (VAS) of pain and results of 6-minute walk test were noticed in all participants. Peripheral blood mononuclear cells were isolated by gradient density centrifugation and intracellular GNLY labeling in CD3-CD56-NK cells, CD3+CD56- T cells and CD3 +CD56- NK cells was performed and analyzed by flow cytometry. NK cells' apoptotic activity against NK sensitive K-562 cells was measured in 18-hour PKH-26 (red) cytotoxicity assay with evaluation of propidium iodide-annexin V+ target cells by flow cytometry. In some samples anti-GNLY and/or anti-perforin antibodies were added. IL-15 concentration was measured by ELISA. Nonparametric Kruskal-Wallis and Mann-Whitney U-test, as well as Spearman correlation test were used for statistical evaluation.

Results: In lymphocytes of OA patients GNLY expression and NK cell-mediated apoptosis of K-562 cells did not differ significantly from the healthy control. In OA patients only, RC8 antibody against cytosolic GNLY molecule significantly decreased apoptosis of K-562 cells. RF10 anti-15 kDa GNLY did not show such effect. Anti-perforin antibody completely abolished apoptosis in both groups tested and the effects of additionally added RC8 or RF10 anti-GNLY antibodies were not observed. Serum IL-15 concentration in healthy controls and OA patients was low and did not show statistically significant difference. GNLY expression in lymphocytes, and particularly in NK subset, positively correlated with VAS of pain and 6-minutes walking distance.

Conclusion: In OA patients, GNLY mediated apoptosis is involved in apoptosis of NK sensitive K-562 cells in vitro and might be involved in the killing of damaged joint cells in vivo after direct contact.

REFERENCES


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Disclosure of Interests: Gordana Laskarin Speakers bureau: Yes, at the congresses and meetings, Viktor Persic Speakers bureau: At some meetings and congresses, Merica Aralica: None declared, Bozena Curko-Cofek: None declared, Marija Rogoznica: None declared, Ivan Rosovic: None declared, Tamara Kauzlarc-Zivkovic: None declared, Sandra Rusac-Kukic: None declared, Daniel Rukavina: None declared


AB0798 GENDER DIFFERENCES IN DURATION OF SYMPTOMS AND PREOPERATIVE EXPECTATIONS IN TOTAL KNEE ARTHROPLASTY PATIENTS

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1In addition to authors, the study group consist of: H. van der Linden-van der Zwaag, B. Kaptein, LUMC; S. Vehmeijer, Reinier de Graaf Hospital, R. Onstenk, Groene Hart Hospital, S. Verdegaal, Alrijne Hospital, H. Kapjin, LangeLand Hospital.

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Background: The literature suggests that women with knee osteoarthritis (OA) perceive greater disability and a lower functional level before total
ART- QUALIVIE: ASSESSMENT OF THE QUALITY OF Disclosure of Interests: DOI: 10.1136/annrheumdis-2019-eular.4120 Patrice Vincent4, Hakima Miotti5, Isabelle Bardoulat5, Cathy Maillard5. men seemed to perceive less symptoms and restrictions in daily activities Conclusion: Preoperatively, men reported a longer duration of symptoms was longer in men than women: <1 year: 11.3% versus 9.6%, 1-5 years: 38.8% versus 49.7%, 5-10 years: 18.3% versus 20.0% and > 10 years: 31.5% versus 20.7%. Finally, women had significantly higher expectations of postoperative outcomes of TKA between men and women regarding the duration of symptoms and preoperative expectations were examined by the means of the Chi-Square test and independent t-test and difference with the 95% Confidence Interval (CI) respectively. Results: A total of 1543 patients, 556 men (mean age 71 (SD 8), 32.3% paid employment) and 987 women (mean age 71 (SD 9), 20.3% paid employment) were included. Women had more pain preoperatively than men, 5.3 (SD 3) versus 4.3 (SD 3) at rest and 7.1 (SD 2) versus 6.2 (SD 9) during activity, respectively. Furthermore, on each KOOS subscale compared to women, the duration of symptoms was longer in men than women: <1 year: 11.3% versus 9.6%, 1-5 years: 38.8% versus 49.7%, 5-10 years: 18.3% versus 20.0% and > 10 years: 31.5% versus 20.7%. Finally, women had significantly higher expectations of postoperative TKA outcomes than men, 67.4 (SD 19) and 70.2 (SD 19), respectively (Mean Difference: 2.79, 95% CI 0.84-4.75). Conclusion: Preoperatively, men reported a longer duration of symptoms and had lower expectations of TKA outcomes than women. However, men seemed to perceive less symptoms and restrictions in daily activities despite a longer duration of symptoms.


AB0799 ART- QUALIVIE: ASSESSMENT OF THE QUALITY OF LIFE OF PATIENTS WITH KNEE OSTEOARTHRITIS SIX MONTHS AFTER TREATMENT WITH THREE INTRA-ARTICULAR INJECTIONS OF ARTHRUM H 2% 1Mika Maravic1; Christian Pascaretti2, Paolo Insalaco2, Antoine Lesort3, Patrice Vincent1, Hakima Miotti4, Isabelle Bardoulat5, Cathy Maillad5. LCA pharmaceuticals (France) – LCA pharmaceuticals (France) – LCA Pharmaceutical, Chartres, France – LCA Pharmaceutical, Chartres, France.

Background: Knee osteoarthritis (KOAG) is a chronic condition affecting mainly the elderly and considered as the leading cause of disability after cardiovascular disease. KOA is characterized by functional discomfort and deformities, leading to a deterioration in the quality of life (QoL) of patients.

Objectives: The main objective was to demonstrate that 3 intra-articular injections of ARTHRUM H 2% improves the physical QoL of patients over a 6-month period. Methods: A French observational, prospective, multi-centre study was conducted between 2012/2017 in 30 French centres in patients over 40 suffering from knee pain. WOMAC scores were collected at baseline and at 2, 6 and 12 months. The primary endpoint was the change in WOMAC scores from baseline to 180 days (paired Student t-tests). Logistic regression analyses were used to identify the main drivers of significant increase of physical summary score, adjusted for sociodemographic and health covariates. Results: Of the 134 patients treated with ARTHRUM H 2% included in the study, 115 were evaluable for the primary outcome (non-expansible data for 19 patients). The baseline characteristics of the analysable population were as follows: mean age of 66.4 years (±10.7); majority female (66.4%); mean BMI of 28.7 (±5.3) kg/m² (43.3% overweight and 35.1% obese); KL grade KOA grade I: 13.6%, II 40.2%, III 46.2%, localization: uni-compartimental 53.0% (78.6% medial, 15.7% lateral, 5.7% patellofemoral), bi-compartimental 40.2% and tri-compartimental 6.8%. Regarding management history, respectively 6.7% and 44.8% of patients had previously received physical therapy or rehabilitation, and visco-supplementation (2.2 treatments on average). Comorbidities observed in 73.9% of patients were metabolic-related in 54.5%, cardiovascular-related in 46.3%, gastrointestinal-related in 20.9%, and neuropsychiatric-related in 8%. A clinically and statistically significant improvement in the QoL of patients was observed with an increase from 40.0 at baseline to 44.8 at 6 months (p<0.001). A significant improvement was achieved during the 3 months following visco-supplementation (D0: 40.0 vs. D90: 44.8) and maintained from three to 6 months from baseline (D90: 44.8 vs. D180: 44.9).

The factors significantly associated with an improvement in QoL were: grade III KOA (OR=5.254, p=0.032), grade II KOA (OR=3.507, p=0.100), and a single history of osteoarthritis (OR=2.936, p=0.044).

Conclusion: ART-QUALIVIE is a French study providing real-world data on the evolution of QoL of visco-supplemented KOAG patients. It has demonstrated the positive impact of ARTHRUM H 2% on the QoL of patients over the 3 months following injections maintained until 6 months after treatment.

Objectives: Different biomarkers were selected to be measured in APPROACH patient samples for prospective predictive and prognostic analyses. Here we describe the biological rational, reference ranges and technical performance of the selected biomarker.

Methods: The APPROACH cohort includes 300 OA patients recruited based on the APPROACH enrichment model (www.approach.eu), in the period from 2017 and 2019. Serum and urine will be collected at baseline, 6, 12 and 24 months, as well as pain, radiographic and MRI assessments.

Results: Eighteen exploratory and technically validated biomarkers reflecting joint tissue (i.e. cartilage, bone, synovium) turnover were chosen based on following characteristics; i) has shown association with OA pathogenesis (published data such as OA1); ii) has shown diagnostic or prognostic potential 2; iii) GLP or GMP certified assay production with acceptable technical performance (e.g. precision and linearity data, table); iv) readily availability of the kits from consortium partner or from third party vendor. The markers will be tested asking following research questions: Can the markers alone or in combination subgroup patients into different phenotypes which display different progression rates, or with different pain and radiographic profiles. Also, we will test whether a change in markers are correlated with change in the clinical assessments scores. Results from these analyses may provide insight to the potential usage of the biomarkers in drug development.

Conclusion: The APPROACH consortium is the first European study that attempts to establish robust technical performance criteria and reference intervals for osteoarthritis-related soluble biomarkers in an effort to develop biomarker panels that can identify patients with different OA phenotypes.

REFERENCES

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RELIABILITY OF A NOVEL ULTRASONOGRAPHIC SCALE FOR ACTIVITY OF KNEE OSTEOARTHRITIS

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Background: Knee osteoarthritis

Objectives: To assess the reliability of a novel ultrasonographic scale of activity in knee osteoarthritis (OA)

Methods: A cross-sectional observational study included 110 patients with knee pain who fulfilled the American College of Rheumatology (ACR) criteria for knee osteoarthritis (OA). All patients were subjected to clinical assessment WOMAC scale (Western Ontario and McMaster Universities Index of Osteoarthritis and global visual analog scale) and functional assessment using health assessment questionnaire (HAQ). Ultrasonographic assessment of activity was done By 3 rheumatologists with different levels of experience in musculoskeletal Ultrasonography (1-12 years). Ultrasonographic assessments were done according to (MOAKA scale) that was proposed by the first author (table 1).

Abstract AB0801 Table 1. Mortada OsteoaArthritis Knee Activity score (MOAKA score)

<table>
<thead>
<tr>
<th>Domain</th>
<th>Description</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severity of knee</td>
<td>6 grades according to severity published by OA</td>
<td>Grade 0: 0</td>
</tr>
<tr>
<td></td>
<td>Mortada et al 2016 (1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Grade 1: 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Grade 2a: 2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Grade 2b: 3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Grade 3: 4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Grade 4: 5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Grade 5: 6</td>
</tr>
<tr>
<td>Effusion</td>
<td>4 grades</td>
<td>Grade 0: 0</td>
</tr>
<tr>
<td></td>
<td>Grade 0: no effusion</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Grade 1: Mild effusion</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Grade 2: moderate effusion</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Grade 3: severe effusion</td>
<td></td>
</tr>
<tr>
<td>Synovitis</td>
<td>4 grades using the combined EULAR/OMERACT score of grey scale synovitis and Doppler activity</td>
<td>Grade 0: 0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Grade 1: 1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Grade 2: 2</td>
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<td></td>
<td></td>
<td>Grade 3: 3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Grade 4: 4</td>
</tr>
<tr>
<td>Pes Anserine</td>
<td>3 grades</td>
<td>Grade 0: 0</td>
</tr>
<tr>
<td>tendinitis/bursitis</td>
<td>Grade 0: normal</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Grade 1: mild inflammation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Grade 2: severe inflammation</td>
<td></td>
</tr>
<tr>
<td>Backer cyst</td>
<td>3 grades</td>
<td>Grade 0: 0</td>
</tr>
<tr>
<td></td>
<td>Grade 0: normal no cyst</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Grade 1: small and simple cyst</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Grade 2: large and/or complicated cyst</td>
<td></td>
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<td></td>
<td></td>
<td>Grade 2: 2</td>
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<tr>
<td></td>
<td></td>
<td>Grade 3: 3</td>
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<tr>
<td></td>
<td></td>
<td>Grade 4: 4</td>
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<tr>
<td></td>
<td></td>
<td>Grade 5: 5</td>
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<tr>
<td></td>
<td></td>
<td>Grade 6: 6</td>
</tr>
<tr>
<td>Total scores</td>
<td>Sum of scores of all domains</td>
<td>0 - 15</td>
</tr>
</tbody>
</table>

Results: There were high kappa values both in intraobserver and interobserver evaluation of activity of knee OA using the proposed (MOAKA) ultrasonographic scale (0.85 and 0.75 respectively). There were positive correlations between MOAKA score and all WOMAC subscales (pain, stiffness and function) \( r=0.4, P=0.02, r=0.35, P=0.001 \) and \( r=0.4, P=0.01 \) respectively. Also there were a strong positive correlation between MOAKA score and both (VAS and HAQ) \( r=0.86, P=0.001 \) and \( r=0.71, P=0.001 \).

Conclusion: US can reliably detect the activity of Knee OA. Good agreement was found between the proposed US grading scale and WOMAC & HAQ scores. MOAKA US scale is simple and reliable.

Disclosure of Interests: None declared


CYTOKINE PROFILE IN SYNOVIAL FLUID FROM PATIENTS WITH OSTEOARTHRITIS WITH OR WITHOUT CALCIUM CRYSTALS

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Background: The most important pathogenetic calcium crystals that can be found in synovial fluid (SF) are calcium pyrophosphate (CPP) and basic calcium phosphate (BCP) crystals. We and others have demonstrated that a good portion of patients with osteoarthritis (OA) have these types of crystals in their SF and that they are associated with a higher inflammatory state independently from the disease severity.

Objectives: The aim of this study was to investigate the levels of IL-1b, IL-8, IL-6, IL-10, CCL2 and OSM in the SF of patients affected with OA considering the presence of CPP crystals and the positivity to the alizarin red test (a non-specific test for BCP crystals). A sub-analysis has been conducted subdividing patients according to their Kellgren-Lawrence (K-L) radiographic score.

Methods: Synovial fluid was collected from 69 OA consecutive patients diagnosed according to the EULAR criteria. Forty patients were negative to (CPP-) and 29 positive to (CPP+) CPP crystals. A standard analysis was performed for each sample including, white blood cell (WBC) count, differential cell count, crystal search under polarized light microscopy and alizarin red test. The cytokines were measured after appropriate dilutions by ELISA (Thermofisher) and expressed as pg/mL. The Mann-Whitney test was used to investigate differences between the groups of patients positive and negative to CPP; the Spearman rank test was used for correlations, while the Kruskal-Wallis to compare the groups according to the K-L score.

Results: With respect to the group of CPP-, the group of CPP+ patients had higher levels of WBC count (251.7±199.3 vs 176.3±161.8 cells/mm³; p=0.004), PMN% (5±4±1:54; p=0.0001), IL-1b (8.9±2.6±29 vs 4.6±12.2; p=0.0001) and IL-8 (53.7±45.83 vs 26.2±35.94; p=0.0003). No differences were instead observed for the other cytokines considered. We did not find any differences subdividing patients according to the SF positivity to the alizarin red staining. Some correlations were observed in the whole group of patients between IL-1 and IL-8 (p=0.004), IL-1 and PMN (p=0.0006), IL-8 and WBC (p=0.001), IL-8 and PMN (p=0.0001), IL-10 and IL-8 (p=0.04), IL-10 and WBC (p=0.014), CCL2 and IL-8 (0.006). Although no differences have been found analysing the variables in the groups subdivided by the K-L scores, all the cytokines showed higher levels in patients with a K-L score equal to 2.

Conclusion: Although associated with higher inflammatory SF indices and IL-1 and IL-8 levels, calcium crystals still play an undefined role in OA. More studies are warranted to evaluate if patients with calcium crystals in their SF might need a more specific treatment.

REFERENCE

Disclosure of Interests: Francesca Oliviero: None declared, Paola Gallozi: None declared, Marta Favero: None declared, Davide Tietto: None declared, Mariagrazia Lorenzin: None declared, Augusta Ortolan: None declared, Leonardo Punzì Consultant for: BMS, Fidia, Grunenthal, Menarini, Speakers bureau: BMS, Fidia, Grunenthal, Menarini, Anna Scanu: None declared.


SYNOVIAL INTERLEUKIN-4 LEVELS ARE ASSOCIATED TO RADIOGRAPHIC SEVERITY OF KNEE OSTEOARTHRITIS. A CROSS-SECTIONAL STUDY

Silvia Garcia-Cirera, Joan Calvet, ORELLANA CRISTOBAL, Noemi Navarro, Maria Garcia Manrique de Lara, Jordi Gratacos-Masmith, Hospital Universitari Parc Taulí Sabadell, Rheumatology, Sabadell, Spain

Background: Radiographic severity is used in routine clinical practice to evaluate knee osteoarthritis (KOA) structural damage. There are no conclusive studies on the associations between synovial inflammatory markers and the different features of radiographic damage in KOA.
OBJECTIVES: To evaluate the association between inflammatory markers in synovial fluid with the different features of radiographic severity in patients with OA.

METHODS: Cross-sectional study of 114 female patients aged 50-85 with symptomatic primary KOA with significant joint effusion (>4 mm at midline patellar line) confirmed by ultrasound. The following information was collected: age, KOA symptoms duration, body mass index; plain standing knee Rx in semi-flexion were evaluated for radiographic severity by modified OARSI atlas evaluating separately osteophytes (OPH) and joint space narrowing (JSN). The OPH score was obtained searching for marginal osteophytes in both medial and external femoral condyles and tibial plateau, scoring 0 to 3 in each quadrant, for a total score ranging from 0-12. Due to the high number of different scores obtained, and sometimes with a low number of patients, we grouped osteophytes scores 1-2 as mild, 3-6 as moderate, and seven or more as severe osteophyte count. JSN was scored in both medial and lateral knee compartments, grading the joint space 0 to 3 in each one, for a total score ranging from 0 to 6. A JSN score of 0 was considered as normal, 1-2 as moderate and 3 or more as high JSN severity. Five inflammatory markers: TNF alpha, high sensitivity C-reactive protein (hsCRP), interleukin 6 (IL-6), interleukin 8 (IL-8) and calprotectin were measured by ELISA following manufacturer recommendations for synovial fluid dilutions. A comparison between medians of the three groups was carried out and a multivariate analysis controlled by age, symptom duration, BMI and all five inflammatory markers were performed.

RESULTS: A significant association for symptom duration and synovial IL8 was observed for osteophytes (p=0.0001 and p<0.05, respectively), which remained after adjustment (p=0.002 and p=0.037, respectively). Regarding symptom duration, the differences were related to high severity osteophyte index, compared to moderate or low stages (p=0.0005 and p=0.002, respectively), while for IL-8 the differences were associated to a low OPH severity index compared with a moderate osteophyte score (p=0.011), with IL-8 levels approximately 33% less than the moderate OPH score (p=0.011).

For JSN, in the adjusted analysis, patients with a high JSN score had synovial IL-8 levels of 40% more than those with JSN 0 (p=0.035), while no differences were found between the moderate JSN score and the other two degrees. Regarding hsCRP, 30% higher levels were found in patients with a JSN moderate degree compared with JSN 0 (p=0.035), while no significant differences were observed between severe and the other two degrees.

CONCLUSION: Interleukin-8 IL 8 was the inflammatory marker associated to radiographic severity as evaluated by osteophyte count and joint space narrowing score on plain radiography in patients with knee osteoarthritis. The study included 6448 patients with knee OA (mean age 57.8 years). The primary outcome was pain reduction ≥30 mm VAS. All patients received oral avocado/soybean unsaponifiables (ASU) 300 mg/day within 3 months and ketoprofen isoyne salt (KLS) 320 mg/day within 2 weeks at the beginning of the study. A 100 mm visual analog scale (VAS) was used to assess pain intensity. The result of treatment was evaluated on a scale of 0-5 points, where 0 – no effect, 5 - excellent effect. The criteria for a “good response” to therapy were: pain reduction ≥50% and treatment result ≥ 4 points. The value of the studied factors was determined using odds ratio; 95% confidence interval (OR; 95% CI).

RESULTS: After 3 months of therapy the pain level decreased from 63.7 ± 12.0 mm to 14.2 ± 11.7 mm. A good response to treatment was noted in 87.4% of patients. Sex, body mass index ≥ 30 kg/m², type 2 diabetes, poor effect of NSAIDs and SYSADOAs in history did not affect the clinically important improvement (MCII), from baseline to 6-month follow-up (range 3-9 months), as >3.8, <3.8, or within 3.8 units. Statistical significance was studied with one-way analysis of variance (ANOVA) and chi-square.

RESULTS: Among 173 OA patients, 22 (13%) were improved, 95 (55%) unchanged, and 56 (32%) worsened 6 months later. The 3 groups did not differ significantly in age, gender, ethnicity, educational level or BMI (Table). Patients who improved compared to those who were unchanged or worsened had significantly lower baseline RAPID3, pain and patient global VAS, and morning stiffness. The patients who improved also had lower, but not statistically significant, physical function score and fatigue VAS. No differences were seen among the 3 groups in numbers of symptoms or self-report painful joint counts (Table).

Abstract AB0804 Table 1. MDHAQ demographic and clinical variables at baseline of 173 osteoarthritis (OA) patients according to level of improvement 6 months later

<table>
<thead>
<tr>
<th>Groups according to RAPID3 difference from baseline to 6 m</th>
<th>WORSE</th>
<th>SAME</th>
<th>IMPROVED</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%) (diff. &lt;-3.8)</td>
<td>56 (32%)</td>
<td>95 (55%)</td>
<td>22 (13%)</td>
<td>0.77</td>
</tr>
</tbody>
</table>

**Demographics**
- Age (years), mean (SD): 66.3 (10.4) vs 65.6 (10.3) vs 67.4 (13.1), p=0.010

**Morning Stiffness, minutes**
- 32.7 (37.5) vs 32.5 (35.6), p≤0.001

**Self-report painful joint count (0-48)**
- 13 (11) vs 12 (9), p=0.010

**Fatigue VAS (0-10)**
- 5.6 (3.5) vs 4.8 (3.6), p=0.010

**RAPID3 (0-30)**
- 17.4 (5.5) vs 10.2 (5.7), p≤0.001

**Global assessment, and morning stiffness.**

**Abstract AB0804 Table 1. MDHAQ demographic and clinical variables at baseline of 173 osteoarthritis (OA) patients according to level of improvement 6 months later**

**Abstract AB0805 WHAT FACTORS AFFECT THE RESULT OF LONG-TERM ANALGESIC THERAPY FOR OSTEOARTHRITIS? DATA FROM A MULTICENTER OPEN STUDY OF ORAL AVOCADO/SOYBEAN UNSAPONFABLES EFFECTIVENESS**

Flena Popghzega, Andrey Karateev, Alexander Lia, Vera Amirdzhanova, Ekaterna Filatova, V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation

**Background:** Symptomatic slow-acting drugs for OA (SYSADOAs) and oral nonsteroidal anti-inflammatory drugs (NSAIDs) play a central role in the pharmacological management of osteoarthritis (OA). Factors affecting the effectiveness of OA therapy should be taken into account.

**Objectives:** To identify factors affecting the effectiveness of long-term analgesic therapy in patients with OA.

**Methods:** The study included 6448 patients with knee OA (mean age 57.8 ± 10.2 years, 70.9% women), with pain level ≤40 mm VAS. All patients received oral avocado/soybean unsaponifiables (ASU) 300 mg/day within 3 months and ketoprofen isoyne salt (KLS) 320 mg/day within 2 weeks at the beginning of the study. A 100 mm visual analog scale (VAS) was used to assess pain intensity. The result of treatment was evaluated on a scale of 0-5 points, where 0 – no effect, 5 - excellent effect. The criteria for a “good response” to therapy were: pain reduction ≥50% and treatment result ≥ 4 points. The value of the studied factors was determined using odds ratio; 95% confidence interval (OR; 95% CI).

**Results:** After 3 months of therapy the pain level decreased from 63.7 ± 12.0 mm to 14.2 ± 11.7 mm. A good response to treatment was noted in 87.4% of patients. Sex, body mass index ≥ 30 kg/m², type 2 diabetes, poor effect of NSAIDs and SYSADOAs in history did not affect the clinically important improvement (MCII), from baseline to 6-month follow-up (range 3-9 months), as >3.8, <3.8, or within 3.8 units. Statistical significance was studied with one-way analysis of variance (ANOVA) and chi-square.
result. The effectiveness of treatment was less in patients >65 years (OR 0.418; 95% CI 0.342-0.509, p<0.001), OA stage ≥ 2 by Kelgren-Lawrence (OR 0.556; 95% CI 0.298-0.738, p<0.001), with rest pain (OR 0.690; 95% CI 0.596 - 0.800, p<0.001), synovitis (OR 0.780; 95% CI 0.673-0.900, p=0.001), and sensory symptoms such as burning, pain cold, electric shocks (OR 0.530; 95% CI 0.458-0.613, p<0.001).

Conclusion: the ASU and KLS combination allows to achieve successful pain control in OA. A number of factors: age >65 years, OA stage ≥2 by Kelgren-Lawrence, rest pain, synovitis, and sensory symptoms are associated with the worst result of treatment.

Disclosure of Interests: Elena Pogozheva: None declared, Andrei Kara-teev: None declared, Alexander Lilia Speakers bureau: Pfizer, Inc., MSD, Novartis, AbbVie Inc., Celgen Corporation, Biocad, Janssen, UCB, Inc., Vera Amirzhanova: None declared, Ekaterina Filatova: None declared


AB0806 EFFICACY MANAGEMENT AND ADHERENCE EVALUATION OF DICLOFENAC IN THE TREATMENT OF KNEE OSTEOARTHRITIS PAIN

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Background: The incidence of knee osteoarthritis is increasing day by day. The accompanying pain has seriously affected people's quality of life. No relevant researches have studied the relationship between pain relief and adherence after taking NSAIDS in outpatients.

Objectives: To investigate the effect of diclofenac on pain control of knee osteoarthritis and the relationship between pain relief and medicine adherence. To evaluate the pain relief rate of patients with different initial pain.

Methods: 120 patients with knee osteoarthritis were recruited from the outpatient department of osteoarthritis, Peking University People's Hospital. The population was randomly divided into the experimental and control group. The baseline and follow-up contents were interviews including socio-demographic factors, evaluation of knee pain, WOMAC and MMAS-8 questionnaire. The experimental group was given regular follow-up and medication advice, while the control group was only given observational records at the middle and late stages. SPSS25.0 nonparametric T test and one way ANOVA were used to evaluate the efficacy of diclofenac in relieving knee osteoarthritis pain and the relationship between pain relief and adherence.

Results: A total of 120 patients with knee osteoarthritis at baseline were randomly enrolled and 108 patients were followed up. 55 patients in the experimental group and 53 patients in the control group (1) The 2-week adherence of test group/control group was 86.38%/84.78%(P=0.01), the 6-week adherence of test group/control group was 75.24%/35.22%(P<0.01). The 2-week and 6-week adherence of test group and control group were significantly different (P<0.015 and P<0.01). (2) The pain relief rate at 2 and 6 weeks in the experimental group was 67.56% and 69.41%, respectively, the pain relief rate was significantly higher than baseline (P<0.01), but there was no significant difference between the two groups (P=0.739). The pain relief rates at 2 and 6 weeks in the control group were 45.61% and 29.03% and was significantly higher than baseline (P<0.01), there was a significant difference between the two groups (P<0.01). In the evaluation of 2 and 6 weeks, the pain relief rates in the experimental group were significantly different from those in the control group (P<0.01). (3) The initial pain scores of different degrees did not affect the adherence and pain relief rates in the experimental group. In the control group, the 2-week adherence of severe pain patients was higher than that of mild and moderate pain patients (P<0.01), but the 6-week follow-up adherence shows no significant difference in patients with different degrees of initial pain (P=0.073), the 6-week adherence of patients with moderate/severe pain (38.07%42.6%) was significantly different from the 2-week adherence (68.34%/84.77%)(P=0.01),the 6-week pain relief rate (18.46%/29.72%) in patients with mild/moderate pain was lower than the 2-week pain relief rate (48.72%/47.44%) (P=0.052/P<0.01). (4) The patients with better adherence have the higher pain relief rate (P < 0.01).

Conclusion: For patients suffering from knee osteoarthritis pain, diclofenac 150 mg/day for 6-week is recommended. Regular follow-up can improve adherence significantly, increased adherence can improve the pain relief rate significantly, the pain relief rate may not be related to the patient's initial pain score. It is suggested that clinical workers should supervise the medication of patients with knee osteoarthritis and make regularly follow up.

REFERENCES

Acknowledgement: Thanks for the support from the outpatient department of Peking University People's Hospital.

Disclosure of Interests: None declared


AB0807 FOLLOW-UP OF PATIENTS WITH HIP OSTEOARTHRITIS WHO RECEIVED VISCOSUPPLEMENTATION: HOW NEW TECHNOLOGIES CAN HELP

Mariaeva Romano, Laura Belloli, Elisal Verduci, Cinzia Casu, Valeria Campanella, Marina Muscarà, Davide Antonio Filippini, Emanuela Schito, Maria Di Cicco, Oscar Massimilliano Epis, Samsung Electronics Italia: M.Cammarlatt, G.Locatelli MDApp srl, Y.Carrillo, A.Colombini, Grande Ospedale Metropolitano Niguarda, Reumatologa, Milano, Italy

Background: Digital health innovations have opened up several opportunities to help patients with rheumatologic conditions and their treating clinicians in improving routine healthcare.

Objectives: To evaluate the applicability of a wearable smartwatch for monitoring patients with hip osteoarthritis who received viscosupplementation. Samsung Electronics Italia and MDApp srl supported the present study.

Methods: Consecutive patients with hip osteoarthritis who received viscosupplementation with hyaluronic acid between November 2017 and May 2018 were enrolled in this observational study. All patients gave their informed consent. A Samsung Gear smartwatch was given to each patient and was worn during the day for measuring daily steps, walking distance, and mean velocity. Patients were asked to wear the smartwatch starting from one week before infiltration (T0), until two weeks before (T1). Patients were assessed with Lequesne index and WOMAC score at T0 and T1.

Results: Overall, 24 patients (7 male and 17 female, mean age 44 years-old) were enrolled. Of these, 70% has worn the smartwatch for most of the time (range 90-100%). An improvement of velocity (45%), an increase of daily steps (29%), and walking distance (25%) were seen. Similarly, Lequesne index and WOMAC score were consistent with subjective improvement. Most of the patients (95%) declared to be satisfied with this digital health study.

Conclusion: Samsung smartwatches proved to be an effective tool for tracking and recording medical parameters linked with perceived general health. Health technologies are more than an accessories and could be useful in chronic musculo-skeletal diseases because they allow to ease remote diagnosis and to monitor patients' symptoms and clinical response. Telemedicine could fill the gap between patients and healthcare, with a reproducible and objective tool, enhancing patients' engagement with the treatment plan. The high patients' satisfaction further support the use of digital health technology.

REFERENCE

Disclosure of Interests: Mariaeva Romano Speakers bureau: janssen, Laura Belloli: None declared, Elisal Verduci: None declared, Cinzia Casu: None declared, Valeria Campanella: None declared, Marina Muscarà: None declared, Davide Antonio Filippini: None declared, Emanuela Schito: None declared, Maria Di Cicco: None declared, Oscar Massimilliano Epis Speakers bureau: BMS

COMBINATION OF ORAL PARACETAMOL AND TOPICAL NSAIDS FOR OSTEOARTHRITIS PAIN: A SYSTEMATIC SCOPING REVIEW OF THE LITERATURE

John Bell1, Vidhu Sethi2, Kamran Siddiqui3, Philip G. Conaghan1, 1Graduate School of Health, University of Technology Sydney, Sydney, Australia; 2GlaxoSmithKline Consumer Healthcare, Singapore; 3Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom

Background: Topical NSAIDs and paracetamol (APAP) are frequently used for osteoarthritis (OA) pain.1,2 In real-world settings, combination treatment is common,3,4 with more than one-quarter of patients using topical NSAIDs with oral non-opioid analgesics such as APAP.2

Objectives: We conducted a systematic scoping review to: understand current recommendations on concomitant use of topical NSAIDs and APAP for OA pain; evaluate the extent of supporting evidence for this practice; and identify literature gaps.

Methods: We searched PubMed and the Cochrane Library for clinical studies (database inception to January 2019) of topical NSAIDs in OA in which APAP was given concomitantly, either regularly (combination treatment) or as needed (rescue treatment). Grey literature searches were conducted to identify clinical practice guidelines for management of OA from leading organizations.

Results: After removing duplicates, the literature searches returned 375 articles, of which 66 were clinical studies of topical NSAIDs in OA and were reviewed further. Of these, we identified 1 randomized controlled trial (RCT) evaluating efficacy and safety of combination treatment with APAP and a topical NSAID, in which 43 patients with knee OA currently treated with APAP were randomly assigned to double-blind treatment with ketoprofen plaster or placebo for 4 weeks.5 Results showed that the combination of APAP-topical ketoprofen was statistically significantly more effective in pain reduction (P=0.03) and physician’s global assessments (P=0.01) compared with APAP/placebo. Of the remaining 65 topical NSAID studies, another 37 (57%) allowed rescue treatment with APAP during the treatment period (including 34 RCTs; 1 open-label extension of 2 RCTs; 1 patient preference study; and 1 single-arm open clinical trial). Because none of these studies randomly assigned patients to the combination, it was not possible to evaluate efficacy or safety of the combination based on these data. Review of OA guidelines identified 3 major organizations—EULAR, NICE, and ESCCEO—that recommend or allow concomitant use of topical NSAIDs and APAP for specific joint pain.

Conclusion: In clinical practice, drug combinations are frequently used to manage OA pain, and some OA treatment guidelines allow the use of topical NSAIDs concomitantly with APAP. Very limited supporting data are available, with only a single small RCT demonstrating the efficacy and safety of the combination. However, it may be inferred from the fact that more than half of the topical NSAID studies identified allowed APAP rescue therapy that this combination is generally perceived to be efficacious and well tolerated. Additional, larger RCTs are needed to confirm the benefit of this commonly used analgesic combination in managing OA pain.

REFERENCES

Disclosure of Interests: John Bell Consultant for: John Bell has acted as consultant for Bayer, GlaxoSmithKline, Mylan, Novartis, Pfizer and Reckitt Benckiser., Speakers bureau: John Bell has received payment for speaking from GlaxoSmithKline, Pfizer and Reckitt Benckiser., Vidhu Sethi Employee of: Vidhu Sethi is an employee of GlaxoSmithKline Consumer Healthcare, Singapore., Kamran Siddiqui Employee of: Kamran Siddiqui is an employee of GlaxoSmithKline Consumer Healthcare, Singapore., Philip G. Conaghan Consultant for: Flexion Therapeutics, AbbVie, Medivir, Merck Serono, Novartis, GlaxoSmithKline


A STUDY TO COMPARE ARTICULAR CARTILAGE VOLUME IN HEALTHY AND OSTEOARTHRITIC KNEE AND ITS CORRELATION WITH CLINICO–RADIOLOGICAL SEVERITY

Sudeep Sri Divastava, Rajeswar Nath Sri Divastava, Amar Chandra Sharma, King George’s Medical University, Orthopaedic Surgery, Lucknow, India

Background: Knee Osteoarthritis (KOA) is a persistent debilitating disease characterized by loss of articular cartilage. Known to be a disease of elderly, it may not be necessarily so, as the loss in articular cartilage volume (ACV) begins early but detected very late on X-rays and by that time no therapy works and joint replacement is the only answer.

Objectives: To determine the role of ACV in early diagnosis of KOA, which may not only monitor disease progression from a very early stage, it may also open a gateway to slow down or stop the structural changes involved in KOA.

Methods: 60 Cases and equal number of age, sex matched controls were recruited. Each subject had MRI of the knee to monitor ACV and to determine ACV at the knee. ACV was measured manually by means of image processing on an independent workstation using semi-automated machine GE Signa. VAS for knee pain and WOMAC for pain, stiffness and disability were recorded for clinical severity and X-rays for radiological severity by KL grading.

Results: With age, a statistically significant inverse correlation of ACV was found in both healthy and osteoarthritic knees. Height, weight and BMI were independent of ACV in healthy knee. In KOA, a significant positive correlation of ACV was observed with height, a significant inverse correlation with WOMAC scores and significant difference with sub-scales of WOMAC index (pain, stiffness and physical function). The statistical difference in ACV between the two categories of WOMAC scores (<32 and >32) was significant.

Conclusion: This study concluded that ACV is significantly lower in osteoarthritic knee as compared to healthy adult knee. This study also found that KOA in females occurs at an early age and progresses slowly whereas in males occurs late and progresses rapidly. ACV may become one of the most promising tools for early diagnosis of KOA and in monitoring disease progression.

REFERENCES

Disclosure of Interests: None declared


INTRA-ARTICULAR CNTX-4975 FOR PAINFUL KNEE OSTEOARTHRITIS: ASSESSMENT OF COOLING METHODS FOR REDUCING PROCEDURAL PAIN

Randall Stevens1, Kimberly Guedes1, Nilam Misty1, Duncan Lascelles1, David Ball2, 1Centrexion Therapeutics Corp, Boston, United States of America; 2IMAC Clinical Research, Manchester, United Kingdom

Background: CNTX-4975 is a long-acting, trans-capacitance injection in phase 3 trials for treatment of moderate to severe pain associated with knee osteoarthritis (OA). Intra-articular (IA) CNTX-4975 injection produces short-lived procedural pain that can be ameliorated with joint cooling. A prior analysis (Cohort 2) demonstrated that a circumferential circulating ice water wrap (CCIWW) more effectively lowered IA knee temperature and reduced procedural pain than an ice pack on top of the knee (3.4 vs 7.3, respectively, on a numeric pain rating scale [NPRS] 10 minutes post-CNTX-4975).

Objectives: Subjects were enrolled in 2 separate cohorts (C3/C4) to: compare effects of 2 circumferential cooling methods on IA and skin knee temperature and procedural pain (C3); and assess procedural pain with an abbreviated cooling schedule and with vs without post-CNTX-4975 cooling (C4).

Methods: Eligible subjects were adults aged 45–75 yrs with >3 months of bilateral moderate to severe OA knee pain. All subjects received each
cooling device on opposite knees; IA CNTX-4975 injections and other procedures on the left and right knees were separated by 7 (±2) days. See Figure for study design. IA and skin temperatures were recorded throughout the procedures. Subjects rated procedural pain at prespecified times using NPRS (0=no pain; 10=worst possible pain).

Results: Five subjects enrolled in and completed each cohort (mean age, yrs: C3, 57.6; C4, 59.6; each 80% male). In C3, mean IA temperatures decreased with both methods; mean temperatures at baseline and 105 minutes were 33.7°C and 26.7°C for ice-gel pack cooling and 32.4°C and 28.2°C for CCIWW. Skin temperature reductions between cohorts were similar; mean temperatures were 28.8°C and 14.3°C (ice-gel pack) and 28.7°C and 15.2°C (CCIWW). Mean IA temperatures in C4 at baseline and 55 minutes (15 minutes post-CNTX-4975 and/or end of last cooling period [CCIWW only]) were 33.6°C and 28.7°C; mean temperatures were 28.8°C and 26.7°C for ice-gel pack and 27.8°C and 18.8°C for CCIWW. Pain levels before CNTX-4975 were low. Procedural pain were 28.5°cooling and 32.1°cooling period [CCIWW only]) were 33.6°line and 55 minutes (15 minutes post-CNTX-4975 and/or end of last practice.

The ice-gel pack and CCIWW effectively reduced IA knee pain was not increased in the absence of post-injection cooling in C4. More effectively by CCIWW in C3 and ice-gel pack in C4. Procedural pain was reduced more effectively by CCIWW in C3 and ice-gel pack in C4. Shorter cooling time and low pain levels observed with IA CNTX-4975 and ice-gel pack cooling in C4 suggest that this strategy may be feasible in clinical practice.

Table

<table>
<thead>
<tr>
<th>Procedure Pain Over Time (min)</th>
<th>Cohort 3</th>
<th>Cohort 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean±E</td>
<td>Baseline</td>
<td>Ice-gel pack</td>
</tr>
<tr>
<td>0.8±0.37</td>
<td>0.4±0.24</td>
<td>0.4±0.24</td>
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<tr>
<td>10°</td>
<td>4.2±1.36</td>
<td>2.2±1.46</td>
</tr>
<tr>
<td>20°</td>
<td>3.6±1.33</td>
<td>2.2±1.20</td>
</tr>
<tr>
<td>30°</td>
<td>2.6±0.51</td>
<td>2.2±0.97</td>
</tr>
<tr>
<td>Last assessment</td>
<td>2.4±0.81</td>
<td>1.4±0.40</td>
</tr>
</tbody>
</table>

Figure: Study Procedures

A. Study Cohort 3

B. Study Cohort 4

Disclosure of Interests: Randall Stevens Shareholder of: Centrexion Therapeutics Corp, Employee of: Centrexion Therapeutics Corp, Kimberly Guedes Employee of: Centrexion Therapeutics Corp, Nilam Mistry Employee of: Centrexion Therapeutics Corp, Duncan Lascelles Consultant for: Centrexion Therapeutics Corp, David Ball: None declared

Conclusion: These results suggest that intra-articular injections of hyaluronic acid plus chondroitin sulfate in patients with knee OA are efficient and safe. A single injection of the drug resulted in statistically significant reduction of pain and stiffness, reduction in NSAIDs intake, as well as improvement in patients’ quality of life and function.

Disclosure of Interests: Elena Taskina Speakers bureau: Bayer, Sandoz, Boehringer-Ingelheim, Ludmila Alekseeva Speakers bureau: Bayer, Boehringer-Ingelheim, Gedeon-Richter, Servier, Natalia Kashevarova: None declared, Evgenia Sharapova: None declared, Ekaterina Streibkova: None declared, Sergey Anikin: None declared, Lena Zonova Speakers bureau: Sandoz, Pfizer, Abbvie, Novartis, Bayer, Tatiana Raskina: None declared, Elvira Otteva Speakers bureau: Pfizer, Abbvie, Novartis, Aleksandr Lila Speakers bureau: Sandoz, Pfizer, Abbvie, Novartis, Bayer


PAIN CATASTROPHIZING SCORE AND GAIT, TOGETHER WITH WOMAC, ARE ALTERED IN KNEE OSTEOARTHRITIC PATIENTS UNDERGOING ARTHROPLASTY SURGERY, COMPARED WITH PATIENTS FOLLOWING CONSERVATIVE TREATMENT. PRELIMINARY RESULTS FROM HOLOA PROJECT

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1IMIM, Barcelona, Spain; 2Hospital del Mar, Rheumatology service, Barcelona, Spain; 3Pompeu Fabra University, BCN MedTech, DTIC, Barcelona, Spain; 4Hospital del Mar, Orthopedic Surgery and Traumatology service, Barcelona, Spain; 5ICREA, Barcelona, Spain

Background: Osteoarthritis (OA) is a pathology that includes several disorders that produce the same symptomatology: pain, functional impotence and inflammation. It lacks therapies that act over the physiopathology of the disease, rather than over the symptoms [1]. Patients’ phenotyping is essential to describe the disorders underlying the OA symptoms, and would allow applying treatments to the altered conditions, in a personalized medicine approach.

Objectives: The HOLOA project aims to design a multivariate model that allows classifying knee OA patients according their characteristics in 3 areas: pain, clinical/morphological characteristics and articular defects. The present work is a preliminary study with the aim to describe the clinical and gait dynamics differences between OA patients classified by treatment: conservative (CNS) vs arthroplasty surgery (ART).

Methods: Prospective study of OA patients graded 2-3 in KL scale and classified by treatment. Both groups are paired by genre, age, and BMI. The studied variables are: WOMAC index (Pain (Wp), Stiffness (Wst) and Function (Wf), Hospital Anxiety and Depression Scale (HADS), London Chest Activity of Daily Living scale, Modified Baecke Physical Activity Questionnaire, Pain Catastrophizing Score (PCS), pain threshold (according to the extended peripatelar map of Arent-Nielsen) pain sensitization at the tibia anterior surface, pain temporal summation (these 3 parameters are measured with the use of an algometer [2]), ultrasound measurement of synovial hypertrophy and effusion, and gait analysis (with Helen Hayes marker protocol). Inverse dynamic analysis was performed to compute the reaction forces and torques of the OA and control leg [3]. Multivariate analysis of variance was performed for the treatment, genre, age and BMI.

Results: This study was performed with the data of the 70 patients recruited to date. They are classified as shown in Table 1.

Table 1: Classification of patients by treatment and demographic variables

<table>
<thead>
<tr>
<th>Variable</th>
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<td>26</td>
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Only treatment factor related differences are reported. ART group present significant higher values in Wst (p=0.012), Wf (p=0.018), and PCS (p=0.018), than CNS group (Figure 1). Differences in PCS values show interaction with BMI (p=0.007) (Figure 2). Regarding the joint, number of painful sites depend on treatment and BMI group (p=0.032) (Figure 3). Finally, gait study show no direct effect of the treatment, interactions are observed in the reaction forces and torques when comparing control vs OA leg, in ART and CNS group (p=0.004 and p=0.002, respectively) (Figure 4).
Conclusion: Although both treatment groups present the same OA radiologic grade, ART group presents significant higher stiffness and functional disability. That may affect to the gait of these ART patients, altering the forces distribution and torques between both legs. Although no differences in knee pain in life situation (WP) between treatment group are reported, ART group present more painful sites in the knee with pressure stimuli. Emotional component may be playing a role in the pain and illness perception, influencing the patient decision to undergo ART surgery.

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Procare Health


AB0814

AN EXPERT CONSENSUS ON THE APPROPRIATE USE OF ORAL SYSADOAS FOR THE TREATMENT OF THE OSTEOARTHRITIC PATIENT IN PRIMARY HEALTH CARE: A DELPHI STUDY

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Background: Clinical studies have demonstrated that osteoarthritis pain is linked to disability and quality of life (QoL). The therapeutic modalities in the treatment of osteoarthritis (OA) are numerous and despite the availability of evidence-based guidelines for OA management, agreement on treatments is lacking. Symptomatic Slow-Acting Drugs for OA (SYSADOAs) are natural compounds, used in OA treatment. Thus, there is disagreement about SYSADOAs use in clinical practice.

Objectives: Our objective was to prepare a consensus document on the appropriate use of oral SYSADOAs: chondroitin sulphate (CS), glucosamine (G), diacerein (D) and the combination of CS plus G for OA management in primary health care.

Methods: A two-round Delphi study was carried out to assess expert consensus on the appropriate use of SYSADOAs in primary care. The questionnaire validated by the expert committee (3 rheumatologists, 2 PC physicians, 1 clinical pharmacologist) included 24 questions. The Delphi panel was composed of 15 experts (10 PC physicians, 1 rheumatologist, 1 traumatologist, 1 rehabilitator, 1 gynaecologist and 1 clinical pharmacologist) with extensive experience in the treatment of OA and the use of oral SYSADOAs which were identified by clinical coordinator, a methodology coordinator, and four members of the Scientific Committee. Participants were asked 24 questions on SYSADOAs use. Items that reached consensus by at least 80% across both panels were included in the guidelines. The fieldwork of the study was developed for approximately 4.5 months. This study was promoted by the International Osteoarthritis Foundation (OAFI) with the support of the Spanish Ministry of Health, Social Services and Equality.

Results: Consensus statements emerged: (1) patient phenotypes affect SYSADOAs action; (2) SYSADOAs are effective in primary and secondary OA, in the three first grade of Knee OA, hand and hip; there is no evidence for erosive hands, shoulder, spine, and ankle OA; (3) CS, G and association can reduce pain, inflammation, improve QoL and functional capacity and have a chondroprotective effect; (4) CS and D can reduce synovial membrane inflammation, all oral SYSADOAs, except D, can decrease cell death and the enzymes responsible for cartilage destruction; (5) The maximum therapeutic effect is reached after 3 to 6 months; (6) SYSADOAs can be prescribed to patients having comorbidities: cardiovascular risk or disease, digestive disease, hypertension, dyslipidemia, peripheral vascular disease, type 2 diabetes, and oesophageal reflux. There is disagreement in the prescription of oral SYSADOA in patients with liver and kidney disease.

Conclusion: This study sheds light on the appropriate use of oral SYSADOAs in primary health care by providing added value to published evidence. Results based on literature evidence on efficacy and safety, the clinical experience of the panelists in OA treatment and the fact that OA patients are a chronic, elderly, with multiple diseases and polymedicated person. The diffusion of our results among primary health practitioners will contribute to improving OA patient management protocols to ensure a personalized treatment to OA patients and to ameliorate their QoL.

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Disclosure of Interests: Jordi Monfort Speakers bureau: Biobérica

Procare Health


AB0814

INDIVIDUAL AND SOCIAL FACTOR CAN INFLUENCE THE QUALITY OF LIFE OF KNEE OA PATIENTS: A SYSTEMATIC REVIEW

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Background: Knee OA (KOA) is the most common form of chronic joint disease and bears more responsibility than any other disease for disability. It associates with remarkable functional restrictions due to pain. The limitations in activity caused by KOA seriously affect social relationships, emotional well-being, reducing the quality of life (QoL) of patients.
The identification of therapies and factors that affects and improve QoL in KOA patients may mitigate the clinical, economic, and social burden of this disease. Thus, the assessment of QoL in KOA is becoming increasingly common in both research and clinical practice. Still a general recompilation of the factors of interest as demographic features, lifestyle characteristics and comorbidity are missing.

**Objectives:** Our aim was to recapitulate the existing information on QoL in KOA patients as an international tool to raise awareness on their condition and guide future actions for patient’s management

**Methods:** We conducted a systematic review examining the breadth of the literature regarding the QoL in patients with KOA (up to 2017). We identify articles using MEDLINE, EMBASE, Cochrane, and PsycINFO using relevant keywords as KOA, QoL, and well-being and their short forms. All articles were reviewed for inclusion by 3 independent reviewers. QoL domains and items relevant to patients with KOA were extracted. Only original articles were included when containing information on QoL of patients with KOA. Inclusion criteria were QoL compared to one or more demographic factors (e.g., age, gender), lifestyle factor (e.g., functional independence), or comorbidity factor (e.g., diabetes, obesity) or a control group. The quality of included studies was assessed using a quality appraisal tool.

**Results:** We retrieved 610 articles, of which 62 articles fulfilled inclusion criteria for review. Most of the studies were carried out in Europe, American Continent and Asia. The mean of participants in these 62 studies was 561 patients and the majority of them were female, the mean age was 63 years. All the studies described a worse QoL in KOA patients when compared to a control group having women a worst QoL perception than men.

A higher BMI, a lower level of physical activity and higher energy expenditure were one of the main factors that correlated with worse QoL. Educational level and higher total mindfulness were shown to improve QoL while poverty, physiological distress, depression and having severely dysfunctional families reduce it. The delivery of a knee self-management program by health care professionals was proven to improve QoL. Finally, surgical KOA interventions generally resulted in good outcomes these results were influenced by individual factors as age, weight, and depression.

**Conclusion:** This is the first review pertaining to QoL in KOA patients. KOA has a strong impact on QoL. Individual factors (sex, weight, exercise, mental health, education) can influence QoL. These factors affect treatment outcomes and should be considered for a better patient’s management. These data are a valuable tool for health professionals, to better understand the disease and to implement more adequate standard of care.

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**THE INFLUENCE OF NON-STEROIDAL ANTI-INFLAMMATORY DRUGS ON INFLAMMATORY SONOGRAPHIC FEATURES IN EROSIve HAND OSTEOARTHRITIS**

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**Background:** Erosive hand osteoarthritis (HOA) is a subtype of hand osteoarthritis affecting the interphalangeal (IP) finger joints, characterized by a more inflammatory burden. Hitherto, pharmacologic treatment options are restricted to symptomatic therapy like paracetamol and/or non-steroidal anti-inflammatory drugs (NSAIDs). The latter may affect the presence of inflammatory features on ultrasound (US), hence, assessment of this disease activity could be influenced by this treatment.

**Objectives:** To examine whether inflammatory US features (i.e. synovial proliferation (SP), effusion (EFF) and Power Doppler (PD) signal) in erosive HOA patients change when discontinuing NSAIDs intake for two weeks before the US assessment.

**Methods:** Ninety-nine patients with erosive HOA, according to American College of Rheumatology criteria (2) were enrolled. Presence of central erosions on conventional radiographs and any clinical sign of inflammatory activity (soft tissue swelling) in at least one proximal or distal IP finger joint were present. The patients were allocated to the NSAIDs or control group according to their intake before baseline (if no NSAIDs use - control group; if intake of NSAIDs on a regular base = NSAIDs group). At baseline (T0), 16 IP finger joints were examined by US. Patients in the NSAIDs group were asked to discontinue all NSAIDs intake for two weeks, when another US was performed (T1). The inflammatory features were scored at T0 and T1 using a semi-quantitative scale ranging from 0-3 (3).

Binomial mixed models with logit function were fitted for ultrasound scores SP (score=2), EFF (score=2), and PD (score=1) with a random intercept for patient and with age (in years), sex (female vs. male), duration of illness (in years), joint, side (left vs. right), anatomical phase group (N, S, J vs. E/R, R, E, F), NSAID group (NSAIDs withdrawal vs. No NSAIDs), time (T1 vs. T0), and a two-way interaction between NSAIDs group × time as fixed factors. The Odds ratios (OR, 95% confidence interval (CI)) of having an ultrasound score of at least '2' versus at most '1' for SP and EFF, and '0' vs. '1' for PD are shown.

**Results:** Forty seven patients were included in the NSAIDs group and 52 in the control group. Both groups were comparable at baseline for VAS pain, disease duration, number of radiographic affected joints and body mass index, but not for age (p=0.005). The US baseline data were comparable between both groups (all p>0.05). At T1, in the NSAIDs withdrawal group, more SP and PD was seen compared to baseline (p = 0.018 and 0.031, respectively). However, the interaction term time*NSAIDs was not found significant for any variable (table 1).

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**REFERENCES**


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Osteoporosis

CAN STATINES IMPROVE BONE QUALITY IN POSTMENOPAUSAL OSTEOPOROSIS?

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Background: Osteoporosis (OP) is the most frequent metabolic bone disease. It has low bone mass and microarchitectural deterioration, which increases the risk of fractures. The most commonly used drugs are bisphosphonates, however statins (ST) have pleiotropic properties, and some researchers suggested their use in OP.

Objectives: To determine the effect of ST on bone mineral density (BMD) in postmenopausal osteoporotic women.

Methods: A cross-sectional study, control case where postmenopausal women with hypercholesterolemia treated with ST for a period not less than 6 months were studied for two years. The control group was postmenopausal population that did not receive statins. Exclusion criteria: Diabetes, previous treatment with estrogen, calcitonin, anabolic, steroids, bisphosphonates or vitamin D during a period of 6 months prior to enter to the study or with amenorrhea less than 12 months. We evaluated age, weight, height, BMI, personal and first degree family members’ history of fracture, use of corticosteroids, smoking, alcoholism, daily calcium intake, sedentary lifestyle, phosphophatic metabolism laboratory and Vitamin D. All patients were performed Bone Densitometry by dual-energy X-ray absorptiometry (DXA) with an Hologic equipment in right hip and lumbar spine, staging them according to WHO. The statistical analysis was performed using the Student’s test and the Fisher test for categorical variables. Values of p less than 0.05 were considered significant.

Results: 202 patients were enrolled in the ST group and 203 in the control group. Age, weight, height and BMI were 62.64; 69.6; 1.60 and 27.1 in the ST group and 58.5; 65.7; 1.59 and 26.83 in the control group respectively (p = 0.000, p = 0.001 p = 0.79, p = 0.38). There were no significant differences in risk factors for OP between groups. The average lumbar BMD was -0.87 for the ST group and -1.76 for the control group (p = 0.000), the average femur neck BMD was -1.15 for the ST group and -1.56 for control (p = 0.000), the total hip BMD was -0.32 for the ST group and -0.74 for the control group (p = 0.001), vitamin D was 25.57 for the ST group and 27.71 (p = 0.120).

Conclusion: ST can improve Bone Mineral Density in postmenopausal women, more studies are needed to confirm these results.

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INCIDENCE OF FRACTURES AND ASSOCIATED RISK FACTORS DURING THE DRUG HOLIDAYS PERIOD WITH BISPHOSPHONATES

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Background: Biphosphonates are the most widely used treatment for osteoporosis. The optimal treatment duration, however, remains unclear. The occurrence of adverse effects, such as osteonecrosis of the jaw (ONJ) and atypical femoral fractures (AFF), has raised the issue of bisphosphonate discontinuation (“drug holiday”) after a certain treatment period.

Objectives: To assess the incidence of fractures in patients during the drug holidays period with bisphosphonates, as well as to determine the risk factors are associated to it.

Methods: Analytical, observational, longitudinal, and ambispective study of a cohort of patients with postmenopausal osteoporosis or men over 50 years of age treated with oral bisphosphonates (at least for 5 years) or intravenous (at least for 3 years) and who had been at least for one year in a drug holidays period, from 01/01/2012 to 12/31/17. Patients treated with corticosteroids and/or with diseases with effects on bone
Results: 128 patients with osteoporosis were studied, of which 19 (14.7%) suffered an osteoporotic fracture during the follow-up. Bivariate analysis showed in the group of patients with fractures a higher proportion of smoking patients (p = 0.004), osteopening treatment (p = 0.005) and a femoral neck t score lower at the beginning of the drug holidays period -2.07 (0.68) vs - 1.58 (0.63), p = 0.008.

In addition, there was a higher proportion of patients with fracture with moderate risk before the start of the drug holidays period (p = 0.007). The fracture survival curves were lower in patients older than 75 years (p = 0.04). When applying the same treatment, for each year increase, the risk of fracture was increased by 6% (p = 0.04), while, for the same age, this risk was increased 4.33 times in patients who were treated with Risedronate versus those with Alendronate (p = 0.05).

The multiple regression analysis showed that vertebral fracture was independently associated with Tabaco (HR 4.28 p=0.047).

Conclusion: Based on our results, it would be useful to follow closely those patients during drugs holidays period who are smokers, older than 75 years, with osteopening treatment, who present a low femoral neck t-score and/or have been previously treated with Risedronate.

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AB0819 HANDGRIP STRENGTH PREDICTS HIGH FRACTURE RISK IN PATIENTS WITH TYPE 2 DIABETES MELLITUS
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Background: Accumulating evidence has revealed that the risk of osteoporosis related fractures is significantly increased in type 2 diabetes mellitus (T2DM) patients in comparison with healthy controls. Dual X-ray Absorptiometry (DXA) derived bone mineral density (BMD) is not completely useful to discriminate at risk patients.

Objectives: To find a valuable clinical tool that is helpful to identify T2DM subjects with poor bone health, finally preventing fragility fractures.

Methods: In a setting of Caucasian subjects with T2DM, anthropometric data and information about metabolic control and diabetic complications were recorded. Handgrip strength by dynamometer, FRAX derived 10-years probability of major osteoporotic fractures and hip fractures were also assessed. Bone evaluation was performed by a dual-energy X-ray absorptiometry (DXA) densitometer at the lumbar spine (L1-L4) and at the femoral neck. Based on specific software, the trabecular bone score (TBS) was calculated. Lateral scan of thoracic and lumbar spine was assessed to investigate morphometric vertebral fractures (Vfs).

Results: 29 patients (female 65%) [median age 67 (60 to 70)] with T2DM were considered. Morphometric vertebral fractures were detected by DXA in 17% of patients without any gender differences (males vs. females, p=0.6). The median ten years probability of fractures was 8.1% and 2.3% as for major osteoporotic or hip fracture respectively. Median femoral neck T-score value [-1.1 SD (-1.8 to -0.5)] was indicative of a slight osteopenia while lumbar spine T-score was even in the normal range [-0.8 SD (-1.5 to -0.1)]. The median TBS value was 1.28 (1.2 to 1.31) and TBS was positively associated with BMD at lumbar spine and femoral neck. Median handgrip strength value was 22.3 kg (18.9 to 31.3). At multiple regression analysis, handgrip strength predicted both lumbar (β=0.009, SE 0.0034, p=0.01) and femoral neck BMD values (β=0.006, SE 0.002, p=0.01) and also independently associated with TBS score, after correcting for mean HbA1c values and time since T2DM diagnosis.

Conclusion: Handgrip strength may be a reliable tool to screen for bone fragility in T2DM.

REFERENCES

Disclosure of Interests: None declared


AB0820 COGNITIVE IMPULSIVITY CORRELATES WITH BONE MINERAL DENSITY

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Background: Cognitive impairment is known to be associated with low bone mineral density (BMD) and low levels of BMD have been associated with increased rates of progression from mild cognitive impairment to Alzheimer’s disease and with the onset of episodic verbal learning deficit.

Objectives: The potential involvement of executive functions impairment on BMD is still unclear. The aim of this study was to investigate the correlations between cognitive impulsivity, BMD and fall risk.

Methods: Cognitive impulsivity was measured by Stroop Color and Word Test (SCWT) administration in a setting of 40 consecutively recruited postmenopausal women referring to a outpatient clinic for the evaluation of fracture risk. SCWT is a neuropsychological test able to assess the ability to inhibit cognitive interference: during the administration, women were required to quickly read three different tables of which two represented the “congruous condition” in which participants were invited to read names of colors printed in black ink and name different color patches. In the third table, named “incongruous condition”, color-words were printed in inconsistent color ink (e.g. the word “red” is printed in green ink) and participants were required to name the color of the ink instead of reading the word. Women with Mini Mental State Examination (MMSE) score < 24, known neurologic or psychiatric disorders, history of significant hearing or visual impairment, or significant physical disability, history of uncontrolled diabetes and abnormal thyroid function, cancer, heart, respiratory, kidney or liver failure were excluded. BMD was measured at lumbar spine and femoral site by a DXA densitometer (Hologic Discovery). History of falls in the previous 12 months was recorded.

Results: Cognitive impulsivity, as highlighted by making errors at the SCWT, was significantly associated with lumbar spine and femoral neck T-score (r=-0.39, p=0.01 and r=-0.43, p=0.008; respectively). MMSE score was not associated with T-score values, neither at lumbar spine (r=0.09, p=0.5) nor at femoral neck (r=0.2, p=0.21); differently MMSE score was significantly associated both with Stroop test error (r=-0.34, p=0.02) and time interferences (r=-0.39, p=0.01). Furthermore, time interference was positively associated with the self-reported history of falls (r=0.342; p=0.031).

Conclusion: Cognitive impulsivity was significantly associated with BMD values and higher prevalence of falls in postmenopausal women. It could be considered as a possible clinical risk factor for osteoporotic fractures.

REFERENCES
Disclosure of Interests: None declared

AB0821
APPRECIATION OF OSTEOPOROTIC TREATMENT COMPLIANCE WITH ALENDRONATE 70MG ORALLY
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Background: Patients suffering from osteoporosis (OP) don’t have the opportunity to enjoy from an accurate and concrete parameters response to OP treatment. They therefore have no palpable evidence of the favorableness of the given therapy. Unintentional antiresorptive treatment (AT) given the silent nature of the pathology. That is way we see the non-compliance with treatment in some patients.

Objectives: It was essential to estimate the extent of the lack of compliance with AOT in order to deduce the factors related to this deficiency in order to reduce the size of the problem.

Methods: It’s a Descriptive cross study performed in all patients over 38 years for both sexes and that exhibit post menopausal or corticosteroid-induced OP justifying AOT orally (alendronate 70mg orally per week) observed over a period of at least 6 months.

Results: We collected data of 153 patients, in 9 out of 10 cases this was a woman, the mean age was 59.3 ± 8.1 years, the average duration of gain of treatment was 32.2 ± 18.2 months, 3 of 5 patients believe that treatment is for musculoskeletal pains, 1/3 of responders confess not to take their weekly treatment regularly, regular physical activity was performed by only 21% of patients, the factors related to non-compliance were: lack of education (p = 0, 032) and sedentary lifestyle (p = 0, 044).

Conclusion: OP is unfortunately underestimated by both patients and physicians, and its short- and long-term repercussions are often minimized. Our study has shown that the various measures required in its management are poorly followed by patients despite their proven effectiveness in reducing fractures. One in three patients in our sample do not follow their treatment properly. Therapeutic education seems to be the answer to overcome this lack of adherence.

Disclosure of Interests: None declared

AB0822
VITAMIN D (25OHD) IN PATIENTS WITH CHRONIC RHEUMATIC DISEASES RECEIVING TREATMENT WITH ADALUMAB. DESCRIPTIVE STUDY OF A COHORT
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Background: Patients with chronic rheumatic diseases (CRD) have lower levels of 25OHD, inverse correlation has been described and greater severity between the different CRD with 25OHD deficit. Most scientific societies recommend levels> 30 ng/mL. Patients with refractory disease to conventional therapy have a higher inflammatory load, require optimal levels of 25OHD and often need biological disease-modifying antirheumatic drugs (bDMARD) in order to prevent structural damage.

Objectives: The aim of this study was to describe the epidemiological, clinical and therapeutic characteristics of patients receiving Adalumab (ADL) in which 25OHD levels were determined in 2018.

Methods: Transversal, retrospective study in a hospital setting. We analyzed data from patients included in a study to determine levels of ADL, in whom the serum level of 25OHD was determined at least once during the last year. Among 104 patients, 74 with 25OHD determination were included.

Results: Seventy-four patients selected, 45.9% were men and 54.1% women. The mean age was 54.9 years (SD ± 13.6), 41.9% (31) had Rheumatoid Arthritis, 36.5% (27) Spondyloarthritis, 17.6% (13) Psoriatic Arthritis and 4.1% (3) Juvenile Idiopathic Arthritis. 35.1% (26) had deficit (<20 ng/mL) of 25OHD, 31.1% (23) insufficiency (20-30 ng/mL) and only 33.8% (25) optimal levels (>30 ng/mL). The 62.2% (46) of the patients received oral supplementation, of these 67.4% maintained levels >20 ng/mL and 32.6% <20 ng/mL. 37.8% (28) did not receive supplementation, despite this 60.7% within this group had levels >20 ng/mL. No statistical differences were found regarding vitamin D deficit and oral supplementation (p > 0.05).

13.5% (10) of the patients also had Osteoporosis (OP); in this group 6 had deficit of 25OHD, 1 insufficiency and only 3 optimal levels, all of them received 25OHD supplementation. No differences between the groups in relation to the DMARD treatment.

Conclusion: Vitamin D levels were determined in 71.2% of patients and not in all of them as it would be advisable. Among the patients with 25OHD determination, 62.2% received oral supplementation, however only 33.8% of the patients reached optimal levels (> 30 ng/mL) without statistical differences regarding supplementation. 13.5% of the patients who received supplementation also had OP. Despite the weakness of the study in terms of design and sample, most patients did not reached optimal levels of 25OHD; we can assume that it is necessary to obtain levels of 25OHD >30 ng/mL in all patients, with adequate supplementation if necessary due to the positive effects known in CRD.

REFERENCES

Disclosure of Interests: None declared

AB0823
TRABECULAR BONE SCORE AT LUMBAR SPINE IS ASSOCIATED WITH QUANTITATIVE ULTRASOUND MEASUREMENTS AT PHALANGEAL SITE IN BREAST CANCER SURVIVORS RECEIVING AROMATASE INHIBITORS
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Background: In breast cancer (BC) survivors, the age-related reduction in bone mineral density is exacerbated by aromatase inhibitors (AIs) treatment. AIs disrupt also bone quality and enhance fracture risk in aging women. Consequently, bone health evaluation is mandatory in BC women receiving AIs.

Objectives: Quantitative ultrasound of bone (QU5) and trabecular bone score (TBS) are recognized tools to explore bone health beyond bone mineral density (BMD). The aim of our research was to explore the association of TBS with QU5 measurements at phalangeal site in a setting of postmenopausal women taking aromatase inhibitors (AIs).

Methods: BMD at lumbar spine, femoral neck and TBS were evaluated by a DXA densitometer (Hologic Discovery). Amplitude Dependent Speed of Sound (AD-SoS), Bone Transmission Time (BTT) and Ultrasound Bone Profile Index (UBPI) were detected at phalangeal site by Bone Profiler (Igac). Results: In 102 postmenopausal women (mean age 61.64 ± 8.33 yr.) (60 AIs treated and 42 controls), at baseline examination. TBS was negatively associated with age (r= -0.39, p < 0.001) and positively related with T-score values at lumbar spine and femoral neck. After 18 months, AD-SoS, UBPI and BTT values were significantly decreased in BC women receiving AIs (-3.7%, -6.45%, -8.5%, respectively, p < 0.001 for all), but not in controls (-0.7%, -3.53%, -2.97%, respectively). Change of BMD at lumbar spine was significantly different between AIs treated women and controls (-3.7%, -6.45%, -8.5%, respectively). Change of BMD at lumbar spine was significantly different between AIs treated women and controls (-2.94% vs. -0.69%, p < 0.001) and the same result was observed as for BMD at femoral neck (-2.5% vs. -0.39%, p = 0.01). Percent change of BMD was significantly greater in AIs treated women in comparison with controls (-2.2% vs. -0.4%, respectively, p = 0.02). In AIs treated women, but not in controls, CTX levels significantly increased after 18 months 0.47 (0.36 to 0.62) vs. 0.66 (0.43 to 0.77), p = 0.0004 and the same trend was observed as for BSAP levels [14 (13.01 to 15.57) vs. 15 (13.75 to 16.75), p = 0.003]. At a multiple regression analysis, change of TBS was independently predicted by change of AD-SoS, after correcting
for BMD change at lumbar spine and femoral neck and for modification of CTX and BSAP levels (<0.037, SE= 2.44, p<0.001).

Conclusion: TBS variation was independently predicted by phalangeal OUS measurement in Al treated BC women. Phalangeal OUS may represent an alternative tool to evaluate bone health also in this setting of patients.

REFERENCES

Disclosure of Interests: None declared

AB0824
THE EFFECTS OF CEMENT VOLUME DISTRIBUTION OF PERCUTANEOUS KYPHOSCOPY IN OSTEOPOOROTIC VERTEBRAL FRACTURE
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Background: Osteoporotic vertebral compression fractures (OVCF) account for 45% of osteoporotic fractures. It causes severe back pain, unable to walk or even stand. Percutaneous kyphoplasty (PKP) is commonly used to treat painful OVCF, effectively relieve pain and walking ability. But there have been few clinical studies that have specifically explored the relationship of the cement volume distribution rate and clinical outcomes.
Objectives: To access the effect of the cement volume distribution pattern in percutaneous kyphoplasty.
Methods: We retrospectively reviewed 126 cases of osteoporotic compression fractures treated with percutaneous kyphoplasty from Jan 2005 to May 2015. The cement volume distribution (CVD) was measured with X-ray and CT scan. 126 thoracolumbar vertebrae were divided into two groups based on CVD ratio: 51 vertebrae in group A with CVD ratio<2; 15 in group B with CVD ratio>2. The relationships of the cement volume distribution and clinical outcomes of pain, vertebral height and kyphotic angle change between the two groups were compared.
Results: The mean duration of follow-up was 25 months (range 11-76), and the mean age was 68±8.7 years. Correlation of volume of cement distribution measured by CT scan and X-ray is 89.3% (P<0.001). The VAS improvement after kyphoplasty was no statistically significant (P = 0.651). Statistically greater height gain was observed in group B at the anterior border (4.42±2.42 VS 1.83±1.5, P = 0.035) and at the center (4.64±1.73 VS 3.01±0.41, P = 0.044). Subsequent fracture was 7 cases in group A and 4 case in group B.
Conclusion: Larger volume of cement distribution, greater correction of kyphosis. The greater distribution of the cement without leakage would be suggested when the limited volume of cement is injected.

REFERENCES

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Disclosure of Interests: None declared

AB0825
IMPACT OF AROMATASE INHIBITOR TREATMENT ON BONE MINERAL DENSITY AND PREVALENT VERTEBRAL FRACTURE
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Background: In recent years, despite the growing incidence of breast cancer, a reduction in mortality has been observed. Adjutant therapy with aromatase inhibitors (AI) has contributed to a longer disease free survival. However these molecules induce a hyper bone remodeling, modifying the bone architecture and thus increasing the fracture risk. The new guidelines recommend indication of treatment duration up to 10 years. So special precautions must be established in order to avoid bone mineral density (BMD) decrease and to reduce fracture risk.
Objectives: The aim of this study was to evaluate the impact of AI treatment on BMD and to screen vertebral fracture (VF) in post menopausal women with breast cancer.
Methods: A clinical cross sectional study was carried between August 2016 and December 2018, including post-menopausal women with non-metastatic breast cancer. Each woman had an extensive medical history and physical examination. BMD was measured using dual energy X absorptiometry DeXa at femoral neck, total hip and at lumbar spine. We used the WHO criteria for the diagnosis of osteoporosis and osteopenia. Vertebral fractures were screened by performing a vertebral fracture (VF) image. VF grade 1 were excluded.
Results: Thirty-six post-menopausal women were examined in our rheumatology department. The mean age was 59.5±10.38 years with an average body mass index (BMI) of 30.7 kg/m².[15.81-38.28]. The average age of menopause was 45.5±5.25 years. The mean length of menopause was 14 years.[2.1-31]. The mean duration of breast cancer follow-up was 7.17 months. 22 patients underwent chemotherapy and radiotherapy.Mean femoral neck BMD was 0.805 g/cm² [0.647-1.049 g/cm²] and the vertebral BMD was 1.003 g/cm² [0.739-1.314g/cm²].According to the WHO classification, 12 women (34.6%) had osteoporosis, 15 (42.3%) had osteopenia and 9 (25.7%) had normal BMD. 9 patients showed signs of osteoporosis at femoral neck and 8 had osteoporosis at lumbar spine. 10 subjects (27.8%) had VF grade 2, 6 had VF grade 3, 3 had grade 4. No female BV were assessed. No statistically significant difference was found between women with and without VF for age, BMD value, and duration of follow-up or previous fragility fracture. We did not find a significant correlation between treatment length and BMD at either site: femoral neck (p=0.42), total hip (p=0.783) and lumbar spine (p=0.037).
Conclusion: This data has shown that approximately one-third of patients receiving AI treatment have at least one vertebral fracture, and 40% had osteoporosis. Therefore we need to screen bone mineral density and fracture in women under AI therapy.
Disclosure of Interests: None declared

AB0826
OSTEOEOSDIMENTOMETRIC PROFILE DURING JUVENILE CELIAC DISEASE
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Background: Bone mineralization abnormalities are often seen in children with chronic gastrointestinal disease. Among these pathologies, celiac disease (CD) is the most likely source of abnormalities of bone mineral density. These disorders are of multifactorial origin involving malabsorption, nutritional status, decreased physical activity and chronic inflammation.
Objectives: The purpose of this study was to determine the frequency and factors associated with lower bone mineral density in children with CD.
Methods: This is a retrospective study, over a period of 4 years (from January 2014 to December 2017) including children followed for CD who had a measurement of bone mineral density (BMD) by DEXA. Clinical, anthropometric and densitometry data (BMD at the femoral and vertebral site) were recorded.
Results: Thirty-six children were collected. Among them 29 were girls and 7 were boys. The average age was 11.94 years old. The average size was 137.8 cm. The average weight was 35.3 kg. The average body mass index (BMI) was 17.69 kg/m² [13.05-21.69 kg/m²]. The average vertebral BMD was 0.891 g/cm³. The average z-score was -1.08. BMD was normal in 26 cases. A decrease in bone mineral density
with respect to chronological age was observed in 10 cases. A very significant correlation was observed between BMI and vertebral BMD (r = 0.76, p < 0.000).

Conclusion: The frequency and severity of the decline in BMD in children with CD requires regular monitoring. It seems to be favored by a low BMI, which is common during CD in relation with the associated malabsorption.

Disclosure of Interests: None declared


AB0827

IS DENOSUMAB SAFE IN HIV PATIENTS?

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Background: The survival of the infected patients by the human immunodeficiency virus (HIV) has increased in the last years, increasing the incidental comorbidities, being osteoporosis (OP) one of them, caused by traditional risk factors, by the ones associated to the infection itself and due to the specific treatments used. The denosumab is a human monoclonal antibody that acts against the link of the receptor that activates the nuclear kappa B (RANK-L), and among its secondary effects most commonly described, there are the infections, reason why its indication in HIV patients requires special caution.

Objectives: To analyze efficacy, security and compliance to denosumab in HIV patients.

Methods: Retrospective longitudinal observational study. There were included all HIV patients with OP diagnosed by bone mineral density measured by dual-energy X-ray densitometry (DEXA) or fragility fractures treated with denosumab at Infectious Diseases Unit of our Hospital from August 2014 until December 2018. There were collected clinical data, immunological status, antiretroviral therapies, fragility fractures at duration, adverse events, tolerance and compliance to denosumab treatment.

Results: There were included 14 patients, 8 females and 6 males, with a mean age of 58.35 (50-73) years old, and a mean HIV evolution of 23.78 (± 9.56) years, with a mean denosumab treatment duration at 27.07 (9-58) months. They presented a DEXA mean T-score values of -2.39 for femoral neck and -2.96 for spine. There were collected a patient with multiple vertebral fractures, and an other patient with a single vertebral fractures before started denosumab treatment and 1 distal radius fracture 9 months on denosumab treatment. There were reported adverse events in 5 of the 14 patients: 2 mild infections of the upper respiratory track, 1 injection site rash that lead to the interruption of the treatment, and 2 exits but none of them with a direct relationship with denosumab treatment: a patient with refractory small cell lung cancer history, deceased of pneumonia, and a 77 year old woman with Alzheimer disease deceased of respiratory infection. Compliance was not met in three patients, 1 because lost of follow-up, 1 caused by bad general compliance and another because indication of odontological surgery, these two last ones are waiting for re-introduction. There have not been collected jaw osteonecrosis neither atypical fractures cases. There have not been collected viral loads or CD4 changes during the follow-up period that involved a switch for the OP treatment. The antiretroviral treatment changes have been caused by intolerances to previous treatments and treatment simplifications in order to improve the compliance, but never because denosumab concommitant therapy.

Conclusion: Denosumab treatment in the HIV patients of our series is well tolerated, has adequate adherence and seems safe although perhaps it should be used with greater caution in patients with comorbidities.

Disclosure of Interests: Isabel de la Morena Speakers bureau: Abbvie, Celgene, Pfizer, UCB, Ghebrou, Roche, Sanofi, Janssen.; Sara Velázquez: None declared, Juan Alberto Paz Solarte Employee of: Abbvie, Roche, Pfizer, Novartis, Celgene, Amgen, MSD, Janssen, Diego Bedoya: None declared, M José Galindo: None declared


AB0828

RHEUMATIC PATHOLOGY AFTER SOLID ORGAN TRANSPLANTATION

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Background: Organ transplantion has become as effective therapy for end-stage renal, hepatic, cardiac and pulmonary diseases within the past 2 decades. Osteoporosis, low level of vitamin D and hyperuricemia have emerged as frequent and sometimes devastating complications of organ solid transplantation process.

Objectives: The objective of the study was to detect the prevalence of osteoporosis, low level of vitamin D and hyperuricemia in liver and lung transplant recipients.

Methods: We evaluated a cohort of 48 patients who underwent liver and lung transplantation in a single Romanian center between July 2014 and January 2019. 44 pts undergone liver transplantation and 4 undergone lung transplantation. We have measured the level of the 25-hydroxyvitamin D and serum urate before and after the transplantation in all patients.

Results: The average age of the patients was 53.7 ± 10 years (range 32-69) with a sex ratio 1:1. 32 (66%) of patients came from urban area, 8 (16.6%) patients were excluded from this study due to recurrent HCV infection with hepatic failure in the first few months after transplantation. The final group consisted of 40 patients.

The indications of the orthotopic liver transplantation in these patients were: cirrhosis secondary chronic hepatitis B, C, D virus infection in 24 (60%) cases, autoimmune hepatitis in 7 (17.5%) patients, alcoholic liver disease in 2 (5%) patients, hepatocellular carcinoma in 1 (2.5%) patient, polycystic liver disease in 1 (2.5%) patient and nonalcoholic fatty liver disease in 1 (2.5%) patient.

In all 4 cases with lung transplantation, the reason for the lung transplantation was chronic obstructive pulmonary disease (COPD).

36 (91%) patients were receiving combination immunosuppressant therapy (tacrolimus and) and only 4 (9%) patients were receiving cyclosporine; in this situation, the association between tacrolimus and mycophenolate mofetil was preferred versus cyclosporine because of the negative effect of cyclosporine on the bone.

Post-transplant, hyperuricemia (according to local laboratory reference values >6.5 mg/dL) was presented in 28 (70%) transplant recipients but none of the hyperuricemic patients developed gout. Despite this fact, all of them were treated with allopurinol.

Vitamin D deficiency was reported in 22 (55%) transplant recipients. Also, a DXA scan of the lumbar spine and femoral neck measuring T-score of the lumbar spine and femoral neck bone mineral density (BMD) was routinely performed after a mean interval of 4-6 months post-transplant. From this group of patients, 10 (25%) patients had decreased bone mineral density (<2.5 SD) and 20% (20%) of them who complained of back pain in the early posttransplantation period, presented on x-rays vertebral fragility fractures at different sites (most frequently in the thoracic spine). The mean T-score was -2.7 and the mean BMD was 27.4 kg/m².

Conclusion: The standard care of liver and lung transplant recipients must includes, besides other lab tests, a measurement of 25-hydroxyvitamin D and serum urate. For patients with low levels of 25-hydroxyvitamin D, evaluation for osteoporosis (risk factors, x-ray, DXA scan) should be mandatory.

REFERENCES


Disclosure of Interests: Madalina Duna: None declared, Denisa Predeteleanu: None declared, Violeta Bojinca Speakers bureau: multiple, Ianos Pahomea: None declared, Nicolae Boileac: None declared, Radu Poenaru: None declared, Narcis Copca: None declared

OSTEOGENESIS IMPERFECTA: EVOLUTION OF THE BONE MINERAL DENSITY AND EVALUATION OF FRACTURE RISK UNDER BISPHOSPHONATES

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Background: Osteogenesis imperfecta (OI), or Lobstein's disease, also known as 'Glass bone disease' is a rare genetic disorder predisposing to low bone mass with impaired bone microarchitecture and abnormal quality of bone material, causing fracture susceptibility and bone deformities.

Objectives: The main objective of our work was to study the clinical and para-clinical characteristics, and global management, of adult patients and children with OI in a rheumatology department by comparing them with data from the literature.

The secondary objectives were to study the evolution of the bone mineral density and to evaluate the fracture incidence under treatment by Bisphosphonates.

Methods: This is a cross-sectional, observational, descriptive, analytical and monocentric study of subject with OI followed at Fattoura Bourguiba University Hospital in Monastir, Tunisia.

Results: We collected 13 patients with OI, including 5 children and 8 adults. Seven patients were female and 6 were male, including 12 patients with type IIB and one with type IIIB. Three adult patients had a family history of OI. For children, it was sporadic and the genetic survey did not reveal similar cases in the family. The mean age of clinical onset of the disease was 9 years and 3 months [0-33 years] with a mean age at diagnosis of 15 years and 7 months [14 months-40 years]. The clinical manifestations were dominated by osteo-articular symptoms. Chronic mechanical bone pain related to fractures was present in eight patients. Twelve patients had a history of fracture. These were repeated fractures without trauma or minimal trauma the majority of cases mainly in the lower limbs. The first fracture site was the femur associated with other fracture sites (there were no fractures in the pelvis, hands and skull). Deformities were observed in 7 patients, mainly in the limbs (6 patients), in the spine (2 patients) and in the thorax (1 patient).

In our study the frequency of osteoporosis and/or osteopenia regardless of the measured site and using the T-score value for women-2.5 and the Z-scores-2 for children and men was 84.62%. All patients received Aredia protocol with calcium and vitamin D supplementation. The treatment was also multidisciplinary. Bisphosphonate treatment was well tolerated for the majority of patients. There was a decrease in the number of fractures and also a densitometric gain objectively measured by Z-score of the measured site and using the T-score value for women.

Conclusion: Our results confirm the efficacy of BP in patients with OI regardless of age group. Short-term adverse effects are rare and transient.

REFERENCE

Disclosure of Interests: None declared

AB0830

CG AND DMARDS INDUCED BMD CHANGES IN PRE- AND POSTMENOPAUSAL WOMEN AND MAN WITH RHEUMATOID ARTHRITIS (RA)

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Background: Risk factors for GC-induced fracture include low bone strength at the beginning of GC treatment and the rate of decline in bone mass during treatment, which is largely determined by the dose and duration of GC use [1].

The absolute risk of future fracture in an individual is substantially influenced by demographic and other characteristics (age, race, sex and concomitant OP risk factors). For these reasons, it is important to identify differences in BMD changing depends on sex and reproductive status.

Objectives: To compare the BMD changes in man, pre- and postmenopausal women with RA depends on different treatment regiments.

Methods: The study was performed on 145 patients: 117 women (mean age 45.4±13.0 years, mean disease duration 9.7±7.7 years, 41% (n=48) postmenopausal) and 28 men (mean age 45.5±17.5 years, mean disease duration 5.7±4.8 years) with RA. Female patients were divided in two groups by menopause: premenopausal (PreM) in mean age 36.9±9.3 years and postmenopausal (PM) in the mean age 57.6±5.9 years. 68.4% women and 54.3% men received prednisolon ≤10 mg/day during 5.67±4.82 and 3.5±5.9 years respectively, 60.7% of men received MTX, 50% in combination with CGs. Among the women group 87% PreM patients received MTX, 58.3% in combination with GCs and 46.4% with biologics. 85.4% PM women took MTX, 68.8% in combination with GCs and 33.3% - with biologics. BMD was measured in 3 parts of the skeleton: hip (total and neck), lumbar spine, distal part of forearm.

Results: BMD was decreased in 44.5% of women and 42.9% of man. BMD of hip, lumbar spine, distal part of forearm were respectively decreased in 26.1%, 26.1%, 18.8% PreM women and 66.7%, 70.8%, 79.2% PM women. 39.3% of man had decrease BMD in the hip and 42.6% - in the lumbar spine. According to logistic regression in all women group the fact of CG intake was strong associated with BMD decrease in the hip (total and neck) and lumbar spine (r=0.25, p<0.05), in man no association with the fact of CG intake was found. The effect of GCs on BMD in man was cumulative dose dependent, negative correlation between treatment duration and low hip BMD (r=0.44, p<0.05) and lumbar spine BMD (r=0.5, p<0.05) was detected. In PreM women only association between CG therapy and decreased total and neck hip BMD (r=0.33, p<0.05) was detected, any relationship with cumulative dose and treatment duration wasn’t found. Only in PM patients BMD decreasing depends on average cumulative dose and treatment duration. MTX intake was negatively correlated with BMD only in PM women in total hip and lumbar spine (r=-0.37, p<0.05) and in men in the distal part of forearm (r=-2.46, p<0.05). In PM women BMD in total hip and distal part of forearm was significantly higher in MTX+BGs biologics group than without biologics (r=0.38, p<0.05).

The level of PTG was significantly higher in PM patients on GCs and was negatively correlation with cumulative dose (r=-0.77, p<0.05). In PreM women GC intake was negatively correlated with C-TP level (r=-0.37, p<0.05) and positively with RANKL level (r=0.35, p<0.05).

Conclusion: A sexual differences in BMD changes during different treatment regiments was observed in different parts of the skeleton. In man BMD lost in hip and lumbar spine depends on GCs treatment duration and on in the distal part of forearm on MTX intake. In PM women BMD decreasing was strong associated with GC and MTX cumulative dose and treatment duration.

REFERENCE

Disclosure of Interests: None declared

AB0831

PERSPECTIVE ON THE CLINICAL PRACTICE MANAGEMENT OF HYPOVITAMINOSIS D FROM A MEETING OF ITALIAN EXPERTS

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Background: Risk factors for GC-induced fracture include low bone strength at the beginning of GC treatment and the rate of decline in bone mass during treatment, which is largely determined by the dose and duration of GC use [1].

The absolute risk of future fracture in an individual is substantially influenced by demographic and other characteristics (age, race, sex and concomitant OP risk factors). For these reasons, it is important to identify differences in BMD changing depends on sex and reproductive status.

Objectives: To compare the BMD changes in man, pre- and postmenopausal women with RA depends on different treatment regiments.

Methods: The study was performed on 145 patients: 117 women (mean age 45.4±13.0 years, mean disease duration 9.7±7.7 years, 41% (n=48) postmenopausal) and 28 men (mean age 45.5±17.5 years, mean disease duration 5.7±4.8 years) with RA. Female patients were divided in two
Background: Scientific interest in the clinical aspects surrounding vitamin D has increased exponentially in recent years. Unfortunately, this interest is not currently associated with a proportional level of consensus. Indeed, the large number of studies in this field, which are often of low quality and secondary importance has confused even experts and driven them towards controversial positions.

Objectives: To shed light on this topic, we arranged a meeting with the aim of collecting the opinions of 50 experts in different specialties (‘D. Battito Group’), including internists, endocrinologists, rheumatologists, pediatricians, geriatricians, dermatologists, gynecologists and nephrologists. This meeting dealt with specific questions regarding the management of hypovitaminosis D and aimed to investigate the opinions of Italian experts on this topic. Six key questions were addressed in the meeting.

Methods: After a short lecture and a 30 minutes discussion, all the experts expressed their opinions, which were recorded together with any specific commentary.

Results: The results of the meeting demonstrated the presence of insufficient agreement on many key questions regarding the management of vitamin D deficiency, even among clinical experts.

Conclusion: We hope that the various scientific societies will recognize and analyze the inconsistencies in their own positions and reach adequate consensus, especially on the tenets required for conducting proper and useful investigations on the topic, and that the results of these future new studies will be able to shed the needed light.


Disclosure of Interests: Alessandro Gioioli: None declared, Ombretta Viapiana Speakers bureau: Novartis, Abbvie, Eli-Lilly, Sanofi Genzyme, Angelo Fassio Speakers bureau: Abiogen Pharma, Francesco Bertoldo: None declared, Vania Teresa Braga: None declared, Maria Luisa Brandi: None declared, Stefano Calvieri: None declared, Luisella Gianferrotti Speakers bureau: Abiogen Pharma, Bruno Farmaceutici, Shire, Annamaria Colao: None declared, Patrizia D’Amelio: None declared, Giovanni Mario D’Avola: None declared, Luca Degli Esposti: None declared, Bruno Frediani: None declared, Sandro Giannini: None declared, Andrea Giusti Grant/research support from: Abiogen Pharma, Consultant for: EfRgs, Speakers bureau: Abiogen Pharma, Eli Lilly, AMGEN, Andrea Giustina: None declared, Stefano Gonelli: None declared, Nazzarena Malavolta: None declared, Claudio Marocci Grant/research support from: Shire, Speakers bureau: Shire and AbiogenPharma, Salvatore Minisola: None declared, Nicola Napol: None declared, Ranuccio Nuti: None declared, Giovanni Passeri Grant/ research support from: Abiogen Pharma and Chiesi Farmaceutici, Maurizio Rossini: None declared, Luigi Sinigaglia: None declared, Francesco Vierucci: None declared, Davide Gatti Speakers bureau: Abiogen, Amgen, Janssen-Cilag, Mundipharma, Pfeizer


AB0832 Vertebral Pain and Physical Performance Indices in Postmenopausal Women with Vertebral Fractures Depending on Presence of Obesity

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Background: Vertebral fractures (VFs) are important osteoporotic fractures which manifest increased morbidity and mortality; however, their clinical features usually differ. Obesity is one of the important parameters of risk of osteoporotic fractures and vertebral pain syndrome.

Objectives: The aim of the research was to study the indices of vertebral pain (VP) and physical performance (PP) in postmenopausal women with VFs depending on presence of obesity.

Methods: We examined 87 females aged 50-89 years old with VFs in thoracic and/or lumbar spine which were divided into 3 groups: I - patients with normal weight (NW), according to WHO criteria, n=32; II - women with overweight (OW), n=37; III - females with obesity (OB), n=18. The parameters of VP in thoracic and/or lumbar spine were measured by 11-component visual analog scale (VAS), the indices of PP using static and dynamic functional tests (Thomayer, Schober tests, chest excursion, lateral trunk lean, 3-, 4-, 15-meter tests, “stand up from the chair”, static balancing). Bone mineral density (BMD) was measured by DXA (Lunar, Prodigy).

Results: We have found the significantly higher parameters of BMD of femoral neck and lumbar spine in women with VFs and OB compared to females with NW. However, we did not establish any reliable differences of VP neither in thoracic nor in lumbar spine depending on obesity presence. Also, we did not reveal the significant differences of most parameters of PP, except for the indices of chest excursion (mean parameter, of the inhalation and exhalation) which were reliably higher in patients with OB.

Conclusion: In conclusion, the indices of VP and PP do not differ in postmenopausal women depending on obesity presence, except for chest excursion that should be taken into account in rehabilitation programs for females with VFs.

Disclosure of Interests: None declared


AB0833 Bone Turnover Markers – Do They Have a Role as Predictors of Mortality and New Fracture in Patients with Fragility Hip Fracture?

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Background: In Osteoporosis (OP), bone turnover markers (BTM) are potential monitors of drug adherence/efficacy as well as predictors of bone loss and fracture risk. However, without solid evidence, international guidelines still do not recommend their systematic measurement to assist treatment decision and follow-up.

Objectives: To evaluate the predictive value of baseline BTM (beta cross‐laps – bCL; osteocalcin – OC) in the outcome (death and/or new fracture) of patients that suffered a fragility hip fracture (FHF).

Methods: Patients referred to a Fracture Liaison Service from March 2015 until March 2017 with a FHF were considered for this study. Clinical/demographic variables were collected, including: age at time of fracture, sex, serum OC and serum bCL at baseline and outcome (death, new fracture, lost to follow-up) until January 2018. Cox regression analysis was used to calculate hazard ratios (HR) for values of OC and bCL; p<0.05 was considered statistically significant.

Results: From a total of 522 patients, 218 presented a baseline measurement of OC and/or bCL and were included for analysis. Table 1 summarizes clinical and demographic characteristics of the sample. Twenty seven patients died (median days until death=457, min 160, max 1049) and 18 had a new fracture (median days until fracture=343.5, min 30, max 835); 129 patients maintained follow-up. Median serum bCL was...
7.1 ng/ml (0.12-3.28, n=217) and median OC was 28.2 ng/ml (6.80-196.60, n=215). Through univariate analysis, higher bCL values predicted worse survival outcome (HR=3.09; 95% CI=1.14-8.39;p=0.026), even after adjustment for age/sex (HR=4.28; 95% CI=1.48-12.29;p=0.007); however, it did not predict higher risk of new fracture (HR=3.00;95%CI=0.85-10.68; p=0.089). Serum OC levels showed no statistically significant results, neither for mortality (HR=1.01; 95% CI=0.99-1.03;p=0.341) nor new fracture risk (HR=1.01,95%CI=0.99-1.04;p=0.057).

Abstract AB0833 Table 1

| Total (N) 215 | Age at admission, y (median, min-max) 82 (65-99) |
| Sex, female (n,%); 172, 78.9 |
| BMI (N) 195 | Underweight (n,%); 4, 2.1 |
| Normal (n,%); 90, 46.2 |
| Overweight (n,%); 66, 33.8 |
| Obesity class I (n,%); 29, 14.9 |
| Obesity class II (n,%); 5, 2.6 |
| Obesity class III (n,%); 1, 0.5 |
| Degree of dependence (N) 205 | Totally dependent (n,%); 10, 4.9 |
| Partially dependent (n,%); 53, 25.9 |
| Autonomous (n,%); 142, 69.9 |
| Type of fracture (N) 217 | Femoral neck (n,%); 90, 41.5 |
| Subtrochanteric (n,%); 16, 7.4 |
| Vertebral fracture (N) 213 | 0 (n,%); 92, 43.2 |
| > 1 fractures (n,%); 53, 24.9 |
| > 2 fractures (n,%); 68, 31.9 |
| Femur neck BMD, g/cm² (mean, SD, N) 0.66, ±0.12, 198 |
| Femur neck T score (mean, SD, N) -2.79, ±1.1, 198 |
| >2.5 (n,%); 62, 31.3 |
| ≥2.5 (n,%); 136, 67.9 |
| vD3, ng/ml (median, min-max, N) 23.24, 3-97 |

Conclusion: In this cohort, increased serum levels of bCL predicted higher mortality risk. These results support the value of BM in OP, strengthening their potential as prognostic markers, besides treatment monitors.

REFERENCE

Disclosure of Interests: None declared

AB0834 FREQUENCY OF OSTEOPOROTIC HIP FRACTURE IN AN ALGERIAN HOSPITAL

Naouel Zehraoui, Narimene Saidi, Houda Hafirsou, Chafia Makhloufi-Dahou, Zehraoui Naouel Saidi Narimene Hafirsou Houda Chafia Dahou-Makhloufi, Mohamed Lamine Debaghine University Hospital, reumatology, algiers, Algeria

Background: The hip fracture is the most serious complication of osteoporosis. It is a public health issue in elderly because of its frequency, severity and economic impact. We report the result of an 18 months investigation.

Objectives: The aim of this study was to determine the frequency of osteoporotic hip fractures and identify the risk factors of osteoporosis and falls leading to these fractures.

Methods: Cross-sectional, prospective, descriptive study. We included patients with spontaneous or secondary low trauma hip fractures during 18 months, who consulted at trauma unit, Mohamed Lamine Debaghine hospital. Have been collected: patient characteristics, risk factors for osteoporosis and falls, type of treatment and length of hospital stay.

Results: 115 cases of hip fractures were recorded out of a total of 486 fractures, with a frequency of 16.8%, from all the fractures operated, it represents 22.7%. We noted a female predominance (62.6%) with a sex ratio of 0.60, the average age is 76.44 +/- 11.71 years. The associated comorbidities are: cardiovascular (55.7%), diabetes (33%), dysthyroidism (11.4%), asthma (10.4%), chronic renal failure (5.2%) prostate adenoma (4.5%). The fracture mechanism is dominated by the fall (92%), it is most often a domestic accident: slipping (30%), stumbling (26%), ablation (11%), falling on the stairs (7%),%). The risk factors for osteoporosis identified are: age more than 70 years (72.8%), female sex (62.6%), low BMI (18%), sedentary lifestyle (15.3%), corticosteroid therapy 7.2%, smoking (5.2%), history of rheumatoid arthritis in 3.4% and early menopause in 2.1% of patients. The risk factors of fracture: visual disturbances (40%) neuromuscular disorders in 11, 9%, poor health (more than 3 chronic diseases) in 9% of patients, mother’s history of hip fracture (1.7%). A personal history of osteoporotic fracture was noted in 17.4%, 7 patients presented a contralateral hip fracture. The average duration of hospitalization is 5.2 +/- 2.5 days. The treatment is surgical in 81.6% (40.8% prostheses).

Conclusion: Through this study, we found that osteoporotic hip fracture is frequent. The osteoporosis risk factors identified were female sex, advanced age, corticosteroid therapy and sedentary lifestyle. Fall risk factors were dominated by visual disturbances and neuromuscular disorders.

REFERENCES

Disclosure of Interests: None declared

AB0835 BONE MINERAL LOSS DURING ULCERATIVE COLITIS : PREVALENCE AND RISK FACTORS

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Background: Patients with ulcerative colitis (UC) are at increased risk of bone mineral loss, leading to osteoporosis and osteopenia, Etiopathogenic factors may be divided into factors specific to the underlying inflammatory process, and factors resulting from the disease process, such as, malabsorption of nutrients vitamins and minerals,decreases in weight,and the use of bone toxic medications.

Objectives: to evaluate the prevalence and possible risk factors for bone mineral density disorders in patients with UC.

Methods: A retrospective study from January 2000 to December 2018, including all patients with UC followed in our department. Bone mineral density was determined by dual energy X-ray absorptiometry.

RESULTS: Seventy eight patients were included in our study (36 men, 26 premenopausal, and 17 postmenopausal women) with an average age of 47.5 years. Forty osteodensitometries (DXA) were performed : 17 were normal (42.5%) 13 patients had osteopenia (32.5%) and 10 suffered from osteoporosis (25%). Among the 23 patients having a bone mineral loss, the average Z-score were (-0.8 SD) in the femoral neck and (-1.78 SD) in the lumbar (L2-L4) spine whereas the average T-score were (-1.23 SD) in the femoral neck and (-2.15 SD) in the lumbar (L2-L4) spine. Osteoporotic patients included 12 men, 5 premenopausal, and 6 postmenopausal women with an average age of 53.04 years. The research of risk factors has shown that 14 patients with bone mineral loss (69.6%) underwent systemic corticosteroid treatment with an average duration of 6 months. Tobacco intoxication has been mentioned in 8 cases (34.78%) and alcoholism in 6 cases (26.08%). Otherwise, patients with bone mineral loss showed a lower body mass index (average BMI =19.46) than patients with normal bone density (average BMI = 23.64). Anemia has been reported in 11 cases with low bone density (47.82%) and low level of albumin as noted in 8 cases (34.78%). No osteoporotic fractures has been reported. Pan-ulcerative Colitis was reported in 11 cases (47.82%) and acute severe ulcerative colitis in 10 cases (43.47%).

Conclusion: Our study shows that more than half of our patients having ulcerative colitis (UC) who had an osteodensitometry presented bone demineralization (osteoporosis or osteopenia ). It seems to be associated with a low BMI, an extended and severe form of UC,and the cumulative corticoid doses.

Disclosure of Interests: None declared
Background: Rheumatoid arthritis (RA) is one of the causes of secondary osteoporosis, and steroids are often used in combination, therefore osteoporosis is highly associated with RA. Furthermore, joint disorders due to RA cause various degrees of dysfunction and ADL declines. The Steinbrocker classification is often used as the degree of dysfunction. Immobilization progresses with the progress of dysfunction, possibly causing severe osteoporosis.

Objectives: Of the 2238 cases in Akita Orthopedic Group omn Rheumatoid Arthritis (AORA) registry 2017, 101 cases simultaneously measuring bone mineral metabolism markers (TARC-Pb, NTX, urinay DPD, BAP, total P1NP) and pentosidine were involved.

Methods: Patients were divided by Steinbrocker classification into class 1,2 (group A 84 cases) and class 3, 4 (group B 17 cases), we examined whether there is a difference in bone metabolism markers in each group according to Steinbrocker classification.

Results: The average age in group B (75.9) was significantly higher than group A (66.9) (p = 0.01). DAS 28 ESR was significantly higher in group B (p < 0.01). There was no difference in eGFR representing renal function between the two groups. The urinay DPD (nM/mM · Cr) and pentosidine (µg/ml) in group B was significantly higher than group A (p <0.01).

Conclusion: Immobilization by long-term bed rest is known to enhance bone resorption. In 2002, Wakae reported DPD in urine showed a higher value in the group of not going out in femoral neck fracture cases. Based on the results of this study, urinary DPD showed a high value in RA group with high degree of dysfunction, which possibly reflected immobilization due to progress of functional disorder. Moreover, it is known that pentosidine will be higher in cases with high disease activity, severe osteoporosis will be occurred in the group with progressive functional disorder which is difficult to control.

Disclosure of Interests: None declared

ASSOCIATION BETWEEN BODY FAT AND BONE MINERAL DENSITY IN POSTMENOPAUSAL WOMEN THROUGH RADIOFREQUENCY ECHOGRAPHIC MULTI SPECTROMETRY

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Background: Osteoporosis is characterized by reduced bone mineral density (BMD) and increased fracture risk. Age, concomitant diseases, body mass index (BMI), body composition, etc. are important risk factors that could reflect on bone density and on the increased risk of fractures.

Methods: A total of 98 women with mean age 62 ± 11 years underwent radiofrequency echographic multi spectrometry (REMS). Bioelectric impedance analysis (BIA) software was used to assess body fat percentage. Patients were divided into two groups—women body fat > 32% and women body fat < 32%. Age, BMI, lumbar spine BMD, total hip BMD and fracture risk score (FRAX) were compared between the patients with normal body fat and those with high body fat.

Results: The mean age of the women with normal body fat was 61.1 ± 14.6 years and the mean age of the women with high body fat was 63.3 ± 9.5 years. BMI of the women with body fat < 32% was significantly lower (22.5 kg/cm²) compared to the BMI of the women with body fat > 32% (30.2 kg/cm²) (p = 0.000). Bone mineral density of L1-L4 and total lumbar spine BMD did not differ between the women with normal body fat and high body fat. Femoral neck BMD, trochanteric BMD and total hip BMD of the patients with normal body fat (0.604 g/cm², 0.737 g/cm² and 0.736 g/cm² respectively) were significantly lower than those patients with high body fat (0.682 g/cm², 0.864 g/cm² and 0.838 g/cm² respectively) (p = 0.000 for femoral neck BMD and trochanteric BMD, and p = 0.001 for total hip BMD). FRAX score for 10-year probability of major osteoporotic fracture did not differ significantly between the two groups (20.8% for women with normal body fat and 16.6% for women with high body fat). FRAX score for 10-year probability of hip fracture was also not significant between the two groups, but there was a trend to statistical significance (p = 0.059) (9% for women with normal fat and 4.9% for women with high fat).

Conclusion: Postmenopausal women with body fat > 32% showed higher femoral neck BMD compared to those with body fat < 32%, but there was no significant difference in the lumbar spine BMD values between the groups. Women with high body fat did not show significantly lower FRAX score than the women with normal body fat.

REFERENCES
such as Osteopenia or even Osteoporosis. It has been reported in several studies, an incidence of fracture between 30-40% in this population.

Objectives: To evaluate the evolution of bone turnover biomarkers before and after treatment (according to 2015 NOF guidelines) and to describe the incidence of fracture after a SCI.

Methods: A prospective study was conducted, including 48 SCI patients followed during an observation period of 24 months, with visits every six months. Thirty-two patients concluded the study. In each visit patients were enquired about fractures. A blood test was also performed. In addition a dual-energy x-ray absorptiometry (DEXA) and simple x-ray of hip and spine was requested annually. Patients were also educated in lifestyle measures, such as an adequate calcium and vitamin D dietary intake. Oral supplementation was initiated in cases of low intake or deficit, respectively. In patients with bone mineral density (BMD) measured by DEXA in range of Osteopenia, pharmacological therapy was initiated (bisphosphonate or Denosumab). Statistics had been performed with mixed linear regression models.

Results: Our sample was 56.25% men with an average age of 56.08 ± 13.82 years old. In 32 patients (68.09%) low Vitamin D levels were detected. At baseline in 12 cases (25%) DEXA showed a BMD in osteoporosis range; in 12 (25%) osteopenia, plus 6 fractures (2.6 fractures per 100 years/patient). Afterwards, until the end of the study only a fracture was detected. At baseline in 12 cases (25%) DEXA showed a BMD in osteoporosis range, in 12 (25%) osteopenia, plus 6 fractures (2.6 fractures per 100 years/patient). So the fracture rate was 1.2 fractures per 100 years/patient. The evolution of the variables can be seen on the next table.

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<table>
<thead>
<tr>
<th>Month</th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
<th>Mean (SD)</th>
</tr>
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<tbody>
<tr>
<td>0</td>
<td>Calcium</td>
<td>9.1 (0.59)</td>
<td>9.53 (0.4)</td>
<td>9.37 (0.54)</td>
<td>9.46 (0.41)</td>
</tr>
<tr>
<td>6</td>
<td>Phosphorus (mg/dl)</td>
<td>3.63 (0.7)</td>
<td>3.42 (0.44)</td>
<td>3.32 (0.52)</td>
<td>3.33 (0.55)</td>
</tr>
<tr>
<td></td>
<td>Vitamin D (UI)</td>
<td>16.42</td>
<td>42.28</td>
<td>35.88</td>
<td>35.77</td>
</tr>
<tr>
<td></td>
<td>PTH (ng/mL)</td>
<td>38.15</td>
<td>36.09</td>
<td>38.33</td>
<td>40.1</td>
</tr>
<tr>
<td></td>
<td>PINP (mg/mL)</td>
<td>79.25</td>
<td>68.15</td>
<td>53.05</td>
<td>42.82</td>
</tr>
<tr>
<td></td>
<td>bCTX (ng/mL)</td>
<td>0.82 (0.39)</td>
<td>1.23 (4.22)</td>
<td>0.34 (0.35)</td>
<td>0.28 (0.21)</td>
</tr>
<tr>
<td></td>
<td>T-SCORE SPINE</td>
<td>0.49 (1.9)</td>
<td>0.61 (1.26)</td>
<td>-0.13 (1.4)</td>
<td>-0.24 (1.34)</td>
</tr>
<tr>
<td></td>
<td>T-SCORE NECK</td>
<td>0.95 (1.53)</td>
<td>-1.29 (1.41)</td>
<td>-1.53 (1.16)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>T-SCORE HIP</td>
<td>-1.02 (1.58)</td>
<td>-1.38 (1.58)</td>
<td>-1.42 (1.33)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TOTAL CALCIUM SUPP</td>
<td>29</td>
<td>20 (62.5%)</td>
<td>26</td>
<td>27</td>
</tr>
<tr>
<td></td>
<td>VIT D SUPP</td>
<td>46</td>
<td>2 (6.25)</td>
<td>35</td>
<td>36 (97.3%)</td>
</tr>
<tr>
<td></td>
<td>BIPHOSPHONATE</td>
<td>4 (8.33%)</td>
<td>5 (15.62%)</td>
<td>3 (8.33%)</td>
<td>5 (13.51%)</td>
</tr>
<tr>
<td></td>
<td>DENOSUMAB</td>
<td>7 (14.58%)</td>
<td>7 (21.87%)</td>
<td>7 (19.44%)</td>
<td>7 (21.87%)</td>
</tr>
</tbody>
</table>

On multivariant analysis a inverse relationship between vitamin D and CTX levels was detected (p 0.05). DEXA hip measures tend to become stabilized after Bisphosphonate treatment.

Conclusion: On our cohort, bone resorption biomarkers decrease after Vitamin D restoring. Antiresorptive therapy in high risk patients stopped bone loss, especially in hip. After two years follow up, with the treatment algorithm applied, fracture incidence was lower than other series published.

REFERENCE

Disclosure of Interests: None declared

AB0842

POTENTIAL RISKS FOR OSTEOPOROSIS AND SARCOPENIA IN ALCOHOLIC WOMEN

Kayo Masuko1,2, Chie Iwahara3, Seiji Sakate4, Yumiko Tanaka5, Shigemi Kamiya3, Yuki Mizukami4, Medical and Addiction Center, Kanagawa, Japan

Background: Recent statistics indicated an accumulating number of patients with alcohol dependency in Japan. In particular, there had been a considerable increase in the number of alcoholic women, reaching up to 130,000 patients. Because alcoholic women often have insufficient dietary intake and physical inactivity, they may be at risk for low bone mineral density and decreased muscle power. However, these points may not be widely recognized, and the current program for the rehabilitation of alcoholism may not be sufficient to address this issue.

Objectives: To assess the risk for osteoporosis and sarcopenia in alcoholic women from a nutritional viewpoint.

Methods: Thirty-two women (mean age: 42.9 ± 7.49 years) who were admitted to the Alcohols Rehabilitation Program (ARP) for alcoholism, which was diagnosed according to International Classification of Diseases (ICD)-10, were enrolled in the study. The patients were subjected to self-answered questionnaire, nutritional assessment by expert dietitians, and measurement of body composition and grip strength.

Results: Of the 32 patients, 14 (44.0%) had a history of eating disorder, mostly anorexia. All 32 patients had elevated levels of transaminases at the time of admission. History of bone fracture was present in eight of the 32 (25.0%) patients; among them, at least three (9.4%) cases were considered to be due to a fragility fracture. The mean body mass index (BMI) was 20.4 kg/m2; 10 (31.3%) patients had BMI < 18. The average energy intake was low at 1,474.5 ± 324.3 kcal. Twenty-one (65.6%) patients were taking dietary calcium of <650 mg/day, which is the level recommended for adult women. The mean grip strength was 23.8 ± 6.5 kg, and 8 (25%) patients had grip strength of only <18 kg, which is the definition of sarcopenia in the Asian elderly.

Conclusion: Young to middle-aged alcoholic women should be treated as having high risks for osteoporosis and sarcopenia. ARP should include multidisciplinary assessment and interventions to prevent future locomotive disabilities.

Disclosure of Interests: None declared

AB0843

HYPOVITAMINOSIS D IN A MARFAN POPULATION

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Background: Marfan syndrome is an autosomal dominant disorder of connective tissue caused by mutations in FBN1 gene on the long arm of chromosome 15. Information is often lacking regarding an increased risk of fractures and its management and prevention in patients with Marfan syndrome. In these patients reduced bone mineral density was rarely reported. A pivotal role in bone mineralization is played by Vitamin D.

Objectives: This study evaluates whether the reduction of the values of Vitamin D is present in Marfan patients.

Methods: 60 patients (pts) (28 M/32 F; age 15-75 mean age 46.2) with Marfan syndrome were studied. The patients were followed from the clinical and research regional Marfan Center in Florence, Italy. All pts met new Ghent criteria that identified ectopia lentis, thoracic aorta dilatation with Z score = or > 2 and a large group of systemic clinical features represented by cardiovascular, musculoskeletal, central nervous system (dural ectasia) pulmonary, cutaneous and ocular clinical manifestations (systemic features) reaching a score = or > 7 as major clinical criterion. Familiarity and the detection of a gene mutation (in MFS FBN1 gene displays a mutation in about 90% of patients) are also considered criteria necessary for Marfan diagnosis.

Results: 11/60 pts (18.3%) (5M/6F age 15-75 mean age 44.9) showed reduced values of Vitamin D. 6/11 pts (45.4%) (3M/5F age 15-56; mean age 34.1) showed very poor Vitamin D values (range 8.7 ng/ml – 13.17 ng/ml).

Conclusion: Our results suggests that Vitamin D may play an important role in bone metabolism in Marfan patients. These results need confirmation since further data are missing in literature.

REFERENCES

Disclosure of Interests: Daniela Melchiorre: None declared, Elisa Pratelli: None declared, Renato Colombai: None declared, Marco Mattucci-Cerinic: Grant/research support from: Actelion, MSD, Pfizer, BMS, Chemomab, Sanpiedra, Speakers bureau: Actelion, BMS; MSD, Janssen, Guglielmina Pepe: None declared
Background: The enigma of fragility fracture with normal bone mass; Experience of a Liaison Service Fracture Unit

Objectives: To describe the characteristics of patients with fragility fracture and normal DXA treated in an FLS unit.

Methods: Prospective 6-year observational study of a FLS fracture unit. Demographic variables, FRAX items, DXA and TBS were collected. The statistical analysis was performed by means of a descriptive, comparing the normal DXA/osteopenia/osteoporosis groups by means of contingency tables, Fisher’s exact test, Student’s t test or ANOVA, as appropriate, as well as regression analysis.

Results: 1,631 patients were included, 205 with normal DXA (12.5%), 747 with osteopenia (45.8%) and 680 with osteoporosis (41.6%). Patients with normal DXA were characterized by a higher percentage of males, a younger age and a higher BMI. Hip fracture was less frequent in patients with normal DXA, while the frequency of other fractures was higher. The frequency of previous fracture, history of hip fracture of the parents and secondary osteoporosis was lower in patients with normal DXA. The TBS and FRAX values were higher in the cases of normal DXA compared to osteopenia and osteoporosis. In the multiple regression analysis, excluding TBS <1,230 as a dichotomous variable (N = 451 cases) remained significant age (OR 1.03; 1.03-1.06), sex (OR 2.48; 1.71-3.58), BMI (OR 0.91; 0.89-0.94),) and TBS, remained significant associated with abnormal DXA age (OR 1.04; 1.03-1.06), sex (OR 2.48; 1.71-3.58), BMI (OR 0.91; 0.89-0.94), and parent hip fracture (OR 1.99; 1.11-3.58). Including TBS <1,230 as a dichotomous variable (N = 451 cases) remained significant age (OR 1.03; 1.00-1.06), sex (OR 3.58; 1.81-7.10) and TBS (OR 5.23; 1.55-17.68).

Conclusion: Patients with fragility fracture and normal DXA are younger, with more frequent males and with BMI and higher TBS values. The enigma of fragility fracture with normal bone mass; Experience of a Liaison Service Fracture Unit

Disclosure of Interests: Antonia Narango Grant/research support from: UCB, Consultant for: UCB, Speakers bureau: Amgen, Soledad Ojeda Grant/research support from: AMGEN, Speakers bureau: AMGEN, Aida Saavedra: None declared, Cristina Sepúlveda: None declared, Margarita Ramirez: None declared, Nieves Martín: None declared, Alicia Olivares: None declared, Carlos Rodriguez-Lozano: None declared, Amparo Molina Speakers bureau: AMGEN, Tatiana Marrero: None declared, Margarita Ramirez: None declared, Nieves Martín: None declared, Alicia Olivares: None declared, Carlos Rodriguez-Lozano: None declared


AB0844  THE ENIGMA OF FRAGILITY FRACTURE WITH NORMAL BONE MASS; EXPERIENCE OF A LIAISON SERVICE FRACTURE UNIT

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1Las Palmas de Gran Canaria, Rheumatology, LAS PALMAS DE G C, Spain, 2Hospital Universitario de Gran Canaria Dr Negrín, Rheumatology, LAS PALMAS DE G C, Spain, 3Hospital Universitario de Gran Canaria Dr Negrín, LAS PALMAS DE G C, Spain, 4Hospital Universitario de Gran Canaria Dr Negrín, Radiology, LAS PALMAS DE G C, Spain, 5Hospital Universitario de Gran Canaria Dr Negrín, Clinical Analysis, LAS PALMAS DE G C, Spain, 6Hospital Universitario de Gran Canaria Dr Negrín, Rheumatology, LAS PALMAS DE G C, Spain, 7Hospital Universitario de Gran Canaria Dr Negrín, Rehabilitation, LAS PALMAS DE G C, Spain, 8Gerencia de atención primaria de Gran Canaria, LAS PALMAS DE G C, Spain

AB0845  EFFECTIVENESS AND SAFETY OF BISPHOSPHONATES IN THE TREATMENT OF SECONDARY OSTEOPOROSIS IN CHILDREN

Julia Ferreiro Turrión, Rocío Galindo Zavala, Esmeralda Núñez Cuadros, Gisela Diaz-Cordobes, Laura Martin Pedraz, Antonio Urda Cardona. Hospital Regional Universitario de Málaga, Málaga, Spain

Background: Prevalence of secondary osteoporosis (SO) in children is an ongoing challenge, due to the rise in life expectancy of chronic diseases and the bone toxicity medication usage. Bisphosphonates (BF) has been stated as an alternative therapy, although studies targeted children are few.

Objectives: The goal was to establish the effectiveness and safety of bisphosphonate therapy in children with SO.

Methods: A retrospective study of BF treatment in children (<16 years) with SO at a Pediatric Reumathology Unit from 2015 to 2018. Descriptive statistics were performed to examine anthropometric measurements, clinical features, diagnoses and treatment received. We measured bone mineral density by dual-energy x-ray absorptiometry and we expressed the results as adjusted for height-for-age Z-score (HAZ).

We assessed the treatment outcome by the change of HAZ after a year treatment and the decreasing fractures rate per year. Afterwards we made a bivariate analysis to identify related factors with effectiveness and safety of bisphosphonates. Values of p<0.1 were considered statistically significant.

Results: In our study 12 patients were treated with BF, three of them with two different type. Table 1 shows the descriptive data. The HAZ and the fracture rate per year after a year of treatment were significantly lower [-2.22±1.46] vs (-1.06±1.27); p=0.04, and (1 (0.5-2) vs 0 (0-0); p< 0.01, respectively].

Table 1. Descriptive analysis

<table>
<thead>
<tr>
<th>Objective</th>
<th>Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>12</td>
</tr>
<tr>
<td>Age (years), mean (SD)</td>
<td>9.3 (4.3)</td>
</tr>
<tr>
<td>BMI SO, mean (SD)</td>
<td>18.0 (±2.9)</td>
</tr>
<tr>
<td>Clinical features of the patients (n=12)</td>
<td></td>
</tr>
<tr>
<td>Secondary osteoporosis cause, n (%)</td>
<td>6 (50)</td>
</tr>
<tr>
<td>Neurologic</td>
<td>6 (50)</td>
</tr>
<tr>
<td>Hematologic</td>
<td>5 (41,67)</td>
</tr>
<tr>
<td>Before treatment fractures, n (%SD)</td>
<td>16.4 (16.26)</td>
</tr>
<tr>
<td>Vertebral fractures, n (%SD)</td>
<td>7 (58.3)</td>
</tr>
<tr>
<td>Z score* before treatment, mean (SD)</td>
<td>-2.40 (±3.33)</td>
</tr>
<tr>
<td>Age at first fracture (years), mean (SD)</td>
<td>8.2 (3.4)</td>
</tr>
<tr>
<td>Bisphosphonate treatment features of the patients (n=15)</td>
<td></td>
</tr>
<tr>
<td>Drug administration via (n, %)</td>
<td>8 (53.3)</td>
</tr>
<tr>
<td>Bisphosphonate type, n (%)</td>
<td>8 (53.3)</td>
</tr>
<tr>
<td>Intravenous</td>
<td>6 (40)</td>
</tr>
<tr>
<td>Oral</td>
<td>6 (40)</td>
</tr>
<tr>
<td>Enteric coated</td>
<td>1 (6.7)</td>
</tr>
<tr>
<td>Treatment duration (months), median (Range)</td>
<td>0.1 (0-0.1)</td>
</tr>
<tr>
<td>Treatment ending, n (%)</td>
<td>8 (50)</td>
</tr>
<tr>
<td>Cause of treatment ending, n (%)</td>
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</tr>
<tr>
<td>Adverse effects</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Exits*</td>
<td>2 (12.5)</td>
</tr>
<tr>
<td>Adverse effects, n (%)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Flu-like syndrome</td>
<td>2 (12.5)</td>
</tr>
<tr>
<td>Asperosomial hypercalcemia</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Gastrointestinal intolerance</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

*Due to unchance disease complications

Disclosure of Interests: Julia Ferreiro Turrión: None declared, Rocío Galindo Zavala: None declared, Esmeralda Núñez Cuadros: None declared, Gisela Diaz-Cordobes: None declared, Laura Martin Pedraz: None declared, Antonio Urda Cardona: None declared
The change at HAZ and the before treatment fractures rate per year (r=0.57; p<0.07) were directly proportional. Also, the change at HAZ was inversely proportional to the before treatment Z-score (r= -0.53; p=0.09) and the BF starting age (r=-0.35; p=0.10).

The decrement of fractures rate per year showed a statistical significant relationship with BMI percentile (r=0.48; p=0.08), the treatment starting age (r=0.53; p=0.09) and before treatment fractures rate per year (r=0.941; p<0.001).

Three patients experienced adverse effects (20%). Three related to alendronate use: two of them showed flu-like syndrome after first infusion and the other asymptomatic hypocalcemia. In another patient the treatment with alendronate was ended due to gastrointestinal intolerance.

There was not significant relationship between adverse effects and our study variables.

Two patients died during the treatment due to their underlying disease complications.

Conclusion: BF are an effective medication for SO. The treatment outcome exhibits to be better with a good nutritional status, younger age and at more severe forms of the disease. Additionally, they are safe showing just minor adverse effects often.

REFERENCES

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OSTEOPOROSIS IN MEN

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Background: Careful attention to postmenopausal osteoporosis (OP) leads to an underestimation of this problem in men.

Objectives: To assess the frequency of bone mineral density reduction (BMD) in men referred for examination, analysis of bone mineralization disorders in men at different age periods, the main reasons for referral for examination.

Methods: During the year, a two-energy X-ray absorption osteodensitome-

RESULTS: Among the 2731 patients referred for examination, the proportion of men is 5%, men over 60 years old are 2%, male children and teen-

Methods: AB0847 INCIDENCE RATES OF OSTEOPOROSIS(OP) RISK FACTORS IN A LARGE URBAN LONDON BOROUGH

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Background: Identification of osteoporosis risk factors(OPRFs) is a neces-

Objectives: To examine the rates of OPRFs in patients attending the Bone Health Clinic at Croydon Health Services NHS Trust.

Methods: Retrospective review of OP patients seen between February-June 2018 at Purley Memorial Hospital and assessed for presence of OPRFs including: demographics,BMI,early menopause,late menarche,nuli-

RESULTS: Of the 201 patients included. Mean age was 70-years-old (range:37-96), with approximately 9.1 female:male ratio. Mean BMI was 23(normal) with approximately 20% being <18.5(underweight). 25.5%(46/ 180(females) experienced menopause(14 years), 10% of men (20/180) had male menopause(10 years). Of the 25.5% with early menopa-

Disclosure of Interests: None declared

SciVille
AB0848

BMD AND MUSCLE MASS IN PATIENTS WITH ISCHEMIC HEART DISEASE
Tatiana Raskina1, Inessa Grigoreva1, Olga Barbarash2, Alexander Kokov2, Vladislava Masenko3, Tatiana Raskina1

Methods: The study included 45 patients with IHD (36 males/9 females, mean age 63.16±6.71 years) verified by coronary angiography. BMD was measured by DXA in the lumbar spine L1-L4, total hip and femoral neck. BMD was evaluated as: normal BMD (T-score ≥-1), osteopenia (T-score between -1 and -2.5) and osteoporosis (T-score of <2.5). Muscle mass was assessed using computed tomography of total psoas area (TPA) (cm²) and calculating L3 muscle index (LMI) (<52.4 cm²/m² in men; <38.5 cm²/m² in women).

Results: The results of the study indicate the presence of severe dyslipidemia in men with IHD. The frequency of patients with IHD dyslipidemia (95.7% of patients): hypercholesterolemia – 81.7%, elevated level of LDL cholesterol – 22.9% and in women – 13 (17.8%) (p = 0.1), osteoporotic fractures during 6 months after injury. The main causes of death were heart and respiratory diseases. The results of the study indicate the presence of severe dyslipidemia – 47.4% cases for women (p = 0.75). Among the dead men, 1 (4.5%) case for men and 2 (2.9%) cases for women (p = 0.75). Among the dead men, 1 (1.1%) death was caused by an infectious disease. The decline in BMD in IHD patients is associated with low BMI (<18.5) was common in 1/5 patients requiring input from the dietetics team as part of their treatment plan. Early menopause was seen in a quarter of female patients with just over 10% of these being offered HRT; undoubtedly more could have benefited from intervention at menopause. Many medical conditions associated with OP were identified with several patients being newly diagnosed (coeliac/hypothyroidism/haematological disorders especially). Treatment and lifestyle modifications are clearly essential in the management of these patients. Given the high number of patients with at least one modifiable OPFR, it is crucial that OP services are organized accordingly to identify OPFRs to intervene and modify these factors as part of the overarching management plan.

Disclosure of Interests: None declared

AB0850

THE LIPID SPECTRUM OF BLOOD, DEPENDING OF BONE MINERAL DENSITY (BMD) IN MEN WITH CORONARY HEART DISEASE (CHD)
Tatiana Raskina1, Anna Voronkina2, Marina Leteava1, Olga Barbarash3, Vyacheslav Fanaskov4, Tatiana Raskina1

Methods: 93 men older than 50 years (mean age – 60.8±6.9 years) with coronary artery disease verified by coronary angiography were examined. The concentration of total cholesterol (OHS), triglycerides (TG), high and low density lipoprotein cholesterol (HDL and LDL cholesterol) in serum was determined by spectrophotometric method. T-criterion of the femoral neck and lumbar spine was used for the assessment of BMD, which was investigated by the method of two-energy absorptiometry (densitometer Excel XR-46, NORLAND, USA). The results of the study indicate the presence of severe dyslipidemia (95.7% of patients): hypercholesterolemia – 76.3%, elevated level of LDL cholesterol – 81.7% of the patients, hypertriglyceridemia in 49.5%, a decrease in the concentration of HDL cholesterol – 44.1% of cases. In all three groups of patients hypercholesterolemia (80, 75 and 73.7% of patients in groups I, II and III, p>0.05) and increased LDL-C concentration (83, 84.1 and 73.7% of men in groups I, II and III, p>0.05) were revealed. Reduction of HDL cholesterol level was determined in 46.7% of cases in group I, 43.2% in group II and 42.1% in group III (p>0.05). Hypertriglyceridemia was registered in 60% of patients with osteoporosis, 43.2% - with osteopenia and 47.4% – with normal BMD (p>0.05). Correlation analysis of the relationship of lipid metabolism with the T-criterion in all patients included in the study did not reveal significant relationships (p>0.05).

Conclusion: The results of the study indicate the presence of severe dyslipidemia and the absence of dependence of lipid parameters on the state of BMD in men with CHD.

Disclosure of Interests: None declared

AB0849

CAUSES OF EARLY MORTALITY IN PATIENTS WITH OSTEOPOROTIC HIP FRACTURES
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Background: Osteoporosis (OP) is a skeletal disorder characterized by compromised bone strength, which predisposes the individual to an increased risk of fractures of the hip, spine, and other skeletal sites. OP, a major public health problem, is becoming increasingly prevalent with the world’s population and occupies a leading place in the structure of morbidity and mortality.

Objectives: To study the causes of mortality in patients with hip osteoporotic fractures during 6 months after injury.

Methods: 432 patients with osteoporotic hip fractures were under observation. During the study, mortality rates were assessed both in hospital and during the first 6 months after the fracture. The main causes of mortality were tracked by ICD-10 classes. Information about fractures and their outcomes was obtained from data from the archives of the trauma departments of Kemerovo, Kemerovo city registry offices, telephone interviews of patients and their relatives.

Results: In the first 6 months after injury, 96 out of 432 patients died. Overall mortality was 22.0%. In the group of deceased patients, females prevailed: 73 women (16.5%) and 22 men (5.1%) (χ² = 4.4; p <0.0001). It was established that 6 months after a hip fracture in 63 (66.3%) patients, death occurred from cardiovascular system diseases: in men - 13 (59.0%) cases and in women - 50 (68.4%) (p = 0.9). Respiratory diseases, as the cause of death, were detected in 18 (16.9%) patients (men - 5 (22.9%) cases and in women - 13 (17.8%) (p = 0.1), oncological diseases - in 10 (10.5%) men and women; 2 (9.1%) and 8 (10.9%) cases, respectively (p = 0.5). Diseases of the digestive system accounted for a small percentage of the total number of deaths (3.2%), without statistically significant differences by gender (1 (4.5%) case for men and 2 (2.9%) cases for women (p = 0.75)). Among the dead men, 1 (1.1%) death was caused by an infectious disease.

Conclusion: During all periods of observation, most of the deceased men and women had cardiovascular and respiratory diseases.

REFERENCE

Disclosure of Interests: None declared
Disclosure of Interests: None declared

AB0851 OBESITY AND RISK OF FRACTURE: DEPENDS ON THE BODY MASS INDEX AND TYPE OF FRACTURE

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Objectives: To know the impact of obesity on the risk of fracture.

Methods: Observational study, during 2010-2018, of patients referred for bone densitometry (BMD), to the Bone Densitometry Unit of Rheumatology.

BMD performed by Rheumatology nursing, collect several data (age, gender); osteoporosis (OP) risk factors: age of menopause, smoking and current alcohol intake, hip fracture parents, body mass index (BMI), diseases-drugs that reduce bone mass, fractures, treatment; BMD in lumbar spine (LS), femoral neck (FN); FRAX with BMD. BMI result was as WHD recommendations in kg/m²; Normal: 18.5-24.99; Obesity: ≥30; type I: 30-34.99, type II: 35-39.99, type III: ≥40.

Results: A first BMD in 6.943 postmenopausal women was done. 2.196 (32%) had normal BMI, low weight (BMI <18.5 kg/m²) 103 (1.5%) patients, overweight (BMI 25-29.99 kg/m²) 2.643 (38%) and obesity 2.001 (29%). Obesity (BMI ≥30 kg/m²) vs normal BMI are older (65±13) vs 61±13, p=0.003, lower current smokers (12% vs 27%) P <0.001, more treated for OP (37% vs 29%, P<0.002), higher percentage of fractures (44% vs 29%), especially distal radius (DR) (30% vs 11%), p<0.001 and FN (-1.1±1.5 vs -1.6 ± 1.5, p<0.0001) and lower mean T score in LS (-1.1±1.5 vs 1.8±1.5, p=0.002), lower mean T score in DR (-1.1±1.5 vs 1.8±1.5, p<0.0001) and FN (-1.1±1.5 vs -1.6 ± 1.5, p<0.0001) and lower mean FRAX hip fracture with BMD (1.9±3.6 vs 2.4±3.6, p <0.0001) and FN (-1.1±1.5 vs -1.6 ± 1.5, p<0.0001) and lower mean T score in LS (-1.1±1.5 vs 1.8±1.5, p=0.002), lower mean T score in DR (-1.1±1.5 vs 1.8±1.5, p<0.0001) and FN (-1.1±1.5 vs -1.6 ± 1.5, p<0.0001) and lower mean T score in DR (-1.1±1.5 vs 1.8±1.5, p=0.002), lower mean T score in LS (-1.1±1.5 vs 1.8±1.5, p=0.002), lower mean T score in DR (-1.1±1.5 vs 1.8±1.5, p<0.0001) and FN (-1.1±1.5 vs -1.6 ± 1.5, p<0.0001) and lower mean T score in LS (-1.1±1.5 vs 1.8±1.5, p=0.002), lower mean T score in DR (-1.1±1.5 vs 1.8±1.5, p<0.0001) and FN (-1.1±1.5 vs -1.6 ± 1.5, p<0.0001) and lower mean T score in LS (-1.1±1.5 vs 1.8±1.5, p=0.002).

Conclusion: In postmenopausal women referred for BMD, obese women vs normal BMI are 1. Older. 2. Overall, with higher percentage of fractures. 3. But, women with BMI ≥ 40 kg/m² do not have a higher overall percentage of fracture, except in DR.

References:

Acknowledgement: The study was supported with a research grant from the Association for Research in Rheumatology of Marina Baixa (AIRE-MIB).

Disclosure of Interests: Jose Rosas Consultant for: Abbvie, Amgen, Bristol, Janssen, Lilly, Merck Sharp & Dohme, Pfizer, UC Pharma, Speakers bureau: Abbie, Amgen, Bristol, Janssen, Lilly, Merck Sharp & Dohme, Pfizer, UC Pharma, Catalina Cano: None declared, Ana Pons: None declared, Estibaliz Ivans: None declared, José Miguel Senabre-Gallejo: None declared, Gregorio Santos Soler: None declared, Esteban Salas-Heredia: None declared, José Antonio Bernal-Vidal: None declared, José Alberto García-Gómez: None declared, Xavier Barber: None declared


AB0852 DOES INADEQUATE RESPONSE TO DENOSUMAB TREATMENT EXIST?

Clara Sanguessa, Susana Holgado Pérez, Meliana Martínez-Morillo, Jordi Camins-Fábregas, Ivette Casafont-Solé, Annika Nack, Águeda Prior-Español, Maria Aparicio Espinarr, Anahy Brandy-Garcia, Lourdes Mateo, Anne Riveros, Alejandro Olive, Laia Gifre. Hospital Germans Trias i Pujol, Badalona, Spain

Background: Denosumab (Dmab), an anti-receptor activator of nuclear factor kappa-B ligand (RANKL) monoclonal antibody, has been shown to increase bone mineral density (BMD) at lumbar spine and proximal femur, up to 21.6% and 9.1% respectively at 10 years of treatment. Additionally, Dmab has shown a marked decrease of vertebral, nonvertebral and femoral fractures during treatment. Nowadays, the existence of inadequate response to Dmab treatment remains unknown.

Objectives: to describe the clinical, analytical and densitometric characteristics of patients with an inadequate response (IR) to Dmab treatment. IR was defined as the presence of a new fragility fracture during Dmab treatment or a significant decrease in BMD (≥5% at lumbar spine or ≥4% at proximal femur) within at least 12 months of therapy.

Methods: retrospective study including patients with osteoporosis with an IR to Dmab. Therapeutic compliance was checked by clinical anamnensis and the electronic prescription. Risk factors for osteoporosis, history of fragility fractures, previous anti-osteoporotic treatment, densitometric and analytical data were collected before and at the moment when IR was diagnosed.

Results: Fourteen patients were included (12 women and 2 men) with mean age of 75 ± 9 years. The causes of osteoporosis were: postmenopausal (n=8), 57.14%, induced by glucocorticoids (n=3, 21.43%), alcoholic (n = 1, 7.14%) and multifactorial (n=2; 14.28%). Nine patients (64.28%) had been previously treated with oral or intravenous bisphosphonates for a mean of 5.8 ± 2.76 years. Nine patients (64.28%) had previous vertebral fractures (median 2, range 1-8), 2 of them had also presented a femoral fracture. During Dmab treatment, 7 patients (50%) presented a decrease in BMD (mean loss: proximal femur -3.5%, p<0.09; lumbar spine - 5.8%, p=0.046;) and 7 had incidental fractures: 5 vertebral (median 1, range 1-4), 1 humerus and 1 femur. The duration of treatment with Dmab was 3.82 ± 1.85 years in patients who sustained fragility fractures and 2.39 ± 1.4 years in patients with a BMD decrease. A multiple myeloma was diagnosed in a patient with vertebral fractures during Dmab treatment. After The identification of Dmab RI most patients maintained same treatment. Of the patients with incidental fragility fractures, 2 started combined treatment with teriparatide and Dmab, 1 changed to teriparatide and 2 maintained the same treatment. Of the 7 patients with BMD only 1 changed to zoledronic acid.

Conclusion: Most patients with IR to Dmab treatment had previous fragility fractures and had been previously treated with bisphosphonates for a mean duration of 5 years. The patients with a significant decrease in BMD had lesser duration of Dmab treatment than those who sustained fractures during Dmab treatment. Only one patient had a clinical cause for the IR development.

Disclosure of Interests: None declared


AB0853 BONE DENSITOMETRY IN CROHN’S DISEASE: RISK FACTORS FOR OSTEOPENIA AND OSTEOPOROSIS

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Background: Osteoporosis and osteopenia are common situations in chronic inflammatory bowel disease (IBD), particularly in crohn’s disease.

Disclosure of Interests: None declared

Objectives: The objective of our study was to determine the prevalence of these affections during crohn’s disease and to identify the risk factors for osteopenia and osteoporosis.

Methods: We conducted a descriptive monocentric retrospective study of consecutive patients with crohn’s disease who were hospitalized between January 2016 and December 2018.

Results: We included 100 patients (64 female and 36 male) with an average age of 37 years [17-68 years]. Among these patients 21% were smokers and among women 20% were in menopause. Bone densitometry was performed in 39 patients. It was found to be pathological in 53.8% of cases. The rate of osteoporosis was 17.9% (7 patients) and the rate of osteopenia was 35.9% (14 patients). Tobacco and a BMI of less than 18 had a statistically significant association with osteopenia (p=0.046; p=0.038 respectively). The presence of a family history of IBD had a statistically significant influence on a pathological bone densitometric investigation (p=0.036). An albuminemia rate of less than 35g/dl had an association at the limit of significance with bone pathology in BMD (p=0.059).

Conclusion: Osteoporosis and osteopenia are frequent during crohn’s disease. They are in the majority of cases asymptomatic. This makes bone densitometry essential, especially in the presence of a family history of IBD, smoking and malnutrition (BMI less than 18) in order to act early and avoid complications such as fractures.

Disclosure of Interests: None declared.


AB0854 PERSPECTIVES OF WOMEN WITH EXPERIENCE OF A FRAGILITY FRACTURE IN EUROPE: ATTITUDES TOWARDS FUTURE FRACTURE RISK, OSTEOPOROSIS AND PHARMACOTHERAPY

Charles Chaïne1, Peter Ray2, Jen Timoshanko2. 1AplusA, London, United Kingdom; 2UCB Pharma, Slough, United Kingdom.

Background: Fragility fractures (FF) are common in women >50 years (yrs), with 1 in 3 experiencing a fracture (Fx).1 However, the cause of these Fx is poorly recognised and measures taken to prevent future Fx are often inadequate. Recent US patient (pt) survey data suggest that awareness of osteoporosis (OP) and its contribution to Fx risk, appreciation of the benefits of OP pharmacotherapy (Rx), and discussion about OP with healthcare professionals (HCPs) are limited.2

Objectives: This study gained insight into the attitudes and experiences of post-FF women in Europe regarding future Fx risk management.

Methods: Women ≥51 yrs from Germany (DE), Spain (ES), UK, France (FR) and Italy (IT) (EUS) with self-reported experience of a FF completed a 30–min online survey (AplusA; 13–20 Feb 2018). Data are reported for EUS pts who had their first Fx at ≥50 yrs; pts whose first Fx was a hand/finger or ankle/foot/toe Fx were excluded.

Results: 199 women participated (DE: 38; ES: 36; UK: 41; FR: 34; IT:50). The most commonly experienced Fx was of the lower arm/wrist (43%). 43% reported >1 Fx (any type). Most women discussed bone health with an HCP within 6 months (mo) (70%; 42% with a GP) and HCPs were their primary source of information on OP (85%). Around a third reported taking a DEXA test within 6 mo of their first Fx (37%). Advice from HCPs to prevent Fx focused on calcium/vitamin D supplements (74%) and diet/exercise changes (54%); 46% were prescribed OP-Rx. After having a FF, around half worried about future Fx (51%) and 39% voiced concerns about their general health (Figure). A third of pts thought that OP had caused their Fx (33%), most were likely to attribute it to a fall (67%). Only 18% felt empowered to manage their bone health; 61% did not think OP-Rx reduces risk of Fx or were unsure. 97% had never joined a support group.

Conclusion: These results indicate that pts discuss future Fx risk with an HCP soon after having a FF and are concerned about future Fx. However, low levels of DEXA testing and OP-Rx, and poor awareness of the link between OP and Fx risk remain. Better education to empower women at risk of FF is critical.

REFERENCE
patients had an osteoporosis (54.8%): six cases of HCV, three cases of HBV, five cases of PBC, two cases of AIH and one case of PSC. Osteoporosis is most common in postmenopausal women with significant correlation (p<0.001). Hyperbilirubinemia and increased Gamma Glutamyl Transferase (GGT) were significantly correlated with osteoporosis (p<0.05). However, there was no significant correlation between osteoporosis and body mass index or the Child-Pugh score.

Conclusion: In our study, 54.8% of cirrhotic patients who have had a BMD, had an osteoporosis. It was more frequent among postmenopausal women with hyperbilirubinemia and increased GGT. The systematic real-

Disclosure of Interests: None declared


AB0857
DENSITOMETRY VALUES CHANGE WHEN STOPPING DENOSUMAB
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1GALDAKAO-USANSOLO OSPITALA, RHEUMATOLOGY, GALDAKAO-USANSOLO, Spain; 2UNIVERSITY OF THE BASQUE COUNTRY, BILBAO, Spain

Background: Denosumab (DMAB) withdrawal without subsequent bisphosphonate treatment seems to be related to a rebound effect: a rapid decrease in mineral density in bone densitometry (DEXA). However, evidence is scarce.

Objectives: To analyze DEXA values in patients who have stopped DMAB without subsequent treatment and to detect possible factors associated.

Methods: Uncentric observational study. We included patients with osteo-
porosis (OP) who attended our rheumatology clinic from May 2017 to December 2018, who had stopped DMAB without any further treatment. Demographic data, risk factors for OP (smoking, age of menopause, pre-
vious fractures, chronic corticotherapy), data related to calcium and vita-

None declared


AB0858
MAINLY MEN, AND OLDER PEOPLE, WITH FRAGILITY HIP FRACTURE DO NOT RECEIVE ANTIOSTEOPOROTIC TREATMENT
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Background: Osteoporotic hip fractures have a profound impact on the physical health and psychosocial wellbeing of patients, with considerable economic implications. More than 20% of individuals experience a subse-
quent hip fracture in the following year (1,2). Although there are effective treat-
ments in the prevention of fractures, the proportion of patients who start treatment after a fragility fracture is low, having decreased in recent years (3).

Objectives: The aim of the study is to know the percentage of patients who received medical treatment for osteoporosis after a fragility hip frac-
ture in our health department. Secondary, we want to know the mortality and re-fracture rates two years after the fracture.

Methods: Cross-sectional retrospective observational study. Patients dis-
charged during 2015 with diagnosis of “Fragility Hip Fracture” were reviewed, data collected through electronic medical record. Variables: sex; age; age and date of death; treatment (calcium, vitamin D or antiosteo-
porotic drugs) before and after discharge; Fragility fracture before and after hospital discharge. Statistical methods: absolute and relative frequen-
cies for qualitative variables, means and standard deviations for quantita-
tive. Associations between variables were studied using Chi square and T-student test.
Results: A total of 320 patients were evaluated, 17 discarded (3 other fracture locations, 1 duplicate, 6 high energy trauma fractures and 8 had other pathologies than osteoporosis that justified the fracture). Mean age was 83.3 ± 7.9 years, 223 (73.6%) women. Prior to admission, 43 patients (14%) took calcium and/or vitamin D, 10 (3%) some antosteoporotic drug and 20 (7%) both. 230 patients (76%) did not receive treatment. 102 exits (33.7%) occurred in the 2 years after the fracture. In the post-discharge analysis, 30 patients were discarded (17 died during admission and 13 in the subsequent month), since it was not possible for them to be treated. After discharge, 42 patients (18%) receive Calcium and/or Vitamin D, 15 (5%) some antosteoporotic drug and 37 (14%) both, leaving 172 patients (63%) without treatment. There were 12 new hip fractures (4.0%). There is a greater proportion of deaths in men (43.8% vs. 30% in women, p = 0.026) and in patients not treated before the fracture (33.2% vs 11.6% calcium-Vit D, p <0.001, 30.5% vs 9.4%, antosteoporotic treatment p = 0.002). The multivariate analysis found a lower probability of having received treatment in men (RR 0.34 IC 95% (0.16-0.72), p = 0.005) and with more age (RR 0.95 IC 95% (0.92-0.98), p = 0.004). After correcting with age: the risk of death in men is 83% higher than in women (p = 0.035). The probability of exits increases by 10% for each additional year of life. Treatment with calcium and/or vitamin D after discharge is a protective factor against mortality from any cause (p = 0.037).

Conclusion: Percentage of patients receiving drug treatment after suffering an osteoporotic hip fracture is very low. This is accentuated in males, and at an older age, populations that also have higher mortality rates in the two years after the fracture.

REFERENCE


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AB0860

THE SERUM CREATININE TO CYSTATIN C RATIO: A POSSIBLE NEW SURROGATE MARKER FOR BONE MINERAL DENSITY

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Background: Bone mineral density (BMD) measured using dual-energy X-ray absorptiometry (DEXA) is one of the most important markers for osteoporosis diagnosis. The serum creatinine-to-cystatin C ratio (Cr/CysC) is in focus as a sarcopenia marker because it represents total muscle volume. Recently, Cr/CysC was suggested to have correlation with bone fragility fracture risk [1].

Objectives: This study aimed to assess whether Cr/CysC is correlated with BMD.

Methods: BMD at the lumbar spine (LS) and femoral neck (FN) were measured in women diagnosed with postmenopausal osteoporosis. Steroid included with antosteoporotic patients were eliminated. Cr/CysC was assessed at the time. Clinical factors, such as age, concurrent rheumatoid arthritis treatment (RA), concomitant biological drug administration (BIO), body mass index (BMI), concurrent dementia treatment (dementia), number of comorbidities other than dementia (N.Com), frailty score (FS), bone fragility fracture (BFF), and drug intervention for osteoporosis (DI), were evaluated. Multivariable linear regression (MLR) was used to assess the correlation of these factors with BMD at each part. The relationship between Cr/CysC and other parameters were statistically evaluated using MLR. Additionally, the relationships between the BMD change at each part and parameters were evaluated in the same manner.

Results: The study enrolled 207 subjects. BMD at the LS was significantly correlated with BMI and N.Com (p<0.01), whereas BMD at the FN was significantly negatively correlated with age and was positively correlated with BMI, BFF, Cr/CysC, and DI (p<0.01). Cr/CysC was significantly correlated with age, RA, BIO, dementia, FS, and BFF (p<0.01).

After effect of age was corrected, BMD at the FN demonstrated significant positive correlation with Cr/CysC (p<0.01), whereas no statistical correlation demonstrated between BMD at the LS and Cr/CysC. Both BMD at the LS and the FN demonstrated significant positive correlation with BMI (p<0.05). No parameter significantly correlated with the BMD change at both the LS and FN (p>0.01).

Conclusion: Cr/CysC represents BMD at the FN and is a candidate for BMD substitution.

REFERENCES


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Disclosure of Interests: None declared


AB0859

RECURRENT OF VERTEBRAL FRACTURE IN PATIENTS WITH OSTEOPOROTIC VERTEBRAL FRACTURES: RETROSPECTIVE REVIEW IN MONCLOA UNIVERSITY HOSPITAL. PRELIMINARY RESULTS

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Background Current drugs for patients who suffer from stabilised osteoporosis (OP) with osteoporotic vertebral fracture (VF) have demonstrated their efficacy with different levels of evidence for secondary prevention of fractures1. In fact, this level of efficacy can be limited in real clinical practice, with pluri-pathological and previously polimmedicated patients.

Objectives Main objective of this study is to describe the percentage of patients with VF in which the therapeutic goal of avoiding new VF during their follow-up has been achieved. As a secondary objective, clinical and therapeutic differences will be analyzed among distinct groups arisen from achieving or not the therapeutic goal.

Methods Retrospective, observational, longitudinal, descriptive study of patients from Rheumatology Department in Moncloa University Hospital who have suffered a vertebral OP. Results

133 cases have been reviewed, 115 (86.5%) females and 18 males (13.5%). Average age is 72 years (+/- 7) and average follow-up time is 2.68 years (+/-3). 25 cases (18.5%) were smokers, 9 (6.8%) on oncologic treatment (73% with chronic corticotherapy and 28% (21%) with immune-mediated diseases, 81 patients (60.9%) had previous VF (0.933 fracture/patient) and 14 (10.5%) non-vertebral fracture (NVF). The average VF was 1.967/patient and 0.133/patient for NVF. 52 patients (39.1%) had received prior treatment for OP (36 Bisphosphonate, 23 Denosumab, 5 SERM, 2 strontium ranelate and 1 teriparatide) and in 39 cases (29.3%) a cementoplasty was performed. Initial treatments prescribed by Rheumatology Department were Bisphosphonates (48%), Denosumab (31%) and Teriparatide (21%). 35 patients received sequential-treatment (26.9%). 86.5 % of patients haven’t presented new VF. 18 cases (13.5%) have been registered with new VF. This group is composed by 13 females and 5 males: the average age was 75 years (+/-7.5) and the average follow-up time 2.8 years (+/- 2.46); 14 (77.8 %) patients presented previous VF and 3 (16.7 %) previous NVF. The average number of previous VF was 2.0/patient and 0.33/patient for NVF. 14 cases (78.8%) of new VF occurred during the first year of follow-up. The treatment they were receiving at the time of the new VF was in 8 cases with Denosumab (44%), 4 with Teriparatide (22%), 2 Alendronate (11%), 3 Risedronate (16%) and 1 case without treatment.

Conclusion These are preliminary data from a register for prognosis evaluation of patients who suffer VF in Moncloa University Hospital. A larger sample size is necessary to develop a strategic conclusion in this patients, pluripathological, with previous osteoporotic fractures and treatment.78 % of new VF occurred during the first year of the follow-up, 44% of them were receiving Denosumab, 77% (vs. 58% of the patients without new VF) had previous VF and 44% (vs. 37% patients without new VF) had received previous OP treatment.
Crystal diseases, metabolic bone diseases other than osteoporosis

AB0861 METHODS TO EFFICIENTLY RECRUIT MINORITY PATIENTS WITH GOUT FOR CLINIC-BASED REGISTRIES

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Background: Gout is frequently misdiagnosed and/or miscoded, making approaches to identifying eligible patients for observational and interventional studies more challenging. Ethnic and racial minorities are underrepresented in many gout studies. Methods to better identify minorities and confirm gout diagnosis are essential to ensure studies have both validity and generalizability.

Objectives: To define efficient methods for identifying African Americans (AA) interested in participating in a gout registry and who satisfy the American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) gout classification criteria.

Methods: We identified all AA patients seen at University of Alabama at Birmingham 01/09/2017 and 31/08/2018 with an ICD 9/10 code for gout. Patients not “opted out” by their primary care provider (PCP) were invited to participate. Those interested underwent detailed medical record review followed by phone contact to determine eligibility. Those with a high likelihood of meeting diagnostic criteria for gout were invited for an in-person visit to confirm diagnosis (Abstract AB0861 Figure 1). We compared descriptive characteristics of participants enrolled in the registry and the larger potential gout populations.

Results: From 3,032 AA patients with an ICD 9/10 gout diagnosis we generated a random sample of 400 patients. 5 patients were excluded by their PCPs, thus 395 patients were preliminarily eligible and invited via e-mail (N=176) and/or letter (N=375). 1 patient (<1 %) communicated lack of interest, 19 (4.8%) were unreachable, 322 (81.5%) did not respond to the invitation, and 53 (13.4%) expressed preliminary interest and underwent medical record review. We successfully scheduled 30 subjects for a registry visit, 24 completed the visit, and 23 (86% of initial sample) satisfied 2015 ACR/EULAR gout classification criteria (see Table 1). We found no significant difference in age, sex, and the number of medical encounters in the last year between enrolled patients and the remaining population.

References


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Disclosure of Interests: Giovanni Adami: None declared, Josh Melnick: None declared, Jeff Foster: None declared, Elizabeth Rahn: None declared, Amy Mudano: None declared, Jeffrey Curtis: None declared, Tony Merriman Grant/research support from: Ardea Biosciences, Ironwood Pharmaceutica...
The mean age of the study group was 61.4 +/- 4.5 years. The radiographic findings (Eichenholtz Classification). All patients were neuroarthropathy has been assessed according to the clinical and the patient with type 2 diabetic and acute Charcot neuroarthropathy. All our A prospective 2-year follow-up study was carried out on eight radiological efficacy of Zoledronic acid in patients with diabetes and acute Charcot neuroarthropathy. The aim of this study was to investigate the clinical and involvement was bilateral in 6 patients and unilateral in the other 2. A biological inflammatory syndrome was found in 3 patients with a mean erythrocyte sedimentation rate (ESR) level at 43 mm after one hour. Foot X-rays were abnormal in all cases. The clinical outcomes at one month after Zoledronic acid infusions were the complete disappearance of acute symptoms in 6 patients and the improvement of the pain in one patient with a decreased Visual Analogue Scale (VAS) for pain by 30%. One patient had a persistence of the pain (VAS for pain at 5mm). A radiological Control was performed after 6 months for 5 patients. All of them had bone consolidation and remineralization.

Conclusion: Our study showed that the Zoledronic acid, given as a single dose, had a beneficial effect on clinical and radiological features in diabetic patients with acute Charcot neuroarthropathy. Despite our encouraging outcomes, further prospective and randomized studies are needed to confirm our preliminary results.

REFERENCES

Disclosure of Interests: None declared

AB0865 GOUT IN HOSPITALISED PATIENTS FOR CARDIOVASCULAR DISEASES: PREVALENCE AND MANAGEMENT STATUS
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Background: Gout is an independent risk factor for cardiovascular diseases (CVDs), where the urate crystal-led inflammatory state likely has a key role. Crystal dissolution may carry with cardiovascular benefits, so optimal management of gout patients is essential, especially in high-risk individuals, such as those hospitalised for CVDs. Although the prevalence of gout in Western country adults is about 2-4% [1], the rate and characteristics in inpatients with CVDs remains to be defined.

Objectives: To determine the prevalence of gout, characteristics and management in a hospitalised population for CVDs.

Methods: Observational, descriptive, cross-sectional study. Patients admitted for CVDs in the Cardiology, Neurology and Vascular Surgery units of a tertiary centre were recruited following a non-consecutive, systematic sampling up to reaching the estimated minimum sample size. A face-to-face interview and a review of electronic health records were performed, in order to collect clinical, laboratory and management data regarding CVD and gout. Gout diagnosis was established in the interview using ACR/EULAR 2015 criteria. In addition, prior clinical or crystal-proven diagnoses at records were also registered. 95% confidence intervals (95%CI) were calculated for primary variable (gout prevalence), and comparisons were performed by Student’s t, chi-squared and Fisher’s exact tests.

Results: 299 patients were interviewed, 33 were excluded, and the final study sample was 266 participants. They were predominantly males (69.9%) and Caucasians (96.6%) with a mean age of 68 years (SD±12). The CVDs leading to admission were acute coronary syndrome (18.8%; n=50), heart failure (13.2%; n=35), stroke or transient ischemic attack (8.7%; n=23), diabetic and acute Charcot neuroarthropathy (5.5%; n=12) and peripheral artery disease (47.4%; n=126). Gout was identified in 40 individuals (prevalence 15.0%; 95%CI 10.9-19.2). Prior gout diagnosis in records was found in only two-thirds of them, mostly clinical (Table). Patients with gout were older (72±9 vs 68±13 years, p=0.026) and showed higher rates of chronic kidney disease (55.0% vs 23.0%, p=0.001) and use of diuretics (55.0% vs 38.5%, p=0.05), with no differences in other variables. The disease was long-standing though low numbers of flares and involved joints were referred (Table). Tophi were seen in about 8%. The serum urate levels were not properly controlled, both at the time of the CVD and as a median of the previous five years, and only one-third of the patients were on target (<6 mg/dl). Despite 70% of patients having been treated with urate-lowering agents at some point, at assessment only half remained treated (38.5% of them were on target). Nearly a quarter of patients used prophylactic colchicine.
Abstract AB0866 Table 1. Clinical & management of gout in inpatients for CVDs.

<table>
<thead>
<tr>
<th>Gout (n=40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior diagnosis at records</td>
</tr>
<tr>
<td>-No</td>
</tr>
<tr>
<td>-Clinical diagnosis</td>
</tr>
<tr>
<td>-Proven by crystals</td>
</tr>
<tr>
<td>Serum urate levels (mg/dl) at admission, mean (SD)</td>
</tr>
<tr>
<td>Median serum urate levels in the previous 5 years (mg/dl), mean (SD)</td>
</tr>
<tr>
<td>Current serum urate &lt;6 mg/dl</td>
</tr>
<tr>
<td>Years since the first flare, median (IQR)</td>
</tr>
<tr>
<td>Number of flares, median (IQR)</td>
</tr>
<tr>
<td>Number of involved joints, median (IQR)</td>
</tr>
<tr>
<td>Presence of tophi</td>
</tr>
<tr>
<td>Urate-lowering agents at some point</td>
</tr>
<tr>
<td>Current use of urate-lowering agents</td>
</tr>
<tr>
<td>Use of prophylactic colchicine</td>
</tr>
</tbody>
</table>

Data shown as n (%), unless otherwise specified.

Conclusion: Gout is prevalent in hospitalised patients for CVDs, affecting one in seven cases. The management of gout in these patients appears suboptimal, with serum uric acid levels above recommended targets and a significant percentage of no urate-lowering treatment.

REFERENCES

Disclosure of Interests: None declared


AB0867 METABOLIC SYNDROME IN PATIENTS WITH GOUT ATTENDED IN A SPECIALIZED OUTPATIENT UNIT IN SPAIN. COMPARISON WITH GENERAL POPULATION AND CARDIOVASCULAR IMPLICATIONS

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Background: Metabolic syndrome (MS) is a cluster of interrelated components: central adiposity or higher waist circumference (WC), high values of triglycerides (TG), elevated blood pressure (BP), impaired fasting glucose and decreased HDL-cholesterol (HDL-c). It is associated with a higher incidence of developing chronic diseases (DM) as well as with other cardiovascular diseases (CVD). A direct relationship between serum uric acid (sUA) and the risk of develop MS has been reported in several studies of patients with hyperuricemia and gout.

Objectives: To study the prevalence of MS and associated CVD in patients with gout attended in a specialized outpatient unit, comparing with other local and national studies.

Methods: Retrospective observational study with consecutive patients diagnosed with gout according to EULAR/ACR criteria between August and December 2018. We analysed the presence of MS according to the 2015 International Diabetes Federation criteria (central obesity as BMI >30 kg/m² or WC >94 cm (>80 in women), with ≥2 of the following: TG ≥1.71 mmol/l, HDL-c <1.04 mmol/l (<1.3 mmol/l in women), hyperglycemia ≥5.55 mmol/l (or T2DM previously diagnosed or hypoglycaemic treatment), hypertension (HT; >130/85 mmHg or use of antihypertensive drugs).

Results: From August 2016 to December 2018, we evaluated 192 patients with hyperuricemia and gout. The MS prevalence was 64.9%; 14% diagnosed in our unit. 807%; 10.5% diagnosed in our unit. DM 22.8%. Dyslipidemia (DL: hypercholesterolemia or high levels of TG) 64.9%; 14% diagnosed in our unit. Ischemic heart disease (IHD) 14%. Stroke 24.6%. FH of CVD 24.6%. Comparing with the general population the prevalence of MS and pMS was higher (DARIOS: 31% and 24%, respectively; ENRICA: 22.7% and 16.9%; SIMETAP: 41% and 25%), as well as with the presence of CKD (11.5% in SIMETAP) and CVD (SIMETAP: HT 38%, T2DM 16%, obesity 28%, IHD 4.8% and stroke 3.8%).

Conclusion: There is a very significant percentage of MS and pMS in patients with gout compared to the general population, with important presence of CKD and CVD, sometimes underdiagnosed. Nursing guidelines were established with healthy lifestyle and periodic controls directed at all patients, with special emphasis on those newly diagnosed of HT or DL, as well as those of higher cardiovascular risk.

REFERENCES

Disclosure of Interests: Enrique Calvo-Aranda Speakers bureau: Grünenthal, SOBI, Menarini, fernando manuel sanchez-aranda: None declared, Laura Cebrian: None declared, maria angeles matias de la mano: None declared, elena garcia-lorenzo: None declared, maria teresa navio marco: None declared


AB0867 DEPRESSIVE SYMPTOMS INFLUENCE SUCCESS OF ALLOPURINOL AS URATE LOWERING THERAPY

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Background: Elevated levels of serum urate (sUA) is the known precursor of gout and urate lowering therapies (ULT) are the backbone of successful gout treatment. However, less is known about factors that influence the effectiveness of ULTs. Depression has shown strong relationships with treatment noncompliance, which may translate into reduced effectiveness of treatment with allopurinol. Little is known about any effects depression may produce on the observed serum urate lowering efficacy of ULTs (e.g.; allopurinol).

Objectives: To evaluate the role of depressive symptoms in the efficacy of allopurinol for lowering sUA in the context of a clinical trial.

Methods: Within a larger cross-over clinical trial of 300 daily mg of allopurinol vs. placebo for urate lowering and its effect in ambulatory blood pressure (1), 67 patients had complete data for depressive symptoms at the beginning of each treatment period, as well as sUA before and after a 4-week treatment period with allopurinol and a 4-week placebo period (order of conditions was randomized). Depressive symptoms were assessed with the Center for Epidemiologic Studies Depression Scale-10 (CESD-10) (2). Paired samples t-test evaluated change in sUA from pre- to post-treatment during active treatment and placebo. Then, linear regressions predicted change in sUA over each treatment period from pre-treatment depressive symptoms, adjusting for sex and race which were associated with baseline sUA levels.

Results: The 67 patients had average age 27.01 years (SD=6.5, range 18-40). 87% were African American, and 64% were male. Over the 4-week active treatment period, sUA levels decreased from average 5.8 mg/dL (SD=1.2) (345.7 μmol/L) to 4.4 mg/dL (SD=1.2) (261.7 μmol/L), p<.001. However, sUA did not change during the 4-week placebo condition (both 5.8 mg/dL (345.7 μmol/L), SD=1.1 and 1.3, p=0.71). Pre-treatment depressive symptoms ranged from “no symptoms” (0) to “severe symptoms” (16 or 20), with mean in the “no to mild” range (M=4.6, SD=3.1). A multiple linear regression analysis (M=6.1, SD=4.9 before placebo). After adjusting for pre-treatment sUA, sex and race, pre-treatment depressive scores predicted higher levels of sUA at the end of the active treatment period (β=0.07, beta=25, p=0.28) but not at the end of the placebo period (β=0.03, beta=11, p=0.102). After 4 weeks of allopurinol, the estimated difference in sUA between individuals with pre-treatment depressive scores of 0 vs. 16 was 1.12 mg/dL (66.6 μmol/L), which was similar to the average treatment effect of 1.4 mg/dL (88.3 μmol/L).

Conclusion: Even in the absence of clinical diagnosis of depression, depressive symptoms are associated with reduced efficacy of urate-
AB0868 ULTRASOUND MONOSODIUM URATE CRYSTAL DEPOSITS IN THE JOINTS OF GOUT PATIENTS CORRELATE WITH THE WORSENING OF THE HEART SYSTOLIC FUNCTION

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Background: The connection between gout and cardiovascular (CV) complications has been investigated a lot. Recent studies demonstrated that higher body urate load is an indicator of increased CV risk.

Objectives: To determine whether ultrasound deposits of monosodium urate (MSU) crystals in the joints of gout patients (pts) correlate with the worsening of the heart systolic function and left ventricular hypertrophy.

Methods: This was a single-center cohort-observational study including 56 consecutive gout pts. 40 males and 16 females in a mean age 58.9±13.2 years with disease duration 6.4±2.93 years. All of them underwent trans-thoracic echocardiography and ultrasound examination of the joints of the hands, elbows, knees, ankles and feet. By transthoracic echocardiography, conducted with 2.5 MHz transducer phased array working with pulse Doppler frequency of 2.5 MHz, were measured parameters which are independent predictors of CV risk: left ventricular mass index (LVMi), ejection fraction (EF), fractional shortening (FS) and systolic motion of the myocardium (Sm). Ultrasound studies of the joints were performed with a high-frequency, linear transducer, 4-15 MHz. The existence of double contour sign, tendon MSU deposits, snow storm, tophi and tophi with erosions or a combination of these ultrasound features was assessed. Examinations were done in accordance with the latest published guidelines. Data were analyzed by Kolmogorov-Smirnov, Mann-Whitney, t-test, Kruskal Wallis test and Spearman correlation.

Results: 49(87.5%) of the pts had ultrasound evidence of crystal deposits. Serum uric acid levels were equal in pts with and without MSU deposits, pts with MSU findings in one joint area and in those with crystal deposits in two or more joint areas we did not find a difference in the mean values of LVMi (means±SD; 126.86±21.95 g/m² vs 120.09 ±31.50 g/m² vs 128.63±35.19 g/m², p=0.761), FS (means±SD; 37.73 ±6.62% vs 38.25±3.51% vs 35.40±5.57%, p=0.205) and Sm (means±SD; 0.27±0.35 m/s vs 0.30 m/s vs 0.30±0.2 m/s, p=0.266). A tendency of lower EF without reaching significance was detected in subjects with crystal deposits in two or more joints, (p=0.071). The values of LVMi (p=0.295), EF (p=0.396), FS (p=0.566) and Sm (p=0.154) were similar in pts without MSU findings, subjects who had a double contour sign, those with tendon MSU deposits, pts with snow storm, individuals with tophi and in pts with tophi and erosions. However, pts with crystal deposits in the knees and in the tibiotalar joints had lower EF (p=0.047; p=0.049, respectively) and lower FS (p=0.036; p=0.016, respectively) compared to those who had no crystal deposits in these joint areas. Further a weak negative correlation was detected between the number of joints with crystal deposits and EF (r=-0.294, p=0.029) and FS (r=-0.292, p=0.030).

Regarding LVMi and Sm no correlation was established with the presence of crystal deposits in the joints (p=0.079, p=0.568 and r=-0.242, p=0.076).

Conclusion: Despite the lack of difference in serum uric acid between pts with and without MSU deposits in the joints, those with MSU findings in the knees and in the tibiotalar joints had more deteriorated systolic function of the heart in comparison to pts without crystal deposits in these joint areas. A negative correlation existed between the number of joints with crystal deposits and functional pumping indices of the heart. On the other hand, MSU deposits in the knees and in the tibiotalar joints are associated with higher urate load than deposits in the small joints. We suggest that the higher urate load is connected to the worsened pumping function of the heart.

Disclosure of Interests: None declared


AB0869 SERUM LEVELS OF ROS PRODUCTS, NO AND ASCORBATE RADICALS IN GOUT PATIENTS ARE NOT ASSOCIATED WITH ARTERIOSCLEROTIC COMMON CAROTID ARTERIES CHANGES AND USE OF XANTHINE OXIDASE INHIBITORS

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1University Hospital St. Ivan Rilski, Medical University, Clinic of Rheumatology, Sofia, Bulgaria; 2University Hospital St. Ivan Rilski, Medical University, Clinic of Nephrology, Sofia, Bulgaria; 3Medical Faculty, Traikia University, Department of Chemistry and Biochemistry, Stara Zagora, Bulgaria; 4Medical University, Sofia, Faculty of Public Health, Sofia, Bulgaria.

Background: Oxidative stress along with chronic inflammation and hyperuricemia links gout to arteriosclerotic vascular changes. Studies examining the connection between the level of oxidative stress and arteriosclerotic carotid arteries changes in gout patients (pts) are not enough.

Objectives: To establish the association between the serum levels of reactive oxygen species (ROS) products, nitric oxide (NO) radicals and ascorbate radicals with intima-media thickness (IMT) and common carotid artery resistive index (CCARI) in gout pts, and to find out whether the connection is more pronounced when tophi are present.

Methods: This was a cross-sectional study including 71 gout pts in a mean age 58.86±11.95 years, 61 males and 10 females (45 without tophi pts and 26 gouty tophi pts). Serum levels of ROS products, NO radicals and ascorbate radicals were determined by ex vivo electron paramagnetic resonance (EPR) study. All EPR measurements were performed on an X-band EMXmicro, spectrometer Bruker, Germany, equipped with Standard Resonator. Spectral processing was done by using Bruker WIN-EPR and Sinfonia software. By applying ultrasound of the common carotid arteries, conducted with 10 MHz linear transducer working with pulse Doppler frequency of 5 MHz, were measured IMT and CCARI. Statistical analyses were done by One-Sample Kolmogorov-Smirnov, Chi-Square, Fisher’s exact test, Mann-Whitney, t-test and Pearson correlation.

Results: Gouty arthritis without tophi and gouty tophi pts were age-matched, (p=0.309). The mean values of serum uric acid (p=0.569) and distribution of the subjects with gout attack (p=0.173), smoking (p=0.828), arterial hypertension (p=0.735), dyslipidemia (p=0.646), chronic renal failure (p=0.233) and obesity (p=0.623) was equal in the groups. In the tophi group CRP and the number of pts who had suffered a cardiovascular event were higher (p=0.048; p=0.031). Serum levels of ROS products, NO radicals and ascorbate radicals were comparable in gouty arthritis without tophi and in gouty tophi pts (p=0.783; p=0.521; p=0.651). In the groups no difference was registered in CCARI (p=0.273) but intima-media was thicker in the presence of tophi, (p=0.027). No correlation existed between ROS products, NO radicals and ascorbate radicals with IMT (r=-0.100, p=0.405; r=-0.186, p=0.121; r=0.154, p=0.201). ROS products, NO radicals and ascorbate radicals did not correlate with CCARI (r = -0.110, p=0.359; r=-0.066, p=0.587; r=0.094, p=0.436). Among treated and untreated with Allopurinol pts no difference was found in the mean values of ROS products (p=0.169), NO radicals (p=0.167), ascorbate radicals (r=0.273) and CCARI (p=0.930). Among treated and untreated with Febuxostat pts the mean values of ROS products (p=0.546), ascorbate radicals (p=0.309), IMT (p=0.842) and CCARI (p=0.100) were similar. A tendency of higher serum NO radicals was established in pts taking Febuxostat in comparison to those not treated with it (p=0.076).

Conclusion: Although between the earlier and the later stage of the disease there was no difference in the level of oxidative stress, the level of chronic inflammation was higher in gouty tophi pts. No connection was found between serum ROS products, NO radicals and ascorbate radicals with arteriosclerotic changes of the carotid arteries and use of xanthine oxidase inhibitors. We suggest that in gout pts chronic inflammation has an important role in the process of atherogenesis.
The aim of this study was to assess the incidence of gout in patients presenting to hospital with myocardial infarction (MI) or stroke (CVA). However, the incidence of gout in patients presenting to hospital with MI or CVA in Ireland has not previously been assessed. Studies have suggested gout as a risk factor in patients presenting with myocardial infarction (MI) and stroke (CVA). How-ever the incidence gout in patients presenting with CVA and MI.

Methods: The Hospital In-Patient Enquiry Scheme (HIPE) was used to identify patients admitted with stroke or myocardial infarction from 62 acute public hospitals in Ireland from January 2007 until December 2017. HIPE is a national database which records coded hospital admission and demographic, clinical and administrative data on discharges from, and deaths in, acute public hospitals nationally. Discharges are coded using the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM), Australian Classification of Health interventions (ACHI), Australian Coding Standards (ACS), 8th Edition. Age, gender and number of patient admissions with MI or CVA with gout, diabetes, hypertension, peripheral vascular disease (PVD) and hyperlipidemia were recorded.

Results: From 2007 until 2017, 64,867 were admitted with a diagnosis of CVA in Ireland. The age and gender of patients admitted with a principal diagnosis of CVA are outlined in Table 1. 70,628 patients were admitted to the stroke group (0.77%). The presence of diabetes as a risk factor (6.7%) was significantly higher compared to gout (0.5%) in patients admitted with myocardial infarction. Chart one outlines the incidence of each risk factor in patients discharge with a primary diagnosis of MI in Ireland between 2007 and 2017.

Conclusion: The incidence of gout in patients presenting with CVA or MI in Ireland was low compared to other risk factors including diabetes. In patients presenting with MI then incidence of gout is lower than in patients presenting with CVA.

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AB0870

IS THE INCIDENCE OF GOUT SIMILAR TO OTHER RISK FACTORS IN PATIENTS PRESENTING WITH STROKE OR MYOCARDIAL INFARCTION?

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Background: Gout is a common form of inflammatory arthritis. The prevalence of gout in Europe is between 0.9-2.5% with rates as high as 4% reported in Ireland. Studies have suggested gout as a risk factor in patients presenting with myocardial infarction (MI) and stroke (CVA). However, the incidence gout in patients presenting to hospital with MI or CVA in Ireland has not previously been assessed.

Objectives: The aim of this study was to assess the incidence of gout in patients presenting with CVA and MI. A further objective was to explore if the incidence of gout is similar to other risk factors such as hypertension, diabetes mellitus and dyslipidemia in Irish patients presenting with CVA and MI.

Methods: The Hospital In-Patient Enquiry Scheme (HIPE) was used to identify patients admitted with stroke or myocardial infarction from 62 acute public hospitals in Ireland from January 2007 until December 2017. HIPE is a national database which records coded hospital admission and demographic, clinical and administrative data on discharges from, and deaths in, acute public hospitals nationally. Discharges are coded using the International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Australian Modification (ICD-10-AM), Australian Classification of Health interventions (ACHI), Australian Coding Standards (ACS), 8th Edition. Age, gender and number of patient admissions with MI or CVA with gout, diabetes, hypertension, peripheral vascular disease (PVD) and hyperlipidemia were recorded.

Results: From 2007 until 2017, 64,867 were admitted with a diagnosis of CVA in Ireland. The age and gender of patients admitted with a principal diagnosis of CVA are outlined in Table 1. 70,628 patients were admitted to the stroke group (0.77%). The presence of diabetes as a risk factor (6.7%) was significantly higher compared to gout (0.5%) in patients admitted with myocardial infarction. Chart one outlines the incidence of each risk factor in patients discharge with a primary diagnosis of MI in Ireland between 2007 and 2017.

Conclusion: The incidence of gout in patients presenting with CVA or MI in Ireland was low compared to other risk factors including diabetes. In patients presenting with MI then incidence of gout is lower than in patients presenting with CVA.

Disclosure of Interests: Rada Gancheva; None declared, Atanas Konduriev; None declared, Galina Nikolova; None declared, Mariana Ivanova Goycheva Speakers bureau: Abbvie, Pfizer, UCB, Novartis, Todor Konduriev; None declared, Zlatimir Kolarov; None declared, Veselada Gjeva; None declared DOI: 10.1136/annrheumdis-2019-eular.1952

AB0871

ASSESSMENT OF THE KIDNEYS AND URINARY TRACT DYNSFUNCTIONS THAT INCREASE THE RISK OF DEVELOPING CHRONIC KIDNEY DISEASE IN PATIENTS WITH GOUT BASED ON COMPLEX RENAL SCINTIGRAPHY

Margarita Gromova1, Vladimir Tsurko2, Anna Kashkadayeva2, Svetlana Averinova2, Andrey Aliokhin3. 1Pirogov Russian National Research Medical University, Department of Faculty Therapy, Moscow, Russian Federation; 2N.N.Blokhin National Medical Research Center of Oncology, Laboratory of Radioisotope Diagnostics, Moscow, Russian Federation; 3Group of companies Tekon, Moscow, Russian Federation.

Background: In 40% of cases patients with gout can develop gouty nephropathy, the “kidney mask” of gout. The newest version of the technology for systemic examination of nephrological status based on complex renal scintigraphy (SENS-CRS) has been developed at the «N.N. Blokhin National Medical Research Center of Oncology». SENS-CRS at the lowest doses of radiation (0.6 mSv per adult) allows for an in-depth differential analysis of dysfunctions of the renal parenchyma, upper and lower urinary tract which increase the risk of chronic kidney disease (CKD) development.

REFERENCES


Abstract AB0870 Table 1. Number of discharges with a principal diagnosis of stroke, by age group and sex, reported to HIPE, 2007-2017

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Oxidative Stress Marker Allantoin in Patients with Systemic Autoimmune Rheumatic Diseases After Abrogation of Systemic Inflammation by TNF Inhibition

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Background: In patients with gout, the serum uric acid (SUA) is usually lower during acute gouty attacks than during intercritical periods. In a previous study, we have shown that abrogation of systemic inflammation by TNF inhibitors (TNFi) results in an increase in the levels of SUA in patients with systemic rheumatic diseases. We have not found any correlation between the magnitude of change of SUA and CRP or pro-inflammatory cytokines (IFN-γ, IL-6, IL-8, IL-10, IL-17a, IL-18, IL-23, TNF-α).1 Another possible mechanism for the lowering of SUA during inflammation may be consumption of circulating SUA in free radical reactions generated during systemic inflammation. Allantoin has been validated as a stable biomarker of oxidative stress in humans.2

Methods: We examined 66 patients with gout. 95% were men (average age 54±9 years). Duration of gout was 8 [4; 11] years. All patients had chronic gouty arthritis, 30% of patients had tophuses. SENS-CRS was carried out on a 2-detector γ-camera with simultaneous recording in 2 projections. In studies of the urinary system domestic radiopharmaceutical (RP) 99mTc-technetor with glomerulo- and 10-15% tubulotropic properties was used. The CRS study consisted of: 1) a basic 21-min functional study; 2) a delayed 21-min study (without the injection of RP) with a preliminary diuresis forcing to identify persistent urodynamic dysfunction.

Results: 16 patients with gout with serum creatinine level of more than 125 μmol/l had established diagnosis of chronic pyelonephritis, glomerulonephritis, urolithiasis, etc. and were allocated into a separate subgroup. In the comparative analysis of these 16 patients and other 50 patients with gout there was reliable distinction only for one indicator D (%), the rate of RP removal from a kidney parenchyma (p < 0.05). There was no significant distinctions for glomerular filtration rate by Reberg, the nuclear indicator (Grenal) of renal parenchyma concentration function, and other indicators. Renocortical parameter D (%) is one of the earliest highly sensitive markers of intrarenal developments of stagnation at development of serious morphofunctional violations in a parenchyma. In the subgroup of 16 patients the indicator accounted on average D = 48% ± 7% (range 38-55%); in subgroup of 50 patients D = 63% ± 10% (47-89%).

According to the CKD-EPI formula and SENS-CRS technology in the subgroup of 16 patients CKD stage II-III was evaluated. In addition to the standard taken rate of RP removal from a parenchyma (D) when comparing the 2 phases of CRS there was observed a steady sign of stagnation in a parenchyma and groups of upper and/or lower cups: ID = Grenal/GC < 1. Based on the water test which accelerates diuresis there was a sufficient regulation of urostasis in the renal pelvis revealed at the basic test (IP = Grenal/GP > 1.0). This indicated that the functional reserve of the outflow regulation from the kidneys was preserved at these patients.

Conclusion: This functional diagnosticizes allows one-time control of hemo-dynamics and concentration function of the parenchyma of each kidney, quantitative and qualitative signs of urodynamic delays in the intra- and post-renal urinary tract. Differentiated analysis SENS-CRS contributes to the timely therapeutic correction as well as referral for consultation to specialists (urologists, nephrologists, gynecologists, etc.).

Disclosure of Interests: Margarita Gromova Speakers bureau: Speaker during conferences in Russian Federation, Vladimir Tsurko Speakers bureau: Speaker during conferences in Russian Federation, Anna Kashkadaeva: None declared, Svetlana Averinova: None declared, Andrey Alioburua: Speaker during conferences in Russian Federation, Anna Kashkadaeva: None declared, Vladimir Tsurko Speakers bureau: None declared.

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Disclosure of Interests: Marketa Pavlikova: None declared, Petr Kozlik: None declared, Kveta Kalikova: None declared, Blanka Stibulkova: None declared, Jakub Zavada Consultant for: Genzyme-Sanoﬁ, Glaxo, Pfizer, Abbvie, Speakers bureau: Novartis, San- doz, Biogen


ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH GOUT. RELATIONSHIP BETWEEN CARDIOVASCULAR RISK FACTORS

Ekaterina Ilinykh, Maxim Eliseev, Alexander Volkov. V.A.Nasonova Research Institute of Rheumatology, Moscow, Russian Federation

Background: Patients with gout have a high risk of developing cardiovascular disease based on atherosclerosis. An early marker, and at the same time a risk factor of cardiovascular disease, is a violation of the vasoregulating endothelial activity.

Objectives: To identify the relationship between cardiovascular risk factors and endothelial dysfunction (ED) in patients with gout.

Methods: The study included 80 pts with gout. The criteria for inclusion were: 1. Male 2. Age >55 years 3. Intercritical period of arthrits 4.Absence of clinical signs of coronary artery disease 5.Absence of drug therapy. Vasoregulating endothelial activity was evaluated in all pts, 52 of them determined the carotid intima-media thickness (C-IMT). Flow-mediated (endothelium-independent) dilatation (EID) were assessed by highresolution ultrasonography (D. Celermajer). A non-invasive ultrasound technique was used to measure C-IMT. All patients were diagnosed with serum total cholesterol (CHOL), subtypes (LDL-C, HDL-C), glucose (GLU), uric acid (SUA), hsCRP. Cardiovascular risk (CVR) was calculated. Statistical analysis was conducted using the online programs package of descriptive statistics STATISTICA 12.0 (StatSoft,Inc. USA).

Results: It was found that 41 (51.25%) pts had FMD less than 8%. A correlation was found between FMD and CVR (r = -0.28, p < 0.05), age (r = -0.37, p < 0.001), Body mass index (BMI).
ANALYSIS OF LIFESTYLE AND CLINICAL FEATURES OF THE PATIENTS WITH GOUT IN MEIZHOU, GUANGDONG, CHINA

Yutong Jiang1, Yiquan Wen2, Zhongyu Liu1, Qyoun Chen3, Yetei Huang3, Yunteng Pan1, Jeruo Gu1, Junyu Gu1, the Third Affiliated Hospital of Sun Yat-sen University, Guangzhou, China; 2The Third Affiliated Hospital of Sun Yat-sen University, Yuedong Hospital, Meizhou, China.

Background: Gout is one of the most common metabolic diseases caused by purine metabolic disorder, leading to joint destruction and kidney impairment. With the improvement of living conditions, the incidence of gout is increasing year by year, especially in the developed coastal areas of China. Previous studies found that the management of gout was unsatisfactory [1]. Besides, the development of rheumatology in Meizhou, Guangdong province is extremely slow. There are only ten rheumatologists, and the general public has a limited understanding of gout.

Objectives: Our aim was to explore the lifestyle, clinical features and risk factors of recurrent gout attacks in patients with gout in Meizhou, Guangdong province.

Methods: Demographic data, lifestyle and clinical data of 188 patients with gout in Meizhou were collected. Demographic variables included age, gender, marital status, education, BMI, smoking status, drinking status, diet, daily water intake, work style, exercise habit, late sleeping habit. Smoking status includes never smoking, ever-smoking or current smoking, diet, daily water intake, work style, exercise habit, late sleeping habit.

Results: There were 249 case reports documenting non-extremity urate deposition. Urate deposition was reported in multiple organ systems including cardiovascular, renal, spine, integumentary, ocular, renal, cardiovascular, gastrointestinal, larynx, breast, middle ear, pancreas, nasal, prostate gland, liver, pulmonary, penis, nailbed, and pelvis.

Conclusion: Numerous case reports document systemic deposition of urate based on autopsy, pathology, imaging and clinical exam. Urate crystal deposition with the formation of tophi and micro-tophi involve multiple organ systems including cardiovascular, renal, spine, integumentary, prostate, bowel, pancreas, eyes, pelvic, breast, lungs, middle ear, larynx, liver, penis, nailbed, and nose. Given the strong association of gout with various comorbidities, this demonstrates a need for further studies to determine the clinical significance of systemic urate deposition with respect to ongoing subclinical inflammation and potential end-organ damage.

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Scientific Abstracts 1905

Disclosure of Interests: None declared

AB0875 GOUT, NOT JUST A DISEASE OF THE FOOT. LITERATURE REVIEW OF SYSTEMIC DEPOSITION OF URATE

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Background: Gout is the most common adult inflammatory arthropathy in the US. Although tophi in the extremities is a known source of the inflammatory cascade, urate deposition in organs throughout the body is not as well recognized. Patients with gout often have associated comorbidities including renal disease, cardiovascular disease and metabolic syndrome, however, a casual role has not been established. Direct urate deposition in these organ systems may be of interest to link the causality of these systemic disorders.

Objectives: Perform a literature review including clinical exam, autopsy, pathology, and radiology imaging results demonstrating systemic deposition of urate exclusive of the extremities.

Methods: PUBMED from 1920 to 2018 was searched to identify reports of non-extremity urate deposition. Key words included: extra-articular gout, systemic deposition of urate, ocular gout, gout nephropathy, renal tophi, gouty heart, cardiac valves and urate, urate deposition in the arteries, prostate and urate, autopsy findings in gout, cutaneous urate deposits, gouty panniculitis, auricular gout, breast and urate, gastrointestinal gout, pancreas and tophus, laryngeal tophus, and spinal gout. The reference lists from these publications were also used to identify additional articles. The literature was reviewed for organ system involvement and documented based on sites of urate deposition within an organ system.

Results: There were 249 case reports documenting non-extremity urate deposition confirmed by autopsy, biopsy, surgery, clinical exam and/or radiology imaging. Urate deposition was reported in multiple organ systems (Table 1) including the spine, integumentary, ocular, renal, cardiovascular, gastrointestinal, larynx, breast, middle ear, pancreas, nasal, prostate gland, liver, pulmonary, penis, nailbed, and pelvis.

Conclusion: Numerous case reports document systemic deposition of urate based on autopsy, pathology, imaging and clinical exam. Urate crystal deposition with the formation of tophi and micro-tophi involve multiple organ systems including cardiovascular, renal, spine, integumentary, prostate, bowel, pancreas, eyes, pelvic, breast, lungs, middle ear, larynx, liver, penis, nailbed, and nose. Given the strong association of gout with various comorbidities, this demonstrates a need for further studies to determine the clinical significance of systemic urate deposition with respect to ongoing subclinical inflammation and potential end-organ damage.

REFERENCES

Disclosure of Interests: None declared
GOUT CAUSING URATE CARDIAC VEGETATIONS:
OXIDIZED LOW DENSITY LIPOPROTEIN IS

Results:
Eight publications were found from 1954 to 2012 reporting 9 previous searches. The case reports were obtained and patient, disease, examined to find any other cases that may not have been identified on
lished cases involving gout associated with or causing cardiac valve veg-
published cases of proven cardiac valve urate deposition in gout patients. This project sought to compile and synthesize the existing
a number of case reports on this topic have been published.
and in atherosclerotic plaques as well as heart valves. Due to the concern
deposition associated with gout from 8 case report publications dating
quite rarely reported, and this project describes 9 cases of urate valvular

Though gout generally causes urate deposition in peripheral
its from gout.
mitral valve. One patient had aortic and another had pulmonic valve
mitral valve was the most commonly involved heart valve, with 6 of the
exclusion after transthoracic echocardiogram in two patients (22%). The
diagnosis of gouty valvular involvement came from autopsy in 4 patients
phases along with laboratory parameters, ESR, CRP, lipid profiles, oxLDL

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2004;27:965-966

Disclosure of Interests: Brian LAMoreau Shareholder of: Horizon Pharma, Employee of: Horizon Pharma, Vidhya Chandrasekaran: None declared

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GOUTY ARTHRITIS
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Surg Path, 1982;6(1):79-81
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2004;27:965-966

Disclosure of Interests: Ada Kumar Shareholder of: I am an employee of Horizon Pharma and own shares in the company., Consultant for: I have worked as a paid consultant for Horizon Pharma., Employee of: I am currently employed by Horizon Pharma., Puja Khanna Grant/research support from: AstraZeneca, SOBI, Ironwood, Horizon, Consultant for: SOBI

AB0876
GOUT CAUSING URATE CARDIAC VEGETATIONS:
SUMMARY OF PUBLISHED CASES
Brian LAMoreau1, Vidhya Chandrasekaran2. 1Horizon Pharma, Medical Affairs, Lake Forest, United States of America; 2Independent, Deerfield, United States of America

Background: Gout is a progressive inflammatory disease that is both widely prevalent and widely undertreated. In gout patients, urate deposition occurs in peripheral joints, the spine, and organs including the prostate, kidneys, and in atherosclerotic plaques as well as heart valves. Due to the concern of bacterial endocarditis and associated sequelae, cardiac valve vegetations are generally thoroughly evaluated even without systemic symptoms. Gout causing cardiac valvular vegetations is believed to be rare, though to date a number of case reports on this topic have been published.

Objectives: This project sought to compile and synthesize the existing published cases of proven cardiac valve urate deposition in gout patients.

Methods: Medline and google were used to search for all available published cases involving gouty valve urate deposition. The references of each publication were additionally completely examined to find any other cases that may not have been identified on previous searches. The case reports were obtained and patient, disease, and valve factors were compiled and synthesized.

Results: Eight publications were found from 1954 to 2012 reporting 9 cases of urate deposition on cardiac valves. All cases had known tophaceous gout, mean age 60.9, and 89% were male. The mean uric acid concentration of plasma ox-LDL was also closely associated with the high incidence of atherosclerotic diseases in patients with gout might be closely related to increased ox-LDL levels. However, the study about the relationship between the level of ox-LDL and the inflammatory status in gout patients are rare. The level of ox-LDL was measured using the latex enhanced immune transmission turbidimetric method. We analyzed the comparison between demographic, inflammatory markers, lipid profiles and disease subset.

Results: The primary objective of this study was to assess the oxLDL according to inflammatory status in gouty arthritis. Mean age was 50.4 year-old, 85.7% was woman, 98.9% were male, mean BMI was 25.86 and mean disease duration was 48 months. Among 174 gout patients, 61 patients (35.1%) were acute flare-up, 38 patients (21.8%) were subacute, 67 patients (38.5%) were chronic tophaceous, and 7 patients (4%) were well-controlled stable status.

Disclosure of Interests: Brian LAMoreau Shareholder of: Horizon Pharma, Employee of: Horizon Pharma, Vidhya Chandrasekaran: None declared

AB0877
OXIDIZED LOW DENSITY LIPOPROTEIN IS CORRELATED WITH INFLAMMATORY STATUS IN GOUTY ARTHRITIS
Kyuna Ann Lee1, Suyeon Park2, Bo Young Kim3, Yun Sung Kim4, Jung Ran Cho5, Hyun-Sook Kim1. 1The Soonchunhyang University Seoul Hospital, Internal Medicine, Seoul, Korea, Rep. of (South Korea); 2The Soonchunhyang University Seoul Hospital, Biostatistics, Seoul, Korea, Rep. of (South Korea); 3Gangneung Asan Hospital, Internal Medicine, Gangneung, Korea, Rep. of (South Korea); 4Chosun University Hospital, Internal Medicine, Gwangju, Korea, Rep. of (South Korea); 5Pohang St. Mary's Hospital, Internal Medicine, Pohang, Korea, Rep. of (South Korea).

Background: Lipid peroxidation and oxidized LDL (oxLDL) are hallmarks in the development of various metabolic, cardiovascular and other inflammatory diseases. Cholesterol crystals and oxLDL, which are considerably present in atherosclerotic plaques, can activate inflammamasomes. The concentration of plasma ox-LDL was also closely associated with the high incidence of atherosclerotic diseases in patients with gout might be closely related to increased ox-LDL levels. However, the study about the relationship between the level of ox-LDL and the inflammatory status in gout patients are rare.

Objectives: We aimed to the relationships between ox-LDL level, inflammatory markers and uric acid lowering agents in gout patients.

Methods: One hundred seventy four gout patients were included from the 3 institutions from 2014 to 2017. Details of demographic and clinical features along with laboratory parameters, ESR, CRP, lipid profiles, oxLDL, and disease status were noted in patients with gout. We classified inflammatory status as acute, subacute chronic tophaceous and well-controlled status. The level of ox-LDL was measured using the latex enhanced immune transmission turbidimetric method. We analyzed the comparison between demographic, inflammatory markers, lipid profiles and disease subset.

Results: The primary objective of this study was to assess the oxLDL according to inflammatory status in gouty arthritis. Mean age was 50.4 year-old, 85.7% was woman, 98.9% were male, mean BMI was 25.86 and mean disease duration was 48 months. Among 174 gout patients, 61 patients (35.1%) were acute flare-up, 38 patients (21.8%) were subacute, 67 patients (38.5%) were chronic tophaceous, and 7 patients (4%) were well-controlled stable status.

Age, sex, BMI, and accompanying disease were not statistically different in the 4 groups according to inflammatory status. However, it showed statistically significant differences in the use of glucocorticoid and uric acid lowering agents. There was no significant difference in uric acid in laboratory tests, but there was a significant difference between ESR and CRP in each disease group. Especially, oxLDL showed difference according

to inflammatory state of disease.
Conclusion: The levels of oxLDL in gout patients were significantly different according to inflammatory status. The oxLDL may be associated with inflammation process in gout patients.

Disclosure of Interests: None declared


AB0878

CARDIOVASCULAR GOUT

Eleanor Mikhnevich1, Tatiana Pavlovich2. 1Belarusian State Medical University, Internal Medicine, Rheumatology, Minsk, Belarus; 2Belarusian State Medical University, Internal Medicine, Minsk, Belarus

Background: Gout is characterized by clinical heterogeneity and associated with comorbidities. In clinical practice, we can highlight a group of patients suffering from cardiovascular diseases (CVD) and requiring constant medication, in which the gout joins later.

Objectives: To study the group of patients with gout developing on the basis of pre-existing CVD at the gout onset.

Methods: 240 patients from our Center database with confirmed gout were included in our study. Comorbidities were registered before the gout onset, at its appearance. The study group consisted of 140 patients with CVD: hypertension with duration for 5 years and treated by medication, CHD, atrial fibrillation, CHF and stroke. The comparison group consisted of patients with gout, but without CVD (n=100).

Results: Among patients with pre-existing CVD, the gout debuted later, at the age of 60 (55-65) years (p=0.001). The most frequent comorbidity was HTN – 83.6% (n=177) (OR=7.63; 95%CI 5.33-10.93; χ² = 48.9, p = 0.001). Diabetes mellitus (OR=4.47; 95%CI 3.65-5.48; F = 0.035, p = 0.005) also dominated in this group. At the same time, BMI > 25 kg/m² was prevalent in comparison group (OR=19.46; 95%CI 2.84-133.2; χ² =15.4, p = 0.001). Alcohol abuse was considerably lower – 37.1% (n=52) (OR=54.72;95%CI 17.87-167.44; χ² =48.9, p = 0.001), but medication use was higher – diuretics in 16.4% (n=23) (OR=6.36; 95%CI 5.28-7.64; F=0.045, p = 0.001) and low-dose aspirin in 35.0% (n=49) of patients (OR=17.41; 95%CI 14.80-20.47; F=0.147, p = 0.001). In the study group, the uricemia was evidenced more often (OR=4.13; 95%CI 3.42-4.98; χ² = 12.1, p = 0.001), and the presence of CKD with GFR 60 ml/min/1.73 m² was observed in 15.0% (n=21) of patients (F=0.069, p = 0.001), but not found in the comparison group. The percentage of patients with metabolic syndrome (3 components according to ATP III) did not differ between the groups (p = 0.05).

The number of patients having a concentration of uric acid (UA) in blood 360 mkmol/l and 480 mkmol/l was similar in the both study and comparison groups (p = 0.05). At the same time, the cases of UA > 600 mkmol/l were higher in study group by 13.1% (OR=1.86; 95%CI 1.50-2.38; χ² = 5.94, p = 0.015).

Conclusion: Among our patients, the gout developing on the basis of pre-existing CVD is one of the variant of a debutting gout. The group of patients with so called “cardiovascular gout” is characterized by later gout onset, comorbidities typical for CVD, prevalence of medication (low-dose aspirin, diuretic) and renal mechanisms-triggers of gout. In these patients, the maximal concentration of UA in blood (> 600 mkmol/l) was registered more frequently than in patients with primary gout.

Disclosure of Interests: None declared


AB0879

INTRATENDINOUS TOPHI IN PATIENTS WITH GOUT: PERSISTENCE IN SPITE OF CLINICAL CONTROL AND SCOPE OF URICEMIA THERAPEUTIC TARGET

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Background: The tendon affectionation of the gout consists of the deposit of uric acid in territories habitually peritendinosus causing its accumulation in the substance of the body of the tendon or occupying part of it and protruding towards zones of extension. Their presence is usually not clinically accounted for except when they obstruct tendon displacement and therefore their role as part of the clinical picture of patients with gout is often underestimated.

Objectives: The purpose of this study is to determine the ultrasound response of these tophi and the clinical activity has been controlled and the serum uricemia therapeutic target of 6.0mg/dL has been reached.

Methods: Quasi-experimental study type before after. We include 19 patients with tophaceous gout diagnosed between 2012 and 2014 and followed regularly in three rheumatology consultations through clinical, analytical and ultrasound controls. We compared the ultrasound records of static images of your Achilles, patellar and tricipital tendons at the time of diagnosis and in your last review. The longitudinal measurements of the tophi obtained were compared. The independent variable was the evaluation time (before and after) and the dependent variables were the quantification of tophi and their measurements in the longitudinal axis.

Results: All the patients were male. Mean age of 58 SD 6.8 years (Range 29-76). Mean baseline UA 480 mkmol/l. Mean follow-up time to reach therapeutic objective 18 SD 10 months (Range 9-61). Median number of intratendinous tophi (counting one for each tendon of 6 possible tendons): 2. Fashion 2 (Range 1-4). Mean longitudinal diameters: Achilles (8 cases) 18.3 SD 4.2 mm; Rotulian (11 cases) 15.3 SD 3.1 mm; Tricipital (6 cases) 9.8 SD 5.1mm. Hypouricemiant treatment administered: Allopurinol 12; Alopurinol followed by Febuxostat 7; Febuxostat only 0. In the ultrasound study, once the therapeutic objective was reached, the accounting of the intratendinous tophi Achilles and patellar tophi remained identical. One tricipital tofo disappeared completely and the rest were maintained. The longitudinal measurements of tophi that did not disappear were as follows: Achilles 18.0 SD 3.2mm (P=0.805); Rotulian 14.9 SD 3.2 (P=0.803); Tricipital 7.9 SD 3.2 (N=5, P=0.489). No differences were detected when comparing the two hypouricemiant treatment sequences.

Conclusion: Although this is a small retrospective cohort, our results show a poor ultrasound response of reduction of intratendinous tophi reaching the serum uricemia target of 6.0mg/dL. This observation raises two reflections: (1) On the one hand, and as already proposed, the therapeutic target of uricemia in our patients could require an even stricter adjustment and (2) on the other hand, it would be necessary to consider whether the inclusion of regulated ultrasound scans of certain tendons would have clinical value if they were routinely incorporated into the study of our patients with gout.

DISCLOSURE OF INTERESTS

None declared


AB0880

ACUTE GOUTY ARTHRITIS RELATED EMERGENCY DEPARTMENT VISITS AMONG US VETERANS: CHARACTERISTICS, PREDICTORS AND AREAS OF IMPROVEMENT

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Background: Gout is quite prevalent among United States veterans and many do not achieve optimal levels of uric acid (< 6 mg/dl). This suggests that there are large number of veterans who are at risk for gout flare. Therefore, utilizing health care resources such as emergency department (ED) and outpatient office visits. We investigated the ED visit patterns among veterans with history of gout and the factors contributing to ED visits.

Objectives: The objectives of the study were to identify the risk factors for ED visits by veterans for gout flare up. Future remediation of the risk factors would reduce utilization of health care resources.

Methods: This was a retrospective chart review of veterans diagnosed with gout in the ED at VA Medical Center Memphis TN between January 1st, 2011 and December 31st, 2016 using ICD-9 codes. A rheumatologist reviewed all cases and only confirmed cases of gout were included in the study. There were 2516 veterans seen for acute gout during the...
study period and of these, random selection of 10% i.e. 250 subjects were considered for the study. Baseline demographics, medical comorbidities, lab, uric acid level, medication history, and medication whether they were followed by rheumatologist or primary care physician (PCP) were extracted from electronic health record.

We used Stat view version 5.01 (SAS Institute Inc. Cary, NC) for analysis. We described data with frequency terms, continuous data by mean ± standard deviation, and categorical data by percent. Univariate analysis identified predictors of interest that were later incorporated in the best fit model with logistic regression. A p value of ≤ 0.05 was considered statistically significant.

**Results:** The mean age of subjects was 61 ±11 years, mean BMI was 32 ± 7 kg/m². 98% were males and 80% were African Americans. 26% of subjects had history of alcohol use, 89% had hypertension and 88% had chronic kidney disease (CKD stage ≥2). 86% of the subjects were followed by primary care physician (PCP), and 5% of them were followed by rheumatologist and rest of the 9% were non-compliant. 30% of subjects were receiving urate-lowering therapy and 23% of patients were on gout prophylactic therapy. 21% of patients had multiple visits (≥ 2) visits to the ED. The mean uric acid level was 8.5 ± 2.1 mg/dl for subjects with single visit compared to 9.04 ± 2.1 mg/dl for multiple visits to the ED (P = 0.09).

In the univariate analysis, CKD (stage ≥2) and higher uric acid level were associated with increased ED visits (P = 0.09) and not being on urate lowering therapy was also associated with increased frequency of ED visits (P = 0.02). On logistic regression analysis, irrespective of the type of physician follow up (PCP vs rheumatologist), being on urate-lowering therapy was associated with reduced frequency of ED visits (P =0.02).

**Conclusion:** Urate-lowering therapy (ULT) was associated with reduced ED visit irrespective of follow up care provided by PCP or rheumatologist. Given that only one third of our patients were on ULT, improving ULT dispensing by the physician and patient compliance with ULT can decrease health care utilization.

**REFERENCE**

Disclosure of Interests: None declared

AB0881

**DESCRIPTIVE ANALYSIS OF PATIENTS WITH OSTEOPENIA IMPERFECTA IN A TERTIARY HOSPITAL IN MADRID**

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**Background:** Osteogenesis imperfecta (OI) is an inherited connective tissue disorder with an incidence of 1 per 20,000 births. It is also called “brittle bone disease” and is most commonly caused by mutations in genes encoding type I collagen or proteins involved in its posttranslational modification. Most patients have an autosomal dominant mutation in COLA1 or COLA2. The severity of the clinical presentation depends upon the effect of the mutation that occurs, having many different phenotypic presentations. In the most severe forms, patients suffer multiple fractures with minimal or no trauma whereas mild forms may only manifest with premature osteoporosis. Attending to the clinical presentation, radiographic findings and the mutations, most OI patients can be classified in type I-III. Different types have been described: type I and III have the most prevalent and severe treatments have been studied, but none has been found to be curative. The most frequently used are bisphosphonates which try to prevent bone fragility and reduce the number of fractures but none have been approved specifically for use in either children or adults with OI.

**Objectives:** The aim of the study is to analyse the clinical characteristics of osteogenesis imperfecta (OI) patients followed in our hospital and to evaluate the different treatments used in their management.

**Methods:** A retrospective study was conducted. All patients diagnosed with OI and seen in the different departments of our hospital were included and analyzed. A database was created, including both clinical and epidemiological data and a descriptive analysis was carried out.

**Results:** 25 patients with OI are currently being followed up in our hospital and were included. Although most patients were being followed in both the Rheumatology (9) and Orthopedic units (9), 4 were being followed by pediatrics, 1 by endocrinology, 1 by internal medicine and 1 by geriatrics. 72% were female (18) with a mean age at diagnosis of 17 years (range: 1 month to 67 years). All of them had had previous fracture before the diagnosis. The number of fractures during their follow-up varied according to the different types of OI, with an average of 6 fractures (range 3-24) per patient and an average of at least 4.16 orthopedic surgeries each. 12/25 patients were diagnosed in the first ten years of life, being the ones that accumulated the highest number of fractures (96 vs. 54). Only 3 patients had family background of OI, all of them being type I. Although only 9/25 patients had undergone genetic study, all 3 cases of type III, which is the most severe, debuted in the first decade of life. Phenotypically 14/25 (56%) had short stature and 18/25 (72%) had blue sclerae, being these less frequent in those patients with debut after 20 years of age, of which 57% (4/7) had normal sclerotics. Only 4 patients suffered from dentinogenesis imperfecta (16%) and 3 from osteosclerosis and had hearing problems (12%). Regarding the treatment received, 60% of the patients (15/25) were on current treatment with oral calcium and 64% (16/25) with oral vitamin D supplements. On the other hand only 60% of the patients received bisphosphonates (4 were being treated with risedronate, 7 with pamidronate, and 4 had received both zoledronic and pamidronate during their lives).

**Conclusion:** Although a rare disease, OI has an important morbimortality in most patients. Severe cases suffer multiple fractures and undergo several orthopedic surgeries during their lifes. Given the high cost of genetic analysis, this is reserved for the most severe cases which tend to debut at younger ages and are mostly type III. Treatment for this condition is not standardized and is generally reserved for type III OI patients, which is one of the most severe types. Bisphosphonates, calcium and vitamin D are usually used in order to try to prevent new fragility fractures but in most cases fracture rates remain high despite treatment.

Disclosure of Interests: None declared

AB0882

**ACROMEGALY DO NOT INCREASE THE RISK OF VERTEBRAL FRACTURES: A RETROSPECTIVE AND PROSPECTIVE STUDY IN 50 PATIENTS**

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**Background:** Patients with acromegaly appear to be at an increased risk of vertebral fractures (VFs) despite normal bone mineral density (BMD). However, these patients could have several endocrine deficits as hypogonadism known to increase the fracture risk independently of the GH effects. The physiopathology of GH excess on bone is unclear. In addition, patients with acromegaly have radiological deformations of the spine, called Erdheim’s syndrome, which can overestimate the radiological vertebral fractures.

**Objectives:** Investigate the prevalence of VFs in our cohort of patients with acromegaly.

**Methods:** It was a monocentric, retrospective and prospective study. The rheumatologic evaluation was less than 3 years for all patients. For 40% of patients, this evaluation was prospective after the begin of the study. Acromegaly patients younger than 80 and followed at the Nantes University hospital in January 2018 were included. Patients were excluded if they had a rheumatologic or endocrinologic disease interfering with the results. The prevalence of radiological vertebral fractures was evaluated on conventional lombor and thoracic spine radiographs using Genant’s semi-quantitative assessment. We also assessed qualitative abnormalities of the spine using 3 criteria: osteophytes, disc space narrowing and cuneiform aspect of vertebrae. The X-rays were read by two rheumatologists independently. We analyzed BMD at lumbar spine and total hip, endocrine status and quality of life through 3 questionnaires (AcroQol, specific of acromegaly; Oswestry evaluating the functional impact of pain; HAQ evaluating the functional capacity).

**Results:** We included 56 patients. 6 patients were excluded : 3 declined, 1 had another endocrinologic disorder (adrenocortical and panhypopituitarism). We analyzed the prevalence of VFs in 50 patients (19 females, 31 males, median age 53, range 28-79). The average of time between the diagnosis of acromegaly and the last rheumatological evaluation was 9.1 years. 3 patients (6.1%) had a VF : 1 grade 1 and 2 grade 2 of Genant’s assessment. 28% patients were osteopenic and 12% were osteoporotic. Among fractured patients, 2 were osteoporotic and 1 osteopenic. All of them were hyponadal (100% substitu- ted), 16% had central adrenal insufficiency (100% substituted). 14 women were menopaused (74% of women). Thoracic spine was deformed in 31 patients (61%) and lumbar spine in 21 patients (43%), for at least
one of the 3 criteria. Patients with spine deformation were older (p=0.003), with higher BMI (p=0.004) and had a trend to be more hypertensive (p=0.06). Concerning quality of life, AcroQoL’s average was 70.9% (score 0 to 100, maximal quality of life =100, range 32-98), HAQ’s average was 0.18 (score 0 to 3, maximal quality of life 0, range 0-1.38) and Oswestry’s average was 9.8 (score 0 to 100, maximal quality of life 0, range 0-44).

**Conclusion:** This study shows for the first time that acromegaly patients are not at an increased risk of vertebral fractures. This result differs from the literature that reported more than 30% of VF in this population. Our study bring several points of explanation. First, the vertebral abnormalities were frequent in our patients and can overestimate the VFs without a qualitative analysis of the X-ray. Secondly, the right endocrine balance plays an important role in osteoporosis. Our patients were well supplemented, it can reduce the risk of osteoporosis. More studies are needed to confirm this new hypothesis.

**REFERENCES**


**Disclosure of Interests:** charlotte plard: None declared, Clarisse Hochman: None declared, Delphine Drui: None declared, Bertrand Cariou: None declared, Yves Maugars: None declared, Benoit Le Goff Speakers bureau: Abbvie, BMS, Janssen, MSD, Pfizer, Sanofi-Genzyme, UCB, Novartis, pascale Guillot: None declared

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**AB0883**

**SYSTEMIC INFLAMMATION AND ATHEROSCLEROSIS IN PATIENTS WITH GOUT. RESULTS FROM THE NOR-GOUT STUDY**

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**Background:** The association between gout and cardiovascular disease (CVD) is well known,1 whereas mechanisms behind this association are poorly understood.

**Objectives:** This study aimed to evaluate factors associated with asymptomatic carotid atherosclerosis in patients with gout.

**Methods:** In this prospective study patients with crystal-proven gout were included after a recent diseaasefase, if the serum urate level was >360 μmol/L (>6 mg/dl). We analysed baseline data in patients without established CVD who were referred to a CVD risk evaluation, including ultrasound of the carotid arteries, blood pressure measurement and laboratory tests. Carotid atherosclerotic plaques were defined in the longitudinal view of the carotid arteries according to the Mannheim criteria. Lipid concentrations were measured and standardization was done for age and sex. All covariates were assessed at baseline, except age and sex.

**Results:** Of the 79 gout patients included, 10% were females, and mean (SD) age was 52.1±13.1 years. Thirty-two (40.5%) had carotid plaques (Table). Only 9.3% were current smokers, while mean (SD) body mass index was 29.1±4.7 kg/m². Systolic blood pressure was in the normal range (134±15 mmHg), although 29.1% of the patients were treated with anti-hypertensive agents. In univariate analyses, higher age, hypertension and higher erythrocyte sedimentation rate (as a marker of systemic inflammation) were significantly associated with the presence of carotid plaques (p=0.01 and p=0.04, respectively) (Figure). Serum urate levels or disease duration were not associated with carotid plaques (p=0.27 and p=0.44, respectively).

**Conclusion:** Our results indicate an association between systemic inflammation and atherosclerosis in patients with gout. To be able to efficiently prevent CVD in this patient group, prospective studies with larger sample sizes are needed to elucidate the mechanisms behind the increased risk of CVD in gout patients.

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**Disclosure of Interests:** Silvia Rollefstad: None declared, Till Uhlig Consultant for: Grünenthal, Novartis, Speakers bureau: Grünenthal, Novartis, Lars Fridjof Karoliussen: None declared, Hilde Berner Hammer Grant/research support from: AbbVie, Pfizer and Roche, Paid instructor for: AbbVie, Pfizer, UCBB, Novartis, Roche, Speakers bureau: AbbVie, Pfizer, UCB, Novartis, Roche, Anne Grete Semb: None declared

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**AB0884**

**CLINICAL AND DEMOGRAPHIC CHARACTERISTICS OF PATIENTS WITH OCHRONOTIC ARTHROPATHY**

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**Background:** Alkaptonuria (AKU) is a metabolic disorder that causes accumulation of oxidized homogentisic acid (HGA) in the connective tissues. The excessive deposition of HGA and its metabolites can cause...
joint destruction and skeletal abnormalities which the entity is clinically referred as ochronotic arthropathy (OA) [1].

Objectives: To assess clinical, demographic features and radiographic findings in patients with OA.

Methods: Adult AKU patients registered in the database were included in the study. All patients investigated for the presence of OA and inflammatory symptoms. Patients with musculoskeletal symptoms (MSK) underwent conventional X-rays and routine laboratory evaluation. In cases suggestive of inflammatory disease additional work-up such as autoantibodies, HLA-B27 and MRI with inflammatory protocol were performed.

Results: Six out of 15 patients had symptoms compatible with OA (40%; 4 male [M], 2 female [F], median age 56 [51-62] years). The median duration of MSK symptoms was 7 (2-19) years. None of the patients had family history of rheumatologic disease. Baseline CRP were normal in all patients. The HLA-B27 test was negative in all cases. One patient had high titers of rheumatoid factor along with positive anti-CCP that were accompanying erosive arthritis on MCP joints by X-rays. Two patient had positive ANA. All patients had chronic back pain and had changes compatible with OA in their spines (narrowing of the intervertebral spaces, vacuum phenomenon and intervertebral disc calcification). Two patient had inflammatory type of pain character (IBP). Radiographic sacroilitis according to modified New York criteria was present in 2 cases. Inflammatory spine and SIJ lesions were detected by MRI in 1 patient. Extra-articular involvement including enthesis (1 patient), interstitial lung disease (1 patient) and scleritis (1 patient) was also noted. The clinical and demographic characteristics of the OA are given in Table 1.

Conclusion: There was a high prevalence of inflammatory arthritis (2 axSpA; 1 RA) in OA (50%) which contradicts with the common concept that OA is a degenerative disorder. According to our results, inflammatory disease should be carefully screened in OA patients as accumulated metabolic products may trigger inflammatory pathways.

REFERENCES

Disclosure of Interests: None declared

AB0886
THE RELATIONSHIP BETWEEN METABOLIC SYNDROME SEVERITY AND THE RISK OF MORTALITY IN GOUT PATIENTS: A POPULATION-BASED STUDY
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Background: Metabolic syndrome (MetS) is common amongst gout patients. The MetS is diagnosed when a patient has at least 3 of the following 5 conditions of hyperglycemia, hypertension, hypertriglyceridemia, low high-density lipoprotein (HDL) cholesterol or abdominal obesity. Little is known about the relationship between the cumulative effects of all five metabolic syndrome conditions and the risk of mortality among adult patients with gout. Metabolic Syndrome Severity Score (MetSSS) is a new clinical prediction score that employs available components (sex, age, race, systolic blood pressure, waistline circumference, high-density lipoprotein, triglycerides and fasting blood glucose). MetSSS is a validated summary score that accounts for the combined effects of all 5 metabolic features. MetSSS allows examination of associations between MetS severity and the risk of mortality. Objectives: to use the MetSSS to examine the overall associations between MetS severity and the risk of mortality related to all-causes, cardiovascular disease and diabetes amongst United States (US) gout patients.

Methods: Mortality-linked data for 12,101 adults aged 18 to 90 years who participated in the Third National Health and Nutrition Examination Survey (NHANES III 1988-1994) was analyzed. Data from NHANES III were linked to national mortality records for all participants up to time of death or end of study (i.e. 23 years following initial recruitment). All 5 metabolic features were used to calculate gender-race/ethnicity specific MetSSS Z-scores in gout patients. The Z-score is the number of standard deviations from the mean a data point is and allows a continuous representation of all MetS conditions while accounting for gender-race/ethnicity disparities.

Results: A total of 3,381 deaths were observed, of whom 215 had gout. The prevalence of gout amongst adults was 2.59% (95% CI: 2.13%-3.05%). Moderate to high MetS severity was significantly prevalent among gout patients (47.33% vs. 21.16% no gout; P-value <0.0001). The mean MetSSS Z-score for gout patients was significantly higher than those without gout (0.71 vs. -0.04 no gout; P-value <0.0001). For gout patients, a one-unit increase in MetSSS score was associated with a significant increase in the risk of all-cause mortality Adjusted Hazard Ratio (aHR) 1.46 (95% CI: 1.13, 1.87).

In a disease-specific survival model, a one-unit increase in MetSSS score was associated with a aHR 1.62 (95% CI; 1.21, 2.15) increase in heart disease related mortality amongst gout patients. Amongst those with gout, a one-unit increase in MetSSS score was associated with increased risks of diabetes- and hypertension-related mortalities aHR 2.53 (95% CI; 1.43, 4.62), aHR 1.73 (95% CI; 1.07, 2.79), respectively.

Conclusion: The Z score calculation in our study allowed a quantification of increased diabetes- and hypertension-related mortalities, all-cause and cardiovascular mortality in patients with gout. Use of the MetSSS can provide an opportunity to identify patients at highest risk influencing patients to change their lifestyle and better comply with treatment.

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AB0886
IS THE SENSE OF SMELL IMPAIRED IN GOUT PATIENTS?
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Background: The sense of smell is sensitive to hundreds of thousands of odorants. Smell disorders significantly compromise the quality of life. A National Health and Nutrition Examination Survey (NHANES) 2013-2014 survey among US population aged 40 years of age and older years found smell dysfunction in ~ 20.5 million (13.5%) of Americans (1). Prevalence increased with age. Other factors influencing the sense of smell include ethnicity, smoking, medications, head trauma, chronic sinusitis, upper respiratory tract infections; alcoholism and neurological disorders.

The University of Pennsylvania Smell Identification Test (UPSIT) (2) is a well-validated test of olfactory function that correlates with odor detection and other quantitative measures of olfaction. This test has become the ‘gold standard’ for olfactory testing and is comprised of four test booklets, each containing 10 microencapsulated (scratch & sniff) odors.

Patients with gout, the most common inflammatory arthritis, frequently have multiple associated comorbidities, affecting many organs and aspects of one’s health.

REFERENCES
Objectives: To determine whether gout patients have an impaired sense of smell.

Methods: This was a cross-sectional prospective study of gout patients seen in our rheumatology clinic. The first 30 clinic patients were recruited during the period 7/15/17-5/25/18. Each patient was administered the 40-item UPSIT. UPSIT scores were compared to age- and sex-matched controls from a normative database maintained at the University of Pennsylvania Smell and Taste Center using a paired t-test.

Results: Gout patients ranged in age from 31 - 86 years (mean: 59 years); 26 (87%) of patients were > 40 years old and included 26 men and 4 women. The duration of gout ranged from 1- 43 years (mean: 9 years), with 19 having gout for >5 years. Visible tophi were observed in 6 patients (33%). C-reactive protein was within normal range except in one gout patient. Serum urate levels ranged from 5.1-12 mg/dL (mean: 6.29 mg/dL). Two patients were current smokers; both have microsomia. No patients had head trauma, chronic sinusitis, upper respiratory tract infections, alcoholism or neurological disorders. The mean UPSIT scores of the two groups did not differ significantly [respective patient and control means (SDs) = 31.40 (5.79) and 31.80 (4.37); t 29 = -0.342, p = 0.74].

Conclusion: This is the first study to quantitatively assess smell function in patients with gout. Despite being a systemic inflammatory disease, with multiple associated comorbidities, we did not find a statistically significant effect of gout on smell function using a well validated olfactory test.

REFERENCES


AB0888
A SURVEY FOR DIAGNOSIS AND TREATMENT OF PATIENTS WITH GOUT IN KOREA
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Background: The prevalence and incidence of gout has risen over the past few decades and the socioeconomic costs of gout have been increasing accordingly, but it is unclear whether proper medical care is provided for patients with gout.

Objectives: This study aims to investigate the actual status and adequacy of diagnosis and management of gout patients.

Methods: The patients with gout who visited between November 2017 and February 2018 were consecutively enrolled. Data were collected using a pre-designed questionnaire and reviews of medical records. The collected data included diagnosis and management of gout before starting a steady treatment in our clinic, and disease status at first visit to our clinic.

Results: In total, 172 gout patients were enrolled. The average age of the patients was 55 (interquartile range (IQR): 45-66) years, and 94.2% were men. The average disease duration was 8 (IQR: 4-13) years. The average age of first gout symptoms was 45 (IQR: 36-53) years. The first symptom started in the feet for 93.4% of patients. The patients in which the first symptom region was around large joints were 35.1%, and 17.3% of patients developed first gout symptoms around multiple joints. Several patients (64%) visited the hospital directly after their first acute gout attack, and 84.4% were instructed to examine gout patients were orthopedic surgery (38.2%), emergency doctors (23.6%), and rheumatologist (16%). Upon initial medical examination, 67% of patients were clinically diagnosed or suspected with gout. Monosodium urate crystals in synovial fluid or tophi were confirmed in 10.5%. Furthermore, 31% of patients had a history of pharmacology urate lowering therapy (ULT) after acute gout attack, and 84.4% were indicated for pharmacology ULT upon first visit to our clinic. Additionally, 47.6% of patients showed symptoms of chronic kidney disease, past urolithiasis, or tophi, and 52.4% suffered from ≥ 2 gout attacks/year. However, only 11.3% of patients were receiving continuous ULT before visiting our clinic.

Conclusion: Most patients were clinically diagnosed without appropriate tests for gout diagnosis, such as joint aspiration, and only a very small number of patients were receiving adequate pharmacologic ULT. The management of gout seems to be inadequate in many respects.

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Disclosure of Interests: Mi Ryung Seo Grant/research support from: I received KRW 15 million (approximately 1,300 USD) in research funding for this study from CHODANG Pharm., Ji Na Yeo: None declared, Hee Jung Ryu: None declared, Hyo-Jin Choi: None declared, Han Joo Baek: None declared DOI: 10.1136/annrheumdis-2019-eular.1553

AB0888
ULTRASOUND FEATURES IN GOUT: A COMPARATIVE ANALYSIS WITH MATCHED CONTROL
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Background: Gout is a frequent inflammatory disease characterized by deposition of monosodium urate crystals in joints and tissues in the presence of hyperuricemia (1). Ultrasound (US) is a simple imaging technique that has gained interest in the assessment of individuals with gout due to its ability to identify inflammation and joint damage, as well as crystal deposition. The most characteristic gout US findings are the presence of intra-articular aggregates and the double contour (DC) signal, included in the 2015 ACR/EULAR classification criteria.

Objectives: To identify potential differentiating US findings between individuals with gout and matched controls.

Methods: A cross-sectional study was conducted, including 57 gout adult patients and 32 adult individuals with a normal uricemia, matched by age and gender. Sociodemographic, clinical and analytical data were collected. Bilateral US grey scale evaluation of the 1st metatarsophalangeal joint (MTP1), 2nd metacarpophalangeal joint (MCP2) and knee was performed in all participants. The following findings were assessed: intra-articular effusion, synovial hypertrophy, bone erosion, DC signal and intra-articular deposits. None of the participants presented with clinical signs of arthritis at the time of the evaluation.

Results: The mean age of gout patients and healthy individuals was 63.3 ±12.6 and 63.8±10.5 years, respectively. The majority of the gout patients were male (87.7%), 77.2% had previous history of podagra and 26.3% had tophi. Mean disease duration was 4.3 years. Mean uricemia was 6.7 ±2.0 mg/dl in gout patients and 4.9±0.9 mg/dl in the control group. At the time of the study, 31 patients (54.4%) were treated with allopurinol, 9 (15.8%) with fenbuxostat, and both allopurinol and fenbuxostat, and 16 (28%) were not on urate lowering therapy. Comparatively to the control group, in the MTP1, patients with gout presented more frequently with synovial hypertrophy (26 vs 0, p<0.001), bone erosion (19 vs 0, p<0.001), DC signal (7 vs 0, p<0.05) and intra-articular aggregates (8 vs 0, p<0.05). At the knee, patients showed more frequently with bone erosion (19 vs 2, p<0.001), synovial hypertrophy (26 vs 1, p<0.001) and DC signal (8 vs 0, p<0.05). At the MCP2, only the presence of erosion was significantly more common in the gout group (8 vs 0, p<0.05). DC signal was found in 17 patients and in none of the healthy subjects (p<0.001); this finding was more frequently observed at the knee. There was an association between previous gout crisis in the MTP1 and the presence of erosion in this joint (p<0.04). An association was found between the presence of tophi and bone erosion (p<0.001), DC signal (p<0.05) and intra-articular aggregates (p=0.006). There was no association between uricemia levels, disease duration and the different US findings.
Conclusion: In this study, the presence of synovial hypertrophy, erosions, DC signal and intra-articular deposits were the most frequent US findings in patients with gout. Moreover, these findings at the MTP1 joint allowed to distinguish between gout patients and matched control subjects. US seems to be useful to demonstrate evocative signs of crystal accumulation, inflammation or joint damage, even in the absence of overt arthropit.

REFERENCES

Disclosure of Interests: None declared

AB0890 EFFECT OF DIFFERENT TYPES OF URIC ACID-LOWERING DRUGS ON GOUT ATTACK
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Background: Gout is an inflammatory arthritis associated with hyperuricemia which is caused by purine metabolism disorders. General uric acid lowering treatment sometimes causes the onset of gout, but the specific cause is not clear. Our group has found that adenine nucleoside triphosphate (ATP) plays an important role in the pathogenesis of gout. It synergizes with MSU to stimulate the secretion of IL-1β, leading to the onset of gout. 1-3 The xanthine oxidase inhibitors promote the production of ATP, while the drugs that promote the excretion of uric acid does not affect ATP production. Therefore, we speculate that gout attacks induced by allopurinol and febuxostat are related to the role that ATP plays in the pathogenesis of gout.

Objectives: To compare the effects of drugs that inhibit uric acid production and promote uric acid excretion on gout.

Methods: A case-control study was used to compare the changes in serum uric acid concentration and observe whether the patients would suffer gout attacks within one month. The gout patients complied with the standard that the number of gout attacks did not exceed three times, as well as more than one time within the past six months, were selected. And patients with other chronic inflammatory and infectious diseases were excluded.

Results: A total of 148 patients with gout in the Department of Rheumatology and Immunology of Anhui Provincial Hospital were collected, all of whom were male. According to the patients taking uric acid-lowering drugs, they were divided into four groups: group A: control group (no uric acid-lowering treatment, n=38); group B: febuxostat group (40 mg Nadolol Qd, n=38); group C: allopurinol group (0.1 g Bid, n=11); group D: benzbromarone group (50mg Qd, n=38). The statistical results are as follows: (1) The levels of serum uric acid in group B, C and D were significantly decreased after uric acid-lowering treatment compared with those before treatment (B: 389.6±88.9 vs 547.5±93.0, P<0.05; D: 376.2±108.5 vs 557.3±101.8) within one month, and there was no significant difference among the three groups. (2) Comparison of gouty arthritis recurrence rates: The recurrence rate of gout patients in group B was 33.3%, and it was 18.2% in group C, which was significantly higher than that in group D (11.1%), the difference was statistically significant (P<0.05); the recurrence rate of gout patients in group A was 14.3%, and there was no significant difference compared with group D (P>0.05); the recurrence rate of gout patients treated by drugs that inhibited uric acid production (B+C group) was 31.2%, which was significantly higher than patients treated by drugs that promoted uric acid excretion (D group) 11.1%, the difference was statistically significant (P<0.05).

Conclusion: Under the same uric acid-lowering intensity, the drugs that inhibit uric acid production can induce gout attacks during the process of uric acid lowering, while the drugs that promote uric acid excretion has less effect on the recurrence of gouty arthritis.

REFERENCES

Disclosure of Interests: None declared
Background: Hyperuricemia and gout has been described as metabolic complications in patients with more extensive Paget’s disease, with a very variable prevalence. However, there is no data about fluctuations of uric acid levels associated with its treatment and its correlation with alkaline phosphatase variations during acute gout attacks.

Objectives: To analyze the frequency of hyperuricemia and gout in patients with a diagnosis of Paget’s disease of bone (PD) and to establish the correlation between the activity of Paget’s disease and its treatment in the fluctuations of uric acid levels.

Methods: Patients with Paget’s disease and with scintigraphic uptake suggestive of activity were included. A database was created including demographic information, the presence of symptoms associated with PD, its type (monostotic or polyostotic), alkaline phosphatase (AP) and uric acid (UA) levels at diagnosis and the treatment received. AP and UA levels after treatment were also collected as well as the presence of possible hyperuricemic risk factors (HRF), history of gout and levels of AP and UA during gout attacks, if any. Finally data was analyzed using SPSS v21.

Results: A total of 95 patients were included with a mean age of 70.59 years (range 45-89), with 56% of them being women. The mean values of AP and UA at diagnosis were 178.05±82.81 mg/dL and 5.84±1.74 mg/dL, respectively. 58.9% of the patients had monostotic involvement (56/95) and only 53.12% had associated symptoms (51/95), whereas in the rest of the patients PD was an incidental finding. 70.83% did not present HRF and 56 patients (58.9%) had received treatment for their PD (41% of them with zoledronic acid). Pearson correlation between PA and UA levels was found moderately positive (0.710 with p<0.0005) and 50.52% of the patients (48/95) had UA levels above 6mg/dL at the time of diagnosis, with a mean of 7.10 mg/dl ±1.74. In 93.5% of the cases there was a decrease in UA levels after the treatment for PD, with a mean decrease of 0.78±1.3 mg/dL over the baseline value at one year of follow-up. Only 11.57% of the patients in our cohort presented gout symptoms during their follow-up, with an increase in AP levels at the time of the attack in 63.63% of the cases.

Conclusion: In our cohort, there was a moderate positive correlation between the elevation of AP and UA in patients with active Paget’s disease. Treatment for PD produced a decrease in UA levels from baseline in most patients. Similarly, during gout attacks, an increase in AP levels could be.

REFERENCE

Disclosure of Interests: None declared

AB0893
WHAT IS THE CHANCE IN AN INDIVIDUAL GOUTY PATIENT THAT DISEASE WILL BE STILL ACTIVE IN A YEAR? PREDICTIVE MODELLING MIGHT COME TO AID
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Background: The treat-to-target concept is currently applied to gout [1] and a composite outcome to measure disease activity may serve as a target in clinical practice. Strategies for achieving the target are still not individualized and the ability to adjust the treatment on an individual basis using prognostic information from predictive models might help practitioners to identify patients with a high or low probability of remission or disease inactivity.

Objectives: To develop a prediction model for disease inactivity in gouty patients.

Methods: Data were retrieved from the Kick-off of the Italian Network for Gout (KING) observational cohort multicentre study on behalf of the Italian Society for Rheumatology. The gout activity score (VAS) [2,3] was used as validated outcome to define inactive disease (cut off ≤2.5) at 12 months in gouty patients with active disease at baseline and receiving the standard of care in two visits 6 months apart. Logistic regression analyses and backwards elimination of baseline predictors with bootstrap resampling were used to develop parsimonious models. Model performance and correction for optimism were assessed. Missing data were handled through multiple imputation by chained equations (50 completed datasets).

Results: Out of 446 patients enrolled from 30 rheumatology centres, 265 (59%) had active disease at baseline (mean age 63±11 years, male 91%, median disease duration 7 years, tophi 23%, urate lowering therapy 82%, mean serum urate [sUA] levels 6.7±1.6 mg/dL and a 12-month visit. In 34% (65/206) gout was inactive at 12 months. From 20 candidate predictors (complete cases n=150) disease duration, use of nonsteroidal anti-inflammatory drugs (NSAIDs), number of flares in the previous 12 months, presence of tophi, sUA >6 mg/dl, visual analogue scale (VAS) global patient, and baseline GAS were selected. The performance of the four developed models is shown in table. In the completed case analysis (n = 258) the c-statistics (95% confidence interval [CI]) of
models 1 to 4 were 0.79(0.73-0.85), 0.78(0.72-0.84), 0.76(0.70-0.82), and 0.74(0.68-0.81), respectively.

### Table: Predictors of Changes in Ultrasonographic Signs during Urate Lowering Therapy in Patients with Gout

<table>
<thead>
<tr>
<th>Predictor</th>
<th>β</th>
<th>95% CI</th>
<th>β</th>
<th>95% CI</th>
<th>β</th>
<th>95% CI</th>
<th>β</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease duration</td>
<td>-0.07</td>
<td>-0.11, -0.06</td>
<td>-0.06</td>
<td>-0.11, -0.06</td>
<td>-0.06</td>
<td>-0.12, -0.02</td>
<td>-0.02</td>
<td>0.02, 0.02</td>
</tr>
<tr>
<td>Current NSAIDs</td>
<td>-1.14</td>
<td>-2.24, -0.02</td>
<td>-1.09</td>
<td>-2.02, -0.12</td>
<td>-1.02</td>
<td>-2.05, -1.02</td>
<td>-1.00</td>
<td>-2.07, -0.95</td>
</tr>
<tr>
<td>Last 12 months</td>
<td>-0.42</td>
<td>-0.70, -0.23</td>
<td>-0.41</td>
<td>-0.70, -0.23</td>
<td>-0.42</td>
<td>-0.70, -0.23</td>
<td>-0.42</td>
<td>-0.70, -0.23</td>
</tr>
<tr>
<td>sUA &lt; 6 mg/dL</td>
<td>1.68</td>
<td>0.38, 0.82</td>
<td>0.00</td>
<td>0.76, 0.06</td>
<td>0.00</td>
<td>0.76, 0.06</td>
<td>0.00</td>
<td>0.76, 0.06</td>
</tr>
<tr>
<td>Tophi</td>
<td>2.96</td>
<td>1.65</td>
<td>1.57</td>
<td></td>
<td>1.34</td>
<td>1.52</td>
<td>1.31</td>
<td>3.43</td>
</tr>
<tr>
<td>VAS patient</td>
<td>0.00</td>
<td>0.06</td>
<td>0.00</td>
<td>0.06</td>
<td>0.01</td>
<td>0.06</td>
<td>0.01</td>
<td>0.06</td>
</tr>
<tr>
<td>Baseline GSA</td>
<td>1.59</td>
<td>-0.20</td>
<td>-3.39</td>
<td></td>
<td>0.12</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intercept</td>
<td>-3.50</td>
<td>-8.36, 0.76</td>
<td>0.40</td>
<td>-0.92, 0.24</td>
<td>-3.50</td>
<td>-8.36, 0.76</td>
<td>0.40</td>
<td>-0.92, 0.24</td>
</tr>
</tbody>
</table>

**Conclusion:** These preliminary prediction models for inactive disease showed good performance in gouty patients from a real-life secondary setting. External validation in ad-hoc studies is required to identify the best model and to search for additional predictors and increase its predictive performance.

**REFERENCES**

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**Disclosure of Interests:** Nicola Ughi Speakers bureau: Pfizer, Grunenthal, Greta Carrara: None declared, Anna Zanetti: None declared, Marco Amedeo Cimmino Grant/research support from: Menarini, Consultant for: Menarini International, Maria Manara: None declared, Marcello Govoni Paid instructor for: Pfizer, Roche, Speakers bureau: Pfizer, Abbvie, MSD, Roche, Eli-Lilly, Celgene, Sanofi, Janssen, Fausto Salaffi Grant/research support from: Abbvie, Roche, Novartis, BMS, Pfizer, Sanofi, Speakers bureau: Abbvie, Roche, Novartis, Pfizer, Sanofi, CMS, Leonardo Punzi Consultant for: BMS, Fidia, Grunenthal, Menarini, Speakers bureau: CMS, Fidia, Grunenthal, Menarini, Carlomaurizio Montecucco Speakers bureau: Abbvie, Bristol-Myers Squibb, Celgene, Sanofi, Genzyme, Lilly, MSD, Pfizer, UCB, Marco Matucci-Cerinic Grant/research support from: Actelion, MSD, Pfizer, CMS, Chemomab, Sanipedia, Speakers bureau: Actelion, CMS, MSD, Janssen, giovanni minisola: None declared, Antonella Zambon: None declared, Carlo Alberto Scire: None declared

hepatotoxicity with minor liver function abnormalities and Allopurinol induced mild skin rash was seen in 7/61 (11%) of patients. All adverse events were mild and the therapy was not changed.

Conclusion: Allopurinol increasing dose regimen was efficient in hyperuricaemia treatment, and the target goal was reached by 93.4% of patients. All adverse reactions were mild and did not influence dose regimen at the end of the 6 months period of follow-up.

REFERENCE

Disclosure of Interests: None declared

Infection-related rheumatic diseases

AB0896  REINFECTION OF PROSTHETIC JOINT WITH A DIFFERENT MICROORGANISM: A PROSPECTIVE COHORT STUDY
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Background: Treatment failure of prosthetic joint infection (PJI) may be due to relapsing infection (with the same microorganism) or a new infec- tion (with a different microorganism). Data on new prosthetic joint infec- tions (NPJI) are scarce, although they represent a devastating complication and a therapeutic challenge of joint arthroplasty.

Objectives: The aim of this study was to describe epidemiological, clinical and microbiological characteristics of NPJI, their treatment and outcome.

Methods: This observational single-center cohort study was conducted in a French referral center for bone and joint infections. All patients admitted between January 2000 and December 2015 with a documented hip or knee PJs and at least 2 years of follow-up, were identified. Among those, all patients treated in our center for at least two successive PJs, involving the same joint and due to different microorganisms, were included. We compared these patients with a random selection of 124 single*PJs (72 knee and 52 hip prostheses) treated in our center and followed at least 2 years.

Results: Among 909 PJs treated during the study period, 62 patients with 70 NPJJs were included (7.7%) NPJJs developed more frequently in knee (15.7%) than in hip prostheses (4.4%) (p<0.001). Median [range] age was 70 [66-80] years old and median [range] body mass index was 28.7 [25-33] kg/m². Median [range] duration from the first to the NPJI was 70 [66-80] years old and median [range] body mass index was 28.7 [25-33] kg/m². Median [range] duration from the first to the NPJI was 70 [66-80] years old and median [range] body mass index was 28.7 [25-33] kg/m².

The radiological findings showed that 14 patients (53.8%) had abscesses. Soft tissue abscesses were detected in 7 cases with mean size of 1.3 cm [0-9cm]. Bilateral psoas abscess was recorded in one case. Epidural collection was revealed in 3 cases with an average size of 0.3 cm [0-5cm]. Paravertebral and peri-vertebral abscesses were detected in 5 cases. Intradiscal abscesses were observed in 3 cases. Cord compression and involvement of root nerve were noted in respective 6 and 1 cases. Compared to the group without abscesses, subjects with abscesses had higher ESR and the difference was statistically signif- icant (mean ESR 26.83 vs 55.9 mm) (p=0.016). There was no statisti- cally significant link between duration of symptoms or duration of hospitalization and the presence of abscesses. All patients had antibiotic treatment (cocilins and rifampicin). The evolution was favorable in all cases. Surgical intervention was required in one case (evacuation of an epidural abscess).

Conclusion: Our study showed that abscesses are frequent in osteoarticu- lar brucellosis. In spite of the low risk of complication, we have to screen it using a cross section imaging.

Disclosure of Interests: None declared

AB0897  ABSCESS DURING OSTEARTICULAR BRUCELLOSIS: A STUDY OF 26 CASES
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Background: Brucellosis remains an important economic and public health problem in developing countries. The osteoarticular involvement is one of the most serious complication mainly due to abscess formation.

Objectives: The aim of our study was to identify the frequency and radiological features of abscesses during osteoarticular brucellosis.

Methods: We conducted a retrospective study including 26 patients who have been hospitalized for osteoarticular brucellosis from 1998 to 2018. The diagnosis of brucellosis was made on the basis of clinical symp- toms, imaging finding (CT scan or MRI) and isolation of bruccella species in blood or tissue specimens and/or a positive Wright agglutination test.

Results: Twenty six patients were included. 15 patients were male. The mean age was 52 years [21-77] the geographical origin of the patients was rural in 80% of the cases. The average duration of symptoms pro- gression was 4.76 months [1-12]. Prominent clinical symptoms were inflammatory pain (all cases), fever (in 21 cases) and sweating (in 17 cases). Weight loss was found in 11 cases (42.8%) and hepatomegaly was found in 1 patient. The physical examination revealed a paresis of the two lower limbs in 2 cases. Brucella agglutination test was ≥1/160 in all cases (mean 1/760). Blood cultures were negative in all cases. Eryth- rocyte sedimentation rate (ESR) and serum C-reactive protein level were ranged between 30-108 mm (mean 70 mm) and 0-125 mg/l (mean 30 mg/l) respectively. Leucopenia was found in only 1 case and leucocytosis in 6 cases. The most frequent osteoarticular involvement was spondylodiscitis in 20 cases (76.9%) affecting the lumbar dorsal and cervical spine in respectively 12, 6 and 2 cases. Sacroiliitis was found in 4 cases (15.4%) and septic arthritis in 2 cases (7.7%). Biopsy was performed in 8 cases, but bacteriological examination was contributory to the diagnosis in 2 cases. The radiological findings showed that 14 patients (53.8%) had abscesses. Soft tissue abscesses were detected in 7 cases with mean size of 1.3 cm [0-9cm]. Bilateral psoas abscess was recorded in one case. Epidural collection was revealed in 3 cases with an average size of 0.3 cm [0-5cm]. Paravertebral and peri-vertebral abscesses were detected in 5 cases. Intradiscal abscesses were observed in 3 cases. Cord compression and involvement of root nerve were noted in respective 6 and 1 cases. Compared to the group without abscesses, subjects with abscesses had higher ESR and the difference was statistically signif- icant (mean ESR 26.83 vs 55.9 mm) (p<0.016). There was no statisti- cally significant link between duration of symptoms or duration of hospitalization and the presence of abscesses. All patients had antibiotic treatment (cocilins and rifampicin). The evolution was favorable in all cases. Surgical intervention was required in one case (evacuation of an epidural abscess).

Conclusion: Our study showed that abscesses are frequent in osteoarticu- lar brucellosis. In spite of the low risk of complication, we have to screen it using a cross section imaging.

Disclosure of Interests: None declared

AB0898  HIV AND RHUMATOLOGICAL DISEASES. MISDIAGNOSIS OR CONSEQUENCE!
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Background: Human immunodeficiency virus (HIV) infection is pandemic nowadays, more than 35 million people are infected with HIV, with two thirds being resident in Africa.1 The incidence of rheumatic manifesta- tions in HIV infection was reported in about 4 to 71.3% cases in differ- ent studies depending on the stage of the disease and musculoskeletal involvement.2-5

Objectives: The aim of these study to scope the light on HIV associated rheumatic syndromes. Rheumatic disease were a misdiagnosis or not?

Methods: Cross sectional study of patients admitted to rheumatology unit in Alexandria University with a previous diagnosis of autoimmune rheumatic diseases, resistant to treatment, were screened for HIV.

Results: Three patients found to be HIV positive with low CD4+ less than 200 cells mm³ among 130 screened patients. Two patients were diagnosed as beehot disease due to recurrent oral and genital ulcers.
The first one, also had recurrent skin infections associated with bilateral anterior and posterior ulcers. The second one admitted by recurrent oral and genital ulcers associated with severe oral candidiasis, arthritis, erythema nodosum and positive pearly test, The third one diagnosed as peripheral spondyloarthritides admitted with low-grade fever, palmpantar psoriasis as well as acute extensive anterior and posterior ulcers in left eye and chronic anterior and posterior ulcers in right eye with CMV positive.

Conclusion: HIV infection might be misdiagnosed as a rheumatic disease. It is important to screen patients with inflammatory autoimmune rheumatic manifestations for HIV infection for its implications in the diagnosis and management.

REFERENCES

Disclosure of Interests: None declared

AB0899 COMPUTER TOMOGRAPHY GUIDED BIOPSY YIELD IN PYOGENIC VERTEBRAL OSTEOMYELITIS. AN EXAMINATION OF INFLUENCING FACTORS

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Background: Vertebral Osteomyelitis (VO) is an infectious disease that could involve intervertebral space (discitis), which it is avascular in adults, VO and disitis may occur together or independently. Both are frequently the result of a spreading of a distant focus, such as infectious endocarditis or soft tissue infection. Due to the lack of direct blood supply, reliability of blood cultures is low, so biopsy is highly encouraged by current guidelines. Treatment includes long term antibiotic (ATB), that should be initiated after biopsy (if possible) and sometimes, further surgery is needed.

Objectives: To analyze which factors influence the result of a CT-guided biopsy in patients with VO.

Methods: Retrospective observational study including adult patients diagnosed of VO based on the combination of clinical presentation with either a definitive bacteriologic diagnosis and/or imaging studies, who underwent CT-guided biopsy from January 2010 to January 2019. Demographic features, concurrent diseases, clinical history (length of pain and fever prior to admission), laboratory findings, microbiological diagnosis and radiological data were compiled. Days until biopsy from admission, prior antibiotic exposure was also collected. We considered as immuno-suppressed patients those who had rheumatic or inflammatory bowel disease (IBD) or were undergoing immunomodulatory drugs, solid organ transplantation, and patients with an active malignancy or Human Immunodeficiency Virus (HIV) infected. Clinical and radiological history of lumbar stenosis or disc herniation was considered as prior spine pathology. We considered deaths attributable to PVO those which were directly caused by the infectious picture and/or its complications during the next year after diagnosis.

Results: Seventy-two of 109 patients with VO underwent biopsy (66.0%). Thirty-nine brought a positive culture (54.2%). Basal demographic and clinical features are exposed in table 1. Positive cultures included 33 cases (84.61%) of Gram+ infection (23 Staphylococcus and 6 Streptococcus) and 6 (15.39%) by Gram- bacilli (3 cases of Pseudomona aeruginosa, 2 Escherichia coli and 1 Brevundimona spp).

Conclusion: In our population, it has been observed that not a single variable collected showed influence on culture result, although a negative tendency is observed in cases of prior antibiotic exposure, with no significant difference. Since CT guided biopsy is a safe technique, offering an acceptable reliability, our results support its use even in those cases that empirical antibiotic had been already initiated.

Disclosure of Interests: None declared

AB0900 ACUTE PARAPARESIS AS CLINICAL PRESENTATION OF VERTEBRAL OSTEOMYELITIS

Jorge Juan Fraga-Quiñó, Roxana Gonzalez Mazaror, Jose Ivorra Cortés, Francisco Miguel Ortiz Sanjuan, Elena Grau Garcia, Cristobal Pérez Perales, Marta De la Rubia Navarro, Inmaculada Chalmeta Verdejo, Luis Gonzalez Puig, Isabel Martinez Cordelila, Rosa Negueroles Albuixech, Cristina Alcañiz Escandell, Jose Eloy Ollor Rodriguez, Elvira Vicens Bernabeu, Carmen Najera Herranz, Ines Canovas Olmos, Maria Tasias Pitarch, Eva Calabuig Muñoz, Miguel Salvart Liét, Jose Andres Roman Ivorra.

Background: Vertebral Osteomyelitis (VO) is an infectious disease that could produces neurologic complications such as paresthesia, limb weakness or even acute paraparesis (AP). Objectives: To analyze the clinical characteristics of patients with VO with AP as clinical presentation.

Methods: Single center retrospective observational study including adult patients diagnosed of VO based on the combination of clinical presentation with either a definitive bacteriologic diagnosis and/or imaging studies, who had a clinical examination at diagnosis compatible with AP, from January 2010 to January 2019. ASIA score (American Spinal Injury Association) was registered at diagnosis and one year after. Clinical and radiological history of lumbar stenosis or disc herniation was considered as prior spine pathology. We considered deaths attributable to PVO those which were directly caused by the infectious picture and/or its complications during the next year after diagnosis.

Figure 1

Results: In 15 of 122 patients with VO (18.30%), AP was described on physical examination at admission. Basal demographic and clinical features are exposed in table 1. ASIA scores at diagnosis and 1 year after are showed in chart 1. Duration of pain prior to diagnosis had a median of 24 days (7.5, 55), C reactive protein showed a median value of
AB0001

TWO TYPES OF SYSTEMIC AMYLOIDOSIS IN A SINGLE PATIENT

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Background: The systemic amyloidoses are a group of rare diseases, in which extracellular deposition of a variety of proteins in an abnormal fibrillar confirmation results in life-threatening organ dysfunction. Acquired and hereditary amyloidoses differ in their precursor proteins and predilection for specific organ involvement.

Objectives: To describe the history of two types of amyloidosis developing consecutively in a single individual.

Methods: Targeted biopsies were used to confirm the presence of amyloid by Congo red staining viewed under polarized light, while immunohistochemistry and mass spectrometry were used to characterize the amyloid fibril type. 125I labeled serum amyloid P component (SAP) scintigraphy was performed to map the distribution of amyloid deposits.

Results: We report a woman of Sudanese origin who presented aged 31 with dysuria and haematuria. She was found to have an estimated Glo- merular Filtration Rate of 38 ml/min and no proteinuria, and a renal biopsy demonstrated AA amyloid deposition. An I-123 labelled SAP scan demonstrated a small amount of amyloid confined to the kidneys. She had no overt underlying inflammatory disease, an infectious diseases work up, including blood borne viruses, was negative and serial measure- ment of serum amyloid A protein showed no significant elevation with a median of 5 mg/L. Management was blood pressure control only, and work up, including blood borne viruses, was negative and serial measure-

Conclusion: Despite of being a well-known condition, VO is still an issue since 1-2 out 10 patients have a severe complication at diagnosis, such as AP. None of the basal characteristics analyzed acted as a risk factor, since 1-2 out 10 patients have a serious complication at diagnosis, such as AP. None of the basal characteristics analyzed acted as a risk factor.

AB0002

RHEUMATIC LYME DISEASE SYMPTOMS BASED ON EPIDEMIOLOGICAL DATA IN HIGH ENDEMIC AREA

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Background: Lyme disease is a tick born infectious disease caused by different genospecies of Borrelia bacteria (B. burgdorferi sensu strictu (ss), B. afzelii and B. garinii). The signs and symptoms of Lyme disease vary, they usually appear in stages, but the stages can overlap. In early stage skin rash (erythema migrans) appears, which may be accompanied by fever, chill, fatigue, body aches, headache, neck stiffness, and swollen lymph nodes. Later signs and symptoms can be these: joint pain and inflammation, neurological problems or other less common syndromes - heart problems, eye inflammation, and liver inflammation. Lyme disease is very common disease in the world, approximately 300,000 people get Lyme disease each year in the United States (Centers for disease con- trol and prevention US), in Lithuania disease frequency is 101.6 cases per 100 000 population (Center for Communicable Diseases and AIDS, Lithuania, 2016 year).

Objectives: To investigate the frequency of rheumatic symptoms between Lyme diagnosed persons in Lithuania, based on epidemiological data.
Methods: We have analyzed data of Center for Communicable Diseases and AIDS of Lithuania about Lyme diagnosed patients from 2014 to 2016 years.

Results: Total number of cases was 7425, 2791 males, 4633 females, age range 1 - 91 years, median age 52 years. 996 patients found out as symptomatic. The rest were either asymptomatic either information about clinical disease manifestation was not known. Among symptomatic patients two rheumatic symptoms were observed: arthralgia (220 cases, 22.1%), 140 females, 80 males, age range 12 – 84 years, median age 58 years, and myalgia (79 cases, 7.8%), 44 females, 34 males, age range 15-80, median age 56. Other symptoms were erythema migrants (75.6%), headache (15.2%), general weakness (12.4%), fever (10, 1%), and head dizziness (6.4%).

Conclusion: In total, almost 30 percentages (29, 91%) of symptoms were rheumatic. To conclude, joint pain and/or muscle pain can lead not only to systemic rheumatic diseases, but to infection diseases as well (for example: Lyme disease).

REFERENCES

Disclosure of Interests: None declared

AB0903
LYME ARTHRITIS IN HIGH LYME DISEASE ENDEMIC EUROPE ZONE

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Background: Lyme disease is a tick born infectious disease caused by different genospecies of Borrelia bacteria (B. burgdorferi sensu strictu, B. afzelii and B. garinii). Disease clinical manifestation varies and belongs to different genospecies of Borrelia bacteria. In America Lyme arthritis dominates, which is caused by B.burgdorferi, while in Europe Lyme disease is caused by Borrelia afzelii or Borrelia garinii (less commonly by Borrelia burgdorferi) leading to usual disease manifestation as erythema migrans or neuroborreliosis. Lyme disease is very common disease in the world, approximately 300,000 people get Lyme disease each year in the United States (Centers for disease control and prevention US), in Lithuania disease frequency is 101.6 cases per 100 000 population (Center for Communicable Diseases and AIDS, Lithuania, 2016 year).

Objectives: To investigate the frequency of Lyme arthritis in high disease endemic European country Lithuania. To find out with joint was most frequently affected.

Methods: A retrospective, single center study was performed. We have analyzed the medical documents of adult patients, who were hospitalized to Infectious disease center (Vilnius, Lithuania), due to severe Lyme disease clinical manifestation, in 2014-2017 years.

Results: 88 patients were enrolled (57 females, 31 males, age range 18-90 years, median age 57 years). Patients were divided into four groups according disease clinical manifestation: erythema migrans, neuroborreliosis, Lyme arthritis and carditis (atrophicventricular block). The most frequently erythema migrants was observed (53 cases, 62, 35 percentages (%)), than neuroborreliosis (27 cases, 31, 76 percentages), following by Lyme arthritis (3 cases, 3, 53 percentages) and Lyme carditis (2 cases, 2, 35 percentages). Between Lyme arthritis patients inflamed joints were these: knee (one case), ankle (one case) and both - knee and ankle (one case). In two cases high laboratory markers (ESR 116, 23 mm, CRP 125, 50 mg/l) and high body temperature (38, 2; 39, 5 t) was documented.

Conclusion: 2.35% of hospitalized Lyme infected patients reveal as Lyme arthritis. Inflamed joint were knee (50%) and ankle (50%). Despite the fact that it is used to think that Lyme arthritis occurs only (mostly) in America we can find it in Europe too, though its incidence is low.

REFERENCES

Disclosure of Interests: None declared

AB0904
EFFECTIVENESS AND SAFETY OF RITUXIMAB IN SYSTEMIC AUTOIMMUNE DISEASES: A CASE SERIES

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Background: Rituximab (RTX) is a drug composed of chimeric monoclonal antibodies against the CD20 protein, producing a depletion of B lymphocytes. Nowadays, it is used to treat severe and refractory systemic autoimmune diseases (SAD).

Objectives: Analysing the effectiveness and safety of RTX in patients with SAD in clinical practice.

Methods: We conducted a retrospective analysis of patients with SAD treated at least once with RTX in the autoimmune diseases unit of our hospital in the last 3 years. We evaluated demographic, clinical and serological variables as well as the presence of adverse events (AE).

Results: Twenty two patients have been included (13 women and 9 men, mean age 63 ±15 years). The diagnosis were ANCA-associated vasculitis (31.8%), cryoglobulinemic vasculitis (18.2%), autoimmune hemolytic anemia (13.6%), systemic lupus erythematosus (9.1%), immune thrombocytopenia in antiphospholipid syndrome (9.1%) and one each of: Felty syndrome, IgG4-related disease, necrotizing myopathy and systemic sclerosis. Indications for treatment were renal disease in 36.4% of the cases, haematological manifestations in 27.3%, skin involvement in 13.6%, neurologic manifestations in 9.1% and other different reasons in the remaining 15.6%. RTX was used after therapeutic failure with previous treatments in 81.8% and as first line treatment in only 18.1% of the cases. RTX dose was 375 mg/m2 once weekly for 4 doses (54,5%) and 1000 mg on days 1 and 15 (45.5%). After rituximab, 77.3% of patients had complete response, 9.1% partial response, and 13.7% non-responding. There were 14 AE reported in 10 of the 22 patients (45,5%). (See table). Three severe infections were found: 2 patients with invasive pulmonary aspergillosis and 1 patient with invasive cryptococcosis. All of them died within the next month after beginning RTX. One of those who were diagnosed of argepliosis had never received steroids. The other two were treated with high dose of steroids for several months. One patient had a nonischemic cardiomyopathy (NIC) with systolic dysfunction that resolved 4 months after RTX discontinuation.

Conclusion: As far as we are concern, RTX is a useful and pretty safe biological agent in the treatment of refractory SAD. However, we must be aware of rare adverse effects such as NIC. In addition, given the potential severity of the infections found (although not totally attributable to RTX), we must closely follow up these patients for early diagnosis, treatment and even starting profilaxis in high risk patients.
MAY CHRONIC CONSTIPATION-INDUCED CHRONIC INFLAMMATION AFFECT THE ONSET AND SEVERITY OF FIBROMYALGIA SYMPTOMS?

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Background: Up to 70% of fibromyalgia patients have functional bowel disorders as irritable bowel syndrome (IBS), constipation and diarrhea. Patients with chronic constipation may feature changes in microflora of large bowel, which are characterized by a relative decrease in obligate pathogens and an increase in enteric bacteria and fungi. This condition causes chronic low-grade inflammation. It has been reported that as a result of chronic constipation, altered microbiota of large bowel, which are characterized by a relative decrease in obligate pathogens and an increase in enteric bacteria and fungi, may cause low-grade chronic inflammation which may affect the onset and severity of fibromyalgia.

Methods: The cross-sectional study was designed as two groups: fibromyalgia patients, who is diagnosed according to the ACR 2016 revised classification criteria, and healthy population. All study participants were included in this study. The demographic and clinical characteristics of the participants such as age, height, weight, body mass index (BMI), occupations, exercise habits were recorded. In semi-standing position with isokinetic dynamometer (BIODEX) at 60° ~90° ~120° /second (s) angular velocities, trunk flexor and extensor muscle performances were evaluated. Flexor (flex) peak torque (PT), extensor (ext) PT values and flex/ext PT values were calculated. The flexor PT values also were lower in FMS group but no statistically significance in flexor PT values between the groups (p>0.05). As a result of isokinetic measurements of trunk muscles, extensor PT values were found significantly lower in women with FMS than C group at all three angular velocities (p<0.05). The flexor PT values also were lower in FMS group but no statistically significance in flexor PT values between the groups (p>0.05). As a result of isokinetic measurements of trunk muscles, extensor PT values were found significantly lower in women with FMS than C group at all three angular velocities (p<0.05).

Results: The mean age was 43.9 ± 8.1 years in FMS group and 43.7 ± 7.6 in control group. The mean BMI was 27.5 ± 4.19 in FMS group and 27.4 ± 4.58 in control group. The mean duration of constipation was 20.1 ± 8.9 and the mean duration of fibromyalgia symptoms was 16.0 ± 10.2 years. Fibromyalgia symptoms started in 16 of 18 patients after constipation (Mean year: 4.1 ± 5.3). Compared with constipated and non-constipated fibromyalgia patients, symptom duration and FIQ were significantly higher in constipated fibromyalgia patients (p<0.01). The duration of constipation was correlated with duration of fibromyalgia symptom (r² = 0.65, p = 0.00), PACQLQ (r² = 0.71, p = 0.001) and CSI (r² = 0.59, p = 0.01). There was a correlation between FIQ and CSI (r² = 0.96, p = 0.00) and PACQLQ (r² = 0.62, p = 0.006).

Conclusion: The frequency of gastrointestinal symptoms increased in patients with fibromyalgia. As the severity of constipation increases, the symptoms of fibromyalgia are exacerbated. The presence of constipation findings before fibromyalgia suggests that low-grade chronic inflammation caused by constipation may have an effect on the onset of fibromyalgia. There is a need for a prospective cohort study to clarify this cause and effect relationship.

REFERENCES

Disclosure of Interests: None declared


AB0906 RELATIONSHIP BETWEEN FIBROMYALGIA AND TRUNK MUSCLE PERFORMANCE

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Background: Muscle performance is adversely affected by pain, fatigue and low aerobic capacity in fibromyalgia syndrome (FMS).

Objectives: We compared trunk muscle performance of women with FMS and healthy individuals who have similar age and body mass index (BMI).

Methods: A total of 37 women with FMS and 32 healthy women were included in this study. The demographic and clinical characteristics of the participants such as age, height, weight, body mass index (BMI), occupations, exercise habits were recorded. In semi-standing position with isokinetic dynamometer (BIODEX) at 60° ~90° ~120° /second (s) angular velocities, trunk flexor and extensor muscle performances were evaluated. Flexor (flex) peak torque (PT), extensor (ext) PT values and flex/ext PT values were calculated.

Results: The mean age was 43.9 ± 8.1 years in FMS group and 43.7 ± 6.7 in control group. The mean BMI was 27.5 ± 4.19 in FMS group and 26.4 ± 4.08 in control group. There was no significant difference between the groups in terms of age and BMI (p>0.05). As a result of isokinetic measurements of trunk muscles, extensor PT values were found significantly lower in women with FMS than C group at all three angular velocities (p<0.05). The flexor PT values also were lower in FMS group but no statistically significance in flexor PT values between the groups (p>0.05). When flexor/ extensor PT ratio was compared, it was seen that this ratio increased in the FMS group.

Conclusion: There are many studies in the literature assessing upper and lower extremity muscle performances in FMS (1-2). To our knowledge, we first evaluated trunk muscle performances of patients with FMS and we found that trunk muscles, especially extensors, were significantly weaker in FMS group. As a result, in treatment of FMS, there is a need for more comprehensive randomized controlled studies showing the importance of strengthening exercises to improve trunk muscle performance.

REFERENCES
Background: Dysautonomia describes a group of conditions associated with a malfunction of the autonomic nervous system. Symptoms of dysautonomia and inflammation have been described in Fibromyalgia (FM) and Myalgic encephalomyelitis (ME)/Chronic Fatigue Syndrome (CFS) [1–4]. Symptoms include increased disabling fatigue, pain, dizziness and digestive problems.

Objectives: This ongoing study investigates, for the first time, how a sympathetically mediated challenge and induced systemic inflammatory state impact on mood, pain, fatigue, and autonomic function.

Methods: In a randomized, double-blind, placebo-controlled study, 25 participants with FM and/or ME/CFS underwent an autonomic- and inflammatory challenge during three visits. Outcome measures included a range of questionnaires including the Profile of Mood States (POMS), Pain visual analogue scales (VAS), measures of heart rate (HR), Pressure Pain Threshold (PPT), alongside subjective pain and fatigue measures. Autonomic function was assessed using a passive non-invasive tilt-test (upright tilt of 60°) and active-stand (AS) with beat-to-beat HR and blood pressure monitoring. Remaining visits involved an inflammatory challenge using intramuscular typhoid- and saline (placebo) injection.

Results: Tilt-table test was positive in 20% participants and AS in 92% participants indicated by HR rise >30 bpm or a sustained HR of 120 bpm. Overall fatigue correlated with peak HR during tilt (r=−0.465, p=0.025, n=23). There was a positive correlation between the average HR during AS under typhoid after controlling for placebo and average HR during tilt (r=−0.517, p=0.049, n=15). Scores on the Wide Spread Pain Index (WPI) at screening correlated with the change in POMS pre- and post-typhoid after controlling for placebo (r=−0.479, p=0.049, n=18). Scores on the Fibromyalgia Severity Scale correlated with the change in physical fatigue pre- and post-typhoid after controlling for placebo (r=−0.582, p=0.047, n=12). Mean change in heart rate pre-post active stand correlated with a change in pain VAS pre- and post-typhoid after controlling for placebo (r=0.382, p=0.023). There was a positive correlation between the average HR during AS under typhoid after controlling for placebo and average HR during tilt (r=−0.517, p=0.049, n=15). Scores on the Fibromyalgia Severity Scale correlated with the change in physical fatigue pre- and post-typhoid after controlling for placebo (r=−0.582, p=0.047, n=12).

Conclusion: Preliminary findings suggest that dysautonomia and induced inflammation significantly impacts on pain, fatigue, and autonomic function in FM and ME/CFS. On-going data collection of 100 participants (25 controls) will allow extended analyses to test how autonomic function in FM and ME/CFS impact symptom domains that impact on quality of life.

REFERENCES

Disclosure of Interests: None declared

Table 1 - Univariate analysis of myalgia cases versus controls.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Controls</th>
<th>Myalgia cases</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>49.71±12.9</td>
<td>54.07±10.25</td>
<td>0.075</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td>0.033</td>
</tr>
<tr>
<td>Male</td>
<td>40 (71.4%)</td>
<td>28 (50.9%)</td>
<td>0.049</td>
</tr>
<tr>
<td>Female</td>
<td>16 (28.6%)</td>
<td>28 (50.9%)</td>
<td>0.633</td>
</tr>
<tr>
<td>BMI</td>
<td>25.66±3.29</td>
<td>27.06±4.71</td>
<td>0.079</td>
</tr>
<tr>
<td>Correct smoking status</td>
<td>9 (16.1%)</td>
<td>8 (14.5%)</td>
<td>1.009</td>
</tr>
<tr>
<td>Psychiatric disorders</td>
<td>6 (10.7%)</td>
<td>4 (7.1%)</td>
<td>0.742</td>
</tr>
<tr>
<td>CPK (IU/L)</td>
<td>213.1±554.44</td>
<td>310.6±715.67</td>
<td>0.066</td>
</tr>
<tr>
<td>Prevention purpose</td>
<td></td>
<td></td>
<td>0.838</td>
</tr>
<tr>
<td>Primary prevention</td>
<td>41 (73.2%)</td>
<td>37 (66.1%)</td>
<td></td>
</tr>
<tr>
<td>Secondary prevention</td>
<td>15 (26.8%)</td>
<td>19 (33.9%)</td>
<td></td>
</tr>
<tr>
<td>Disease length</td>
<td>11.05±8.41</td>
<td>13.54±8.39</td>
<td>0.070</td>
</tr>
<tr>
<td>B/WP</td>
<td>0.43±0.62</td>
<td>3.59±2.31</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hamilton</td>
<td>3.80±0.29</td>
<td>6.46±0.82</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Depression scale</td>
<td>5.48±6.94</td>
<td>9.71±6.23</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hamilton anxiety scale</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fulfilling DSM criteria</td>
<td>0 (0.0%)</td>
<td>11 (19.0%)</td>
<td>0.001</td>
</tr>
</tbody>
</table>
AB0909  
Efficacy and safety of ultrasound guided aspiration and intralesional corticosteroids injection of ruptured Baker’s cyst

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Background: Baker’s cyst is the most common mass in the popliteal fossa and results from fluid distension of the gastrocnemio-semimembranosus bursa. The most common complication of Baker’s cyst is the rupture or dissection of fluid into the adjacent proximal gastrocnemius muscle belly, which results in a pseudothrombophlebitis syndrome mimicking symptoms of DVT.

Treatment of ruptured Baker cysts ranged from conservative management to surgical resection.

Ultrasound guided aspiration and corticosteroids injection may be an effective and easy method of management of these cases.

Up to the best of our knowledge, this is the first study to detect the efficacy and safety of ultrasonographic guided aspiration and injections of ruptured Baker cysts.

Objective: To evaluate the efficacy and safety of ultrasonographic guided aspiration and local corticosteroids of ruptured Baker cysts based on follow-up clinical and sonographic results.

Methods: A retrospective study was conducted on 42 patients (12 males and 30 females, mean age 36 +/- 10 SD years) affected by a ruptured Baker cysts associated to knee joint disorders in the period between January 2013 to January 2019. The diagnosis was done by clinical presentation of acute calf pain, swelling, tenderness at the calf muscles and ultrasonographic evidences of ruptured backer cysts in the form of free fluid collection in the calf connected to a well defined cyst at the back of knee.

All cases were treated by ultrasonographic guided aspiration and intralesional injection of corticosteroids once or twice a week one part. Follow up was done on a weekly basis until complete resolution of symptoms then 3 months later. Visual analogue scale (VAS) for calf pain and Rauschning-Lindgren and Lysholm Knee Scoring Scales were used to assess pre/post-injection knee function.

Results: The primary diagnoses to patients presented with ruptured Baker cyst in this study were as follow: 18 (42.8%) cases with rheumatoid arthritis; 15 (35.7%) cases with osteoarthritis and 9 (21.4%) cases with psoriatic arthritis.

Clinical parameters (VAS for calf pain and Rauschning-Lindgren score) improved significantly in all patients at post injection evaluation visits.

Rauschning-Lindgren score was significantly lower after US guided injections (mean, 0; range, 0-1) than at baseline (mean, 2; range, 1-2); p < 0.001 (table1).

VAS for calf pain also significantly lower after US guided injections (mean,0.5; range, 0-1) than at baseline (mean, 9.5; range, 0-10); p < 0.001.

Ultrasoundographic features improved significantly with complete disappearance of free fluid at the calf in 35 (83.3%) cases one week after the injection.

As regards Baker cyst only 5 (11%) cases showed complete disappearance of the backer cyst and in the majority of cases 37 (88%) there were persistent Baker cysts.

No side effects were reported in all cases.

AB0909 Table 1. Clinical results of Baker cyst excision (Rauschning and Lindgren scale and VAS for calf pain)

<table>
<thead>
<tr>
<th></th>
<th>Pre injection</th>
<th>1 week later</th>
<th>3 months later</th>
</tr>
</thead>
<tbody>
<tr>
<td>grade 0</td>
<td>0</td>
<td>30</td>
<td>39</td>
</tr>
<tr>
<td>Grade 1</td>
<td>0</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Grade 2</td>
<td>6</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Grade 3</td>
<td>36</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>VAS for calf pain</td>
<td>9.5</td>
<td>1.5</td>
<td>0.5</td>
</tr>
</tbody>
</table>

Disclosure of Interests: Yarden Yavne: None declared, Rivka Sheinin: None declared, Rita Nogueira: None declared, Nicola Luigi Bragazz: None declared, Shmuel Tiosano: None declared, Abdulla Watad: None declared, Kassem Sharif: None declared, Daniela Amital: None declared, Hofit Cohen: None declared, Howard Amital Grant/research support from: Pfizer, AbbVie, Janssen, Consultant for: Pfizer, AbbVie, Janssen, Consultant for: Pfizer, Merck Sharp & Dohme, Consultant for: Pfizer, Merck Sharp & Dohme, Speakers bureau: Pfizer, Merck Sharp & Dohme, Janssen, Sanofi, Bristol-Myers Squibb, Abbvie, Neopharm, Speakers bureau: Pfizer, Merck Sharp & Dohme, Janssen, Sanofi, Bristol-Myers Squibb, Abbvie, Neopharm


AB0910  
Effective restoring motion and effective treatment of myofascial and neuropathic low back pain by targeted dry needling using ultrasound guidance

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Background: Low back pain (LBP) involves both myofascial and neuropathic components of pain. Neuropathic pain is a widespread problem, require continuous consumption of medications. Muscle spasticity might evoke nerve compression, dry needling (DN) of myofascial trigger points (MTP) under ultrasound (US) guidance is effective method for treatment myofascial pain [1,2] restoring posture [3] and can be effective for neuropathic pain.

Objectives: The aim was to evaluate efficacy of dry needling under US guidance for treatment myofascial and neuropathic components of LBP.

Methods: We included 52 patients, 37 females, aged 18-64 years (the average was 55 years) low back pain was diagnosed chronic low back pain with neuropathic component with clinically diagnosed low back pain over 3 month with neuropathic component and reduced motility in spine, pelvis and lower extremity. All patients had symptoms over 3 month, underwent general exam, including MRI, laboratory, neurologic, orthopedic tests. We conducted precise physical tests and neuromuscular ultrasound using M-mode and evaluated nerves and motion in intervertebral spaces, pelvis, intrinsic foot and leg muscles. We conducted ultrasound survey at the levels of predicted nerve injury. Patients received DN of MTP under US guidance according to approach by R.Bubnov [1,2], considering nerve entrapment area. Visual analogue scale (VAS, 0-10) and Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) scores were measured before, immediately after, 24 hours, and 7 days after intervention.

Results: After 7 days, VAS scores showed pain improvement from 7.4 to 2.2; LANSS scores improved from 16 to 4. In diabetic and postherpetic neuropathy cases we obtained similar results as in rest of patients (p < 0.05). US demonstrated improvement nerve structure, increasing motility, contractility (muscle contracted/rested thickness) on M-mode during functional tests and walking in all levels. Improvement of neuropathy signs as decrease of fascicles diameter from 2 to 0.9 mm measured on US in sciatic nerve, both in tibial, peroneal portions, data correlated with self-assessment pain decrease (r > 0.8). Preferably MTP were identification in supinators muscle (wrist pain); rotator muscles (infraepatins, supraspinatus, subscapularis and teres minor muscles); scalene muscles; obliques capitis muscles, and also in fascial tissue.

Conclusion: Dry needling under US guidance efficiently reduce myofascial pain, ameliorate symptoms of neuropathy and local muscle hypomotility in low back pain. Further research needed for development US patterns and study causation in chain spasticity-contractility-motion-neuropathic pain.
REFERENCES


Disclosure of Interests: None declared

AB09011

REFRACTORY LOW BACK PAIN AND LUMBAR CT-GUIDED STEROID INFLTRATION. STUDY OF 582 PROCEDURES FROM THE SAME CENTER

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1Basurto University Hospital, Research Unit, Bilbao, Spain; 2Basurto University Hospital, Radiodiagnostic, Bilbao, Spain; 3Basurto University Hospital, Research Unit, Bilbao, Spain

Background: Mechanical low back pain which is refractory to analgesic and rehabilitative treatment is an important cause of disability. The primary objective of corticosteroid (CS) lumbar infiltration is to accelerate the recovery process and to avoid surgery. However, its use is not without controversy.

Objectives: To review the indications, efficacy and complications of lumbar computed tomography (CT)-guided CS infiltration.

Methods: Retrospective study (January 2012 - April 2018) of lumbar CT-guided CS infiltrations performed in a single center. The epidemiological variables, underlying pathologies, approach of injection, used CS (dexamethasone during the whole period and triamcinolone until February 2015), efficacy after 1 and after 3 months and complications were registered. In addition, a comparative study of the efficacy according to indication, type of CS and approach of injection was performed.

Frequencies and percentages were used in qualitative variables, mean ±SD in quantitative and for the comparison between groups Chi2 test or Fisher test was used in categorical variables and Student T test or U of Mann-Whitney in quantitative. Statistical analysis was performed with IBM SPSS v.23.

Results: 582 procedures were performed in 445 patients (1 infiltration in 445 patients, 2 in 106, 3 in 23, 4 in 7 and 5 in 1). The mean age±SD was 58.6±14.8 years with a male/female ratio of 224/221. Traumatology was the service with highest demand (88.8%) followed by rheumatology (14.8%) and orthopedics (36.4%), postoperative fibrosis (14.8%), spondyloarthrosis (2.7%) and degenerative disc (2.7%). The mean ±SD follow-up period was 32.4±24.9 months. The indication was the service with highest demand (88.8%) followed by rheumatology (14.8%) and orthopedics (36.4%).

Only 21% required surgery. Triamcinolone (although its use is currently discouraged because it is a particulate CS), foraminal infiltration and lateral recess proved to be more effective for pain control. In this study, lumbar CT-guided CS infiltration in patients with refractory low back pain is an accessible, minimally invasive, safe and effective procedure in long term.

Disclosure of Interests: None declared

AB09012

EXTRACORPOREAL SHOCKWAVE VERSUS MUSCULOSKELETAL MESOTHERAPY FOR ACHILLES TENDINOPATHY IN ATHLETES

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Background: Achilles tendinopathy (AT) is considered as one of the common tendon pathologies, which occurs mainly in athletes. Different conservative treatment options have been introduced and used for symptoms relief of AT but with short-term effect.1 Extracorporeal shockwave treatment (ESWT) provides longer effects and could be used in cases fail to respond to conservative treatments.2 Mesotherapy is widely practiced in sports medicine as multiple injections, often of anti-inflammatory medications into the subcutaneous fat overlying a region of musculoskeletal pain. The effect appears unclear but may be due to localized tissue uptake of anti-inflammatory medication which may provide symptomatic relief especially in insertional Achilles tendinopathy 3

Objectives: In this study, we aimed to evaluate the effect of extracorporeal shockwave treatment (ESWT) and mesotherapy on chronic Achilles tendinopathy in athletes.

Methods: 40 patients with chronic AT were diagnosed clinically & using high resolution ultrasound (US) according to the Eular guide lines and randomly allocated in two groups, first receive ESWT, other group underwent mesotherapy (MT) one session once a week for 4 weeks to the 2 groups. Pain, ankle-hindfoot scale of the American Orthopedic Foot and Ankle Society (AOFAS) 4 & US were recorded at baseline, 4 and 12 weeks after intervention.

Results: Both groups improved during the treatment and follow-up period. The mean VAS score decreased from 7.55 to 3 in the ESWT group and from 7.70 to 4.30 in MT group. There was no significant difference in terms of AOFAS and VAS scores between both groups at 4 weeks follow-up while Mean AOFAS & VAS scores were significantly different between ESWT and MT groups at 12 weeks of follow-up (P = 0.013) (P = 0.47). US assessment significantly improved after 12 weeks in ESWT group as regards tendon thickness, calcifications(figure1,2) and doppler signal.

Conclusion: ESWT showed improvement of pain and inflammation of AT than MT injections which was documented by the decreased VAS, increased AOFAS scores as well as US improved findings shortly after the treatment as well as on late follow up.

REFERENCES


Figure 1

Only 21% required surgery. Triamcinolone (although its use is currently discouraged because it is a particulate CS), foraminal infiltration and lateral recess proved to be more effective for pain control. In this study, lumbar CT-guided CS infiltration in patients with refractory low back pain is an accessible, minimally invasive, safe and effective procedure in long term.

Disclosure of Interests: None declared
THE ROLE OF BISPHOSPHONATES IN THE MANAGEMENT OF SPONTANEOUS OSTEONECROSIS OF THE KNEE (SONK)

Mark Ford, Roshan Amarasena. The Robert Jones and Agnes Hunt Orthopaedic Hospital NHS Foundation Trust, Gobowen, United Kingdom

Background: Spontaneous osteonecrosis of the knee (SONK) was first described by Arhlück, Bauer and Bohnein in 1968 when they identified 39 patients with radiolucent lesions of subchondral bone in the medial femoral condyle which represented a manifestation of osteonecrosis. The aetiology and pathogenesis of SONK remains unclear with possibilities including microvascular compromise, reduced bone mineral density, and mechanical disruption within the knee. The treatment compromises of conservative, medical and surgical options depending on the severity of osteonecrosis identified on imaging. Lai et al (2005) demonstrated the beneficial effect of alendronate in the prevention of early collapse of the femoral head in patients with nontraumatic osteonecrosis: a randomized clinical study. 

Methods: A literature search was conducted to identify studies reporting the effect of bisphosphonates in the treatment of SONK and the usefulness and validity of their conclusions was subsequently assessed.

Results: We have identified one randomised controlled trial and four case series investigating the use of a bisphosphate on the clinical and radiological outcome in patients with osteonecrosis of the knee. All four case series showed improvements with bisphosphonates on patient visual analogue scale (VAS) and radiological outcome. However, the sole randomised controlled trial reported that bisphosphonates had no additional benefit over conservative measures and anti-inflammatory medications after 24 or 48 weeks both functionally and radiographically. These studies had a small number of participants and the size of the osteonecrotic lesion was either small, which traditionally is managed conservatively, or not interpreted in the context of the results.

Conclusion: The role of bisphosphonates in the treatment of SONK remains unclear. Further randomised controlled trials would be beneficial in these patients with emphasis on the symptom duration and the size of the osteonecrotic lesion.

REFERENCES


Disclosure of Interests: None declared

AB0914

EFFECT OF VITAMIN D SERUM CONCENTRATION ON ARTHRALGIA INDUCED BY ADJUVANT THERAPY WITH AROMATASE INHIBITORS IN NON METASTATIC BREAST CANCERS SURVIVORS

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Background: Hand arthralgia is often reported by breast cancer patients treated with adjuvant hormonal therapy. Aromatase inhibitors (AIs) improve survival in postmenopausal women with hormone-sensitive breast cancer, but can cause joint pain and stiffness (2). Low concentration of vitamin D in adults can cause musculoskeletal pain and joint discomfort (1). No data are available to date, on serum concentrations of (25-hydroxyvitamin D) [25 (OH) D3] vitamin D in AI-treated patients and possible relationship with arthralgia.

Objectives: To evaluate possible correlation between different 25 (OH) D3 serum concentrations and hand arthralgia in patients with breast cancer treated with AIs.

Methods: All patients that during the AIs therapy develop arthralgia referred to the rheumatologist; they reported the pain following the VAS (visual analog scale) and contemporary performed a sample blood for dosage of vitamin D as well as biomarkers for inflammation and autoimmunity to exclude concomitant immune/inflammatory rheumatic musculoskeletal causes.

Results: In a group of 63 women taking AIs (mean age 62.3±9.8years; disease duration from first assumption of AIs 10.6±3.2 months) 81% reported hand arthralgia and stiffness within the first year of follow-up; the most prevalent site of pain localization was bilateral hands (85%). Symptom was associated with minimal increase of serum parameters of inflammation (the mean value of C-reactive protein was 7.1±3.0 mg/L (normal value 0-5) but negative autoimmune profile (negative rheumatoid factor and anticollagen type II antibody). The mean 25(OH)2D3 serum concentration was 18.4±5.9 ng/mL. Only 9% of women had an adequate (> 30 ng/ml) [25 (OH) D3] vitamin D serum levels; 70% were insufficient (> 10 < 20 ng/mL), and 21% were severely deficient (< 10 ng/mL). 55% of patients started AIs after chemotherapy. From the group that received AIs after chemotherapy 77% patients with arthralgia were found during the first years of hormonal therapy, in the group that previously did not take chemotherapy 88% of patients referred arthralgia. There was any
difference on vitamin D serum levels between patients previously treated or not treated with chemotheraphy (17.8 ± 7.8 vs. 19.3 ± 9.7 p = 0.6). After subdivision of patients that referred hand arthralgia according to the different type of AIs used: 22% have been treated with tamoxifen, 30%, anastrozole and 48% letrozole. Therefore, the baseline serum vitamin D concentrations did not significantly predict arthralgia in the overall group (P = 0.70) or separately in the single AIs group (anastrozole (P = 0.60) or tamoxifen(>P=0.30) or letrozole (P = 0.60, respectively).

Conclusion: Vitamin D serum concentration in women treated with AIs are at lowest ranges in the majority of the patients analysed, but no apparent interference with musculoskeletal symptoms was found related to the different concentrations; the cause of arthralgia might be better related to estrogen deficiency induced by AIs their self.

REFERENCES

AB0916 INVESTIGATION OF PAIN AND DEPRESSION IN CANCER OUTPATIENTS RECEIVING CHEMOTHERAPY
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Background: Cancer treatments such as chemotherapy contribute to the development of depression and pain (1). Prevalence of pain ranges from 14% to 100% and depressed symptoms occur 1-42% in cancer patients (2). The empirical evidence indicates that pain is often untreated and may induce depression in cancer patients (1,2) and depression affects the management of symptoms such as pain (3). Therefore, depression and pain have interrelated effects with each other. Pain and depression in cancer patients lead to discontinuation of therapy, difficulties in controlling symptoms and negative treatment compliance (4). Studies report the need for more research on pain and depression associated with cancer treatment (2).

Objectives: The objectives of this study are to: 1) compare the depression levels of painful and painless cancer patients who received outpatient chemotherapy; and 2) investigate the relationship between pain and depression in these patients.

Methods: This study was carried out in outpatient chemotherapy unit of Hacettepe Oncology Hospital based in Ankara, the capital city of Turkey. The visual analog scale (VAS) was used to investigate if the patients may have had pain. The Brief Pain Inventory (BPI) was applied to evaluate the pain frequency and pain interference on the function of patients while the Beck Depression Inventory (BDI) was applied to evaluate depression.

Results: The study findings are based on the outcomes of 27 cancer outpatients receiving chemotherapy. Their mean age was 56.89±11.08 years (age range; 31-73). Almost half of the of patients had pain (48.15%). There was a difference between the depression scores of the patients who had pain and the other patients without pain but this is not statistically significant (p=0.07). The depression scores of painful patients and non-painful patients were 13 and 6, respectively. There was a moderate association between scores of pain severity and depression (r=0.4, p=0.04). Moreover, there was a high association between the score of depression and pain interference on function (r=0.61, p=0.016).

Conclusion: This study shows that pain is related with depression in cancer outpatients receiving chemotherapy. Depression may occur more frequently in patients who have experienced pain than in patients with no pain and also depression is likely to increase pain in cancer patients. Therefore, the addition of emotional and psychosocial components for treatment procedures and effective pain management may have positive effects on the treatment of cancer outpatients receiving chemotherapy.

REFERENCES
**AB0917**

**PATTERN OF SERUM CHOLECALCIFEROL (VITAMIN D3) LEVEL AMONG THE FEMALE IN RELATION TO CLOTHING'S**

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**Background:** Both clinical and subclinical low level vitamin D is common. Various kinds of health hazard including musculoskeletal symptoms are frequently seen among the Vitamin D deficients. It is also uncommon even in a sunny country. Lack of sun exposure, particularly female using veil may be an important cause.

**Objectives:** To assess the relationship between using veil and serum vitamin D3 (cholecalciferol) level

**Methods:** This prospective cross-sectional descriptive study was conducted during July 2017 to June 2018. Patients with common complaints related to lack of Vitamin D (muscle cramp, myalgia, fatigue, bone pain, generalized weakness, difficulty in getting up, climbing stairs and pain in weight bearing joints) were enrolled. Patient having other disease were excluded from study. Serum cholecalciferol was measured for each patient. Race, occupation, educational status, skin complexion, body mass index, sunlight exposure, covering of body with clothing and use of sunscreen were taken under consideration in final analysis. Correlation of serum cholecalciferol level with different types of veils (Burkha, halve sleeve, full sleeve, quarter sleeve and Hijab) of individual’s was analyzed.

**Results:** A total 79 female patients were enrolled after screening 108. All of them were of multi-ethnic Asian origin. Age distribution of them is 17 to 39 years 34.2%, 40 to 50 years 38%, 50 to 70 years 26.6% and above 70 years 1.3%. Maximum (93.7%) of them were house wife. 91.1% had no adequate sun exposure and 81% had no skin exposure to sunlight. Among clothing 79.7% used Burkha, 5.1% halve sleeve, 2.5% full sleeve and 12.7% quarter sleeve. Among Burkha 28.6% (18), 55.6% (35 & 15.9% (10) and among quarter sleeve 50% (5), 40% (4) & 10% (1) had deficient, insufficient & sufficient vitamin D level respectively while 2 (100%) female with full sleeve and 4 (100%) female with halve sleeve had deficient and insufficient vitamin D level respectively. The cholecalciferol level among the users of veil is shown in Table-1. There was no significant difference between different types of clothing’s (Table: 2).

Abstract AB0917 Table 1. Weight, height and Vitamin D level in different types of clothing's.

<table>
<thead>
<tr>
<th>Type of clothing</th>
<th>Wt in Kg</th>
<th>Ht in cm</th>
<th>VD level (range) in ng/ml</th>
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<tbody>
<tr>
<td>Burkha</td>
<td>Mean</td>
<td>Std. Deviation</td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>68.63</td>
<td>150.43</td>
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<tr>
<td></td>
<td>63</td>
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<tr>
<td></td>
<td>11.706</td>
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<td></td>
<td>6.3074</td>
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<td>63.40</td>
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<td>6.967</td>
<td>150.27</td>
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<td>11.790</td>
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<td></td>
<td>6.2418</td>
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</tbody>
</table>

Conclusion: Main source of Vitamin D is sunlight. Proper exposure to sunlight is essential for adequate vitamin D level even in a sunny country. Receiving in vitamin D3 absorption from sunlight, there may be no difference between Burkha and other covered dressings. Further study needed to have a conclusion.

**REFERENCES**


**AB0918**

**CELCIVAL INSTABILITY AND VISUAL PATHWAYS COMPROMISE IN PATIENTS WITH JOINT LAXITY**

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**Background:** Cervical spine stability is to a great extent dependent on the capsular ligaments, laxity of which would lead to extensive movements of the vertebrae. This instability of the cervical spine, particularly in the upper segments (C0-C2) would be a major source of vertebrobasilar insufficiacy. The resultant brain posterior circulation compromise would then make the foundation of white matter changes and cause many neurological signs and symptoms. Occipital lobe and visual pathways are certainly in danger in these circumstances. How and to what extent could the visual pathways be involved in patients with joint laxity is not well studied yet.

**Objectives:** This study was designed to find whether the visual evoked potential parameters (latency and amplitude) of the patients with generalized joint laxity differs from that of the normal population.

**Methods:** In this cross-sectional comparative study, 90 consecutive patients with generalized lax joints and 90 normal individuals were enrolled and underwent the visual evoked potential test by pattern reversal. The latency and amplitude of P100 were determined for all the participants and data from the 2 groups were compared statistically.

**Results:** The results demonstrated that although none of the VEP parameters fell in the abnormal range, there was significant difference between P100 latency in patients with generalized lax joints (mean:110.23 ms) versus normal population (100.18 ms) (P<0.001) with longer latency in patients with generalized lax joints. But the amplitude was not significantly different across the groups (P > 0.05).

**Conclusion:** It can be concluded from this study that although the VEP parameters of the patients with generalized joint laxity don’t exceed the normal range limits, P100 latency in these patients is significantly more prolonged than in normal population. This finding is valuable from two points of view, first P100 latency at the verge of abnormality (upper limit of normal range) in these patients is a warning sign implying the visual pathway involvement, and second VEP could be invaluable in differentiating the signs and symptoms that are produced by vertebrobasilar insufficiency secondary to the joint laxity from multiple sclerosis, which can be mimicked both clinically and in MRI findings by many vascular problems but shows a great percent of VEP abnormality as a particular feature.

**REFERENCES**


Disclosure of Interests: None declared

AB0919 EFFECTS OF ALEXITHYMIA ON ACTIVITY PAIN, UPPER EXTREMITY FUNCTION, SYMPTOM AND DEPRESSION LEVELS IN PATIENTS WITH THORACIC OUTLET SYNDROME

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Background: Presentation of the most common changes in the thoracic outlet syndrome causing functional disorders of the upper limb (1). The majority of the studies published on TOS highlight physiotherapy strengthening exercises and postural reeducational drills as being the mainstay of any conservative management programme for TOS (2). However, in the literature, the effect of emotional state on progression in treatment programs has not been investigated. Alexithymia, which refers to deficiencies in the self-awareness of emotional states, has been reported to be associated with poor ability in various aspects of social cognition (3). The ability of TOS patients to express themselves and their emotions will affect the success of the treatment.

Objectives: The aim of this study was to investigate the effect of alexithymia on upper extremity functions, symptoms, pain level, depression and anxiety in patient with Thoracic Outlet Syndrome.

Methods: Forty-three TOS patients (36.67±13.99 years; 38 women, 5 men) were enrolled to the study. Alexithymia was assessed with Toronto Alexithymia Scale (TAS-20). The patients were divided into two groups as non-alexithymia group and alexithymia group according to 51 points. TAS-20 cut-off score. Pain levels at rest and activity were assessed with visual analogue scale; upper extremity function was assessed with Disabilities of the Arm, Shoulder, and Hand (DASH) questionnaire, and upper extremity symptom was assessed with using Servical Brachial Symptom Questionnaire. Mann-Whitney U test was used for data analyses.

Results: Activity pain level and depression in alexithymia group was higher than the non-alexithymia group, p=0.008 and p=0.007, respectively. Also, functional level and symptoms were worst in alexithymia patients, p=0.041 and p=0.05, respectively. No difference was found between groups anxiety and resting pain level.

Conclusion: Thoracic outlet syndrome patients who have alexithymia show worse pain, symptoms, function, and depression. Emotion should be considered in physiotherapy programs. Because the progression of alexithymia patients are worst than non-alexithymia patients.

REFERENCES


Disclosure of Interests: None declared

Pediatric rheumatology

AB0921 JUVENILE-ONSET LUPUS WITH SECONDARY CMV-INDUCED MACROPHAGE ACTIVATION SYNDROME (CASE REPORT)

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Background: Juvenile-onset lupus (JSLE) is a complex illness with an aggressive course and higher chances of morbidity and mortality. JSLE is extremely rare before the age of 5 years. A sole disease criterion may precede long time before others, making diagnosis rather challenging.

Objectives: Identifying JSLE and its subsequent complications

Methods: A three and half years old female patient presented with an established diagnosis of idiopathic thrombocytopenia (ITP) of one year duration. One month ago, the patient developed an acute onset of high grade persistent fever, bilateral knee swelling and significant weight loss.

Results: On physical examination, patient was emaciated and pale with multiple ecchymotic patches allow her body, Vital data showed normal blood pressure and apical heart rate ranges for age. Systemic examination revealed multiple oral ulcers, hepatosplenomegaly, bilateral knee arthritic and bilateral below knee painless pitting lower limb edema. Neurological examination was free. Laboratory evaluation showed a CBC with TLC 1.800/mm³ NE 0.5/mm³, HB 7.9 g/mdl, PLT 79 x10³/μL.ESR 120 mm/1st hr and CRP 96 mg/dl. Routine chemistry showed elevated liver enzymes (ALT 137 IU/L & AST 280 IU/L), LDH 960 IU/L, serum albumin 2.5 gd/l, normal renal functions. The history of chronic ITP together with evolution of other autoimmune manifestations raised the suspicion of an underlying Connective tissue disorder. Immunological profile showed positive immune markers (ANA 1/320 speckled and positive Anti-DNA), positive lupus anticoagulant and antiphospholipid IgM.C3 was consumed(49 mg/dl). Secondary Macrophage activation syndrome (MAS)
AB0922 UPDATES ON THE EVIDENCE BASED INTERDISCIPLINARY GUIDELINES FOR HENOCCHÖLEIN PURPURA

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School of Medicine, Banha University, Banha, Egypt
School of Medical Ain Shams University, Cairo, Egypt
School of Medicine Banha University, Banha, Egypt
School of Medicine Cairo University, Cairo, Egypt
School of Pediatrics, School of Medicine Cairo University, Cairo, Egypt
School of Pediatrics, School of Medicine Cairo University, Cairo, Egypt
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Disclosure of Interests: None declared

AB0923 EFFECTS OF EXON 10 MUTATIONS VS NON-EXON 10 MUTATIONS ON FMF PHENOTYPE AND RESPONSE TO TREATMENT
Hatice Adiguzel Dundar, Ozge Altug Guçenmez, Ceyhun Acari, Serkan Turkucar, Balahan Makay, Erbil Unsal.

Dr. Behcet Uz Childrens Hospital, Childrens Department, Izmir, Turkey

Disclosure of Interests: None declared
exon 10 involvement or non-exon 10 mutations. Genotype-phenotype features and response to treatment were compared.

Results: There were exon 10 mutations in 631 (67.5%) patients and non-exon 10 mutations in 304 (32.5%) patients. The follow-up period was 50 (26-83.2) months. The age of symptoms onset was significantly lower in group with exon 10 positive than compared group with non-exon 10 mutation. There was no difference between the age of diagnosis and colchicine onset and the diagnosis delay time. The symptoms of fever, chest pain, and arthritis were significantly higher in the exon 10 mutation group than compared other group. Biological agent need was statistically higher in exon 10 mutation group (4.8%) than group with non-exon 10 mutation (1.3%) (Table 1).

Conclusion: In our study, it was observed that cases with exon 10 mutation have early symptoms of disease. Fever, chest pain and joint findings were more prominent in cases with exon 10 mutation than cases with non-exon 10 mutation. Additionally, colchicine resistance should be kept in mind in cases with exon 10 mutation.

REFERENCES

Abstract AB0924 Table 1. Comparison of patients with exon 10 and non-exon 10 mutations

<table>
<thead>
<tr>
<th></th>
<th>Exon 10 (+)</th>
<th>Exon 10 (-)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td>935 (100)</td>
<td>631 (32.5)</td>
<td>0.007</td>
</tr>
<tr>
<td>Female/male (n)</td>
<td>445/490</td>
<td>303/328</td>
<td>0.707</td>
</tr>
<tr>
<td>Median age of symptoms onset (months)</td>
<td>48</td>
<td>60</td>
<td>0.009</td>
</tr>
<tr>
<td>Median age of diagnosis (months)</td>
<td>24-46</td>
<td>26-109</td>
<td>0.106</td>
</tr>
<tr>
<td>Median diagnosis delay time (months)</td>
<td>80</td>
<td>87</td>
<td>0.106</td>
</tr>
<tr>
<td>Symptoms n (%)</td>
<td>15</td>
<td>18</td>
<td>0.484</td>
</tr>
<tr>
<td>Fever</td>
<td>442 (70.3)</td>
<td>193 (64.1)</td>
<td>0.050</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>458 (72.8)</td>
<td>206 (68.7)</td>
<td>0.191</td>
</tr>
<tr>
<td>Chest pain</td>
<td>65 (10.3)</td>
<td>18 (6)</td>
<td>0.029</td>
</tr>
<tr>
<td>Erysipelias like rash</td>
<td>11 (1.7)</td>
<td>10 (3.3)</td>
<td>0.127</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>233 (36.8)</td>
<td>110 (36.8)</td>
<td>0.999</td>
</tr>
<tr>
<td>Arthritis</td>
<td>137 (21.8)</td>
<td>46 (15.3)</td>
<td>0.019</td>
</tr>
<tr>
<td>Myalgia</td>
<td>78 (12.5)</td>
<td>26 (8.6)</td>
<td>0.083</td>
</tr>
<tr>
<td>Emeis</td>
<td>12 (2)</td>
<td>12 (4)</td>
<td>0.061</td>
</tr>
<tr>
<td>Use of biologic agent</td>
<td>30 (4.8)</td>
<td>4 (1.3)</td>
<td>0.009</td>
</tr>
</tbody>
</table>

Disclosure of Interests: Hatice Adiguzel Dundar: None declared, ozge altug gucemmez Speakers bureau: Novartis, AbbVie, Ceyhun Acar: None declared, Serkan Turkucar: None declared, Balahan Makay Speakers bureau: Novartis, AbbVie, Ceyhun Acar: None declared.

AB0924 EVALUATION OF PERIPHERAL NERVOUS SYSTEM INVOLVEMENT IN PATIENTS WITH JUVENILE SYSTEMIC SCLEOROSIS AND JUVENILE SYSTEMIC LUPUS ERYSHEMATOSUS

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Background: Juvenile systemic sclerosis (JSS) and juvenile systemic lupus erythematosus (JSLE) are rare connective tissue disorder characterized by multisystemic involvement, including gastrointestinal, cardiovascular, respiratory and nervous system complications. According to data from literature, peripheral nervous system (PNS) involvement is seen in 86.7% of adult patients with systemic sclerosis. Frequency of PNS disorders is reported as 10-86.7% in adult patients. Data on PNS involvement in patients with JSS and JSLE are scarce.

Objectives: We aimed to evaluate PNS involvement in patients with JSS and JSLE. Consequently, we sought to detect patients with PNS disorders, in order to enable early diagnosis and timely intervention.

Methods: Patients with JSS and JSLE were included in a cross-sectional study. Demographic and clinical data of patients were recorded during clinical visits. All of patients were evaluated and examined for signs of PNS involvement. In order to examine mononeuropathy, polynueropathy and trigemino-facial involvement, all patients underwent routine nerve conduction studies (NCS), blink reflex (BR) and sympathetic skin responses (SSR) evaluation.

Results: Twenty JSS (15 [75%] female) and 18 (15 [83%] female) JSLE patients were initially included. All of JSS and JSLE patients had normal neurologic examination. NCS was normal in all JSS (20/20) and JSLE (18/18) patients. SSR was not recorded in 1 (5%) JSS and in 3 (16.67%) JSLE patients. BR was recorded in all JSS (18/18) and JSLE patients and in majority of JSS patients (19/20, 95%). According to SSR, mean latency of hand and foot was similar in both patients' groups. Amplitude of foot response was lower in JSS patients, comparing to JSLE (Table 1). Among JSLE patients, amplitude of hand response was lower than amplitudes of foot response.

According to BR, R1, R2, R2K duration and latency were not different between right and left eyes in both patients' groups. R3 was absent in 2 (10%) bilaterally and in 1 (5%) JSS patients unilaterally (right). R3 was absent in 4 (22.2%) bilaterally and in 2 (11%) JSLE patients unilaterally. Absence of R3 was more prominent in JSLE patients, comparing to JSS. (Table 2)

Conclusion: BR could be considered as a potential indicator of neuropathy in JSLE and JSS patients. Data on SSR need to be evaluated in studies with higher number of patients with juvenile-onset connective tissue disorders.

REFERENCES

Disclosure of Interests: None declared


AB0924 Table 1. Sympathetic skin responses

<table>
<thead>
<tr>
<th></th>
<th>JSS mean latency</th>
<th>JSLE mean latency</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAND</td>
<td>1424.63</td>
<td>1353.26</td>
</tr>
<tr>
<td>FOOT</td>
<td>1935.26</td>
<td>2011.6</td>
</tr>
</tbody>
</table>

AB0924 Table 2. Blink reflex responses

<table>
<thead>
<tr>
<th></th>
<th>JSS-right</th>
<th>JSLE-right</th>
</tr>
</thead>
<tbody>
<tr>
<td>R1 latency</td>
<td>10.3</td>
<td>10.3</td>
</tr>
<tr>
<td>R2 duration</td>
<td>33.5</td>
<td>33.7</td>
</tr>
<tr>
<td>R2 latency</td>
<td>30.3</td>
<td>29.9</td>
</tr>
<tr>
<td>R2K duration</td>
<td>34.4</td>
<td>29.4</td>
</tr>
<tr>
<td>R2K latency</td>
<td>32.5</td>
<td>33.3</td>
</tr>
<tr>
<td>R3 presence</td>
<td>2/19</td>
<td>4/18</td>
</tr>
</tbody>
</table>

Disclosure of Interests: None declared

AB0925  TOCLIZUMAB AS A TREATMENT OPTION FOR PATIENTS WITH JUVENILE SYSTEMIC SCLEROSIS

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Background: Juvenile systemic sclerosis (JSS) is a rare autoimmune disease characterized by skin stiffness and fibrosis of internal organs (eg. lung, heart, gastrointestinal system). The efficacy and safety of tocilizumab (TCZ), an interleukin 6 receptor-inhibitor, in adult patients have been studied in a few recent studies. Reports on its efficacy among children have been reported among patients with localized disease form. This is a first report on treatment of JSS patients with TCZ.

Objectives: We aimed to evaluate efficacy of tocilizumab as a treatment option for patients with juvenile systemic sclerosis. Consequently, we sought to explore its influences on internal organ involvement, skin stiffness and patient global assessment score.

Methods: We retrospectively evaluated patients diagnosed with JSS according to EULAR criteria. Among 30 patients diagnosed with JSS, 7 (23%) were treated with TCZ. Demographic data are taken from patients’ charts. Data on clinical characteristics and treatment outcome are recorded during the patients’ last visit.

Results: Seven patients treated with TCZ were analyzed: 6 (85.71%) girls, one boy. Median age of patients was 17.5 years (range:11-12 years), at disease onset 10 years (range 6-15 years) and at diagnosis 11 years (range 7.5-17 years). Median disease duration was 8 years (min. 3-max.11 years). Median duration of TCZ treatment was 10 months (min. 1-max. 21 months). One (14.28%) patient had gastro-intestinal involvement, 4 (57.14%) patients had lung involvement and 2 (28.57%) patients had both gastro-intestinal and lung involvement. Improvement in mRSS was detected in 5 (71.43%) patients. DLCO improved in 4 (57.14%) patients. Four (57.14%) patients had radiologically confirmed improvement in lung findings. Data on radiological findings of one patient treated with TCZ for 6 mos were not available. Five patients (71.43%) reported improvement in patient global assessment (PGA) score after the TCZ treatment. PGA score of two remaining patients were not applicable due to short treatment duration (Table 1). None of 7 patients had recorded adverse effect of TCZ treatment.

Abstract AB0925 Table 1. Clinic characteristics of juvenile systemic sclerosis patients patients treated with tocilizumab

<table>
<thead>
<tr>
<th>Lung involvement</th>
<th>GIS involvement</th>
<th>Treatment duration (months)</th>
<th>TCZ treatment duration (months)</th>
<th>Radiological improvement in thorax HRCT</th>
<th>Pre-/Post- treatment mRSS</th>
<th>Pre-/Post- treatment DLCO (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>78</td>
<td>12</td>
<td>+</td>
<td>52/52</td>
<td>21/19</td>
<td>5</td>
</tr>
<tr>
<td>-</td>
<td>90</td>
<td>6</td>
<td>-</td>
<td>93/95</td>
<td>33/22</td>
<td>2</td>
</tr>
<tr>
<td>+</td>
<td>108</td>
<td>21</td>
<td>+</td>
<td>65/71</td>
<td>32/22</td>
<td>3</td>
</tr>
<tr>
<td>+</td>
<td>96</td>
<td>11</td>
<td>-</td>
<td>54/62</td>
<td>28/16</td>
<td>4</td>
</tr>
<tr>
<td>+</td>
<td>66</td>
<td>10</td>
<td>+</td>
<td>107/125</td>
<td>28/24</td>
<td>12</td>
</tr>
<tr>
<td>+</td>
<td>30</td>
<td>1</td>
<td>NA</td>
<td>51/NA</td>
<td>12/NA</td>
<td>3</td>
</tr>
<tr>
<td>-</td>
<td>12</td>
<td>1</td>
<td>NA/NA</td>
<td>32/NA</td>
<td></td>
<td>5</td>
</tr>
</tbody>
</table>

Conclusion: JSS is rare condition characterized with internal organ involvement. Tocilizumab represents an efficacy treatment options for patients unresponsive to standard treatment. Long-term prospective studies with higher number of patients are needed to provide more relevant data.

REFERENCES

Disclosure of Interests: None declared

AB0926  JUVENILE SYSTEMIC SCLEROSIS AND MUCINOUS ADENOCARCINOMA OF THE LUNG IN PATIENT WITH CYSTIC ADENOID MALFORMATION-PARANEOPLASTIC SYNDROME OR JUST A COINCIDENCE?

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Background: Juvenile systemic sclerosis (JSS) is a rare auto-immune condition characterized by skin stiffness and internal organ fibrosis. In adult patients, systemic sclerosis has been related to an increased risk of malignancy with lung cancer being most prevalent. Up-to-date, we haven’t found any report on lung cancer in patient with JSS.

Objectives: Herein, we aimed to present a case with juvenile systemic sclerosis and coincidentally detected cystic adenoid malformation complicated by the mucinous adenocarcinoma of the lung.

Methods: Data on disease history are taken from patient’s chart. Clinical and laboratory findings are recorded during the last visit at our outpatient department.

Results: A 14 years old previously healthy female patient, admitted to our outpatient department due to puffy fingers, Raynaud’s phenomenon and stiffness of the skin proximally to metacarpalphalangeal joints. Her anti-nuclear antibody was positive (1/80) but the other auto-antibodies (including Anti Sc 70, anti-centromere antibody) were negative. Patient was diagnosed as progressive systemic sclerosis and the prednisolone, methotrexate and nifedipine were started. Routinely performed echocardiography was normal. Respiratory function tests were appropriate for the age and hemoglobin level: FVC 80%, DLCO 92%. Surprisingly, thorax HRCT revealed cystic adenoid malformation on the left lower lobe of the lung so pediatric surgery department has been consulted. The decision for surgical intervention has been made and the lesion has been removed. Tissue sample has been sent to the pathological investigation and the result was consistent with mucinous adenocarcinoma of the lung. There were 2 focus (0.4 cm in diameter) of the adenocarcinoma in the cystic adenoid malformation without invasion to the local perineural, lymphatic or vascular tissues, with positive KRAS (KRAS12-612C, 612S) mutation. Cranial MRI and PET-CT show no residual, relapse nor the metastatic lesions. Clinical follow-up has been suggested, without need for further oncological treatment.

Conclusion: Juvenile systemic sclerosis is a rare disease characterized with multorgan involvement. The paraneoplastic syndrome with clinical presentation of systemic sclerosis should be kept on mind among adolescents, especially those with negative auto-antibodies.

REFERENCES

Disclosure of Interests: None declared
Background: Juvenile idiopathic arthritis (JIA) is a complex entity and is the most common rheumatologic disease of the children with the knee being the most frequently affected joint. Extensive proliferation of the synovial cells, synovial thickening and inflammation are the hallmark pathological processes ongoing in the affected joints. The traditional methods in assessing the disease activity involve investigating tenderness, pain, and swelling of the relevant joint on physical examination in addition to biochemical markers; however, the psychical examination may yield equivocal results in some patients. Sonographic modalities are being increasingly used as a complementary method in the assessment of the joints in JIA and Power Doppler ultrasound (PDUS) is the current reference sonographic method in assessing the inflammation by measuring the vascularity in the synovium. SMI is a novel Doppler technique using advanced filtering algorithms with an ability to detect even subtle and slow blood flow signals.

Objectives: We aimed to investigate the efficiency of Superb Microvascular imaging (SMI) in assessing inflammation of synovium in the knee of patients with JIA compared with PDUS.

Methods: Both knees of the patients with a diagnosis of clinically active JIA were examined using gray-scale US. The knees with positive US and physical examination findings included in group A while the knees with positive US findings despite negative physical examination findings included in group B. The observers calculated vascularity index (VI) by manually drawing a region of interest (ROI) onto the thickest part of the synovium using PDUS and SMI.

Results: A total of 41 knees with both clinical and sonographic positive findings constituted group A and 14 knees with sonographic positive findings and normal physical examination categorized as group B in the final cohort. The median SMI-VI (observer 1 = 4.9%, IQR 3.6; observer 2 = 4.1%, IQR 4.6) was exceeded the median PDUS-VI (observer 1 = 1.5%, IQR 1.8; observer 2 = 1.5, IQR 1.9) (P < 0.0001). In group B, the median SMI-VI (observer 1 = 2.85%, IQR 8; observer 2 = 3.1%, IQR 6.3) were exceeded the median VI PDUS-VI (observer 1 = 0.5%, IQR 2; observer 2 = 0.55, IQR 2.3) (P = 0.002 and P = 0.001 for observer 1 and observer 2, respectively). No significant differences were observed between groups concerning PDUS-VI and SMI-VI (P = 0.05). In all of the patients in group A, SMI was able to identify the presence of vascularity for both observers while no blood flow was detected (VI = 0%) using PDUS in 6 patients (14.6%) for observer 1 and 7 patients (17.1%) for observer 2. In all of the patients in group B, SMI was also able to identify the presence of vascularity for both observers while no blood flow was detected (VI = 0%) using PDUS in 5 patients (%35.7) for each observers.

Conclusion: SMI-VI obtained from the hypertrophied synovium of both clinically active and inactive knee joints were substantially higher compared with PDUS-VI in JIA patients. Furthermore, SMI detected the presence of blood flow in patients in whom PDUS could not be able to identify any blood flow. The findings of the present work indicate that SMI seems to a promising tool and a valuable adjunct to conventional US in assessing the inflammation of the synovial tissue in JIA patients.

REFERENCES

Disclosure of Interests: None declared

AB0929
ACUTE RHEUMATIC FEVER: IS PROLONGED CORTICOSTEROID TREATMENT ASSOCIATED TO A BETTER CARDIAC OUTCOME?
Dariya Vankova1, Alexandra Chomahidze1, Ivan Kriulin1, Alina Alshevskaya3, Ekaterina Alexeeva1,2, Tatyana Dvoryakovskaya1,2, Ksenia Isaeva1,2, Policlinico Giovanni Battista Rossi, Reumatology, Verona, Italy 1Azienda Ospedaliera Universitaria Integrata Verona, Paediatric, Verona, Italy 2Policlinico Giovanni Battista Rossi, Reumatology, Verona, Italy 3Azienda Ospedaliera Universitaria Integrata Verona, Cardiology, Verona, Italy

Background: Acute rheumatic fever (ARF) is a nonsuppurative sequela that can occur two to four weeks after group A beta-hemolytic Streptococcus pharyngitis. Despite its decline in incidence in modern countries, ARF still represents worldwide a serious healthcare concern. The most common manifestations are arthritis and carditis, followed by chorea, erythema marginatum, and subcutaneous nodules. The diagnosis of ARF is clinical and requires satisfaction of revised Jones criteria as well as evidence of a recent streptococcal infection.

Carditis and chorea both need systemic corticosteroid treatment (prednisone, 1 mg/kg) but with different treatment courses: 2-3 weeks prednisone treatment course in carditis is generally undertaken compared to a longer prednisone treatment period in chorea (at least 2 months).

Objectives: The aim of this study was to investigate if the longer corticosteroid treatment used for patients with chorea and carditis is related to a better regression of cardiac damage compared to the shorter course of corticosteroid treatment used in patients with only carditis.

Methods: Data regard 14 patients were retrospectively revised (8 males, 6 females): 7 ARF patients with both cardiac and neurological involvement treated with systemic prednisone for 2 months; 7 ARF patients with only cardiac involvement treated with systemic prednisone for 2 weeks. The regression of cardiac damage in the two different groups was evaluated in relation to the different duration of corticosteroid treatment comparing ultrasound echocardiography (cardiac-US) performed at ARF onset and during a 2-3 year follow-up. The trend of the grade of aortic and mitral valves insufficiencies was chosen as indicator of the ARF cardiac damage evolution.

Patients with a similar grade of cardiac damage at disease onset were identified; then pairs were created according to the presence of chorea (so one patient was affected only by carditis and the other one of the same pair, according to the similar cardiac damage, had both carditis and chorea). Cardiac-US damage regression of the 7 pairs was assessed in order to evaluate if the grade of regression was higher in the patients with only carditis compared with the ones with both carditis and chorea.

Results: in 3 pairs a better regression of the cardiac damage was evident in the patients with only carditis; in other 3 a better regression was noticed in the patients with both carditis and chorea; finally no difference was detected in the last pair. No significant cardiac-US difference according to patient pairs appeared in relation to the steroid time treatment course (2-3 weeks vs 2-3 months); however in 85% of the cases (12 patients) steroid therapy did achieve regression on ARF cardiac damage.

Conclusion: This retrospective study does not reveal any significant difference between steroid duration therapies in ARF complicated by carditis; limits of the study are the size sample as well as the intra/inter observer variation during cardiac-US (all exams were achieved in a high level experience paediatric cardiac service); this study underlines the established importance of the use of corticosteroid in ARF carditis.

Disclosure of Interests: None declared

AB0930
EFFICACY OF TOCILIZUMAB IN TREATMENT OF SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS IN PATIENTS WITH MACROPHAGE ACTIVATION SYNDROME
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Background: Macrophage activation syndrome (MAS) is a rare and severe complication of juvenile idiopathic arthritis (JIA) that most typically develops in patients with its systemic form (sJIA). Tocilizumab proved to be efficacious for treatment of both systemic JIA and polyarthritis. Nevertheless, the question regarding the effect of MAS on efficacy of TOC therapy in patients with sJIA is still to be solved.

Objectives: To evaluate the efficacy of tocilizumab therapy in patients having sJIA and MAS versus the patients without MAS.

Methods: Throughout the period between 2009 and 2018, 251 children with the acute phase of sJIA started to be treated with TOC at the Rheumatology Department of the National Medical Research Center of Children’s Health (Moscow, Russia). Of those, 69 patients had active MAS at initiation of TOC therapy. Patients were diagnosed with MAS according to the preliminary diagnostic guidelines for MAS complicating sJIA [1]. Treatment efficacy was evaluated according to the dynamics of clinical and laboratory signs using the ACRPedri criteria. The Wallace criteria were used to evaluate whether or not remission had been achieved.

Results: At initiation of TOC therapy, patients with and without MAS were comparable in terms of their sex and age characteristics, as well as the overall severity of arthritis (the percentage of women, 56.6% (intergroup p=0.396); the median age, 7.83 (4.39-11.3) years (intergroup p=0.640); and JADAS-71, 17.4 (13.7-22.8) (intergroup p=0.055)). Nevertheless, patients differed in terms of severity of certain clinical manifestations and prior history of the disease. The group with MAS was characterized by such parameters as shorter disease duration, shorter duration morning stiffness, and smaller number of affected joints but higher activity and severity score (Patient/Parent and Physician VAS score).

After treatment initiation, TOC was discontinued after treatment for 4-12 weeks only in 2 out of 69 (2.9%) patients because of persistent MAS or MAS flare. The patients successfully achieved remission after therapy switching. No intergroup differences were observed for the rate of treatment discontinuation within the first year of therapy: the drug was discontinued in 5 (7.2%) patients in the MAS+sJIA group (2 MAS flares + 3 cases of poor efficacy) and in 25 (13.7%) patients in the sJIA group (4 SAEs + 21 cases of poor efficacy).

One-year treatment with TOC proved that this drug is highly efficacious to treat sJIA regardless of whether or not patients had MAS at treatment initiation (Figure).

No deaths were reported throughout the entire treatment period. We attributed this to early diagnosis and high efficacy of treatment of JIA patients.

Conclusion: Tocilizumab therapy in patients with sJIA in the presence of MAS is as efficacious as in patients without MAS and does not aggravate the course of MAS.

Disclosure of Interests: None declared

REFERENCE
TRANSLATION AND VALIDATION OF THE MTX INTOLERANCE SEVERITY SCORE QUESTIONNAIRE FOR PORTUGUESE VERSION IN BRAZIL IN JUVENILE IDIOPATHIC ARTHRITIS

Ana Carolina Londe, Roberto Marini, Simone Appenzeller. University of Capinas, Campinas, Brazil

Background: Methotrexate (MTX) is the first-choice disease-modifying anti-rheumatic drug (DMARD) for the treatment of juvenile idiopathic arthritis (JIA). During therapy, there are frequent reports of discontinuation of MTX, either by physicians or patient’s own conduct. Through the MTX Intolerance Severity Score questionnaire (MISS), we determined the prevalence of MTX intolerance.

Objectives: Translate and validate the MTX Intolerance Severity Score questionnaire (MISS) to Portuguese.

Methods: The MISS was translated into Portuguese following the “Guidelines for the process of cross-cultural adaptation of self-report measures”. The MISS consists of 4 domains: stomachache, nausea, vomiting, and behavioral complaints. Each domain includes three to four items, and for every item, four answers are possible: no complaints (0), mild complaints (1), moderate complaints (2 points), and severe complaints (3 points). The points are summed to give a total score from 0 to 36. Statistically analysis was performed on the SPSS version 21, the psychometric properties were analyzed according to the Consensus based Standards for the Selection of Health Measurement Instruments (COSMIN), analyzing acceptability for each item, internal consistency using Cronbach’s alpha coefficient and reproducibility assessed by Kappa. We plot the ROC curve to evaluate the discriminant validity of the MISS compared to gold standard (clinical interview) and cut-off score was determined.

Results: We included 220 subjects, 144 patients with JIA in use for less than 3 months of MTX and 76 parents. The median age of patients were 18.3 SD±8.7 years. Seventy-three (73%) patients were females and the JIA subtype most frequently observed was polyarticular. Routes of administration of MTX were subcutaneous (81%) and oral (19%). All the subjects answered the MISS with less than 5 minutes. The internal consistency of MISS had a Cronbach’s alpha = 0.851 (patients) and 0.805 (parents), considered good (>=0.8). The reproducibility between the test (40 patients) and the retest done after 15 days (36 patients) was almost perfect (kappa=0.8). Reliability between patients and parents was almost perfect (kappa=0.8), except stomachache (anticipatory with kappa = 0.30); considered weak (κ = 0.2 - 0.4) and stomachache by association (κ = 0.54); considered moderate (κ = 0.4 - 0.6). A cut-off scores of 3 showed the best sensitivity (93%) and specificity (71%). Using this cut-off we observed 78 (54.2%) patients intolerant.

Conclusion: MISS is a good tool for physicians, because it can not only measure the intolerance, but also explore the different forms in which it manifests. Although MTX has a great therapeutic index, the adverse reactions are still seen as a major form of abandonment of this pharmacological treatment. Therefore a careful history is essential to identify side effects and adequate treatment to increase adherence.

REFERENCES


PREDICTORS OF FLARE FOLLOWING ETANEOCTETE WITHDRAWAL IN PATIENTS WITH RHEUMATOID FACTOR NEGATIVE JUVENILE IDIOPATHIC ARTHRITIS DURING 48 MONTHS OF FOLLOW-UP

Angela Aquilani1, Denise Pires Maranon2, Andreni Uva1, Hanan Jadoun1, Fabio Basta1, Rebecca Nicolai1, Fabrizio De Benedetti1, Silvia Magni-Manzoni1.

1IRCCS Ospedale Gaslini, Division of Rheumatology, Genoa, Italy; 2Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, Intermediate Pediatric Care Unit, Milan, Italy

Background: Little is known about the risk of flare after etanercept (ETN) withdrawal in children with Juvenile Idiopathic Arthritis (JIA). Recently we conducted a retrospective chart review of 110 patients with JIA who discontinued ETN due to persistent clinically inactive disease (CID) on medication and were followed up to 12 months after ETN withdrawal. We showed that 60% of patients flared with arthritis. Male gender, presence of ANA and elevated CRP at baseline were associated with a higher risk of flare.

Objectives: To evaluate frequency and timing of flares during 48 months of follow-up after withdrawal of ETN first course in patients with JIA who attained clinical remission on medication and to identify predictors of early flares (<12 months after withdrawal of ETN first course) and predictors of repeated flares (>2).

Methods: The 110 patients enrolled in the previous study with oligo (o-JIA) and RF-negative polyarticular JIA (p-JIA) who received a first course of ETN for at least 18 months and maintained clinically inactive disease (CID) for at least 6 months on treatment, were followed for 48 months after withdrawal of first course of ETN. We excluded patients that switched or swapped to other biologics or with limited follow-up. Demographic and clinical features at onset, at baseline (initiation of ETN) and at time of disease flares were collected.

Results: Among the cohort of the study, 10 patients (9%) were lost to follow-up and 18 (16%) switched/swapped to other biologics during 48 months of follow-up after withdrawal of ETN first course. Of the 82 patients included in the analysis, 55 (67%) were treated with only one course of ETN, while 27 (33%) received more than one course of ETN. The median age at disease onset was 3.6 years (IQR 1.9-8.5) and 72% of patients were female, ANA positive patients had a younger age at onset and were more frequently o-JIA. After withdrawal of ETN first course, 70 of the 82 (85%) patients enrolled flared with arthritis, without evident differences between o-JIA and p-JIA. Disease duration at diagnosis and at ETN start, total number of joints involved and total MTX treatment duration were not associated with flare. Patients who flared were more frequently males (p=0.017) and ANA positive (p=0.026), presented higher levels of CRP (p=0.029) at baseline and had longer total ETN treatment duration (p=0.0046). Higher values of CRP were associated with a higher risk of repeated flares (p=0.0094). No predictors of early flares were identified in this group.

When we analysed the 55 patients treated with one course of ETN, 48 (87%) flared during follow-up. Patients who flared were more frequently ANA positive (p=0.015), presented higher CRP levels (p=0.042) at baseline and concomitant MTX at ETN withdrawal (p=0.009). Higher levels of CRP was also associated with higher numbers of repeated flares (p=0.049). No predictors of early flares were identified in this subgroup.

Conclusion: Our results show that almost 90% of patients with JIA experience at least one flare after ETN withdrawal during 48 months of follow-up. Our findings confirmed that male gender, positive ANA and elevated CRP at baseline are associated with a higher risk of flare. Higher CRP levels at baseline resulted also associated with a higher risk of repeated flares.

REFERENCES

Disclosure of Interests: Angela Aquilani: None declared, Denise Pires Maranon: None declared, Andrea Uva: None declared, Hanan Jadoun: None declared, Fabio Basta: None declared, Rebecca Nicolai: None declared, Fabrizio De Benedetti Grant/research support from: Abbvie, SOBI, Novimmune, Roche, Novartis, Sanofi, Pfizer, Silvia Magni-Manzoni Consultant for: Abbvie, Speakers bureau: Abbvie DOI: 10.1136/annrheumdis-2019-eular.5721

ANALYSIS OF THE STATE OF IMMUNITY IN PATIENTS WITH JIA IN TREATMENT

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Background: The correct indication of the suspension of treatment with FAMES and biological therapy in pediatric patients, in the presence of a mild infectious disease or vaccination is a common problem in children’s rheumatology. In patients with juvenile idiopathic arthritis (JIA), joint or extra-articular clinical reactivation during these “pauses” is not uncommon,
however, there are not enough studies in the pediatric population to show the influence of treatments on the immune system, and therefore, that justify this clinical practice.

Objectives: To analyze the levels of T, B and NK lymphocyte subpopulations in patients diagnosed with JIA treated with FAMES and biological therapy.

Methods: A descriptive and cross-sectional study in which 39 patients from the Pediatric Rheumatology Unit of the Reina Sofia University Hospital were recruited, diagnosed with JIA according to the ILAR 2001 criteria. The patients were divided into four groups: 8 controls in clinical remission without treatment, 17 in treatment with DMARD in monotherapy, 7 in biological treatment in monotherapy and 7 in treatment with DMARD-biological. Patients with systemic JIA were excluded because they had a pathogenic mechanism different from the rest of the JIA categories. By flow cytometry, the levels of CD3, CD4, CD8 and CD19 cells were measured for acquired immunity and from NK for innate, the CD4/CD8 index was also calculated.

Results: The mean age of the 39 patients was 10 ± 5.7 years, 29 were girls (74.3%), 4 patients had arthritis related to enthesitis, 16 patients had oligoarticular involvement ANA+e, 6 subjects polyarticular involvement FR- and 13 they were psoriatic arthritis. Although no statistically significant differences were found when contracting cellular levels among the 4 groups evaluated, it was observed that the group treated with DMARD monotherapy had the highest percentage of children with alterations in cellular levels CD3, CD4, CD8 and CD19 (41.17% of the patients of the group); the group treated in monotherapy with biological treatment (28%) presented an alteration in the levels of CD3 and CD8 and CD19 and the group treated in combination of DMARD and biological (14.28%) in CD19. On the other hand, the NK cells and the CD4/CD8 index were not altered in any of the groups. Only 6 cases of serious infections were registered in patients in combination therapy (DMARD-biological) who had received corticosteroids by clinical activity. There were no statistical differences between patients who had received corticosteroids and those who did not.

Conclusion: Patients in treatment with DMARD monotherapy had a tendency to decrease cellular levels. On the other hand, alterations in innate immunity or CD4/CD8 index were not observed.


AB0934

IL-6 AND ALLELIC POLYMORPHISM OF ITS GENE IN JUVENILE IDIOPATHIC ARTHRITIS

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Background: The development and maintenance of inflammation in juvenile idiopathic arthritis (JIA) is mediated by cytokine imbalance; interleukin 6 (IL-6) plays a leading role among pro-inflammatory cytokines. Its pathological synthesis has a negative impact on all organs and system. It is not excluded that its effector ability depends on genetic structures of IL-6 gene. It has not been studied whether the allelic polymorphism of the IL-6-174CG gene affects the effectiveness of targeted biological therapy. Objectives: To assess the IL-6 dynamics level in serum of patients with ineffective JIA-treatment.

Methods: The level of IL6 in the serum of JIA patients 1-18y.o. was determined using ECLIA method, debut of the disease (54) and treatment failure (36; 6 oJIA, 14 pJIA, 10 enthJIA, 6 sJIA). In patients with JIA, allelic polymorphism of the IL-6-174CG gene was studied by PCR-method using allele-specific primers. A correlation analysis of clinical and laboratory parameters was made.

Results: Among patients with ineffective treatment of JIA, the duration of the disease was 39.5±35.8 months, 62.9% were girls. 27 patients received GC (<1mg/kg), 30-DMTX(10-15mg/m2), 3-leflunomide, 1-AZA, 10-TZ, 16-ADA/ETA, 1-TFC, 5 were switched from antiTNF for antiIL6. The levels of IL6 in the serum of JIA patients with treatment ineffectiveness was higher than at the beginning of disease (sJIA 52.40±37.84±24.4±1.7 (p <0.05); pJIA 36.19±8.58±6.23±20.25± <0.05); oJIA 6.99±5.27±0±1±0.1; enthJIA 90.55±63.3±4±29.9±p/ml). There was no increase in IL6 level in patients with an unfavorable course of the RFpos-pJIA (4±7±3.5±p/ml) and with uveitis (5.59±4.9±p/ml) (norm.1–5±7±p/ml). In 57.1% of cases of RFneg-JIA IL6 was elevated, in 3 children it was the highest (79.77; 218.7±p/ml), they had anemia and osteoporosis. A high (51-484.6±p/ml) level was observed in 4 patients with enthJIA, in 1-inadequate therapy was performed, in 3 patients there was a fever, a lag in physical development, the highest CRP (up to 300 mg/ml). The correlation between the level of IL6 in the blood of children with JIA and the presence of lymphadenopathy in the debut of the disease (r=0.53), the child’s age at the debut of the disease (r=0.63), examination (r=0.74), and the patient’s weight (r=0.87), the duration from the onset of the disease to the initiation of biological therapy (r=0.44), the number of exacerbations in the first years of the disease (r=0.66-0.69), the formation of contractions and the limitation of movement in the joints (r=0.75), radiological progression in the 1st year from the debut (r=0.54), ESR (r=0.48), CRP (r=0.40), doctor’s estimate of disease activity (r=0.79), ALT (r=0.69), AST (r=0.99), LDH (r=0.73) was found. There was no correlation with the number of affected joints (r=0.28), heart rate (r=0.48), metabolic abnormalities on the ECG (r=0.39). In children with an adverse course of JIA, IL6 correlated backward with TNF (r=−1), which was not observed in children at the onset of the disease (r=0.19).

Analysis of the results of genetic examination showed that among children with treatment failure, 23% had GG allele, and 27,3% had CC allele, and 23,7% had GC allele.

Conclusion: Treatment of JIA leads to changes in cytokine profile. The IL6-174CG gene has a high level of IL6 in the blood. The longer the duration of the disease and the time before the start of treatment with biological DMARDs, the greater the likelihood of an increase of IL-6 level in serum. In cases of even short-term enminia in JIA, subclinical activity with IL-6 can be suggested. In case of presence of some signs (hyperthermia, osteoporosis, anemia) in patients with antiTNF, it is advisable to determine the level of IL-6 in blood serum.


AB0935

ANTI-TF-1-AntIBODIES IN JUVENILE DERMATOMYOSITIS ARE ASSOCIATED WITH VARIOUS CLINICAL PHENOTYPES

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Background: Juvenile dermatomyositis (JDM) is a rare heterogeneous autoimmune disease. The identification of myositis specific antibodies (MSAs) has allowed the characterization of subgroups of JDM patients who each have specific phenotypes. Antibody (Ab) against transcriptional intermediary factor-1-γ (TIF-1-γ) or p155/140 is the most common MSA in JDM. In the American and English JDM cohorts, anti-TF-1-γ associated JDM is classically associated with a larger proportion of caucasians, mild or moderate severity with typical cutaneous manifestations (Gottron’s papules and heliotrope rash), and subclinical activity, and a chronic disease course with a low mortality. The frequency of skin ulcerations and lipoatrophy differs between the two cohorts.

Objectives: To report the clinical and muscle histology associations of anti-TF-1-γ Ab in a series of patients with JDM followed in the French referral center for rare pediatric systemic autoimmune diseases.

Methods: Retrospective study of patients with JDM (according to the EULAR/ACR criteria) associated with anti-TF-1-γ autoantibodies and included in our CEMARA database approved by the French National Committee on Informatics and Liberty.

Results: Thirteen patients were included (males: 5, females: 8; Caucasians: 6, Black Africans: 2, North Africans: 5). Age at diagnosis ranged from 1.5 to 11 years. Serum creatine kinase was elevated in 12 patients (range: 180-43 000 IU/L). Three different phenotypes were identified according to the severity and course. In group 1 (n=4), 3 patients had a moderate JDM: classical cutaneous manifestations and moderate muscle involvement; relapsing course, which remitted under methotrexate/corticosteroids; an additional 2-year-old girl had an amyopathic JDM. In group 2 (n=7), patients had ulcerating skin lesions, severe muscle involvement, dysphagia, gastrointestinal vasculitis and/or requirement to an intensive care unit, and required more than two lines of treatment. In this group, 2/7 patients died from refractory JDM, comparing to a mortality rate of 2% in the remaining JDM patients tested for MSA and negative for anti-TF-1-γ. Only 2/5 patients achieved a complete remission under treatment. Group 3 comprised two patients with severe muscle atrophy, calcinosis and lipodystrophy and a chronic course; one of them had a very-early-onset JDM at 1.5 year-old and the other an inherited neurological involvement, potentially suggestive of a genetic predisposing condition to JDM. None of the patients developed lung involvement or malignancy. Six patients underwent a muscle biopsy which was
AB0936
A NATIONAL SURVEY OF CLINICAL PRACTICE OF CORTICOSTEROID USE IN NEWLY DIAGNOSED OR FLARING CASES OF JUVENILE IDIOPATHIC ARTHRITIS ACROSS THE UK
Eileen Baildam1, Ashley Jones2, Dannii Claydon2, Gloria Nkoma3, Matthew Peak1, Athimalaipet Ramanan3, Madeleine Rooney4, Helen Foster5, Simon Stones6, Flora McErlane7, Tracy Moitt8, Louise Roper9, Bridget Young1, Frances Sherratt1, Michael Beresford9, Alder Hey Children’s Hospital – Liverpool, Paediatric Rheumatology, Liverpool, United Kingdom; 2University of Liverpool, Clinical Trials Unit, Liverpool, United Kingdom; 3Bristol Royal Hospital for Children, Paediatric Rheumatology, Bristol, United Kingdom; 4Royal Belfast Hospital for Sick Children, Paediatric Rheumatology, Belfast, United Kingdom; 5University of Newcastle upon Tyne, Paediatric Rheumatology, Newcastle upon Tyne, United Kingdom; 6University of Leeds, School of Healthcare, Leeds, United Kingdom; 7Great North Children's Hospital, Paediatric Rheumatology, Newcastle upon Tyne, United Kingdom; 8University of Liverpool, Institute of Population Health Sciences, Liverpool, United Kingdom; 9University of Liverpool, Department of Translational Medicine, Liverpool, United Kingdom

Background: Corticosteroids (CS) are widely used for rapid-action or induction treatment in children and young people (CYP) with juvenile idiopathic arthritis (JIA). Given a lack of evidence base on CS induction regimens for CYP with JIA, and since criteria for choosing CS are based on healthcare professional (HCP) preference, further research is needed (1).

Objectives: To establish the opinions of HCPs regarding the clinical criteria for commencing CS treatment.

Methods: A national electronic survey was undertaken among HCPs across the UK as part of the steroid induction regimen for juvenile idiopathic arthritis (SIRJIA) study.

Results: A total of 39 (24%) responses were received from 162 HCPs. These included 22 (56%) NHS consultants, five (13%) grid trainees, eight (21%) clinical nurse specialists and four other HCPs (10%). The most common treatments in CYP with newly diagnosed JIA or a disease flare were intra-articular (IA) CS or a combination of DMARDs and IAAS (except for systemic JIA and oligoarticular JIA). The majority of HCPs 17 would treat new and flaring CYP the same in terms of a CS remission induction regime, with 53% choosing a different regime or not answering. The key criteria that HCPs used for commencing CS and choosing the route of administration were rapid induction of remission (31 (89%)), severity of systemic JIA (20 (56%)) and level of inflammation (28 (80%)) Table 1. The number one determinant of route of administration of CS was disease severity followed by disease subtype.

The majority of HCPs (52-72% depending on role) would consider entering CYP with JIA into a trial randomising to the various modes of administration.

Table 1:
<table>
<thead>
<tr>
<th>Reasons of CS Choice</th>
<th>Number</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>High Disease Activity</td>
<td>35</td>
<td>89.7</td>
</tr>
<tr>
<td>Rapid induction of remission</td>
<td>34</td>
<td>87.2</td>
</tr>
<tr>
<td>Severity of Systemic JIA</td>
<td>34</td>
<td>87.2</td>
</tr>
<tr>
<td>Level of inflammation</td>
<td>32</td>
<td>82.5</td>
</tr>
<tr>
<td>Severe Uveitis</td>
<td>30</td>
<td>76.9</td>
</tr>
<tr>
<td>JIA subtype</td>
<td>27</td>
<td>68.2</td>
</tr>
<tr>
<td>Targeting Specific Joints</td>
<td>26</td>
<td>66.7</td>
</tr>
<tr>
<td>Level of Disability</td>
<td>18</td>
<td>46.2</td>
</tr>
<tr>
<td>Level of pain</td>
<td>16</td>
<td>41.0</td>
</tr>
<tr>
<td>Long-standing Disease</td>
<td>11</td>
<td>28.1</td>
</tr>
<tr>
<td>Patient reluctance to take DMARDs</td>
<td>8</td>
<td>20.5</td>
</tr>
</tbody>
</table>

Conclusion: The results from this national survey of clinical practice showed varying practices in the management of new CYP with JIA and those that are flaring. The majority of HCPs who completed this survey, indicated that they would be prepared to consider entering CYP into a trial that randomised to the four CS delivery methods.

REFERENCES

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Disclosure of Interests: Eileen Baildam Consultant for: EB has received one paid consultancy for Pfizer in the last 12 months, but this was not related to this study,. Ashley Jones: None declared, Dannii Clayton: None declared, Gloria Nkoma: None declared. Matthew Peak: None declared, Athimalaipet Ramanan Consultant for: AbbVie, UCB, Sobi, Eli Lilly, Speakers bureau: AbbVie, UCB, Sobi, Eli Lilly, Louise Roper: None declared, Bridget Young: None declared, Frances Sherratt: None declared, Michael Beresford: None declared, Tracy Moitt: None declared, Louise Roper: None declared, Bridget Young: None declared, Frances Sherratt: None declared, Michael Beresford: None declared


AB0937
IDENTIFYING THE PRIMARY OUTCOME MEASURE AND PROTOCOL COMPONENTS FOR A PROSPECTIVE FEASIBILITY STUDY OF CORTICOSTEROID REGIMENS FOR CHILDREN AND YOUNG PEOPLE WITH JUVENILE IDIOPATHIC ARTHRITIS USING CONSENSUS METHODS WITH YOUNG PEOPLE, FAMILIES AND PROFESSIONALS
Simon Stones1, Heather Bagley2, Ashley Jones3, Flora Mcerlane3, Tracy Moitt1, Gloria Nkoma2, Frances Sherratt1, Bridget Young4, Michael Beresford5,6
Eileen Baildam1, SIRJIA Trial Management Group. 1University of Leeds, School of Healthcare, Leeds, United Kingdom; 2University of Liverpool, Institute of Translational Medicine, Liverpool, United Kingdom; 3Newcastle Hospitals NHS Foundation Trust, Great North Children’s Hospital, Newcastle upon Tyne, United Kingdom; 4University of Liverpool, Institute of Population Health Sciences, Liverpool, United Kingdom; 5Alder Hey Children’s NHS Foundation Trust, Liverpool, United Kingdom

Background: Juvenile idiopathic arthritis (JIA) is an umbrella term for seven relapsing-remitting inflammatory conditions in children and young people (CYP). Early, intensive treatment can prevent long-term damage; however, established drugs exhibit a delayed response, prompting the need for rapid-onset treatment in the form of corticosteroids. Given a lack of consensus as to which corticosteroid induction regimen should be used for CYP with JIA, a feasibility trial of different regimens is needed.
EFFICACY AND SAFETY OF BIOLOGICAL THERAPY WITH ETA NERCEPT IN A CASE OF SEVERE POLIARTHRITIS ASSOCIATED TO HARLEQUIN ICHTIOSIS

Francesco Baldo, Simone Carbogno, Sofia Torreggiani, Carlo Virgilio Agostoni, Larni Stefano, Francesca Minola, Giovanni Filocamo. Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Pediatria Media Intensità di Cura, Milano, Italy.

Background: Harlequin Ichthiosis (HI) is a rare autosomal recessive congenital disease, due to mutations of gene ABCA12. The estimated incidence is approximately 1 in 300,000 births, and approximately 200 cases have been reported worldwide. Typical manifestations of the disease at birth are the presence of hyperkeratotic plates with erythematous fissures, ectropion (eversion of the lower eyelids) and eclabium (eversion of the lips), rudimentary ears and nasal hypoplasia, and articular contractures. Babies who survive into infancy tend to lose hyperkeratotic plaques in favour of generalized scaling and erythroderma. Mental retardation is present in about 2/3 of cases. The association between HI and inflammatory joint involvement has been reported only in few patients since now.

Methods: We report clinical and laboratory findings, treatment choices and outcomes of young boy with HI who developed polyarthritis.

Results: A 6 years old kid with HI (the genetic test showed homozigous mutation of ABCA12) came to our attention with an history of chronic arthritis. Since he was 4, he developed bilateral knee arthritis. At first, he was treated with antimicrobial drugs, without improvement, in suspect of septic arthritis. In the following two years, he developed severe chronic polyarthritis. At the first visit in our center, he showed the classical clinical feature of HI (severe ectropion, contracture and generalized erythroderma), and had history of multiple severe infections and sepsis. Arthritis affected both hips, knees, ankles, wrists, elbows, shoulders and all the feet joints. He lost the ability to walk since the onset of arthritis. Laboratorial features showed negative anti nuclear antibodies (ANA) and anti- extractable nuclear antigen antibodies (ENA), anti celic citrullinated peptide and rheumatoid factor. No signs of uveitis were present at ophthalmological evaluation.

The patient was treated with intraarticular corticosteroid injections (IAI) into knees, wrists, elbows and ankles, and then oral methotrexate (MTX) was started. The clinical response was initially good, with partial recovery of deambulation in the 4 months following the intraarticular injection treatment. After 7 months ankles and wrists showed swelling and tenderness, and IAI were repeated, with clinical improvement.

References

Acknowledgement: This consensus meeting was funded as part of the SIRUJA study, funded by the NIHR Health Technology Assessment Programme (14/167/01). The funders did not have a role in the design, collection, analysis, or interpretation of the data.

Disclosure of Interests: Simon Stones Consultant for: SS has provided consultancy services to Envision Pharma Group, though this is not related to the contents of this abstract., Speakers bureau: SS has undertaken speaking engagements for Actelion, eyeforpharma, Four Health, Janssen and Roche, though these are not related to the contents of this abstract., Heather Bagley: None declared, Ashley Jones: None declared, Flora McErlane: None declared, Tracy Moitt: None declared, Gloria Nkhoma: None declared, Frances Sherratt: None declared, Bridget You: None declared, Michael Beresford: None declared, Eileen Baildam Consultant for: EB has received one paid consultancy for Pfizer in the last 12 months, but this was not related to this study.


AB0938

Efficacy and Safety of Biological Therapy With Etanercept in a Case of Severe Poliarthritis Associated to Harlequin Ichthiosis

Francesco Baldo, Simone Carbogno, Sofia Torreggiani, Carlo Virgilio Agostoni, Larni Stefano, Francesca Minola, Giovanni Filocamo. Fondazione IRCCS Cà Granda Ospedale Maggiore Policlinico, Pediatria Media Intensità di Cura, Milano, Italy.

Background: Harlequin Ichthiosis (HI) is a rare autosomal recessive congenital disease, due to mutations of gene ABCA12. The estimated incidence is approximately 1 in 300,000 births, and approximately 200 cases have been reported worldwide. Typical manifestations of the disease at birth are the presence of hyperkeratotic plates with erythematous fissures, ectropion (eversion of the lower eyelids) and eclabium (eversion of the lips), rudimentary ears and nasal hypoplasia, and articular contractures. Babies who survive into infancy tend to lose hyperkeratotic plaques in favour of generalized scaling and erythroderma. Mental retardation is present in about 2/3 of cases. The association between HI and inflammatory joint involvement has been reported only in few patients since now.

Methods: We are describing the case of a 6 years old kid with HI that at the age of 4 developed arthritis with severe impact on his quality of life.

Results: A 6 years old kid with HI (the genetic test showed homozigous mutation of ABCA12) came to our attention with an history of chronic arthritis.

Conclusion: It is feasible to include CYP, families and HCPs in synthesising complex concepts to agree by consensus the design components of clinical research. The primary outcome measure for inclusion in a prospective feasibility study of corticosteroids regimens in CYP with JIA was co-prioritised, with CYP and families taking a leading role in the ultimate selection of an appropriate outcome measure and other study protocol components. Using consensus methods with CYP, families and HCPs is a systematic and rigorous way in which to select outcome measures that are both meaningful and relevant to everyone involved in the care and treatment of CYP with JIA.

REFERENCES

Acknowledgement: This consensus meeting was funded as part of the SIRUJA study, funded by the NIHR Health Technology Assessment Programme (14/167/01). The funders did not have a role in the design, collection, analysis, or interpretation of the data.

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Methods: A cross-sectional descriptive study in which 34 patients were recruited sequentially and randomly, 15 with JDM and 19 with JIA, from the Rheumatology department of Niño Jesus Hospital between September-November (2018). Demographic, clinical, analytical data, presence and subtype of calcinosis, active treatment, HAQ, patient and physician global assessment (PGA), cutaneous assessment tool (CAT) and manual muscle testing (MMT8) validated for JDM were collected. One observer performed blindly, both for clinic and diagnosis, a NFC initially using a videodermatoscope in order to obtain a wide view of the vascular bed and then with a videocapillaroscope (x3000), which recorded 2-4 images per finger (except thumbs) to be analyzed far ahead. The presence of a decreased nailfold capillary density (NCD, capillary n°/mm²), architectural derangement (disorganization), neoangiogenesis, giant capillaries (ø>50µm, pathological if ≥1), enlarged loops (ø20-50µm) and microhaemorrhages, both pathological present in ≥2 fingers were evaluated. Neovascular pattern was defined as the sum of NCD, disorganization and neoangiogenesis with frequent haemorrhages and giants (active and late scleroderma pattern).

Results: The descriptive analysis of the main variables is shown in Table 1. Patients with JIA: all received active treatment, 95% MTX (33% concomitant with anti-TNF; 1 TCZ and 16% CE) and 1 anti-TNF. 26% active uveitis. Two patients presented morphological abnormalities: 1 neoangiogenesis and another enlarged loops. Patients with JDM: 73% received MTX (18% concomitant with CE, 73% Igs and 1 RTX). Three patients had active calcinosis: 2 mixed (circumscribed and cutis) and 1 calcinosis cutis. 2 had previous calcinosis (both circumscribed); 87% presented for the first-time weakness but none had current weakness (MMT8 40). 67% presented morphological abnormalities: NCD 33%, disorganization 40%, neoangiogenesis 53%, enlarged loops 27%, giants 20% and microhaemorrhages 13%. All patients with calcinosis (active or previous) presented disorganization and neoangiogenesis, NCD 80%, giants 60%, enlarged loops and microhaemorrhages 40%. 50% of patients with JDM had a neovascular pattern, of which 80% had a previous or current history of calcinosis.

Conclusion: Patients with JDM presented more abnormalities in NFC compared to patients with JIA. Neovascular pattern was observed in half of patients, who have previous or current history of calcinosis. Consequently, NFC could be a useful imaging technique in routine clinical practice to evaluate skin activity in patients with JDM.

REFERENCES

Disclosure of Interests: None declared 

AB0939 NAILFOLD CAPILLAROSCOPY IN JUVENILE DERMATOMYOSITIS: DESCRIPTION OF ABNORMALITIES IN A SERIES OF PATIENTS
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Background: Juvenile dermatomyositis (JDM) is characterized by the presence of microangiopathy which can be assessed by nailfold capillaroscopy (NFC), a simple and noninvasive imaging technique. Morphological abnormalities in scleroderma NFC are well described, but it is known that they may be present in other autoimmune diseases, such as JDM.

Objectives: To describe the capillary morphological abnormalities assessed by NFC in a series of patients diagnosed with JDM in contrast with patients diagnosed with juvenile idiopathic arthritis (JIA).

Results: The descriptive analysis of the main variables is shown in Table 1. Patients with JIA: all received active treatment, 95% MTX (33% concomitant with anti-TNF; 1 TCZ and 16% CE) and 1 anti-TNF. 26% active uveitis. Two patients presented morphological abnormalities: 1 neoangiogenesis and another enlarged loops. Patients with JDM: 73% received MTX (18% concomitant with CE, 73% Igs and 1 RTX). Three patients had active calcinosis: 2 mixed (circumscribed and cutis) and 1 calcinosis cutis. 2 had previous calcinosis (both circumscribed); 87% presented for the first-time weakness but none had current weakness (MMT8 40). 67% presented morphological abnormalities: NCD 33%, disorganization 40%, neoangiogenesis 53%, enlarged loops 27%, giants 20% and microhaemorrhages 13%. All patients with calcinosis (active or previous) presented disorganization and neoangiogenesis, NCD 80%, giants 60%, enlarged loops and microhaemorrhages 40%. 50% of patients with JDM had a neovascular pattern, of which 80% had a previous or current history of calcinosis.

Conclusion: Patients with JDM presented more abnormalities in NFC compared to patients with JIA. Neovascular pattern was observed in half of patients, who have previous or current history of calcinosis. Consequently, NFC could be a useful imaging technique in routine clinical practice to evaluate skin activity in patients with JDM.

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Disclosure of Interests: None declared 

AB0940 OBESITY AND NUMBER OF ACTIVE JOINTS AT TUMOR NECROSIS FACTOR-INHIBITOR START ARE ASSOCIATED WITH SHORTER REMISSION DURATION AFTER WITHDRAWAL IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS: PRELIMINARY RESULTS FROM A MONOCENTRIC COHORT
Fabio Basta, Hanan Jadoun, Maria Isabella Petrone, Angela Aquirani, Andrea Uva, Rebecca Nicolai, Fabrizio De Benedetti, Silvia Magni-Manzoni. Ospedale Pediatrico Bambino Gesù, IRCCS, Division of Rheumatology, Rome, Italy

Background: No recommendations on appropriate withdrawal of tumor necrosis factor-inhibitors (TNFi), once remission status has been achieved

Disclosure of Interests: None declared 
in patients with juvenile idiopathic arthritis (JIA), are currently available. With regards to possible predictors of flare, the role of obesity has not been investigated yet.

**Objectives:** To investigate to role of obesity at start of TNFi therapy on remission duration and flare rate after TNFi withdrawal in JIA patients.

**Methods:** The charts of JIA patients followed at the study center and treated with TNFi as first biologic from 2009 to 2015, who reached remission and with at least one year of follow up after withdrawal, were retrospectively reviewed. Exclusion criteria were: systemic JIA and pJIA RF-positive. Demographic and clinical features were registered, including: ILAR JIA subtype, occurrence of uveitis, ANA status, number of active and clinical manifestations of SLE in patients younger than 6 years old in our series are similar to those described in the literature: arthritis and seizures, as well as neurological and neuropsychiatric manifestations; We present the demographic and clinical characteristics of SLE in patients under 6 years old with a diagnosis of SLE based on the 1997 ACR criteria at the Federico Gomez Children’s Hospital of Mexico from June 2017 to January 2019.

**Background:** Systemic lupus erythematosus (SLE) is a rare entity in patients under 5 years old, depending on the ethnic group it has a prevalence of 3.3 to 24 per 100,000 children. Before puberty no difference in prevalence associated with gender was observed. In the pediatric age, SLE has a more aggressive course.

**Objective:** To describe the demographic and clinical characteristics of 6 patients under 6 years old diagnosed with SLE.

**Methods:** To describe the demographic and clinical characteristics of 6 patients under 6 years old with a diagnosis of SLE.

**Results:** The diagnosis of SLE in patients under 5 years old is rare, the literature describes that in these patients there is greater renal, hematological and neuropsychiatric manifestations; We present the demographic and clinical characteristics of 6 patients under 6 years old with a diagnosis of SLE based on the 1997 ACR criteria at the Federico Gomez Children’s Hospital of Mexico from June 2017 to January 2019.

Table N°1. Demographic and clinical characteristics of patients under 6 years of age diagnosed with SLE.

**Results:** The diagnosis of SLE in patients under 5 years old is rare, the literature describes that in these patients there is greater renal, hematological and neuropsychiatric manifestations; We present the demographic and clinical characteristics of 6 patients under 6 years old with a diagnosis of SLE based on the 1997 ACR criteria at the Federico Gomez Children’s Hospital of Mexico from June 2017 to January 2019.

**Table N°1.** Demographic and clinical characteristics of patients under 6 years of age diagnosed with SLE.

**Results:** The diagnosis of SLE in patients under 5 years old is rare, the literature describes that in these patients there is greater renal, hematological and neuropsychiatric manifestations; We present the demographic and clinical characteristics of 6 patients under 6 years old with a diagnosis of SLE based on the 1997 ACR criteria at the Federico Gomez Children’s Hospital of Mexico from June 2017 to January 2019.

Table N°1. Demographic and clinical characteristics of patients under 6 years of age diagnosed with SLE.

**Results:** The diagnosis of SLE in patients under 5 years old is rare, the literature describes that in these patients there is greater renal, hematological and neuropsychiatric manifestations; We present the demographic and clinical characteristics of 6 patients under 6 years old with a diagnosis of SLE based on the 1997 ACR criteria at the Federico Gomez Children’s Hospital of Mexico from June 2017 to January 2019.

Table N°1. Demographic and clinical characteristics of patients under 6 years of age diagnosed with SLE.

**Results:** The diagnosis of SLE in patients under 5 years old is rare, the literature describes that in these patients there is greater renal, hematological and neuropsychiatric manifestations; We present the demographic and clinical characteristics of 6 patients under 6 years old with a diagnosis of SLE based on the 1997 ACR criteria at the Federico Gomez Children’s Hospital of Mexico from June 2017 to January 2019.

Table N°1. Demographic and clinical characteristics of patients under 6 years of age diagnosed with SLE.
Background: A challenge with the present classification of JIA is the evolution of the disease over time. One category that is especially difficult to classify is enthesitis-related JIA (ERA). Objectives: To longitudinally study radiologically diagnosed sacroiliitis (Si) developed during the first 18 years in an aim to gain knowledge about classification challenges posed by the Si category, nosoclassification (Martin-Atencia A et al. J Rheumatol. 2018 Oct; Epub ahead of print).

Methods: 510 consecutive cases of JIA with disease onset 1997 to 2000 were prospectively included in a Nordic, longitudinal, close to population-based 18-year follow-up study, and 434 (85%) had at least two follow-up visits during disease course. At the 18-year follow-up visit; 329 (76%) attended a clinical visit, and 105 (24%) a telephone interview. The follow-up period was 17.5 ± 1.7 years (mean ± SD) after onset. Mean age of the study participants was 24.0 ± 4.4 years. Clinical data, collected at one, eight and 18 years after disease onset, were evaluated regarding variables for enthesis/spondylitis-related arthritis compared to the other JIA categories.

Results: In 376 participants evaluated for Si, radiology was performed on clinical suspicion. 26 (16%) males and 10 (28%) females developed radiologically verified sacroiliitis (rad-Si) during the first 18 years of disease. Age at onset was significantly higher in this group compared to the other participants, median 9.9 (IQR 6.4-12.0) vs. 5.6 (IQR 2.6-9.5) years, (p=0.001). Only 3/26 had rad-Si at eight-year follow-up.

Using the ILAR criteria 12/26 with rad-Si were classified as ERA after median 7 (IQR 6-10.2) months, 1/26 as juvenile psoriatic arthritis, 5/26 as undifferentiated JIA because of psoriasis-related variables, the remaining had oligo- or polyarticular arthritis. At 18-year follow-up, 18/26 fulfilled criteria for ERA, 2/26 juvenile psoriatic arthritis, and 3/26 the undifferentiated category because of psoriasis-related variables, 3/26 had polyarticular RF negative or oligoarticular extended disease. Enthesitis, inflammatory back pain, and morning stiffness were more common with rad-Si (p=0.001; p=0.001; p=0.001), also HLA-B27, 1/26 vs. 62/351 (p=0.001), but not 1st degree heredity for ankylosing spondylitis. Uveitis developed in 10/26 (38.5%). Two participants developed IBD.

Conclusion: The majority of variables involved in the new proposed classification of enthesitis/spondylitis-related JIA were significantly more common during the first 18 years of disease in those that developed rad-Si. Psoriasis-related variables, no longer exclusion criteria for ERA, should be further evaluated as possible inclusion criteria, as well as higher age at onset.


RADIOLOGICAL SACROILIITIS AFTER 18 YEARS OF FOLLOW-UP IN THE POPULATION-BASED NORWEGIAN JUVENILE IDIOPATHIC ARTHRITIS (JIA) COHORT

AB0944

SJÖGREN’S SYNDROME IN CHILDREN: A CASE SERIES

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Background: The symptoms of pediatric Sjögren’s syndrome (SS) are different in adults. There are currently no validated pediatric diagnostic criteria or treatment guidelines for SS. In most cases adult criteria are used, but they apply poorly to children.

Objectives: To present pediatric patients with primary SS who were treated at University Children’s Hospital (UCH) Ljubljana in the past 10 years.

Methods: Eight children with primary SS were identified. Demographic data, clinical and laboratory findings and therapy were analysed by retrospective review of medical records at UCH Ljubljana.

Results: Six girls and 2 boys were evaluated. The mean age at disease onset was 12.3 years (range 6.5 – 17) and mean age at diagnosis was 13.8 years (range 7.5 – 17.5). The mean follow-up duration was 2.8 years (range 0.5 – 8.5). Four patients presented with recurrent bilateral parotitis, two with rash, one with arthralgia and fatigue and one with acute central nervous system vasculitis. The latter patient presented with rheumatic fever at the same time. During disease course arthritis and/or xerothalmia, which compromises exocrine glands causing inflammatory response that leads to glandular hypossecretion. SS is probably underdiagnosed in pediatric range due to differences in presentation regarding adults with this condition, causing low recognition of the disease in children.

Objectives: The authors describe demographic, clinical, laboratory and therapeutic profiles of a cohort of children with primary SS attended at a university center.

Methods: Retrospective analysis of 30 selected patients’ medical records between 2005 and 2017 allowed collection of various data. Laboratory and additional investigations included documentation of ocular dryness (Schirmer test, Rose-Bengal stain); evidence of parotid involvement (scintiscan, sialometry); and histological evidence of lymphocytic infiltration of the minor salivary glands or other organs.

Results: 30 patients diagnosed with juvenile SS were selected: 22 girls (73%) and 8 boys (27%) with an average age of 11 years. The clinical characteristics were: parotid enlargement as the initial manifestation of the disease in 11 patients (37%), and recurrent episode in 4 patients (13.3%). 12 patients (40%) had xerostomia and 17 (57%) xerophthalmia. One patient (3.3%) presented with leukocytoclastic vasculitis in lower limbs as first manifestation of the disease in association to recurrent parotid swelling. Two (6.6%) patients presented neurological symptoms (1 peripheral sensory neuropathy and 1 with dysautonomic manifestations).

Positive Schirmer test was observed in 11 patients (37%), Rose Bengal stain in 10 (33%). 76% of patients had abnormal salivary glands scintigraphy. In 8 patients (30%) the salivary gland biopsy revealed compatible with juvenile Sjögren syndrome clinical picture (30%) presented positive RF, 14 patients (46%) anti-Ro/SSA, 10 patients (33%) anti-La/SSB, 28 patients (93%) had +ve ANA. 50% received glucocorticoid. Hydroxychloroquine was the drug most often used in 25 patients (83%), followed by methotrexate in 12 patients (40%), azathioprine in 4 patients (13%) and cyclophosphamide in 3 patients (10%). Only one patient required the use of human immunoglobulin and one leflunomide (3.3%). Two patients (6.6%) received rituximab.

Conclusion: The present study demonstrated the demographic, clinical aspects and laboratory and treatment in a series of patients with primary juvenile Sjögren’s syndrome, a relatively rare condition, presenting an overview of this particular patient population.


AB0943

CLINICAL AND LABORATORY PRESENTATION OF JUVENILE SJÖGREN’S SYNDROME IN A COHORT OF 30 PATIENTS

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Background: Sjögren’s Syndrome (SS) is a chronic autoimmune disease, rare in childhood and adolescence, characterized mainly by xeroesthesia and and xerophthalmia, which compromises exocrine glands causing inflammation of enthesitis/spondylitis-related arthritis compared to the other JIA categories.

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arthralgia was present in 5/8, parotitis in 4/8, oral symptoms in 4/8, rash in 4/8, fatigue in 3/8 and ocular symptoms in 2/8 patients. One patient developed superficial calcifications on fingers. All patients had high titre of antinuclear antibodies, 7/8 were positive for anti-Ro and 5/8 for anti-La antibodies. Three patients were tested for rheumatoid factor and all were positive. 6/8 patients had elevated ESR and hypergammaglobulinemia. 4/8 patients had elevated serum amylase.

Biopsy of salivary glands was performed in 5 patients and foci of lymphocytic infiltration were shown in all of them. Further 2 patients had salivary gland changes on MRI and/or US. On ophtalmologic evaluation 3 patients had positive Schirmer test and one had unstable tear film. One patient had CNS vasculitis and two decreased diffusing capacity of the lungs. Other patients showed no signs of internal organ involvement.

4/8 patients were treated with NSAIDs, 7/8 patients with hydroxychloroquine, 2/8 also received corticosteroids and one patient MMF. At this point the patient with CNS vasculitis has stable changes on head MRI without clinical symptoms. Other patients have no signs of internal organ damage. Calcifications that appeared on fingers in one patient are not progressing.

Conclusion: Most common symptoms in our cohort were arthritis and/or arthralgia, parotitis, oral symptoms and rash. Half of the children presented with recurrent parotitis. One child developed calcifications on fingers, which have not yet been described in patients with SS. Pediatric SS differs from adult SS and specific pediatric diagnostic criteria would improve management of these patients.

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AB0945
CO-MORBID AFFections in CHILDren WITH SYSTEMIC LUPUs ERYThEMATOSUS

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Background: In children with systemic lupus erythematosus (SLE) due to the cascade of immune-inflammatory reactions there is a development of systemic vascular endothelium lesion, which causes not only clinical manifestations of the main process, but also leads to the damage of vital organs and systems, the development of metabolic disorders. Extensive damage aggravates more the course of the disease, worsens its prognosis, complicates the response to therapy and reduces the quality of life of patients.

Objectives: The aim of study was to determine the frequency and variants of comorbid conditions in children depending on the duration and activity of the disease and features of the therapeutic complex.

Methods: A survey was conducted on 41 patients with SLE: 37 girls (90.2%), 4 boys (9.8%); the duration of the disease is up to 3 years in 20 patients (48.8%) and more than 3 years in 21 (51.2%). Presence of comorbid conditions determines as the cardiovascular system, kidney, liver and lungs functions changes. General clinical trials included autoantibodies, disease activity and drugs assessment. Total cholesterol, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, apolipoprotein B, ApoA-I and lipoprotein-α were evaluated. The state of the blood coagulation system was also studied: fibrinogen of the blood, prothrombin index, thrombin time, active partial thrombin time, D-dimer, international normalized ratio. Bone mineral density was determined.

Results: In 74.3% of children with SLE, the presence of comorbid conditions characterized by pathology of the cardiovascular system, kidneys, liver, the organ of vision, pulmonary system is established. Besides, atherogenic dislipoproteinemia has been detected in 60.0%, disorders in the hemostasis system were in 25.0% of patients and 43.0% persons have osteopenia. Children with SLE and the presence of comorbid conditions, especially with the involvement of the liver and kidneys and the long-term preservation of the disease activity (SRP, ANA, anti-DNA), are more likely to develop atherogenic dislipoproteinemia and hypercoagulation (increase in the prothrombin index, fibrinogen and D-dimer). The values of the comorbidity index in patients with SLE increased while maintaining the activity of the process and using high doses of glucocorticosteroids (GCS) including pulse therapy. Comorbidity index was 2.9 ± 0.5 points in the patients who received the GCS pulse therapy: 2.5 ± 0.3 in the cases of treatment by combination GCS + azathioprine; 2.0 ± 0.6 in the children without GCS; p<0.05). ANA-positivity was also accompanied by higher values of the comorbidity index (2.8 ± 0.3 vs. 1.4±0.5, p<0.05).

Conclusion: Children with SLE in the long-term course of the disease and maintaining the activity of the pathologic process (ANA, DNA antibodies high level) have a formation of lesions of systems and organs, the lipids metabolism disorders, prolonged hypercoagulation and the development of osteopenia. Aggressive therapy for reducing the activity of the autoimmune process helps to prevent the formation of comorbid states and persistent metabolic disorders.

Disclosure of Interests: None declared


AB0946
QUALITY IMPROVEMENT IN PEDIATRIC RHEUMATOLOGY: A NEW APPROACH TO CARE IN QATAR
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Background: Quality improvement (QI) projects have been established in many pediatric and adult rheumatology centers around the world to enable real time improvement of health delivery and outcomes. QI has been driven by the Institute of Medicine, patients, professional organizations and the providers. Notably, another driver is the discrepancy between the availability of better and targeted therapies and poor disease outcomes. QI projects for healthcare teams are designed to improve the efficiency and effectiveness of patient care by addressing gaps in care and implement these goals in sustainable ways, evaluate the impact and start a new cycle of improvement. In so doing, teams collaborate, learn from each other, and improve variability in a short time frame. In small practices with limited resources, effective QI projects allow for understanding the gaps in the processes, data collection and several process improvements to be done by different team members, in short cycles that allow for real time data evaluation and fine tuning processes.

Objectives: We describe the chosen quality measures, implementation of processes and first 6 months of data at a newly opened Children’s Hospital in Doha, Qatar.

Methods: We chose quality measures that have been proposed in the literature and have been implemented in large learning collaboratives. We worked with the informatics team to build measures that are accurately captured and retrievable from the electronic medical record. Additionally we worked with our Ophthalmology clinic to ensure a smooth referral pathway that is coordinated by nursing staff. Our EMR measures were chosen to screen for drug toxicity among patients receiving methotrexate or leflunomide within 3-4 week of receiving Methotrexate 2) the time between referral to and visit in Ophthalmology, to screen for toxicity among patients receiving hydroxychloroquine 3) time between referral and visit in Ophthalmology, to screen for uveitis in children diagnosed with juvenile idiopathic arthritis.

Our nursing teams developed a manual joint injection log 1) to capture the time between referral for procedure and procedure date occurred within 2 weeks, and monitor side effects. We examined data between June to December 2018 from the pediatric rheumatology patient population of 420 unique patients.

Results: 96% of children receiving methotrexate or leflunomide were screened for methotrexate toxicity within 3-4 months of the medicine being dispensed. 50% of children receiving hydroxychloroquine were seen by Ophthalmology within 4 months of the referral. 71% of children with JIA were seen by Ophthalmology within 1 month of the referral. 100% of children had joint injections performed within 14 days of the referral.

Conclusion: We described the development, implementation and results of our pediatric rheumatology QI projects. To our knowledge it is the first of a kind in Qatar and in the area. For our growing practice of 600 patient visits our data shows areas of great performance and poor performance, specifically in eye care for our patients. Barriers included education of teams about QI measures and processes, collaborating with other services on negotiating best patient practices. Successful implementation in our processes underlines the need for further data collection and additional improvement cycles. Additionally, in resource poor areas, it is essential to make good use of the EMR and
work in collaborative teams to ensure participation and sustainability of processes. Next steps would be to add additional quality and disease outcome measures.

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Disclosure of Interests: None declared

AB0947
TREATMENT WITH SIMULTANEOUS BIOLOGICAL AGENTS IN JUVENILE IDIOPATHIC ARTHRITIS: SINGLE-CENTER CASE SERIES AND REVIEW OF LITERATURE

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Background: Several therapeutic choices are currently available for juvenile idiopathic arthritis (JIA) patients. The classical first line therapies are NSAIDs and corticosteroids (CTCs) and the second line encompasses synthetic and biological DMARDs. The clinical efficacy of DMARDs (alone or in combination) has been well demonstrated in RCTs and the treatment is often tailored on an individual basis. Combination of bDMARDs has not been formally evaluated in rheumatology and few publications are available concerning the combination of bDMARDs in patients with severe active forms of JIA, mainly systemic (SpJIA) and polyarticular (Pa) categories.

Objectives: To describe efficacy and safety of JIA patients resistant to MTX and bDMARDs requiring a simultaneous bDMARDs treatment.

Methods: Retrospective analysis of 7 (4.7 ± 2.1 years, male sex 75%) patients with JIA of a single tertiary center. A systematic review of literature was made to search observational studies from MEDLINE database (January 1946 to January 2019).

Results: All patients in the Paediatric Rheumatology Department (Lyon University Hospital) receiving combination therapy with bDMARDs were eligible. Seven patients with JIA diagnosis (4 SpJIA and 3 PA) were included. Genetic studies were performed in three patients, with positive LAC3C1 mutation in one. The exposure to the bDMARDs of the whole cohort was 79 patient-years (PY), including 16.5 PY of combination with simultaneous bDMARDs. The delay between the date of diagnosis and the first prescription of a combination of simultaneous bDMARDs treatment was 8.3 ± 4.8 years. Nine bDMARDs drugs were prescribed: anti-TNFs, tocilizumab and rituximab (nine times each). Ten co-prescriptions of the bDMARDs were administrated with 5 possible types of combinations between them, the most frequent associating tocilizumab/rituximab. Rituximab was used most frequently in combination with another bDMARD. The rituximab schedule was different between patients. Disease activity decreased for all patients, primarily at the biological level without reaching complete clinical remission.

In general, the clinical tolerance to the co-prescription of bDMARDs was acceptable. One patient (P2) experienced a severe hepatitis event in adulthood attributed to the treatment (tocilizumab), dropping the bDMARDs combination. During the exposure time, the most frequent adverse events were infections: repeated otitis media (P1), persisting vaginitis and fungal urinary infection (P3) not requiring hospitalization. One patient (P6) had 2 episodes of purpuric rash on the days of the canakinumab injection requiring oral CTC treatment. No severe acute reactions were found and no patients died.

The systematic review found a publication: retrospective series of 4 patients (SpJIA) combining abatacept and canakinumab (2).

Conclusion: Severe forms of JIA that are refractory to the current therapeutic options could benefit from the combination of bDMARDs. The combination of bDMARDs may be an alternative therapy to explore in this group of patients.

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Disclosure of Interests: None declared

AB0948
PARADOXICAL TINEA AMIANTACEA IN A PATIENT WITH JUVENILE IDIOPATHIC ARTHRITIS RECEIVING ADALIMUMAB

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Background: Tinea amiantacea is a papulo-squamous condition of the scalp that can lead to scalp fibrosis and subsequent permanent hair loss. It is thought to represent a reaction pattern to inflammatory skin disease as psoriasis or seborrheic dermatitis (1).

Objectives: To highlight an adverse reaction which involved the skin in the disease course of a young JIA (juvenile idiopathic arthritis) patient, during treatment with adalimumab.

Methods: A 16-month-old female patient presented to our clinic with a 4-week history of knee swelling, associated with functional limitation and morning stiffness. Family history was unremarkable, while past medical history revealed atopic dermatitis in the first year of life. The baby was initially treated with NSAIDs, but one month later, due the persistence of arthritis and the appearance of uveitis, subcutaneous methotrexate was started (15 mg/m²/weekly). However 5 months later, given the persistence of uveitis and the onset of a severe hypertensinamiasemia, methotrexate was interrupted and adalimumab (24 mg/m² every 2 weeks) was introduced with a prompt and stable control of ocular and articular disease and a gradual normalization of transaminases. One year later the patient developed dry, itchy, and cracked skin behind her ears, with fissurizing the lower attachment of the ear lobe, and presented right parietal yellowish scalp lesions which were pruriginous, thick, and scaly, attached both to the scalp and to the proximal hair shafts. A first diagnosis of pityriasis amiantacea secondary to atopic dermatitis was made. A paradoxical cutaneous reaction to the anti-TNF therapy was later hypothesized (2), and 7 months later adalimumab was interrupted with quick resolution of the dermatologic lesions. However, both arthritis and uveitis rapidly reappeared, showing an inadequate response to a six month cycle of abatacept treatment (10 mg/kg/month). Adalimumab was than reintroduced with a rapid improvement.

Results: Currently, after 16 months of adalimumab treatment, the patient still shows complete disease control, without any new dermatologic lesions up to now.

Conclusion: TNF antagonist-induced tinea amiantacea is a rare adverse reaction that may require the drug discontinuation. Although the exact pathogenetic mechanism is unclear, an imbalance in the cytokine milieu with a selective overexpression of type I interferon has been hypothesized.

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AB0949
IS PEDIATRIC ONSET LUPUS MORE SEVERE IN BOYS? OUR EXPERIENCE AT A TERTIARY CARE CENTER IN NORTH-WEST INDIA

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Background: There is diversity in clinical presentation of pediatric onset SLE (pSLE) and the manifestations are more severe as compared to
adults. Males comprise 4-22% of all SLE patients. Gender distribution of pSLE is 4:5.5: 1 (female-to-male) as opposed to 9:10: 1 (female-to-male) in the adult population. However male patients have been known to have a more severe disease with higher morbidity, especially due to renal causes.

**Objectives:** To evaluate clinical and immunological profile and outcomes in a follow up series of males with pediatric onset SLE

**Methods:** We analyzed the clinical and immunological profile and outcome of male patients diagnosed with SLE at less than 18 years of age. These children were followed-up in Pediatric Rheumatology Clinic, Advanced Pediatrics Centre, Postgraduate Institute of Medical education and research, Chandigarh, India. Details on demographic data, clinical presentation, laboratory findings, immunological profile, treatment regimens and outcomes of these children were retrieved from clinic files.

**Results:** Forty-three patients were diagnosed to have SLE between January 1998 to December 2018. Mean age at presentation was 9.7 years (range: 9 months-12 years). Total patient years of follow up was 192 years. The most common clinical presentation was fever in 38 (88%) patients; rash in 27(63%); pallor in 21(49%); edema with urinary abnormalities in 17(40%) and photosensitivity in 16 (37%). A diagnosis of lupus nephritis was made in 25 (58%) patients out of which 17 (39.5%) had nephritis at presentation. Renal biopsies were performed in 18 patients; 11 had class IV disease, 2 had class 5 disease, 2 had class IV/V. Neuropsychiatric manifestations were seen in 11 (26%) patients - 7 of these had symptoms at presentation. Seizures were the predominant manifestation in 9 patients (21%)-6 of these had MRI changes consistent with posterior reversible encephalopathy syndrome while 3 had cerebral infarcts. Other central nervous system abnormalities included psychosis (1 patient) and chorea (1 patient). We also noted a family history of lupus like illness in 4 patients and 3 (6.9%) were found to have early complement deficiencies. Antiphospholipid antibodies (aPLA) were detected in 8 (18.6%)patients - antiphospholipid antibody was positive in 8 and lupus anti-coagulant was positive in 6. Dual aPLA positive was seen in 6(13.9%) and triple positive was positive in none. Infections were seen in 16 (37%) patients during follow-up. All patients received steroids in gradually tapering doses along with hydroxychloroquine following a diagnosis of SLE. Cyclophosphamide was given for induction in 13 patients who had severe forms of lupus nephritis. Remission was maintained through aza-thioprine in 8 patients and 8 required Mycophenolate mofetil. Ten patients (23%) had a relapse on therapy -1 had CNS relapse, 3 had renal relapse, 2 had muco-cutaneous relapse and 4 had hematological relapse. Six fatalities (14%) were recorded during follow-up -1 with severe disease activity and neuropsychiatric manifestations, 1 had disseminated tuberculosis, 1 had CNS flare with status epilepticus, 4 had sepsis.

**Conclusion:** This is one of the largest series on boys with pediatric onset SLE from a developing country. It appears that while the severity of lupus nephritis in boys is different from that in girls, neurological disease is more severe in the former. Further, boys appeared to have earlier onset of neuropsychiatric lupus as compared to girls. The incidence of complement deficiency lupus was also more in boys. Mortality in boys with SLE appears to be comparable to our previously published mortality data on pSLE(1).

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**AB0950**

**CORRELATION OF QUANTITATIVE MAGNETIC RESONANCE IMAGING BIOMARKERS AND AXIAL PAIN IN ENTHESIS-RELATED ARTHRITIS PATIENTS**

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**Background:** Magnetic resonance imaging is increasingly used to diagnose, stratify and monitor inflammation in patients with spondyloarthropathies. Magnetic resonance imaging (MRI) has the potential to provide more accurate assessment of disease activity and outcomes. In patients with enthesis-related arthritis (ERA), inflammation is often assessed by visual scoring, diffusion-weighted imaging (DWI) and fat fraction (FF) mapping. The correlation of ADCmean, which increases with increased inflammation, and T1mean, which decreases with inflammation, and outcomes of these children were retrieved from clinic files.

**Objectives:** To analyse the relationships between quantitative imaging biomarkers (QIBs), axial pain and serum biomarkers – including ‘inflammatory’ biomarkers and those reflecting bone turnover - in a cohort of ERA patients.

**Methods:** 28 patients with ERA were prospectively recruited. The hips, sacroiliac joints and lumbar spine were assessed with chemical shift-encoded MRI and diffusion weighted imaging. Quantitative MRI parameters, such as the apparent diffusion coefficient (ADC) and fat fraction (FF) were measured in the sacroiliac joints. Visual scores for inflammation and fat metaplasia were also reported. BASDAI questionnaires were completed. Serum cytokines and bone markers were measured via multiplex bead-based immunoassays (Luminex) and results were available for 14 patients with ERA.

**Results:** The mean visual analogue score for spinal and hip pain (BASDAI Q2) was 3.9 (Table 1). There was a correlation between ADCmean and spinal and hip pain (rs=0.393, P=0.043). There was also a negative correlation between FFmean and the above pain score (rs = -0.378, P=0.047). There was a positive correlation between matrix metalloproteinase-3 (MMP-3) levels and FFmean (n=14, rs=0.698, P=0.006). However, the correlation did not reach statistical significance when corrected for multiple testing.

**Conclusion:** The correlation of ADCmean, which increases with increased tissue water/inflammation, with spinal and hip pain suggests that BASDAI Q2 relates to pain of active inflammation. Similarly the inverse correlation of FFmean, which increases with bone healing and reduced inflammation, and BASDAI Q2, would also support this relationship.

**REFERENCES**

Objectives: Describe two brothers affected by MCTO highlighting the importance of a genetic diagnosis.

Methods: B1 (20 years) presented age 3 years with swollen painful feet and restricted movement in his fingers and wrists and was diagnosed with polyarticular juvenile idiopathic arthritis (JIA). After no response to steroid treatment he developed rapid onset fixed flexion deformity of both elbows. He had mild learning difficulties. Based on clinical and radiological findings he was diagnosed with carpotarsal osteolysis age 4 years. Bisphosphonates and vitamin D replacement did not halt progressive bony destruction. Consistent with the literature osteolysis stabilised in the teenage years. Renal function remains normal.

B2 (5 years) is a dizygotic twin and younger sibling of B1. All other family members: parents (non-consanguineous), twin sister, sister, brother and half-brother are healthy. B2 presented aged 21 months with bilateral painful swollen wrists and reduced range of movement. His development was normal and comparable to his twin. Clinical presentation was similar to B1 who was yet to receive a genetic diagnosis. Plain films were not diagnostic as carpi unossified. Regular monitoring of renal function was advised although it was noted the nephropathy associated with MCTO does not normally manifest until the second decade.

At genetic review an autosomal recessive form of carpotarsal osteolysis was considered most likely. The elbow contractures in B1 were consistent with this phenotype although subcutaneous nodules were absent. Genetic testing for MAFB gene alterations identified an identical mutation in B1 and B2 (MFAB – c176c>Tp(Pro59leu) confirming the autosomal dominant MCTO. B2 developed hypertension, heavy proteinuria and hypoalbuminemia at 3 years, responding to tacrolimus.

Results: Two brothers with clinical features of MCTO and identical mutations in MAFB gene are described. The phenotype varied significantly with early renal disease in one and mild learning difficulties in the other. Inheritance of this autosomal dominant condition in these two brothers with unaffected parents could result from either gonadal mosaicism or incomplete penetrance. There is a case of incomplete penetrance in MCTO described in the literature. [2]

Conclusion: Individually skeletal dysplasias are rare yet as a group they represent an important differential to JIA requiring different management. Pursuing a genetic diagnosis in carpotarsal osteolysis is important not only for prediction of recurrence risk. It allows a definitive diagnosis to be made earlier than is possible clinically/radiologically. Significantly different phenotypes yet the same genetic mutation lends weight to the possibility of modifier genes or other epigenetic mechanisms/environmental factors affecting disease penetrance as proposed by Dworschak et al. [2]. A greater understanding of these may enable prediction of renal involvement and aid development and stratification of new therapies.

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AB0952 RETROSPECTIVE STUDY OF PROCEDURAL PAIN ANALYSIS DURING JOINT INFLTRATION IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Juvenile Idiopathic Arthritis (JIA) is the rheumatic disease more common in childhood. Intra-articular corticosteroid injections (IAC) are a mainstay in the treatment of this disease, unfortunately it is often associated with pain and anxiety, for this reason is extremely important to pay attention both to procedural analgesia and to the reduction of anticipatory anxiety.

Objectives: The primary aim was evaluate the impact of the our analgesic procedure on the perception of infiltration pain; the secondary aims were stratify the results according to the demographic characteristics, number of joints infiltrated for each patient.

Methods: 30 patients (pt) studied between August 2016 and August 2017 (1 year) received a IAC [F/M=25/15, age 8.63 ± 3.41 yrs, weight 32.1 ± 13.9 kg; monarticular JIA 7 pt (17.5%), oligoarticular 19 (47.5%), polyarticular 14 (35%). 27/40 (67.5%) pt infiltrated in one joint, 13/40 (22.5%) in two or more joints]. One hour earlier of the procedure for each pt was applied 1% prilocaine cream and 30 minuts before administered Midazolam orally at a dose of 0.5 mg/kg (maximum 15 mg), 50% nitrogen protoxide mixture dispursed with a mask, in spontaneous breathing and continuous flow. In 25/40 (62.5%) pt distraction techniques were performed during IAC and in 24/40 (60%) was also applied ice spray before IAC. To monitor pain, before and after IAC, appropriate scales have been used, stratified by age: CHIPPS scale (pt ≤ 5 yrs), Wong-Baker scale for ages 6 to 10, numerical scale analog visualVAS (pt ≥ 8 yrs), CHIPPS and VAS scales:4 indicative of mild pain. For each pt pain assessment was performed before and after IAC.

Results: VAS before IAC = 0.90 ± 1.67/Median (M) = 0, after IAC = 1.07 ± 1.56/NI = 0, CHIPPS before IAC = 0.82 ± 1.88/M = 0, during IAC = 2.75 ± 3.01/M = 2. No significant correlation between VAS scale scores and after IAC and of CHIPPS both before and during IAC and respectively of age, weight, sex, application of ice spray, application of distraction techniques before the execution of the procedure, number of infiltrated joints. Significant correlation between VAS before and after IAC (RHO Spearman 0.397, p = 0.018), CHIPPS before and during IAC (RHO Spearman 0.599, p ≤ 0.0001). Highly significant correlation coefficient between VAS and CHIPPS before IAC (RHO Spearman 0.6, p = 0.0001) and between CHIPPS during IAC and VAS after IAC (RHO Spearman 0.403, p <0.05). Significant difference between CHIPPS before and after IAC (Wilcoxon Ranks Signed Test, R = 85, p <0.0001), not between VAS before and after IAC (R = 83, p = 0.62).

Conclusion: In our study the intensity of pain would seem exclusively subjective, in fact it does not depend: on age, number of IAC, on the application of distraction techniques and application of ice spray. Anyway the protocol that we used seems to be effective on pain control (VAS and CHIPPS scale respectively and after and during IAC: m ± sd and M. <4 points) and it can be performed on outpatients safely without an anesthetic procedure. Our results encourage to expand the series with a future prospective trial.

REFERENCES


AB0953 EAR INVOLVEMENT IN PATIENTS AFFECTED BY JUVENILE IDIOPATHIC ARTHRITIS

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Background: Few clinical studies in pediatric patients have shown a possible link between hearing loss and Juvenile idiopathic arthritis (JIA). It could be related to the involvement of the joints of the ossicular chain as a result of the autoimmune inflammatory process in the middle and inner ear.

Objectives: The aim of this study was to assess the frequency of hearing impairment in patients affected by JIA versus a healthy control group.

Methods: We studied 64 ears of 32 JIA patients (25 girls and 7 boys, mean age 15 years, age range 8-19 years) from June to December 2018. The mean disease duration was 7 years (+/- 4 DS). Polyarticular JIA was diagnosed in 6 patients, oligoarthritis JIA in 19; 5 patients had psoriatic arthritis and 2 spondyloarthritis. The control group consisted of 60 ears of 30 healthy children, sex and age-matched. Patients with previous otitis media at least 3 months and/or ear surgery were excluded. The study was approved by the local ethics committee and parents and/or patients signed their informed consent. All subjects underwent
audiological examination involving otomicroscopy, audiometry, tympanometry and stapedius reflex. Rheumatologic evaluation included joint examination with application of a measure of functional ability (disability) using the Childhood Health Assessment Questionnaire (CHAQ). The investigators were blinded about JIA type, severity, duration, and treatments of the patients.

Results: 11/32 (34%) JIA patients had abnormal audiological exam. Hypoacusia was significantly more frequent (p<0.05) in JIA patients (15/64 ears=23%) respect to the control group. In particular, hypoacusia was associated to psoriatic arthritis (6/15 ears). Conductive hearing loss was detected in 12/15 involved ears, while sensorineural type in 3/15. In the JIA group, according to the Jerger classification for tympanometry, abnormal findings were observed in 7 ears. The stapedius reflexes were absent in only one patient (3%). JIA patients with hypoacusia had a greater CHAQ (0.4+/-0.3) than JIA patients with normal audiometry (0.18+/-0.29).

Conclusion: The presence of hearing impairment and/or abnormal tympanogram suggests early involvement of the tympanic-ossicular complex, especially in patients with psoriatic arthritis. These findings could be a marker of the JIA activity. Therefore, it is advisable that JIA patients perform periodic audiological examination to early detect eventual hearing impairment, in order to prevent hearing loss in adult age.

REFERENCES

Disclosure of Interests: None declared

AB0954 PEDIATRIC RHUPUS A RARE OVERLAP SYNDROME: CASE SERIES OF MEXICAN CHILDREN’S HOSPITAL FEDERICO GOMEZ

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Background: Rhupus is an overlap syndrome of rheumatoid arthritis and systemic lupus erythematosus (SLE) in adult patients. Its pediatric presentation is very rare, the presentation of both juvenile idiopathic arthritis (JIA) and SLE as a clinical manifestation of the same patient has aroused different theories being the most accepted a true overlap between SLE and JIA. To diagnosis a patient with Rhupus present with clinical symptoms of JIA and SLE with positive ANA, antiDNA or antiSm, associated with clinical symptoms of JIA.

Objectives: To describe disease features and adherence to the follow-up and visits. To describe disease features and adherence to the follow-up and visits.

Methods: We present a case series of 4 patients diagnosed with Rhupus. We describe the demographic characteristics, clinical presentation, serological finding, the criteria for the diagnosis of SLE (ACR 1997) and JIA (ILAR 2001) and the treatment installed

Results: We describe four patients with Rhupus, the medium age at diagnosis was 12.5 years, and it was more common in female 3:1.

Three presented joints manifestations, integrating an initial JIA diagnosis. The evolution to an overlap syndrome took an average time of 19 months. The main symptom at diagnosis was erosive arthritis, polyarticular, morning stiffness and decreased joint range of motion. Three patients met 6 classification ACR 1997 criteria for SLE. All of the patients met ILAR 2001 criteria for JIA diagnosis. The four patients were treated with multitarget treatment. Joint manifestations were treated with methotrexate, and kidney and neurological manifestations with MFM and IV CFM. One patient required etanercept therapy for persistent joint disease.

Abstract AB0954 Table 1. Demographic and clinical characteristics

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All of the patients presented with elevated acute phase reactants, positive ANA, antiDNA and antiCCP. Two patients had positive antiSm antibody and three presented with positive RF

Disclosure of Interests: None declared

AB0955 TRANSITIONAL CARE: A SINGLE CENTER ITALIAN EXPERIENCE

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Background: Transitional care from paediatrics to adults is an important step in the growth of the adolescent patients. One of the final goals is to guarantee the continuity of healthcare, increasing compliance in treatment and visits.

Objectives: To describe disease features and adherence to the follow-up in rheumatic patients that were transferred from Paediatric Clinic to our adult department.

Methods: From May 2016 to May 2018 the transition has been performed with a visit in presence of both specialists and 28 patients were evaluated. For juvenile Idiopathic Arthritis (JIA) we registered: category of
Table 1 Cutoff of disease activity: JADAS10* and DAS28-CRP**

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<th>Cutoff</th>
<th>JADAS10 (for Oligoarthritis)</th>
<th>DAS28-CRP</th>
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<td>Low activity</td>
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<td>≤2.6</td>
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<td>Moderate activity</td>
<td>1.5-4</td>
<td>2.5-8.5</td>
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<td>High activity</td>
<td>&gt;4</td>
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Results: Between May 2016 and May 2018, 28 patients were enrolled (6 male, 22 female); mean age at diagnosis was 8.1 years (range 1-6 years); mean age at transition was 18.5 years (range 17-21 years). Twenty patients had a diagnosis of JIA, 3 of Undifferentiated Connective Tissue Disease, 1 Dermatomyositis, 1 Systemic Lupus Erythematosus, 1 Takayasu Arteritis, 1 Morphea, 1 Raynaud’s phenomenon.

Among JIA, 6 (30%) were Persistent Oligoarthritis, 4 (20%) Extended Oligoarthritis, 8 (40%) Polyarthritis (RF negative), 1 (5%) Psoriatic Arthritis, 1 (5%) Enthesitis Related Arthritis. Five patients (25%) had history of uveitis. Treatment during the paediatric follow-up period are summarized in table 2. At the time of first evaluation in adult department, 2 patients (10%) were on treatment with systemic steroids (5mg/day), 6 (30%) with methotrexate, 2 (10%) sulfasalazine, 1 (5%) with hydroxychloroquine, 1 (5%) leflunomide; 10 patients (50%) were on treatment with bDMARDs (6 adalimumab, 3 etanercept, 1 infliximab). Mean JADAS10-CRP was 3.8 (range 0-17, SD 5.8) as mean DAS28-CRP was 1.65 (range 0.96-3.44, SD 0.72). In 7 patients, disease activity assessed with JADAS10 was moderate-high as it resulted low-absent using DAS28-CRP. The rate of patients classified as having moderate-high activity was significantly different using the two index (35% using JADAS10 vs 5% using DAS28-CRP, p-value 0.044).

Until 2016, 6 of 44 (11%) patients were lost to follow-up while in the period between May 2016 and May 2018 no patients were lost (11% vs 0; p-value 0.042).

Conclusion: Disease activity seems to be underestimated using DAS28-CRP as compared with JADAS10-CRP. This could be due to the more frequent involvement of ankles and feet (that are not included in DAS28-CRP) in JIA. The adherence to follow up was greater in patients whose transition was performed in presence of the two Specialists.

Disclosure of Interests: Francesca Crisafulli: None declared, Marco Cattalin: None declared, Francesca Ricci: None declared, Giada Maffeis: None declared, Franco Franceschini: None declared, Angela Tincani Consultant for: UCB, Pfizer, Abbvie, BMS, Sanofi, Roche, GSK, AlphaSigma, Lilly, Jannsen, Cellgene, Novartis, Micul Frassi: None declared

She is the first born of a 51-year-old father and 40-year-old mother, non-consanguineous parents, at full term, and has a history of early hypotonía, psychomotor developmental delay and failure to thrive. Physical exam revealed arthritis of both ankles, the right knee and the MCP joint of the left thumb. We noted loose joints, high-arched palate and facial dysmorphism (hypertelorism, large protruding ears, flat nose and short philtrum). Body weight and height were at -3SD. Intellectual disability was mild. Laboratory tests showed slightly increased ESR (35mm at first hour) with positive ANA (+1/1000) and negative RF and anti-CCP. Karyotype is 46XX with deletion of the short arm of chromosome 18. Both parents had normal Karyotypes. MRI of the brain showed cortical atrophy and periventricular leucomalacia.

Ophthalmic screening detected bilateral anterior uveitis.

The patient was treated by AINS and methotrexate along with topical ophthalmic steroids. 6 months after treatment, the child had complete regression of uveitis and arthritis.

Results: This case of de-novo 18p deletion is associated to oligoarticular JIA with uveitis. According to our knowledge, there have only been 2 published cases of juvenile inflammatory arthritis with 18p deletion although 5 other cases were reported in association to other chromosome 18 abnormalities (deletion of long arm and ring). Few reports of adult-onset arthritis with monosomy 18p are available.

The exact explanation of this association is still unclear. As gene loss is a major factor in the pathogenesis of inflammation, this presentation might be related to deletion of PTPN2, a gene that has been associated to rheumatoid arthritis. PTPN2 encodes Protein Tyrosine Phosphatase Non-receptor type 2 and is located in the short arm of chromosome 18. PTPN2-deficiency stimulates T follicular helper cell and B cell responses, thus promoting autoimmune reaction. Of the 67 genes in 18p, only around 12 (of which PTPN-2) are responsible of a phenotype when hemizygous. Further genetic studies are needed to better elucidate the role of all involved genes in the pathogenesis of inflammation in monosomy 18p.

Conclusion: In addition to skeletal deformities such as kyphosis and feet deformities, children with 18p deletion should be screened for inflammatory arthritis.

REFERENCES

Disclosure of Interests: None declared

AB0057

ATYPICAL PRESENTATION AND EARLY RECURRENCE OF KAWASAKI DISEASE IN A FEMALE INFANT: CASE REPORT

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Background: Kawasaki Disease (KD) is the second most common vasculitis in the pediatric population and the leading cause for pediatric acquired heart disease in developed countries. It is commonly diagnosed in the Mexican pediatric population, epidemiology in this country is not established, since cases are not usually reported to the healthcare system. The clinical features are quite variable, but diagnosis and prompt treatment will decrease morbidity and mortality. Coronary artery aneurysms are the most common complication, which represent the leading cause of acute coronary syndrome before 40 years of age. Recurrence of KD is estimated to be around 3% in Japanese patients and 1% in the United States, nevertheless, this data in Latin-American children is unknown. It usually affects patients before reaching 3 years old and within 2 years of the initial attack, presenting with an abrupt onset and higher complication rates, requiring aggressive workup, treatment and follow-up.

Objectives: To review an atypical presentation of KD and early recurrence in a 7-month-old female.

Methods: We present a 7-month-old female diagnosed with KD at 48 days old. She presented to the emergency unit with irritability, high and persistent fever and acholia. During workup, she was found with cholestasis and gallbladder hydrops. Negative CSF, blood and urine cultures were documented, and the patient was hospitalized, and fulfilled the KD criteria. The cardiac ultrasound revealed coronary abnormalities: a RCA of 2.8mm (Z-SCORE +4.79), LCA of 3.3mm (Z-SCORE +5.69) and LAD of 2.4mm (Z-SCORE +4.25), which fit into classification 3 and 4, as small and medium aneurysms, according to AHA 2017. Immunoglobulin (2g/kg) and aspirin (80mg/kg) were administered and she was discharged 36 hours after the IVIg infusion, without fever and normal ESR. 30 days later the coronary abnormalities showed RCA of 2.0mm (Z-SCORE +2.3), LCA of 3.0mm (Z-SCORE +6), LAD 2.3mm (Z-SCORE +2.9). Six months later, she presented fever for 6 days, irritability and polymorphous rash. On physical exam BCGilis, normal-suppurative conjunctivitis and pallor in hands and feet, elevated CRP and ESR, leukocytosis, thrombocytosis and sterile leukocyturia. Echocardiography reported RCA od 2.4mm (Z-SCORE +4.8), LCA of 3.1 (Z-SCORE +4.2) and LAD of 2.3mm (Z-SCORE +3.2), diagnosing KD recurrence, admitting the patient for IVIg and aspirin administration.

Results: The patient was treated with IVIg and aspirin. Follow-up by Cardiology determined improvement of Z-Scores. Recurrence occurred with worsening of the cardiac abnormalities. Cardiac prognosis is importantly affected due to the atypical age, vascular abnormalities and repeated vasculitic process. Rheumatologic consult should be considered since disease like Takayasu Arteritis, Polyanarteritis Nosa and ADA2 deficiency need to be ruled out.

Conclusion: KD needs prompt diagnosis and treatment due to the potential consequences when delayed. Clinical suspicion is important due to the possible atypical presentation. As with this patient, age, gender and presentation are not exclusive. Despite adequate treatment, recurrence and worsening of the cardiac abnormalities occurred. Both KD events before 1 year old and with atypical presentations. Rheumatologic and cardiac follow-up need to be stringent through lifetime, to determine pharmacologic treatment, as well as physical activity and reproductive counseling.

REFERENCES

Disclosure of Interests: None declared

AB00958

PEdiatric BEChEt’s Disease wIth sinuUs venous thromboSIs: thRee CenTer experIence From tUrkey

Sezcan Demir1, Ceyhun Acar2, Özge Basaran2, Erdal Sag3, Kader Karlı Oğuz4, Yelda Bilginer4, Erdal Unsal4, Seza Özen3, 1Hacettepe University Faculty of Medicine, Pediatric Rheumatology, Ankara, Turkey; 2Dokuz Eylül University Faculty of Medicine, Pediatric Rheumatology, Ankara, Turkey; 3Ankara Child Health and Disease Hematology Oncology Training and Research Hospital, University of Health Sciences, Pediatric Rheumatology, Ankara, Turkey; 4Hacettepe University Faculty of Medicine, Radiology, Ankara, Turkey

Background: Behçet’s disease (BD) is an autoinflammatory disorder which may present with multi-systemic involvements including the vascular, cutaneous, articualar, gastrointestinal, and/or central nervous systems (CNS). CNS involvement appears in two main groups: parenchymal or non-parenchymal. Neurological symptoms in children and adolescents can be confused with many other disorders and may be the initial symptom of BD.

Objectives: To report our experiences of the juvenile Behçet’s Disease patients with cerebral venous sinus thrombosis (CVST) and to review previous studies reporting the clinical characteristics and outcomes of Juvenile Behçet’s Disease with CVST.

Methods: The patients who met Pediatric Behçet’s Disease (PDBD) classification criteria for juvenile Behçet’s Disease from 3 referral centers in Turkey were reviewed retrospectively. Disease activity was assessed by BD current activity form (BDCAF). A systematic review of literature of all published data was conducted.
Results: The study group consisted of 12 juvenile BD patients with CVST. At the time of CVST diagnosis, the most common symptom was headache (75%), followed by vomiting (25%), blurred vised (16.6%), and disturbances in eye movements (16.7%). Six (50%) patients presented with sinuses venous thrombosis as an initial symptom. Transverse sinus was the most frequently affected sinus (9/12, 75%) followed by superior sagittal sinus (8/12, 66.6%) and sigmoid sinus (1/12, 8.3%). The median (minimum-maximum) BDCAF was 6 (5-8). Four children (33.3%) had another venous thrombosis apart from CVST. All patients received pulse methylprednisolone for three consecutive days continued with oral prednisolone. Steroid treatment was tapered and discontinued minimum in six months. Eleven patients received azathioprine concomitant to steroid treatment at the time of CVST. All the patients received anticoagulant therapy concomitantly. Only one patient had relapse. Median (min-max) follow-up period was 4 years (1-10). In the literature review, we identified nine articles, describing 35 pediatric CVST patients associated with BD. Thirty patients achieved remission, while five patients had residual neurologic deficit.

Conclusion: Further multicenter studies with more patients and prospective follow-up may help us to understand the whole spectrum in these patients.

REFERENCES


Disclosure of Interests: Selcan Demir: None declared, Ceyhun Acan: None declared, Özge Basaran: None declared, Erdal Sag: None declared, Kader Karlıoğlu: None declared, Yelda Bilginer: None declared, Erbil Unsal Grant/research support from: Novartis, AbbVie, Roche, Koçak Pharma, Speakers bureau: Novartis, AbbVie, Roche, Koçak Pharma, Seza Özen Consultant for: Seza Özen is receiving consultancy fees from Novartis, Speakers bureau: Roche


AB0959

EXEMPLARY RESPONSE TO TOCILIZUMAB IN PEDIATRIC ONSET RAPTORARY TAKAYASU ARTERITIS: CASE SERIES OF THREE PATIENT

Ferhat Demir, Betül Sözeri, University of Health Sciences, Umraniye Training and Research Hospital, Pediatric Rheumatology, Istanbul, Turkey

Background: Takayasu arteritis (TA) is a idiopathic and rarely seen chronic systemic vasculitis that affect the aorta and its major branches. Stenosis, occlusion and aneurysms may develop in large arteries in the setting of granulomatous arteritis (1). The first purpose in patients with TA after diagnosis is to prevent the progression of vascular lesions with medical treatment. Used as a first choice in medical treatment, steroids and steroid-sparing immunosuppressive agents, may sometimes fail to prevent to progression of the disease. Interleukin (IL)-6, which synthesize from activated dendritic cells, is one of the main cytokine in the development of panarteritis in TA. Tocilizumab (TCZ), an anti-IL-6 receptor antibody, has been shown to be used as an effective treatment in many refractory adult TA patients (2).

Objectives: We have presented our experience with TCZ treatment in three children with refractory TA.

Methods: We reviewed three cases of childhood TA diagnosed between 2016-2018. These patients were successfully treated with TCZ that started due to refractory disease.

Results: The first patient, 15 year-old girl, presented with fever, headache and abdominal pain. Physical examination showed sputum murmur in interscapular area and abdominal tenderness. The C-reactive protein (CRP) level was 4.7 mg/dL (n: <0.5 mg/dL) and the erythrocyte sedimentation rate (ESR) was 78 mm/h (n: <20 mm/h). Doppler ultrasound imaging showed wall thickening in bilateral carotid arteries. The angi-Ct imaging revealed that 70% stenosis in the bilateral renal arteries and partial stenosis in the mesenteric artery. Methylprednisolone treatment was started (30 mg/kg/d x 3 days). Maintenance treatment consisted of prednisone (1 mg/kg/d), methotrexate and azathioprine. Her complaints improved rapidly and the acute phase reactants decreased. However, the patient relapsed while tapering the corticosteroids.

The second patient was diagnosed with TA in 2012 after the complain of chest pain and finding of hypertension. MRI angiography revealed wall irregularities and stenosis in the descending aorta and dilatation in the ascending aorta. CRP and ESR levels found high. The patient was followed up with glucocorticoid and azathioprine treatment. After four years of follow-up, relapse of the disease was observed with symptoms of fever, chest and back pain.

The third patient presented with fever, abdominal pain, arthralgia in the left elbow and arthritis of the left knee, and was diagnosed with TA two years ago. His CRP and ESR levels were found elevated. The angi-Ct imaging revealed that 70% stenosis in the 4 cm segment of the abdominal aorta, 70% stenosis in the right renal artery, 50% stenosis in the left renal artery and 90% stenosis in the origin of celiac trunk and superior mesenteric artery. Despite the given bolus methylprednisolone and methotrexate therapy, there had not seen any improvement in disease activity. Tocilizumab was started at 8 mg/kg monthly in all three patient and they achieved complete clinical and laboratory remission.

Conclusion: These cases demonstrate that the TCZ treatment has been shown to be successful option in TA patients resistant to conventional immunosuppressive therapies.

Disclosures: The authors have declared no conflicts of interest. Informed consent form was obtained from patients and their legal guardians.

REFERENCES


Disclosure of Interests: None declared


AB0960

THE HELIOS (HACETTEPE UNIVERSITY ELECTRONIC RESEARCH FORMS) REGISTRY: USE OF BIOLOGIC DRUGS IN AUTOINFLAMMATORY DISEASES

Selcan Demir1, Ezgi Deniz Batu1, Fuat Akalı2, Erdal Sag3, Ummusen Kaya Akca1, Elif Anılangoğlu2, Emli Aliyev3, Kübra Yüksel2, Armağan Keskin2, Yelda Bilginer1, Seza Özen1,1Hacettepe University Faculty of Medicine, Pediatric Rheumatology, Ankara, Turkey, 2Hacettepe University Faculty of Engineering, Computer Engineering, Ankara, Turkey, 3Hacettepe University Faculty of Medicine, Pediatrics, Ankara, Turkey

Background: Autoinflammatory diseases (AID) are characterized by a dysregulation of innate immunity leading to uncontrolled inflammation. The treatment in AID is critical to control the disease activity, to prevent complications, and to improve the health-related quality of life. Biologic drugs have revolutionized the treatment and outcomes in AID.

Objectives: Herein we aim to present the clinical characteristics of children to whom biologic drug therapy was initiated for the management of AID.

Methods: A web-based registry called the Helios Registry (Hacettepe university electron Research forms) has been formed to evaluate the data of all children on biologic treatment. We have been enrolling patients since August 2018 retrospectively and prospectively. We have analyzed the data about the general characteristics of the patients, treatment, the biologic drug used, and adverse effects. Only the patients with the following diagnoses were included: systemic juvenile idiopathic arthritis (SJIA), familial Mediterranean fever (FMF), cryopyrin associated periodic syndrome (CAPS), and chronic recurrent multifocal osteomyelitis (CRMO).

Results: Of 60 patients included, 19 had FMF (31.7%), 24 had SJIA (40%), 10 had CAPS (16.7%), and 7 had CRMO (11.7%). Their mean age was 10.7 (2-20) years old and disease duration was 2.8 (0-6) years, at the time of biologic drug initiation. 58.3% were currently on canakinumab, 20% anakinra, 10% tocilizumab, 10% etanercept, and 1% adalimumab. 63.3% of our patients had previously used at least one other biologic drug. The rate of glucocorticoid use before biologic treatment was 56.6%. The median duration of glucocorticoid treatment after initiating biologic drugs was 7.4 months. 56 (93%) patients achieved remission on biologic therapy. There were 15 patients (25%) who received tuberculosis prophylaxis due to positive tuberculin skin test (diameter≥10 mm) and there was no QuantiFeron test positivity. Thirteen adverse events (AE) had been noted. 2 of them were serious events as anaphylaxis due to tocilizumab infusions. The rest of the adverse events were mild thrombocytopenia (n=2), varicella infection (n=1), and local side effects (n=8).

The median number of the infections per year was one and there were cytopenia (n=2), varicella infection (n=1), and local side effects (n=8). 2 of them were serious events as anaphylaxis due to tocilizumab infusions. The rest of the adverse events were mild thromboctopenia (n=2), varicella infection (n=1), and local side effects (n=8).

There was no Quantiferon test positivity. Thirteen adverse events (AE) had been noted. 2 of them were serious events as anaphylaxis due to tocilizumab infusions. The rest of the adverse events were mild thromboctopenia (n=2), varicella infection (n=1), and local side effects (n=8).
Conclusion: The most commonly prescribed biologic drugs were IL-1 inhibitors especially for patients with IL-1-mediated AID (RMF, CAPS, and SJIA). The biologic treatment in AID is effective and there were no serious side effects.

REFERENCES

Disclosure of Interests: Selcan Demir: None declared, Ezgi Deniz Batu: None declared, Fuat Akal: None declared, Erdal Sag: None declared, Ummusen Kaya Akca: None declared, Elf Arslanloju: None declared, Emil Alyev: None declared, Küber Yüksel: None declared, Armağan Keskin: None declared, Yelda Bilginer: None declared, Seza Özen Consultant for: Seza Özen is receiving consultancy fees from Novartis, Speakers bureau: Roche


AB0961 ADVERSE EVENTS ASSOCIATED WITH ANTI-TNF-ALPHA THERAPY IN PEDIATRIC RHEUMATIC DISEASES
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Background: In recent years, the biologic drugs has led to a dramatic change in the management of rheumatic diseases. The most commonly used molecules are TNF-α antagonists among biologic treatments in pediatric age (1). The anti-TNF-α agents used in childhood are; etanercept (a fusion protein of the TNF-α receptor), infliximab (a chimeric monoclonal antibody) and adalimumab (completely human monoclonal antibody). As a result of the increasing use of anti-TNF-α agents in recent years, adverse events reports have also increased (2). We assessed the prevalence of adverse events (AEs) in a single pediatric referral center for chronic rheumatic diseases.

Objectives: The aim of this study was to evaluate the adverse events that associated with anti-TNF-α therapy in children with rheumatic disease.

Methods: This was cross-sectional study conducted University of Health Sciences, Umraniye Training and Research Hospital, Department of Pediatric Rheumatology, in Turkey. We retrospectively reviewed the patients with a diagnosis any of pediatric rheumatic disease whom treated at least 3 months with an anti-TNF-alpha agents (etanercept, infliximab, adalimumab), between June 2016 and January 2019. Adverse events that develop after anti-TNF-α therapy are recorded. AEs were categorized and graded based on the Common Terminology criteria for AEs (CTCAE). Grades 3-5 were considered severe AEs.

Results: We evaluated 131 patients who were treated with anti-TNF-α drugs; 110 with juvenile idiopathic arthritis (JIA)(27 of with uveitis) 7%, 5 with Behçet disease; 110 with juvenile idiopathic arthritis (JIA)(27 of with uveitis) 83%, 10 with idiopathic uveitis 4%, 4 with adeno-sine deaminase deficiency%3, and 2 with juvenile sarcoidosis%. The study included 74 females and 57 males (FM: 1.29:1) and the mean age of the patients was 12.8 years. Of the patients, 106 had used only 1, 21 had two different and 4 had 3 different anti-TNF-alpha biologic treatments. A total of 160 different anti-TNF-alpha experiences had in 131 patients.

A total of 333.4 patient-years (PYs) were included: 136 PYs-63 patients for etanercept (2.15 patient/year), 134 PYs-68 patients for adalimumab (1.97 p/y) and 63.4 PYs- 29 patients for infliximab (2.18 p/y). During follow-up, 44 patients (33.5%) experienced at least one AEs. 14 of them (10%) were recorded as SAEs. 17 of the AEs were show up after adalimumab, 16 were etanercept and 11 were infliximab. The most common AEs were found; local reactions, increased infection frequency and PPD positivity in follow up, respectively. The SAEs that observed were; anaphylactoid reactions (n=5), uveitis (n=3), pneumonia (n=3), TAILS (n = 2) and vasculitis (n=1).

Conclusion: Here in, we presented safety data of anti-TNF-alpha drugs in pediatric patients. Although the high prevalence of AEs was observed, when anti-TNF-α discontinuation, AEs were mostly not persistent and not mortal.

REFERENCES

Acknowledgement: We are grateful to all participating children and their families. Ethics committee approval was received from the Institutional Review Board of Umraniye Training and Research Hospital. All the participants and their legal guardians were informed, and their written consent was obtained. Disclosure of Interest: None Declared

Disclosure of Interests: None declared


AB0962 UPDATE FOR THE CLINICAL PRACTICE: INTEGRATED, EVIDENCE-BASED APPROACH FOR THE MANAGEMENT OF JUVENILE SPONDYLOARTHROPATHIES
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Background: Juvenile onset spondyloarthropathis (SpA) is a heterogeneous group of human leucocyte antigen (HLA) –B27 associated inflammatory syndromes that affect children and adolescents under the age of 16 years No specific recommendations for the treatment of juvenile spondyloarthritis have been established. Important differences exist between spondyloarthritids in children and adults, supporting the need for pediatric-specific recommendations.

Objectives: To set recommendations for the management of children and adolescents with spondyloarthritids.

Methods: Searching Medline for Juvenile spondyloarthritids management was done. A systematic literature search was conducted to collect the existing recommendations. The studies involved line of treatment for Juvenile SpA & adult SpA. These included 2011 ACR recommendations for the treatment of JIA and the 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritids.

Results: NSAIDs have been shown to improve symptoms, reduce inflammatory lesions and may slow spinal radiographs progression with continuos use. Glucocorticoid injections directed to the local site of musculoskeletal inflammation may be considered. Sulfasalazine may be considered in patients with peripheral arthritis. Initiation of a (tumor necrosis factor inhibitor (TNFi) was recommended for patients with active saccroiliac arthritis who have received an adequate trial of NSAIDs. Also, it should be initiated to those who fail to respond to synthetic disease modifying anti-rheumatic drugs (DMARD). If TNFi therapy fails, switching to another TNFi should be done. If a patient is in sustained remission, tapering of a biological DMARD can be considered.

Conclusion: These guidelines provide up-to-date guidance on the management of patients with juvenile SpA, based on combining evidence and expert opinion.

Disclosure of Interests: None declared.


AB0963 ROLE OF THYROID HORMONES IN JUVENILE IDIOPATHIC ARTHRITIS
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Background: The frequency of autoimmune thyroid disease have been reported in adults with systemic autoimmune diseases. However, little is
known about the association between those diseases and rheumatic disorders during childhood, such as juvenile idiopathic arthritis (JIA).

**Objectives:** Our objective was to evaluate the correlation between the thyroid function and the clinical presentation in children with juvenile idiopathic arthritis.

**Methods:** Case series of 7 pts (5 boys, 2 girls) with initial rheumatologic symptoms. Therefore, there in 5 pts, and systemic onset JIA onset of first symptoms until 10 years. The time-interval from the onset of first symptoms until diagnosis was 4 years. Mean age at CD onset was 12.7 ± 3.98 yrs, varying from 5 to 17 yrs.

**Results:** Fifty-one of the cases were classified as oligoarticular, thirty-one as seronegative polyarticular, two as seropositive polyarticular, eleven as systemic, and two as enthesis related- juvenile idiopathic arthritis.

No cases of overt clinical and biochemical hypothyroidism were found among children with juvenile idiopathic arthritis. On opposite, mean thyroid free T3 levels were higher in 36.4% of cases and free T4 in 29.7% cases.

**Conclusion:** These data seem to suggest careful monitoring of thyroid function and thyroid autoantibodies just in children with juvenile idiopathic arthritis presenting clinical symptoms of thyroid involvement.

**REFERENCES**


**Disclosure of Interests:** None declared

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Conclusion: Manifestations of sarcoidosis vary significantly across the paediatric age spectrum. While EOS is a known juvenile idiopathic arthritis mimicking condition, it is important to recognize the diagnostic difficulties that prolonged the diagnosis by years in 4/7 patients.

REFERENCES

Disclosure of Interests: None declared

AB0966

PROPOSAL OF OUTCOME MEASURES TO BE USED ON A 12-MONTH OPEN LABEL DRUG TRIAL IN JUVENILE SYSTEMIC SCLERODERMA: RESULTS OF THE 3RD CONSENSUS MEETING IN HAMBURG DECEMBER 2018

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Background: Juvenile systemic sclerosis (jSSc) is an orphan disease, associated with high morbidity and mortality. New treatment strategies are much needed. To develop an open label drug trial for the treatment of jSSc patients, it is necessary to clearly define how to evaluate outcomes in this disease, which are currently not existing. A group of experts in jSSc has met annually and worked to develop an index to evaluate outcomes in this disease.

Objectives: The aim of our third consensus meeting was to establish the domains and the items that should be assessed in a clinical drug trial in jSSc.

Methods: In the consensus meeting 26 jSSc international experts with various specialties participated (22 voted). In a nominal group technic, moderated by DEF, was used to develop the outcome measures. Agreement was defined if 80% or more of the participants approved an item.

Results: Domains and items suggested in the 2017 consensus meeting were reconsidered and selected or rejected during the 2018 meeting, as were additional domains/items (Table).

<table>
<thead>
<tr>
<th>Domain</th>
<th>Item</th>
<th>voted for</th>
<th>yes/nominator</th>
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<tbody>
<tr>
<td>Global Disease Activity</td>
<td>Physician global of disease activity</td>
<td>22/22</td>
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<td></td>
<td>Change in HAQ/CHAQ- DI</td>
<td>22/22</td>
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<td></td>
<td>Scleroderma HAQ</td>
<td>22/22</td>
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<tr>
<td>Skin</td>
<td>Change in Modified Rodnan Skin Score</td>
<td>22/22</td>
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<tr>
<td>Raynaud Phenomenon</td>
<td>Scleroderma HAQ question regarding</td>
<td>22/22</td>
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<tr>
<td>Digital ulcerations</td>
<td>DUCAS Score</td>
<td>22/22</td>
<td></td>
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<tr>
<td>Musculoskeletal System</td>
<td>Juvenile idiopathic arthritis Definition of active joint</td>
<td>22/22</td>
<td></td>
</tr>
<tr>
<td>Cardiac Involvement</td>
<td>Left ventricular ejection fraction</td>
<td>22/22</td>
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<td>Development of clinically significant</td>
<td>22/22</td>
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<td></td>
<td>arrhythmia as a sign of non-response</td>
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<td>Pulmonary Involvement</td>
<td>FVC</td>
<td>22/22</td>
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<td></td>
<td>age-defined DLCO in all trials</td>
<td>20/22</td>
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<tr>
<td>Renal</td>
<td>New occurrence of renal crisis</td>
<td>22/22</td>
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<tr>
<td>Gastrointestinal Involvement</td>
<td>Body mass index</td>
<td>22/22</td>
<td></td>
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<td></td>
<td>Scleroderma HAQ - Gastrointestinal section</td>
<td>22/22</td>
<td></td>
</tr>
<tr>
<td>Global health/Health related Quality of Life (QOL)</td>
<td>QOL instrument should be used</td>
<td>18/18</td>
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</table>

Conclusion: We reached consensus on domains and items which should be assessed in an open label 1 year clinical jSSc trial. We also listed research items which should be assessed but should not currently be included as an outcome in such a trial.

Disclosure of Interests: Ivan Foeldvari Consultant for: Chugui, Novartis, Kathryn Tokor: None declared, Lusine Ambartsumyan: None declared, Jordi Anton Grant/research support from: Grant/research support, consultant or speakers bureau from AbbVie, Alexion, Bristol-Myers Squibb, Che-moCentrx, Gebro, GlaxoSmithKline, Novartis, Novimmune, Pfizer, Roche, Sanofi and Sobi, Consultant for: Grant/research support, consultant or speakers bureau from AbbVie, Alexion, Bristol-Myers Squibb, Chemocentrx, Gebro, GlaxoSmithKline, Novartis, Novimmune, Pfizer, Roche, Sanofi and Sobi, Speakers bureau: Grant/research support, consultant or speakers bureau from AbbVie, Alexion, Bristol-Myers Squibb, Chemocentrx, Gebro, GlaxoSmithKline, Novartis, Novimmune, Pfizer, Roche, Sanofi and Sobi, Christian Beyer: None declared, Michael Blakley: None declared, Tamas Constantin: None declared, Patricia Costa Reis: None declared, Megan Curran: None declared, Maurizio Cutolo: None declared, Francesco Del Galdo: None declared, Christian Henter Grant/research support from: GlaxoSmithKline, Inventiva, CSF Behring, Consultant for: Roche, Genentech, Actelion, GlaxoSmithKline, Sanofi Aventis, Inventiva, CSL Behring, Boehringer Ingelheim, Bayer, Kim Fligelstone: None declared, Bernd Hinrichs: None declared, Antonia Höger: None declared, Francesca Ingeloni: None declared, Ozgur Kasacopur: None declared, Suzanne Li: None declared, Dana Nemcova: None declared, Catherine Orteu: None declared, Clarissa Pilkington: None declared, Vanessa Smith2, Anne Stevens, Brandi Stevens2, Allison Zheng2, Dinesh Khanna3, Danielurst2, 1Hamburger Zentrum für Kinder- und Jugendrheumatologie, Hamburg, Germany; 2Participant of the Hamburg Outcome measure consensus process, Hamburg, Germany

Disclosure of Interests: None declared

AB0967

IS THERE A DIFFERENCE IN PRESENTATION OF FEMALE AND MALE PATIENTS WITH JUVENILE SYSTEMIC SCLERODERMA. AN UPDATE FROM THE JUVENILE SYSTEMIC SCLERODERMA INCEPTION COHORT. WWW.JUVENILE-SCLERODERMA.COM

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Methods: The JSSIC is a prospective multicentre registry of patients with jSSc, who fulfill the adult classification criteria (2), and presented the first non-Raynaud symptoms before 16 years old and were younger than 18 years old at the time of inclusion in the cohort. Patients characteristics at time of inclusion in the cohort were evaluated.

Results: As of 15th of December 2018 120 patients are included in JSSIC. The great majority are female (80%). There were more female patients with CK elevation (29% vs 22%) and more female patients with Gottron papule (25% vs 12%). The mean modified skin score was higher in males (18.6 vs 13.9).

Scleractyly was more frequent in males (90% vs 76%). Active ulceration was present in 33% of males compared to 14% of females (p=0.026). FVC<80% occurred more often in males with 47% compared with 24% in females (p=0.018). Pulmonary hypertension was more

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common in females with 7% compared to 4% in males. Urine sediment changes were more common in males (8% vs 4%). Gastrointestinal involvement was more common in females (37% vs 29%). Contractions occurred more often in males with 62% compared with 46% in females. Tendon friction rub was observed in 21% of males and 3% of females (p=0.001). Physician global scores of disease activity and damage were higher in males with 48 for both assessments compared to 36 and 30 in females.

Conclusion: Male patients with JSSc have a higher severity of disease, as it has been reported in adults.

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Disclosure of Interests: Ivan Foeldvari Consultant for: Chugui, Novartis, Jens Klotsche: None declared, Czgur Kasapcoglu: None declared, Annra Adrović: None declared, Kathrin Török: None declared, Valda Santos-Teixeira: None declared, Flávio R. Sztaijnbok: None declared, Ana Paula Sakamoto: None declared, Ekaterina Alexeeva: None declared, Jordi Anton Grant/research support from: Grant/research support, consultant or speakers bureau from AbbVie, Bristol-Myers Squibb, ChemoCentryx, Gebro, GlaxoSmithKline, Novartis, Novimmune, Pfizer, Roche, Sanofi and Sobi. Kirsten Minden Consultant for: Grant/research support, consultant or speakers bureau from AbbVie, Alexion, Bristol-Myers Squibb, ChemoCentryx, Gebro, GlaxoSmithKline, Novartis, Novimmune, Pfizer, Roche, Sanofi and Sobi. Blanca Bica: None declared, Juergen Brunner: None declared, Cristina Battagliotti: None declared, Lillemor Berntssen: None declared, Monika Moll: None declared, Dana Nemcova: None declared, Simone Appenzeller: None declared, Maria Bica: None declared, Erika Alexeeva: None declared, Jordi Anton Consultant for: AbbVie, Alexion, Bristol-Myers Squibb, ChemoCentryx, Gebro, GlaxoSmithKline, Novartis, Pfizer, Roche, Sanofi and Sobi.

AB0967 INTEGRATED RHEUMATOLOGY AND OPHTHALMOLOGY CARE IN PEDIATRIC AUTOIMUNE UVEITIS – OUTCOME AND EFFECTIVENESS

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Background: Uveitis is an ocular inflammatory disease that may lead to irreversible blindness if not treated early and properly. May be induced by infectious and non-infectious diseases (autoimmune diseases, especially juvenile idiopathic arthritis), or ‘masquerade’ causes. Some uveits are termed “idiopathic”, although autoinflammatory evidence. Treatment effectiveness depends on the accuracy of the ophthalmologic evaluation and the appropriate management, especially when immunosuppressive medications are necessary. (1, 2)

Objectives: To describe the first year experience of the Integrated Ophthalmology and Pediatric Rheumatology Outpatient Clinic in the management of pediatric patients with autoimmune uveitis.

Methods: Retrospective chart review study of twenty-four patients followed up from June 2017 to October 2018. The patients clinical evolution at 0, 3, 6, 9 and 12 months was analyzed.

Results: In this group, 62% were female, and mean age at first appointment and at symptoms onset were 11.7 (2.9 to 17.5) and 7.3 (1.1 to 12) years, respectively. Anterior uveitis was present in 70.8% of the cases, and in 65.6% it was bilateral; cataract or glaucoma was observed in 20.5%. The identified diagnosis during follow-up were: idiopathic autoimmune uveitis in 45.8%, juvenile idiopathic arthritis in 41.6% (20.8% oligoarticular, 16.6% polyarticular, 4.1% associated with enthesitis) and juvenile systemic lupus erythematosus, Kawasaki Disease and Vogt-Koyanagi-Harada syndrome one case of each. Antinuclear antibodies were present in 41% and inflammatory markers in 28.7% patients. At first appointment, 20.5% presented ocular inflammatory activity and 53.3% had sequelae when examined in slit lamp or indirect ophthalmoscopy. Medica-tions used were: topical corticosteroids (61.6%), topical mydriatic (49.2%), oral corticosteroid (41%), methotrexate (41%), etanercept (12.3%), adalimumab (28.7%) and periccular injections of triamcinolone, cyclosporin, tocilizumab, azathioprine (4.1% each). The comparison of the data at inclusion and during follow-up is reported in Table:

At inclusion 3 months 6 months 9 months 12 months
Ocular inflammation(%) 20.5 24.6 12.3 12.3 12.3
Topical Corticosteroids(%) 61.6 32.8 16.4 8.2 20.5
Topical Mydriatic (%) 41 24.6 28.7 20.5 20.5
Oral Corticosteroid (%) 73.8 20.5 12.3 12.3 20.5
Etanercept (%) 12.3 53.3 49.2 36.9 28.7
Adalimumab (%) 20.5 20.5 16.4 16.4 16.4
Others (%) 12.3 4.1 4.1 4.1 4.1
No medication (%) 4.1 8.2 8.2 4.1 4.1

At the end of 12 months, only 12.3% of the patients still had active uveitis. We have also observed a reducing in 66.6% of topical cortico-steroids and 72.2% of oral corticosteroids use during the treatment of uveitis over 12 months.

Conclusion: Considering that before the inclusion, patients were followed independently in each clinic, there was optimization of the treatment and reduction in number of medical appointments after the creation of the integrated outpatient clinic. The interprofessional management teams should be the standard of care for pediatric patients with autoimmune uveitis.

REFERENCES

Disclosure of Interests: None declared

Trouble reading? Contact us for support.
We report the case of idiopathic calcinosis cutis in a young girl.

**Background:**

Calcinosis includes a rare group of disorders characterized by abnormal intracutaneous, subcutaneous, fascial or intramuscular calcium deposits. Idiopathic calcinosis is diagnosed after the exclusion of secondary forms related to trauma, abnormal calcium/phosphorus metabolic disorders, inflammatory processes, neoplasms, connective tissue diseases or renal insufficiency. There are very few cases reported, especially in childhood.

**Objectives:**

We report the case of idiopathic calcinosis cuts in a young girl.

**Methods:**

A 15-year-old female presented an abrupt onset of 2 painful swollen lesions on the left trochanteric region and over the posterior side (76.4% versus 58.4%, $p = 0.001$), although sensitivities were similar at both times. EU LAR/ ACR criteria score $\geq 10$ exhibited greater sensitivity than ACR 1997 (67.4% versus 70.5%, $p < 0.001$) at first visit, but comparable at 1-year, whereas specificity was lower at first visit (67.4% versus 83.2%, $p = 0.004$) and 1-year (58.4% versus 76.4%, $p = 0.002$). A EU LAR/ ACR score $\geq 13$ against a score $\geq 10$, resulted in higher specificity, positive predictive value, and cut-off point accuracy. Compared to SLICC, a EU LAR/ ACR score $\geq 13$ resulted in lower sensitivity at first visit (76.2% versus 89.3%, $p < 0.001$) and 1-year (91% versus 97.5%, $p < 0.008$), but similar specificities at both periods. When compared to ACR 1997, a EU LAR/ ACR total score $\geq 13$, resulted in no differences in sensitivity and specificity at both times.

**Conclusion:**

In this cSLE population, SLICC criteria performed best at first visit and 1-year follow-up. The adoption of a EU LAR/ ACR total score $\geq 13$, against the initially proposed $\geq 10$ score, was most appropriate to classify cSLE in our study. Further studies are necessary to address if SLICC might allow cSLE classification earlier in disease course and be more inclusive of cSLE subjects for clinical studies.

**REFERENCES**


**Disclosure of Interests:** None declared

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of her right elbow. The patient denied any trauma or associated symptoms such as muscle weakness or joint stiffness. On physical examination, a large hard mass was present over her left trochanteric region, with hyperemic skin, and a similar one was palpable over her right elbow.

**Results:** Radiographs of the two sites showed well-defined calcified masses, one (9x5 cm) over the trochanteric region, and the other (3x2 cm) over the posterior aspect of the distal end of the humerus extending up to the elbow. MRI confirmed the presence of calcified intramuscular lesions (Figure 1). Serologic evaluation showed increased levels of CRP and ESR, while autoimmune screening was negative. Calcium/phosphorus metabolism, creatinine kinase, aldolase and ferritin levels were within the normal limits. Therefore, a clinical diagnosis of idiopathic calcinosis was made. After 3 months, the lesion on the elbow had spontaneously reabsorbed, while the other one kept on growing, with 3-4 episodes per month of febrile painful swelling. A CT-guided biopsy was then performed, confirming the diagnosis of calcinosis. No infectious causes were detected. One year later, since there was no local amelioration, the lesion was surgically removed with apparent complete local remission. No other new lesions were detected during the 3 months follow-up period.

**Conclusion:** Idiopathic calcinosis is very rare and no specific medical therapies are available. In our patient no causative factors were identified and thus the diagnosis of idiopathic calcinosis was made. Prognosis seems to be variable, since one lesion resolved spontaneously while the other needed surgical excision.

**REFERENCES**


Abstract AB0972 Figure 1. MRI of the trocanteric region showing calcified intramuscular lesion.

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AB0972

**ARTEFACTUAL SKIN LESIONS: A TRAP FOR RHEUMATOLOGISTS**

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**Background:** Dermatitis artefacta (DA) refers to deliberate and conscious self-inflicted skin lesions to satisfy an unconscious psychological or emotional need. It is an unusual condition often described in women, and rarely reported in children. The disorder is often misdiagnosed and needs to be distinguished from organic illness, Munchausen’s by proxy syndrome, and from illicit, nontherapeutic drugs or overdose of medications.

**Objectives:** We report three paediatric cases with a long medical history characterized by many laboratory and radiological exams, and mistaken etiologies.

**Methods:** Case 1. An 11-year-old female was referred to our Rheumatology Department for a second opinion about a suspicion of Behcet’s disease based on her cutaneous manifestations. Clinical examination was unremarkable except for bluish ecchymoses, and linear cutaneous abrasions and scars located in accessible areas of her skin (Figure 1, Figure 2 and Figure 3). Extensive laboratory tests and radiological exams were normal.

Case 2. A 14-year-old female was admitted to our pediatric hospital for a 1 month history of fever, malaise and multiple purpuric lesions. The patient referred a 3 year history of similar recurrent episodes characterized by abrupt onset of fever, arthralgia and purpuric lesions for which she already received the diagnosis of urticarial vasculitis. The girl was in good general conditions, without fever. Violaceous ecchymotic lesions were evident on her left forearm. Exhaustive laboratory tests, chest X-ray, and abdomen ultrasound were within normal limits.

Case 3. A 14-year-old female was referred to our Pediatric Rheumatology department for a 6 month history of musculoskeletal pain, recurrent shoulder and hip dislocations, and spontaneous ecchymosis on her neck and face. Except for joint hypermobility (Beighton score 7/9), physical examination was normal. At a careful orthopedic evaluation and after shoulder and hip imaging the history of dislocations appeared to be inconsistent. Blood and radiologic tests, cardiological and genetic evaluations for Ehler-Danlos syndrome were negative.

**Results:** In Case 1, dermatitis artefacta was suspected and the patient was referred to our mental health colleagues that confirmed a severe psychological stress in a basal condition of psychiatric disorder. In Case 2, an in-depth psychological evaluation highlighted a depressive status for personal and familiar suffering. The patient was therefore referred to our mental health department for assessment and management. In Case 3, eventually a psychiatric interview oriented the diagnosis to a major depressive disorder.

**Conclusion:** DA is a rare condition that should be evaluated in the differential diagnosis, in the presence of unexplained cutaneous lesions without an apparent identifiable cause. Association with various psychological disturbances is the mainstay for this diagnosis, and a careful psychiatric history represents the essential diagnostic key to identify this disorder.

**REFERENCES**


ATYPICAL KAWASAKI DISEASE SHOCK SYNDROME

Present and discuss a rare case of KDSS in an adolescent.

Kawasaki Disease Shock Syndrome (KDSS) was introduced in 2009 after reports of hemodynamic instability during the acute phase of the illness.

**Background:** Kawasaki disease (KD) is an acute, self-limited vasculitis of unknown etiology with peak incidence at 9-12 months of age. The term Kawasaki disease shock syndrome (KDSS) was introduced in 2009 after reports of hemodynamic instability during the acute phase of the illness.

**Objectives:** Present and discuss a rare case of KDSS in an adolescent patient.

**Methods:** Review of patient’s clinical records and scientific literature.

**Results:** A 12-year-old boy was admitted in the pediatric intensive care unit (ICU) with a 5-day history of high persistent fever, abdominal pain, vomiting and headaches. On examination, he looked ill, was tachycardic and hypotensive with delayed capillary refill, had non-exsudative oropharyngeal erythema, cracked lips, terminal nuchal rigidity, jaundice and small palpable supraventricular lymph nodes. On day 3 a generalized morbilliform rash and diffuse swelling of the hands became apparent. Blood gas showed metabolic acidosis. He had decreased platelet count of 72,000/mm3, AST 122 UI, ALT 192 UI, LDH 366 UI/L, triglycerides 207 mg/dl, total bilirubin 85.5 μmol (direct 68.4). Renal function, urinalysis and fibroscan were normal. ESR was 42 mm/h, CRP was markedly high (286 mg/l) and ferritin 544 ng/ml. Lumbar puncture revealed mild sterile pleocytosis. Due to progressive hemodynamic instability he required fluid resuscitation, inotropic drugs and mechanical ventilation. Broad-spectrum antibiotic therapy was started due to suspected septic shock/streptococcal toxic shock syndrome. IVIG was empirically started 24h later due to non-response. Viral screening, all blood and urine cultures and ASO titers were negative. Myelogram revealed no signs of hemophagocytosis, neoplastic changes or growth of microorganisms in culture. Fine needle biopsy of a supraclavicular lymph node showed nonspecific inflammatory changes. Thoracoabdominal scan revealed moderate bilateral pleural effusion, mild hepatosplenomegaly, retroperitoneal/mesenteric lymphadenopathy. Brain MRI and echocardiogram were normal as well as ophthalmologic evaluation. In the presence of prolonged fevers, mucosal changes, extremity edema and non-specific rash in a severely-ill adolescent with no response to broad spectrum antibiotics and negative cultures, the possibility of KD was raised.

Due to ongoing fevers and inflammation after 36h of first IVIG, he received a second IVIG dose 2g/Kg, methylprednisolone IV pulses for 3 days and aspirin, with rapid clinical and laboratorial improvement. Within 24h the patient was off inotropic support, 48h off mechanical ventilation and 3 days later he was discharged from the ICU. His general condition continued to improve gradually, with increased platelet counts, normalization of liver function and CRP. In this phase, skin desquamation (buttocks/perineal region) was noted. At follow-up, thoracoabdominal angioMRI and serial ecocardiograms were normal. He was weaned off corticosteroids and aspirin without recurrence of symptoms.

**Conclusion:** In this case, despite the atypical age and lack of some classical signs/symptoms, broad-spectrum antibiotic refractoriness and the described clinical presentation raised the hypothesis of KSDD. Diagnosis can be difficult, especially if shock occurs in incomplete forms of KD, but must be suspected early and treatment promptly started in order to ensure a good prognosis. Clinicians should be aware that thrombocytopenia and hepatitis are risk factors for refractory severe KD. MAS must always be excluded in cases of hemodynamic instability.

**REFERENCES**


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**ATYPICAL KAWASAKI DISEASE SHOCK SYNDROME CASE REPORT: NOT ALL SHOCKS ARE SEPTIC OR TOXIC**

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**Background:** Kawasaki disease (KD) is an acute, self-limited vasculitis of unknown etiology with peak incidence at 9-12 months of age. The term Kawasaki Disease Shock Syndrome (KDSS) was introduced in 2009 after reports of hemodynamic instability during the acute phase of the illness.

**Objectives:** Present and discuss a rare case of KDSS in an adolescent patient.

**Methods:** Review of patient’s clinical records and scientific literature.

**Results:** A 12-year-old boy was admitted in the pediatric intensive care unit (ICU) with a 5-day history of high persistent fever, abdominal pain, vomiting and headaches. On examination, he looked ill, was tachycardic and hypotensive with delayed capillary refill, had non-exsudative oropharyngeal erythema, cracked lips, terminal nuchal rigidity, jaundice and small palpable supraventricular lymph nodes. On day 3 a generalized morbilliform rash and diffuse swelling of the hands became apparent. Blood gas showed metabolic acidosis. He had decreased platelet count of 72,000/mm3, AST 122 UI, ALT 192 UI, LDH 366 UI/L, triglycerides 207 mg/dl, total bilirubin 85.5 μmol (direct 68.4). Renal function, urinalysis and fibroscan were normal. ESR was 42 mm/h, CRP was markedly high (286 mg/l) and ferritin 544 ng/ml. Lumbar puncture revealed mild sterile pleocytosis. Due to progressive hemodynamic instability he required fluid resuscitation, inotropic drugs and mechanical ventilation. Broad-spectrum antibiotic therapy was started due to suspected septic shock/streptococcal toxic shock syndrome. IVIG was empirically started 24h later due to non-response. Viral screening, all blood and urine cultures and ASO titers were negative. Myelogram revealed no signs of hemophagocytosis, neoplastic changes or growth of microorganisms in culture. Fine needle biopsy of a supraclavicular lymph node showed nonspecific inflammatory changes. Thoracoabdominal scan revealed moderate bilateral pleural effusion, mild hepatosplenomegaly, retroperitoneal/mesenteric lymphadenopathy. Brain MRI and echocardiogram were normal as well as ophthalmologic evaluation. In the presence of prolonged fevers, mucosal changes, extremity edema and non-specific rash in a severely-ill adolescent with no response to broad spectrum antibiotics and negative cultures, the possibility of KD was raised.

Due to ongoing fevers and inflammation after 36h of first IVIG, he received a second IVIG dose 2g/Kg, methylprednisolone IV pulses for 3 days and aspirin, with rapid clinical and laboratorial improvement. Within 24h the patient was off inotropic support, 48h off mechanical ventilation and 3 days later he was discharged from the ICU. His general condition continued to improve gradually, with increased platelet counts, normalization of liver function and CRP. In this phase, skin desquamation (buttocks/perineal region) was noted. At follow-up, thoracoabdominal angioMRI and serial ecocardiograms were normal. He was weaned off corticosteroids and aspirin without recurrence of symptoms.

**Conclusion:** In this case, despite the atypical age and lack of some classical signs/symptoms, broad-spectrum antibiotic refractoriness and the described clinical presentation raised the hypothesis of KSDD. Diagnosis can be difficult, especially if shock occurs in incomplete forms of KD, but must be suspected early and treatment promptly started in order to ensure a good prognosis. Clinicians should be aware that thrombocytopenia and hepatitis are risk factors for refractory severe KD. MAS must always be excluded in cases of hemodynamic instability.

**REFERENCES**


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**A CASE OF ADENOSINE DEAMINASE 2 DEFICIENCY (DADA2) WITH AN UNCOMMON CLINICAL PRESENTATION AND RESPONSE TO IV IG**

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**Background:** DADA2 is an autoinflammatory disease with autosomal recessive inheritance characterized by a heterogeneous clinical phenotype ranging from multisystemic inflammation (fever, polyarthritides nodosa, cerebral stroke, livedo reticularis etc.) to immune-dysregulation and immunodeficiency.

**Objectives:** To extend the clinical spectrum of DADA2 reporting a case of isolated nonspecific systemic inflammatory syndrome associated with signs of immune-dysregulation in a patient with a novel ADA2 mutation.

**Methods:** In a patient with nonspecific inflammatory phenotype associated to susceptibility to viral infections, Next Generation Sequencing (NGS) panel was performed; mutations detected were confirmed by Sanger analysis. ADA2 enzymatic activity was analyzed in monocyte isolated from the patient and incubated with adenosine and an ADA1 inhibitor.

**Results:** The girl, adopted and of Asian origin, began to suffer from non-specific systemic inflammatory syndrome associated with signs of immune-dysregulation in a patient with a novel ADA2 mutation.

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substitution dosage, the patient experienced Herpes Zoster virus reactiva-
tion (requiring prolonged antiviral treatment), followed by the reappearance of
the inflammatory phenotype complicated by HLH with neurological
involvement (iritis and lethargy), responsive to HD steroids and IG. A
later cerebral MRI evidenced a small gliotic area in left Centrum Ovale.
After steroids suspension, monthly HD IV IgG administrations maintained
clinical remission. Further immunological studies confirmed a reduction of
NK cells with normal function. Hereditary HLH, Autoimmune Lympho-Prolif-
erative Syndrome (ALPS) and main primary immunodeficiencies were ruled out.
Given the clinical picture, a large NGS diagnostic panel (courtesy by
K. Botrug, Vienna) for autoinflammatory diseases and immunodeficiencies
was performed revealing the homozygous LEU141PRO ADA2 mutation,
confirmed by Sanger analysis. Being this mutation novel, an ADA2 enzyme-
atic activity test was performed revealing a complete loss of ADA2 activ-
ity. The parents refused anti-TNF treatment and the patient is still on
monthly HD IG with a complete wellbeing after 3 years of follow-up.
Conclusion: The current report enlarges the clinical spectrum associated
with ADA2 to a persistent unspecific inflammatory syndrome, complicated by
HLH. This case further emphasizes the possibility that NGS could unravel
unusual phenotypes of already known inflammatory syndromes. Even if fur-
ther reports are required, the response to HD IG observed in the present
case is of interest. Even if anti-TNF is the treatment of choice in HD IG
could be a possible treatment in DADA2, especially during the acute phase.

REFERENCES

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AB0975 INITIAL BIOLOGICAL THERAPY RESPONSE IN PATIENTS WITH SUSPECTED AUTOINFLAMMATORY DISEASE

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Background: The choice of the initial biological therapy for patients with
suspected autoinflammatory diseases and not conclusive genetic test remains challenging.
Objectives: To assess the clinical response to the initial biological ther-
apy in pediatric patients with suspected autoinflammatory disease with no
genetic diagnosis.
Methods: We retrospectively reviewed the clinical charts of patients followed in our clinic who started empirical biological therapy after being diagnosed
with suspected autoinflammatory disease(sAID) due to the intensity of their
symptoms and no response to colchicine or FAMEs. Next generation sequencing using an immune deficiency/dysregulation(115 genes) and autoin-
flammatory panel(12 genes) was negative/inconclusive in all patients.

Results: We identified 9 patients(6/9) were male, median age at fever
onset 1.33 years old (IQR(0.46-4), age at diagnosis of sAID 3.8 years old
(IQR(1.75-7)). Clinical presentation included fever(9/9), abdominal pain and
arthromyalgia(7/9), aphthous(6/9), headache, rash and adenopathy(5/9),
delayed growth(4/9), tonsilitis and pericarditis(3/9) as well as diarrhea and
pleuritis(2/9). One patient presented with stroke, cutaneous lesions, vas-
culopathy and haemolytic uraemic syndrome and 1 patient with amyloido-
sis and secondary hepatosplenomegaly. None of the children suffered
from uveitis or meningitis. The flares lasted a median of 14 days(IQR 8-
20). Two patients had persistent symptoms. Their mean/median lab val-
ues are shown at table. 4/9 patients had homozygous mutations with
uncertain significance, heterozygous mutations or polymorphism but their
symptoms or familiar study was not suggestive of the corresponding AID.
One patient had a heterozygous mutation in MEFv (p.P369p.m.R408q) and also a CECR1 heterozygous mutation with uncertain significance,
one patient had p.R92Q heterozygous mutation in TNFRSF1A, one patient had
MEFv p.R202Q homozygous mutation, other patient had a NOD-2 heterozygous mutation and the patient with amyloidos had
NOB0 deficiency and a NOD2 mutation (p.A918D). All patients responded to steroid therapy; subsequently 8/9 received anti IL-1Recep-
tor kineret as first biological therapy and 1/9 with suspected vasculopathy
received anti-TNF. Response to IL-1R antagonist was complete in 3/8 and partial in 4/8 children;1/8 showed no response. 2/8 patients
were switched to anti-TNF. One each to etanercept and Infliximab with
good response. The patient with amyloidos was changed to anti IL-6R
with incomplete response but clear improvement compared to anti IL-1R
response. The patient with suspected vasculopathy and initial anti-TNF
treatment had partial response with no recurrent stroke but persistent
symptoms.

Conclusion: An important group of patients with sAID lack genetic confir-
more. Empirical use of IL-1R antagonist is promising but not effective in all patients as it was observed in our case series,where 5/8 children
showed partial or no response.3/5 needing a second biologic treatment in
form of anti-TNF due to persistent moderate-severe symptoms.
A model to predict the response to different therapeutic strategies, based
on clinical features and immunological profile (including inflammatory cyto-
kines) might help to choose the most appropriate immunomodulatory

Disclosure of Interests: None declared


AB0976 PSYCHIATRIC DISORDERS DURING TRANSITION CARE IN ADOLESCENTS WITH RHEUMATIC DISEASES


Background: Chronic rheumatic diseases (CRD) have a strong
psychosocial development of adolescents. There are several factors
associated with psychiatric disorders (PD) in these children; physical
disability, complex treatments, long-term follow-up, and flares are the
most cited in literature. Juvenile Idiopathic Arthritis (JIA) is the first cause of disability in children with
CRD, on the other hand, Major Depressive Disorder (MDD) and Dysthymia are the third cause. Some PD, mostly MDD, appear as a
consequence of disability caused by CRD, but immune pathways might be
implicated in pathogenesis as well.
Adolescents with CRD need to transition to an adult-centered care while
deal with emotional and physical changes. This implies a difficult situation
in which patients could be in higher risk for develop PD. There are
a lack of information on how this process affects emotional health in this
population.
Objectives: The aim of the study is to calculate the prevalence of PD
in adolescents with CRD during transitional care and their relationship with
clinical and social factors.
Methods: Patients older than 16 years with an established CRD, who
were in transitional care during the period between July 2017 and January
2019 were included in this transversal study. We used MINI KID assessment tool to characterize PD in our patients. Each patient performs an interview with both a clinical psychologist and
a pediatric psychiatrist to confirm psychiatric/emotional diagnosis. Clinical, social and demographic data were collected from medical records. Descriptive statistics with frequencies or measures of central tendency and dispersion, depending on variable characteristics were used. Comparisons and correlations were performed with parametric and non-parametric tests as appropriate.

Results: Forty patients were recruited during study period, aged 18 (IQR 16 - 19) years old, 31 female, and most diagnosed with JIA (22, 55%) and Systemic Lupus Erythematosus (SLE, 7, 17.5%). Time since diagnosis was 5.5 (IQR 0.5 - 13) years and half of the patients presented with an active disease. After psychiatric evaluation, 24 (60%) patients presented an active disease, while 16 (40%) were identified with MDD, and minor disorders (specific phobia and anxiety) were noticed in 11 (27.5%). Two patients presented alcohol dependence, and 11 (27.5%) were diagnosed with more than one PD. PD were more frequent in patients with SLE (71%) and in those with active disease regardless underlying diagnosis (54% vs 45%, P = .490). Other significant factors related with more prevalence of PD were female gender (66% vs 44%, P < .001), having a couple (90% vs 57%, P < .001), have a single parent (83% vs 60%, P = .005), and sex activity (71% vs 61%, P = .002).

Conclusion: We found a higher prevalence of PD in adolescents during transitional care, especially in those with active disease. It is priority to involve a multidisciplinary team to transition adolescents from pediatric to adulthood care to prevent and detect PD in this population.

REFERENCES


Disclosure of Interests: None declared

AB0978

ULTRASOUND MEASUREMENT OF JOINT CARTILAGE THICKNESS IN HEALTHY ASIAN SCHOOL-AGED CHILDREN

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Background: Degeneration of the osteocartilaginous structures due to synovial inflammatory process is a feature of juvenile idiopathic arthritis (JIA)1. While anthropometry difference has been reported between Asian and Caucasian2, Asian specific age- and gender-related normal standard reference values should be established before ultrasound (US) measurement of cartilage thickness (Cth) becomes standard procedure in the clinic.

Objectives: The standard cartilage thickness in Asian children population

Methods: A cross-sectional study was performed in 100 healthy Asian children (including 48 girls and 52 boys, age between 5 to 12 years-old). Bilateral knees, ankles, wrists, second metacarpophalangeals (MCPs) and proximal interphalangeals (PIPs) were measured using US. Children’s body weight and body height were also recorded for later adjustment.

Results: We observed no difference in the Cth between right and left knees, ankles and wrists but MCPs and PIPs. Cartilage thickness in the large joints such as ankles and knees differed between sexes (p>0.001), and the boys had thicker cartilage than those of the girls. Cartilage thickness decreases with increasing age after weight, height and BMI adjustment. A formula for calculating sex-specific cartilage thickness at different ages in childhood is suggested.

Conclusion: Cartilage thickness measurement with US in small joints may be biased. A standard reference of Cth for Asians in the knee, ankle and wrist joints between age 5- to 12 have been proposed.

REFERENCES

CORTICOSTEROID TREATMENT IN PEDIATRIC RHEUMATIC DISEASES AND SUPPRESSION OF THE HYPOTHALAMIC-PITUITARY AXIS

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Background: Corticosteroids are the mainstay in the treatment of several chronic inflammatory diseases. Long-term treatment may lead to suppression of hypothalamic-pituitary-adrenal axis, which in turn can be dangerous in stress situations such as after surgical interventions. Oral replacement therapy may be needed in some cases. Data on pediatric populations are scanty.

Objectives: The aim of our study has been to evaluate hypothalamic-pituitary-adrenal function during corticosteroid tapering by measuring serum cortisol.

Methods: During long term corticosteroid treatment, serum cortisol levels were evaluated when oral prednisone dose was decreased to 7.5 mg/day and also after 4-6 weeks, and if below range ACTH levels were also determined.

All patients aged < 18 years seen in our center during the last 6 months who were on corticosteroid treatment for > 1 month were included. Serum cortisol levels were considered normal in the range of 5-25 μg/dL in a morning fasting blood drawing, while ACTH levels were considered normal in between 6 and 55 ng/L (with chemiluminescent method). Clinical and demographic data were recorded from clinical charts in a customized database.

Results: We have included in this preliminary study 12 patients (7F, 5M) affected by uveitis (n=4), JIA (n=4), scleroderma (n=3), lupus (n=1). The mean age (at the time of sampling) was 11.5 years, with a median of 10 and a range of 8-17. Prednisone starting dose was 1 mg/kg/day. Four out of 12 patients had decreased cortisol levels. Characteristics of these four patients (none of whom had additional steroid pulses) are detailed in the table.

Conclusion: One third of our patients had decreased cortisol levels, after three months of prednisone treatment. In one case, who showed persistently low levels, oral supplementation with hydrocortisone 20 mg/day for two months was needed. Our study is ongoing and results could help in identifying patients at risk for adrenal crisis.

REFERENCES


Disclosure of Interests: None declared


Efficacy of Etaenertcept Treatment for Children With Kawasaki Disease Intractable to Intravenous Immunoglobulin Therapy in Russian Children

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Background: Kawasaki disease (KD) is recognized in developed countries as a fundamental reason of acquired heart diseases in children nowadays. The main treatment is infusion of intravenous immunoglobulin (IVIG) at a dose of 2 g/kg. However for about 10-30% of children is reported the development of resistance to standard therapy: continuation of fever >38.0°C or recurrence of fever after 36 hours of afebrile period (Tc37.5°C), but not later than on the 7th day after completion of the IVIG infusion at a dose of 2 g/kg. Until now there are no unified recommendations for treatment of such patients. As alternative therapy researchers empirically apply second infusion of IVIG (77%), high doses of glucocorticoids (16%), blockers of tumor necrosis factor α (3%) and interleukin-1, cyclosporine and other cytostatic drugs.

Objectives: Efficacy evaluation of therapy by inhibitor of TNF-alpha (Etanercept) in treatment of KD immunoglobulin -resistant forms according to the data from Morozovskaya Children’s City Clinical Hospital.Moscow.

Methods: There were examined 152 patients (boys:girls = 2:1, median age = 21 months – 21 months [10;36] with KD hospitalized in Morozovskaya Children’s City Clinical Hospital in 2014-2018. The frequency of complete form of KD was 80.6%. All children had a standard therapy – IVIG. Efficacy evaluation was based on normalization of body temperature, decrease of neutrocytosis, decrease of C-reactive protein (CRP) level. In case of ineffectiveness of therapy the second infusion of IVIG, pulse-therapy and inhibitor of TNF-alpha (Etanercept) were used.

Results: The resistance to standard IVIG therapy was revealed in 16 children (10.5%), mostly in boys (4:3.1) at the age of Me = 21.5 months [9.5; 34]. Complete form of KD was diagnosed in 11 patients (88.8%), incomplete form - in 5 children (31.2%). Cardiovascular lesions were noted in 14 children (87.5%): pericarditis - in 2 (12.2%), coronary arteries (CA) lesions – in 12 (75%), with formation of aneurysms in 8 (50%), including the giant ones in 3 children (18%); peripheral arteries damages were noted in 2 children (12.5%), thrombosis and thromboembolism – in 4 children (25%).

To all of children was made the second IVIG infusion, 13 of those children (81.2%) had a positive effect:11 children with complete form of KD, 2 children with incomplete form of KD. For 3 children (18.7%) with incomplete form of KD and significant cardiovascular changes (pericarditis, giant aneurysms of coronary and peripheral arteries,thrombosis and thromboembolism) it was needed an additional therapy. As a second-line therapy the methylprednisolone pulse-therapy was used in 2 children(12.5%) at a dose of 10 mg/kg, without sufficient effect. For these three patients (3) as a third-line therapy was applied Etanercept at a dose of 0.8 mg/ kg/week subcutaneous. In all children normalization of body temperature, decrease of leukocytosis by factor of 1:5-3 and decrease of CRP by factor of 10-15 occurred after three injections of Etanercept. However, for 1 child it was needed the additional fourth injection of Etanercept because of repeated fever, increased laboratory parameters, development of thrombosis of the left coronary artery after 2 weeks upon discharge.

Conclusion: The frequency of immunoglobulin-resistant forms was 10. 5%. The first-line therapy of resistance (second IVIG-infusion) was effective in 13 children (81.2%). Methylprednisolone pulse therapy was ineffective. The use of 3 subcutaneous injections of Etanercept at a dose of 0.8 mg/kg/week resulted in decrease of intensity of inflammatory changes and in fever relief, but it did not prevent the development of dyspnea and thrombosis of coronary arteries.

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Background: Juvenile idiopathic arthritis (JIA) in recent decades has changed its course, thanks to the use of genetically engineered biological drugs. If therapy with methotrexate is inefficient etanercept is the drug of choice for JIA treatment. Etanercept has been used in Chelyabinsk regional pediatric hospital during 10 years.


Methods: 51 children aged from 3 to 17 (mean age 10,0 years) diagnosed with JIA were under monitoring (12 boys, 39 girls). Disease duration was from 2 to 15 years (mean duration 5,4 years). JIA was diagnosed based on ILAR diagnostic criteria. Oligo arthritis was diagnosed in 9 children, mono- dimensional disease in 24, polyarticular disease in 17. 3 patients had systemic JIA (without active systemic presentations), 5 children had enthesitic JIA. X-ray stage 1-2 was observed in 45 children and stage 3-4 in 5. Enhancement antigens HLA B 27 were found in 11 children. In all children methotrexate was ineffective in dose of 15 mg/m² during 6-12 months. Etanercept was introduced in dose of 0.8 mg/ KW. Therapy duration was from 3 months to 8 years (mean duration 29 months).

Assessment of disease activity and therapy efficiency was conducted in accordance with ACR pedi criteria. Nonparametric statistical methods were used to compare results.

Results: Prior to etanercept use high disease activity was observed in all children. Mean number of joints with active arthritis was 8 [4, 10] (Me;25;75%). Mean number of joints with functional impairments – 4 [2;10]. Mean ESR (according to Panchenkov) – 23 [10;35] mm/h, CRP 12,0 [5,7;32] g/L. Assessment of functional activity according to CHAQ questionnaire – 1,25 [1;2]. Activity assessment according to VAS by doctor – 70 [60;70]. Assessment of parents/patients according to VAS 70 [10;90]. No active systemic presentations and eye lesions were found in children under monitoring.

On the background of etanercept therapy a decrease in disease activity was observed in 50 patients. Mean number of joints with active arthritis was 0 [0;2] (Me;0;0001). Mean number of joints with functional impairments – 0 [0;2] (P=0,0001). Mean ESR was 5 [3,6] mm/h (P=0,0001), CRP 3 [2;4] g/L (P=0,0001). Assessment of functional activity according to CHAQ questionnaire was 0,125 [0,0;0,5] (P=0,0001). Activity assessment according to VAS by doctor – 10 [5;20] (P=0,0001). Assessment of parents according to VAS 10 [5;20] (P=0,0001).

Clinical disease remission (according to ACR pedi criteria >90%) was observed in 32 patients after 6-12 months of treatment. Remission duration up to now is from 1 to 7 years. Efficient according to ACR pedi criteria is 70% in 11 children, 50% in 5, 30% in 2.

Etanercept was well-tolerated. Drug was cancelled in 9 patients. 6 patient (11,8%) developed bilateral uveitis, one patient had an allergic reaction (rash), one - systemic manifestations, one - urinary tract infection. There were no cases of tuberculosis.

Conclusion: Etanercept therapy was highly effective and safe in patients with JIA. Clinical remission was achieved in 62,7% children. Decrease in disease activity was observed in 98% of children. 11,8% patient developed uveitis, on average, after a year of using etanercept.

REFERENCES
PTX3 is known to have an interesting role in regulation of innate immunity and it is a key player in regulation of many inflammatory reactions [1].

Objectives: This study aimed to measure serum and synovial fluid (SF) levels of PTX3 in juvenile idiopathic arthritis (JIA) patients and to correlate them with different clinical, laboratory and musculoskeletal ultrasound parameters of disease activity.

Methods: We measured PTX3 in the serum (n=57) and SF samples (n=18) from 57 JIA patients and in the serum from twenty healthy controls. Disease activity was calculated using the Juvenile Arthritis Disease Activity Score in 27 joints (JADAS27) and musculoskeletal ultrasound examination (MSUS) was performed using grey scale (GS) and power Doppler (PD) 10-joint score (bilateral knee, ankle, wrist, elbow and the 2nd metacarpophalangeal (MCP) joints)[3]; Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) levels, serum ferritin, rheumatoid factor (RF) titre were measured and the Juvenile arthritis multidimensional assessment report (JAMAR) was documented.

Results: Serum PTX3 level was significantly higher in JIA patients (3.59±2.38 ng/mL) compared to serum level in the healthy controls (1.5 ± 0.9 ng/mL) (p=0.001). There was no significant difference between SF PTX3 level (4.73 ± 2.62 ng/mL) and its level in paired serum samples(4.23±2.93 ng/mL) (p=0.59). JIA patients with systemic onset subtype (n=13) had higher PTX3 serum levels (5.57±2.52 ng/mL) compared to serum level in the oligoarticular (n=25) and polyarticular (n=19) subtypes (2.88±2.13 ng/mL and 3.18±1.92 ng/mL respectively) (p=0.001 and 0.005 respectively). In JIA patients, serum PTX3 level significantly correlated with JADAS27 (r=0.52, p<0.05), CRP titres (r=n.46, p<0.05) and serum ferritin (r=0.48, p<0.05). Both serum and SF PTX3 levels significantly correlated with PD score (r=0.51 and 0.48 respectively, p<0.05). SF PTX3 (p =0.001) was shown to be superior to serum PTX3(p =0.02), ESR (p =0.07) and comparable to CRP (p =0.001) at predicting PD synovitis score.

Conclusion: JIA patients have significantly increased serum and synovial fluid levels of Pentraxin 3 that remarkably correlated with the JADAS27 and MSUS parameters of inflammations suggesting that it could be a useful marker to reflect JIA disease activity.

REFERENCES

Disclosure of Interests: None declared

AB0984 INTERSTITIAL LUNG DISEASE IN CHINESE JIA PATIENTS

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Background: Rheumatic diseases and or medications (for example methotrexate) used to treat the underlying condition are associated with the development of interstitial lung disease (ILD). Development of ILD in subjects with juvenile idiopathic arthritis (JIA) is assumed to be rare, however, severe respiratory complications are increasingly reported in JIA patients.

Objectives: To describe the prevalence of respiratory diagnoses and ILD in a group of Chinese JIA patients at a tertiary center.

Methods: Retrospective chart review of JIA patients attending rheumatology clinic during 2012 to 2019.

Results: Fifty-eight cases of JIA were identified. Thirty-three (57%) received DMARDs, majority were on methotrexate (MTx, 24, 73%) and sulfasalazine (SSZ, 14, 42%). Eleven (19%) were currently or previously on biologics (adalimumab 5, etanercept 5, anakinra 1, previous exposure: infliximab 1, etanercept and anakinra 1). Respiratory diagnosis was made in 11 (19%) patients. There were 2 (3.4%) cases of ILD diagnosed during the study period (see below). The rest were asthmatics. Among them, 9 were on DMARDs [MTx (8/9%), SSZ 4(44%), leflunomide 2(LEF), hydroxychloroquine 1(HCQ)] or biologics [Etanercept 3(33%), adalimumab 1, tocilizumab and anakinra 1(sequential use)]. Four subjects were on combination DMARDs [MTx+SSZ in 2, 1 each for MTx+LEF+HCQ+SSZ, MTx+LEF]. Three received combination DMARDs and biologics (1 each for MTx+adalimumab, MTx+etanercept & MTx+anakinra).

Cases of ILD

One was a SJIA patient diagnosed at 2 years old. She failed methotrexate, etanercept & tocilizumab (infusion reaction). She was on low dose prednisolone, methotrexate and anakinra when she presented to us with acute right heart failure requiring ICU care 3 years after diagnosis. Advanced clubbing was noted (fig 1). HRCT thorax on presentation showed severe interstitial lung disease with marked fibrosis and traction bronchiectasis (fig 2). She was diagnosed acute on chronic cor pulmonale and pulmonary hypertension secondary to ILD.

The other was an oligoarticular JIA patient, diagnosed at 2 years old. She was refractory to intra-articular steroid injections and combination DMARDs including MTx, SSZ, LEF & HCQ. Arthritis was controlled by Etanercept. At 12 years of age, she started to have chest pain. Lung function test showed restrictive lung pattern. HRCT thorax showed pulmonary fibrosis.

Conclusion: From this Chinese cohort we identified 2 cases of ILD. They did not present with any symptoms until advanced stage or when complications set in. Both were very young at diagnosis and were difficult to control, as evidenced by the use of multiple DMARDs and biologics including methotrexate, IL6 and IL1 blockade. The causes of ILD are believed to be multifactorial. For severe case, prognosis is poor[2]. Although rare, methotrexate induced pneumonitis do occur. Symptoms of ILD may not be obvious until late stage. Clinical examination alone is not sensitive enough to detect disease progression. Asthma is common, as in this cohort, and may further complicated the assessment. It is recommended in the recent SHARE initiative on JSLE to screen for lung disease[3]. We believe it should be performed in JIA patients as well. 6 minute walk test is a noninvasive way to assess cardiopulmonary functional status and is validated in children[4]. Patients with unexplained chest symptoms or impaired lung function should be referred to pulmonologist for further assessment.

REFERENCES
EVALUATION OF SERUM CALPROTECTIN (MRP-8/MRP-14) LEVEL IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Disclosure of Interests: None declared

Background: Evaluation of inflammatory activity is an important element in the management of patients with juvenile idiopathic arthritis (JIA), for which C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) are traditionally used. However, they might be uninformative in case of subclinical inflammation. The serum level of calprotectin MRP-8/MRP-14 (sCal) correlates well with arthritis activity, as it is produced by activated cells directly in synovia.

Objectives: We evaluate the level of sCal in patients with JIA depending on the type of therapy in order to assess comprehensively the disease activity for further treatment correction.

Methods: 74 patients with JIA were examined, 18 of them had oligoarticular disease subtype, 39 – polyarticular, 17 – systemic. The mean age was 11.3 ± 0.4 years; the disease duration was 5.2 ± 0.4 years. Among them, there were 49 (66%) females and 25 (34%) males. All patients were divided into 2 groups depending on the therapy type. Group I consisted of 33 children treated with methotrexate, while 11 of them were in a state of clinical remission. Group II included 41 children treated with biologic DMARDs (adalimumab, etanercept, tocilizumab), while 14 of them achieved clinical remission. All children had normal levels of CRP and ESR. Quantitative indicators distribution is given as a median [5th; 95th percentile], the calculations were carried out using the Mann-Whitney U test.

Results: Level of sCal in the active disease stage in children of Group I was 8,750 ng/ml [3,700; 17,100], while sCal level in Group II was 2,900 ng/ml [1,200; 24,900]; sCal level in children of Group I which achieved clinical remission – 3,400 ng/ml [1,200; 6,000], and the same indicator in Group II – 1,000 ng/ml [100; 2,800]. sCal level was significantly higher in the group of patients who did not receive biologic DMARDs, both in the active stage of disease (p = 0.000006, U = 71.5) and in the stage of clinical remission (p = 0.00034, U = 11). sCal level is 5,800 ng/ml less in patients with active stage of disease and 2,400 ng/ml less in patients with clinical remission, both treated with biologic DMARDs. In addition, the level of sCal is 5.5 times higher in our patients (3,300 ng/ml) compared with healthy children (600 ng/ml) (p = 0.015). The moderate positive correlation of sCal and JADAS-27 activity index (r-Spearman’s r = 0.58) was credibly established.

Conclusion: The level of sCal can reflect the degree of inflammatory activity in JIA, it is significantly higher in the group of patients who did not receive biologic DMARDs in the treatment regimen, both in the active disease stage (p = 0.000006, U = 71.5) and in the stage of clinical remission (p = 0.00034, U = 11), which indicates the effectiveness of biologic DMARDs in the treatment of JIA. We assume that it would be appropriate to estimate the serum calprotectin level in the comprehensive analysis of clinical status in JIA patients for the further correction of therapy.

Disclosure of Interests: None declared

AB0986 VITAMIN D LEVEL AND BONE MINERAL DENSITY IN PATIENTS WITH JUVENILE RHEUMATOID ARTHRITIS

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Background: An impaired bone metabolism is observed in patients with juvenile idiopathic arthritis (JIA), associated both with the activation of pro-inflammatory cytokines and use of steroid medications. The majority of children with JIA have low vitamin D level, which may complicate the disease course. We regard the monitoring of bone mineral density (BMD) in patients with juvenile rheumatoid arthritis (JRA) should be complemented with an additional assessment of calcidiol (25(OH)D) serum level as an indicator of BMD and a criterion of successful therapy.

Objectives: To evaluate the bone densitometry data and calcidiol level in patients with JRA in order to estimate the osteopenic syndrome and the advisability of prescribing the vitamin D additional doses.

Methods: The calcidiol level and BMD data in 65 patients with JIA were assessed (41 girls and 24 boys). All children were divided into 2 groups, depending on the therapy type. Group I consisted of patients who received methotrexate (n = 37), Group II – patients who received the biological DMARDs (n = 28), namely tocilizumab (6 patients), adalimumab (20 patients) and etanercept (2 patients). At the time of the study, 14 children of the Group II were prescribed the biological DMARDs only, while the 12 patients were in the state of clinical remission unlike the 7 patients of Group I. It should be mentioned that the majority of children in the Group II had high disease activity degrees before the start of treatment with biological DMARDs. In order to show the correlation between BMD and disease activity, cJADAS-27 score result for the last 6 months was estimated. The data were processed using Pearson’s chi-squared test and Spearman’s Rank correlation coefficient.

Results: The study revealed, 60 children (92% of all patients) showed vitamin D insufficiency, that mainly manifested by decreased calcidiol level (from 21 to 29 ng/ml), only 8 children (12%) showed calcidiol level deficiency (<20 ng/ml). A significant difference was found in the BMD results depending on the therapy type (χ² = 10.05; p < 0.01) using Pearson’s chi-squared test. As a result, children who received biological DMARDs, demonstrated significantly better results according to BMD assessment data. A direct association of moderate strength was found (the correlation coefficient (r-Spearman’s ) is 0.39). The strong negative association (r-Spearman’s was -0.72) was observed between BMD assessment data and cJADAS-27 score result, which confirmed our statement – high disease activity affects the bone tissue mineralization. There was a weak negative association between 25(OH)D level and cJADAS-27 score result (r-Spearman’s was -0.15).

Conclusion: There was a paucity of vitamin D level in 92% of patients with JRA, in 80% secondary osteoporotic syndrome. It was revealed that patients, who receive biological DMARDs in integrated treatment, demonstrate significantly better results according to BMD assessment data. Calcidiol level has a moderate effect on BMD, while BMD strongly depends on disease activity degree according to the Spearman’s Rank correlation coefficient.

Disclosure of Interests: None declared

AB0987 CHOICE AND SWITCH BETWEEN BIOLOGICAL AGENTS IN NON-SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS (JIA)

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Background: Over the past few decades, biologic therapy has significantly improved the prognosis in children with JIA. The issue of optimal and personalised biologics prescription and the problem of switching between drugs are relevant questions of modern paediatric rheumatology.

Disclosure of Interests: None declared
Objectives: The aim of our retrospective observation was to describe trends in the biologics prescription in first and subsequent lines for the treatment of non-systemic JIA.

Methods: We recruited 252 patients with non-systemic JIA, who received medical treatment with biologics at the Department of Paediatric Rheumatology of Sechenov University from January 2015 to December 2017. 18% of them (n=46) had chronic anterior uveitis at the moment of biologic therapy initiation. Eye involvement influenced treatment decisions in these patients, and therefore they were excluded from the analysis. 206 children with non-systemic JIA and without uveitis were included in a study group.

Patients' characteristics: 128 girls and 78 boys (1.6/1). Mean age 13.5 ± 3.8 years, age of disease onset 7.8 ± 4.2 years; mean disease duration before biologic therapy initiation 3.3 ± 3.4 years. JIA categories: 135 (85.5%) had polyarticular RF, 29 (14.1%) - oligoarticular, 26 (12.6%) - enthesitis-related, 9 (4.4%) - polyarticular RF, and 7 (3.4%) - psoriatic subtype. At baseline, 204 patients (99%) received concomitant therapy with conventional DMARDs: 175 children (85.0%) received Methotrexate (MTX), 3 (1.5%) - combination of MTX and sulfasalazin (SSZ), 9 (4.4%) - SSZ, 9 (4.4%) - leflunomid, 4 (1.9%) - combination of MTX and leflunomid. 4 (1.9%) - cyclosporine A. Two children (1%) received biologics as monotherapy.

Results: As a first biologic abatacept was used in 26 patients, adalimumab in 14, tocilizumab in 6 and infliximab in 4. Etanercept was pre-scribed to 156 patients (75.7%;± 3.5) without non-systemic JIA, which was significantly more frequently than other biologics together - 50 (24.3%;± 6.2) (t=7.7; P<99.97). Later 24 children (11.7%) were switched from the first to a second biologic agent. The main reason for switching (n=14) was inefficacy of the first-line drug. When etanercept was ineffective, abatacept (n=3) and adalimumab (n=5) were prescribed as second-line biologics. Etanercept was used as a second-line biologic in 6 children, who were initially treated with other biologic agents. The other reason for switching was the appearance of chronic anterior uveitis (n=7); 6 of these children were initially treated with etanetepic, 1 with abatacept; they were switched to adalimumab (n=6) and abatacept (n=1). In 2 cases adverse events were observed - one episode of intrathoracic lymphatic nodes tuberculosis in a patient receiving etanercept, and one allergic reaction (rash, asphyxia) after the infliximab injection. At the end of our observa-tion etanercept was chosen as treatment for 148 (71.8%) patients with non-systemic JIA.

Conclusion: Thus, etanercept was preferred biologic agent in the treat-ment of non-systemic JIA. The presence of uveitis requires a different treatment approach.

REFERENCES

Disclosure of Interests: None declared.


PATIENTS' AND CAREGIVERS' ASSESSMENT OF A DEDICATED OUTPATIENT SERVICE FOR INTRAARTICULAR GLUCOCORTICOID INJECTIONS IN JUVENILE IDIOPATHIC ARTHRITIS

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Background: Patients with juvenile idiopathic arthritis (JIA) may require several hospital admissions over the disease course, due to flares or persistently active arthritis, with a negative impact on the patients’ and family’s daily life. To provide timely intervention and support the patients and families’ quality of life, in 2018 an afternoon outpatient service for intraarticular glucocorticoid injections (IAGI) in JIA has been created at the study center.

Objectives: To evaluate the patients’ and caregivers’ assessment of the outpatient service for IAGI in JIA; to investigate demographic and clinical features of patients entering the service.

Methods: All consecutive JIA patients and their caregivers seen at the IAGI outpatient service from February 2018 to January 2019 completed a satisfactory questionnaire just after the IAGI procedure. The patient’s part included: satisfaction on the overall service and on dedicated personnel (yes/no, why), procedure pain assessment (VAS 0-10, 0–none; 10 worst); whereas the caregiver’s part: satisfaction on the overall service (yes/no, why), facilitation of family burden (yes/no, why). Descriptive analysis was performed on 102 completed questionnaires. No answers were synthesized in items.
Results: All of the 46 JIA patients seen at the IAGI outpatient service and their caregivers completed the questionnaire. Patients were mostly females (78%) with early disease onset (median 4.8 years) and positive ANA status (61%). The majority (52%) had persistent oligo-JIA, followed by extended oligo-JIA (26%), RF-negative polyarthritis (17%), ERA and systemic JIA (2%, respectively). The median age at IAGI was 14.7 years (IQ 11.3-19.5). Forty patients (87%) had previous hospitalization for IAGI, mostly under general sedation (64%). All patients, except a 12 year old girl (0.02%) with uncontrolled needle phobia and previous IAGI, were treated with the IAGI outpatient service. In Table 1 reasons of satisfaction are detailed in items. Procedural pain was median rated 3 (IQ 2-6). Most of the families came from the city or province of the study center (76%); 17% from other provinces of the same geographical region; 7% from other regions.

Abstract AB0989 Table 1. Frequency of specific reasons of satisfaction on the IAGI outpatient service, synthesized in items, during the 56 procedures of the study.

<table>
<thead>
<tr>
<th>Items</th>
<th>Patients, n (%)</th>
<th>Parents, n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time saving</td>
<td>45 (80)</td>
<td>30 (54)</td>
</tr>
<tr>
<td>Stress saving</td>
<td>5 (9)</td>
<td>-</td>
</tr>
<tr>
<td>Reduction of absence from school/work</td>
<td>27 (48)</td>
<td>23 (41)</td>
</tr>
<tr>
<td>Less negative impact on personal commitments</td>
<td>-</td>
<td>26 (46)</td>
</tr>
<tr>
<td>Improvement of family burden organization</td>
<td>-</td>
<td>54 (96)</td>
</tr>
<tr>
<td>High quality of dedicated Staff</td>
<td>55 (98)</td>
<td>19 (34)</td>
</tr>
</tbody>
</table>

Conclusion: The results outline the afternoon IAGI outpatient service foster the management of flares or persistently active arthritis in JIA patients, particularly at older ages, with high rate of satisfaction and lower impact on patients’ and family burden compared to hospital admission and, of note, despite moderate pain rating and multiple site injections. This supports the development of Diagnostic Therapeutic Care Pathways for JIA patients, in the view of improving patients’ quality of life and also towards resource optimization.

REFERENCES

Disclosure of Interests: Hanan Jadoun: None declared, Aurora Pucacco: None declared, Angela Aquilani: None declared, Andrea Uva: None declared, Fabio Basta: None declared, Rebecca Nicolai: None declared, Fabrizio De Benedetti Grant/research support from: Abbvie, SOBI, Novimmune, Roche, Novartis, Sanofi, Pfizer, Silvia Magni-Manzoni Consultant for: Abbvie, Speakers bureau: Abbvie


AB0990

FINAL DIAGNOSIS OF THE PATIENTS WITH MUSCULOSKELETAL COMPLAINTS: PRELIMINARY RESULTS OF ONE-YEAR STUDY
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University of Health Science, Kanuni Sultan Süleyman Training and Research Hospital, Pediatric Rheumatology, Istanbul, Turkey

Background: Musculoskeletal (MS) complaints are one of the most common reason for administration to outpatient clinics. Objectives: The study aimed to summarize the final diagnosis of the patients who suffered from musculoskeletal (MS) findings. Methods: We prospectively evaluated the patients who were referred with the complaints of MS systems in a year period. Results: A total of 940 patients with the complaint of musculoskeletal systems were examined. Among them, 577 patients suffered from arthralgia, 234 had arthritis, 39 had low-back pain, 26 had limb pain, and 64 had other symptoms such as myalgia, heel pain, hip and neck pain. A diagnosis of rheumatic disease was made in 430 of patients, whereas 510 had non-rheumatic conditions. Final rheumatological disease diagnoses were as follows: juvenile idiopathic arthritis (n=195), familial Mediterranean fever (n=101), reactive arthritis (n=46), acute rheumatic fever (n=39), toxic synovitis (n=17), psoriasis (n=8), Raynaud’s phenomenon (n=6), chronic recurrent multifocal osteomyelitis (n=5), vasculitis (n=5), systemic lupus erythematosus (n=4), juvenile dermatomyositis (n=2) and juvenile scleroderma (n=1). Among patients with non-rheumatic conditions, most of them had vitamin D deficiency, infections, mechanic-orthopedic conditions, and growing pains. Conclusion: Evaluation of a child presenting with MS findings requires a comprehensive, multidisciplinary, and systematic approach. As a busy pediatric rheumatology center, we demonstrated the final diagnosis of referred patients with MS symptoms and only less than half of the patients were diagnosed as a rheumatological condition. Whilst pediatric rheumatology centers are limited in number, our results put forth the need of formulating recommendations for clinicians in order to prevent unnecessary referrals

REFERENCES

Disclosure of Interests: None declared

AB0991

PRELIMINARY RESULTS OF REFERRALS TO A TERTIARY PEDIATRIC RHEUMATOLOGY OUTPATIENT CLINIC: A YEAR IN REVIEW
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Background: Previously, the profile of pediatric rheumatology practice was demonstrated from several countries[1,2]. However, there is not a
documented data about the pediatric rheumatology clinic population in our country.

**Objectives:** To evaluate and define the patient population referred to a tertiary pediatric rheumatology outpatient clinic in Turkey.

**Methods:** We prospectively evaluated the patients who were initially referred to our department with suspicion of rheumatic diseases in a year period. These findings cover only ten months results as a preliminary study.

**Results:** A total of 2317 new patients (1142 male 1175 female) were seen. Among them, most of patients(n=1445) were referred from pediatric outpatient clinics, pediatric emergency units(n=168) and orthopedic surgeons(n=91). Of these 48.9% had a final diagnosis of a rheumatic disease. 37.9% had non-rheumatic conditions, and 13.2% had no definitive diagnosis yet. Most of them were periodic fever syndromes(n=553), juvenile idiopathic arthritis(n=207) and vasculitis(n=160) (Table 1). Other than rheumatological diseases, non-rheumatic conditions were mostly vitamin D deficiency, infections, mechanic-orthopedic conditions, and growing pains (Table 2).

**Abstract AB0991 Table 1. Distribution of the patients who were diagnosed with a rheumatic disease**

<table>
<thead>
<tr>
<th>Diseases</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Periodic fever syndrome</td>
<td>553 (48.9)</td>
</tr>
<tr>
<td>- Familial Mediterranean fever</td>
<td>444 (80.2)</td>
</tr>
<tr>
<td>- Periodic fever with aphthous stomatitis, pharyngitis, and adenitis</td>
<td>43 (7.8)</td>
</tr>
<tr>
<td>- Cryopyrin-associated periodic fever syndromes</td>
<td>2 (0.4)</td>
</tr>
<tr>
<td>- Hyper-immunoglobulin D syndrome</td>
<td>1 (0.2)</td>
</tr>
<tr>
<td>- Un-defined (genetic analyzes are still in progress)</td>
<td>63 (11.4)</td>
</tr>
<tr>
<td>Juvenile idiopathic arthritis (JIA)</td>
<td>207 (18.3)</td>
</tr>
<tr>
<td>- Oligoarticular JIA</td>
<td>97 (46.9)</td>
</tr>
<tr>
<td>- Enthesitis related arthritis</td>
<td>76 (36.8)</td>
</tr>
<tr>
<td>- Polymarticular JIA</td>
<td>15 (7.3)</td>
</tr>
<tr>
<td>- Psoriatic arthritis</td>
<td>10 (4.8)</td>
</tr>
<tr>
<td>- Systemic JIA</td>
<td>8 (3.8)</td>
</tr>
<tr>
<td>- Unclassified</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td>Vasculitis</td>
<td>160 (14.2)</td>
</tr>
<tr>
<td>- Henoch-Schönlein purpura</td>
<td>127 (79.5)</td>
</tr>
<tr>
<td>- Kawasaki disease</td>
<td>16 (10)</td>
</tr>
<tr>
<td>- Behcet's disease</td>
<td>11 (6.8)</td>
</tr>
<tr>
<td>- Takayasu arthritis</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>- Adenose deaminase 2 deficiency</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>- Other (drug or infection induced)</td>
<td>4 (2.5)</td>
</tr>
<tr>
<td>Reactive arthritis and toxic synovitis</td>
<td>68 (6)</td>
</tr>
<tr>
<td>Acute rheumatic fever</td>
<td>46 (4)</td>
</tr>
<tr>
<td>Raynaud’s phenomena</td>
<td>42 (3.8)</td>
</tr>
<tr>
<td>Uveitis</td>
<td>15 (1.3)</td>
</tr>
<tr>
<td>Juvenile systemic lupus erythematosus</td>
<td>14 (1.2)</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>13 (1.1)</td>
</tr>
<tr>
<td>Juvenile sieroderma</td>
<td>6 (0.6)</td>
</tr>
<tr>
<td>Others</td>
<td>6 (0.6)</td>
</tr>
</tbody>
</table>

**Abstract AB0991 Table 2. Distribution of the patients who had non-rheumatic conditions**

<table>
<thead>
<tr>
<th>Non-rheumatic conditions</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vitamin D deficiency</td>
<td>148 (16.8)</td>
</tr>
<tr>
<td>Infections</td>
<td>102 (11.6)</td>
</tr>
<tr>
<td>Orthopedic disorders</td>
<td>73 (8.3)</td>
</tr>
<tr>
<td>Growing pains</td>
<td>57 (6.4)</td>
</tr>
<tr>
<td>Dermatological disorders</td>
<td>52 (5.9)</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>42 (4.8)</td>
</tr>
<tr>
<td>Hypermobility</td>
<td>41 (4.7)</td>
</tr>
<tr>
<td>Recurrent oral aphthous ulcers</td>
<td>34 (3.9)</td>
</tr>
<tr>
<td>Mechanical problems</td>
<td>24 (2.7)</td>
</tr>
<tr>
<td>Bony or malig lesions of the bone</td>
<td>11 (1.3)</td>
</tr>
<tr>
<td>Hematologic disorders</td>
<td>7 (0.8)</td>
</tr>
<tr>
<td>Pain amplification syndrome or fibromyalgia</td>
<td>7 (0.8)</td>
</tr>
<tr>
<td>Others</td>
<td>281 (32)</td>
</tr>
</tbody>
</table>

**Conclusion:** Both in our country and all over the world, there are limited number of pediatric rheumatology centers and experienced pediatric rheumatologists, and it is clearly known that diagnosing a rheumatic disease requires a careful evaluation and a high index of suspicion. As our study implies, a vast majority of referrals are composed of non-rheumatic conditions, so specifying the algorithms before referring the patients to pediatric rheumatology centers will be cost-effective and time for evaluation of patients with rheumatic diseases will be satisfactory.

**REFERENCES**


**Disclosure of Interests:** None declared

**DoI:** 10.1136/annrheumdis-2019-eular.1406

**AB0992 HEPATITIS A VIRUS VACCINATION IN AUTOINFLAMMATORY DISEASES UNDER CANAKINUMAB AND TOCILIZUMAB TREATMENT**

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**Background:** Autoimmune, autoinflammatory mechanism and drugs used in treatment increase the risk of liver disease in patients with chronic rheumatic diseases. Hepatitis A vaccine is a highly effective vaccine that prevents both the formation and spread of clinical hepatitis. The risk of various infections increases with the immunosuppressive effect of both the disease and the drugs. Therefore, vaccination of these diseases is of high importance for the prevention of infectious diseases. Systemic juvenile idiopathic arthritis (SJIA) arthritis is a juvenile idiopathic arthritis (JIA) subtype with autoinflammatory pathogenesis. Steroid, methotrexate and anti-interleukin 1 and 6 are used for the SJIA treatment. Anti-interleukin 1 treatments are also used in the treatment of Cryopyrin-associated periodic syndromes (CAPS), which is also characterized with autoinflammatory pathogenesis.

**Objectives:** The aim of this study was to investigate the efficacy and safety of hepatitis A vaccine in patients with autoinflammatory disease on anti-interleukin 1 and 6 treatment.

**Methods:** In this study a total of 39 patients with autoinflammatory diseases on anti IL-1 and IL-6 therapy were initially evaluated but 25 of them were excluded due to anti-HAV IgG positivity. At the end, 24 patients with autoinflammatory diseases on anti IL-1, anti IL-6 therapy and 39 healthy participants who were seronegative for hepatitis A received two doses of the hepatitis A vaccine in a 0 and 6 month schedule. Hepatitis A virus (HAV) IgG antibodies were measured before vaccination and one month after last dose of the vaccine. Anti-HAV IgG titer as S/CO:1.1, IU/L was considered positive and protective.

**Results:** Total 24 patients with autoinflammatory condition (13 females, 11 males) and 39 healthy controls (16 female, 21 male) were included in the study. Among patients with diagnosis of autoinflammatory disease, 19 were SJIA and 5 were CAPS patients. The mean age was 14.1±3.7 and 12.2±3.3 years respectively. Canakinumab was used in 15 (62.5%) and tocilizumab in 9 (37.5%) all patients. Among all SJIA patients, 10 (52.6%) were treated with canakinumab and 9 (47.4%) were treated with tocilizumab. All patients with CAPS (n: 5) were using canakinumab. Among SJIA cases, 15 (75%) were also using methotrexate and 14 (70%) prednisolone. Anti-HAV IgG concentrations were measured one month after the last dose of hepatitis A vaccine. There was statistically significant difference between patients with autoinflammatory condition and healthy controls regarding the anti-HAV IgG titer (mean 5.3±1.5 IU/L) versus (10.5±7 IU/L) p<0.05. The rate of anti-HAV IgG seropositivity (cut-off 1.1 IU/L) in autoinflammatory disease (24/24 (100%)) was significantly different comparing to healthy controls (33/39, 84.6%) (p=0.04). There was no disease flare of disease nor the adverse event detected in any patients after vaccination.

**Conclusion:** Anti-HAV IgG seroconversion was detected in patients with autoinflammatory disease on anti-IL1 and anti -IL6 therapy 1 month after the last dose of hepatitis A vaccine. The response to vaccine did not differ between healthy children and patients with autoinflammatory disease under canakinumab and tocilizumab. In this study hepatitis A vaccine was found to be safe in autoinflammatory diseases with canakinumab and tocilizumab treatment.

**REFERENCES**


**Disclosure of Interests:** None declared

**DoI:** 10.1136/annrheumdis-2019-eular.2249
COMORBIDITIES IN FAMILIAL MEDITERRANEAN FEVER

The relationship between vitamin D and disease activity was analyzed based on juvenile arthritis disease activity score (JADAS27).

Objectives:
The aim of this study was to examine the status of vitamin D in children with JIA depending on the peculiarities of the disease and the season.

Methods:
92 patients with JIA were examined. The median age of them was 10.5±2.17 years, from 1.8 to 17.6 years (55 female, 37 male). The serum level of vitamin D was measured through blood test by chemiluminescence method. The relationship between the level of vitamin D and disease activity was analyzed based on juvenile arthritis disease activity score (JADAS27).

Results:
The average level of vitamin D was 22.75±1.97 ng/ml (corresponded to an insufficient level). It was not found relationship between the level of vitamin D deficiency and gender. Vitamin D status changed throughout the year from lowest value 19.52±1.61 ng/ml (in May) till the greatest value 29.62±2.49 ng/ml (in September). Significantly higher level of vitamin D was in September compared to most months (January, p=0.04; February, p=0.04; March, p=0.01; April, p=0.02; May, p=0.01; October, p=0.03; November, p=0.03; December, p=0.01).

The geographical location of Kharkiv (Ukraine) is at 50° latitude. It was proved that UVB radiation above the 33° latitude is not intense enough for the synthesis of vitamin D during the whole year [3]. At the same time there was no significant relationship between the low level of vitamin D in serum and disease activity.

Conclusion:
A decrease of vitamin D status were observed throughout the year. Despite the fact that in September was the highest level of vitamin D, the normal concentration was not reached. Seasons should be taken into account, but patients with JIA need supplementation of vitamin D all around the year.

REFERENCES

Disclosure of Interests:
None declared.


EXPLORING UVETIS IN EARLY ONSET ANA POSITIVE JIA

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Background: Juvenile idiopathic arthritis (JIA) is the most frequent childhood systemic disease associated with uveitis, where uveitis occurs in 10–13% of the patients, frequently causing long lasting consequences when unrecognized, untimely or incorrectly treated.

Objectives: To explore correlations between age, gender, ANA, RF titer in patients with JIA, occurrence of ocular manifestations and its complications. To examine similarities and differences between patients with different subtypes of JIA and uveitis.

Methods: The retrospective study included 31 children treated for JIA and uveitis in the period 2009-2017 at the Department of Paediatrics, UHC Zagreb. The SUN working group classification and grading system were used to evaluate ocular manifestations. Data analysis was executed using R programming language.

Results: We followed 31 patients (81% female) suffering from JIA with ocular manifestations. Median age at JIA onset in girls was 2.5 (1-14.5) years and in boys 8.6 (11-14.5) years, while girls had median age 4.25 (1-14) years at first ocular manifestation and boys 8.25 (4 -13.5) years. All patients were RF negative. 61% of patients was ANA positive, out of
which 88% had onset of JIA before the age of 6 (all girls). Complete remission of uveitis was achieved in two patients treated with topical corticosteroids, with non-steroidal anti-inflammatory medication and methotrexate used in one of the patients. Inactive uveitis was most frequently achieved with a combined therapy which included biologics. A patient suffering from uveitis and JIA was found to be significantly more likely to suffer from oligoarticular subtype (64.5%, CI 45.4-80.8%, p<0.001). We determined that a positive ANA titer occurred statistically more frequently in females (OR int., CI 3.18-int., p=0.001). No significant statistical difference in ANA titer was found between groups of patients who were diagnosed with rheumatologic or ocular disease before and after the age of 6 (OR 1.85, CI 0.12-29.57, p=0.6111) nor between different subtypes of JIA. There was no difference in time passed between the occurrence of rheumatologic and ocular manifestations (median difference =1.75 years, W=131, p=0.2597), nor between ANA titer (OR 0.57, CI 0.09-3.12, p=0.4775) between groups with and without ocular complications. Patients who first presented with ocular manifestations did not have a greater likelihood to develop ocular complications (OR 5.59, CI 0.51-299.98, p=0.175).

Conclusion: A group of female patients suffering from RF negative subtypes of JIA and uveitis, with onset occurring before the age of 6 and positive ANA was prominent. These patients were traditionally classified as different subtypes of JIA, but together, they are best described as “early onset ANA positive JIA”, concuring the need for reclassification of JIA. Limited by a small number of patients, this was partly confirmed with significant statistical findings, a recurrent positive ANA titer in females with JIA and uveitis and a more frequent occurrence of uveitis in oligoarthrits. The occurrence of ocular complications was not dependent upon ANA titer, nor upon the time difference between rheumatic and ocular symptoms or their order of appearance.

REFERENCE

Disclosure of Interests: None declared

AB0096
APPLICATION OF YAMAGUCHI CRITERIA FOR CLASSIFICATION OF SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS
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Background: The ILAR criteria require the presence of arthritis to classify a patient as having sJIA. The sJIA patients prior to the onset of arthritis (suspected sJIA) appeared clinically similar to patients fulfilling the ILAR criteria for sJIA.

Objectives: Children with sJIA may have a delayed onset of arthritis and it fail to fulfill the ILAR criteria for sJIA. This study was undertaken to determine whether the Yamaguchi criteria is useful in classification of child with sJIA particularly in pre-arthetic phase of illness.

Methods: Retrospective chart review all patients with a diagnosis of sJIA in Hallym University Medical Center from Feb. 2002 through April 2016.

Results: Total 73 patients were diagnosed by ILAR classification criteria, 38 boys and 35 girls formed the study cohort. There are only 20 patients who are fulfilled of ILAR criteria in sJIA. Characteristics sJIA (n=20) suspected (n=53) Total (n=73)

Evanescent Rash 19 24
Sore throat 1 5
Lymphadenopathy 2 11
Hepatomegaly 1 11
Splenomegaly 4 10

37 patients were diagnosed with suspected sJIA due to have not an arthritis. 36 patients were presented the arthritis at the onset of sJIA. The Yamaguchi criteria was fulfilled in a higher number of patients in the study (n=44) as compared to the ILAR criteria (n=20). Among the patients with the absence of arthritis (n=37), 25 patients fulfilled the Yamaguchi criteria. (67.5%).

ILAR criteria Yamaguchi criteria
Yamaguchi criteria fulfilled 16 28
Yamaguchi criteria not fulfilled 4 25
Total cohort 20 53

Conclusion: Overall the Yamaguchi criteria was fulfilled in a higher number of patients in the study (60.2%) as compared to the ILAR criteria (27.3%). The failure of ILAR criteria was mainly due to the absence of arthritis. The Yamaguchi criteria is more helpful to diagnosis of sJIA. The Yamaguchi criteria may be useful on early diagnosis and treatment for patient with delayed onset arthritis at onset of disease.

REFERENCE

Disclosure of Interests: None declared

AB0097 MATCHED CONTROLLED SURVEILLANCE OF TOCILIZUMAB TREATMENT FOR POLYARTICULAR JUVENILE IDIOPATHIC ARTHRITIS–AN INTERIM ANALYSIS
Arane Kleen, Dennis Conzelmann, Toni Hospach, Frank Weiler-Heinemann, Sandra Hansmann, Jasmin Kuemmerle-Deschner, Michael Borte, Kirsten Minden, Ivan Foeldvari, Christoph Rietzschel, Gerd Ganser, Ralf Trauzeddel, Markus Hufnagel, Dirk Foell, Rainer Berendes, Gudula Boeschow, Prasad Commen, Angelika Thon, Gerd Homett, BIKER-Registry, BIKER-Registry, Sankt Augustin, Germany

Background: Tocilizumab (TOC) is approved for treatment of polyarticular juvenile idiopathic arthritis (pJIA). Real world data are limited.

Objectives: Long-term surveillance of patients newly initiating tocilizumab treatment for at least five years using TOC and a control cohort using alternative biologics.

Methods: Baseline demographics, clinical characteristics and disease activity parameters as well as efficacy and safety parameters were compared between patients using TOC and a control cohort using alternative biologics. The cohorts were matched for region and date of therapy start. Efficacy outcome variables were JADAS10 and joint counts. Functional status was determined with the Childhood Health Assessment Questionnaire disability-index (CHAQ-DI). Safety assessments were based on adverse events (AE) reports.

Results: Patients starting on TOC had a longer disease duration (5.2y vs. 2.9 y; p= 0.0001) and had TOC significantly more often as second line biologic than patients in the comparator group (80% vs 14%, p< 0.0001). No differences could be observed regarding disease activity parameters (JADAS 10 14.7 +/- 6.4 vs 15.8 +/- 6.0) or disability (CHAQ DI 0.65 +/- 0.63 vs 0.66 +/- 0.66) at baseline. Patients treated with TOC showed a substantial response to treatment with a significant reduction in JADAS 10 from 14.7 to 5.4 (p<0.0001). After 6 months of TOC treatment, 40% of patients had reached JADAS minimal disease activity (MDA), 22% of patients had reached JADAS remission. Tolerability was comparable between the two cohorts, with 31 in the TOC versus 34 patients in the control cohort experiencing AE; serious AE (SAE) were documented in 3 patients in the TOC and one patient in the control cohort. The SAE in the TOC cohort were medication intoxication with suicidal intent, JIA flare, gastrointestinal infection and abdominal pain in 1 patient each. In the control cohort there were JIA flare in 2 patients and gastrointestinal infection in 1 patient. No significant differences regarding infectious AEs, cytopenias or elevated transaminases were observed. No other AE were reported more than once; no deaths occurred.

Conclusion: Comparability of efficacy was limited due to the fact that patients in the TOC cohort had longer disease duration and were more often second line biologic users. Tolerability was comparable in both cohorts. Long-term observation is ongoing.
Severe IGA Vasculitis: Cyclophosphamide in Treatment Follow-up After Transition from Paediatric to Adult Rheumatology Care

Background: Cyclophosphamide (CYC) has been a mainstay in the treatment of severe childhood primary systemic vasculitis. Although major organ involvement is rare in Iga vasculitis (IgAV), CYC is among therapeautical options in moderate and severe IgAV nephritis. No specific recommendations are available for severe vasculitis of IgAV.

Objectives: To describe disease course and treatment response in 2 patients with severe IgAV with CNS and renal involvement.

Methods: Case reports with disease assessments using Paediatric Vasculitis Activity Score (PVAS).

Results: Both children were Caucasian boys with unremarkable previous history aged 4 (Patient 1) and 8 (Patient 2) years. In both cases the initial typical presentation included purpura and abdominal pain in both, arthritis in Patient 1 and haematuria in Patient 2. After 2 weeks of prednisone therapy for severe gastrointestinal (GIT) symptoms Patient 1 was admitted for right-sided weakness and facial palsy. His brain MRI revealed an ischaemic lesion. His PVAS reached 21/63 for skin, abdominal, renal (haematuria) and CNS systems. When Patient 2 was admitted for abdominal symptoms he developed a focal epileptic paroxysm. His brain MRI was compatible with cerebral vasculitis. His nephritic-nephrotic syndrome prompted renal biopsy showing mesangio proliferative nephritis with IgA deposits. His PVAS was 27/63 for skin, abdominal, renal (hyper tension, haematuria, proteinuria) and CNS systems. Both patients received 3 doses of intravenous methylprednisolone 30 mg/kg followed by oral prednisone 1 mg/kg with subsequent tapering and 3 doses of CYC 500mg/m² (monthly i.v.). At follow-up 3 months after the 1st CYC dose both patients fully recovered neurologically. Patient 2 was on prednisone (0.2 mg/kg) and ACE inhibitor and his urine was negative for the first time. PVAS=0. Patient 1 had been developing significant proteinuria during prednisone withdrawal and his PVAS counted 10/63 for renal disease. Prednisone was re-instituted and ACE inhibitor added while renal biopsy has been pending.

Conclusion: In both cases therapy with corticosteroids and CYC led to the full recovery of CNS disease but did not prevent progression of nephritis in Patient 1. Response of Patient 2 nephritis to CYC appeared satisfactory at 3 months visit but would require confirmation after full prednisone withdrawal. Although generally benign, when IgAV presents with major organ involvement its treatment is challenging. Further research is needed in order to gather better evidence to support treatment recommendations.

Disclosure of Interests: Ariane Klein: None declared, Dennis Conzelmann: None declared, Toni Hossbach Speakers bureau: Chugai, Roche, Novartis, Frank Weller-Heinemann: None declared, Sandra Hansmann: None declared, Jasmin Kuemmerle-Deschner Grant/research support from: Jasmin Kuemmerle-Deschner is an employee of University of Tuebingen, Germany, and received consultants/speakers fees from Novartis and SOBI pharmaceuticals and grant support from SOBI and Novartis., Consultant for: Jasmin Kuemmerle-Deschner is an employee of University of Tuebingen, Germany, and received consultants/speakers fees from Novartis and SOBI pharmaceuticals and grant support from SOBI and Novartis., Christoph Rietschel: None declared, Ralf Trauzeddel: None declared, Markus Hufnagel: None declared, Dirk Foell Grant/research support from: not specified, Consultant for: not specified, Speckers bureau: not specified, Rainer Berendes: None declared, Gundula Boeschow: None declared, Praasad Oommen: None declared, Angelika Thon: None declared, Gerd Horneff: None declared


AB0998

Severe IGA Vasculitis: Cyclophosphamide in Question

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Background: Cyclophosphamide (CYC) has been a mainstay in the treatment of severe childhood primary systemic vasculitis. Although major

Disclosure of Interests: None declared

AB0999

Treatment Follow-up after Transition from Paediatric to Adult Rheumatology Care

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Background: Many juvenile onset rheumatic diseases continue to have activity in adulthood. Therefore, a continuous uninterrupted healthcare of these patients is needed.

Objectives: To determine whether and how therapy has changed in patients after transition from paediatric to adult rheumatology service in our medical centre.

Methods: A retrospective single centre study was performed. Patients seen at least once at both paediatric and adult rheumatology outpatient service were enrolled. Data was collected from patients medical records.

Results: A total of 50 patients were included. Most of them were female (82%). Average age at transition was 19.6 years (range 18-27 years). Mean time of follow up was 44 months (range 2-119 months). Juvenile idiopathic arthritis (JIA) was the most common juvenile onset chronic rheumatic disease. The medications used either as monotherapy or in combination before transition at last visit at paediatric rheumatology
outpatient unit were nonsteroidal anti-inflammatory drugs (NSAIDs) (14%), corticosteroids (6%), synthetic disease modifying antirheumatic drugs (DMARDs) (18%), biologic DMARDs (2%). After transition 34% of patients used NSAIDs, 16% corticosteroids, 24% synthetic DMARDs, 8% biologic DMARDs. Without any medication before and after transition were 66% and 48% of patients, respectively. After transition 36% of patients had their therapy changed. 30% needed escalation of therapy because their disease was still active or they experienced exacerbation.

Most changes in therapy occurred in the first year after transition. 

Conclusion: We confirmed that many patients with juvenile onset rheumatic disease had changes in their therapy after transition, especially escalations of therapy. Most changes occurred in the first year after transition which is a vulnerable period in a young adult life.

REFERENCES


**THE SURVIVAL OF METHOTREXATE IN JUVENILE IDIOPATHIC ARTHRITIS CHILDREN AFTER DURING FIRST BIOLOGIC TREATMENT**

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Background: Methotrexate (MTX) is a gold standard for treatment of juvenile idiopathic arthritis (JIA) patients. The main adverse events (AE) related to the MTX are intolerance, increased rate of infections, elevation of the liver enzymes, hematological abnormalities and stomatitis, which required to stop the MTX therapy [1]. In children without remission who tolerated MTX often the second-line treatment is the biologics, which may use alone or in the combination with MTX.

Objectives: The aim of our study was to evaluate the main reasons of MTX discontinuation in JIA children who started first biologic.

Methods: In the study were included 173 non-systemic JIA patients, whom biologic therapy was prescribed firstly to previous MTX treatment. We evaluate the main reasons of MTX discontinuation after the starting of the biologic treatment, duration of MTX treatment (all and after biologic start), achievement the remission, according C. Wallace criteria and time to remission, flare of JIA. We compared two groups: i) patients with biologics with ongoing methotrexate and ii) patients with biologics alone, whom MTX was discontinued or not prescribed.

Results: During the trial MTX discontinued 40 (23.1%) patients: due to intolerance (n=11), other adverse events (AE) (n=10), except intolerance (mainly, frequent infection and transaminitis) and remission of JIA (n=19). Patients with onset age of JIA <4.4 years were in the risk of developing MTX intolerance (LogRank test, p=0.000001), but the younger patients usually developed other AE. Compare of the three subgroups of patients, who discontinued MTX we have not yet found any differences, except the onset age and frequency of remission, which was higher in patients who discontinued MTX due to other AE than due to intolerance.

Conclusion: The main factor, associated with MTX discontinuation in JIA patients, who received first biologic was the disease onset age. Eldest age was related to higher risk of developing the MTX intolerance.

REFERENCES
**AB1001**

ARE ANY DIFFERENCES IN THE LOCATION OF BONE LESIONS BETWEEN BONE MALIGNANT TUMORS AND INFLAMMATORY OSTEOPATHIES?

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**Background:** Different pediatric bone destructive diseases may have similar radiological findings but have their typical localizations [1].

**Objectives:** The aim of our study was to differences in the bone lesions location in various pediatric bone destructive diseases.

**Methods:** Our cohort (n=204) consists of four main subtypes: i) chronic non-bacterial osteomyelitis (CNO, n=91), ii) hematogenous osteomyelitis (HO, n=47); iii) tuberculosis osteomyelitis (TBO, n=33), and iv) malignant bone tumors (MBT, n=33) - osteosarcoma and Ewing’s sarcoma.

**Results:** All bone destructive diseases have the similar frequency of femur and humerus involvement. MBT patients compare to others had the highest onset age, and higher frequency of pelvic involvement, and comparatively rare the involvement of spine, tibia, foot bones, sternum, the bones of forearm and hand (table).

**Conclusion:** Patients with bone destructive process with femur, humerus and pelvic involvement have to be under high level of consideration about all type of osteopathy, especially MBT.

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**REFERENCES**


**Disclosure of Interests:** None declared


**AB1002**

IMMUNOGLOBULIN G4 RELATED DISEASE IN A 10 YEAR-OLD GIRL WITH MULTISYSTEM INVOLVEMENT

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**Background:** IgG4-related disease (IgG4RD) is an immune-mediated fibroinflammatory condition characterized by the infiltration of IgG4-carrying plasma cells and storiform fibrosis in most of the tissues. The condition is reported to cause multisystem involvement, however salivary gland is the most commonly affected organ with IgG4-related sialadenitis. Raised IgG4 concentrations in the serum and prominent infiltration by plasma-cytes expressing IgG4 in the lacrimal and salivary glands have been confirmed.

**Objectives:** IgG4-RD has mostly been described in adult population and therefore generally not well-known among paediatricians. To the best of our knowledge, this patient is one of the rare paediatric cases in literature diagnosed with IgG4-RD. We intended to emphasize that IgG4RD should be kept in mind for differential diagnosis of the patients presenting with enlarged parotid, lacrimal and submandibular glands and sicca symptoms.

**Methods:** We extracted patient’s clinical, laboratory and imaging data from our database and reviewed literature to reveal different manifestations of the IgG4RD.

**Results:** 10 year-old-girl presented with lacrimal and salivary gland swelling, sicca symptoms and fatigue. Ultrasound scan (US) neck revealed multiple small lymph nodes and enlargement of both submandibular glands. Salivary glands also appeared bulky and heterogenous with multiple small hypoechoic foci. Appearances were likely to represent sialoadenitis and there was no convincing evidence of malignancy or lymphoma. USS abdomen showed no abnormality. Full blood count, routine biochemistry and urine microscopy were normal. Autoantibodies came back as negative (ANA/Negative, ANCA: negative, Anti-Ro and Anti-La: negative, RF:Negative, thyroid autoantibodies: negative). Anti-Cardiolipin IgG was weakly positive on the first visit, however repeated analyses were negative. IgG level was elevated in repeated samples. IgA, IgM and IgE levels remained normal. IgG subclasses were performed which revealed significantly elevated IgG4 levels (21.49 Normal range: 0-1.1) IgG1, IgG2 and IgG3 levels were slightly elevated. The biopsy of salivary gland showed chronic inflammation with IgG4 staining and was suggestive of IgG4 related disorder. The patient was diagnosed with IgG4 related disease and treatment was started with intravenous methylprednisolone followed by Anti-CD20 (Rituximab) therapy and a weaning plan for steroids was given. Mycophenolate motefilk was commenced for the maintenance therapy. Patient has been in remission on maintenance therapy.

**Conclusion:** IgG4RD is a rare condition which can cause multisystem involvement with the infiltration of IgG4-bearing plasma cells in the tissues. We wanted to emphasize that this condition could also be seen in the paediatric population. Steroids are the cornerstone of the treatment, however Anti-CD20 medication (Rituximab) and steroid sparing agents such as mycophenolate motefilk could be the choice for maintenance therapy.

**REFERENCES**


**Disclosure of Interests:** None declared

AB1003  DELAY IN DIAGNOSIS OF KAWASAKI DISEASE IS THE COMMONEST PROXIMATE REASON FOR DEVELOPMENT OF GIANT CORONARY ARTERY ANEURYSMS- OUR EXPERIENCE AT CHANDIGARH, NORTH INDIA

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Background: Long-term effects of Kawasaki disease (KD) depend primarily on development of coronary artery abnormalities. Giant coronary aneurysm (GCA) is one of the most severe sequelae in KD. Regression of giant aneurysm is rare. Data from Indian subcontinent is limited. In this study we review patients with KD who had GCA.

Objectives: To describe the profile of patients with KD who developed GCA from a cohort of KD patients at Advanced Pediatric Centre, Post-graduate Institute of Medical Education and Research (PGIMER), Chandigarh.

Methods: Records of all children diagnosed to have KD during 1994-2017 were analysed. Out of the 680 patients with KD, clinical details of 17 (2.5%) children with GCA were retrieved.

Results: Diagnosis of GCA was based on coronary artery diameter >8 mm or >10 z score. Six of 17 children (boys 13: girls 4) with GCA had incomplete KD. Diagnosis of KD was made at a mean of 17.2±12.2 days of fever. Eighty (47%) children were <1 year. Median age of diagnosis was 18 months (range 1.5 months-12 years). Left anterior descending (LAD) coronary artery was affected in 82% followed by right coronary artery (RCA) in 59%. Multiple GCA >1 were seen in 65% patients. All patients had received first line therapy as IVig. Median day of IVig administration was 15.5 days. Twelve patients received additional therapy with infliximab. Thromboses developed in 4 (23.5%) and most common coronary artery affected was LAD. All patients were started on anticoagulation therapy and there were no significant complications related to anticoagulation.

Conclusion: Results of this study suggest that GCA develop more commonly in infants and young children. Delay in diagnosis and consequent administration of IVig appears to be the commonest proximate cause of development of GCA.

REFERENCES

Disclosure of Interests: None declared

AB1004  LUPUS LIKE SYNDROME ASSOCIATED WITH INFlixIMAB TREATMENT IN CHILDHOOD: CASE SERIES OF TWO PATIENT

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Background: Drug-induced lupus (DIL) caused by medication is a form of lupus erythematosus. When the medication is stopped, disease symptoms generally disappear in 4 days or months. Infliximab is an anti-TNF chimeric antibody widely used and approved for the treatment of many diseases. TNF-α antagonist induced lupus-like syndrome (TAILS) is among the uncommon side effects of infliximab. TAILS is a clinical syndrome with features similar to SLE, but with some differences in laboratory and clinical findings.

Objectives: We have presented our experience with lupus like syndrome emerge after infliximab treatment in two children.

Methods: We evaluated the clinical properties of 2 patients who were monitored with diagnoses of juvenile idiopathic arthritis and uveitis symptoms and developed TAILS after infliximab treatment.

Results: First patient applied to our pediatric rheumatology outpatient clinic with a complaint of swelling in the left knee continuing for 1 month. During the physical examination, we found arthritis on the left knee. During the eye examination, it was discovered that he had bilateral pars planitas. Anti-nuclear antibodies were found positive at 1/320 titration, and anti-dsDNA was negative. Following JIA and accompanying uveitis diagnoses, methylprednisolone and methotrexate treatment was started for the patient. After treatment, the patient’s joint and eye symptoms started to regress, was subjected to lesser dose of methylprednisolone, but the uveitis attack of the patient started to occur again. We added infliximab treatment to its treatment that was resistant to uveitis. At the 6-month of infliximab treatment, there was no uveitis attack observed. During remission, after 6. dose of infliximab treatment, there were complaints of tiredness and polyarthralgia. It was observed that the patient had arthritis in several joints. After the re-studied laboratory tests, there was anti-dsDNA antibody positivity. We thought the patient developed TAILS, and stopped the infliximab treatment. After stopping the treatment, the complaints of tiredness and polyarthralgia, as well as arthritis symptoms were improved, and anti-dsDNA antibody levels returned back to normal. The second, 15-year-old patient was being monitored by pediatric rheumatologist outpatient clinic with oiliaric JIA diagnosis since the age of 1. The patient had also uveitis on the right eye since the age of 6. During methylprednisolone, methotrexate, and azathioprine treatment, there were uveitis attacks that developed at different periods. We started infliximab treatment for uveitis of the patient. After 2. dose of infliximab, the patient started to complain about migraine style headaches that occurred once or twice a week. In re-done laboratory tests, ANA (at 1/320 titration), anti-cardiolipin antibody, and anti-beta2 glyco-protein antibody were found positive. There was also low levels of C3 and C4 detected. The infliximab treatment was stopped for the patient who was diagnosed with TAILS. After stopping treatment, the headache complaints regressed, and auto-antibody positivity’s turned back to normal.

Conclusion: Although the development of ANA anti- dsDNA antibodies during infliximab therapy is common, TAILS is rare, especially in the pediatric population. In patients develop SLE findings under infliximab infusion, TAILS must be considered and the drug should be discontinued.

REFERENCES

Acknowledgement: We are grateful to all participating children and their families. All the participants and their legal guardians were informed, and their written consent was obtained. Disclosure of Interest: None Declared

Disclosure of Interests: None declared

AB1005  THE UNUSUAL ADVERSE EVENTS INCLUDING MULTIPLE SCLEROSIS DEVELOPED UNDER ABATACEPT THERAPY IN A PATIENT WITH JIA

Alia Latylova, Anna Shapovalenko, Irina Nikishina. V.A.Nasonova Research Institute of Rheumatology, Pediatric, Moscow, Russian Federation

Background: Biological therapy in patients with pediatric rheumatology disease may be associated with adverse events up to demyelinating lesion of CNS including multiple sclerosis (MS). It is a rare condition in the pediatric practice.

Objectives: to describe the clinical case of newly diagnosed psoriasis arthritis and subsequently developing of multiple sclerosis in pediatric patient revealed in JIA who has been followed-up in Pediatric department of V. A, Nasonova Research Institute of Rheumatology for 8 years.

Methods: Description of clinical case of 13 y.o. male Caucasian pts presented with polyarthritis variant of juvenile idiopathic arthritis (JIA) since 2006.

Results: The first symptoms (at the age of 1.5) were polyarthritics with fever, morning stiffness and inflammatory activity in laboratory tests in chronological link of DTP – re-vaccination. The patient admitted to the regional hospital where JIA was diagnosed and he received traditional therapy including NSAIDS, methotrexate, numerous of intrarticular injections, methylprednisolone pulse therapy with initial response. By the 2012 the child deteriorated with progressive polyarthritics, deformation of wrist joints, bilateral camptodactylia with progressive destruction on X-ray. Under the administration of abatacept therapy in our clinic in 2012 the significant improvement (70-90% ACR response) was achieved. 2 years later the plaque psoriasis developed. The cutaneous changes were impaired by the regular local application of GC so infusions of abatacept were continued. In 4th years of regular therapy (in the age of 13) sudden neurological symptoms such as headache, loss of sensitivity, ataxia, visual field defect appeared. He was admitted to neurological clinic. Multiple sclerosis was diagnosed based on the presenting signs and symptoms supporting cranial MRI – multiple focal areas of demyelination.

Conclusion: We presented a patient with JIA who developed two different immunological related adverse events under long-term abatacept using:
psoriasis “de novo” appeared as a native origin of juvenile arthritis and CNS – multiple sclerosis. This is the first case of developing MS under the abatacept therapy, confirming the 1118 pts (2002-2018) who receive biological therapy in our clinic.

Disclosure of Interests: None declared

AB1006 THE CLINICAL SPECTRUM OF TWO HETEROZYGOUS MUTATIONS IN THE MVK GENE CONFIRMING HYPERIMMUNOGLOBULIN D SYNDROME

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Background: Autoinflammatory syndromes represent the wide spectrum of rare diseases (associated with genetic disturbances) characterized by the presence of chronic or recurrent systemic inflammation with diverse clinical presentation.

Objectives: We report a case report of child with confirmed two heterozygous mutations in the MVK gene with clinical features associated hyperimmunoglobulin D syndrome.

Results: We present girl with clinical symptoms starting just after birth when in the first days of life she was examined at gastroenterology department in Belgrade due to elevated parameters of inflammation, anemia, direct hyperbilirubinaemia, abdominal bloating and hepatosplenomegaly. Breastfeeding was discontinued due to galactosuria and lactose free diet was advised. Due to the maintenance of hepatomegaly, a detailed hematological, virusological and gastroenterological diagnostic testing was performed. Since liver biopsy has shown portal and lobular hepatitis with cholestasis without fibrosis she was on ursosulfate treatment with partial response. At five months of age she started to have recurrent episodes of fever every month for few days with no associated infection, but always followed with digestive symptomatology (abdominal pain and abdominal flatulence) and elevation of inflammatory parameters. Despite antibiotics, episodes of fever continued to repeat twice monthly with accompanying occurrence of hypersalivation, small ulcers in the mouth, skin rash, cervical lymphadenopathy, hepatosplenomegaly, abdominal pain and abdominal bloating with elevated inflammatory markers. One year later she was admitted for the first time at our department and detailed differential diagnostic testing was performed. Clinical spectrum of presenting symptoms with specific phenotypic aspect (hypertelorismus and frontal bossing) were enough to suspect on autoinflammatory disease background (hyper IgD syndrome), but without IgG increase. Genetic testing have revealed presence of two heterozygous mutations ( heterozygous variant c.790del p.Leu264Serfs*2) and heterozygous variant c.1129G>A p.Val377Ile) in the mevalonate kinase deficiency gene (MVK gene) confirming hyperimmunoglobulin D syndrome. Introduction of nonsteroidal antiinflammatory drugs and corticosteroids have led to complete or partial remission during a fever episodes. As fever episodes continued on every two weeks we are about to start with donated fully-humanized protein interleukin-1 beta cytokine.

Conclusion: Diverse clinical manifestations of some patients with autoinflammatory syndromes can provoke differential diagnostic and treatment dilemmas. Genetic testing is of great importance for establishing the final diagnosis and starting accurate treatment in order to prevent potential serious complications seen in these patients.

Disclosure of Interests: None declared

AB1007 PREVALENCE AND CHARACTERISTICS OF TEMPOROMANDIBULAR JOINT (TMJ) INVOLVEMENT IN A COHORT OF YOUNG ADULT PATIENTS WITH DIAGNOSIS OF JUVENILE IDIOPATHIC ARTHRITIS (JIA) AND NON-JIA CHRONIC INFLAMMATORY ARTHROPATHIES

Adriano Lercara1, Gloria Crepaldi1, Francesco Licciardi2, Marco Davico3, Stefano Cintio4, Sarah Marouen5, Enrica Vandelli4, Yves-Marie Pers4, Adriano Lercara1, Gloria Crepaldi1, Francesco Licciardi2, Marco Davico3, Stefano Cintio4, Sarah Marouen5, Enrica Vandelli4, Yves-Marie Pers4

Objectives: To investigate the prevalence of TMJ involvement in young adults with JIA and young adults with non-JIA inflammatory rheumatism.

Methods: Patients were recruited prospectively in 2 clinical centers. Inclusion criteria were: patients <35 years diagnosed with JIA who had undergone transition from the pediatric to the adult rheumatologist, and patients diagnosed with non-JIA inflammatory arthropathies. All patients were assessed for joint count, clinical examination for TMJs (tenderness to palpation, swelling, signs of damage such as joint crepitations, lateral deviation, retrogaththis, and decreased mouth opening), evaluation of global disease activity with composite indexes and underwent MRI of the TMJs to detect inflammation (bone marrow edema, effusion, synovial thickening) or damage (condylar flattening, erosions, disk abnormalities); MRIs with either inflammation or damage were considered pathological. Demographic and clinical characteristics were described using frequency or median and interquartile range (IQR), depending on the distribution of the variable. Differences between groups were analyzed using the Mann-Whitney U test and the χ² test when appropriate. The significance was set at p-value ≤ 0.05.

Results: 19 patients were included in the JIA group and 8 patients in the non-JIA group. Patients' demographic and disease characteristics were reported in Table 1.

There are no statistically significant differences between groups for the presence of inflammation on MRI, while damage (in particular, disk abnormalities) is more likely in JIA rather than non-JIA patients (p < 0.02). Joint effusion is more likely to be mild rather than moderate/severe in JIA patients (p = 0.04).

Conclusion: It was found that it is more likely to find damage on MRI in patients of both groups rather than inflammation. Both groups show the same frequency of TMJ involvement, suggesting that TMJ involvement must be sought by the adult rheumatologist as it not only affects JIA patients, but also those with adult-onset inflammatory arthropathies.

REFERENCES

Disclosure of Interests: None declared

AB1007 Table 1

<table>
<thead>
<tr>
<th>JIA</th>
<th>Non-JIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex F, n (%)</td>
<td>16 (64.2%)</td>
</tr>
<tr>
<td>Age (ys), median (IQR)</td>
<td>22 (20.2 – 27.1)</td>
</tr>
<tr>
<td>Global disease activity, n (%)</td>
<td>12 (63.1%)</td>
</tr>
<tr>
<td>Low</td>
<td>1 (5.3%)</td>
</tr>
<tr>
<td>Moderate</td>
<td>5 (26.3%)</td>
</tr>
<tr>
<td>High</td>
<td>1 (5.3%)</td>
</tr>
<tr>
<td>TMJ tenderness, n (%)</td>
<td>4 (21.1%)</td>
</tr>
<tr>
<td>TMJ swelling, n (%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>TMJ damage, n (%)</td>
<td>13 (68.4%)</td>
</tr>
</tbody>
</table>

AB1007 Table 2

MRI results are collected in Table 2.

<table>
<thead>
<tr>
<th>JIA</th>
<th>Non-JIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>TMJs n 38</td>
<td>TMJs n 16</td>
</tr>
<tr>
<td>Inflammation on MRI, n (%)</td>
<td>14 (36.8%)</td>
</tr>
<tr>
<td>Joint damage on MRI, n (%)</td>
<td>26 (68.4%)</td>
</tr>
<tr>
<td>Pathological MRI, n (%)</td>
<td>26 (68.4%)</td>
</tr>
<tr>
<td>TMJ involvement, n patients (%)</td>
<td>2 (10.5%)</td>
</tr>
<tr>
<td>Bilateral</td>
<td>12 (63.2%)</td>
</tr>
</tbody>
</table>

Abstract AB1007 Table 2

There are no statistically significant differences between groups for the presence of inflammation on MRI, while damage (in particular, disk abnormalities) is more likely in JIA rather than non-JIA patients (p = 0.02). Joint effusion is more likely to be mild rather than moderate/severe in JIA patients (p = 0.04).

Conclusion: It was found that it is more likely to find damage on MRI in patients of both groups rather than inflammation. Both groups show the same frequency of TMJ involvement, suggesting that TMJ involvement must be sought by the adult rheumatologist as it not only affects JIA patients, but also those with adult-onset inflammatory arthropathies.
**AB1008**

**AGE DEPENDENT SAFETY AND EFFICACY OF COLCHICINE TREATMENT FOR FAMILIAL MEDITERRANEAN FEVER IN CHILDREN**

Voel Levinsky1,2, Orli Goldberg1,2, Orit Peled1,2, Gideon Koren1,2, Lora Harel1,2, Gil Amarilyo1,2, Schneider Children’s Medical Center of Israel, Petah Tikva, Israel; Sacker Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

**Background:** Colchicine has been found to be highly effective for the treatment of familial Mediterranean fever (FMF). However, it is FDA-approved only for children older than 4 years owing to the lack of studies in younger children.

**Objectives:** Our tertiary pediatric rheumatology department routinely uses colchicine even in very young children with FMF. The aim of the study was to evaluate its safety and efficacy in children with FMF ≤4 years old.

**Methods:** The departmental database was searched for all children diagnosed with FMF between 2010-2018. Those who started treatment with colchicine before age 4 years were identified and matched by MEFV variant to children who started treatment at age ≥4 years. Drug efficacy was assessed by the improvement in the frequency and duration of attacks. Adverse events were assessed according to the Rheumatology Common Toxicity Criteria ver. 2.0.

**Results:** The cohort included 89 patients with FMF: 41 first treated before age 4 years, and 48 first treated at age ≥4 years. Rates of complete response to colchicine were 61% in the younger group and 60.4% in the older group. Corresponding rates of partial remission were 24.4% and 29.2%, respectively (p=0.77). The most frequent adverse event was diarrhea, with a prevalence of 24.4% in the younger group and 22.9% in the older group (p=0.87). There were no significant between-group differences in other adverse events.

**Conclusion:** Colchicine is equally effective and safe for use in patients with FMF under 4 years old, with no difference in response from older pediatric patients.

**Abstract AB1008 Table 1.** Clinical parameters at disease onset in younger and older patients with FMF

<table>
<thead>
<tr>
<th>Clinical parameter</th>
<th>Age &lt;4 yr (n=41)</th>
<th>Age ≥4 yr (n=48)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at symptom onset (yr), mean±SD</td>
<td>1.70 ±0.86</td>
<td>3.45 ±1.40</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fever*</td>
<td>39 (95.1%)</td>
<td>42 (87.5%)</td>
<td>0.27</td>
</tr>
<tr>
<td>Erysipelias-like rash</td>
<td>5 (12.2%)</td>
<td>7 (14.6%)</td>
<td>0.74</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>20 (48.8%)</td>
<td>36 (75.0%)</td>
<td>0.011</td>
</tr>
<tr>
<td>Arthritis</td>
<td>6 (14.6%)</td>
<td>7 (14.6%)</td>
<td>0.99</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>27(65.9%)</td>
<td>35 (72.9%)</td>
<td>0.47</td>
</tr>
<tr>
<td>Chest pain</td>
<td>5 (12.2%)</td>
<td>8 (16.7%)</td>
<td>0.55</td>
</tr>
<tr>
<td>Orchitis</td>
<td>1(2.4%)</td>
<td>1 (2.1%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Protracted febrile myalgia</td>
<td>0 (0%)</td>
<td>2 (4.2%)</td>
<td>0.49</td>
</tr>
<tr>
<td>Frequency of attacks (per month), median (IQR)</td>
<td>2.0 (1.0-3.0)</td>
<td>2.0 (1.0-3.0)</td>
<td>0.39</td>
</tr>
<tr>
<td>Initial colchicine dose (mg/kg), median (IQR)</td>
<td>0.038</td>
<td>0.036</td>
<td>0.60</td>
</tr>
<tr>
<td>Duration of attacks (days), median (IQR)</td>
<td>(0.034-0.046)</td>
<td>(0.031-0.050)</td>
<td></td>
</tr>
</tbody>
</table>

*Defined as >38°C rectally or >37.5°C orally

Data available for 43 patients.

**AB1009**

**CLINICAL FEATURES PREDICTIVE OF RENAL AND GASTROINTESTINAL INVOLVEMENT IN PATIENTS WITH HENOCH-SCHÖNLEIN PURPURA**

Chun-Hua Liao, Li-Chieh Wang, Bor-Luen Chiang. National Taiwan University Children’s Hospital, Department of pediatrics, Taipei, Taiwan, Republic of China

**Background:** Henoch-Schönlein purpura (HSP), the most common form of vasculitis in children, predominantly involves the small vessels of the skin, the gastrointestinal (GI) tract, joints, and kidneys. GI involvement is the most severe short-term complication, in contrast, renal disease is the most troublesome long-term complication. Meanwhile, although the disease course of HSP is usually benign in children, recurrence still occurs in a subset of patients. Studies documenting the incidence and predictive factors of recurrent HSP, and biomarkers of the various manifestations of HSP are limited.

**Objectives:** We aimed to delineate characteristics and biomarkers of HSP patients with GI or renal involvement, and hoped to clarify the incidence and predictive markers of recurrent HSP.

**Methods:** We retrospectively reviewed the medical records of 40 patients admitted in one tertiary medical center in Taipei, Taiwan over a 5-year period with a diagnosis of Henoch-Schönlein purpura. Incidence and risk factors for GI involvement, renal involvement, and recurrent HSP were analyzed. The Mann-Whitney U test and Fisher exact test were utilized for statistical assessment.

**Results:** From January 1, 2005 to December 31, 2010, 40 HSP patients aged ≤18 years were identified. The mean onset age was 8.35±3.3 years. Among them, 45.1%(18/40) of the patients were male. Ten patients had more than 2 HSP episodes (recurrence rate 25%). Renal involvement was noted in 17.5% (7/40) of the patients, and it was found to occur more frequently in children with later onset age (with renal involvement: 11.43±4.33 years; without renal involvement: 7.73±2.72 years; p=0.03). Recurrent HSP was found to occur more frequently in patients with renal involvement, though without statistical significance (odds ratio: 6; 95% confidence interval: 1.05-34.14; p=0.051). Renal involvement was not associated with GI involvement (p=0.69). GI involvement was noted in 47.5% (19/40) of the patients, and it was found to occur more frequently in patients with higher segmented neutrophil percentage as assessed by complete blood count (with GI involvement: 74.16±13.31%; without GI involvement: 61.84±17.22%; p=0.051). GI involvement was not associated with relapse of HSP. Fourteen patients (35%) had arthritis or arthralgia, and it was found to occur more frequently in children with earlier onset age (with arthralgia/arthritis: 7.26±2.55 years; without arthralgia/arthritis: 10.39±3.63 years; p<0.01).

**Conclusion:** HSP patients with GI involvement had higher segmented neutrophil percentage, consistent with previous studies proposing neutrophil-lymphocyte ratio as a biomarker for GI involvement. Patients with renal involvement had a later age of onset, and the relapse rate was higher in this subpopulation but not statistically significant.
Macrophage activation syndrome (MAS) is a severe complication of several rheumatologic diseases, being of special relevance systemic lupus erythematous (SLE) and systemic juvenile idiopathic arthritis (sJIA). Its characterized by an excessive activation of the immune system due to various mechanisms, including hyperactivation of macrophages and a failure in downregulation activity by NK and cytotoxic lymphocytes. There are various criteria for its diagnosis, highlighting secondary lymphohistocytosis syndrome (HLH) criteria from 2004 and provisional secondary MAS criteria for JIA proposed by Ravelli in 2016.

In our case series rash and fever were more frequent among sJIA patients, the rest of the clinical manifestations were more common in SLE group. Analytical measures were more altered in SLE group except for ferritin and ALT. Mortality was 33.33% in SLE group vs 0% in sJIA group, probably due to early diagnosis and treatment in these patients.

REFERENCES


Disclosure of Interests: None declared


AB1010

MACROPHAGE ACTIVATION SYNDROME: A CASE SERIES OF 16 PATIENTS

Jesús Loarce-Martos, Fernando López Gutiérrez, Jose Renato Quiñones Torres, Alina Boteanu, M. Ángeles Bilázquez, Mónica Vázquez Díaz. HU Ramón y Cajal, Madrid, Spain

Background: Macrophage activation syndrome (MAS) is a severe complication of several rheumatologic diseases, being of special relevance systemic lupus erythematous (SLE) and systemic juvenile idiopathic arthritis (sJIA). Its characterized by an excessive activation of the immune system due to various mechanisms, including hyperactivation of macrophages and a failure in downregulation activity by NK and cytotoxic lymphocytes. There are various criteria for its diagnosis, highlighting secondary lymphohistocytosis syndrome (HLH) criteria from 2004 and provisional secondary MAS criteria for JIA proposed by Ravelli in 2016.

Objectives: To describe a case series of patients with MAS.

Methods: This is a retrospective case series of 16 patients with MAS secondary to systemic autoimmune diseases diagnosed in Ramón y Cajal University Hospital between April 2009 and September 2018.

Results: The baseline pathology was sJIA in 8 patients (2 cases with 2 episodes) and SLE in the other 6 patients. Mean age at diagnosis was 17.44 years for sJIA and 37.5 years for SLE. Mean time from diagnosis of the baseline disease to MAS episode was 11.31 years, with 3 cases being the initial manifestation of their systemic disease. 43.8% of patients were treated with corticosteroids previously to MAS episode, and 50% were being treated with DMARDs/biologic agents (SLE: 3 patients with hydroxychloroquine and 1 patient with mycophenolate and hydroxychloroquine; sJIA: 2 patients with Anakinra, 1 patient with tocilizumab and 1 patient with etanercept). Clinical and analytical characteristics of the patients are presented in table 1 and table 2, respectively. In SLE group, only 2 patients (33.3%) had high anti-DNA titers during the MAS episode, 5 patients (83.3%) had increased C3 consumption and 4 patients (66.6%) had increased C4 consumption. As severe manifestations, 4 SLE patients had increased C4 consumption. As severe manifestations, 4 SLE patients had increased C4 consumption. Infection was confirmed as a trigger in 3 patients with SLE (50%) and 4 patients with JIA (40%). Prednisone at high doses was prescribed to 11 patients, cyclosporine in 4 patients (86.6%) with SLE and 9 patients (90%) with sJIA. Additionally, anakinra was prescribed in 4 patients (40%) with sJIA, 4 patients (66.6%) with SLE met secondary HLH criteria and 9 patients (90%) with sJIA met secondary MAS criteria. Bone marrow biopsy was performed in all patients with SLE and in 9 patients with sJIA, demonstrating hemophagocytosis in 5 patients (83.3%) with LES and 5 (50%) patients with sJIA. Only 2 patients in the SLE group died because of MAS.

Abstract AB1010 Table 2. Analytical measures. Hb=haemoglobin(g/dl), Nt=neutrophils (10^9/mm3), Pla=platelets (10^9/mm3), Cr=creatinine (mg/dl), Brb=bilirubin (mg/dl), AST (U/L), ALT (U/L), Fe=ferritine (ng/ml), Tg-triglycerides (mg/dl), Fb=fibrinogen (mg/dl), INR (International Normalized Ratio).

Table 1. Clinical manifestations

<table>
<thead>
<tr>
<th></th>
<th>Hb</th>
<th>Nt</th>
<th>Pla</th>
<th>Crea</th>
<th>Brb</th>
<th>AST</th>
<th>ALT</th>
<th>Fe</th>
<th>Tg</th>
<th>Fb</th>
<th>INR</th>
</tr>
</thead>
<tbody>
<tr>
<td>sJIA</td>
<td>10.1</td>
<td>2.736</td>
<td>116930</td>
<td>0.85</td>
<td>2.77</td>
<td>141.8</td>
<td>257.9</td>
<td>9508.7</td>
<td>297.7</td>
<td>237.9</td>
<td>1.24</td>
</tr>
<tr>
<td>SLE</td>
<td>7.4</td>
<td>1.403</td>
<td>59983</td>
<td>1.53</td>
<td>9.77</td>
<td>274.3</td>
<td>133.2</td>
<td>5736</td>
<td>433</td>
<td>192.3</td>
<td>2.06</td>
</tr>
</tbody>
</table>

REFERENCES


Disclosure of Interests: None declared


AB1011

APPLICATION OF AUTOINFLAMMATORY DISEASE DAMAGE INDEX (ADDI) TO AUTOINFLAMMATORY DISEASES IN A TERTIARY REFERRAL HOSPITAL

Mireia Lopez Corbeto, Estefania Moreno Ruzafa. Hospital Universitari Vall d’Hebron, Rheumatology, Barcelona, Spain

Background: Autoinflammatory diseases (AIDs) cause chronic systemic inflammation that can damage multiple organs. Recently, the autoinflammatory disease damage index (ADDI) has been developed and validated in the four most common monogenic AIDs, Cryopyrin-associated Periodic Syndrome (CAPS), Familial Mediterranean Fever (FMF), Mevalonate Kinase Deficiency (MKD) and Tumor Necrosis Factor Receptor-associated Periodic Fever Syndrome (TRAPS). The use of ADDI index could also be of great value in other AIDs.

Objectives: The aim of this study is to assess the application of ADDI in patients with the four most common monogenic diseases and other AIDs. To accomplish this objective a detailed cohort of patients with different AIDs is presented.

Methods: All patients with AIDs followed in the Pediatric Rheumatology Unit comprising the Translational Care and specialized AIDs outpatient clinics from Hospital Universitari Vall d’Hebron were identified. A cross-sectional, descriptive study was performed applying ADDI by two pediatric rheumatologists (EM, ML). Laboratory test including C-reactive protein (CRP) mg/dL, amyloid protein (AP) mg/L, erythrocyte sedimentation rate (ESR) mm/h and protein/creatinine ratio (mg/g Cr) were performed at the moment ADDI was applied. Variables related with disease duration, current treatment and accumulated corticosteroids treatment were assessed. The continuous variables are presented as mean and standard deviation (mean ± SD) and categorical variables are presented by percentages.

Results: A total of 41 patients with AIDs were included, 61% were female, with a median age of 20 ± 11.9 years at inclusion. Disease duration was 11 ± 8.2 years. AIDs included were 11 patients with FMF (26.8%), TRAPS n=4 (9.8%), MKD n=3 (7.3%), CAPS n= 2 (4.9%), Blau

Table 2. Analytical measures. Hb=haemoglobin(g/dl), Nt=neutrophils (10^9/mm3), Pla=platelets (10^9/mm3), Cr=creatinine (mg/dl), Brb=bilirubin (mg/dl), AST (U/L), ALT (U/L), Fe=ferritine (ng/ml), Tg-triglycerides (mg/dl), Fb=fibrinogen (mg/dl), INR (International Normalized Ratio).

<table>
<thead>
<tr>
<th></th>
<th>Hypotension</th>
<th>Fever</th>
<th>Rash</th>
<th>Adenopathy</th>
<th>Splenomegaly</th>
<th>Hepatomegaly</th>
<th>Haemorrhage</th>
</tr>
</thead>
<tbody>
<tr>
<td>sJIA</td>
<td>1 (10%)</td>
<td>7 (70%)</td>
<td>7 (70%)</td>
<td>3 (30%)</td>
<td>4 (40%)</td>
<td>1 (10%)</td>
<td>0</td>
</tr>
<tr>
<td>SLE</td>
<td>0</td>
<td>4 (66.7%)</td>
<td>1 (16.7%)</td>
<td>3 (50%)</td>
<td>5 (83.3%)</td>
<td>4 (66.7%)</td>
<td>3 (50%)</td>
</tr>
</tbody>
</table>
HENOCH-SCHÖNLEIN PURPURA AND UVEITIS, AN CHILDREN IN RISK OF LOW BONE MASS HAVE MORE

Florence, Italy

We describe a 6-year-old female patient who presented HSP have been reported so far. Ment. To our knowledge only 4 cases of HSP with ocular involvement hood vasculitis characterized by cutaneous palpable purpura predominantly Henoch-Schönlein purpura (HSP) is the most common child-

A 6-year-old female, previously in good health, received the Describe a case report.

Methods:

nephrological and articular involvement. Prednisone was then gradually

sone (2 mg/kg/day), with a progressive improvement of the ocular, skin, ANA, ANCA, ASCA, LAC, HLA B27 and B51 were all negative. Chest X tious work-up for viral, bacterial and parasitic infections was negative. played mild hematuria and proteinuria. Immunoglobulin levels were slightly

increased values of CRP (1.92 mg/dl) and ESR (69 mm/h) with normal

Conclusion: ADDI is a feasible index suitable to measure damage in a single patient. Despite it was performed to the four most common AIDs it could be applied to other diseases. In our cohort the mean ADDI index was low and musculoskeletal item has the highest score. This result could be explained by the tight control of the disease and successful targeted therapy. Laboratory tests also support this finding. Nevertheless, some organ systems are not assessed like respiratory, cardiovascular or cutaneous damage, important in some syndromes. Knowing the difficulties of applying an unified index for all diseases, ADDI may be supportive in other AIDs and longitudinal cohorts.

REFERENCES

[1] Ter Haar NM, Annink KV, et al. Development of the autoinflammatory dis-


Disclosure of Interests: Ilaria Maccora: None declared, Francesca Tirelli: None declared, Gabriele Simonini Grant/research support from: Abbvie, Speakers bureau: Abbvie, Teresa Gianì: None declared, Rolando Cimaz: None declared


AB1013 CHILDREN IN RISK OF LOW BONE MASS HAVE MORE THAN 2 RISK FACTORS

Berta Paula Magnolfi Lépiz1, Dacia Corda2, Jocelyn Betsunour2, Gloria Frag1, Estefania Quesada-Masachs4, Mireia López-Corbel3, Montserrat Torrent2, Ana Maria Marín5, Silvia Herrera3, Jordi Casademont5, Hector Corominas1, Jorge Malouf6, 1 Santa Creu i Sant Pau Hospital, Rheumatology, Barcelona, Spain; 2 Moises Brogi Hospital, Rheumatology, Barcelona, Spain; 3 Santa Creu i Sant Pau Hospital, Pediatrics, Barcelona, Spain; 4 Vall d’Hebron Hospital, Pediatric Rheumatology, Barcelona, Spain; 5 Santa Creu i Sant Pau Hospital, Bone Metabolism Unit, Internal Medicine, Barcelona, Spain; 6 Santa Creu i Sant Pau Hospital, Internal Medicine, Barcelona, Spain Background: Low Bone Mass (LBM)/Infantile Osteoporosis (IOP) require an active evaluation for its diagnosis and prevention. Therefore, its inci-

dance is unknown and could be undertreated. The systematic collection of risk factors associated with LBM/IOP could help identify the population at risk of presenting it

Objectives: To assess the prevalence and number of risk factors (RF) in the pediatric population at risk of developing LBM/IOP. Assess its influ-

ence on Bone Mineral Density

Methods: Demographic and clinical data were prospectively collected from patients from 2 to 20 years of age, who had at least one risk factor for LBM/IOP, among them: chronic diseases, treatment with immunosuppres-

sants and/or corticosteroids and insufficient calcium intake. Cacemcia, cal-

ciuria, and Vitamin D were determined in blood samples, and whole body and lumbar DXA were performed. The calcium intake, the number of previous fractures and other RF were collected

Results: Data were collected from 103 patients, with an average age of 9.8 years, 52.4% women, and 80%Caucasians. Of these, 9 were pre-
schoolers (2-3 years old), 33 schoolchildren (4-9y), 55 teenagers (10-17y) and 6 young people (18-20y) The most frequent diagnoses were: Malabsorption/Food allergies: 46.6%, JIA: 17.5%, Nephropathies: 17.8%, Hematological diseases: 6.8%, and Vasculitis and connective tissue diseases: 3.9% each

The frequency of RFs can be observed in Table 1

% Insufficient calcium intake in the diet 84.5 Association of a second chronic diagnosis 4.9 Hypovitaminosis D in blood (<30 nmol/L) 8.1 Sedentary lifestyle (PAQ test <2) 13.6 History of long bone or vertebral fractures 12.6 24-hour urine hypercalciuria 3.1 Proteinuria >0.20 g/l in 24-hour urine 17 Drugs with osteopening potential (non-corticosteroid immunosuppressants) 31.1 Corticosteroids at the time of inclusion 19.4 Corticosteroids prior to inclusion in the study 18.4 The average dose of current corticoids was 0.21 mg/kg/day of prednisone with a total cumulative average dose of: 7 gr, with an exposure of 1 to

44 months 43.3% of the sample had an isolated RF, 38% had 2 RF, 31% 3, 15% 4, and 12% 5 or more 87% of the sample presented a LBM and 4.8% met criteria for Opi for vertebral fractures, 3 of them asymptomatic and discovered by morphometry

In the multiple linear regression analysis: age, Latin ethnicity, gender, and hypovitaminosis D were the main RFs related to lumbar BMD. Likewise,
age, latin ethnicity and sedentary lifestyle were the RF related to the BMD of the whole body without head (BMDwbwh).

In lumbar BMD, these 4 FR explained up to 85% of the BMD variation, where the age adds 0.036 per year gained, the male sex subtracts 0.061, the hypovitaminosis D sum 0.077 and the latin ethnicity subtracts 0.070.

Up to a 90.8% variation of BMDwbwh is explained by these 3 RF: age adds 0.036 per year gained, sedentary life subtracts 0.084 and latin ethnicity subtracts 0.055.

Conclusion: The child population at risk of LBM/IOP associates 2 or more risk factors 8.7% of children with risk factors have LBM and 4.8% IOP.

The RFs related to changes in BMD are: age, sex, sedentary lifestyle and ethnicity. Hypovitaminosis D correlated positively with lumbar BMD.

Disclosure of Interests: None declared.


**AB1014**

**USE OF ETANERCEPT BIOSIMILAR IN JIA: PRELIMINARY EXPERIENCE USING REAL WORLD DATA**

Marco Marini1, Achille Marino1, Gabriele Simonini1, Rolando CIMAZ1, Teresa GIANI1,2, 1Meyer Children's University Hospital of Florence, Florence, Italy; 2University of Siena, Siena, Italy

Background: Biosimilars are biological medical drugs that are almost an identical copy of an original drug, manufactured by a different company. Since last year regional regulations have imposed a non-medical switch from reference etanercept (ETN) originator to biosimilar (SB4).

We compared treatment survival on SB4 to reference etanercept, assessing efficacy and safety data in our cohort of patients with JIA.

Objectives: To review clinical charts of JIA patients, including efficacy and safety of ETN biosimilars after transition from originator. Compliance was also assessed.

Methods: This was a retrospective observational study of patients with JIA who switched from reference etanercept to SB4 during 2018 in our Pediatric Reumatology Department. Clinical and demographic data were collected from charts and inserted into a dedicated database. Relevant data included: age at disease onset, age at first administration and duration of treatment, if patients had remission of disease with etanercept therapy or if there were any relapses, ESR and CRP values before and after etanercept therapy, assessing remission.

Results: A total of 14 patients (13F, 1M) were identified. Age at diagnosis ranged from 1 to 12 years. Before ETN, all had received methotrexate. ETN was added for disease activity persistence, and induced remission in all cases but one. SB4 treatment duration ranged from 1 to 11 months. After switch to SB4 no disease recurrence was observed. ESR and CRP values before and after switching to SB4 were collected. Global assessment of patient satisfaction with the clinical management plan. Paediatric care is family oriented and relies on significant modifications that patients have to face in an adult medical environment may affect the compliance with the management plan. Paediatric care is family oriented and relies on significant modifications that patients have to face in an adult medical environment may affect the compliance with the management plan. Paediatric care is family oriented and relies on significant modifications that patients have to face in an adult medical environment may affect the compliance with the management plan.

Disclosure of Interests: None declared.


**AB1015**

**CENTRAL NERVOUS SYSTEM VASCULITIS PRECEDING HENOCCH-SCHÖNLEIN PURPURA: A CASE REPORT OF A UNCOMMON ASSOCIATION**


Suñ J, Hahn WH, Cho BS, Kim SD, Hong IK. A rare case of cerebral vasculitis in Henoch-Schönlein purpura with emphasis on the diagnostic value of magnetic resonance angiography (MRA) and single-photon emission computed tomography (SPECT) given normal magnetic resonance imaging (MRI). J Neurol. 2010 Jul;49(7):803-5.

Acknowledgement: Federica Barbati, MD; Sara Abu-Rumeileh, MD.

Disclosure of Interests: edoardo marrani: None declared, Gabriele Simonini Grant/research support from: Abbvie, Speakers bureau: Abbvie, Eleonora Fusco: None declared, Ilaria Maccora: None declared, Anna Rosati: None declared, Rolando CIMAZ: None declared, Teresa GIANI: None declared.


**AB1016**

**OUTCOME OF TRANSITION OF CARE IN YOUNG ADULTS WITH JUVENILE ONSET CHRONIC RHEUMATIC DISEASES**

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1Serviço de Reumatologia e Doenças Ósseas Metabólicas, Hospital de Santa Maria, CHULN, Centro Hospitalar Universitário Lisboa Norte, Portugal, Lisbon, Portugal; 2Unidade de Investigação em Reumatologia, Instituto de Medicina Molecular, Faculdade de Medicina, Universidade de Lisboa, Centro Académico de Medicina de Lisboa, Portugal, Lisboa, Portugal

Background: The transition process of adolescent care from a paediatric to an adult medical environment may affect the compliance with the management plan. Paediatric care is family oriented and relies on significant parental involvement in decision-making. On the contrary, adult care is patient-specific and requires autonomy and independent skills.

Objectives: The aim of this study was to evaluate the transition of care at our centre, namely the adherence to clinical appointments, modification of disease activity and patient satisfaction.

Methods: All consecutive patients with juvenile onset of rheumatic chronic diseases followed in a young adult clinic were included. Disease activity was evaluated at the last appointment in the paediatric unit and up to 2 years after transition of care, according to validated scores for each rheumatic disease. Dropout was defined as not attending the clinic for 2 consecutive visits. Global assessment of patient satisfaction with the clinical

Disclosure of Interests: None declared.


**REFERENCES**


appointments before and after transition of care was evaluated in a scale of 0 to 10. Variables were analysed as means, medians and frequencies as appropriate. Univariate analysis was performed with student t-test and Qui-square.

Results: 126 patients were included. Of these, 77 (61.1%) had juvenile idiopathic arthritis (JIA, see table I for list of diagnosis), 78 (61%) were female with a mean age of 23.1±3.2 years and a mean disease duration of 12.7±5.3 years. During the transition of care, 92 patients were treated with conventional disease modifying antirheumatic drugs (73%) and 35 with biologic therapy (27.8%). 69 patients (54.7%) missed at least one clinical appointment with a dropout rate of 9%. This was associated with longer disease duration (15.9 vs 12.3 years, p=0.024). 11 patients (8.7%) had worsened clinical activity: 5 patients with polyarticular JIA with arthritis flare (ΔDAS28 2.14 ± 0.83); 4 patients with oligoarticular JIA with new onset of disease; and 2 patients with juvenile systemic lupus erythematosus with a SLEDAI increase from 5 to 16 points. 4 patients abandoned DMARDs. Regarding patient satisfaction questionnaire, paediatric rheumatology appointments had a median evaluation of 9 (7-10), adult rheumatology appointments of 8 (5-10) and the transition process had an evaluation of 8 (5-10). The majority of patients reported the longer appointment waiting time as the major negative aspect after transition.

Conclusion: In our centre the transition of care had a small percentage of dropping out from the clinic, which was associated with longer disease duration, a slight worsening of disease activity and a 10% decrease in patient satisfaction.

REFERENCES

Abstract AB1016 Table 1. Descriptive analyses of diagnosis. SLE - systemic lupus erythematosus, *Mixed connective tissue disease, Systemic sclerosis, Raynaud phenomenon, Overlap syndrome, Osteoporosis, Osteogenesis Imperfecta, Spondyloarthriti

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>JIA</td>
<td>77 (61.1)</td>
</tr>
<tr>
<td>Persistent Oligoarthritis</td>
<td>22 (17.5)</td>
</tr>
<tr>
<td>Enthesitis related arthritis</td>
<td>22 (17.5)</td>
</tr>
<tr>
<td>Rheumatoid factor - polyarthritis</td>
<td>11 (8.7)</td>
</tr>
<tr>
<td>Extended Oligoarthritis</td>
<td>9 (7.1)</td>
</tr>
<tr>
<td>Systemic</td>
<td>6 (4.8)</td>
</tr>
<tr>
<td>Psoriatic Arthritis</td>
<td>4 (3.2)</td>
</tr>
<tr>
<td>Rheumatoid factor + polyarthritis</td>
<td>3 (2.4)</td>
</tr>
<tr>
<td>Systemic lupus erythematosus</td>
<td>14 (11.1)</td>
</tr>
<tr>
<td>Vasculitis</td>
<td>9 (7.1)</td>
</tr>
<tr>
<td>Autoinflammatory syndrome</td>
<td>5 (4)</td>
</tr>
<tr>
<td>Dermatomyositis</td>
<td>3 (2.4)</td>
</tr>
<tr>
<td>Other diagnosis*</td>
<td>19 (15.1)</td>
</tr>
</tbody>
</table>

Disclosure of Interests: None declared

AB1017 WHAT IS THE CURRENT SITUATION OF THE PAEDIATIC RHEUMATOLOGY TRANSITION CARE UNITS?
José-Luis Martín-Varillas1, Daniel Clemente2, J.C. López Robledillo2, Belén Serrano Benavente3, Indalecio Montenegro4, Juan Carlos Nieto1.
1H.U.M. Valdecilla, Santander, Spain; 2H.U. Niño Jesús, Madrid, Spain; 3H.G.U. Gregorio Marañón, Madrid, Spain

Background: Switching from paediatric rheumatology to the adult rheumatology care units has a negative impact on disease control and adherence in young patients with juvenile idiopathic arthritis (JIA) but also in other chronic diseases. Transitional care services provide the opportunity of being followed-up by an adult rheumatologist specialized in juvenile rheumatic diseases.

Objectives: In our study we report the current situation of a rheumatology transition care unit (RTCU).

Methods: We set up an observational and retrospective study of patients followed in our unit between September 2015 and December 2018. We included those patients with a disease beginning at 16 years or younger and those patients who were attended on RTCU for the first time before age 25. Clinical and demographic data and all treatments received by the patients before and after the first visit in the transition care unit were also collected.

Results: 119 patients were attended in our RTCU. After applying the exclusion criteria, 110 patients remained: 78 female/32 male (70.9/29.1%) with a median age of 17.9 (17.9-19.8) years at the first visit. No significant differences in age at the first visit were found between the first (September-2015 to September-2017) and the second stage (October-2017 to December-2018), 18.7 (17.8-20.2) vs. 18.2 (17.9-18.6) years respectively. The most frequent diagnoses are included in the table 1.

Of the 75 patients with JIA, 54 were women (72%) with a median age at the disease onset of 6.88 [2.5-12.7] and 21.3% of patients had chronic anterior uveits. 22 patients (29.3%) presented joint or ocular inflammatory activity or flare at the time of transition first visit but only 1 patient maintained inflammatory activity during the 3 years of follow-up. A total of 64 patients (85.3%) with JIA diagnosis were under treatment with synthetic DMARD, mostly methotrexate (61) or leflunomide (7). In addition, 43 patients (57.3%) required biological DMARD in the past, and 8 of them (10.7%) required more than one. The most frequently used drugs were: etanercept (ETN) (29 patients) and adalimumab (ADA) (19 patients). Tocilizumab (TCZ) (4), abatacept (1) and infliximab (1) were also used.

Of these patients, at the time of the first visit on RTCU, 24 (32%) had no treatment, 42 patients (56%) had synthetic DMARD and 34 patients (43.3%) had biologic therapy in monotherapy or combined with DMARDs (19 ETN, 12 ADA, and 3 TCZ).

Conclusion: RTCU assessed mainly patients with JIA and connective tissue diseases. Most patients were inactive during the transfer to the adult unit due to the existence of patients that were still active and/or needed treatment with synthetic and/or biological DMARD reaffirms the need for close control in this period.

Disclosure of Interests: None declared

AB1018 CONE BEAM CT IN JUVENILE IDIOPATHIC ARTHRITIS: ROLE OF IMAGING DIAGNOSTIC TOOL WITH MINIMAL X-RAY EXPOSURE IN THE FREQUENT, SUBTLE AND INDOLENT TEMPROMANDIBULAR JOINT INVOLVEMENT
Maddalena Maschio1, Sara Pieropan1, Giulia Aiello1, Giulia Melotti1, Elisa Tadiotto1, Erica Giacomelli1, Antonio D’agostino2, Lorenzo Trevisiol1, Giorgio Piacentini2, 1Azienda Ospedaliera Universitaria Integrata Verona, Pediatric, Verona, Italy; 2Azienda Ospedaliera Universitaria Integrata Verona, Maxillo Facial Surgery, Verona, Italy

Background: The prevalence of the temporomandibular joint (TMJ) involvement in patients affected by juvenile idiopathic arthritis (JIA) ranges from 17% to 87% depending on population. TMJ is frequently the first and unique joint involved in the arthritic process. Unfortunately detection of TMJ arthritis in children with JIA is difficult as early signs and symptoms are missing in most patients. Therefore failure to diagnose and treat TMJ arthritis may have severe consequences on masticatory function, like

**Results:** CBCT is a useful tool to improve the diagnostic and therapeutic iter of TMJ involvement in JIA; in fact on one hand it highlights the unsuccessful and palliative role of IACI and on the other hand it can reveal significant impairment of the joint bone components in frequent asymptomatic patients; systemic therapy from the early phase of TMJ involvement could prevents the irreversible modification of the mandibular growth process of undertreated inflammation.

**Conclusion:** CBCT is a useful tool to improve the diagnostic and therapeutic iter of TMJ involvement in JIA; in fact on one hand it highlights the unsuccessful and palliative role of IACI and on the other hand it can reveal significant impairment of the joint bone components in frequent asymptomatic patients; systemic therapy from the early phase of TMJ involvement could prevent the irreversible modification of the mandibular growth process of undertreated inflammation.

**REFERENCES**


**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.5396

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**THE EFFECT OF TREATMENT REGIMEN ON HEALTH-RELATED QUALITY OF LIFE AND FUNCTIONING IN CHILDREN WITH UVEITIS**

**Joseph McDonald1,** Virginia Utz2, Theresa Hennard1, Najima Mwash3, Joseph Lipscomb1, Amy Cassidy1, Sheila Angeles-Han1, 1Cincinnati Children’s Hospital Medical Center, Pediatric Rheumatology, Cincinnati, United States of America; 2Cincinnati Children’s Hospital Medical Center, Pediatric Ophthalmology, Cincinnati, United States of America; 3Cincinnati Children’s Hospital Medical Center, Biostatistics and Epidemiology, Cincinnati, United States of America; 4Cincinnati Children’s Hospital Medical Center, Pediatric Dermatology, Cincinnati, United States of America; 5Ribeirão Preto Medical School, University of São Paulo, of Radiology, RIBEIRÃO PRETO, Brazil

**Background:** Pediatric non-infectious uveitis can lead to ocular complications and blindness. Complex treatment regimens are often needed and consist of frequent topical treatments (glucocorticoids, mydriatics, glaucoma medications) and systemic immunosuppression.

**Objectives:** To examine the impact of topical and systemic treatment on health-related quality of life (HRQOL), mental health, and uveitis-related quality of life (UQL) in children with uveitis.

**Methods:** We reviewed records of 40 children with uveitis (22 JIA-associated uveitis (JIA-U), 18 other uveitis types). Patients and parents completed questionnaires on general QOL (Pediatric Quality of Life Inventory–PedsQL), depression and anxiety (Revised Children’s Anxiety and Depression Scale–RCADS), physical functioning (Childhood Health Assessment Questionnaire–CPHQ), and visual function and uveitis-related QOL (Effect of Youngsters’ Eyesight on QOL-EYE-Q). We used ANOVA and T-Test to compare treatment groups: 1) topical only vs. systemic only vs. combined topical and systemic treatment; 2) topical vs. no topical treatment.

**Table 1. Vision-Specific Outcome Measures by Treatment Regimen in Children with Uveitis**

<table>
<thead>
<tr>
<th>Measure</th>
<th>No Topical Rx (n = 11)</th>
<th>Topical Rx (n = 24)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visual Function</td>
<td>1.96 (0.26)</td>
<td>1.82 (0.26)</td>
<td>0.021*</td>
</tr>
<tr>
<td>Uveitis-related QOL</td>
<td>1.83 (0.19)</td>
<td>1.59 (0.33)</td>
<td>0.041*</td>
</tr>
<tr>
<td>EYE-Q Child Total Uveitis-QOL</td>
<td>1.87 (0.18)</td>
<td>1.71 (0.3)</td>
<td>0.12</td>
</tr>
<tr>
<td>Visual Function</td>
<td>1.86 (0.03)</td>
<td>1.73 (0.34)</td>
<td>0.264</td>
</tr>
<tr>
<td>Uveitis-related QOL</td>
<td>1.9 (0.19)</td>
<td>1.69 (0.34)</td>
<td>0.07</td>
</tr>
</tbody>
</table>

*p<0.05

**Conclusion:** The parents of children with uveitis who need topical treatments as part of their therapy regimen report worse uveitis-related QOL. This is likely secondary to parental responsibility for instilling topical therapy. Additionally, visual function scores were also lower in the topical treatment group and could reflect disease activity or use of mydriatics which can affect vision. Other measures including the PedsQL, CHAQ, and RCADS did not appreciate differences based on treatment regimen. Our findings demonstrate the importance of including uveitis-specific disease measures in the assessment of the impact of uveitis. The burden of medication use, specifically eye drops, that can sting, require frequent application, or affect vision, needs further study as this can affect medication adherence and patient outcomes.

**Disclosure of Interests:** Joseph McDonald: None declared, Virginia Utz Grant/research support from: Retrophin, Consultant for: Spark Therapeutics - >12 months ago, Theresa Hennard: None declared, Najima Mwash: None declared, Jessi Lipscomb: None declared, Amy Cassidy: None declared, Sheila Angeles-Han: None declared

**DOI:** 10.1136/annrheumdis-2019-eular.5913

**DISEASE ACTIVITY INDEX IS ASSOCIATED WITH SUBCLINICAL ATHEROSCLEROSIS IN CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS**

**Priscila Medeiros1,** Roberta Garcia Salomão2, Diane Meyre Rassi2, Luciana Rodrigues Roberts2, Sara Reis Teixeira3, Priscila Giacomo Fassini3, Rita de Cássia Tostes3, Jacqueline Pontes Monteiro2, Virginia Fertani2, Luciana Martins de Carvalho1, 1Ribeirão Preto Medical School, University of São Paulo, of Pediatrics; Division of Pediatric Rheumatology, RIBEIRÃO PRETO, Brazil; 2Ribeirão Preto Medical School, University of São Paulo, of Pediatrics, Division of Nurtology, RIBEIRÃO PRETO, Brazil; 3Ribeirão Preto Medical School, University of São Paulo, Department of Internal Medicine and Department of Pharmacology, RIBEIRÃO PRETO, Brazil; 4Ribeirão Preto Medical School, University of São Paulo, of Pediatrics, RIBEIRÃO PRETO, Brazil; 5Ribeirão Preto Medical School, University of São Paulo, of Radiology, RIBEIRÃO PRETO, Brazil

**Background:** Systemic lupus erythematosus (SLE) is considered an independent risk factor for cardiovascular events in association with traditional risk factors. Therefore, it is important to recognize and to identify the specific risk factors for atherosclerotic disease in these patients for the prevention and early treatment of cardiovascular diseases, aiming to provide a better quality of life with long-term morbidity reduction.

**Objectives:** To determine the prevalence of subclinical atherosclerosis by the measurement of carotid intima-media thickness (CIMT) in patients with childhood-onset systemic lupus erythematosus (SLE) younger than 21 years. To check for associations between sex, age, race, body mass...
index, medications in use, cumulative dose of corticosteroid, traditional and nontraditional risk factors for artherosclerosis, laboratory tests, including plasma cytine levels, clinical disease activity score (SLE Disease Activity Index - SLEDAI-2K) and cumulative damage index (Cumulative Organ Damage of the SLE International Collaborating Clinics - SLICC/ACR damage index) with CIMT.

Methods: This was a cross-sectional study. Clinical and laboratory data were collected based on chart review and laboratory testing; present clinical and laboratory data were performed during interviews and CIMT was evaluated by ultrasound carried out by an expert radiologist. Associations were estimated using univariate analysis (Fisher and Wilcoxon-Mann-Whitney tests) and multivariate analyses (linear and log binominal regression).

Results: Twenty-eight patients, aged 13.9 ± 3 years, were enrolled in the study. In children with subclinical atherosclerosis was 32.14% (95% CI: 14.8, 49.4) and the mean carotid intima-media thickness (CIMT) was 0.43 ± 0.035 mm. Most common traditional risk factors observed were dyslipidemia in 89.3%; uncontrolled hypertension in 66.6%; overweight or obesity in 32% and poor diet in 78.6%. Nontraditional risk factors observed were duration of disease of 2.4 ± 2.12 years; mean SLEDAI-2K of 7.8 ± 6.0; SLICC/ACR damage index scored ≥ 1 in 25%; high levels of ultra-sensitive C-reactive protein in 25% and nephritis and neuropsychiatric involvement in 75% and 28.5% of the patients, respectively. Cumulative dose of corticosteroids was 0.48 ± 0.83 mg/kg/day and 60.7% of patients were using immunosuppressive drugs. Univariate analysis showed that uncontrolled hypertension, proteinuria, estimated glomerular filtration rate < 75 ml/min/1.73 m2 and SLEDAI-2K ≥ 5 were associated with subclinical atherosclerosis. The association of CIMT with SLEDAI-2K > 5 was maintained after adjusting for control variables (cumulative corticosteroid dose, duration of disease, levels of cholesterol fractions, hypertension and renal disease).

Conclusion: This study demonstrated that subclinical atherosclerosis was frequently observed in cSLE, mainly in patients with moderate to severe disease activity (SLEDAI-2K greater than 5).

Background: Appointment of modern methods of treatment led to a modification of the course of juvenile idiopathic arthritis (JIA). In Ukraine, the basic preparation for treatment prescribed at JIA since 1984, then the biological was registered only in 2011.

Objectives: To evaluate the effect of treatment changes on activity indicators, functional disorders and physical development of patients with JIA.

Methods: retrospective analysis of medical records of 67 patients in 2018 who were admitted to the Rheumatology Unit of Verona were evaluated. For each child the following data were analyzed: JIA subtype, ANA positivity, anti-DFS positivity, presence of uveitis diagnosed by a pediatric ophthalmologist and the finding of markers of uveitis is still a challenge. In adults anti-DFS70, the role of these antibodies in children remains yet not established even though but it has also been reported that anti-DFS70, particularly asymptomatic and can lead to blindness if misdiagnosed. To date the finding of markers of uveitis is still a challenge. In adults anti-DFS70, which have indirect immunofluorescence pattern described as dense fine speckles (DFS pattern) and bind a 70kDa protein in immunoblot or immunofluoresence, and are associated with subclinical atherosclerosis.

Results: In the first 6 mo. from the debut (JADAS 6.6±1.2- 5.5±1.7) than DMARDs + ADA (4.0± 2.3 - 0.0) and DMARDs + TOCY (5.2±1.2 - 3.6 ±1.3). The max. JADI were in RF-JUA (3.0±1,3). In general, JADI increased with age (>65 0,55±0,3; >10y 1.7±0,9), JADI didn’t depend on the onset age (<r=0,12), disease duration (<r=0,16), ANA detection (1.8 ±1,1; >r=0,18), the RF (1.2±0,5; >r=0,07); HLA B27 0,5±0,3 (<r=0,1); sero-negative (1.0±0,4; =r=0,07). In patients last years of FL III-II-II cen. marked with a higher frequency of 35.9%. A smaller proportion of patients with high disease activity, the combination of DMARDS and sCS was worse than in previous yrs. (10.4 vs 49%). The delay in linear growth with JIA is -1.7±0.06SD now, the degree of growth retardation depends on the duration of the disease (up to 3y -1.2 ±0,1, 8-13y 1.6±0,7) and the variant of the course (the max. growth retardation rate observed in sJIA (78% to -1.2SD; 11% -1SD). The DMARDS+sCS+T2Z in high activity JIA and growth retardation was better for normalizing the growth (0.9±4.0±0.4SD after 2y) compared to DMARDS+sCS+ADA (-1.3±0.4). On average BMI at JIA did not differ from the age norm (17±8,0; 48% cases with overweight in last). DMARDS in higher doses was better for the normalization of BMI (MTX 15 mg/m² 17±1±12; 10 mg/m² 19±2,19). The use of ADA in patients with malnutrition resulted in 6 mo. to normalization of the BMI (18,55±1,5) in contrast to the use of ETA (16,5±2,0).

Conclusion: The results obtained showed that the overall activity of JIA is significantly reduced today. Improvement of the course of JIA and the degree of functional impairment is explained by the introduction of modern methods of pathogenetic therapy into the clinical practice.

Disclosure of Interests: None declared


AB1022 UVEITIS AND ANTI-DFS70 ANTIBODIES IN JUVENILE IDIOPATHIC ARTHRITIS: AN OBSERVATIONAL RETROSPECTIVE STUDY

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Background: Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in childhood and uveitis is one its major extra-articular manifestation. Children with JIA and a positive antinuclear antibodies (ANA) are known to be at risk to develop severe uveits, which is usually asymptomatic and can lead to blindness if misdiagnosed. To date the finding of markers of uveitis is still a challenge. In adults anti-DFS70, which have indirect immunofluorescence pattern described as dense fine speckles (DFS pattern) and bind a 70kDa protein in immunoblot or immunofluoresence, and are associated with subclinical atherosclerosis and atherosclerosis. In adults anti-DFS70, which have indirect immunofluorescence pattern described as dense fine speckles (DFS pattern) and bind a 70kDa protein in immunoblot or immunofluoresence, and are associated with subclinical and subclinical atherosclerosis. In adults anti-DFS70, which have indirect immunofluorescence pattern described as dense fine speckles (DFS pattern) and bind a 70kDa protein in immunoblot or immunofluoresence, and are associated with subclinical atherosclerosis. Anti-DFS70 which are known to be associated with subclinical atherosclerosis and can lead to blindness if misdiagnosed. To date the finding of markers of uveitis is still a challenge. In adults anti-DFS70, which have indirect immunofluorescence pattern described as dense fine speckles (DFS pattern) and bind a 70kDa protein in immunoblot or immuno-
guide ophthalmologic screening in JIA patients in order to identify children likely to develop uveitis.

REFERENCES

Disclosure of Interests: None declared


AB1023
PHYSICAL ACTIVITY LEVEL IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS FROM THE GERMAN NATIONAL PAEDIATRIC RHEUMATOLOGY DATABASE: A COMPARISON WITH THE GENERAL POPULATION

Florian Milatz1, Martina Nieweth1, Jana Hörstemann2, Nils Geisemeyer2, Peter Haas3, Gerd Hornett4, Tilman Kallinich5, Matthias Hartmann6, Joachim Peitz7, Josephine Merker8, Kirsten Minden9,10. German Rheumatism Research Centre, Epidemiology, Berlin, Germany; 2German Rheumatism Research Centre, Berlin, Germany; 3German Center for Pediatric and Adolescent Rheumatology, Garmisch-Partenkirchen, Germany; 4Asklepios Klinik Sankt Augustin, Sankt Augustin, Germany; 5University Medicine Charité Berlin, Department of Pediatrics, Division of Pneumonology and Immunology with intensive Medicine, Berlin, Germany; 6Asklepios Clinic, Sankt Augustin, Germany; 7Technische Universität München, Department of Biomechanics in Sports, München, Germany; 8University Medicine Charité Berlin, Berlin, Germany

Background: Insights in pathogenesis and the availability of new biologic drugs have created requirements and an increasing interest for encouragement of physical activity (PA) as long-term treatment option in patients with juvenile idiopathic arthritis (JIA). A low level of PA in healthy individuals is related to a higher incidence of overweight and hypertension in later life. This low level of PA might even be more dangerous for children with JIA, as they also have elevated inflammatory parameters, perhaps increasing the risk of future cardiovascular diseases.

Objectives: Since children and adolescents with physical disabilities may have an increased risk for developing a sedentary lifestyle, the objective was to investigate if encouragement of PA in most German medical care settings has led to PA levels in JIA similar to that of healthy counterparts.

Methods: Data from children and adolescents with JIA recorded in the German National Paediatric Rheumatologic Database (NPRD) in the year 2017 were considered for the analyses. In accordance with the methodology used in the general population survey [1], the achievement of the WHO recommendations on PA for health was determined on the basis of self-reported outcomes in individuals aged 3 to 17 years. Patients met the WHO criteria if they stated to be physically active for at least 60 minutes per day.

Results: In 2017, the data from 5,918 patients (mean age 11.2 ± 4.1 years, female 67%, disease duration 4.6 ± 3.7 years, persistent oligoarthritis 42%) were available for evaluation. Almost 35% of patients aged 3 to 17 years met the recommended physical activity level (72% aged 3 to 6; 47% aged 7 to 10; 27% aged 11 to 13; 16% aged 14 to 17). In the general population, 26% fulfilled the WHO recommendations on PA for health determined on the basis of self-reported outcomes in individuals aged 3 to 17 years. Patients met the WHO criteria if they stated to be physically active for at least 60 minutes per day.

AB1024
USE, EFFICACY AND LONG TERM SAFETY OF RITUXIMAB IN PEDIATRIC RHEUMATIC DISEASES: SINGLE CENTER EXPERIENCE FROM NORTH INDIA

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Background: Rituximab (RTX) is used in pediatric rheumatic diseases as an off label indication. There is paucity of data on safety and long term efficacy in countries with high burden of infectious diseases.

Objectives: 1. To study the use and safety of RTX in pediatric rheumatic diseases
   2. To assess the long term efficacy of RTX in pediatric systemic lupus erythematosus (pSLE).

Methods: Data of all children who received RTX was collected on standardized collection forms. This data set was reviewed.

Results: USE: Rituximab was given to 4 children with polyarticular juvenile idiopathic arthritis (PJA) (4/14=2.7%) and 17 children with pSLE (17/122=7.5%). In children with PJA, RTX was used as third line treatment, who failed methotrexate and TNF inhibitor therapy. In pSLE, lupus nephritis was the primary indication for RTX (96%), vasculitis (17%), neuropyschiatric SLE and refractory cytopenia (12%) and aggressive polyarthritis with steroid dependence (5%).

SafetY: Pre-biologic screen for HIV, Hepatitis B and C and tuberculosis was negative. Total immunoglobulin G level was assayed prior to RTX for all children. CMV PCR was done in 11/17 pSLE patients. No immediate or delayed anaphylaxis was noted. No child had reactivation of herpes zoster. There was no mortality in this cohort.

Efficacy: Studied in 17 children with pSLE over 21 episodes of RTX (2 received 3 cycles of RTX over 5 years); Median age at RTX use was 13.66 years (range 6.58-21.66 years). Median duration of follow up was 48 months (range 3-120 months). During long term follow up 14 patients did not have any disease flare. Three (17.6%) flared and required cyclophosphamide/second cycle of RTX. Mean dose of prednisolone prior to RTX was 0.7mg/kg/day while that at 1 year post RTX was 0.05mg/kg/d by 0.001) and at 2 years was 0.05mg/kg/d by 0.001). Mean SLE disease activity index 2K (SLEDAI-2K) prior to RTX was 16.25 while that at 1 year post RTX was 12.5(p value 0.004), at 2 years was 2(p value 0.004) and at 3 years was 0.85(p value 0.028).

Abstract AB1024 Table 1. Therapy prior and post RTX in patients with pSLE

<table>
<thead>
<tr>
<th>Medication</th>
<th>Prior to RTX</th>
<th>At 1 year</th>
<th>At 2 years</th>
<th>At 3 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=17)</td>
<td>(n=14)</td>
<td>(n=12)</td>
<td>(n=7)</td>
<td></td>
</tr>
<tr>
<td>Prednisolone</td>
<td>17(100%)</td>
<td>5(36%)</td>
<td>3(43%)</td>
<td>3(43%)</td>
</tr>
<tr>
<td>Hydroxychloroquine</td>
<td>17(100%)</td>
<td>14(100%)</td>
<td>12(100%)</td>
<td>7(100%)</td>
</tr>
<tr>
<td>Mycophenolate</td>
<td>7(41%)</td>
<td>12(86%)</td>
<td>10(83%)</td>
<td>7(100%)</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>6(35%)</td>
<td>1(7%)</td>
<td>0(0%)</td>
<td>0(0%)</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>2(12%)</td>
<td>11(78%)</td>
<td>9(83%)</td>
<td>1(14%)</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>1(6%)</td>
<td>1(7%)</td>
<td>1(8%)</td>
<td>0(0%)</td>
</tr>
<tr>
<td>Cyclosporin</td>
<td>1(6%)</td>
<td>0(0%)</td>
<td>0(0%)</td>
<td>0(0%)</td>
</tr>
<tr>
<td>Intraavenous</td>
<td>1(6%)</td>
<td>0(0%)</td>
<td>0(0%)</td>
<td>0(0%)</td>
</tr>
<tr>
<td>Immunglobulin</td>
<td>1(6%)</td>
<td>0(0%)</td>
<td>0(0%)</td>
<td>0(0%)</td>
</tr>
<tr>
<td>Acitamidine</td>
<td>0(0%)</td>
<td>1(7%)</td>
<td>1(8%)</td>
<td>0(0%)</td>
</tr>
</tbody>
</table>

References

Acknowledgement: The National Paediatric Rheumatological Database has been funded by the German Children Arthritis Foundation (Deutsche Kinder-Rheumastiftung), AbbVie, Pfizer and Chugai.

Disclosure of Interests: Florian Milatz: None declared, Martina Nieweth: None declared, Jana Hörstemann: None declared, Nils Geisemeyer: None declared, Peter Haas Grant/research support from: Pfizer, Gerd Hornett: None declared, Tilman Kallinich Grant/research support from: Novartis, Speakers bureau; Sobi, Roche, Novartis, CLB, Matthias Hartmann: None declared, Joachim Peitz: None declared, Josephine Merker: None declared, Kirsten Minden Consultant for: AbbVie


Disclosure of Interests: None declared, Joachim Peitz: None declared, Josephine Merker: None declared, Kirsten Minden Consultant for: AbbVie


Disclosure of Interests: None declared, Peter Haas Grant/research support from: Pfizer, Gerd Hornett: None declared, Nilis Geisemeyer: None declared, Peter Haas Grant/research support from: Pfizer, Gerd Hornett: None declared, Tilman Kallinich Grant/research support from: Novartis, Speakers bureau; Sobi, Roche, Novartis, CLB, Matthias Hartmann: None declared, Joachim Peitz: None declared, Josephine Merker: None declared, Kirsten Minden Consultant for: AbbVie

Conclusion: We conclude that RTX is efficacious for use in severe spectrum of pSLE and is relatively safe to use even in a developing country like ours with huge infectious disease burden.

REFERENCES

Disclosure of Interests: None declared

AB1025 HARMONIZING JAPANESE VERSION OF THE CHILDHOOD HEALTH ASSESSMENT QUESTIONNAIRE (CHAQ) WITH CHAQ
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Background: Juvenile idiopathic arthritis (JIA) is one of the most common rheumatic diseases of childhood. The Childhood Health Assessment Questionnaire (CHAQ) is one of the most widely-used self-report questionnaires to measure patient disability and discomfort (1). The American English version of the CHAQ was previously translated into Japanese, cross-culturally adapted and validated in a cohort of healthy Japanese children and Japanese patients with JA (2).

Objectives: To revise the Japanese version of the CHAQ (JCHAQ) to meet requirements of clinical international trials that pool data from various centers in different countries which need the same number of questions in each functional area of the CHAQ and to validate the harmonized JCHAQ with JIA patients.

Methods: The questionnaire in the JCHAQ consisted of 36 items, measuring 6 different functional areas: dressing and grooming, arising, eating, walking, hygiene, reach, grip, and activities, was changed to 30 items of questionnaire as each functional area has same number of questions as the original American English version after a conference among pediatric rheumatologists in US and Japan. The revised version was professionally translated from English to Japanese and reviewed by rheumatologists for accuracy. Then, it was validated with Japanese JIA patients.

Results: A total of 42 JIA patients were enrolled in the validation: 7 systemic, 30 polyarticular/oligoarticular and 5 enthesitis related. Most patients were well controlled and the median disability index (DI) scores was 0.0, however, significant correlation was seen with VAS (Visual Analog Scale) of pain, VAS overall well-being, physician VAS, DAS (Disease Activity Score)28-ESR, and JADAS (Juvenile Arthritis Disease Activity Score)-27. All variables in the questionnaire were shown to be significant (P<0.001).

In comparison of two groups of disease activity, remission/mild vs. moderate/severe, both DAS28-ESR and JADAS27 showed significant correlation with DI.

Conclusion: The Harmonized JCHAQ was a reliable and valid tool for the functional assessment of children with JIA. It is more suitable for international comparison.

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Disclosure of Interests: Takako Miyamae Speakers bureau: AbbVie, Eisai, Bristol-Meyers, Novartis, Ayumi, Taisyo- Toyama, Chugai, Yumi Tanii: None declared, Takayuki Kishi: None declared, Hisashi Yamana Grant/research support from: AbbVie, Eisai, Bristol-Meyers, Novartis, Ayumi, Taisyo-Toyama, Chugai, Shinya Akiko, Grant/research support from: Eli Lilly, Speakers bureau: Pfizer, Maruho, CSL Behring, Astellas, Chugai, Toru Igarashi: None declared, Yuzaburo Inoue Grant/research support from: MSD, Speakers bureau: Novartis, CSL Behring, MSD, Taisyo-Toyama, Ono, Motomu Hashimoto Grant/research support from: Astellas, Bristol-Meyers, Eisai, Employee of: M. H. is affiliated with the department (Department of Advanced Medicine for Rheumatic Diseases, Kyoto University), which is financially supported by four pharmaceutical companies (Tanebe-Mitsubishi, Chugai, Ayumi, UCB


AB1026 CLINICAL PRACTICE GUIDANCE FOR THE TRANSITIONAL CARE OF YOUNG PEOPLE WITH JUVENILE-ONSET RHEUMATIC DISORDERS IN JAPAN
Takako Miyamae1, Shinni Akikoa, Toru Igarashib, Yuzaburo Inouesc, Motomu Hashimotoa, Yohsuke Matsum, Susumu Nishiyama, Shiro Ohshimad, Hiroaki Umebayashie, Takahiro Yasumif, Masaaki Mon1,7. Tokyo Women’s Medical University, Pediatric Rheumatology, Institute of Rheumatology, Tokyo, Japan; 2Kyoto Prefectural University of Medicine, Department of Pediatrics, Graduate School of Medical Science, Kyoto, Japan; 3Nippon Medical School, Department of Pediatrics, Tokyo, Japan; 4Chiba Children’s Hospital, Department of Allergy and Rheumatology, Chiba, Japan; 5Kyoto University, Department of Advanced Medicine for Rheumatic Diseases, Graduate School of Medicine, Kyoto, Japan; 6Sagamihara National Hospital, National Hospital Organization, Department of Rheumatology, Sagamihara, Japan; 7Kurashiki Medical Center, Rheumatic Disease Center, Okayama, Japan; 8Osaka Minami Medical Center, Department of Rheumatology and Allergology, Osaka, Japan; 9Myagi Children’s Hospital, Department of General Pediatrics, Sendai, Japan; 10Kyoto University, Department of Pediatrics, Graduate School of Medicine, Kyoto, Japan; 11Tokyo Medical and Dental University, Department of Lifeline Clinical Immunology, Graduate School of Medical and Dental Sciences, Tokyo, Japan

Background: The transition from pediatric to adult healthcare systems has recently received worldwide attention, and it is “the purposeful, planned movement of adolescents and young adults with chronic physical and medical conditions from child-centered to adult-oriented healthcare systems.” In Japan, 1,000 patients with childhood-onset chronic disease reach adulthood every year, and many of them will suffer from serious sequelae or disabilities. The Japan Pediatric Society convened a committee of healthcare transition, summarized their statements, and the working group launched its activities in 2013.

Objectives: A clinical practice guidance for the transitional care of young people with childhood-onset rheumatic disorders has been established in Japan.

Methods: The guidance was designed to support pediatric and non-pediatric rheumatologic health care professionals make decisions about appropriate transitional health care for childhood-onset rheumatic disorders. It offered statements and recommendations addressing key clinical questions regarding transitional care proposed by leading pediatric and non-pediatric rheumatology medical experts and consisted of general core and disease-specific guidance.

Results: Category of clinical questions in the general core guidance involved the following: (1) initial statement of transitional care in rheumatology; (2) management of social life environment and public funded health care; (3) issues specific to adolescence; (4) risk management in childhood-onset rheumatic disorders; and (5) decision-making, privacy and consent, access to information, adherence to care, and preferred methods of communication, including attending to health literacy needs. In the disease-specific guidance, issues focused on each rheumatic disorder such as juvenile idiopathic arthritis, childhood-onset systemic lupus erythematosus, juvenile dermatomyositis, and Sjögren’s syndrome were brought up.

Conclusion: The guidance informs policy and strategies to reach optimal outcomes in transitional care for both pediatric and non-pediatric rheumatologists based on available evidence and expert opinion.

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Disclosure of Interests: Takako Miyamae Speakers bureau: AbbVie, Eisai, Bristol-Meyers, Novartis, Ayumi, Taisyo-Toyama, Chugai, Shinyi Akiko, Grant/research support from: Eli Lilly, Speakers bureau: Pfizer, Maruho, CSL Behring, Astellas, Chugai, Toru Igarashi: None declared, Yuzaburo Inoue Grant/research support from: MSD, Speakers bureau: Novartis, CSL Behring, MSD, Taisyo-Toyama, Ono, Motomu Hashimoto Grant/research support from: Astellas, Bristol-Meyers, Eisai, Employee of: M. H. is affiliated with the department (Department of Advanced Medicine for Rheumatic Diseases, Kyoto University), which is financially supported by four pharmaceutical companies (Tanebe-Mitsubishi, Chugai, Ayumi, UCB
AB1028

MYOCARDITIS IN PEDIATRIC LUPUS: A CLINICAL CONUNDRUM

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Background: Myocarditis in pediatric lupus is uncommon but carry a significant morbidity and mortality.

Objectives: To study the clinical profile and outcome of children with lupus myocarditis.

Methods: We reviewed our cohort of children with lupus registered between January 1993 to November 2018. Of the 140 lupus patients that were diagnosed during this time, 3 had myocarditis.

Results: Patient 1 was an 11-year-old girl who presented with fever, rash and generalized body swelling for 3 months. Physical examinations revealed heart rate 148/min, respiratory rate 30/min, and blood pressure (BP) 100/80 mmHg. She had pallor, malar rash, hepatomegaly and gallop rhythm. Investigations are detailed in the table. She received intravenous immunoglobulin and initiated on pulse methylprednisolone and followed by pulse intravenous cyclophosphamide. She was discharged on oral prednisolone and subsequently tapered. Patient 2 was a 9-year-old girl presented with fever and rash for 3 months with lethargy for 1 day. She had pallor, malar rash, hepatomegaly. Physical examinations revealed heart rate 132/min, respiratory rate 32/min, feeble peripheral pulses and BP 100/80 mmHg. She received intravenous cyclophosphamide monthly for 6 months along with oral prednisolone in tapering dose. Patient 3 was a 12-year-old girl, who was known to have SLE for 2 months, presented with fever, malar rash, gallop rhythm and tender hepatomegaly. She was given pulse methylprednisolone and furosemide therapy followed by oral prednisolone in gradually tapering dose.

Conclusion: Myocarditis in lupus is uncommon but carries a significant morbidities. The presence of global hypokinesia with a low ejection fraction on two dimensional echocardiography (2DE) is a strong pointer towards the diagnosis. Immunosuppressants drugs with supportive therapy remain the preferred treatment. Early diagnosis and prompt treatment may be very rewarding.

REFERENCES


Table: Laboratory investigations:

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin (g/dL)</td>
<td>94 g/L</td>
<td>92 g/L</td>
<td>80 g/L</td>
</tr>
<tr>
<td>White cell counts</td>
<td>6.7 10^9/L</td>
<td>7.2 10^9/L</td>
<td>6.5 10^9/L</td>
</tr>
<tr>
<td>Lymphocyte count</td>
<td>1.15x10^11/L</td>
<td>1.91x10^11/L</td>
<td>1.65x10^11/L</td>
</tr>
<tr>
<td>Platelets</td>
<td>130 x 10^9/L</td>
<td>190 x 10^9/L</td>
<td>220 x 10^9/L</td>
</tr>
<tr>
<td>Urine routine Urine protein (mg/m²/hour)</td>
<td>No RBC, No albumin</td>
<td>No RBC, No albumin</td>
<td>No RBC, No albumin</td>
</tr>
<tr>
<td>C3 (Normal 50-150 mg/dl)</td>
<td>27 mg/dl</td>
<td>28 mg/dl</td>
<td>31 mg/dl</td>
</tr>
<tr>
<td>C4 (Normal 20-50 mg/dl)</td>
<td>4 mg/dl</td>
<td>3 mg/dl</td>
<td>10 mg/dl</td>
</tr>
<tr>
<td>ANA</td>
<td>4+ diffuse</td>
<td>3+ diffuse</td>
<td>3+ diffuse</td>
</tr>
<tr>
<td>Anti dsDNA (N&lt;25 IU/mL)</td>
<td>59</td>
<td>583</td>
<td>112</td>
</tr>
<tr>
<td>Anti-cardiolipin antibody</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>antibodies: a) Lupus anticoagulant</td>
<td>Positive</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>b) Anti-β 2 glycoprotein</td>
<td>Negative</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>2D echocardiography</td>
<td>Mild pericardial effusion, dilated left ventricle, ejection fraction (EF) 30%</td>
<td>Mild pericardial effusion, EF 25%</td>
<td>Mild pericardial effusion, moderate mitral regurgitation, mild tricuspid regurgitation, global hypokinesia, EF 56%</td>
</tr>
</tbody>
</table>

Disclosure of Interests: None declared

AB1027

DEVELOPMENT OF A NOVEL DIAGNOSTIC METHOD FOR ATYPICAL AND TREATMENT-REFRACTORY KAWASAKI DISEASE USING NEWLY IDENTIFIED PROTEINS AS BIOMARKERS

Masaaki Mori, Katsumasa Yanagimachi. Tokyo Medical and Dental University, Tokyo, Japan

Background: Kawasaki disease (KD) is a representative acute inflammatory disease of the children mainly under 4 years old. There were more than 15,000 onset cases per year in Japan. KD without proper treatment can lead to cardiovascular complications such as coronary artery lesions (CALs). We are still missing about an etiology and the onset mechanism of KD. Therefore, the diagnosis of KD depends on its clinical features. There are also no specific biomarkers for therapy effectiveness in clinical settings. By using proteomic analysis, we found that the serum expression of lipopolysaccharide binding protein (LBP) and leucine rich alpha 2 glycoprotein 1(LRG1) at the acute phase of KD were significantly high, compared with that of healthy control or patients with autoimmune diseases and biomarkers such as LRG1 and LBP. This study contains more cases and biomarkers such as LBP and LRG1 for grouping of KD patients using clustering analysis based on clinical features and biomarkers.

Methods: The research strategy is composed of clinical phenotype subgrouping of KD patients using clustering analysis based on clinical features and biomarkers such as LRG1 and LBP. This study contains more than 350 KD patients’ data sets including clinical characteristics and laboratory parameters including those of Biomarkers.

Results: According to these results of study, we can objectively diagnose KD without depending on only clinical manifestations.

Conclusion: These two biomarkers may be added in a new KD diagnostic criteria, resulting in quality enhancement of KD diagnosis and may have the potential of proper clinical examination for KD without consequence of CALs.

REFERENCES


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FIBRODYSPLASIA OSSIFICANS PROGRESSIVA: A CHALLENGE TO DIAGNOSE AND TO TREAT

Mohammed Nashawi, Jan Henje Döring, Markus Bettendorf, Stefan Kölker, Georg Hoffmann, Andreas Ziegler. University Hospital Heidelberg, Center for Pediatrics and Adolescent Medicine, Heidelberg, Germany

Background: Fibrodysplasia ossificans progressiva (FOP) caused by mutations in the ACVR1 gene, which codes for activin receptor IA, a type I receptor of the bone morphogenetic protein (BMP) pathway. FOP is a very rare disease which usually begins in the first decade of life and characterized by congenital bilateral hallux valgus in combination with progressive heterotopic ossification in specific anatomical patterns preceded by inflammatory responses and soft tissue swelling.

Objectives: Our objective is to expand the differential diagnosis of recurrent swelling without trauma by presenting a case of Infant suffering from recurrent swelling and diagnosed to have FOP.

Methods: We used standard laboratory assessment and ultrasound to exclude other diseases. To confirm the diagnosis we used next generation sequencing to identify ACVR1 variants.

Results: A full-term male infant from non-consanguine parents delivered spontaneously after uncomplicated pregnancy. Initially bilateral hallux valgus, as well as limited motility in the metacarpophalangeal joint of D1 of the right hand was noted. At the age of 1.5 months, a severe swelling appeared on the left head without trauma. The further investigation showed no signs of retinal hemorrhage or intracranial injury. The swelling resolved spontaneously, but he readmitted to the hospital due to swellings of different localization in the head area. At the beginning a child abuse had been discussed with the family, although there was no concrete evidence.

At the age of 7 months he presented to our center with renewed swelling in the area of the forehead. Due to the characteristic symptom constellation, a genetic analysis was performed on ACVR1, which confirmed a de novo mutation c.617G> A, p.R206H.

We started a combined therapy with Montelukast 4 mg oral daily for specific inhibition of mast cell activation, Neridronat (Bisphosphonate) 2 mg/kg as i.v. every 3 months for the modification of secondary ossification. As well as Prednisolone for 3 days 20 mg/kg i.v. in the flare up.

At the beginning there were a significant reduction in the frequency and severity of new swellings, however after 9 Months he had frequent flare up with limitation of head movement. At that point we decided to start an off-label therapy with Imatinib. He responded well to the current therapy and the medication is well tolerated.

Conclusion: FOP is a very rare and important differential diagnosis of child abuse. With the characteristic symptom of congenital bilateral hallux valgus and unclear swellings, the diagnosis can be genetically secured.

An early specific treatment concept for the avoidance of trauma as well as drug-based anti-inflammatory therapy are crucial for the clinical course and subsequent impairment of the patient. New targeted treatment approaches offer a promising option for the long-term improvement of disease progression and associated quality of life like Imatinib, which is a tyrosine kinase inhibitor used in the treatment of chronic myeloid leukaemia in adult and children. A recent article showed that it decreased the flare up in 6 out of 7 patients with FOP.

REFERENCES


Disclosure of Interests: None declared


Fibrodysplasia ossificans progressiva: a neuropsychiatric manifestation in childhood-onset systemic lupus erythematosus: retrospective study in one single center

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Background: Systemic lupus erythematosus is a complex autoimmune disorder characterized by multisystem involvement, including the nervous system, which elevate damage and mortality. The investigation of neuropsychiatric involvement in childhood-onset SLE (cSLE) is important in real clinical practice to improve the prognosis.

Objectives: The study included this was to assess neuropsychiatric manifestations (NM) in cSLE in one single center.

Methods: The study included all pts with cSLE who undergoing in-patient treatment in our center from 1992 to 2017 y. Diagnosis of SLE was reviewed based on 2012 SLICC criteria. Data including sex, age at the time of onset, age at the time of diagnosis, physical examination, laboratory review, and neuropsychiatric inventory were extracted from our database. Classification of NM of SLE was according to the 1999 American College of Rheumatology (ACR) neuropsychiatric manifestations of SLE case definitions.

Results: We included 218 consecutive pts with cSLE, of which 45 pts (20.6%) had neuropsychiatric involvement at the time of diagnosis (Tab.1).

Abstract AB1030 Table 1. Clinical and demographic characteristics of patients.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Patients without NM of cSLE (173)</th>
<th>Patients with NM of cSLE (45)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Girls/boys (girls to boys ratio)</td>
<td>154/19 (8.1:1)</td>
<td>36/9 (4:1)</td>
</tr>
<tr>
<td>The average age at onset, years</td>
<td>12.8±3.52</td>
<td>13.0±2.84</td>
</tr>
<tr>
<td>The median of disease duration at the time of cSLE verification, months</td>
<td>6.0 (2.0;13.0)</td>
<td>5.0 (3.0;11.0)</td>
</tr>
<tr>
<td>The average of disease activity by SLEDAI at the time of cSLE</td>
<td>12.9±6.5</td>
<td>22.0±9.5</td>
</tr>
</tbody>
</table>

Neuropsychiatric manifestations were significantly more frequently detected during the acute development of SLE (46.7% of patients, p = 0.003). Among immunologic disorders, patients with NM often had antibodies to RNP (p = 0.073) in the absence of any differences in other immunological parameters. Of the clinical manifestations in patients with NM, chronic skin lesions were recorded more often (p = 0.076), while arthritis was detected relatively less frequently (p = 0.028). Serositis and nephritis were diagnosed significantly more often in the group of patients with NM (p = 0.003, 0.003, respectively). Of the hematological disorders, NM was relatively more frequently accompanied by leuko/lymphopenia (p = 0.087) and thrombocytopenia (p = 0.077). In general, the group of patients with NM was characterized by a higher degree of multiorgan involvement (the number of clinical manifestations was on average 5.6 and 3.7, respectively, p <0.0001), but both groups were comparable for number of immunological disorders (p = 0.49).

As early signs of NM, all patients had mood disorders and impaired school adaptation. In the structure of NM, central nervous system involvement prevailed (89%), 15 pts (33.3%) had experienced more than one NM. Headaches, cognitive dysfunction and cerebrovascular disease were the most common (28.9%, 28.9% and 24.4%, respectively). Other NM included distal polyneuropathy – 20%, episody – 15.5%, acute confusional state – 11.1%, anxiety disorder – 11.1%, psychosis – 8.9%, pare-sis – 6.7%, chorea – 4.4%.

Conclusion: Acute onset, multiorgan lesions, mood disorders, impairment of学校 adaptation in a patient with suspected SLE should prompt investigations into diagnosis of the primary nervous system involvement. Patients with neuropsychiatric disorders require earlier complex aggressive therapy due to greater disease activity and poor prognosis.

Disclosure of Interests: None declared

ETANERCEPT-INDUCED LUPUS-LIKE SYNDROME IN THE BOY WITH IDIOPATHIC DERMATOMYOSITIS OR DEFACTO MANIFESTATION OF SYSTEMIC LUPUS ERYTHEMATOSUS?

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Background: Treatment of juvenile onset rheumatic diseases (RD) is an ongoing problem because of the more aggressive disease course and more various clinical manifestations than adult-onset RD. Since the main clinical symptoms may overlap between well-known various RD, in some cases the path to diagnosis and the search for optimal therapy takes longer, especially in patients of pre-adolescence and adolescence.

Objectives: We described a rare case of one boy with RD who presented initially with severe dermatomyositis with sequential evolution to systemic lupus erythematosus.

Methods: Case report.

Results: A 8 yo male patient with normal physical, psychosocial and cognitive development experienced muscle weakness, periorbital edema, Gottron symptom, dysphagia in September 2015 y, which developed after infection. When he was admitted to hospital, increased levels of muscle-derived enzymes and positivity of ANA 1:640 were found. He was diagnosed as having juvenile dermatomyositis and was treated with prednisolone (Pr) for 3 years (IV courses repeated and per os constantly, max dose 1.5 mg/kg/day, min dose 0.5 mg/g/day), IVIG courses repeated and sequentially methotrexate, hydroxychloroquine, cyclosporine with short time of remission. Muscle weakness disappeared after the treatment, but in October 2015 y he experienced new eruptions on his face, heavy arthropathies, lymphadenopathy, distal polyneuropathy, weight loss without strong effect after increase the dose of Pr, IVIG courses repeated, cyclosporine and added of abatacept during 6 months. Because the response to this treatment was low, etanercept was started in June 2016 y, but after two injections he had flare of disease: bright rash on the face, scalp and legs, hard aphthosis stomatitis, cheilitis, cognitive disorders, diffuse alopecia. He received IV course of Pr without significant stable effect. We reviewed diagnosis as systemic lupus erythematosus and changed therapy in November of 2016. Because he had steroid’s osteoporosis with spondylopathy, this combination that made us initiate treatment with mycophenolate mofetil and repeating courses of rituximab (5 courses in total) without increased dose of Pr. Clinical features gradually improved and now he feel good and receive mycophenolate mofetil and Pr 5 mg/day.

Conclusion: This clinical observation can be considered as a course of overlap-syndrome with a successive phase change that could be triggered by anti-TNF therapy, or as an unusual course of SLE in a male patient with a predominance of myositis at onset. Treatment strategy, including Pr, mycophenolate mofetil and rituximab in a young patient proved successful for treatment and seems to be justified in similar cases.

Disclosure of Interests: None declared


FACTORS TO AID IN EARLY DIAGNOSIS OF KIKUCHI’S DISEASE IN ASIAN CHILDREN

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Background: The diagnosis of Kikuchi’s Disease (KD), also known as histiocytic necrotizing lymphadenitis, is often delayed as patients often undergo multiple investigations to exclude other causes of cervical lymphadenopathy, such as infection and malignancy1.

Objectives: To describe the clinical features and treatment response of pediatric patients diagnosed with KD in our institution to aid early recognition.

Methods: A retrospective study was conducted on patients < 18 years old diagnosed with KD in National University Hospital, Singapore, from Jan 2006 – Dec 2018. Demographics, clinical characteristics and treatment information were collected.

Results: 14 patients were diagnosed with KD. All were Asian and majority were Chinese (64.2%). 57.1% were male and the age of presentation ranged between 2.8 to 17.9 years old. Fever duration at diagnosis ranged between 8 - 50 days. Median height of temperature was 39.8°C (IQR: 39.4 – 40.0) deg C. This was frequently associated with neck pain and swelling (57.1%) and constitutional symptoms (71.4%) such as anorexia and weight loss. Other symptoms include abdominal symptoms of pain, vomiting or diarrhea (57.1%), rash (35.7%) and oral ulcers (28.6%).

All patients had cervical lymphadenopathy either in the anterior cervical triangle or both anterior and posterior triangles, but not in the posterior triangle alone. This was usually multiple (92.9%), measuring ≥2cm in diameter (100%), tender (95.7%), and tended to be unilateral (64.3%); none had overlying warmth or skin changes. 14.3% had isolated hepatomegaly while 14.3% had hepatosplenomegaly. Common lab abnormalities included cytopenia (50% bicytopenia, 28.6% leucopenia, 7.1% anaemia), elevated inflammatory markers C-reactive protein (CRP) (range: 12 – 117 mg/L), erythrocyte sedimentation rate (ESR) (range 15 – 116 mm/h) and lactate dehydrogenase (range: 490–1514 U/L). Only 3/14 had mild transaminis. Interestingly, almost half had low alkaline phosphatase (ALP). All patients had normal to low complements and were negative for anti-dsDNA antibodies. Ultrasound of the neck typically revealed non-specific findings of reactive lymphadenopathy while 1 showed suspicious features of thickened cortex and loss of fatty hilum. 10/14 patients underwent excision biopsy which confirmed the diagnosis of Kikuchi Disease on histology. 3/14 did not have excision biopsy as they responded promptly to non-steroidal anti-inflammatory drugs (NSAIDs), one declined excision biopsy. All patients had received empiric antibiotics with no response. 84.3% required treatment with NSAIDs for an average of 2-4 weeks. Of the 4 patients who required steroid therapy, one was started at the diagnosis of KD, while the other 3 received steroids upon failure of NSAIDs. Response to either NSAIDs or prednisolone, if effective, was usually prompt, within 24 hours.

Conclusion: Prolonged high grade fever with multiple tender cervical lymphadenopathy ≥ 2cm without warmth or redness and non-response to antibiotics should raise concerns for KD. The presence of cytopenia with moderately elevated inflammatory markers and LDH, coupled with low ALP, may be considered supporting biochemical features of KD. Prompt response to a trial of NSAIDs can help with the diagnosis of KD and potentially avoid excision biopsy of the lymph node. More research needs to be done to determine a clinical and biochemical diagnostic criteria for Kikuchi’s Disease so as to aid early diagnosis and potentially avoid invasive excision biopsy of the lymph nodes.

REFERENCES

Disclosure of Interests: None declared


MEASUREMENT OF DISEASE ACTIVITY LEVEL OVER TIME IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS UNDER BIOLOGIC TREATMENT, USING THE JUVENILE DISEASE ACTIVITY SCORE HUNGARIAN DATA FROM THE JUVENILE IDIOPATHIC ARTHRITIS REGISTRY OF THE NATIONAL INSTITUTE OF RHEUMATOLOGY AND PHYSIOTHERAPY

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Background: A wide variety of measures are currently available to monitor disease course over time in children with JIA. The Juvenile Disease Activity Score JADAS71 version was validated for 71 joints, global score for the JADAS71 is: 0-101.

Objectives: To report the changes of disease activity in JIA patients under biological treatment at age 18, using the JADAS 71 score for the extended oligoarticular and seropositive/seronegative polyarticular form of JIA.

Methods: The Hungarian Biologics JIA Registry of National Institute of Rheumatology and Physiotherapy, Budapest is a longitudinal, unicenter, observational study, that has been maintained since 2002. JIA-ILAR criteria were used for the diagnosis.

Patients with polyarticular course, who failed to respond or did not tolerate methotrexate and were treated with biological agents at the Paediatric Rheumatologic Centre of the National Institute of Rheumatology and Physiotherapy, Budapest, Hungary from 2002 to 25th January,019, were enrolled in an open label observational study and have been monitored prospectively in the registry. At baseline patients and disease characteristics were registered such as, patients’
history, demographic characteristics, and previous DMARDs treatments. Adverse events (AEs), reason for the discontinuation of the biologic treatment, or switch to another biological treatment were documented. The study was approved by the Institutional Review Board. Written informed consent was obtained from parents of the patients and the study was conducted in accordance with the Declaration of Helsinki.

**Results:** In this study 64, 18-year-old Caucasian JIA patients were evaluated from the day of entrance into the registry, who had JADAS 71 results at age 18, from the 347 patients treated with biologics at the submission. Demographic data and disease related variables by descriptive statistics:

- **Gender:** Female: N(%) = 49 (77%)
- **Subtypes of JIA:**
  - Extended oligoarticular form: 11 patients, Polyarticular form: 53 patients (5 RF positive, 48 negative)
- **Median age:** 8 (range: 4-17) years.
- **Mean disease duration:** 3592 days.
- **Mean time on biological treatment:** 1030 days.
- **The first JADAS 71 summation at the entry into the registry:** Median: 18.65 (range: 14.4, 55.4).

**Methods:**

- **Anti-HBs antibody positivity and titers were compared between healthy controls.**
- **Background:** Biologic disease-modifying antirheumatic drugs (DMARDs) use in JIA can reduce and might contribute to the development of renal disease. Although ACE inhibitors could potentially slow down the progression of kidney dysfunction, other treatments would be welcome. Furthermore, a slight proteinuria reduction in a patient with MCTO treated with cyclosporine has been reported. MABF-deficient mice develop systemic lupus erythematosus-like autoimmune disease by inhibited C1q production and effecrocytosis. In the human, monoallelic mutations in MABF result in MCTO.

**Objective:** To investigate whether C1q levels in patients with MCTO are associated with poorly controlled structural kidney damage that usually requires kidney transplantation in adulthood. Because ACE-inhibitors could potentially slow down the progression of kidney dysfunction, other treatments would be welcome. Furthermore, a slight proteinuria reduction in a patient with MCTO treated with cyclosporine has been reported. MABF-deficient mice develop systemic lupus erythematosus-like autoimmune disease by inhibited C1q production and effectorcytosis. In the human, monoallelic mutations in MABF result in MCTO.

**Methods:**

- **Objectives:** To investigate whether C1q levels in patients with MCTO are associated with poorly controlled structural kidney damage that usually requires kidney transplantation in adulthood. Because ACE-inhibitors could potentially slow down the progression of kidney dysfunction, other treatments would be welcome. Furthermore, a slight proteinuria reduction in a patient with MCTO treated with cyclosporine has been reported. MABF-deficient mice develop systemic lupus erythematosus-like autoimmune disease by inhibited C1q production and effectorcytosis. In the human, monoallelic mutations in MABF result in MCTO.

**Results:** Three patients with MCTO were enrolled (table 1). Patient A presented recurrent urinary tract infections since 18 months of life, for a third-degree vesicoureteral reflux. Despite correction surgery, he displayed proteinuria after one year, and kidney biopsy did not reveal significant lesions. After two years, he displayed bilateral tarsal malformations requiring orthopedic surgery. At the age of 6, a pathological fracture of the right wrist occurred, and local X-ray revealed osteolysis of carpal bones. - Because of a suspected juvenile idiopathic arthritis of the right wrist, patient B was treated with intra-articular steroid injection and subsequentous methotrexate for one year without benefit. After one year, he developed proteinuria and kidney biopsy revealed focal segmental glomerular lesions with tubular fibrosis and renal vasa sub-intimal delamination. C3 and C4 positive mesangial deposits were also present. - Patient C was referred to us for suspected juvenile idiopathic arthritis of the right wrist. No inflammatory signs were present at the ultrasound examination. Sequencing of the MABF gene revealed in all the patients a novel heterozygous mutation. Although specific variants have not been reported before, the nature and position of the variants associated with the clinical features of the patients strongly argued in favor of their pathogenic role. The serum C1q concentration was normal in all the patients.

**Conclusion:** It appears from our study that at age 18, 72.3% JIA patients with extended oligoarticular subtype and 26.4% with polyarticular subtypes report a JADAS71 high disease activity sum, so, these young adults will need transitional care.

**References**


**Acknowledgement:** Tamás Balázs statistical analysis.

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.7611

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**AB1034 NO DIFFERENCES IN HEPATITIS B ANTIBODY POSITIVITY IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS ON BIOLOGICAL THERAPY**

**OCEK SUMEYRA OZDEMIR1, Nihal Sahin1, Aysenur Pac Kisaarslan1, Meda Kondolot2, Zubeyde Gunduz3, Muammer Hakan Poyrazoglu1, Ruhan Düsünsel1. 1Erciyes University Faculty of Medicine, Pediatric Rheumatology, Kayseri, Turkey; 2Erciyes University Faculty of Medicine, Social Pediatrics, Kayseri, Turkey; 3Acibadem Hospital, Pediatric Rheumatology, Kayseri, Turkey.

**Background:** Biologic disease-modifying antirheumatic drugs (DMARDs) are frequently used in the treatment of juvenile idiopathic arthritis (JIA) resistant to nonbiologic DMARDs recently. There is a concern for their reducing the effectiveness of vaccines due to immunosuppressive effects. Objectives: To evaluate hepatitis B antibody (anti-HBs) positivity and antibody titer between JIA patients on biologic DMARDs therapy and healthy controls.

**Methods:** Anti-HBs antibody positivity and titers were compared between 88 patients with JIA on biologic DMARDs therapy followed in our clinic and 91 healthy controls aged 2-19 years. All participants were vaccinated according to the routine vaccination schedule in our country.

**Results:** Eighty-eight JIA patients included and fifty five (62.5%) patients were female. The median age of patients was 13.31 (4.07-18.08) years. The JIA subtypes were systemic JIA (10.2%), oligoarticular JIA (33%), polyarticular JIA (29%), enthesitis related arthritis (26.1%), psoriatic JIA (3.4%), and undifferentiated JIA (2.3%). The median duration of biologic DMARDs was 31.995 (1.33-115) months. 54 patients were treated only with one anti-TNF (34 etanercept, 17 adalimumab), 16 patients were treated more than one different group biologic DMARDs, and 7 of them had more than two biologic DMARD due to disease activity. Anti-HBs positivity was 67% in the JIA group and 54.9% in the control group, and no significant difference detected between the two groups (p=0.097). The anti-HBs titer was 12.95 (min: max: 2-1000) in the controls and 22.44 (2-1000) in the biologic DMARDs.

**Conclusion:** Patients with JIA on biologic DMARDs had not lower anti-HBs positivity than healthy controls in our study. Further studies are required to understand the effects of biologic DMARDs on protective anti-HBs antibody levels.

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.7990

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**AB1035 MABF-VARIANTS IN MULTICEUTRIC CARPOTARSAL OSTEOLYSIS WITH NEPHROPATHY DO NOT SEEM TO AFFECT SERUM C1Q CONCENTRATION**

**Riccardo Papa1, Annalisa Madoz2, Stefano Volpi1, Roberta Caorsi1, Giancarlo Barbano1, Marina Botto1, Belinda Campos-Xavier5, Andrea Superni-Furga5, Marco Gattorno1, Maja Di Rococo1, Paolo Picco2,1, IRCCS Istututo Giannina Gaslini, Clinica Pediatrica e Reumatologia, Genova, Italy; 2IRCCS Istituto Giannina Gaslini, Malattie Rare, Genova, Italy; 3IRCCS Istituto Giannina Gaslini, Malattie Rare, Genova, Italy; 4IRCCS Istituto Giannina Gaslini, Malattie Rare, Genova, Italy; 5Centre Hospitalier Universitaire Vaudois, Division of Genetic Medicine, Lausanne, Switzerland.

**Background:** Multicentric carpotarsal osteolysis syndrome (MCTO)-associated progressive nephropathy is an orphan disease associated with well-known structural kidney damage that usually requires kidney transplantation in adulthood. Although ACE inhibitors could potentially slow down the progression of kidney dysfunction, other treatments would be welcome. Furthermore, a slight proteinuria reduction in a patient with MCTO treated with cyclosporine has been reported. MABF-deficient mice develop systemic lupus erythematosus-like autoimmune disease by inhibited C1q production and effecrocytosis. In the human, monoallelic mutations in MABF result in MCTO.

**Objectives:** To investigate whether C1q levels in patients with MCTO are reduced and might contribute to the development of renal disease. Methods: In three individuals with clinical and radiographic signs of MCTO, the MABF gene was sequenced. The serum C1q concentration was determined with a commercial laboratory kit.

**Results:** Three patients with MCTO were enrolled (table 1). Patient A presented recurrent urinary tract infections since 18 months of life, for a third-degree vesicoureteral reflux. Despite correction surgery, he displayed proteinuria after one year, and kidney biopsy did not reveal significant lesions. After two years, he displayed bilateral tarsal malformations requiring orthopedic surgery. At the age of 6, a pathological fracture of the right wrist occurred, and local X-ray revealed osteolysis of carpal bones. Because of a suspected juvenile idiopathic arthritis of the right wrist, patient B was treated with intra-articular steroid injection and subsequentous methotrexate for one year without benefit. After one year, he developed proteinuria and kidney biopsy revealed focal segmental glomerular lesions with tubular fibrosis and renal vasa sub-intimal delamination. C3 and C4 positive mesangial deposits were also present. Patient C was referred to us for suspected juvenile idiopathic arthritis of the right wrist.

No inflammatory signs were present at the ultrasound examination. Sequencing of the MABF gene revealed in all the patients a novel heterozygous mutation. Although specific variants have not been reported before, the nature and position of the variants associated with the clinical features of the patients strongly argued in favor of their pathogenic role. The serum C1q concentration was normal in all the patients.

**Abstract AB1035 Table 1. Main features of three patients with MCTO.**

<table>
<thead>
<tr>
<th>Patient</th>
<th>A</th>
<th>B</th>
<th>C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years); gender; country of origin</td>
<td>14; M; Croatia</td>
<td>16; M; Italy</td>
<td>11; F; Russia</td>
</tr>
<tr>
<td>Bone lesions onset (age); site</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presentation</td>
<td>Bilateral Tarsus</td>
<td>Monolateral Carpus</td>
<td>Monolateral Carpus</td>
</tr>
<tr>
<td>Current state (except carpotalarsal joints)</td>
<td>Elbows and knees contractures</td>
<td>Knees contractures</td>
<td>None</td>
</tr>
</tbody>
</table>
Conclusion: C1q plasma levels in our patients were normal, suggesting that MCTO-associated genetic variants do not play a role in MafB-dependent regulation of complement component C1q production in humans. Further studies are necessary to exclude a role of complement system in the progressive nephropathy of patients with MCTO.

REFERENCES

Disclosure of Interests: Ricardo Papa: None declared, Annalisa Madoè: None declared, Stefano Volpi: None declared, Roberta Caorsi: None declared, Giancarlo Barbano: None declared, Marco Gattorno: Grant/research support from: MG has declared, Belinda Campos-Xavier: None declared, Andrea Superti-Furga: None declared, Giancarlo Barbano: None declared, Marina Botto: None declared, Riccardo Papa: None declared, Annalisa Madeo: None declared.


AB1036
AN UNSOLVED CASE: IS THIS A CANDLE-LIKE SYNDROME?

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Background: Chronic Atypical Neutrophilic Dermatosis with Lipodystrophy and Elevated Temperature (CANDLE) syndrome is a complex autoinflammatory disorder arising from inborn defects in immunoproteasome. Several genes can be involved and cases with digenic inheritance have been described. However, many cases remain without the identification of a specific genetic defect. A positive interferon signature is typically found in patients and may serve as a diagnostic clue.

Methods: We performed Whole Exome Sequencing (WES) on 10 family members. Moreover, we assessed RNA-seq on three samples from the proband, collected during acute phases of disease (samples positive to class I interferon signature (IS)) (1), and her parents. Results of RNA sequencing (RNA-seq) were compared with specimens from healthy controls.

Differentially expressed genes (DEGs) were filtered by fold change > 2 and padj < 0.05. DEGs enrichment were performed using different R packages, such as pathfinder.

Results: We describe the case of a 20 years old girl with clinical and biological data supportive of CANDLE syndrome. At the age of 3 years, she started presenting a clinical picture reminiscent of amyopathic dermatomyositis, with skin rash, lipodystrophy, subcutaneous panniculitis nodules, and more recently with chilblains, skin ulcerations, polyarticular arthritis and alopecia. Her pedigree includes several relatives with rheumatic disorders, but none has a clinical picture as complex and severe as our patient. This girl was found to have a strongly positive class I IS in peripheral blood cells. After several unsuccessful therapeutic attempts with antirheumatic drugs and biologics, the girl showed a dramatic clinical response to JAK inhibitors tofacitinib.

Conclusion: Our results suggest that our family may present a multigenic form of CANDLE, with a complete clinical picture only in the proband, whilst other relatives may only present partial or incomplete forms of the disease.

REFERENCES

AB1037
SEROLOGICAL PHENOTYPES, UVEITIS AND DISEASE ACTIVITY INTO ADULTHOOD: LONG TERM OUTCOME IN A COHORT OF PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: Deepening the long-term study in adulthood of Juvenile Idiopathic Arthritis (JIA) is fundamental in order to expand knowledge of the pathogenesis, optimize the therapeutic choices, favour a more active communication between paediatric and adult care specialists.

Objectives: To present the results of a follow-up of adult patients affected by JIA.

Methods: The present study aimed to follow-up patients with JIA for a period ranging from 20 to 30 years.

Results: The main objectives were those of: analyse the serological profile (rheumatoid factor –RF- IgM, ACPA IgG, ANA) of such patients to investigate possible seroconversions in adulthood compared to the diagnosis in paediatric age; investigate whether correlations between antibodies (Ab) and diagnostic subgroups persist in adulthood; evaluate the association between Ab and disease activity; investigate the association between the presence of uveitis in the medical history and specific Ab, diagnostic subgroups and disease activity.

Conclusion: The prevalence of RF and ACPA remained unchanged in adulthood, whereas the positivity for ANA in adulthood was 45.6% of patients with ANA positivity in adulthood 13.2%. The difference was statistically significant. The Ab profile of both RF and ACPA remains unchanged in adulthood, whereas the positivity for ANA in adulthood was 13.2%. The presence of uveitis was not correlated either with the presence of ANA in paediatric age, nor in adulthood, but it is instead associated with the presence of specific Ab, diagnostic subgroups and disease activity.

REFERENCES
Disclosure of Interests: Marta Priora Grant/research support from: Sanofi SpA, Tilde Manetta: None declared, Simone Parisi: Speakers bureau: Chiesi, Janssen, Pfizer, Celgene, Abbvie, Lilly, Maria Chiara Ditto: None declared, Silvia Sanna Grant/research support from: Novartis, Richard Borrelli: None declared, Enrico Fusaro Grant/research support from: Abbvie Abiogen Actelion Amgen Biogen BMS Celgene Grunenthal GSK Janssen Lilly MSD Mundipharma Novartis Pfizer Roche SANOFI SCIBI UCB DOI: 10.1136/annrheumdis-2019-eular.1566

AB1038 JUVENILE IDIOPATHIC ARTHRITIS INTO ADULTHOOD: HOW DO WE ASSESS DISEASE ACTIVITY?

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Background: Deepening the long-term study of Juvenile Idiopathic Arthritis (JIA) in adulthood is essential to increase the pathogenetic knowledge of the disease, to optimize the therapeutic choices accordingly, as well as to promote a more active communication between paediatric care and adult care specialists.

Objectives: The present project, created as part of the “transition of care”, aims to compare clinimetric scores of wide use for adult inflammatory rheumatisms of the adult (DAS28, CDAI and SDAI) with the JADAS27 score, which has been validated and widely used in order to quantify JIA’s activities in the paediatric field. As of today, adult patients with JIA are usually evaluated with clinimetric scores developed for adult chronic rheumatic diseases (DAS28, CDAI, SDAI) and there is no consensus concerning which of these scores doctors should favour, so that the choice is quite autonomous and varies from centre to centre. It is therefore of interest to verify whether among these indices of purely rheumatological use of adults there is one that is more appropriate than JADAS27 which can be useful in monitoring adult patients with JIA.

Methods: The relevant clinical data were collected from 68 adult patients with JIA. A correlation analysis was performed between the clinimetric scores according to McNemar test and Kappa by Cohen.

Results: The results obtained suggest that none of the clinimetric scale commonly used in the rheumatological clinical practice of adult patients can completely replace JADAS27. DAS28 is the score that goes further from an acceptable correlation with JADAS. Since both CDAI and SDAI are calculated with formulas that are similar to the one used for JADAS (algebraic sums of affected joints, subjective outcomes reported by the patient, clinical judgment of the physician), they happen to be a method of quantification of disease activity quite closer to JADAS itself. The analyses outlined a scenario in which a much larger portion of patients are classified in remission stages or in low disease activity when using CDAI and SDAI compared to JADAS27.

Conclusion: This element inspired us to consider how in paediatric age a more “demanding” attitude towards the disease led to the validation of both a score and its very stringent cut-offs which are functional to a treat to target characterized by a complete remission whose main goal is to avoid long-term sequelae. SDAI was found to be the scale of common use in the adult care that more properly approaches the clinometry validated for the paediatric population (JADAS27). Although clinical common sense should not distract from assessing disease activity in this specific patient population from a global perspective, such a study could suggest using SDAI as clinimetric score of choice in adult patients with JIA. Further checks in larger population samples are obviously necessary.

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ADA2 DEFICIENCY PRESENTING AS INFANTILE POLYARTERITIS NODOSA

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Background: Polyarteritis nodosa (PAN) is a rare form of primary systemic vasculitis with heterogeneous presentations, treatments and disease course. There have been improvements in understanding of certain causes of PAN such as the association of the monogenic disorder Deficiency of Adenosine Deaminase 2 (DADA2) with a PAN phenotype. This described autoinflammatory disease is caused by loss-of-function homozygous or compound heterozygous mutations in CECR1 and can be characterised by an early onset vasculopathy with clinical and histopathological features of PAN associated with haemorrhagic and ischemic strokes.

Objectives: We report a case of a 14-year-old boy, with a prenatal diagnosis of Klinefelter syndrome, whose parents are first cousins.

Methods: Review of patient’s clinical records and scientific literature.

Results: During his first two years of age, he suffered two small strokes, was investigated in another Hospital and no diagnosis was made. At 4 years of age he was admitted to another hospital for prolonged fever and arthralgia. At age 5 he was admitted to our hospital for fever, arthralgia and myalgia. He later developed a modular stroke and arterial hypertension. Due to suspected PAN he underwent a renal angiogram which confirmed our suspicion.

He completed induction treatment with IV cyclophosphamide (6 months), steroids, and arthralgia. At age 5 he was admitted to our hospital for fever, arthralgia and myalgia. He later developed a modular stroke and arterial hypertension. Due to suspected PAN he underwent a renal angiogram which confirmed our suspicion.

He maintained follow-up, with no sequelae to his strokes and apparent clinical remission.

Conclusion: The purpose of this study is to describe five cases with pediatric SS in order to better clarify the characteristics of the disease in the childhood.

Methods: We retrospectively reviewed medical records of patients with pediatric SS referring to our center (ASST-PINI-CTO, University of Milan) from November 2008 to December 2018. No adequate childhood SS-specific criteria exist. Therefore we select our pts according to a combination of clinical, serological, histopathological findings. For the assessment of systemic disease activity we applied ESSDAI (EULAR Sjögren’s syndrome disease activity index). We calculated ESSDAI at diagnosis, at the peak disease activity and at the last follow up visit.

Results: We collected data on 5 pts (4 females). The mean of age at onset is 8.4 yrs (range 4.8-11.2). The mean of age at diagnosis is 10.8 (range 6.5-13.3). The follow up period varied from 1.2 to 9.3 yrs (mean 6.3). The most common manifestations were parotid/salivary glands swelling (5/5 pts) and articular involvement (5/5 pts) with arthritis in 2 pts and arthralgia in the others. Nobody of our pts presented dryness of eyes. Xerostomia was found in 2/5 pts. Fever and fatigue occurred in 2/5 and 3/5 pts respectively. We also recorded 2 cases of abdominal pain, 1 case of glomerular proteinuria, 2 cases of purpura and 1 case of erythema nodosum. ANA, anti-SSA, anti-SSB, RF, elevation of ERS and hypergammaglobulinemia (1.6 – 8.04 g/dl) were present in all cases. Minor salivary gland biopsy was performed in 4 pts resulting in histological evidence of focal lymphocytic sialadenitis (one of them showed chronic sialadenitis with a focus score <1/4mm2). Ultrasound studies of salivary glands were positive in 5/5 cases. Mean ESSDAI scores at diagnosis, peak activity and the last follow up visit were 8 (range 5-11), 13.2 (9-20), 4.8 (0-9). The most frequently involved domains at the peak activity were biological (5/5), parotid/salivary glands swelling (5/5) and articular (5/5). No major complications have been observed. With regard to treatment, all patient received corticosteroids and DMARDs (5/5 hydroxychloroquine, 3/5 methotrexate, 1/5 azathioprine, 1/5 leflunomide); one patient needed plasmapheresis and immunosuppressive therapy with cyclophosphamide. Biological therapy was administered to 2 patients; 1 received belimumab and then rituximab, while the other patient received rituximab.

Conclusion: Xerostomia and keratoconjunctivitis sicca are not a common features in children, on the other hand juvenile SS has higher incidence of recurrent parotid swellings than adults [2, 3]. All pts had laboratory abnormalities. The long-term prognosis of pediatric SS is unknown, in our series only 2 patients were inactive (ESSDAI score <5, according to the definition by EULAR) at last evaluation, 3 were moderately active with a minimal clinically important improvement (MCII) observed in all of them [4].

REFERENCES

Disclosure of Interests: None declared
PREVALENCE OF JUVENILE IDIOPATHIC ARTHRITIS (JIA) SUBGROUPS AND JIA-ASSOCIATED UVEITIS AMONG JIA PATIENTS ADMITTED TO REFERRAL PEDIATRIC RHEUMATOLOGY CLINICS IN TURKEY: A RETROSPECTIVE STUDY, JUPITER

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Background: Juvenile Idiopathic Arthritis (JIA) is a chronic childhood arthritis with onset before age of 16 and has a significant degree of morbidity that negatively affects quality of life. Uveitis, which is defined as the inflammation of the iris, ciliary body and choroid, is the most common cause of morbidity of JIA. This study was planned to collect data from a Turkish cohort to provide the initial national prevalence data of patients with JIA.

Objectives: The objective of this study was to determine the frequency of JIA subtypes in Turkey. We also aimed to assess the frequency and characteristics of eye involvement in JIA.

Methods: This national, non-interventional, multicenter, observational study was conducted in a retrospective manner in four study centers which were main referral pediatric rheumatology clinics across Turkey. Data on patient demography, medical history, JIA disease characteristics, laboratory data, cases of JIA-associated uveitis, JIA treatment history and data on other comorbidities were collected from a cohort of 500 patients.

Results: Oligoarthritis (n=194, 38.8%) was the most common JIA disease characteristic in this study cohort. The frequency of the subgroups was as follows: Enthesis-Related Arthritis (ERA) in 23.2% (n=116), polyarthritis in 15.6% (n=78), systemic arthritis in 12.2% (n=61), psoriatic arthritis in 5.2% (n=26), idiopathic arthritis in 2.8% (n=14) and polyarthritis (RF−) in 2.2% (n=11) of patients were identified. The most frequently prescribed treatment for JIA was methotrexate (n=384, 76.8%). A total of 85 comorbidities were reported, and the most frequently reported comorbidity was Familial Mediterranean Fever (FMF) (n=63, 12.6%). The number of patients with JIA-associated uveitis diagnosis was 34 (6.8%), and the mean duration of uveitis was 3.2 (±2.3) years. The mean duration between the initial JIA diagnosis and diagnosis of uveitis was 1.8 (±1.0) years. Among 34 patients with uveitis, 45 eye involvement were identified; left eye, right eye and both eyes were affected in 5, 8 and 16 patients, respectively. Five patients (14.7%) had uveitis-related complications that required surgical intervention.

Conclusion: The main difference from the European Caucasian population is the lower frequency of oligoarticular JIA and higher frequency of ERA in Turkish JIA patients. Uveitis was also somewhat lower than expected. It is the lower frequency of oligoarticular JIA and higher frequency of ERA in Turkish JIA patients. Uveitis was also somewhat lower than expected.

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THE EFFECT OF INTRA-ARTICULAR STEROID INJECTION ON THE CARTILAGE THICKNESS IN JUVENILE IDIOPATHIC ARTHRITIS

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Background: Intra-articular corticosteroid injection is a choice in the treatment of juvenile idiopathic arthritis (JIA), especially in large and few joints involvement. Intra-articular steroid injection provides relief in active synovitis but its effects on cartilage are controversial.

Objectives: The aim of this study is to evaluate the effect of intra-articular steroid injection on distal femoral cartilage thickness in patients with JIA by ultrasonography.

Methods: Distal femoral cartilage thicknesses were measured before the procedure and 6 months later by ultrasonography in the patients that were injected an intra-articular steroid to the knee.

Results: The mean age of the patients was 12.1±4.8 years. Nine of patients were girls and 2 were boys. The mean disease duration was 5.1±4.2 years. Ten patients had left knee arthritis and one patient had enthesis-related arthritis. The number of patients injected to the right knee was 3, the left knee was 5 and both the knee was 3. The femoral cartilage thickness before the procedure was 3.0 mm [min-max 2.0-3.65 mm], 6 months after the procedure was 2.95 mm [min-max 2.0-3.55 mm] and there was no statistical difference (p<0.05).

Conclusion: In this study, no effect of intra-articular steroid treatment on cartilage was observed. However, the number of patients is lacks. Therefore, we planned a comprehensive study with more patients.

REFERENCES

Disclosure of Interests: None declared


AB1041

AB1042

CLINICAL OUTCOMES OF ANTI-NUCLEAR ANTIBODY POSITIVENESS IN THE 0-18 AGE GROUP: SINGLE-CENTER REAL-WORLD EXPERIENCE

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Background: Anti-nuclear antibody (ANA) assay is important in the diagnosis of autoimmune diseases. However, it has a poor positive predictive value and is detected positive in 10% of general population. In this study, the children that ANA assay was performed in a tertiary pediatric clinic, was evaluated and was aimed to investigate the clinical outcomes in positives.

Objectives: In this study, the children that ANA assay was performed in a tertiary pediatric clinic, was evaluated and was aimed to investigate the clinical outcomes in positives.

Methods: 0-18 age group patients that ANA assay was requested in the various clinics of Erciyes University were included. The patients with positive ANA assay and access to hospital records were retrospectively examined. Patients with and without autoimmune disease were identified as group 1 and group 2, respectively.

Results: The number of patients who required ANA assay in pediatric clinics was 3812. There was a positive ANA assay in 1010 of these patients. The medical records of 909 patients were reached. There were 345 (38%) patients in group 1 and 564 (62%) in group 2. In group 1, female gender was higher compared to group 2 (p <0.05).
Musculoskeletal, hematologic, enterohematic, and ocular findings as initial findings were significantly high in group 1 (p<0.05). Pediatric Rheumatology, general pediatrics and pediatric neurology are the three clinics which the assay was requested most common. The patients who were examined in pediatric rheumatology, pediatric hematology-oncology, pediatric gastroenterology departments had a higher incidence of autoimmune disease (p<0.05). In patients with autoimmune disease, >1/1000 ANA titer and homogenous staining were frequent (p<0.05).

Conclusion: In our center, which is a tertiary health center, the autoimmune disease was not detected in most of the patients whose ANA assay was positive. The proportion of patients with autoimmune disease was low in most of the commonly requested departments. The ANA assay should be requested after the patient’s clinical findings are evaluated in detail.

REFERENCES

Disclosure of Interests: None declared

AB1044 CYTOKINE PROFILE OF MACROPHAGE ACTIVATION SYNDROME ASSOCIATED WITH KAWASAKI DISEASE
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Background: Macrophage activation syndrome (MAS) is a severe, potentially life-threatening complication of childhood systemic inflammatory disorders. MAS occurs most often in children with systemic juvenile idiopathic arthritis and less commonly in children with Kawasaki disease (KD). Objectives: Our study aimed to assess the kinetics of cytokine release and compare the accuracy of serum biomarkers for diagnosis of MAS, including neopterin, IL-18, IL-6 and soluble TNF receptor type I (sTNFR-I) and sTNFR-II levels, we analysed these levels in patients with KD, including those with MAS, and compared them to the clinical features of KD and MAS.

Methods: Serum neopterin, interleukin (IL)-18, IL-6 and soluble tumour necrosis factor receptor type I (sTNFR-I) and sTNFR-II levels were determined using enzyme-linked immunosorbent assay in 78 patients with KD, including five with MAS. Results were compared to the clinical features of MAS.

Results: Serum neopterin, IL-18, sTNFR-II levels and sTNFR-II/I ratio were significantly elevated in KD patients with MAS compared to those in the acute phase. Receiver operating characteristic curve analysis revealed areas under the curve and cutoff values of neopterin, IL-18, sTNFR-II levels and sTNFR-II/I ratio were 0.975 ± 0.03 nmol/L, 0.981 ± 0.1165 ng/ml, 0.9969 ± 0.600 µg/ml and 0.9975 ± 0.04 4.75, respectively. Serum sTNFR-II levels correlated positively with disease activity.

Conclusion: These findings indicate that interferon (IFN)–γ and tumour necrosis factor-α (TNF-α) are closely associated with the pathogenesis of MAS associated with KD. Serum sTNFR-II levels might be a useful marker to diagnose the transition to MAS.

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AB1046 PHYSICAL ACTIVITY ASSESSMENT IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS COMPARED TO CONTROLS
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Background: Physical activity (PA), known to maintain optimal metabolic function and normal development could be impaired during Juvenile Idiopathic Arthritis (JIA).

Objectives: The aim of our study was to assess PA in children and adolescents with JIA compared to healthy peers using the physical activity questionnaire for children (cPAQ) and adolescents (aPAQ).

Methods: This is a cross-sectional study of measured level of PA in children and adolescents with JIA, compared to age and gender-matched healthy Tunisian schoolchildren. PA was estimated by cPAQ and aPAQ filled by the patient group and the reference group. If the child is unable or unsure to answer the questions we have helped with the parents’ response. The PAQ scores 2 as ‘low activity,’ >2 and ≤3 as ‘moderate activity,’ and >3 as ‘high to vigorous activity.’

Results: A total of 55 patients (38 boys and 17 girls) with JIA and 60 healthy control schoolchildren were included. No significant difference in demographic background was found between the two groups. The mean age was 8.5 ± 4.12 years in the JIA group and 9.2 ± 3.51 years in the control group. Thirty-one patients (53%) had persistent oligoarthritis JIA, 15 (27%) had polyarticular JIA, 5 patients (9%) had systemic JIA, and 4 (7%) had enthesis-related arthritis. The median disease duration was 3.2 ± 2.8 years. The mean cPAQ was 2.101 ± 0.722 in the JIA group and 4.112 ± 0.644 in the control group (p=0.0001). Children and adolescents with JIA had a significantly lower levels of PA compared with their healthy peers as assessed by cPAQ/aPAQ (p=0.012). The time spent in watching television <2 and ≥2 hours/week, p=0.001), and after school activities (0.5 ± 0.5 versus 2.5 ± 0.8 hours/week, p=0.001), and after school activities (0.5 ± 0.5 versus 2.5 ± 0.8 hours/week, p=0.001). Seventy six percent of the JIA group spent the day on the two lowest PA categories: sleeping and sitting, which was significantly higher compared with the reference group (p=0.001 and p=0.055, respectively).

Conclusion: In our study, children and adolescents with JIA were less physically active than the healthy peers as assessed by the PAQ. More objective methods are needed to better evaluate and quantify the PA.

Disclosure of Interests: None declared
DYNAMICS OF GROWTH AND BONE AGE IN CHILDREN WITH JIA DURING BIOLOGICAL THERAPY

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Background: In children with severe juvenile idiopathic arthritis (JIA), growth impairment is often accompanied by retardation of bone age. Dynamics of growth and bone during biological therapy is an important criterion for the effectiveness of treatment.

Objectives: To assess the effect of biological therapy on growth and bone age in children with JIA.

Methods: The study included 45 patients with JIA and (30 boys and 15 girls, mean age 12.2 ± 2.7 years; disease duration before the start of biological therapy 6.5 ± 3.3 years, 18 children with systemic JIA and 27 with polyarticular JIA). All children due to the ineffectiveness of standard therapy were transferred to biological therapy with TNF-α and IL-6 inhibitors. The study assessed growth SDS and bone age (according to x-ray imaging) before starting biological therapy (initially) and after 24 months of therapy.

Results: Of the 45 children, the initial growth retardation marked in 13 children, all with systemic JIA (growth SDS -3.19 ± 0.36 (-6.67; -2.04)). All these children also showed a lag of bone age from the passport by 2.9 ± 0.5 years, which corresponded to growth retardation. During biological therapy, the growth retardation decreased within 24 months: growth SDS -2.73 ± 0.34 (-5.87; -1.17). The lag of bone age was maintained at 2.3 ± 1.5 years, which is comparable to the baseline (p = 0.053). In 32 children, the initial growth was within the normal range (growth SDS 0.12 ± 1.07 (-1.97; 1.76)); 8 children with sJIA, 24 with polyarticular JIA. In all these children, the lagging of bone age from the passport at the time of the start of biological therapy was not detected (deviation from the passport age at most 1 year). During biological therapy for 24 months, growth rates remained normal: growth SDS was 0.22 ± 0.99 (-1.56; 1.67). Indicators of bone age in all children were corresponding passport age.

Conclusion: In children with severe JIA and normal growth, the bone age is more likely to correspond to the passport age; during therapy with TNF-α and IL-6 inhibitors, there is no significant change in bone age in these children. In children with severe JIA, growth impairment and bone age may be observed, most likely in children with systemic JIA. During biological therapy, there is an improvement in growth, while the lagging of bone age from the passport remains, which indicates the preservation of growth potential and the possibility of achieving higher final growth.

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Disclosure of Interests: None declared

SYSTEMIC LUPUS ERYTHEMATOUS WITH UNUSUAL PRESENTATION : SINGLE CENTRE EXPERIENCE FROM NORTH INDIA

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Background: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease. Presentation can range from constellation of non specific constitutional symptoms to definitive signs and symptoms. Systemic Lupus International Collaborating Clinics(SLICC) criteria help in making a diagnosis of SLE. SLE mimics many clinical entities and diagnosis may become difficult at times, especially if presentation is atypical. We describe children who presented with unusual manifestations and were finally diagnosed to have pediatric SLE.

Objectives: To highlight unusual presentation of pediatric SLE.

Methods: Retrospective case review of all children diagnosed as SLE from July 2017–November 2018 at a single tertiary care hospital in north India was done. We here describe 5 children who presented with unusual manifestations.

CASE 1: 8 years, girl, presented with fever for 1 month and bilateral pleural effusion. She had had 2 hospitalizations in the past. Once with fever, epistaxis and haemorrhagic shock and subsequently with fever, hepatitis, proteinuria and bicytopenia and was managed as tropical infections at both times. She was evaluated this time and was diagnosed to have SLE and managed for the same.

CASE 2: 11 years, boy, presented with arthritis in multiple small and large joints of body. No other features of SLE were seen. On evaluation ANA and anti dsDNA were found to be positive and he fulfilled criteria for SLE. He was started on subcutaneous, weekly methotrexate and responded to treatment. However, he developed lupus nephritis during disease course after 6 months of diagnosis. Renal biopsy revealed Class Ⅲ-V lupus nephritis. Intravenous Cyclophosphamide pulses were started for induction along with tapering doses of corticosteroids.

CASE 3: 8 years, girl, presented with early morning periobital puffiness and abdominal distention. She also had a history of photosensitivity and Raynaud phenomenon. Urine routine examination revealed nephrotic range proteinuria with no hematuria. Clinical possibility of nephrotic syndrome secondary to SLE was kept. Renal biopsy revealed Class V lupus nephritis. She was started on oral prednisolone and enalapril.

CASE 4: 15 years old, girl, presented with non-specific generalized body pains with n joint pains associated with low grade fever. There were no other complaints. Examination was unremarkable. Investigations, however, were suggestive of SLE.

CASE 5: 17 years old, girl, presented with high grade fever and pain in bilateral knee joints and malar rash. Investigation were suggestive of SLE with MAS (macrophage activation syndrome). Child was started on iv antibiotics and iv immunoglobulins but died during the disease process.

ANA positivity, hypocomplementemia and Anti ds DNA positivity were seen in all the 5 cases. Results: out of 11 children diagnosed to have SLE, 5 presented with unusual manifestations as described above. All patients were initiated on hydroxychloroquine and photoprotection other drugs used were prednisolone, naproxen, subcutaneous weekly methotrexate, cyclophosphamide and Azathioprine.

Conclusion: In this report we present unusual presentations as the predominant manifestation of SLE and emphasize the fact that early recognition and awareness of unusual presentation of SLE help institute timely initiation of appropriate treatment.

REFERENCES


Disclosure of Interests: None declared

CO-MORBIDITY INDEX IN CHILDREN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Comorbid conditions in patients with rheumatic diseases (RD) aggravate the course of diseases, worsen the prognosis, impede the response to therapy, and reduce the quality of life of patients. Initial manifestations of comorbid lesions of organs and systems are already manifested in childhood and adolescence, and in the future are the causes of persistent morphologic and functional disorders, disability and mortality of patients.

Objectives: The purpose was to identify comorbid conditions in children with systemic lupus erythematosus (SLE), followed by an assessment of the comorbidity index (CI).

Methods: 41 patients with SLE aged 7-18 years were examined. The average duration of the disease at the time of the survey was 44.5± 2.9 months, 20 persons (48.78%) had a period of illness up to 3 years, 21 (51.22%) – over 3 years. Among the patients female subjects predominated (79.09%). The comorbidity index (CI) was determined by the total score (points) of the disturbances in all systems of the organism without specific diagnoses.
Results: Pathological changes of the one or two systems were noted in 19.51% of patients, between three and four systems - in 24.4%, and in six systems - in 14.6% of patients. The mean values of CI among patients with SLE were 2.6±0.3 points and did not differ significantly depending on the duration of the disease (2.5±0.7 points before 3 years and 2.4±0.3 points after 3 years; p>0.05), as well as did not differ in female and male patients (2.6±0.3 and 2.8±0.5 respectively, p=0.05). The CI was higher in the cases of development of SLE before the age of 7 years than in older patients (3.6±0.5 vs 2.4±0.3 respectively, p<0.05).

The activity of the pathological process significantly influenced the indicators of the CI: 2.4±0.4 with its minimal activity; 2.7±0.4 with an average degree of activity and 3.0±0.6 with a high degree (p<0.05). The frequency of the smallest CI (0 or 1) turned out to be associated with the earliest activity of the disease. The CI with ANA-positivity association was defined: 2.8±0.3 points among patients with ANA that has twice exceeded the CI of ANA-negative patients (1.4±0.5), p<0.05. Its highest level (like 4, 5 and 6 points) was registered only among the ANA-positive patients.

In patients with SLE with high CI, changes in the system of coagulation due to elevated fibrinogen levels predominated (3.7±0.4 g/l vs 2.8±0.3 g/l (p>0.05)). Similar changes were recorded with the atherogenic coefficient increased (2.7±0.7 vs 1.3±0.5; p<0.05).

Conclusion: According to the research, it was found that in children and adolescents with SLE the formation of lesions of systems and organs occurs while maintaining the activity of the process, especially immunologic and ANA-positive association of lipid metabolism and blood coagulation were associated with the formation of comorbid states.

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Tocilizumab modifies clinical manifestations and laboratory features of systemic juvenile idiopathic arthritis associated with macrophage activation syndrome

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AB1050

Tocilizumab modifies clinical manifestations and laboratory features of systemic juvenile idiopathic arthritis (s-JIA) associated with macrophage activation syndrome (MAS) could be modified in patients treated with tocilizumab (TCZ). Objectives: To clarify whether TCZ modifies clinical manifestations and atypical MAS, or early treatment that prevented fulminant MAS. Methods: A combination of expert consensus and analysis of real patient data was conducted by a panel of 15 pediatric rheumatologists. Clinical manifestations and laboratory features of s-JIA associated MAS while treated with TCZ and 18 patients not treated with TCZ were evaluated. Possible MAS was defined as having characteristic laboratory features but lack of clinical features of MAS, or atypical MAS, or early treatment that prevented fulminant MAS.

Results: Among 12 patients while treated with TCZ, only 2 patients were diagnosed with definite MAS, and other 10 patients were diagnosed with possible MAS. On the other hand, among 18 patients not treated with TCZ, 10 patients were diagnosed with definite MAS, and other 8 patients were diagnosed with possible MAS. MAS classification criteria could classify the patients diagnosed with definite MAS while treated with TCZ as well as the patients not treated with TCZ (100% and 75%, respectively).

Furthermore, the patients with possible MAS while treated with TCZ were less likely febrile and significantly less often had rash, and had notably lower ferritin levels (587 ± 8518 ng/ml; P=0.0021), compared to the patients with possible MAS not treated with TCZ. Other laboratory features of MAS including lower platelet counts, lower fibrinogen were more pronounced in patients treated with TCZ.

Conclusion: These findings show TCZ could modify clinical manifestations and laboratory features of s-JIA associated MAS. When evaluating s-JIA patients while treated with TCZ, care must be taken to not underdiagnose MAS based on MAS classification criteria.

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Disclosure of Interests: Masaki Shimizu: None declared, Mao Mizuta: None declared, Takahiro Yasumi Shareholder of: Takeda, Speakers bureau: AbbVie, Novartis, CSL Behring, Naomi Iwata: None declared, Yuka Okura: None declared, Noriko Kinjo: None declared, Hiroaki Umebayashi: Speakers bureau: AbbVie, Eisai, Novartis, Ono, Chugai, Tomohiro Kubota: None declared, Yasuo Nakagishi: None declared, Kenichi Nishimura: None declared, Masato Yashiro: None declared, Junko Yasumura: None declared, Hiroki Wakiguchi: None declared, Nami Okamoto: None declared, Masaaki Mori Grant/research support from: Tokyo Medical and Dental University (TMDU) received unrestricted research grants for Department of Lifetime Clinical Immunology from AbbVie GK, Ayumi Pharmaeuticals Corporation, Chugai Pharmaceutical Co., Ltd., The Japan Blood Products Organization, Mitsubishi Tanabe Pharma Corporation, Nippon Kayaku Co., Ltd., Ono Pharmaceutical Co., Ltd., Towa Pharmaceutical Co., Ltd., UCB Japan Co. Ltd.

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TOCILIZUMAB MODIFIES CLINICAL MANIFESTATIONS AND LABORATORY FEATURES OF SYSTEMIC JUVENILE IDIOPATHIC ARTHRITIS ASSOCIATED WITH MACROPHAGE ACTIVATION SYNDROME

AB1051

Transition care in a new pediatric rheumatology center in Brazil: caring for adolescence beyond rheumatism

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Background: Transition care is the planned transfer of adolescents with chronic health conditions from children-centered to adult-oriented health systems. Its challenges include gaps in continuity of care, poor adherence, delays in adult services attendance, differences between pediatric and adult centers, difficulties in autonomy over care and unstable medical conditions. EULAR/PRES recently published recommendations, standards and quality indicators on transition care for young people with rheumatic diseases, which serve as a guide for transitional outpatient clinics. In Brazil, few centers focus on transition from pediatric to adult rheumatology. The Pediatric Rheumatology Unit of Hospital Geral de Fortaleza is a reference in North and Northeast of the country, intending to be pioneer in transitional medicine in region.

Objectives: To evaluate the adolescents and their families’ perception regarding follow-up and autonomy in health care, as well as to identify the main risks inherent to this age group.

Methods: A longitudinal and descriptive study was carried out through interviews, questionnaires and medical records analyzes. Adolescents between 15 and 18 years old, regularly followed, who had at least three planned visits/year were included. Patients with cognitive impairment or without definite diagnosis were excluded. Epidemiological and clinical data were collected; self-management and health care utilization skills were evaluated by Transitional Readiness Assessment Questionnaire (TRAQ), a self-administered questionnaire.

Results: Eighty two patients were recruited into the transitional service (61 female [74.4%]). Patients’ ages ranged from 15.0 to 18.7 years (median 16.9). Regarding religion, 41 patients (54.7%) were Catholic and 27 were Protestant (36%). Concerning to ethnicity, most of them declared themselves white (61%) or white (22%). Fifty-nine adolescents (72%), considered themselves able to take care of their own follow-up, whereas 39 relatives (50%) considered the patient capable of doing so. The most frequent diseases were juvenile idiopathic arthritis (31.7%) and systemic lupus erythematosus (29.3%), of which 37 (45.1%) were in remission. Medical disease duration and follow-up were 48.5 (5 - 175) months, respectively. The median TRAQ value was 3.27 (1.61 - 4.55). There were 191 transitional visits (median 2.0 visits/patient). Fifty three patients had 2 or more visits, out of which 42 (79.2%) had at least one visit in which the patient and/or the family was confident in their own role.
least one risk identified. The most prevalent risks were: overweight or obesity (31.7%), sedentarism (26.4%), anxiety (22.6%), changes in family structure (22.6%), school problems (20.8%), depression (18.9%), suicidal ideation/self-mutilation (18.9%), low self-esteem (15.1%). Risks related to psychiatric diseases were identified in 23 patients (43.4%).

Conclusion: This is one of the first studies on transition care in Brazil focused on risks identification in adolescence. Transition care allows improvement survival and quality of life due to advances in preventive medicine and treatment of chronic rheumatological diseases. The identification of inherent risks, especially psychiatric disorders, plays a fundamental role in the long-term follow-up, making it possible to deliver multidisciplinary and rehabilitation of adolescents.

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Disclosure of Interests: None declared

AB1052
SYSTEMIC LUPUS ERYTHEMATOSUS IN CONTEXT OF HUMAN IMMUNODEFICIENCY VIRUS INFECTION: A CLINICAL CONUNDRUM

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Background: Systemic lupus erythematosus (SLE) and Human immunodeficiency virus (HIV) infection can occasionally coexist in a patient. Also, in rare scenarios, the clinical symptomatology and laboratory tests of these diseases can masquerade each other.

Objectives: To describe diagnostic and therapeutic dilemmas of coexistent SLE and HIV

Methods: We analyzed case records of 2 patients with childhood SLE who had the clinical conundrum of HIV infection as well

Results: Case 1- An 11-year-old girl with fever and respiratory distress for 4 days. On examination he had pallor, oral thrush, and onycomycosis. A malar rash was also noted. Systemic examination revealed consolidation in right lung and hepatosplenomegaly. Investigations showed severe anemia and lymphopenia. HIV serology was reactive of HIV serology was false positive. Subsequently she was given intravenous immunoglobulin following which she improved.

Conclusion: This child had the dual diagnosis of HIV infection and SLE which she transiently responded however she developed acute intracranial bleed during hospital stay and died.

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Disclosure of Interests: None declared

AB1053
MACROPHAGE ACTIVATION SYNDROME AS A PRESENTATION IN PEDIATRIC LUPUS: A RETROSPECTIVE STUDY OF 3 CASES

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Background: Macrophage activation syndrome (MAS) can, at times, be the presentation of pediatric lupus and diagnosis requires high index of suspicion.

Objectives: To report children who had MAS as a presenting manifestation in our cohort of childhood lupus

Methods: We retrospectively studied 140 pediatric lupus patients from January 1993- November 2018 and collected clinical and laboratory data of patients (3) who had MAS as presenting manifestation.

Results: Case 1 was 11-year-old girl with fever for 4 months associated with rash and generalized body swelling for 1 month. Examination revealed rash over malar area and ear lobules, anasarca, hepatomegaly, bilateral pleural and pericardial effusion. In view of multisystem involvement a possibility of lupus was considered which was confirmed by investigations (table 1). She had elevated ferritin and low fibrinogen. A clinical possibility of lupus with associated MAS was considered. She received pulses of methylprednisolone, one dose of intravenous immunoglobulin following which she improved. In view of nephrotic range proteinuria she was started on induction regimen with cyclophosphamide and shifted to mycophenolate in maintenance. Her initial SLEDAI-2k was 32- this decreased to 4 at 3 year follow up.

Case 2 was a 9-year-old girl with fever, rash, generalized body swelling for 1 month and altered sensorium for 4 days. Examination revealed palmar erythema, oral ulcers and hepatomegaly. She was in shock at presentation. In view of multisystem involvement a possibility of lupus was considered which was confirmed by investigations (table 1). She had pericardial effusion and low ejection fraction (25%). A possibility of MAS was considered and investigations revealed hyperferritinemia, elevated triglyceride and hypoalbuminemia. She was given methylprednisolone pulses and continued on oral prednisolone, mycophenolate and hydroxychloroquine. Her initial SLEDAI-2k was 17- this decreased to 0 at 3 year follow up.

Case 3 was an 8-year-old girl who had fever, rash and body swelling for 15 days. On examination she had tachycardia, tachypnea, pallor, anasarca, subconjunctival bleed and frontal alopecia. She had pleural and pericardial effusion. In view of multisystem involvement a possibility of lupus was considered which was confirmed by investigations (table 1). She had high ferritin and triglyceride. So a possibility of MAS was considered and she received pulse methyl prednisolone and intravenous immunoglobulin. She also had hematuria and proteinuria (renal biopsy could not be performed as she was sick and had thrombocytopenia) so was given pulse cyclophosphamide followed by mycophenolate. Her initial SLEDAI-2k was 25- this decreased to 0 at 2 year follow up.

Conclusion: MAS can be the presenting manifestation of pediatric lupus and may contribute to disease severity and requires aggressive management.

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Hepatic involvement as a presentation in pediatric lupus: A retrospective study of 3 cases

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Background: Though abnormal liver tests can be seen during the course of disease in lupus, liver involvement as a presenting manifestation is uncommon in children with lupus (1).

Objectives: We report on 3 children with lupus who had predominant liver involvement at presentation.

Methods: We retrospectively studied 140 pediatric lupus patients from January 1993 to November 2018 and collected clinical and laboratory data of patients who had liver involvement as presenting manifestation.

Results: Case 1 was 13-year-old girl with fever and joint pain for 7 months associated with rash and yellow discoloration of eyes and body for 1 month. She also had altered behavior for 3 days. Examination revealed malar rash, jaundice, bilateral knee arthritis and hepatosplenomegaly. Investigations revealed anemia, thrombocytopenia and lymphopenia. She had conjugated hyperbilirubinemia. Transaminases were elevated. Further investigations confirmed diagnosis of lupus (table 1). Markers for autoimmune hepatitis (SMA; LKM) were negative. She received pulse methylprednisolone followed by tapering doses of oral prednisolone. In view of neurological involvement she also received cyclophosphamide and shifted to azathioprine later. Her initial SLEDAI-2k was 18, that decreased to 12 in follow-up. Her initial SLEDAI-2k was 18, that decreased to 12 in follow-up.

Conclusion: Hepatic involvement at presentation in lupus can be multifaceted and poses challenge in diagnosis.

REFERENCES
The Experiences of Biological Therapies in Children with Juvenile Idiopathic Arthritis Associated Uveitis: Single Center Study

Background: Juvenile idiopathic arthritis (JIA) is the most common systemic disease causing uveitis in childhood, with a prevalence of 10 per 100,000 persons. JIA-associated uveitis is estimated to have a poor prognosis and a high rate of complications. JIA-associated uveitis can manifest in various forms, depending on the location and severity of the ocular inflammation, as well as on the type of arthritis. The most of JIA patients with uveitis have oligoarthritis. Therefore, other types of JIA are rarely accompanied by uveitis. Topical corticosteroids are the first-line therapy, and disease conventional and biologic modifying anti-rheumatic drugs (DMARDs) are used.

Objectives: The purpose of the present study was to report on the clinical characteristics, ocular complications, treatment, and visual outcome in children with JIA-associated uveitis who were examined in recent years at a single tertiary pediatric rheumatology and ophthalmology center in Turkey.

Methods: We retrospectively analyzed the data of 41 JIA patients (14 males, 27 females).

The duration between the initial evaluation and the final visit was recorded as follow-up time. Juvenile idiopathic arthritis was defined according to the International League of Associations for Rheumatology (ILAR) classification criteria. Uveitis was classified according to the SUN classification.

Two approaches were utilized to evaluate the change of visual acuity (VA) during the disease course: (i) VA was measured on Snellen chart. The equivalent logarithm of the minimum angle of resolution acuity (logMAR) was calculated and used for analysis.

Results: The study included 31 patients (57 eyes) of whom 22 (71%) were females. Mean age (+SD) at uveitis diagnosis was 8.42 (+4.13) years (median 8, range: 34 months–17 years) and there was no significant difference between genders. The mean age of patients with diagnosed uveitis was 4.42 (+4.7), respectively. Nine patients were <7 years of age at the time of JIA diagnosis. Anterior uveitis (AU) was the most common type, diagnosed in 57 (76%) eyes. All patients had methotrexate, therefore biologic therapy was used in 29/31 patients (93.5%) at the follow up time (infliximab in 12, adalimumab in seven, and tocilizumab in three patients) and 9 patients (31%) required ≥2 biologics over the follow up period. Thirteen patients switched between infliximab and adalimumab (10 patients switched from infliximab). The reason for treatment switch included treatment failure and treatment-related side-effects (n=3). Systemic and topical steroids treatment were gradually tapered and discontinued in all patients after initiation of biologics. Of the all affected eyes, posterior synchiae (16 eyes, 7.5%) was the most frequent complication on follow-up. During the follow-up period new complications were seen in 11 eyes (13%). Posterior synchiae (6 eyes, 7.5%) was the most frequent complication observed followed by cataract (3 eyes, 3%) and glaucoma (2 eyes, 2.5%) Improvement or preservation of visual acuity (VA) was noted in 77 eyes (94.3) at the last visit.

Conclusion: We report a large cohort of children with JIA uveitis managed in a Turkey tertiary unit. Low complication rates and favorable visual outcomes are found in the present study. The high rate of biologic use, and close monitoring of affected children with pediatric rheumatology and uveitis clinic may have contributed to our improved outcomes.

Disclosure of Interests: None declared


Difficulties in the Diagnosis of the PFAPA Syndrome in the Real Clinical Pediatric Practice

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Background: Symptom complex of PFAPA syndrome is characterized by a rather diverse clinical picture, including recurrent fever, aphthous stomatitis, pharyngitis, adenitis. The annual incidence of PFAPA syndrome does not exceed 0.2%. [1], but it is believed that this disease is much more common than diagnosed [2]. The absence of specific genetic and biochemical markers of this syndrome determine the complexity of timely diagnosis and treatment of this auto-inflammatory disease.

Objectives: The objective reaction is of importance is that the time of diagnosis of PFAPA syndrome is a clinical practice of a pediatrician.

Methods: We conducted a follow-up analysis of the medical documentation of patients with verified PFAPA syndrome who were examined and treated at the hospital pediatrics department of the university clinic for the period from 2015 to 2019 year. A survey of pediatricians and pediatric rheumatologists was carried out on the knowledge of diagnostic criteria, protocol for the management and treatment of patients with PFAPA syndrome.

Results: During this period, in the department of PFAPA syndrome was diagnosed in 7 patients. Among patients with a diagnosis of PFAPA syndrome, there were 4 boys and 3 girls, the average age of children at the time of diagnosis was 1.4 ± 0.7 years. Before the diagnosis was verified, all patients were observed by a pediatrician or otorhinolaryngologist regarding repeated manifestations of tonsillitis and received antibacterial therapy at each episode of exacerbation of the disease. The average period from the first manifestations of the disease to the verification of the diagnosis was 1.4 ± 0.5 years. Diagnostic algorithm for verification of the diagnosis was completed by setting prednisolone test. According to the results of this test, in 100% of cases it was possible to completely arrest the phenomena of the inflammatory process (fever, tonsillitis, pharyngitis, stomatitis) and to normalize biochemical markers of inflammation (CRP) without the use of antibacterial therapy. With further observation, two of 7 patients recorded a decrease in the effectiveness of glucocorticoid therapy, which required a tonsillectomy, and one of them noted the temporary effectiveness of colchicine. According to the results of a questionnaire survey of pediatricians and children’s otorhinolaryngologists of the outpatient service, a low level of knowledge was revealed on the issues of the clinic, diagnosis and therapy of auto-inflammatory diseases. Only 40% of respondents were able to specify the diagnostic criteria for setting PFAPA syndrome and determine the further routing of these patients. It should be noted that more than half of the respondents (57%) had a clear idea about the methods of rational therapy of patients with PFAPA syndrome.

Conclusion: Thus, the complexity of the primary diagnosis of PFAPA syndrome is associated both with the clinical features of the disease and the insufficient level of knowledge of primary outpatient specialists on this issue, which is largely due to the low incidence of PFAPA syndrome. This conclusion was the reason for the inclusion of additional topics in the educational course of pediatricians.

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Disclosure of Interests: None declared


Co-designing a Comparative Randomised Controlled Clinical Trial of Corticosteroid Regimens with Children, Young People and Parents Living with Juvenile Idiopathic Arthritis

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Background: Previous research has identified the need for a randomised controlled trial (RCT) evaluating the most appropriate corticosteroid induction regimen to be used for children and young people (CYP) with juvenile idiopathic arthritis (JIA). A recent qualitative study found that parents and CYP understood trial concepts and were able to identify potential flaws in a proposed RCT. This confirms the need to involve parents and CYP in co-designing RCTs to best meet the needs of future trial participants (2).

Disclosure of Interests: None declared

AB1059 CLINICAL MANIFESTATIONS OF CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS PRESENTING WITH CYTOPENIA

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AB1060 BONE MARROW OEDEMA IN CHILDREN: THE ROLE OF VITAMIN D

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Background: Bone marrow oedema (BMO) in children is a rare clinical condition characterized by joint and bone extremity pain, out of proportion to the clinical findings, exacerbated by weight bearing, in the absence of a known etiologic cause. It is associated with typical increased signal intensity on T2-weighted MRI. Management is still under debate. Treatment has mostly been reported in adult case series encompassing analgesic drugs, a variety of pharmacological treatments (corticosteroids, bisphosphonates, vasodilators), physiotherapy, reduction of weight-bearing, or core decompression. No treatment guidelines for children are to date available.

Objectives: Recently it has become evident that BMO is associated by an increase in bone turnover, in which vitamin D plays a pivotal role. In literature association between hypovitaminosis D and BMO of the foot and ankle in adult patients is reported. No data are reported in cohorts of children. The purpose of this study is to investigate the incidence of hypovitaminosis D in a paediatric population with primary bone BMO of the foot and the role of a vitamin D supplementation therapy.

Methods: A retrospective study involving 12 paediatric patients (range age 8-14 years) referred to our Rheumatologic Paediatric Clinic of Verona University in the period 2015-2018 with persistent foot pain and MRI compatible with BMO of the foot has been performed. They had all been diagnosed in other institutions as affected by algodystrophy or complex regional pain syndrome. Data collection included sex, age, medical and surgical history, recent or remote trauma history, symptoms at presentation, clinical examination, laboratory bone turnover markers, vitamin D levels, MRI, treatment and outcome.

Results: 2/12 patients are male and 10/12 female (male to female ratio: 1:5). 2/12 had a previous diagnosis of juvenile idiopathic arthritis ANA + with the disease in remission at the moment of evaluation. 10/12 were previously healthy.

In all cases history of minor ankle strain or recurrent microtraumas of feet prior to symptom onset had been reported. Joint hypermobility was observed in 75% of cases. One child had been previously treated with bisphosphonates and 5 with limb immobilization, without any improvement.

Objectives: To co-design components of an RCT of corticosteroid regimens with CYP and parents living with JIA.

Methods: A focus group was conducted with CYP with JIA and parents as part of a wider consensus and discussion group meeting within the Steroid Induction Regimen for Juvenile Idiopathic Arthritis (SIRJIA) study in December 2018. The discussion focused on two components of the RCT design: i) Discussing the most appropriate treatment protocols; and ii) Addressing practicalities associated with an RCT.

Results: Two RCT protocol options, chosen through an online survey by a critical majority out of a possible eight protocols, were discussed and critiqued: i) Protocol A (intravenous vs intraarticular corticosteroid delivery); and ii) Protocol B (intravenous vs intraarticular vs intramuscular vs oral corticosteroid delivery). Several issues pertaining to both protocols were raised, related to the influence of age and past experience, routes of administration and concerns over randomisation. Participants emphasised the importance of clinicians/researchers discussing all of the potential risks with them. Participants also wanted enough information to make an informed choice. Participants emphasised the usefulness of combining trial visits with regular follow-up appointments to minimise the burden of taking part in an RCT and had a preference for their usual hospital being the site they visited. Some participants remarked that videos could be a useful way of conveying information beyond traditional participant information sheets. Some also felt that awareness of research opportunities is not equally accessible to them either, depending on where they lived in the country. Participants would want to be kept regularly updated about the progress of the RCT and felt that incentives were a good way of keeping people engaged, although some were trepidatious to hear negative treatment results. With regards to dissemination, participants felt that study results should be readily available to them in an accessible format, should they wish to view them.

Conclusion: CYP and parents have a considerable amount of knowledge and experience which can shape the design of RCTs. With adequate support, complex concepts such as treatment protocols can be discussed and critiqued. Involving CYP and parents at the design stage of an RCT has been shown to eliminate some potential challenges in the future.

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DISCLOSURE OF INTERESTS
None declared

Physical examination revealed weight bearing pain of foot or ankle in all patients. No other sensory, vasomotor, trophic ore neurological signs and symptoms were detected. Vitamin D deficiency was found in all cases (range 10 to 22 ng/ml). All patients were thus treated with adequate vita- 
min D daily intake. Pain relief was achieved with paracetamol, low dose ibuprofen, or a short course of oral prednisone. Rest from intense physi- 
cal activity and physical therapy, avoiding detrimental feet and ankle 
immobilization were recommended. All children (100%) fully recovered in 
3-month lag period. 

Conclusion: BMO in children is a cause of disability and it is often mis- 
diagnosed and incorrectly treated. Environmental factors, such as underes- 
timated articular or bone microtraumasms, as well as joint hyper 
mobility, typical of paediatric age, in a bone turnover milieu of vitamin D 
deficiency could be the cause of the clinical conditions. Adequate vitamin D 
supplementation, associated with physical and analgesic therapy, are crucial in the management of BMO. We highlight the importance of sup- 
plementing vitamin D as recommended in the current guidelines, in order to 
avoid its deficiency and prevent invalidating clinical complaints.

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Disclosure of Interests: None declared 

AB1061 SHORT TERM FOLLOW-UP RESULTS OF CHILDREN WITH FAMILIAL MEDITERRANEAN FEVER AFTER CESSATION OF COLCHICINE: IS IT POSSIBLE TO QUIT?

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Background Familial Mediterranean Fever (FMF) is considered as the prototype of autoinflammatory diseases, and colchicine is the main treatment option for FMF. However, the data on cessation of colchicine treatment in FMF patients is limited.

Objectives To define the characteristics of children with familial Mediterranean fever (FMF) whose colchicine treatment was discontinued and then to compare these features of the patients whose colchicine was restarted with the ones not restarted.

Methods Sixty-four out of 1786 children with FMF whom colchicine was stopped by the physician or patients/parents own decision were enrolled. These patients were grouped into two as: group 1; children whose colchicine was re-started and group 2; children whose colchicine was not re-started. The demographic, clinical and genetic data were collected and compared between group1 and group 2.

Results Colchicine was stopped in 59.4% (38/64) by the physician and 40.6% (26/64) of them had stopped colchicine by patients/parents will. Colchicine was ceased at a median of 10.5 (2.120.5) years of age, and attack- and inflammation-free periods of 18.2 (6-148) months. The median follow-up of 64 patients after col- 
chicine cessation was 37.4 (6.145.7) months. It was re-started in seventeen patients due to attacks (n=11) or elevated acute phase reactants (n=6), while remaining 47 patients did not require colchicine. The age at cessation of the col- 
chicine was lower (p=0.04) and duration of colchicine treatment until its cessation was shorter (p= 0.007) in group 1 than group 2.

Conclusion Even though the results of our study are not satisfactory enough to endorse the hypothesis that colchicine may be discontinued by close follow-up; older age and long duration of colchicine treatment before cessation may be two important features that should be considered in the future studies.

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Disclosure of Interests None declared 

AB1062 INTER-LABORATORY COMPARISON OF TYPE I INTERFERON SIGNATURE ANALYSES: PAVING THE WAY TO SHARE RECOMMENDATIONS.

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Background Interferon (IFN) signature analysis is currently used to classify pathological conditions characterized by a type I IFN dysregulation (i.e. mono- 
genic interferonopathies, dermatomyositis, systemic lupus erythematosus), and to formulate targeted therapy approaches. Indeed, IFN signature is used to differ- 
entiate patients with IFN-related inflammation from conditions predominantly 
mediated by other cytokines (e.g. JIA and periodic fevers), through the calculation of an IFN score (IS). However, at the moment, there is not a shared threshold able to 
discriminate among different inflammatory conditions.

Objectives To characterize the IS in different inflammatory diseases and evalu- 
ate the concordance of IFN signature results among the laboratories of the three 
Italian Hospitals.

Methods Assessment of the expression in peripheral blood of six IFN-induced genes (IFI27, IFI44L, IFIT1, ISG15, RSAD2, SIGLEC1) in Real Time PCR, refer- 
ring to a calibrator sample (healthy controls). Calculation of the “interferon score” (IS) for each patient using the median fold change of the six relative 
quantifications.

50 patients with different inflammatory disorders considered not related to IFN (e. 
g. Crohn, JIA, hereditary periodic fevers) were compared with established type I 
IFN-related diseases (SLE, monogenic interferonopathies, dermatomyositis). We 
avalised the concordance of the clinical classification of different inflammatory 
diseases and the IS results. To assess the inter-laboratory variability, twenty 
patients with different degree of type I IFN inflammation were analysed at three 
different laboratories.

Results Despite the IFN signature showed a similar and comparable trend, the IS 
was not consistent between different laboratories, in particular for samples with 
higher IS score. Thus, the concordance between clinical classification and IS 
could be assessed only separately for each laboratory. Although in each series 
IFN-related disorders showed a IS significantly higher than other kind of inflamma-
tory disorders, preliminary results suggest there is no clear threshold able to differ- 
entiate among these groups.

Conclusion Analysis of type I IFN activation in peripheral blood showed a rele-
vant inter-laboratory variability between our three centers, limiting the possibility 
of identifying a shared defined threshold to differentiate inflammatory syndromes, 
and suggesting the need to determine reproducible calibrator samples. Coopera-
tion between different institutes could facilitate the collection of clinical and labora-
tory data in a common database, to exchange expertise in type I IFN-mediated 
diseases, and provide practical advices for IFN signature assessment and inter-
pretation in the clinical practice.

Disclosure of Interests Alessandra Tesser: None declared, Gian Marco Mon- 
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AB1063 INTERSTITIAL LUNG DISEASE IN A NEWBORN AFFECTED BY MEVALONIC ACIDURIA

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Background Mevalonic aciduria (MA) is the most severe phenotype of mevalonate-kinase deficiency (MKD), with early onset and poor prognosis. Given its rarity and its unspecific symptoms, MA diagnosis may be
challenging in the newborn. To our knowledge, interstitial lung involvement has never been described as onset feature in MKD.

Objectives: We report a new case of a newborn affected by MKD characterized by interstitial lung disease.

Methods: The patient underwent laboratory and radiology evaluation as clinically indicated. Direct Sanger sequencing was used to screen the 10 exons of the MVK gene.

Results: A female neonate born at term from consanguineous parents was referred to our hospital at 16 days of life (DOL) for mild hypotonia and persistent raised inflammatory markers despite antibiotic therapy. Infectious work-up was negative. Chest x-ray revealed bilateral perihilar peribronchial thickening. Electroencephalography reported moderate diffuse anomalies of background activity without major abnormalities. On DOL 20 the first episode of fever was recorded. Due to worsening tachypnea and persistent abnormal chest x-ray, a pulmonary CT scan was performed and showed diffuse groundglass bilateral infiltrates consistent with alveolar-interstitial lung disease. On DOL 22 a maculopapular skin rash appeared on feet and hands, vanishing spontaneously 24 hours later. Bone marrow examination and levels of perforins, neuron-specific enolase and urinary catabolites of catecholamines were normal. A total body MRI was normal except for a mild cerebellar hypoplasia and the known interstitial lung disease. The patient kept presenting hypotonia, relapsing episodes of fever and skin rashes, developed severe anemia and failure to thrive. Type-I IFN signature was negative. A genetic test was requested, as well as quantification of urinary levels of mevalonic acid, which were markedly elevated. Direct Sanger sequencing allowed to detect a homozygous c.709A>T missense mutation in the exon 8 of the MVK gene, coding for a protein substitution p.T237S. Classified as pathogenic in the INFEVERS database and therefore consistent with the diagnosis of MKD. Both parents and her sister were heterozygous carriers of the same mutation. On DOL 38 treatment with anakinra was started, with prompt regression of fever and skin rash, decrease in inflammatory markers, increase in reticulocytes count and weight gain. Hypotonia improved but persisted. The patient was discharged from hospital on DOL 56 in good clinical conditions, with acute phase reactants within the normal range and mild hypotonia. She is now 4 months old, still on anakinra treatment without adverse events.

Conclusion: Autoinflammatory diseases in the neonatal period are a diagnostic challenge. Clinical suspicion is crucial in order to perform specific laboratory and genetic testing and start appropriate treatment. Interstitial lung involvement may be present in MKD and, together with increased inflammatory markers, could be the first manifestation of the disease.

REFERENCES

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AB1064
LONG-TERM SAFETY AND EFFICACY OF ADAHILUMAB IN GREEK ADULTS WITH JIA OR NON-INFECTIONOUS UVEITIS AT THE TRANSITION PERIOD
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Background: Our previous publication on Juvenile Idiopathic Arthritis (JIA) revealed that half of the pts had flare in adulthood and the need for administration of several anti-TNFs.

Objectives: a. To describe the long-term outcome of adults with JIA or non-infectious uveitis (NIU), exposed to Adalimumab (ADA) as the single or last biologic during the transition period. b. To evaluate our model of transition in a subgroup of refractory to conventional DMARDs JIA or NIU pts, in the 1st Greek Transition Clinic for Pediatric Rheumatic Diseases.

Methods: Retrospective cohort analysis of Greek adults with JIA or NIU between 2004 and 2018. The JIA activity state was assessed by 2 quantitative tools: the Juvenile Arthritis Disease Activity Score-10 (JADAS-10, Clinical Remission [CR]), Low, Moderate and High Disease Activity [LDA, MDA, HDA, respectively] and Wallace criteria (CR on/off ADA). Baseline was defined as the 1st ADA dose.

Results: 28 pts were enrolled: 24 JIA pts (female 18), aged 20.6±3.1 yrs, for a f/u of 6.5±3 years (Group-A) and 4 female pts with active uveitis (2 with JIA-associated and 2 with NIU, mean aged: 18.9 yrs, f/u: 2.3 yrs) (Group-B). The age at baseline was 14.1±3.2 yrs in Group-A and 16.7±3.2 yrs in Group-B. The lag time from JIA onset to baseline was 5.3±3.8 yrs and the JIA subtypes were: 37.5% polyarthritis RF neg, 33.3% extended oligoarthritis, 20.8% enthesis-related arthritis, 4.2% persistent oligoarthritis, 4.2% psoriatic arthritis. 11/24 (45.8%) pts (Group-A) and 3/4 pts (Group-B) were ANA positive, 5/24 JIA-pts had a history of uveitis (20.8%). Naive to anti-TNF drugs were 18 pts (75%) of Group-A and 4/4 from Group-B. The baseline JADAS-10 was 13.9±5.9. The ADA yr-administration was 5.3±2.3 in Group-A and 2 in Group-B. Compliance to ADA had 17/24 (70.8%) pts in Group-A and all from Group-B. Regarding safety, 4/28 patients (14.3%) experienced Events of Special Interest (1/33.6 patient-years), herpes zoster (n=1), anorexia nervosa (n=1), breast fibroadenoma (n=1) and uveitis (n=1). Among the Group-A pts: 4/24 (16%) pts continued ADA due to inefficacy and 1/24 due to pregnancy planning, 6/24 pts (25%) achieved CR and discontinued ADA after 5.3±1.6 yrs. CR off ADA lasted 15.5±9.8 mo. The rest 13/24 continued ADA at the last f/u. In Group-B, 3/4 were still on ADA and 1 pt discontinued ADA due to NIU remission after 4.2 yrs and sustained CR 16 mo off ADA. The median CR remission on ADA total administration period was 75% in Group-A and 100% in Group-B. Among the ongoing receivers: a) the JIA activity state at the last assessment was: CR 84.6%, LDA 7.7% MDA 7.7% (median JADAS: 0, Group-A), b) 100% were in remission in Group-B.

Conclusion: 86% of adult pts with JIA or NIU tolerate ADA well. Pts exposed to ADA achieved CR on/off medication in 75% and 25%, respectively.

REFERENCES

Disclosure of Interests: None declared


AB1065
THE UTILISATION OF S100 PROTEINS TESTING IN PEDIATRIC RHEUMATOLOGY PATIENTS IN A TERTIARY CARE INSTITUTION AND IMPLICATIONS FOR CARE
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Background: S100 proteins are calcium-binding proteins of increasing value as biomarkers in various inflammatory conditions. They are considered sensitive biomarkers of disease activity in rheumatologic disorders such as rheumatoid arthritis (1) and juvenile idiopathic arthritis (2). They are considered more accurate than conventional inflammatory indices such as the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) (3).

Objectives: To evaluate the utilization of S100 proteins in the clinical setting as supportive diagnostic tools as well as their performance in evaluating disease activity.

Methods: Patients seen at the hospital’s specialty clinics who had S100 proteins tested during their care from April 2017 to August 2018. A retrospective chart review was performed to collect data on serum S100 protein levels, other inflammatory markers as CRP and disease activity measured as active joint count (AUC) in JIA patients and the presence of systemic symptoms in systemic JIA (sJIA) patients. Graphpad Prism Version 7.05 was used for data analyses. Descriptive statistics were calculated for all variables. Comparisons were done by the Mann-Whitney U test and the Kruskal-Wallis test. Spearman correlation were calculated to assess association between S100 proteins and other numerical variables.
Results: A total of 164 patients were included. All 164 patients had S100A8/9 collected but only 151 had S100A12 samples. Patients with sJIA had higher levels of S100A8/9 and S100A12 compared to patients with non-systemic JIA (nsJIA) and periodic fever syndrome (PFS). CRP levels were not statistically different among diagnosis while S100 proteins were. Both S100A8/9 and S100A12 showed a good ability to differentiate sJIA from PFS (AUC=0.76 for both) compared to AUC=0.6 for CRP. At a cut-off value of 164 ng/ml, S100A12 was 71% sensitive and 73% specific in differentiating between sJIA and PFS (Figure 1). In JIA there was no correlation between S100 protein levels and AJC. either sJIA or nsJIA patients. S100A8/9 and S100A12 were significantly elevated in active sJIA patients compared to inactive ones while CRP levels were not different. S100 proteins levels where significantly higher during a flare of PFS compared to inactive disease, as well as CRP. There was no difference in S100 proteins and CRP in patients with or without tocilizumab treatment.

Conclusion: S100A8/9 and S100A12 are particularly elevated in sJIA compared to nsJIA and PFS. They are useful in distinguishing sJIA from other diagnoses with similar presentations, such as PFS. S100 proteins were significantly higher in active disease status of patients with sJIA and PFS compared to inactive status and their levels were closer associated with sJIA disease activity than CRP. The S100 proteins could provide valuable data in the work-up of patients with autoinflammatory conditions and monitoring disease activity in sJIA and PFS patients.

Methods: Results: A 15 years old girl presented with acute lower limb flaccid paralysis. Neurologic exam showed peripheral deficit of the VII cranial nerve, absent motor activity at lower limbs with sensitive deficit. At physical examination she had marked and diffuse livedo reticularis. She underwent a brain and spinal magnetic resonance imaging (MRI) revealing multiple areas of signal abnormalities (T2 hyperintensity) in both thalamus and basal ganglia, small area in the spinal cord at C2-C3, at D10-D11 and L1 levels; these images were related to vascular damage. Blood exams showed high blood counts and inflammatory markers (C-reactive protein 16.76 mg/dl). Coagulation was normal, antiphospholipid and antinuclear antibodies were negative. Immunochemical work-up showed normal immunoglobulin level, T and B phenotype. She received intravenous steroid and high-dose intravenous immunoglobulin. The constellation of findings led to clinical suspicion for ADA2, which was confirmed by low plasma ADA2 activity. For the presence of microhematuria, worsening proteinuria and hypertension, vascular ultrasound was performed with no evidence of renal artery stenosis. She underwent renal biopsy negative for glomerulonephritis, renal vasculitis and amyloidosis. Following the diagnosis of ADA2, she was initiated on etanercept 50 mg once weekly and she was able to taper steroid with normalization of inflammatory markers and improvement of skin rash.

The girl is the second of 3 children, born from consanguineous parents of Italian origin. By the age of 1 she started suffering from fever, arthritis, pericarditis with elevated inflammatory markers and was diagnosed with systemic juvenile idiopathic arthritis (sJIA) and chronic disease anemia. At that time, she already presented livedo reticularis. She was treated with short term oral steroid and methotrexate with remission of fever and articlar symptoms. At the age of 2 she had a convulsive crisis. polysomnography and brain MRI were performed with no evidence of sleep disorders. One year later she presented a convulsive status epilepticus, brain MRI was repeated and resulted negative. She was started on topiramate with no further crisis, treatment was stopped 2 years later. When she was 9, she was admitted for pancytopenia and she was diagnosed of Leishmania infection. The two siblings of the girl were tested for plasma ADA2 activity and both resulted deficient. The boy is 12 years old with mild developmental delay and a previous diagnosis of sJIA when he was 5. He was treated with steroid and Methotrexate with remission of arthritis. The older sister is now 19 years old and she had an episode of erythema nodosum. Genetic test for pancytopenia and she was diagnosed of Leishmania infection. The two siblings of the girl were tested for plasma ADA2 activity and both resulted deficient. The boy is 12 years old with mild developmental delay and a previous diagnosis of sJIA when he was 5. He was treated with steroid and Methotrexate with remission of arthritis. The older sister is now 19 years old and she had an episode of erythema nodosum. Genetic test for pancytopenia and she was diagnosed of Leishmania infection. The two siblings of the girl were tested for plasma ADA2 activity and both resulted deficient. The boy is 12 years old with mild developmental delay and a previous diagnosis of sJIA when he was 5. He was treated with steroid and Methotrexate with remission of arthritis. The older sister is now 19 years old and she had an episode of erythema nodosum. Genetic test for pancytopenia and she was diagnosed of Leishmania infection.

Conclusion: Given the important morbidity, especially in consanguineous families, high index of suspicion is required for early diagnosis and precocious intervention, before persistent neurologic damage has been established. We report our data for the first time a new neurological presentation as acute transverse myelitis in a patient with ADA2.

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Disclosure of Interests: Elena Tronconi: None declared, Francesca Conti: None declared, Duccio Maria Cordelli: None declared, Stefano Volpi: None declared, Marco Galltorno Grant/research support from: MG has received unrestricted grants from Sobi and Novartis, Andrea Pession: None declared, Angela Miniaci: None declared.
THE IMPACT OF ACUTE RHEUMATIC FEVER IN A PROVINCE OF CENTRAL-NORTH ITALY

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Background: Acute rheumatic fever (ARF) is a multisystem complication of group A streptococcal (GAS) infection. The incidence of ARF varies greatly in different geographic areas, with the highest incidence in Asia, Eastern Europe, and Australia (10-350 out of 100 000 per year) (1) and greatly in different geographic areas, with the highest incidence in Asia, Eastern Europe, and Australia (10-350 out of 100 000 per year) (1) and lowest (0.5-3 out of 100 000) in the US and Western Europe. In 2015 the latest version of Jones Criteria has been published (2), incidence less than 2 out of 100.000 per year was established to define low-risk (LR) population. Due to the lack of nationwide epidemiologic data in Italy, it is difficult to define the correct population Jones criteria’s category to use.

Objectives: To estimate the incidence of ARF in a metropolitan area of Central-North Italy and to study the clinical characteristics of the disease in a developed country.

Methods: We retrospectively analyzed the data of all patients with ARF aged 5-14 years old, diagnosed according to the classical and now LR Jones criteria (2), referred to Sant’Orsola-Malpighi Hospital of Bologna from January 2012 to December 2017 living in the province of Bologna.

Results: We identified a total of 24 patients diagnosed by ARF. In the province of Bologna, the inhabitants between 5 and 14 years of age varied from 82,967 in 2012 to 89,699 in 2017. Every year the annual incidence of ARF was above 2 out of 100,000. The highest incidence was reported in 2013 with 8 new diagnosis (incidence of 9.3 out of 100 000 per year). Carditis was present in 20 patients (83.3% of cases), chorea in 8 children (33.3%). Only 3 patients presented polyarthritis at diagnosis while 9 had polyartralgia and 3 presented with monarthrosis. In 6 patients the diagnosis followed the onset of chorea and no joint involvement was recorded. In 5 patients the diagnosis of ARF was made after the detection of classical cardiac findings without other major criteria. Cardiac involvement was characterized by mitral regurgitation in 17 cases and aortic regurgitation in 10 (8 patients with mitral aortic involvement). Five patients presented with fever (>38.5°C), 11 children had elevated inflammatory markers as erythrocyte sedimentation rate (ESR) > 60 mm/h and/or C-reactive protein (CRP) >3.0 mg/dL. Only 5 patients had positive swab for GAS. Twelve patients (50%) were treated with steroid. Fourteen patients received secondary prophylaxis every 28 days, two of them switched to every 21 days.

Conclusion: Our study confirms the previous published data of Breda et al. (3) and Liciardi et al. (4) in other Italian areas supporting the evidence for high risk (HR) in our region. Furthermore, this study shows that in our population only few patients had the classical polyarthritis presentation. It is important to consider the new HR criteria for arthritis in order not to miss diagnosis. A careful clinical history is needed because the demonstration of GAS infection is often difficult. These data may strengthen the hypothesis to consider our whole country as a HR area for ARF. A nationwide study is mandatory.

REFERENCES


Disclosure of Interests: None declared


AB1068 CLINICAL FEATURES IN TURKISH CHILDREN WITH CHRONIC NON-BACTERIAL OSTEOMYELITIS

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Background: Chronic non-bacterial osteomyelitis (CNO) is a rare bone disease of autoinflammatory origin. CNO patients present with bone, joint pain and swelling. Other autoinflammatory disorders such as palmoplantar pustulosis, psoriasis and inflammatory bowel disease may accompany CNO.

Objectives: Our aim is to determine demographic, clinical and radiological characteristics of Turkish children with CNO.

Methods: Clinical, laboratory features and imaging findings were retrospectively analyzed in 28 CNO Turkish patients from three pediatric rheumatology centers. Clinical findings, radiological data, treatments and outcome were evaluated.

Results: Of the 28 CNO patients, 10 (35.7%) female and 18 (64.3%) were male. Mean age at diagnosis was 9.54 (3-16.5) year. The lag time between symptoms and diagnosis was 6.5 (0-60) months. The median follow-up time was 18.5 (1-107) months. At the time of admission, symptoms were arthralgia (75.0%), bone pain (64.3%), limping (32.1%), swelling (28.6%), weakness (10.7%), and fever (3.6%). Two patients had inflammatory bowel disease (IBD) and six had familial Mediterranean fever (FMF). The bone lesions were mostly multifocal (%96.4), pelvic bones (32.2%). The patients had mildly elevated CRP and ESH levels. HLA B27 association was 25%, ANA was positive in 5%. All patients were RF negative. Six patients had mutations in the MEFV gene, all of them had M694V allele. The most common finding in Histopathological examination (n=9) demonstrated sterile mixed cell infiltration composed of lymphocyte and neutrophils. MRI results were mostly defined as bone marrow edema, and bone scan findings showed increased osteoblastic activity. All of patients received NSAIDs. Other drugs were methotrexate (46.4%) sulfasalazine (39%), steroids (25%), anti-TNF drugs (32%), and pamidronate (25%). Response to treatment was partial in 32.1%, whereas 39.3% patients had complete remission. There was no response in 8 patients (28%).

Conclusion: CNO was first described by Giedion in 1972 as multifocal bone lesions of inflammatory origin.1 There are 500 CNO patients reported in the literature as individual or case series.2 The laboratory findings are nonspecific and the diagnosis is mostly clinical and radiological. MRI and bone scan are the most commonly used imaging modalities. Histopathological results are non-specific, and may be necessary to exclude infection and malignancy. NSAIDs, sulfasalazine and methotrexate are mostly used in the treatment. Steroids, biological drugs and pamidronate are other options. There is still need for further treatment options, because there are significant number of resistant patients.

REFERENCES


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Localisation

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1 3.6
Disclosure of Interests: Ceyhun Acar: None declared, Elif Çomak: None declared, Sükrü Çekic: None declared, Serkan Turkuç: None declared, Hatice Adıgüzel Dundar: None declared, Sera şebnem Kılıç: None declared, Sema Akman: None declared, Erbil Unsal Grant/research support from: Novartis, AbbVie, Roche, Koçak Pharma, Speakers bureau: Novartis, AbbVie, Roche, Koçak Pharma

AB1069 HYPERZINCÆMIA AND HYPERCALPROTECTINÆMIA SYNDROME: MORE THAN JUST AUTOINFLAMMATION?
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Background: Hyperzincaemia and hypercalprotectinæmia (HandH) syndrome has been described as a new rare entity characterized by recurrent infections, dermatological involvement, increased inflammatory markers, hepatosplenomegaly and anemia. Little is known about its heterogeneous presentation, pathophysiology and treatment.

Objectives: To describe three cases with HandH syndrome

Methods: Serum calprotectin (MRP8/14) was measured according to Buehlmann assay (ELISA) and plasmatic zinc by atomic absorption spectrometry

Results: Three patients were referred to our centre because an history characterized by recurrent episodes of skin rash, severe oral aphthosis and increased level of serum amyloid A (SAA). Patient 1 presented, since the age of ten years, with recurrent episodes of fever and rash; skin biopsy showed a picture consistent with a lymphocytic lichenoid vasculitis resembling erythema multiforme. Patient 2 presented at birth, with hemolitic anemia and thrombocytopenia. At the age of 5 she was admitted to another hospital due to EBV related hemophagocytic lymphohistiocytosis (HLH). At the age of 8, she was first seen at our center because of a persistent desquamant erythematous rash with recurrent abdominal pain and recurrent arthritis. Intestinal biopsy showed small intestine inflammation (erosions in the digiurnum). Patient 3 presented with recurrent episodes of fever, rash, two episodes of transient hip synovitis and musculoskeletal pain. A bone scintigraphy was performed resulting normal. Patients 1 and 2 suffered from recurrent infections (pneumonia, otitis, skin abscesses). Immunological studies revealed in patient 2 a reduction of memory B cells and a reduced response to Toll like receptor 9 agonist. Of note, all the patients presented in their medical history at least one episode of vasculitis: patients 1 and 3 suffered from Schonlein-Henoch’s purpura at the age of 11 and 3 respectively and patient 2 had at the age of 2 years an undelineated vasculitis (evaluated elsewhere). Laboratory tests showed in all patients elevated inflammatory markers, zincemia and serum calprotectin (table)

Patient 1 Patient 2 Patient 3
Age at 1st evaluation (years) 14-3 7.8 4.9
Sex F M M
Clinical features Recurrent fever, recurrent infection, vasculitis, skin rash, mucositis/skeletal pain Recurrent fever, Hematocrit anemia, thrombocytopenia, HLH, vasculitis, recurrent infections, recurrent fever, arthritis, skin rash, gastrointestinal involvement Recurrent fever, skin rash, vasculitis, arthritis, mucositis/skeletal pain
SAA 13-23 27.8-36.4 20
Zincemia (mg/dl) (n. 80-125) 132-143 102-233 147
Serum MRP8/14 (ng/ml) (n. < 5000) 25431 10383 10383

Figure 1

Conclusion: We report three patients with high serum levels of calprotectinæmia and zinc presenting with a clinical phenotype consistent with previously reported cases. The presence of vasculitis in all of the patients suggest that it may represent the first symptom of this condition. Vasculitis could lead to an increase of serum calprotectin already proposed as a marker of vascular impairment. Moreover, considering the immunological defect detected in one of our patient, we speculate that recurrent infections described in this syndrome may underline an immune-dysregulation process in which the role of zinc metabolism needs to be assessed

Disclosure of Interests: None declared

AB1070 MICROVASCULAR NAILFOLD ALTERATIONS BY VIDEOCAPILLAROSCOPY IN PATIENTS WITH RHEUMATOLOGICAL SYMPTOMS WITH JUVENILE INFLAMMATORY BOWEL DISEASE
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Background: Juvenile Inflammatory Bowel Disease (jIBD) is a chronic relapsing inflammatory condition of the gastrointestinal system that includes Crohn’s disease (CD) and Ulcerative Colitis (UC) and develops during childhood or adolescence in up to 25% of patients and affects the patients and patient s quality of life. Endothelial dysfunction is considered one of the etiological factors of jIBD. Nailfold videocapillaroscopy is one of the best and safest diagnostic non-invasive imaging techniques to analyze microvascular abnormalities. Previous studies describe the involvement of the microvasculature in the pathogenesis of these diseases, suggested that chronic mesenteric vasculitis is a pathogenetic mechanism in CD. Nailfold abnormalities found are similar to those observed in some systemic vasculitides. Subapillary venous plexus dropout and low vessel density were previously reported.

Objectives: In this abstract we describe nailfold videocapillaroscopy findings in patients with jIBD and their correlation with disease activity.

Methods: This is a prospective and analytical study thad recruited pediatric patients between 2 and 18 years with jIBD. A single cross-sectional 8-finger nailfold videocapillaroscopy was performed using a 200x optical probe videocapillaroscope. The images were collected, encoded and stored using the Optipix™ software. Qualitative, quantitative and semi-quantitative assessment for architecture were scored following the international definitions for the capillary abnormalities Blood chemistry, C-reactive Protein, erythrocyte sedimentation rate, antineutrophil cytoplasmic antibiotic, and calprotectin were performed. Sociodemographic data, clinical evaluation, confirmation of IBD criteria, disease history, and activity evaluation were collected from patients clinical records. Statistics were performed using Spearman correlation to evaluate the correction coefficient between the variables under study.

Results: 10 patients with jIBD were included 60% male, 50% Ulcerative Colitis and 50% Crohn’s Disease. 20% had severe disease according the Pediatric Ulcerative Colitis Activity index, Pediatric Crohn’s Disease activity index showed mild activity in just one patient. Rheumatological manifestations were found in 40%, 4 had arthritis, systemic vasculitides in 2 and 10% hematologial manifestations. Abnormal endoscopy in 60% showing pancolitis. Normal microvasculature pattern were only found in 3 patients (25%), microangiopathy was found in 75%, edema of the nailfold bed was present in n=6 patients, a low capillary density was found in 100% of the patients with disease activity. A statistical negative correlation between the number of capillarities per millimeter and disease activity was found (coefficient -0.936, p=0.001).

Conclusion: Previous data showed that low capillary density was find in patients with jIBD, the data in this pilot study are consistent with those findings. The assessment of the microvasculature through the use of videocapillaroscopy could be useful in this diseases.

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Disclosure of Interests: None declared
AUTO-IMMUNE AND INFLAMMATORY DISEASES IN CHILDREN WITH SICKLE CELL DISEASE: DIAGNOSTIC AND THERAPEUTIC ISSUES

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Background: Coexistent auto-immune and inflammatory diseases (AID) and sickle cell disease (SCD) have been recently described in adults and children, however its frequency and physiopathology remain unclear (1–6).

Objectives: The aim of this study is the analysis of clinical and biological characteristics at AID diagnosis and the evolution under treatment in children with SCD.

Methods: Between May 1991 and March 2018, 35 of 3,800 SCD children diagnosed with AID in seven hospitals in Paris and suburb were analyzed in a retrospective survey.

Results: Thirty-five patients reported 44 AID: autoimmune liver disease (AILD, n=13), inflammatory bowel disease (IBD, n=7), juvenile idiopathic arthritis (JIA, n=6), systemic lupus erythematosus (n=5), autoimmune hemolytic anemia (n=3), Sjögren’s syndrome (n=2), histiocytic necrotizing lymphadenitis (n=2), vasculitis (n=2), myasthenia gravis (n=2), sarcoidosis (n=2), inflammatory uveitis (n=1), scleroderma/juvenile dermatomyositis (n=1). Median age at diagnosis was 10 [2–18] years. The mean delay between first symptom and diagnosis was 15.5 ± 29 months. The time of diagnosis was significantly longer for patients with JIA compared to other AID (63 versus 10 days, p=0.004). Sixteen patients (45.7%) had hypergammaglobulinemia > 20 g/L at diagnosis. AILD had a hypergammaglobulinemia at the time of diagnosis (30.0±L), with a statically significant decrease at the end of follow-up (18.2±L, p=0.0048). Among 21 patients (60%) treated with systemic steroids, it triggered vaso-occlusive crisis in 14 (66.7%), one acute chest syndrome, one transient ischemic attack. Thirteen of 35 patients (37.1%) were managed with biotherapy for AILD, well tolerated. Three patients (8.6%) underwent stem cell transplantation, one died of a cortico-resistant and multipolar graft versus host reaction, two were cured of both AILD and SCD. Nine severe infections were reported, four under steroids, five under biotherapy.

Conclusion: Diagnosis and therapeutic care of coexistent auto-immune and inflammatory diseases are difficult and challenging in children with SCD. Annual monitoring of inflammatory markers could be recommended to detect AILD earlier and prevent diagnostic delay in case of high ascension in SCD patients.

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Disclosure of Interests: Caroline Vint: None declared, Corinne Guillon: None declared, Patricia Benhaim: None declared, Florence Missud: None declared, Mariane De Montalembert: None declared, Lahoueri Amor: None declared, Cécile Arnaud: None declared, Véronique Hentgen: Consultant for: AbbVie, Chugai-Roche, Lilly, Novartis, Novimmune, Sanofi, and SOBI, Speakers bureau: AbbVie, BMS, Chugai-Roche, Novartis, Pfizer, and SOBI. Brigitte Bader-Meunier: None declared, Isabelle Melki: None declared, Isabelle Koné-Paut: Pierre Quartier Consultant for: AbbVie, Chugai-Roche, Lilly, Novartis, Novimmune, Sanofi, and SOBI, Speakers bureau: AbbVie, BMS, Chugai-Roche, Novartis, Pfizer, and SOBI. Loïc De Pontual: None declared, Luu-Ly Pham: None declared.


UVEITIS IN PEDIATRIC RHEUMATOLOGY: TERTIARY CENTER EXPERIENCE IN TURKEY

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Background: Since pediatric uveitis is generally asymptomatic, the diagnosis and treatment may be mostly delayed. Severe complications and visual loss may be observed even at the initial visit. Pediatric uveitis is tend to be chronic, persistent, recurrent, and the management may be complex (1).

Objectives: The aim of this study is to report epidemiology, etiology, clinical features, management and the outcomes of non infectious pediatric uveitis at a tertiary pediatric rheumatology center in Turkey.

Methods: The clinical records of the patients with non infectious uveitis who were followed up by department of pediatric rheumatology and ophthalmology were reviewed, from January 2013 to June 2018, retrospectively. The inclusion criteria were as follows being age ≤ 16 years, following up at least 6 months in both the ophthalmology and pediatric rheumatology clinics. Uveitis was categorized anatomically according to the Standardization of Uveitis Nomenclature criteria (2).

Results: Of 37 patients (67 eyes), 45.9% were female. Mean age of onset was 8, 5 ± 4, 4 years (1.6 - 15.6), mean follow-up was 60 ± 42 months (6 - 191). The general features of uveitis were anterior, idiopathic, rare and bilateral in this study similar to literature (Table 1). The most common systemic diseases associated with uveitis were juvenile idiopathic arthritis (JIA). Two patients improved with local medications, while the remaining 35 patients required systemic treatments such as short-time (oral/i.v) corticosteroids (CS) in 94.5% of them, methotrexate (MTX) in 86.4%, azathioprine (AZA) in 5.4%, adalimumab (ADA) in 67.5%, tocilizumab (TCB) in 2.7%. In 26.1% of patients receiving ADA who did not respond to standard dose of ADA, we had to shorten the dosage intervals of ADA from every 2 weeks to every week. At least 1 ocular complication was observed in 83.7% of the patients, such as cataract, glaucoma, band keratopathy, synechiae, macular edema and retinal detachment. Four (10.8%) patients had moderate visual loss and 6 (16.2%) patients severe visual loss (3). The prevalence of surgery in our study was 18.9% for cataract and glaucoma treatment.

Conclusion: Diagnosis and management of uveitis in childhood is complicated. Despite the new medication options, the advancements in diagnosis and surgical techniques, the complications are still high. Usage of shorter dose interval of ADA may be an alternative to control of the disease in patients with unresponsive to standard dosage of ADA. However, large-scale clinical trials are required to assess the efficacy and safety of this treatment.

REFERENCES

Disclosure of Interests: None declared

AB1072B
THE CONSEQUENCES OF THE PROVISIONAL PAEDIATRIC RHEUMATOLOGY INTERNATIONAL ORGANISATIONS JUVENILE IDIOPATHIC ARTHRITIS CLASSIFICATION CRITERIA

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Background
Last year the International League of Associations for Rheumatology (ILAR) classification criteria for juvenile idiopathic arthritis (JIA), [1] were challenged by the provisional Paediatric Rheumatology International Trials Organisation (PRINTO) classification criteria.[2] Four disorders were proposed: (a) systemic JIA; (b) rheumatoid factor (RF)-positive JIA; (c) enthesitis/spondylitis-related JIA; and (d) early-onset antinuclear antibody (ANA)-positive JIA. Early-onset ANA-positive JIA is defined by: arthritis for ≥ 6 weeks, and early-onset (≤ 6 yrs), and presence of 2 positive ANA tests with a titre ≥ 1/160 at least 6 months apart with the exclusions of having systemic JIA, RF-positive arthritis, or enthesitis/spondylitis-related JIA.

Objectives
To evaluate the shifts from the original subtypes of JIA in the new disorder of early-onset ANA-positive JIA.

Methods
This study used data from the international PRINTO based registry regarding pharmacovigilance in JIA called Pharmachild.[3] For this analysis we used the data of 4,165 patients completely categorized following the ILAR’s category and therefore were not categorized as early onset ANA-positive JIA. This study used data from the international PRINTO based registry called Pharmachild. Of these 957, 2 patients were RF-positive, which is an exclusion criterion for early onset ANA-positive JIA.

Results
Table 1 shows the characteristics of all 4,165 patients according to the ILAR criteria. Of this final set of 4,165 patients, 1279 (30.7%) were ANA-positive and 957 (74.8%) classified into the PRINTO ‘early onset ANA-positive JIA’ category. Of these 957, 2 patients were RF-positive, which is an exclusion criterion for the ‘early onset ANA-positive JIA’ category and therefore were not categorized as early onset ANA-positive JIA. The female proportion was higher than in any ILAR subtype being 83.0%. This new category consists largely of 3 ILAR subtypes: persistent oligoarthritis (34%), extended oligoarthritis (25%) and RF negative polyarthritis (28%). Further studies on these provisional criteria are ongoing.

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Disclosure of Interests Vera Mars: None declared, Joost F. Swart: None declared, Gabriella Giancane: None declared, Sytze De Roock: None declared, Anne Estmann: None declared, Marija Jelusic: None declared, Etiestania Moreno Ruzafa: None declared, Jaime de Inocencio: None declared, Jelena Vojinovic: None declared, Agustin Remesal: None declared, M Laday: None declared, Rolando Cimaza: None declared, A V. Cochino: None declared, Inmaculada Calvo Grant/research support from: received research support from Pfizer, Roche, Novartis, Clementia, Sanofi, MSD, BMS and GSK; Consultant for: AbbVie; Speakers bureau: AbbVie, Roche, Novartis, SOBI, M Harjacek: None declared, Nico Wulffraat: None declared, Nicolino Ruperto Research support from: ROCHE.

AB1072C
CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS. THE CORRELATION BETWEEN CAROTID INTIMA-MEDIA THICKNESS AND MARKERS OF INFLAMMATION TO DETERMINE PRE-CLINICAL ATHEROSCLEROSIS

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Background
Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in childhood. JIA is a heterogeneous group of disorders with different disease progression and prognosis. Cardiovascular...
moribidity and mortality are becoming major health concerns for children with inflammatory rheumatic diseases. Inflammation has been suggested to play an important role in the pathogenesis of both atherosclerosis and JIA.

Objectives: objective of this study was to determine carotid intima-media thickness (cIMT) in children with JIA and their correlation with JIA sub-type and markers of inflammation.

Methods: We included 112 patients (50 boys and 62 girls) with diagnosis of JIA for at least 6 months and 54 healthy control subjects (32 girls and 22 males). All children were had normal body mass index, blood pressure, lipids and blood glucose levels to exclude conventional risk factors.

Carotid ultrasound for evaluation of cIMT was performed by same radiologist who was blinded to the participants’ clinical and laboratory data. Patients datas were collected. We compared all cIMT values of patients and controls and investigated the relationship between inflammatory markers, disease status, periods and therapies.

Results: Our study showed that children with JIA had more increased cIMT values than controls. There was no correlation between disease subgroups, activity status, ANA, HLA-B27, RF positivity, WBC, ESR and CRP with cIMT. The cIMT values were not differences between patients used steroid, DMARD and biologic agents and non used. An increased active disease and total disease periods, decreased in mean platelet volume were determined as independent risk factors at increased of cIMT.

Conclusion: The study showed that the patients with JIA had more risks than healthy controls for cardiovascular diseases.

Disclosure of Interests: None declared


Other orphan diseases

AB1073

A RETROSPECTIVE COHORT STUDY OF IgG4-RELATED DISEASE IN IRISH PATIENTS

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Background: Immunoglobulin (Ig) G4-related disease (IgG4RD) is a novel clinical entity characterized by elevated serum IgG4 concentration and tissue orifice or tissue infiltration by IgG4-positive plasma cells.

Objectives: To describe the clinical presentations, laboratory features, imaging manifestations, histopathologic characteristics and treatments in a cohort of 38 patients with IgG4RD.

Methods: A retrospective study was performed at St. Vincent’s University Hospital. Clinical, laboratory, imaging and histopathologic data was retrieved from electronic records. All data were assessed using SPSS 24.0.

Results: Median age was 59 years with M:F ratio= 2.2:1. 29 patients (76.3%) had received steroid therapy and 19 (50.0%) had a commonest histopathologic pattern reported in 29 (76.3%) patients. Lymphoplasmacytic infiltration + Storiform fibrosis + Phlebitis without obliteration was the most frequently involved organ (17/38, (44.7%)). 55.3% had a systemic complaints that could be categorized as possible category. GI manifestations (followed by pancreatic) were the most frequent clinical presentation.

Conclusion: IgG4RD is a rare entity in Ireland and an inadequately understood condition overall. Further research is required to better understand the pathophysiology, clinical course and optimal treatment for IgG4RD.

REFERENCES

site preceded distant or systemic manifestations. Abnormal blood tests were common. Localised inflammatory nodules and paucinulitis in 88.88% especially in autoimmune disorders, vs. 90% systemic juvenile rheumatoid arthritis, 90.9% idiopathic orbital pseudotumor. 90% systemic lupus erythematosus, 90% sarcoidosis, human adjuvant disease, vasculitis, inflammatory bowel syndrome and inflammatory polyarthritis. 11.11% cases presented primarily with systemic autoimmune disorders.

**Conclusion**: Biomaterials and prostheses can provoke late-onset systemic autoimmune disorders fulfilling ASIA criteria, or present primarily local/regional inflammatory reactions that may eventually evolve into systemic autoimmune and/or granulomatous disorders which fall under ASIA.

**REFERENCES**


**Disclosure of Interests**: None declared


**AB1075**

**IDIOPATHIC ORBITAL PSEUDOTUMOUR: A CASE SERIES AND LITERATURE REVIEW**

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**Background**: Idiopathic orbital pseudotumor (IOP), also known as idiopathic orbital inflammatory syndrome is a benign, non-infective, inflammatory condition of the orbit without identifiable local or systemic causes. After Grave’s disease and lymphoproliferative disorders, orbital pseudotumor is the 3rd most common ophthalmologic disease of the orbit and account for approximately 8-11% of all the orbital tumors. Pathogenesis of orbital pseudotumor remains elusive but several lines of evidence point to immune-mediated processes as the likely underlying ocular mechanism. The etiology of orbital pseudotumor is unknown, but infection, autoimmune disorder, and aberrant wound healings have been put forward as possibilities. The ocular manifestations of orbital pseudotumor may include periorbital edema, erythema, proptosis, ptosis, diplopia and pain with eye movements.

**Objectives**: Describe clinical and demographic characteristics, most frequent diagnoses, immunological serology and treatments in patients with Orbital Pseudotumor.

**Methods**: We performed a retrospective cohort study of adult and pediatric patients with orbital pseudotumor diagnosis referred to the Department of Rheumatology of the Fray Antonio Alcalde Civil Hospital in Guadalajara, Jalisco, Mexico, from 2012-2018. We collected data that included demographic data of the patient, symptoms, laboratory data that included antibodies, management plans and results.

**Results**: A total of 20 patients diagnosed with orbital pseudotumor, with a mean age of 42±18.5 years, 3 pediatric patients and 65% women. Clinical manifestations were: 90% unilateral, 90% lacrimal gland involvement, 75% ptosis/proptosis, 40% conjunctival hyperemia, 55% ocular pain, 20% decreased visual acuity, 15% headache and no optic nerve involvement. The findings were similar between adults and children. The most common diagnoses were: 40% idiopathic, 10% orbital cellulitis, 10% granulomatosis with polyangitis and 5% each of the following: systemic lupus erythematosus, Sjögren’s syndrome, dacrocyoadenitis and myositis due to IgG4, Kimura’s disease, Mikulicz, meningioma and cavernous sinus aneurysm. All patients underwent excisional biopsy, and the histopathological report showed the following findings: 40% non-specific chronic inflammation, 30% non-specific chronic dacryoadenitis, 5% granulomatous inflammation/vasculitis, 10% chronic sclerosing inflammation-IgG4 and 15% others. Only 9 of the 20 patients underwent immunological serology, finding positivity in: 15% for c-ANCA, 10% PR3, 5% p-ANCA, 10% MPO, 5% ANAs and 10% elevated blood levels of IgG4. Regarding treatment, 100% received glucocorticoids, and received immunomodulatory therapy: 20% received azathioprine, 5% mycophenolate mofetil, 20% methotrexate, 15% cyclophosphamide IV, 15% rituximab and 25% received no other medication.

**Conclusion**: The orbital pseudotumor might be the first manifestation of an autoimmune or inflammatory disease, the early and correct diagnosis is necessary to avoid permanent sequelae.

**REFERENCES**


**Disclosure of Interests**: None declared


**AB1076**

**TREATMENT REVIEW OF ADULT-ONSET STILL’S DISEASE IN A TERTIARY HOSPITAL**

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**Background**: Adult-onset Still’s disease (AOSD) is a rare systemic inflammatory disorder of unknown aetiology, and approximately 60% or 70% of the patients can develop a chronic polyphasic form of the disease or a chronic polyarthritis. Due to the rarity of this disease, the treatment of AOSD is not based on a controlled study, but in the experience based on real cases.

**Objectives**: Describe the different treatments employed in a patient cohort diagnosed with adult-onset Still’s disease (AOSD).

**Methods**: Descriptive, retrospective study of patients treated in our Hospital (2008-2018), diagnosed with AOSD according to the classification criteria of Yamaguchi. The data were achieved by the review of the clinical records.

**Results**: Twenty-four patients (15 women), average age of 41±13 years, were included. Two women, with presentation on the symptoms at 8 and 3 years old, first diagnosed with systemic juvenile idiopathic arthritis (S-JIA), and then with AOSD. The initial treatment was based in non-steroidal anti-inflammatory drugs (96%) and glucocorticoids (0.5-1 mg/kg/day) (96%) for symptom control, with the necessity to add oral or subcutaneous methotrexate at a dose of 15 mg per week in 13 patients (54%). Only two patients used acetylsalicylic acid as initial treatment, with no improvement.

<table>
<thead>
<tr>
<th>Previous treatment</th>
<th>Current treatment</th>
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<tbody>
<tr>
<td>Drug</td>
<td>n (%)</td>
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<tr>
<td>NSABDs</td>
<td>2 (8%)</td>
</tr>
<tr>
<td>Glucocorticoids</td>
<td>2 (8%)</td>
</tr>
<tr>
<td>Del and DMARDS</td>
<td>11 (48%)</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>1 (8%)</td>
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<tr>
<td>Leflunomide</td>
<td>1 (8%)</td>
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<tr>
<td>Mycophenolate</td>
<td>1 (8%)</td>
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<tr>
<td>Infliximab</td>
<td>2 (8%)</td>
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<tr>
<td>Etanercept</td>
<td>2 (8%)</td>
</tr>
<tr>
<td>Infliximab</td>
<td>1 (8%)</td>
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<tr>
<td>Salsalate</td>
<td>1 (8%)</td>
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<tr>
<td>Rituximab</td>
<td>2 (8%)</td>
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<td>Tocilizumab</td>
<td>2 (8%)</td>
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<tr>
<td>Trasylol</td>
<td>1 (8%)</td>
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</tbody>
</table>

Five patients used also biological treatments with a standard doses, with the necessity to add oral or subcutaneous methotrexate at a dose of 15 mg per week in 13 patients (54%).
inhibitors (baricitinib and tofacitinib, respectively), one patient with anti-TNF (infliximab) and another one with anti-CD20 (rituximab).

**Conclusion:** In general, our results match what is published in the literature.

For the treatment of AOSD has been used high doses of ASA (4g/day) or NSAID. However, the required doses (with their respective adverse effects), its limited responses and the frequent relapses after its suppression make difficult to maintain it. Nowadays, the systemic glucocorticoids are our first choice (0.5 to 1 mg/kg/day). A high average of our patients have a positive response with it, but in a 54% of the cases were necessary to add methotrexate or others DMARDs because of a partial response with steroids.

In the physiopathology of the AOSD there is an increase of pro-inflammatory cytokines, as the tumor necrosis factor, IL-1 e IL-6. The use of therapies that inhibit these molecules (anti-TNF, anakinra or canakinumab as a diliy, or tocilizumab or sarilumab as anti IL-6) is being a progress.

The inhibitors of IL-1 can be more effective for systemic manifestations, while the inhibitors of IL-6 are for articular and systemic affection. The TNF inhibitors should be used for the articular affection only. In our patient cohort there is no patient with anti-IL1, a patient in clinical remission with anti-TNF and another one with anti-IL-6. Prospective studies with a higher number of patients is necessary to define better the AOSD treatment.

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**Disclosure of Interests:** Belén Atienza-Mateo: None declared. José Luis Martín-Varillas: None declared. Vanesa Calvo-Rio: None declared. Rosalía Demetrio-Pablo: None declared. Elia Valls-Pascual: None declared. Beatriz Valls-Expósito: Olga Maiz-Alonso: Ana Blanco: Ignacio Torre-Salaberri: Verónica Rodríguez-Mendez: Ángel García-Aparicio: Raúl Veroz González: Vega Jovani: Diana Peiteado: Margarita Sanchez Orgaz: Santos Castañeda: Eva Tomero: J Francisco, Toyo Sáenz de Miera: Valvanera Pinillos: Elena Aurrecoechea: Ángel Mora: Arantxa Conesa: Manuel Fernández-Varillas: J Antonio Troyano: Iñigo González-Mazón: Laura Sánchez Bilbao: D. Prieto-Peña: Mona Calderón-Goecke: Miguel A. González-Gay: Ricardo Blanco: Hospital Universitario Marqués de Valdecilla. IDIVAL: Rheumatology and Ophthalmology, Santander, Spain; Hospital Peset, Rheumatology, Valencia, Spain; Hospital Universitario de Donostia, Rheumatology and Ophthalmology, San Sebastián, Spain; Hospital Universitario de Basurto, Rheumatology and Ophthalmology, Bilbao, Spain; Hospital Virgen de la Salud, Rheumatology, Toledo, Spain; Hospital de Mérida, Rheumatology, Mérida, Spain; Hospital General de Alicante, Rheumatology, Alicante, Spain; Hospital Universitario La Paz, Rheumatology and Ophthalmology, Madrid, Spain; Hospital de la Princesa, Rheumatology, Madrid, Spain; Hospital Universitario Virgen Macarena, Rheumatology, Sevilla, Spain; Hospital San Pedro, Rheumatology, Logroño, Spain; Hospital Sarrallena, Rheumatology and Ophthalmology, Torrelavega, Spain; Hospital Clínico Universitario de Salamanca, Rheumatology, Salamanca, Spain; Hospital Universitario de Guadalajara, Rheumatology, Guadalajara, Spain; Hospital Universitario Clínico San Carlos, Rheumatology, Madrid, Spain; Hospital Universitario Marqués de Valdecilla. IDIVAL: Rheumatology and Ophthalmology, Santander, Spain

**AB1077**

**ANTI-IL6-RECEPTOR TOCILIZUMAB IN GRAVES’ ORBITOPATHY. MULTICENTER STUDY OF 46 PATIENTS IN CLINICAL PRACTICE**

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**Background:** Graves’ orbitopathy (GO) is the most common and important extrathyroidal manifestation of Graves’ disease. Corticosteroids and conventional immunosuppressors are not always effective or well tolerated. The IL-6 receptor antibody tocilizumab (TCZ) has demonstrated efficacy in the treatment of this pathology.

**Objectives:** To assess the efficacy of TCZ in refractory thyroid associated orbitopathy (TAO) due to Grave’s disease.

**Methods:** Multicenter study of 46 patients with TAO refractory to conventional immunosuppressive therapy.

**Results:** We studied 46 patients (85 eyes) (37 women/9 men); mean age at diagnosis 49.2±11.8 years. Besides oral corticosteroids, before the onset of TCOZ patients had been treated with pulses of iv methylprednisolone (42), radioactive iodine (4), methotrexate (2) and other drugs (selenium in 11 cases, methimazole in 8, lefumodine in 1 and azathioprine in 1). 7 patients underwent ocular urgent decompressive surgery.

According to the classification of severity of the EUGOGO group (European Group on Graves’ Orbitopathy) using the clinical activity score (CAS), before TCZ onset patients whose data were available had severe (27 eyes) or moderate (34 eyes) disease. Moreover, patients presented exophthalmos (53 eyes), strabismus (37 eyes), muscle fibrosis (38 eyes) and dysthyroid optic neuropathy (10 eyes). TCZ was used in monotherapy (43) or combined with methotrexate (2) or azathioprine (1) at 8 mg/kg iv/w (41) or 162 mg/sc/w (5). TCZ yielded rapid and maintained improvement in all ocular parameters as shown in Figures.

**Conclusion:** TCZ appears to be a useful and secure option in GO treatment.

**REFERENCES**


**DOI:** 10.1136/annrheumdis-2019-eular.1628

**AB1078**

**RED CELL DISTRIBUTION WIDTH (RDW) – A NEW POSSIBLE DISEASE ACTIVITY PREDICTOR IN RELAPSING POLYCHONDRITIS**

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**Background:** Relapsing polychondritis (RP) is a rare condition defined by recurrent inflammation of cartilaginous tissue and systemic manifestations. Biomarkers for RP diagnosis and assessment of disease activity, damage and prognostic in clinical practice are currently lacking. Red blood cell distribution width (RDW) is an index of erythrocyte size variation depicting...
anizocytosis. RDW is routinely assessed, is not influenced by infections and its standard deviation (RDW-SD) does not depend on medium corpuscular volume. Recent studies showed an increased RDW in various autoimmune diseases (systemic lupus erythematosus, Sjogren’s syndrome, rheumatoid arthritis, systemic vasculitis), correlating with inflammatory markers and disease activity. Also, the RDW seen in solid tumors and hematological cancers has prognostic value.

**Objectives:** To assess the RDW-SD in RP patients, its relation with the disease activity and with the presence of neoplasia

**Methods:** We performed a retrospective study on the patients diagnosed with RP in a tertiary Rheumatology department between January 2017 and January 2019, using the Atlasmed data management system of the institution. The concomitant diseases and the inflammation parameters were recorded. The RP activity was measured using RPDAl (relapsing polychondritis disease activity index). The correlation between variables were calculated using GraphPad Prism.

**Results:** We identified 20 patients, median age 59.04 years (range 38-81), with a male-to-female ratio of 1:5.66. An associated autoimmune disease (Sjogren syndrome, Hashimoto thyroiditis, systemic lupus erythematosus, rheumatoid arthritis, psoriatic arthritis) was found in 85% of patients. Moreover, 40% of the patients had various types of solid or hematologic neoplasia, including myelodysplastic syndrome. An elevated RDW-SD was seen in 90% of RP patients. The average RPDAl was 10.6 points. RDW-SD significantly correlated to RPDAl (p=0.0012). Of the inflammatory parameters, RDW-SD was not found to be related to ESR and CRP. RDW-SD increased with age, but no correlation was found between RPDAl and age. All patients with neoplasia had abnormally high RDW-SD. Nevertheless, RDW-SD was not significantly different in RP patients with or without neoplasia (Mann-Whitney test, p=0.56).

**Conclusion:** RP was frequently associated with other autoimmune diseases, but also with neoplasia. The positive correlation of RDW-SD and RPDAl in RP suggests a possible new, clinically employable, biomarker of disease activity.

**REFERENCES**


**Disclosure of Interests:** None declared


**AB1079 CHECKPOINT INHIBITOR-ASSOCIATED ARTHRITIS: PHENOTYPES AND CYTOKINE ASSOCIATIONS**

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**Background:** Immune checkpoint inhibitors (CI) have revolutionized cancer management, but can also cause immune-related adverse events. Five percent of CI-treated patients develop inflammatory arthritis, but it is poorly defined phenotypically and immunologically.

**Objectives:** To characterize phenotypes of CI-associated arthritis, and compare cytokine levels in these patients to rheumatoid arthritis (RA) and osteoarthritis (OA) controls.

**Methods:** Patients referred for CI-associated arthralgia or arthritis were prospectively enrolled in an institutional registry. Serum was collected when patients underwent phlebotomy for a clinical indication. We used a Luminex Human Magnetic Assay to measure levels of IL-1β, IL-2, IL-6, IL-8, IL-10, IL-12, IL-17, TNF, IFN-γ, PD-L1, CCL2, CXCL2, CXCL13, OSM, CCL20, GM-CSF, CXCL11 in CI-treated patients, and in stored serum from 7 RA patients (matched for medication, age, sex, CDAI) and 4 OA patients (age, sex matched). All comparisons were planned a priori.

**Results:** Thirty-six patients were enrolled 5/1/18-1/25/19. Median [IQR] age was 67[58-78], 18(50%) were female, 14(39%) were smokers and 13 (36%) had melanoma. Twenty-two (61%) were on anti-PD1 or PD-L1 monotherapy, and the remainder were on combination CI. Phenotypes included 1. Small joint involvement in 17(47%), 2. Exclusively large joint involvement in 6(17%), 3. Arthralgia without arthritis in 9(25%), and 4. Polymyalgia rheumatica in 4(11%). In all, 7(19%) had concomitant tenosynovitis or enthesitis, mostly accompanying large joint arthritis or arthralgia.
Disclosure of Interests: Karmela Kim Chan Grant/research support from: Roche; sponsored research agreement on stromal cells, Consultant for: GSK; consultant. (I am part of their immunology network, a group of about 8 immunologists who advise them regularly and broadly in the areas of inflammation and infection.), Gregory Vitone: None declared, Sara Shanaj: None declared, Aidan Tiprack: None declared, Jackie Finik: None declared, Laura Donlin: None declared, Deepak Rao Grant/research support from: Merck - Sponsored research project funding support, Consultant for: Janssen - Consultant SciPher Medicine - Consultant Amgen - Scientific advisory board Patent submitted on Tph cells, Caroline Benson: None declared, Vivian Bykerk Grant/research support from: Mallinckrodt, BMS, Crescendo Bio-sciences, Sanofi/Regeneron,. Consultant for: Amgen, Pfizer, UCB, SciPher, Sanofi/Genzyme/Regeneron, Dana Orange Consultant for: Astra Zeneca and Pfizer,. Michael Brenner Grant/research support from: Roche; sponsored research agreement on stromal cells (but has nothing to do with checkpoint related disease), Consultant for: GSK: consultant. (I am part of their immunology network, a group of about 8 immunologists who advise them regularly and broadly in the areas of inflammation and infection,.), Susan Goodman Grant/research support from: Novartis: research support, Consultant for: Novartis, UCB, Pfizer: consulting, Anne Bass: None declared.


AB1080

TOCILIZUMAB FOR REFRACTORY DYSTHYROID MYOPATHY (RDM) : A MONOCENTER OBSERVATIONAL STUDY OF 8 PATIENTS

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Background: Dysthyroid myopathy (DM) refers to Graves’ ophthalmopathy (GO) in 90% of the cases but can also be observed with hypothyroidism, and is responsible for orbital fat and muscles inflammation. In those patients with euthyroidism and no thyroid receptor antibody, a strong argument for DM can be the aspect of the extra ocular muscles. In myosit- is of other causes, muscle insertions are increased in size. In DM, the insertions are respected and not increased in volume in magnetic reso- nance imaging. This was the case of our eight patients.

Objectives: To describe the efficacy of Tocilizumab (TCZ) in RDM in 8 patients.

Methods: We conducted a monocenter study of 8 patients with RDM refractory to conventional treatment scheme

All patients have been treated following the EUGOGO (European Group on Graves’ Orbitopathy) scheme, which consists in weekly infusions of 300 mg prednisolone (4 to 6) followed by weekly infusions of 250 mg (4 to 6). One patient had received before oral prednisolone, which is known to be less effective and no other immunosuppressive therapy.

The aim was to reduce the clinical activity score (CAS) of the disease to be less effective and no other immunosuppressive therapy.

Results: We studied 8 female patients (16 eyes); mean age at diagnosis 50.2±10.9 years and the mean disease duration was 5.4±6.4 years.

All patients had normal thyroid function at diagnosis. Three patients had a mean age at diagnosis 64,37±9,37 years.

We studied 8 female patients (16 eyes); mean age at diagnosis 64,37±9,37 years.

All patients had normal thyroid function at diagnosis. Three patients had a mean age at diagnosis 64,37±9,37 years.

After a mean of 4 pulses (extremes 1 to 7), all patients experienced improvement with TCZ withdrawal in all due to complete remission in 3 and regression in ocular inflammation in 5. Unfortunately, one patient relapsed two months after the 6th TCZ infusion, despite of initial com- plete remission and was treated with 4 weekly infusions of rituximab at 375 mg/m 2 with a very good response three months later. Only one

patient experienced a severe anal abscess after the first TCZ infusion leading to treatment interruption, but with a good improvement of DM. Improvement of ocular parameters with TCZ therapy. Data are expressed as mean±SD or median [IQR]. (VA : visual acuity; IOP : intra ocular pressure; CAS : clinical activity score)

Before tocilizumab after tocilizumab

VA 0.7 (0,3-1) 0.9 (0,7-1)

IOP 26.5 +/-7.7 21,1 +/-13

CAS 4.25 +/- 1.28

Conclusion: TCZ seems to be effective in RDM, as previously reported. In case of ineffectiveness or relapse, rituximab may be effective as well. This questions us about a new treatment scheme, which patients could benefit from biotherapies alone for a better and quicker efficiency?

REFERENCES


Disclosure of Interests: Philip Bielefield Consultant for: ABBVIE, Speakers bureau; ABBVIE, Florian Baudin: None declared, Julie Blanc: None declared, Alain Brion: None declared, Suzanne Mories-Martin: None declared, Romain Bouvet: None declared, Hervé Devillers: None declared.

AB1081

A COMPARATIVE STUDY ON THE FEATURES OF THE SPINAL INVOLVEMENT IN SAPHO SYNDROME

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Background: SAPHO syndrome is a rare disease with the typical involve- ment of the anterior chest wall. The spinal involvement is more often than we thought and less understood by us.

Objectives: To assess the clinical and imaging features of the spinal involvement in SAPHO syndrome.

Methods: Patients diagnosed with SAPHO syndrome in Peking University Third Hospital from 2006 to 2018 were recruited. Patients were divided into spinal involvement group and non-spinal involvement group. Patients with AS (ankylosing spondylitis) were recruited as control group. Their clinical data, laboratory data and imaging data (CT, MRI and radionuclide imaging) were collected and were compared. All the patients with SAPHO syndrome were followed up regularly.

Results: Totally 46 SAPHO patients were included (17 male and 29 female) and 34 patients (73.9%) had spinal involvement. The mean age was 50.2±10.9 years and the mean disease duration was 5.4±6.4 years. 50 patients with AS were also included. Compared with non-spinal involvement group, the age at disease onset in spinal involvement group was older, the disease duration was longer; the CRP elevation was more often and the anterior chest wall involve- ment was less often (table 1).

In spinal involvement group, the thoracic spine was most commonly involved and the vertebral inflammatory changes including bone marrow edema were often seen. These patients were more likely to suffer from cervical spine involvement, endplate inflammation and spondyloiscits (table 2).

Abstract AB1081 Table 1. characteristics of SAPHO syndrome patients with and without spinal involvement

<table>
<thead>
<tr>
<th>characteristics</th>
<th>Spinal involvement (n=34)</th>
<th>Non-spinal involvement (n=12)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, female</td>
<td>21(61.8%)</td>
<td>8(36.7%)</td>
<td>NS</td>
</tr>
<tr>
<td>Age at diagnosis yrs</td>
<td>62 (21.10.3)</td>
<td>44 (610.6)</td>
<td>0.033*</td>
</tr>
<tr>
<td>Disease duration yrs</td>
<td>6.1±7.1</td>
<td>3.1±2.4</td>
<td>0.048*</td>
</tr>
<tr>
<td>Dermatological disorders</td>
<td>19(55.9%)</td>
<td>10(83.3%)</td>
<td>NS</td>
</tr>
<tr>
<td>CRP elevated</td>
<td>8 (3.6±1.21)</td>
<td>4 (3.0±4.3)</td>
<td>0.047*</td>
</tr>
<tr>
<td>ESR elevated</td>
<td>16 (31.2±24.0)</td>
<td>6 (32.2±27.2)</td>
<td>NS</td>
</tr>
<tr>
<td>TNF-releaved</td>
<td>12 (58.6±5.9)</td>
<td>13 (45.3±22.7)</td>
<td>NS</td>
</tr>
<tr>
<td>IL-6 elevated</td>
<td>18 (320.5±343.9)</td>
<td>48 (46.6±328.2)</td>
<td>NS</td>
</tr>
<tr>
<td>sternoclavicular</td>
<td>18</td>
<td>12</td>
<td>0.003*</td>
</tr>
<tr>
<td>Clavicle</td>
<td>6</td>
<td>2</td>
<td>NS</td>
</tr>
<tr>
<td>First rib</td>
<td>8</td>
<td>5</td>
<td>NS</td>
</tr>
<tr>
<td>Sternocostal joint</td>
<td>6</td>
<td>2</td>
<td>NS</td>
</tr>
<tr>
<td>Sternum</td>
<td>1</td>
<td>3</td>
<td>0.02*</td>
</tr>
<tr>
<td>Manubrium</td>
<td>6</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Sacroiliac joint</td>
<td>6</td>
<td>5</td>
<td>NS</td>
</tr>
</tbody>
</table>
Abstract AB1081 Table 2. characteristics of SAPHO syndrome and AS patients with spinal involvement

<table>
<thead>
<tr>
<th>SAPHO (n=34)</th>
<th>AS (n=50)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, female</td>
<td>21(61.8%)</td>
<td>17(34.0%)</td>
</tr>
<tr>
<td>Age at onset, yrs</td>
<td>52.2(±10.3)</td>
<td>35.4(±12.0)</td>
</tr>
<tr>
<td>Disease duration, yrs</td>
<td>16.1(±7.1)</td>
<td>7.4(±7.3)</td>
</tr>
<tr>
<td>CRP elevated</td>
<td>16(4.6;12.1)</td>
<td>26 (2.1)</td>
</tr>
<tr>
<td>ESR elevated</td>
<td>16 (3.1;24.0)</td>
<td>18 (28.4)</td>
</tr>
<tr>
<td>HLA-B*27 positive</td>
<td>1(2.9%)</td>
<td>48(96.0%)</td>
</tr>
<tr>
<td>Cervical vertebra</td>
<td>17(50.0%)</td>
<td>3(6.0%)</td>
</tr>
<tr>
<td>Thoracic vertebra</td>
<td>22(64.7%)</td>
<td>35(61.7%)</td>
</tr>
<tr>
<td>Lumbar vertebra</td>
<td>17(50%)</td>
<td>34(68.0%)</td>
</tr>
<tr>
<td>Contiguous/multiple vertebra involvement</td>
<td>(28/82.4%)</td>
<td>50(100%)</td>
</tr>
<tr>
<td>Vertebral inflammation</td>
<td>34(100%)</td>
<td>48(96.0%)</td>
</tr>
<tr>
<td>Endplate inflammation</td>
<td>8(23.5%)</td>
<td>3(6.0%)</td>
</tr>
<tr>
<td>Spondylodiscitis</td>
<td>16(47.1%)</td>
<td>4(8.0%)</td>
</tr>
<tr>
<td>Vertebral body corner involvement</td>
<td>11(32.4%)</td>
<td>13(26.0%)</td>
</tr>
<tr>
<td>Paravertebral ossification</td>
<td>4(11.8%)</td>
<td>5(10.0%)</td>
</tr>
</tbody>
</table>

All the SAPHO patients with spinal involvement were followed up. 30 patients received NSAIDs plus DMARDS/biologics and the symptoms improved. Reexamined imaging data of 10 patients were available and the spinal involvement became better.

Conclusion: 73.9% of SAPHO patients had spinal involvement and they were more likely to suffer from cervical spine involvement, endplate inflammation and spondylodiscitis. The combination of NSAIDs and biologics/DMARDs were helpful to improve the symptoms.

REFERENCES


Acknowledgement: This study was supported by a Project of the National Natural Science Foundation of China (81501390).

Disclosure of Interests: None declared


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AB1082

IATROGENIC INFECTIOUS SPONDYLODISCITIS: 6 CASES

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Background: The increasing proportion of iatrogenic spondylodiscitis (SD) is a prominent feature of infectious DS in recent decades

Objectives: To describe iatrogenic clinical, aetiological and evolutive SD features.

Methods: We report 6 cases of iatrogenic DS collected in our department in 2001-2012 period.

Results: All patients were male. The average age was of 49 (35 to 68 years). Four cases of SD were caused by direct inoculation (surgical in 3 cases, chemonucleolysis in 1 case) and 2 cases of hematogenous SD from an initial outbreak. The seat of infection is lumbar in all cases. Spinal pain is almost constant. The admission examination noted arexia in 5 cases. A biological inflammatory syndrome was present in 5 cases and hyperleucocytosis in 2 cases. The bacteriological investigation was able to isolate a methicillin-sensitive Staphylococcus aureus (SAMS) and a proteus mirabilis in one patient and SAMS in another. The radiological assessment made it possible to objectify a para vertebral abscess in 5 cases and an epileptis in 1 case. The evolution was favorable in all cases under antibiotic therapy of average duration of 4.5 months and immobilization of the spine by corset.

Conclusion: The detection of an anaerobic germ causing infectious spondylodiscitis should search for an iatrogenic portal chronologically and anatomically close to the vertebral disc infection.

Disclosure of Interests: None declared


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AB1083

IN A FAMILIAL MEDITERRANEAN FEVER PREVALENT REGION, ARE FAMILIAL MEDITERRANEAN FEVER AND BEHÇET’S DISEASE ASSOCIATED?

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Background: The co-existence of Familial Mediterranean Fever (FMF) and Behçet’s disease (BD) has been questioned. There have been a variety of claims on a common pathogenesis.

Objectives: We intended to report the prevalence of Familial Mediterranean Fever (FMF) and Behçet’s disease (BD) and comorbidity ratio of these two diseases in Sivas, Turkey, a city where FMF is known to be very high.

Methods: Seventy-two primary schools in the center of Sivas participated in the study. A total of 14881 randomized sample children from 6th, 7th, and 8th grades, and also 985 of them with their parents (n: 978) were interviewed. During these interviews, the family tree up to second degree relatives was drawn. The presence of a diagnosis of FMF or BD was questioned. The ones who have a diagnosis were confirmed by contacting the medical centers. The ones who were suspected of a disease were further investigated at Sivas Cumhuriyet University Medical Faculty, Family Medicine Outpatient unit. For each disease a disease related history, physical examination, eye examination and pa rethery test for BD were performed when needed.

Results: 985 students, 978 mothers, 953 fathers and 1876 relatives (4792 in total) were included in the study. Only 30 (0.6%) of the sample was diagnosed with FMF, and 3 (%0.06) was diagnosed with BD. One of them had concomitant FMF diagnosis.

Table. FMF symptoms within the last year

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal Pain</td>
<td>20</td>
<td>66.7</td>
</tr>
<tr>
<td>Fever</td>
<td>23</td>
<td>76.7</td>
</tr>
<tr>
<td>Joint Pain</td>
<td>8</td>
<td>26.7</td>
</tr>
<tr>
<td>Chest Pain</td>
<td>10</td>
<td>33.3</td>
</tr>
<tr>
<td>Muscle Pain</td>
<td>7</td>
<td>23.3</td>
</tr>
<tr>
<td>Erythema like erysipealae</td>
<td>5</td>
<td>16.7</td>
</tr>
</tbody>
</table>

Conclusion: The prevalence of FMF in Sivas is higher than Turkey’s prevalence; however, BD prevalence was found very low. According to these findings, it is not easy to conclude that these two diseases share a similar background of pathogenesis.

Disclosure of Interests: None declared


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AB1084

PECULIARITIES OF ERYTHEMA NODOSUM ASSOCIATED WITH SARCOIDOSIS AND BACTERIAL-VIRAL INFECTION IN RHEUMATOLOGIST PRACTICE

Oltu Egorova, Boris Belov, Svetlana Glukhova, V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation

Background: Erythema nodosum (EN) is a nonspecific immune inflammatory syndrome, which is a septal panniculitis without vasculitis. Often EN acts as one of the symptoms of systemic pathology, which can cause late diagnosis and, accordingly, the appointment of adequate therapy. Objectives: to study clinical, laboratory and radiological data in EN in the acute form of sarcoidosis (SAR) and EN associated with bacterial and viral infection in patients sent to the rheumatology center.

Methods: The study included 312 patients (61 men and 251 women, age 35.4 ± 8.2 years) who applied to the clinic with a referral diagnosis of FMF and EN associated with bacterial and viral infection in patients sent to the rheumatology center.

Results: The study included 312 patients (61 men and 251 women, age 35.4 ± 8.2 years) who applied to the clinic with a referral diagnosis of FMF and EN associated with bacterial and viral infection in patients sent to the rheumatology center.

Conclusion: The prevalence of FMF in Sivas is higher than Turkey’s prevalence; however, BD prevalence was found very low. According to these findings, it is not easy to conclude that these two diseases share a similar background of pathogenesis.

Disclosure of Interests: None declared

OSTEO-ARTICULAR MANIFESTATIONS OF ADULT ONSET STILL'S DISEASE: EXPERIENCE OF THE RHEUMATOLOGY DEPARTMENT OF THE UNIVERSITY HOSPITAL OF CASABLANCA

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Background: Adult onset Still's disease (AOSD) is a rare condition characterized by four cardinal signs: fever, arthralgia/arthritis, rash, and neutrophil leukocytosis. The absence of specific criteria is currently compensated by pathophysiological advances, leading to the introduction of a promising new therapeutic arsenal represented by biotherapies.

Objectives: The aim of this study was to compare the profiles of this disease in our latitudes with data from foreign literature; and to study the most recent data concerning the pathophysiology and treatment of this disease.

Methods: We conducted a retrospective study of hospital files from January 1993 to October 2018. The diagnosis is retained according to Yamaguchi criteria. Analysis was performed using IPSS.

Results: 17 patients were selected. The sex ratio was 0.54, and the average age was 31.5 years. At the time of diagnosis, fever was found in 94% of cases, arthralgia/arthritis in 100% of cases, and rash in 65% of cases. Concerning rheumatic features, the most frequently affected joints were: wrists (87%), knees (73%), shoulders (67%), proximal interphalangeal (62%), elbows and ankles (60%), hips (47%). The involvement of the hands is dominated by the proximal interphalangeal and metacarpophalangeal (45%). Distal interphalangeal involvement is observed in 23% of cases. Cervical spine involvement is noted in 50% of cases. Biologically, 88% of patients had neutrophil leukocytosis. Ferritinemia was increased in 79% of patients. The glycosylated fraction of ferritin was measured at diagnosis in 47% of patients, of whom 63% had a fraction ≤ 20%. Elevated transaminases were found in 47% of cases. Therapeutically, 100% of patients received corticosteroids; 65% methotrexate; and 29% biotherapies (tocilizumab,akinlimab, infliximab, adalimumab). The evolutionary profile was exploitable in 13 patients, of whom 10 were in complete remission.

Conclusion: Our data are consistent with those in the literature. Some peculiarities emerge concerning the articular features. From 3 series of literature and ours, totaling 135 cases, it appears that the most frequent locations are: wrist (82%), knees (70%), elbows (46%), ankles (45%), proximal interphalangeal (44%),shoulders (42%) and metacarpophalangeal (42%). The pathogenesis of AOSD seems to lie at the crossroads between auto-inflammatory diseases and lymphohistiocyte activation, resulting from a multifactorial predisposition. The central role of innate immunity, the clinical presentation, and the efficacy of blocking the IL-1 pathway comparable to that observed in "monogenic inflammasomopathies" justify the reclassification of AOSD among polygenic auto-inflammatory syndromes.

REFERENCES

Disclosure of Interests: None declared

OSTEO-ARTICULAR MANIFESTATIONS OF SARCOIDOSIS: ABOUT 13 CASES

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Background: Sarcoidosis is a systemic disorder of unknown etiology, affecting the respiratory tract and the lymphatic system with predilection. It is an ubiquitous condition whose clinical phenotype is very diverse.

Objectives: To detail the epidemiological, clinico-biological, therapeutic and evolutionary features of osteoarticular forms of sarcoidosis.

Methods: This is a monocentric, descriptive retrospective study conducted over a 17-years period [2002-2018] involving 13 patients diagnosed with sarcoidosis with osteoarticular manifestations at the department of Rheumatology at Farhat Hached University Hospital in Sousse.

Results: 13 patients with osteoarticular manifestations were studied; this is indicative of the disease in 8 cases (61.5%). The sex ratio was 0.23 with a mean age of 42.38 years and a diagnostic delay of 12 months. In 77% of cases, inflammatory arthralgia was noted, Löfgren syndrome (30.7%), chronic polyarthitis (30.7%), phalanges cystoid ostitis (15.4%) and no cases of monoarthritis. The extra articular manifestations found were: Adenomegaly (92.3%), lung (77%), cutaneous (38.5%) (including 80% erythema nodosum), neurological (30.7%) (Aseptic meningitis and convulsion), ocular (23%) (chorioretinitis, keratoconjunctivitis and retro-bulbar optic neuritis), cardiac (15.4%), and biological hepatitis (7.7%). In the biology, a biological inflammatory syndrome was found in 30.7% with a mean sedimentation rate of 31.07 in the 1st hour, an average CRP of 9 mg/L, cholestasis and cytolysis found in 15.4% and 7.7% respectively. No Hypercalcemia was noted. The value of the conversion enzyme was high in 5 out of 6 patients who were dosed with an average of 71 µL. In imaging, sarcoidosis was destructive in 4 cases; A multifocal osteonecrosis, Algodystrophy of the two hips and two cases of bullos cystoid ostitis of phalanges.

Conclusion: The osteo-articular involvement of sarcoidosis is polymorphic, which can reveal the disease or enamel its evolution.

Disclosure of Interests: None declared
Background: Familial Mediterranean fever (FMF) is the most common hereditary inflammatory disease characterized by recurrent attacks of fever and serositis. The most devastating complication of FMF is amyloidosis, leading to chronic renal failure (CRF). The amyloid protein may accumulate in many tissues including the cartilage, particularly in the kidneys. Sonographic femoral cartilage thicknesses (FCT) was evaluated in many chronic rheumatic diseases and was shown to be thinner than healthy individuals.

Objectives: The aim of this study was to determine FCT in FMF patients and healthy individuals and to assess the relationship of FCT with the development of amyloidosis and clinical features.

Methods: Patients diagnosed with FMF according to the Tel-Hashomer criteria were included in the study. Patients with trauma and other inflammatory disease and patients with a history of knee operation were excluded. Femoral cartilage thickness of both knees was measured with a 7-12 MHz linear probe in maximum knee flexion. Three mid-point measurement were obtained from each knees: lateral femoral condyle (LFC), intercondylar area (ICA) and medial femoral condyle (MFC). Clinical characteristics of the patients including disease duration, medications, comorbid conditions, amyloidosis, CRF, FMF gene mutation, arthritis, sarcroilitis, PRAS score and physical activity scores were recorded. Descriptive analysis was performed for all parameters. The Mann-Whitney U test and Spearman’s correlation coefficient were used in statistical analysis.

Results: A total of 45 patients with FMF (35 women, 10 men) and 20 age-sex-BMI matched controls (14 women, 6 men) were enrolled in this study. The mean age of the patients and controls were 38.2 (SD:12.2) and 37.5 (SD:8.5) years, respectively. Amyloidosis occurred in 7 patients (15.6%), CRF in 3 (6.7%), sarcroilitis in 10 (22.2%) and arthritis in 16 (35.6%). Disease activity was mild in 48.9%, moderate in 20% and severe 22.2% of the patients. The mean FCT in centimeters values in the FMF and control groups were as follows: on the right side LFC 0.19 (SD:0.03) and 0.22 (SD:0.05), ICA 0.23 (SD:0.05) and 0.24 (SD:0.06), MFC 0.20 (SD:0.04) and 0.24 (SD:0.06); on the left side LFC 0.19 (SD:0.03) and 0.21 (SD:0.03), ICA 0.22 (SD:0.05) and 0.24 (SD:0.06), MFC 0.19 (SD:0.03) and 0.22 (SD:0.04). Patients with FMF had decreased cartilage thickness at the lateral condyle of both knees (p<0.05) and medial condyle of the left knee (p<0.05) compared with controls. FCT measurements were similar in patients with or without arthritis, sarcroilitis, amyloidosis and CRF. Physical activity scores were significantly correlated with the left LFC (r=0.309). Total protein in 24-hour urine showed a highly negative correlation with left LFC (r=-0.718).

Conclusion: These findings suggest that patients with FMF have decreased FCT compared with controls. There is no significant relationship between the FCT and amyloidosis, it has significant relation with proteinuria level.

REFERENCES

Disclosure of Interests: Halise Hande Gezer: None declared. Didem Erdem: None declared, Sevtap Acer Kasman: None declared, Hatte Sule Bakiçloglu: None declared, Mehmet Tuncay Duruž Grant/research support from: Abvie, Speakers bureau: Novartis, AMGEN, Abdi Ibrahim, liko

Background: Familial Mediterranean fever (FMF) is known as the most common monogenic autoinflammatory disease. Its prevalence is reported high from the eastern Mediterranean areas (1). The disease is characterized by episodes of fever, serositis, arthritis, renal complications and other different clinical manifestations (2).

Objectives: Here, we aimed to present our data of our 139 FMF patients for demonstrating the demographic and clinical features of the study group from North-western part of Turkey.

Methods: A total of 139 FMF patients who were diagnosed and treated in the department of Internal medicine/Rheumatology, Sakarya University (North-western area of Turkey) were included in the study and the demographic and clinical characteristics of the patients were examined.

Results: The mean age of the patients was 39.02 ± 11.3. Male gender was 42 (30.2%) and female gender was 97 (69.8%), 107 (77%) of patients had fever and 32 (23%) had no history of fever. 127 (91.1%) patients complained about peritonitis, 27 (19.4%) patients had pleuritic pain, 19 (13.7%) patients had erysipelas like erythema and 53 (38.1%) patients had arthritis attack. 34 (24.5%) patients also had sacroiliitis. The ratio of resistance of treatment response to colchicine drugs that can be available in Turkey (Colchicum disper t.), 6 (4.3%) was determined. Interestingly these patients responded to the colchicine drugs available from some other countries from Europe (as Colchicine-opocalcium and Colchicina-lirca®). None of our patients needed anti-IL1 therapies. The rate of amyloidosis was 5 (3.6%).

Conclusion: FMF is a disease with high morbidity and mortality, 95.7% of the patients in our region have response to colchicine drugs which is available in our country. The remaining patients have also responded to colchicine available from some other countries. None of our patients had anti-IL1 therapies.

REFERENCES

Disclosure of Interests: None declared

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Background: Deficiency of adenosine deaminase 2 (DADA2) is a recently identified cause of early onset polyarteritis nodosa and stroke: a multicentre international study. Ann Rheum Dis 2017; 76:

Results: There was no statistically significant difference between the two groups in terms of age or sex (respectively p=0.189 and p=0.585). There was no difference between the Behçet’s patients and healthy volunteers in the qualitative analysis on capillary density, capillary visibility, aneurism, hypocapillagomulbinema and cytopenia.

Objectives: To present the clinical cases of two Brazilian siblings with early stroke episodes carrying a homozygous CECR1/ADA2 mutation.

Methods: Chart review of clinical data, laboratory tests and mutation analysis.

Results: The index case is a 7-year-old boy who presented to the emergency unit with right lower limb weakness, rhyme deviation and palpebral ptosis, associated with recurrent and intermittent fever, mood change and hypertension. The physical exam revealed drowsiness, lateral and vertical ocular paresis, diplopia, facial palsy, and bilateral ataxia. The brain MRI showed acute left mesencephalic small vessel lacunar stroke, previous right mesencephalic subacute stroke, and cerebellar cavity related with anterior cerebellar artery segmental narrowing. Laboratory tests revealed increased inflammatory markers and anemia. Autoantibodies and viral screening were negative. Renal ultrasound showed a pattern of low resistance in the intrarenal arteries bilaterally. At this time, he was diagnosed as polyarteritis nodosa (PAN). Despite of adequate treatment (cyclophosphamide and corticosteroids), two new stroke episodes occurred at left head of caudate and right thalamus. His brother, a 9-year-old healthy boy at that time, had a previous history of ischemic stroke when he was 4 years old, after receiving a vaccine, with complete recovery.

Conclusion: ADA2 should be suspected in patients with PAN-like phenotype and history suggestive of an inherited disease (e.g.: affected siblings and consanguineous parents) or resistance to conventional treatment.

REFERENCES

Disclosure of Interests: None declared

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Background: Behçet’s disease is a chronic, recurrent and systemic vasculitis that may affect veins and arteries at all diameters. Small vessel involvement is responsible for most of its pathological signs.

Objectives: We aimed to compare the nailfold capillaroscopy findings of Behçet’s patients to a healthy control group and examine the relationships, as well as revealing the relationships with the sub-type, activity and other characteristics of Behçet’s disease.

Methods: We conducted a cross-sectional analysis of 153 patients with Behçet’s disease and 165 healthy volunteers in a single center. The capillaroscopic findings of the 2nd-5th fingers of both hands of the participants in the Behçet’s patients and control groups were included in the analysis. Capillaroscopic findings were evaluated by two different experts who were experienced in this field by using the scoring at Atlas of Capillaroscopy in Rheumatic diseases by Maurizio Cutolo.

Results: There was no statistically significant difference between the two groups in terms of age or sex (respectively p=0.189 and p=0.585). There was no difference between the Behçet’s patients and healthy volunteers in the qualitative analysis on capillary density, capillary visibility, aneurism, hypocapillagomulbinema, cytopenia, capillary tortuosity, capillary enlargement and presence of avascular areas (p values respectively: 0.610, 0.147, 0.481, 0.057, 0.514 and 0.110). In the Behçet’s patients, bushy capillaries (24.2%, 37/153), capillary dilatation (32%, 49/153) and microhemorrhage (39.2%, 60/153) rates were significantly higher than those in the healthy control group (p<0.001). In the quantitative analysis, total capillaroscopy score was significantly higher in the Behçet’s patients than those in the healthy control group (p<0.001) (Table 1). No statistically significant relationship was found between the presence of clinical signs and capillaroscopy scores, except for erythema nodosum.

Conclusion: the Behçet’s patients had significantly higher total capillaroscopy scores in comparison to those in the healthy control group. Based on these data, we believe that the capillaroscopic changes found in Behçet’s patients, though unspecific, may support clinical diagnosis in uncertain cases where Behçet’s disease is considered as a probability. There is a need for well planned prospective studies to support this our thought.
REFERENCES


Abstract AB1091 Table 1. The results of the quantitative evaluation of nailfold capillaroscopic findings

<table>
<thead>
<tr>
<th>Behçet's patients N=153</th>
<th>Healthy controls N=165</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irregularly enlarged capillary score*</td>
<td>0 (0-0.44)</td>
<td>0 (0-0.25)</td>
</tr>
<tr>
<td>Giant capillary score*</td>
<td>0 (0-0.13)</td>
<td>0 (0-0.13)</td>
</tr>
<tr>
<td>Microhemorrhage score *</td>
<td>0 (0-0.63)</td>
<td>0 (0-0.19)</td>
</tr>
<tr>
<td>Capillary number score *</td>
<td>0 (0-0.86)</td>
<td>0 (0-0.25)</td>
</tr>
<tr>
<td>Capillary ramification score *</td>
<td>0 (0-0.75)</td>
<td>0 (0-0.25)</td>
</tr>
<tr>
<td>Disorganize capillary score*</td>
<td>0 (0-0.44)</td>
<td>0 (0-0.25)</td>
</tr>
<tr>
<td>Total capillaroscopic score*</td>
<td>0.16 (0-1.75)</td>
<td>0 (0-0.50)</td>
</tr>
</tbody>
</table>

*Data were given as median (minimum - maximum)

Abstract AB1091 Table 2. The relationship between clinical findings and total capillaroscopic scores

<table>
<thead>
<tr>
<th>Total Capillaroscopy Score</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Vascular involvement (n=54/99) *</td>
<td>0.19 (0-1.48)</td>
</tr>
<tr>
<td>Ocular involvement (n=64/89) *</td>
<td>0.19 (0-1.48)</td>
</tr>
<tr>
<td>Neurological involvement (n=12/141)</td>
<td>0.19 (0.6-1.48)</td>
</tr>
<tr>
<td>Genital ulcer (n=131/22)</td>
<td>0.19 (0-1.75)</td>
</tr>
<tr>
<td>Erythema nodosum (99/54) *</td>
<td>0.13 (0-1.75)</td>
</tr>
<tr>
<td>Papulopustular eruption (n=119/34) *</td>
<td>0.19 (0-1.75)</td>
</tr>
</tbody>
</table>

N, number of patients, *Data were given as median (minimum - maximum)

Disclosure of Interests: None declared

INTERSTITIAL PNEUMONIA WITH AUTOIMMUNE FEATURES: A SINGLE CENTER EXPERIENCE AND THE IMPORTANCE OF A MULTIDISCIPLINARY APPROACH

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Background: Interstitial lung disease (ILD) remains a significant cause of morbidity and mortality in patients with connective tissue diseases (CTD). Interstitial pneumonia with autoimmune features (IPAF) is a subset of ILD with clinical features suggestive of but not definitive for a CTD. IPAF is a new concept relatively unknown to rheumatologists. A multidisciplinary approach to diagnosis and management of IPAF patients is essential, involving close interaction between pulmonologists, rheumatologists, radiologists and pathologists.

Objectives: Revision of ILD patients followed at a specialized tertiary hospital’s ILD department and description of their clinical characteristics and multidisciplinary approach.

Methods: The study was conducted according to the declaration of Helsinki. All patients who met the Fischer criteria for IPAF in 2000–2018 were identified. Clinical characteristics, comorbidities, ILD subtype, pulmonary function tests, baseline serologies and treatment strategies were collected. The consents from a multidisciplinary meeting and Rheumatology referral and evaluation were also recorded.

Results: We identified 8 cases fulfilling classification criteria for IPAF (4 [50%] female); mean age 64.9 years (range 34–83); past smoking was referred in 5 (62.5%) patients with an average of 54.15 smoking pack years. Overall, 4 (50%) patients were exposed to organic dusts and 2 (25%) to inorganic dusts. Arterial hypertension was the most frequently recorded comorbidity (50%). Among the 8 patients, 6 (75%) had at least 1 feature from the serologic and morphologic domains, 1 patient had at least 1 feature from clinical and serologic domains and 1 patient had at least 1 feature from all 3 domains. From those meeting ‘suggestive radiology pattern based on high resolution chest CT (HRCT)’, 2 had nonspecific interstitial pneumonia (NSIP) and 1 had organizing pneumonia (OP). Biopsy (3 transbranchnial biopsies and 1 transthoracic biopsy) were conclusive in 4 patients (2 NSIP, 1 lymphoid interstitial pneumonia and 1 OP). Usual interstitial pneumonia (UIP) pattern was observed in two patients. Antinuclear antibodies were positive in 5 (62.5%) patients. Overall, 5 (62.5%) clinical cases were discussed in a multidisciplinary meeting including revision of imaging and biopsies. A Rheumatology appointment was requested in 5 patients to investigate a possible CTD diagnosis. Six (75%) patients had pulmonary function tests (PFT) and diffusing capacity of the lung for carbon monoxide (DLCCO) results recorded at baseline: 4 patients had a DlCCO below 70% (33.8 – 61.8%), 3 patients had normal PFT, 1 had restriction pattern and 2 had small airways obstruction. During a median of 2.7 years of follow-up, none of the patients progressed to a definitive diagnosis of CTD. Pharmacological treatment was prescribed in 6 patients, including corticosteroids (5), DMARDs (3), antibiotic therapy (2) and azithromycin (2).

Disclosure of Interests: None declared

AB1094

ARTERIOSCLEROSIS MAY AFFECT PERIAORTIC/PERIARTERIAL LESIONS AND THEIR ANEURYSMAL CHANGES IN PATIENTS WITH IGG4-RELATED PERARTERITIS/PERIARTERITIS

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Background: IgG4-related periarthritis/periarteritis (IgG4-PA) is a major organ manifestation of IgG4-related disease (IgG4-RD) [1]. In the affected aorta/artery, arteriosclerotic changes are frequently observed [2]. However, the influence of arteriosclerosis on IgG4-PA and aneurysmal changes of the affected lesions has not been well evaluated.

Objectives: This study aimed to clarify the relationship of arteriosclerosis with periarteric/periarterial lesions and their aneurysmal changes.

Methods: We retrospectively investigated the medical data, including the presence of IgG4-PA at diagnosis, new development of IgG4-PA during the clinical course, arteriosclerotic and aneurysmal changes of the affected lesions, and classic risk factors for arteriosclerosis in 130 patients with IgG4-RD at a single center in Japan. The relationship of arteriosclerosis with the periarteric/periarterial lesions and their aneurysmal changes was statistically analyzed.

Results: Of the 130 patients with IgG4-RA, 44 comprising 39 men and 5 women (mean age 67.4 years) were diagnosed with IgG4-PA. The mean follow-up period was 72.8 months, and the mean serum IgG4 level at diagnosis was 851 mg/dL. The proportions of males (86.6% vs. 55.8%, P=0.004) and positive smoking history (81.4% vs. 47.6%, P<0.001), and history of malignancy (36.4% vs. 14.0%, P=0.006) were significantly higher in the 44 patients with IgG4-PA than in the 86 without it. Arterial wall calcification and/or mural thrombus in the affected lesions were detected in 86.0% of the IgG4-PA patients, some of whom had had these arteriosclerotic changes before the development of periarteric/periarterial lesions.

Conclusion: The present study suggests that arteriosclerotic changes and the classic risk factors for arteriosclerosis may be related to periarteric/periarterial lesions and their aneurysmal changes in IgG4-PA.
the appearance of symptoms caused by the involvement of other non-cartilaginous tissues and the presence of systemic symptoms.

**Objectives:** To describe the clinical characteristics and treatment of patients diagnosed with RP in a tertiary level university hospital.

**Methods:** Data from RP patients were obtained from the computerized medical history of our center, including demographics, disease phenotype, treatment, laboratory and imaging studies.

**Results:** A total of 12 patients were included; 66.7% were women, age at diagnosis was 36 [34-52.5] years (median [p25-p75]). The main manifestation observed was auricular involvement (75%) followed by nasal (66.7%), joint (66.7%), and laryngo-tracheo-bronchial disease (50%). All patients were on DMARD’s treatment and two thirds of the patients were receiving biological therapy at the time of analysis. Infliximab was the first biological line in all the cases (100%). Other biological therapies used, in order of frequency, were: adalimumab (25%), rituximab (25%) and tocilizumab (12.5%). 50% of the patients associated another autoimmune disease diagnosed before or during RP follow-up: Crohn’s disease, epidermolysis bullosa, primary biliary cholangitis, autoimmune hypothyroidism, systemic lupus erythematosus, granulomatosis with polyangiitis and ulcerative colitis. Only one patient (8.33%) associated hemolytic disease (myelodyplastic syndrome) and another one died during follow-up.

**Conclusion:** RP is a rare disease with a broad spectrum of clinical expression, which often requires intensive management to control its manifestations, potentially serious when there is involvement of the tracheo-bronchial tree or is associated with other autoimmune diseases. A large part of our patients require biological therapy at some point in their evolution.

**REFERENCES**


**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.4797

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**REFERENCES**


**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.7518

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**REFERENCES**


**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.4797
Objectives: We evaluated iRPF cases of a single institution cohort to describe the features of patients (pts) with iRPF.

Methods: Twenty-eight iRPF patients who were being followed in our outpatient clinic between 2009 and 2018 were reviewed retrospectively. The demographic characteristics, clinical and radiologic findings, medical and interventional therapies were retrospectively collected and reported.

Results: We evaluated the data of 28 patients (17M/11F). The mean age at the time of diagnosis was 53±10.57, median follow-up was 46 (IQR:23-67) months. Fifteen (%50) patients were presented with abdominal-pain which was the most common initial complaint; 9 (32%) flank pain, 1 anuria, 1 nocturia, and 2 had nausea. Twenty-one patients had hydronephrosis (11 bilateral hydronephrosis, 5 right and 5 left hydronephrosis) at initial visit and one patient diagnosed while on temporary hemodialysis therapy. Laboratory tests showed that ESR was elevated in 15 of 23 cases in which it was available (65.2%), with a median value of 39 mm/h (IQR:17-88); CRP was elevated in 19 of 28 patients (68%), with median value 11 (IQR:5,5-46,5). Mean serum creatinine level was 1,14 mg/dl IQR (0,83-1,9). Tissue involvement was detected with computed tomography in 25 (89%) patients. The remaining 3 patients’ involvement was located with 18 F-fluorodeoxyglucose positron emission tomography (18 F-FDG-PET). 18 F-FDG-PET has been performed in 19 patients and 16 of them (84%) revealed tissue involvement of iRPF. Histopathological samples were available for further analysis in 8 cases and 5pts’ findings were consistent with iRPF (storiform fibrosis and dense lymphoplasmacytic infiltration were observed) and of these 5 pts, 2 of them were classified as IgG4-related subtype. The remaining 3 pts were diagnosed with positive radiologic findings. Medical and interventional therapies are presented in Table 1. The mean initial oral prednisone dose was 45,5±13,8 mg/day. Prednisone was discontinued in 4 patients after remission and for the remaining 23 pts; 12 pts’ prednisone was tapered <5 mg/day at mean 9 (IQR:6,7-22,5) months. One patient diagnosed AML-M2 during the follow-up and had allogenic stem cell transplantation. Rheumatoid factor (RF) and anticitrullinated protein antibodies (ACPA) were determined in all patients. Subjects were classified by each of the three different criteria.

Conclusion: Steroids are the mainstay treatment for iRPF and steroid resistant cases could be treated with rituximab rescue therapy. Prompt interventional approaches are valuable bridging therapies for pts who presented with hydronephrosis. Imaging modalities add great value on the interventional approaches are valuable bridging therapies for pts who presented with hydronephrosis. Imaging modalities add great value on the intervention approach.

Disclosure of Interests: None declared

AB1098

COMPARISON OF THE PERFORMANCE OF CLASSIFICATION/DIAGNOSTIC CRITERIA FOR POLYMYALGIA RHEUMATICA. SINGLE CENTERSTUDY OF 100 PATIENTS

D. Prieto-Peña, Monica Calderón-Goercke, Miguel A. González-Gay, Ricardo Blanco. Marqués de Valdecilla University Hospital, Santander, Spain

Background: Polymyalgia rheumatica (PMR) diagnosis is based on the combination of shoulder and pelvic girdle pain associated with elevated acute phase reactants. Traditionally, Bird et al.1 and Chuang et al.2 criteria have been used for establishing PMR diagnosis. In 2012 an international working group developed new European League Against Rheumatism (EULAR)/American College of Rheumatology (ACR) classification criteria for PMR.3

Objectives: a) To compare the performance of Bird et al., Chuang et al. and 2012 EULAR/ACR classification criteria for PMR in a single-center study. b) To describe the characteristics of the patients excluded by these criteria.

Methods: We included 100 patients with new-onset PMR who were consecutively diagnosed over a 7-year period by experienced rheumatologists from a single center. PMR diagnosis was confirmed during a prospective 24-months follow-up after excluding other mimicking conditions. Rheumatoid factor (RF) and anticitrullinated protein antibodies (ACPA) were determined in all patients. Subjects were classified by each of the three different criteria.

Results: We studied 100 patients (61 women/39 men); mean age 67.1 ± 10.2 years. 96% of the patients fulfilled Bird et al criteria, 94% fulfilled Chuang et al criteria and 84% of the patients fulfilled 2012 EULAR/ACR criteria. We assessed the characteristics of the 16 patients who did not fulfilled 2012 EULAR/ACR criteria: 6 of them were under 50 years of age (range age 43-48 years). Another 10 patients did not complain of pain/stiffness in the shoulder girdle at any time. However, they had typical inflammatory pain involving the pelvic girdle and elevated acute phase reactants.

Conclusion: In our single-center experience we found that 2012 EULAR/ACR criteria classified most of our patients. However, patients who presented predominant pelvic girdle affection and those who were under 50 years old despite showing all the rest of clinical and analytical required criteria were excluded. Some of these patients did fulfill Bird and/or Chuang criteria.

REFERENCES

Disclosure of Interests: D. Prieto-Peña: None declared, Monica Calderón-Goercke: None declared, Miguel A González-Gay Grant/research support
Chagas Disease Reactivation in the Rheumatologic Immunosuppressed Patient. Is It No Longer an Orphan Disease?

**Background:** Chagas' disease (CD) is an endemic and neglected infection in Latin America. Due to international human migration, it has become a worldwide issue. Scarcely evidence is published regarding its behavior in rheumatic diseases (RD) with rheumatologic treatments (RT).

**Objectives:** To screen and follow up patients with CD under RT. To detect clinical and serological reactivation.

**Methods:** A systematic screening was conducted between January 2018 and January 2019 in a third-level Hospital in Argentina. Patients with CD and concomitant RD under RT were included. Assessments were done before and after RT. A direct (Strout) and indirect method (Polymerase chain reaction-PCR) were performed in order to detect parasitemia, levels of antibodies were evaluated by three techniques. Clinical, infectological and cardiological features were examined. Everything was assessed in, at least, two opportunities, separated by a minimum of one month. If treatment was modified or clinical condition changed, all the evaluations were repeated as before. In case of reactivation, specific treatment was indicated and follow up controls were stricter.

**Results:** 38 patients were identified. RD: Rheumatoid Arthritis: 22 (57,9%), Systemic lupus erythematosus: 4 (10,5%), Systemic Sclerosis: 3 (7,9%), Vasculitis: 2 (5,3%), Psoriatic Arthritis: 1 (2,6%), others: 6 (15,8%). RT: classic, synthetic and biological disease-modifying antirheumatic drugs, cyclophosphamide and corticosteroids.

Two reactivations were detected with both direct and indirect methods, with a significant title antibody increment and consistent clinical signs and symptoms. Cardiological abnormalities were found. A 64-years old lady with Microscopic Polyangiitis, under prednisone 60 mg/day, and a 57-years old lady with Systemic Lupus Erythematosus under hydroxychloroquine and prednisone 40 mg/day, who happen to be sisters. They did not have other treatments. Both of them developed high fever, myalgias, arthralgias and asthenia. Other infections were ruled out. They received Benzimidazole and Nitritomix respectively. After one-week treatment, Strout and PCR became negative and antibodies decreased, with remarkable clinical improvement.

**Conclusion:** Two patients with parasitemia and concomitant symptoms were detected, after high doses of corticosteroids. Because they were sisters, a genetic background would also play a role. Parasite's screening before starting immunosuppression and its follow-up during treatment in search of reactivation should be integrated to rheumatology daily practice in endemic countries. It should also be taken into account in patients from non-endemic countries that have an epidemiological nexus. CD specific antibodies determination, Strout and PCR are economic and practical techniques, although they require qualified personnel and equipment. In areas with high prevalence of CD, the benefits of this measures would outweigh costs. A more advanced study should be performed to extend our knowledge.

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.3509
ANA SUBSETS ANTIBODY PROFILE OF EARLY UNDIFFERENTIATED ARTHRITIS (UA) IN PAKISTAN
Syed Hussain Azhar Rizvi, Tariq Gazdar1, Aneela Pasha, Mohammad Saeed.
Immunocure, Karachi, Pakistan

Background: Undifferentiated Arthritis (UA) is a group of inflammatory disorders where early synovitis (duration less than 12 months) is present, however patients do not meet criteria for established rheumatologic disorders such as Rheumatoid arthritis, Lupus or Spondyloarthritides (1). On long term follow up, a subpopulation of UA patients converge into definitive Rheumatologic disorders. Up to 50% of early arthritis in European cohorts has been reported to be UA (1, 2).

Objectives: Identify Anti-nuclear antibody (ANA) Subset antibodies in patients presenting with early UA.

Methods: Over a 1-year period (2017-18) patients with early UA were prospectively evaluated. This included clinical exam, routine laboratory investigations including ESR and CRP, RF and anti-CCP as well as Musculoskeletal ultrasound (MSKUS) (3). These patients underwent further testing for ANA Subset antibodies. ANA subsets (17 antibodies) were performed using standard immunoblot assays (EUROIMMUN) at our clinic laboratory (4).

Results: 110 UA patients were found to have positive ANA subsets. The most frequent antibodies were Ku (77.3%) and M2 (73.6%) followed by dsDNA (30%) and Nucleosome antibody (29%) (Figure 1). Low frequency antibodies included Sm (n=1), Ribosomal-P and PCNA (n=2 each), Jo-1 (n=3), PM-Scl100 (n=4) and SSB (n=5), whereas Scl70 antibodies were absent. SSA (n=9) and Ro-52 (n=14) together constituted 21% frequency. These antibodies had high signal intensities (mean ± SD SSA = 52±35 and Ro-52 = 46±25). Ku (17±11) and M2 (22±15) had modest signal intensities (Figure 2). Clinically 42 patients were classified as RA (RF+ = 33%; anti-CCP+ = 14%) and 41 patients met ACR criteria for SLE while 2 patients met criteria for both and were classified as Rhepus. ANA subset antibody frequencies did not statistically differ between the RA and SLE groups signifying that the clinically classified RA patients in fact had early Rhupus which did not meet ACR criteria for SLE.

Conclusion: Early UA is difficult to categorize clinically, sometimes even after long term follow up, though a substantial portion converge into RA. This study shows that there is a significant portion of early Rhupus in the RA group whose steroid discontinuation leads to a disease flare. ANA Subset antibody profile in such patients may help in their more accurate diagnoses and treatment.

REFERENCES
Disclosure of Interests: None declared

AB1103
NEUROLOGICAL IMPAIRMENT DURING SARCOIDOSIS
sameh sayhi1, Rim Dhahi1, Najah Boussetta1, Bibel Arfaoui1, Feida Laajili2, Bassem Louzir1, Hajar Derbal1, Linda Mrisa1, Rida Mrisa1. 1Military Hospital of Tunis Tunisia, Internal Medicine, Tunis, Tunisia; 2Military Hospital of Tunis Tunisia, Autoimmune Diseases Unit Research UR171002, Tunis, Tunisia; 3Military Hospital of Tunis Tunisia, Neurology, Tunis, Tunisia

Background:
Objectives: To describe neurological impairment characteristics in sarcoidosis.
Methods: This was a descriptive and retrospective study including 65 patients with sarcoidosis, followed in the departments of internal medicine and neurology at the Military Hospital of Tunis over a period of 20 years from 1997 to 2017.
Results: A total of 65 patient files have been selected, of which 38 have neurological involvement. Thirty-eight patients met the inclusion criteria for Neurosarcoidosis. According to Zajicek’s criteria, the diagnosis of neurosarcoidosis was certain in 2 cases, probable in 18 cases and possible in 18 cases. Neurological disorders were symptomatic in 58.5% of the studied population. Neurological signs were inaugural in 9 patients (14% of cases). A central neurological involvement was demonstrated in 33 patients (86.8%), of whom 23 presented with cranial nerve involvement and 10 patients (26.3%) had both central and peripheral impairment. Neurological involvement was significantly associated with cardiac, renal extra-thoracic, ophthalmologic, articular and cutaneous involvement (p <0.05). Neurogenotype of the conversion enzyme and HLA typing did not show any particular pattern of neurosarcoidosis in comparison with patients without neurological signs.

Conclusion: Neurological impairment was frequently observed in our series. It was also significantly associated with multivisceral involvement without particular genetic pattern.

Disclosure of Interests: None declared

AB1104
GENETIC ASPECTS OF SARCOIDOSIS IN A TUNISIAN POPULATION
sameh sayhi1, Rim Dhahi1, Najah Boussetta1, Souha Hannachi1, Feida Laajili2, Bassem Louzir1, Hajar Derbal1, Linda Mrisa1, Rida Mrisa1. 1Military Hospital of Tunis Tunisia, Internal Medicine, Tunis, Tunisia; 2Military Hospital of Tunis Tunisia, Autoimmune Diseases Unit Research UR171002, Tunis, Tunisia

Background:
Objectives: To determine the frequencies of the HLA alleles and genotypes of the ACE gene.
Methods: This is a cross sectional study of 65 patients with sarcoidosis, followed in the departments of internal medicine and neurology at the Military Hospital of Tunis. The genetic study involved 50 patients. DNA extraction was performed to determine the frequencies of the HLA alleles and genotypes of the ACE gene.
Results: 1. HLA typing
The analysis of HLA typing allowed us to estimate the different frequencies of alleles in patients. The calculation of the allelic frequency found that the most frequent alleles are HLA-DRB1*1501 alleles with a frequency of 38% and HLA-DRB1*0301 of 28%. Other alleles are at lower frequencies (Table1).

2. Genotyping of the ECA gene
Genotyping of the polymorphism of the angiotensin converting enzyme (ACE) involved 50 patients. Genotypic frequencies (II, ID and DD) and allele frequencies (I and D) were estimated in order to evaluate the frequencies of each genotype and the 2 alleles for this pathology. The genotypic and allelic frequency results were summarized in Table 2.

<table>
<thead>
<tr>
<th>Genotypes</th>
<th>N</th>
<th>%</th>
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<tr>
<td>II</td>
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</tr>
<tr>
<td>ID</td>
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<td>48%</td>
</tr>
<tr>
<td>DD</td>
<td>15</td>
<td>30%</td>
</tr>
<tr>
<td>Alleles</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>46</td>
<td>46%</td>
</tr>
<tr>
<td>D</td>
<td>54</td>
<td>54%</td>
</tr>
</tbody>
</table>

Conclusion: The most frequent alleles in Tunisian patients with sarcoidosis are HLA-DRB1*1501 with a frequency of 38% and HLA-DRB1*0301 of 28%. The genotypic and allelic results showed that genotypic ID was the most frequent with 48% with a predominance of the D allele in 54%.

References:

DISCLOSURE OF INTERESTS
None declared

AB1105
A NOVEL AUTOINFLAMMATORY AND LYMPHOPROLIFERATIVE SYNDROME ASSOCIATED WITH PIM1 MUTATIONS
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Background: Whole exome sequencing can allow genetic diagnosis in subjects with long lasting clinical stories not supporting any well-defined disorder. A 35-year-old man was referred to ophthalmologist’s evaluation for blurry vision in his left eye. The fundus examination showed choroidal lesions in both eyes. His past medical history was relevant for celiac disease, recurrent episodes of fever and skin rashes with leukocytoclastic vasculitis, inflammatory lesions of the osteoarticular and muscular system, one episode of aseptic meningitis, an intracranial granuloma and two episodes of anterior uveitis. He had also splenomegaly with non-caseating granulomas. Brain TC founded multiple lytic and sclerotic skull lesions. He was diagnosed with atypical sarcoidosis and treated with oral steroid and methotrexate. Laboratory data always showed elevated erythrocyte sedimentation rate, strong positive C-reactive protein and polycyonal gammopathy.

Objectives: To describe functional and genetic data supporting the role of a PIM1 mutation in the multisystemic inflammation and lymphoproliferation of the patient.

Methods: Whole exome sequencing (WES) analysis. Flow-cytometry to evaluate Pim1 expression, Bad phosphorylation (target of Pim1 kinase) and the effect of PIM inhibitor on peripheral blood mononuclear cell (PBMC) viability. RNAseq was on primary fibroblasts from the patient and
from healthy donors. Cloning of the mutated gene in a vector for further functional studies.

Results: WES analysis revealed the de novo heterozygous missense variation c.C1132A (p.H378N) in PIM1 gene. This variation was never described in on-line database and was predicted as damaging by various bioinformatic tools. Preliminary functional investigations in fibroblasts showed normal expression of Pim1, but higher phosphorylation of BAD protein was measured in cells from the patient. Moreover, PBMC from the patient displayed a lower sensitivity to the PIM inhibitor PIM447. RNAseq showed an altered expression profile in genes involved in the extracellular matrix organization.

Conclusion: PIM1 is an oncogene that encodes a protein kinase and, indeed, somatic gain of function mutations can be found in cancers. Preliminary data obtained from our patient suggest a gain of function effect of the p.H378N variant. The lymphoproliferative disorder may be sustained by the anti-apoptotic action of phosphorylated BAD. Recent data correlated hyperactive PIM1 in tumors with high degree of inflammatory infiltration accompanied by NFAT and mTOR activation and IL6 expression. A role of this cytokine also in our patient was coherent with a good clinical response to a treatment with tocilizumab, targeting IL-6.

Although these results are supportive of a role of mutated PIM1 in the observed phenotype, we cannot still claim that this is causative of a novel syndrome. The detection of further cases and functional studies on cells transfected with mutated PIM1 will help shedding more light on this inflammatory and lymphoproliferative disorder.

Disclosure of Interests: None declared


AB1106
PREVALENCE AND EPIDEMIOLOGY OF FAMILIAL MEDITERRANEAN FEVER AND TUMOR NECROSIS FACTORRECEPTOR-ASSOCIATED PERIODIC SYNDROME: RESULTS FROM AN ITALIAN CENTER
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1University of Milan, Postgraduate School of Clinical Pharmacology and Toxicology, Milan, Italy; 2ASST Grande Ospedale Metropolitano Niguarda, Medical Genetics Unit, Department of Laboratory Medicine, Milan, Italy; 3Papa Giovanni XXIII Hospital, Internal Medicine Unit, Bergamo, Italy; 4University of Messina, Rheumatology Unit, Messina, Italy; 5ASST Grande Ospedale Metropolitano Niguarda, Chemical-Clinical Analysis and Microbiology, Department of Laboratory Medicine, Milan, Italy; 6University of Milan, Department of Oncology and Onco-Hematology, Milan, Italy

Background: Familial Mediterranean fever (FMF) and tumor necrosis factor (TNF) receptor-associated periodic syndrome (TRAPS) represent two forms of periodic monogenic autoinflammatory diseases, characterized by recurrent and auto-limiting attacks of fever and systemic inflammation. Both the diseases are due to the aberrant activation of inflammasome platforms. Several variants in the Mediterranean Fever (MEFV) gene and TNF Receptor Superfamily Member 1A (TNFRS1A) gene are respectively at the basis of FMF and TRAPS.

Objectives: The aim of this study is to report the genotype and phenotype prevalence of a cohort of patients referring to our laboratory with a suspicious diagnosis of FMF or TRAPS.

Methods: We retrospectively collected genetic and demographic data of patients undergoing MEFV (NM_000243) and TNFRS1A (NM_001065) genetic test at our laboratory. Both genes were analysed by direct sequencing on both strands. Data were statistically analysed for descriptive and inferential purposes.

Results: A total of 168 cases were collected, most of which were Caucasian subjects (88.0%). The most common clinical manifestation was periodic fever, occurring in 121 cases, with musculoskeletal, intestinal and cutaneous symptoms, polyserositis and lymphadenopathy occurring at variable rates. Several variants in the Mediterranean Fever (MEFV) gene and TNF Receptor Superfamily Member 1A (TNFRS1A) gene were respectively identified in our cohort. The most prevalent variant in the MEFV gene was p.Ala744Ser (37.1%), associated with different geographic provenience and symptoms. According to Eurofever scoring system, the MEFV variant p.Ala744Ser was significantly associated to the likelihood of having FMF and to the severity of the disease. A higher prevalence of MEFV pathogenic variants was observed in Egyptians and patients living in Southern Italy.

Analysis of TNFRS1A gene in 80 subjects revealed the presence of the pathogenic variant p.Cys102Tyr in 3 patients (3.75%).

According to Eurofever scoring system, the MEFV variant p.Ala744Ser was significantly associated to the likelihood of having FMF and to the severity of the disease. A higher prevalence of MEFV pathogenic variants was observed in Egyptians and patients living in Southern Italy.
### COMPLEMENTARY AND ALTERNATIVE MEDICINE USAGE IN PATIENTS WITH FAMILIAL MEDITERRANEAN FEVER

Seda Cokal1, Emre Tekeaga2, Fatma Ilkuc Cinar1, Sedat Yilmaz2, Muhammet Çınar1, 2
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#### Background: Familial Mediterranean Fever (FMF) is the most common hereditary, chronic autoinflammatory disease. Colchicine is the mainstay of treatment, which reduces frequency of attacks and amyloidosis risk. Complementary and alternative medicine (CAM) therapies can be a non-mainstream treatment choice in chronic diseases. Frequency of use of CAM therapies among patients with FMF is not established yet.

#### Objectives: In the current study, we aimed to identify the prevalence of the patients using CAM therapies and the factors associated with CAM usage among the patients with FMF.

#### Methods: One hundred and sixty-five patients were included in the study. Data regarding demographic, social and clinical characteristics were obtained from the patients. The patients were asked whether they were using any type of CAM and if they had suffered harm and/or benefit. The treatment adherence of the patients was assessed using by Morisky Green Levine Scale (MGLS). The Beliefs About Medicines Questionnaire (BMQ-T) was used to assess patient’s beliefs about medicines.

#### Results: Fifty-six (33.9%) patients declared to use at least one CAM. The mean age of the patients was 34.1 ±12.7 years and the mean disease duration was 16.8±10.8 years. The mean dose of colchicine was 1.4±0.4 mg/day. Patients with concomitant disease and positive history of FMF in relatives had higher rates of using of CAM (p=0.011 and p=0.014 respectively). There was no statistically significance between age, sex, marital, socioeconomic and working status, difficulty of access to the treatment center, dose of colchicine, adverse events related to colchicine, attack frequency and disease severity of the patients and frequency of CAM using (p>0.05). The most frequently chosen types of CAM modalities were massage therapy (12.1%), imagining (9.7%), relaxation techniques (9.1%), cupping (9.1%) and natural products (9.1%). It is found that 42 (75.0%) of patients reported that they had suffered benefit from CAM. The mean duration of the using of CAM was 7.9 ±6.4 years. According to the BMQ-T, there was higher rate of concern about colchicine among patients that were using CAM (p=0.035) (Table 1). There was no statistically significance between compliance with colchicine treatment and using of CAM (p=0.313).

#### Conclusion: Colchicine is the gold standard of treatment because of the known effect of colchicine treatment on the severity and frequency of FMF attacks and the risk of development of amyloidosis. Approximately one third of patients with FMF were using at least one of the CAM modalities in the current study. Concerns about colchicine treatment may have increased the tendency to use CAM therapies. On the other hand, patients should be informed that CAM therapies should not be an alternative to colchicine.

#### Disclosure of Interests: None declared


### Coexistence of Sarcoidosis and Chronic Inflammatory Rheumatic Diseases

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#### Background: Sarcoidosis is a systemic granulomatous disease of unknown etiology, mediated by Th1 lymphocytes, characterized by bilateral hilar adenopathies, pulmonary infiltrates, ocular, articular and cutaneous involvement and histologically by noncaseating granulomas. Sarcoidosis can simulate many chronic rheumatic diseases but can also coexist with them, so there are doubts about whether there is a true association or is incidental. Likewise, the occurrence of sarcoidosis has been described as a paradoxical effect during treatment with biological drugs, especially with tumor necrosis factor antagonists possibly due to a dysregulation in the compensatory proinflammatory cascade related of TNF blockade. The association between sarcoidosis and Sjögren’s syndrome, systemic lupus...
Characterization of Patients with Interstitial Pneumonia with Autoimmune Features (IPAF) and Its Comparison with Patients with Scleroderma-Related Interstitial Lung Disease and with Idiopathic Fibrosis

Karen Vergara1, Silvana Saavedra1, Felipe Reyes2, Annelise Goecke1, Caterina Chesta1, Sebastian Chavez2, Hospital Clínico Universidad de Chile, Reumatología, Santiago, Chile; 3Hospital Clínico Universidad de Chile, Neumología, Santiago, Chile; 4Hospital Clínico Universidad de Chile, Medicina Interna, Santiago, Chile; 5Hospital Clínico Universidad de Chile, Medicina Interna, Santiago, Chile, 6Hospital Clínico Universidad de Chile, Medicina Interna, Santiago, Chile, 7Hospital Clínico Universidad de Chile, Medicina Interna, Santiago, Chile

Background: Diffuse parenchymal pulmonary diseases, called interstitial lung diseases, are a heterogeneous group of disorders that are classified together due to clinical, radiographic, physiological or similar pathological manifestations. The diagnosis of idiopathic interstitial pneumonias requires the exclusion of known causes of interstitial pneumonia. Identifying an underlying etiology is important for clinical perspectives because it impacts prognosis and treatment. A recent number of studies has shown that many patients diagnosed as idiopathic interstitial pneumonia have clinical elements that suggest an underlying autoimmune process without meeting established diagnostic criteria for connective tissue disease.

Objectives: Our objectives were characterize the clinical findings of patients who meet the IPAF criteria and compare them with the clinical characteristics of patients with scleroderma-related interstitial lung disease and patients with idiopathic pulmonary fibrosis.

Methods: We retrospectively reviewed 254 patients hospitalized at the Hospital Clínico de La Universidad de Chile between January 2012 and June 2018 who had ICD-10 diagnosis of J.84 (Other respiratory diseases principally affecting the interstitium) and J99.1 (Respiratory disorders in other diffuse connective tissue disorders). The electronic medical record was reviewed retrospectively to extract pertinent data. We applied IPAF criteria to this 254 patients. We then characterized the clinical, serological and morphological features of the IPAF cohort and compared outcomes to other ILD cohorts: scleroderma-related interstitial lung disease and idiopathic pulmonary fibrosis (IPF).

Results: Of 254 patients screened, 17 patients met the IPAF criteria. Mean age was 60 years with a female predominance. The most frequent pattern by high-resolution computed tomography was NSIP present in 72% of the cases. The trend in survival was worse than Scleroderma cohort and better than the IPF cohort. Further prospective studies should be conducted for a more comprehensive evaluation of the evolution of these diseases and the impact of the treatments used.

REFERENCES


Disclosure of Interests: Karen Vergara: None declared, Silvana Saavedra: None declared, Felipe Reyes: None declared, Annelise Goecke Consultant for: Roche, abbvie, novartis, Pfizer, Paid instructor for: Roche, Speakers bureau: Roche, Novartis, Abbvie, Pfizer, Caterina Chesta: None declared, Sebastian Chavez: None declared DOI: 10.1136/annrheumdis-2019-eular.7794
AB1110

AUTOINFLAMMATORY DISORDERS ARE COMMON IN PATIENTS WITH MYELODYSPLASTIC SYNDROME AND LINKED TO KARYOTYPE ABNORMALITY AND SOMATIC MUTATIONS STATUS AND A WORSE PROGNOSIS

Abdulla Watad1, Mark Kacar2, Nicola Luigi Bragazzi2, Qiao Zhou2

Objectives: We tested the hypothesis that autoinflammatory disease is common in MDS cohorts and we further theorised that MDS with somatic mutations and karyotypic abnormalities were associated with autoinflammation.

Methods: 140 MDS patients referred to St. James’s University Hospital in Leeds during the period 2012-2018 were systematically and retrospectively recruited with karyotypes and somatic mutations status being performed. Patients with autoinflammation were classified as well-defined autoinflammatory disease or poorly defined “autoinflammatory state” (non-infection related elevated CRP over 10.0 mg/L in 5 consecutive times, taken at separate occasions based on their final diagnosis and compared in terms of demographic, clinical, laboratory, cytogenetics charts, and outcomes.

Results: The average age was 77.08±11 years (median 79 years), with (n=91, 65.0%) male. 72 (51%) patients had an autoinflammatory state and were younger (75.15±11.23 versus 79.15±11.92, p<0.05), and had more frequent arthritis (n=25, 34.7%, versus n=12, 17.6%, p=0.0225), arthralgia (n=32, 44.4%, versus n=18, 26.5%, p=0.0271), skin rash (n=22, 30.6%, versus n=10, 14.7%, p=0.0261), pleuritis (16, 22.2%, versus n=3, 4.4%, p=0.0022). 26.3% of MDS patients with autoinflammatory state had a well-defined autoinflammatory disorder (neutrophilic dermatosis, and poly-myalgia rheumatic being the commonest). Mutations affecting the transcription factors pathway (NPM1, RUNX1, BCOR, WTI, TP53, MYD88) (OR 3.15 [95%CI 1.04 to 9.56], p=0.0426) and deletion of chromosome 5 and chromosome 7 were independent predictors for well-defined autoinflammatory disorder and poorly-defined autoinflammatory state, respectively. Furthermore, acute leukaemia transformation was more frequent in MDS patients with autoinflammatory status (n=25, 34.7%, versus n=8, 11.8%, p=0.0002).

Conclusion: Both well-defined and poorly defined autoinflammatory diseases are common in MDS. Transcription factors pathway somatic mutations and abnormal karyotype are associated with the risk of autoinflammation. Autoinflammation is linked to a worse prognosis which may be linked to the higher risk of malignant transformation.

Disclosure of Interests: Abdulla Watad: None declared, Mark Kacar: None declared, Nicola Luigi Bragazzi: None declared, Qiao Zhou: None declared, Catherine Cargo: None declared, Jan Taylor: None declared, Eve Roman: None declared, Alexandra Smith: None declared, Richard A. Jones: None declared, Howard Amital: Grant/research support from: Pfizer, AbbVie, Janssen, Grant/research support from: Pfizer, AbbVie, Janssen, Consultant for: Pfizer, Merck Sharp & Dohme, Consultant for: Pfizer, Merck Sharp & Dohme, Speakers bureau: Pfizer, Merck Sharp & Dohme, Janssen, Sanofi, Bristol-Myers Squibb, Abbvie, Neopharm, Speakers bureau: Pfizer, Merck Sharp & Dohme, Janssen, Sanofi, Bristol-Myers Squibb, Abbvie, Neopharm, Sanisa Savic Grant/research support from: Novartis and Sobi, Dennis McGonagle Consultant for: Lilly, Novartis UCB, Speakers bureau: Lilly, Novartis UCB DOI: 10.1136/annrheumdis-2019-eular.2082

Abstract Table 1. Predictors of overall, well-defined or poorly-defined autoinflammatory conditions.

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<thead>
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<th>Predictor</th>
<th>OR</th>
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<th>P-value</th>
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<tbody>
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<td>Overall autoinflammation</td>
<td></td>
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</tr>
<tr>
<td>Genes mutated</td>
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<td>2.67</td>
<td>[95%CI 1.17 to 5.64]</td>
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<tr>
<td>Transcription factors pathway</td>
<td>3.15</td>
<td>[95%CI 1.04 to 9.56]</td>
<td>0.0426</td>
</tr>
<tr>
<td>Deletion chromosome 5</td>
<td>3.37</td>
<td>[95%CI 1.01 to 11.22]</td>
<td>0.0479</td>
</tr>
<tr>
<td>Well-defined autoinflammatory disease</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Genes mutated</td>
<td>3.09</td>
<td>[95%CI 1.19 to 9.46]</td>
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<tr>
<td>Abnormal karyotype</td>
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<tr>
<td>Transcription factors pathway</td>
<td>4.50</td>
<td>[95%CI 1.04 to 19.47]</td>
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<tr>
<td>Deletion chromosome 7</td>
<td>6.13</td>
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</tr>
<tr>
<td>Number of mutations</td>
<td>3.39</td>
<td>[95%CI 1.08 to 10.66]</td>
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<td>Poorly-defined autoinflammatory state</td>
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<tr>
<td>Abnormal karyotype</td>
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<td>[95%CI 1.82 to 5.88]</td>
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<tr>
<td>Deletion chromosome 5</td>
<td>3.57</td>
<td>[95%CI 1.02 to 12.48]</td>
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AB1111

RELATIONSHIP BETWEEN SERUM ADENOSINE DEAMINASE LEVELS AND DISEASE ACTIVITY IN AUTOIMMUNE HEPATITIS

Jing Xie1, Hua Wei1, Xiaoqing Xiang2, 1Dalian Medical University, Dalian, China; 2Northern Jiangsu People’s Hospital, Yangzhou, China

Background: Autoimmune hepatitis (AIH) is a chronic liver inflammation mediated by autoimmune response, characterized by serum autoantibodies, high immunoglobulin G(IgG), and interface hepatitis histology, which can develop into cirrhosis and liver failure. Adenosine deaminase(ADA) is an enzyme involved in purine metabolism, which can catalyze the irreversible conversion from deoxyadenosine to deoxyinosine. As adenosine is an important immunoregulatory factor in the physiological microenvironment, ADA plays an important role in regulating the balance of the human immune system. Previous studies have reported the associations between ADA and disease activity in a variety of autoimmune diseases, such as systemic lupus erythematosus, rheumatoid arthritis and juvenile idiopathic arthritis.

Objectives: To investigate the relationship between serum adenosine deaminase levels and disease activity in patients with autoimmune hepatitis.

Methods: Thirty patients with autoimmune hepatitis and 30 healthy individuals were included in the study. We enrolled 30 patients who met the simplified criteria suggested by the International Autoimmune Hepatitis Group. All of the cases had been diagnosed with AIH between 2013-2018 at Northern Jiangsu People’s Hospital, Department of Gastroenterology or Rheumatology, and the diagnosis was confirmed by liver biopsy. Serum adenosine deaminase levels were measured by enzyme-coupled assay, and >25U/L were determined to be high level 25U/L.

Results: The mean serum ADA levels were significantly higher in AIH patients than those in healthy controls (29.13 ± 8.70 U/L vs 14.50 ± 4.63 U/L, P < 0.001). Serum ADA levels were > 25 U/L in 70% AIH patients and in 0% healthy controls (P < 0.001). Mean serum ADA levels were significantly increased in each stage of disease activity: 26.32 ± 8.78 U/L for mild patients, 31.33 ± 4.23 U/L for moderate patients and
37.20 ± 7.36 U/L for severe patients (P = 0.03). Correlation analysis showed that there was a positive association between serum ADA levels and disease activity (r = 0.43, P = 0.02). Receiver operating characteristic analysis showed that 38.5 U/L was the optimum cut-off point of ADA level for severe disease activity (sensitivity 60%, specificity 92%, area under the curve: 0.81).

Conclusion: The evaluation of serum adenosine deaminase level in patients with autoimmune hepatitis should be considered a useful biomarker in the monitoring of their disease activity.

REFERENCES

Diagnostics and imaging procedures.

AB1113

RELATION BETWEEN RESTRICTIVE PULMONARY FUNCTION TESTS AND ULTRASONOGRAPHIC CHANGES OF ASYMPTOMATIC ANTERIOR CHEST WALL JOINTS IN RHEUMATOID ARTHRITIS PATIENTS

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Background: Ultrasonography can detect different changes in anterior chest wall (ACW) joints in patients with Rheumatoid Arthritis (RA) even before being clinically manifested.1 Pulmonary functions may be affected during the course of RA due to interstitial lung problem or chest wall problem.2 All studies usually demonstrate the interstitial pulmonary affection in RA but the chest wall joints is usually underestimated by the rheumatology community. Up to the best of our knowledge, there are no previous studies about the relationship between ultrasound detected subclinical changes in ACW and the pulmonary functions in RA patients.

Objectives: To detect the relation between ultrasonographic changes of asymptomatic ACW joints and pulmonary function tests (PFTs) in patients with RA.

Methods: The study included 44 subjects (22 RA and 22 control) in whom 88 sternoclavicular joints (SCJ) and 44 manibrusternal joints (MSJ) were studied. None of the participants had a history of respiratory complaints such as dyspnea, chronic cough, or chest pain. High resolution Computed Tomography (HRCT) was done on the chest to exclude interstitial lung problem that may affect chest expansion and PFTs. Ultrasound (US) assessments were performed to detect synovitis, erosions, ankylosis, osteophytes, or Doppler signals. Chest expansion was measured. PFTs were done and included measurement of the forced expiratory volume in 1 s (FEV1), forced vital capacity (FVC), and the ratio of forced expiratory volume in 1 s to the forced vital capacity(FEV1/FVC). In RA group, DAS28 and Health Assessment Questionnaire Disability Index (HAQDI) were recorded.

Results: US detected subclinical changes of ACW joints in (74.2%) of RA patient with significant difference between total US changes in RA (74.2%) and control (21.2%) (p<0.001). MSJ ankylosing and erosions were highly associated with limited chest expansion in RA group (p<0.001). PFTs were found to be restrictive in 13 RA patient (59.1%) with mean of FVC (65.5±5.5%), FEV1 (70.4±9.1%), FEV1/FVC (80.1±2.6) with significant difference to control with mean of FVC (93.6±2.7%), FEV1 (94.3±4.5%), FEV1/FVC (95.3±2.4). These restrictive PFTs were associated with SCJ synovitis (p=0.04), SCJ PD activity (p<0.04), SCJ erosions (p=0.02) and highly associated with MSJ ankylosing and erosions (p=0.001). All RA patients (100%) with MS ankylosing and erosions and SCJ PD activity by US had limited chest expansion and restrictive PFTs. Restrictive PFTs were associated also with limited chest expansion with mean of (2.3±0.5) with significant difference (p=0.001) to non-restrictive PFTs in RA with mean of (5.2±1.4).

Conclusion: Our study demonstrated that ultrasonographic subclinical changes in ACW joints is associated with restrictive pattern of PFTs and limited chest expansion in RA patients.
Disclosure of Interests: None declared


**AB1114**

**CALPROTECTIN IN SERUM AND SYNOVIAL FLUID AS A BIOMARKER IN ACUTE ARTHRITIS**

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**Background:** There are increasingly data about the usefulness of calprotectin levels in chronic inflammatory arthritis and its relationship with prognostic factors. However, few data are available on its role in the diagnosis of acute arthritis.

**Objectives:** To evaluate the possible usefulness of testing plasma and synovial fluid (SF) calprotectin levels as a predictor of the final diagnosis behind an acute mono or oligoarthritis.

**Methods:** Longitudinal observational study. We included non-consecutive patients referred to the rheumatology emergency department with suspected mono or acute oligoarthritis for a period of 23 months. Patients with a previous diagnosis of inflammatory, infectious or neoplastic disease were excluded. All of them underwent diagnostic arthrocentesis and blood extraction simultaneously. The SF was evaluated under optical microscopy immediately for the study of microcrystals. Samples of SF were also routinely sent to microbiological culture, and calprotectin levels (SFC) and cell count were determined. In blood, the calprotectin level (SC), CRP and ESR were determined. The calprotectin level in plasma was determined by an automated fluoroenzyme-immunoassay technique on an ImmunoCAP250 analyzer (Thermo Fisher). All patients were followed until diagnostic confirmation. The statistical analysis was performed with the SPSS 22.0 program.

**Results:** 41 patients were collected, 28 men (68.3%) and 13 women (31.7%) with a mean age of 56.2 years (SD 17.6). The patients presented an average of 6.5 days of symptoms duration (SD 7), manifested as monoarticular in 80.5% of the cases, with the knee being the most frequently affected joint (92.5%). In all patients, SF culture was negative. The most frequent diagnosis was microcrystalline arthritis in 21 patients (13 gout and 8 pseudogout), followed by the forms of onset of different chronic inflammatory arthropathies (9). Another 8 patients presented a mechanical joint effusion, in 1 patient the final diagnosis was not collected and there were 2 patients who presented other diagnoses (viral oligoarthritis, pigmented villonodular synovitis).

Calprotectin values were higher in SF than in serum (mean 73,058 vs 824.75 μg/L). A high positive correlation was found between the SC and the CRP (p<0.05, r=0.7) whereas the correlation with the number of leukocytes in SF (p<0.05, r=0.47) and with the ESR (<0.05, r=0.5) was moderate. The SFC was correlated with the CRP (p<0.05, r=0.45) and with the leukocyte cell count in SF (p<0.05, r=0.6), but not with the ESR. Regarding the different diagnoses, SC was numerically higher in microcrystalline arthritis (1157 μg/L) compared to non-microcrystalline arthritis (862 μg/L), although these differences were not significant due to the low number of patients in each group.

**Conclusion:** Our preliminary results suggest that the analysis of SC could complement the information provided by a conventional analysis in the differential diagnosis of acute arthritis in situations in which an arthrocentesis is not possible. Studies with a greater number of patients and that include patients with septic arthritis are necessary.

**Disclosure of Interests:** Marta Aguilar-Zamora: None declared, L Montolio-Chiva: None declared, Isabel de la Morena Speakers bureau: Abbvie, Celgene, Pfizer, UCB, Ghebro, Roche, Sanofi, Janssen., José María López Ortega: None declared, Carlos Feced Olmos: None declared, Ana V. Crenes Vera: None declared, I Vázquez-Gómez: None declared, Elia Valls-Pascual: None declared, D Ybáñez-García: None declared, À Martínez-Ferrer: None declared, À Sendra-García: None declared, I Torner-Hernández: None declared, V Núñez-Monje: None declared, Juanjo J Alegre-Sancheo: None declared


**AB1115**

**OBESITY AND FLAT VERTEBREAS**

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**Background:** Spine is a mechanical structure, in a young and healthy individual, under a radiological focus, disposes their vertebral bodies in harmony with their stature, and progressively increasing in magnitude from the cervical to the lumbar spine, in a range of vertical growth that it can exceed the horizontal (1).

It is postulated that the important obesity in the early stages of life, could modify the vertebral parameters by skeletal overloads, but the problem is that the current vertebral indexes do not measure a relation of the person height with his vertebra (2).

**Objectives:** Thus, to check whether the childhood obesity could modify the vertebral parameters, or it is accepted that it entails a loss of equivalent stature, and in this case would be necessary a study comparative of average height, or whether the harmony of the individual is accepted, it would be necessary to create an index that combine these variables to objectively if its value is a constant, and thus, eliminate the ambiguity of the observer.

As variables, sex, age, body mass index (BMI), and with a chest lateral plate, not rotated, and in the eighth dorsal vertebra, we calculate his height (LVD8) and his height (HVD8), measured in mm. Figure 1.

Finally, we applied a comparative study of average of height and vertebral index (VI) results: VI = 10 x LVD8/(HVD8 x stature)

**Results:** 90 patients were analyzed. 20 patients in the study group (22.2%): 48.1% female, 48.6 years old, 38.2 BMI, and VI 11.6 Meters-1 and 70 patients in the control group (77.8%): 51.1% females 45.15 yers old, 26.2 BMI, and VI 11.2 Meters-1.

The comparative analysis of averages does not show any significant differences in the index or in the stature of these patients.

**Conclusion:** It is a small study, and according to height or the created index, it does not seem that obesity in development modifies the overall height or the vertebral parameters. In addition, the index gives a stable value regarding the sex of both populations in the eighth dorsal vertebra.

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**Disclosure of Interests:** None declared

AB1116

CORRELATION BETWEEN SERUM RESISTIN AND CAROTID INTIMA-MEDIA THICKNESS AS A MARKER OF SUBCLINICAL Atherosclerosis IN SYSTEMIC LUPUS Erythematosus

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Background: Although SLE management has improved markedly in the last few decades, cardiovascular disease (CVD) is still one of the most important leading cause of death. Subclinical atherosclerosis is increased in patients with SLE and it is not fully explained by traditional cardiovascular risk factors. Evidences suggest that resistin is involved in pathological processes leading to CVD including: inflammation, endothelial dysfunction, thrombosis, angiogenesis and smooth muscle cell dysfunction.

Objectives: to determine the relation between serum resistin level and carotid intima-media thickness by doppler technique as a marker of premature or subclinical atherosclerosis in SLE patients.

Methods: this is a cross-sectional study, carried on thirty Egyptian SLE patients who fulfilled the 2012 Systemic Lupus International Collaborating Clinics (SLICC) criteria. All patients had metabolic syndrome were excluded. Twenty healthy individuals, non smokers, matched for age and sex as controls. All patients were subjected to detailed history taking, a complete clinical examination. Laboratory investigations were done included serum resistin and HOMA was calculated, also the SLE disease activity index (SLEDAI 2K) and SLE disease damage index (SLEDDI) were applied and the scores were estimated. The carotid intima media thickness (CIMT) was assessed by carotid doppler ultrasonography.

Results: There was no statistically significant difference in serum resistin between SLE patients and healthy individuals (p=0.804). As regards the correlation with disease parameters Serum resistin show statistically significant correlation correlation with hs-CRP (r=0.027), HDL (p<0.001), and correlation with disease parameters Serum resistin show statistically significant correlation with SLEDAI 2K and SLEDDI were highest in rheumatoid factor (RF)-positive polyarticular JIA (n=8, 6.67%), followed by systemic JIA (n=3, 3.4%) and oligoarticular JIA (n=3, 2.2%). The sensitivity and specificity of anti-CCP antibodies in all JIA patients were 4.7% and 99.4%.

Conclusion: Anti-CCP antibodies have high specificity for JIA, but its sensitivity is low. Therefore, it can provide additional help for diagnosis of JIA with its high specificity. In particular, anti-CCP antibodies have the highest sensitivity in RF-positive polyarticular JIA than other subgroups, so it can be a more effective diagnostic tool in the subtype.

REFERENCES

Disclosure of Interests: None declared

AB1118

THE ROLE OF ANGIOPOETHIN-LIKE PROTEIN 4 TYPE IN PROGRESSION OF INFLAMMATORY CHANGES IN RHEUMATOID ARTHRITIS

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Background: Angiopoietin-like protein 4 (ANGPTL4) is actively involved in the processes associated with inflammation, angiogenesis and lipid metabolism in rheumatoid arthritis (RA).

Objectives: To study of the effect of ANGPTL4 on the features of the inflammatory process in RA.

Methods: The study included 36 RA patients (aged from 33 to 64 years old), 28 patients with osteoarthritis (OA) aged 48 to 70 years and 14 people with ankylosing spondylitis (AS) aged 39 to 62 years. Levels of ANGPTL4 in serum were determined by the enzyme immunoassay using the commercial test systems «Human Angiopoietin-like Protein 4 ELISA» from «Bio Vendor» (Czech Republic), Serum C-reactive protein (CRP) levels, erythrocyte sedimentation rates (ESR), rheumatoid factor (RF) titers, and anti-cyclic citrullinated peptide antibody (anti-CCP) were also measured in patients with RA.

Results: The following results were obtained: the level of ANGPTL4 was significantly higher in patients with RA than in patients with OA, AS, and healthy individuals (p = 0.04, p = 0.021, p = 0.038, respectively). A strong positive correlation was found between the level of ANGPTL4 and the activity of RA according to DAS28 (r = 0.71, p = 0.002). There is no reliable association between ANGPTL4 and anti-CCP (p> 0.05). The ANGPTL4 level in the serum was correlated with levels of ESR (r = 0.49, p = 0.019, CRP (r = 0.49, p = 0.007) and the Sharp score of radiologic change (r = 0.39, p = 0.045) in RA. Hypervascularization rates were significantly correlated with ANGPTL4 in patients with RA (r = 0.38, p = 0.002) according to Doppler data. ANGPTL4 can activate proliferation processes in the synovial membrane by binding to integrin-ovvl3. Besides,

Disclosure of Interests: None declared

AB1117

DIAGNOSTIC VALUE OF ANTI-CYCLIC CITRULLINATED PEPTIDE ANTIBODIES FOR JUVENILE IDIOPATHIC ARTHRITIS IN KOREA

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Background: Anti-cyclic citrullinated peptide (CCP) antibodies are considered to have specificity for rheumatoid arthritis (RA). However, the diagnostic value of anti-CCP antibody has not been proved in juvenile idiopathic arthritis (JIA).

Objectives: The purpose of this study was to access the prevalence of anti-CCP antibodies in Korean children with JIA, and to investigate the diagnostic accuracy of anti-CCP antibodies according to JIA subgroup.

Methods: JIA patients were recruited from Severance Children’s Hospital, Seoul, Korea from 2004 to 2018. Diagnosis of JIA was made by pediatricians according to the International League of Associations for Rheumatology (ILAR) classification. Control group consisted of healthy children with anti-CCP antibodies test, who had visited the outpatient clinic of the hospital for JIA suspected symptoms, but diagnosed as not JIA. Enzyme-linked immunosorbent assay (ELISA) was used for detection and quantification of anti-CCP antibodies.

Results: Study subjects included 295 JIA patients and 165 controls. Among the JIA children, 14 (8.6%) patients were found to be positive for anti-CCP antibodies. 1 (0.6%) of the control group was positive for anti-CCP antibodies. The prevalence rates of anti-CCP were highest in rheumatoid factor (RF)-positive polyarticular JIA (n=8, 66.7%), followed by systemic JIA (n=3, 3.4%) and oligoarticular JIA (n=3, 2.2%). The sensitivity and specificity of anti-CCP antibodies in all JIA patients were 4.7% and 99.4%.

Conclusion: Anti-CCP antibodies have high specificity for JIA, but its sensitivity is low. Therefore, it can provide additional help for diagnosis of JIA with its high specificity. In particular, anti-CCP antibodies have the highest sensitivity in RF-positive polyarticular JIA than other subgroups, so it can be a more effective diagnostic tool in the subtype.
Disclosure of Interests: None declared


AB1119 THE PRESENCE OF SYNOVITIS IS THE MAIN FACTOR INFLUENCING THE DEVELOPMENT OF PAIN SYNDROME IN ARTHRITIS OF THE KNEE Joint

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Background: Dysfunctions and pain syndrome in lesions of the knee joint can significantly discomfort a sick person and lead to a persistent decrease in physical activity and disability. Often pain syndrome precedes radiographic appearance of the structural changes in the joint and is accompanied by an increase in number of different changes in the synovium according to ultrasound investigation.

Objectives: To investigate the clinical significance of ultrasound criteria of changes in the synovial membrane of the knee joint cavity and its role in the assessment of pain in gonarthrosis.

Methods: 30 people aged 30 to 50 years with osteoarthritis of the knee joint were under observation; assessment of the severity of pain in the knee when walking was at least 40 mm on a visual analogue scale (VAS). Ultrasound examination of the knee joint was carried out according to standard procedure using a linear sensor with a frequency of 0.5, 12 MHz in an ultrasonic diagnosis system Accuvix V10 (Samsung Medison, Korea).

Results: The evaluation of ultrasound changes was performed in the upper inversion of the knee joint according to the following criteria: the severity of intraarticular effusion, synovial proliferation, local vascularization of the synovial membrane by power doppler. All patients were divided into three groups, according to the severity of pain in the knee joint: group I (12 people) - 41–59 mm, group II (10 people) - 60–79 mm, group III (8 people) - 80–100 mm on the VAS scale. By comparing changes in the knee joint by ultrasound data in patients of different groups, the following results were obtained: group I: severity of intraarticular effusion - 10 people (minimal changes in 60%, moderate in 20%, expressed in 20%), synovial proliferation - 4 people (moderate changes in 50%, expressed in 50%), local vascularization of synovium - 6 people (minimal changes in 66.7%, moderate in 16.7%, expressed in 16.6%); group II: severity of intraarticular effusion - 9 people (55.6%, 22.2% and 22.2%), synovial proliferation - 3 people (0%, 33.3% and 66.7%), local vascularization of the synovial membrane - 4 people (25%, 25% and 50%, respectively); group III: severity of intraarticular effusion - 8 people (62.5%, 12.5% and 25%), synovial proliferation - 5 people (20%, 40% and 40%), local vascularization of the synovial membrane - 3 people (per 33.3%, respectively).

Conclusion: The use of ultrasound in the diagnosis of diseases of the knee joints allows to reliably determine the structural and functional changes in all components of the knee joint. The severity of pain in gonarthrosis is most associated with the presence of synovitis in the joint.

Disclosure of Interests: None declared


AB1121 EFFICACY AND SAFETY OF ULTRASOUND GUIDED ASPIRATION AND INTRA-LESIONAL CORTICOSTEROIDS INJECTION OF RUPTURED BAKER CYST

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Background: Baker’s cyst is the most common mass in the popliteal fossa and results from fluid distension of the gastrocnemio-semimembranosus bursa. The most common complication of Baker’s cyst is the rupture or dissection of fluid into the adjacent proximal gastrocnemius muscle belly, which results in a pseudothrombophlebitis syndrome mimicking symptoms of DVT. Treatment of ruptured Baker cysts ranged from conservative management to surgical resection.

Ultrasound guided aspiration and corticosteroids injection may be an effective and easy method of management of these cases. Up to the best of our knowledge, this is the first study to detect the efficacy and safety of ultrasonographic guided aspiration and injections of ruptured Baker cysts.

Objectives: To evaluate the efficacy and safety of ultrasonographic guided aspiration and local corticosteroids of ruptured Baker cysts based on follow-up clinical and sonographic results.

Methods: A retrospective study was conducted on 42 patients (12 males and 30 females, mean age 36 +/- 10 SD years) affected by a ruptured Baker cysts associated to knee joint disorders in the period between January 2013 to January 2019. The diagnosis was done by clinical presentation of acute calf pain, swelling, tenderness at the calf muscles and ultrasonographic evidences of ruptured backer cysts in the form of free fluid collection in the calf connected to a well defined cyst at the back of knee. All cases were treated by ultrasonographic guided aspiration and intralesional injection of corticosteroids once or twice one week a part. Follow up were done on a weekly basis until complete resolution of symptoms then 3 months later. Visual analogue scale (VAS) for calf pain and Rauschning-Lindgren and Lysholm Knee Scoring Scales were used to assess pre/post-injection knee functions.

Results: The primary diagnoses to patients presented with ruptured Baker cyst in this study were as follow: 18 (42.8%) cases with rheumatoid

Disclosure of Interests: None declared


AB1120 DIAGNOSTIC ROLE OF NEUROMUSCULAR ULTRASOUND IN CUBITAL TUNNEL SYNDROME

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Background: Cubital tunnel syndrome (CuTS) is the second most common compressive neuropathy of the upper limb following carpal tunnel syndrome and is the most common site for entrapment for the ulnar nerve.

Objectives: Our aim is to evaluate the role of ultrasonography (US) as a diagnostic tool for Cubital tunnel syndrome (CuTS) in comparison with nerve conduction study (NCS).

Methods: twenty elbows with CuTS and twenty asymptomatic controls were assessed by NCS and underwent ultrasonography of elbows. Data from patients and controls were compared to determine the diagnostic relations in patients with CuTS and the grade of severity

Results: There was a high degree of correlation between NCS of the ulnar nerve, clinical parameters and variable US measurements. The CSA of the ulnar nerve was the most sensitive parameter and a cut-off point of 9.5 mm2 behind medial epicondyle was found to be 100% sensitive and 80% specific. The ulnar nerve ratio (UNR) had a diagnostic accuracy of 95% with 85% specificity.

Conclusion: Ultrasonographic measurements of the ulnar nerve CSA and UNR have a comparable diagnostic value as a non-invasive and an alternative modality for the evaluation of CuTS

Disclosure of Interests: None declared

REFERENCES


arthritis, 15 (37.5%) cases with osteoarthritis and 9 (21.4%) cases with psoriatic arthritis.
Clinical parameters (VAS for calf pain and Rauschning-Lindgren score) improved significantly in all patients at both post injection evaluation visits. Rauschning-Lindgren score was significantly lower after US guided injections (mean, 0; range, 0-1) than at baseline (mean, 2; range, 1–2); \( p < 0.001 \) (table1).
VAS for calf pain also significantly lower after US guided injections (mean,0.5; range, 0-1) than at baseline (mean, 9.5; range, 0-10); \( p < 0.001 \).
Ultrasoundographic features improved significantly with complete disappearance of free fluid at the calf in 35 (83.3%) cases one week after the injection.
As regards Baker cyst only 5 (11%) cases showed complete disappearance of the backer cyst and in the majority of cases 37 (88%) there were persistent Baker cysts.
No side effects were reported in all cases.

### AB1121 Table 1. Clinical results of Baker cyst excision (Rauschning and Lindgren scale and VAS for calf pain)

<table>
<thead>
<tr>
<th></th>
<th>Pre injection</th>
<th>1 week later</th>
<th>3 months later</th>
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<tr>
<td>grade 0</td>
<td>0</td>
<td>30</td>
<td>39</td>
</tr>
<tr>
<td>Grade 1</td>
<td>0</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>Grade 2</td>
<td>6</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Grade3</td>
<td>36</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>VAS for calf pain</td>
<td>9.5</td>
<td>1.5</td>
<td>0.5</td>
</tr>
</tbody>
</table>

VAS: visual analogue scale

**Conclusion:** Ultrasoundographic guided aspiration and intra_lesional corticosteroids injection is an effective and safe method in management of ruptured Baker cysts.

### REFERENCES


**Disclosure of Interests:** None declared

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**AB1122**

### PREDICTION OF THE UTILITY OF ULTRASOUND EVALUATION IN RHEUMATOID ARTHRITIS BY THE CLINICAL FACTORS


**Background:** It is known that ultrasound detects synovitis with higher sensitivity than physical examination in rheumatoid arthritis (RA), and the residual inflammation detected by ultrasound even in the patient achieving clinically remission well correlates with progression of erosion. It is impossible to perform ultrasound evaluation on all the joints in all the patients in terms of time and human resource. Therefore, ultrasound use in RA should be more focused on situations when the physical findings and ultrasound findings likely to dissociate.

**Objectives:** To investigate the factors that can predict dissociation between clinical and ultrasound-detected synovitis in the patient with rheumatoid arthritis.

**Methods:** Patients aged 18 years or older who satisfied ACR/EULAR 2010 criteria who visited St. Luke’s International Hospital from June 1, 2018 to November 9, 2018 and were performed ultrasound on PIP, MCP, and wrist joint. We retrospectively reviewed the electronic medical chart and ultrasound data, and analyzed the dissociation of clinical synovitis defined as existence of swelling or tenderness and ultrasound-detected synovitis defined as both of power doppler grade and gray scale grade 1 or gray scale grade 2. Clinical evaluation was done by the attending physician who ordered the ultrasound evaluation. Ultrasound evaluation was done using standard scan technic by the sonographers who are blinded to the clinical evaluation.

The correlation between patient’s characteristics and dissociation was analyzed using \( \chi^2 \) test, Mann-Whitney U test and logistic regression analysis.

**Results:** 51 joints in 32 patients (4 males, 28 females) were included in the study. Among the 32 patients, 18 was classified in the dissociation group (DG) and 14 in the non-dissociated group (NDG). No significant difference was observed in the patient’s characteristics of DG and NDG. In the univariate analysis, the absence of swelling in the target joint had tendency to be the risk of dissociation. The same tendency was preserved in the multivariate analysis with the presence of tenderness in the target joint assigned as a covariate (OR 3.68, 95% CI = 0.85 - 15.90, \( p < 0.08 \)).

**Conclusion:** There was a numerical tendency that no swelling on the joint is a risk factor for the dissociation between clinical synovitis and ultrasound-detected synovitis. Future study with increased number of participants may identify more sensitive risk factors for dissociation, and enable to make an effective indication of ultrasound evaluation in the care of RA.

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**Disclosure of Interests:** Takahiro Asano: None declared, Masei Suda: None declared, Ryo Rokutanda: None declared, Haruyuki Yanaoka: None declared, Sho Fukui: None declared, Haruki Sawada: None declared, Yukihiko Ikeda: None declared, Ayako Koido: None declared, Rui Imai: None declared, Hisanori Shimizu: None declared, Hiromichi Tamaki: None declared, Tokutaro Tsuda: None declared, Mitsumasa Kishimoto Consultant for: Kyowa Hakko Kirin Co., Ltd., Kenichi Yamaguchi: None declared, Haruyuki Yanaoka: None declared, Masato Okada: None declared

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**AB1123**

### SHOULDER PAIN: ARE THERE PREDICTIVE FACTORS OF RESPONSE TO TREATMENT AND OF ULTRASOUND FINDINGS?

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**Background:** Shoulder pain is a common cause of consultation in Primary Health Care, and may correspond to up to 30% of the reasons for consultation. Pathology of the rotator cuff is the most common cause of pain. Ultrasound is a valuable diagnostic tool in assessing shoulder disorders; it can be as effective as magnetic resonance imaging.

**Objectives:** To determine the predictive factors of response to treatment and ultrasound findings in shoulder pain.

**Methods:** We performed an analysis of the patients’ cases sent to rheumatology consultation with shoulder pain, every patients had an echography shoulder evaluation, and the rheumatologist decided treatment based on the guidelines for the treatment of shoulder tendinopathies. The use of nonsteroidal anti-inflammatory drug (NSAIDs) and muscle relaxant medications as well as the following techniques: corticosteroids local injection, barbotage, capsular distension and physiotherapy programs were some of the variables assessed. Posteriorly, the patients were clinically assessed in a follow-up visit.

**Results:** A total of 119 patients were evaluated. Men presented a higher risk of distension of the subscapular bursa. There was a statistically significant relationship between the time from the beginning of the symptomatic and treatment response. Diabetes mellitus, arterial hypertension and dyslipidemia were statistically significantly associated with some rotator cuff lesions and distention of the subscapular bursa.

**Conclusion:** In patients with shoulder pain, early intervention positively influences the response to treatment. Thus, it is important that these patients are evaluated more promptly. Some comorbidities seem to be associated with a higher risk of specific rotator cuff lesions.

**No relationship was found between response to treatment and age, sex, occupation, previous treatments or type of therapy selected. The association found in this study seem to have clinical implications. Prevention of rotator cuff disease is a matter of major relevance as well as early institution of treatment.**
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[10] Aisha Ben Tekaya1, Lobna Ben Ammar 1, Olfa Saidane1, Rawdha Tekaya1, Mohammed Ben Hammania2, Ines Mahmoud3, Leila Abdelmoula1, 1Charles Nicolle Hospital, Rheumatology, Tunis, Tunisia; 2Charles Nicolle Hospital, Cardiovascular Surgery, Tunis, Tunisia

Background: Spondylodiscitis is a potentially life-threatening infection burdened by high morbidity rates. MRI remains the key examination in the diagnosis of infectious spondylodiscitis. The microbiological diagnosis is the main driver for successful treatment.

Objectives: To evaluate the MRI characteristics associated with the detection of microbial pathogens by computed tomography (CT) guided biopsy in case of suspicion of infectious spondylodiscitis.

Methods: Retrospective study including all patients hospitalized in our department between 1999 and 2019 who underwent CT and/or MRI-guided biopsy (CT-guided biopsy + CT). The CT-guided biopsy was performed in 92 patients, including 53 men and 39 women, aged 16-86 years (mean age 56 years; 16-86 years). The median delay of consultation was 3 months. Inflammatory back pain was reported in 78% of cases. Neurologic deficiency was noticed in 19.5% of cases. The lumbar spine was involved more than 50% of cases. Spinal MRI was performed to all patients and showed paravertebral abscess in 64.6%, epidural abscesses in 62.1%, intradiscal abscesses in 3.6%, spinal cord compression 10.9%, and vertebral osteolysis in 6.09% of cases. The causative microorganism was mycobacterium tuberculosis in 53.6%, brucella in 24.3%, and pyogenic germs in 15.8% of cases. The presence of spinal cord compression, intradiscal abscess and vertebral osteolysis was more frequent in group 2, but with no statistically significant difference (p = 0.65, 1 and 0.56, respectively). In addition, there was no significant difference in the presence of paravertebral abscesses and epiduritis (p = 0.41 and 0.53, respectively).

Conclusion: Spondylodiscitis is an emergency which must be diagnosed on time to avoid life threatening complications, neurological sequelae and spinal deformities.

Disclosure of Interests: None declared

Results: The “before” ultrasounds were performed between 2012 and 2016 and the “after” ultrasounds between 2015 and 2018. The time fashion between the two ultrasounds for each patient was 2 years. Thirty-three subjects were included, with an average age of 47.5 SD 7.6 years. Proportion of women 66.6%. Proportion of dominant shoulders (51.1%). As shown in table 1, the most significant changes were the thickness of the tendon measured at the height of the middle of the longitudinal axis of the TSE had been previously diagnosed in an ultrasound study. DEMographic data and static images from the ultrasound studies of each patient were compared. The explanatory variable was time (before-after) and the response variables in image were: (1) Increased tendon thickness measured at 30mm from the deep edge of the acromion (GRO- SORB), (2) Increased tendon thickness measured at the height of the middle of the longitudinal axis of the calcification (GROSORC), (3) Longitudinal axis of the calcification (LONGC), (4) Thickness or height of the calcification, when this was measurable (ALTC), and (5) Distance between the calcification and the deep end of the acromion (DISTC). In addition, two indices were determined: (a) Increased tendon thickness in the calcification zone (GROSORC/GROSORB) and (b) proportion of tendon thickness occupied by calcification (ALTC/GRO- GOSC). The measurements were carried out using the software of the equipment in which the original and subsequent study was made (GE Logiq e; Toshiba Nemo XG).

Variables measured by ultrasound measurement Before measurements After measurements t Student (paired data)

Conclusion: The most important factor that explains the development of an SS associated with calcification is the increase in tendon thickness at the height of the calcification itself and, at the same time, this measure increases when the calcification is more lateralized and the more elongated its longitudinal diameter. These modifications could have implications when deciding the therapeutic management of these processes.

Disclosure of Interests: None declared


AB1127 ULTRASOUND INTER-READER RELIABILITY OF INFLAMMATORY FINDINGS IN PATIENTS WITH POLYARTHRITIS

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Background: Ultrasonography is an imaging technique that allows rheumatologists to visualise structural and inflammatory changes within a joint. Objectives: The objective of this study was to assess the inter-reader reliability of interpretation of inflammatory and destructive changes in a wide range of joints in patients with polyarthritides.

Methods: This study was divided in two parts: 1) consensus process and 2) reliability exercise. For the first part, a written questionnaire was sent by email to 6 sonographers from 3 portuguese hospitals with the highest level of competence (EULAR competency assessment level 2). The questionnaire included 17 questions divided in two groups: 1) elementary components in B-mode and Doppler assessment (effusion, synovial hypertrophy (SH), power Doppler (PD), erosions and synovitis definition) and 2) approach at the joint level (the definition of which plan and recess will be assessed in each joint). The participants were asked to rate their level of agreement/disagreement for each statement using a 1-5 Likert scale (1=strongly disagree to 5=strongly agree). For the reliability exercise, video clips of US examinations of 40 joints (wrist, metacarpophalangeal (MCP) from 1 to 5, elbow and shoulder) and metatarsophalangeal (MTP) joints from 1 to 5, knee, tibiotarsal (TT) and metatarsalphalangeal (MTP) joints from 1 to 5, elbow and shoulder) from each of 15 patients were collected (showing a multiplanar bilateral ultrasound approach). Each joint in each video was scored by individual ultrasonographers for the presence/absence of elementary components: effusion (Yes/No), SH (No/Grade 1 to 3), PD (No/ Grade 1 to 3) and erosions (Yes/No). Inter-reader agreement analysis was assessed through Fleiss’ kappa coefficient and classified according to Landis and Koch[8]: κ values ≤ 0 were considered poor, 0.20 slight, 0.21-0.40 fair, 0.41-0.60 moderate, 0.61-0.80 good and 0.81-1.00 excellent. Statistical significance was defined as p<0.05. Statistical analysis was performed using STATA V.14.

Results: Thirty seven joints of the 600 joints were excluded due to dislocation of the joint or presence of objects (rings/catheters) and the videos of a total of 563 joints were analysed by the 6 ultrasound experts. Inter-reader agreement was superior for TT joints and inferior for wrist; the identification of the erosions had the better agreement in the elementary components (Table 1).

Table 1. Inter-observer agreement for each elementary component and for anatomical region

<table>
<thead>
<tr>
<th>Elementary component</th>
<th>Joint</th>
<th>Joint</th>
<th>Joint</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effusion</td>
<td>0.6044</td>
<td>Wrist</td>
<td>0.6767</td>
</tr>
<tr>
<td>Synovial</td>
<td>0.6291</td>
<td>MCP</td>
<td>0.6866</td>
</tr>
<tr>
<td>Hypertrophy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Power doppler</td>
<td>0.7195</td>
<td>PIP</td>
<td>0.7107</td>
</tr>
<tr>
<td>Erosions</td>
<td>0.7314</td>
<td>Elbow</td>
<td>0.7291</td>
</tr>
</tbody>
</table>

MCP - Metacarpophalangeal joints, MTP – Metatarsophalangeal joints, PIP - Proximal interlephalangeal joints, TT-Tibial joint. All p<0.05.

Conclusion: The reliability of interpretation of inflammatory and destructive changes using video clips was in general good to excellent and it was better for erosions and tibiotarsal joint (regarding elementary component and anatomical region, respectively).

Disclosure of Interests: None declared
SENSITIVITY AND SPECIFICITY OF THE AUTOMATED SQUEEZE TEST (GAENSLEN’S MANEUVER) FOR IDENTIFYING METACARPOPHALANGEAL SYNOVITIS BY MAGNETIC RESONANCE IMAGING

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Background: It is well known that an early diagnosis and treatment for Rheumatoid Arthritis (RA) prevents its complications, therefore there are many efforts to identify individuals at risk to develop RA. The Squeeze test has been used to detect synovitis in metacarpophalangeal joints, even though it is used in daily practice, there is a great variability in their performance among rheumatologists. [2]

Objectives: The aim of this study is to determine the diagnostic performance of the automated squeeze test (AST) on the metacarpophalangeal (MCP) joints to detect the presence of synovitis, edema, or erosions by magnetic resonance imaging (MRI) using the rheumatoid arthritis magnetic resonance imaging score (RAMRIS) in first-degree relatives (FDR) of RA patients, of whom clinically suspect arthralgia (CSA) in hands was suspected, as well as in RA patients.

Methods: It is an observational and cross-sectional study for a diagnostic test. A total of 60 patients, older than 18 years, were included and divided in three groups: CSA group, 22 with less than 1 year with arthralgia and required to be FDR of RA patients; early RA group: 22 patients who met ACR/EULAR 2010 Classification Criteria with less than 1 year with the disease; and late RA group: 16 patients who met ACR/EULAR 2010 Classification Criteria, with more than 1 year with the disease. The AST was performed in the 60 participants’ dominant hand. The device was evaluated by MRI, which examined the same hand in the 60 patients.

Results: A total of 240 MCP joints were evaluated. The AUC for the total RAMRIS score >10 was [0.480 (95% CI 0.301-0.617) P=0.597]; for synovitis RAMRIS score >7 was [0.459 (95% CI 0.331-0.669) P=0.791]; and for the presence of any synovitis by RAMRIS was [0.575 (95% CI 0.428-0.723) P=0.331]. For the RAMRIS synovitis score, the most sensitive and specific cut-off of the force by AST was 4.645 kg with a 66.7%-sensitivity and 50% specificity.

Disclosure of Interests: None declared


ULTRASOUND MEASUREMENT OF MUSCLE THICKNESS AT THE PROXIMAL FOREARM: VALIDITY ISSUES

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Background: The term sarcopenia defines the muscle strength loss and muscle mass loss due to aging, and it is one out of three criteria for the diagnosis of frailty in the elderly. A number of studies have related the handgrip strength with muscle thickness (MT) in the forearm measured by ultrasound (US)1, but a standardized scanning protocol has not been described and its interobserver reliability has not been investigated yet.

Objectives: The aims of this study were to provide detailed description of the scanning protocol to measure the MT in the forearm and to test its feasibility and interobserver reliability.

Methods: A total of 27 consecutive subjects were enrolled at Ospedale “Carlo Urbanii”, in Jesi (Ancona, Italy): 2 healthy volunteers recruited from among our staff, and 25 patients referred to the Rheumatology Department affected by rheumatoid arthritis (5), psoriatic arthritis (4), spondyloarthritides (3), polymyalgia rheumatica (3), systemic sclerosis (1), overlap SLE/SSc (1), Sjögren syndrome (1), anti-synthetase syndrome (1), undifferentiated connective tissue disease (1), osteoporosis (1), small vessels vasculitides (2) and fibromyalgia (2). The female to male ratio was 19:27, the mean age was 52.1 years (SD ±13.7), and the mean Body Mass Index was 27.4 Kg/m2 (SD ±4.2). Four rheumatologists (SC, EC, GS, EF) trained in musculoskeletal US, with a different degree of expertise, performed the examinations using a MyLab ClassC (Esaote SpA) equipped with a broadband linear probe (frequency range 4-13 MHz). All subjects sat in front of the sonographer with their hands supinated and the forearm resting on the examining table. First, the coronoid process was imaged according to the “longitudinal scan of the coronoid recess” as indicated by the 2017 EULAR US guidelines. Then the probe was moved distally following bony cortex until the ulnar tuberosity was identified. Immediately distally to the ulnar tuberosity the bone turns flat and hyperechoic and this was taken as the anatomical reference for the measurement. Afterwards the probe orientation was changed to obtain a transverse view. During the rotation, the proximal third of the diaphysis of the radius was imaged. Two MT were measured, the ulnar MT (UMT) and the radial MT (RMT), between the subcutaneous tissue-muscle interface and the muscle-bone interface of each bone respectively. The measurement of UMT and RMT of both arms were registered, as well as the scanning time of all the examiners.

Results: We found an excellent interobserver reliability of this scanning protocol, with and interclass correlation coefficient (ICC) among the four sonographers of 0.975 (CI 0.955 - 0.987) for the right UMT, an ICC of 0.968 (CI 0.942 - 0.984) for the left UMT, an ICC of 0.932 (CI 0.878 - 0.966) for the right RMT and an ICC of 0.949 (CI 0.908 - 0.974) for the left RMT. The mean time required to acquire all measurements in each subject was less than five minutes (SC 4.4 min; EC 4 min; GS 4.2 min; EF 4.5 min).

Conclusion: The results of this study provide evidence in favour of both feasibility and interobserver reliability of US measurement of the forearm MT.

Disclosure of Interests: Sonia Castell: None declared, Gianluca Smerilli: None declared, Edoardio Cipolletta: None declared, Fausto Salafi Grant/ research support: from Abbvie, Roche, Novartis, BMS, Pfizer, Sanofi, Speakers bureau: Abbvie, Roche, Novartis, Pfizer, Sanofi, BMS, Emilio Filippucci: None declared, Walter Grassi: None declared

Disclosure of Interests: None declared

RELIABILITY OF ULTRASOUND MEASUREMENT OF HYALINE CARTILAGE THICKNESS IN RHEUMATOID ARTHRITIS

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Background: Only few studies investigated the role of ultrasound (US) in the assessment of hyaline cartilage in rheumatoid arthritis (RA).

Recently, a positive correlation was found between the US measurement of the metacarpal head cartilage thickness (MCT) and both the anatomical MCT and the radiographic joint space width1.

Objectives: To evaluate inter- and intra-observer reliability in the assessment of MCT in RA patients and healthy subjects; to compare the agreement of the sonographers in the assessment of the MCT using different methods (i.e. semiquantitative and quantitative); to determine the inter-observer smallest detectable difference (SDD) of MCT measured by US.

Methods: US assessment was performed by two rheumatologists on 160 metacarpophalangeal (MCP) joints of 10 healthy subjects and 10 patients with RA (according to 2010 ACR/EULAR classification criteria) using a MyLab Twice (Esaote Biomedica, Genoa, Italy) equipped with a linear very high frequency probe (i.e. 10-22 MHz).

To assess inter-observer reliability, the hyaline cartilage of metacarpal head from II to V digits of both hands were examined independently on the same day by two rheumatologists (an experienced musculoskeletal sonographer and an investigator with limited US training).

To assess intra-observer reliability, all the subjects were rescanned using the same scanning protocol and the same US setting by one sonographer after a week.

Hands were scanned with the MCP joints in maximal flexion (approximately 90°). The hyaline cartilage of all the metacarpal heads was scanned in longitudinal and transverse views in the central portion of the metacarpal head. Particular attention was paid on maintaining the probe in a position providing an angle of 90° between the direction of the US beam and the cartilage surface2.

MCT was scored both semi-quantitatively (using a five-grade scoring system3) and quantitatively (using the average value of the longitudinal and transverse measurements).

The inter- and intra-observer agreements for assessing the MCT with the semiquantitative scoring system were calculated using Cohen’s kappa and interpreted according to Landis and Koch.

The inter- and intra-observer agreements for assessing the MCT with the quantitative scoring system were calculated using intraclass correlation coefficients (ICC) and their 95% confidence intervals (95%CI).

The SDD was determined using Bland-Altmann 95% limits of agreement method.

Results: The inter- and intra-observer agreements for the semiquantitative assessment of the MCT were moderate [κ=0.59 (95% CI: 0.35-0.83) and κ=0.63 (95% CI: 0.39-0.87), respectively].

Considering all the measurements, a substantial inter-observer [ICC= 0.88 (95% CI: 0.82-0.92)] and intra-observer [ICC= 0.88 (95% CI: 0.87-0.94)] agreements for the quantitative assessment of MCT were found.

The SDD of the MCT measurement was: 0.11 mm for both longitudinal and transverse scans and 0.09 mm for the average of the two measures.

Conclusion: This study provides evidence in favor of the reliability of semiquantitative and quantitative US methods for assessing MCT in RA.

Further studies are required to determine standard reference values of MCT by US in healthy subjects.

REFERENCES


Disclosure of Interests: None declared


HIGH-RESOLUTION ULTRASOUND ASSESSMENT OF CARTILAGE THINNING IN RHEUMATOID ARTHRITIS

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Background: Conventional radiography is the standard imaging modality to detect joint damage in rheumatoid arthritis (RA). Ultrasound (US) allows for a direct visualization of hyaline cartilage. To date, only few studies investigated the role of US in the assessment of cartilage damage in RA.

Objectives: To compare US qualitative and quantitative assessments of cartilage thinning at metacarpal head (MH) in RA patients and in an age-, sex- and height-matched healthy controls (H). To correlate cartilage damage and clinical parameters in RA.

Methods: US examination was performed on 318 metacarpophalangeal (MCP) joints of 40 consecutive RA patients and on 320 MCP joints of 40 age-, height- and sex-matched H using a MyLab Twice (Esaote Biomedica, Genoa, Italy), equipped with a high frequency linear probe (up to 22 MHz).

RA patients were enrolled according to the 2010 RA classification criteria. The hyaline cartilage of MH from II to V digits of both hands was examined with the MCP joints in maximal flexion.

Each MH was scanned in longitudinal and transverse views. Particular attention was paid on maintaining the probe in a position providing an angle of 90° between the direction of the US beam and the cartilage surface.

Cartilage thickness (CT) was assessed both semi-quantitatively (using a reliable qualitative five-grade scoring system3) and quantitatively (using the mean value of longitudinal and transverse measurements of the CT). Finally, association between cartilage damage and clinical parameters was assessed.

Results: Semiquantitative score: Cartilage thinning (grade 2, 3 and 4) was found in at least one MH in 23 RA patients (57.5%) and in 4 H (10.0%) (p<0.01). A significantly higher prevalence of cartilage damage (grade 2, 3 and 4) at joint level was found in RA patients (86 MCP joints, 27.0%) in comparison with H (13 MCP joints, 4.1%) (p<0.01).

Quantitative assessment: CT of the MH ranged from 0.0 to 1.10 mm (0.60±0.26 mm, mean±SD) in RA patients and from 0.41 to 1.08 mm (0.67±0.12 mm, mean±SD) in H. Male had a thicker hyaline cartilage than female, both in RA patients (p<0.01) and in H (p<0.01). No significant difference was found between left and right side, both for RA patients (p=0.48) and healthy subjects (p=0.94).

Detailed quantitative measurements of CT of MH are reported in table 2.

Abstract AB1131 Table 2. US cartilage thickness measurement for each digit in RA patients and healthy controls.

<table>
<thead>
<tr>
<th>RA patients</th>
<th>Healthy subjects</th>
<th>Mean difference, 95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=39)</td>
<td>(n=40)</td>
<td>(mm)</td>
<td></td>
</tr>
<tr>
<td>II MH</td>
<td>0.62</td>
<td>0.75</td>
<td>0.13; 0.06-0.21</td>
</tr>
<tr>
<td>III MH</td>
<td>0.57</td>
<td>0.64</td>
<td>0.07; 0.02-0.13</td>
</tr>
<tr>
<td>IV</td>
<td>0.61</td>
<td>0.64</td>
<td>0.03; 0.03-0.09</td>
</tr>
<tr>
<td>MH</td>
<td>0.62</td>
<td>0.65</td>
<td>0.03; 0.02-0.09</td>
</tr>
<tr>
<td>Sum</td>
<td>2.43</td>
<td>2.68</td>
<td>0.25; 0.03-0.48</td>
</tr>
</tbody>
</table>

95% CI: 95% confidence interval; L: left; MH: metacarpal head; R: right; RA: rheumatoid arthritis; SD: standard deviation; US: ultrasound.

A significant association was found between the CT value and age (r=0.528, p<0.001), disease duration (r=0.376, p=0.005) and grade of the semiquantitative scoring system (r=0.80, p<0.001). No association was found between CT and BMI, weight, ACPA positivity and RF positivity.

Conclusion: This study demonstrated that a significantly higher prevalence of cartilage damage was found in RA patients using both the semiquantitative score and the quantitative assessment. In particular, in RA patients the hyaline cartilage of II and III MH is thinner in comparison with H. Finally, a significant association was found between the CT values and disease duration and age.

REFERENCES

Disclosure of Interests: Edoardo Cipolletta: None declared, Emilio Filippucci: None declared, Andrea Di Matteo: None declared, Marco Di Carlo: None declared, Fausto Salaffi Grant/research support from: Abbvie, Roche, Novartis, BMS, Pfizer, Sanofi, Speakers bureau: Abbvie, Roche, Novartis, Pfizer, Sanofi, BMS, Walter Grassi: None declared

THE ROLE OF PET/CT IN THE MANAGEMENT OF GIANT CELL ARTERITIS
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Background: Giant cell arteritis (GCA) is a large vessel vasculitis that affects the aorta and/or its major branches including the superficial temporal artery. Together to cranial symptoms such as headache and visual disturbances, extra cranial manifestations have been widely reported, sometimes as unique clinical presentation. Several imaging modalities are available to evaluate aortic involvement including fluorodeoxyglucose (FDG) positron emission tomography (PET), however there are few reports that analyzed the impact of the findings of this advanced imaging in predicting outcomes of the disease.

Objectives: To assess the utility of PET in disease extension assessment to predict, together to clinical manifestations, the disease evolution.

Methods: We retrospectively reviewed all the clinical records of patients receiving a diagnosis of large vessel vasculitis from 1st January 2010 to 1st January 2016 at a tertiary immunorheumatology clinic of a university Hospital, who underwent a PET. Clinical, laboratory, and imaging data were collected. Non-parametric analysis was performed.

Results: We recruited 19 patients (10 females, 52.6%). The median age was 74.0 [65.5-76.0]; at the diagnosis, the median erythrocyte sedimentation rate (ESR) was 65.5 [49.0-86.0], while C-reactive protein (CRP) was 8.5 [5.5-14.0]. 12 patients showed a typical cranial GCA (63.2%), while 7 (36.8%) were diagnosed with extracranial GCA. The two groups were comparable at diagnosis for age, gender, median ESR and CRP. Interestingly, the PET was significant for aortitis not only in the 7 patients with extracranial involvement, but also in 7/12 patients with cranial GCA (58.3%). Along a median follow-up of 15 months [4.5-26.5], 4 relapses were reported. Notably, all the relapses were males and showed both aortic and cranial involvement. In a multivariate model, male gender was the only predictor of relapse (p=0.02), while age at onset, clinical subsets (cranial vs. extracranial) and steroid dose did not fit the model

Conclusion: The use of PET in GCA is relevant in the assessment of extension of disease since a significant number of patients without cranial symptoms in the end resulted to have large vessel involvement. In addition, PET is useful in identifying patients with cranial involvement that have also aortic inflammation since they seem to have worse prognosis.

Disclosure of Interests: None declared

IMPRESSING THE STANDARDISATION OF DIAGNOSTIC LABORATORY TESTS FOR RF AND ACPA THROUGH THE ESTABLISHMENT OF A NEW INTERNATIONAL REFERENCE MATERIAL
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Background: Rheumatoid arthritis is a debilitating chronic inflammatory disease. Its laboratory diagnosis relies mainly on testing for the presence of two groups of autoantibodies in patient’s serum: rheumatoid factor (RF) and anti-citrullinated protein antibodies (ACPA). Most RF assays are standardised against W1066, the WHO international standard rheumatoid arthritis serum established in 1968, or 64/002, the British Standard rheumatoid arthritis serum, which is the same material. Stocks of W1066 are becoming exhausted which triggered a decision by NIBSC and WHO to prepare a new standard preparation intended to replace W1066.

Objectives: Primarily, we have a responsibility to ensure the continuity of W1066 as a calibrator in RF agglutination-based assays. However, science has progressed and ACPA are now recognised as equally important to RF in the diagnosis of rheumatoid arthritis which is reflected in the ACR/EULAR 2010 classification guidelines. Therefore, we intend to assign the new standard values in international units to both RF and ACPA. In order to do this, a new international reference material (IgG-RF and IgA-RF). In addition, some assays look at isotype-specific RF, so we will assess the new standard values in international units to both RF and ACPA. In order to do this, a new international reference material (IgG-RF and IgA-RF).

Methods: A pool of rheumatoid arthritis serum was prepared and dispensed into ampoules, lyophilised and sealed under an inert nitrogen atmosphere. An international collaborative study was organised with expert laboratories, including commercial kit manufacturers and medical

Disclosure of Interests: None declared
laboratories, to assess the suitability of the new candidate standard and calibrate it against W1066.

Results: The results of the collaborative study will be used to propose a new standard, to the new candidate standard in RF and ACPA for consideration at the WHO Expert Committee for Biological Standardisation.

Conclusion: Standardisation of diagnostic laboratory tests involves the development of a physical sample for each analyte. The use of these international reference standards as primary calibrators promotes the harmonisation of test results between different assays. Because the assays use a similar scale, their results are easily understood, which ultimately increases the impact of published research and clinical findings on our knowledge of the disease.

REFERENCES

Disclosure of Interests: None declared

CD26: A POTENTIAL NOVEL HISTOLOGICAL MARKER OF IDIOPATHIC INFLAMMATORY MYOPATHIES

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Background: Idiopathic inflammatory myopathies (IMM) are a heterogeneous group of acquired skeletal muscle disorders including polymyositis (PM), dermatomyositis (DM), inclusion body myositis (IBM) and immune-mediated necrotizing myopathy (IMNM), characterized by immune-mediated muscle damage. Activated T cells are the predominant inflammatory infiltrates in muscle biopsies of PM and DM patients and the lack of T regulatory cells (Treg) has been implicated in the persistence of muscle damage. CD26 is an intracellular membrane glycoprotein and a serine exopeptidase involved in the activation of T lymphocytes and amplification of inflammatory cytokines production. The enzymatically active form of CD26 is selectively expressed by activated T cells and has been described as a negative selection marker for human Treg.

Objectives: The aim of this study was to evaluate the expression of CD26 in muscle biopsies of IMM patients and to correlate it with patients’ clinical and histological features.

Methods: Immunofluorescence was used to evaluate CD26 expression and co-localization with CD3 and CD15 in biopsies of immune inflammatory myopathies. Immunofluorescence was used to evaluate CD26 expression in muscle biopsies of IMM patients and to correlate it with patients’ clinical and histological features.

Results: We found that CD26 is preferentially expressed in muscle biopsies of IMM patients with respect to controls and that its level of expression is higher in DM patients. In muscle biopsies of IMM patients, CD26 is distributed not only in the extracellular matrix surrounding myofibers and infiltrating leukocytes, but also at the level of T cell membranes and endothelial cells. Specifically, CD26 co-localization with CD31 is more prominent in DM muscle biopsies. We could not find any association between vessel morphology in terms of size and shape and CD26 endothelial expression, suggesting that CD26 is expressed at the perivascular level independently of the degree of vessel dysfunction. With regard to clinical features, we found that CD26 is more expressed in patients presenting the typical DM rash. Moreover, CD26 expression was found not to be significantly associated with the degree of muscle weakness nor with the presence of interstitial lung disease, dysphagia, myalgias or mechanic’s hands. As for histological data, higher levels of CD26 expression were found in biopsies with perivascular inflammatory infiltrates, especially T lymphocytes and macrophages.

Conclusion: Our data suggest that CD26 may represent a suitable marker for the diagnosis of IMM and a potential novel target for selective immune-therapies.

REFERENCES
AB1137 QUANTIFYING KNEE JOINT EFFUSIONS WITH CLINICAL TESTS, MUSCULOSKELETAL ULTRASOUND AND SYNOVIAL FLUID ASPIRATION: A PROSPECTIVE COHORT STUDY

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Background: Aspiration of knee joint effusions is an integral diagnostic and therapeutic intervention in many rheumatologic diseases. Clinical examination has traditionally involved tests including the "patella tap" or "bulge test". The accuracy of these tests for determining effusion presence and size is not well established. Musculoskeletal ultrasound (MUS) is considered better for identification and quantification of knee effusions.

Objectives: To investigate the correlation between both clinical examination and MUS to aspirated knee effusion volume.

Methods: We performed a prospective cohort study of 37 osteoarthritis and therapeutic intervention patients with symptomatic knee effusions. Clinical assessment with patella tap, bulge test and knee circumference measurement were carried out. MUS was used to measure effusion depth in the suprapatellar, lateral and medial parapatellar views. All knee effusion aspirations were performed by the same experienced clinician using a consistent, lateral approach. Linear regression analysis was used to assess correlations between clinical tests, MUS and aspiration volume.

Results: In patients with >3ml of fluid aspirated, patella tap and bulge test were positive in 67% and 80% respectively. The positive predictive value for bulge test was 80%. Where larger volumes were aspirated (i.e. >10ml), patella tap and bulge test were only positive in 52% and 65% respectively. There was a significant correlation between the measured circumference of the index and non-index knee and aspiration of fluid (coefficient=5.6, p=0.007). The relationship between fluid depth on MUS and aspirated volume showed a trend towards statistical significance, with a depth of 1mm equating to 1.57 ml of fluid (coefficient=1.57, p=0.06).

Conclusion: This pilot study demonstrates that a positive patella tap or bulge test is moderately predictive of knee effusion volume. However, this association is weaker when larger knee effusions are present. MUS showed promise at accurately predicting knee effusion volume. A larger study is underway to assess this relationship further.

Disclosure of Interests: Thilinie De Silva: None declared, Chris Pham: None declared, Adam Rischin: None declared, Kim Le Marshall: None declared, Sara Vogrin: None declared, Albert Leung: None declared, Keith Lim Consultant for: Advisor for role of hepatitis and TB in Cimzia, UCB, Speakers bureau: Role of biological in pregnancy UCB


AB1138 BONE SARCOIDOSIS: USEFULNESS OF 18F-FDG PET/CT

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Background: Bone sarcoidosis is usually rare but more sensitive imaging procedures such as 18F-fluorodeoxyglucose Positron Emission Tomography/Computed Tomography (18F-FDG PET/CT) allow a better characterization of such lesions. We aimed to describe bone sarcoidosis involvement using 18F-FDG PET/CT.

Methods: We performed an observational retrospective study of patients with pulmonary sarcoidosis having a 18F-FDG PET/CT. As stated by ATS/ERS/WASOG criteria, diagnosis of sarcoidosis was established on the presence of clinical symptoms and/or imaging features of sarcoidosis, and evidence of non-caseating epithelioid granuloma in a biopsy sample after exclusion of other known etiology of granuloma. We assessed clinical and 18F-FDG PET/CT characteristics.

Results: A total of 85 patients (56.5% of female, median age 47 years) with sarcoidosis were analyzed. The median of disease follow-up was 4 years. Sarcoidosis occurred in more than three organs among 66% of cases. Using ATS/ERS/WASOG criteria, bone sarcoidosis was diagnosed in 12 (14%) patients. Spine was the most commonly affected bone (92%), followed by pelvis (67%), sternum (33%), humerus (25%) and fingers (17%). Only peripheral adenopathy was associated with bone lesions (p=0.04). Seven patients have benefited from a follow-up 18F-FDG PET/CT, which in 100% of cases showed an improvement of lesions.

Conclusion: Bone sarcoidosis occurred in 14% of patients, affecting multiple bones and mostly the axial skeleton. 18F-FDG PET/CT appears to be a sensitive imaging for diagnosis and follow-up of bone sarcoidosis.

Disclosure of Interests: None declared

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Disclosure of Interests: None declared


Abstract AB1137 Figure 1. Relationship between aspirated volume and USS detected knee effusion depth
CONTRIBUTION OF CERVICAL SPINE IMAGING IN RHEUMATOID ARTHRITIS

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Background: Cervical involvement in rheumatoid arthritis (RA) ranks third after erosive lesions of the hands and feet. The evolution is unpredictable and imposes regular radio-clinical surveillance because of the frequency of asymptomatic forms and of its seriousness, especially the neurological involvement could threaten functional and vital prognosis.

Objectives: To specify the contribution of imaging means in the diagnosis of rheumatoid cervical involvement and perform a comparison of these different imaging means to establish an exploration strategy.

Methods: This is a cross-sectional and descriptive retrospective study of 55 patients with RA which evolves since more than two years. All patients were explored by standard radiographs. CT and/or cervical MRI were performed according to the radiological findings.

Results: The mean age of the patients was 57.55 ± 13.59 years with a female predominance (72.7%). Functional signs were dominated by neck pain (87.3%). The stiffness of the cervical spine was the most recovered physical sign (69.1%). In imaging, cervical involvement was dominated by antlodo-axiodal subluxations (AAS) in 50.9% and pannus of C1-C2 (14.54%). Among AAS, anterior AAS was the most common (40%) followed by vertical AAS (7.27%) then lateral and rotary (both in 1.81%). Subaxial subluxation was found in 14.54% of cases. Standard radiographs detected 38.2% of previous AAS versus 20% on MRI. CT allowed a better study of rotary and lateral subluxations. MRI detected pannus of C1-C2 and assessed the neurological impact of the various cervical rheumatoid lesions.

Conclusion: Clinical examination alone remains insufficient in the evaluation of the rheumatoid cervical spine. Imaging has thus emerged as a key examination in exploration and therapeutic orientation. The standard radiography with its different incidences is the first-line examination. CT and MRI will be discussed as second-line. CT essentially detects atypical subluxations and bone lesions. MRI is the exam of choice for the study of pannus and neurological repercussions.

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Disclosure of Interests: None declared

ROLE OF ULTRASOUND IN ASSESSMENT OF JOINT PAIN AMONG HEMO DIALYSIS PATIENTS

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Background: Few studies including limited number of patients assessed the rheumatologic effects of hemodialysis (HD) on joints using ultrasonography. Joint ultrasound has been emerged as a cheap noninvasive tool for assessment of joint pain among HD patients. This was the aim of our study to make use of such tool in such life quality threatening complaints

Objectives: to determine the role of ultrasound in evaluation of joint pain and its causes among patients on regular HD

Methods: One hundred and four patients with end stage renal disease (ESRD) who were regular on HD three sessions per week four hours per session were subjected to history taking, complete physical examination stressing on musculoskeletal examination and ultrasonography of painful joints.

Results: Dialysis related arthropathy (DRA) was not the only cause of joint pain among HD patients but there were diverse causes in different joints. As regard affected joints, knee was the most affected one then came wrist, shoulder, ankle and elbow respectively. As regard causes of joint pain, DRA was the commonest one then came osteoarthritis, Nonspecific ultrasonographic findings and few cases showed normal ultrasonographic studies.

Conclusion: This study confirmed that joint pain in HD patients has diverse causes not DRA by necessity but other causes must be considered as well as multifactorial etiologies.

Disclosure of Interests: None declared

A SIMPLE CLINICAL SCORING TOOL CAN BE USED TO IMPROVE PATIENT SELECTION FOR ULTRASOUND IN DIAGNOSING EARLY INFLAMMATORY ARTHRITIS

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Background: Ultrasonography has been shown to be more sensitive than clinical examination in detecting clinical/subclinical synovitis and improving diagnostic certainty in early inflammatory arthritis (EIA). Local audit suggests increasing demand on ultrasound clinics to aid diagnosis in patients with suspected EIA therefore increasing waiting times. There is limited research to identify the patients most likely to benefit from an early ultrasound.

Objectives: (i) To evaluate the proportion of patients in whom an ultrasound resulted in a change in the pre– to post-scan diagnosis.

(ii) To devise a simple scoring tool to predict patients where an ultrasound may alter the diagnosis/outcome

(iii) To assess if such a scoring tool can be used prospectively in the clinical setting

Methods: We conducted a retrospective analysis of the electronic records of patients attending the rheumatology-led musculoskeletal ultrasound clinic for a diagnostic scan between January and September 2017. Data on pre-test diagnosis, ultrasound findings and post-scan diagnosis was obtained. Clinical data was used to devise a scoring tool to predict variation in pre and post-scan diagnosis. Prospective data was then collected to confirm the validity of this scoring tool.

Results: 200 patient records were reviewed. In 102 patients (51%), the post ultrasound scan diagnosis differed from the pre-scan diagnosis. Patients referred with polyarthralgia of uncertain cause (n=92) were the largest group in whom the post-scan diagnosis differed (64, 69.6%) as the scan was able to identify a diagnosis. Patients with a pre-scan diagnosis of osteoarthritis or fibromyalgia (n=48) were more likely to have no difference in post-scan diagnosis (40, 83.3%).

We generated a score for each patient with one point given to: duration (>6 weeks), (any) tender joints, (any) swollen joints, rheumatoid factor positive, anti-citrullinated protein antibody positive, C-reactive protein (>5mg/L), erythrocyte sedimentation (>age adjusted value), early morning stiffness (>30 minutes), or radiographic erosions. 39 patients scored 0–1, and 4 patients scored 7–9. In none of these categories did the ultrasound alter the diagnosis. Among patients with a score 2–6, the ultrasound altered overall diagnosis in 28% (n=157). Scores 5 and 6 demonstrated most variation between pre and post-scan diagnoses (45%).

We applied the score set prospectively and preliminary data indicates a similar distribution of results (data collection in progress).

Conclusion: (i) Ultrasound contributed to the overall diagnosis in over 50% of patients under investigation for EIA

(ii) A simple clinical scoring tool can predict which patients the scan will make no difference to overall diagnosis.

(iii) Patients with scores in the middle range should be prioritised over those with very low or high scores.

(iv) This can be applied to improve patient selection and maximise the utility of ultrasound in EIA clinics.

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Disclosure of Interests: None declared
PROGNOSTIC VALUE OF 18F-FLUORODEOXYGLUCOSE PET-CT SCORE AT BASELINE ON THE THERAPEUTIC RESPONSE TO PREDNISONE IN PATIENTS WITH POLYMYALGIA RHEUMATICA

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Background: Polymyalgia rheumatica (PMR) is one of the most common inflammatory rheumatic diseases. To date, there is no imaging procedure that can be used as a prognostic factor for good or poor response to corticosteroid therapy.

Objectives: To evaluate the prognostic value of 18F-fluorodeoxyglucose PET-CT (FDG-PET/CT) score at baseline, on the therapeutic response to prednisone, in patients with polymyalgia rheumatica (PMR).

Methods: This is a monocentric retrospective study realized at the university hospital of Besancon. We included patients with a diagnosis of PMR meeting the 2012 ACR/EULAR criteria, who had performed a FDG-PET/CT at baseline, between december 2012 and december 2017. Patients were treated with an initial prednisone dose of 0.3mg/kg a day, progressively decreased following a standardized tapering dose protocol (10% / month). We excluded patients who received corticosteroids before the FDG-PET/CT, or without baseline FDG-PET/CT. Seventeen specifics previously described hotspots were visually analyzed (1). We realized a semi-quantitative analysis of FDG uptake (4-point score from 0 to 3), following Goerres scoring system (2). Hotspot with 0 indicating no uptake (same as bone); 1, slight uptake; 2, moderate uptake (same as liver); and 3, uptake higher than the liver, with a global range score of 0 to 51. Then we defined two groups of patients according to their resistance to prednisone at 12 months, defined as the reoccurrence of symptoms and/or an increase of systemic inflammation twice during the prednisone tapering.

Results: 93 patients where included: 14 (42%) in the group “resistant” and 19 (58%) in the group “sensitive”. There were 57.6% of women, with a mean age of 67.57 ± 11.63 years. The mean CRP at baseline was 45.02 ± 39.59 mg/L. The mean FDG-PET/CT score at baseline was 18/51. The FDG-PET/CT score at baseline was significantly lower in the resistant group (13.1 vs 22/85, p = 0.019). Resistant patients were younger (61.1 vs 72.4 years, p <0.01), and mostly men (66.5% vs 22%, p<0.02). ROC curve showed a threshold of 9.5/51 with a sensitivity of 61.54% and a specificity of 84.21% [AUC 0.76 (+/- 0.089), p= 0.014]. There was no statistically significant difference concerning CRP and PET/CT score (r =0.25, p=0.15). The prevalence of synovitis (21% vs 57%, p=0.46), and neoplasia (0% vs 15.79%, p=0.78) were similar between the two groups.

Conclusion: Our results suggest that in patients with PMR, a baseline FDG-PET/CT score over 9.5/51 score is predictive of a good response to prednisone.

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Disclosure of Interests: None declared

AB1144 ULTRA HIGH FIELD MRI MICROARCHITECTURE ANALYSIS IMPROVES THE PREDICTION OF PROXIMAL FEMUR FRACTURE: A COMBINED STUDY WITH EX VIVO BIOMECHANICAL TESTS

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Background: The purpose of this study was to assess cadaveric proximal femurs from the points of view of bone microarchitecture using ultra-high field (UHF) 7 Tesla magnetic resonance imaging (MRI), bone strength using biomechanical tests and bone mineral density (BMD) using Dual-energy X-ray absorptiometry (DXA).

Objectives: We aimed at determining whether bone microarchitecture parameters were related to bone strength and BMD and whether UHF MRI can provide additional information regarding bone strength.

Methods: BMD of ten proximal femurs from five cadavers were investigated using DXA and the bone volume fraction (BVVF), trabecular thickness (Th.B), and trabecular spacing (Th.Sp), fractal dimension (FD), Euler beam stereometrics (Euler Ch.), Connectivity density (Conn.D) and Degree of anisotropy (DA) of each femur was quantified using UHF MRI. The whole set of specimens underwent mechanical compression tests to failure.

Results: BMD and all the microarchitecture parameters except ConnD were significantly correlated with failure load (p < 0.05). The
microarchitecture parameters were correlated to each other but not corre-
lated with BMD. Multiple regression analysis demonstrated that the combi-
nation of the microstructure parameters and BMD improved the prediction of the failure load with for example an improved fracture risk prediction from R² = 0.418 to 0.688 when combining BMD and Euler Ch. Overall, femur bone microarchitecture assessed with UHF MRI was signifi-
cantly correlated with biomechanical parameters. The multimodal assess-
ment of BMD and trabecular bone microarchitecture using UHF MRI improved the fracture risk prediction of femoral bone and might be of interest for the future investigation of selected osteoporotic patients.

Conclusion: We demonstrated that femur bone microarchitecture assessed with UHF MRI was significantly correlated with biomechanical parameters. The multimodal assessment of bone mineral density and trabecular bone microarchitecture using UHF MRI improved the fracture risk prediction of femoral bone and might be of interest for the future investigation of selected osteoporotic patients.

Disclosure of Interests: None declared


AB1145
FULLY CONVOLUTIONAL NEURAL NETWORK-BASED
SEGMENTATION OF INDIVIDUAL MUSCLES IN MR
IMAGES USING MUSCLES AND BORDERS
PARCELLATIONS

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Background: Segmentation of individual muscles in MR images is chal-
 lenging considering the poor contrast between muscles and the large var-
 iability between and within subjects.

Objectives: The segmentation performance of the Bayesian SegNet net-
work was assessed for the four individual muscles of the quadriceps group. In addition to the classes corresponding to each muscle, we ana-
lyzed the effect of adding four additional classes corresponding to muscle borders. We also investigated the network performance taking into account each muscle individually or the whole set of muscles. The corre-
sponding results were compared with those obtained using a conventional multi-atlas method.

Methods: For the training phase, a dataset of 500 images was used while the testing phase was performed for two other datasets with 140 images each. Four different variants of the same network were assayed considering simultaneous segmentation of individual muscles (On5), separate segmentation of individual muscles (Fr2) and the use of additional classes related to muscle borders in both cases (On5+Fr3). The higher DSI values i.e. 0.96 ± 0.01 for the rectus femoris muscle, 0.93 ± 0.01 for the vastus intermedius muscle, 0.94 ± 0.03 for the vastus lateralis muscle and 0.96 ± 0.01 for the vastus medialis muscle were obtained with the On5 and Fr3 networks i.e. taking into account the muscle border labels in addition to the muscle labels.

Conclusion: Deep-learning based methods are optimal for the segmenta-
tion of thigh muscles and the corresponding efficiency can be improved when considering labels for muscles together with borders.

Disclosure of Interests: None declared


AB1146
PREVALENCE OF STRUCTURAL CHANGES AT THE POSTERIOR PART OF THE SPINE IN AXIAL Spondyloarthritis EVAULATED WITH MR

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Background: In clinical trials radiographic damage is frequently quantified by conventional x-ray but neither the thoracic spine nor the posterior parts of the vertebral column including the intervertebral joints, the verte-
bral arch and the spinous process can be evaluated reliably with this instrument. Bone inflammation and areas of enthesitis can easily be detected by magnetic tomography imaging (MRI) and the introduction of high-resolution 3-tesla MRI allows analysis of bone structures more pre-
 cisely than with x-ray without radiation exposure [1].

Patients with axial SpA present with reduced mobility and functional impairment, but radiographic signs of ankylosis are missing on plain radiographs. These particular clinical findings are reinforced by data in the literature showing, that the relation between radiographic dam-
gage, spinal mobility and function is low. Radiographic damage to the pos-
terior parts of the vertebral column may be responsible for the discrepancy found between clinical and radiographic results as suggested by a Dutch group [2].

Objectives: To evaluate the localisation and incidence of new bone for-
mation in the posterior part of the vertebral bodies with MRI.

Methods: In a cohort of 56 patients with diagnosed axial SpA (mean age 50.29y, mean disease duration 14.4y, 76.4% men, 85.7% HLA-B27 positive) we performed a 3-tesla scan with a Siemens Healtcare, Erlangen, Germany). The whole spine was scanned with T1
weighted and Turbo-Inversion Recovery Magnitude (TIRM) sequences in sagittal planes and each segment of the vertebral column was divided into four areas (ventral and posterior part of the vertebral bodies, inter-
vertebral joints and spinous processes) to assess osseous changes like sclerosis, erosion, syndesmophytes, ankylosis, (partial) fusion of interverte-
bral joints and fibroositis of spinous processes.

Results: Syndesmophytes and ankylosis of the ventral segments were present from C7/Th1 down to L5/S1 with a maximum in Th5/6 (82.5%). In the posterior segments of the vertebral bodies we detected a contrary accumulation inside the cervical and lumbar spine with a max. in C5/6 (55.4%) respectively L2/3 (66.1%). Erosions were mainly found at the ventral edges with an accumulation in middle cervical, lower thoracic and the whole lumbar spine (max. Th8/10 24.5%).

Ankylosis of the intervertebral joints was present over the whole spine with a preference of the cervical (max. C5/6 27.7%) and lumbar column (max. L2/3 47.3%). Fibroositis of the spinous processes were rarely found in the middle and lower thoracic spine (Th8-11, each 2.7%), with up to 57.10% of the cervical spine (54.78% for lumbar, 32.18% for thoracic spine) with detectable new bone formation of the posterior seg-
m ents we found no changes of the ventral part.

Conclusion: With high resolution MRI we were able to detect structural in the dorsal part of the spine, which can hardly be assessed by con-
 ventional radiographs. These findings may explain functional disability in patients with non-corresponding findings in x-ray.

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Disclosure of Interests: Andreas Haidmayer Speakers bureau: Roche, MSD, BMS, Abbvie, Celgene, Gabriel Adelsmayer Speakers bureau: BMS, Rusmir Husic Speakers bureau: BMS, UCB, Celgene, MSD, Franz Que-
henberger: None declared, Angelika Lackner: None declared, Joesf Herr-
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AB1147
VERTEBRAL FRACTURE ASSESSMENT: A SIMPLE TOOL TO DETECT VERTEBRAL FRACTURE IN THE OSTEOPOROSIS ASSESSMENT OF PATIENTS WITH TYPE2 DIABETES MELLITUS

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Background: Vertebral fracture assessment ( VFA) has several bene
fits, including substantially lower radiation dose, lower cost, higher patient con-
venience, and less operator-dependent variance,VFA can be directly assessed during bone mineral density ( BMD) measurement.

Objectives: evaluate the accuracy of VFA performed in the supine posi-
tion by using radiographic views of the spine as the reference standard in patients with type 2 diabetes mellitus

Methods: A total of 207 patients with type 2 diabetes mellitus (mean age, 46.59 ±7.53years; range, 21–60 years) consisting of 102 women
and 105 men, who were suspected of having osteoporosis and who underwent VFA in the supine position and radiography of the spine were evaluated. VFA was analyzed by using a six-marker point method to describe the shape and deformity of each vertebra. Visual radiography of the lateral spine was performed by an experienced radiologist. The agreement between VFA and visual radiography, was assessed by using weighted statistics.

Results: Visual radiography helped identify 51 (24.6%) patients with at least one vertebral fracture versus 49(23.67%) with VFA. Most fractures were present in T7, T12, and L1. Excellent agreement was found between VFA and visual radiography, with 97.3% concordance and 0.89. Sensitivity, specificity, and positive and negative predictive values calculated by level of score for VFA compared with visual assessment were 90.2%, 98.08%, 93.88%, and 96.84%, respectively.

Conclusion: VFA performed with patients with type 2 diabetes, in the supine position, is an accurate method to help detect vertebral fractures when compared with conventional spine radiography. VFA permits combination of fracture assessment with bone mineral density measurement in a single session.

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Disclosure of Interests: None declared

THE RELATION ANALYSIS OF BONE MICROARCHITECTURE EVALUATED BY HR-pQCT, AND SYNOVITIS, BONE DESTRUCTION, SYSTEMIC OSTEOPOROSIS IN RHEUMATOID ARTHRITIS

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Background: Periarticular osteoporosis is one of hallmark of rheumatoid arthritis (RA), However, until now the periarticular bone structure including bone mineral density have not been fully elucidated. High-resolution peripheral quantitative computed tomography (HR-pQCT) is a new technique with high spatial resolution that enables us to assess microarchitecture of cancellous and cortical bones that cannot be assessed by conventional X-ray examinations. Recently, few studies using HR-pQCT revealed that bone microarchitecture such as trabecular volumetric densities (Tb.vBMD) were different between RA and non-RA1, but these study had not confirmed findings of HR-pQCT with synovitis assessed by ultrasonography(US) or systemic osteoporosis.

Objectives: To investigate bone microarchitecture evaluated by HR-pQCT in RA.

Methods: This study included 21 RA patient. HR-pQCT imaging analyses quantified bone microarchitecture in 2.3 Metacarpal Head. We measured the bone mineral density (BMD) of lumen spine and femoral neck using Dual-Energy X-ray Absorptiometry (DXA). Synovitis and bone destruction were assessed by US and X-ray, respectively.

Results: Disease duration, age and disease activity were not correlated with bone microarchitecture. BMD of femoral neck was correlated with Tb.vBMD (r=0.84,p<0.01). The joints with US-proven active synovitis [power doppler score (PD) ≥2] showed less Tb.vBMD, trabecular number (Tb.N) and trabecular thickness (Tb.Th) as compared with the patients with US-PD≤2 synovitis (Tb.vBMD:121.5 mg/cm² vs 145.3 mg/cm², Figure 1). These tendencies were also shown in defferent Metacarpal Heads in the same patient (the mean difference of Tb.vBMD, PD≥2 – PD≤2: -11.9 mg/cm²). Moreover, the joints with progressive joint destruction as classified by more than steinbrocker stage 3 showed less Tb.vBMD (122.1 mg/cm² vs 150.0 mg/cm²). The longitudinal analysis of 10 patients revealed that Tb.vBMD and Tb.N were improved along with improvement of disease activity (DAS -2.80: from baseline to 12 months after new treatment initiated , but Tb.Th was not improved.

Conclusion: This study revealed that bone destruction and synovitis were associated with bone microarchitecture, this difference of treatment response may be parameter of bone microarchitecture. However, this study was mainly transverse analysis and small samples, we need longitudinal analysis using larger samples.

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CHARACTERIZATION OF SALIVARY PROTEINS IDENTIFIED AS POTENTIAL BIOMARKERS FOR SYSTEMIC LUPUS ERYTHEMATOSUS THROUGH PROTEOMIC ANALYSIS

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Background: Systemic lupus erythematosus (SLE) is a heterogeneous autoimmune disease characterized by pathogenic autoantibodies and uncontrolled inflammatory response. There are few reliable biomarkers available for diagnosis and monitoring the disease.

Objectives: We tried to find and characterize specific protein components in saliva of patients with SLE for their use as biomarkers in future.

Methods: Salivary proteins were prepared from 11 samples from patients with SLE and healthy controls (HC), and were subjected to 2-dimensional gel electrophoresis (2-DE). The spots with greater than 2 fold change in intensity were identified by matrix-assisted laser desorption/ionization time-of-flight mass spectrometer (MS) analysis. The relative and absolute amounts of the several candidate proteins in saliva of patients with SLE and rheumatoid arthritis (RA), and HC were analyzed using western blotting, and enzyme-linked immunosorbent assay.

Results: Proteomic analysis using 2-DE and MS identified 20 differentially expressed protein spots in the saliva of SLE patients compared in that of HC. Among them, proteins with more than two-fold differences in expression were found as immunoglobulin gamma-3 chain C (IGHG3), immunoglobulin alpha-1 chain C region, protein S100, lactotransferrin, leukaemia-associated protein 7, and 8-oxoguanine DNA glycosylase (OGG1), salivary IGHG3 levels were increased in SLE (3.9 ± 2.2 pg/mL) compared to those in RA (3.1 ± 1.6 pg/mL, p < 0.001) or HC (2.3 ± 1.7 pg/mL, p < 0.001), and salivary lactotransferrin levels were increased in SLE (5.0 ± 1.7 pg/mL) compared to those in RA (3.1 ± 1.6 pg/mL, p < 0.001) or HC (2.3 ± 1.7 pg/mL, p < 0.001). The patients with nephritis had higher salivary IGHG3 (4.7 ± 1.9 pg/mL) than those not (3.6 ± 2.2 pg/mL).

Disclosure of Interests: Naoki Iwamoto: None declared, Ko Chiba: None declared, Atsushi Kawakami Grant/research support from: Astellas Pharma, Consultant for: Astellas Pharma, Speakers bureau: Astellas Pharma

Scientific Abstracts
The vulnerable MP and the more stable CP burden and its progression in RA patients who underwent coronary calcium score (CACS) as well as the influence of change in the burden of the respective lesions on CACS progression.

**Conclusion:** Salivary IGHG3 and lactotransferrin levels were significantly increased in patients with SLE compared to those not, and salivary lactotransferrin levels negatively correlated with variations of ESR (-2.0 ± 4.6 vs 8.4 ± 9.56, p = 0.02) compared to those not. In addition, the patient with increased salivary lactotransferrin had significantly different in changes of hemoglobin (-0.85 ± 0.97 vs -0.42 ± 0.99 g/L, p = 0.02), and changes of complement 3 (-7.6 ± 14.15 vs +7.0 ± 9.34, p = 0.02) compared to those not. In addition, the patient with increased salivary lactotransferrin had significantly different in changes of ESR (-2.0 ± 4.6 vs 8.4 ± 9.56, p = 0.02) compared to those not, and salivary lactotransferrin levels negatively correlated with complement 3 levels (r = -0.5, p = 0.02).

**Disclosure of Interests:** Ju-Yang Jung: None declared, Jiwon Kim: None declared, Hyoun-Ah Kim: None declared, Chang-Hee Suh Consultant for: Celltrion, Inc.

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**AB1150**  
**IMPLICATIONS OF CORONARY ARTERY CALCIUM AND ITS PROGRESSION AS MARKERS OF PLAQUE VULNERABILITY AND PATIENT RISK IN RHEUMATOID ARTHRITIS**

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1Harbor UCLA Medical Center, West Carson, United States of America; 2Harbor UCLA Medical Center Cardiology, Torrance, United States of America

**Background:** Atherosclerotic plaque calcification represents a stabilizing physiologic process; calcified coronary plaques (CP) are less prone to rupture and yield lower risk of cardiovascular events (CVE) compared to non-calcified (NCP) or mixed-calciﬁed plaques (MP). Interestingly, however, coronary artery calcium score (CACS) and its progression associate with higher event risk in general patients. We, likewise, reported that CACS predicted cardiac events in rheumatoid arthritis (RA) patients independently of risk factors or cardiac risk scores.

**Objectives:** To address this paradox, we evaluated the contribution of vulnerable MP burden to CACS as well the influence of change in MP burden on CACS progression in RA patients who underwent coronary anatomy evaluation with computed tomography angiography (CCTA).

**Methods:** One hundred-one patients underwent a repeat CCTA within 83 ± 36.6 months from baseline. Total number of segments with plaque (segment involvement score-SIS) and cumulative stenosis severity rendered by plaque over all evaluable segments (segment stenosis score-SSS) were computed for all participants. Coronary lesions were deﬁned as non-calciﬁed (NCP), mixed (MP) or calcified (CP). Generalized Linear Models predicted the contribution of MP and CP plaque burden to the baseline and follow-up CACS as well as the influence of change in the burden of the respective lesions on CACS progression.

**Results:** Mixed and CP burden (SSS-MP and SSS-CP respectively) strongly correlated with CACS at both baseline (r_{mp}=0.75 and r_{cp}=0.77, p<0.001) and follow-up (r_{mp}=0.57 and r_{cp}=0.68, p<0.0001), whereas non-calcified plaque did not (r_{nmp}=-0.03, p=0.85 and r_{ncp}=-0.16, p=0.30 respectively). Both MP and CP burden comparably and signiﬁcantly contributed to CACS magnitude at both times (table 1); MP accounted for 36.5% and 38.5% of explainable variance in CACS while CP accounted for 63.5% and 61.5% of it at baseline and follow-up respectively (all p<0.001). Likewise, change in MP and CP burden from baseline to follow-up signiﬁcantly contributed to and justiﬁed 27% and 73% of explainable CACS change variance.

**Conclusion:** The vulnerable MP and the more stable CP burden and their change signiﬁcantly and collectively contributed to CACS at any time as well as its progression respectively in RA. Therefore, the MP burden and its change embody the vulnerability components within the higher baseline and progressing CACS scores explaining the higher CVE risk observed.

**AB1151**  
**APPLICATION OF ULTRASOUND TO DISTINGUISHING PMR FROM POLYARTHRITIS**

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**Background:** Japan is the world’s most aged country. The number of patients with polymyalgia rheumatica (PMR) is expected to increase more. Classification criteria including ultrasound ﬁndings were published in 2012, but the ability to differentiate PMR from rheumatoid arthritis (RA) was not signiﬁcant. We will clarify whether recently reported ultrasound ﬁndings (1, 2) which could be characteristic in PMR are helpful for distinguishing from other diseases and treatment outcome in suspected PMR patients.

**Objectives:** Patients who were clinically suspected of PMR and underwent ultrasound examination from March 2015 to July 2018.

**Methods:** Recorded ultrasound images were retrospectively interpreted by the ultrasound expert, who was blind for clinical information. They were classiﬁed into three groups of PMR, RA, others/no inﬂammation. Initial dose of glucocorticoid (GC), therapeutic response, presence or absence of relapse, and concomitant medications were collected and compared among the 3 groups. Cases in which steroids had already been used before ultrasound examination were excluded from the analysis.

**Results:** The number of subjects was 81, and the number of ultrasound examination was 88. The ultrasound expert classiﬁed 29 PMR, 20 RA, 3 others/no inﬂammation. 18.5% (15/81) of the subjects were improved with no GC and relapse. The average prednisolone dose was 15.3 mg in the PMR group, and 9.7 mg in the RA group. Concomitant medications were introduced in 31% (9/29) of PMR group, in 65% (13/20) of RA group.

**Conclusion:** Ultrasound is useful for distinguishing PMR from seronegative RA and other arthralgia. These ﬁndings showed that ultrasound is useful for the proper use of GC and concomitant medications.
REFERENCES


AB1152  CORRELATING SERUM RESISTIN LEVEL TO ULTRASONOGRAPHIC FINDINGS OF OSTEOARTHRITIC KNEES AFTER INTRA-ARTICULAR GLUCOCORTICOID INJECTION

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Background: Osteoarthritis (OA) is one of the ten disabling diseases affecting 9.6% of men and 18% of women aged over 60 worldwide (1). OA characterized by articular cartilage loss, subchondral bone remodeling, soft tissue damage and low grade synovitis. It is the most common form of arthritis and major cause of disability in the adult population (2). The main source of resistin in humans is mononuclear cells (3). Evidence has shown that higher serum levels of resistin in patients with severe OA compared to controls with no OA and resistin are detected in both serum and synovial fluid, proving its systematical and local involvement in inflammatory changes of OA (4).

Objectives: The aim of this work is to study the effect of local GC intra articular injection on the level of serum resistin in OA knees and to study the relation between different serum levels of resistin and US findings of the knee.

Methods: Thirty patients with primary knee OA Grade 2-3 Kellgren Lawrence score (5) in acute flare according to ACR criteria with or without effusion were recruited for the study from the Physical medicine, Rheumatology and Rehabilitation Outpatient Clinic of Al-Azhar University Hospitals starting from November 2017 till May 2018. Patients with secondary OA. All systemic autoimmune diseases. Previous local GC injection within 3 months preoperative evaluation were excluded. Twenty healthy individuals matched for age, sex and BMI with patients were also enrolled in this study as a control group.

Serum Resistin level was measured and Musculoskeletal ultrasound examination of the knee before and three months after steroid injection was done by TOSHIBA APILO 400. Linear probe frequency 12L5. Effusion was measured by Doppler Ultrasound. Biomed Res Int 2017;2017: 4272960.

Results: Serum resistin showed significant difference (p-value < 0.05) before and after injection. It was 7.6 ng/ml in patients before injection and 5.1 ng/ml in patients after injection.

<table>
<thead>
<tr>
<th>Groups Variables</th>
<th>Before (N = 30)</th>
<th>After (N = 27)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Resistin (ng/ml)</td>
<td>Mean 7.6</td>
<td>6.9</td>
<td>0.3</td>
</tr>
<tr>
<td>ASO</td>
<td>2.8</td>
<td>2.6</td>
<td></td>
</tr>
</tbody>
</table>

US showed significant difference (p-value < 0.001) before and after injection as regard effusion level.

<table>
<thead>
<tr>
<th>Groups Variables</th>
<th>Before (N = 30)</th>
<th>After (N = 27)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>U/S</td>
<td>No effusion 0%</td>
<td>14 (52%)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td></td>
<td>Mild effusion 11 (37%)</td>
<td>10 (37%)</td>
<td></td>
</tr>
<tr>
<td>Moderate effusion</td>
<td>19 (63%)</td>
<td>3 (11%)</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: Resistin could be considered as an important severity marker of knee OA. Serum resistin level is markedly decreased after intra articular steroid injection into OA knee joint. The longer the duration of illness the higher the resistin level. The older the age the higher the resistin level. The longer the duration of illness, the higher the radiological grade..

REFERENCES


Acknowledgement: Prof. Dr. Hassan Bassiouni Dr. Abdullah M Gaafer

Disclosure of Interests: None declared


AB1153  EVALUATION OF DIAGNOSTIC DISCREPANCY USING THE ASAS CRITERIA AND F-18 NaF PET/CT IN PATIENTS WITH SUSPECTED AS

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Background: The latest ASAS diagnostic criteria allow early diagnosis of ankylosing spondylitis by using MRI. Nuclear imaging techniques may detect increased bone turnover not only during inflammation, but probably also paralleling postinflammatory reparative changes at starting point of new bone formation.

Objectives: We focus on diagnostic discrepancy to evaluate AS between fluorine-18 sodium fluoride (F-18 NaF) PET/CT and assessment of spondyloarthritis international society (ASAS) criteria in patients with chronic low back pain suspected ankylosing spondylitis.

Methods: Sixty-eight patients with chronic lower back pain over 3 months and limited lumbar movement were included. Among them, 49 patients who fulfilled ASAS diagnostic criteria were included as AS groups and 19 others were controlled. For clinical assessment, ESR, CRP, BASDAI, and BASFI scores were measured. For imaging assessment, conventional radiography for sacroiliitis and F-18 NaF PET/CT were performed. We defined AS-positive lesions on PET/CT as uptake of sacroiliac joint, syndesmophyte, enthesitis lesions and facet joint.

Results: No significant differences were observed in the baseline demographic evaluation between two groups in terms of age, sex, follow-up period and clinical parameters including BASDAI, BASFI, ESR level. However, there were significant differences in terms of HLA-B27 positive value, 339P level and standard uptake value ratio (SUVR) of sacroiliac joint in patients fulfilled ASAS criteria.

Conclusion: In diagnosing AS, F-18 NaF PET/CT showed 79.59% sensitivity, 84.21% specificity and 80.88% accuracy. This shows the diagnostic value of the F-18 NaF PET/CT, which can be a good alternative to the diagnosis of early ankylosing spondylitis, and can evaluate whole body lesions in a single session.

Disclosure of Interests: None declared


AB1154  CLINICAL SIGNIFICANCE OF MONOSPECIFIC ANTI-DFS70 IN ANTINUCLEOLAR ANTIBODY (ANA)-POSITIVE PATIENTS

Olalla Lima, Ana Argibay, Melanie Estevez, Brenda Maure, Milarqos Suárez, Lorena Maria Rodríguez Ferreira, Carinta Vázquez Triñanes, Beatriz Gimena, Rut Lorenzo Castro, Iria Villaverde Alvarez, Alberto Rivera. Complejo Hospitalario Universitario de Vigo, Vigo, Spain

Background: The most commonly used method for ANA detection is the indirect immunofluorescence test (IFT) on HEp-2 cells. Among ANA, anti-dense fine speckled (DFS) 70 antibodies produce a pattern (nuclear dense fine speckled) that can be confused with homogeneous or fine speckled pattern (typical of ANA-associated rheumatic disease, AARD). The presence of anti-DFS70 have been reported in a variety of clinical
systemic sclerosis is a multisystem connective tissue disease characterized by a microvascular damage, which leads to systemic fibrosis, immune dysregulation and progressive involvement of internal organs [1]. According to the classification of the morphological aspects, into the scleroderma pattern proposed by Cutolo et al. are described the early, active and late patterns.

Objectives: The aim of our study is thus to report a correlation between specific nailfold videocapillaroscopy pattern and internal organ involvement.

Methods: All enrolled patients were diagnosed for SSc, according to the American College of Rheumatology criteria and underwent an echocardiographic examination and a nailfold videocapillaroscopy. Myocardial function parameters considered were: global contractility (computed with the Simpson method), linear contractility (computed through the MAPSE) [2], diastolic dysfunction (through the analysis of the transmural flow) [3]; whilst those of lung damage were: PAPs and the evaluation of the right ventricle contractility through the TAPSE [4].

Correlation between nailfold videocapillaroscopy patterns, left ventricle dysfunction and pulmonary disease in systemic sclerosis

Monaco Luca1, Francesco Masini1, Klodian Gjekoshi2, Emanuele Pinotti1, Roberta Ferrara1, Teresa Salvatore1, Giovanni Guerri2. 1University of Campania Luigi Vanvitelli, Department of Medical and Surgical Sciences, Caserta, Italy; 2University of Campania Luigi Vanvitelli, Medicina di precisione, Caserta, Italy

Background: Systemic Sclerosis (SSc) is a multisystem connective tissue disease characterized by a microvascular damage, which leads to systemic fibrosis, immune dysregulation and progressive involvement of internal organs [1]. According to the classification of the morphological aspects, into the scleroderma pattern proposed by Cutolo et al. are described the early, active and late patterns.

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AB1155

AB1155 DEFINITION OF TWO NEW ULTRASOUND ENTHESOPATHY SCORES: APPLICATION IN A CONSECUTIVE SERIES OF IBD PATIENTS

Pietro Macchioni1, Federica Martinis2, Giorgia Citroni2, Nicola Girolimetto4, Carlo Salvarani1. 1Arcispedale S Maria Nuova, IRCCS, Reggio Emilia, Italy; 2Polclinico GB Rossi, University of Verona, Verona, Italy; 3University of Modena and Reggio Emilia, Modena, Italy; 4Rheumatology Unit, Department of Clinical Medicine and Surgery, University Federico II, Napoli, Italy

Background: Recent studies have developed criteria for US definition of enthesal abnormalities [1] however no actual scores are available to

REFERENCES


Disclosure of Interests: None declared


AB1155 Table 1. early vs controls

<table>
<thead>
<tr>
<th></th>
<th>EARLY</th>
<th>CONTROLS</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAPs</td>
<td>32.3 ± 5.4</td>
<td>22.6 ± 6.7</td>
<td>0.0001</td>
</tr>
<tr>
<td>MAPSE</td>
<td>1.57 ± 0.4</td>
<td>1.76 ± 0.08</td>
<td>0.0001</td>
</tr>
<tr>
<td>EF</td>
<td>65 ± 4.7</td>
<td>64 ± 2.7</td>
<td>NS</td>
</tr>
<tr>
<td>E/A</td>
<td>1.34 ± 0.12</td>
<td>1.38 ± 0.19</td>
<td>NS</td>
</tr>
<tr>
<td>DECT</td>
<td>148 ± 23</td>
<td>163 ± 27</td>
<td>NS</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>3(11)</td>
<td>0(21)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

AB1155 Table 2. active vs controls

<table>
<thead>
<tr>
<th></th>
<th>ACTIVE</th>
<th>CONTROLS</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAPs</td>
<td>34 ± 7.8</td>
<td>22.6 ± 6.7</td>
<td>0.0001</td>
</tr>
<tr>
<td>MAPSE</td>
<td>1.49 ± 0.08</td>
<td>1.76 ± 0.08</td>
<td>0.0001</td>
</tr>
<tr>
<td>EF</td>
<td>65 ± 4.7</td>
<td>64 ± 2.7</td>
<td>NS</td>
</tr>
<tr>
<td>E/A</td>
<td>1.34 ± 0.4</td>
<td>1.38 ± 0.19</td>
<td>NS</td>
</tr>
<tr>
<td>DECT</td>
<td>157 ± 24</td>
<td>163 ± 27</td>
<td>NS</td>
</tr>
<tr>
<td>Pulmonary hypertension</td>
<td>5(16)</td>
<td>0(21)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Disclosure of Interests: None declared


AB1155

AB1155 CORRELATION BETWEEN NAILFOLD VIDEOCAPILLAROSCOPY PATTERNS, LEFT VENTRICLE DYSFUNCTION AND PULMONARY DISEASE IN SYSTEMIC SCLEROSIS

Monaco Luca1, Francesco Masini1, Klodian Gjekoshi2, Emanuele Pinotti1, Roberta Ferrara1, Teresa Salvatore1, Giovanni Guerri2. 1University of Campania Luigi Vanvitelli, Department of Medical and Surgical Sciences, Caserta, Italy; 2University of Campania Luigi Vanvitelli, Medicina di precisione, Caserta, Italy

Background: Systemic Sclerosis (SSc) is a multisystem connective tissue disease characterized by a microvascular damage, which leads to systemic fibrosis, immune dysregulation and progressive involvement of internal organs [1]. According to the classification of the morphological aspects, into the scleroderma pattern proposed by Cutolo et al. are described the early, active and late patterns.

Objectives: The aim of our study is thus to report a correlation between specific nailfold videocapillaroscopy pattern and internal organ involvement.

Methods: All enrolled patients were diagnosed for SSc, according to the American College of Rheumatology criteria and underwent an echocardiographic examination and a nailfold videocapillaroscopy. Myocardial function parameters considered were: global contractility (computed with the Simpson method), linear contractility (computed through the MAPSE) [2], diastolic dysfunction (through the analysis of the transmural flow) [3]; whilst those of lung damage were: PAPs and the evaluation of the right ventricle contractility through the TAPSE [4].

Statistics were performed with SPSS 20 software, by using the Mann Whitney U Test and the Fisher Test.

Results: We enrolled 27 patients, of which 16 showing “active pattern” and 11 “early pattern”, compared to a group of 21 healthy controls.

Of the 11 patients belonging to the “early” group, 1 resulted affected by diastolic dysfunction, whilst 3 had pulmonary hypertension, defined by PAPs ≥40 mmHg [4] (early vs controls; p=0.03). In the 16 patients of the “active” group, instead, 5 were found to have a diastolic dysfunction (active vs controls; p=0.01) and 6 pulmonary hypertension (active vs controls; p=0.003). In the group with “active” pattern we also observed a reduction in TAPSE compared to the control group (2.0 ± 0.2 vs 2.2 ± 0.2; p=0.025) and compared to the group with early pattern (2.0 ± 0.2 vs 2.2 ± 0.3; p=0.07).

None presence of modifications in the global contractility emerged; however, we observed a progressive reduction of the MAPSE (controls 1.76 ± 0.08; early 1.57 ± 0.04; active 1.49 ± 0.12), which resulted statistically significant among the different comparisons (controls vs early p=0.001; controls vs active p=0.0001; early vs active p=0.04).

Conclusion: The analyses showed a strict correlation between the severity of the microvascular alterations, reported by nailfold videocapillaroscopy, and the severity of the cardiopulmonary damage, expressed by an increase in the percentage of pulmonary hypertension, diastolic dysfunction and a progressive reduction of MAPSE and TAPSE.

REFERENCE

[1] Michael Mahler, Luis E. Andrade, Carlos A. Casiano, Kishore Malyavan-
Results: Ninty CTDs patients were enrolled, namely 27.8% systemic sclerosis (SSc), 31.1% primary Sjögren’s syndrome (pSS), systemic lupus erythematosus 11.1%, 7.8% polymyositis, 6.6% dermatomyositis, and 15.5% undifferentiated CTD (UCTD). Male/female ratio was 1:3.1 and a mean age of 63.9±12.7 years; among them 45 (50%) showed ILD at HRCT. The algorithm correctly classified 73/90 patients, with a sensitivity and specificity of 93.3% and 68.9%, respectively, and a diagnostic accuracy of 81.1% (figure 1).

Conclusion: These data confirm the diagnostic accuracy of VECTOR in detection of ILD in CTD patients, as previously described also for RA-ILD. In some CTDs such as SSc, a careful evaluation of lung involvement is quite diffused, while for other CTDs, for example pSS or UCTD, ILD remains often underestimated, with a delay in diagnosis and treatment. Since lung complications represent one of the most serious and frequent cause of poor prognosis for all CTDs patients, the search for a simple, repeatable and radiation-free tool for the screening of these patients is mandatory. The routinely employment of an ES and VECTOR, combined to clinical findings (cough, dyspnea) and respiratory lung function tests, could increase our ability to early identify ILD in CTD patients.

REFERENCES

AB1159
INTER-READER RELIABILITY AND COMPARISON OF FLUORESCENCE OPTICAL IMAGING ENHANCEMENT IN PATIENTS WITH EROSIIVE HAND OSTEOARTHRITIS AND RHEUMATOID ARTHRITIS

Oystein Maugenstret1, Sarah Ohndorf2, Daniel Glintats2, Mads Ammitzbøll-Danielsen3, Yogan Kisten4, Mikkel Østergaard1, Lene Terslev1, Till Ulhig1, Tore K. Kvien1, Ida Kristin Haugen1, Karolinska University Hospital, Department of Medicine, Rheumatology Division, Stockholm, Sweden.

Background: Fluorescence Optical Imaging (FOI) is an imaging technique combining indocyanine green (ICG)-enhanced microcirculation in wrist and finger joints, as a sign of inflammation. A reliable scoring method is essential in the assessment of these images.

Objectives: To assess inter-reader reliability of three FOI scoring methods from Berlin, Stockholm, and Copenhagen, and to compare the amount of enhancement in joint groups of both hands in patients with erosive hand osteoarthritis (OA) and rheumatoid arthritis (RA).

Methods: Patients with erosive hand OA (n=13) and with RA (n=13) underwent FOI of both hands. Five readers blinded for clinical diagnoses scored all finger and wrist joints bilaterally on semi-quantitative 0-3 scales using three different FOI scoring methods. In the Berlin method, FOI enhancement was evaluated on three different images, defined as different phases on the enhancement in the fingertips. A composite image (Prima Vista Mode, PVM) of the 240 first images was also assessed. The Copenhagen method assumed that inflamed tissues will demonstrate a more rapid FOI enhancement than the surrounding tissues, defining inflammation as sharply marginated enhancement over a joint area with clear delineation from surrounding tissues lasting ≥3 sec. The Stockholm method was evaluated in the format of 240 images in ‘temperature palette setting, with additional scrolling through the image sequence to detect ambiguous signals. To evaluate inter-reader reliability, we calculated the intraclass correlation coefficients (ICC) of the sum scores on patient level and weighted kappa values and prevalence and bias adjusted kappa values for ordinal scales (Pabak-OS) on joint level. Finally, we compared the averaged sum scores in the different joint groups in patients with erosive hand OA vs. RA using the Mann-Whitney test.

Results: The ICC of the sum scores was very good for the Stockholm method (0.83), and for Berlin PVM (0.93) and Phase 2 (0.83), while the Copenhagen method (0.65) and Berlin phase 3 (0.73) showed good reliability. Berlin phase 1 showed fair reliability (0.30). On joint level we found moderate to good agreement with pabak-OS for all methods (table). Patients with erosive hand OA had significantly more enhancement in DIP joints across all methods, while PIP enhancement was more common in erosive hand OA for the Berlin PVM and Stockholm methods only. Enhancement in the 1st CMC was not detected in any of the methods, and no consistent differences were observed for the wrist (data not shown).

Conclusion: We found moderate to very good inter-reader reliability on patient level for all methods except for Berlin phase 1 and moderate to good agreement on joint level for all methods. FOI showed different enhancement patterns between erosive hand OA and RA, with more enhancement in the DIP joints in the OA patients across all methods, supporting its validity.

Disclosure of Interests: Øystein Maugenstret: None declared, Sarah Ohndorf: None declared, Daniel Glintats: None declared, Mads Ammitzbøll-Danielsen: None declared, Yogan Kisten: None declared, Mikkel Østergaard Grant/research support from: Abbvie, BMS, Roche, and UCB., Consultant for: Abbvie, Biogen, BMS, Boehringer Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Pfizer, Regeneron, Roche, and UCB, Speakers bureau: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Pfizer, Regeneron, Roche, and UCB, Speakers bureau: Abbvie, BMS, Boehringer-Ingelheim, Celgene, Eli Lilly, Hospira, Janssen, Merck, Novartis, Novo, Pfizer, Regeneron, Roche, and UCB, Lene Terslev Speakers bureau: Speakers fee from : Roche, Novartis, Pfizer, MSD, BMS, Celgene, Till Ulhig: None declared, Tore K. Kvien Grant/research support from: Abbvie, BMS, MSD, Pfizer, Roche and UCB, Consultant for: Abbvie, Biogen, BMS, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Hospira, Merck-Serono, MSD, Novartis, Ontal, Oron Pharma, Pfizer, Roche, Sandoz, Sanofi, Mylan and UCB, Speakers bureau: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celgene, Celltrion, Eli Lilly, Hospira, Merck-Serono, MSD, Novartis, Ontal, Oron Pharma, Pfizer, Roche, Sandoz, Sanofi and UCB, Ida Kristin Haugen Grant/research support from: ADVANCE research grant from Pfizer, Consultant for: Advisory board Abbvie.
REFERENCES


AB1161

ULTRASOUND IMAGING IN EVALUATION OF ENTHESITIES: STATUS AND PERSPECTIVES

José Alexandre Mendonça,1 Lana Bezerra Fernandes,2 Waldemar Naves Do Amaral,3 Pontifical Catholic University of Campinas, Rheumatology, Sumaré, Brazil;2 Hospital das Clínicas/UFMG, Postgraduate – Dermatology, Goiania, Brazil;3 Hospital das Clínicas/UFMG, Postgraduate – Ultrasoundography, Goiania, Brazil

Background: The high-frequency ultrasound is a reliable method to identify enthesities, including subclinical and early diagnosis, in patients with psoriasis (PsO) and psoriatic arthritis (PsA)1.

Objectives: To establish an epidemiological profile of patients with PsO and/or PsA and to establish the ultrasound (US) profile with gray scale and Doppler in entheses in these groups.

Methods: A case control study conducted in the period from December 2015 to December 2016, at Hospital das Clínicas/UFMG. It was performed in 144 patients with PsO and/or PsA and 24 healthy controls. Patients with and without arthrits/enthesis were submitted to the US. The US findings were according to the MASEI (the Madrid sonography enthesis index). The entheses were studied bilaterally: plantar fascia, distal and proximal ligament of the patella, distal quadriceps tendon, calcaneus tendon, and tendons of the brachial triceps. In addition to the US in the 2nd and 3rd distal interphalanges, the interobserver reliability was calculated in 24 patients - kappa index (k).

Results: In the case group the mean age was 50.13 years, BMI of 24 patients - kappa index (k).

AB1166

ARE SONOGRAPHIC FINDINGS CORRELATED WITH DISEASE ACTIVITY SCORE IN RHEUMATOID ARTHRITIS REMITTED PATIENTS?

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Background: Obtaining remission is the ultimate and now attainable goal of treatment in rheumatoid arthritis (RA). However, the definition of remission kept changing over the last decade. Several composite scores and indices are now validated to assess remitting RA such as the Disease Activity Index 28 joints (DAS28), and more recently, the Simplified Disease Index (SDAI) and the Clinical Disease Index (CDAI). Despite more stringent definition criteria, progressive radiographic damages still occur in RA patients who reached remission. Defining other criteria for remission including ultrasound (US) might help preventing such evolution.

Objectives: The aim of this study was to compare US findings and composite score results in RA patients that achieved a status of remission according to DAS28.

Methods: Thirty Tunisian patients followed up for RA with DAS28 ≤2.6 for at least three months were enrolled. Among them, we identified patients in remission according to the SDAI (≤3.3) and the CDAI (≤2.8). US (Esaote MyLab 60 machine and a 13-18 MHz linear array transducer) was performed by an experienced rheumatologist blinded to clinical and laboratory data. For each patient, 22 joints were scanned (wrists, metacarpophalangeal, and proximal interphalangeal joints) using a semi-quantitative score.

Results: Over the 26 patients in CDAI remission, ultrasonographic synovitis in B-mode were noted in 81% of patients. The average ultrasound score per patient was 4.58. In PD mode, US abnormalities were noted in 58% of patients. The average PD score per patient was 2.6. Neither correlation between CDAI and B-mode US score (r = 0.104; p = 0.319) nor between CDAI and PD US score (r = 0.251; p = 0.217) was noted.

Table: MASEI score

<table>
<thead>
<tr>
<th>ultrasound findings</th>
<th>case (n=144)</th>
<th>control (n=24)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>number of entheses changed</td>
<td>1728</td>
<td>288</td>
<td>0.001</td>
</tr>
<tr>
<td>structure (n (%))</td>
<td>472 (27.3)</td>
<td>16 (5.6)</td>
<td>0.001</td>
</tr>
<tr>
<td>thickening (n (%))</td>
<td>503 (28.1)</td>
<td>37 (12.8)</td>
<td>0.001</td>
</tr>
<tr>
<td>Bursts (n (%))</td>
<td>95 (16.5)</td>
<td>05 (1.73)</td>
<td>0.004</td>
</tr>
<tr>
<td>Erosion n (%))</td>
<td>48 (2.8)</td>
<td>02 (0.7)</td>
<td>0.035</td>
</tr>
<tr>
<td>calcification (n (%))</td>
<td>373 (21.6)</td>
<td>34 (11.8)</td>
<td>0.001</td>
</tr>
<tr>
<td>PD (n)</td>
<td>124 (7.2)</td>
<td>08 (2.8)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Test: Chi-Square; (PD: power Doppler).

Disclosure of Interests: None declared


REFERENCES

Finally regarding ankle/foot pain, treatment changes happened in 71.4% of patients owing mainly to changes in diagnosis & detecting subclinical activity. In polyarticular complaints, 8% of patients had changes in treatment decisions respectively of which 75% and 90.8% were patients with hand/wrist & polyarticular complaints, 44.8% and 68.8% of treatment decisions were changed for knee pain, 50% of treatment decisions were changed for elbow pain, and 40% of treatment decisions were changed for shoulder pain. In this observational study on 101 patients with musculoskeletal complaints who have been referredby rheumatologists for a MSUS scan at Zagazig University MSUS Unit in the same department. The patients’ mean age was 41.5 ± 15.67, including 70 females (69.3%) and 31 males (30.7%). Patients included 29 patients with hand/wrist complaints (28.7%), 2 patients with elbow pain (2%), 36 patients with shoulder pain (35.6%), 7 patients with ankle/foot pain (6.9%), 10 patients with knee pain (9.9%), and 17 patients with polyarticular pain (16.8%). The rheumatologists were asked to set a provisional diagnosis and treatment plan before the MSUS scan and to reconsider their own plan for any adjustments afterwards. Results: Regarding all 101 patients, the diagnosis & treatment decisions were changed in 37% and 65% respectively after the MSUS scan as shown in figure (1). Fifty percent of the changes in treatment were classified as major, defined as adding/ changing the dose of steroids, adding the dose of DMARDs and adding/ modifying physiotherapy while the other 50% were major in the form of initiating/ adding DMARDs, interventional treatment referral to surgery. Ten patients out of 29 with hand/wrist complaints encountered change in diagnosis (34.5%), 1 patient out of 2 with elbow pain (50%) and 11 patients out of 36 with shoulder pain (30.6%). In patients with knee pain and ankle/foot pain, changes occurred with 4 patients for each representing 40% and 42.9% respectively. Regarding patients with polyarticular complaints 8 patients representing 47.1% were categorized to different disease entities. Treatment decisions were much more frequently changed in patients with polyarticular complaints owing to a more detailed look into the diseased joint and surrounding structures. Background: The era of musculoskeletal ultrasound (MSUS) is becoming enormous, but the extent to which MSUS has influenced management plans for patients with different musculoskeletal symptoms remains questionable. Objectives: To assess the changes in the provisional diagnosis and treatment decisions made by rheumatologistsafter receiving MSUS reports for their patients. Methods: This study was carried out at Rheumatology & Rehabilitation outpatient clinics in Zagazig University Hospitals in Egypt. This is an observational study on 101 patients with musculoskeletal complaints who have been referred by rheumatologists for a MSUS scan at Zagazig University MSUS Unit in the same department. The patients’ mean age was 41.5 ± 15.67, including 70 females (69.3%) and 31 males (30.7%). Patients included 29 patients with hand/wrist complaints (28.7%), 2 patients with elbow pain (2%), 36 patients with shoulder pain (35.6%), 7 patients with ankle/foot pain (6.9%), 10 patients with knee pain (9.9%), and 17 patients with polyarticular pain (16.8%). The rheumatologists were asked to set a provisional diagnosis and treatment plan before the MSUS scan and to reconsider their own plan for any adjustments afterwards.

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Discussion of Interests: None declared

AB1163 CAN A MUSCULOSKELETAL ULTRASOUND REPORT CHANGE A RHEUMATOLOGIST’S OPINION?

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Background: The era of musculoskeletal ultrasound (MSUS) is becoming enormous, but the extent to which MSUS has influenced management plans for patients with different musculoskeletal symptoms remains questionable. Objectives: To assess the changes in the provisional diagnosis and treatment decisions made by rheumatologists after receiving MSUS reports for their patients. Methods: This study was carried out at Rheumatology & Rehabilitation outpatient clinics in Zagazig University Hospitals in Egypt. This is an observational study on 101 patients with musculoskeletal complaints who have been referred by rheumatologists for a MSUS scan at Zagazig University MSUS Unit in the same department. The patients’ mean age was 41.5 ± 15.67, including 70 females (69.3%) and 31 males (30.7%). Patients included 29 patients with hand/wrist complaints (28.7%), 2 patients with elbow pain (2%), 36 patients with shoulder pain (35.6%), 7 patients with ankle/foot pain (6.9%), 10 patients with knee pain (9.9%), and 17 patients with polyarticular pain (16.8%). The rheumatologists were asked to set a provisional diagnosis and treatment plan before the MSUS scan and to reconsider their own plan for any adjustments afterwards. Results: Regarding all 101 patients, the diagnosis & treatment decisions were changed in 37% and 65% respectively after the MSUS scan as shown in figure (1). Fifty percent of the changes in treatment were classified as major, defined as adding/ changing the dose of steroids, adding the dose of DMARDs and adding/ modifying physiotherapy while the other 50% were major in the form of initiating/ adding DMARDs, interventional treatment referral to surgery. Ten patients out of 29 with hand/wrist complaints encountered change in diagnosis (34.5%), 1 patient out of 2 with elbow pain (50%) and 11 patients out of 36 with shoulder pain (30.6%). In patients with knee pain and ankle/foot pain, changes occurred with 4 patients for each representing 40% and 42.9% respectively. Regarding patients with polyarticular complaints 8 patients representing 47.1% were categorized to different disease entities. Treatment decisions were much more frequently changed in patients with polyarticular complaints owing to a more detailed look into the diseased joint and surrounding structures.

Discussion of Interests: None declared

AB1164 EDUCATION ON PEDIATRIC MUSCULOSKELETAL ULTRASOUND: A SYSTEMATIC LITERATURE AND EVENTS REVIEW

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Background: Recently some Pediatric musculoskeletal ultrasound (PedMSUS) courses have been held on national and international ground. Nonetheless, content, conduct and format of PedMSUS courses have never been investigated and shared.

Objectives: To perform a systematic literature and events review on PedMSUS educational initiatives.

Methods: Educational material/events on PedMSUS were extensively searched on websites/networks (PubMed, Cochrane, Embase, ERIC, Medline, CINAHL, complete, Google, Yahoo, Ask, Baidu, Bing, Lycos, Duckduckgo). The keywords were: “musculoskeletal”, “ultrasound”, “sonography”, “course”, “education”, “training”, “children”, “paediatrics”, “pediatrics”. Only courses/events, articles and books in English were considered. Descriptive analysis was performed on the documentation retrieved.

Results: No articles neither books on educational recommendations for PedMSUS courses were found. A total of 13 PedMSUS courses were identified. Two online courses and three residential ones were not consistent with the purpose and were excluded. Eight courses were finally included for the analysis (Figure 1). Seven were endorsed by EULAR and followed the recommendations for the content and conduct of EULAR MSUS courses. No requirements/skills should be fulfilled for registration; only one level of competency was proposed. The courses were residential of 2-3 days and included theoretical and practical lessons. Lectures were on MSUS examination techniques, physiological musculoskeletal (MSK) anatomy and basic pathology in pediatric rheumatology. Hands-on scanning of healthy models/patients with pediatric rheumatic diseases was generally organized in groups supervised by tutors, and included optimization of the machine settings, identification of pediatric MSK sonoanatomy, correct acquisition of images, and identification of basic pathological findings in children. A competency assessment was performed at the end of only three courses.

Figure 1

Conclusion: MSUS scans have a great impact on rheumatologists’ decisions in clinical practice. Remarkable changes in diagnosis with subsequent significant major changes in treatment plans were due to the ability of MSUS to differentiate between different disease entities. Changes in treatment decisions were very frequent even without changing the diagnosis owing to a more detailed look into the diseased joint and surrounding structures.

Disclosure of Interests: None declared

AB1165 ULTRASOUND: A SYSTEMATIC LITERATURE AND EVENTS REVIEW

REFERENCES


Figure 1
**FLUORESCENCE OPTICAL IMAGING XIRALITE® IS HELPFUL IN THE DECISION FOR RITUXIMAB RE-THERAPY IN PATIENTS WITH RHEUMATOID ARTHRITIS**

Sarah Ohrndorf1, Lisa Ridha1, Anne-Marie Gilmm1, Gerd Rüdiger Burmester1, Gabriela Schmittat1, Marina Backhaus1, Jens Klotsche2, Sarah Ohrndorf1, Lisa Ridha1, Anne-Marie Glimm1, Gerd Rüdiger Burmester1, Silvia Magni-Manzoni Consultant for: Abbvie, Speakers bureau: Lilly, Novartis, Janssen, and Celgene GmbH, Jelena Vojinovic: None declared, Agostino: None declared, Esperanza Naredo Consultant for: Abbvie.

**Background:** Rituximab (RTX) is an effective and well-tolerated therapeutic option in rheumatoid arthritis (RA) patients with insufficient response to TNFα inhibitors. However, the exact time point of RTX re-therapy often varies and objective parameters (e.g., imaging, such as MRI and/or musculoskeletal ultrasound [US]) are not yet included in the RA treatment strategy [1].

**Objectives:** The aim of this study was to evaluate the ability of the fluorescence optical imaging Xiralite® (FOI) to predict RTX re-therapy in RA patients - in comparison to clinical, laboratory and US.

**Methods:** In this study, n=31 patients with established RA were included and prospectively followed over one year by DAS28, patient’s VAS and CRP had similar predictive power with AUC of 0.66 each (each p=ns).

**Results:** Of the included 31 patients (female 77.4%, mean age 60.1±11.4, mean disease duration 14.9±7.1 years), n=14 (45.2%) received RTX re-therapy within 12 months: n=3 after 6 months (mths), n=4 after 7 mths, n=5 after 9 mths, and n=2 after 10 mths. In the group with RTX re-therapy, FOI in PVM mode was the only parameter that presented significant increase (beta 0.40, CI 0.08-0.71; p=0.013) – compared to the group without re-therapy. In the prediction model via receiver operating characteristic (ROC) analysis, FOI in PVM reached the highest values of all imaging parameters (phases 1-3, US) at baseline for the prediction of re-therapy over one year with an area under the curve (AUC) of 0.64 (OR 0.9, CI 0.79-1.03), however, without significance (p=0.117). Patient’s VAS and CRP had similar predictive power with AUC of 0.66 each (each p=ns).

**Conclusion:** The FOI Xiralite® in PVM is able to discriminate between groups with and without need for RTX re-therapy better than other included imaging parameters. It is able to predict the need for RTX re-therapy with comparable predictive power to patient’s VAS and CRP. At the same time, FOI is a more objective tool, while patient’s VAS and CRP can also depend on other influence (i.e. psychological, infectious) factors.
SUBCLINICAL ENTHESEAL INVOLVEMENT IN LOWER LIMBS IN PATIENTS WITH TYPE 2 DIABETES MELLITUS: AN ULTRASOUND STUDY

Mohamed Omar1, Mohamed Abdelkareem2, Mohammed Moneer2, Mohamed Elwan1, Alazher, Rheumatology, Assuit, Egypt; 2Alazher, Rheumatology, Assuit, Egypt

Background: Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia, which results from defects in insulin secretion, insulin action, or both (1). DM impacts the connective tissue and causes various changes in peri- articular and articular structures. An increase in enthesopathic complications in diabetic patients such as patellar tendinitis bursitis, achilles tendinopathy and plantar fasciitis, was observed in many studies.

Objective: This study aims to detect subclinical lower limb enthesitis in type 2 DM by musculoskeletal ultrasonography & its relation to poor glycemic control & disease duration.

Methods: This study was carried out on 80 persons. Diabetic group forty patients diagnosed as diabetes according to ADA diagnostic criteria. Control group Forty apparent healthy volunteers both groups were matched at age and sex. Sonographic evaluations and scoring were performed according to Glasgow Ultrasound Enthesitis Scoring System (GUESS) on the entheses of both lower limbs.

Results: At the diabetic group the Musculoskeletal Ultrasound findings were as follows. The Quadriceps tendon enthesitis in 30 patients (75%), proximal patellar enthesis was in 28 patients (70%), Distal patellar enthesis in 22 patients (55%), Achilles enthesis in 27 patients (67.5%) & plantar aponeurosis enthesis in 25 patients (55%). There is a statistically significant difference between age and Ultrasound findings p. value <0.05. There is a statistically significant correlation between disease duration and (proximal patellar ligament, Achilles tendon, quadriceps tendon and plantar fascia) thickness p. value<0.05.

Conclusion: Enthesal abnormalities can be documented by ultrasonography in clinically asymptomatic patients with Diabetes. These findings could be related to a subclinical enthesal inflammation.

REFERENCES


Disclosure of Interests: None declared
**Results:** Demographics were 60.2±8.3 years of age, 65% female, BMI of 28.6±4.5 of kg/m²; 60% with Kellgren and Lawrence (KL) grade 2 and 40% with a KL grade 3. Semi-quantitative OMERACT ultrasound scores revealed a good to excellent IRR (Kw=0.73 -0.88) for osteophyte and moderate to good IRR (Kw=0.42-0.66) for synovitis. Conversely, quantitative measures of ultrasound pathologies had excellent IRR (ICC=0.84-0.95) except for synovial hypertrophy (ICC=0.67-0.72).

A significant association was found between semi-quantitative ultrasound measurements and MRI outcomes, the absolute feature-specific agreement is called into question. These is moderate to good IRR between operators with varying experience using the OMERACT knee scoring image atlas for osteophyte and synovitis. While quantitative ultrasound measurements showed excellent IRR and significant association with MRI quantitative outcomes, the absolute feature-specific agreement is called into question.

**REFERENCES**


**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.2134

**AB1168**

**SIGLEC1/C1D169 IS A SENSITIVE MARKER FOR MONOMERIC INTERFERONPATHIES**

**Banu Orak** 1,2, **Marc Nikolaus** 1,2, **Ellen Knierim** 1,2, **Angela Kaindl** 1,2, **Manuela Theophil** 1,2, **Axel Panzer** 4, **Barbara Zieba** 5, **Frédéric Ebstein** 5, **Elke Krüger** 5, **Nadine Unterwalder** 6, **Christian Meisel** 6, **Tilmann Kallinic** 1,2.

**Background:** Monomeric Interferonopathies are a rare group of inflammatory diseases that are difficult to diagnose in the onset phase given the lack of well-defined disease-markers. A correlation with interferon-stimulated genes (ISG) has been reported for SIGLEC1 (syn. CD169), in systemic lupus erythematosus (SLE). Furthermore, expression of SIGLEC1 on monocytes is the second highest ISG in SLE.

**Objectives:** To study the relevance of SIGLEC1 as a putative marker for early detection of interferonopathies.

**Methods:** Clinical data, classical inflammatory markers, blood count values and genetic information were obtained from the medical files of eight patients with genetically confirmed monomeric interferonopathies. SIGLEC1 expression was measured by flow cytometry with a highly standardized quantitative assay with a reference range in healthy controls less than 2500 SIGLEC1 molecules/monocyte. Additionally, transcriptional level of SIGLEC1, IFI44L, IFI27, ISG15 and RSAD2 as type I Interferon stimulated genes were assessed by real-time PCR.

**Results:** Eight patients with interferonopathies carried mutations in the genes TREX1 (n=3), IFIH1 (n=2), SAMHD1 (n=2) and RNASE2HB (n=1). Mean age of patients was 12 years (range 6 months to 49 years). Six of eight patients showed neurological symptoms consistent with Aicardi-Goutieres-Syndrome presenting developmental delay and microcephaly. Five patients showed abnormalities on cranial MRI including periventricular calcifications and corpus callosum thinning. Two patients were diagnosed with Singleton-Mertens Syndrome presenting abnormal ossification of extremities and dental anomalies. One patient with homozgyous TREDX1 mutation presented with postnatal glaucoma, microcephaly, sensorimotor polyneuropathy and recurrent fever with persistent chilblain lesions. All patients had elevated SIGLEC1 levels (mean molecules/monocyte +/- SD: 10272 +/- 3746) without high levels of standard inflammatory markers. In six patients, elevated SIGLEC1 expression showed dysregulation of the type 1 interferon pathway prior to genetic testing. The relative expression (ΔCt) of all ISG’s was significantly elevated in comparison to healthy controls (SIGLEC1 p= 0.0167, ISG15 p=0.0015, RSAD2 p=0.0067, IFI44L p=0.0001, IF27 p=0.0056).

**Conclusion:** We report high expression of SIGLEC1 in monomeric interferonopathies like Aicardi-Goutieres-Syndrome. Therefore, SIGLEC1 qualifies as an accessible and cheap diagnostic marker to screen patients with suspected interferonopathy.

**Disclosure of Interests:** Banu Orak: None declared, Marc Nikolaus: None declared, Ellen Knierim: None declared, Angela Kaindl: None declared, Manuela Theophil: None declared, Axel Panzer: None declared, Barbara Zieba: None declared, Frédéric Ebstein: None declared, Elke Krüger: None declared, Nadine Unterwalder: None declared, Christian Meisel: None declared, Tilmann Kallinic: Grant/research support from: Novartis, Speakers bureau: Sobi, Roche, Novartis, CLB

**DOI:** 10.1136/annrheumdis-2019-eular.5506

**AB1169**

**ASSOCIATION OF ANXIETY, DEPRESSION WITH ULTRASONOGRAPHIC EVALUATION OF THE JOINTS, DISEASE ACTIVITY, FUNCTIONAL DISABILITY AND QUALITY OF LIFE IN PATIENTS WITH RHEUMATIC DISEASES:**

**Rita Osipyants** 1, **Victoria Nadtocheeva** 2, **Madina Bogdanova** 3, **Marina Kanevskaya** 4, **Temuri Mirlashvili** 5, **Department of Internal Diseases, RUDN University; Ermanshantsev City Clinical Hospital, Moscow, Russian Federation; 6Department of Internal Diseases, RUDN University, Moscow, Russian Federation; 7FSBI “Polyclinic N6” of the Administrative Department of the President of the Russian Federation, Moscow, Russian Federation; 8Sechenov Moscow Medical University, Moscow, Russian Federation; 9Ermanshantsev City Clinical Hospital, Moscow, Russian Federation

**Objectives:** The aim of this study is to evaluate anxiety and depression disorders and to study their correlation with disease activity, ultrasonographic (US) finding indicative of synovitis, functional status and quality of life in patients (pts) with rheumatic diseases.

**Methods:** 39 pts (F/M–29/10) with rheumatoid arthritis (RA, n=17),ankylosing spondylitis (AS, n=10), psoriatic arthritis (PsA, n=12) were included. All RA pts fulfilled the ACR/EULAR 2010, AS pts - the ASAS, PsA pts - the CASPAR criteria. 20 pts (8 RA, 6 AS, 6 PsA) were performed US examinations (Minrad DC-N6 (China), C5-2, L10-13 MHz probes) included bilateral of the hip and knee joints. Each joint was scored according to the OMERACT definitions of pathology. Functional status (BASFI), disease activity indices (DAS28-CRP, ASDAS-CRP, DAPSA), anxiety and depression levels (Hads-A, Hads-D) and quality of life (RAPID3, EQ-SD) were assessed. The Mann-Whitney U-test was applied for intergroup comparison and correlation was evaluated using a Spearman’s Rank two-tailed test (R value is shown).

**Results:** Median age of 39 pts – 52 (44;61) years and the body mass index (BMI) 28.6±4.5 of kg/m2; 60% with Kellgren and Lawrence (KL) grade 2 and 40% with a KL grade 3. Semi-quantitative OMERACT ultrasound scores revealed a good to excellent IRR (Kw=0.73 -0.88) for osteophyte and moderate to good IRR (Kw=0.42-0.66) for synovitis. Conversely, quantitative measures of ultrasound pathologies had excellent IRR (ICC=0.84-0.95) except for synovial hypertrophy (ICC=0.67-0.72).

**References:**


**Disclosure of Interests:** Banu Orak: None declared, Marc Nikolaus: None declared, Ellen Knierim: None declared, Angela Kaindl: None declared, Manuela Theophil: None declared, Axel Panzer: None declared, Barbara Zieba: None declared, Frédéric Ebstein: None declared, Elke Krüger: None declared, Nadine Unterwalder: None declared, Christian Meisel: None declared, Tilmann Kallinic: Grant/research support from: Novartis, Speakers bureau: Sobi, Roche, Novartis, CLB

**DOI:** 10.1136/annrheumdis-2019-eular.2134
A PHASE IV, MULTICENTER, SINGLE-ARM, OPEN-LABEL STUDY TO EVALUATE THE IMPACT OF APRIMO CARNO METAL AND WHOLE-BODY MRI OUTCOMES IN PATIENTS WITH PSORIATIC ARTHRITIS (MOSAIC): RATIONALE, DESIGN AND METHODS

Mikkeli Östergaard1, Walter P. Maksymowczyk2, Mikaël Boesken3, Olga Kubassova4, Priscila Nakasato5, Benoît Guerette6, Lichen Teng7, Philip J. Mease8, 1University of Copenhagen, Copenhagen, Denmark; 2University of Alberta, Edmonton, Canada; 2BiSpiegel and Friedrichberg Hospital, Copenhagen, Denmark; 3Image Analysis Group, London, United Kingdom; 4Celgene Corporation, Summit, United States of America; 5Swedish Medical Center and University of Washington School of Medicine, Seattle, United States of America

Background: Phase III clinical trials have shown apremilast (APR) reduced PsA signs/symptoms and improved physical function, but no study has addressed its impact on structural disease progression. MRI is a highly sensitive, validated tool to assess inflammatory and structural changes, as it can detect soft tissue inflammation, bone marrow edema (BME) lesions, bone erosion and proliferation in peripheral joints and axial skeleton. Whole-body (WB)-MRI, a relatively novel technique in musculoskeletal studies, allows assessment of all peripheral/axial joints and entheseal changes in 1 examination. Recent, consensus-based and semi-quantitative scoring methods were developed and validated. This study is the first to systematically use new state-of-the-art MRI scoring methodologies to assess PsA inflammatory and structural changes in a global clinical trial.

Objectives: To assess APR efficacy on inflammatory indices and imaging outcome measures associated with PsA structural progression by conventional static MRI and dynamic contrast-enhanced (DCE)-MRI of the most affected hand and WB-MRI.

Methods: The study aims to enroll 120 biologic-naive adults with PsA for ≥3 mos to ≤5 yrs and prior treatment with ≥2 conventional DMARDs. Subjects must have ≥3 swollen and ≥3 tender joints, involvement (>1 swollen joint or >1 dactylitis) and ≥1 active enthesis site. After 4-wk screening, all eligible patients will receive APR 30 mg twice daily (titrated during the first 5 days) as monotherapy or in combination with methotrexate for 48 wks, with a 4-wk observational follow-up. Conventional MRI and optional DCE-MRI of the most affected hand and WB-MRI of the entire body will be performed at Wks 0, 24 and 48. The primary endpoint is change from BL to Wk 24 in OMERACT PsA MRI (PsAMRIS) composite score of BME + synovitis + tenosynovitis. Other imaging endpoints include change from BL to Wk 48 in PsAMRIS composite score (BME + synovitis + tenosynovitis) and change from BL to Wks 24 and 48 in PsAMRIS composite score (BME + synovitis), PsAMRIS composite inflammation score (BME + synovitis + tenosynovitis + periarthritis inflammation). PsAMRIS total damage score (erosion + bone proliferation), WB-MRI indices (including peripheral joint inflammation index and peripheral enthesis inflammation index), hip and knee inflammation MRI scores (HIKRISS, KIKRISS), OMERACT heel enthesis MRI indices, axial inflammation indices (SPARCC, CanDen), DEMRIO-Volume and DEMRIO-Inflammation and other DCE-MRI-derived parameters. Clinical parameters will include HLA-C21, cDAPSA, SPARCC Enthesitis Index, Leeds Dactylitis Index, Leeds Dactylitis Index, PASDAS, PGHS, PGHA, Patient's Assessment of Pain, HAQ-DI, and BASDAI and impact of disease (PsAID12). Safety and tolerability also will be assessed.

Results: The study protocol was approved by an independent ethics committee and is now enrolling in the USA. Selected countries in Europe and Russia will also participate. MRI, clinical and patient-reported outcomes will be analyzed.

Conclusion: This study will provide important evidence of APR’s impact on inflammatory/structural changes by assessing PsA structural progression by conventional static MRI and dynamic contrast-enhanced (DCE)-MRI of the most affected hand and WB-MRI. This study will provide important evidence of APR’s impact on structural disease progression. MRI is a highly sensitive, validated tool to assess inflammatory and structural changes, as it can detect soft tissue inflammation, bone marrow edema (BME) lesions, bone erosion and proliferation in peripheral joints and axial skeleton. Whole-body (WB)-MRI, a relatively novel technique in musculoskeletal studies, allows assessment of all peripheral/axial joints and entheseal changes in 1 examination. Recent, consensus-based and semi-quantitative scoring methods were developed and validated. This study is the first to systematically use new state-of-the-art MRI scoring methodologies to assess PsA inflammatory and structural changes in a global clinical trial.

REFERENCES
ARE CIRCULATING BLOOD BIOMARKERS FOR INFLAMMATORY RHEUMATIC DISEASES GENDER-DEPENDENT? – SYSTEMATIC REVIEW BASED ON OMICS DATA

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Background: Inflammatory rheumatic diseases (IRDs) are thought to be multifactorial diseases. Female-male ratio in IRDs differs according to the disease. In Rheumatoid Arthritis (RA) and Systemic Lupus Erythematosus (SLE) female prevalence is higher opposing to Ankylosing Spondylitis (AS). Until recently, differences on gender bias observed in predisposition to IRDs, and to their pathophysiology have been understudied and neglected. Recent research using omics approaches shows that gender-bias is widespread in a diversity of pathologies. The integration of omics results, despite the extremely complex crosstalk among the several biomolecules involved, places these methods at the lead of medical research, overcoming limitations and increasing the forecasts of targeted methodologies.

Objectives: The purpose of this systematic review is to aggregate existing omics results on biomarkers for RA, SLE and AS to raise awareness about whether gender can actually play a role on their profiles.

Methods: Two searches were conducted on PUBMED database (22nd November 2018) with a final output of 81268 articles. Both searches were sorted by best matches and for the second thousandth articles ranked no relevance was found for the aim of this review. The first 1000 articles were further analyzed based on the title, abstract and content. Three articles having relevant results were selected from the first thousand publications. Ten more were identified from the cross-references of both searches. The PICO (P, population; I, intervention; C, comparison; O, outcome) concept was used to perform the analysis according to: Patients: adults (>18 years old) with RA, SLE or AS (SpA); Intervention: any –omic study; Comparison: gender information regarding results; Outcomes: identified genes, proteins or metabolites.

Results: Dectin-2, MCP-1 and DC-SIGN polymorphisms where proposed as possible accounts for gender-associated differences in susceptibility to RA. Sex-differentiated and sex-interaction analyses of a GWA study revealed strong evidence of association in both sexes, highlighting links with RA only in one of the genders. Several transcriptomic studies pointed to gender differences on biomarkers profiles for the three diseases. For instance, different expression levels of TNFα, IL-6, IL-17, IL-18, IFNγ as well as X or Y chromosome-linked genes were found in SLE and/or AS. In AS, male patients with syndesmophytes showed higher levels of TNFα and men without syndesmophytes presented higher levels of VEGF, IL-6, TNFα and IL-18 both compared to females-matched. In RA patients, microRNAs 222, 532, 98, and 92a were found significantly down regulated in PBMC of female versus male. Six genes displayed a gender-based expression among male and female SLE patients.

Conclusion: Blood biomarkers signatures for the IRDs analyzed in this study have been shown gender-biased. These will contribute for a better understanding of these diseases pathophysiology and probably to different gender approaches regarding diagnosis, monitoring and therapeutic approach.

REFERENCES

ENDOCARDIAL LESIONS IN PATIENTS WITH RHEUMATIC DISEASES: CASE REVIEW

Sergio Rodríguez Montero, Consuelo Ramos Giráldez; PLAZA NAHIA, Jose Luis Marenco. Valme Hospital, Rheumatology, Sevilla, Spain

Background: The infection of a native or prosthetic heart valve usually occurs in patients with structural valvular anomalies that predispose to turbulent flows. Manifestations such as arthralgia, arthritis or back pain appear in up to 40% of patients, which acts as a confounding factor when this infection occurs in patients with rheumatic diseases. On the other hand, in the latter patients, noninfectious endocarditis has been described, which adds even more complexity to the diagnosis.

Objectives: To describe the characteristics of endocardial lesions in patients with rheumatic diseases.

Methods: Patients attending clinics at the Department of Rheumatology were analyzed to determine how many of them required hospitalization for causes directly related to endocardial lesion, from January 2015 until December 2018. The following information was recorded: age, sex, type of rheumatic disease, duration of the disease, immunosuppressive treatment, characteristics of endocardial lesions, complications of endocardial lesions, and cardiovascular risk factors.

Results: All patients were identified from an electronic database. Results regarding to demographic and clinical data are as follows:

Conclusion: The spectrum of endocardial involvement in patients with rheumatic diseases is variable. In this case review, we found lesions of different origin: infectious, thrombotic and tumoral. The appearance of fever of unknown origin in patients with rheumatic diseases, requires ruling out an endocarditis, needing transesophageal echocardiography in case the transthoracic study, which is less sensitive, is negative. It is striking the case of patient 3, a systemic sclerosis with calcinosis in limbs, whose endocardial wart, was studied histologically, revealing in its composition mainly calcium and fibrin. We have not found a bibliographic reference of calcium endocarditis in systemic sclerosis.

In conclusion, patients with rheumatic diseases can develop infectious endocarditis, but also thrombotic valvular vegetations, as well as myxomas. Whose consequences, from their clinical debut, may pose life-threatening situations for the patient. The presence of fever, stroke or embolic events in these patients should put us on the track of an underlying endocardial involvement.

REFERENCES

Disclosure of Interests: Sergio Rodríguez Montero: None declared, Consuelo Ramos Giráldez: PLAZA NAHIA: Jose Luis Marenco. Valme Hospital, Rheumatology, Sevilla, Spain

Table 1: Patients attending clinics at the Department of Rheumatology for causes directly related to endocardial lesion, from January 2015 until December 2018. The following information was recorded: age, sex, type of rheumatic disease, duration of the disease, immunosuppressive treatment, characteristics of endocardial lesions, complications of endocardial lesions, and cardiovascular risk factors.

<table>
<thead>
<tr>
<th>Age</th>
<th>Sex</th>
<th>Rheumatic disease</th>
<th>Baseline Treatment</th>
<th>Endocardial lesions</th>
<th>Complications</th>
<th>Clinical evolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>1° case</td>
<td>27</td>
<td>Male</td>
<td>Dermatomyositis</td>
<td>Methotrexate + glucocorticoids</td>
<td>Digital ulcer + Staphylococcus Aureus</td>
<td>Infectious endocarditis</td>
</tr>
<tr>
<td>2° case</td>
<td>64</td>
<td>Male</td>
<td>Rachailgia</td>
<td>Digital ulcer + glucocorticoids</td>
<td>Staphylococcus</td>
<td>Infection endocarditis</td>
</tr>
<tr>
<td>3° case</td>
<td>53</td>
<td>Female</td>
<td>Systemic Sclerosis</td>
<td>Tocilizumab + glucocorticoids</td>
<td>Nonbacterial thrombotic endocarditis</td>
<td>Acute ischemia right upper limb</td>
</tr>
<tr>
<td>4° case</td>
<td>13</td>
<td>Female</td>
<td>Autoimmune</td>
<td>Glucocorticoids, Ischemic stroke</td>
<td>Aortic myxomatosis</td>
<td>-</td>
</tr>
<tr>
<td>5° case</td>
<td>48</td>
<td>Female</td>
<td>Thrombocytopenia</td>
<td>Glucocorticoids, Splenectomy</td>
<td>Aortic myxomatosis</td>
<td>Systemic lupus ANA and anti-DNA</td>
</tr>
</tbody>
</table>

declared, Jose Luis Marconc© Speakers bureau: abbie, pfizer, novartis, jannsen


Table 1

<table>
<thead>
<tr>
<th>Segment</th>
<th>RA patients</th>
<th>Controls</th>
<th>Comparison (χ²-test)</th>
</tr>
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<tbody>
<tr>
<td>L1-L2 Left</td>
<td>1 (3.0%)</td>
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<td>χ²=0.157, df=1, p=0.692</td>
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<tr>
<td>L2-L3 Left</td>
<td>0 (0.0%)</td>
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<tr>
<td>L3-L4 Left</td>
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<tr>
<td>L4-L5 Left</td>
<td>2 (6.1%)</td>
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<td>L4-L5 Right</td>
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<td>Total L1-S1 score</td>
<td>9 (27.2%)</td>
<td>11 (19.0%)</td>
<td>χ²=0.046, df=1, p=0.838</td>
</tr>
</tbody>
</table>

Table 1: Correlation coefficients between twelve spine score. Fusion scores and stability with the highest score in all joint combinations.

Bayesian logistic mixed models were fitted with age, sex, and disease duration included as fixed effects. The model selection was based on the Bayesian information criterion. The χ²-test was used to compare the performance of the different models. The null hypothesis was rejected if the p-value was less than 0.05.

Conclusion: The present study of patients with RA shows that the US examination of both hands only for assessing disease activity is highly correlated for with the 46-joint evaluation at all time points, both regarding GS and Doppler sum scores. Using hands as a reduced joint set US assessment of inflammation could be an option to increase the feasibility of US in routine clinical practice.

Disclosure of Interests: Dolores Ramos-Bello: None declared, Hilde Berner Hammer Grant/research support from: Abbvie, Pfizer and Roche.

Paid instructor for: Abbvie, Pfizer, UCB, Novartis, Roche, Speakers bureau: Abbvie, Pfizer, UCB, Novartis, Roche, Mette Bjørndal Axelsen: None declared, Mikkel Østergaard Grant/research support from: Abbvie, Celltech, Merck, Novartis, Synovis, Wii, Orion, Pfizer, Regeneron, Roche, and UCB, Speakers bureau: Abbvie, BMS, Boehringer-Ingehelm, Celgene, Eli Lilly, Hospira, Jansen, Merck, Novartis, BMS, MSD, Abbvie, Roche, Novartis, Biogen, Pfizer, Consultant for: Eli Lilly, Speakers bureau: Orion Pharma, Biogen, Pfizer, CellTrion, Merck, Samsung Bioepis, Susanne Juul Pedersen: None declared, Lene Terslev Speakers bureau: Speakers fee from: Roche, Novartis, Pfizer, MSD, BMS, Celgene


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Table 1: Prevalence of FJ degenerative changes in patients with RA and age and sex-matched peers.

Results: Prevalence of facet joints changes in patients with RA and group of age and sex-matched controls were not significantly different at any spinal level or in total L5-S1 score. Marginal erosions, that are characteristic feature of joint change in RA, were not found in any subject with RA in our sample. In subjects with RA, individuals with affected FJs and without affected FJs have no difference in any disease parameters and markers (Tables 1 and 2).

Conclusion: In our samples of CT scans we did not find a difference in facet joints changes between the subject with RA and control group. The occurrence of FJs changes among subjects with RA had no correlation with disease duration and activity. According to the findings, we may assume, that facet joints of the lumbar spine are not involved in the inflammatory process of RA, and patients' low back pain is not due to inflammation in this region of the spine.

FACET JOINTS INVOLVEMENT IN RHEUMATOID ARTHRITIS: A CROSS-SECTIONAL STUDY

Tatiana Reitblat1, Lina Linov2, Fadi Badeer3, Azara Simonovich3, Leaard Kalichman2, Barzilai MC, Rheumatology Unit, Ashkelon, Israel, 2Barzilai MC, Radiology, Ashkelon, Israel, 3Recanati School for Community Health Professions, Faculty of Health Sciences at Ben-Gurion University of the Negev, Department of Physical Therapy, Beer-Sheva, Israel

Background: Even it is accepted among rheumatologists that rheumatoid arthritis (RA) does not involve the facet joints (FJs) of the spine, the issue is still under debate. Studies that described a prevalence of the FJs in rheumatoid arthritis patients are scarce.

Objectives: To compare the prevalence of FJs changes between patients with RA and age and sex-matched peers.

Methods: We compared computed tomography (CT) scans of 34 patients with RA, who suffered from low back pain, and 70 age and sex-matched controls-people without RA, with low back pain. The changes in FJs were evaluated according to the score proposed by Kalichman et al: joint space narrowing, marginal osteophytes, articular process hypertrophy, subchondral sclerosis, inter-joint vacuum phenomenon, and subchondral cysts. The characteristic joint changes of RA were also evaluated.

Disease activity characteristics, duration of RA, age, and gender were taken from patients' clinical charts.

Results: Prevalence of facet joints changes in patients with RA and group of age and sex-matched controls were not significantly different at any spinal level or in total L5-S1 score. Marginal erosions, that are characteristic feature of joint change in RA, were not found in any subject with RA in our sample. In subjects with RA, individuals with affected FJs and without affected FJs have no difference in any disease parameters and markers (Tables 1 and 2).

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ABSTRACT AB1175

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CRP– C-reactive protein; ESR – Erythrocyte sedimentation rate; DAS-Disease Activity Score; CDAI – Clinical Disease Activity Index; SDAI – Simple Disease Activity Index.

REFERENCES


Disclosure of Interests: Tatiana Reibltal Consultant for: Abbvie, Eli Lilly, Lina Linov. None declared, Fadi Badee: None declared, Azaria Simono- vich: None declared, Leonid Kalichman: None declared


AB1176

CORRELATION OF THE FINDINGS OF ULTRASOUND EXAMINATION OF THE LUNGS AND INTERSTITIAL LUNG FIBROSIS IN PATIENTS WITH SYSTEMIC SCLEROSIS

Nikola Raganovic, Institute of Rheumatology, Belgrade, Serbia

Background: Interstitial lung disease is one of the most severe complications in patients with systemic sclerosis (SSc), especially in those with diffuse form of this disease. Carbon monoxide diffusion capacity (DLCO) measurement is an important diagnostic method for assessing lung fibrosis. In recent years, ultrasound (US) lung examination has been used to evaluate the presence of interstitial changes (B lines) in the lungs.

Objectives: Determine whether there is a statistically significant difference in positive US findings on the lungs between the groups of subjects with a diffuse SSc and limited SSc, and whether there is a statistically significant difference in the presence of pulmonary fibrosis between these two groups of subjects. Then determine whether there is a correlation between the presence of B lines on the US examination of the lungs and the finding of lung fibrosis in patients with diffuse and limited SSc.

Methods: The study included 55 patients of both sexes with SSc from the Institute of Rheumatology (28 with diffuse and 27 with limited SSc), aged between 43 and 79 years. Data on the presence of pulmonary fibrosis were based on clinical findings and reduced lung diffusion parameters (DLCO less than 75%). An US examination of the lungs was performed for all patients and the number of B lines in all lung segments was determined. Positive US finding was the finding of 3 or more B lines in at least two adjacent fields of US scanning or more than 5 B lines in any single field of ultrasonics scanning.

Results: There was a statistically significant difference in positive US findings on the lungs between the groups of subjects with diffuse SSc and limited SSc (85.7% versus 44.4%, p <0.001). A statistically significant difference was observed in the presence of pulmonary fibrosis between the groups of subjects with diffuse SSc and limited SSc (85.7% versus 55.6%, p <0.05). It has also been shown that there is a highly statistically significant correlation between the presence of B lines on US examination of the lungs and findings of lung fibrosis in patients with diffuse and limited SSc (r = 0.700, p <0.001).

Conclusion: The conducted study confirmed that there is a highly statistically significant correlation between the presence of B lines in the US examination of the lungs and the findings of lung fibrosis in patients with diffuse and limited form of SSc. The study also found that patients with diffuse SSc had significantly more frequent positive US findings on the lungs, as well as a more frequent presence of pulmonary fibrosis compared to the patients with limited SSc. Introducing US into a routine protocol for monitoring patients with SSc diagnosis would provide a simple, inexpensive, fast and accurate orientation to the development of fibrotic changes in the lungs.

REFERENCES


Disclosure of Interests: None declared


AB1177

HOW TO DEFINE RHUPUS SYNDROME: SYSTEMATIC REVIEW OF THE CURRENT LITERATURE

Elena Rubini, Silvia Grazietta Foddai, Massimo Radin, Irene Cecchi, Daniela Rossi, Savino Sciascia, Dario Roccattelo, University of Turin, Turin, Italy

Background: Systemic lupus erythematous (SLE) is a chronic autoimmune disease characterized by the presence of multi-systemic manifestations in patients with immunologic anomalies. While joint involvement is present in up to 90% of patients with SLE [1], only a small subset of patients develops erosive arthritis. The term rhupus refers to the coexistence of erosive symmetrical polyarthritis, typical manifestation of rheumatoid arthritis (RA), and clinical signs of SLE in the presence of anti-double-stranded DNA (anti-dsDNA) and/or anti-Smith antibodies (anti-Sm) [2]. However, to date, no consensus exists on how to define the rhupus syndrome.

Objectives: In this study we aim to investigate the definition of rhupus by systematically reviewing the current literature.

Methods: A detailed literature research has been developed a priori to identify articles that reported findings from rhupus patients. The search strategy was applied to Ovid MEDLINE In-Process and Other Non-Indexed Citation 2000 to present. Studies that included rhupus patients were systematically analyzed by two independent reviewers (ER and SGF). Disagreements were resolved by consensus; if consensus could not be achieved, a third party (MR) would provide an assessment of eligibility.

Table 1

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
<th>Patients</th>
<th>RA</th>
<th>SLE</th>
<th>Anti-dsDNA</th>
<th>Anti-Sm</th>
<th>Anti-citrullinated peptide antibodies</th>
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<tbody>
<tr>
<td>Study 1</td>
<td>Case-control</td>
<td>50</td>
<td>30</td>
<td>20</td>
<td>70%</td>
<td>50%</td>
<td>80%</td>
</tr>
<tr>
<td>Study 2</td>
<td>Retrospective</td>
<td>100</td>
<td>60</td>
<td>40</td>
<td>80%</td>
<td>60%</td>
<td>90%</td>
</tr>
</tbody>
</table>

Results: We analyzed clinical and serological data of 176 patients with diagnosis of rhupus derived from a total of 16 studies. All works considered the presence of autoantibodies specific for SLE by including anti-nuclear antibodies (ANA), anti-dsDNA, and anti-Sm antibodies. Only 67% of patients had ANA positivity (113/176), 64% showed anti-dsDNA in serum (113/176) and 17% were positive for anti-Sm antibodies. No heterogeneous data were available on pattern or title of these autoantibodies. Only two studies did not assay ANA or anti-dsDNA. Twelve out of 16 studies tested the occurrence of anti-citrullinated peptide antibodies (ACPAs) that have been reported in 73 patients (41%), rheumatoid factor (RF) was detected in 149 patients (84%) resulting from 13 out of 16 studies. Among clinical criteria of rhupus, an erosive arthritis has been observed in 155 patients (88%), only one study did not take into account the joint erosion. Hematological and cutaneous disorders (64% and 86%,
PLANTOGRAPHIC ASSESSMENT OF FOOT DEFORMITIES IN PATIENTS WITH RHEUMATOID ARTHRITIS

Russka Shumnaliev, Simeon Monov. Clinic of Rheumatology, Department of Internal Medicine, Medical University-Sofia, Sofia, Bulgaria

Background: In almost one third of the patients with rheumatoid arthritis (RA) the disease begins with involvement of the small joints of the feet with high risk for developing significant foot deformities with disease progression. Irreversible structural changes occur as a result of synovitis combined with mechanical stress. The pain and the impaired static cause functional disability in these patients and the orthotic correction is often limited and with no evidence for effectiveness.

Objectives: To assess the foot structure and determine the incidence of foot deformities in patients with RA with different disease duration ranging from 3 months to more than 10 years.

Methods: Forty two RA patients (32 women and 10 men) underwent assessment of the foot structure under an axial load and while walking on a pressure measuring plate as well as a 3D scan of the feet.

Results: The most common foot deformities found in the study group included hallux valgus deformity in 73.81%, flattening of the medial longitudinal arch in 64.29% and valgus deformity of the calcaneus in 35.71% of the patients.

Conclusion: The introduction of the plantography in the clinical practice offers the opportunity for early diagnosis of foot deformities in patients with RA and indicates the necessity of correction through orthotics or surgery.

Disclosure of Interests: None declared

AB1179

TYPES OF JOINT LESIONS IN REACTIVE ARTHROPATHY

Volha Sirotka1, Uladzimir Sirotka2, Alexander Litvyakov1. 1Vitebsk State Order of Peoples’ Friendship Medical University, Department of internal diseases №1, Vitebsk, Belarus; 2Vitebsk State Order of Peoples’ Friendship Medical University, Department of traumatology, orthopedics and military field surgery, Vitebsk, Belarus

Background: Differential diagnosis of ReA has certain difficulties, especially at an early stage in the absence of confirmation of trigger infection. Radiographic signs of joint damage when the response are not specific and appear not earlier than 3-6 months from the onset of the disease; enthesitis this method is not visualized, making it difficult to timely diagnosis of ReA [1]. To determine the tactics of patient management and selection of adequate therapy is no less important to determine the duration and characteristics of the course of ReA.

Objectives: To study the ultrasonic features of joint lesions in reactive arthropathy depending on the course of the disease.

Methods: We examined 66 patients with ReA who met the preliminary international criteria were examined (4th International Workshop on Reactive Arthritis, Berlin 1999). Women were 26 (39%), men - 40 (61%), median age - 34 years (31-42), median duration of ReA- 1 year (0.3-3.25). Among the patients there were 40 (61%) people with acute ReA and 26 (39%) people with chronic ReA. All patients had confirmed chlamydial infection (PCR and IFA). Patients underwent a comprehensive clinical and laboratory examination, MRI and ultrasound of the knee joints. Statistical processing of the information package.

Results: The MRI of the affected joints clearly visualized inflamed entheses and the presence of local osteitis with an erosive defect of the closing plate of the bone (Fig.1).

In patients with acute ReA were visualized: thickening of entheses more than 3 mm (98%), hypo-, anechogenic areas in the projection of the tendon-ligamentous apparatus and places of its fixation (74%), the formation of a bone defect under them with a contour of reduced echogenicity (erosion of acute inflammation - 66.8%) and uneven edges, pronounced effusion (75%), lack of strengthening of local blood flow in the projection of synovia and joint structures (Fig.2).

In patients with chronic ReA, the following were visualized: thickening of entheses to 3 mm (65%), hyperechogenic inclusions in the projection of the tendon-ligamentous apparatus and its fixation sites (53%), the formation of a bone defect under them with a contour of increased echogenicity (erosion of chronic inflammation - 46.9%) and uneven edges, slight effusion (28%), the absence of strengthening of local blood flow in the projection of synovia and joint structures (Fig.3).

Disclosure of Interests: None declared

REFERENCES

Figure 1

Figure 2

Figure 3
REFERENCES


Disclosure of Interests: None declared

AB1180 ULTRASOUND SEMIOTICS OF DEFEATS OF THE JOINTS IN REACTIVE ARTHRITIS AND OSTEARTHROSIS

Volha Sirotska1, Uladzimir Sirotska2, Alexandr Libyakov1. 1Vitebsk State Order of Peoples’ Friendship Medical University, Department of internal diseases, Vitebsk, Belarus 2Vitebsk State Order of Peoples’ Friendship Medical University, Department of traumatology, orthopedics and military field surgery, Vitebsk, Belarus

Background: The most common cause of knee joint damage in people of working age is osteoarthritis. However, in recent years, cases of reactive arthropathy, which often takes a chronic course, have become more frequent [1]. Given the current possible ultrasonic equipment, relevant is the study to study the ultrasonic features of defeat of joints with ReA and OA.

Objectives: To study the ultrasonic features of joint lesions at osteoarthritus and reactive arthritis.

Methods: We studied 55 patients with ReA and 22 patients with OA. Among patients with ReA were 25 women and 20 men, median age was 31 years (18 to 47), the median duration of the current Illipe - of 2.86 (0.07-29.0) months. Among patients with OA were examined in 15 women and 7 men, median age was 56.5 years (43-61), the median duration of flow OA - 139 months (12-360 months). All patients with ReA at the time of the study or in history had confirmed genital chlamydial infection. All patients were multiplescule dynamic study of the knee by the ultrasonic device expert class using a sensor with a frequency of 12 MHz.

Results: As a result of the ultrasound examination of the 110 joints with ReA, we have identified: pronounced synovitis in 69 (62.7%) joints, but the absence of pathological vascularization in the projection of the synovia; narrowing of the joint space 73 (66,4%) joints; heterogeneous structure of the ligament in 82 (75%) joints, tenosynovitis in 20 (18%) joints, thickening entheses in 89 (80.9%) joints; hypoechoic inclusions in projection entheses in 39 thickening entheses in 89 (80.9%) joints, hypoechoic entheses in 72 ture of the ligament in 82 (75%) joints, tenosynovitis in 20 (18%) joints, via; narrowing of the joint space 73 (66,4%) joint; heterogeneous struc-

Fig.2 (a,b,c) Ultrasound examination of knee joints in a patient with OA

Conclusion: Ultrasound criteria of joint damage in ReA are: no hypervas-

REFERENCES


Disclosure of Interests: None declared

AB1181 ULTRASOUND PATHOLOGICAL PATTERNS AT CARPAL TUNNEL LEVEL IN RHEUMATOID ARTHRITIS AND IDIOPATHIC CARPAL TUNNEL SYNDROME

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Background: High-frequency ultrasound (US) has proven to be a useful imaging tool for the evaluation of carpal tunnel pathology. US impact in the assessment of idiopathic carpal tunnel syndrome (CTS) has been widely investigated, but only few studies have been carried out with the aim of revealing the pathologic conditions responsible for CTS in rheuma-

Fig.1 (a,b,c) Ultrasound examination of knee joints in a patient with ReA

As a result of the ultrasound examination of the 44 joints with osteoarthritis, we have identified: a decrease in the thickness of the cartilage and narrowing of the joint space of degree 1 in 14 (31.8%) joints, reduc-

Results: CTS was diagnosed in 21 out of 112 wrists (18.75%) and in 14 out of 56 RA patients (25%). Enlarged median nerve was found in 4 out of 21 wrists with RA and CTS (19%), in 6 out of 84 wrists of patients without CTS (7.1%) and in 22 out of 24 wrists of patients with idiopathic CTS (91.7%). Flexor tenosynovitis was found in 6 out of 21 wrists with RA and CTS (28.6%), in 8 out of 84 wrists of patients without CTS (9.2%) and in 4 out of 24 wrists with idiopathic CTS (16.7%). Palmar radio-carpal synovitis was found in 4 out of 21 wrists with CTS (19%), in 10 out of 84 wrists of patients without CTS (11.9%) and in 1 out of 24 wrists with idiopathic CTS (4.2%). Marked bone profile irregularities were detected in 3 out of 21 wrists with CTS (14.3%), in 22 out of 84 wrists without CTS (26.2%) and in none of the patients without RA. In RA patients, positive intra-neural PD signal was found in 9 out of 21 wrists with CTS (42.8%) and
in 12 out of 84 wrists without CTS (14.3%). In idiopathic CTS, PD signal was found in 15 out of 24 wrists (62.5%).

**Conclusion:** US allowed a detailed identification of the pathological findings at carpal tunnel in both RA and idiopathic CTS patients. When CTS was diagnosed, different US patterns were distinguished being median nerve less frequently enlarged and synovitis more frequently detected in RA patients. Finally, a positive association was found between the presence of intra-neural PD signal and clinical diagnosis of CTS independently of the diagnosis of RA.

**REFERENCES**


**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.5725

**AB1182**

THE CORRELATION BETWEEN THE ULTRASOUND-DETECTED SYNOVITIS OF SMALL JOINTS AND THE DISEASE ACTIVITY IN PATIENTS WITH RHEUMATOID ARTHRITIS

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**Background:** In patients with rheumatoid arthritis (RA), small joints, especially metacarpophalangeal (MCP), and interphalangeal (PIP) joints are frequently affected. Ultrasound (US) is a sensitive method for detecting joint inflammation in patients with RA. So far, what degree does the synovitis of every small joint contribute to the disease activity in RA was not clear.

**Objectives:** The purpose of the present study was to compare the correlation between the ultrasound-detected synovitis of small joints and the disease activity in RA.

**Methods:** 211 RA patients with DAS28-ESR >2.6 were included in this study. Thirty joints, including bilateral metacarpophalangeal (MCP) 1-5, proximal interphalangeal (PIP) 1-5 and metatarsophalangeal (MTP) 1-5 joints, were evaluated by ultrasound scan in all patients. Disease activity was assessed by DAS28-ESR, DAS28-CRP, CDAI, SDAI. Synovitis was detected by using semi-quantitative scoring systems (0-3) for grey scale (GS) and power Doppler (PD). All correlations among US variables and clinical variables were assessed using Spearman’s rank correlation test.

**Results:** Their median age was 51.82 years, median disease duration was 60 months, with 84.3% females. The mean (SD) DAS28-ESR and DAS28-CRP were 4.59±1.51 and 4.18±1.39, respectively. The whole GS scores of MCPs (MCP1-5 joints) showed highest correlation with the disease activity (r=0.404-0.452, p<0.01), including DAS28-ESR, DAS28-CRP, CDAI, SDAI, followed by PD (r=0.318-0.331, p<0.01) and MTPs (r=0.277-0.301, p<0.01). Similarly, the whole PD scores of MCPs also showed highest correlation with the disease activity (r=0.332-0.396, p<0.01), followed by PIPs (r=0.211-0.242, p<0.01), and then the least MTPs (r=0.198-0.222, p<0.01). In individual joint, GS score showed better correlation with disease activity than PD score. In 30 joints, MCP3 joint exhibited the highest correlation between GS score and DAS28-ESR (r=0.411, p<0.01), DAS28-CRP (r=0.459, p<0.01), SDAI (r=0.444, p<0.01). MCP2 joint exhibited the highest correlation between GS score and CDAI (r=0.421, p<0.01). While MCP5 joint exhibited the highest correlation between PD score and DAS28-ESR (r=0.353, p<0.01), DAS28-CRP (r=0.399, p<0.01), CDAI (r=0.368, p<0.01), SDAI (r=0.377, p<0.01). In 30 joints, PIP1 joint showed lowest correlation between GS (r=0.166-0.199, p<0.01) and PD (r=0.134-0.143, p<0.01) score and disease activity.

**Conclusion:** In small joints of RA patients, the ultrasound-detected synovitis of MCPs had best correlation with disease activity, compared with PIPs and MTPs. In individual joint, MCP2, MCP3, and MCP5 joint had the best correlation between ultrasound-detected synovitis and disease activity, while PIP1 joint showed lowest correlation.

**REFERENCES**


**AB1183**

ULTRASOUND POWER DOPPLER AND GREY-SCALE JOINT INFLAMMATION: WHAT DO THEY REVEAL ABOUT RHEUMATOID ARTHRITIS?

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**Background:** Grey-scale (GS) and Power Doppler (PD) imaging are routinely performed when assessing rheumatoid arthritis (RA) joint inflammation using ultrasound (US). While PD vascularity is often regarded as an US feature of more active joint inflammation, the true clinical significance of GS joint inflammation in RA is less understood.

**Objectives:** To gain further insight into US PD and GS joint inflammation through studying their relationship with two distinct, yet important outcome measures: (i) DAS28 – a disease activity measure and (ii) US-detected erosion - a structural joint damage measure.

**Methods:** In this cross sectional study, US PD and GS joint inflammation were graded semi-quantitatively (0-3), while bone erosion(s) was scored dichotomously (1=yes/0=no) at each joint recess. At the patient level, PD and GS scores were correlated with DAS28 and US erosion scores respectively using Pearson’s correlation coefficient, while linear regression was used to characterize the relationship between variables.

**Results:** 1080 joints and 1800 joint recesses from bilateral elbows, wrists, MCPJs, thumbs’ IPJs, PIPJs, ankles and MTPJs were scanned in 30 adult RA patients (baseline characteristics: 76.7% Chinese; 93.3% female; mean (SD) DAS28, 3.58 (1.20); mean (SD) disease duration, 70.3 (61.2) months). PD scores were correlated (r=0.46, P<0.0104) with DAS28 but not with US erosion scores. GS scores were correlated (r= 0.64, P<0.0001) with US erosion scores but not with DAS28 (table 1). Scatter plots for these variables are presented in Figure 1. Results of simple linear regressions showing PD as a predictor of DAS28 (coefficient (95% CI), 0.167 (0.048, 0.286); P<0.0104) and GS as a predictor of US erosion (coefficient (95% CI), 0.223 (0.125, 0.322); P<0.0001) are summarized in table 2.

**Acknowledgement:** The authors thank all the colleagues in our department for kind cooperation in this project and the patients for participating in this study.

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.5549

Figure 1
correlation with DAS28. In contrast, GS joint inflammation is associated with structural joint damage and has strong correlation with US-detected erosion.

REFERENCES


Abstract AB1183 Table 1. Pearson’s correlation for the ultrasound and clinical variables

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<th>Variables</th>
<th>Correlation coefficient</th>
<th>P-value</th>
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<tr>
<td>PD score</td>
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<tr>
<td>GS score</td>
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<td>0.2634</td>
</tr>
<tr>
<td>Correlation with number of joint recesses with ultrasound-detected erosion(s)</td>
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<td></td>
</tr>
<tr>
<td>PD score</td>
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<td>0.2302</td>
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<tr>
<td>GS score</td>
<td>0.64</td>
<td>0.0001***</td>
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</table>

Statistically significant: * p<0.05; *** p<0.001

Abstract AB1183 Table 2. Linear regression for the ultrasound and clinical variables

<table>
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<th>Coefficient (95% CI)</th>
<th>P-value</th>
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<td>Prediction of DAS28</td>
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<tr>
<td>PD score</td>
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</tr>
<tr>
<td>GS score</td>
<td>0.016 (-0.012, 0.044)</td>
<td>0.2634</td>
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<tr>
<td>Prediction of number of joint recesses with ultrasound-detected erosion(s)</td>
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</tr>
<tr>
<td>PD score</td>
<td>0.371 (-0.222, 0.963)</td>
<td>0.2302</td>
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<tr>
<td>GS score</td>
<td>0.223 (0.125, 0.322)</td>
<td>0.0001***</td>
</tr>
</tbody>
</table>

Statistically significant: * p<0.05; *** p<0.001

Disclosure of Interests: None declared

Figure 1

Results: Demographic, densitometric, TBS and 3D-DXA parameters are shown in table 1. Of the 73 subjects included, 38 (52%) had pathogenic mutations in ALPL. Between premenopausal women and men above 50 years, 9 subjects (29%) with ALPL mutations had osteopenia and 4 (13%), osteoporosis whereas 4 (13%) and 2 (6.5%) were detected in the HPP-GT group, respectively (p<0.05). Between premenopausal women and men under age 50, only 2 (5%) showed low BMD (Z-score < -2). BMD at femoral neck was significantly lower in the HPP + GT group compared to the HPP- GT group (0.864 ± 0.18 vs 0.948 ± 0.16 (p=0.014), similar findings were found for Wards area (0.695 ± 0.14 and 0.781 ± 0.16, p=0.021) and a trend was observed at the femoral diaphysis (p=0.076), BMD at the LS and TBS assessment did not show differences. Major, hip FRAX and T-FRAX were superior in the HPP + GT group. In terms of the parameters of bone metabolism, ALP levels were lower in the HPP + GT (p= 0.0004), serum phosphate levels were higher in this group (p=0.01) and the rest did not show differences. The 3D-SHAPER software was applied in a subgroup of 52 subjects: volumetric BMD at the PF was lower in the HPP + GT (873.6 ± 84.4 g/cm² vs 819.4 ± 95.3 g/cm²; p = 0.035) with no differences in trabecular vBMD (p=0.117).

Conclusion: HPP + GT group showed lower BMD at femoral neck and wards area and this trend was also observed at the diaphysis. At the femur, vBMD was also lower in this group. No differences in BMD at the lumbar spine and in TBS were found. These findings and its value for predicting the risk of fractures, specially in atypical femoral fractures, must be elucidated.

Disclosure of Interests: Carolina Tomero: None declared, Monica Coronado: None declared, Ludovic Humbert: None declared, Sara Garcia-Carazo: None declared, Carmen Lancha: None declared, Domenico Monachello: None declared, Luis Dominguez-Gadea: None declared, Alejandro Balsa: Pilar Aguado, 1 La Paz University Hospital, Rheumatology, Madrid, Spain; 2 La Paz University Hospital, Nuclear medicine, Madrid, Spain; 3 Galgo Medical, Madrid, Spain

Background: Scarcie evidence exists on the assessment of bone mineral density (BMD) in adult Hypophosphatasia (HPP). Recent studies suggest that dual-energy X-ray absorptiometry (DXA) could not appropriately predict their fracture risk and note the importance on further explore bone microstructure.

Objectives: To evaluate BMD at the lumbar spine (LS) and proximal femur (PF) assessed by DXA, the trabecular bone score (TBS) at the femur, vBMD was also lower in this group. No differences in BMD at the lumbar spine and in TBS were found. These findings and its value for predicting the risk of fractures, specially in atypical femoral fractures, must be elucidated.

Disclosure of Interests: Carolina Tomero: None declared, Monica Coronado: None declared, Ludovic Humbert: None declared, Sara Garcia-Carazo: None declared, Carmen Lancha: None declared, Domenico Monachello: None declared, Luis Dominguez-Gadea: None declared, Alejandro Balsa Grant/research support from: Abbvie, Pfizer, Novartis, BMS, Nordic, Sanofi, Consultant for: Abbvie, Pfizer, Novartis, BMS, Nordic, Sanofi, Sandoz, Lilly, Paid instructor for: Pfizer, Speakers bureau: Pfizer, Novartis, UCB, Nordic, Sanofi, Sandoz, Lilly, Pilar Aguado: None declared

AB1184 BONE MINERAL DENSITY, TRABECULAR BONE SCORE AND 3D-DXA ASSESSMENT IN ADULT PATIENTS WITH A POSITIVE AND NEGATIVE GENETICAL TESTING FOR HYPOPHOSPHATASIA

Carolina Tomero1, Monica Coronado2, Ludovic Humbert3, Sara García-Carazo1, Carmen Lancha2, Domenico Monachello2, Luis Dominguez-Gadea3, Alejandro Balsa1, Pilar Aguado1, 1 La Paz University Hospital, Rheumatology, Madrid, Spain; 2 La Paz University Hospital, Nuclear medicine, Madrid, Spain; 3 Galgo Medical, Madrid, Spain

Background: Scarcie evidence exists on the assessment of bone mineral density (BMD) in adult Hypophosphatasia (HPP). Recent studies suggest that dual-energy X-ray absorptiometry (DXA) could not appropriately predict their fracture risk and note the importance on further explore bone microstructure.

Objectives: To evaluate BMD at the lumbar spine (LS) and proximal femur (PF) assessed by DXA, the trabecular bone score (TBS) at the LS and the fracture risk assessment (FRAX and adjusted by TBS, T-FRAX) in patients with persistent low alkaline phosphatase levels (ALP) and HPP genetically confirmed (HPP TG +) compared to a group of subjects with the same biochemical abnormality and a negative HPP genetic test (HPP TG -). As a secondary objective, to assess the cortical and trabecular bone at the PF using DXA-based 3D modeling.

Methods: Seventy-three subjects with persistent low ALP levels - at least two values < 35 IU/L and none > 45 IU/L - and a genetic test for HPP performed were included. Individuals were distributed into 2 groups according to their genetic status. BMD was measured using GE-LUNAR iDXA and TBS. The 3D-SHAPER software was employed in a subgroup of 52 subjects matched by age, gender and body mass index. A clinical questionnaire and a battery of lab measures to assess risk factors for Osteoporosis were also performed.

Results: Demographic, densitometric, TBS and 3D-DXA parameters are shown in table 1. Of the 73 subjects matched by age, gender and body mass index. A clinical questionnaire and a battery of lab measures to assess risk factors for Osteoporosis were also performed.
or with nodules of Schmorl, in isolation or in a maximum of two vertebral bodies, to distinguish it from Scheuermann’s disease (2). Image 1.

**Objectives:** Current vertebral indexes, don’t measure a relation between a person height and his vertebra, and if the harmony of the individual is accepted, an index that combines these variables must be created in order to guaranteeing the objectivity of the resultant value.

![Image 1](https://via.placeholder.com/150)

**Methods:** Patients attending physician since 1994, both sexes, 20-55 years old, in whom Type II collagen disease or vertebral dysplasia was suspected, were selected for the study. A control group was created in 2054 formed within 3 days after the onset of symptoms, but our short series did not show any significant difference compared to the previous imaging, on average 6 days after the beginning of their symptoms. 4 early signs in favour of the diagnosis of infectious sacro ilios could be identified: fat infiltration in front of the sacroiliac joint in 86% of cases, bulging and elevation of the anterior part of the joint capsule in 43%, swelling of the piriform (71%) and iliac (71%) muscles on the sacroiliac side. All patients had at least 1 positive sign out of 4, 86% had at least 2. In 1 case, signs of osteitis were present. In 4 out of 7 cases, the injection of iodized contrast medium did not provide any additional element compared to the non-injected sequences. 5 patients underwent an MRI after the scan, which confirmed the signs in favour of the infectious nature of sacroiliitis. MRI detected in one case an aspect of osteomyelitis of the sacrum and iliac bone, but also a hypersignal of the joint space on the T2 sequences (80%) and a better visualization of abscesses.

In the literature, there is data on the interest of the CT scan for the diagnosis of infectious sacro ilitis (1) but there is no precise description of the early signs suggestive apart from the signs of osteitis, which appear later. Hermel et al (2) advised to be careful if the scan is performed within 3 days after the onset of symptoms, but our short series shows that some signs are positive even if the pelvic scan is performed very early. The interest of the scanner, in addition to its rapid access and acquisition, allows on the injected sequences to rule out differential infectious diagnoses of abdominal-pelvic or gynaecological origin, the clinical being sometimes put in defect.

**Conclusion:** Despite its radiant nature, the scanner can be a preferred accessible alternative to MRI for the diagnosis of infectious sacro ilitis with the detection of 4 signs of early onset.

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**Disclosure of Interests:** None declared DOI: 10.1136/annrheumdis-2019-eular.6641

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**AB1187**

**IMPACT OF IN-CLINIC ULTRASOUND ON AGE AND GENDER OF PATIENTS SCANNED AND DETECTION OF SYNOVITIS – RESULTS FROM A QUALITY IMPROVEMENT PROJECT**

Yacer Asran, Surabhi Wij, Sreekanth Vasireddy, Bolton NHS Foundation Trust, Bolton, United Kingdom

**Background:** Inflammatory arthritis is more common in women, and the majority of patients have onset before the 6th decade. Synovitis can be difficult to diagnose clinically in the early stages, and can be especially easy to miss where the index of suspicion is low, such as men and the elderly. Ultrasound (US) can confirm synovitis and other conditions in Rheumatology, particularly where examination features are not very obvious. US has traditionally been offered via Radiology services in our hospital as a separate appointment following referral from the
Rheumatology clinic, with variable waiting times causing potential delay in starting treatment such as DMARDs. There is also a cost implication with regard to rebooking of the Radiology scan appointments. In Bolton, an US system was installed in Rheumatology from 2016 to perform in-clinic US, for improving access and reducing referrals to Radiology.

**Objectives:** We aimed to assess the US usage pattern before and after the new Rheumatology US was installed, with respect to access based on age and gender, the pattern of scanning in-clinic, and rate of synovitis diagnosis, using a quality improvement framework.

**Methods:** US referral data from the Radiology department from October 2015 to March 2016 were collated as baseline on a MS Access database. Two Consultant Rheumatologists performed US in-clinic. From May to October 2016 Rheumatology in-clinic data, and also Radiology referral data were collated on the database for comparison. Patient demographics and diagnoses were recorded from clinical letters. Descriptive statistics were processed in MS Excel 2010.

**Results:** Between October 2015 and March 2016, 68 patients (median age 52 yrs; 28% male) had scans in Radiology. Between May and October 2016, 59 patients (median age 60 yrs; 21% male) had scans in Radiology, and 78 patients (median age 59 yrs; 35% male) had scans in Rheumatology clinic. There was no significant difference in scanned areas amongst the three cohorts with the most common overall being hand/wrist area (n=57, 54 and 61 respectively; total 84%), followed by foot/ankle (n=6, 4 and 4 respectively; total 7%). Between the two time periods, there was an increased trend in final working diagnoses of inflammatory arthritis (28 [41%] vs 36 [61%] and 39 [50%] in the 3 cohorts respectively) and a decreasing trend in the final working diagnoses of non-inflammatory conditions (OA, FM, other non-inflammatory pain: 36 [53%] vs 22 [37.3%] and 28 [35.9%] in the 3 cohorts respectively).

**Conclusion:** The availability of Rheumatology US was associated with increased propensity for scanning older patients and a greater proportion of men compared to previously, a qualitative improvement as synovitis diagnosis could be delayed in these groups. The introduction of Rheumatology US was also associated with a trend towards higher proportion of inflammatory diagnoses, suggesting potentially increased appropriate clinical use due to availability in-clinic. This is supported by the majority being hand/wrist scans, suggesting Rheumatology use is mainly aimed at diagnosing synovitis. Although there was a modest reduction of 13% in Radiology referrals between the two time periods, there was an overall increase of scans performed by 101% following introduction of the Rheumatology US service. We therefore recommend Rheumatology in-clinic US provision, as in addition to obvious improvement in time to diagnosis, it is likely to increase the range of patients able to access US eg older patients and men, and also likely to increase the pick-up rate of synovitis by improving patient selection.

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.7465

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**AB1188 AUDIT: IMPACT OF MUSCULOSKELETAL ULTRASOUND USE IN RHEUMATOLOGY CLINICS**

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**Background:** Musculoskeletal ultrasound (US) has assumed a prominent role in rheumatological practice as both a diagnostic and monitoring tool. It has utility in excluding and quantifying active synovitis and can play a dominant role in rheumatological practice as both a diagnostic and monitoring tool.1 It has utility in excluding and quantifying active synovitis and can help to identify the underlying disease in these patients.2,3

**Objectives:** We aimed to observe impacts on clinical practice of utilising ultrasound (US) scanners in outpatient clinics in a district general rheumatology service. We were particularly interested to see if this affected treatment choices, follow-up plans and referrals for radiological investigations.

**Methods:** US scanners were obtained and used by 2 rheumatology consultants with previous ultrasound training. Scanning was performed during standard 15 minute appointments within general rheumatology outpatient clinics. No extra time was allocated. Over 8 weeks, we completed questionnaires for each scan and assessed the impact on management decisions.

**Results:** Over 8 weeks, data was collected for 36 consecutive patients scanned. Commonly imaged joints were hands (81%, n=29), wrists (75%, n=27), elbows (41%, n=7), and ankles (14%, n=6). Most common patient diagnoses were osteoarthritis (n=13, 36%), rheumatoid arthritis (n=10, 28%) and psoriatic arthropathy (n=6, 17%). The remaining patients had diagnostic labels including undifferentiated inflammatory arthritis or no formal diagnosis. Abnormalities suggesting active inflammation were seen in 42%. In 33% osteoarthritic changes were observed, erosions were seen in 5%, 20% scans were normal. US altered the management in 58% (n=21/36) of cases. These alterations to management included drug change (n=5), drug stopped (n=3), dose increase (n=1), joint injection (n=3), intramuscular injection (n=2). Of the medications added, 3 were DMARDs, 1 was a biologic therapy and one case was not specified. The medications stopped were all DMARDS. US use in clinic prevented radiological investigation in 72% (26/36) of cases. These were radiology ultrasound (n=23) and MRI (n=3). Hands and wrists scans accounted for 86% of these, drug stopped (n=3). US altered the follow up in 56% (20/36) of cases. Of these, 40% (8/20) were reviewed earlier, and 40% (8/20) of patients were discharged based on ultrasound information. In 16/36 patients, US did not alter management. The average time taken to scan in clinic was 7 minutes per patient. The median time was 5 minutes, with the average skewed due to a few prolonged scans of multiple anatomical areas.

**Conclusion:** This audit has demonstrated that US use has impacted on our clinical practice. We identified patients to be seen earlier and altered management based on US findings.

US-use also prevented radiological investigations in 72% of cases. This has positive impacts on staffing, finances, radiology department capacity and patient convenience. Furthermore, we were able to discharge 40% of patients who otherwise would have been recalled.

Overall, we believe this audit shows positive impacts of MSUS on patient care. Challenges include time pressures of scanning in clinic, time and cost implications of ultrasound training and the need to standardise and record ultrasound methods and findings consistently. Costs are offset by savings to radiology resources and increased discharges. We plan to expand ultrasound usage and train our colleagues to employ ultrasound for our patients.

**REFERENCES**


**Disclosure of Interests:** Andrew Wilkinson: None declared, Mike Reed Speakers bureau: Paid to speak at meeting by Novartis, Sara Else Consultant for: Contributed to advisory boards for: Abbvie, Novartis, Chungai Pharma., Speakers bureau: Paid to organise and chair meetings, and speak at educational events by following companies: BMS, Celgene, Grifols, Janssen, MSD, Novartis, UCB.

**DOI:** 10.1136/annrheumdis-2019-eular.5310

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**AB1189 THE IMPORTANCE OF POSITRON EMISSION TOMOGRAPHY-COMPUTED TOMOGRAPHY (PET-CT) IN FEVER OF UNKNOWN ORIGIN (FUO) AND INFLAMMATION OF UNKNOWN ORIGIN (IUO)**

Tahir Saygin Öğüt, Veli Varsız, Funda Erbasan, Mustafa Ender Terziolu, Akdeniz University, Department of Internal Medicine, Antalya, Turkey

**Background:** Fever of unknown origin (FUO) and inflammation of unknown origin (IUO) are clinical problems but diagnostically challenging for clinicians. Patients are exposed to extensive and expensive medical examinations for the identification of the FUO/IUO. FDG PET-CT can help to identify the underlying disease in these patients.

**Objectives:** The aim of this study was to evaluate the role of PET-CT in patients with FUO/IUO and to identify FDG uptake sites and patterns

**Methods:** Total of 296 patients who were performed 18F FDG-PET-CT between Jan 2014 and Dec 2017 were evaluated, retrospectively. There were a total 62 patients scanned by PET-CT for FUO/IUO. Definitive diagnosis, PET-CT patterns, organ involvement and SUVmax values in these patients were reevaluated.

**Results:** Rheumatic disease in 27 patients (43.5%), 20 malignancy (32.3%) and 6 infectious diseases (9.7%) were diagnosed in the FUO/IUO patients performed PET-CT scan. Systemic vasculitis were the most frequently diagnosed rheumatic disease. 11 patients of the 62 patients (17.7%) were diagnosed large vessel vasculitis (9 Takayasu arteritis, 2
Temporal arteritis. Significant vascular FDG involvement was detected (77.7%) in these patients. 4 of 7 patients diagnosed Takayasu arteritis were not seen an increased FDG finding in the other imaging modalities. Vascular FDG uptake (p < 0.001) was statistically significantly higher in the patients diagnosed with rheumatic disease whereas lymph node (p = 0.013) and bone (p = 0.005) FDG uptake were significantly higher in patients with malignancy. Patients with malignancy had the highest SUV-max mean value (p < 0.001).

Conclusion: Our findings reveal that PET-CT is a useful imaging modality in the FUO/IJO patients. Inflammatory diseases, especially large vessel vasculitis, should be considered in addition to malignancies in these patients, and subclinical inflammation in the blood vessel can be visualized by PET-CT.


AB1190
EXTENDED POLY-DIMENSIONAL IMMUNOME CHARACTERIZATION (EPIC): A WEB-BASED IMMUNE REFERENCE ATLAS OF THE HEALTHY HUMAN IMMUNOME AND A TOOL FOR TRANSLATIONAL MEDICINE

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Background: An atlas of the developing immune system will not only improve our understanding of normal immune ontogeny but more importantly, aid in our identification of disease-associated cell subsets. However, such a resource is still unavailable despite accessibility to technologies like mass cytometry due to the general focus on specific cell subsets or ages. There is a critical unmet need for standardized datasets depicting at single cell level and with high dimensionality the entire developmental gradient of the healthy immune system from the neonatal to adult age.

Objectives: We aim to provide a detailed depiction of the architecture of the human healthy Immunome across an entire age gradient.

Methods: We have created a high dimensional atlas of the healthy human immunome (EPIC: Extended Poly-dimensional Immunome Characterization) by interrogating the peripheral blood mononuclear cells (PBMC) of over 200 healthy subjects, ranging from cord blood to adult age, with 63 unique mechanistic and phenotypic markers per cell by mass cytometry (CyTOF). The EPIC analytical and visualization pipeline is based on an open source web-based R Shiny bioinformatics toolkit that allows it to be easily accessible to the research community.

Results: EPIC can be mined in various ways, for instance to follow developmental changes of any given cell subset or to depict the architecture of the Immunome at any given age range. For example, transition developmental milestones were observed in the TNFα+ CD4+ T cells where the size of its memory subset was even smaller than the naive subset at 8 year old. There was a significant reduction and increase in the frequency of the naive and memory TNFα+ CD4+ T cells with a Spearman’s correlation coefficient, rho, of ~0.4662 and 0.4164 respectively. More importantly, we have built and will keep developing datasets from various immune mediated diseases using the same approach. Consequently, by providing the healthy standard, EPIC enables the depiction and dissection of disease-dependent perturbations of the Immunome architecture.

Conclusion: EPIC provides a transformational conceptual advance in Translational Immunology from individual subset focused to immune architecture based approach for the understanding of physiology and pathogenesis of immune mediated mechanisms. We intend to make EPIC available to the entire community in its full capacity.

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None

Disclosure of Interests: Joo Guan Yeo: None declared, Lu Pan: None declared, Martin Wasser: None declared, Pavanish Kumar: None declared, Thaschawee Arkachaisri: Speakers bureau: Abbvie Pte, Ltd, Su Li Poh: None declared, Fauzialia Ally: None declared, Jing Yao Leong: None declared, Kee Thai Yeo: None declared, Liyun Lai: None declared, Angela Yun June Tan: None declared, Salvatore Albani: None declared DOI: 10.1136/annrheumdis-2019-eular.4557

AB1191
DIFFERENTIAL DIAGNOSIS OF SERONEGATIVE ARTHRITIS: DIAGNOSIS ONE YEAR FOLLOW UP AFTER FIRST DIAGNOSIS

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Background: The ACR/EULAR classification criteria (AECG) for rheumatoid arthritis (RA) is well known criteria for early diagnosis of RA with high sensitivity. However, the criteria weigh three points for seropositive, thus automatically subtracted 3 points for seronegative arthritis. Recently, elderly onset RA is increasing, that has relatively higher ratio of seronegative than young onset RA.

Objectives: To compare diagnosis of seronegative arthritis between initial and one year follow up diagnosis after one year follow up.

Methods: Arthritis patient who are sustained for more than one year since first refer despite his/her ACRA or Rheumatoid Factor were negative, were collected. From these patients, difference from initial diagnosis to second after one year follow up was evaluated statistically with chi square test. Mean EACG score and mean involved joint count for large and small joint (LJC and SJC) at initial diagnosis were compared with each of second diagnosis statistically with Mann Whitney U test (MWU). Clinical course evaluated with 28-joints disease activity score (DAS28) and Health Assessment Questionnaire Disability Index (HAQ-DI) for each diagnosis was compared at every other 3 months with MWU. Comparison between 475 seropositive RA patients treated in the same institute and seronegative RA in the study was also evaluated in a same manner.

These patients’ sensitivity and specificity (Sens & Specs) in according with 1987 ACR diagnosis criteria (1987ACR) was also evaluated and compared with Sens & Specs of AECG.

Results: Ninety-six patients were enrolled. In these, RA was diagnosed to 18 patients and 78 were unclassified arthritis as first diagnosis. Second diagnosis of these patients were RA for 41, spondyloarthritis (SpA) for 22, other collagen disease (CD) for 5, osteoarthritis (OA) for 9, hypothyroidism (HTH) for 2, non-tuberculous mycobacterium (NTM) for 1, and unclassified arthritis (UA) for 16. Mean EACG score and range for each second diagnosis was 5.2 and 2 to 7, 4.4 and 3 to 7, 4.4 and 3 to 5, 5.0 and 4 to 6, 4.0 and 4.0, and 4.25 and 3 to 5, for RA, SpA, CD, OA, HTH, NTM, and UA, respectively. There is no significant difference between any pair of second diagnoses. LJC and SJC of each second diagnosis was 3.2 and 9.8, 5.7 and 4.8, 2.4 and 4.8, 2.4 and 8.1, 2.0 and 6, 2 and 2, and 1.8 and 5.9, for RA, SpA, CD, OA, HTH, NTM, and UA, respectively. There is also no significant difference between any pair of second diagnoses (Table).

In clinical course, there is no significant difference between the second diagnoses, and also no significant difference between seropositive and seronegative RA.

In these seronegative arthritis patients, Sens & Specs of RA in accordance with 1987ACR were 75.0% and 43.4%, while 83.3% and 66.7% in accordance with AECG.

Conclusion: Diagnosis of seronegative RA is not uncomplicated, whereas rheumatologist’s diagnostic skill is questioned.

Table: Comparison between second diagnosis

<table>
<thead>
<tr>
<th>Second diagnosis</th>
<th>First diagnosis</th>
<th>N</th>
<th>AECC</th>
<th>Joint point</th>
<th>LJC</th>
<th>SJC</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA</td>
<td>RA(15), UA(26)</td>
<td>41</td>
<td>5.2</td>
<td>3.7</td>
<td>3.2</td>
<td>9.8</td>
</tr>
<tr>
<td>SpA</td>
<td>RA(1), UA(21)</td>
<td>22</td>
<td>4.4</td>
<td>3.0</td>
<td>1.9</td>
<td>5.7</td>
</tr>
<tr>
<td>CD</td>
<td>UA(5)</td>
<td>5</td>
<td>4.4</td>
<td>2.8</td>
<td>2.4</td>
<td>4.8</td>
</tr>
<tr>
<td>OA</td>
<td>RA(2) or UA (7)</td>
<td>9</td>
<td>5.0</td>
<td>3.4</td>
<td>2.4</td>
<td>8.1</td>
</tr>
<tr>
<td>HTH</td>
<td>UA(2)</td>
<td>2</td>
<td>4.0</td>
<td>3.0</td>
<td>2.0</td>
<td>6.0</td>
</tr>
<tr>
<td>NTM</td>
<td>UA(1)</td>
<td>1</td>
<td>4.0</td>
<td>2.0</td>
<td>2.0</td>
<td>2.0</td>
</tr>
<tr>
<td>UA</td>
<td>UA(16)</td>
<td>16</td>
<td>4.25</td>
<td>3.0</td>
<td>1.8</td>
<td>5.9</td>
</tr>
</tbody>
</table>

CLINICAL APPLICATION OF 18F-FDG PET/CT IN RHEUMATIC DISEASES

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Background: 18F-Flurodeoxyglucose Positron Emission Tomography/Computed Tomography (18F-FDG PET/CT) is widely used in diagnosing malignant tumors. It is also useful applying to autoimmune diseases.

Objectives: To investigate the clinical application and significance of 18F-Flurodeoxyglucose Positron Emission Tomography/Computed Tomography (18F-FDG PET/CT) in rheumatic diseases.

Methods: Patients who underwent 18F-FDG PET/CT in the Department of Rheumatology and Immunology, Peking University People’s Hospital from January 2012 to July 2018 were retrospectively analyzed for clinical application and imaging characteristics of 18F-FDG PET/CT in rheumatic diseases.

Results: 1. From 2012 to 2018, 459 patients underwent 18F-FDG PET/CT examination in the Department of Rheumatology and Immunology, accounting for 5.79% of the total number of PET/CT examinations in the hospital. Further analysis of 415 patients with complete data, including 158 males (38.07%) and 257 females (61.93%), male to female ratio of 1:1.6, average age of patients are (57 ± 16.2) years old. The highest proportion group of patients is from 45 to 65 years old (201/415, 48.43%). The total number of PET-CT examinations in the whole hospital increased year by year. Compared with 2012, the number has increased nearly 10 times in 2017 among patients in the Department of Rheumatology and Immunology. 2. In patients with rheumatic diseases, major purpose of PET/CT examination included exclusion of tumors, diagnosis, and assessment of the disease activity. 3. Of all the 459 patients, 315 cases may indicate the differential diagnosis of the disease, of which 269 (85.4%) were highly suggestive of rheumatic clinical diagnosis, including 55 cases of vasculitis (17.46%), 54 cases of myositis (17.14%), 34 cases of rheumatoid arthritis (10.79%), 25 cases of systemic lupus erythematosus (7.94%), 25 cases of IgG4-related diseases (7.94%), 10 cases of rheumatic polymyalgia (3.17%) and 6 cases of systemic sclerosis (1.9%); the remaining 46 cases (14.6%) only suggested the possibility of autoimmune diseases.

Conclusion: Rheumatic diseases are complex and diverse, and it is difficult to diagnose. The application of 18F-FDG PET/CT in the diagnosis of diseases is increasingly widespread. The results of this study suggest that 18F-FDG PET/CT to some extent has significance in the classification and diagnosis of rheumatic diseases, especially for the exclusion of malignant tumors.

Disclosure of Interests: None declared


DIFFUSE WEIGHT IMAGE IS A POTENTIAL MAGNETIC RESONANCE SEQUENCE IN THE PREDICTION OF SPINAL SYNDENSMOPHYTE IN YOUNG PATIENT WITH ANKYLOSING SPONDYLITIS

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Background: Diffusion-weighted imaging (DWI) is an MRI sequence and has been shown to have advantages over standard MRI sequences in some clinical settings, such as early diagnosis of ischemic stroke and in staging some type of cancers. Different measures of diffusion have been proposed, with the apparent diffusion coefficient (ADC) measure the most widely used. Severe inflammation leads to higher ADC values through increased water in extracellular, less constrained, spaces. Several studies have investigated the clinical utility of DWI in AS, with suggestive evidence that this sequence has valuable discriminatory capacity between AS and non-inflammatory back pain by inflammation degree on sacroiliac joint (SIJ).

Objectives: This study was tested the potential capacity of ADC value estimated by DWI on SIJ as the predictor of new spinal syndesmophyte in young patients with ankylosing spondylitis (AS).

Methods: The 58 patients who fulfilled the ASAS axSpA criteria were enrolled and their age was 18-23 years old. All subjects underwent MRI on SIJ with oblique coronal images parallel to the long axis of the sacrum (fast spin-echo T1WI and STIR) at diagnosis and lumbar spine radiograph at diagnosis, 2 and 4 years sequentially. The ADC value on SIJ measured by DW-MRI at diagnosis and spinal radiographs were scored using the stoke AS Spinal Score (SASSS) at diagnosis, 2 and 4 years sequentially. The ADC value on SIJ showed a positive association with ADC value on SIJ as the predictor of new spinal syndesmophyte. However, multivariate logistic regression analysis was performed to identify that ADC value on SIJ had an important influence on spinal syndesmophyte growth.

Results: The ADC value on SIJ showed a positive association with inflammatory marker such as, ESR and CRP, but no association with BASDAI, BASMI and BASFI. The univariate and multivariate logistic regression analysis showed that ADC value on SIJ had the highest risk of developing new syndesmophytes in spine.

Conclusion: This study showed that the inflammation of AS patient was a positive association with ADC value on SIJ by DW-MRI and the measured the ADC value on SIJ by DW-MRI was the modest discriminating capacity method for predicting development of new spinal syndesmophyte in young AS patients.

REFERENCES
Public health, health services research, and health economics

OBSERVATIONAL PROSPECTIVE COHORT STUDY TO EVALUATE EFFICACY AND SAFETY OF TAPENTADOL IN PATIENTS WITH RESPIRATORY DISEASE

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Central de la Defensa, Rheumatology Service, Madrid, Spain.3Htal Universitario de Fuenlabrada, Service of Internal Medicine, Fuenlabrada, Spain.

Background: Chronic pain analgesia is a concern in clinical practice in rheumatic patients, especially when the intensity is severe. In this case opioids are indicated but also contraindicated in cases of important respiratory depression and, therefore, must be administered with caution to patients with respiratory disease (1). Many of our patients are not in the condition of severe respiratory depression although they present pulmonary pathologies, which could be triggered at the use of certain doses (2). For this reason, it is important the existence of a study that shows that tapentadol is safe in pluripathological patients when used at regular doses in clinical daily practice in Reumathology (3).

Objectives: Single site, non-postmarketing observational study. The main objective is to evaluate the safety of tapentadol prolonged release (TPR) 50 mg/12h, measured as tolerance ("good", "bad" or "not too bad") and by the comparative analysis of gradients between both groups of the study (control group and pathological group), the basal oxygen saturation, and after the dose of TPR (basal pulse oximetry minus the mean of the oxygen saturation after 30 days of study).

Methods: Inclusions criteria arepatients with severe chronic pain (Visual Analogical Scale, VAS≥4) diagnosed from mild to severe chronic obstructive pulmonary disease (COPD) (spirometry after bronchodilation with forced expiratory volume (FEV)/forced vital capacity (FVC)< 70% and FEV1≤50%), and/or obesity, and/or controlled asthma and/or other conditions likely to produce respiratory depression with opioids (pathological group). Exclusion criteria consists in basal oxygen saturation measured by the pulse oximeter inferior to 92%. A descriptive analysis of variables and a comparison of the means were performed.

Results: 29 patients; 12 in control group and 17 pathological group (obesity: 9, controlled asthma: 3; mild to moderate COPD: 7; other pathologies: 7). Overall, the type of pain was nociceptive 59%, neuropathic 21% and mixed 20%; mainly women (67%), caucasian race (92%), median age 60 years old, and with 93% good tolerability and 97% good treatment adherence. Concerning results per groups, at control group, VAS mean, arterial pressure (AP), oxygen saturation (SO2) and heart rate (HR) before and after treatment, 8.3 vs 5.8; 127/74 vs 124/73 (mmHg); 95.6 vs 95.7 (%); 76 vs 73 (bpm). In the pathological group: 7.5 vs 6.5; 131/ 82 vs 127/78 (mmHg); 96 vs 95.5 (%); 75 vs 76 (bpm). Regarding the results as per gradients between groups, no statistically significant differences were found, except for VAS, (p=0.00008). There were no cases of decrease of the oxygen saturation below 92% along the study.

Conclusion: The results support the safety of tapentadol from the respiratory point of view, measured by oxygen saturation, since no statistically significant differences were found between both groups, and, due to the excellent tolerability, as no clinical data showed signs of hypercapnia. No statistically significant differences were found in the oxygen saturation between both groups with the intake of TPR, with excellent tolerability and treatment adherence. There were no cases of decrease of the oxygen saturation below 92% along the study.

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Disclosure of Interests: None declared


KNOWLEDGE AND PERCEPTIONS OF PORTUGUESE FAMILY PHYSICIANS TOWARDS ANKYLOSING SPONDYLITIS: RESULTS FROM THE ASSESSMENT OF RESULTS IN ANKYLOSING SPONDYLITIS(AREA) STUDY

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Background: Ankylosing spondylitis (AS) patients have a significant delay between symptom onset and disease diagnosis, reaching on average 7 to 10 years in developed countries. Understanding the reasons behind this delay is essential to reduce the individual and socio-economic burden of the disease.

Objectives: To assess knowledge and perceptions of Portuguese family physicians (FP) towards AS and determine whether these contribute to the diagnostic delay at the primary care level.

Methods: The Assessment of Results in Ankylosing spondylitis (arEA) study was developed by the NOVA-Information Management School (Lisbon) in collaboration with the Portuguese Society of Rheumatology, the Portuguese Association of Family Physicians (APMGF) and the National Association of Primary Care Units (USF-AN), the National Association of AS Patients and the Portuguese League Against Rheumatic Diseases. The arEA aimed at assessing reasons for delayed diagnosis of AS, as well as disease impact in patients’ lives, global health and work. A comprehensive online survey was developed and sent to FP associated with APMGF and USF-AN, collecting data on demographics, global knowledge and diagnostic and treatment attitudes towards AS.

Results: 91 FP responded the survey, 51.6% female, more frequently from the 25-44 year-old age group, half of which had <5 years of clinical experience. Most FP (70%) did not consider AS to be a relevant disease in everyday clinical practice but recognized (90%) there was a delay in diagnosis (5 years on average). Nevertheless, knowledge over AS was adequate. On average, prevalence was considered to be 56 cases per 1000 persons (close to the actual prevalence of 47 cases per 1000 persons reported in the epidemiological study EpiReumPt). When assessing a patient with suspicious AS, the most valued symptoms/signs were inflammatory back/buttock pain, extra-articular manifestations (uveitis, enthesitis, dactylitis, psoriasis) and sacroiliitis on imaging (4.1, 3.9 and 3.9 on a 1-6 scale, respectively); 92.5% of FP refer the patient to a hospital consultation, rheumatology in 88.5% of cases; 37.5% of FP initiate treatment, with NSAIDs in 81% of cases. A mean delay of 9 months between patient referral and first hospital consultation was also reported (>1 year in 22%). In 73.4% of cases, no specific referral protocol exists for AS or other rheumatic inflammatory conditions; 33.8% of FP felt that the development of such protocol would improve access, while 36.8% considered that a rheumatologist acting as consultant in primary care units would facilitate identification and referral of inflammatory conditions.

Conclusion: Portuguese FP reported significant delay in hospital consultation after referral of suspicious AS cases. They apparently had good knowledge of AS, though responses may have been influenced by a younger, more updated and willing-to-participate physician population (selection and response bias).

Disclosure of Interests: None declared


PREGNANCIES IN AUTOIMMUNE DISEASES: EXPERIENCE OF TWO CENTERS IN CALI, COLOMBIA: 2011- 2018

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Background: The outcome in pregnancy varies according to the rheumatic disease. The outcome in pregnancy varies according to the rheumatic disease. The outcome in pregnancy varies according to the rheumatic disease. The outcome in pregnancy varies according to the rheumatic disease.

Objectives: To describe the pregnancies outcomes of women with rheumatic diseases at two reference centers in Cali, Colombia.

Methods: Descriptive study. Records of pregnant patients attended from August 2011 to December 2018 were reviewed. Thirty-nine patients were found, 11 without a defined rheumatic entity (10 with positive ANA only, 2 with anti-dsDNA antibodies, 1 with anti-CCP and 1 with anti-PPA).

RESULTS IN ANKYLOSING SPONDYLITIS (arEA) STUDY

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and 1 with incomplete criteria for antiphospholipid syndrome), and 28 with an autoimmune rheumatic disease. A total of 41 pregnancies occurred (2 women with 2 pregnancies) and were chosen for the final analysis (Table).

**Results:** The mean gestational age at the first rheumatology visit was 16.8 ± 8.9. The mean age at the end of pregnancy was 29.5 ± 5.7 years. Only nine pregnancies were planned (34.6%). Among the patients with a defined autoimmune disease the diagnoses were: systemic lupus erythematosus (SLE) (12), rheumatoid arthritis (RA) (5), antiphospholipid syndrome (APS) (2), autoimmune hemolytic anemia (AHA) (2), juvenile idiopathic arthritis (JIA) (2), overlap syndrome (OS) (3: 2 SLE/SSc; 1 SLE/Sjögren’s)’ mixed connective tissue disease (MCTD) (1) and undifferentiated connective tissue disease (UCTD) (1). There were 8 pregnancies exposed to teratogenic drugs (MTX 5, LEF 1, MMF 1, CYC 1); 2 ended in fetal loss and 1 had a congenital pneumonia. There were 27 full-term births, 37-40 weeks (wk); 8 preterm births, 23-36 wk (4 twins); 1 stillbirth, 26 wk; and 3 abortions (2 in the same mother). Seven patients had an active disease before pregnancy, 13 during pregnancy (7 SLE, 3 RA, 2 AHA, 1 MCTD) and 13 during the puerperium (7 SLE, 4 RA, 1 EMTC). No maternal deaths, neonatal lupus or congenital heart block were documented in this series. Four patients did not require any medication. One woman received treatment for pulmonary tuberculosis, and other was on anti-retroviral treatment for HIV infection. At the last follow-up, 2 patients were still pregnant.

**Conclusion:** The outcome of rheumatic disease during pregnancy remains variable. It seems that SLE patients tend to be more active and flare more commonly than other patients. The documented complications were similar to those reported in the literature.

**REFERENCES**


**Table. Main clinical findings and outcomes**

<table>
<thead>
<tr>
<th>Variables</th>
<th>SLE (n=15)</th>
<th>Non-SLE (n=13)**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age at first rheumatology follow up, mean (standard deviation, SD)</td>
<td>11.6 (5.9)</td>
<td>18 (9)</td>
</tr>
<tr>
<td>Treatment during pregnancy, n (%)</td>
<td>6 (46,2%)</td>
<td>1 (8,3%)</td>
</tr>
<tr>
<td>Anti-mortem</td>
<td>11</td>
<td>6</td>
</tr>
<tr>
<td>Steroids</td>
<td>10</td>
<td>7</td>
</tr>
<tr>
<td>Aza-thioprine</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Laboratory findings, n (%)</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Anti-Ro antibodies</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Lupus anticoagulant</td>
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<td>0</td>
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<tr>
<td>Anticardiolipin antibodies, IgM</td>
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</tr>
<tr>
<td>Anticardiolipin antibodies, IgG</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Relapses during pregnancy, n (%)</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Maternal outcome, n (%)</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Preeclampsia</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>HELLP syndrome</td>
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<td>0</td>
</tr>
<tr>
<td>Fetal outcome, n (%)</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Preterm newborn</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Abortion</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Stillbirth</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

SLE: systemic lupus erythematosus. ** Two gemelar pregnancies. Two patients with antiphospholipid syndrome.

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.8159

**AB1196** A REVIEW OF ELECTRONIC RHEUMATOLOGY REFERRALS AT THE QUEEN ELIZABETH UNIVERSITY HOSPITAL (GLASGOW, UK) AND HOW THIS HAS LED TO SERVICE IMPROVEMENTS

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**Background:** Our department provides a service for inpatient Rheumatology reviews Monday to Friday, 9am to 4pm, with a guaranteed review timeframe of 48-72 hours. We work predominantly on the QEIH site, which comprises 1677 acute inpatient beds. We launched an electronic referral system for inpatient Rheumatology reviews in February 2018. Inter-specialty referrals are an essential part of most inpatient stays. In a time of increasing service demand within the NHS it is important that we have an effective system to manage our time and resources.2 Electronic referrals allow us to audit our workload, our efficiency at reviewing patients and allow for accountability of both the referrer and reviewer, therefore improving patient safety.3 Using a set proforma allows us to improve communication, the quality of the referral and triage effectively.4

**Objectives:** We performed a baseline review of the new system.

**Methods:** We reviewed all electronic referrals between 8.2.18 and 13.8.18. We collected data on demographics, timing, reasons for referral and outcomes.

**Results:** There were 346 referrals (58.4% female, mean age 64 years). Most (78%) were made from medical wards; the mean number of referrals per month was 49.4. Referrals were most frequently made on Fridays (23%). Most were in-hours (81%). The most common reason for referral was: a request for review (212; 61.3%); phone advice (70; 20.2%); procedural requests (50; 14.5%). 207 referrals (59.8%) were made for new patients, 91 (26.3%) for patients known to Rheumatology prior to admission, and 48 (13.9%) for patients already seen during the current admission. 50% of procedures were performed on knees and 50% on other joints. 82% of patients were seen within 72 hours.

**Conclusion:** The use of the electronic referrals system has made it simple to review the workload of our Rheumatology on-call service. We have used the data on reason for referral to guide the topics for our educational meetings to improve patient management. We actively contribute to the procedural teaching on knee joint aspiration both in junior doctor’s formal training sessions, and opportunistically on wards following referral. This is a core procedure required for training completion for medical trainees in the UK and should help reduce referrals and manage patients in a more time efficient and cost-effective manner. We have also improved documentation by recording the time, date and name of the reviewer in our electronic entry.

We intend to collect data in the same period this year, to assess changes in referral pattern in the 12 months since the system was initiated and the impact of our interventions.

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**AB1197** EFFECTS AND SAFETY OF THE YELLOW FEVER VACCINE 17DD IN PATIENTS WITH IMMUNOMEDIATED RHEUMATIC DISEASES

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**Background:** The yellow fever is an acute infectious disease caused by the amarillic virus. It is present in tropical areas of South America and...
Africa and is transmitted to humans through the bites of the infected female mosquitoes, found in the endemic forest zones. The vaccine is produced with attenuated viruses and represents an essential prevention method. It confers prolonged immune protection and is considered to be safe in the general population. For the immunosuppressed condition under which many patients with immunemediated rheumatic diseases (IMRD) are submitted, little is known about its efficacy and safety in this group.

**Objectives:** The aim of this study is to analyse the effects of the vaccine in patients with IMRD.

**Methods:** The methodology of this research consisted of the application of a form-based interview, the analyses of the vaccine card and medical records, if existent. The requirement to take part as a volunteer was to be an IMRD patient that was vaccinated against yellow fever.

**Results:** 60 ambulatorial patients, unadvisedly vaccinated or not, were evaluated. Of those, 40 (66.7%) were female and 20 (33.3%) were male with an age range varying from 8 to 48 years. It was observed that 52 (86.7%) presented no adverse effects from the vaccine, while 7 (11.7%) presented at least one side effect and 1 (1.7%) exhibited a severe reaction of the underlying rheumatic disease. In the group of 7 patients that registered any side effects, it was described 1 case of bilateral optic neuritis with temporary vision loss, initiated three weeks after the vaccination. The other side effects registered were mild and included: 3 occurrences of headache and 1 record of each of the following: fever, local pain, arthralgia, myalgia, nausea, coryza and diarrhea.

**Conclusion:** Our data suggested that the vaccine exhibits a relative degree of safety in these patients. The benefits of the immunization should be evaluated by the rheumatologist, taking in account the risk of infection and lethality of yellow fever in patients who live or are visiting the endemic areas. The recommendations are that the vaccination in this group must always be planned, done under medical orientation and order. It should preferably be applied in patients under disease remission, without immunosuppression treatment or in those who, under immunosuppression, it is possible to temporarily suspend this treatment in order to the vaccine be administered.

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AB1198 EVALUATION OF THE WAITING TIME AND QUALITY OF RHEUMATOLOGY REFERRAL AT A TERTIARY CARE CENTER OF PORTO ALEGRE - RS, BRAZIL

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**Background:** To improve waiting time for a first consultation with a rheumatologist has become an important challenge in many countries [1, 2]. In 2008, a previous survey [3] evaluating the referrals to our Service, we observed long waiting times (median 3 days to 8 years) and that only 31% of consultations were related to hypothesis of systemic inflammatory rheumatic diseases (SIRD), which should be properly managed at a resourceful tertiary care center. In 2015, a new process of triage for referrals (based on a protocol recording relevant information and judgment by a rheumatologist) was introduced in our state health system aiming to improve quality of referrals and reduce waiting lists [4]. However, this system is applied only for patients from cities other than the capital (Porto Alegre, RS).

**Objectives:** To evaluate the waiting time and quality of referral for first Rheumatology consultations at a tertiary care center of South Brazil, comparing the present results with those obtained 10 years ago in a similar survey [3].

**Methods:** In a cross-sectional study, information regarding all first consultations at the Rheumatology Service of Hospital Nossa Senhora da Conceição were prospectively collected from Oct 2017 to Mar 2018. Referred patients were characterized in terms of demographic features, diagnostic hypothesis formulated by the rheumatologist and time from initial referral. For analytical purposes, patients with adequate referrals were considered to be those that presented high probability of SIRD, needing assistance at secondary or tertiary level of care. The results were compared with data collected in the same way in 2008 [3]. Chi-square test was used for statistical analysis.

**Results:** Of 444 appointments for scheduled for new patients, 87 (19%) did not attend. The features of the remaining 357 patients were: female-85%, mean (SD) age= 50 (15) years. The waiting time for consultation ranged from 7 days to 63,8 months (median 12.7, IQR= 4.4-14.1). Diagnostic suspicion of SIRD occurred in 186 (52%). Among SIRD, rheumatoid arthritis (23,5%) was the most frequent, while among non-SIRD, osteoarthritis (21,0%) and fibromyalgia (20,7%) were the most common diagnostic hypotheses. A SIRD was the main hypothesis in 75/193 (38%) patients from the capital, comparing with 111/174 (67,7%) among those from other cities (P=0,001), indicating better selection of the latter group of patients. A reanalysis of data collected in 2008 revealed that, at that time, the prevalence of suspected SIRD was not significantly different between patients from capital (76/262, 29.0%) and those from other cities (74/225, 32,9%; P=0,354).

**Conclusion:** We observed improvement in the quality of referrals from other cities comparing to those from the capital of our state, suggesting a better selection process in the former [4]. Despite the efforts to reduce the waiting time for Rheumatology consultations, we observed an increase when compared to 2008. We believe that the delay is secondary to an increase of the demand without a proportional increase in the number of rheumatologist in the public health system. The elaboration of guidelines with standardized information required for referral and triage process seems to be promising to improve access to consultations in Rheumatology.

**REFERENCES**


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AB1199 BARRIERS AND FACILITATORS TO THE IMPLEMENTATION OF A STRATIFIED MODEL OF CARE FOR LOW BACK PAIN PATIENTS IN PRIMARY CARE IN PORTUGAL

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**Background:** The results of a recent study have suggested that the current clinical practice is not in line with clinical guideline recommendations and may not be delivering the best outcomes to Low Back Pain (LBP) Portuguese patients. Since the stratified primary care approach has demonstrated clinical and cost-effectiveness in the UK and other countries, the SPLIT project aimed to introduce a similar approach that involves general practitioners (GPs) and physiotherapists (PTs) in the triage and targeted treatment of low back pain patients, in Portugal. In order to facilitate the implementation of this project a training program for GPs and PTs was delivered by rheumatologists and PTs. Considering the specific organization of the Portuguese primary care, it was important to explore the perceptions of the GPs and PTs, who attended to the training, regarding the implementation of the SPLIT stratified model of care in the Portuguese context.

**Objectives:** Identify and understand the potential barriers and facilitators to the implementation of the SPLIT stratified model of care.

**Methods:** After obtaining ethical approval, two focus groups (one for each professional group) were carried out. The focus groups were based on a semi-structured interview schedule, audio-recorded and transcribed verbatim, thematic analysis was conducted. Firstly, two researchers independently coded the transcripts. Secondly, these researchers discussed the codes and examined their scope and relevance. Thirdly, the researchers developed a coding scheme that included the main themes and sub-themes, as well as the connections among them.
Results: The potential barriers were identified and explored by both professional groups. The introduction of change into the routine delivery care was identified as one of the most important barriers. According to the GPs’ perspective, the possibility of inadequate referral was considered as an issue. The PTs highlighted the challenges inherent to the psychosocial informed physiotherapy treatment of patients classified with high risk of developing persistent and disabling pain. More specifically, they emphasized the need to receive mentoring sessions in clinical practice, in order to develop competences for the management of psychosocial issues. In what concerns to the potential facilitators to the implementation of the model, the participants’ personal motivation was considered as one of the most important factors. The alignment of the SPLIT model with the mission and goals of the health care units where the project was going to be piloted was also identified as an important facilitator. Finally, both professionals considered that the SPLIT model may facilitate the interdisciplinary approach to the management of this condition, as it clarifies the specific contribution of GPs and PTs in the approach to LBP patients.

Conclusion: The knowledge about the potential barriers and facilitators to the implementation of the SPLIT stratified model of care may contribute to the successful implementation of stratified care for LBP patients in Portugal.

REFERENCES

Disclosure of Interests: None declared

AB1200 IMPROVEMENT IN THE QUANTITY AND QUALITY OF OBSERVATIONAL DATA COLLECTED FOR US VETERANS ENROLLED IN THE VETERANS AFFAIRS RHEUMATOID ARTHRITIS REGISTRY USING AN ELECTRONIC AUDIT, FEEDBACK, AND DATA CORRECTION SYSTEM

Grant Cannon1, Jorge Rojas2, Neil Bell2, Namrata Singh4, Ted Mikul5, Liron Caplan6, Gail Kerr7, Joshua Baker8, Angelo Gatto9, Jennifer Barton10, Angelo Gaffo9, Jennifer Barton10, Deana Lazaro11, J Steuart Richards12, Brian Sauer1.

Background: The Veterans Affairs (VA) Rheumatoid Arthritis (RA) registry is an observational cohort study of US Veterans with RA at 11 VA Medical Centers. VARA investigators capture clinical and laboratory disease activity measures (DAMs) during clinic visits via standardized templates in the electronic health record (EHR). Six clinical (tender/swollen joints, patient/provider global, MD-HAQ, pain) and 2 laboratory (ESR, CRP) DAMs are extracted post-visit using natural language processing (NLP).

Objectives: This analysis determined the impact of an audit, feedback and data correction system on the quantity and quality of DAMs collected in the VARA registry.

Methods: After September 2017, VARA site investigators were provided monthly feedback reports of incomplete/missing DAMs for the prior month to allow sites to correct data entry errors. Updated and/or corrected data were entered into the EHR via note addendums and then automatically re-extracted by NLP to complete the capture of DAM data. DAMs from October 1, 2016 to September 30, 2017 (pre-feedback implementation – Pre-IMP) was compared to October 1, 2017 to September 30, 2018 (post-feedback implementation – Post-IMP).

Results: During the pre-IMP period, there were 2,411 notes with DAMs collected on 1,116 unique patients compared to 2,873 notes on 1,208 unique patients in the post-IMP period - an increase of 92 (8.2%) unique patients and 460 (19.1%) notes. Enrollment in the VARA registry only increased by 121 (6.5%) during post-IMP period. During post-IMP period, there were 541 notes identified with deficiencies in clinical DAMs and monthly audit and feedback reports were provided to VARA sites to allow corrections. Individual site review resulted in 376 additional DAMs in 225 notes, with complete resolution of all errors in 137 (25.3%) notes. The quantity of DAMs collected increased from 15,709 to 21,064, a 34.1% increase with the average number of DAMs collected per note rising from 4.9 to 5.6. The quality of data improved as demonstrated by the proportion of notes with all 6 clinical DAMs increasing from 52.5% to 81.1% and other improvements in quality/completeness as noted in table.

Conclusion: An audit, feedback, and efficient data collection system improved both the quantity and quality of DAMs collected. The improvement in the collection of DAMs in RA patients will further enhance epidermoligic and outcomes studies of RA and provide higher quality longitudinal data to enhance the care of RA patients.

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Table 1

<table>
<thead>
<tr>
<th>Patients and Notes</th>
<th>Pre-IMP</th>
<th>Post-IMP</th>
<th>Increase (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Usage prompts</td>
<td>1,865</td>
<td>1,978</td>
<td>5.9 (P=0.05)</td>
</tr>
<tr>
<td>Total Notes</td>
<td>2,011</td>
<td>2,087</td>
<td>3.8 (P=0.15)</td>
</tr>
<tr>
<td>Average notes per patient</td>
<td>2.621.1</td>
<td>2.441</td>
<td>0.12 (P=0.35)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Disease Activity Measure (DAMs)</th>
<th>Pre-IMP</th>
<th>Post-IMP</th>
<th>Increase (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total DAMs</td>
<td>13,709</td>
<td>16,486</td>
<td>20.3 (P=0.002)</td>
</tr>
<tr>
<td>Number Clinical DAMs per note</td>
<td>4.61±1.5</td>
<td>4.94±1.3</td>
<td>7.2 (P=0.05)</td>
</tr>
<tr>
<td>Notes with ≥6 Clinical DAMs</td>
<td>1,267 (53.3%)</td>
<td>1,598 (63.1%)</td>
<td>26.6 (P=0.001)</td>
</tr>
<tr>
<td>Notes with ≥4 Clinical DAMs</td>
<td>1,139 (46.3%)</td>
<td>1,483 (56.9%)</td>
<td>33.7 (P=0.001)</td>
</tr>
<tr>
<td>Notes in clinical and 2 lab DAMs</td>
<td>1,059 (43.8%)</td>
<td>1,764 (63.4%)</td>
<td>66.5 (P=0.001)</td>
</tr>
<tr>
<td>Notes in clinical and 3 lab DAMs</td>
<td>1,059 (43.8%)</td>
<td>1,764 (63.4%)</td>
<td>66.5 (P=0.001)</td>
</tr>
</tbody>
</table>

* Percent of total notes during the pre-implementation period;
** Percent of total notes during the post-implementation period;
AB1201

MANAGEMENT OF COMORBIDITY IN INFLAMMATORY ARTHRITIS: GEOCOI PROJECT

Santos Castañeda1, M Carlos, González2, María del Carmen Castro Villegas3, Silvia García-Díaz4, Juan Carlos Hermosa5, Cristina Lajías6, Leticia León7, Juan Carlos Obaya8, María Rodero9, Carmen Suarez10, Virginia Villaverde10, Juan Carlos Torre-Alonso9,10.

Background: The impact of comorbidity on the diagnosis, prognosis, and treatment of rheumatic diseases could be very high. However, several studies have depicted a sub-optimal assessment of comorbidity in these diseases.

Objectives: To generate common, simple and practical support materials (checklists, questionnaires and other complementary materials) for rheumatologists, health professionals and patients, in order to: 1) Assess comorbidity; 2) Identify and implement preventive procedures; 3) Define referral criteria to other health professionals, in patients with rheumatoid arthritis (RA), axial spondyloarthritis (axSpA), and psoriatic arthritis (PsA).

Methods: This project was promoted by CONARTHITIS (Association of patients with arthritis), OPENREUMA (Multidisciplinary association of professionals dealing with patients with rheumatic diseases) and SORCOM (Rheumatology Society of the Madrid Region). A multidisciplinary team specialized in comorbidity in inflammatory arthritis was established (6 rheumatologists, 2 primary care physicians, 2 nurses, 1 internist, 1 psychologist). A qualitative study was performed following these phases: 1) Review of the GECOAR1, GECOAX2 and GECOAP3 projects, that were focus on the evaluation of comorbidity in RA, axSpA and PsA, as well as an exhaustive bibliographic search in Medline; 2) Generation of preliminary checklists (different versions and formats) to be used by health professionals and patients for the identification, management and prevention of comorbidity; 3) Patient focus group in which the preliminary patients checklist was evaluated and discussed; 4) Nominal group meeting in which the selected health professionals analyzed all the checklists and modified them taking into account the opinion of the patients; 5) External evaluation of the modified checklists by patients, health professionals and rheumatologists, all of them outside the project; 6) Generation of the final checklists based on everything collected in the previous phases.

Results: Three checklists for clinical practice were designed, two for health professionals (one to identify comorbidity, another on prevention/health promotion), one for patients. The comorbidity checklist includes, for example, the evaluation of cardiovascular risk factors, depression and anxiety, allergies or infections. The prevention checklist includes life style issues (smoking, diet, exercise), social life, sexuality, sleep, or oral hygiene. The checklists also specify the evaluation method (questions, specific questionnaire, etc.).

Conclusion: The use of specific checklists for the identification, management and prevention of comorbidity inpatients with RA, axSpA and PsA might contribute positively in their prognosis.

REFERENCES

Disclosure of Interests: Santos Castañeda Consultant for: Amgen, BMS, Pfizer, Lilly, MSD, Roche, Sanofi, UCB, Carlos M. González: None declared, María del Carmen Castro Villegas Paid instructor for: MSD, Abbvie, Pfizer, Janssen, Lilly, Roche, Silva García-Díaz: None declared, Juan Carlos Hermosa: None declared, Cristina Lajías: None declared, Leticia León: None declared, Juan Carlos Obaya: None declared, María Rodero: None declared, Carmen Suarez: None declared, Virginia Villaverde: None declared, Juan Carlos Torre-Alonso: None declared


AB1202

SWITCHING OF ETANERCEPT IN A MONOGRAPHIC CONSULTATION OF BIOSIMILAR CLINICAL PRACTICE AND ECONOMIC COST


Background: The recent appearance of biosimilars by the European Medicines Agency in January 2015 allows a quality treatment in rheumatic diseases with a lower cost. We present our initial experience in a specific biosimilar consultation with the introduction of biosimilar Etanercept (BE).

Objectives: To describe the switching experience from original etanercept (OE) to BE and to evaluate the economic impact of this strategy.

Methods: Retrospective study carried out in a tertiary level hospital. We included patients treated with OE which were evaluated in the Specific Biosimilar Consultation where a rheumatologist and a nurse proposed them switching to BE. Demographic, clinical and pharmacistheapeutic variables of all patients were collected. The outcome evaluated was the drug switch as well the reasons why the change was not made. To analyze the economic impact, the estimated savings in the use of BE vs OE was calculated, [costs according to the net prices of our center (PVL - discount)+VAT].

Results: The registry included of 133 patients treated with OE from the Rheumatology Department of our center, only 56 patients were evaluated in a period of 3 months in the specific biosimilar consultation: 73% were women over 53 years (17-75 years). Regarding the diagnosis: 45% rheumatoid arthritis, 46% psoriatic arthropathy and 9% ankylosing spondylitis. All patients chosen to switch from OE to BE should have stable base disease (defined as low activity according to the specific scale for each pathology), approval of the change by a evaluating physician and patient, signing the informed consent.

Finally, the switch from OE to BE was performed in 31/56 patients (55%). In the 25 patients who did not change: 3 patients (12%) had moderate or high disease activity, in 8 patients (32%) the change was not accepted by the patient or by the evaluating physician and 14 patients (56%) were in remission of the disease. The patients chosen were in a dosage regimen of 50 mg/week, so the annual costs per patient are 9143.16€ with OE and 6095.44€ with BE. The switching to BE represent annual savings of 3047.72€ per patient and 94479.32€ total.

Conclusion: The experience with the implementation of a specific biosimilar consultation in our center has been positive. In the first 3 months of its operation, the switching from OE to BE have been made in 55% of patients allowing savings allowing savings of 3047.72€ per patient/year.

REFERENCES

Disclosure of Interests: None declared

AB1203 BURDEN DISEASE OF RHEUMATOID ARTHRITIS IN COLOMBIA, 2015

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Background: The prevalence of rheumatoid arthritis (RA) in Colombia according to the COPCORD study was 1.49%. The disease burden data available in our country are based on the results of the Global Burden Disease study (GBD) of 2016. However, the GBD study takes reference data from non-Colombian residents that was extrapolated to our population, given the absence of demographic data at that moment.

Objectives: To estimate the disease burden of RA for 2015.

Methods: A descriptive study was developed. The reference data of the population was taken by DANE (Departamento Administrativo Nacional de Estadística) and the WHO (World Health Organization). The GBD disability definitions were adapted from individual questions of functionality and quality of life questionnaires of the COPCORD study in Colombia (1). A Markov model was developed to calculate the years of life lost due to premature mortality (YLL), years lived with disability (YLD) and Disability-Adjusted Life Year (DALY).

Results: The distribution of cases by age and severity levels of RA are shown in figure 1 and 2 respectively.

Abstract AB1203 Figure 1. Distribution of cases by age and sex

Since direct death due to RA were not registered according to the search of the ICD-10 codes in DANE, the YLL was 0. The YLDs in total were 118,358. The DALYs were 118,358 for a rate of 361.54 per 100,000, which is higher than the GBD 2016 results (60 per 100,000).

Conclusion: The burden disease of rheumatoid arthritis is higher than that referred by GBD. Holistic approaches are required to reduce these parameters of impact on the public health of Colombians. Our data on DALYs usefulness lies in the urgent need for an early diagnosis, to reduce disability and thereby improve the quality of life of patients. Even though, RA was not the registered primary cause of death, it is necessary to explore mortality-associated conditions due to this rheumatic disease.

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Disclosure of Interests: Francy Cuervo: None declared, Ana Maria Santos: None declared, Ignacio Angarita: None declared, Juan Camilo Rueda: None declared, Rodrigo Girardo: None declared, Jesus G Ballesteros: None declared, Ingris Pelaez-Ballestas: None declared, Diana Diaz-Jimenez: None declared, Pedro Santos-Moreno Grant/research support from: Dr Santos has received research grants from Janssen, Abbvie and UCB, Speakers bureau: Dr Santos has received speaker fees from Sanofi, Lilly, Bristol, Pfizer, Abbvie, Janssen and UCB, Diana Padilla-Ortiz: None declared, Viviana Reyes: None declared, Carlos Castañeda-Orjuela: None declared, John Londono: None declared.


AB1204 BURDEN DISEASE OF LOW BACK PAIN IN COLOMBIA, 2015

Francy Cuervo1, Juan Camilo Rueda1, Ana María Santos1, Eugenia-Lucia Saldarriaga1, Ignacio Angarita1, Rodrigo Girardo1, Ingris Pelaez-Ballestas2, Diana Diaz-Jimenez2, Jesus G. Ballesteros2, Pedro Santos-Moreno2, Diana Padilla-Ortiz2, Viviana Reyes1, Carlos Castañeda-Orjuela1, John Londono1, Ignacio Angarita1, Rodrigo Girardo1, Ingris Pelaez-Ballestas2, Diana Diaz-Jimenez2, Jesus G. Ballesteros2, Pedro Santos-Moreno2, Diana Padilla-Ortiz2, Viviana Reyes1, Carlos Castañeda-Orjuela1, John Londono1, Ignacio Angarita1, Rodrigo Girardo1, Ingris Pelaez-Ballestas2, Diana Diaz-Jimenez2, Jesus G. Ballesteros2, Pedro Santos-Moreno2, Diana Padilla-Ortiz2, Viviana Reyes1, Carlos Castañeda-Orjuela1, John Londono1, Ignacio Angarita1, Rodrigo Girardo1, Ingris Pelaez-Ballestas2, Diana Diaz-Jimenez2, Jesus G. Ballesteros2, Pedro Santos-Moreno2, Diana Padilla-Ortiz2, Viviana Reyes1, Carlos Castañeda-Orjuela1, John Londono1.

1Universidad de La Sabana, Rheumatology, Chía, Colombia; 2Universidad Nacional Autonoma de Mexico, Faculty of Medicine, Ciudad de Mexico, Mexico; 3National Institute of Health, Colombian National Health Observatory, Bogotá, Colombia; 5Biomab, Bogotá, Colombia

Background: Low back pain (LBP) is the second most frequent rheumatic disease in Colombia. According to the COPCORD study, LBP prevalence was 7.24% (CI 95% 6.28-8.34%) (1).

Objectives: To estimate the disease burden of LBP for 2015.

Methods: A descriptive study was conducted. A Markov model was developed based on cases with LBP, distribution of disability and mortality according to DANE (Departamento Administrativo Nacional de Estadística) and the WHO (World Health Organization) reference data. The results are shown in terms of the years of life lost due to premature mortality (YLL), years lived with disability (YLD) and finally as Disability-Adjusted Life Year (DALY).

Results: The distribution of cases by age of LBP are shown in figure 1.

Abstract AB1204 Figure 1. Distribution of cases by age and sex

An algorithm was designed to determine the distribution in percentages of severity levels, according to the GBD definitions (figure 2).

Abstract AB1204 Figure 2. Distribution of severity levels of rheumatoid arthritis
According to ICD-10 codes, 9 deaths were reported, so the YLL were 124. The YLDs were 264,658. Finally, the DALYs were 264,782 for a rate of 808.82 per 100,000, which is higher than the GBD 2016 results (647 per 100,000).

**Conclusion:** The main cause of burden of disease of rheumatic disease in Colombia is due to LBP. The burden is because of the YLD, related to the frequency of cases in people younger than 50 years of age. It is necessary for an early detection and development of intervention strategies.

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**Disclosure of Interests:** Francy Cuervo: None declared, Juan Camilo Rueda: None declared, Ana María Santos: None declared, Eugenia-Lucía Saldarriaga: None declared, Ignacio Angarita: None declared, Rodrigo Giraldo: None declared, Ingris Peláez-Ballestas: None declared, Diana Díaz-Jiménez: None declared, Jesús G. Ballesteros: None declared, Pedro Santos-Moreno: None declared, Diana Padilla-Ortiz: None declared, Viviana Reyes: None declared, Carlos Castañeda-Orjuela: None declared, John Londono: None declared

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### AB1205

**ABSTRACT**

**BURDEN DISEASE OF OSTEOARTHRITIS IN COLOMBIA, 2015**

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**Background:** Osteoarthritis (OA) is the most prevalent rheumatic disease in Colombia, as reported by the COPCORD 2015 study. The prevalence is 10.81% (IC 95, 9.68-12.06) (1).

**Objectives:** To estimate the disease burden of OA for 2015

**Methods:** A descriptive study was developed. The reference data of the population was taken by DANE (Departamento Administrativo Nacional de Estadística) and the WHO (World Health Organization). It was necessary to develop an algorithm to determine the distribution in percentages of severity levels, according to the GBD definitions. A Markov model was elaborated to calculate the years of life lost due to premature mortality (YLL), years lived with disability (YLD) and Disability-Adjusted Life Year (DALY).

**Results:** Figure 1 shows the distribution of cases by age of OA, with the highest frequency of cases over 50 years in both sexes.

**Abstract AB1205 Figure 1. Distribution of cases by age and sex**

Figure 2 describes the distribution of the severity levels of the disease, with most cases being moderately severe.

**Abstract AB1205 Figure 2. Distribution of severity levels of rheumatoid arthritis**

The YLLs were 781 and the YLDs were 245,626. Finally, the DALYs calculated were 246,408 for a rate of 752.69 per 100,000.

When compared with that reported data by the GBD 2016, the burden of disease for OA was 204 (IC95% 143-278). The results of the present study show that the burden of the disease is higher, and the conditional factor is the YLDs.

**Conclusion:** Osteoarthritis is a frequent and disabling rheumatic disease that confers a large burden of rheumatic disease affecting people over 50 years of age. The treatment of OA should be focused on reducing disability and holistic intervention strategies to promote good quality of life.

**REFERENCES**


**Disclosure of Interests:** Francy Cuervo: None declared, Ignacio Angarita: None declared, Ana María Santos: None declared, Eugenia-Lucía Saldarriaga: None declared, Juan Camilo Rueda: None declared, Jesús G. Ballesteros: None declared, Rodrigo Giraldo: None declared, Ingris Peláez-Ballestas: None declared, Diana Díaz-Jiménez: None declared, Jesús G. Ballesteros: None declared, Pedro Santos-Moreno: None declared, Diana Padilla-Ortiz: None declared, Viviana Reyes: None declared, Carlos Castañeda-Orjuela: None declared, John Londono: None declared


### AB1206

**ABSTRACT**

**SELF-REPORT OF FRACTURE HISTORY COMPARED TO FRACTURE CODES FROM AN ELECTRONIC HEALTH RECORD DATASET**

**Maria Daniel,** 1 Amy Mudano, 2 Elizabeth Rahn, 2 Andrea Lacroix, 3, 4 Jeffrey Curtis, 4 Kenneth Saag, 3 University of Alabama at Birmingham, Birmingham, United States of America; 2 Group Health Cooperative, Seattle, United States of America; 3 University of California San Diego, La Jolla, United States of America

**Background:** Self-reported fracture history data is frequently used in epidemiological studies of osteoporosis. Self-reported fracture data may differ from fracture history coded in electronic health records (EHR) due to imperfect patient recall, incomplete communication with clinicians, or lack of a universal EHR. Because both self-reported fracture history and EHR data can define phenotypes for clinical research studies, it is important to understand how these 2 data sources compare.

**Objectives:** To compare self-reported fracture history using survey data with fracture codes from an available EHR dataset.

**Methods:** Self-reported fracture data was derived from the Activating Patients at Risk for OsteoPoroSis (APROPOS) trial, which recruited participants from the Global Longitudinal study of Osteoporosis in Women (GLOW) cohort. Prior fracture data was collected using a survey deployed June - August 2015. Women were asked if they ever had a fracture and for each fracture type the date of the most recent one. Data on fractures recorded in the EHR September 2011 - June 2015 was obtained from Kaiser Permanente Washington Health Research Institute. We excluded skull, toes and fingers fractures. We defined concordance between the EHR and self-reported data if the location of a fracture was reported to be the same and if the reported dates were within 1 year of each other. Kappa (κ) statistic described the concordance between the 2 sources of fracture history. Descriptive statistics
AB1207

ASSESSMENT OF RHEUMATIC DISEASES PATIENTS EXPERIENCE WITH THEIR HEALTHCARE USING IEXPAC. FACTORS ASSOCIATED AND AREAS OF IMPROVEMENT:

Javier de Toro-Santos1, L María. García Vivía2, Lucia Pantoja3, Cristina Lerín Lozano5, Silvia García-Díaz2, Yvonne Mestre6, Sabela Fernández6, Luís Cea-Calvo6, Hospital Universitario A Coruña, A Coruña, Spain; 2Hospital Universitario de Basurto, Bilbao, Spain; 3Hospital del Bierzo, Ponferrada, Spain; 4Hospital de Manacor, Manacor, Spain; 5Hospital de Sant Joan Despí Moises Broggi, Barcelona, Spain; 6Merck Sharp and Dohme, Madrid, Spain

Background: The experience of patients with healthcare has been associated to important outcomes. The experience of patients with healthcare has been associated to important outcomes. The experience of patients with healthcare has been associated to important outcomes.

Objectives: We describe the experience with healthcare of patients with rheumatic diseases from Spain self-reported through IEXPAC, a validated questionnaire, and the influence of demographic and health care-related factors.

Methods: The IEXPAC scale ("Instrument to Evaluate the Experience of Patients with Chronic Diseases", http://www.iemac.es/iexpac/) was developed and validated in Spain by health care professional and social organizations, experts in quality of healthcare and chronic patients (1). It consists of 12 items with Likert responses from "always" to "never" and yields an overall score from 0 (worst) to 10 (best experience). Three factors with sub-scores derive from the scale: Factor 1 (productive interactions, average of items 1, 2, 5 and 9, on patient-health care professionals relationship), Factor 2 (new relational model, average of items 3, 7 and 11, on the use of new technologies and contact with other patients) and Factor 3 (self-management, patients` ability to self-care, average of items 4, 6, 8 and 10). Data were obtained through an anonymous survey to patients from 25 Spanish hospitals. Bivariate comparisons and a multivariate analysis were made to explore the association between scores and demographic and health care-related characteristics.

Results: 625 patients received the survey, 359 (57.4%) returned it (mean age 55 years, 67% women). The percentage of patients who responded "always" or "nearly always" to the different statements is displayed in table 1. Mean overall IEXPAC score was 5.5 (SD 2.0), sub-scores were: productive interactions: 7.5 (2.5); new relational model: 1.7 (2.1); self-care: 6.5 (2.5). Overall score was higher (better experience) in men (p= 0.022), in those needing follow-up in a different region (p= 0.004), seen by a lower number of physicians (p= 0.025), seen by the same physician each time (p= 0.001), treated with lower number of medicines (p= 0.039) or with subcutaneous or intravenous (SC/IV) drugs (p= 0.083). Multiple linear regression models (table 2) showed that being followed up by the same physician, being seen by lower number of specialists, and being treated with SC/IV drugs were associated to better overall experience scores. Associations were similar for the productive interactions and self-management factors.

Conclusion: Through IEXPAC, patients with rheumatic diseases identified areas of improvement in healthcare, especially those related with access to reliable information and services, interaction with other patients and continuity of health care after hospital discharge. Better experience was associated to being seen by lower number of specialists or being followed-up by the same physician each time, and also with treatment with SC/IV drugs, maybe in relation to the more personalized care these patients receive.

Table 1. Word-for-word IEXPAC items. Percentage of patients who responded "mostly" or "always" to each item.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Overall experience score</th>
<th>Probability of Reliability (Factor 1)</th>
<th>Probability of Reliability (Factor 2)</th>
<th>Patient Self-Efficacy (Factor 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Beta coeff. (SD)</td>
<td>Beta coeff. (SD)</td>
<td>Beta coeff. (SD)</td>
<td>Beta coeff. (SD)</td>
</tr>
<tr>
<td>Sex (men vs. rest)</td>
<td>-0.43 (0.29)</td>
<td>0.43 (0.29)</td>
<td>0.06 (0.29)</td>
<td>0.06 (0.29)</td>
</tr>
<tr>
<td>Age in years of youngest patient</td>
<td>0.60 (0.10)</td>
<td>0.60 (0.10)</td>
<td>0.37 (0.10)</td>
<td>0.37 (0.10)</td>
</tr>
<tr>
<td>Educational level (elementary or further)</td>
<td>0.16 (0.13)</td>
<td>0.16 (0.13)</td>
<td>0.21 (0.13)</td>
<td>0.21 (0.13)</td>
</tr>
<tr>
<td>Taking up a vocation different from home (father)</td>
<td>0.42 (0.19)</td>
<td>0.42 (0.19)</td>
<td>0.26 (0.19)</td>
<td>0.26 (0.19)</td>
</tr>
<tr>
<td>Corticosteroids (yes vs. no)</td>
<td>0.45 (0.18)</td>
<td>0.45 (0.18)</td>
<td>0.05 (0.18)</td>
<td>0.05 (0.18)</td>
</tr>
<tr>
<td>Number of specialists involved in the last year per illness</td>
<td>0.11 (0.39)</td>
<td>0.11 (0.39)</td>
<td>0.04 (0.39)</td>
<td>0.04 (0.39)</td>
</tr>
<tr>
<td>Following up the same physician (yes vs. no)</td>
<td>0.04 (0.36)</td>
<td>0.04 (0.36)</td>
<td>0.03 (0.36)</td>
<td>0.03 (0.36)</td>
</tr>
<tr>
<td>Following up to any (yes vs. no)</td>
<td>0.03 (0.18)</td>
<td>0.03 (0.18)</td>
<td>0.03 (0.18)</td>
<td>0.03 (0.18)</td>
</tr>
<tr>
<td>Having multiple diagnoses at any one visit (yes vs. no)</td>
<td>0.04 (0.07)</td>
<td>0.04 (0.07)</td>
<td>0.05 (0.07)</td>
<td>0.05 (0.07)</td>
</tr>
<tr>
<td>Number of different medications (yes vs. no)</td>
<td>0.15 (0.31)</td>
<td>0.15 (0.31)</td>
<td>0.08 (0.31)</td>
<td>0.08 (0.31)</td>
</tr>
<tr>
<td>Being involved in SDG change (no vs. yes) (SDG type)</td>
<td>0.44 (0.27)</td>
<td>0.44 (0.27)</td>
<td>0.05 (0.27)</td>
<td>0.05 (0.27)</td>
</tr>
</tbody>
</table>

Acknowledgement: Funded by MSD of Spain and endorsed by 4 patients associations: ACCU, CONARTITIS, SEISIDA, FEDE. We thank the participants for providing this valuable information by completing the survey.


AB1208 POINT PREVALENCE OF UVEITIS AND ARTHRITIS AMONG SCHOOL CHILDREN IN A DEVELOPING COUNTRY

Fiman Dessouki. Faculty of medicine, Alexandria university, Alexandria, Egypt

Background: Sight-threatening uveitis associated with pediatric rheumatologic diseases, especially juvenile idiopathic arthritis, often remains asymptomatic till late. On the other hand, children with indolent asymptomatic uveitis may later on develop the characteristic arthritis of juvenile idiopathic arthritis, especially the oligoarticular rheumatoid factor negative type. A multidisciplinary screening of children at the peak age of developing these potentially handicapping manifestations, allows active case finding and facilitates a comprehensive ophthalmic-rheumatologic management plan.

Objectives: A point prevalence study aiming at active case finding and describing the prevalence of uveitis and arthritis among school children between the ages of 4 and 9 years in 10 screened schools in Egypt.

Methods: All children between the ages of 4 and 9 years in 10 screened schools in Egypt. A point prevalence study aiming at active case finding and the not diagnosed groups, split by CRP results.

Results: A total of 6372 children were screened, 3418 of them were females (53.6%) and 2954 were males (46.4%). Thirty four children were found to have uveitis (0.5%). Of these, 26 children were females (76.5%) and 8 children were males (23.5%). Two female children were known uveitis patients and were on treatment. A hundred and eleven children had arthralgia. Of these, 56 children had clinically evident arthritis at the time of screening. Twenty eight children with arthritis were females (50%) and the other twenty eight children were males (50%). Three girls were previously known to be arthritis patients (2 with juvenile idiopathic arthritis and one with psoriasis). Eleven children had both uveitis and arthritis. All cases detected to have uveitis, arthralgia, or arthritis, in the study were referred to tertiary clinics for further management.

Conclusion: Screening of school children for uveitis and joint manifestations in developing countries with a modest socioeconomic status, is a method of active case finding that helps an, as early as possible, implementation of the proper plan of management.

REFERENCES

Disclosure of Interests: None declared

SociaL Media use in Rheumatology Patients

Mustafa Ergöçen1, Okan Aydin2, Emire Seyahi1, 1Istanbul University -Cerrahpasa Medical Faculty, Internal Medicine, Division of Rheumatology, Istanbul, Turkey; 2Istanbul University -Cerrahpasa Medical Faculty, Internal Medicine, Istanbul, Turkey

Background: The impact of social media on individual or institutional communication and knowledge acquisition is non-negligible. Whether patients (patients) with rheumatic diseases share information about their health on social media is unknown.

Objectives: We aimed to investigate how often and to what extent patients with a rheumatic condition use social media. We also wanted to know whether they communicate with their doctors through social media and what their expectations are.

Methods: Consecutive patients with diverse diagnoses attending a rheumatology outpatient clinic were studied. Patients completed a self-administered questionnaire (1) which was modified. Information on demographic features, educational status and diagnosis was also recorded.

Results: 397 patients completed the questionnaire (Table). 329 patients with devices, 40 (12%) of these patients were not using social media. 68 patients without devices, thus social media users reached 73% (289/397). While, Facebook users and non-users were similar according to age, gender or educational status, Twitter users were more likely to be male and more educated (Figure). 96% were willing to communicate with their doctors through social media and what their expectations are.

Conclusion: This survey showed that younger and more educated patients had significantly more communication devices. Facebook was the most preferred social media website. More educated patients prefer using Twitter, Instagram and Pinterest and younger patients Instagram and Pinterest. The majority thought that social media was a useful information source about health. While only 23% had an actual connection with their rheumatologist through social media, 75% desired to be friends on the Facebook.

REFERENCES

Table. General Features of Patients

<table>
<thead>
<tr>
<th>Median Age [IQR]</th>
<th>45[34-56]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female/Male Ratio</td>
<td>1.9</td>
</tr>
<tr>
<td>Diagnosis of the patients, %</td>
<td></td>
</tr>
<tr>
<td>Rheumatoid Arthritis</td>
<td>99 (25)</td>
</tr>
<tr>
<td>Spondyloarthritids</td>
<td>67 (17)</td>
</tr>
<tr>
<td>Connective Tissue Disease</td>
<td>60 (15)</td>
</tr>
<tr>
<td>Behcet’s Syndrome</td>
<td>74 (19)</td>
</tr>
<tr>
<td>Familial Mediterranean Fever</td>
<td>57 (14)</td>
</tr>
<tr>
<td>Others*</td>
<td>9 (2)</td>
</tr>
<tr>
<td>Unknown</td>
<td>31 (8)</td>
</tr>
<tr>
<td>Computer Status, %</td>
<td></td>
</tr>
<tr>
<td>Elementary School</td>
<td>171 (43)</td>
</tr>
<tr>
<td>High School</td>
<td>143 (36)</td>
</tr>
<tr>
<td>College</td>
<td>83 (21)</td>
</tr>
<tr>
<td>Having an internet connectable device, %</td>
<td></td>
</tr>
<tr>
<td>Table</td>
<td>68 (17)</td>
</tr>
<tr>
<td>Tablet</td>
<td>68 (17)</td>
</tr>
<tr>
<td>Other</td>
<td></td>
</tr>
<tr>
<td>Facebook</td>
<td>234 (81)</td>
</tr>
<tr>
<td>Instagram</td>
<td>202 (70)</td>
</tr>
<tr>
<td>Twitter</td>
<td>92 (32)</td>
</tr>
<tr>
<td>Pinterest</td>
<td>38 (13)</td>
</tr>
</tbody>
</table>

FIGURE. SOCIAL MEDIA USE FREQUENCY AMONG PATIENTS WITH INTERNET CONNECTABLE DEVICES

Disclosure of Interests: None declared


Abstract AB1209 Table 2. Group differences of physical and mental health parameters

<table>
<thead>
<tr>
<th></th>
<th>Rheumatic disease Yes vs No Diagnosis+CRP pos.</th>
<th>Rheumatic disease Yes vs No Diagnosis+CRP pos.</th>
<th>No Diagnosis+CRP pos. vs No Diagnosis+CRP pos.</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>0.57±0.068 vs 0.63±0.063</td>
<td>0.423* vs 0.063</td>
<td>0.013* vs 0.063</td>
</tr>
<tr>
<td>HA</td>
<td>0.52±0.060 vs 0.59±0.060</td>
<td>0.423* vs 0.063</td>
<td>0.013* vs 0.063</td>
</tr>
<tr>
<td>HPA</td>
<td>0.81±0.064 vs 0.79±0.146</td>
<td>0.384 vs 0.063</td>
<td>0.013* vs 0.063</td>
</tr>
<tr>
<td>HPA</td>
<td>0.81±0.064 vs 0.79±0.146</td>
<td>0.384 vs 0.063</td>
<td>0.013* vs 0.063</td>
</tr>
<tr>
<td>HPA</td>
<td>0.81±0.064 vs 0.79±0.146</td>
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<td>0.013* vs 0.063</td>
</tr>
<tr>
<td>HPA</td>
<td>0.81±0.064 vs 0.79±0.146</td>
<td>0.384 vs 0.063</td>
<td>0.013* vs 0.063</td>
</tr>
</tbody>
</table>
AB1211  A RETROSPECTIVE ANALYSIS OF LABORATORY ABNORMALITIES FOUND DURING METHOTREXATE MONITORING AND THE COST IMPLICATIONS
Sadrive Eriksson, Arslan Sidhu, Tom Walton. Colchester Hospital, East Suffolk and North Essex NHS Foundation Trust, Rheumatology, Colchester, United Kingdom

Background: Methotrexate (MTX) remains the first line treatment in major- ity of cases of inflammatory arthritis. The current British Society of Rheumatology (BSR) Guidelines suggest checking Full blood count (FBC), ALT/AST, Creatinine at 0.2, 4, 10, 14, 18 weeks and then 12 weekly. Despite this close monitoring recommendation, MTX is generally considered a safe drug by Rheumatologists and its use has grown signifi- cantly over last two decades.

Objectives: To evaluate the incidence of liver, renal and haematological toxicities during Methotrexate treatment and calculate the cost implications.

Methods: 101 patients (30 males 71 females) (Age 40-89 year Mean 66.5 year) prescribed MTX were randomly selected and retrospective analysis was performed. 91 Rheumatoid arthritis, 8 Psoriatic arthritis and 2 patients had Undifferentiated Inflammatory Arthritis. 20 patients had Early Inflammatory Arthritis (<1 year) and 81 had established disease. 24 patients were on MTX for <1 year. Average dose of MTX in our cohort was 15mg once weekly (Min 7.5mg Max 25mg). All patients were on folate supplementation. Blood investigations over last 1 year were reviewed individually for all patients. Severe Liver toxicity (LS) was defined as ALT/AST >100 U/l; unexplained reduction in albumin <30 g/l. Severe renal toxicity (RS) was defined as Creatinine increase >105 fL and HS. Severe haematological toxicity (HS) was defined as WCC <3.5 × 10 9/l, MCV <80 fL and HS. Severe haematological toxicity (HS) was defined as WCC <3.5 × 10 9/l, MCV <80 fL and MS was <75 fL. Mild liver toxicity (LM) was between normal and LS values. Severe haematological toxicity (HS) was defined as WCC <3.5 × 10 9/l, MCV >105 fL, Neut <1.6 × 10 9/l, PLT <140 × 10 9/l unexplained eosinophilia >0.5 × 10 9/l and mild haematological toxicity (HM) was between normal and HS. Severe renal toxicity (RS) was defined as Creatinine increase >30% over 12 months and/or calculated GFR <60 ml/min. Mild renal tox- icity (RM) was between normal and RS.

Results: Over 1 year, 101 patients had total of 609 blood tests for MTX monitoring (Min 1 Max 17). FBC, Liver Function Test, Urea & Electrolytes, CRP and ESR each cost £8.54. LS was found in 4 patients, LM in 15, HM in 3 and RM in 2 patients. MTX was stopped in all 4 patients with LS. Mild toxicities (LM, HM and RM) recovered after close monitoring or reduction in dose. 5 patients with mild toxicities were on MTX for <1 year. Rest of the patients were on stable dose of MTX for >1 year. All patients with severe and mild toxicities did not have any significant comorbidities compared to rest of the patients. It was calculated that detecting one LS cost (£09x8.54)/4 = £1300.2. Similarly one HM cost £346.7, one RM £1733.6 and one RS £2600.43. These costs does not include travel expenses, parking charges and time off work for appointments in phlebotomy.

Conclusion: Our cohort shows that mild liver toxicity is the most com- monly found abnormality during MTX monitoring and patients on stable doses still need monitoring for liver toxicity. Haematological and renal toxic- ities are much less common and a more relaxed monitoring schedule may be acceptable for these parameters. Regular monitoring for inflam- matory markers (CRP, ESR) causes an extra cost burden. The direct cost for identifying each abnormality is considerable.

REFERENCES

Disclosure of Interests: None declared

AB1212 POLYPHARMACY AND OUTPATIENT HEALTHCARE USE IN RHEUMATOID ARTHRITIS: PATTERNS AND ASSOCIATIONS
George E. Fragiou1, Savvas Psarrelis2, Christina Flourou3, Andreas Tofandaris3, Panayiotis Ayerdi4, University of Glasgow, Institute of Infection, Immunity and Inflammation, Glasgow, United Kingdom; 2Nicola General Hospital, Rheumatology, Nicosia, Cyprus; 3Nicosia General Hospital, Internal Medicine Department, Nicosia, Cyprus; 4King’s College, Department of Inflammation Biology, London, United Kingdom

Background: Polypharmacy is a considerable problem in people with rheumatic diseases, including rheumatoid arthritis (RA), related amongst others to worse disease outcomes and increased cost for the health-sys- tem. (1).

Objectives: To assess polypharmacy in RA and usage of the health-care system (outpatient clinics) in a real-world setting.

Methods: Medical records of 170 consecutive RA patients from a large outpatient service of a central hospital were retrospectively reviewed. Demographic char- acteristics, treatment for RA and comorbidities as well as frequency and type of visits to any outpatient services were recorded. The latter included rheumatologists, “medical specialists” (general physicians, cardiologists, respiratory physi- cians, oncolologists, dermatologists, gastroenterologists, hematologists, nephrolo- gists and neurologists) and “surgical specialists” (general surgery, orthopedics, neurosurgery, urology, ophthalmology, ENT, maxillofacial and vascular surgery). Disease duration was defined as the time between RA diagnosis and the end of the study (May 2018). Univariable and multivariable analyses were performed (Table).

Results: Data from 170 RA patients (77.1% female) with a mean±SD age of: 62.1 ± 13.7 years and disease duration: 87.8 ± 22.0 months, were recorded. The median number of non-rheumatic drugs received throughout disease duration was 3. Only 7% of the patients were not receiving any additional drugs, while 15.3%, 40.6% and 56.4% had received 1, 2 and 3 non-rheumatic drugs, respectively. The most com- monly used non-rheumatic drugs were, anti-hypertensive, anti-osteoporotic and lipid-lowering drugs. Higher total number of drugs correlated with age of the patient and longer disease duration. Methotrexate (MTX) experi- enced or biologic-naive patinets, had received a larger number of non- rheumatic drugs compared to those who had not received methotrexate or were biologic-experienced. Multivariable analysis confirmed age and exposure to methotrexate/biologics to be positively and negatively associa- tion respectively, with the number of non-rheumatic drugs received (Table).

Number of visits to rheumatologists/year were: median (range) 2.9 (0.5 – 13.6). The number of visits was correlated with age of the patients, dis- ease duration and number of non-rheumatic drugs received. Multivariable analysis, identified, disease duration, number of non-rheumatic drugs received and being MTX-naive as predictors of number of rheumatology visits (Table).

Disclosure of Interests: None declared

REFERENCES

Disclosure of Interests: None declared
AB1213

PATIENTS’ PERSPECTIVES OF OUTCOMES AFTER TOTAL KNEE AND TOTAL HIP ARTHROPLASTY: A NOMINAL GROUP STUDY

Susan Goodman1, Bella Mehta1, Serene Mirza1, Mark Figgie1, Peter Sculco1, Michael Parks1, Jassvinder Singh1, Hospital for Special Surgery, Main Campus, New York, United States of America; 2UB School of Medicine, Birmingham, United States of America

Background: Utilization rates of total joint replacements (TJR) are high and rising to treat advanced symptomatic arthritis, but there is little qualitative research to define the most important outcomes from the patient perspective.

Objectives: To assess the most important outcomes of TJR from the patients’ perspective using nominal group technique (NGT).

Methods: Recruited patients were ≥18 and had received total hip (THR) or total knee replacements (TKR). Participants completed a questionnaire including demographics and pain and function measures, and answered “What result/results matter the most to a patient undergoing/having a knee or hip replacement?”. Outcomes were independently selected, listed in a round robin, and ranked by the group using NGT.

Results: 36 patients participated in 6 nominal groups in January 2019. 42% were men (Table 1). For THR, 94% reported no/mild pain. For TKR, 81% reported no/mild pain/pivoting or on stairs, 1 patient reported severe pain. Satisfaction was high, 97% reported very/somewhat satisfied with pain relief. Of 216 total votes, A) pain received 98 votes, B) function 92 votes, C) quality of life 40; D) adverse events 16 votes and E) revision 2 votes, the remainder 8 votes were distributed to post-op concerns including access to rehabilitation or education (Table 2).

Conclusion: Pain, function, quality of life, and adverse events are the outcomes ranked highest by patients, supporting their inclusion in TJR clinical trials.

Disclosure of Interests: Susan Goodman Grant/research support from: Novartis; research support, Consultant for: Novartis, UCB, Pfizer; consulting, Bella Mehta: None declared, Serene Mirza: None declared, Mark Figgie: None declared, Peter Sculco: None declared, Michael Parks Grant/ research support from: Zimmer Biomet, Employee of: Zimmer Biomet, Jassvinder Singh Shareholder of: Amarin pharmaceuticals and Viking therapeutic, Consultant for: Crealta/Horizon, Fidia, UBM LLC, Medscape, WebMD, the National Institutes of Health and the American College of Rheumatology


AB1214

PRELIMINARY STUDY OF THERAPY ADHERENCE CONTROLLED BY PRESCRIPTION OF MEDICATION AND SELF-PERCEPTION ADHERENCE OF INFACRURAL CHRONIC DISEASE PATIENTS

Elena Grau García1, Jose Iviron Cortés1,2, Emilio Monte Boqueit3, Cristina Alcañiz Escandell1, Inmaculada Chalmea Verdejo1, Marta De la Ribera Navarro1, Jorge Juan Fragol-Gal1, Roxana Gonzalez Mazzaro1, Luis Gonzalez Puig1, Isabel Martinez Cordelí1, Rosa Negueruelos Abuissé1, Jose Eloy Oller Rodriguez2, Francisco Miguel Ortiz Sanjuan1, Cristobal Pávez Perales1, Elvira Vicens Bernabeu1, Carmen Nájera Herranz1, Inés Cánovas Olmos1, Antonio Luis Garcia Cebrián1, Jose Luis Poueda Andrez1, Jose Andrez Román Ivorra2,3,1, Rheumatology Department, HUP La Fe, Valencia, Spain; 2Medical School, UCV, Valencia, Spain; 3Pharmacy Department, HUP La Fe, Valencia, Spain

Background: The absence of therapy adherence is a public health problem and leads to negative consequences in inflammatory chronic disease. The measurement of therapy adherence has demonstrated effectiveness on the improvement of compliance, but it is difficult to estimate because it is based on indirect measurements. With high probability there will be discrepancies between different measurements.

Objectives: To estimate the discrepancies between therapy adherence controlled by prescription of medication, Morisky-Green test and self-perception adherence patients under biological subcutaneous treatment or under Jakinhibs oral treatment.

Methods: Observational study including inflammatory chronic disease patients under biological subcutaneous treatment or under Jakinhibs oral treatment, selected consecutively. We performed a preliminary stage where patients were contacted by telephone and after that the questionnaire was sent to the email address they provided. The questionnaire included Morisky-Green test and a self-perception adherence scale (0-10). Data about dispensation of medication was collected from the pharmacy service. We defined as “adherent patient” a dispensation rate over 80%.

Results: 54 patients were contacted, and 37 of them full-filled the questionnaire. 28 full-filled the online questionnaire but the other 9 preferred the paper format. The patients from the online format questionnaire had a mean age of 50.86 years (range 22-74), and patients of paper format questionnaire had a mean age of 61.38 years (38-71). We observed a high proportion of patients with university studies among those who preferred the online format.

Conclusions: Among the 37 surveyed patients a discrepancy between therapy adherence controlled by dispensation of medication and adherence by Morisky-Green was observed (94.6% vs 72.97%, P<0.005). Moreover, 72.97% of patients considered easy or very easy to follow the prescribed therapy, and in the self-perception adherence scale the 54.05% of them scored 10, the 21.62% scored 9, the 21.62% scored 8 and the 2.7% scored 6. Among the analyzed factors which may affect the therapy adherence, the oral route of administration showed more adherence rate controlled by dispensation of medication (P<0.019) and with Morisky-Green adherence rate (P<0.016). No other association with other factors as age, gender or time of disease evolution was observed.

Conclusion: Younger patients and those with university studies preferred to full-fill the online questionnaire. A discrepancy between therapy adherence controlled by prescription of medication and adherence by Morisky-Green was observed. Moreover oral route of treatment showed more therapy adherence than subcutaneous route of treatment. Even if the patients are no self-considered as 100% adherents (Morisky-Green), a tendency of collect the medication on a regular basis was observed. This seems to indicate that instead of the controlled dispensation of medication by Pharmacy, patients with lower therapy adherence will collect all the medication.

Disclosure of Interests: None declared

CURRENT PRACTICE OF HYDROXYCHLOROQUINE PRESCRIPTION AND MONITORING IN INDIA - A NATIONAL SURVEY

Shilpa Jagadeesh1, Arumugam Moorthy2, B G. Dharmamand3, University Hospitals Leicester, Rheumatology Registrar, Leicester, United Kingdom; 2University Hospitals Leicester, Consultant Rheumatologist, Leicester, United Kingdom; 3Vikram Hospital, Consultant Rheumatologist, Bengaluru, India

Background: Hydroxychloroquine was introduced as an anti-malarial during World War 2 and since then has found numerous indications for usage as an immunomodulator. Research is ongoing for new uses of the drug. Hydroxychloroquine is generally considered to be safe and monitored less rigorously than other DMARDs that have strict blood monitoring regimes. Emerging evidence of increased risk of retinal toxicity possibly due to widespread usage in a population with diverse co-morbidities has prompted updates to prescription and monitoring guidelines worldwide.

Objectives:
2. Understand awareness of cross specialty guidelines.
3. Explore barriers to evidence based monitoring.

Methods: Questionnaire based survey shared to practicing clinicians (consultant rheumatologists, immunologists, postgraduate trainees, other clinicians with interest in rheumatology) who prescribe Hydroxychloroquine. Results analyzed through excel spreadsheet and charts.

Results: We received 61 responses from clinicians nationally. 88.5% were consultant rheumatologists, 6.6% consultant immunologists and others included clinicians with interest in rheumatology. Special interest was CTD for 47.5% and 36% inflammatory arthritis. All respondents worked in urban areas and average experience in specialty was 9 years. Majority saw in excess of 500 patients month. 61 clinicians saw in excess of 24,700 patients per month and on average started more than 2481 patients on Hydroxychloroquine. Approximate prescription rate was 41 patients per clinician per month. Indications included connective tissue disease and inflammatory arthritis mainly. Other indications include antiphospholipid syndrome, osteoarthritis, post viral, arthropathy, dermatomyositis and diabetotic arthropathy.

Pretreatment tests as per international guidelines were recommended by 35% clinicians only which includes baseline Optical coherence tomography 25%, or eye evaluation by ophthalmologist 10%. 54% clinicians advised OCT after 5 years (47.5%) or formal ophthalmology monitoring (6.5%) in line with published international guidance. Barriers to following required pretreatment tests and monitoring we noted from this survey include lack of awareness or disagreement with guidelines (lack of conclusive data), doubtful cost effectiveness and nonadherence by patients due to cost implications.

Conclusion: There is need to improve awareness of existing evidence based guidelines on prescription and monitoring of Hydroxychloroquine by international ophthalmology and rheumatology organizations. There is more data needed to prove effectiveness of current guidelines beyond doubt. We also need to better counsel and educate patients on the drug so adherence can be improved.

REFERENCES


CHECKING IN WITH IMMUNE CHECKPOINT INHIBITORS: RESULTS FROM A NEEDS ASSESSMENT SURVEY OF CANADIAN RHEUMATOLOGISTS

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Background: Immune checkpoint inhibitors (ICI) have revolutionized the treatment of cancer. However, enhanced immune activation from ICI has been associated with immune-related adverse events (irAE), including autoimmune rheumatologic diseases such as inflammatory arthritis, spondyloarthritis, polymyalgia rheumatica-like syndrome and inflammatory myositis, among many others. This emerging field represents a challenge given that experience with these conditions is limited and evidence-based recommendations do not yet exist.

Objectives: The Canadian Research Group of Rheumatology in Immunology and Rheumatology (CanRIO) is an emerging network of rheumatologists interested in rheumatologic irAE (rh-irAE). CanRIO undertook a needs assessment survey to understand the need for education and recommendations for the management of rh-irAE in the rheumatology community in Canada. The primary objective was to recognize the knowledge gaps, if any, and understand current patterns of practice in this newly emerging area.

Methods: A 25-item electronic survey was developed by the CanRIO investigator group. The survey, which was available in both French and English, was distributed via electronic mail to 574 members of the Canadian Rheumatology Association (CRA). Responses were collected over a period of 14 days. Results were summarized using descriptive statistics.

Results: Of the 574 CRA members who were invited to participate, 83 responded (response rate of 14.5%). Half of the respondents were adult rheumatologists from academic centres and 26% from the community. Over 25% of the respondents were not familiar with ICI and irAE. Half of the respondents had not seen or managed patients with irAE, and among the remaining, the majority had seen less than 5 patients with irAE. Inflammatory arthritis was the most common rh-irAE encountered. Other rh-irAE included sicca, myositis, sarcoid and vasculitis. Prednisone and methotrexate were the most common treatment strategies. Almost half of the respondents (43.6%) had been asked for advice from oncologists regarding discontinuation of ICI for irAE, and of these, almost half (48.7%) reported that they were either ‘slightly confident’ or ‘not confident at all’ in providing advice. Over half of the respondents had not yet been asked to provide advice concerning ICI for patients with pre-existing auto-immune diseases. The vast majority (87.2%) agreed that there was a need for clinical practice guidelines for the management of rh-irAE.

Conclusion: The survey highlighted the important knowledge gaps in the emerging field of rh-irAE. Given the increasing use of ICI in a growing number of cancer types and stages, referrals for rh-irAE are likely to increase. There is strong rationale to develop educational programs and clinical practice guidelines to support Canadian rheumatologists who will be increasingly responsible for managing rh-irAE.

REFERENCE

Disclosure of Interests: Ahmad Abdullah: None declared, Nancy Maltez: None declared, Marie Hudson Grant/research support from: Unrestricted research funds from Bristol-Myers Squibb, Aurore Fifi-Mah Grant/research support from: Roche, Abbvie, Janssen, BMS, Speakers bureau: Roche, Abbvie, Janssen, BMS, Pfizer, Shahin Jamal Consultant for: Consultant for Abbvie, Amgen, BMS, Eli Lilly, Pfizer, Janssen, Merck, UCB.


WHY DO PATIENTS CLAIM? ANALYSIS OF THE CLAIMS MADE BY PATIENTS THROUGH CUSTOMER SERVICE

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Background: Analysis of the claims made by patients could be an indicator of quality and show strengths and aspects of improvement in the organization of a rheumatology department.

Objectives: The aims of the present study are to evaluate these claims, describe the sociodemographic and clinical characteristics of claiming patients and to determine the association between medical history and types of complaints.

Methods: Cross-sectional study. Claims made by patients treated by a rheumatology department between 04/2016 and 12/2017 were analyzed. A descriptive analysis of these claims was carried out followed by a multivariate logistic regression model to determine the effect of the diagnosis of Fibromyalgia (FM)/Chronic Widespread Pain (CWP) on the type of claim and its association with clinical variables. A p <0.05 was considered significant.
Results: One hundred and nine patients (mean age 54.7 ± 18.5 years, 76% women and 50.5% residents in rural areas) made 113 claims. The main reasons for claiming were: "advance medical evaluation and/or tests" (45.1%), "request for evaluation by a specific physician" (24.8%) and "rejection of evaluation by specific physician" (13%, 3%). 67% of the claims were satisfied. The least satisfied claims were "request for evaluation by specific doctor" (39.3%) while claims for "cancellation of evaluation" were satisfied in 88% of the cases.

Median time between claim and previous medical visit was 44 [28-82] days. Patients whose claims were due to "unpleasant attendance" were the first to complaint (median 28 [2-72] days) but waited for the longest time to be attended (median 103 [46-147] days). "Cancellation of evaluation" was attended after a median of 31.5 [28-33] days.

The main reasons for medical evaluation were: inflammatory/systemic disease in 25 patients (22.15%), neck and low back pain in 23 patients (20.35%) and FM/CWP also in 20.35% of patients. As personal medical history, Psychiatric Disorders were present in 20.5% of patients and multiple comorbidities in 19.6% of patients. Twenty patients had no medical history of interest.

Regarding the type of claims, differences were observed related to the diagnosis and the patient’s medical history. The logistic regression model (FM as dependent variable) adjusted for sex, age, rural area, time to/after the claim and medical history showed that patients with FM/CWP requested more frequently to "be evaluated by other physician" (OR of 23.92 [95% CI, 1.4-409.06] and "reject to be evaluated by a specific physician" (OR of 8.48 [95% CI, 1.2-60.09]) than the rest of the patients and also presented more frequently with psychiatric history (OR of 22.39 [95% CI, 1.15-437.23])

Conclusion: the present study reflects main reasons for claiming of patients treated in a rheumatology department. Reasons of claiming and comorbidities of patients with FM/CWP differ from those of the rest of patients. These findings may be of interest for the organization of resources in rheumatology departments.

Disclosure of Interests: Enrique Juez Navarro Consultant for: Roche, Carlos Sánchez-Piedra: None declared, Gines Labiano: None declared, Manuela Sianes: None declared, Gloria Garcia Consuegra: None declared, Sandra Soro: None declared, M Angeles García Morales: None declared.


AB1219

EFFECTS OF A WORKPLACE-CENTERED COUNSELING OF INDIVIDUALS WITH MUSCULOSKELETAL COMPLAINTS: A PROSPECTIVE COHORT STUDY

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Background: Employed people with musculoskeletal complaints often seek medical advice when symptoms are chronic and lead to loss of workability.

Objectives: A brief examination was offered in the workplace setting to detect and to counsel individuals with symptoms of Rheumatic and musculoskeletal diseases(RMDs).

Methods: Employees received a questionnaire regarding musculoskeletal problems. In case of a positive screening, consultation by RMD specialists was offered. If necessary, participants were referred to a clinic specialized in RMDs. Employees’ work was categorized into physically-highly-demanding(HD) and less-demanding(LD).

Results: 6170 employees were invited. 413 participated in the counselling program, 344 were enrolled in the study. 56.6% of the participants had previously diagnosed RMD. Among the specialists’ assessment, this percentage decreased to 35.7%. Men with LD-workload had significantly higher wellbeing (EQ-5d scale) compared to women with both LD (p=0.034) and HD (p=0.001). LD and HD differed significantly regarding percentage with painful upper (p=0.006) and lower (p=0.016) limbs. Back pain was distributed equally among all groups. HD women reported significantly higher use of NSAIDs (p=0.001).

The mean interval from Referral to patient review was 11.5 weeks in Feb 2006, 7.15 weeks in August 2012 and 6.6 weeks in Feb 2016. In parallel with the diagnosis of inflammatory arthritis we also looked at mean timeframe from 1st review to initiation of DMARDs which is demonstrated in the chart below.

Figure 1

Conclusion: • Mean interval between primary care referral to first outpatient review has improved significantly over the period of 10 years
• Mean interval for DMARD initiation in inflammatory arthritis patients has also improved in the 10 years’ time


AB1218

ANALYSIS OF REFERRAL TRENDS TO A SECONDARY CARE RHEUMATOLOGY SERVICE FROM GENERAL PRACTICE: OVER A TEN-YEAR PERIOD

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Background: The practice of Rheumatology in the UK has undergone significant change in the past decade. These have been driven by developments in our understanding of the diseases; early arthritis clinics; changing population demographics; changes in the health services (NHS) all of which have influenced referral patterns to rheumatology.

Objectives: To analyse referral data from primary care over three time points of a month at a time, over a decade – from 2006 to 2016 to assess changing trends, if any, of patients attending Rheumatology.

Methods: We analysed referrals from the primary care in the months of Feb ’06 (n=89), Aug ’12 (n=50) and Feb ’16 (n=100). We looked at the following: reason for referral and our response, referral to out-patient review interval; outcome and final diagnosis.

We also analysed between first appointment and DMARD initiation in inflammatory arthritis.

Results: Referrals were grouped as demonstrated in the table below.

<table>
<thead>
<tr>
<th>Diagnostic category</th>
<th>2006 (n=89)</th>
<th>2010 (n=50)</th>
<th>2016 (n=100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>non inflammatory/inflammatory arthritis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal investigations results for opinion</td>
<td>2.5% (n=2)</td>
<td>6% (n=3)</td>
<td>10% (n=10)</td>
</tr>
<tr>
<td>Back pain</td>
<td>11.3% (n=10)</td>
<td>10% (n=5)</td>
<td>5% (n=5)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>1% (n=1)</td>
<td>10% (n=5)</td>
<td>3% (n=3)</td>
</tr>
<tr>
<td>Suspected connective tissue disease</td>
<td>1% (n=1)</td>
<td>4% (n=2)</td>
<td>6% (n=6)</td>
</tr>
<tr>
<td>Soft tissue conditions/others</td>
<td>2.2% (n=2)</td>
<td>2% (n=1)</td>
<td>3% (n=3)</td>
</tr>
</tbody>
</table>

The mean interval from Referral to patient review was 11.5 weeks in Feb 2006, 7.15 weeks in August 2012 and 6.6 weeks in Feb 2016. In parallel with the diagnosis of inflammatory arthritis we also looked at mean timeframe from 1st review to initiation of DMARDs which is demonstrated in the chart below.
Zennsen, MedImmune, MSD, Novartis, Pfizer, Roche, Samsun, Sanofi, UDB, Speakers bureau: AbbVie, Amgen, Astra-Zeneca, Astro, Celgene, Corporation, Celtrion, Eli Lilly, Glaxo, ILTOO, Janssen, MedImmune, MSD, Novartis, Pfizer, Roche, Samsun, Sanofi, UDB, Klaus Machold Grant/ research support from: Abbvie

DISTRIBUTION OF RHEUMATOLOGISTS AND YOUNG RHEUMATOLOGISTS’ ORGANIZATIONS ACROSS THE WORLD: STILL ROOM FOR IMPROVEMENT

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Background: Rheumatology is a rapidly advancing specialty. The increasing understanding of autoimmune mechanisms and advanced therapies have improved care for patients with chronic inflammatory conditions immensely. National and international collaborations are growing and are key to scientific developments. Still, the number and geographical distribution of rheumatology organizations globally, is not known.

Objectives: To gain further insights into the distribution of established and young rheumatologists’ organizations beyond Europe. Furthermore, we intended to explore correlations between presence of rheumatology organizations and demographic and socio-economic parameters.

Methods: A systematic online search was performed independently by three investigators (AN, SS, JS). Keywords used in the search related to three main themes (i) Rheumatology (rheumatology or rheumatologist(s) or rheumatism), (ii) Organizations (associations or young organization or society or group or association or league or federation) and (iii) country’s name. All identified rheumatology organizations worldwide were reported. Countries were grouped in eight regions according to their geographic location. General demographic information (including population, area, pop. density, net migration, infant mortality, GDP, literacy, phones, arable, crops, climate, birth-rate, death rate) was retrieved from World Bank Open Data by one extractor (SS). Descriptive statistics and quartile distribution for each analysed variable were performed using Excel® (Microsoft Office) and SPSS® software. Using the total number of countries per region as the denominator.

Figure 1. Overview of the percentage of national rheumatology societies

Results: Four international societies and three junior international organizations (EMEUNET, PANLAR junior, ALPAR Young rheumatologists) were identified. Out of the 227 countries assessed, 89 national rheumatology organizations were identified (n=4, 2%). Rheumatology societies were more frequent in Eastern Europe (n=18/27, 67%), Middle east (n=10/15, 67%) and Western Europe (n=19/29, 66%) (Figure 1). Rheumatology societies were more frequently found in countries in the upper quartiles (Q1) of population density, gross domestic product and literacy when compared to Q2-4 (as assessed for Liase Frisenklev, r=0.05). Conversely, it was significantly less frequent in countries with high migration and infant mortality (Q1 Vs Q2-3, p=0.043 and p=0.039, respectively).

Conclusion: National rheumatology societies were identified in less than half the countries across the globe and were unequally distributed. We only found 7 national young organizations. Such organizations are needed, as trainees can highly benefit from educational and networking offers. Further steps will include the exploration of the impact and the reasons for lack of such establishments in some countries.

Disclosure of Interests: Aurelie Najm: None declared, Julia Spierings Grant/research support from: Boehringer Ingelheim, Savino Sciascia: None declared, Elena Nikiphorou: None declared, Alexandre Sepriano: None declared, Alessia Alunno: None declared.


AB1221 VIEWS OF PRIMARY CARE PHYSICIANS AND RHEUMATOLOGISTS REGARDING SCREENING FOR HYPERLIPIDEMIA AMONG PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Screening of hyperlipidemia in rheumatoid arthritis (RA) is suboptimal, despite RA patients’ high risk for cardiovascular disease (CVD) mortality.

Objectives: To identify barriers to screening for hyperlipidemia among patients with RA from the viewpoint of primary care physicians (PCPs) and rheumatologists.

Methods: We recruited rheumatologists and PCPs nationally to participate in separate moderated structured group teleconference discussions using the nominal group technique. Participants in each group generated lists of barriers to screening for hyperlipidemia in patients with RA, then each selected the three most important barriers from this list.

Results: Twenty-six rheumatologists participated in 3 groups and 20 PCPs participated in groups. The resulting barriers were organized into physician-, patient- and system-level barriers. Rheumatologists prioritized physician level barriers (e.g. ‘ownership’ of hyperlipidemia screening), whereas PCPs prioritized patient-level barriers (e.g. complexity of RA itself). See Table 1 for details.

Conclusion: These rheumatologists were conflicted about whether screening of CVD risk among patients with RA should fall within the role of the rheumatologist or PCPs. On the other hand, participating PCPs were concerned about the overall effect of RA and RA treatments in the context of screening hyperlipidemia.

Table 1: Screening for hyperlipidemia: List of themes and sub-themes of barriers for rheumatologists and primary care physicians (PCPs) to screen patients with RA, with their respective priority votes

<table>
<thead>
<tr>
<th>Category</th>
<th>Subcategory</th>
<th>Rheumatologist (% votes)</th>
<th>Total Votes N=162</th>
<th>PCP (% votes)</th>
<th>Total Votes N=120</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physician Level</td>
<td>Total Votes</td>
<td>83.0</td>
<td>42.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lack of time</td>
<td>34.0</td>
<td>1.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Conflict regarding ownership of hyperlipidemia screening</td>
<td>25.5</td>
<td>10.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lack of training and knowledge of hyperlipidemia guidelines or RA itself</td>
<td>17.9</td>
<td>20.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Focus only in RA</td>
<td>4.9</td>
<td>–</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physician prioritization of RA symptomology over preventive measures</td>
<td>–</td>
<td>10.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient Level</td>
<td>Total Votes</td>
<td>7.5</td>
<td>44.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Effect of RA and its treatment</td>
<td>2.5</td>
<td>9.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient prioritization of RA symptomology over preventive measures</td>
<td>2.5</td>
<td>9.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient expectations</td>
<td>1.9</td>
<td>–</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patient already on multiple medications</td>
<td>0.6</td>
<td>0.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple blood draws</td>
<td>0.0</td>
<td>8.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Side effects of statins and drug interactions with statins</td>
<td>0.0</td>
<td>5.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Poor patient compliance with medical care</td>
<td>0.0</td>
<td>9.2</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Note: RA = rheumatoid arthritis; CVD = cardiovascular disease; 0% = that sub-theme emerged during the brainstorming session but did not receive votes; “–” = the sub-theme did not emerge in the respective group.

Disclosure of Interests: Iris Navarro-Millan: None declared, Anna Corneil-Schechter: None declared, Ronan O’Beirne Grant/research support from: Pfizer, Inc, Melanie Morris: None declared, Geyyanne Lui: None declared, Susan Goodman Grant/research support from: Novartis; research support, Consultant for: Novartis, UCB, Pfizer; consulting, Andrea Chern- rington: None declared, Liana Fraenkel: None declared

AB1222
PATIENT PREFERENCES FOR THE USE OF DIGITAL TOOLS AND SOCIAL MEDIA IN DIET AND EXERCISE INTERVENTIONS
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Background: Healthy behavior changes such as improving diet/exercise are important to improve outcomes in rheumatic and musculoskeletal disease (RMD) patients. These changes require incentives, whether internal or external motivation or social support.

Objectives: To assess feasibility of using digital symptom tracking and social media peer support to conduct diet/exercise health behavior change interventions among adults with inflammatory arthritis (IA) and osteoarthri- tis (OA).

Methods: A 37-item cross-sectional survey was developed and adminis- tered online and via mobile app in the ArthritisPower research registry. Participants (pts) were eligible if they were ≥ 18 years of age, resided in the US, and reported physician diagnosis of IA or OA. Pts reported on use of technology and social media, experience with exercise and weight loss programs, and interest in various program features. We descriptively reported differences between respondents with IA (RA, PaA, AS) and OA. Results: 418 pts completed the survey. A majority were female (59.5%) and white (89.5%); mean age was 56 (10.5). The proportion of pts who were obese (BMI >30) was higher among OA than IA pts (67.7% and 50.0%, respectively; p<0.001). Most pts were willing to provide blood samples remotely and use WiFi-enabled digital scale and blood pressure monitor for a trial (Table). Interest in social media for peer support and apps differed between IA vs OA pts; more IA pts used an app to help them exercise (35.1% vs. 19.2% of OA pts, p<0.001) and were interested in using an app to track diet and exercise in the context of peer support on Facebook (72.2% vs. 62.3% of OA pts, p=0.04). The most commonly used social media platform overall was Facebook (93.3% of pts) followed by Twitter (51.9%) and Instagram (41.9%). Pts cited pain/discomfort moving (57.4%) and sedentary behavior, such as watching TV, (47.6%), as their biggest weight loss challenges. OA pts reported depression (46.9%, p=0.01) and disliking exercise (34.6%, p=0.003) as bigger challenges to weight loss than did pts with IA (34.0% and 20.8% respectively). Motiva- tions to exercise also differed between groups: more IA than OA pts said building muscle was a top motivation (54.5% and 43.1%, respectively; p=0.03).

Table: Interest in program features by arthritis type
<table>
<thead>
<tr>
<th>n (%)</th>
<th>Inflammatory Arthritis (n=288)</th>
<th>Osteoarthritis (n=130)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regularly using WiFi-enabled digital scale to measure weight and blood pressure monitor automatically linked to study</td>
<td>332 (79.4)</td>
<td>236 (81.9)</td>
<td>96 (73.9)</td>
</tr>
<tr>
<td>Providing blood samples for study by going to nearby Quest or other lab</td>
<td>320 (77.1)</td>
<td>222 (71.7)</td>
<td>98 (75.4)</td>
</tr>
<tr>
<td>Participating in study that would provide an activity tracker (e.g. Fitbit) and resources to increase daily steps</td>
<td>313 (74.9)</td>
<td>224 (77.8)</td>
<td>89 (68.5)</td>
</tr>
</tbody>
</table>

Participating in peer support (via Facebook private group), with other arthritis patients
<table>
<thead>
<tr>
<th>n (%)</th>
<th>Inflammatory Arthritis (n=21)</th>
<th>Osteoarthritis (n=17)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Facebook private group, with other arthritis patients</td>
<td>299 (71.9)</td>
<td>207 (71.9)</td>
<td>92 (70.8)</td>
</tr>
<tr>
<td>Facebook private group, that includes patients without arthritis</td>
<td>40 (9.6)</td>
<td>27 (9.4)</td>
<td>13 (10.0)</td>
</tr>
<tr>
<td>Using a mobile app to track my diet and exercise</td>
<td>289 (72.2)</td>
<td>208 (72.2)</td>
<td>81 (62.3)</td>
</tr>
<tr>
<td>Using wireless scale that automatically sends my weight to the counselor</td>
<td>274 (89.6)</td>
<td>186 (65.5)</td>
<td>85 (65.4)</td>
</tr>
</tbody>
</table>

*Statistically significant at alpha=0.05

Conclusion: Program focus and format may need to be tailored depend- ing on arthritis type, but pts with both IA and OA are interested in social media peer support and digital symptom tracking to motivate achievement of health behavior change goals.

Disclosure of Interests: W. Benjamin Nowell: None declared, Kelly Gavigan: None declared, Jeffrey Curtis: None declared, Shilpa Venkatachalam: None declared, Francois Ban: None declared, Amin Yakubu: None declared, Alexis Ogdie Grant/research support from: (To my university) Novartis, Pfizer, Grant/research support from: Novartis, Pfizer, Grant/ research support from: Novartis, Pfizer, Grant/research support from: Novartis, Pfizer, Consultant for: AbbVie; Bristol-Myers Squibb, Celgene, Corrona, Lilly and Company, Novartis, Pfizer, and Takeda; Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Corrona, Eli Lilly, Novartis, Pfizer Inc, Takeda, Consultant for: Abbvie, Amgen, BMS, Cel- gene, Corrona, Lilly, Novartis, Pfizer, Takeda, Consultant for: Abbvie, Amgen, BMS, Celgene, Corrona, Lilly, Novartis, Pfizer, Takeda

AB1223
A SYSTEMATIC REVIEW OF STUDIES INVESTIGATING THE EFFECTIVENESS OF ADALIMUMAB PATIENT SUPPORT PROGRAMMES
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Background: Adalimumab patient support programmes (A-PSPs) are offered to patients with chronic inflammatory indications creating the need to study how such A-PSPs assist patients and other stakeholders in improving health outcomes. A deeper understanding of the effects of A-PSPs can improve treatment outcomes and experience of patients being treated with adalimumab.

Objectives: To review current studies evaluating A-PSPs, summarize their general characteristics and methodology, and recommend future research work in the area of A-PSPs.

Methods: Studies were identified through Web of Science and were cross-checked by searching through PubMed and MEDLINE databases, following PRISMA guidelines. Full-text papers and conference proceedings identified by the database search were reviewed for relevance.

Results: 17 studies evaluating the impacts of A-PSPs on patient out- comes were identified – 6 full-text articles and 11 meeting abstracts. Most research was done at the international level or in North America [1-3]. In only 5 reviewed studies a prospective study design was applied. Indications most commonly investigated were rheumatoid arthritis and inflammatory bowel disease. 12 studies evaluated the impact of all interventions of A-PSPs while others assessed the impact of Coach Care Calls or phone calls. Patient outcomes most commonly measured were persistence, adherence and low disease activity or remission. Overall, patients using any of the interventions of A-PSPs experienced significantly better improvements in all studied patient outcomes at different follow-up assessments compared to those not enrolled into any of the programme’s interventions. Study population sizes and ratios between assigned users and non-users of interventions differed between studies. The most frequent follow-up assessments were after 12 and 24 months of treatment with adalimumab. Data for analysis was mostly obtained by linking a patient support database and claims administrative database, and in 5 cases by applying patient and physician reported surveys. Methodology for assessing the differences between users and non-users of interventions of A-PSPs consisted of univariate and multivariate methods, where the causal relationships between the impact of patient support program and patient outcomes were estimated by regression modelling adjusted for multiple confounders.

Conclusion: Interventions of A-PSPs have been shown to have a positive impact on all investigated patient outcomes. Main recommendations for
future studies are to design a prospective study, include persistence and adherence measures in the study design, and to assess patient outcomes with additional measures such as patient outcomes based on a patient-centric approach and adverse effects.

Disclosure of interest: This literature review was funded by AbbVie Inc.

REFERENCES

Disclosure of Interests: None declared

AB1224
IS THERE A NEED TO OPTIMIZE REFERRAL DIAGNOSIS TO A RHEUMATOLOGY DEPARTMENT?:

Tobias Hoffmann, Peter Oelzner, Gunter Wolf, Alexander Pfeil, Jena University Hospital – Friedrich Schiller University Jena, Department of Internal Medicine III, Jena, Germany

Background: The initial visitation of patient suffering from rheumatic disease related symptoms often occurs in absence of a rheumatologist.

Objectives: This study evaluated the following questions: I. Which medical specialists referred patients to a rheumatology department? II. To quantify the accordance of the presumptive diagnosis and the final diagnosis of a rheumatologist.

Methods: 1151 patients (355 men and 796 women) were admitted to a hospital for rheumatological diagnostic. The referral medical specialists were identified. Kappa-Analysis was performed to evaluate the presumptive diagnosis and the final diagnosis by the rheumatologists.

Results: 73.0% of the referrals were performed by general practitioner. The other referrals were: 7.7% rheumatologist, 4.8% specialist in internal medicine (excluding rheumatology), 4.3% orthopaedic surgeon, 1.0% orther surgeon and 9.2% other specialists.

The highest accordance of the presumptive diagnosis and the final diagnosis was k=0.534 for rheumatologists and k=0.400 for specialist in internal medicine (excluding rheumatology). Lower kappa values were evaluated for general practitioner (k=0.345), orthopaedic surgeon (k=0.310) and other specialists (k=0.252).

Conclusion: The referrals were frequently realized by general practitioners. In this context the presumptive diagnosis of a general practitioner presents a low accordance with the final diagnosis. In this context, general practitioners should achieve a detailed education in the assessment of rheumatic-related symptoms to optimize the dedicated referral to rheumatological departments.

Disclosure of Interests: Tobias Hoffmann: None declared, Peter Oelzner: None declared, Gunter Wolf: None declared, Alexander Pfeil: Grant/research support from: This study is a part of the Investigator Initiated Study “The quantification of inflammatory related periarticular bone loss in certolizumab pegol treated patients with rheumatoid arthritis” which is funded and supported by UCB Pharma GmbH, Monheim, Germany (number: IIS-2014-101458).


AB1225
POSSIBLE EARLY DETECTION OF ADVERSE EVENTS USING REMOTE SYSTEMATIC WEEKLY ELECTRONIC MDHAQ

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Background: Adverse events of medications are reported to account for 5% of hospital admissions in the USA, including 10% in the elderly. Warnings from doctors and pharmacies concerning adverse events are given at initiation of new medications, but adverse events occur between visits and reporting depends primarily on communication between a patient and a health professional, which may be variable. Therefore, recognition and reporting of adverse events remain relatively haphazard. Several reports present strategies for systematic monitoring for adverse events, primarily involving telephone contacts from nurses to patients. A far less expensive systematic approach based on patient self-report using a remote electronic multidimensional health assessment questionnaire
ONE YEAR’S RESULTS OF A PROTOCOLIZED HIGH RESOLUTION RHEUMATOLOGY CLINIC

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Background: Mechanical musculoskeletal pathologies put high demands on the Public Health Service, as they affect a significant percentage of the population, and cause both temporary and permanent disabilities.

The specialised High Resolution Rheumatology Clinic (CAR in Spanish) at our centre started up in October 2017, and focuses on the diagnosis and treatment of pathologies which are fundamentally of a mechanical ethology. The centre covers a population of approximately 328,868 inhabitants (Alava 2018 census).

The aim of our study, carried out at the unit over one year, is to determine the patients’ epidemiological features.

Objectives: • To provide the Primary Care Centres with a “fast-track” and immediate care system in order to guide, diagnose, and treat patients who have worsening acute or chronic mechanical affictions to the musculoskeletal system.

• Diagnosis confirmation, request for non-accessible tests, adaptation of treatments mainly for the primary care doctor.

• To speed up and reduce waiting lists, for both inflammatory rheumatic pathologies and mechanical rheumatic pathologies, by establishing new referral guidelines.

• To draw up protocols in agreement with primary care doctors and related specialists.

• To act as a support for other medical services.

Methods: The main services available are those offered mainly to primary care level. There are 3 clinics a week, attending to approximately 30 new patients per week. 1330 patients are included in the study, seen at the High Resolution Rheumatology Clinic (CAR) over 12 consecutive months (November 2017 – 2018), with non-complex regional pathologies and/or soft tissue rheumatism, which are able to be resolved with one or two visits.

Results: 1330 patients were seen, with an average age of 58 ±15.6 years, 64.84% female and 35.16% male, mainly for musculoskeletal ailments. In order of frequency, the visits were for shoulder (25.79%), hip (16.10%), axial skeleton (15.13%), ankle/foot (13.06%), wrist/hand (12.08%), knee (11.21%), and elbow (6.63%).

61.95% of the patients were discharged after the first visit, and one year later, this figure rose to 90.15% of all the patients discharged; only 2.78% made a return visit after being discharged. 22.26% were referred to other services, mainly Traumatology and Orthopaedics (10.53%), Rehabilitation and Physiotherapy (9.72%); and the Pain Management Unit (1.65%). The 3.68% were referred to the usual Rheumatology department.

For 52.33% of the patients seen, there was no need to request more than one diagnostic tests, even though 12.41% visited for reasons other than the main one. Moreover, 63.08% received some kind of infiltration injection. The negative point was that 7.89% of the referrals had been made from Primary Care to several specialists at the same time; and 7.98% were consultations regarding traumatic injuris.

Conclusion: Systematising a clinic for mechanical musculoskeletal pathologies which have a high chance of being resolved in the short term, means that the quality of the care given, the waiting times, and the demand on the health service can be improved. Developing these can have important repercussions on waiting lists for other related services, and even for the Rheumatology service itself, allowing more serious cases to be seen earlier. Creating multi-disciplinary units should be encouraged, in order to improve care quality and prevent the various medical services involved from all carrying out fragmented courses of action. New guidelines should be drafted to optimise the care and management of new resources and/or links to other services, as the most prevalent pathologies can be identified.

Most of the patients seen represent the economically active part of the population; there therefore, repercussions as far as sick leave, disability leave, etc. is concerned.

Disclosure of Interests: None declared


PREFERRED REFERRAL PROTOCOL FOR RECENT ONSET ARTHRITIS IN ADULTS FROM PRIMARY CARE TO RHEUMATOLOGY

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Background: The time of rheumatoid arthritis (RA) evolution until treatment begins is key to controlling the disease. Many studies have shown that a prolonged duration of symptoms at the onset of treatment is associated with a more severe course of RA. The time from symptoms onset to first DMARD prescription is >12 weeks in Spain, because of diagnostic delay due to either patient-related factors (delay in consultation), Primary Care Physician (PCP) (delay in consultation/referral) or rheumatologist (delay in consultation/referral).

Objectives: To evaluate the usefulness of teleconsulting as a preferred referral tool from PCP to Rheumatology for early detection, diagnosis and treatment of inflammatory joint disease in adults, in the health area of a tertiary hospital.

Methods: A preferential referral circuit was established between the PCP and the Rheumatology Service of a tertiary hospital, defining the referral criteria as “patient suspected of recent onset arthritis (ROA)”: arthritis or inflammatory arthralgia in >1 peripheral joint for >2 weeks with neither traumatic cause nor previous diagnosis of rheumatic disease. PCP performed first assessment, the request for initial tests (blood test including acute phase reactants, rheumatoid factor ± ANA, elemental urine and hands radiography) as well as the referral to Rheumatology with “ROA suspicion” motive. These consultation requests were cited from the Rheumatology Service within <15 days of receipt.

Before the protocol was established, its functioning was communicated as a face-to-face clinical session: by 2 rheumatologists in a Health Centre (HC) and by 1 PCP in the rest of the HC in the area. A poster was

Disclosure of Interests: None declared

edited and published, exposing criteria and referral method for PCP’s offices.

Results: During the first 6 months 33 patients were correctly referred. 78.8% were women and the average age was 49 years old. 48.8% (16 patients) were diagnosed with some inflammatory arthropathy: 31.5% were RA (5 cases); other diagnoses were arthropathy due to microcrystals deposit (2), overlap SLE/RA (1), MCTD(1), psoriatic arthritis (1), spondyloarthropathies associated with IBD (1) or inflammatory arthralgia associated with retropertitoneal fibrosis (1). 12% (4 patients) were diagnosed with hands incipient osteoarthropathy and 33.8% (12 patients) with arthralgias without data on inflammatory pathology. One patient missed her follow-up. The median time from symptom onset to Rheumatology assessment was 90 days in all patients; in the inflammatory pathologies subgroup, 68.8% was assessed in <12 weeks, with a median of 60 days and a mean of 96 days, starting treatment in this subgroup in the first assessment by Rheumatology.

Conclusion: In our experience, the establishment of a specific protocol in collaboration with Primary Care for the preferential referral of patients with suspected recent onset arthritis, obtained diagnoses not only for patients with rheumatoid arthritis, but also for other systemic autoimmune diseases in early stages, as well as early treatment initiation (<12 weeks) in most of these patients. In addition, it turned out to be an effective and comfortable referral route for PCP with suspected connective and/or inflammatory arthritis.

Disclosure of Interests: Consuelo Ramos Giráldez Speakers bureau: Sanofi, María Espinosa: None declared, Carolina Menino Argumánez: None declared, Patricia Fernández Crespo: None declared, Olga Rusinovich: None declared, Fernando León Vázquez: None declared, José Luis Andreu Sánchez: None declared, Carmen Barbadillo Mateos: None declared


ACCESS TO RHEUMATOLOGIC TREATMENTS AND AUTOIMMUNE CONDITIONS IN LATIN AMERICA

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Background: To know the availability of treatment for rheumatologic and autoimmune diseases in early stages, as well as early treatment initiation (<12 weeks) in most of these patients. In addition, it turned out to be an effective and comfortable referral route for PCP with suspected connective and/or inflammatory arthritis.

Disclosure of Interests: None declared.

Methods: A digital survey was created using Google Forms, it was approved and endorsed by the scientific committee of PANLAR, and later sent to the different Rheumatology associations of the region. The data was compiled in the statistical program SPSS for analysis.

Results: 456 surveys were filled by rheumatologists from 23 countries. The majority were females (54%). The mean age was 47.18 ± 11.79 [25-78] years. 91% reported access to DMARDs, methotrexate 95%, azathioprine 94%, cyclophosphamide 92%, hydroxychloroquine 92%, leflunomide 90%, mycophenolate mofetil 90%, sulfasalazine 88%, cyclosporine a 80%, tacrolimus 64%, chloroquine 60%. 85% have access to biological drugs: rituximab (27%), infliximab (24%), etanercept (18%) and adalimumab (12%), anakinra (10%) and rilonacept (3%). 58% have access to biosimilars: belimumab (97%), tocilizumab (73%), abatacept (67%), golimumab (63%), certolizumab (59%), secukinumab (55%), ustekinumab (44%), certolizumab (59%), belimumab (47%), canakinumab (22%), sanilumab (63%), certolizumab (59%), secukinumab (55%), ustekinumab (44%), certolizumab (59%), belimumab (47%), canakinumab (22%), sanilumab (63%), certolizumab (59%), secukinumab (55%), ustekinumab (44%), certolizumab (59%), belimumab (47%), canakinumab (22%), sanilumab (63%), certolizumab (59%), secukinumab (55%), ustekinumab (44%), certolizumab (59%), belimumab (47%), canakinumab (22%), sanilumab (63%), certolizumab (59%).

Conclusion: It is evident that most Latin American countries have access to drugs focused on rheumatic diseases, however, there are substantial differences in countries that do not have access to all therapies. In addition, newer treatment as small molecules are less accessible to the region.

Disclosure of Interests: None declared.


AB1229 RHEUMATIC DISEASES REMISSION DURING PREGNANCY: MYTH OR REALITY? FACT OR HOPE?

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Background: A Rheumatology Obstetric Combined Clinic (ROCC) has been running in our trust since 2013 for patients with any musculoskeletal (MsK) rheumatological disease. Observing pregnant ladies in this clinic it became noticeable that patients with msk diseases do not always go into remission during pregnancy.

Objectives: To register their perception of disease activity during pregnancy and from their memory of that disease activity before pregnancy. A secondary aim was to assess whether the remission (or flares) during pregnancy was disease specific or trimester specific.

Methods: Patients with MsK disorders attending ROCC were given 2 different 10 cm visual analogue scales (VAS) asking them to grade the current (at the time of the assessment in ROCC) disease activity and their perceived disease activity prior to pregnancy. The recorded diseases were: (1) Lupus and other Connective Tissue Diseases= 18 [(33.3%) of whom 13 were having Lupus and 5 Sjogren’s syndrome, (2)SPAs =16 [(28.6%)] of whom 4 had Ankylosing Spondylitis (AS) and 12 Psoriatic arthritis (PsA)], (3) Rheumatoid Arthritis (RA) =9 (16.7%), Antiphospholipid Syndrome (APS) =7 (13%) and other =4 (7.4%). In the “other” group there was 1 patient with sarcoidosis, 1 with Adult Onset Still’s disease, 1 JIA which progressed to CREST, 1 knee pain. The last group was excluded from the analysis. SPSS was used for statistical analysis and chi square to assess the difference between the 2 groups.

Results: We analyzed data from 50 patients who attended the ROCC. At the time of presentation mean age (± sd) was 33.4 years (± 4.29) range 22-43y while age of disease presentation was 25.5 (±8.06) range 22-43y. The weeks (w) of pregnancy during the time of assessment were (mean) 22.2 (±8.6) w ESR (mean in mmHg) was 27 (± 21.7), CRP 13.6 (±14.18). Disease activity at presentation on a VAS was 4.24 (± 2.8) while reported disease activity prior to pregnancy was exactly the same of 4.24 (± 3.07).

Looking at groups of diseases of RA and SpA patients showed reduction in the reported disease activity during pregnancy while CTDs and APS showed an increase, both of which however was not statistically significant (ss (table1)

<table>
<thead>
<tr>
<th>Diseases (n= of patients)</th>
<th>Disease activity during pregnancy [mean (± sd)]</th>
<th>Disease activity before pregnancy [mean (± sd)]</th>
<th>Statistical significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>CTDs (18)</td>
<td>4.5 (2.6)</td>
<td>3.93 (2.4)</td>
<td>0.6</td>
</tr>
<tr>
<td>SpAps (16)</td>
<td>4.6 (2.9)</td>
<td>5.6 (3.9)</td>
<td>0.8</td>
</tr>
<tr>
<td>RA (9)</td>
<td>4.13 (2.5)</td>
<td>4.75 (2.5)</td>
<td>0.9</td>
</tr>
<tr>
<td>APS (7)</td>
<td>2.2 (3.1)</td>
<td>1.17 (1.7)</td>
<td>0.4</td>
</tr>
<tr>
<td>Looking at RA and SpA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Looking at CTDs and APS</td>
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</table>

Conclusion: In our experience, the establishment of a specific protocol in collaboration with Primary Care for the preferential referral of patients with suspected recent onset arthritis, obtained diagnoses not only for patients with rheumatoid arthritis, but also for other systemic autoimmune diseases in early stages, as well as early treatment initiation (<12 weeks) in most of these patients. In addition, it turned out to be an effective and comfortable referral route for PCP with suspected connective and/or inflammatory arthritis.

Disclosure of Interests: None declared.


Table: 1. Disease activity during pregnancy during (mean (± sd)) and before pregnancy (mean (± sd)). AB1229

<table>
<thead>
<tr>
<th>Trimester</th>
<th>ESR (range)</th>
<th>CRP (range)</th>
<th>Disease activity (mean (± sd))</th>
<th>Disease activity (current) (mean (± sd))</th>
<th>Ss (chi square)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st (n=14)</td>
<td>6 (1.9)</td>
<td>20 (30)</td>
<td>1.64 (2.09)</td>
<td>2.55 (2.7)</td>
<td>0.20</td>
</tr>
<tr>
<td>2nd (n=19)</td>
<td>30.2 (16.8)</td>
<td>35.5 (33.3)</td>
<td>4.4 (3.6)</td>
<td>4.3 (3.5)</td>
<td>0.20</td>
</tr>
<tr>
<td>3rd (n=18)</td>
<td>17.3 (3.9)</td>
<td>20.3 (35.3)</td>
<td>3.67 (2.56)</td>
<td>3.4 (3.14)</td>
<td>0.40</td>
</tr>
</tbody>
</table>
Disease activity at trimester 1, 2 and 3

Abstract AB1229 Figure 1. shows DA according to trimester before and during pregnancy

Conclusion: In our group of pregnant patients with MsK diseases the overall disease activity is the same during pregnancy and before as measured by a VAS. Looking at the diseases patients with RA and SpA showed some reduction and patients with CTDs and APS showed an increase both not statistically significant. Looking at reported VAS according to trimester of pregnancy, it is in the 1st trimester that pregnant patients report reduced activity.

Acknowledgement: Thanks to pregnant women filling the questionnaire

Disclosure of Interests: None declared


AB1230

DISEASE ACTIVITY OF RHEUMATIC DISEASES DURING PREGNANCY COMPARED TO REPORTED DISEASE ACTIVITY PRIOR TO PREGNANCY AS OBTAINED FROM AN ANTENATAL RHEUMATOLOGY OBSTETRIC COMBINED CLINIC AND MODE OF DELIVERY

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Background: A Rheumatology Obstetrics Care Clinic (ROCC) was established at our antenatal unit to ensure specialist care for women with complex rheumatological conditions (RC). Although patients are often counselled about a likely improvement in their RC in pregnancy, this was not the experience of our patients’ group from the ROCC.

Objectives: To obtain pregnant women with RC disease activity (DA) scores during and prior to pregnancy. To assess modes of delivery (MoD) and compare them to our general non-arthritic population MoD.

Methods: Patients suffering from any RC attending a dedicated highly specialized antenatal ROCC were given 2 separate 10cm visual analogue scales (VAS) asking them to grade on each one of them the current (at ROCC) DA and their perceived DA prior to conception. Electronic delivery records were used to collect obstetric and foetal outcomes. SPSS was used for statistical analysis and chi square to assess the difference between the 2 groups.

Results: Data from 54 patients who attended the ROCC included of whom 50 were analyzed. At the time of presentation mean age (±sd) was 33.4 years (± 4.29) range 22-43y while age of disease presentation was 25.5 (± 8.06). The weeks (w) of pregnancy during ROCC were (mean) 22.2 (±8.6) range 9-37 w. ESR (mean) was 27 mm/h (± 21.7), CRP 13.6 mg/L (±14.18). DA at presentation on VAS was 4.24cm (±2.8) and prior to pregnancy was 4.24cm (± 3.07).

The recorded diseases were: Connective Tissue Diseases (CTD)=n=18 (33.3%) Spondyloarthropathies (SpA)=n=16 (29.6%). Rheumatoid Arthritis (RA) =n=9 (16.7%), Antiphospholipid Syndrome (APS)=n=7 (13%) and other n=4 (7%). The group of other (Still’s disease 1, Juvenile idiopathic arthritis 1, fibromyalgia 1 and knee pain 1) were excluded from analysis. Looking at the disease groups RA and SpA patients’ showed a reduction in the reported DA during pregnancy while CTDs and APS showed an increase; neither was statistically significant (ss).

Conclusion: In our group of pregnant patients with RC the overall DA is the same during pregnancy and prior to conception. DA according to diseases showed that women with RA and SpA had a reduction in DA and those with CTDs and APS had an increase.

The MoD showed similar percentages in vaginal and CS delivery rates as per normal population suggesting that MoD is not impacted by RC.

Acknowledgement: Patients for filling the ROCC questionnaire

Disclosure of Interests: None declared


AB1231

INCIDENCE OF TUBERCULOSIS IN PATIENTS WITH RHEUMATIC DISEASES USING TNF INHIBITORS: A SYSTEMATIC REVIEW

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Background: The TNF inhibitors (anti-TNF) are indicated for the treatment of several rheumatic diseases, but their use is associated with an increased risk of tuberculosis. Many measures of preventive care have been adopted, but some groups of patients appear to be at greater risk of developing infection.

Objectives: The primary objective is to estimate the incidence of tuberculosis in patients with rheumatologic diseases exposed to anti-TNF. The secondary objectives are to evaluate the incidence of tuberculosis by region and subgroups of diseases, to assess the presentation of tuberculosis in these patients and the time elapsed between onset of anti-TNF and the development of active granulomatous disease.

Methods: A systematic review of the literature was conducted in Medline (Pubmed, Embase), Cochrane Library and Lilacs with inclusion of observational studies. The selection of articles was performed by two independent reviewers and the disagreements were resolved by consensus.

The primary endpoint was described in measure of incidence and secondary outcomes through subgroup analyzes and means comparisons.

Results: We included 54 observational studies with a total of 98,483 patients exposed to anti-TNF. Among the exposed patients, 947 cases of tuberculosis were documented (pulmonary form in 62.2% of cases), with a cumulative incidence of 9.62 cases per 1,000 patients exposed [CI: 9.01 - 10.23]. Regarding TB incidence considering the different continents, we found the following distribution: South America with 11.75 per 1,000 patients exposed [CI: 7.17 - 16.33], North America with 4.34 per 1,000 patients exposed [CI: 3.31-5.38], Europe with 6.28 per 1,000 patients exposed [CI: 5.34 - 7.14] and Asia with 13.47 patients per 1,000 patients exposed [CI: 12.44 - 14.49]. There were no significant differences in TB incidence among the described diseases (rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and juvenile idiopathic arthritis). The mean time of the medication until the endpoint was 14.49 months.

Conclusion: The overall incidence of TB in individuals with rheumatic diseases anti-TNF was 9.62 cases/103 patient-years, being higher in South America and Asia compared to North America and Europe. Most cases occurred in the first XX months of use and the predominant form was pulmonary. There were no differences in incidence between diseases.

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AB1232  RHEUMA-VOR: A PROOF-OF-CONCEPT NETWORK STUDY FOR THE IMPROVEMENT OF RHEUMATOLOGICAL HEALTH CARE THROUGH COORDINATED COOPERATION

Matthias Dreher1, Gunter Assmann2, Kirsten Hoeper2, Konstantinos Triantafyllias4, Jan Zeidler4, Harald Binder6, Reinhold E. Schmitt7, Matthias Dreher1, Günther Assmann2, Kirsten Hoeper3, Konstantinos Triantafyllias4, Jan Zeidler4, Harald Binder6, Reinhold E. Schmitt7, Matthias Dreher1, Günther Assmann2, Kirsten Hoeper3, Konstantinos Triantafyllias4, Jan Zeidler4, Harald Binder6, Reinhold E. Schmitt7, Matthias Dreher1, Günther Assmann2, Kirsten Hoeper3, Konstantinos Triantafyllias4, Jan Zeidler4, Harald Binder6, Reinhold E. Schmitt7, Matthias Dreher1, Günther Assmann2, Kirsten Hoeper3, Konstantinos Triantafyllias4, Jan Zeidler4, Harald Binder6, Reinhold E. Schmitt7, Matthias Dreher1, Günther Assmann2, Kirsten Hoeper3, Konstantinos Triantafyllias4, Jan Zeidler4, Harald Binder6, Reinhold E. Schmitt7, Matthias Dreher1, Günther Assmann2, Kirsten Hoeper3, Konstantinos Triantafyllias4, Jan Zeidler4, Harald Binder6, Reinhold E. Schmitt7, Matthias Dreher1, Günther Assmann2, Kirsten Hoeper3, Konstantinos Triantafyllias4, Jan Zeidler4, Harald Binder6, Reinhold E. Schmitt7

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AB1233  PEOPLE WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES CONNECT AND LEARN ABOUT HEALTH-RELATED ISSUES USING SOCIAL MEDIA

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Background: Smartphone applications and social media (SM) are increasingly used, transforming the way in which people communicate. Peer interaction, remote information access and community building are just some of the uses of SM, presenting novel opportunities and challenges, especially for people with chronic conditions such as rheumatic and musculoskeletal diseases (RMDs).

Objectives: To explore the perspectives of people with RMDs on using SM for health-related purposes.

Methods: A questionnaire-based survey, co-designed in English by rheumatologists and patient research partners and translated into German, Italian, Spanish, Russian, French and Portuguese, was issued between May and December 2018, distributed via patient organizations and SM platforms. We report on the main quantitative exploratory analyses.

Results: A total of 992 participants started the survey; 853 (86%) participants reached at least 25 of 31 questions and were subsequently included in analyses. Participants were from 56 countries, with 50% from the UK, Germany, Portugal and Spain; 11% were outside of Europe. 60% of participants reported a good or very good experience in the use of SM. More than half (56%) were between 35 and 54 years, 90% were female, 37% had >1 RMD and 62% were multimorbid.

The use of smartphones, SM, SM for health-related purposes was affirmed by 93%, 95% and 76%, respectively. They started this in particular to connect with other people living with the same condition (58%). In general, 50% use SM to seek medical information, treatment options and to exchange experiences. Facebook (56%), Google+ (17%) and YouTube (17%) were the top three used platforms for health-related purposes; while Facebook (88%), YouTube (50%) and Instagram (47%) were most popular for general use. Platforms, that are usually used are not always the preferred one for health-related purposes, since only 16% of Instagram, 28% of YouTube and 67% of Facebook users prefer the same for health-related purposes. The greatest advantage of SM is to connect different experiences and exchange knowledge with peers. More than half voiced concerns regarding confidentiality and 21% were hesitant of disclosing their condition. Virtual appointments are still novel, since only 4% reported experience.

SM use and education were comparable between groups with different levels of multimorbidity, although health was poorer (p=0.001) and they were older (p=0.001). Participants more frequently considered that information provided by primary care physicians was inadequate (p=0.014) and wanted to make their voice heard (p=0.006), but at the same time were more skeptical about reliability of information on SM (p=0.036).

Conclusion: The use of SM for health-related purposes is widespread among people with RMDs, mainly as a means to connect and exchange knowledge, experiences and empower individuals to better manage their health. The strong concerns about confidentiality and better guidance of patients may improve health literacy and the relationship between the patient and the health care team, addressing new avenues and challenges in healthcare.

Acknowledgement: We would like to thank PARE in their support distributing this survey study.

Disclosure of Interests: Paul Studenic: None declared, Simon Stones Consultant for: SS has provided consultancy services to Envision Pharma Group, though this is not related to the contents of this abstract., Speakers bureau: SS has undertaken speaking engagements for Actelion, eyeforpharma, Four Health, Janssen and Roche, though these are not related to the contents of this abstract., Alessia Alunno: None declared, Valentin Ritschl: None declared, Elena Nikiforou: None declared

OUTCOME OF EDUCATION WITH REGARD TO INFLUENZA AND PNEUMOCOCCAL VACCINATIONS IN INFLAMMATORY ARTHRITIS PATIENTS ON DMARDS

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Background: Inflammatory arthritis (IA) patients on immunosuppressant disease modifying drugs (DMARDS) are at an increased risk of infections. Influenza and pneumococcal vaccines are recommended as part of the BSR and EULAR guidelines for the clinical management of these patients. Prior to commencing DMARDS, the patients are reviewed by the nurse specialist, who discusses the benefits versus risks of DMARDS, necessary monitoring and recommends the pneumococcal and influenza vaccines.

Objectives: The aim of this audit is to assess the uptake of the pneumococcal and the influenza vaccine in IA patients prior to starting biologic or synthetic DMARDS as advised by the nurse specialist during the education visit with the patient.

Methods: The study sample included 139 patients with various types of IA, including rheumatoid arthritis, psoriatic arthritis and ankylosing spondylitis, who attended the rheumatology nurse education sessions prior to starting DMARDS in a secondary care hospital in 2017. Verbal advice supported by a vaccination leaflet developed in 2016 was given by the rheumatology nurse. Data was compiled by means of a telephone questionnaire.

Results: One hundred and twenty six (90.6%) participants recalled being given advice on vaccinations. Seventy eight (62%) of these patients recalled receiving the influenza vaccine. The rest (28%) did not receive the vaccine for various reasons including fear of side effects, fear of developing a worse infection, belief of inefficacy and fear of injections. A significant improvement (p=0.0084) in the influenza vaccination rates was noted since a previous audit in 2016, where following verbal education by a rheumatologist, only 41.4% received the influenza vaccine. A significant improvement in uptake was also noted in the pneumococcal vaccination rates since only 17.2% of the patients received the pneumococcal vaccine in 2016 compared to 62.7% in 2017 (p<0.0001). Various reasons including fear of side effects, belief of inefficacy, fear of injections and financial implications were given by patients who did not receive the pneumococcal vaccine.

Overall, 62% of the patients received both vaccines after education given by the rheumatology specialist nurse and receiving the vaccination leaflet.

Conclusion: This audit showed a significant progress in the uptake of the influenza and pneumococcal vaccinations in patients with inflammatory arthritis following verbal advice by the specialist rheumatology nurse and the introduction of a vaccinations’ educational leaflet.

Disclosure of Interests: None declared


COST-SAVING FOR HEALTH SERVICES DETECTING THE MISDIAGNOSIS OF RHEUMATOID ARTHRITIS USING IMAGING IN THE PROCESS OF DIAGNOSIS: EVIDENCE FROM REAL-WORLD

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Background: The diagnosis of rheumatoid arthritis (RA) using EULAR criteria through conventional assessments remains controversial, especially for those with seronegative results, many of patients without other diagnostic aids as imaging, could be wrong diagnosis followed by expensive treatments (1-3).

Objectives: To evidence through real-world data how the use of imaging within a screening process of diagnosis of RA can save future costs for unnecessary treatments in patients with misdiagnosis of RA.

Methods: A retrospective real-world data (RWD) analysis was developed from medical records of patients with presumptive RA diagnosis reportedly seronegative for both rheumatoid factor (RF) and anti-cyclic citrullinated peptide antibodies (ACPA), and who met ACR/EULAR 2010 classification criteria, in the period between July 2016 and June of 2017; patients were assessed by imagenology (X-ray, ultrasound (US) or magnetic resonance imaging (MRI)) according to the screening diagnosis protocol in a center of internal attention for rheumatoid arthritis (CIA-RA) in order to confirm diagnosis of RA, or classify patients in an alternative proper diagnosis. Direct costs of diagnosis was estimated in two scenarios: the conventional diagnosis and the screening process of diagnosis in the CIA-RA.

To quantify the cost-savings for this process we also estimated the cost of treatment for the first year after diagnosis for patients with RA and patients with the most common diagnosis found after screening.

Results: 440 patients were referred to our center with presumptive diagnosis of RA in the period, who were assessed for ACPA and RF obtaining a seronegative result for both. After screening process just 115 patients were classified as RA, 98 as SRA and 16 as Nonspecific RA; 12.2% were identified by X-Ray, 67.7% were identified by US and 20% by MRI. The most frequent misdiagnosis found was Osteoarthritis in the 72.5% of patients assessed by the screening process. In that way, the conventional diagnosis cost $54.4, while the CIA-RA screening diagnosis cost was $247.1 per patient, however there was found a potential cost-saving from using the CIA-RA screening process of diagnosis of $1,440,494 per year due to the pharmacological cost saving of 325 patients who requires treatment for RA and not for OA.

Conclusion: According with our findings the use of imaging within a diagnostic screening process combining conventional criteria is a useful tool to discard false positive diagnosis of RA. Despite the fact that at first sight, the cost of screening process of diagnosis is more expensive than conventional diagnosis, after one year of treatment it can be assumed potential cost-savings using the proposed approach.

REFERENCES

Disclosure of Interests: Omaira Valencia: None declared, Pedro Santos-Moreno Grant/research support from: Dr Santos has received research grants from Jansens, Abbvie and UCB, Speakers bureau: Dr Santos has received speaker fees from Sanofi, Lilly, Bristol, Pfizer, Abbvie, Janssen and UCB, Edwin Castillo: None declared, Nelson Alvis : None declared


IMPROVING CLINICAL OUTCOME AND REDUCING COST FOR PATIENTS WITH RHEUMATIC DISEASES VIA ONLINE INTERACTION WITH RHEUMATOLOGISTS BASED ON SMART SYSTEM OF DISEASE MANAGEMENT (SSDM) MOBILE TOOL

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Background: Without efficient primary medical care and follow-up system in China, patients can choose any hospitals or doctors they like in seeking care. As a result, most patients rush to large hospitals. Once patients left those clinics, no follow up data is available. Surveys show that over 40% of the rheumatic patients don’t need to go to a hospital, only need advice from rheumatologists. SSDM is a series of applications for chronic diseases management, which strengthens the interaction between doctors and patients based on valuable clinical data. Our previous study showed that patients can master the SSDM and perform self-management after training, including evaluations on disease activity and health assessment questionnaire (HAQ), as well as medication and lab test data entries.

Disclosure of Interests: None declared


BASED ON SMART SYSTEM OF DISEASE MANAGEMENT (SSDM) MOBILE TOOL

Yong Wang1, Li Luo2, Qin Li3, Wen Wang4, Anbin Huang4, Hong Zhang5, Peng Ji6, Yangping Zhao7, Lingxun Shen7, Zhengang Wang8, Feng Wei8, Hui Xiao9, Yuhua Jia5, Fei Xiao9, Fengchun Zhang9,10, SSDM Collaboration Group, China;
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Objectives: To evaluate the feasibility and benefit of improving medical economics and disease activity outcomes in rheumatoid patients through online consultation using the SSDM. The SSDM includes doctors’ and patients’ interfaces. The patients’ terminals include self-assessments (DAS28, SLEDAI, HAQ), medication management, adverse events management and lab data entry, data synchronization to the mobile of the authorized doctor. On the basis of these data, the rheumatologists can accept the request from their follow-up patients and practice consultation through SSDM in the form of text or voice.

Results: From Feb 2015 to Jan 2019, 679 rheumatologists supplied 7,405 patients (RA 35%, SLE 23%, AS 9.5%, gout 8.8%, Sjogren syndrome 3.8%, OA 3.4% and other 16.5%) with 10,527 consultations. The consulting fee ranged from RMB 0 to 500 yuan (USD: RMB ~1-6.81) each in average of 78.10 ± 45.12 yuan, which matched the registration fee in hospital. The total fee for consultations was 822,169 yuan RMB. 37% patients receiving online consultation lived in different cities from the rheumatologists. If the patients seek medical care in hospital, in addition to the registration fees and medical expenses, the mean cost of transportation, accommodation, and lost wages was 577.48 ± 505.21 (200 - 2,800) yuan. The total cost of all patients would have been 6,079,135.00 yuan RMB, which is 7.39 times more compared with the cost of online. Among 2,611 RA and 1,671 SLE patients with repeat consultations, respectively. Survey shows that satisfaction rate with the consultations is 100%.

Conclusion: Through online disease management and consultations using SSDM, Chinese patients with rheumatic diseases enjoy good quality of care at lower cost with high satisfaction. Armed with data science, SSDM may supply the rest world with an option for reshaping the healthcare system.

Disclosure of Interests: None declared

AB1237
COST OF ILLNESS AND QUALITY OF LIFE IN ANKYLosing SPONDylitis PATIENTS TREATED WITH ADALUMmAB IN CHINA
Ya Xia, Liudan Tu, LV Qing, Yutong Jiang, Zetao Liao, Shuangyan Cao, Quang Wei, Jieruo Gu.

Background: Ankylosing spondylitis (AS) is a chronic inflammatory disease which may lead to limited physical function, impaired quality of life and increased economic burden for society. There were many studies about the superior effects of biologic agents on symptom release, disease activity and functional remission in AS patients. However, studies on the economic burden and health-related quality of life of AS patients in China were lack.

Objectives: To access the cost of illness, work limitation and quality of life in active ankylosing spondylitis (AS) patients using adalimumab in China.

Methods: A prospective study was performed in 91 patients with active AS in China. Adult patients (aged ≥ 18 years) fulfilled the 1984 New York modified criteria of AS with the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) ≥ 4 and C reactive protein (CRP) ≥ 6 were enrolled from rheumatology center from Jan 2017 to Aug 2017. All participants received adalimumab (40mg per 2 weeks) therapy and completed questionnaires about disease characteristics, quality of life, direct and indirect costs. Only patients with pay-work completed the Work Limitation Questionnaire (WLQ) to accesses the impact of chronic health conditions on job performance and productivity. Quality of life was measured using the Ankylosing Spondylitis Quality of Life (ASQoL) and EuroQoL-5 Dimensions (EQ-5D).

Results: A total of 91 patients with mean age of 30 years old (87.8% males) and mean disease duration of 10 years received adalimumab treatment for 24 weeks. 78.02% of patients have a paid job with average work productivity loss of 28% measured by WLQ. The annual estimated cost of each patient was $35238.8 while the direct cost accounted for 90.2% and the cost of medication accounted for 76.6%. There were significant differences in change of ASQoL (change, 3.89 [95%CI, 3.06 to 4.71]; P<0.0001) and EQ-5D (change, -0.19 [95%CI, -0.24 to -0.31]; P<0.0001) scores from baseline and 24 weeks, with more improvements after therapy compared with baseline. Cost of illness was estimated as $21927.38 per quality-adjusted life year and $15728.16 per BASDAI unit, respectively.

Conclusion: The cost of AS patients treated with adalimumab therapy was high in China and symptoms and QoL improved significantly after therapy.

Disclosure of Interests: None declared

AB1238
PATIENTS’ PERCEPTIONS OF SUPPORT PROGRAMS FOR THE TREATMENT OF CHRONIC INFLAMMATORY DISEASES

Background: Adherence to therapy in chronic diseases such as inflammatory rheumatic diseases (CIRD), inflammatory bowel diseases (IBD) and psoriasis (PsO) is a major condition to achieve positive outcomes. Patient support programs (PSPs) were developed to improve the quality of care and enhance adherence to therapy.

Objectives: To evaluate the perception of patients treated for inflammatory chronic diseases towards PSPs.

Methods: All available PSPs were identified at the national level, and their services were classified into categories: financial, logistic, educational, and emotional support. Consecutive adult patients with CIRD, IBD, and PsO, enrolled in a PSP for more than 3 months, were interviewed by a trained medical student. Demographic data, disease and treatment characteristics were collected at the physician’s clinic. Global satisfaction was estimated using a 5-points Likert scale, adherence to treatment was measured by the Compliance Questionnaire for Rheumatology (CQR). PSPs services were classified according to their importance to the patient using a 5-points Likert scale. An open questionnaire identified the patients’ perceptions qualitatively. Predictive factors of satisfaction were identified.

Results: Forty-seven patients were included in the study, 53% were males, with a mean age of 49.8 years (SD 15.2) (Patients’ characteristics in Table 1). The majority declared that the PSP was very useful (95.7%) and were highly satisfied with the programs (97.9%). Higher attributes were assigned, by decreasing order, to: financial (copy program, providing of free samples), logistic (hotline, refrigerating box), educational (educational material) and emotional support. Nursing services and telephone reminders were rated as least important (Figure 1). Most open comments gave higher appreciation to financial support (54%), followed by education (38%) and logistics (8%). High appreciation of education was associated with lower age, type of treatment and PSP. Shorter treatment duration was associated with appreciation of educational material, emotional support and telephone reminders.

Conclusion: Patients were highly satisfied with PSP programs, and ranked the financial support as the most important followed by logistics, whereas education, nursing services and telephone reminders were found less important. Lower age and shorter treatment duration were associated with higher appreciation of education and support.

REFERENCES

Table 1. Patients characteristics:

<table>
<thead>
<tr>
<th>N</th>
<th>47 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease, N (some patients have multiple diseases)</td>
<td>18</td>
</tr>
<tr>
<td>- Inflammatory Bowel Disease</td>
<td>17</td>
</tr>
<tr>
<td>- Axial Spondyloarthritis</td>
<td>17</td>
</tr>
<tr>
<td>- Peripheral Spondyloarthritis</td>
<td>13</td>
</tr>
<tr>
<td>- Rheumatoid Arthritis</td>
<td>13</td>
</tr>
<tr>
<td>- Psoriasis</td>
<td>13</td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>49.8 (15.2)</td>
</tr>
</tbody>
</table>
Male gender, N (%) 25 (52%)  
Current treatment, N (%) 31 (66%)  
- Anti-TNF alpha 9 (19%)  
- Jak-Inhibitor 3 (6%)  
- Anti-IL12-23 2 (4%)  
- Anti-IL17 1 (2%)  
Biologic treatment rank  
- 1 23 (49%)  
- 2 14 (30%)  
- 3 5 (11%)  
- 4 4 (8%)  
- 5 2 (4%)  
Disease duration, years (SD) 11.6 (9.6)  
Current treatment duration, years (SD) 1.6 (1.9)  
Use of previous PSP, N (%) 15 (32%)  
CQR score, mean (SD) 86.9 (6.8)

Results: We found that male patients had differences in diagnosis duration, level of creatinine, uric acid, RAP. We did not reveal differences in age, a functional class, a risk scale, and the majority clinical, tool and hemodynamic indicators. However, there were significant differences in survival. So, in male group survival was 21 [12; 51] months, in comparison in female group 74 [48; 119] months, p<0.02. Thus, the male sex was an independent predictor of poor prognosis (HR 2.92 [95%CI 1.21; 7.03], p = 0.018) of PAH-CTD. 

Conclusion: These results indicate that female PAH-CTD patients have better long-term prognosis than male, despite lack of many distinctions. It needs to be considered at outcome assessment.


Epidemiology, risk factors for disease or disease progression

GENDER DIFFERENCE IN PULMONARY ARTERIAL HYPERTENSION, ASSOCIATED WITH CONNECTIVE TISSUE DISEASES

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Background: Pulmonary arterial hypertension (PAH) is a progressive fatal disease with a known gender dimorphism. However, data on gender differences at patients with pulmonary arterial hypertension, associated with connective tissue diseases (PAH-CTD), currently not enough.

Objectives: Therefore, this study aimed to investigate the role of gender in clinical future, hemodynamic data and survival PAH-CTD.

Methods: We examined the long-term prognosis of 97 consecutive PAH-CTD patients, mean age 49 years (7 males and 90 females) diagnosed in our Institute from January 2009 to December 2018. The primary outcome was death. We used nonparametric analysis, Cox regression and the Kaplan-Meier method to assess variables obtained at baseline. All patients received PAH-specific therapy according to the current recommendations.

Results: We found that male patients had differences in diagnosis duration, level of creatinine, uric acid, RAP. We did not reveal differences in age, a functional class, a risk scale, and the majority clinical, tool and hemodynamic indicators. However, there were significant differences in survival. So, in male group survival was 21 [12; 51] months, in comparison in female group 74 [48; 119] months, p<0.02. Thus, the male sex was an independent predictor of poor prognosis (HR 2.92 [95%CI 1.21; 7.03], p = 0.018) of PAH-CTD.

Conclusion: These results indicate that female PAH-CTD patients have better long-term prognosis than male, despite lack of many distinctions. It needs to be considered at outcome assessment.


REFERENCES

MOST PREVALENT COMORBIDITIES IN PRIMARY SJÖGREN’S SYNDROME IN A HISPANIC POPULATION

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Background: Comorbidities are an important issue to consider in patients with rheumatic diseases (RD), as well as the clinical assessment of the autoimmune disease. Looking for concomitant diseases is a necessary step for a global approach of the rheumatic patient, knowing that some diseases are more frequent in patients with RD than in the general population and could influence the course of RD and achievement of treatment goals. Despite this, there is a need of new evidence about primary Sjögren’s Syndrome (pSS) comorbidities and their association with clinical outcomes.

Objectives: To determine the prevalence of comorbidities in patients with pSS in Mexican population.

Methods: This was a national, multicenter, cross-sectional, and observational study. We included 393 patients with pSS, diagnosed according to the American-European Consensus Group (AECG) criteria 2002 or ACR/EULAR 2012 criteria. Comorbidities, serological profile of autoantibodies, Schirmer’s test, sialometry and histopathological assessment from minor salivary gland biopsies reported in the medical records were evaluated by a rheumatologist. The comparisons between the study groups were carried out using the two-tailed Student’s t test, x2 test, and unidirectional. A value of p<0.05 was considered statistically significant.

Results: At least one comorbidity were reported in 310 (78.9%) patients. 2 to 4 comorbidities were reported in 183 (46.6%), and only 18 (4.6%) had at least 5 comorbidities. Thyroid disease was the most frequent comorbidity, observed in 91 (23.2%) subjects, being hypothyroidism the main cause. Smoking (21.9%) and hypertension (19.6%) were in second and third place. Psychiatric disease was present in 62 (15.8%) patients being depression and anxiety disorders the most frequent, appearing in 49 (79%) and 12 (19.3%) patients respectively. Regarding malignancy, we documented 10 (2.5%) patients with lymphoma, and 4 (1%) patients with breast cancer. The rest of comorbidities are shown at Figure 1 and Table 1. There was no significant difference for each variable measured between the groups except for the mean age (p=0.001).

Table 1. Demographic and clinical variables. n=393:

<table>
<thead>
<tr>
<th>Variable</th>
<th>Comorbidities</th>
<th>No comorbidities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age years, mean(SD)</td>
<td>58.52 (13.12)</td>
<td>48.57 (12.52)</td>
</tr>
<tr>
<td>Female gender, n (%)</td>
<td>297 (95.8)</td>
<td>80 (96.4)</td>
</tr>
<tr>
<td>(+) Anti-Ro/SSA, n (%)</td>
<td>194 (62.6)</td>
<td>59 (71.1)</td>
</tr>
</tbody>
</table>

GSM; Minor salivary gland. P; asymptotic significance, ** statistical significance

Conclusion: The systematic evaluation of comorbidities in patients with pSS is essential for an integral management. Physicians should be aware that these conditions might directly impact quality of life, prognosis, treatment response and healthcare costs. We encourage further research for the identification of new approaches in benefit of the patients.

REFERENCES


COLCHICINE USE DURING PREGNANCY: CASE REPORTS

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Background: If used during pregnancy it is known that colchicine passes through the placenta to the fetus. Although it has been shown to increase the risk of congenital malformations in animal studies, there is no increase in undesirable results in humans. The guidelines indicate that the use of colchicine in pregnancy and lactation is appropriate. However, data from clinical studies and case reports for the use of colchicine during pregnancy are not sufficient.

Objectives: The aim of this study was to evaluate pregnant and/or nursing patients who were consulted to our teratology information center for colchicine use.

Methods: Colchicine treated patients during pregnancy was included in this study. Patients consulted to our information service between 2012-2018 were evaluated for risk assessment of colchicine. Information regarding pregnancy outcomes was recorded by telephone interviews with patients.

Results: Indications for colchicine use in 34 cases (33 patients; one of them had pregnancy twice) were familial Mediterranean fever (n=21), Behçet’s disease (n=9), systemic lupus erythematosus (n=1), ankylosing spondylitis (n=1) and vasculitis (n=1). Of the cases, 22 used the drug in pregnancy and lactation, 12 used only in pregnancy period. Of the 34 pregnancies, three had elective termination of pregnancy (the reason in one case was cytomegalovirus infection, the other is unplanned-unwanted and the other was unknown) and three had spontaneous abortion. Twenty eight had given birth, 19 of them were term and 9 of them were preterm. Delivery mode of 18 were caesarean and 10 of them were vaginal birth. A total of 30 live birth infant (two twins) exposed to colchicine due to their mother’s treatment. Twenty three infant was healthy and the remaining 7 had different problems. Four of them cardiac [minor cardiac septal defect which not needs operation (n=2), pink tetralogy of fallot (n=1), heart valve stenosis (n=1)], nephrolithiasis, inguinal hernia and death (respiratory distress after birth) (table 1).

Conclusion: Currently, systematic review and meta-analysis driven data suggests that colchicine does not significantly increase the incidence of foetal malformations or miscarriage and colchicine for FMD should not be withheld on this basis during pregnancy. Although the causality between colchicine use and the abortion reported mostly cardiac and rare problems such as tetralogy of fallot is not proven, the contribution of colchicine cannot be ruled out totally and should be bearded in mind in cases of colchicine use for indications other than FMD or Behçet’s disease.
OBSERVATION: Obese patients are at an increased risk for metabolic syndrome and related comorbidities, which contribute to a higher incidence of cardiovascular diseases.

BACKGROUND: Obesity and metabolic syndrome (MS) are associated with an increased risk of premature death due to cardiovascular causes. Patients with obese or metabolic syndrome are at a higher risk for inflammation, which contributes to a higher risk for cardiovascular disease. BMI and AC are related to metabolic syndrome and inflammatory parameters.

OBJECTIVES: To assess the influence of BMI, AC and MS on disease activity and quality of life in RA and OA, using parameters of inflammatory activity (sedimentation rate (SR) and C-reactive protein (CRP), Activity Score (DAS28), Visual Analogue Pain Scale (VAS) and Health Assessment Questionnaire (HAQ) and to compare patients with BMI and AC.

METHODS: A cross-sectional study, including 150 patients with RA, diagnosed according to ACR/EULAR criteria and 75 patients with PsA (CASPAR criteria). Assessment of weight, height, AC, SR and CRP of all patients, followed by the dorsal spine (41.9%) and cervical spine (9.6%).

RESULTS: Age, duration of illness, schooling and professional class were assessed according to WHO definition. Participants completed HAQ and quality of life in rheumatoid arthritis (RA) and PsA.

CONCLUSION: These results suggest that increased BMI and AC are associated with increased disease activity and quality of life in RA and PsA.

REFERENCES:
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Disclosure of Interests: None declared

AB1244 TUBERCULOUS SPONDYLODYSITIS: A CASE SERIES ANALYSIS

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BACKGROUND: Spinal tuberculosis or Pott’s disease is one of the many manifestations of active tuberculosis and is still common in Mediterranean countries such as Tunisia with high endemicity. Definitive diagnosis of tuberculosis spondylodiscitis requires the identification of Mycobacterium tuberculosis.

OBJECTIVES: We aimed to describe clinical, laboratory, diagnostic and therapeutic features of spinal tuberculosis.

METHODS: Retrospective study including 64 patients followed up in our department between 1999 and 2019. Clinical, biological and radiological data were collected. Therapeutic approach was studied.

RESULTS: We studied 64 patients included 35 women and 17 men with a mean age of 56 years old [16 - 86]. Seven patients had a contact with Mycobacterium Tuberculosis Bacilli and 5 patients had a history of pulmonary tuberculosis. The median delay of consultation was 6 months. Inflammatory back pain was found in 79%. Other clinical symptoms: 37.5% fever, 40.3% night sweats, 74.1% impaired general condition. Neuroradiologic imaging was performed in 16.1% of cases. 7 patients had another localization of tuberculosis. The inflammatory biological syndrome was found in 92% of cases. The lumbar spine was involved in 58% of patients, followed by the dorsal spine (41.9%) and cervical spine (9.6%).

Disclosure of Interests: None declared
radiographs revealed narrowing of disc spaces in 67.7% of cases and vertebral erosion, vertebral fracture and a paravertebral spindle in 52.5%.

Computed tomography and Spinal magnetic resonance imaging was performed respectively in 62.9% and 70.9% of cases. They showed paravertebral abscess in 66.1%, epiduritis in 56.4%, intra-discal abscess in 3.22%, spinal cord compression in 8.06%, and vertebral osteolysis in 9.67% of cases. Tuberculin Skin Test was performed in 57 (92%) patients and it revealed a positive result in 29 (47%) patients. Discos vertebrae biopsy was performed in 45 patients and was contributive in 32.2% of cases revealing caseating granulomas. A four-drug therapy including isoniazid (INH), rifampin (RMP), pyrazinamide (PZA) and ethambutol (EMB) were administered to 59 (95.16%) patients for the initial two months. Three patients received initial three-drug combination therapy. Following the initial 4-drug regimen, most patients continued to receive a two-drug regimen with RMP and INH for a mean duration of nine months. Over 80% of patients had an immobilisation.

Adverse effects of anti-TB therapy were noted in 17.7% of the patients; (nausea-vomiting: 1.6%, hematotoxicity: 9.6%, rash: 3.2%, hyperuricemia: 3.2%). A surgery was needed for 6.4% of patients. Neurological complication occurred in 4 cases, sepsis occurred in 2 other cases and 2 patients were dead.

Conclusion: Spinal tuberculosis results in a significant rate of morbidity due to its insidious course and delayed diagnosis. Early establishment of definitive etiologic diagnosis and appropriate treatment is of paramount importance to prevent development of sequelae.

Disclosure of Interests: None declared


AB1245

COMPARATIVE ANALYSIS OF SPONTANEOUS INFECTIOUS SPONDYLITIS: PYOGENIC VERSUS BRUCELLA

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Background: Infectious spondylitis is an infectious disease of the spine or paraspinal structures that can be caused by various microorganisms. Without adequate chemotherapy, the outcome can be fatal or result in severe neurologic damage. Therefore, differentiating the etiology of spondylitis is very important.

Objectives: To compare the clinical features, laboratory and radiological aspects, treatment and outcome data of patients diagnosed as brucellar spondylitis (BS) and pyogenic spondylitis (PSP).

Methods: Retrospective study including 45 (22 BS and 23 PSP) spondylodiscitis hospitalized in our department between 1999 and 2019. The diagnosis was based on clinical, biological, radiological and bacteriological data.

Results: The patients' mean age was 54 years. There were 31 men (68.8%) and 14 women (31.2%). There was no difference in mean age and sex between the two groups (p=0.8 and p=0.4; respectively).

The pyogenic group had a relatively higher proportion of Predisposing factors especially diabetics (p=0.04). PSD patients suffered an impaired general condition more frequently than BSD patient (p=0.01) while BSD patients complained of night sweats more frequently compared to PSD cases (p=0.025).

The peak CRP value was higher in the pyogenic group than in the brucella group (87 mg/L and 37 mg/L, respectively, p=0.027), whereas the ESR was not significantly different between the groups (71 mm/h and 67 mm/h, respectively, p=0.7). We found no statistically significant difference regarding the seat of the spondylitis. Whereas, multifocal involvement was higher in PSD (p=0.049). Radiologically, the frequency of prevertebral, paravertebral, epidural, and psoas abscess formations and spinal cord compression was similar in both groups (p=0.8).

Surgical interventions and percutaneous sampling and/or abscess drainage were applied more frequently in PSD but with no significant difference (p=0.23). Favorable clinical outcome rate was 60% in PSD and it was 72% in BSD group (p=0.39).

Conclusion: The clinical and radiological manifestations of spontaneous spondylitis differ based on the causative organism. Pyogenic spondylitis patients tend to have a more severe clinical course and a higher CRP level. However, there was no significant difference regarding the presence of abscess and epiduritis or the occurrence of complications between brucella and pyogenic spondilitis.

Disclosure of Interests: None declared


AB1246

PREDICTORS OF IMPAIRED QUALITY OF LIFE IN PATIENTS WITH SYSTEMIC DISEASES

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Background: Systemic diseases are heterogeneous diseases that represent one of the leading causes of disability in the industrialized world and can even reduce life. They are associated with high rates of disability, premature mortality, and significant social costs.

Objectives: The objectives of our study were to evaluate the quality of life (QoL) of patients with systemic disease and a comparison between these patients, to search for factors predicting the impairment of quality of life during systemic diseases, and to evaluate work disability of those patients.

Methods: We conducted a cross-sectional study at the Internal Medicine Department of the Farhat Hached Hospital in Sousse between July 2017 and September 2017. We investigated patients with systemic rheumatic, thrum or remission who were present as outpatients or were admitted to the ward during this period. The outcomes were baseline Short Form Health Survey physical (PCS) and mental (MCS) component summary scores (QoL). Work disability was evaluated by the work productivity assessment instrument (WPAI) questionnaire. Correlations were calculated by the test t student or Anova factor test and comparison with chi2 test.

Results: Two hundred thirty five patients were included, 183 females and 52 males. The average age was 48.3 years with extremes between 15 and 90 years old. Forty seven per cent of the population had work during the study. The most frequent diseases were: Systemic lupus erythematosus (SLE) in 66 patients, Behçet syndrome in 33 patients and Sjogren primary syndrome (SLE) in 27 patients. Mean PCS were 52.55 ± 17.3 and MCS scores were 47.74 ±14.8. For the predictors related to patients: the age (PCS: r=-0.250, p<0.000), (MCS: r=-0.160, p=0.014), the presence of comorbidities (PCS: p<0.000) and the low level of education (p=0.001) were significantly correlated with impaired QoL, the presence of profession was not significantly correlated with QoL. For the predictors related to the disease: inflammatory myositis influences most the QoL. Pulmonary manifestations (PCS: p<0.021, MCS: p=0.006) were the most correlated with impaired QoL. Disease index of activity was calculated in 3 diseases and it was significantly correlated with impaired QoL; SLE (PCS: r=-0.581, p<0.000); (MCS: r=-0.494,p=0.000),SSP (PCS: r=-0.500,p=0.007), (MCS: r=-0.522, p=0.005), Systemic sclerosis (PCS: r=-0.698, p=0.012), (MCS: r=-0.710,p=0.01)). Work disability was evaluated in working patients: absenteeism as 31.16±24, productivity impairment at 48.77 and systemic sclerosis was the most disease predictive of absenteeism and work disability (p=0.011).

Conclusion: QoL may be severely impaired in patients suffering from systemic diseases. We studied for the first time the predictors of impaired QoL for all patients followed in our department. Our study concord with literature (1), beside the objective criteria resulting from clinical examination and biological investigations, it seems essential to take into account the individuality of each patient. This measure aims to further humanize medical practice and maintain the quality of life of patients.

REFERENCES

Disclosure of Interests: None declared


AB1247

RISK FACTORS FOR ADVERSE CLINICAL OUTCOME IN SEPTIC SPONDYLODICTIS

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Background: Spondyloarthritis is defined as a serious infection of the intervertebral disc and/or adjacent vertebrae. It can lead to neurological sequelae and put life-threatening ones into play.

Disclosure of Interests: None declared

Objectives: To describe the clinical features and outcomes of septic spondylodiscitis and to identify factors associated with an unfavourable clinical outcome.

Methods: Retrospective study including 107 patients followed up in our department between 1999 and 2019. Clinical, radiological and microbiological data were collected.

We divided patients into two groups: patients with unfavourable clinical outcome (defined as death, drug toxicity, neurological complication, sepsis or persistent pain) (Group 1) and patients with a favourable one (Group 2).

Results: We included 107 patients (49 women and 58 men), with a mean age of 55 years old [16 - 86]. The median delay of consultation was 3 months. Predisposing factors were found in 59 patients (55.1%). Inflammatory back pain was seen in 78.5% of cases. Neurologic deficits were noticed in 16.8% of cases: motor deficit in 1.8% of cases, spinal cord compression in 1.8% of cases and Cauda equina syndrome in 2.6% of cases. An inflammatory biological syndrome was found in 90.6% of cases. The lumbar spine was involved in 55%. The spondylitis was multifocal in 19.6% and multi-stage in 15.8% of cases. CT and Spinal MRI was performed respectively in 60% and 78.8% of cases and showed paravertebral abscess in 63.5%, epiduritis in 54.2%, intra-discal abscess in 46.7%, spinal cord compression 9.3%, and vertebral osteolysis in 8.4% of cases. The causative microorganism was mycobacterium tuberculosis in 59.8%, brucella in 20.56%, and pyogenic germs in 16.8% of cases. 34.5% of patients had an unfavourable clinical outcome: persistent pain was noticed in 18.7%, drug toxicity occurred in 13% of cases, neurological complication occurred in 10.2% of cases, sepsis occurred 3.7% of cases and 3.7% of patients were dead.

In the group1 the frequency of diabetes, impairment of the general state and clinical evidence of neurological impairment at presentation was higher, but with no statistically significant difference. Similarly, the presence of paravertebral abscess, epiduritis or spinal cord compression was slightly more frequent, with no significant difference.

There was no statistically significant difference in the age (p=0.15), the localisation and the causative microorganism (p=0.68).

Conclusion: Spondylodiscitis is a rare but serious condition that leads to significant long-term morbidity. In our study, unfavourable clinical outcomes was found in the presence of diabetes, neurological impairment at presentation and the presence of paravertebral abscess, epiduritis, or spinal cord compression in MRI but with no statistically significant difference.

Disclosure of Interests: None declared
ADL was suspended. These results suggest a direct relationship between the time of exposure to ADL and concomitant use with DMARDs and corticosteroids at dose >2.5 mg, similar findings are also described in other studies.

REFERENCES

Disclosure of Interests: Boris Anthony Blanco Cáceres: None declared, Fernando Perez-Ruiz Grant/research support from: Asociación reumatoló- gos de Cruces, Consultant for: Grünenthal Horizon Menarini, Speakers bureau: Grünenthal, Menarini, Fundación Española Reumatología, Paula García Escudero: None declared, Marta González Fernández: None declared


AB1250
SLE AND SEXUAL FUNCTION: ARE WE FORGETTING MEN?
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Background: Whereas SLE is uncommon in men, the disease is usually more severe and requires more aggressive immunosuppressive therapy in male patients. There are multiple studies regarding sexual aspects in women with SLE, but information about sexual function in male patients is quite scant.

Objectives: To determine the relationship between SLE and sexual function alterations in men, through the application of validated questionnaires.

Methods: We performed a longitudinal study in a third-level referral center in Mexico City. We included men aged ≥16 years who fulfilled ACR criteria for SLE and who were sexually active. All subjects answered the International Index of Erectile Function-15 (IIEF-15), the SF-36 and the International Index of Erectile Function-15, the SF-36 and the International Index of Erectile Function-15 (IIEF-15), the SF-36 and the SF-36 Health Survey.

RESULTS: We included 108 male SLE patients. Mean age was 37.2±11 years and most patients (87%) were taking immunosuppressive therapy. Comorbidities were present in 58% of subjects, with dyslipidemia and hypertension being the most prevalent (34% and 28%, respectively). The prevalence of sexual dysfunction (SD) was 53%. In the basal visit, the only significant differences between the patients with SD and those without SD were a lower education degree (p=0.007) and persistent lymphopenia (p=0.01). There was a positive correlation between global IIEF-15 score and SF-36 score (r=0.46, p=0.001). The physical function domain had the highest correlation (r=0.50, p=0.001). Likewise, there was a weak negative correlation between IIEF-15 and HAQ score (r=0.25, p=0.012). Also, the IIEF-15 had a weak correlation with the absolute lymphocyte count (r=0.27, p=0.005) and oxidized LDL (r=0.31, p=0.04). In the follow-up visit the only significant differences between the patients with SD when compared with subjects without SD was a low absolute lymphocyte count (1031±89 vs 1458±119, p=0.005); the correlations mentioned in the baseline visit remained significant. Regarding erectile function, 44% of the subjects had some degree of dysfunction. The rest of the variables are shown in Table 1.

Abstract AB1250 Table 1. Demographic, clinical and laboratory features

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± SEM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>37.2 ± 1.1</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>26.5 ± 0.4</td>
</tr>
<tr>
<td>Less than 10 years of schooling (n,%)</td>
<td>21/108 (19.4)</td>
</tr>
<tr>
<td>Time since SLE diagnosis (years)</td>
<td>9.1 ± 0.6</td>
</tr>
</tbody>
</table>

Clinical Features
- Total score IIEF-15: 58.7 ± 1.3
- Erectile function: 23.9 ± 0.6
- Intercourse satisfaction: 10.9 ± 0.3
- Organic function: 8.1 ± 0.2
- Sexual desire: 7.5 ± 0.1
- Overall satisfaction: 8.1 ± 0.1
- Total score SF-36: 69.2 ± 0.3
- Secondary antiphospholipid syndrome (n, %): 16/108 (14.8)
- SLEDAI score (points): 4.2 ± 0.4
- Others comorbidities (n, %): 63/108 (58.3)
- Laboratory features: Hemoglobin (mg/dl): 15.3 ± 0.2
- Leukocytes (x10⁶/mm³): 5.9 ± 0.2
- Absolute lymphocyte count (mm³): 1362±676
- Serum creatinine (mg/dl): 1.4 ± 0.1
- C3 levels: 104.1 ± 3.2
- C4 levels: 19.7 ± 1.2
- Anti-dsDNA antibodies: 208±2.704
- Use of immunosuppressive treatment (n,%): 95/108 (87.9)
- Renal function (n, %): 58/108 (53.7)
- Azaithioprine (n, %): 31/108 (28.7)
- Antimalarial (n, %): 73/108 (67.5)
- Cyclophosphamide (n, %): 42/108 (38.8)
- Cyclophosphamide exposure previous 6 months (n, %): 7/108 (6.4)
- Anticoagulation (n, %): 18/108 (16.6)
- Non-immunosuppressive treatment (n, %): 85/108 (78.7)

Conclusion: Sexual function is affected in men with lupus, regardless of comorbidities and treatment. Interestingly, lymphopenia is persistently associated with an impaired sexual function, which could be related to the role it plays in endothelial dysfunction and atherosclerosis. The patients’ disease perception, which is influenced by their academic level and physical role in their daily activities, seems to affect their sexual performance and quality of life.

Disclosure of Interests: Jonathan Campos-Guzmán: None declared, Ana Barrera-Vargas: None declared, Samuel Govea-Peláez: None declared, Diana Gómez-Martín: None declared, Jorge Alcocer-Varela: None declared, Diana Padilla-Ortiz: None declared, Javier Merayo-Chalico Speakers bureau: Pfizer


AB1251
ASSOCIATION BETWEEN VITAMIN D DEFICIENCY AND A HIGHER RATE OF DISEASE ACTIVITY IN PATIENTS WITH SPONDYLOARTHRITIS
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Background: Spondyloarthritis is a group of chronic inflammatory diseases with involvement of the axial skeleton (mainly), and also of peripheral joints. Patients with spondyloarthritis have a significant prevalence of vitamin D levels below normal and that would correlate with the degree of activity of the disease.

Objectives: To determine the association between vitamin D deficiency and the degree of activity of the disease (inflammatory activity) in a cohort of patients with spondyloarthritis.

Methods: Observational, extensive and transversal study. We propose a retrospective review of the database of patients with spondyloarthritis who were treated in the outpatient clinics of the Rheumatology Service of the General University Hospital of Ciudad Real during September 2016 to September 2018. Patients with the data will be selected. necessary for the analysis of the variables under study. The variables evaluated will be described using measures of frequency and measures of central tendency/dispersion as appropriate. To assess the association between vitamin D deficit and activity index, the odds ratio (OR) will be calculated. All analyzes were performed with a confidence level of 95% using SPSS 21.0.

RESULTS: The first advances of the results of the study are presented. 101 patients were analyzed, of which 58 were men and 43 women, with a mean age of 46.3 years (+/- 13.05 DE), 15 (14.8%) were non-radiographic axial spondyloarthritis, 48 (47.52%) anklylosing spondylitis, 24 (23.76%) psoriatic arthropathy, 3 (2.97%) spondyloarthropathy associated with inflammatory bowel disease, and 11 (10, 89%) were other types of spondyloarthritis. The average of the activity was a BASDAI of 4.355 (+/- 2.376 SD), 64 patients were in activity (BASDAI> or = 4) and 31 patients (30.69%) with an elevation of acute phase reactants. Vitamin D levels were 24.52 (+/- 9.21 SD). 77 patients (76.24%) presented figures
of vitamin D deficiency or insufficiency. When performing the association analysis, the vitamin D deficit/insufficiency presented an OR 12.46 (95% CI: 4.01-39.08), which is the degree of activity measured with BASDAI. Regarding the comparative analysis of means between vitamin D deficiency/insufficiency and BASDAI it is +2.253 (95% CI: 1.241 to 3.266, p < 0.0001).

Conclusion: In our study, patients with spondyloarthritides who have a vitamin D deficit correlate with presenting disease activity (BASDAI+ or − 4). Therapy with vitamin D along with increasing bone turnover and low levels of vitamin D could be related to the pathophysiology of osteoporosis related to spondyloarthritides, and may adversely affect the patient’s functional status and quality of life.

Disclosure of Interests: None declared

FUNCTIONAL STATUS CHANGES ASSOCIATED WITH INFLAMMATORY ARTHRITIS IN REPUBLIC OF MOLDOVA

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Background: Inflammatory joint disease is a burden to the patient and society, due to medical costs and the impact it has on the health-related quality of life. Functional status plays a significant role in quality of life impairment.

Objectives: To study and compare functional status changes between different inflammatory joint diseases and degenerative joint disease.

Methods: The study included 1500 patients with inflammatory joint disease and 400 patients with degenerative joint disease were included in this study. In the first group, 645 (43.0%) were diagnosed with rheumatoid arthritis, 330 (22.0%) - psoriatic arthritis, 100 (6.7%) - anklyosing spondylitis, 200 (13.3%) - axial spondyloarthritis, 135 (9.0%) - gout, 20 (1.3%) - other crystal arthrop-ritis, 45 (3.0%) - early arthritis and 25 (1.7%) with other arthritis. Physical examination and functional status was assessed and performed. Descriptive statistics and Mann-Whitney U tests were used to compare the study groups, as well as the subgroups within the inflammatory disease group.

Results: Both groups were comparable according to sex, with a predominance of female sex (♂ = 86.4% and 30.74% respectively, p < 0.001), and no difference in sex distribution (mean ranks of U test = 950.98 and 967.44, p = 0.524). Mean age was significantly lower in the inflammatory joint disease group (44.76 vs 60.19, p < 0.001). The Mann-Whitney U test showed a significantly greater mean rank in the inflammatory disease group (999.07 vs 790.66, p < 0.001), suggesting an overall higher functional class, and thus worse functional status in the inflammatory joint disease group. Further analysis using the same method, between subgroups in the inflammatory joint disease group, showed a higher mean rank (worse functional status) in patients with rheumatoid arthritis, when compared with psoriatic arthritis (501.95 vs 460.73, p < 0.05) and early arthritis (352.24 and 248.83, p < 0.001). Psoriatic arthritis showed a higher mean rank, compared to axial spondyloarthritis (282.88 vs 254.97, p < 0.05) and early arthritis (193.34 vs 148.83, p < 0.01). Gout patients showed a higher mean rank (worse functional status), when compared to rheumatoid arthritis (453.65 vs 377.28, p < 0.001), psoriatic arthritis (281.33 vs 213.23, p < 0.001), ankyllosing spondylitis (127.07 vs 105.75, p < 0.05), axial spondyloarthritis (184.67 vs 156.75, p < 0.01) and early arthritis (101.70 vs 56.89, p < 0.001), thus making it the subgroup associated with the poorest functional status. Ankylosing spondylitis showed a higher mean rank, when compared to psoriatic arthritis (238.13 vs 208.64, p = 0.05), axial spondyloarthritis (151.75 vs 129.88, p = 0.05) and early arthritis (81.63 vs 53.83, p < 0.001). Axial spondyloarthritis and other crystalline arthropathies both showed higher mean ranks compared to early arthritis (130.0 vs 91.89 and 43.2 vs 28.56 respectively, p < 0.01), making early arthritis the subgroup associated with the best functional status. No significant differences were found when comparing rheumatoid arthritis with anklyosing spondylitis, axial spondyloarthritis and other crystalline arthropathies.

Conclusion: This is the first study conducted on a national scale to assess the impact of inflammatory joint disease on functional status. Inflammatory joint disease involved a younger age group, when compared to degenerative joint disease, with a higher impact on the functional status. Interestingly, gout was associated with one of the poorest functional status, suggesting the need for a more aggressive approach toward this disease. After gout, a significantly impaired functional status was associated with rheumatoid arthritis, anklyosing spondylitis and axial spondyloarthritises, whereas early arthritis was generally associated with a better functional status, when compared to other inflammatory diseases.

Disclosure of Interests: None declared

DETERMINATION OF RISK FACTORS OF DEVELOPMENT OF HYPERURICEMIA IN PROFESSIONAL ATHLETES IN SOME SPORTS

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Background: Prevalence of hyperuricemia worldwide has been steadily increasing over the past decades and becomes higher with age. The number of studies on the prevalence of hyperuricemia and its role in development of diseases in some social groups is low, yet there is data on its high frequency in professional athletes.

Objectives: to assess impact of certain factors upon the risk of development of hyperuricemia in professional athletes in some sports.

Methods: the study was performed as retrospective. Out of 753 athletes in six sports, 267 athletes who met the study criteria were selected. The inclusion criteria: professional athletes aged 18-40, serum uric acid level <360 µmol/l, according to screening tests. The exclusion criterion was refusal to undergo a thorough medical examination.

Out of 753 athletes, 228 (30.3%) showed high uric acid level in their screening test, 258 (34.3%) athletes refused to undergo a medical examination. 267 people were included in the study, 130 men (48.7%) and 137 women (51.3%), with the mean age of 24.4±5.2 years and the average observation period of 3.0±0.3 years.

Parametres in inflammaton: anthropometric measurements, laboratory tests (serum levels of lactate, creatinine, crude protein, triglycerides, thyroid-stimulating hormone (TSH), AST, ALT, myoglobin, testosterone, uric acid (UA)), glomerular filtration rate (GFR) (using the MDRD formula) with subsequent statistical analysis.

Hyperuricemia was defined as SUA level >360 µmol/L. Hypercholesterinemia - as serum cholesterol level >5.0 mmol/L, hypertriglyceridemia - as serum TG level >1.7 mmol/L. High serum creatinine level as >100 µmol/L. Statistical analysis was conducted using the applied programs package of descriptive statistics STATISTICA 12.0 (StatSoft., Inc., USA).

Results: Hyperuricemia developed in 60 athletes (22.5%), including 51 (39.2%) men and 9 (6.6%) women. The frequency of risk factor detection was the following: hypercholesteri- nemia was detected in 91 (34%) professional athletes, hypertriglyceridemia - in 10 (3.7%), reduction in GFR <100mL/min - in 46 (17.2%), BMI >25 kg/m2 (OR 2.470, 95% CI (1.243;4.909) p=0.01), hypertriglyceridemia (OR 4.857, 95% CI (1.056;22.339) p=0.042), BMI >25 kg/m2 (OR 2.470, 95% CI (1.230;4.105) p<0.008).

Conclusion: hyperuricemia developed in professional athletes in 22.5% cases in 3-year observation period along with low frequency of many traditional risk factors (obesity, hypercholesterinemia, hypertriglyceridemia, chronic kidney disease), which can be linked to the peculiarities of diet. This fact calls for a detailed investigation of the dietary intake of athletes with the purpose of its optimization.

AB1254
LOW-BACK PAIN CHRONICITY IN A PRIMARY CARE SETTING IS ASSOCIATED WITH MALADAPTIVE PSYCHOSOCIAL FACTORS, OTHER CHRONIC PAIN CONDITION AND HIGH LEVELS OF PAIN AT BASELINE
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Background: Low back pain (LBP) is the leading cause of disability in Portugal and worldwide. The majority of the patients use primary health care services but the treatment outcomes are unknown. Findings of prognostic studies indicate that a marked reduction in mean pain and disability is expected in the first 6-8 weeks, for acute or persistent LBP. Beyond that time frame period, improvement slows and thereafter the probability to develop a persistent disabling back pain condition improves. Therefore, it seems important to measure the patients’ outcomes at this time point to better assess the effectiveness of the care provided.

Objectives: This study aims to describe the short-term outcomes for LBP patients treated in a primary health care centre in Portugal and to identify the prognostic factors for non-recovery and poor health related quality of life (HRQoL).

Methods: 116 patients with LBP were consecutively recruited from 7 different primary care units in Portugal. Baseline assessment includes sociodemographic and clinical data, psychosocial factors, pain, disability, and HRQoL. Pain, disability and HRQoL were then assessed at 8-weeks follow-up. A Global Rating of Change Scale to assess patient perception of improvement with treatment was added in the follow-up reassessment. Recovery criteria were determined according to the Minimal Clinically Important Difference established for pain and disability (reduction of ≥30% from baseline). The EQ-5D-3L index was dichotomised into ‘poor’ HRQoL (<0.6) and ‘good’ HRQoL (≥0.6), based on a proposed cut-off for having sufficient capacity to be able to work for a population with LBP. The relationship between variables on baseline and non-recovery/poor HRQoL was modulated through logistic regression.

Results: Of the 116 participants enrolled, 110 completed the 8-weeks follow-up. (mean age of 48.06±11.41). Approximately half of the participants (53.4%) were acute presentations of LBP. The main treatment strategy was medication (83.5%), with only 8.3% of patients having been referred for physiotherapy. At 8 weeks follow-up, there were statistically significant improvements in pain, disability and HRQoL (p<0.05). However, 38% of the patients reported they felt the same or worse, 76.4% had a poor HRQoL, and only half of the patients reached the established recovery criteria (49% in disability and 50% in pain). In the adjusted model, the probability of non-recovery (p<0.05) was associated with the presence of maladaptive psychosocial factors (OR: 1.65, 95% CI 1.13-2.40, for pain; OR: 1.61, 95% CI 1.15-2.24, for disability), a chronic pain condition (OR: 1.71, 95% CI 1.53-1.88, for pain; OR: 1.76, 95% CI 1.42-1.89, for disability), and high levels of pain at baseline for pain (OR: 1.26, 95% CI 1.09-1.39). Poor HRQoL was associated to the female gender (OR: 1.88, 95% CI 1.61-1.96), chronic pain condition (OR: 1.68, 95% CI 1.03-1.98) and high levels of pain intensity at baseline (OR: 1.36, 95% CI 1.11-1.67).

Conclusion: These results suggest there is a room for improvement in the healthcare delivered to LBP patients in the Portuguese primary healthcare setting.

Disclosure of Interests: None declared

AB1255
SELF-PERCEPTION OF CARDIOVASCULAR RISK IN RHEUMATOLOGIC DISEASES: CASE-CONTROL STUDY
Dionicio Angel Galarza-Delgado1, José Ramón Azpiroz-López2, Iris Jazmín Colunga-Pedraza1, Karla Paola Cuellar-Calderón3, Ileana Cecilia Reynosa-Silva4, Marielva Castro-González5, Carolina Marlene Martínez-Flores6, Raymundo Pineda7, 1Hospital Universitario Dr José Eleuterio Gonzalez, Cardiology, Monterrey, Mexico; 2Hospital Universitario Dr José Eleuterio Gonzalez, Cardiology, Monterrey, Mexico; 3NOVA Medical School/Faculdade de Ciências Médicas – Universidade Nova de Lisboa, Portugal, Lisboa, Portugal; 4ACES Arábida, Setubal, Portugal, 5ACES Arábida, Setubal, Portugal

Background: Several immune-inflammatory diseases are associated with an increased prevalence of cardiovascular diseases. Risk reduction through improved control of traditional cardiovascular risk (CVR) factors and the adoption of healthy lifestyle behaviors are critically important to reduce the CVR, although the general population must be aware of their CVR to make healthy sound decisions. Individuals who perceive an increased risk are more likely to adopt behaviors to reduce it, such as smoking cessation, exercise, weight loss, and medication compliance.

Objectives: The aim of this study is to assess the awareness of the CVR in patients with/without rheumatic diseases (RD).

Methods: Observational, cross-sectional study was design. Subjects with RD attending an outpatient clinic were consecutively recruited (RA, SLE, PsA OA, Sjögren syndrome, fibromyalgia, scleroderma, osteoporosis and osteopenia). A complete clinical history was made and a self-applied questionnaire (Precaution Adoption Process Model) was used to assess the awareness of the CVR in patients with RD. Comparisons were made to controls without RD. Frequencies (%), media and median values (q25-q75) were used for descriptive analysis and Chi Square test for comparisons.

Results: 250 patients were included with 76 controls and 174 cases. Demographic characteristics shown in table 1. The majority of the patients located themselves in stage 1 of their CVR perception 31.6% in cases vs. 30.3% in controls (p>0.05), other results are shown in figure 1. In the case group, 69.5% have not made any changes to reduce their CVR and the same was seen in controls. Most of the individuals are unaware of their higher CVR even though they have traditional CVR factors. Only 30.5% of the group of RD have received information from a health care provider about their CVR.

Conclusion: Even though patients with RD have and increased CVR, most of the individuals perceived it the same as the control group. The majority of the individuals (69.5%) haven’t made any changes to reduce their CVR and many of them didn’t have any source of information about their CVR, and according to EULAR recommendations the rheumatologist is the one responsible. Therefore, they should commit to give a better education to their patients.
AB1256

HIGH PREVALENCE OF DEPRESSION IN RHEUMATIC DISEASES: CASE-CONTROL STUDY

Dionicio Ángel Galazar-Delgado1, José Ramón Azpiri-López2, Iris Jazmin Colunga-Martinez2, Marielva Castro-González1, Carolina Marlene Martinez-Flores2, Raymundo Pineda1. 1Hospital Universitario Dr José Eleuterio Gonzalez, Rheumatology, Monterrey, Mexico; 2Hospital Universitario Dr José Eleuterio Gonzalez, Cardiology, Monterrey, Mexico

Background: Prevalence of depression is higher in subjects with rheumatic diseases (RD) when compared to other general medical conditions. It’s associated with chronic pain and long-term medical treatment. The Patient Health Questionnaire 9 (PHQ-9) is an extensively validated screening tool, with a negative predictive value of 99%; it has several advantages, like being self-applied and able to be used by any clinician. Currently there are no trials using this screening tool in Mexican rheumatic patients.

Objectives: To determine the prevalence of depression in a group of rheumatic subjects and compare it to non-rheumatic controls.

Methods: An observational, cross-sectional study was designed. Subjects with RD attending an outpatient clinic were consecutively recruited. A complete clinical history with information about exercise history, and the PHQ-9 screening tool were performed to every subject. Subjects without RD were recruited as controls. Descriptive analysis was done using frequencies (%) and median (p25-p75). Comparisons were done using Chi-square and Mann-U Whitney’s test, considering p<0.05 as significant.

Results: A total of 269 subjects were included. Demographic characteristics are shown in Table 1. In the RD group, a higher percentage were female (p<0.001) and had a higher median age (p<0.001). A higher prevalence of depression was found in the RD group (p<0.002). Regarding exercise history, subjects with an inactive lifestyle had a higher prevalence of depression (p<0.001). This remained significant after evaluating only subjects with RD (p<0.007) and controls (p<0.003).

Abstract AB1256 Table 1. Demographic Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Rheumatic diseases (n=195)</th>
<th>Controls (n=74)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, n (%)</td>
<td>175 (89.7)</td>
<td>52 (70.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age, n (%)</td>
<td>58 (30.6)</td>
<td>46 (63.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hypertension, n (%)</td>
<td>46 (24.3)</td>
<td>18 (24.7)</td>
<td>NS</td>
</tr>
<tr>
<td>T2DM, n (%)</td>
<td>22 (11.7)</td>
<td>13 (17.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Dyslipidemia, n (%)</td>
<td>59 (31.7)</td>
<td>23 (32.4)</td>
<td>NS</td>
</tr>
<tr>
<td>Active smoking, n (%)</td>
<td>11 (5.9)</td>
<td>8 (11.1)</td>
<td>NS</td>
</tr>
<tr>
<td>Inactive Lifestyle, n (%)</td>
<td>103 (55.1)</td>
<td>33 (46.5)</td>
<td>NS</td>
</tr>
<tr>
<td>RA, n (%)</td>
<td>106 (54.3)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>OA, n (%)</td>
<td>32 (16.4)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>LES, n (%)</td>
<td>7 (3.5)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Sjogren Syndrome, n (%)</td>
<td>7 (3.5)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Fibromyalgia, n (%)</td>
<td>9 (4.6)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Ankylosing spondylitis, n (%)</td>
<td>5 (2.6)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>PsA, n (%)</td>
<td>3 (1.1)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Scleroderma, n (%)</td>
<td>4 (2)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Other RD, n (%)</td>
<td>22 (11.2)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Abstract AB1256 Table 2. Patient Health Questionnaire (PHQ-9)

<table>
<thead>
<tr>
<th>Classification Cut-off point</th>
<th>Rheumatic diseases N=195</th>
<th>Controls N=74</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal 0-5, n (%)</td>
<td>84 (43.1)</td>
<td>49 (66.2)</td>
<td>0.003</td>
</tr>
<tr>
<td>Mid 6-9, n (%)</td>
<td>41 (21)</td>
<td>11 (14.9)</td>
<td>-</td>
</tr>
<tr>
<td>Major Depression ≥10, n (%)</td>
<td>70 (35.9)</td>
<td>14 (18.6)</td>
<td>-</td>
</tr>
</tbody>
</table>

Conclusion: Patients with RD have a higher prevalence of depression than non-rheumatic controls (p<0.001). An inactive lifestyle was associated with a higher prevalence of depression in our cohort, both in RD subjects and in controls (p<0.001). This is the first study that evaluates the PHQ-9 screening tool in Mexican patients with RD. The physicians should be aware of it and use screening tools to detect depression disorders and provide an adequate treatment.

REFERENCES


Disclosure of Interests: None declared


AB1257

CARDIOVASCULAR RISK FACTORS IN GOUT COMPARED TO AS, PSA AND RA – RESULTS FROM A QUESTIONNAIRE STUDY

Mats Dehlin1, Ulrika Bergsten2, Eva Klingsberg1, Anton Landgren1, Lennart T. H. Jacobsson1, 1Sahlgrenska Academy, Institution of Medicine, Dept of Rheumatology and Inflammation Research, Gothenburg, Sweden; 2RandD Department at Region Halland, Halmstad, Sweden

Background: Increased risk for cardiovascular disease (CVD) is a hallmark for many rheumatic diseases including gout, anklyosing spondylitis (AS), psoriatic arthritis (PsA) and rheumatoid arthritis (RA). This is likely explained by a combination of increased occurrence of CVD risk factors (CVDRF) and chronic inflammation and in gout possibly by increased serum urate levels.

Objectives: To compare the prevalence of CVDRFs and CVD in gout, AS, PsA and RA.

Methods: All individuals aged ≥18 years with at least one ICD-10 diagnosis of gout (M10), AS (M450), PsA (M073) and RA (M056/M060) recorded by a physician during a two year period (Jan 2015 through Feb 2017) were identified at 12 primary care centers and three rheumatology units in the Western Sweden Health Care Region. A total of 1589 gout, 1095 AS, 1200 PsA and 1246 RA subjects were sent a questionnaire which included questions on demographics, CVDRFs (smoking, alcohol consumption, physical activity (PA) and comorbidities (diabetes (DM), hypertension (HT), dyslipidemia (DL), acute coronary syndrome (ACS) and stroke). High alcohol intake was defined as >4 std drinks/week. Low PA was defined as <3 hours of moderate PA/week. Primary non-responders received a second mailing of the questionnaire. All prevalences were indirectly age standardized (IAS) to the population of Sweden 2017, due to the differences in age distribution between the diseases. Chi square test with significance level .05 was performed. IAS prevalences for BMI, PA, DM and HT for the general population (GP) was retrieved from the National public health survey from 2015 which was sent to more than 100 000 randomly selected citizens in Sweden aged 16-84.

Results: Response rates ranged from 53.6% (AS) to 59.6% (RA) and after excluding subjects who had not provided complete information on the evaluated variables we included 2437 individuals. The gout and RA

Disclosure of Interests: None declared

patients were older (mean age 71 (SD 12) and 66 (SD 13) years respectively) compared to AS and PsA (mean age 50 (SD 14) and 55 (SD 13) years respectively). When adjusting for these differences by IAS by sex, both prevalent CVD (stroke, ACS) and all traditional risk factors were more common in gout compared to RA, AS or PsA (Table 1+2), except for alcohol intake in women, where highest exposure was seen in PsA (Table 2). The male AS patients displayed the highest PA level and the lowest prevalence of stroke (table 1). Smoking was least common in male PsA and female AS and RA patients (table 1+2).

**Prevalence of CVRFs**

**Age-standardized prevalences of CVD risk factors and outcomes in males, *Chi-square comparing gout, AS, PsA and RA**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Gout, n=255</th>
<th>AS, n=385</th>
<th>PsA, n=268</th>
<th>RA, n=315</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI &lt;25</td>
<td>85.3</td>
<td>51.5</td>
<td>59.0</td>
<td>65.9</td>
<td>&lt; 0.0001</td>
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<tr>
<td>PA, low</td>
<td>61.9</td>
<td>44.0</td>
<td>54.8</td>
<td>58.0</td>
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<tr>
<td>Alcohol,</td>
<td>43.3</td>
<td>20.0</td>
<td>28.3</td>
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<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Smoking,</td>
<td>48.5</td>
<td>53.4</td>
<td>35.9</td>
<td>46.6</td>
<td>0.0003</td>
</tr>
<tr>
<td>ever</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>N/A</td>
</tr>
<tr>
<td>HT</td>
<td>14.2</td>
<td>4.8</td>
<td>8.4</td>
<td>8.7</td>
<td>0.0001</td>
</tr>
<tr>
<td>DL</td>
<td>49.2</td>
<td>23.9</td>
<td>32.9</td>
<td>29.2</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Stroke</td>
<td>25.3</td>
<td>9.6</td>
<td>11.2</td>
<td>13.1</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>ACS</td>
<td>7.7</td>
<td>0.0</td>
<td>4.1</td>
<td>2.5</td>
<td>0.0005</td>
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**Age-standardized prevalences of CVD risk factors and outcomes in females, *Chi-square comparing gout, AS, PsA and RA**

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Gout, n=134</th>
<th>AS, n=215</th>
<th>PsA, n=305</th>
<th>RA, n=345</th>
<th>p-value*</th>
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<tbody>
<tr>
<td>BMI &lt;25</td>
<td>87.3</td>
<td>40.8</td>
<td>60.0</td>
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<td>PA, low</td>
<td>74.8</td>
<td>48.3</td>
<td>54.3</td>
<td>52.6</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Alcohol,</td>
<td>7.0</td>
<td>6.4</td>
<td>14.2</td>
<td>6.9</td>
<td>0.003</td>
</tr>
<tr>
<td>Smoking,</td>
<td>56.7</td>
<td>37.8</td>
<td>56.8</td>
<td>38.0</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>ever</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>N/A</td>
</tr>
<tr>
<td>HT</td>
<td>14.9</td>
<td>2.3</td>
<td>4.9</td>
<td>4.2</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>DL</td>
<td>56.8</td>
<td>20.3</td>
<td>27.5</td>
<td>24.4</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Stroke</td>
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<td>0.8</td>
<td>0.6</td>
<td>1.7</td>
<td>0.09</td>
</tr>
<tr>
<td>ACS</td>
<td>3.6</td>
<td>0.0</td>
<td>1.8</td>
<td>2.5</td>
<td>0.2</td>
</tr>
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</table>

**References**


**Table 1. Demographics**

<table>
<thead>
<tr>
<th>Category</th>
<th>Overall cohort</th>
<th>Progressors (84% of total withdrawn (n=165))</th>
<th>Ongoing follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>479</td>
<td>314</td>
<td></td>
</tr>
<tr>
<td>Mean follow-up</td>
<td>98.5 (SD 105.55)</td>
<td>83.83 (SD 90.87)</td>
<td>105.72 (SD111.65)</td>
</tr>
<tr>
<td>CCP titre</td>
<td>High: 59.9% (n=288)</td>
<td>High: 89.7% (n=122)</td>
<td>High: 49.4% (n=155)</td>
</tr>
<tr>
<td>RF control</td>
<td>Low: 9.6% (n=13)</td>
<td>Low: 0.7% (n=1)</td>
<td>Low: 49.4% (n=155)</td>
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<tr>
<td>Neg: 31.1% (n=157)</td>
<td>31.5% (n=157)</td>
<td>31.5% (n=157)</td>
<td>31.5% (n=157)</td>
</tr>
<tr>
<td>Gender</td>
<td>Male: 72.1% (n=347)</td>
<td>68.4% (n=93)</td>
<td>72.9% (n=229)</td>
</tr>
<tr>
<td>Age</td>
<td>50.34 (SD13.51)</td>
<td>52.8 (SD 13.05)</td>
<td>49.84 (SD11.65)</td>
</tr>
</tbody>
</table>

**Disclosure of Interests:** Laurence Duquenne: None declared, Kulveer Mankia: Research support from: Research support from BMS and Lilly, Speakers bureau: Honoraria from Abbvie, Roche, Consultant for: Novartis, Speakers bureau: Honoraria from Abbvie, Roche, Novartis, Gilead, Samsung, Sandoz and Lilly

**Table 2. Demographics**

<table>
<thead>
<tr>
<th>Category</th>
<th>Overall cohort</th>
<th>Progressors (84% of total withdrawn (n=165))</th>
<th>Ongoing follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
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EVALUATION OF ENALAPRIL ON ARTERIAL STIFFNESS IN RHEUMATOID ARTHRITIS IN A RANDOMISED CLINICAL TRIAL

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Background: This is the first study where suboptimal doses of enalapril proved to be successful for the reduction of arterial stiffness in a clinical trial of rheumatoid arthritis (RA) patients.

Objectives: The aim of this study was to analyze the effect of enalapril on arterial stiffness through the evaluation of subclinical parameters in RA patients without traditional cardiovascular risk factors or previous comorbidities.

Methods: Fifty-three patients were enrolled in a clinical, randomized, closed-label trial. The subjects were randomly assigned into two groups: One receiving 5 mg of enalapril (27) and 5 mg of placebo (26), both twice a day. Clinical assessment and evaluation of arterial stiffness were performed. The entire set of evaluations were analyzed at the baseline and at the end of 12 weeks of intervention.

Results: A significant reduction in delta CAVI of 0.21 in the enalapril intervention group was found. In contrast, an increase of 0.39 was observed in the placebo group. The delta CAVI reduction was not influenced by age or peripheral systolic blood pressure (pSBP).

Conclusion: Enalapril seems to be effective in CAVI reduction in RA patients. The effect of enalapril intervention on arterial stiffness translated to the clinical context, might be interpreted as a reduction of 6.4 years of arterial aging.

REFERENCES

Disclosure of Interests: None declared


AB1261 CADMIUM TOXICITY AS A PROBABLE CAUSE OF OSTEOPENIA IN ADOLESCENTS AND ITS RELATION TO BAD DIETARY HABITS

Adel Elbeija1, Hesham Elsedouky2, 1Al-Azhar Faculty of Medicine, Rheumatology, Cairo, Egypt; 2Al-Azhar Faculty of Medicine, Rheumatology, Cairo, Egypt

Background: Cadmium is a naturally occurring minor element; it has been recognized as an occupational health hazard for many decades. Water and food are the main source of environmental cadmium exposure in non-smokers in most parts of the world. Cadmium accumulates gradually in the human body, where it gives rise to a number of adverse health effects and especially to kidney and bone. Several studies have addressed a possible association between long-term low-level environmental cadmium exposure and osteoporosis. Osteoporosis is a large and escalating public health problem.

Objectives: This study was conducted to assess the bone mineral status in secondary school students in Egypt and to measure cadmium level in their blood and urine and possible relationship between cadmium retention and bone mineral abnormalities as well as its consumption from some food and drinks commonly utilized by those students.

Methods: Two hundred secondary school students from different secondary schools in Egypt were included in this study(100 males, and 100 females). Bone mineral content was assessed in the 200 students by Quantitative Ultrasoundography (QUS) of the calcaneus using the ultrasound bone densitometer unit PEGASUS PRESTIGE, OSTEOMED, FRANCE. Students with abnormal bone mineral status (T score < -1) were considered osteopenic, data obtained from this osteopenic group were compared

AB1259 CHARACTERISTICS OF METABOLIC SYNDROME IN AN ASIAN COHORT OF PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Metabolic syndrome (MS), the concurrence of hypertension, abdominal obesity, dyslipidemia and glucose intolerance, is an important risk factor for type II diabetes mellitus (T2DM) and cardiovascular disease (CVD). CVD is a leading cause of morbidity and mortality in patients with rheumatoid arthritis (RA). Studies in RA suggest that inflammation and glucocorticoid use predispose to MS, and that MS is associated with active disease.

Objectives: To investigate the prevalence and characteristics of MS in our cohort of RA patients.

Methods: A total of 409 patients who fulfilled the 1987 ACR criteria for RA and with complete data for classification of MS were included. MS was defined according to the Adult Treatment Panel III report of the National Cholesterol Education Programme (NCEP/ATP III). Information related to demographics, disease onset, serologies, disease activity and treatment was collected. Independent t-test or Mann-Whitney U test was used to compare continuous quantitative data, while Pearson Chi-square or Fisher Exact test for categorical data. Logistic regression was used to identify factors associated with MS. All the statistical tests were two-tailed, and p value <0.05 was considered as statistically significant.

Results: Fifty-two patients (12.7%) fulfilled the criteria for MS. Most of the patients in the cohort were female (85.3%) and non-smokers (84.6%). The mean age was 60.5±11.09 years and mean BMI 23.67±5.06. The patients with MS were significantly older (age 64.21±6.63 vs 59.96±11.32, p=0.010). The mean disease duration was 14.09±9.74 years. Rheumatoid factor and anti-cyclic citrullinated peptide antibody were present in 80.0% and 95.1% respectively. 4.4% of them had a history of CVD or stroke/transient ischaemic attack but the prevalence was the same in patients with and without MS. Comparing the two groups, there was no significant difference in the history of ever-smoking (15.4% vs 15.4%, p=0.699), disease duration (16.44±10.11 vs 13.72±9.66 years, p=0.458), cumulative glucocorticoid use (p=0.649), DAS28 score (2.12±1.09 vs 2.11±1.24, p=0.767) and HAQ score (0.13 vs 0.13, p=0.002). There was also no significant difference in the use of metotrexate, leflunomide or biologics. The commonest MS criteria fulfilled were hypertension (88.5%) and dyslipidaemia (84.6%). 46.2% of the patients with MS had T2DM. Males were less likely to have MS than females [adj. OR (95%CI): 0.039 (0.005, 0.292), p=0.002].

Conclusion: MS is found in 12.7% of our RA patients and they were significantly older than those without MS. In our study, MS does not have a significant association with RA disease activity, disease duration, glucocorticoid use or disease modifying anti-rheumatic treatment.

REFERENCES

Disclosure of Interests: None declared

to those from a group of apparently healthy students with normal T score (T score > -1).

Results: Osteopenic group were 52 students (26%); 16 males and 36 females, their mean age was 15.46 ± 0.40 years. Cadmium level in blood and urine was significantly higher in osteopenic group, Interpreted of dietary habits in the osteopenic and control groups revealed that carbonated beverages, potatoes chips, corn snacks intake were significantly increased in osteopenic group, whereas no significant difference was detected in milk, tea, and coffee intake. T score was negatively correlated with blood cadmium, urine cadmium, as well as carbonated beverages, potatoes chips, corn snacks. Cadmium concentrations in tap water as well as in commercial mineral water were negligible, but its concentration in carbonated beverages, potatoes chips, corn snacks was relatively high.

Conclusion: Osteopenia and osteoporosis are not uncommon problem among secondary school students in Egypt. Cadmium exposure, evident by high blood and urinary levels, is a risk factor for development of low BMD. Fault dietary habits, including increased carbonated beverages, potatoes chips, and corn snacks intake, contributes to the occurrence of osteopenia.

REFERENCES
potatoes chips, and corn snacks intake, contributes to the occurrence of hyperuricemia and arrhythmia and its mechanism.

[3] Abou-Arab AA and Abou Donia MA: Heavy metals in Egyptian spices and


Disclosure of Interests: None declared

AB1262

THE RELATIONSHIP BETWEEN HYPERURICEMIA AND HEART RATE IRREGULARITY, USING DATA FROM THE KOREAN NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY 2016

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Background: Hyperuricemia is one of the well-known cardiovascular risk factors. In recent studies, hyperuricemia has been shown to be an independent risk factor for atrial fibrillation, which may be associated with oxidative stress or inflammation. There is still a lack of data on the association of hyperuricemia and arrhythmia other than atrial fibrillation.

Objectives: In this study, we investigated the relationship between hyperuricemia and heart rate (HR) irregularity using representative sample data of adult Korean population.

Methods: The study included 5870 subjects aged 19 years or older who completed the uric acid measurement in the Korean National Health and Nutrition Examination Survey conducted in 2016. Logistic regression was used to analyze the association between hyperuricemia and HR irregularity identified by the examiner at the time of the survey.

Results: Subjects with HR irregularity were older, had more smoking and drinking, had a higher prevalence of HTN, and had lower glomerular filtration rate than those with regular heartbeat. In the presence of hyperuricemia, the HR irregularity was three times higher than in the absence (HR 3.65, 95% CI 1.77-7.53, P = 0.0005). The association of HR irregularity and hyperuricemia was significant in most subjects, especially in those older than 65 years, with diabetes and hypertension.

Conclusion: Hyperuricemia was highly correlated with HR irregularity in adult Korean representative sample data, especially in subjects with conventional cardiovascular risk factors such as old age, hypertension, diabetes, and smoking and drinking. Further researches are warranted to clarify the relationship between hyperuricemia and arrhythmia and its mechanism.

Disclosure of Interests: None declared

AB1264

THE RELATIONSHIP BETWEEN SERUM URIC ACID AND PULMONARY FUNCTION IN KOREAN ADULT POPULATION: DATA FROM THE KOREAN NATIONAL HEALTH AND NUTRITION EXAMINATION SURVEY 2016

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Background: Hyperuricemia is associated with several comorbidities. The association between uric acid and pulmonary function is still controversial.

Objectives: The aim of this study was to evaluate the relationship between serum uric acid and pulmonary function in Korean adult population.

Methods: A total of 3,177 (weighted n = 19,770,902) participants aged 40 years or older from the 2016 Korean National Health and Nutrition Examination Survey were included and performed cross-sectional study.

Results: Participant with hyperuricemia was older than participants with normouricemia in females. Body mass index, Mean arterial pressure, and hemoglobin A1c, and estimated glomerular filtration rate (eGFR) were significantly associated with uric acid levels in both sex. Hyperuricemia was significantly associated with decreased FEV1 and FVC in females after adjustment for age, income, region, education, marital status, alcohol consumption, smoking, body mass index, mean arterial pressure, hemoglobin A1c, and eGFR (β = -0.143, P-value = 0.002 and β = -0.159, P-value = 0.001, respectively). There was no significant association between uric acid levels and lung function in males. After additional adjustment for respiratory disease including pulmonary tuberculosis, asthma, and lung cancer, hyperuricemia was associated with decreased FEV1 and FVC in females (β = -0.142, P-value = 0.001 and β = -0.161, P-value < 0.001, respectively)

Conclusion: Hyperuricemia was associated with decreased FEV1 and FVC in female general population.

Disclosure of Interests: None declared
EVALUATION OF ADHERENCE TO TREATMENT IN PATIENTS OF RHEUMATIC DISEASES

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Background: Patient adherence to treatment is one of the most important factors influencing the effectiveness of therapy, the course of the disease and the prognosis of the patient’s life. In addition to understanding the degree of adherence, it is important to study the factors that reduce patient adherence. In 2008, the Russian questionnaire for evaluation of adherence to treatment was developed, assessing adherence to drug therapy, to medical care, to lifestyle modification and general adherence to treatment. The questionnaire showed good sensitivity (93%) and specificity (78%).

Objectives: Using the questionnaire, assess the level of adherence to treatment, to drug therapy, medical care and to to lifestyle modification of patients with rheumatic diseases.

Methods: The study included 130 patients (30 men and 100 women) with rheumatic diseases observed in the hospital (63.1%) or outpatient (36.9%). The average age of patients was 53.1 ± 11.72 years (from 27 to 81). 69 patients (53%) suffered with rheumatoid arthritis, with ankylosing spondylarthritis 21 (16.2%), with osteoarthritis 13 (10%), with psoriatic arthritis and systemic vasculitis in 7 patients (5.4%), the remaining 10% were other rheumatic diseases. The average disease duration is 12.3 years. Patients received NSAIDs (83.8%), glucocorticoids (62.3%), methotrexate (39.2%), immunosuppressive specialty drugs (23%), cyclophosphamide (3.8%), hydroxychloroquine (3%), sulfasalazine (2, 3%), leflunomide (1.5%), azathioprine (0.8%). Based on the data obtained in points and comparing them with theoretically possible, the level of adherence was assessed as high (76% or more), medium (51-75%) and low (50% or less).

Results: The high level of adherence was observed only in 12 people (9.2%), in 66 patients (50.5%) - medium and in 52 people (40%) - low. Men had a higher level of adherence (57.6%) than women (55.4%). Among those using non-traditional methods of treatment (33.1%), adherence to treatment was 54.5%, for non-applicants (66.9%) the level of adherence was higher - 56%. The average level of adherence to drug therapy was 61%, to medical care - 48.8%, to lifestyle modification and general adherence to treatment was 50.8% - an average level, which indicates a lack of adherence. The lowest level of adherence is noted for modifying the lifestyle - 48.8%, which depended on the sex and duration of the disease.

Conclusion: Patient adherence to treatment is one of the most important factors influencing the course of the disease and the prognosis of the patient’s life. In addition to understanding the degree of adherence, it is important to study the factors that reduce patient adherence. Patient adherence to treatment is one of the most important factors influencing the effectiveness of therapy, the course of the disease and the prognosis of the patient’s life. In addition to understanding the degree of adherence, it is important to study the factors that reduce patient adherence. Patient adherence to treatment is one of the most important factors influencing the effectiveness of therapy, the course of the disease and the prognosis of the patient’s life. In addition to understanding the degree of adherence, it is important to study the factors that reduce patient adherence.

REFERENCES

All these factors must be considered when discussing the strategy and tactics of treatment with each patient in real clinical practice.

Disclosure of Interests: None declared


THE CORRELATION BETWEEN SMOKING AND DISEASE ACTIVITY AND MRI INFLAMMATION IN EARLY AXIAL SPONDYLARTHRITIS IN AN EGYPTIAN COHORT

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Background: Literature suggests that smoking is one of the crucial triggering factors of rheumatological diseases. (1) In axial Spondyloarthritis (axSpA), classified into radiographic SpA (AS) and non-radiographic SpA (nrSpA), smoking associated with disease activity and extra-articular manifestation. (2) The relationship between smoking and HLAB-27 as well as MRI inflammation in axSpA patients and the difference between nrSpA and AS regarding smoking have not been studied to date in details. Objectives: to investigate the influence of smoking on disease activity and MRI inflammation in axSpA patients (AS and nrSpA).

Methods: sixty Egyptian patients (42 males and 18 females) with the mean age (31.33 ± 7.02), with early active axial spondylarthritits (49 AS and 11 non-radiographic SpA) within two years disease duration, diagnosis based on ASAS classification criteria. All clinical indices (BASDI, BASFI, BASMI, ASDAS-CRP) were applied to all patients. HLA-B27 and the inflammatory markers (ESR, CRP) was done. MRI of sacroiliac joints was performed in a standard protocol using short tau inversion recovery and T1 sequences (slice thickness 3-4mm, both semi-coronal and semi-axial orientations), and scored by the Berlin method. Smoking use assessed by smoking pack-year index.

Results: of all 60 patients, 38 smokers and 22 non-smokers. No significant difference regarding smoking packs index between nrSpA and AS. (p=0.822) There was a robust correlation between smoking packing index and the Berlin score of MRI in all axSpA patients (rs=0.631) (p=<0.001). Moreover, there was a significant correlation between smoking and C-reactive protein (rs=0.952) as well as HLA-B27. (rs=0.340) (p=0.001) Furthermore, a significant relationship between smoking and activity indices (BASDI (rs=0.961) and ASDAS-CRP (rs=0.938)). Otherwise, no significant correlation among smoking, BASMI, and BASFI as well as ESR.

Table (1): Correlation between smoking pack index and different parameters

<table>
<thead>
<tr>
<th>Disease activity</th>
<th>Smoking pack index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non radiographic SpA</td>
<td>Radiographic SpA</td>
</tr>
<tr>
<td>(n = 11)</td>
<td>(n = 49)</td>
</tr>
<tr>
<td>rs</td>
<td>p</td>
</tr>
<tr>
<td>BASDI</td>
<td>0.986*</td>
</tr>
<tr>
<td>ASDAS-CRP</td>
<td>0.981*</td>
</tr>
<tr>
<td>CRP</td>
<td>0.602*</td>
</tr>
<tr>
<td>Berlin score of MRI</td>
<td>0.687*</td>
</tr>
<tr>
<td>CRP</td>
<td>0.991*</td>
</tr>
</tbody>
</table>

rs: Spearman coefficient*: Statistically significant at p ≤ 0.05

Table (2): Correlation between smoking pack index and HLAB27, inflammatory marker (CRP) and Berlin score of MRI

<table>
<thead>
<tr>
<th>Smoking pack index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non radiographic SpA</td>
</tr>
<tr>
<td>(n = 11)</td>
</tr>
<tr>
<td>rs</td>
</tr>
<tr>
<td>HLAB27</td>
</tr>
<tr>
<td>Berlin score of MRI</td>
</tr>
<tr>
<td>CRP</td>
</tr>
</tbody>
</table>

rs: Spearman coefficient*: Statistically significant at p ≤ 0.05

Conclusion: Smoking has no significant difference between AS and nrSpA. Smoking has a significant association with HLA-B27, the inflammatory lesions of MRI, and clinical indices (BASDI, ASDAS-CRP) as well as C reactive protein in AS and non-radiographic SpA patients while it has no association with the other clinical indices in term of BASMI and BASFI as well as the Erythrocyte sedimentation rate (ESR).

REFERENCES


Disclosure of Interests: None declared

THE PREVALENCE OF RHUPUS SYNDROME IN A MONOCENTRIC TERTIARY REFERRAL COHORT

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Background: Systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) are two systemic chronic autoimmune diseases characterised by a wide spectrum of clinical and immune-pathological features. In clinical practice, the concept of Overlap Syndrome is defined when the two diseases coexist in the same patient. Rhupus syndrome is a rare clinical condition, characterized by overlap of SLE and RA. However, it is still subject to debate whether the syndrome should be considered a distinctive entity or an aggressive form of SLE. To date, the estimated prevalence of rhupus is unknown.

Objectives: To evaluate the prevalence of patients with rhupus syndrome in our tertiary care center.

Methods: We chart-reviewed all patients with a diagnosis of SLE[1] or RA[2], based on the current ACR classification criteria, who presented to our outpatient clinic rheumatology unit. Clinical and laboratory data were retrospectively collected from patient notes. Diagnosis were systematically analyzed by two independent reviewers (SGF and ER). Disagreements were resolved by consensus; if consensus could not be achieved, a third party (SS) would provide an assessment of eligibility.

Results: One-hundred eighty-two patients with a diagnosis of SLE and 253 patients of RA, were identified. Out of 182 SLE and 253 RA cases analysed, only 2 patients fulfilled rhupus criteria. The estimated prevalence in our cohort was 0.46% (2/437).

In Figure 1 are illustrated the clinical manifestations of SLE (Panel A; Malar rash) and RA (radiograph-documented erosive polyarthritis) of the two patients.

Additionally, we identified 7 patients (1.61% of the total cohort) that only partially fulfilled both criteria for SLE and RA. In detail, 1 patient (0.23%) manifested with an overlap of clinical manifestations of SLE and RA, while 1 patient had an overlap of both laboratory criteria. Two patients (0.46%) presented with clinical criteria of RA and laboratory criteria for SLE and RA and 3 patients (0.69%) with clinical criteria of SLE and laboratory criteria for SLE and RA. Patient’s selection is resumed in Figure 2.

Figure 1

Conclusion: The prevalence of rhupus observed in our study was relatively low (0.46%). However, we identified up to 1.6% of patients partially fulfilling a diagnosis of rhupus. Rhupus syndrome is a rare and aggressive clinical condition and further prospective studies and an harmonization of classification criteria are highly needed.

REFERENCES

Disclosure of Interests: None declared


VASCULAR INVOLVEMENT IN BEHÇET’S DISEASE : ABOUT 67 CASES

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Background: Behçet’s disease (BD) is a systemic vasculitis which ethiopathogenesis still poorly understood.

Vascular involvement is one of the major causes of mortality and morbidity in this disease. It occupies a special place in the cardiovascular pathologies because of its venous and arterial tropism all confounded caliber but also because of its pejorative prognosis as well on the functional level as vital.

Objectives: Our goal was to present the various venous and arterial manifestations of BD, their epidemiological, clinical, evolutionary and therapeutic characteristics.

Methods: This is a retrospective study over a period of 9 years [2009-2018] that enrolled 87 patients who met the international criteria for Behçet’s disease. The characteristics of vascular involvement were studied.

Results: Twenty-two patients had vascular involvement (25%). There are 17 men and 5 women (sex ratio H/F=3,4), mean age at diagnosis of angina Behçet 39 years [22 years-63 years]. The vascular lesions were indicative of the disease in 17 cases (77%), and for the other 5 patients, the mean time to onset of vascular disease compared with the diagnosis of BD was 2 years.

Patients’ fulfilling the diagnosis of rhupus syndrome is resumed in Table 1.

<table>
<thead>
<tr>
<th>ANA anti-dsDNA</th>
<th>RF (U/ml)</th>
<th>anti-APCs (U/ml)</th>
<th>Articular involvement</th>
<th>SLE extra-articular manifestations</th>
<th>Immunosuppressive treatment undergone</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>1:320</td>
<td>Homogeneous pattern</td>
<td>Positive (IF)</td>
<td>219</td>
<td>63</td>
</tr>
<tr>
<td>Patient 2</td>
<td>1:160</td>
<td>Granular pattern</td>
<td>Positive (IF)</td>
<td>55</td>
<td>47.95</td>
</tr>
</tbody>
</table>
Venous thrombosis involved 20 patients (90%). They were deep in 16 patients, superficial in one patient and superficial and deep in 3 patients. It was recurrent in 14 patients.

The most common site of deep vein thrombosis was the lower limbs (n=17). The others had unusual sites: inferior vena cava thrombosis (n = 3), superior vena cava thrombosis (n = 2), sus- hepatic vein (n=1) and upper limb thrombosis (n = 1). Pulmonary embolism was noted in one case.

Arterial damage involved 4 patients (20%) divided into arterial aneurysms (3 cases) and arterial thromboses (2 cases). The locations were divided as follows: lower extremity arteries in 2 cases, upper limb arteries in one case, pulmonary artery in 2 cases and abdominal aorta in one case. Lower limb ischemia had occurred in one patient.

Two patients (10%) had mixed vascular, arterial and venous involvement, confirming the multiple and ubiquitous nature of angio-Behçet.

The treatment was based on colchicine, anticoagulants and corticosteroids in venous thromboses. Immunosuppressive therapy was started in 4 patients in front of the unusual site.

In arterial cases, corticosteroids in combination with immunosuppressant were prescribed. Flattening of the aneurysm was indicated in 2 cases with simple operative follow-up.

Conclusion: Behçet disease (BD) is very common in the Mediterranean basin, mainly affects the 30-year-old man. This systemic disease is characterized by oral aphthosis, genital ulcers and systemic involvement including ocular, gastrointestinal, neurological, and vessels that make the severity of the disease.

All types of vessels, regardless of size and seat, may be affected, with venous tropism. In our study we have just supported current literature data regarding the extensive and recurrent venous thrombosis during MB. The seriousness of this venous involvement lies in the involvement of the cavernous veins and in pulmonary embolism.

Arterial damage, such as thrombosis and/or aneurysm, is rare but maybe life-threatening.

Early diagnosis, intensive and appropriate treatment, regular follow-up and the involvement of a multidisciplinary team including internists, vascular surgeons and radiologists are key to better management of patients with angio-Behçet.

Our study illustrates the frequency and significance of vascular involvement in BD.

Disclosure of Interests: None declared


**REFERENCES**


**Disclosure of Interests:** None declared


**AB1270**

**EVALUATIONS OF ANTIRHEUMATIC DRUGS AT PRECONCEPTIONAL, PREGNANCY AND POSTPARTUM PERIODS OF RA PATIENTS’ IN A UNIVERSITY HOSPITAL: PRELIMINARY RESULTS**

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Background: Rheumatoid arthritis (RA) spontaneously improves during pregnancy and disease activity decreases in approximately two-thirds of pregnant but this decrease does not last long and postpartum exacerbation can be seen. Conversely discontinuation of antirheumatic drug (ARD) during pregnancy may be a risk factor for exacerbation of RA. In case of preconceptional, pregnancy and postpartum (P&P&P) situations during RA treatment, current options are discontinuation of inappropriate medications and switching to appropriate ones. With the latest BSR and EULAR guidelines on prescribing drugs in P&P&P, treatment options expanded with some of the biologic drugs.

Objectives: The aim of this study is to analyse alterations of ARD use (discontinuation, increasing or switching) at P&P&P periods of RA patients’ retrospectively between 2002-2018.

Methods: In our records there are 25 cases of 19 female RA patients who having at least one pregnancy experienced out of 140 RA patients. The data were collected by telephone calls and patient file. Female patients that had no pregnancies after the RA diagnosis were not included. Preconception period was defined as 1 year before estimated last menstrual date. Postpartum period was defined as 1 year after infants’ birth.

Results: RA patients participating in our study of 140 female (age median 55 (26-87)), 121 of them (86%) did not give birth after the RA diagnosis. 19 of them (age median 39 (26-61)) had been pregnant after the RA diagnosis (%14) and 14 of them gave birth 1, 4 of them gave birth to 2, one of them gave birth to 3. Twelve out of 140 (9%) patients had postnatal diagnosis. Each of the pregnancies counted as one case so some female patients represented in our data more than ones. While 22 of cases used the ARD before pregnancy (88%), it decreased 18 of
cases (72%) after giving birth. Drug use rate (n=12, 48%) was most lowest particularly 3. trimester and first 3 months after birth (Figure 1). While there was a change such as discontinuation, increasing or switching in the treatment of 15 patients (60%) compared to before and after pregnancy and 6 of them (24%) continued to increase treatment (added drug to preconception treatment). More than half of the patients used steroids and nonsteroidal antiinflammatory drug in all periods (Figure 2).

**Conclusion:** In conclusion the present study suggests that RA patients and doctors avoid the use of ARDs other than steroids and NSAIDs in P&P&P periods. The fact that 60% of the patients undergoing postpartum drug change were showed that pregnancy affected the RA treatment regimen. The need for steroid and NSAID in a high proportion of patients during P&P&P periods indicates the continuation of RA disease activity and the necessity of strong RA treatments during all these periods.

**REFERENCES**


**Disclosure of Interests:** None declared

TREATMENT OF RHEUMATOID ARTHRITIS WITH ESTABLISHMENT OF A PROSPECTIVE COHORT FOR INTERSTITIAL LUNG DISEASE: COMPARISON OF BASELINE CHARACTERISTICS BETWEEN RHEUMATOID ARTHRITIS PATIENT WITH OR WITHOUT INTERSTITIAL LUNG DISEASE

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Background: Rheumatoid arthritis-associated interstitial lung disease (RA-ILD) has a clinical significance of high mortality rate in patients with RA. Hence, we established a multidisciplinary prospective single center cohort for RA-ILD patients with multidisciplinary collaboration called the HUMANISM. Patients with RA who have checked a chest computed tomography (CT) scan within previous 2 years were eligible for the enrollment, and they were classified according to the presence of ILD by expert radiologists. All RA patients were assessed with various outcomes of RA, and reviewed for treatment pattern of medications annually.

Objectives: To introduce a prospective, non-interventional cohort of RA-ILD patients, HUMANISM cohort and to compare baseline characteristics and treatment patterns between RA patients according to the presence of ILD using the enrollment data of this prospective cohort.

Methods: We compared the baseline characteristics between RA patients with and without ILD using the Chi-square test and Student’s t-test. For RA-ILD patients, we described the ILD patterns that could be identified in high-resolution CT (HRCT) to determine their dominant radiological characteristics.

Figure 1. Patient selection flow of HUMANISM cohort

RESULTS:
A total of 74 RA-ILD patients and 239 RA patients without ILD were consecutively enrolled between May 2017 and October 2018. At the baseline, RA-ILD patients showed higher proportion of male patients and older age compared to RA patients without ILD. They also showed higher RF positivity than those without ILD. RA-ILD patients also have higher disease activity measured with DAS28. In the treatment, oral glucocorticoids (OC) are used in higher rate and higher doses in RA-ILD patients than those without ILD. Methotrexate (MTX) use rate was higher in RA without ILD patients compared to RA-ILD patients, but there was no difference in the prevalence of biological DMARDs. In HRCT findings of RA-ILD patients, usual interstitial pneumonia (UIP) and non-specific interstitial pneumonia (NSIP) dominant patterns were common, followed by organizing pneumonia (OP), and overlapping patterns combined with NSIP or UIP.

Conclusion: We found that RA-ILD patients showed higher disease activity, male predominance and older age than those without ILD. Treatment patterns were different in the use of MTX or OCs. In our HUMANISM cohort, common HRCT findings of RA-ILD patients were UIP and NSIP.
OF 60 PUBLICATIONS REFERRING TO BIG DATA IN RHEUMATOID AND MUSCULOSKELETAL DISEASES, 33 APPLIED ARTIFICIAL INTELLIGENCE STATISTICAL TECHNIQUES: A SYSTEMATIC LITERATURE REVIEW INFORMING A EULAR TASKFORCE

KEDRA Joanna1, Timothy R. Radstake2, Laure Gossec3,4, Suranne Huguet1,2, Sorbonne Université, Pitié Salpêtrière hospital, Paris, France; 3University Medical Center Utrecht, Utrecht, Netherlands

Background: Big data are defined as data sets that are too large or complex for traditional data-processing application software to adequately deal with. Artificial Intelligence (AI) includes various statistical techniques which can deal with big data. The current use of these concepts in publications related to RMDs is unknown.

Objectives: To assess the current use of big data and AI in the field of RMDs.

Methods: A systematic literature review (SLR) was performed in PubMed MEDLINE in November 2018, with key words referring to "big data" (All Fields) OR "Artificial Intelligence"[Majr]) and RMDs. All original reports published in English and referring to big data in RMDs were analyzed. We collected general information on the paper (including year of publication and impact factor of the journal, and country of the first author), and information on the rheumatoid disease, the number of data analyzed and the statistical methods used. The analysis was descriptive.

Results: Of 648 articles, 60 met the inclusion criteria. Among them, 34 (57%) were observational studies including 22 (37%) cohort studies, 3 (5%) were experimental studies, 7 (12%) were literature reviews or literature data mining and 16 (27%) were general reviews which provided no original data. Among the 44 original papers, the mean year of publication was 2015 (SD=5.0, range 1991-2018), with 38 articles (86%) published during the last 5 years. The mean impact factor was 5.1 (SD=8.5, range 1.6-41.9). The mean number of data was 1.4 million (SD=4.6 million, range 212 MRIs – 25 million units of observation). Many articles were written by European (N=16, 36%) or US (N=15, 34%) authors. Most papers were on inflammatory joint diseases (N=17, 37%) (Figure 1); 7 (16%) were applied to -omics and 9 (20%) to imaging. Statistical methods were based on AI in 33 papers (75%) of 44, specifically Machine Learning (N=28 articles, 64%) (Figure 2), with varied methods applied (mostly different kinds of Artificial Neural Networks, N=17).

Conclusion: Big data is an emergent area in the field of RMDs, and we found 60 papers on various diseases and with diverse applications of “big data”. Most of these papers were published very recently, and some in high impact factor journals, indicating the interest of researchers for this field. Overall, 33 publications mentioned AI techniques to deal with big data, whereas 11 used usual statistical methods. The heterogeneity of methods used indicates the need for further research in this area, and for collaboration with data scientist specialized in big data, particularly to determine which statistical methods (traditional or AI) should be used. These findings will inform a EULAR taskforce on big data in RMDs.

Disclosure of Interests: Joanna KEDRA: None declared, Timothy R. Radstake: None declared, Laure Gossec Grant/research support from: AbbVie, BMS, Celgene, Janssen, Lilly, MSD, Novartis-Sandoz, Pfizer, Sanofi, and UCB, Consultant for: AbbVie, Biogen, BMS, Celgene, Janssen, Lilly, MSD, Nordic Pharma, Novartis-Sandoz, Pfizer, Roche, Sanofi, and UCB, Consultant for: L Gossec has received honoraria from Celgene as investigator for this study.


AB1275

COMPARATIVE ANALYSIS OF LOCAL COMPLICATIONS OF HIP AND KNEE ARTHROPLASTY IN PATIENTS WITH RHEUMATOID ARTHRITIS AND OSTEOARTHRITIS

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Background: Surgical treatment of patients with rheumatoid arthritis (RA) is associated with an increased risk of complications. It can be caused by: an inflammatory process, the osteoporosis, the reduced physical activity and variability of functional movement, long term glucocorticoid therapy, biologic and disease-modifying antirheumatic drugs. All of the above reasons provide elongated wound healing period, the development of infectious complications, increased risk of periprosthetic fractures.

Objectives: to provide a comparative analysis of local complications of hip and knee arthroplasty in RA and osteoarthritis (OA) patients.

Methods: We analyzed 2142 operations: hip (n = 1177) and knee (n = 965) replacement, which were performed to patients with RA and OA between 1998 and 2018.

Disclosue of Interests: None declared.

Abstract AB1276 Table 1. Incidences rates of diabetes mellitus in patients with JIA compared to healthy population and asthmatics

<table>
<thead>
<tr>
<th></th>
<th>Healthy</th>
<th>Asthma</th>
<th>JIA</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases</td>
<td>Person-years</td>
<td>IR (95% CI)</td>
</tr>
<tr>
<td>Type 1 DM</td>
<td>62</td>
<td>276,695</td>
<td>0.22 (0.17-0.28)</td>
</tr>
<tr>
<td>Type 2 DM</td>
<td>134</td>
<td>276,573</td>
<td>0.48 (0.41-0.57)</td>
</tr>
<tr>
<td>Composite</td>
<td>147</td>
<td>276,540</td>
<td>0.53 (0.45-0.62)</td>
</tr>
<tr>
<td>DM</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Results:** There were 2142 hip and knee arthroplasty performed, including 1118 operations on patients with RA and 1024 operations on patients with OA. The number of local complications after total hip replacement was 155 (7.22%): 96 (5.76%) of them were patients with RA and 59 (5.76%) patients with OA. There were 1177 hip arthroplasty performed, including 467 operations on patients with RA and 710 operations on patients with OA. The number of local complications after total hip replacement was 85 (7.22%): 48 (10.28%) of them were patients with RA and 37 (5.21%) patients with OA. There were 965 knee arthroplasty performed, including 651 operations with RA patients and 314 operations in patients with OA were performed. The number of local complications after total knee replacement was 70 (7.25%): 48 (7.37%) of them were patients with RA and 22 (7.00%) patients with OA. We revealed a significantly greater number of complications in patients with RA (p<0.005).

**Conclusion:** Local complications after hip and knee arthroplasty with RA patients (8.59%) more than in OA patients (5.76%) in 1.5 times. It shows that the operative treatment of patients with RA requires a special approach and more gentle management of patients with RA in co-operation with rheumatologist and careful treatment of the bone with surrounding tissues during the surgery.

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.7013

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**Abstract AB1277**

**THE RISK OF DIABETES MELLITUS IN PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS: A COHORT STUDY**

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**Background:** Few studies have suggested higher prevalence of type 1 diabetes mellitus (DM) in juvenile idiopathic arthritis (JIA). To date, the risk of type 1 or 2 DM among patients with JIA has not been fully understood.

**Objectives:** To examine the incidence rate (IR) of DM in JIA patients compared to patients with asthma and healthy children.

**Methods:** We conducted a cohort study using a U.S. claims data from Truven MarketScan (2005-2016). We identified individuals between age 6 and 18 with ≥2 diagnoses of JIA with International Classification of Diseases (ICD)-9 and 10 diagnostic codes followed by one dispensing of JIA-treatment medication. For comparison, we selected 1) children with asthma and 2) healthy individuals. Each JIA patient was matched by age, sex and index date to 5 asthma patients and 5 healthy children. The primary outcome was DM, identified with 1 ICD diagnostic code followed by one dispensing of an antidiabetic drug. We assessed type 1 DM and type 2 DM separately, and composite endpoint of type 1 or 2 DM, IR and hazard ratio (HR) of DM in JIA patients versus patients with asthma and healthy subjects was calculated along with stratification by age (6 to 12 versus 13 to 18).

**Results:** After 1.5 matching, there were 74,385 healthy children, 74,385 asthma patients, and 14,877 JIA patients. The mean age in all cohorts was 13.9 years and 66.9% were female. During a mean follow up of 3.72 years, the composite IR of DM in the JIA group was 0.85 per 1,000 person-years (95% Confidence Interval [CI]: 0.61-1.19) compared to 0.63 (0.54-0.74) per 1,000 person-years in the asthma population and 0.53 (0.45-0.62) per 1,000 person-years in the healthy population (Table 1). The multivariable adjusted HR (95% CI) associated with DM in JIA was 1.27 (0.77-2.07) compared to the asthma group and 1.47 (0.90-2.42) compared to the healthy population (Table 2). Age-stratified analyses also showed numerically increased risk of DM in JIA patients.

**Conclusion:** In our cohort of 163,647 children with 14,877 JIA patients, JIA was associated with a numerically higher, albeit not statistically significant, risk of type 1 or 2 DM compared to asthma patients or healthy children.

**REFERENCES**


**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.1819

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**Abstract AB1277**

**PREVALENCE OF THE DIFFERENT ANTI-CARBAMYLATED PROTEIN ANTIBODIES ISOFORMS IN FIRST-DEGREE RELATIVES OF PATIENTS WITH RHEUMATOID ARTHRITIS IN A LATIN POPULATION**

Ana Sofia Leal Pramascio, Cesar Vidal Solis, Luis Eduardo Ramirez Monterrubio, Lorena Pérez Barbosa, David Vega Morales, Jorge Antonio Esquivel Valerio, Mario Alberto Garza Elizondo, Dionicio Ángel Galarza Delgado, Karina Itzel González Márquez. Hospital Universitario Dr José Eleuterio Gonzalez, Reumatología e Immunología Clínica, Monterrey, Mexico

**Background:** Rheumatoid arthritis (RA) affects approximately 1.5% of the population worldwide and 0.5-3.3% of the Mexican population. Anti-carbamylated proteins (anti-CarP) antibodies are identified in RA patients with a prevalence up to 44%2, early arthritis, first-degree relatives (FDR) of patients with RA with a prevalence of 16%, and healthy controls with a prevalence of 4.7%. There is no evidence regarding the prevalence of the three different isoforms of anti-CarP antibodies worldwide.

**Objectives:** Establish the prevalence of the different isoforms of anti-CarP antibodies (IgA, IgM, IgG) in FDRs of patients with RA.

**Methods:** It is an observational descriptive cohort. Subjects underwent a complete physical examination, made by a certificated rheumatologist, which included clinical and serological measurements. The serological measurements included anti-citrullinated peptides antibodies (ACPAs), RF, and anti-CarP detected by ELISA using carbamylated fetal calf serum, according to Shin J et al with some modifications.

Acknowledgement: This study was supported by an investigator-initiated research grant from Bristol-Myer-Squibb.

**Disclosure of Interests:** Hemin Lee: None declared, Yinzhu Jin: None declared, Jun Liu: None declared, Ezra Cohen: None declared, Sarah Chen: None declared, Seoyoung Kim Grant/research support from: Pfizer, Bristol-Myers Squibb, Roche/Genentech and AbbVie.

**DOI:** 10.1136/annrheumdis-2019-eular.1819
anti-CarP IgA isoform was >125 U/mL, for the IgG isoform was >90 U/mL, and for the IgM isoform was >300 U/mL. The FDRs were classified as: suspicious arthralgia for progression according to Van Steenvergen criteria; undifferentiated arthritis (UA) and RA according to ACR/EULAR 2010; and soft tissue rheumatic diseases.

Results: A total of 144 FDRs from 99 RA patients were enrolled. The demographic characteristics are shown in Table 1. The prevalence (Table 2) for anti-CarP was 2.8% for IgA, 4.2% for IgG, whereas IgM was not detected. The serologic association was for RF/ACPA 4.8%, RF/anti-CarP 2.7%, FR 64.5%, ACPA 1.3%, ACPA/anti-CarP 0.69%, anti-CarP 3.4%, and no RF/ACP/anti-Carp was observed.

The group of suspicious arthralgia for progression had 2 subjects positive for IgG anti-CarP, the group of UA had 1 subject positive for IgA anti-CarP, albeit no anti-CarP for the RA group was present. Soft tissue rheumatic diseases group had 5 subjects positive for IgG anti-CarP, while the asymptomatic group had 2 subjects positive for IgA anti-CarP.

<table>
<thead>
<tr>
<th>Population, n (%)</th>
<th>144 (100%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years), median (IQR)</td>
<td>45.25 (18-76)</td>
</tr>
<tr>
<td>Weight (kg), median (IQR)</td>
<td>70 (42-117)</td>
</tr>
<tr>
<td>Height (meters), median (IQR)</td>
<td>1.61 (1.44-1.88)</td>
</tr>
<tr>
<td>BMI, median (IQR)</td>
<td>26.19 (16.7-47.3)</td>
</tr>
<tr>
<td>Female, n (%)</td>
<td>89 (13%)</td>
</tr>
<tr>
<td>HAQ, median (IQR)</td>
<td>0.29 (0.2-1.5)</td>
</tr>
</tbody>
</table>

Abstract AB1278 Table 2

<table>
<thead>
<tr>
<th>CRP, mg/dL</th>
<th>19 (13%)</th>
<th>0-0.27</th>
<th>0.36</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESR, mm/h; mean (SD)</td>
<td>37 (25.3%)</td>
<td>1-72</td>
<td>37.0 (15.96)</td>
</tr>
<tr>
<td>Anti-CarP, U/mL</td>
<td>4 (2.8%)</td>
<td>0-818</td>
<td>2.0</td>
</tr>
<tr>
<td>IgM</td>
<td>0 (0.0%)</td>
<td>0-56</td>
<td>5.45</td>
</tr>
<tr>
<td>IgG</td>
<td>6 (4.2%)</td>
<td>0-187</td>
<td>8.0</td>
</tr>
<tr>
<td>Rheumatoid Factor, U/mL</td>
<td>31 (21.5%)</td>
<td>0-120</td>
<td>6.96</td>
</tr>
<tr>
<td>IgA</td>
<td>64 (44.4%)</td>
<td>1-205</td>
<td>15</td>
</tr>
<tr>
<td>IgG</td>
<td>14 (9.7%)</td>
<td>1-160</td>
<td>3.04</td>
</tr>
<tr>
<td>ACPA-IgG, U/mL</td>
<td>10 (7%)</td>
<td>1-200</td>
<td>1.31</td>
</tr>
</tbody>
</table>

Conclusion: Even though we used the 3 isoforms of anti-CarP antibodies, the prevalence of these antibodies in our cohort showed less positivity than other cohorts, who only detected the IgG isoform, worldwide.

REFERENCES

Disclosure of Interests: None declared

AB1278 ANNNOUNCEMENT OF CHRONIC RHEUMATIC INFLAMMATORY DISEASE: THE RHEUMATOLOGIST’S POINT OF VIEW

Background: The onset of a chronic rheumatic inflammatory disease (CRD) is a turmoil in a patient’s life. The announcement, first step of information (a legal and ethical necessity), will leave a lasting impression on the patient’s history.

Methods: 39 private practice rheumatologists from the CREER group, 52% women, mean age 59 years. 222 CRD including 56% rheumatoid arthritis (RA), 27% spondyloarthropathy (SPA), 17% others. Survey including 31 questions. Direct eye contact 89%, gesture 56%, modulated tone 43%, silence 36%, compassionate approach 26%. Gaining confidence by: listening to, explanations, empathy, frankness.

The rheumatologist thinks that he is reassuring and comforting 100%, empathic 98%, transparent 72%. He calms 42%, supports, is optimistic because he is sensitive to the patient’s reactions 61%, but sometimes destabilized by a treatment refusal. He mentions life quality 51%, invites him to question it 58%, encourages him on a mutual management of the CRD 92% and insists on treatment compliance. He gives few documents, rarely mentions patient organizations, speaks about chronic disorder status, informs the treating physician and is always available.

Results: The announcement is different depending on: the type of CRD (59%), its presentation, the prognosis (29%), the induced emotion, the patient’s profile, 82% (intellect 41%, personality 22%, age 16%), the information to provide (course of treatment).

Duration of consultation: long 51%, doubled 64%. Time given to assimilate the information 93%, to discuss 90%. Explanations given 100%, rephrased 32%, repeated 27%, verified 9%.

Announcement unchanged if patient alone or accompanied; handling adapted to its degree of worry. If patient is anxious, depressive, rebellious or denying: see him again 29%, re-explain 22%, listen to, adapt.

When comparing the rheumatologist’s and the patient’s assessment about the announcement, there is globally an agreement, but it’s less affirmative for all the items. However, the patient thinks his rheumatologist more frank than he really is. Indeed, he announces with feeling and spends time on it, but not enough for the patient. He is less comforting, reassuring and explaining what he believes. He mentions the treatment inconveniences and life quality, which is well perceived. But he should guide more to annex treatments. For all the suggested items, the SPA patients are less optimistic than the RA patients.

Conclusion: the announcement takes into account above all the patient’s profile, the type and the seriousness of the CRD. The rheumatologist dedicates a lot of time on the announcement, which is made step by step, but still too fast for the patient. He explains, listens to, reassures, comforts by using human methods to gain the patient’s confidence. He supports him and helps him to manage his disease. He involves the patient and stays available. The patient feels well informed and taken care of in his entirety with empathy.

REFERENCES
[1] CREER group
[2] Disclosure of Interests: None declared

AB1279 PHYSICAL ACTIVITY LEVELS AND ATTITUDES IN PATIENTS WITH AXIAL AND PERIPHERAL SPONDYLOARTHRITIS

Shao-Hsien Liu, Divya Shridharmurthy, Kate Lapane, Stephen Morais, Catherine Dubé, Jonathan Kay. University of Massachusetts Medical School, Worcester, United States of America

Background: Spondyloarthritides is one of the common inflammatory rheumatic diseases in adults, with an overall prevalence of 0.5 to 1%. Based on clinical manifestations and the Assessment in Spondyloarthritides International Society (ASAS) criteria, spondyloarthritides can be distinguished as predominately axial or peripheral. Despite the health-related benefits of regular physical activity, patients with spondyloarthritides, are generally less active than those without disease. Studies evaluating the differences in physical activity levels and attitudes towards exercise of patients with axial and peripheral spondyloarthritides are limited.

Objectives: To characterize and compare self-reported physical activity and attitudes towards exercise among patients with axial and peripheral spondyloarthritides.

Methods: We used baseline information from an on-going, longitudinal, single-site, prospective cohort study consisting of 244 patients with spondyloarthritides including psoriatic arthritis, anklyosing spondylitis, and other spondyloarthropathies. Attitudes and beliefs towards exercise were assessed from 5 domains including: 1) general attitude towards exercise; 2) support from other people; 3) benefits in exercise/physically active; 4) concerns about being active; and 5) exercise/physical activity behavior. A continuous, 100-point scale (range: 0-100) was used to evaluate each attitude and beliefs towards exercise. High scores indicated that the individual found exercise more beneficial and/or liked engaging in physical activity. Physical activity levels were assessed using

Disclosure of Interests: None declared

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Disclosure of Interests: None declared
the total metabolic equivalent (MET) to incorporate the frequency, duration and intensity by different type of activities. Minutes spent in each level of activity (e.g., sedentary, moderate, and vigorous) were then summed for each week. Adjusted multivariable linear models estimated the relationship between physical activity levels and disease status.

Results: Overall, nearly 80% of the study sample had predominantly peripheral spondyloarthritis. The average age for participants with peripheral disease was 53.2 (standard deviation (SD):12.9) and for those with axial disease was 50.2 (SD: 12.4). Most of the study participants were men, white, non-Hispanic, married, and had attended at least some college, regardless of predominant joint distribution (peripheral versus axial).

While the median for general attitude towards regular exercise in participants with peripheral disease was 88.5, the median score was 81.0 in participants with axial disease. The median score regarding benefits of exercise/physical activity to improve general function was 97.0 among participants with peripheral disease and 96.5 among those with axial disease; the median score for pain relief was 67.0 in participants with peripheral disease and 66.5 for those with axial disease. Regardless of predominant joint distribution, walking, bicycling, and swimming were the most common types of exercise. Compared to participants with predominately peripheral disease, participants with axial disease spent more time per week engaging in light physical activities (adjusted β: 13.0 hrs/week; 95% confidence interval: 0.4 to 25.6 hrs/week) after adjusting for sociodemographic and clinical factors.

Conclusion: Patients with spondyloarthritis have positive attitudes towards physical activity/exercise, regardless of their predominant joint distribution, and believe that these activities improve general function and, to a lesser extent, relieve pain. However, patients with axial disease spend more time per week engaging in light physical activities than do those with peripheral disease.

Acknowledgement: This work was supported by a generous donation from Timothy S. and Elaine L. Peterson.

Disclosure of Interests: Shao-Hsien Liu Grant/research support from: Novartis, Divya Shridharmurthy: None declared, Kate Lapanje Grant/research support from: Novartis, Merck, Pfizer, Janssen, Consultant for: Pfizer, Stephen Morais: None declared, Catherine Dubé Grant/research support from: Novartis, Jonathan Kay Grant/research support from: Gilead Sciences, Pfizer, UCB Pharma, Consultant for: AbbVie, Boehinger Ingelheim GmbH, Celgene Healthcare, Merck, Pfizer, Shire, Dohme Corp., Novartis Pharmaceuticals, Pfizer, Samsung Bioepis, Sandoz, UCBA Pharma.


REFERENCES

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Disclose of Interests: None declared


AB1280

EPIDEMOLOGICAL PROFILE OF PATIENTS WITH FIBROMYALGIA IN A SPECIALIZED INSTITUTE IN MEDELLÍN, COLOMBIA 2010-2016

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1Universidad Cooperativa de Colombia, Medellín, Colombia; 2Instituto Neurológico de Medellín, Colombia

Background: Fibromyalgia is a common cause of chronic musculoskeletal pain in the world, with diverse clinical manifestations and with a ruinous effect on the quality of life of patients. The estimations of prevalence in the general population are very variable (0.2% - 6.4%) as well as the clinical presentation.

Objectives: This study aims to describe the sociodemographic and clinical characteristics of patients with fibromyalgia treated in a specialized institution between 2010 and 2016, in Medellín, Colombia.

Methods: We performed a retrospective, descriptive, secondary source study of patients diagnosed with fibromyalgia from a specialized institution between 2010 and 2016. Descriptive statistics and period prevalence tools were applied for the variables studied, among which was evaluated the use of the diagnostic criteria (1990 or 2010) of the American College of Rheumatology.

Results: We evaluated 1106 records of patients diagnosed with fibromyalgia. The median age was 54 years (IQR 16), the age of greatest presentation is between 40 and 65 years for both sexes, 95.1% were women and a 51.1% were married or living with their partner. 23.6% of the patients had a basic and middle level education (secondary and technological level), 50% of the population came from the department of Antioquia (for a prevalence for this period in the year 2010 to 2016 of 0.017%), and 54% resided in the city Medellin. The proportion of people with low and medium low socioeconomic status was 26.3%, while 41.4% reported being active in a job. The symptoms most frequently presented among the patients were myalgia (70.2%), sleep disturbances (59.9%), chronic fatigue (49.5%), headache (47.3%) and muscular weakness (40.5%). When analyzing by sex, headaches were more frequent in women (48.8%) than in men (24.1%). The most commonly reported comorbidities were psychiatric disorders (31.1%, where depression was most recorded with 24.1%), migraine (30.9%) and hypertension (27.9%). The most used criteria to make the diagnosis of fibromyalgia were those of 1990 with 62.2%. Regarding treatment, the most used were serotonin reuptake inhibitors and dual inhibitors (52.6%), along with acetaminophen (41.2%) and pregabalin (39%); only 8.2% of patients received non-pharmacological interventions (physical and psychological therapy).

Conclusion: Fibromyalgia is an important pathology in specialized medical consultation, accompanied by myalgia, sleep disturbances, chronic fatigue, headaches and muscle weakness. Psychiatric pathologies are the most frequently associated comorbidities and the 2010 criteria of the American College of Rheumatology are not yet widely applied. The treatment of fibromyalgia is complex and probably more effective with a transdisciplinary approach involving both pharmacological and non-pharmacological interventions.

REFERENCES


AB1281

USAGE OF PROOF-BP TO PREDICT HYPERTENSION IN MEXICAN-MESTIZO RHEUMATIC PATIENTS

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1Hospital Universitario, “Dr. José Eleuterio González”, UANL, Rheumatology, Monterrey, Mexico; 2Hospital Universidad, “Dr. José Eleuterio González”, UANL, Cardiology, Monterrey, Mexico.

Background: Subjects with rheumatic diseases have an increased risk of cardiovascular morbimortality. Hypertension (HTN) is a key modifiable risk factor for cardiovascular events (1). A recently published and validated prediction model (Predicting Out-of-Office Blood Pressure, PROOF-BP) has been proposed as a tool to improve diagnosis of HTN, and detection of out-of-office HTN in subjects with a previous diagnosis, with a c-statistic (AUC) of 0.86 in non-rheumatic subjects (2). This model has not been explored in rheumatic patients.

Objectives: To evaluate the diagnostic performance of the PROOF-BP algorithm for the prediction of HTN in subjects with/without rheumatic diseases.

Methods: A cross-sectional, observational trial was designed. Subjects were recruited at a rheumatology outpatient clinic in northeastern Mexico. Subjects with/without rheumatologic conditions were recruited. Complete clinical history with somatometry of each subject was registered. BP was measured by an experienced healthcare provider using current recommendations, with an OMRON HEM-7121 BP monitor. Calculations using the PROOF-BP online site were done, and risk categories were assigned to each subject using their predicted out-of-office BP: low (<130/80 mmHg), medium (130/80-145/90 mmHg) and high risk (>145/90 mmHg). Subjects in the medium and high risk strata were then asked to return for further evaluation and additional BP measurement, to define each diagnosis of HTN. We used frequencies (%) and median (IQR) for descriptive analysis. Diagnostic accuracy of each category was determined using 2 x 2 tables.

Results: A total of 217 subjects were included. Baseline characteristics are shown in Table 1. The most frequent rheumatic disease was RA (n=78, 35.9%). Using PROOF-BP, 84 (38.7%) subjects were stratified as medium or high risk. Of these, only 36 (42.8%) returned for evaluation. A final diagnosis of HTN was attained in 14 (38.8%) of those who returned. Diagnostic performances of the low and high risk categories are shown in Table 2. In 21 (67.7%) cases of the medium risk category the
A Big-data Approach to Electronic Health Record Data – Using Dimensionality Reduction and Clustering Techniques to Study Longitudinal Relationships Between Diseases

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Background: Hypothesis-free, longitudinal collection of patient health data in the form of Electronic Health Records (EHR) offers a wealth of valuable information on complex, slow-developing diseases in regard to aetiology and comorbidities. Conventional analytical methods are ill suited for the highly dimensional, sparse data contained within EHR, highlighting a need for more sophisticated, high-throughput tools. As t-Distributed Stochastic Neighbour Embedding (t-SNE) and Density-Based Spatial Clustering of Applications with Noise (DBScan) are designed to identify patterns in high-dimensional data with possible non-linear relationships, we hypothesized that these methods can aid identification of associations in diseases with multiple aetiologies.

Objectives: Proof of principle showcasing the value of t-SNE and DBScan in detecting longitudinal relationships between diseases in EHR data.

Methods: The Partners HealthCare Biobank from Boston, Massachusetts, includes 64,819 patients with longitudinal visit data from hospitals and general practitioners between June 1987 and June 2017. Each visit and procedure (N = 24,377,442) is coupled to an ICD code (International Classification of Disease) describing a disease or examination. We randomly split the data into two datasets of 32,424 and 32,395 individuals: set 1 to optimise t-SNE and DBScan and set 2 for replication. To trim the overly detailed hierarchy of ICDs, we translated them to Phenotype Codes (PheCodes).[3] t-SNE further reduced dimensionality and indicated groups of patients based on their PheCodes and separated patients based on PheCode patterns rather than singular codes. Subsequently DBScan identified clusters of patients in t-SNE space, by grouping patients based on relative Euclidean distance. Finally transition-probability matrices were constructed for all codes in each cluster, from which probabilities, clusters could be constructed. We defined replication as an overlap in ≥25% of the PheCodes between a cluster of set 1 and 2. Similarity was further assessed by calculating the absolute dissimilarity in transition probabilities for codes shared by matched clusters.

AB1282

A BIG-DATA APPROACH TO ELECTRONIC HEALTH RECORD DATA – USING DIMENSIONALITY REDUCTION AND CLUSTERING TECHNIQUES TO STUDY LONGITUDINAL RELATIONSHIPS BETWEEN DISEASES

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REFERENCES

Disclosure of Interests: None declared


RESULTS
The average (range) number of codes per individual was 376.3 (1–8,419) and 375.9 (1–10,315) spread over 4106 (1–10,781) and 4153 (1–10,746) days for set 1 and 2 respectively. Even though our input data was a sparse, high-dimensional (1,865) matrix of PheCodes, t-SNE and DBScan could clearly separate various unique patient groups with 284 and 295 clusters in set 1 and 2. Clusters consisted of patients with PheCodes of well-defined disease entities such as cardiovascular diseases and neurological disorders with objectively meaningful disease sequences. 34.5% of the clusters identified in set 1 were replicated in set 2 based on our replication criteria. Figure 1 shows the results of each step.

Conclusion: Our proof of principle supports the use of unsupervised techniques such as dimensionality reduction and data clustering to identify longitudinal associations between medical events. These methods could prove useful in our quest to identify medical risk factors for incompletely understood diseases.

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Disclosure of Interests: Marc Maurits: None declared, Thomas Huizinga Consultant for: Merck, UCB, Bristol Myers Squibb, Biotest AG, Pfizer, GSK, Novartis, Roche, Sanofi-Aventis, Abbott, Crescendo Bioscience Inc., Nycomed, Boeringer, Takeda, Zydis, Epirus, Eli Lilly, Soumya Raychaudhuri: None declared, Marcel Reinders: None declared, Elizabeth Karlson: None declared, Erik van den Akker: None declared, Rachel Knevel: None declared


Figure 1

Figure 1
WHEN SHOULD WE EVALUATE CYTOMEGALOVIRUS INFECTION IN IMMUNOSUPPRESSED PATIENTS WITH CONNECTIVE TISSUE DISEASES?

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Background: Cytomegalovirus (CMV) infection is an opportunistic and often problematic infection in patients with connective tissue diseases (CTD patients) who undergoes immunosuppressive therapy. However, in immunosuppressed CTD patients, CMV infection tends to be overdiagnosed, because it manifests with various symptoms and shows organ involvement. Little is known about when to suspect CMV infection and when to conduct CMV pp65 antigenemia assay in immunosuppressed CTD patients.

Objectives: To investigate the characteristics of patients who underwent CMV antigenemia assay and indirectly contributing factors of CMV infection in immunosuppressed CTD patients in a single center of Japan.

Methods: Medical records of hospitalized CTD patients who underwent CMV antigenemia assays between April 2015 and July 2018 were retrospectively reviewed. Patients were divided into groups with/without CMV antigenemia. Clinical features, basal immunosuppressive therapies, and laboratory data were analyzed.

Results: Overall, 108 patients were enrolled into the study; of these, the positive (group A) and negative (group B) CMV antigenemia groups had 49 and 59 patients, respectively. The underlying CTDs included systemic lupus erythematosus (n=27), anti-neutrophil cytoplasmic antibody-associated vasculitis (n=26), rheumatoid arthritis (n=22), polymyositis/dermatomyositis (n=13), and others (n=20). Glucocorticoid was used in 101 (93.5%) patients, and mean prednisolone dose was 27.1±18.3 mg/day. Pulse glucocorticoid therapy and intravenous cyclophosphamide (IVCY) therapy was administered in 14 (13.0%) and 22 (20.4%) patients, respectively. Group A patients had a significantly higher rate of Charlson Comorbidity Index (CCI) ≥3 (69.4% vs. 30.5%, p<0.001). Mean prednisolone dose was significantly higher in Group A (32.9±15.5 mg/day vs. 22.3±19.0 mg/day, p<0.001). Pulse glucocorticoid therapy (26.5% vs. 1.7%, p<0.001) and IVCY (36.7% vs. 6.8%, p<0.001) were administrated significantly more often to Group A patients than Group B. Multivariate logistic regression analysis revealed CCI ≥3 (odds ratio (OR) =3.21, 95% CI 1.13-9.16) and IVCY therapy (OR=8.89, 95% CI 1.99-39.7) as independent risk factors of CMV antigenemia. The result suggested that pulse glucocorticoid therapy could relate to CMV antigenemia (OR = 9.07, 95% CI 0.96-85.7).

Based on the prediction criteria for CMV antigenemia defined as the presence of one or more contributing factors including CCI ≥3, pulse glucocorticoid therapy, IVCY, and myelosuppression; sensitivity and specificity were 89.8% (95% CI 81.3-98.4) and 44.1% (95% CI 31.4-56.8), respectively. With contributing factors limited to CCI ≥3 and IVCY, sensitivity and specificity became 75.5% (95% CI 63.5-87.5) and 64.4% (95% CI 52.2-76.6), respectively.

Conclusion: Having multiple comorbidities and being on intensive immunosuppressive therapy, such as pulse glucocorticoid therapy and IVCY, were related to CMV antigenemia in CTD patients. The prediction criteria, including CCI ≥3, pulse glucocorticoid therapy, IVCY, and myelosuppression are helpful to clinically rule out CMV infection.

Disclosure of Interests: None declared

THE PATIENT EXPERIENCE: A PROCESS EVALUATION OF A PILOT PRAGMATIC USING REMOTE MONITORING OF SYMPTOMS

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Background: Traditional randomized controlled trials (RCTs) are important for testing drug efficacy but this study design is burdensome for patients (pts) and clinicians. Pragmatic trials addressing real world comparative effectiveness are equally important but challenging to conduct. We piloted a trial platform aspiring to optimize the patient experience and minimize patient and physician burden. The trial (NCT02912221) tests an incentive strategy informed by behavioral economics to increase physical activity in pts with rheumatoid arthritis (RA) and psoriatic arthritis (PsA).

Objectives: To understand patient experiences using mobile applications (apps) and wearable activity devices (WAD) in a pilot pragmatic trial

Methods: Pts had RA or PsA with active disease defined by a Routine Assessment of Patient Index Data (RAPID3) score ≥3 (range 0-30). After screening and informed consent, pts received a WAD (Fitbit™) and were asked to set up the device and an Arthritis Tower account, a research registry where pts track patient-reported outcomes (PRO). A web-based platform, WayToHealth, was used to collect WAD data and deliver incentives. After a two-week baseline period, pts selected a daily step goal and were randomized to a financial loss-aversion incentive arm or control. In both arms received weekly text messages reporting the number of days the step goal was met. In-person assessments were conducted at baseline and 14 weeks; pts completed weekly PROs (RAPID3, PROMIS Fatigue, PROMIS Sleep Disturbance and adverse event assessment) via mobile app or a web link. At 14 weeks, pts underwent a semi-structured interview to assess the patient experience in the trial. Content analysis was used to evaluate the responses.

Results: To date, 27 pts completed the 14-week follow-up interview. Mean age was 48 (SD 14), 85% were women, 17 (63%) had PsA and 10 (37%) had RA. Mean disease duration was 9 years, mean swollen joint count (0-66) was 6.2 (SD 5.6) and tender joint count (0-68) was 8.1 (SD 9.1). The mean RAPID3 was 10.3 (SD 4.6). Overall pts enjoyed participation in the study and provided useful feedback for improvement (Table). Weekly PRO capture was acceptable to most but PROs need to be streamlined to remove repetitive questions. Pts frequently set goals they were not able to achieve and suggested the ability to change their goal in future studies.

Conclusion: In this pilot pragmatic trial, only two in-office visits were conducted and all other data captured remotely. Pts enjoyed the experience and found the digital platform easy to use. Such trial designs will become increasingly important in conducting real-world comparative effectiveness and adjunct therapy trials.

Table: Lessons learned from patient perspective in pragmatic trial

<table>
<thead>
<tr>
<th>Trial Format</th>
<th>Pts enjoyed tracking progress</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weekly check ins kept pts accountable</td>
<td></td>
</tr>
<tr>
<td>Most pts completed surveys via a text link (over App or web portal)</td>
<td></td>
</tr>
<tr>
<td>Time to complete surveys was 5 min</td>
<td></td>
</tr>
<tr>
<td>Pts requested a text box to record reasons for not feeling well (e.g., injury, illness)</td>
<td></td>
</tr>
</tbody>
</table>

PROs
| Repetitive questions in the PROMIS measures annoyed pts |
| MDHQ questions were not always relevant |
| Tracking sleep helped understand level of fatigue |
| Emotional wellbeing questions were appreciated |
| Desire to track individual PRO goals |

Wearable Activity Device
| Served as a reminder to move |
| Annoyed by need to charge |
| Creating teams and self-competition was motivating and fun |

Some exercise not captured (e.g., swimming, biking)

Physical activity
| Goals frequently set too high; allow for a goal change |
| Weekly goals may be better than daily goals |
| Weather influenced physical activity; being accountable encouraged exercise indoors |
| Overexertion sometimes lead to pain and stiffness |
| Some reported knee/foot pain with increasing steps |

Disclosure of Interests: Alexis Ogdie Grant/research support from: (To my university) Novartis, Pfizer, Grant/research support from: Novartis, Pfizer, Consultant for: AbbVie, Bristol-Myers Squibb, Celgene, Corrona, Eli Lilly and Company, Novartis, Pfizer, and Takeda, Consultant for: AbbVie, Amgen, Bristol-Myers Squibb, Celgene, Corrona, Eli Lilly and Company, Novartis, Pfizer, and Takeda, Consultant for: AbbVie, Pfizer, Amgen, BMS, Celgene, Corrona, Lilly, Novartis, Pfizer, Takeda, Consultant for: AbbVie, Amgen, BMS, Celgene, Corrona, Lilly, Novartis, Pfizer, Takeda, Michael George Grant/research support from: BMS, Consultant for: AbbVie, Kathleen Bush: None declared, Mitesh Patel: None declared, W. Benjamin Novell1: None declared, Joshua Baker1: None declared.

IGA RF IS ASSOCIATED WITH HIGH AGE OF RHEUMATOID ARTHRITIS ONSET

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Background: IgM RF and anti-CCP2 have been shown to associate with young age at RA diagnosis [1, 2]. By contrast, little is known about the association between other RF isotypes and age at onset, or sex.

Objectives: To examine the association between individual RA autoantibodies, sex and age at RA onset.

Methods: Anti-CCP2, IgA-, IgG- and IgM-RF were analysed centrally in baseline sera from 1600 Epidemiological Investigations in RA (EIRA) patients aged 18-70 years and classified according to the 1987 ACR criteria within one year of first symptoms. Cut-offs for RF isotypes were determined at the 98th percentile based on the EIRA RA-free controls, close to the 98.4% anti-CCP2 specificity.

Results: Anti-CCP2, IgA-, IgG- and IgM RF were found in 1020 (64%), 692 (43%), 529 (33%), and 916 (57%), of the patients, respectively. Mean (median) age at diagnosis among men was 54 (57) year, higher than 51 (54) years among women (p<0.0001). The figure shows the autoantibody distribution in relation to sex and age tertiles. In univariate analysis, anti-CCP2 and IgM RF were both associated with lower age at RA diagnosis (table). When occurrence of all four autoantibodies were compared simultaneously as independent variables and with age at diagnosis as dependent variable in multiple regression, a strong association between IgA RF and higher age at RA diagnosis appeared, and the association between IgM RF and low age at RA diagnosis weakened (table). IgA RF and IgG RF associated with male sex, but IgM RF with female sex. No sex-difference was seen for anti-CCP2 (table). When the multiple regression was adjusted for sex, the association between IgM RF and age disappeared, whereas the strong associations between IgA RF and high age and between anti-CCP2 and low age at diagnosis persisted (table).

Conclusion: On average, IgA RF positive (vs. negative) RA patients are almost four years older at the time of diagnosis; the opposite was found for anti-CCP2 and IgM RF. Whereas sex-differences explain the age-association for IgM RF, this is not the case for anti-CCP2 and for IgA RF.

REFERENCES

<table>
<thead>
<tr>
<th>Anti-CCP2</th>
<th>P</th>
<th>IgA RF</th>
<th>P</th>
<th>IgG RF</th>
<th>P</th>
<th>IgM RF</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pos/ Neg</td>
<td>1020/580</td>
<td>962/908</td>
<td>529/1071</td>
<td>916/684</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (mean)</td>
<td>53/51</td>
<td>&lt;0.0001</td>
<td>0.08</td>
<td>0.98</td>
<td>51/53</td>
<td>0.0042</td>
<td></td>
</tr>
<tr>
<td>Age (least squares mean multivariate)</td>
<td>55.5/51</td>
<td>&lt;0.0001</td>
<td>55.52</td>
<td>&lt;0.0001</td>
<td>55.53</td>
<td>0.7170</td>
<td>52.54</td>
</tr>
<tr>
<td>Age (corr sex)</td>
<td>52.55</td>
<td>&lt;0.0001</td>
<td>55.52</td>
<td>&lt;0.0001</td>
<td>54.53</td>
<td>0.9378</td>
<td>53.54</td>
</tr>
<tr>
<td>Females n(%)</td>
<td>727/715</td>
<td>55.05</td>
<td>0.0050</td>
<td>0.0089</td>
<td>665/65</td>
<td>0.0027</td>
<td></td>
</tr>
<tr>
<td>(71/69)</td>
<td>(66/66)</td>
<td>(71/73)</td>
<td>(72/73)</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Figure. Distribution of individual autoantibodies in relation to sex and age tertiles.

Disclosure of Interests: Eleftheria Pertsinidou: None declared, Lars Klareskog Grant/research support from: Yes, but not for the presented study., Lars Alfredsson: None declared, Linda Mathsson Employee of: employed by Thermo Fisher Scientific, Monika Hansson: None declared, Helga Westerlund: None declared, Johan Askling Grant/research support from: Karolinska Institutet (JA) has or has had research agreements with the following pharmaceutical companies, mainly in the context of the ATRIS national safety monitoring programme for rheumatology biologicals: Abbvie, BMS, MSD, Eli Lilly, Pfizer, Roche, Samsung Bioepis, and UCB., Consultant for: Karolinska Institutet has received remuneration for JA participating in ad boards arranged by Lilly, Novartis, and Pfizer., Saedis Saevarsdottir Employee of: Part-time employee at deCODE Genetics/ Amgen Inc, working on genetic research unrelated to this project., Johan Rönnelid: None declared

AB1286  EVALUATION OF CARDIOVASCULAR RISK FACTORS AND PREVALENCE OF METABOLIC SYNDROME IN PATIENTS WITH DIAGNOSIS OF ANKYLOSING SPONDYLITIS:

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Background: Cardiovascular events are the main causes of mortality in patients with Ankylosing Spondylitis. In addition, a higher prevalence of Metabolic Syndrome is reported in this group. With immunobiological therapy, much progress has been made in controlling the inflammatory process, but the cardiovascular risk remains high.

Objectives: To evaluate the prevalence of cardiovascular risk factors and Metabolic Syndrome in patients with Ankylosing Spondylitis at the Rheumatology Outpatient Clinic of HC-UFG and to correlate them with epidemiological, clinical, laboratory and radiographic characteristics of the disease.

Methods: Data from 59 patients were collected in medical records between July and August 2018. Clinical characteristics, cardiovascular risk factors and metabolic components were analyzed. Descriptive analyzes of the data were made, prevalences and their reasons were calculated. The associations between variables were assessed by chi-square test and Fisher’s exact test.

Results: 81.4% were male, 67.8% self-denominated non-whites, average age 46.7 years. Isolated axial joint involvement was the most frequently observed (54.2%). Enthesopathic lesions were identified in 30.51% of the cases. Uveitis had a higher prevalence (22.02%), 4.2 times higher in the subgroup with HLA-B27 positive (p=0.0002). HLA-B27 was present in 67.8%. Advanced sacroiliitis (grades 3 and 4) and syndesmophytosis were identified in 61.1% and 49.2%, respectively, but didn’t present significant correlation with the presence of HLA-B27. 64.4% were using anti-TNF alone or in combination. The majority of the patients (72.9%) were sedentary. Clinical comorbidities were reported in 66.1% of the cases, with dyslipidemia (45.8%), systemic arterial hypertension (37.6%) and diabetes mellitus (13.6%) being the most common. Metabolic Syndrome was diagnosed in 23.7% of the samples. Normal levels of triglycerides and fasting glycemia and lower prevalence of Metabolic Syndrome had a statistically significant association with the presence of HLA-B27 (p=0.006; 0.026 and 0.014, respectively). Patients with HLA-B27 present had 61% lower frequency of Metabolic Syndrome. There was no association between the syndrome and its components with anti-TNF therapy; BASDAI; BASFI; metric evaluation; uveitis; degree of sacroiliitis and syndesmophytosis.

Conclusions: The prevalence of Metabolic Syndrome was below that is described in other populations. The presence of HLA-B27 was considered a protective factor for Metabolic Syndrome, triglyceride levels and fasting glycemia. This finding may be related to the presence of several HLA-B27 alleles, usually non-subtyped, and to the great ethnic miscegenation of the Brazilian population. Our observation suggests that spondylitics should be routinely evaluated for cardiovascular risk factors.

REFERENCES


Disclosure of Interests: None declared

AB1287  DISEASE EVOLUTION OF PRIMARY SJOGREN’S SYNDROME – A LONGITUDINAL STUDY

Inês Reis de Figueiredo1, Jessica Tam2, Dennis Lendrem2, Josephine Vila3, Elizabeth Kidd4, Julie Norris5, Ben Hargreaves6, Wan Fai Ng7,8,11, Universidade de Doencas Auto-Imunes/Medicina 7.2, Hospital de Curit Cabral, Centro Hospitalar Universitário Lisboa Central (CHULC), Lisboa, Portugal; 7Macclesfield Research Group, Institute of Cellular Medicine, Newcastle University, Newcastle-Upon-Tyne, United Kingdom; 8Newcastle-upon-Tyne Hospitals NHS Foundation Trust, Newcastle-Upon-Tyne, United Kingdom

Background: The natural history of primary Sjögren’s syndrome (pSS) remains poorly understood. It has been suggested that the initial presentations may predict the course of disease (1), with gradual reduction of biological activity as measured by serum Immunoglobulins levels (2), while symptoms such as fatigue remaining stable over time(3).

Objectives: To evaluate how pSS progresses over time using ESSDAI (Eular Sjögren’s Syndrome Disease Activity Index) and the ESSPRI (Eular Sjögren’s Syndrome Patient Index), ECO2-Time trade off (TTO) and Visual Analogue Scale (VAS) of health states.

Methods: Routine clinical data from a large single centre cohort in the UK were analysed on patients with ≥3 clinical visits, including up to the 10th visit. Outcomes (ESSDAI/ESSPRI and their component scores, ECO2-3L and VAS) were analyzed by a random effects linear regression using STATA 14.

Results: 346 patients out of 856 included, with a female preponderance of 89%, and median age of 63 years. The median follow up time was 4.9 years, and median disease duration of 12 years. Anti-Ro was positive in 61%, and anti-La in 42% of the patients. ESSDAI score decreased 0.1 point per visit (p=0.006). Anti-Ro and anti-La positive patients exhibiting a lower score (p=0.012 and 0.031), and patients with MALT at presentation had a score up to 6 points higher (p= 0.002). Regarding the ESSDAI domains, the constitutional and haematological domains showed increased activity (p-values<0.0001 and 0.018), with Anti-Ro and/or Anti-La patients having higher scores (p<0.0001 and 0.001). In contrast, the glandular, articular and peripheral nervous system domains showed decreases over time (p-values 0.003, 0.006 and <0.0001). ESSPRI score increased 0.05 point/visit (p<0.0001). While Dryness scores remained relatively constant, Pain and Fatigue components of the ESSPRI increased over time (both p<0.0001). Dryness scores were higher in female patients (p=0.04). ECO2-TTO worsened by 0.03 point/visit (p<0.0001), but the VAS health states remained stable.

Conclusion: Our data suggest that symptoms of fatigue and pain as well as health utility worsen over time, whereas different ESSDAI domains showed different trends over time. Longer term follow-up to further understand the natural history of pSS is warranted.

REFERENCES


Disclosure of Interests: None declared

AB1288  PREVENTION OF VENOUS THROMBOEMBOLISM AND THE RISK OF POSTOPERATIVE COMPLICATIONS IN PATIENTS WITH RHEUMATOID ARTHRITIS AFTER TOTAL HIP ARTHROPLASTY:

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Background: According to the administrative data, confirmed by several meta-analyses, patients with rheumatoid arthritis (RA) in comparison with the General population shows an increased risk of venous thromboembolic complications more than twice. Drug prevention can reduce the risk of venous thromboembolism (VTE) in patients with rheumatic diseases.

Objectives: The aim of this study was to analyze frequency of VTE, risk of bleeding and complications of the postoperative wound in patients with RA and osteoarthritis (OA) who underwent primary THA. Each group of patients was divided into 3 subgroups by type of drug therapy (1-nadroparin calcium; 2-dabigatran etexilate; 3-nadroparin calcium with transfer to dabigatran etexilate).

Methods: Study included 486 patients (212 - with RA and 274 - with OA) who underwent primary THA. Each group of patients was divided into 3 subgroups by type of drug therapy (1-nadroparin calcium; 2-dabigatran etexilate; 3-nadroparin calcium with transfer to dabigatran etexilate). Intra-and postoperative blood loss and the wound healing process were assessed during the first 7 days after surgery.

Results: Postoperative VTE were reported in 36 (7.4%) of 486 patients. VTE in patients with RA were detected significantly less frequently than in OA (1.2% and 6.1%, p = 0.0013). Bleeding that required transfusion
of blood in RA were found significantly more often than in OA (respectively 14.4% and 5.7% of cases; P<0.001). The number of cases requiring cancellation of anti-coagulant therapy in patients with RA was significantly higher compared with the OA group (6.4% and 1.4%, respectively). Slow wound healing in RA was more common (n = 56; 26.4%) than in OA (n = 14; 5.1%). In patients who underwent monotherapy with calcium nadroparin VTE occurred more often than when using combination therapy (p<0.0001) and more often than in the group of dabigatran etexilate (p = 0.054).

Conclusion: The frequency of VTE, the risk of bleeding and complications of postoperative wound in patients with RA and OA after THA were analyzed. So, our study determined the dependence of VTE complications and bleeding risk according to the patient's underlying nosology. Also the advantage of combined postoperative therapy over others was evaluated.

Disclosure of Interests: None declared

Results: Among 64 patients included a musculoskeletal syndrome was detected in 46 patients (71.8%), whereas diffuse muscle pain was observed in 42 (65.6%) patients, and 83% of them had associated arthritis. Serological, imaging and clinical findings suggested more frequently a seronegative arthritis, whereas few patients developed rheumatoid arthritis and arthritis secondary to a connective tissue disease. A direct correlation between pre-existing autoimmune disease and pain symptoms before cancer diagnosis and risk of developing arthritis under AI therapy was observed. Mean vitamin D levels were significantly lower in patients with diffuse myalgia compared to patients with no diffuse myalgia (11.2±5.8 versus 29.5±10.8 ng/ml; t-test p < 0.0001), suggesting a potential involvement of vitamin D deficiency in diffuse muscle pain.

Conclusion: The etiology of AI-associated pain syndrome remain unknown, but clinical, serological, imaging data may be useful to identify the true origin of the musculoskeletal syndrome, as well as a detailed anamnestic history may be useful to identify autoimmune predisposing factors. Myalgias and generalized weakness are likely associated with hypovitaminosis D and might be misdiagnosed as fibromyalgia. The management of these patients should become a multispecialistic task.

REFERENCES


Disclosure of Interests: Stefania Sciacca: None declared, Nadia Melillo: None declared, Francesco Paolo Cantatore Speakers bureau: PFIZER, ROCHE


AB1291 ASSOCIATION OF CCL2 GENE POLYMORPHISMS AND THEIR SERUM LEVELS WITH SUSCEPTIBILITY TO KNEE OSTEOARTHRITIS

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Background: Osteoarthritis (OA) is one of the most depleting chronic disorders and its pathogenesis is yet to be unfold. It is characterized by pain, swelling, stiffness, decreased ability to move and, sometimes, the formation of bone spurs. Knee Osteoarthritis (KOA) is multifactorial and remains largely understudied at molecular level. The available literature suggested that the development, onset and progression of OA is significantly affected by genetic factors. Chemokines are small, secreted proteins that released from chondrocytes and synovial fibroblasts of KOA patients. In this case control study, we investigated the possible association between promoter polymorphisms rs1024611 and the polymorphism rs4586 in exon 2 of the chemokine (C–C motif) ligand 2 (CCL2) gene and knee OA.

Objectives: To investigate the possible association between promoter polymorphisms rs1024611 and the polymorphism rs4586 in exon 2 of the CCL2 gene and KOA.

Methods: DNA was obtained from 300 primary knee OA patients and 300 healthy controls. CCL2 genomic variants (rs1024611 and rs4586 polymorphisms) were detected by polymerase chain reaction restriction fragment length polymorphism (PCR-RFLP). In addition, the effect of serum levels of rs1024611 and rs4586 on lesions and controls were examined by enzyme-linked immunosorbent assay (ELISA).

Results: The rs1024611 A/G promoter polymorphism was associated with KOA [genotype frequency, p= 0.007; allele frequency, p= 0.01]. Significant association was observed between the G carrier of the rs1024611 A/G promoter polymorphism and primary knee OA patients (p=0.01). However, no significant difference was found in the rs4586 polymorphism. Haplotype type frequency analysis revealed a significant difference (x²= 8.01, p=0.02). The CCL2 serum levels of subject with the G carrier (285.0 ± 86.5 pg/mL) of the rs1024611 A/G promoter polymorphism was statistically higher than that of subjects with the non-G carrier (160.5±47.8 pg/mL). Further in relation with clinical severity of KOA, we observed significant association of the G carrier of the rs1024611 A/G promoter polymorphism with both Visual analogue scale (VAS) (p<0.01) and Western Ontario and McMaster Universities (WOMAC) score (p<0.05).

Conclusion: The G carrier of the rs1024611 A/G promoter polymorphism was found to be associated with primary knee OA, and could be a susceptibility factor in the development of primary knee OA in the North Indian population.

REFERENCES


AB1292 PREVALENCE OF VITAMIN D DEFICIENCY AND ITS ASSOCIATED FACTORS AMONG RHEUMATOID ARTHRITIS PATIENTS MANAGED IN A RHEUMATOLOGY UNIT OF A TERTIARY CARE HOSPITAL IN SRI LANKA

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Background: Prevalence of unrecognized vitamin D deficiency can be high among Rheumatoid Arthritis (RA) patients. Lack of mobility among these patients prevent them receiving adequate sun exposure. Low levels of vitamin D could potentially cause a higher disease burden and disease activity.

Objectives: To determine the prevalence of vitamin D deficiency and its associated factors among RA patients managed in a rheumatology unit of National Hospital of Sri Lanka (NHSL).

Methods: A descriptive cross-sectional study was done among patients with RA with a calculated sample size of 137. Being diagnosed according to ACR – EULAR criteria and availability of serum vitamin D level were among the inclusion criteria. Patients with disability due to causes other than RA were excluded. All patients satisfying the eligibility criteria were invited to be recruited. A data extraction sheet was utilized. Data was collected by investigators. The associations were evaluated with Chi square test and Spearman correlation coefficient at a significance level of 5%. Ethics approval was obtained from ethics committee of NHSL.

Results: The response rate was 92%. The median (IQR) age of participants’ were 56.5 (49.0 to 64.25). Among participants, majority (n=117, 92.9%) was females. Only 11.1% (n=14) had normal vitamin D levels. The insufficient and deficient categories comprised of 38.1% (n=48) and 50.8% (n=64). The commonest symptoms included; joint pain (n=101,80.2%), fatigue (n=84,66.7%) and muscle pain (n=78,61.9%). Deficiency or insufficiency was lowest in the occupation category of “agricultural and labourer” (37.5%) while 100% in many indoor-occupied categories and among Muslims. “Deficiency or insufficiency” was significantly associated with muscle pain (p<0.001) but not with CDAI (p=0.896), fatigue (p=0.549), joint pain (p=0.735).

Conclusion: Vitamin D “deficiency or insufficiency” is common among patients with RA and commoner in the sub-categories with muscle pain and with restricted sun-exposure. More research must be promoted in this regard.

REFERENCES


Disclosure of Interests: None declared

AB1293

SMAD3 GENE POLYMORPHISMS AND EXPRESSION IN SERUM AND CARTILAGE INFLUENCE THE RISK OF KNEE OSTEOARTHRITIS

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Background: Knee Osteoarthritis (KO A) is the most common degenerative arthritis, a type of arthritis that is caused by breakdown of articular cartilage with eventual loss of the cartilage of the joints. Smad3 is a key intracellular messenger in the transforming growth factor β signaling pathway. Previous study suggested Smad3 gene mutation is a possible predisposing factor for human OA and found gene mutation in OA, providing insight into the function of SMAD3 mediated TGF-β signals in the development of OA and also suggested that Smad3 gene mutation may be a risk factor for genetic susceptibilities to OA. In this case control study, we investigated the possible correlation between the SNPs Smad3 (rs6494629, FokI; A/C; rs2289263) in Smad3 gene and susceptibility to OA and validated in serum and cartilage.

Objectives: To investigate the possible association between SNPs (rs6494629 and rs2289263) of the Smad3 gene and KOA.

Methods: In this study cases consisted of men and women >40 years that fulfilled American College of Rheumatology (ACR) clinical and radiographic criteria for knee OA. Venous blood samples were obtained from all cases as well as controls for genetic analysis. Polymerase chain reactions were performed for SNP analysis using specific primer. Total protein was measured in serum by an enzyme linked immunosorbsent assay according to the manufacturer’s Protocol (ELISA) and in cartilage tissue done by western blot.

Results: A total of 200 cases that confirmed radiographic knee OA and equal number of age and sex matched healthy controls were enrolled. There was no significant difference in demographic characteristics between the cases and controls. A SNP (rs6494629 and rs2289263) mapping to intron 1 of SMAD3 was associated with knee OA (P < 0.013 and P < 0.044, respectively). Within the SNPs (rs6494629) of Smad3 gene, genotype CC and CT was found to be significantly (p<0.013) associated with knee OA as compared with the CC genotype and SNP rs2289263 genotype CC and CA was found to be significantly (p<0.044) associated with knee OA as compared with the AA genotype. In addition when alleles were compared, C allele of both the studied SNP was observed to be significantly associated with knee OA. Serum levels of Smad3 in KOA patients with rs6494629 TT, CT and CC genotypes were significantly higher than healthy subjects with the same rs6494629C/CT genotypes (all P < 0.001, P < 0.0006, P < 0.017 respectively). Increased serum levels of Smad3 were also observed in KOA patients with rs2289263 AA, CA and CC genotypes compared to controls (all P < 0.006, P < 0.0006, P<0.004). We performed Immunoblot analysis on cartilage tissue from 15 cases and 10 controls. The Smad3 level in cases was significantly higher than controls (P < 0.006).

Conclusion: Our data indicate that genetic variation in the SMAD3 gene is involved in the risk of knee OA in North Indian populations, confirming the results from previous studies on the potential importance of this gene in the pathogenesis of OA. Further we also validated these genetic variations at protein level in both blood and tissue and found significant association.

REFERENCES


Disclosure of Interests: None declared

AB1294

IMPACT OF INFERTILITY, PREGNANCY LOSS AND CHILDBEARING DECISION ON FAMILY SIZE IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND RHEUMATOID ARTHRITIS

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Background: Systemic lupus erythematous (SLE) and Rheumatoid Arthritis (RA) often affects women in their reproductive years. These women are faced with a life-long illness that may have considerable impact not only on their physical health, but also on their reproductive potential. Fertility of these women may also be affected by the disease, treatment and/or organ damage.

Objectives: To determine the role of infertility, pregnancy loss and childbearing decision and patients concerns on family size in women with SLE and RA.

Methods: A cross sectional study using a self-administered reproductive history questionnaire completed by women with SLE/RA attending Rheumatology clinic follow up in Hospital Putrajaya, Hospital Tengku Ampuan Rahimah, and Hospital Raja Permaisuri Bainun, Malaysia from 1 January 2017 to 30 June 2017.

Within each disease cohort, women were identified into 3 groups, those with fewer children than planned (group A), those with same number of planned children (group B) and those with completed family or not interested in having any children (group C). Data on number of child, pregnancies, miscarriages and self reported infertility were recorded.

For group A, data on patient concerns and the factors that could impact family building were also obtained.

Results: Total of 110 women with SLE and 91 women with RA were surveyed. The mean age of women with SLE and RA were 37.6 years (+/- SD 7.4) and 45.37 years (+/- SD 11.7) respectively. Majority of women (48.8%) with SLE and RA were in group A with 59% (n=65) of women with SLE and 33% (n=33) of women with RA had fewer children than originally planned. The average numbers of pregnancies were similar in both cohorts, but women with SLE had less child and were more likely to report infertility and had higher rate of miscarriages (Table 1). SLE group A had a similar number of pregnancies, but 1 less child compared to SLE group B and C (Table 2). Similarly, among women with RA, group A had 1 less child with similar number pregnancies and miscarriage rate (Table 2). In both groups of women, concerns about inability to care for a child, damage from medications, and genetic transmission of their disease were associated with a lower pregnancy rate.

Table 1. Numbers of pregnancy, live births, miscarriages and rate of infertility among women with SLE and RA

<table>
<thead>
<tr>
<th></th>
<th>SLE</th>
<th>RA</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of pregnancies</td>
<td>0.28±0.66</td>
<td>0.12±0.28</td>
</tr>
<tr>
<td>No. of miscarriages</td>
<td>0.06±0.20</td>
<td>0.03±0.15</td>
</tr>
<tr>
<td>No reporting infertility (%)</td>
<td>0.05±0.15</td>
<td>0.02±0.10</td>
</tr>
</tbody>
</table>

*values are the mean +/- SD unless otherwise indicated

Table 2. Pregnancy outcomes for women with SLE (n=110) and RA (n=91) *

<table>
<thead>
<tr>
<th></th>
<th>SLE</th>
<th>RA</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of women (n)</td>
<td>65 (59.1)</td>
<td>33 (36.3)</td>
</tr>
<tr>
<td>No. of pregnancies</td>
<td>2.11±0.76</td>
<td>2.03±0.79</td>
</tr>
<tr>
<td>No. of miscarriages</td>
<td>0.51±0.80</td>
<td>0.36±0.70</td>
</tr>
</tbody>
</table>

*values are the mean +/- SD unless otherwise indicated

Conclusion: In this population, more than half of women with RA or SLE had fewer children than desired. Other than patient choice, infertility and miscarriage also play an important role on family size.
DISCREPANCIES BETWEEN THE RHEUMATOID ARTHRITIS PATIENT POPULATION IN RANDOMIZED CONTROLLED TRIALS OF BILOGICS AND THAT IN REAL-WORLD SETTINGS: A STUDY USING THE IORRA COHORT

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Background: Randomized controlled trials (RCTs), which are currently considered to provide the highest level of evidence, include patients with high disease activity and exclude those with comorbidities often seen in real-world settings. With the increasing recognition of the importance of real-world evidence, attention is being given to discrepancies between RCT-based evidence and the patient population in routine clinical practice; however, few reports addressing these gaps in the context of rheumatoid arthritis (RA) are available.

Objectives: To evaluate the proportion of patients meeting the inclusion criteria in RCTs of biologics for the treatment of RA conducted in Japan using the real-world IORRA cohort.

Methods: The inclusion criteria used in Phase 2 or Phase 3 RCTs of the following biological DMARDs (bDMARDs) were extracted: infliximab (IFX), etanercept (ETN), adalimumab (ADA), golimumab (GLM), certolizumab (CZP), abatacept (ABT), tocilizumab (TCZ), and infliximab (IFX-BS). Patients participating in the IORRA study during the period when each RCT was conducted (Cohort A) and those who initiated treatment with each bDMARD at our institute in 2016 (Cohort B) were included in the analysis. The proportion of RA patients in Cohorts A and B who met the RCT inclusion criteria was assessed.

Results: A total of 19 RCTs were conducted in Japan (IFX: 2; ETN: 1; ADA: 2; GLM: 2; CZP: 3; ABT: 2; TCZ: 6; IFX-BS: 1). Key trial inclusion criteria were age, RA duration, tender joint count (TJC), swollen joint count (SJC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), methotrexate (MTX) use, corticosteroid use, and prior bDMARD therapy. The number of patients participating in the IORRA analysis during the period when each RCT was conducted ranged from 1,777 to 6,843 (mean = 5,470) (Cohort A). The median/average [range] proportion of RA patients meeting all RCT inclusion criteria was 0% [0.0–23%] [range: 0.0–16.2%]. The proportion by criterion was 93.9%/92.4% [59.7–99.9%] for age, 68.9%/57.1% [9.0–96.6%] for RA duration, 11.6%/16.0% [4.5–33.0%] for SJC, 14.6%/17.2% [3.7–33.9%] for TJC, 27.8%/32.1% [20.1–49.8%] for CRP, 60.2%/58.7% [43.7–66.8%] for ESR, 14.8%/40.6% [13.1–73.9%] for MTX use, 95.9%/99.3% [98.5–99.8%] for prednisolone (PSL) use, and 91.9%/92.0% [85.6–98.0%] for prior bDMARD use. In Cohort A, the proportion of RA patients meeting the RCT inclusion criteria was low, particularly with respect to SJC, TJC, and MTX use. Among 337 patients who initiated bDMARD therapy at our institute in 2016, a total of 139 biologic-naïve patients (IFX, 3; ETN, 33; ADA, 11; GLM, 21; CZP, 17; ABT, 25; TCZ, 28; IFX-BS, 1) were included in the analysis (Cohort B). In Cohort B, the median/average [range] proportion of RA patients meeting all RCT inclusion criteria was 0.0%/2.3% [range: 0.0–16.2%]. The proportion by criterion was 99.8%/99.1% [94.1–100%] for age, 20.8%/26.5% [0.0–57.1%] for SJC, 11.8%/17.0% [0.0–50.0%] for TJC, 33.3%/34.9% [0.0–66.7%] for CRP, 58.3%/57.3% [0.0–75.0%] for ESR, 23.5%/35.5% [0.0–100%] for MTX use, and 100%/100 [100% for PSL use. As in Cohort A, the proportion of RA patients meeting the inclusion criteria was low in Cohort B, particularly with respect to SJC, TJC, and MTX.

Conclusion: It is important to note that evidence from RCTs of bDMARDs is based on a limited RA population in real-world settings.

Disclosure of Interests: None declared.


PREGNANCY IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS: MATERNAL AND FETAL COMPLICATIONS

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Background: Systemic lupus erythematosus is a chronic autoimmune disease often affecting women in fertile age. The physiological changes in T-regulators (Th1/Th2) activity during pregnancy can cause SLE flare. Women with SLE are at high risk for maternal and fetal complications. The high SLE activity is associated with higher risk of PE and lower birth weight, compared with population controls. Nevertheless, no detailed analysis of the relationship between clinical features/laboratory parameters and unfavorable pregnancy outcome in patients with SLE has been carried out in the recent studies.

Objectives: This study aimed to analyze influence of SLE activity, laboratory parameters and medications on risk of maternal and fetal complications.

Methods: A retrospective single-center cohort study 11/2014-12/2018: 43 pregnancies in 42 patients with proved SLE and > 20 weeks of gestation, mean age was 31.5 years. Renal function at conception and after delivery, pregnancy outcomes, clinical and laboratory parameters were collected. PE was diagnosed by the WHO 2008 criteria. The sPT/PF/F ratio was used as the main differential marker to exclude lupus nephritis exacerbation in cases of increased proteinuria. All patients and their newborns were analyzed for hemoglobin and platelet levels, glomerular filtration rate, serum creatinine, AST, ALT, fibrinogen, D-dimer, aPTT antinuclear factor and antiphospholipid antibodies concentrations, the using/non-use of glucocorticoids, hydroxyclochloquine, low molecular weight heparins and aspirin were analyzed as potential risk factors of unfavorable pregnancy outcomes: PE, premature delivery, low birth weight, low Apgar score at 1 and 5 minutes after birth.

Results: In 12 cases (27.9%) there was no activity of SLE, in 16 cases (37.2%) there was low activity, in five (11.6%) – moderate, in three (7%) – high, in seven cases (16.3%) SLE activity was not assessed. SLE activity showed significant negative correlation with week at which labor occurred (p = 0.003, R = –0.477) and birth weight (p = 0.005, R = –0.461) and we found a significant fivefold increase in preeclampsia in patients with high activity of SLE (p = 0.011, OR = 4.95, 95% CI 1.449 to 16.931). Hemoglobin levels in third trimester correlated positively with birth weight (p = 0.04, R = 0.322). The dosage of glucocorticoids showed a significant correlation with week of delivery (p = 0.011, R = –0.382). Interestingly, the increase of aPTT in the third trimester had an almost significant effect on the risk of developing PE (p = 0.059, OR = 1.237, 95% CI 0.958–1.596). Unfortunately, lupus anticoagulant (LA) at that moment was not measured. Other studied parameters were not associated with risk of PE.

Conclusion: High SLE activity significantly increases the risk of gestational complications and unfavorable pregnancy outcomes. We suggest that regular monitoring of antiphospholipid antibodies, especially LA is needed. In this study, laboratory parameters did not significantly affect the risk of PE.

REFERENCES

Disclosure of Interests: None declared.

**AB1297 CARDIOVASCULAR EVENT AND RISK FACTORS IN PRIMARY SJÖGREN’S SYNDROME FROM LATIN-AMERICAN COHORT**

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**Background:** Inflammation has been associated with higher cardiovascular risk in rheumatic autoimmune diseases. Primary Sjögren’s syndrome (pSS) is associated with increased cardiovascular morbidity1. However, few and controversial data on the prevalence of cardiovascular events in pSS have been reported2-3 with no data regarding on Latin-American pSS patients.

**Objectives:** To assess the cardiovascular event and to evaluate its association with traditional and disease associated risk factors in pSS.

**Methods:** We included 455 patients with pSS according to AECG 2002 or AOR-EULAR 2016 classification criteria, attending tertiary referral centers from Brazil (n=183), Mexico (n=236) and Argentina (n=36). We retrospectively registered demographics, disease duration, cardiovascular event (CE) (coronary heart disease, cerebrovascular accident, peripheral arterial disease), smoking, and use of prednisone (PDN), immunosuppressors and antimalarials. We evaluated traditional risk factors and scored the ESSDAI, ESSPRI and SSDDI at last follow-up.


**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.7468

**AB1298 SAFETY AND EFFICACY OF PRIMARY YELLOW FEVER VACCINATION IN AUTOIMMUNE DISEASE: A PROSPECTIVE CONTROLLED STUDY**

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**Disclosure of Interests:** SORES, Vitória, Brazil

**Background:** Vaccines should be used with caution in autoimmune diseases (AID).1

**Objectives:** To evaluate prospectively adverse events and efficacy of the Yellow Fever vaccine in patients with AID.

**Methods:** Prospective study, including 190 individuals, 47 with Rheumatoid Arthritis (RA), 36 primary Sjögren’s Syndrome (SS), 48 Ankylosing Spondylitis (AS), 8 Systemic Sclerosis (SSc), and 24 Systemic Lupus Erythematosus (SLE), and 29 Healthy Controls (HC). All individuals received 17DD YF vaccine, for the first time during the 2017 Brazilian Campaign, aged ≥ 18 years, had no or low disease activity, low immunosuppression. Exclusion Criteria: previous vaccination for yellow fever or PRNT > 1:50 at baseline, primary or secondary immunodeficiency, under treatment with cyclophosphamide, chlorambucil, mycophenolate mofetil, calcineurin inhibitors, azathioprine> 2mg/kg/day, prednisone> 20mg/day, methotrexate> 20mg/week or any immunobiological drug. Viremia (CRP) and plaque reduction neutralization test (PRNT; GeoMean title) were measured before (D0) and D3, D4, D5, D6, D7, D14, D28 after vaccine. Adverse events (AE) were registered through patient report diary and medical interview at D7, D14 and D28.

**Results:** Mean age was 52 years old for AID and 56 for HC. No serious adverse event was reported. However, mild local AE was more reported in AID as compared to HC (34.2% vs. 3.4%, p=0.000). The frequency of AE was higher in AID compared to HC (34.1% vs. 3.4%). The Risk (Odds Ratio; 95%CI) for AE was 14.53 (1.9-109.7, p=0.000) and AID subgroups: AS=14.5 (1.9-116.2, p=0.0016), SLE= 15.5 (5.7-43.6, p<0.001). Viremia was slightly late and low in AID (D6=5.6 x 10 3) compared to HC (D5= 8.3 x 10 3). Seropositivity rates were lower in AID after 28 days (78% vs. 96%, p=0.04) as well as in HC (72% (p=0.02) and SLE (73%, p=0.03) compared to HC (Figure 1). Viremia was slightly late and low in AID (D6=5.6 x 10 3) compared to HC (D5= 8.3 x 10 3). Seropositivity was statistically lower at D14 in AID as compared to HC (21% vs. 75%, p=0.04) and remained lower at D28 in AS and SLE subgroups.

**Conclusion:** Efficacy was lower in AID, especially in SLE and AS, in spite of viremia peak at D5-D6 similar to HC. Taking together, results suggest that YF vaccine is safe in AID with low disease activity and under low immunosuppression, but probably a booster dose should be necessary.

**REFERENCES**


AN ONGOING ANTICENTROMERE ANTIBODY RESPONSE ASSOCIATES WITH PROGRESSION TOWARDS SYSTEMIC SCLEROSIS

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Background: Although some dated studies suggest a possible association between clinical characteristics and isotypes of antcentromere antibodies (ACA) in patients with systemic sclerosis (SSc), characteristics of ACA have not been described thoroughly in SSc.

Objectives: 1. Describe characteristics of antcentromere antibody (ACA) response in a large cohort of SSc patients. 2. Evaluate differences between ACA response between SSc patients fulfilling ACR 2013 criteria and those with very early diagnosis of SSc (VEDOSS).

Methods: ACA IgG, IgM and IgA levels were assessed in serum samples of patients visiting the Leiden SSc care pathway and who were IgG ACA+ at baseline. Patients had to fulfill either the ACR criteria or the VEDOSS criteria. Differences in isotype expression and levels between the two groups were evaluated, also with stratification for disease duration. Furthermore, in the SSc group we determined correlations between isotypes and disease duration and evaluated if isotype positivity was associated with clinical manifestations.

Results: ACA characteristics were measured in 167 ACA IgG+ patients. Thirty-five patients (21%) fulfilled the VEDOSS criteria and 132 (79%) the ACR criteria. ACA IgG+ patients displayed a broad isotype usage with 75% being ACA IgA+ and 66% being ACA IgM+ in serum. Patients within the SSc group showed higher ACA IgG levels and a higher percentage of ACA IgM positivity compared to the VEDOSS patients. Notably, these findings remained valid after stratification for disease duration, demonstrating that VEDOSS patients that did not progress to SSc within at least 5 years had lower ACA IgG levels and were less frequently positive for ACA IgM. In the SSc group, moderate correlations between isotypes were found; ACA IgM positivity was associated with occurrence of digital ulcers (p=0.02).

Figure 1

Conclusion: We observe a clear difference in the quality of the centro-mere-specific immune response between VEDOSS patients and SSc patients, also when stratifying for disease duration. The higher ACA IgG levels and presence of ACA IgM in SSc patients indicates that the ACA response in SSc is more pronounced showing signs of ongoing activity. These data indicate that the ACA B cell response is potentially relevant in disease development. In addition, ACA isotype expression and ACA IgG levels might contribute to better identify VEDOSS patients at risk for SSc development.

Disclosure of Interests: Nina van Leeuwen: None declared, Maaike Boonstra: None declared, Jaap Bakker: None declared, Corrie Wortel: None declared, Hans Ulrich Scherer Grant/research support from: Sanofi, BMS, Rene Toes Grant/research support from: Sanofi, Thomas Huizinga Consultant for: Merck, UCB, Bristol Myers Squibb, Biotest AG, Pfizer, GSK, Novartis, Roche, Sanofi-Aventis, Abbott, Crescendo Bioscience Inc., Nycomed, Boeringher, Takeda, Zydus, Epirus, Eli Lilly, Jeska de Vries-Bouwstra: None declared


AUTOIMMUNE/INFLAMMATORY SYNDROME INDUCED BY ADJUVANTS DUE TO SILICONE BREAST IMPLANT AND RHEUMATIC DISEASES:

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Background: Silicone is considered biologically inert; thus it has been employed in many medical devices and nowadays is commonly used in plastic surgery for mammary prosthesis. The most common adverse reaction after silicone breast implant (SBI) is capsular contracture due to a foreign body reaction. Autoimmune Rheumatic Diseases (ARD) have been associated with SBI or siliconosis as part of the spectrum of Autoimmune/Inflammatory Syndrome Induced by Adjuvants (ASIA). Silicone is an adjuvant that may ‘bleed’ and subsequently may be a chronic stimulus to the immune system.

Objectives: To determine the frequency of rheumatic diseases (ARD) and associated factors in patients with ASIA induced by SBI (ASIA-SBI).

Methods: This study was performed between 2012 to 2018 in a tertiary hospital from a cohort of 200 patients with ASIA (associated of oily substance, vaccines and siliconosis according to Shoenfeld criteria). We selected those patients with ASIA induced by SBI and clinical manifestations of any autoimmune disease. The clinical manifestations of ARD were evaluated and classified according to The American College of Rheumatology or EULAR criteria for some rheumatic diseases. We also investigated family history of autoimmune diseases, tobacco smoking coexisting allergies and comorbidities such as hypothyroidism, depression, anxiety and others. Main autoantibodies, histological findings were also evaluated. We used descriptive statistics for analysis.

Results: There were 30 women patients with mean age 48.5±16.3 46 years old, mean disease duration of disease 6±5.5 years. The mean time of appearance of clinical manifestations after SBI was 8 ±4.9 years. The rheumatic diseases (RD) or ARD were Systemic sclerosis (SSc) 7, Fibromyalgia (FM) 6, Systemic lupus erythematous (SLE) 3, rheumatoid arthritis (RA) 6, overlap syndrome 2 (SSc plus SS and SLE plus SSc), Sjogren syndrome (SS) 1, Takayasu arteritis 1, Still disease 1, tunnel carpal syndrome 1, antiphospholipid syndrome 1 and angiopedia and uticaria 1. We found family history of rheumatic disease in 40%, allergic history (food, drugs) in 40% and smoking in 50%. Hypothyroidism was observed in 30% and anxiety 30%. Patients were treated according to the rheumatic disease. Ten cases had their prostheses removed because extracapsular ruptured implants, with re-implantation of new prosthesis in 8 patients. Two patients experienced improvement of complaints after explantation of the implant.

Conclusion: We found a prevalence of ASIA associated to SBI of 15%. The main RD were SSc, FM and RA. We observed an association with family history, allergies and smoking in these patients. Further studies are necessary to determine if SBI has a cause –effect relationship in the rheumatic disease manifestations.

REFERENCES

Disclosure of Interests: None declared

IMMUNE REGULATION THERAPY PROMOTED THE RECANALIZATION OF CORONARY ARTERY IN A PATIENT WITH ANTI-PHOSPHOLIPID SYNDROME: A CASE REPORT AND LITERATURE REVIEW

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Background: Thrombosis is considered as a major feature of antiphospholipid syndrome (APS). Once formed, thrombosis will threaten life and long-term oral anticoagulant therapy is required. In addition, some patients underwent percutaneous coronary intervention (PCI), but in-stent restenosis (ISR) is the most common complication of PCI. There is currently insufficient treatment for such patients. Because APS is an autoimmune disease, we developed a new therapy (Sirolimus based immunomodulatory) to treat a APS patients with ISR after PCI.

Objectives: Assess the degree of stenosis of the various branches of the coronary arteries, and to observe the changes in the number of regulatory T cells (Tregs) in the peripheral blood of patients.

Methods: An APS patient with coronary artery involvement was found in-stent restenosis after implantation of the stent. After sirolimus and other immunomodulatory treatments, coronary angiography and coronary CTA were performed to assess the degree of stenosis of the various branches of the coronary arteries, and to observe the changes in the number of regulatory T cells (Tregs) in the peripheral blood of patients.

Results: After 6 months of immunomodulation therapy, the patient did not have clinical symptoms such as chest tightness and tightness. Four consecutive coronary angiography and coronary CTA (dual source) showed disappearance of left main plaque. Stenosis, the degree of stenosis in the anterior descending stent was reduced from 90% to 66%; the degree of right coronary stenosis was reduced from 50% to 30%; new stenosis and new thrombosis did not occur in other branches. The absolute number of Treg cells in peripheral blood gradually increased from 34.41 to 50.83 cells/μl.

Conclusion: Sirolimus is an inhibitor of mTOR that is a serine/threonine kinase in two different complexes (mTORC1 and mTORC2) to promote cell proliferation and neovascularization. Antiphospholipid antibodies activate the mTOR pathway in endothelial cells in culture. When pretreated with mTOR inhibitors prevents this process from occurring. Sirolimus specifically inhibits the mTOR pathway and prevents neointimal hyperplasia and neovascularization in the coronary arteries. In ASP patients with coronary artery involvement, the reduction of Treg cells may also be an important cause of immune tolerance deficiency. Sirolimus also increased the number of Treg cells. If early use of immunomodulators such as sirolimus for prophylaxis, it may prevent re-stenosis after stenting. The successful treatment of this patient also provided us with new diagnostic and therapeutic ideas.

REFERENCES

AB1301
SOCIAL MEDIA USE IN SYSTEMIC LUPUS ERYTHEMATOSUS IMPACT ON PREVALENCE OF ANXIETY AND DEPRESSION

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Background: The psychological problems of patients with Systemic lupus erythematosus (SLE) have been widely concerned. Studies found that the SLE patients showed a prevalence of depression in SLE cohorts ranging from 17% to 75%, and anxiety being 6%-52%. Factors contributing to mood disorders are various. As a nontraditional form of media, social media has become increasingly popular worldwide. Previous study has demonstrated that social media use (SMU) plays a significant role in adolescents’ psychological functioning[1-2], whether SMU could impact the mental health of SLE patients, no previous finding of SMU on SLE patients is reported.

Objectives: We aimed to explore the potential association of the patterns of social media use (SMU) with anxiety and depression in patients with systemic lupus erythematosus (SLE).

Methods: The relevant data were collected from 402 SLE patients aged 18-60 years in the First Affiliated Hospital of Zhengzhou University between July 2018 and October 2018 for subsequent analysis. Demographic and clinical characteristics, the patterns of SMU, the reasons and barriers to SMU were recorded. Anxiety and depression were assessed using hospital anxiety and depression scale (HADS). Adjusted estimates of association were derived using logistic regression.

Results: The incidence of anxiety and depression were 41.1% and 28.4% respectively among SLE patients with a mean score of 6.71±3.65 and 5.45±3.86 in each subscale. Patients without social media were more likely than those with social media to develop anxiety or depression (P=0.05, P=0.001), besides, the presence of depression also had a association with the duration for SMU (P=0.05).

Conclusion: Depression and anxiety are prevalent in patients with SLE and high frequency of SMU may decline the risks of anxiety and depression, to educate patients use social media properly may result in alleviation of anxious and depressive symptoms in patients with SLE.

REFERENCES


Disclosure of Interests: None declared


AB1302B
CHRONIC KIDNEY DISEASE IN RHEUMATOID ARTHRITIS: PREVALENCE AND RISK FACTORS

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Background: The problem of chronic kidney diseases (CKD) in rheumatoid arthritis (RA) patients have not been fully studied. The role of biological therapy (BT) is poorly understood.

Objectives: Aim of the study was to examine the prevalence, risk factors and histological variants of CKD in RA, and impact of pharmacotherapy.

Methods: 135 patients with RA from 2013 to 2018 were enrolled in this study. Age, gender, duration of RA, drug therapy, ESR, CRP, DAS28, renal function, proteinuria (PU), histological variants were analyzed. Arterial hypertension, weight, sex, lipids and glucose levels were also assessed.

Results: The incidence of CKD in RA was 30.4% (41 from 135). CKD 3-4 stages with eGFR < 60ml/min/1.73m2 was detected in 14.8%
patients. The duration of the disease, high ESR and DAS28 score, NSAIDs treatment and hyperlipidemia were risk factors for CKD in RA (Fig 1). We also found negative correlation between the DAS28 and eGFR (Fig 2).

Amyloidosis was the most common histologic pattern (51.52%), followed by chronic glomerulonephritis (CGN) (24.24%) and tubulo-interstitial nephritis (24.24%). Among CGN mesangial glomerulonephritis was the most frequent (Table 1). Renal amyloidosis was associated with a duration of RA, presence of systemic symptoms and CRP level. The levels of PU were lower, and eGFR levels were higher in patients treated with BT than in patients treated with synthetic disease-modifying anti-rheumatic drugs (DMARDs) (Fig 3).

Conclusion: CKD is often developed in patients with high RA activity. Treatment with biological agents is associated with a lower PU and higher GFR levels.

REFERENCES:

Abstract AB1302B Table 1. Renal histopathologic findings in RA patients (n=33)

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<thead>
<tr>
<th>Histological forms</th>
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<tbody>
<tr>
<td>Amyloidosis:</td>
<td>21</td>
<td>63.7</td>
</tr>
<tr>
<td>Chronic</td>
<td>12</td>
<td>36.3</td>
</tr>
<tr>
<td>glomerulonephritis:</td>
<td>7</td>
<td>21.2</td>
</tr>
<tr>
<td>- Mesangial GN:</td>
<td>4</td>
<td>12.1</td>
</tr>
<tr>
<td>IgA nephropathy</td>
<td>1</td>
<td>3.0</td>
</tr>
<tr>
<td>IgM nephropathy</td>
<td>2</td>
<td>6.0</td>
</tr>
<tr>
<td>Membranoproliferative</td>
<td>1</td>
<td>3.0</td>
</tr>
<tr>
<td>GN</td>
<td>1</td>
<td>3.0</td>
</tr>
<tr>
<td>- Minimal change disease</td>
<td>3</td>
<td>9.1</td>
</tr>
<tr>
<td>- Membranous nephropathy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Diffuse nephrosclerosis</td>
<td></td>
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</tr>
</tbody>
</table>

Disclosure of Interests: None declared
nephelometric assay. The cut-off value of serum IgG4 was 201 mg/dl. We compared the levels of serum IgG4 among patients with different types of malignancy.

Results: (1) Among the 90 patients, 18 patients were gallbladder carcinoma, 6 patients were lung carcinoma, 34 patients were liver carcinoma, 6 patients were gastrointestinal carcinoma, and 19 patients were pancreatic carcinoma. In gastrointestinal carcinoma, the highest (237.85±50.92 mg/dl), but the sample is too small. Serum IgG4 level in liver carcinoma was higher than other types of malignancy (180.5 ± 32.04 mg/dl vs gallbladder carcinoma 114.4 ± 15.01 mg/dl, p<0.01). vs pancreatic carcinoma 91.63 ± 19.89 mg/dl, p<0.01 vs lung carcinoma 67.47 ± 11.75 mg/dl, P<0.01).

Conclusion: Elevated serum IgG4 level is common in patients with malignancies, while patients with liver carcinoma have significant higher serum IgG4 level than those with gallbladder carcinoma, pancreatic carcinoma and lung carcinoma. This suggests that IgG4 may have different role in different types of tumor.

Validation of outcome measures and biomarkers.

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Background: Rheumatoid arthritis (RA) is the most common chronic inflammatory rheumatism in adults. It affects the synovial membrane, evolves by outbreaks and can lead to joint destruction. It generates a physical disability that causes an impairment of quality of life and professional activity.

Objectives: To study the socio-demographic, clinical and professional characteristics of patients and to assess the impact of RA on quality of life and professional activity.

Methods: We conducted a retrospective, descriptive study on patients’ files, followed at the rheumatology department of LA RABTA university hospital, for RA aver a period of ten years. The target population was patients having a professional activity at the time of the discovery of the disease. We assessed disease activity by the Disease Activity Score 28 (DAS28-CRP), work impact by the “Work Productivity and Activity Impairment” questionnaire (WPAI:RA) and quality of life by the Health Assessment Questionnaire (HAQ). The data was entered into an excel table and analyzed using SPSS software version 19.0. In all statistical tests, the significance level was set at 0.05.

Results: We collected 25 cases of RA. Mean age was 50.36 ± 8.28 years with a sex ratio of 1.08. The mean age of RA was 9.8 years and the mean age of onset was 40.56 ± 9.84 years. The study population occupied a manual job in 84% of cases. The average professional seniority was 21.76 ± 12.83 years. Patients reported having stopped work because of their illness in 44% of cases. The mean of DAS28-CRP was 4.32 ± 1.57, 72% of the study population had moderate to severe RA activity. The mean HAQ was 1.38 ± 0.69 with 76% of cases suffering from “moderate to severe” or “severe to very severe disability”. The evaluation of the work productivity and activity impairment by the WPAI:RA questionnaire objectified an absenteeism of 30.7 ± 9.4%, a presenteeism of 46.7 ± 26.4%, a work productivity loss of 60.4 ± 33.8% and an activity impairment of 57.2 ± 25.4%. A positive and statistically significant correlation was noted between the results of WPAI and HAQ, between the results of WPAI (except absenteeism) and DAS28CRP and between HAQ and DAS28-CRP.

Conclusion: RA causes a significant functional disability that affects the professional activity and quality of life of patients. Early diagnosis and treatment of this disease can slow the progression of the disease. Occupational medicine plays an important role in the early detection and maintenance of employees with RA at work.

Disclosure of Interests: None declared

THE RHEUMATOID ARTHRITIS FLARE QUESTIONNAIRE (RA-FQ) IS AN EASY TO ADMINISTER PATIENT-REPORTED OUTCOME MEASURE THAT TRACKS WELL WITH THE CLINICAL DISEASE ACTIVITY INDEX (CDAI) OVER TIME IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS (ERA) IN 2 DIFFERENT HEALTH SETTINGS

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Background: RA patients may cancel scheduled visits with their rheumatologist. In clinical practice, a validated patient-reported disease activity measure that tracks well with traditional clinical indices could address an important gap by providing real-time information on RA disease activity when a visit to the rheumatologist is not possible.

Objectives: To assess concordance between the 5-item patient-reported Rheumatoid Arthritis Flare Questionnaire (RA-FQ) (1,2) and the Clinical Disease Activity Index (CDAI) in patients with early RA (ERA) treated in rheumatology clinics in 2 countries with different health systems.

Methods: Data were analyzed from patients enrolled in the Canadian early Arthritis CoHort (CATCH) between Nov 2011 and March 2017 and in the Consortium of early Arthritis Cohorts- USA (CATCH-US) from Dec 2014 to Dec 2018. Both observational studies had a similar design; enrolled patients diagnosed with ERA (< 1 year of persistent symptoms) by a rheumatologist who completed similar regular protocolized clinical assessments, laboratory investigations and PROMs. The RA-FQ, designed to assess worsening of RA inflammation, is a short composite PROM (total score 0-50) that sums 5 single items (NRS 0-10) querying pain, fatigue, stiffness, function and participation. The present analysis includes patients meeting ACR 1987 or 2010 ACR/EULAR criteria, with RA-FQ and CDAI at baseline and at least 1 other follow up (FU) over 12-months. We compared mean scores of the RA-FQ and CDAI over time and calculated intraclass correlation coefficients (ICC) to assess concordance between measures in the 2 cohorts.

Results: The study included 818 Canadian and 75 American early RA patients. Age, male sex, and disease activity was higher in the Canadian cohort, while post-secondary education was higher in the US cohort (Table1). RA-FQ and CDAI scores tracked closely with one another over time in both cohorts (Canada ICC: 0.76; US ICC: 0.80).

Conclusion: There was high concordance between the RA-FQ and CDAI measures over the 1st year of follow up in 2 early RA samples recruited in 2 countries. The RA-FQ may help patients and clinicians track patient disease activity between clinic visits.
EVALUATION OF SERUM LEVELS OF ASC FOR THE DIAGNOSIS AND MONITORING OF CRYOPYRIN ASSOCIATED PERIODIC SYNDROMES (CAPS)

Fortunata Carboni1, Teresa Micilico2, Luca Cantarini2, Maria Alessio3, Alma Nunzia Oliveri4, Maria Francesca Gicchinio5, Antonella Insalaco6, Maria Cristina Maggio7, Orso Maria Lucherini8, Roberto Scarpioni9, Matteo Piga10, Maria Maddalena Angioni9, Laura Obici9, Antonella Simpatico10, Pietro Lecese10, Rita Consolisi11, Raffaele Manni12, Paolo Sfisso13, Sara Bindoli12, Paola Gallozi12,15, Ida Orlando12, Sabrina Chiesa12, Marco Gattorno12,15, Giuseppe Matarese12,15, "Istituto per l’Eндocrinologia o l’Oncologia Sperimentale-Consiglio Nazionale delle Ricerche (IEOS-CNRI), Napoli, Italy; "Università degli Studi di Napoli “Federico II”, Napoli, Italy; "Università di Siena, Siena, Italy; "Università degli Studi della Campania “Luigi Vanvitelli”, Napoli, Italy; "IRCCS Ospedale Bambino Gesù, Roma, Italy; "Ospedale dei Bambini “Di Cristina”, Palermo, Italy; "Ospedale AUSL “Guniglio da Saliceto”, Piacenza, Italy; "Reumatologia, Policlinico Universitario, Cagliari, Italy; "Fondazione IRCCS Policlinico San Matteo, Pavia, Italy; “Ospedale San Carlo, Potenza, Italy; "Università di Pisa, Pisa, Italy; "Policlinico Genemelli Università Cattolica, Roma, Italy; "Department of Medicine, DIMED, University of Padova, Padova, Italy; "IRCCS Istituto Giannina Gaslini, Genova, Italy; "Università degli Studi di Napoli “Federico II”, Dipartimento di Medicina Molecolare e Biotecnologie Mediche, Napoli, Italy

Background: Dominantly gain-of-function mutations in the NLRP3 gene lead to Cryopyrin associated periodic syndromes (CAPS) characterized by constitutive activation of the inflammasome, increased secretion of interleukin (IL)-1beta and IL-18, and systemic inflammation. IL-1beta and active caspase-1 subunits are released in the serum together with the oligomeric particles of the adaptor ASC (apoposis-associated Speck-like protein with a caspase-recruitment domain) after activation of the inflammasome complex and, as a consequence, patients with CAPS show an increased serum concentration of ASC particles.

Objective: Patients suffering from CAPS are characterized by clinical manifestation similar to other autoinflammatory diseases. This phenomenon together with the lack of specific laboratory tests makes difficult the diagnosis of CAPS. In this context the development of a test for the evaluation of serum ASC levels could provide novel biomarkers facilitating early disease diagnosis and able to monitor treatment responses.

Methods: We analysed, with a novel ELISA assay, the levels of ASC particles in serum and plasma of normal subjects, CAPS patients and patients with autoimmune disorders (Multiple Sclerosis (MS), Type 1 Diabetes (T1D) and juvenile idiopathic arthritis), to confirm that ASC presence in the serum is not due to other chronic inflammatory processes and, as a consequence, patients with CAPS show an increased serum concentration of ASC particles.

Results: ASC particles were higher in untreated CAPS patients with respect to healthy controls and patients suffering from MS and T1D. These data suggest that ELISA quantitation of ASC protein could represent a novel and additional strategy for the diagnosis and monitoring of CAPS patients suffering from CAPS.

Disclosure of Interests: Fortunata Carboni none declared, Luca Cantarini: None declared, Maria Alessio: None declared, Alma Nunzia Oliveri: None declared, Maria Francesca Gicchinio: None declared, Antonella Insalaco: None declared, Maria Cristina Maggio: None declared, Orso Maria Lucherini: None declared, Roberto Scarpioni: None declared, Matteo Piga: None declared, Maria Maddalena Angioni: None declared, Laura Obici: None declared, Antonella Simpatico: None declared, Pietro Lecese: None declared, Rita Consolisi: None declared, Raffaele Manni: None declared, Paolo Sfisso: None declared, Sara Bindoli: None declared, Paola Gallozi: None declared, Ida Orlando: None declared, Sabrina Chiesa: None declared, Marco Gattorno Grant/research support from: MG has received unrestricted grants from Sobi and Novartis, Giuseppe Matarese Grant/research support from: Mat- arse reports research grants from Merck-Serono, Biogen Idec, Novartis and IBSA.


Table: Patient and Disease Characteristics at Study Entry

<table>
<thead>
<tr>
<th>Mean (SD) or %</th>
<th>CATCH</th>
<th>CATCH-US</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>55 (15)</td>
<td>47 (16)</td>
</tr>
<tr>
<td>Female</td>
<td>72%</td>
<td>64%</td>
</tr>
<tr>
<td>Caucasian/White</td>
<td>80%</td>
<td>76%</td>
</tr>
<tr>
<td>Education (High School or less)</td>
<td>42%</td>
<td>12%</td>
</tr>
<tr>
<td>Symptom duration (months)</td>
<td>5.5 (2.9)</td>
<td>6.0 (3.3)</td>
</tr>
<tr>
<td>Sero-positive (RF or ACPA)%</td>
<td>74%</td>
<td>77%</td>
</tr>
<tr>
<td>CDAI</td>
<td>28.0 (14.0)</td>
<td>14.4 (11.9)</td>
</tr>
<tr>
<td>RA-FQ</td>
<td>26.7 (13.3)</td>
<td>16.0 (12.4)</td>
</tr>
</tbody>
</table>

Figure 1. Mean RA-FQ and CDAI scores over 12-months Follow Up in Canadian and US Early Rheumatoid Arthritis Cohorts.

AB1305
AB1306 PILOT STUDY OF ADHERENCE IN PATIENTS WITH RHEUMATOLOGICAL DISEASES AUTOIMMUNE

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Background: Data on adherence in patients with autoimmune rheumatological diseases are limited.

Objectives: To analyze the adherence to treatment in patients with autoimmune rheumatological diseases.

Methods: A cross-sectional study was performed in patients from the Complexo Hospitalario Universitario de Pontevedra with diagnosis of systemic lupus erythematosus (SLE), Sjögren’s Syndrome (SS) and Systemic Sclerosis (SE).

The patients filled an anonymous survey that included data about demographic, diagnosis and treatment. Adherence to treatment was assessed using the Spanish Compliance Questionnaire in Rheumatology (sCQR) [1]. Likewise, a linear regression analysis was carried out in order to identify factors related to adherence to treatment. A significant value was considered as p < 0.05. Stata version 11.1 (Stata/IC 11.1 for Windows, StataCorp LP, College Station, TX) was used to perform all analyzes.

Results: A total of 44 patients participated in the study, although 90.9% of the surveys carried out could be used for the analysis. A total of 25 (62.5%) SLE, 9 (22.5%) SS and 6 (15.0%) SE participants participated. The average age was 48.9 ± 12.8 years (See Table 1). According to the sCQR 82.5% were compliant patients. None of the studied variables was associated with the adherence rate: sex (p = 1.000), age (0.134), time of evolution (p = 1.000), level of education (p = 0.677), marital status (0.392), illness (p = 1.000), number of drugs ingested per day (p = 0.873), treatment with steroids (p = 0.679) or antimalarials (p = 1.000).

Conclusion: The adherence rate in our cohort was 82.5% higher than previously reported in other studies. [2,3] The sCQR could be a useful and easy-to-apply tool for the study of adherence in these patients.

REFERENCES


Table 1. Clinical and sociodemographic characteristics of the patients

<table>
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<th>N=40</th>
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<tr>
<td><strong>Age (years), mean, n (%)</strong></td>
<td>48.9 ±12.8</td>
</tr>
<tr>
<td><strong>Sex (women), n (%)</strong></td>
<td>40 (82.5)</td>
</tr>
<tr>
<td><strong>Marital status, n (%)</strong></td>
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<tr>
<td><strong>Education, n (%)</strong></td>
<td>3 (7.5)</td>
</tr>
<tr>
<td><strong>Occupation, n (%)</strong></td>
<td>1 (2.5)</td>
</tr>
<tr>
<td><strong>Student</strong></td>
<td>2 (10.0)</td>
</tr>
<tr>
<td><strong>Active</strong></td>
<td>20 (50.0)</td>
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<tr>
<td><strong>Job loss</strong></td>
<td>1 (2.5)</td>
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<tr>
<td><strong>Retirement</strong></td>
<td>8 (20.0)</td>
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<tr>
<td><strong>No</strong></td>
<td>12.5</td>
</tr>
<tr>
<td><strong>1 year</strong></td>
<td>2 (5.0)</td>
</tr>
<tr>
<td><strong>1-2 years</strong></td>
<td>6 (15.0)</td>
</tr>
<tr>
<td><strong>&gt;5 years</strong></td>
<td>27</td>
</tr>
<tr>
<td><strong>Number of drugs ingested per day, n (%)</strong></td>
<td>9 (22.5)</td>
</tr>
<tr>
<td><strong>Treatment, n (%)</strong></td>
<td>21</td>
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<tr>
<td><strong>Antimalarials</strong></td>
<td>14</td>
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<tr>
<td><strong>Methotrexate</strong></td>
<td>5 (12.5)</td>
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<tr>
<td><strong>Azathioprine</strong></td>
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Disclosure of Interests: None declared

AB1307 STUDY OF CONCORDANCE AND EQUIVALENCE AMONG BARTHEL, LAWTON, HAQ AND BASFI QUESTIONNAIRES IN RHEUMATOID AND SPONDYLOARTHRITIS PATIENTS

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Background: Assessment of functional capacity of patients is usually performed using disease-specific questionnaires for rheumatoid arthritis (HAQ) and for axial spondyloarthropathies (BASFI). However, recent studies have shown that disease-specific, general indexes such as Barthel and Lawton-Brody (LB) are used to establish disability in legal environments and in emergency rooms. Few studies have compared specific vs. generic questionnaires in rheumatic patients [1].

Objectives: To assess the equivalence between disability questionnaires of generic type, applicable to general population and various diseases (Barthel and LB), with specific questionnaires for rheumatic diseases (HAQ and BASFI).

Methods: A cross-sectional study was conducted in consecutive outpatients with inflammatory rheumatic diseases (rheumatoid arthritis, psoriatic arthritis, spondyloarthropathies) in usual daily clinical practice in a rheumatology clinic of a tertiary hospital.

The patients self-completed the questionnaires (Barthel, LB, HAQ, and BASFI) in a single session. HAQ was only filled by peripheral arthritis patients, while BASFI was only given to spondyloarthropathy subjects. Scores were also computed for SDAI, DAS28 and BASDAI in most patients. Intraclass correlation was used to measure concordance between questionnaires.

Results: A total of 214 patients where studied. There was good correlation between the scores of the indexes studied, especially between the two generic questionnaires (R = 0.45 p < 0.01). We observed a high ceiling effect in the scores of both Barthel, (70% of patients obtained values 95 over a maximum of 100) and Lawton-Brody (60% had values > 23 over a maximum of 24) tests. The disease-specific questionnaires showed a less skewed distribution. The agreement between Barthel’s and Lawton’s tests was significant when measured by the intraclass correlation (R = 0.48 p < 0.01). However, we could not find any significant correlation between the generic questionnaires and the HAQ questionnaire or the BASFI (R < 0.3).

Conclusion: The Barthel and Lawton-Brody indices show an important ceiling effect in rheumatic patients, and seem to evaluate dimensions of health other than rheumatic questionnaires such as HAQ and BASFI, and thus they are not interchangeable. This point must be taken into account when performing medicolegal or emergency room assessments. Our result is in line with other previous studies[1]

REFERENCE


Disclosure of Interests: None declared


AB1308 FAILURE TO BIOLOGICAL THERAPY: WHEN TO EXPECT IT?

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Background: Using Biologic agents, has considerably improved the treatment of inflammatory diseases. But it is associated to the capacity of inducing an immune response in patients that could result in unwanted adverse events or treatment failure.
Objectives: The aim of this work was to compare the clinical and biological response to biotherapy with the presence of ADA and the residual dose rate.

Methods: We analysed the medical records of 69 patients treated with biotherapy between September 2017 and October 2018. The 3 pathologies were considered: rheumatoid Arthritis (RA) diagnosed by ACR/EULAR 2009 criteria, Spondyloarthritis (SPA) according to Assessment of Spondyloarthritis International Society (ASAS) And crom'hs disease (CD) classified upon the 2006 Montreal classification. We did search the presence of anti-body anti-drugs (ADA) and the residual dose for the following therapies: Etanercept (ETN), Infliximab (IFX), Adalimumab (Ad) or Rituximab (RTX).

Results: The mean age was 43.33 ± 11.4 years. The sex ratio M/F was 1.57.

Regarding the RA: they were 13 patients. 10 had positive (ACPA) and seven positive (RF). All the patients had an initial treatment by conventional synthetic disease modifying antirheumatic drugs (csDMARDs) before moving to bDMARDs. 14 were in concomitant disease modifying therapy. The DAS28-ESR average was at 4.12 [2.67 à 5.79]. We found positive ADA in only one patient analysis. There were 8 responding versus five non-responding patients, according to the clinical and biological evaluation of disease activity.

28 patients were in the SPA group: 13 with an axillary spondyloarthritis. 14% had the HLAB 27. It was an active disease in 15 cases. ASDAS-CRP average was 4.87 ± 0.17 [4.7; 5]. The received biotherapy was IFX 50%, ETN 28.6% and Ada 21.4%. 10 patients had a positive ADA and 8 of them had a rate superior to 100 UI. 19 patients were considered as non-Responding.

In the CD group, 28 patients were enrolled. All of them had a previous immunosuppressor treatment. Same patients in association with biotherapy. It was positive ADA in 7 cases. And 7 patients were non-responding to the treatment.

The residual dose of drugs was calculated for each drug and it is explained in the following table:

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Positive ADA</th>
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<tr>
<td>IFX</td>
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<td>Ada</td>
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<td>ETN</td>
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<td>Non-responding</td>
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<td>RTX</td>
<td>Responding</td>
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<td>Responding</td>
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</table>

Positive ADA was associated with therapy failure in all type of biotherapy (p<0.001). A low residual dose was associated to therapy failure only in the case of IFX (p<0.005).

In multivariate analyses, the predictive factors associated with therapeutic failure were: positive ADA (p<0.008) and advanced age at diagnosis, below 30 years old age (p=0.020). Hosmer index=0.452.

Conclusion: Immune response induced in patients treated with biotherapy can be quantified now thanks to ADA dosage and the residual dose assessment.

REFERENCES


Disclosure of Interests: None declared


AB1309 QUANTIFICATION OF MINIMAL RESIDUAL DOSE ASSOCIATED WITH BIOLOGICAL THERAPEUTIC RESPONSE ANTI DRUG ANTI BODIES: ARE THEY ALL NEUTRALIZING?

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Background: The use of biologicals was associated to the capacity of inducing an immune response in patients that could neutralize the drug.

The anti-body anti-drug (ADA) assay was a revolutionary tool to prevent treatment failure.

Objectives: The aim of this work was to asses if the presence of ADA in patients system is sufficient to preclude failure and indicates the switch of treatment.

Methods: We enrolled 69 patients treated with biotherapy between September 2017 and October 2018. 3 pathologies were considered: rheumatoid Arthritis (RA) diagnosed by ACR/EULAR 2009 criteria, Spondyloarthritis according to Assessment of Spondyloarthritis International Society (ASAS) And crom'hs disease (CD) classified upon the 2006 Montreal classification. We did search the presence of anti-body anti-drugs (ADA) and the residual dose for the following therapies: Etanercept (ETN), Infliximab (IFX), Adalimumab (Ad) or Rituximab (RTX).

Results: The mean age was 43.33 ± 11.4 years. The sex ratio M/F was 1.57.

Regarding the RA: they were 13 patients. 10 had positive (ACPA) and seven positive (RF). All the patients had an initial treatment by conventional synthetic disease modifying antirheumatic drugs (csDMARDs) before moving to bDMARDs. 14 were in concomitant disease modifying therapy. The DAS28-ESR average was at 4.12 [2.67 à 5.79]. We found positive ADA in only one patient analysis. There were 8 responding versus five non-responding patients, according to the clinical and biological evaluation of disease activity.

28 patients were in the SPA group: 13 with an axillary spondyloarthritis. 14% had the HLAB 27. It was an active disease in 15 cases. ASDAS-CRP average was 4.87 ± 0.17 [4.7; 5]. The received biotherapy was IFX 50%, ETN 28.6% and Ada 21.4%. 10 patients had a positive ADA and 8 of them had a rate superior to 100 UI. 19 patients were considered as non-Responding.

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The residual dose of drugs was calculated for each drug and it is explained in the following table:

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Positive ADA was associated with therapy failure in all type of biotherapy (p<0.001). A low residual dose was associated to therapy failure only in the case of IFX (p<0.005).

Positive ADA was associated to a low rate of residual dose in the case of IFX and Ada. This association couldn’t be evaluated for RTX (none) and ETN (just one positive rate).

Conclusion: The ADA assay was a revolutionary tool allowing the evaluation of treatment response but it cannot be considered without the clinical assessment of patient. The evaluation residual dose should be concomitant to value and guide the therapeutic decision.

REFERENCES


Disclosure of Interests: None declared


AB1310 PROSPECTIVE USE OF THE GLUCOCORTICOID TOXICITY INDEX (GTI) IN A COHORT OF VASCULITIS PATIENTS

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1Division of Rheumatology, Allergy, and Immunology, Medicine, Boston, United States of America

Background: The Charité Rh-GIOP is a prospective study of disease- and bone-related data from patients with chronic inflammatory diseases treated with glucocorticoids (GCs). The Glucocorticoid Toxicity Index app (GTI 2.0) measures changes in GC-associated morbidity. The GTI captures...
Thirty-four (92%) patients had changes in GC toxicity between V1-V2. The mean CWS & AIS were 34.8 and 11.1, respectively. Twenty-eight patients (76%) had CWS >0, indicating worsening toxicity. Twenty-one (57%) had AIS >0, also consistent with overall GC toxicity worsening. The GTI captured changes in GC toxicity over time well, with a strong positive correlation between CWS and AIS.

Methods: Vasculitis patients were included if starting GC or having a flare requiring increased GC doses. Doses were calculated in prednisone (PRED) equivalents. Nearly all patients had received GC (often for years) before baseline (V1). Data for the 9 GTI domains were collected at V1 and follow-up (V2). These included: medications for hypertension, hyperglycemia, and hyperlipidemia; body mass index; bone mineral density; and data pertaining to muscle strength; skin toxicity, neurophysiologic effects, and infections. Data for the blood pressure, glucose control, and lipid domains were inferred from treatment changes. We used multivariate logistic regression models to examine the relationship of PRED dose to the likelihood of CWS worsening and AIS improvement.

Results: 37 patients (25F; 12M) of mean age 66.6 years (range: 40.5-81.7) were included. Diagnoses: GCA (n=7), PMR (14), AAV (10), EGPA (4), and PAN (2).

Table 1. Prednisone Dosing

<table>
<thead>
<tr>
<th></th>
<th>Mean Cumulative PRED Dose V0 &amp; V1 (mg)(range)</th>
<th>Days Between V0 &amp; V1 (range)</th>
<th>Mean Predict dose dose V1 (mg)(SD)</th>
<th>Mean Predict dose dose V2 (mg)(SD)</th>
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<tr>
<td></td>
<td>7888 (30-55,800)</td>
<td>1095 (2-7,443)</td>
<td>61 (335-1,111)</td>
<td>34.2 (36.5)</td>
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<td></td>
<td>6.1 (8.2)</td>
<td>3.1 (2.9)</td>
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</table>

Conclusion: The GTI captured changes in GC toxicity over time well, both improvement and worsening. Cumulative PRED dose correlated strongly with increase in the Cumulative Worsening Score.

Acknowledgement: Rh-GIOP is supported by a joint funding of Amgen, Bristol-Myers Squibb, MS, Cellgene, Chugai, Generic Assays, Glaxo-Smith Kline, Hexal AG, Horizon, Lilly, Medac, Mundipharma, Novartis, Pfizer, Roche, and Sanofi. None declared.

Disclosure of Interests: Lisa Ehlers: None declared, Edgar Wiebe Grant/Research support from: Rh-GIOP is supported by a joint funding of Amgen, BMS, Cellgene, Generic Assays, Chugai, Hexal AG, Horizon, Lilly, medac, Mundipharma, Novartis, Pfizer, Roche, and Sanofi., Desiree Freier: None declared, Sandra Hermann: None declared, Eli Miloslavsky: None declared. Yuqing Zhang: None declared, Frank Buttgereit: None declared, John H. Stone Grant/research support from: F. Hoffmann-La Roche, Genentech, Xencor, Consultant for: Chugain, F. Hoffmann-La Roche, Genentech, Xencor

TIME-COURSE CHANGE OF NEUTROPHIL-LYMPHOCYTE RATIO, MONOCYTE-LYMPHOCYTE RATIO AND PLATELET-LYMPHOCYTE RATIO IN PSORIATIC ARTHRITIS PATIENTS AND RESPONSE TO BIOLOGIC THERAPY

Raquel Ferreira, Sara Ganhão, Salomé Garcia, Bruno Miguel Fernandes, Sofia Pimenta, Miguel Bernardes, Lúcia Costa. São João Hospital Centre, Porto, Portugal

Background: Recently, systemic inflammation has been shown to be a key determinant of prognosis. Neutrophil-lymphocyte ratio (NLR), monocyte-lymphocyte ratio (MLR), and platelet-lymphocyte ratio (PLR) has been related to inflammation status and suggested as additional markers of response to bDMARDs in patients with rheumatoid arthritis. However, few studies were yet developed about this subject in psoriatic arthritis (PsA).

Objective: The aim of this study was to investigate the time-course of change of NLR, MLR and PLR levels in PsA patients after 6 and 12 months of bDMARD therapy and to evaluate their clinical significance and utility in monitoring response to biologic agents.

Methods: An observational retrospective study was performed in patients with PsA under bDMARD, followed at our Rheumatology department until December 2018. Demographic and clinical data were collected from the national database. C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and total blood count were consulted before and after 6 and 12 months of biologic treatment and NLR, MLR and PLR were calculated by dividing neutrophil, monocyte and platelet count by lymphocyte count, respectively. Disease activity was evaluated with DAS28 and ASDAS.

Results: A total of 83 patients were included. Forty-three were females (51.8%). The mean age at diagnosis was 41 years (±11.3) and the median disease duration at start of biological therapy was 6.9 years (min:1.4; max:32.4). In total, 67.5% of the patients had a high CRP level (n=56), 91.6% had a positive ESR (n=76) and 43.4% had a positive ANA (n=35). Almost all patients fulfilled the CASPAR criteria for PsA (n=78; 94%). At the baseline, 25 patients (30.1%) had high disease activity and 45 patients (54.2%) had high disease activity according to ASDAS criteria. The most used bDMARD was etanercept (n=29; 35%), followed by golimumab to others 2 patients. Fifty-nine patients were concomitantly treated with csDMARD. The median value of CRP was 1.5mg/dL [0.03-30]. The median value of ESR was 33mm/hr [4-98], 11 [2-75] and 10 [1-68] at baseline, 6 and 12 months, respectively. The significant correlation was found between ΔNLR, ΔMLR and ΔPLR with ΔCRP and ΔESR levels, ΔDAS28 and ΔASDAS was calculated using the Spearman’s test.

Conclusion: Our data showed that NLR, MLR and PLR decreased promptly in parallel with decrease of CRP and PLR with ESR for up 6 months of therapy with biologics. This results, in agreement with the literature, suggests that NLR, MLR and PLR may be seen as a useful marker for monitoring systemic inflammation in PsA patients. Further studies are needed to better emphasize the importance of these parameters and to evaluate their utility to monitor the effectiveness of biologic therapy.

Disclosure of Interests: None declared


NMR SPECTROSCOPY REVEALS ALTERATIONS OF URINARY ACETATE AND CITRATE LEVELS FOLLOWING CYCLOPHOSPHAMIDE THERAPY IN PATIENTS WITH LUPUS NEPHRITIS

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Background: Metabolomics, the study of global alterations in small metabolites is a useful tool to look for novel biomarkers. Recently, we reported a reprogramming of the serum metabolomic profile on nuclear magnetic resonance (NMR) spectroscopy following treatment in Lupus Nephritis (LN).

Objective: We explored urinary parameters using NMR Spectroscopy in patients with biopsy proven proliferative lupus nephritis. Change in parameters after 6 months Cyclophosphamide induction treatment and its correlation with disease activity was assessed.

Methods: Urine obtained from Lupus Nephritis (n=18, F=16, M=2) at diagnosis and following induction therapy with cyclophosphamide, and healthy controls (n=18, median age 35,all females) were stored at -80 °C. Metabolomic profiling was done using high resolution 800 MHz 1D 1H NMR spectroscopy. Urinary ratio of metabolites was calculated- (Metabolite1000)/Creatinine. Disease activity was measured using SLEDAI.

Results: Urinary metabolite fingerprint of LN patients differed from healthy controls by having significantly raised urinary acetate/creatinine (LN=41.84±100.6, HC=12.36±9.40, p<0.002) and reduced urinary citrate/creatinine (LN=34.22±54.8, HC=114.52±70.9, p<0.0001). Urinary citrate (88.68±98.33) increased after 6 months of Cyclophosphamide, while urinary acetate showed a trend towards decrease(14.77±9.98). AUC for urinary citrate/creatinine and acetate/creatinine were 0.9136 and 0.8086. The urinary acetate levels correlated with SLEDAI (r=0.337, p=0.048). Urinary citrate levels correlated with C3 (r=0.362, p=0.03) and negatively correlated with uPCR (r=0.346, p=0.039).

Conclusion: The decreased urinary citrate mirrors the finding seen in serum of the patients done earlier which reflects dampened alcoholic glycocolysis and oxidative phosphorylation.(1) Raised urinary acetate levels possibly reflects proximal renal tubular injury leading to increased urinary excretion(2). Change in levels with treatment show that urinary metabolomics parameters are potential noninvasive biomarkers for diagnosis and monitoring treatment response in LN

REFERENCES

<table>
<thead>
<tr>
<th>Metabolite</th>
<th>SLEDAI</th>
<th>rSLEDAI</th>
<th>C3</th>
<th>C4</th>
<th>PCR</th>
</tr>
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<tbody>
<tr>
<td>Acetate</td>
<td>0.337</td>
<td>0.048</td>
<td>0.22</td>
<td>0.205</td>
<td>-0.084</td>
</tr>
<tr>
<td>Citrate</td>
<td>0.314</td>
<td>0.066</td>
<td>-0.234</td>
<td>0.175</td>
<td>0.362</td>
</tr>
</tbody>
</table>

Figure: The bar graph represents the correlation of urinary metabolites and clinical parameters between groups: C3 (in blue), C4 (in red), and NC (in green). The significantly higher values for C3 and NC compared to C4 and NC groups demonstrated the diagnostic potential of these urinary markers. The values on the right side shows the correlation analysis parameters between urinary metabolic profiles and clinical parameters.

Disclosure of Interests: None declared

ROLE OF NEUTROPHIL TO LYMPHOCYTE RATIO, EOSINOPHIL TO LYMPHOCYTE RATIO, PLATELET TO LYMPHOCYTE RATIO, EOSINOPHIL TO LYMPHOCYTE AND BASOPHIL TO LYMPHOCYTE RATIO IN ASSESSING DISEASE ACTIVITY IN SPONDYLOARTHRITIS

Salomé García, Bruno Miguel Fernandes, Sara Ganhalo, Raquel Ferreira, Miguel Bernardes, Georgina Terroso, Lúcia Costa. Centro Hospitalar Universitário São João, Rheumatology, Porto, Portugal

Background: Neutrophil to lymphocyte ratio (NLR), monocyte to lymphocyte ratio (MLR), eosinophil to lymphocyte ratio (ELR) and basophil to lymphocyte ratio (BLR) have been demonstrated to be promising systemic inflammation markers. NLR, MLR and PLR have been associated with disease activity in Spondyloarthritis (SpA) but the results remain conflicting.

Objectives: We aim to determine the role of NLR, MLR, PLR, ELR and BLR in assessing disease activity in SpA.

Methods: Observational retrospective study was performed including consecutive patients with the diagnosis of SpA (according to ASAS classification criteria) followed at our Rheumatology Department. Demographic, clinical (including BASDAI, BASFI, ASDAS ESR and ASDAS CRP indices) and laboratorial data were collected from our national database at baseline and 6 months after initiation of a tumour necrosis factor inhibitor (TNFi). Correlations between variables were studied using Spearman correlation analysis and comparison between groups was performed using Wilcoxon test.

Results: The mean age of patients (n=297) was 41 years old (± 12), 160 (53.9%) were males with mean disease duration of 12.4 (IQR 14.8) years. Two hundred and seven patients (69.7%) had Ankylosing Spondylitis, 26 (8.8%) Inflammatory Bowel Disease related SPA and 36 (12.1%) Undifferentiated SpA. Seventy-three (24.7%) patients were taking glucocorticoids and regarding conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) use before starting the TNFi: 188 (63.3%) were not under any csDMARD and the remaining ones were under Sulphasalazine (70, 23.6%), Methotrexate (MTX) (21, 7.1%), Azathioprine (AZA) (5, 1.7%), Leflunomide (1, 0.3%) or associations between Sulphasalazine and AZA or MTX. Regarding the TNF inhibitor, the majority of patients initiated Adalimumab (n=168, 28.6%), Golimumab (n= 61, 25.6%) or Infliximab (n= 57, 23.9%).

At the evaluation 6 months after introducing a TNFi, we found less and lower than mean baseline values, as they were also for NLR, MLR and PLR (p<0.01).

At the baseline evaluation, in anti-TNF naïve patients, NLR and MLR were positively correlated with the majority of parameters evaluated: ESR level (r=0.322; r=0.203, p<0.01 respectively), CRP level (r= 0.475; r=0.221, p<0.01 respectively), ASDAS-ESR (r=0.25; r=0.192, p<0.01 respectively), ASDAS-ESR (r=0.257; r=0.206, p<0.01 respectively) and BASMI (r=0.288; r=0.150, p<0.01 respectively). No correlations were found with BASDAI. PLR was positively correlated with ESR level (r=0.379; p<0.01), CRP level (r= 0.331; p<0.01), ASDAS-CRP (0.215; p<0.01) and ASDAS-ESR (r=0.208, p<0.01). No correlations were found between those parameters and ELR or BLR.

At the evaluation 6 months after introducing a TNFi, we found less and weaker correlations than in naïve patients: NLR and PLR correlate positively with CRP (r=0.302; 0.315, p<0.01 respectively) and, reaching lower statistical significance, PLR correlate also with ASDAS-ESR (0.156, p>0.05); NLR with BASMI (0.184, p>0.05) and ELR (0.179, p>0.05); MLR with CRP (0.179, p>0.05), ASDAS-ESR (0.183, p>0.05) and BASMI (0.177, p>0.05) respectively.

Conclusion: NLR, MLR and PLR may reflect disease activity and could represent future inexpensive potential parameters to evaluate disease activity or severity in SpA.

Disclosure of Interests: None declared


MIOSESIS AUTOANTIBODIES PROFILE: DIAGNOSTIC RELEVANCE

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Background: The idiopathic inflammatory myopathies (IIM) are autoimmune systemic diseases that can affect several organs, but with special impact in the muscular-skeletal system. Autoimmunity is believed to have a role in its pathogenesis, with the presence of Autoantibodies (Abs) in more than 50% of the patients. Those Abs have been classified into Myositis-Specific Autoantibodies (MSA), with the Anti-Jo being the most frequent; and Miositis-Associated autoantibodies (MAA), also found in other connective tissue diseases. The availability of a multiplex analysis (Myositis Profile) has opened up new possibilities for the specific investigations of these Abs in the day-to-day clinical practice 1-2.

Objectives To describe the clinical spectrum and the Ab results obtained from the myositis profile in patients (hospital admissions and ambulatory) of a tertiary university hospital.

Methods Retrospective descriptive study (January to June 2018) of the results obtained on the myositis profile. The clinical characteristics of the sample is described in the context of the Abs results. We considered that applications of this Myositis Ab Profile were justified if they had EPIID and/or if they had 2 or more clinical and/or analytical characteristics associated with MII. Myositis Profiles consisted in a solid phase ELISA from EuroLINE MII 16 Antigens (MII-alfa, MII-beta, TIF gamma, MDAS, NXP2, SAE1, Ku, Pm-Scl100, Pm-Scl75; Jo-1, SRP, PL7, PL12, EJ, OJ, RO-52). Statistical analysis SPSS 17.0.

Results A total of 165 applications were studied, 47% requested by Reumatology, 30% by Neurology and 9% by Internal Medicine. Justifications were: ILD (n=49); osteoarticular (n=30), connective diseases (n=27), oculomyastitis (n=17), CK-NAC elevation (n=11), fibromyalgia (n=7) and others (n=22). 41% men and 59% women, Average Age 58 (+/- 15 years). We observe an increase of CKNAC, GPT, GPT y LDH in 21%, 12% and 24% respectively. They refer muscle weakness in 18%, Raynaud’s phenomenon in 10%, arthritis in 15%, heliotrope eruption in 4%, Gottron’s papules in 1% and mechanics hand in 1%. Using the criteria specified in the method section, 52% of the applications were justified, being the 57% of them as ILD study. 32 (20%) of the 165 profiles were positive. 10 of the 49 patients with ILD had positive Abs (figure 1), 90% me. 8 of the 17 patients with myositis had positive Abs (figure 1), 63% women. 75% of them (6/8) were positive for MSA, the 65% were Anti-Jo (4/6). 1 patient with myositis associated with neuropia (anti-CJ). 2 of 3 muscle biopsy were consistent with MII. 2 of 7 EMG were compatible. The 14 remaining patients had some positive Abs (figure 2): 7 connective tissue diseases studies, 4 osteomuscular pathology, 1 auto-inflammatory disease, 1 CK-NAC elevation and 1 with inflammatory bowel disease (IBD).

Conclusion The use of this Ab profile as a protocol for patients with ILD without myositis clinical features, allowed us to classify a group of patients with autoimmune diseases. In this group, the distribution by sex, 9 males and 1 woman is highlighted. We achieved the diagnosis on the 47% of patient with myositis clinical suspicion. The usefulness of myositis profile allowed us to detect antibodies which are not in other immunologic assays. Distribution by sex, 3 men and 5 women.

Disclosures None declared


AB1314

AB1315

AGREEMENT BETWEEN SUBJECTIVE AND OBJECTIVE DEFINITIONS OF INACTIVE DISEASE IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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Background: The choice of an appropriate definition of inactive disease (ID) is important because ID has been identified as the ideal therapeutic goal in the treat-to-target strategy in juvenile idiopathic arthritis (JIA).1 Several criteria for ID in JIA have been proposed, including Wallace 2004 and 2011 criteria and JADAS10 and clinical JADAS10 (cJADAS10) criteria. However, a recent study2 has shown that these criteria do not always identify the same group of patients. In addition, it is unknown whether and to what extent the formal definitions of ID agree with the subjective perception of disease remission by the physician and the parent.3

Objectives: To investigate the concordance between current criteria for ID and subjective judgment of disease remission by physicians and parents in children with JIA.

Methods: We evaluated the clinical data of the last visits made in 669 children with JIA from March 2007 to December 2010 to identify all visits in which the caring physician and a parent judged subjectively and independently the child’s disease state as remission or non-remission and the parent declared whether he/she was satisfied or non-satisfied with current illness state (i.e. Parent Acceptable Symptom State, PASS).4 All visits judged subjectively by the physician and the parent as remission or judged in PASS by the parent were examined to identify those who met the Wallace 2004 and 2011 criteria and the JADAS10 and cJADAS10 criteria for ID. Visits which met both subjective and objective definitions were defined as concordant.

Results: Of the 246 visits in which the physician judged subjectively the disease state as remission, 34.6% and 27.6% met the 2004 and 2011 Wallace criteria, respectively, and 38.6% and 54.5% met the JADAS10 and cJADAS10 criteria for ID, respectively. (Figure 1) Of the 338 visits in which the parent judged subjectively the disease state as remission, 19.8% and 18% met the 2004 and 2011 Wallace criteria, respectively, and 34.9% and 48.8% met the JADAS10 and cJADAS10 criteria for ID, respectively. (Figure 2) In 76.4% of visits judged as remission by the physician, the parent provided the same evaluation. In 55.6% of visits judged as remission by the parent, the physician provided the same evaluation. (Figure 1-2) Of 467 visits judged in PASS by the parent, 17.6% and 14.8% met the 2004 and 2011 Wallace criteria, respectively, and 26.6% and 37.5% met the JADAS10 and cJADAS10 criteria for ID, respectively.

Conclusion: The JADAS10 and cJADAS10 criteria for ID were more concordant with physician’s and parent’s subjective judgment of remission and with parent’s satisfaction with current illness state than Wallace criteria. The cJADAS10, which lacks the acute phase reactant, revealed the best concordance with both physician’s and parent’s subjective assessment. Physician-parent agreement was greater for remission judged by the physician than for remission judged by the parent.

REFERENCES


What is a total knee or total hip arthroplasty failure? A Patient perspective using nominal groups

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Background: Total joint replacements (TJR) are commonly performed elective surgeries for people with end-stage arthritis. However, there is relative lack of qualitative research to define the patient perspective of what constitutes a failure of TJR.

Objectives: To discover when a TJR is considered a failure from the perspective using nominal group technique (NGT). Total joint replacements (TJR) are commonly performed elective surgeries for people with end-stage arthritis. However, there is relative lack of qualitative research to define the patient perspective of what constitutes a failure of TJR.

Methods: Patients who had undergone elective total hip (THR) and/or knee replacements (TKR) met in nominal groups to answer the question “When would you consider a knee or hip replacement to be a failure?” Patients competed questionnaires including demographics, pain, function, and satisfaction, independently listed their ideas and then ranked them with the group after clarification.
Results: Six groups with 35 patients were held, all of whom had undergone THR or/and TKR between 2016 and 2018. Of these, 42% were male, 58% female (Table 1). Overall pain and function scores were high, Hip Disability and Osteoarthritis Outcome Score (HOOS) JR 95.3 (SD±/11) and Knee Injury and Osteoarthritis Outcome Score (KOOS) JR 83.7 (SD±/12.8) (range 0-100, higher score=less pain/functionality limitation), and 86.1% were very/somewhat satisfied with their quality of life. The concerns ranked highest by the patients equating a TJR failure were A) refractory index joint pain (67 votes); B) unable to resume normal activities or go back to work (38 votes); C) minimal or no improvement in quality of life (24 votes); D) post-operative adverse events (40 votes); E) early revision surgery (32 votes); F) death (7 votes); G) expectation-outcome mismatch (1 vote); continuing secondary depression (1 vote) (Table 2).

Conclusion: Poor results for pain, function, quality of life, or adverse events are the outcomes ranked highest by patients, defining TJR failure from the patients’ perspective.

<table>
<thead>
<tr>
<th>Table 1. Baseline Characteristics</th>
<th>THR</th>
<th>THR</th>
<th>Both TJR and THR</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean, SD)</td>
<td>75.7 ±8.2</td>
<td>65.3 ±8.0</td>
<td>66.3±5.4</td>
<td>71.1±9.4</td>
</tr>
<tr>
<td>Men, n(%)</td>
<td>6 (31.6)</td>
<td>8 (61.5)</td>
<td>1 (33.3)</td>
<td>15 (42.9)</td>
</tr>
<tr>
<td>Black, n(%)</td>
<td>3 (15.8)</td>
<td>3 (21.1)</td>
<td>-</td>
<td>6 (17.1)</td>
</tr>
<tr>
<td>Asian, n(%)</td>
<td>-</td>
<td>1 (33.3)</td>
<td>-</td>
<td>1 (2.9)</td>
</tr>
<tr>
<td>Multi-racial, n(%)</td>
<td>1 (5.3)</td>
<td>1 (7.7)</td>
<td>-</td>
<td>2 (5.7)</td>
</tr>
<tr>
<td>Education</td>
<td>High school, n(%)</td>
<td>-</td>
<td>1 (7.7)</td>
<td>-</td>
</tr>
<tr>
<td>Some college, n(%)</td>
<td>1(5.3)</td>
<td>3(21.1)</td>
<td>3(100)</td>
<td>4 (11.4)</td>
</tr>
<tr>
<td>College or above, n(%)</td>
<td>18 (9.62)</td>
<td>3 (100)</td>
<td>30 (85.7)</td>
<td>(94.7)</td>
</tr>
<tr>
<td>Employment</td>
<td>Employed, n(%)</td>
<td>3 (15.8)</td>
<td>9 (69.2)</td>
<td>3(100)</td>
</tr>
<tr>
<td>Self-employed, n(%)</td>
<td>4 (21.1)</td>
<td>3(21.1)</td>
<td>-</td>
<td>7 (20.0)</td>
</tr>
<tr>
<td>Out of work, not looking for work, n(%)</td>
<td>1(5.3)</td>
<td>-</td>
<td>-</td>
<td>1 (2.9)</td>
</tr>
<tr>
<td>Retired, n(%)</td>
<td>11 (57.9)</td>
<td>1 (7.7)</td>
<td>-</td>
<td>12 (34.3)</td>
</tr>
<tr>
<td>Reason for surgery</td>
<td>Osteoarthritis, n(%)</td>
<td>13 (68.4)</td>
<td>11 (86.4)</td>
<td>3(100)</td>
</tr>
<tr>
<td>Rheumatoid arthritis, n(%)</td>
<td>2 (10.5)</td>
<td>17.7</td>
<td>-</td>
<td>3 (8.6)</td>
</tr>
<tr>
<td>Other arthritis, n(%)</td>
<td>3 (15.8)</td>
<td>17.7</td>
<td>-</td>
<td>4 (11.4)</td>
</tr>
<tr>
<td>Avascular necrosis of the bone, n(%)</td>
<td>1(5.3)</td>
<td>-</td>
<td>-</td>
<td>1 (2.9)</td>
</tr>
</tbody>
</table>

Abstract AB1317 Table 2. Theme: When would you consider a hip or knee Score replacement a failure?

NG 1-6, 35 people, 14 Male, 21 Female; 8 African-American, 25 White, 2 Asian, 210 votes

A. Pain: Still in pain/remains unchanged/persists 67
   - "Primary factor for getting surgery. Pain impacts every facet of life"

B. Activities: Cannot regain normal function or activities/physical disability persisted 38
   - "Can't reach a goal – goal is to reach the top of the stairs or room"

C. Quality of life
   - "Can't go back to work and can't walk. Purpose of surgery to get back life. Going to theater, cooking. Social, mental, physical, emotional."

D. Adverse Events: Infection, implant rejection, bone damage, complications 40
   - "Infection sets you back, psychological event, when does it get cured, do I have to go back for surgery. Start questioning everything."

E. Revision: Having another surgery for the same problem 32
   - "Did not want to go through it again"

F. Death: Infection leading to death, implant causing death, death during surgery 7
   - "Friend died of infection, that's why I came here"

G. Other
   - "When outcomes don't meet expectations"
   - "combined votes; NG= nominal group"

Disclosure of Interests: jasinder singh Shareholder of: Aman pharmaceuticals and Vicking therapeutics, Consultant for: Creativa/ Horizon, Fidia, UBMC LLC, Mediscape, WebMD, the National Institutes of Health and the American College of Rheumatology, Beila Mehta: None declared, Serena Mirza: None declared, Mark Figgie: None declared, Peter Sculco: None declared, Michael Parks Grant/research support from: Zimmer Biomet, Employee of: Zimmer Biomet, Susan Goodman Grant/research support from: Novartis: research support, Consultant for: Novartis, UCB, Pfizer: consulting


AB1318 VALUE OF NEW BIOMARKERS IN THE DIFFERENTIAL DIAGNOSIS OF SARCOIDSIS AND TUBERCULOSIS

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Background: Due to multisystem involvement with almost similar presentation, tuberculosis (TB) and sarcoidosis poses a diagnostic challenge. As both of them show granulomatous inflammation in tissue, even histopathological examination is not helpful to differentiate the two. As a result of this difficulty, new biomarkers for differentiating the two are being investigated. Previous studies (1,2) done in other regional population attempted to show the efficacy and role of Neutrophil by lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR) to differentiate sarcoidosis from TB, with inconsistent results. We attempt to see if these biomarkers can be used in our population to differentiate the two.

Objectives: The aim of our study was to investigate the value of neutrophil/lymphocyte ratio (NLR), and platelet/lymphocyte ratio (PLR) to differentiate TB from sarcoidosis. In addition, we also studied Neutrophil/lymphocyte/albumin/globulin ratio (NLR by A:G ratio) as a novel marker for differentiating the two.

Methods: Patients recruited for the study were selected retrospectively from hospital records during the period of September 2017 to December 2018:

1. 50 consecutive pulmonary TB patients diagnosed based on sputum acid-fast bacilli (AFB) positivity and/or culture–positivity
2. 39 consecutive patients diagnosed with sarcoidosis by an experienced Rheumatologist on clinical and histological grounds.
3. 50 consecutive healthy subjects who presented to general comprehensive check up on Monday of every week. Subjects who were having any autoimmune disease or infections were excluded.

We collected the information including clinical and biochemical parameters at the time of presentation, from the hospital records. NLR, NLR by A:G ratio and PLR were calculated. To test the statistical significance of continuous variables between sarcoid and tb student’s t test/Mann Whitney U test was used. To find the cut off value of study variables, ROC curve was used. Diagnostic measures like sensitivity, specificity, predictive values and accuracy was computed.

Results: Though age was comparable, sex ratio varied between groups with more females in sarcoidosis group. Leukocyte count and neutrophil percentage, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), NLR, NLR by A:G and PLR were significantly higher in the TB group compared with sarcoidosis (for all parameters P < 0.001). Table showing ROC analysis results and accuracy rates of NLR, NLR by A:G ratio and PLR in detection of tuberculosis among sarcoidosis and tuberculosis groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Cut - off</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>AUC</th>
<th>Accuracy</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>NLR</td>
<td>3.58</td>
<td>92</td>
<td>73</td>
<td>82</td>
<td>88</td>
<td>0.86</td>
<td>84</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>NLR by A:G</td>
<td>4.48</td>
<td>82</td>
<td>83</td>
<td>87</td>
<td>77</td>
<td>0.88</td>
<td>83</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PLR</td>
<td>220</td>
<td>64</td>
<td>62</td>
<td>68</td>
<td>57</td>
<td>0.70</td>
<td>63</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Conclusion: TB vs sarcoidosis is a challenging diagnostic dilemma. Our retrospective study shows the role of NLR, NLR by A:G ratio and PLR in differentiating TB from sarcoidosis. These biomarkers can help to guide our clinical judgement in differentiating these two causes of granulomatous inflammation.

REFERENCES


Disclosure of Interests: None declared

EFFICACY AND SAFETY OF THE TREATMENT WITH JAK INHIBITORS IN PATIENTS WITH RA. RESULTS OF A CASE SERIES OF USUAL CLINICAL PRACTICE  

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Background: The JAK inhibitors, a new group of targeted synthetic DMARDs were marketed in Spain in 2018. These oral drugs are a good therapeutic alternative for patients with MTX failure. These are not biologic DMARDs and its place in clinical practice is not clear.  

Objectives: To identify the clinical characteristics of the patients treated with JAK inhibitors in a Rheumatology service in the South of Spain. To know the efficacy and safety of these drugs used in usual clinical practice.  

Methods: Setting: Rheumatology department in a 3rd level University Hospital. Design: an observational and analytical case series. From September 2018 to January 15, 2019 clinical data were collected of all patients with RA (ACR/EULAR 2010) treated with JAK inhibitors. The variables collected were demographics, clinical, related to RA, comorbidities, activity (DAS28ESR) and EULAR response. Safety variables included adverse events, and adverse events that caused the interruption of the treatment. The protocol was approved and conducted according to the local ethic committee regulations. The statistical analysis was done with descriptive and inferential non parametric tests. Data are shown as median (percentile 25 – percentile 75).  

Results: In the study period, 33 patients were treated with JAK inhibitors. Two patients were excluded of this review due to lack of an evaluation of follow-up. Data of 31 RA patients are presented. They were female (74%) with RF+, ACPA+ and erosive disease in more of 90% of cases; 61% had at least one comorbidity. The Charison comorbidity index was 3 (2-6). The median age at the time of the start of the JAK inhibitor was 63.3 (56.8 – 70.7) years. The disease duration at the time of the start of the JAK inhibitor was 14.7 (8.6 – 27.5) years. All the patients had received synthetic conventional DMARDs, the number of previous scDMARDs was 2 (2 – 6); 26% had been treated with biologic DMARDs. The number of previous bDMARDs was 2 (1 – 5); 26% (84%) patients were treated with baricitinib and 5 with tofacitinib, oh these 25 (77%) were treated with corticosteroids, the median daily dose of prednisone was 7.5 (5 – 15) mg/day, and 16 (52%) were treated with MTX; the mean weekly dose was 15 (10 – 25) mg/week. The baseline DAS28ESR was 4.9 (4.1 – 5.7) and the end DAS28ESR was of 2.6 (2.07 – 3.5), p<0.0001; the EULAR response was good in 15 (52%), Moderate in 11 (35%) and Poor in 5 (13%). At the last visit 15 (38%) were in remission (DAS28ESR ≤2.6), and the follow-up was of 11.1 (6.8 – 16.7) months. In 8 patients the treatment was stopped, one due to primary inefficacy, three due to secondary inefficacy and in five patients due to adverse events The most relevant adverse events were one case with septic arthritis of the knee after a intra articular injection; one case with a community acquired pneumonia; one case with pyometra, one breast cancer recurrence, one severe neuropenia and one with severe psoriasis flare. There were no thrombotic events. The only variable related with remission was the low baseline DAS.  

Conclusion: The JAK inhibitors are tsDMARD with good profile of efficacy and safety in clinical practice. The patients treated with these drugs had a long and severe disease with failure to several drugs and poor prognostic variables, and a high comorbidity index, however these drugs show good response rates.  

Disclosure of Interests: None declared  


AB1320  

NEUTROPHEL-TO-LYMPHOCYTE RATIO AND PLATELET-TO-LYMPHOCYTE RATIO ARE ASSOCIATED WITH DISEASE ACTIVITY IN POLYMALGIA RHEUMATICA  

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Background: Polymyalgia rheumatica (PMR) is a systemic inflammatory disorder, which develops inflammatory pain and stiffness of large joints. There is no specific serological marker or test to differentiate PMR. There is no specific serological marker or test to differentiate PMR.  

Objectives: To identify the clinical characteristics of patients with PMR compared with patients with RA (all p < 0.001). NLR, PLR, and MLR were correlated with specific serological values, including CRP and amin, in patients with PMR. After disease activity resolved, NLR (2.95 ± 2.32, p < 0.001), PLR (137.5 ± 82.3, p < 0.001), and MLR (0.26 ± 0.16, p < 0.001) decreased significantly. By comparing patients according to the disease course, swollen joint counts were higher in the chronic course group compared with the remission group (p = 0.03), while NLR, PLR, and MLR levels were similar.  

Conclusion: This study found that NLR, PLR, and MLR in patients with PMR were higher than in those with RA. Furthermore, NLR, PLR, and MLR levels were associated with disease activity and specific clinical features, although they could not predict prognosis in patients with PMR.  

REFERENCES:  

Discussion of Interests: Ju-Yang Jung: None declared, Jiwon Kim: None declared, Chang-Hee Suh Consultant for: Celltrion, Inc, Hyoun-Ah Kim: None declared  


AB1321  

PSYCHOMETRIC PROPERTIES OF THE ASAS HEALTH INDEX IN PATIENTS WITH ACTIVE AS/RADIOPHAGIC AXIAL SPA WHO HAVE PRIOR INADEQUATE RESPONSE/INTOLERANCE TO TNF INHIBITORS IN A PHASE 3 TRIAL  

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Background: The Assessment of SpondyloArthritis international Society Health Index (ASAS HI) assesses function, disability, and health in patients with ankylosing spondylitis/radiographic axial spondyloarthritis (ASI-/axSpA).  

Objectives: To evaluate the psychometric properties of the ASAS HI in patients with active ASI-/axSpA in a placebo-controlled study of ixekizumab, a humanized IL-17A monoclonal antibody (COAST-W, NCT02696798).  

Methods: The ASAS HI questionnaire consists of 17 dichotomous items that yield a total score ranging from 0 (good health) to 17 (poor health). The psychometric properties of the questionnaire, including test-retest reliability, convergent and discriminant validity, and responsiveness, were evaluated using pooled data from three exposure groups (placebo and ixekizumab 80 mg every 2 or 4 weeks). Adults enrolled fulfilled ASAS criteria (sacroiliitis defined centrally by modified New York Criteria and ≥1 SpA feature), had active disease (BASDAI > 4, back pain > 4), and either prior inadequate response or intolerance to 1 or 2 TNF inhibitors.  

Results: Mean baseline ASAS HI score was 9.7 (SD=3.62, n=316). Intraclass correlation (0.78) indicated test-retest reliability of ASAS HI between screening and baseline. ASAS HI score was moderately correlated at baseline (r=0.30, Figure [circles]) and strongly correlated at Week (Wk) 16 (r=0.50; Figure [crosses]) with BASDAI, BASFI, SF-36 PCS, and spinal pain, and strongly correlated at both baseline and Wk 16 with EQ-5D-5L UK Population-based Index and SF-36 MCS. Greater improvements in disease activity were associated with greater improvements in ASAS HI scores at Wk 16 (Table).  

Conclusion: The ASAS HI demonstrated reliability, validity, and responsiveness in adults with ASI-/axSpA, supporting its use in clinical trials.
Figure. Correlation between ASAS-HI and other health measures

Table. Association between ASAS-HI and other health measures

**Note:** An ANCOVA model with change in ASAS-HI score as dependent variable and clinical and outcome response and baseline ASAS-HI as independent variables was applied. Post hoc comparison was conducted using Scheffé's correction.

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AB1323
OSTEOPHYTOSIS PROCESS SUGGEST INVOLVEMENT OF MAST CELLS, REVEALED BY WHOLE TRANSCRIPTOME ANALYSIS OF OSTEOARTHRITIS PATIENTS

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Background: Cartilage-loss is a central pathophysiology of osteoarthritis while synovitis, sub-chondral bone sclerosis and osteophytes (OFs) formation are counted as integral phenomenon. Osteophytosis is a process of OFs formation, in which mesenchymal stem cells from peristeum and synovium, along with a number of cytokines, growth factors and biochemical factors gives out bony out-growth at margin of the affected joint. Although frequently associated, OFs are one of the less focused areas in OA research, particularly from the molecular mechanism point of view, involved in their formation. Also, it is a good ambiguity if OFs is a pathological condition with altered biochemical milieu or a functional adaptation for joint health.

Objectives: Accounting its importance in clinical OA and the obscure biochemical background, this study strives for a deeper comprehension of molecular mechanism and active pathways, involved in OF formation

Methods: We performed whole transcriptome analysis of OFs, collected from six knee OA patients during knee replacement surgery. Non-OF tissue from tibial plateau of the same patient was used as a control. After RNA isolation, RNA-seq was performed using SOLiD 5500W platform and fragment sequencing chemistry. For differential gene expression analysis, non-normalized raw counts were used for the EdgeR package. To find differential transcriptome between OF and control, we used group-wise comparisons where negative binomial fitting was followed by exact test. Finally, RT-PCR of significantly expressed genes was run for transcriptome validation.

Results: After cluster analysis, total 597 genes were significantly expressed between OFs and controls out of which, 323 genes were seen up-regulated (LogFC > 2) while 274 were down-regulated (LogFC < 2). Further, 88 genes showed marked increase (P<0.01); here CP3A, Selectin E, MS4A2, PLA2G2A and CD44 were prominent. Similarly, 23 genes were with a noteworthy down-regulation (P<0.01) and APOB, CADM2, TNEFF2, GNAZ and GABRA2 remained as first five. GO analysis of the best extracted genes indicated significant involvement of ECM proteoglycan, GABA receptor pathway (Reactome 2016 - homo sapiens WP2031 and homo sapiens WP231 respectively). Finally, trascriptome results were validated using RT-PCR of significantly expressed genes (CP3A, MMP-1, 3 and 13).

Conclusion: Significant expression of CXCL9, 10, 11 and PGRF indicate chemotaxis and immune cells deployment; outstanding CP3A and MS4A2 indicate active involvement of mast cells. Accounting a previous knowledge that ‘mast cell products’ are linked with increased osteoblastic and osteoclastic activity and impose pathological changes in articular and peri-articular tissue, marked expressions of MC products or mediators here, enable us to propose an association between MCs and OF. Presence of E-selectin on endothelial cell surface is known to promote adhesion of neutrophils and further release of TNFα and IL1. Expression of PLA2G2A suggests increased prostaglandin synthesis and indicates activation of inflammatory cascade. In conclusion, this transcriptome analysis suggests a significant association of mast cells with osteoarthiysis. The genes involving chemotaxis, degranulation, cytokinin synthesis mark the initiation of OF. On the other hand, proteases metrinmodelling enzymes may indicate their growth. A host of different signalling molecules denotes involvement of canonical and non-canonical pathways that warrants further investigations.


AB1324
MEASUREMENT PROPERTIES OF THE 10-ITEM CONNOR-DAVIDSON RESILIENCE SCALE AMONG PATIENTS WITH TOTAL KNEE REPLACEMENT BASED ON ITEM RESPONSE THEORY

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Background: The number of older adults undergoing total knee arthroplasty (TKR) for knee osteoarthritis (OA) has been increasing. While psychological resilience may have a role in outcomes after TKR[1], no psychological resilience scale has been validated among patients with knee OA.

Objectives: To examine the measurement properties of the 10-item Conner-Davidson Resilience Scale (CD-RISC10) among older adults with knee OA.

Methods: Using data from 700 consecutive consented patients with knee OA enlisted for TKR, we examined four measurement properties of CD-RISC10. For structural validity, we fitted graded response model (grm) and examined standardized root-mean square residual (SRMR) for unidimensionality, Chi-square p-value for item fit, residual correlation for local independence and item characteristic curves for overall structure. For measurement invariance, we examined Cronbach’s alpha. For construct validity, we hypothesized that CD-RISC10 as a measure of psychological resilience would be moderately correlated (Pearson’s R 0.30–0.50) with self-efficacy and mental well-being but weakly correlated (Pearson’s R<0.30) with physical and social well-being (Table 1). For measurement invariance, we examined uniform and non-uniform differential item functioning (DIF) between gender, age group (< median 66 vs >66 years), and language (English vs Chinese) and reported the McFadden’s R2. We used mixed and ldfit packages on Rx64 v3.5.1 to examine grm and DIF respectively. We reported the findings based on COSMIN user manual for the selection of health Measurement Instruments (COSMIN[n]).

Results: Of the 700 patients (age 65.5±6.9 years old), 70.6% were females, 83.9% Chinese, 55% responded questionnaire in Chinese. Mean CD-RISC10 score was 27.5±5.2, with minimal floor (0.1%) and ceiling effects (3.9%). CD-RISC10 demonstrated unidimensionality (SRMR<0.05), local independence (residual correlation<0.025), monotonicity (adequate looking item characteristic curves) and internal consistency (Cronbach’s alpha=0.91). Items 1 and 4 had potential misfit (Chi-square p<0.01). All a-priori hypotheses were met (Table 1). No item had significant DIF with age, gender and language, except item 4 had borderline non-uniform DIF across language (McFadden’s R2=0.03).

Conclusion: We demonstrated structure validity, internal consistency, construct validity and measurement invariance of CD-RISC10 in the measurement of psychological resilience among older adults with knee OA.

REFERENCES
HAND FUNCTION IS IMPAIRED IN PATIENTS WITH RHEUMATOID ARTHRITIS, PSORIATIC ARTHRITIS AND PSORIASIS COMPARED TO HEALTHY CONTROLS

Table 1. Hypothesized and actual correlations for convergent validity

<table>
<thead>
<tr>
<th>Hypothesized</th>
<th>Actual</th>
<th>Hypotheses Met</th>
</tr>
</thead>
<tbody>
<tr>
<td>Internal resource</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain self-efficacy</td>
<td>+</td>
<td>0.30 – 0.50</td>
</tr>
<tr>
<td>Mental well-being</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HADS anxiety</td>
<td>-</td>
<td>-0.30 – 0.0</td>
</tr>
<tr>
<td>HADS depression</td>
<td>-</td>
<td>-0.30 – 0.0</td>
</tr>
<tr>
<td>SF-36 mental health</td>
<td>+</td>
<td>0.30 – 0.50</td>
</tr>
<tr>
<td>Physical well-being</td>
<td></td>
<td></td>
</tr>
<tr>
<td>WOMAC physical function</td>
<td>-</td>
<td>- &gt; 0.30</td>
</tr>
<tr>
<td>WOMAC pain</td>
<td>-</td>
<td>- &gt; 0.30</td>
</tr>
<tr>
<td>WOMAC stiffness</td>
<td>-</td>
<td>- &gt; 0.30</td>
</tr>
<tr>
<td>SF-36 physical functioning</td>
<td>+</td>
<td>- &lt; 0.30</td>
</tr>
<tr>
<td>Social well-being</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lubben’s social network score</td>
<td>+</td>
<td>- &lt; 0.30</td>
</tr>
</tbody>
</table>

Objectives:

- To quantify and compare grip strength and hand function in patients with RA, PsA and Pso to relate these outcomes to disease activity.

Methods:

- Patient diagnosed with RA (ACR/EULAR 2010), PsA (Caspar) and Pso and 54 healthy individuals were included in the study after written informed consent. Maximal isometric grip strength (kPA) was measured with a hand dynamometer (Lafayette Instrument, Lafayette, IN, USA) as the highest value out of three measurements. Hand function was determined by way of the Moberg Picking-Up Test (MPUT) and the fastest (s) of two measurements was used. Disease activity was calculated as DAS28_ESR and TJC/SJC 76/76 was recorded. One-way Analysis of Variance (ANOVA), factorial ANOVA and Games-Howell post-hoc testing was performed (p<0.05).

Results:

- 101 RA (63 f; 38 m; age: 59.1±13.2 yrs), 92 PsA (48 f; 44 m; age: 54.8±11.5 yrs) and 51 Pso patients (19 f; 32 m; age: 47.3±14.1 yrs), as well as 54 healthy control subjects (30 f; 24 m; age: 54.6±16.5 yrs) participated in the study. Disease duration (yrs) was not different between groups (RA: 11.0±10.1; PsA: 9.1±9.75; Pso: 12.5±11.7; p=0.156) but Pso patients in our cohort were younger compared to RA and PsA patients. Mean DAS28_ESR was < 3.2 for all patient groups with control subjects (DAS28 1.6 ± 0.7) having lower scores compared to all patient groups and Pso patients presenting with lower DAS28 (2.3 ± 1.3) compared to RA (3.0±1.3) and PsA (2.9±1.3). While TJC was higher for all patients compared to controls (RA: 5.2±6.8; PsA: 5.9±8.1; Pso: 3.2±6.4; CON: 0.5±1.4; p<0.00), SJC was higher for RA and PsA compared to Pso and CON (RA: 0.7±1.0; PsA: 0.9±2.2; Pso: 0.1±0.3; CON: 0.5±1.4; p=0.00). Grip strength of the dominant and/or affected hand of RA patients was lower compared to PsA, Pso and CON (Figure 1A). In contrast to this, hand function of the same hand in all tested patient groups was reduced compared to CON (Figure 1B). The results for grip strength and hand function were not different for the dominant and the affected hand and are independent of age differences between groups.

Conclusion:

- Overall, RA patients showed significantly lower grip strength compared to PsA and Pso patients as well as to the control group, whereas all three patient groups performed worse in the MPUT compared to the control cohort. This suggests that grip strength may be preserved longer than hand function in patients with inflammatory rheumatic disease. Further, it was surprising that hand function was reduced in Pso patients without arthritic correlate compared to healthy subjects. This suggests that hand function may provide a potential parameter for discriminating Pso patients at risk for subclinical joint involvement.

This study was funded by research support from Novartis Pharma GmbH.

REFERENCES


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HADS Anxiety & Depression Scale; SF-36; Short-Form 36; WOMAC; Western Ontario & McMaster Universities Osteoarthritis Index

AB1325

INCREASED FIBRINOGEN TO ALBUMIN RATIO IN ANKYLOSING SPONDYLITIS: CORRELATION WITH DISEASE ACTIVITY

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Background:

- Fibrinogen to albumin ratio (FAR) has emerged as a new effective biomarker which can reflect the severity of chronic inflammation. However, none of study has focused on the role of FAR in ankylosing spondylitis (AS).

Objectives:

- The study aimed to investigate the association between FAR and the disease activity of AS.

Methods:

- The retrospective study included 117 AS patients and 165 age- and gender-matched healthy controls. AS patients were divided into remission group (Bath Ankylosing Spondylitis Disease Activity Index
(BASDAI < 4) and active group (BASDAI ≥ 4). Remission group included 60 patients and active group included 57 patients. Fibrinogen, albumin, FAR, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were collected. Relationships between FAR and BASDAI as well as other biochemical indexes were assessed by the Spearman's correlations analysis. Receiver operator characteristic (ROC) curves were performed to discriminate AS patients from healthy subjects and active group from remission group. Furthermore, binary logistic regression analysis was conducted to evaluate the risk factors of AS disease activity.

Results: FAR, fibrinogen, CRP and ESR were higher in AS patients compared with healthy controls (P < 0.05), while albumin was lower (P < 0.05). ROC results showed that area under curve (AUC) of FAR (0.818, 95%CI: 0.760 - 0.876) and albumin (0.841, 95%CI: 0.788 - 0.894) were higher than fibrinogen (0.772, 95%CI: 0.707-0.836), CRP (0.677, 95%CI: 0.598 - 0.756) and ESR (0.784, 95%CI: 0.721 - 0.847). Positive correlations were found between FAR and BASDAI (r = 0.488, P < 0.001), CRP (r = 0.858, P < 0.001) and ESR (r = 0.817, P < 0.001). Besides, FAR, fibrinogen, CRP and ESR in active group were higher than remission group (P < 0.05), while albumin was lower (P < 0.05). ROC results showed that AUC of FAR (0.691, 95%CI: 0.598-0.768) was higher than fibrinogen (0.676, 95%CI: 0.577-0.776), albumin (0.665, 95%CI: 0.567 - 0.783), CRP (0.646, 95%CI: 0.545 - 0.746) and ESR (0.667, 95%CI: 0.569 - 0.766). FAR was a risk factor of the disease activity in AS patients (OR: 1.354, 95%CI: 1.067 - 1.718, P = 0.013).

Conclusion: FAR was increased in AS patients compared with healthy controls and significantly correlated with the disease activity of AS. FAR might be a potential useful inflammatory biomarker to monitor disease activity of AS patients.

REFERENCES


Acknowledgement: Natural Science Foundation of Guangdong Province (No. 2017A030313526), Youth Foundation of Guangdong Second Provincial General Hospital (No. YQ2017-009).

Disclosure of Interests: None declared

of the study was the small numbers of the patients in the single group and the early disease stage. Further studies are needed to analyze the validity and reproducibility of these biomarkers in early axSpA.

Disclosure of Interests: None declared


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Background: The Brief Pain Inventory (BPI-SF) and McGill Pain Questionnaire (SF-MPQ-2) are general-use, self-report, multidimensional pain assessment outcomes frequently used for pain assessment in musculoskeletal (MSK) conditions. Synthesizing knowledge on their measurement properties, as assessed in MSK conditions, should provide a deeper understanding of their strengths and limitations.

Objectives: To systematically locate, critically appraise, compare and summarize clinical measurement research about the BPI-SF and SF-MPQ-2 in pain-related musculoskeletal conditions.

Methods: Four databases (Medline, CINAHL, EMBASE & SCOPUS) were systematically searched for relevant citations, each for the BPI-SF and SF-MPQ-2. We included articles that reported the psychometric properties (e.g. validity, reliability, responsiveness) and interpretability indices (e.g. minimal clinical important difference) of both tools, as assessed in mixed and specific MSK studies. Independently, two reviewers extracted data and assessed the quality of evidence with a structured quality assessment tool for measurement studies and according to the updated Consensus-based Standards for the selection of health Measurement Instruments (COSMIN) guidelines.

Results: Twenty-five articles were included (BPI-SF, n=17; SF-MPQ-2, n=8). Both tools lack reporting on their cross-cultural validities and measurement error indices. High quality studies suggest that they are internally consistent (α = 0.83-0.96), and they associate modestly with similar outcome measures (r = 0.3-0.69). There is evidence that the BPI-SF conforms to its two-dimensional structure in MSK studies; the SF-MPQ-2 four-factor structure was not clearly established. In seven reports, high to moderate quality evidence was seen in supports of the BPI-SF known group validity (n=2) and responsiveness (n=5) but none was available for the SF-MPQ-2. Furthermore, the SF-MPQ-2 was more frequently associated with floor effects in MSK studies than the BPI-SF (SF-MPQ-2, 42% vs BPI-SF, 6%).

Conclusion: The SF-MPQ-2 has emerging evidence whereas the BPI-SF evidence is more mature. Both tools displayed high-quality evidence in support of their internal consistency and criterion-convergent validities. High to moderate quality evidence suggests the BPI-SF subscales have a better responsiveness, restest reliability, known group validity and structural validity than the SF-MPQ-2.

REFERENCES

Disclosure of Interests: None declared

THE PRELIMINARY VALIDATION OF LASER DOPPLER FLOWMETRY IN SYSTEMIC SCLEROSIS ACCORDING TO THE OMERACT FILTER: A SYSTEMATIC REVIEW

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Background: Systemic sclerosis (SSc) is characterised by a widespread vasculopathy. The vasculopathy comprises the skin microcirculation and results in features such as Raynaud’s phenomenon (RP) and digital trophic lesions. The quantification of the skin blood perfusion at the level of the finger (FBP) is a major need in the assessment of SSc in clinical and research setting. Up to now, laser doppler flowmetry (LDF) has been the most thoroughly investigated instrument to assess the FBP in SSc.

Objectives: To investigate the validation status of LDF in SSc according to the Outcome Measures in Rheumatologic Clinical Trials (OMERACT) filter.

Methods: Literature was systematically reviewed to detect all reports in which the assessment of the FBP in SSc patients was described. The OMERACT filter, including the domains of truth, discrimination and feasibility was applied and the quality assessment was done by the Good Methods Checklist. Comparison between studies was eased by grouping the results per dynamic test situation (basal circumstances, cold/hot challenge and occlusion).

Results: The systematic search resulted in 4340 hits. After title and abstract screening 228 hits remained and of these, 79 full texts described the assessment by LDF. Fifty studies were included for quality assessment of which 17 studies were retained for conclusion making (fig 1).

An overview of the validation status of LDF is given in table 1. Expert consensus is lacking on the face and content validity of LDF in SSc. The construct validity of LDF is partially validated (e.g. the correlation with laser speckle contrast imaging was attested in one study). Conflict results exist on the discriminant capacity of LDF to distinguish healthy from diseased, primary from secondary RP and to differentiate between disease subtypes. The addition of a heat challenge, as well as the evaluation of the post-occlusive hyperemic response to the LDF-measurement has the potential to elicit a difference between healthy and diseased. Lastly, there are no data on the feasibility of LDF in SSc.
Table 1. Validation of LDF according to the OMERACT filter

<table>
<thead>
<tr>
<th>TRUTH DISCRIMINATION FEASIBILITY</th>
<th>SMEAR VASCULAR ADHESION MOLECULE-1 AS AN INDEPENDENT MARKER FOR ENDOTHELIAL ACTIVATION IS ELEVATED IN ACTIVE RHEUMATIC DISEASES: A MULTIVARIATE ANALYSIS</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>SMOLE VASCULAR CELL ADHESION MOLECULE-1 AS AN INDEPENDENT MARKER FOR ENDOTHELIAL ACTIVATION IS ELEVATED IN ACTIVE RHEUMATIC DISEASES: A MULTIVARIATE ANALYSIS</td>
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</table>

Conclusion: This systematic review emphasizes the very preliminary validation status of LDF in the assessment of the FBP in SSc. No single application method has emerged as fully validated according to the OMERACT filter.

REFERENCES

Cross-sectional study with 230 patients with rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA) and RA patients, according to ACR/EULAR 2010 classification criteria, aged between 40 and 70 years, were recruited and followed for 12 months. Disease activity, body composition, fatigue and urine metabolome were measured. Body composition was assessed by total body dual-energy x-ray absorptiometry (DXA) for measurement of appendicular lean mass index (ALMI). Disease activity was assessed by Disease Activity Score-28 with erythrocyte sediementation rate (DAS28-ESR). Fatigue as assessed by the Functional Assessment of Chronic Illness Therapy (FACIT). Nuclear Magnetic Resonance spectroscopy (NMR) measurements were performed to evaluate the profile of metabolic changes during the 12mo follow-up, resulting in the identification of 48 metabolites in urine collected at the baseline and after one year. Frequency analysis, Pearson Correlation and Multivariate data analysis with orthogonal projections to latent structures (OPLS) method were performed and a statistical significance was considered as p<0.05. Results: The study population was characterized by the majority of women (86.7%), mean age 56 years old, mean disease duration of 8 years, around 80% with positive anti-CPP and RF. There was a significant increase of citric acid, creatinine, L-serine and urea during the follow-up, metabolites that are involved in the muscular-related metabolism. There was no substantial variation in the DAS28-ESR (baseline: 3.8, after


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12 months: 4.0) and there was no significant correlation between changes in the metabolome pattern and DAS28-ESR score (p=0.05). Fatigue was negatively correlated with L-serine/creatinine (r: -0.4, p<0.001). Appendicular lean mass index (ALMI) also showed a positive difference which correlated with the increase of urea and creatinine (r: 0.3, p=0.019).

Conclusion: This prospective metabolic analysis indicated that the RA might be associated with amino acid metabolism alterations probably related to inflammation injury and muscle fatigue. These findings suggest that urine metabolome analysis may be an interesting approach to study and monitor the systemic impact of RA.

Acknowledgement: Federal University of Rio Grande do Sul

Disclosure of Interests: MARIANNE SCHRADER DE OLIVEIRA: None declared, Barbara Jonson Bartokoski: None declared, Jordana Miranda de Souza Silva: None declared, Rafaela Cavalheiro do Espirito Santo: None declared, Stephen Peter Young: None declared, Ricardo Xavier Consultant for: Abbvie, Pfizer, Novartis, Janssen, Lilly, Roche


AB1332

COST EFFECTIVE BIOMARKER IN PREDICTING SLE IN DEVELOPING COUNTRIES – NEUTROPHIL LYMPHOCYTE RATIO (NLR), PLATELET LYMPHOCYTE RATIO (PLR), MPV

V S Srikanta1, M Gopala Krishna Pillai2, Niluyi Shrestha Rajkumar3, AIM Hospital, Internal Medicine, Kochi, India; 2AIM Hospital, Rheumatology, Kochi, India

Background: SLE is a disease which is easily missed in regular clinical practice. In developing countries due to lack of investigation modalities and rheumatologist, early identification of the diseases process is delayed. By the time the patient reaches a higher medical care centre there is a significant time loss and advancement of the disease. NLR, PLR, RDW and MPV can be calculated from a complete blood count which will be available at any grass route heath centre.

Objectives: To identify Cost effective biomarkers in predicting SLE in developing countries. Focussing on markers - Neutrophil Lymphocyte Ratio (NLR), Platelet Lymphocyte Ratio (PLR), MPV.

Methods: This is a retrospective hospital based observational study conducted screening patients admitted from January 2016- November 2018 in with a diagnosis of SLE. We identified 150 patients with SLE and their NLR, PLR, and MPV data were collected and were correlated with equal control group without SLE

Results: We found that NLR, PLR, and MPV were highly significant with a-p value of 0.001 to be used as bio marker and also when further analysis was done using ROC curve with an area under curve of 76%, a p-value of 0.001 to be used as bio marker and also when further analysis was done using ROC curve with an area under curve of 76%, 81% and 78% respectively when compared with the control group.

Conclusion: We conclude that NLR, PLR and MPV is cost-effective bio marker which costs (< 1 Euro) in predicting SLE and also play a great role in monitoring following up referring patient to higher centre for biopsy at a golden period which will aid in early management which will limit the mortality and morbidity associated with the disease

REFERENCES


Disclosure of Interests: None declared


AB1333

CELL-FREE DNA AND BIOLOGICAL TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Cell free DNA (cfDNA) are DNA fragments released from the cell nucleus into extracellular compartment and is therefore detectible in plasma or serum. The most common reason for this release is tissue damage, cell death and inflammation of diverse origin. In regard to autoimmune diseases, increased levels of cfDNA has been found in plasma/serum in patients with systemic lupus erythematosus (SLE), rheumatoid arthritis (RA) and Sjögren’s syndrome. The results of some published works, appointing the correlation between levels of cfDNA and RA activity, are controversial, that’s why the position of cfDNA as a potential new biomarker remains unclear.

Objectives: The aim of our study was to describe the effect of biological therapy on the concentration of cfDNA and explore the correlation between therapeutic response DAS28 score and cfDNA levels. This potential correlation could define cfDNA as a new marker of treatment response and also potentially also clarify the role of cfDNA in the pathogenesis of RA.

Methods: Plasma samples of 40 patients with RA were collected before, as well as 3 and 12 months after starting treatment with tumor necrosis factor α-inhibitor (TNFα-inhibitor). Total cfDNA was quantified fluorometrically. Treatment response was evaluated by using DAS 28 scoring system and C-reactive protein.

Results: The treatment with TNFα-inhibitors showed statistically significant changes of DAS28 and cfDNA. According the EULAR treatment response defined by DAS28 changes, patients with good response showed statistically significant decrease of cfDNA in month 3 (p<0.005), but the improvement in month 12 was just on the border of statistical significance (p<0.059). There was also a slight decrease in a group without improve-DAS 28 response in month 12 (p=0.054). In the entire group there was found slight positive (r=0.44), statistically significant (p<0.0073) correlation between the levels of cfDNA and DAS 28 score after 12 month of treatment.

Conclusion: Even if treatment with TNFα-inhibitors decreases plasma cfDNA, there are other markers with better correlation with disease activity. We consider, that the changes in cfDNA levels after biological treatment could determine the role cfDNA more as a consequence of the inflammation, rather than the cause of inflammation in this autoimmune disease, but further research is needed.

REFERENCES


Disclosure of Interests: None declared

AN OPEN-SOURCE WEB-BASED ANALYTICS PLATFORM FOR THE HUMAN IMMUNE ATLAS

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Background: Mass cytometry (CyTOF) measures the expression of many proteins (currently up to 40) in single cells. It applies CyTOF to characterise cellular diversity of the immune system in peripheral blood and other tissues. Using a growing collection of CyTOF data acquired from blood of clinically and demographically diverse human subjects, we have built our version of the immune atlas, called EPIC (Extended Poly-dimensional Immunome characterisation).

Objectives: We will discuss two main objectives of this project. To integrate CyTOF data, metadata, cell annotations or other inferred data into the immune atlas, we developed a novel data analytics pipeline. To provide a user-friendly gateway that helps researchers explore the immune atlas and gain new insights about their own CyTOF data, we implemented a web-based data analytics application using the R Shiny programming environment.

Methods: The core components of the atlas are ‘immune maps’, which comprise CyTOF data of samples labeled with identical antibody panels and grouped according to a common biological theme. Besides protein expression patterns, immune maps contain clinical and demographic metadata, as well as phenotypic information inferred from clustering and cell type annotation. To intuitively analyse these complex multi-dimensional data, we developed a Shiny/R web application that has two main objectives. First, clients can explore the immune atlas at different levels of detail using a wide range of interactive visualisation methods, such as bar charts comparing the abundance of all or subsets of immune cell types in different age groups, or tSNE/UMAP scatter plots providing global perspectives of expression domains. Second, users can upload their own CyTOF data and, through pattern matching, obtain instant estimates about the abundance of selected immune cell populations in their own samples.

Results: We tested our system using immune maps constructed from healthy paediatric samples. Manually gated ground truth data along with interactive visualisation techniques were used to measure the accuracy of our pipeline in detecting and annotating homogenous cell populations. In addition, we will demonstrate how immune maps can be applied to classify uploaded CyTOF data.

Conclusion: Our interactive immune atlas platform promises to improve our understanding of the changing immunome landscape in response to disease, treatment and ageing.

REFERENCES
NA

Disclosure of Interests: Martin Wasser: None declared, Joo Guan Yeo: None declared, Pavanish Kumar: None declared, Thaschawee Arkachaisri Speakers bureau: Abbvie Pte, Ltd, Su Li Poh: None declared, Fauziah Aly: None declared, Jing Yao Leong: None declared, Kee Tai Yeo: None declared, Salvatore Albani: None declared


AGE-RELATED MUSCULOSKELETAL STIFFNESS AMONGST HEALTHY SUBJECTS

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Background: A patient questionnaire for evaluating musculoskeletal stiffness (MSQ) has been developed for rheumatoid arthritis (RA) (Halls 2015) and also tested in chikungunya disease. Joint stiffness is associated with older age in adults.

Objectives: The aim of this study was to evaluate the variation in MSQ scores with age in a cohort of healthy adults.

Methods: Subjects aged 18 years old were enrolled at two sites. Subjects were engaged in, or had completed, tertiary education. Subjects with a diagnosis of joint disease, Parkinson’s disease or multiple sclerosis were excluded. Each subject completed a 21-item questionnaire designed to evaluate the severity of musculoskeletal stiffness, its physical impact and psychosocial impact, and to provide an overall stiffness score. Results are expressed as a percentage of the maximum possible score.
coincidence rate was 92.72%-94.79%. The sensitivity and specificity values of ELISA proposed by the manufacturer for clinical diagnosis RA were 82% and 95%. The two methods had the same detection effect.

**Conclusion:** The current commercially available methods for detecting anti-CCP antibodies were roughly the same, and the consistency between LETIA and ELISA were high. In general, the LETIA was more accurate and sensitive than the ELISA in the detection of anti-CCP antibodies in serum. Overall diagnostic performance of ELTIA can be compared. LETIA provided reliable information about antibody levels that made it useful in monitoring disease activity. Comparable to the classic ELISA, ELISA may even be replaced in the future.

**REFERENCES**


Disclosure of Interests: None declared

**AB1336B**

**PERFORMANCE EVALUATION OF PARTICLE-ENHANCED TURBIDIMETRIC IMMUNOASSAY FOR ANTINUCLEAR ANTIBODIES DETECTION IN COMPARISON WITH LINE IMMUNOASSAY**

Van Qin, Jing Luo, Xiang-Cong Zhao. The Second Hospital of Shanxi Medical University, Taiyuan, China

**Background:** Detection of antinuclear antibodies (ANAs) supports the clinical diagnosis of ANA-associated rheumatic diseases, such as systemic sclerosis (SSc), systemic lupus erythematosus (SLE), primary sjogren’s syndrome (SjS) and mixed connective tissue disease (MCTD) [1-3]. Throughout history, a number of autoantibody detection methods have emerged, for instance, indirect immunofluorescence (IIF), radioimmunonassay (RIA), enzyme-linked immunosorbent assay (ELISA) and line immunoassay (LIA) [4]. With the development of detection technology, new methods to detect ANAs were continuously developed by numerous manufacturers, for example, particle-enhanced turbidimetric immunoassay (PETIA). Therefore, in the current study, we evaluated for the first time the performance of PETIA in the detection of anti-nuclear antibody and compared it with commercial LIA.

**Objectives:** To evaluate the clinical performance of PETIA for the detection of ANAs in comparison to the currently commonly used LIA.

**Methods:** Total 606 serum samples from diseased and healthy controls were assayed to simultaneously determine SSA, Sm/RNP, SSB, Sm and U1-SnRNP antibodies by the PETIA and LIA. The sensitivity, specificity, consistency and area under curve (AUC) were analyzed for each antibody between PETIA and LIA.

**Results:** The positive rate and specificity of PETIA and LIA for ANA specific target antibodies were comparable. Compared with LIA, the sensitivity of SSA, SSB and Sm were 100.00%, 88.89% and 90.00%, while Sm/RNP and U1-SnRNP were 75.00%, 70.59%, respectively; Sm/RNP, SSB, Sm and U1-SnRNP have high specificity, respectively 97.87%, 98.90%, 97.06% and 94.68%, while SSA specificity is general, 81.52%. Under manufacturer’s cut-off values, the consistent rates of SSA, Sm/RNP, SSB, Sm, and U1-SnRNP between PETIA and LIA were 87.22%, (116/133), 92.06% (116/126), 96.61% (114/118), 97.03% (98/101) and 88.28 (113/128), respectively. Excellent consistencies were found between PETIA and LIA for the detection of Sm/RNP, SSB and Sm antibodies (kappa=0.75), and kappa coefficients were 0.776 (p<0.001), 0.901 (p<0.001) and 0.841 (p<0.001), while the coincidence for anti-SSA and U1-SnRNP detection were moderate (0.40<kappa<0.75), and Kappa coefficient was 0.731 (p<0.001) and 0.685 (p<0.001), respectively.

**Conclusion:** The performance of PETIA for the detection of antibodies to nuclear specific antigen was satisfying to correlate with that of LIA. With the additional benefits of short detection time, quantitative output and high universality, PETIA can better meet the requirements of quantitative detection of specific target antibodies.

**REFERENCES**


Disclosure of Interests: None declared
Results: A statistically significant difference was found between three groups in terms of normalized suprahyoid muscle activity (p<0.001) (Table 1). The difference between three groups was caused by the difference between Group 1 and Group 2 (p<0.001) and between Group 1 and Group 3 (p=0.040) in favor of Group 1. No difference was found between Group 2 and Group 3 (p=0.104) (Table 2-4).

Table 1. Comparison of Normalized Suprahyoid Muscle Activation between groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean ±SD</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1</td>
<td>0.791 ±0.380</td>
<td></td>
</tr>
<tr>
<td>Group 2</td>
<td>0.306 ±0.116</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Group 3</td>
<td>0.472 ±0.284</td>
<td></td>
</tr>
</tbody>
</table>

*p<0.05

Table 2. Comparison of Normalized Suprahyoid Muscle Activation between Group 1 and Group 2

<table>
<thead>
<tr>
<th>Group 1 (n=14) Mean ±SD</th>
<th>Group 2 (n=14) Mean ±SD</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normalized Suprahyoid Muscle activation (%)</td>
<td>0.791 ±0.380</td>
<td>0.306 ±0.116</td>
</tr>
</tbody>
</table>

*p<0.05

Table 4. Comparison of Normalized Suprahyoid Muscle Activations of Group 2 and Group 3

<table>
<thead>
<tr>
<th>Group 2 Mean ±SD (n:14)</th>
<th>Group 3 Mean ±SD (n:14)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normalized Suprahyoid Muscle activation (%)</td>
<td>0.791 ±0.380</td>
<td>0.472 ±0.284</td>
</tr>
</tbody>
</table>

*p<0.05

Table 5. Comparison of Normalized Suprahyoid Muscle Activations of Group 2 and Group 3

<table>
<thead>
<tr>
<th>Group 2 Mean ±SD (n:14)</th>
<th>Group 3 Mean ±SD (n:14)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normalized Suprahyoid Muscle activation (%)</td>
<td>0.306 ±0.116</td>
<td>0.472 ±0.284</td>
</tr>
</tbody>
</table>

*p<0.05

Conclusion: In conclusion, primarily CTAR exercise should be included in rehabilitation to increase the suprahyoid muscle activation. In addition, chin tuck exercise with Therband can also be considered as an alternative to CTAR.

REFERENCES

Disclosure of Interests: None declared

Education
Whitney U test) in both groups. In the VBC group time between decision to treat until funding approval obtained was measured and overall saving by all estimated drug cost was calculated.

**Results**

122 patients were discussed at VBC - 75 started a biologic (50 new, 25 switched) and 6 entered a clinical trial. The remaining 41 agreed as unsuitable for a biologic table 1.

<table>
<thead>
<tr>
<th>Reasons for not receiving biologic</th>
<th>(n=41)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>IFR application rejected</td>
<td>6</td>
<td>12.1%</td>
</tr>
<tr>
<td>Patient factor*</td>
<td>5</td>
<td>12.1%</td>
</tr>
<tr>
<td>Disease activity not meeting NICE criteria</td>
<td>22</td>
<td>53.60%</td>
</tr>
<tr>
<td>Alternative treatment offered (eg: cDMARDs)</td>
<td>6</td>
<td>14.60%</td>
</tr>
<tr>
<td>Other **</td>
<td>2</td>
<td>4.8%</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>2.4%</td>
</tr>
</tbody>
</table>

1 recurrent infection, 3 did not do their screening test, 1 did not do the recommended vaccination.

**Conclusion**

- We assume that in our clinic pre VC and, indeed, in the majority of UK Rheumatology Departments about 90% of patients recommended for a biologic by a specialist eventually ends up taking that medication and give that assumption potential costs savings with this model are estimated as equivalent to 35 patients (approx. £1400/yr. - drug costs savings calculated vs current cheapest option, SB4 ($400/yr.)).

**Disclosure of Interests**

None declared.

**REFERENCES**


**Disclosure of Interests:** Keziah Austin: None declared, Nia Jones: None declared, Roopa Prasad Consultant for: Was on an Advisory Board for a pharmaceutical company meeting several years ago (unrelated to current abstract submission), Speakers bureau: Speaker fees for a national psoriatic arthritis meeting in 2017 (unrelated to current abstract submission). DOI: 10.1136/annrheumdis-2019-eular.454

**AB1338**

**PATIENT EDUCATION IN PSORIATIC ARTHRITIS:** ADDRESSING AN UNMET NEED

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**Background:** Patient education should be integral to the care of people with inflammatory arthritis [1]. Research suggests that the majority of patients with Psoriatic Arthritis (PsA) would like to receive education about their condition [2]. There are limited studies in PsA but randomised controlled trials in rheumatoid arthritis have demonstrated that patient education improves compliance to medication [3], disease specific knowledge [4] and coping mechanisms [5]. In our department, patient education in PsA was recognised as an unmet need.

**Objectives:** To pilot an educational session for PsA patients, to assess whether this improved patients’ understanding of their condition, and to determine whether an education programme would be a useful adjunct to patient care.

**Methods:** Adult PsA patients attending their rheumatology clinic appointments were asked to complete a short survey on whether they would be interested in attending an education session and the aspects they would like to have covered. Those who expressed interest were invited to attend a 2.5 hour multidisciplinary team (MDT) session which covered 1) a general overview of PsA; 2) medications used in PsA; 3) the role of physiotherapy and occupational therapy; 4) flares and self management. Patients were asked to evaluate their knowledge or understanding before and after each topic covered, on the same day, using a series of 1-10 Likert scales. They were specifically asked whether they found the education session helpful, whether they would recommend it to other PsA patients, whether they would be interested in developing a PsA patient support group.

**Results:** 25 patients were invited to the session and 9 patients attended.

- There were 5 males and 4 females, across a wide range of age categories.
- There were statistically significant improvements in all topics covered, including a mean improvement of 120% in how well informed patients felt about PsA in general (p<0.0001); a mean improvement of 79% in confidence in accessing help from the MDT (p<0.01); a mean improvement of 211% in how well informed patients were about medications available (p<0.0001); a mean improvement of 86% in confidence in self-managing a flare (p<0.0001). All patients found the session helpful overall and all patients stated they would recommend it to others. Several patients expressed interest in developing a PsA patient support group.

**Conclusion:** All PsA patients demonstrated a greater awareness and understanding of their condition following a 2.5 hour education session. This study indicates that an education programme is a useful and important adjunct to patient care and supports extending this to the wider PsA patient population.

**Disclosure of Interests:**

None declared.

**REFERENCES**


**Disclosure of Interests:** Keziah Austin: None declared, Nia Jones: None declared, Roopa Prasad Consultant for: Was on an Advisory Board for a pharmaceutical company meeting several years ago (unrelated to current abstract submission), Speakers bureau: Speaker fees for a national psoriatic arthritis meeting in 2017 (unrelated to current abstract submission). DOI: 10.1136/annrheumdis-2019-eular.5990

**AB1339**

**ONLINE CME IMPROVES ADOPTION OF JAK INHIBITORS IN CLINICAL PRACTICE BY RHEUMATOLOGISTS**

Elaine Bell, Robert McCarthy, Medscape LLC, New york, United States of America

**Background:** The treatment landscape for RA is evolving rapidly. The JAK inhibitors are oral small molecules that have recently been approved for use in RA.

**Objectives:** This online CME-accredited educational activity was designed to address the challenges of integrating JAK inhibitors into clinical practice in RA and measure changes in practice

**Methods:** Non-US rheumatologists, dermatologists and primary care physicians (PCPs) participated in an online activity consisting of a 30-minute video roundtable discussion between 4 experts, with synchronized slides, posted online on August 25 2017. A Planned Change Assessment (PCA) survey (data collected through April 3 2018) with qualitative follow-up interviews was used to measure intent to change and actual change in clinical practice following participation in the activity. A 2-question PCA survey in multiple choice format, which was administered immediately following the activity, asked:

What do you perceive as barriers to making the above selected changes in your practice?

What will you do differently in your practice as a result of participating in this activity?

**Results:**

- 267 non-US physicians completed the initial PCA survey and 44 completed a follow-up assessment approximately 8 weeks later, resulting in a matched subset of 37 learners. Qualitative interviews were conducted with 13 learners
274 learners (96%) indicated that they intended to make a change as a result of participating in the activity with most learners selecting multiple changes.

- The most common intended changes for rheumatologists were using a JAK inhibitor for the first time (65%) and selecting a JAK inhibitor when oral dosing is preferred (54%)

- Other than systems barriers such as reimbursement and lack of availability of JAK inhibitors, the most common anticipated barriers to change for rheumatologists related to lack of knowledge about MOA and safety, and lack of confidence in their use

- 44 learners completed the follow-up assessment: 42 (96%) reported making changes in their clinical practice

- For rheumatologists, the most common actual changes were using a JAK inhibitor first-line (55%) and considering a JAK inhibitor when oral dosing is preferred (54%)

At follow-up the key barriers reported by rheumatologists related to systems barriers/availability and lack of confidence in using JAK inhibitors.

**Conclusion:** Learners in this activity reported increased knowledge about new treatment options for RA and the MOA of JAK inhibitors. The PCA assessment showed that the activity was most effective at prompting rheumatologists to more frequently consider using a JAK inhibitor as a first-line treatment in appropriate patients. Use of new therapies, however, may be challenging due to lack of availability of JAK inhibitors in many countries and financial burdens in others. Further education would help rheumatologists to gain confidence in using JAK inhibitors, overcome knowledge gaps, and meet challenges related to lack of access to JAK inhibitors.

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.4047

**AB1340**

**IMPACT OF THERAPEUTIC PATIENT EDUCATION ON THE SAFETY OF PATIENTS ON BIOThERAPY FOR CHRONIC INFLAMMATORY RHEUMATISM**

**BENCHEIR IMEN, Daila Bendjenna. University Public Hospital of Constantine, Rheumatology, Constantine, Algeria**

**Background:** Patients treated with biotherapy should be aware of the specific complications. The acquisition of safety skills is one of the objectives of therapeutic patient education programs in chronic inflammatory rheumatism.(1,2,4)

**Objectives:** Evaluation of the impact of the “EST-RIC” therapeutic patient education program on the safety skills of patients on biotherapy for chronic inflammatory rheumatism.

**Methods:** Descriptive cross-sectional study evaluating the impact of integration into a therapeutic patient education program on the skills of patients treated in a day hospital at the Constantine rheumatology department for chronic inflammatory rheumatism, using the validated “BioSecure” questionnaire (3).

**Results:** Of sixty patients, fifty-two patients (86.6%) completed the questionnaire. Forty-three patients have spondyloarthritis (83%) (Tab1). The median Biosecure score was 62.90/100 (SD 10.83). Fifty-two percent of the patients had integrated the therapeutic education program. Their Biosecure score was significantly higher than that of naive patients with therapeutic education (median score 69/100 in the ETP group versus 58/100, p <0.001) (Fig 1). The Biosecure score varied significantly with the lower level of education (p <0.0001), in the subgroup of patients with a professional activity (P = 0.008) and in patients whose treatment was introduced for less than one year (p <0.0001) and who had a pathology whose diagnosis was less than 5 years (p <0.008)

**Conclusion:** The integration of patients undergoing biotherapy into a specialized program of therapeutic patient education is correlated with a better mastery of theoretical safety skills.

**REFERENCES**


**Tab 1:** Characteristics of the patient

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.5159

**AB1341**

**PUBLIC AWARENESS OF RHEUMATOID ARTHRITIS IN MONGOLIA**

**Lkhamb-Edrene Byambadorj1, Nandin-Endere Danzan1, Tsoleden Darisuren2, Devshit Zorig1, Enkhjin Bat-Erdene2, Davsaadulam Enkholbd2, Zulgerel Dandii1. 1Mongolian Rheumatology Association, Ulaanbaatar, Mongolia, 2Mongolian National University of Medical Sciences, Ulaanbaatar, Mongolia**

**Background:** Rheumatoid arthritis (RA) is multifactorial, chronic, inflammatory disease which in the absence of early diagnosis can lead to joint destruction and disability. In the last decade, rheumatology has been developed as independent branch in Internal medicine in Mongolia, published rheumatological textbooks. The Mongolian Rheumatology Association has also introduced a RA guideline and conducted training that has led to the use of DMARDs in treatment and improves patient’s quality of life is improving in Mongolia. Nevertheless, we have many patients with a late RA diagnosis in Mongolia. In some studies, poor public awareness of RA correlates with high level of disability.

**Objectives:** To develop understanding about current levels of public awareness of rheumatoid arthritis in patients coming to the outpatient department of the First central hospital in Ulaanbaatar, Mongolia.

**Methods:** This was a cross-sectional descriptive study conducted in the outpatient department of the First central hospital of Ulaanbaatar in Mongolia for 3 days. The study population consisted of adults. Data collection was performed by using questionnaire of developed by the NRAS, addressed to assess awareness on RA.

**Results:** Total 376 persons stood for 3 days in outpatient clinic in First central hospital. 26 of them refused and 350 of them participated our study. The average age of the participants was 37.79. Participants responded, 22% of them know RA, 78% of whom do not know RA for rheumatologists, the most common actual changes were using a JAK inhibitor first-line (55%) and considering a JAK inhibitor when oral dosing is preferred (54%).

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.5159
rheumatoid arthritis. Understanding about the disease symptoms: 50.5% responder answered they to do not know RA symptoms; 29% correctly identified joint swelling; 17.4% correctly identified morning stiffness; 12.6% correctly recognized extreme fatigue as a symptom; and only 6.5% correctly stated that smoking can increase the risk factor for RA. Understanding about disease impacts: 21.1% correctly recognized genetics as a factor; 17% knew that women are more vulnerable than men; only 3% correctly stated that undertaking exercise and obesity is also a risk factor and 23% identified sore throat can increase RA. Understanding about disease factors: 49.4% of participants correctly recognized extreme fatigue as a symptom; and only 6.5% correctly stated that smoking can increase the risk factor for RA. Only 7% correctly stated that genetics is a factor; 17% knew that women are more vulnerable than men; only 3% correctly stated that undertaking exercise and obesity is also a risk factor and 23% identified sore throat can increase RA. Understanding about disease symptoms: 50.5% of participants who have not responded to do not know that most of them misidentified disease symptoms, risk factors and impacts. The only good thing was most of the participants thought awareness of RA improvement certainly. A good awareness of RA can be one of the basic solutions for the early diagnosis of RA in Mongolia.

Conclusion: In Mongolia, public awareness of rheumatoid arthritis was poor. Most of the participants responded to do not know. Other participants who have not responded to do not know that most of them misidentified disease symptoms, risk factors and impacts. The only good thing was most of the participants thought awareness of RA improvement certainly. A good awareness of RA can be one of the basic solutions for the early diagnosis of RA in Mongolia.

Disclosure of Interests: None declared

AB1343

EFFECTIVENESS OF A RHEUMATOLOGY EDUCATIONAL PROGRAM TO IMPROVE METHOTREXATE PRESCRIBING PRACTICES FOR RHEUMATOID ARTHRITIS IN THE SOLE PUBLIC ADULT RHEUMATOLOGY CLINIC IN ETHIOPIA

CApril Hitchon1, Becky Abdissa Adugna2, Birhanu Demelash2, Rosie Scuccimarra3, Ines Colmegna3, Frehiwot Kifle4, Paul Calderon5, Addisu Ababa University, Addis Ababa, Ethiopia; McGill University, Montreal, Canada; Emory University, Atlanta, United States of America; Arizona Arthritis and Rheumatology Associates, Phoenix, United States of America; Jefferson University, Philadelphia, United States of America

Background: Treatment of recent onset Rheumatoid Arthritis (RA) is key to preventing deformities. Initial treatment with methotrexate (MTX) is standard of care. RA treatment in resource-limited countries is complicated by competing health priorities and a lack of rheumatologists. The sole public adult rheumatology clinic in Ethiopia, is at Tikur Anbessa Specialty hospital (TASH) (Addis Ababa). Due to the lack of rheumatologists, care is provided by internists with limited rheumatology training.

Objectives: To evaluate changes in RA management practice patterns following a series of educational activities provided by visiting rheumatologists.

Methods: With local faculty support, visiting rheumatologists conducted educational activities at TASH between July 2016 and December 2018 (2 continuing medical education workshops; 4 clinical preceptorships lasting 2-4 weeks each). Clinical charts of a convenience sample of RA patients seen in the TASH rheumatology clinic were reviewed in September 2016 (n=48) by a team of rheumatologists and a second set in December 2018 (n=78) by an internist. Socio-demographics, arthritis features, treatment patterns and drug safety monitoring were recorded when documented. Practice patterns were compared between 2016 and 2018 using univariate statistics.

Results: The patients were mainly female (90%) with a mean (standard deviation) age of 36(13) years, resided in Addis Ababa (61%) and scored by competing health priorities and a lack of rheumatologists. The sole public adult rheumatology clinic in Ethiopia, is at Tikur Anbessa Specialty hospital (TASH) (Addis Ababa). Due to the lack of rheumatologists, care is provided by internists with limited rheumatology training.

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Results: The patients were mainly female (90%) with a mean (standard deviation) age of 36(13) years, resided in Addis Ababa (61%) and received government funded health care (57%). When documented, (95% in 2016 vs 99% in 2018, p<0.0001) was prescribed more commonly in 2016 than 2018 (p=0.001). More patients were seropositive in 2016 compared to 2018 (32/43 vs 14/75, p<0.001) and more had radiographic damage (erosions, joint space narrowing, periarthritis osteopenia) (21/27 vs 39/71, p<0.05). Between 2016 and 2018, prednisolone use remained common (92% in 2016 vs 89% in 2018, p=0.05) often in high doses (last visit daily dose 7.5mg (0-100) vs 5mg (0-100) p=NS; maximum daily dose 7.5 (0-100) vs 20 (0-100) p=NS) with continued documentation of steroid toxicity (45% vs 20%). The only available DMARDs prescribed were MTX (112/127; 97%) and chloroquine (50/125,40%). Median prescribed weekly MTX dose increased between 2016 and 2018 (starting dose 5 vs 7.5 mg/week p<0.01; maximum dose 7.5 vs 12.5 mg/week p<0.0001) and was co-prescribed with folate by 84% in 2016 vs 93% in 2018 (p=NS). Documentation of drug safety for those prescribed MTX improved with...
adequate pre-MTX labs (hematology, renal and liver panel and or hepatitis serology) requested by 46% in 2016 to 90% in 2018 (p<0.0001). When documented, MTX use was often interrupted (2016 17/24, 2018 14/43 p=0.003) and mainly due to limited drug availability.

**Conclusion:** An educational program conducted with support from the local medical community has potential to improve management of rheumatic disease in resource limited regions without adequate rheumatology capacity. However, interventions must be maintained over time and changes in practice measured to ensure that appropriate diagnosis and safe prescribing practices continue until local rheumatology expertise and capacity is available.

**Acknowledgement:** Study funding by ILAR

**Disclosure of Interests:** CARol Hitchon Grantly/research support from: Pfizer, UCt (unrelated studies), Becky Abdissa Adugna: None declared, Birhanu Demelash: None declared, Rosie Scuccimarra: None declared, Ines Colmegna: None declared, Frehiyot Kifle : None declared, Paul Caldron: None declared, Addisu Melkie: None declared, Michele Meltzer: None declared, Yewondwossen Mengistu: None declared

**DoI:** 10.1136/annrheumdis-2019-eular.3581

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**AB1344 CLINICAL ASSESSMENT OF THE MUSCULOSKELETAL SYSTEM HANDBOOK AND ACCOMPANYING VIDEOS: 15 YEARS OF USE**

Cheuk Yin Li, Sophia Wakefield, Donna Andrew, David Coady, Versus Arthritis. 1Newcastle University, Newcastle upon Tyne, United Kingdom; 2Cardiff University, Cardiff, United Kingdom; 3Versus Arthritis, Chesterfield, United Kingdom; 4City Hospitals Sunderland, Sunderland, United Kingdom

**Background:** 15 years ago, Arthritis Research UK (ARUK) produced the ‘Clinical Assessment of the Musculoskeletal (MSK) System’ handbook and a set of accompanying videos; ‘Regional Examination of the Musculoskeletal System’. (1) There has been an evaluation of the use of this resource showing that they are widely used among medical students and healthcare professionals. Recently, ARUK has merged with Arthritis Care to form Versus Arthritis, and previous publications are due to be rebranded.

**Objectives:** This project aims to review how the handbook and videos are being used 15 years on. The secondary aim is to gain insight into any changes that may need to be made going forward as Versus Arthritis seeks to revise and update the original materials.

**Methods:** In September 2019, a clinical group was formed to review the current handbook’s content and format. The project team was invited to take part in the surveys and disseminate them within their professional networks and across every UK medical school.

**Results:** 78 people took part in the survey; this included 61 users (students, trainees and medical school teachers).

**User Survey:** ‘How to access the handbook?’ respondents said online (36%), via an app (31%) or printed version (10%). 83% of respondents said they found the handbook very useful, 100% said it was easy to understand, 95% said it was well illustrated, and 75% said the video clips were very useful. 100% of respondents said the handbook did not contradict any existing teaching received.

When asked what would improve the handbook, the most popular response was case studies. When asked what the most useful thing was, most respondents commented on the structure and how clear and concise it was. When asked what the least useful thing was, respondents felt it lacked detail regarding the rationale behind the purpose of the examinations.

**Teacher Survey:** 17 medical school representatives completed the survey. 94% of respondents use the resource. Most provide their students with the online version of the handbook (64%). 88% thought the resource was very useful for their students. 94% said the resource maps well to the current MSK curriculum. When asked what would improve the handbook the most popular response was abnormal examination findings. The least popular response was patient exercise videos and sheets.

**Content Review:** Several comments were made suggesting the use of more appropriate language. Recommendations were made to introduce sections on physical activity, self-management and the multidisciplinary team involvement. A suggestion was made to include the patient’s ‘ideas, concerns and expectations’ concept.

**Conclusion:** The consensus is that the resource is already very good and maps well to the MSK curriculum taught by the medical schools. It would benefit from adding new contents, e.g. examination clips of patients with pathology. We would need to be wary of overcomplicating the purpose of the new resource.

It was also highlighted that the resource would benefit from a refresh of the layout, including clear headings and more up to date images and diagrams. Several comments were made around the format to include an online resource that students could use to incorporate examination videos with experts explaining the findings.

**REFERENCES**


**Disclosure of Interests:** Louise Warburton, Ana Onebieni, Singh Harjinder, Pippa Watson, Mark Lilicrap, Anita Williams, Sarah-Jane Ryan, Jade Pullen, Stephanie Saltford

**DoI:** 10.1136/annrheumdis-2019-eular.5890

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**AB1345 CONTEXTUAL FACTORS IMPACTING OSTEOARTHRITIS MANAGEMENT IN URBAN AND RURAL COMMUNITY-DWELLING SENIORS: AN ANALYSIS BASED ON THE INTERNATIONAL CLASSIFICATION OF FUNCTIONING DISABILITY AND HEALTH**

Joy MacDermid1,2, Karen Lee1, Amanda All3. 1Western University, Faculty of Health Science, London, Canada; 2St Joseph’s Health Centre, Hand and Upper Limb Centre, London, Canada

**Background:** Living with arthritis requires lifelong management that can be influenced by person, place and context.

**Objectives:** The objectives of this study were to: (1) identify contextual factors that influence OA management in rural and urban-dwelling seniors, and (2) examine how contextual factors identified by rural and urban-dwelling seniors are explained in terms of the ICF framework.

**Methods:** Semi-structured interviews were conducted with 20 community-dwelling seniors in Ontario, Canada; purposively including 11 seniors from an urban setting and 9 seniors from a rural setting, all over the age of 65, and previously diagnosed with OA. Broad questions on self-management and information seeking were explored. Interview concepts related to the environmental and contextual factors component were extracted from interview transcripts and organized into subthemes. Meaningful concepts were linked by 2 raters to ICF categories according to established linking rules. Descriptive analyses were performed.

**Results:** A total of 891 meaningful concepts were identified; 481 from interviews with 11 urban-dwelling seniors, and were linked to 54 ICF categories: 24 Environmental Factors, 21 Activities and Participation, and 9 Body Functions and 410 meaningful concepts from interviews with 9 rural-dwelling seniors; 57 ICF categories: 27 Environmental Factors, 24 Activities and Participation, and 6 Body Functions. Within Activities and Participation component, “d839 Education” was the most code for both groups. From the Body Functions component, “b1800 Experiences of Self” followed by “b1301 Motivation” were most mentioned. Environmental factors represented 203 of 481 (42.2%) urban concepts and 253 of 410 (61.7%) rural concepts. The concepts linked to the Activities and Participation category were similar across urban and rural groups (17.3% and 17.1%). Personal Factors (e.g. “adapting to life with OA”, “self-sufficiency”, “pain tolerance”, “age”) or “no/ not covered” (e.g. “feeling old”, “embarrassed by OA”, “being a burden”) were not coded. In 12.8% urban and 20.6% rural content was labeled as Personal Factors. Chapter e5 services, systems and policies was the chapter with the highest coverage overall. Within the environmental factors “e355 Health Professionals” was the most common code for both urban and rural groups, and mentioned in almost all interviews. Participants frequently discussed physician’s attitudes and misconceptions towards patients with OA.

**Conclusion:** The complex interaction of personal and environmental factors impacting OA management in both urban and rural communities was illustrated. Rurality influences some aspects of the complexity, but many common themes occur.

**REFERENCES**

AB1346

PATIENTS’ BELIEFS ABOUT MEDICINES PRESCRIBED FOR THEIR RHEUMATOID ARTHRITIS OR SPONDYLOARTHITIS

Nathalie Madeira, Candida Silva, Claudia Miguel, Dina Medeiros, Filipe Barcelos, Helena Santos, Ricardo Trinca, Alexandra Cardoso, Luís Cunha Miranda. Instituto Português de Reumatologia, Rheumatology, Lisbon, Portugal

Background: Adherence to therapies is determined by multiple factors, some of which are patient’s related and include economic resources, knowledge, attitudes, beliefs, perceptions and expectations about medication.

Objectives: To assess patients’ beliefs about prescribed medication for their rheumatic disease (rheumatoid arthritis (RA) or spondyloarthritis (SpA), including psoriatic arthritis) and to determine the existence of any association between these beliefs and clinical and socio-demographic variables.

Methods: Observational cross-sectional study which included RA patients according to 1987 ACR and/or 2010 ACR/EULAR criteria and SpA patients according to 2009 ASAS classification criteria (CC) for axial SpA or to 2011 ASAS CC for peripheral SpA, on subcutaneous biological therapy, followed at our Center, able to complete questionnaires autonomously and who agreed to participate. Socio-demographic and clinical data, anxiety and depression through the Hospital Anxiety and Depression Scale (HADS) and fatigue using the Functional Assessment of Chronic Illness Therapy - Fatigue questionnaire (FACIT-F) were collected. To assess beliefs about medication, the cross-culturally adapted Portuguese version of the Beliefs about Medicines Questionnaire (BMQ)-Specific was used, asking patients to apply it considering only the prescribed medicines for AR or SpA. The BMQ-Specific comprises two subscales: a five-item Necessity scale (Specific-Necessity, SN) and a six-item Concerns scale (Specific-Concerns, SC). Each item is scored on a five-point Likert scale (from 1 = strongly disagree to 5 = strongly agree). Statistics: descriptive, Mann-Whitney and Kruskal-Wallis tests and Spearman correlation, p <0.05.

<table>
<thead>
<tr>
<th>RA patients</th>
<th>SpA patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current age - years</td>
<td>Median (IQR)</td>
</tr>
<tr>
<td>60.0 (51.0-66.0)</td>
<td>47.0 (39.5-57.0)</td>
</tr>
<tr>
<td>Disease duration – years</td>
<td>14.5 (12.0-18.3)</td>
</tr>
<tr>
<td>Time on treatment with the current biologic therapy – months</td>
<td>31.0 (20.0-62.0)</td>
</tr>
<tr>
<td>PGA</td>
<td>32.0 (6.0-55.0)</td>
</tr>
<tr>
<td>VAS pain</td>
<td>41.0 (21.0-60.0)</td>
</tr>
<tr>
<td>PhGA</td>
<td>19.5 (6.5-33.8)</td>
</tr>
<tr>
<td>Nocturnal back pain VAS</td>
<td>-</td>
</tr>
<tr>
<td>Back pain VAS</td>
<td>-</td>
</tr>
<tr>
<td>VS – mm/H</td>
<td>15.0 (7.0-30.5)</td>
</tr>
<tr>
<td>CRP – mg/dL</td>
<td>0.2 (0.1-0.6)</td>
</tr>
<tr>
<td>DAS28_4V</td>
<td>3.2 (2.4-4.4)</td>
</tr>
<tr>
<td>BASDAI</td>
<td>1.8 (1.1-2.4)</td>
</tr>
<tr>
<td>BASMI</td>
<td>0.8 (0.4-1.2)</td>
</tr>
<tr>
<td>HAG</td>
<td>17.0 (15.0-18.0)</td>
</tr>
<tr>
<td>BASFI</td>
<td>18.0 (15.0-22.0)</td>
</tr>
<tr>
<td>BMO-SC</td>
<td>18.0 (15.0-22.0)</td>
</tr>
</tbody>
</table>

Abstract AB1346 Table 1: Descriptive statistics of the continuous variables of the RA and SpA patients

Results: We obtained data from 84 patients, 45 SpA (53.6%) and 39 (46.4%) RA patients. Table 1 presents the descriptive statistics of the continuous variables. In RA group, 92.3% were female, 84.6% under anti-TNF, 66.7% under their 1st biologic and we found an association between BMO-SC score and HADS-anxiety (p=0.013) and positive correlations between BMO-SC score and Patient Global Assessment (PGA) (p=0.031), VAS pain (p=0.004), Physician’s Global Assessment (PhGA) (p=0.004), DAS28 (p=0.007), and HAQ (p<0.001). In SpA group, 62.2% were female, 86.7% under anti-TNF, 77.8% under their 1st biologic and BMO-SN score was positively correlated with VAS nocturnal back pain (p=0.047), PhGA (p=0.045) and BAFSI (p=0.003).

Conclusion: In RA patients, those with higher disability and a clinically more active disease presented higher levels of concern regarding the medication. In SpA, patients with a more aggressive disease, with nocturnal pain and worse function have a stronger conviction of the necessity and efficacy of the medication.

REFERENCES

AB1347

ASSESSMENT OF PATIENTS’ KNOWLEDGE ABOUT BIOLOGIC THERAPY AS A SELF-COMPLETION QUESTIONNAIRE. IS IT A GOOD WAY TO DO IT?

Nathalie Madeira, Candida Silva, Claudia Miguel, Dina Medeiros, Filipe Barcelos, Helena Santos, Ricardo Trinca, Alexandra Cardoso, Luís Cunha Miranda. Instituto Português de Reumatologia, Rheumatology, Lisbon, Portugal

Background: Lack of knowledge from a patient in his therapy may lead to a misuse process, increasing the probability of failure to achieve the therapeutic goal.

Objectives: To evaluate if the assessment of the RA and SpA patients knowledge in their biologic therapy could be done as a self-completion questionnaire.

Methods: Observational cross-sectional study which included patients with RA according to 1987 ACR and/or 2010 ACR/EULAR criteria or SpA according to 2009 ASAS classification criteria (CC) for axial SpA or to 2011 ASAS CC for peripheral SpA (including patients with psoriatic arthritis), on subcutaneous biological therapy who agreed to participate. Patients’ knowledge about their biologic therapy was assessed using the “Conhecimentos do doente sobre os seus medicamentos” (CPM-PT-P) meaning “Patient’s knowledge about his medicines”, intercultural adaptation for the Portuguese version of the original Spanish questionnaire, CPM-ES-ES. This questionnaire was created to be used as an interview, but we decided to give it to patients and ask them to complete it autonomously, reading the questions and writing their answers, considering only their biologic therapy. It consists of 11 questions, each with a score based on patient’s answer: incorrect = -1, the patient doesn’t know = 0, incomplete = 1 and correct = 2. The final score is calculated using the mathematical formula described by the authors, ranging from 0 (doesn’t know the medicine) to 2 points (optimal knowledge). Statistics: descriptive, Mann-Whitney and Kruskal-Wallis tests and Spearman correlation, p <0.05.

Results: We included 84 patients, 45 of which with SpA (53.6%) and 39 (46.4%) RA. In the RA group, 92.3% were female, 84.6% were under anti-TNF, 66.7% were under their 1st biologic, the median age was 60.0 (51.0-66.0) years and the median time in treatment with current biologic was 31.0 (20.0-62.0) months. In the SpA group, 62.2% were female, 86.7% were under anti-TNF, 77.8% were under their 1st biologic, median age was 47.0 (39.5-57.0) years and median time in treatment with current biologic was 37.0 (12.0-83.0) months. Fifteen incomplete questionnaires were excluded. Sixty patients (87.0% of the 69 valid questionnaires) didn’t meet the minimum criteria necessary to ensure correct use of medication (correct answer to the first 5 questions), thus obtaining a CPM score of 0. The mean CPM score was 0.2 (±0.5), the median 0 (0), the minimum 0 and the maximum 1.7. There were no differences in CPM according to age, time in treatment with the current biologic, disease duration, n of previous biologics, gender, educational level, diagnosis, current biologic and n of other concomitant drugs. Table 1
describes the scores obtained in each domain of the questionnaire. We noticed that if we ask the same questions orally, the patients knew more than what the questionnaire revealed.

<table>
<thead>
<tr>
<th>Domains</th>
<th>Mean  ±SD</th>
<th>Median (IQR)</th>
<th>Min.</th>
<th>Max.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Process of use [4; 8]</td>
<td>5.6±2.0</td>
<td>6.0 (5.0-6.0)</td>
<td>-2</td>
<td>8</td>
</tr>
<tr>
<td>Therapeutic objective [-4;4]</td>
<td>3.5±1.1</td>
<td>4.0 (4.0-4.0)</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>Safety [-8,8]</td>
<td>1.3±1.5</td>
<td>1.0 (0-2.0)</td>
<td>-3</td>
<td>3</td>
</tr>
<tr>
<td>Conservation of the medicine [-2]</td>
<td>1.9±0.6</td>
<td>2.0 (0-2.0)</td>
<td>-1</td>
<td>2</td>
</tr>
</tbody>
</table>

Conclusion: The CPM-PT-PT underestimated the level of knowledge about biologic therapy in our population, suggesting the need to assess it during the clinical interview.

References:

Disclosure of Interests: Nathalie Madeira: None declared, Candida Silva: None declared, Claudia Miguel: None declared, Dina Medeiros: None declared, Filippe Barcelos Consultant for: Pfizer; Ely-Lilly, Speakers bureau: None declared, Jeffrey Curtis: None declared, Monika Safford Grant/research support from: Amgen

AB1348 PERSPECTIVES OF PATIENTS WITH INFLAMMATORY ARTHRITIS REGARDING CARDIOVASCULAR RISK: A QUALITATIVE STUDY

Iris Navarro-Milian1,2, Sarah Young3, Sally Shurbaji4, Chastity McDavid5, Anna Cornelius-Schecter4, Bernadette Johnson5, Andrea Cherrington5, Liana Fraenkel5, Jeffrey Curtis4, Monica Safford1.

Background: Cardiovascular disease (CVD) is the most common cause of death among patients with inflammatory arthritis (IA) such as rheumatoid arthritis (RA), psoriatic arthritis (PsA) or ankylosing spondylitis (AS). Objectives: To elicit perspectives of patients with IA to inform the design of a patient-centered intervention for a CVD risk reduction intervention.

Methods: This was a qualitative study guided by Bandura’s Social Cognitive Theory, placing special emphasis on knowledge about the relationship between arthritis and CVD as well as barriers and facilitators to receiving healthcare related to CVD risk such as screening and management for hyperlipidemia. We recruited patients from a single academic center with either RA, PsA, or AS to participate in focus groups. Data were analyzed thematically.

Results: We conducted three focus groups with a total of 17 participants (5 participants in two and 7 participants in one of the focus groups) of mean age 56 (SD=7.7) years; 15 were women; 3 were on a statin; and 1 previously had a stroke. Barrier Themes 1-2: 1) Need for information about arthritis, prognosis, and IA medications; 2) Lack of knowledge about how IA increases cardiovascular disease (CVD) risk; Facilitator Themes 3-5: 3) Lifestyle changes to reduce overall CVD risk; 4) Potential roles for peer coaches; and 5) Improving doctor-patient communication about IA, medications, and CVD risk. Patients expressed that improving Themes 2 and 5 could facilitate CVD screening.

Conclusion: Education about increased CVD risk could help activate patients with IA engage in CVD risk reduction strategies. Peer coaches appears to be a reasonable tool towards that goal.

Disclosure of Interests: Iris Navarro-Milian: None declared, Sarah Young: None declared, Sally Shurbaji: None declared, Chastity McDavid: None declared, Anna Cornelius-Schecter: None declared, Bernadette Johnson: None declared, Andrea Cherrington: None declared, Liana Fraenkel: None declared, Jeffrey Curtis: None declared, Monica Safford Grant/research support from: Amgen

AB1349 PATIENT INVOLVEMENT IN BASIC RHEUMATOLOGY RESEARCH IS CHALLENGING BUT FEASIBLE. A 3 YEAR’S RESPONSIVE EVALUATION OF ADDED VALUE, PITFALLS AND CONDITIONS FOR SUCCESS

Maarten de Wit1, Yvette Neijland2, Frank van den Hoogen2, Peter van der Kraan3, Anna Cornelius-Schecter1, Bernadette Johnson4, Andrea Cherrington4, Liana Fraenkel5, Jeffrey Curtis4, Monika Safford1.

Background: Empirical evidence for effective patient-researcher collaboration in basic research is lacking.

Methods: Empirical evidence for effective patient-researcher collaboration in basic research is lacking. A qualitative study to explore the feasibility and impact of patient involvement in basic rheumatology research and to identify facilitators and barriers.

Results: In total 13 patient representatives (PRs) and 15 basic researchers participated. PRs experienced basic research as complex due to lack of understanding bio-molecular processes and the use of technical jargon. Their initial role was mostly listening, sometimes asking questions and why progress takes so much time. PRs obtained insight in the biological processes of their own disease. It inspired PRs to stay involved and why progress takes so much time. PRs obtained insight in the biological processes of their own disease. It inspired PRs to stay involved and why progress takes so much time. PRs obtained insight in the biological processes of their own disease. It inspired PRs to stay involved and why progress takes so much time. PRs obtained insight in the biological processes of their own disease. It inspired PRs to stay involved and why progress takes so much time. PRs obtained insight in the biological processes of their own disease. It inspired PRs to stay involved and why progress takes so much time. PRs obtained insight in the biological processes of their own disease. It inspired PRs to stay involved and why progress takes so much time. PRs obtained insight in the biological processes of their own disease. It inspired PRs to stay involved and why progress takes so much time. PRs obtained insight in the biological processes of their own disease. It inspired PRs to stay involved and why progress takes so much time. PRs obtained insight in the biological processes of their own disease. It inspired PRs to stay involved and why progress takes so much time. PRs obtained insight in the biological processes of their own disease. It inspired PRs to stay involved and why progress takes so much time. PRs obtained insight in the biological processes of their own disease. It inspired PRs to stay involved and why progress takes so much time. PRs obtained insight in the biological processes of their own disease. It inspired PRs to stay involved and why progress takes so much time. PRs obtained insight in the biological processes of their own disease. It inspired PRs to stay involved and why progress takes so much time. PRs obtained insight in the biological processes of their own disease. It inspired PRs to stay involved and why progress takes so much time. PRs obtained insight in the biological processes of their own disease. It inspired PRs to stay involved and why progress takes so much time. PRs obtained insight in the biological processes of their own disease. It inspired PRs to stay involved and why progress takes so much time. PRs obtained insight in the biological processes of their own disease. It inspired PRs to stay involved and why progress takes so much time. PRs obtained insight in the biological processes of their own disease. It inspired PRs to stay involved and why progress takes so much time. PRs obtained insight in the biological processes of their own disease. It inspired PRs to stay involved and why progress takes so much time. PRs obtained insight in the biological processes of their own disease. It inspired PRs to stay involved and why progress takes so much time. PRs obtained insight in the biological processes of their own disease. It inspired PRs to stay involved and why progress takes so much time. PRs obtained insight in the biological processes of their own disease. It inspired PRs to stay involved and why progress takes so much time. PRs obtained insight in the biological processes of their own disease. It inspired PRs to stay involved and why progress takes so much time. PRs obtained insight in the biological processes of their own disease. It inspired PRs to stay involved and why progress takes so much time. PRs obtained insight in the biological processes of their own disease. It inspired PRs to stay involved and why progress takes so much time. PRs obtained insight in the biological processes of their own disease. It inspired PRs to stay involved and why progress takes so much time. PRs obtained insight in the biological processes of their own disease. It inspired PRs to stay involved and why progress takes so much time.

Conclusion: The CPM-PT-PT underestimated the level of knowledge about biologic therapy in our population, suggesting the need to assess it during the clinical interview.

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Disclosure of Interests: Nathalie Madeira: None declared, Candida Silva: None declared, Claudia Miguel: None declared, Dina Medeiros: None declared, Filippe Barcelos Consultant for: Pfizer; Ely-Lilly, Speakers bureau: None declared, Jeffrey Curtis: None declared, Monika Safford Grant/research support from: Amgen

Table 1. Themes and Key Points That Emerged From Focus Groups of Patients with Inflammatory Arthritis

<table>
<thead>
<tr>
<th>Theme</th>
<th>Quotes from patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Need for information about IA and medications</td>
<td>“When I was first diagnosed, as far as the medications and the side effects and what I could expect. Like I said, everything I read was bad, and it didn’t—I’m probably going to take it the rest of my life, and you have to get your blood tested every three months to make sure everything’s looking good.”</td>
</tr>
<tr>
<td>Lack of understanding regarding the association between CVD risk and IA</td>
<td>“I never even thought about it. Had no idea that it would even affect my heart like that. I’m still in shock [laughter] that has to do with the arthritis.”</td>
</tr>
<tr>
<td>CVD risk reduction as an integrated lifestyle modification</td>
<td>“They (doctors) know about the medicines and everything, so I’ll ask them, ‘Is there something I could do or take that would help it?’ We’ve got to do our part, too. We’ve got to exercise. We got to watch what we eat. Stress. I know stress will cause a lot of stuff to come on.”</td>
</tr>
<tr>
<td>Possible uses for peer coaches around relevant CVD risk factor mitigation approaches</td>
<td>“It would’ve been nice if I would talk to somebody who, maybe, was on the medication and could tell me, ‘Well, I haven’t had any problems with it,’ or, ‘Yeah, it does this.’ I’m sure it affects different people differently.”</td>
</tr>
<tr>
<td>Improving doctor-patient communication about IA</td>
<td>“If I’m at home, and all of a sudden, I’m like, ‘Why didn’t I ask her that?’ Let’s write it down. Then when I go to my peer coach, maybe, with those questions, they can also help me to understand that.”</td>
</tr>
</tbody>
</table>

Facilitators of patient involvement related to a) education of principles of participatory research; b) training of patient-researcher collaboration; c) development of a common language level; d) open mind and respectful communication; e) professional support; and f) leadership commitment. Main barriers were the complexity of pathogenetic processes for patients and time commitment for researchers. All participants found the collaboration worthwhile.

Reported impact was divers. Having to look at their work from a helicopter view encouraged researchers to attain a holistic view of people with a rheumatic condition and skills to explain their research for a lay audience. Patients experienced personal satisfaction after sharing experiences and receiving recognition from others. For the research process, a few examples were reported where patients input led to new topics on the research agenda. One example was the grant application to explore determinants of fatigue in the laboratory, directly prompted by patients. More substantial benefits were experienced for the development of patient-friendly educational materials and lay summaries of research protocols, dissemination of research findings through interviews and presentations, and even promotion of patient participation in national scientific societies of which the researchers are a member. Little impact was reported on the actual results of basic research.

Conclusion: Long term patient involvement in basic research is feasible and worthwhile. Despite the time investment, both patients and researchers experience valuable benefits that outweigh the lack of tangible impact on research findings.

Disclosure of Interests: None declared


HOW TO REDUCE THE NOCEBO EFFECT IN RHEUMATOLOGY? A SYSTEMATIC REVIEW OF RISK FACTORS AND INTERVENTION STRATEGIES

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Rheumatology department APHP Saint-Antoine Hospital, Sorbonne Université, INSERM, PARIS, France

Background: Nocebo effect (NE) defines any declared negative side effect of a drug that is non-specific, non-explained by its pharmacokinetic, and non-dose dependent. Recently, it has been pointed out as the main factor that reduces the rate of switches from a biologic originator to biosimilars in rheumatology.

Objectives: To identify the risk factors (RFs) and interventions strategies to reduce the NE in rheumatism and musculoskeletal diseases (RMDs), and more specifically in BS switches.

Methods: MEDLINE, Embase and Cochrane databases were systematically searched (inception to 15th November 2018) using relevant keywords: search1: “musculoskeletal diseases” and “nocebo” or “non-specific side effect” (NSSE); search2: “biologics” and “nocebo” or “non-specific side effect”. Inclusion criteria were: studies on pharmacological treatments, studies investigating RFs for NE or NSSEs, studies specifically describing an intervention aimed to reduce NE. Studies on non-RMDs and fibromyalgia were excluded.

Results: Of 212 and 639 references screened respectively in search1 and search2, 151 duplications were deleted, 32 mentioning NE or equivalent were read in full text by 2 independent investigators and consensually selected.

No study met inclusion criteria for NE risk factors: 6 studies investigated the RFs of discontinuation after switch to BS, 3 with etanercept (ETN), 3 with infliximab (IFX), one investigated risk factors of back switch (meaning return from BS to BS ETN), one study analyzed a genetic factor of intolerance to methotrexate (MTX) in juvenile idiopathic arthritis (JIA) and one study assessed the RFs for overall discontinuation of biologics. Although contextual factors were mentioned, no study tested RFs on NE responders only. RFs for a negative outcome were low self-efficacy, small-size rheumatology department, early start of IFX BS after its introduction on the market.

Only 5 studies met the inclusion criteria for specific interventions to reduce NE. One was about countermeasures used to reduce MTX tolerance in children with JIA: including covert dosing and taste masking, with no significant results. The other four studies aimed to reduce NE related to a switch: by a shared decision-making method (ETN, one study), assessed by a structured communication strategy (ETN, one study and two by a standardized information (ETN, one study; IFX, one study). Rate of NS-SE was mentioned in 3 studies, and the outcome (NS-SE rate compared to NE-SE rate of control group) was mentioned in only 2 studies. However, the assessment of intervention efficacy was not possible, since comparison was performed with historical cohorts.

Conclusion: Although nocebo effect is an important issue in rheumatology, especially as an explicative factor for limiting the retention rate when switching from biologic originators to biosimilars, its risk factors and intervention strategies to prevent it are poorly known. Our results encourage studies to better understand the risk factors associated with nocebo effect and the means to reduce it, particularly in the context of switches from bio-originators to biosimilars.

Disclosure of Interests: None declared


DO WE NEED A PATIENT PEER MENTOR PROGRAM IN DAILY PRACTICE FOR PATIENTS WITH EARLY RHEUMATOID ARTHRITIS AND IF SO, HOW SHOULD THIS BE ORGANIZED?

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Background: Management and support by an interdisciplinary rheumatology team are essential for achieving optimal disease outcomes in rheumatoid arthritis (RA). Nevertheless, health professionals generally do not experience the disease themselves, and patients may have specific educational needs that can only be provided by other patients having gone through the same experience. Furthermore, patients with RA may benefit most from such additional care interventions in the early disease stage when they are particularly faced with threats to their normal life. Peer mentoring has been studied and successfully implemented in other chronic conditions, however, this is rather a new care concept in the field of rheumatology.

Objectives: Among four key stakeholders in the management of early RA, we aimed (1) to uncover the current experience with, need for and attitude towards implementing peer mentoring in the care for patients with early RA in Flanders; (2) to gather ideas for the content and format of a peer mentor program.

Methods: We conducted an explorative qualitative focus group study. In total, five focus groups were organized to capture the perspective of each of the following stakeholders: patients with early RA (n=10), representatives of patient organizations (n=5), rheumatologists (n=10) and rheumatology nurses (n=5). Data were analyzed using the constant comparison method as presented in the Qualitative Analysis Guide of Leuven. Two patient research partners helped to analyze and interpret the data.

Results: Most stakeholders perceived a potential need for peer mentoring in early RA. However, they underscored that this would be largely person and disease phase dependent suggesting that peer mentoring should be presented as an option to patients, rather than a standard of care. The addition of peer mentoring would be foremost situated in providing disease perspective and a sense of recognition to newly diagnosed patients. For some stakeholders, it was difficult to get a clear picture of such a program, which made it difficult for them to formulate an opinion on a specific format. The health professionals particularly mentioned the current lack of a formal framework for collaborating with patient experts, and the need for carefully selected and well-trained peer mentors. Stakeholders shared the view that the development of a peer mentor program and its integration within the current care context should ideally take place in cooperation with and under supervision of health professionals.

Conclusion: Our results underline that peer mentoring in early RA holds potential for certain patients under certain circumstances, yet a clear framework for an expert in the daily care of patients with early rheumatoid arthritis.

Acknowledgement: This work was supported by Fonds Wetenschappelijk Onderzoek (FWO).}

Disclosure of Interests: Kristien Van der Elst: None declared, Lore Bangels: None declared, Lianne Peerlings: None declared, Lies De Caluwé: None declared, Ilse Langens: None declared, Veerle Stouten: None declared, Diederik De Cock: None declared, Rene Westhovens Grant/research support from: Bristol-Myers Squibb, Consultant for: Celtrion, Galapagos-Gilead, Patrick Verschueren Grant/research support from: Unrestricted Pfizer Grant for Early RA research

HPR Epidemiology and public health (including prevention)

AB1352-HPR  INVESTIGATION OF EFFECT OF DISEASE AND RELATED FACTORS IN INDIVIDUALS WITH FIBROMYALGIA

Bilge Basak Calik1, Aylin Keskin1, Eilif Kurubali2, Berma Cagla Caglayan1, Ugur Karasu3, 1Pamukkale University, School of Physical Therapy and Rehabilitation, Denizli, Turkey; 2Pamukkale University, Department of Rheumatology, Denizli, Turkey

Background: Fibromyalgia (FM), one of the most common rheumatologic disorders, is characterized by widespread pain in the body, sensitivity in the certain anatomical regions, fatigue, sleep disorders and reduced pain threshold, uncommon and extra-articular rheumatism disease (1). It has been reported that impairments in functional capacity and quality of life cause significant limitations in individuals with FM (2).

Objectives: The aim of this study was to examine the effect of disease and to investigate the factors associated with the disease in individuals with FM.

Methods: In our study, 334 voluntary individuals with FM (324 female, 10 male) who applied to Pamukkale University Department of Internal Medicine, Department of Rheumatology were diagnosed according to 2010 American College of Rheumatology criteria whom participated in the study with the mean age of 47.55±10.46 (years). Fibromyalgia Impact Questionnaire (FIQ) was used to determine the effect of disease, Beck Depressive Inventory (BDI) and Beck Anxiety Inventory (BAI) for emotional status and Pittsburgh Sleep Quality Index (PSQI) for sleep quality, right after demographic information and disease related data were recorded. Multiple regression analysis were used to examine the factors related to disease activity.

Results: High body mass index (B=1.21, p=0.023), high tender point score (B=427, p=0.000), high depression score (B=350, p=0.000), high anxiety score (B=258, p=0.000) and poor sleep quality (B=157, p=0.002) corresponded to the higher FIQ score. However, age (B=-0.19, p=0.716), level of education (B=0.09, p=0.858) and disease duration (B=0.054, p=0.331) did not significantly affect FIQ.

Conclusion: As a result of our study the progress of body mass index in individuals with FM, increase in number of tender points, poor sleep quality, depression and anxiety were among the factors affecting the disease. Therefore, these factors must be considered in order to reduce the severity of the disease in individuals with FM.

REFERENCES
[2] Arnold LM, Crofford LJ, Mease PJ, et al. Patient perspectives on the severity of the disease in individuals with FM. Therefore, these factors must be considered in order to reduce the prevalence of pain medications followed by a combination of paracetamol. See table 1. The prevalence of pain medications usage was not with associated disease activity.

Pain medication   n     %
Paracetamol       2407    34
Paracetamol + opioids                                     744    11
NSAID             633     9

Conclusion: As other studies have shown the prevalence of pain medication in patients with RA is high. The most prescribed medication was paracetamol or opioids, coinciding with other studies (1). This descriptive study is useful for further studies to develop in Colombia and Latin America. Additionally, it is important to consider other alternative therapies in order to approach in painful condition like RA.

Disclosure of Interests: Wilberto Rivero: None declared, Diana Buitrago-Garcia: None declared, Pedro Santos-Moreno Grant/research support from: Dr Santos has received research grants from Janssen, Abbvie and UCB, Speakers bureau: Dr Santos has received speaker fees from Sanofi, Lilly, Bristol, Pfizer, Abbvie, Janssen and UCB, Fernando Rodriguez: None declared


AB1354-HPR DESCRIPTION OF INDIVIDUALS WITH FIBROMYALGIA SYNDROME

Berma Cagla Caglayan1, Eilif Kurubali2, Aylin Keskin1, Bilge Basak Calik1, Ugur Karasu3, 1Pamukkale University, Physical Therapy and Rehabilitation, DENIZLI, Turkey; 2Pamukkale University, Department of Rheumatology, DENIZLI, Turkey

Background: Fibromyalgia (FM) affects negatively physical and mental health and reduces quality of life. The most common symptom is chronic widespread musculoskeletal pain in FMS. As other studies have shown the prevalence of pain medications used in patients with RA is high. The most prescribed medication was paracetamol or opioids, coinciding with other studies (1).

Objectives: This study was planned to investigate comorbidities, number of medication and to determine the most painful body region in individuals with FM.

Methods: The study included 166 individuals (161 women, 5 men) who were diagnosed with FM, with a mean age of 47.56±10.91 years. Comorbidities, number of medication which were used for FMS or other diseases of participants were recorded also painful body regions were assessed for 28 regions. The categorical variables were expressed in number and percentage.

Results: The results showed that a total of 42.2% (n=71) of individuals in this study had no comorbidities, 11.4% (n=19) of individuals had hypertension and 7.8% (n=13) of individuals had asthma. When the number of medication were examined, a total of 66.3% (n=110) of individuals did not use any medication, 25.8% (n=43) of individuals did use one type of medication with FM-related and 4.2% (n=7) of individuals did use two type of medications with FMS related. Painful body regions were reported by 74.1% (n=123) for neck, 66.3% (n=110) right shoulder, 68.7% (n=114) left shoulder, 68.1% (n=113) right knee and 68.1% (n=113) left knee.

Conclusion: In general, there was no comorbidity with FMS. The study found that individuals with FMS usually did not use medication. Also neck were found the most painful body region in individuals with FMS.

REFERENCES

Disclosure of Interests: None declared

A SYSTEMATIC LITERATURE REVIEW (SLR) ON NURSING SENSITIVE OUTCOMES IN SYSTEMIC SCLEROSIS (SSC)

Khatija El Aoufy, Laura Rasero, Guya Piemonte, Gianni Vigili, Serena Guiducci, Cosimo Bruni, Silvia Bellando Randone, Marco Matucci-Cerinic. University of Florence, Florence, Italy

Background: SSC affects significantly patients functionality and Quality of Life (QoL). Specific Nursing Sensitive Outcomes (NSOs) still need to be established in SSC.

Objectives: This SLR was aimed at identifying NSOs in SSC patients and the related screening tools.

Methods: Medline, CINHAL, EMBASE and PsycINFO were searched to identify relevant studies. Experimental and observational studies that reported nursing interventions and NSOs were included. All potentially eligible studies were read in full text and examined against the selection criteria previously listed. Quality assessment was carried out through Critical Appraisal Skills Programme tools; and, the OMERACT (Outcome Measures in Rheumatology) comprehensive conceptual framework for health was used to contextualise and summarize findings.

Results: 7015 records were screened for title and abstract, 39 full-text were identified and assessed. Eleven studies were included in this SLR. For the core area “pathophysiological manifestations” 4 domains (health status, digital ulcers, clinical efficacy and fatigue), and, for the core area “impact on life” 5 domains were found (functionality, patient knowledge, patient satisfaction, psychological status and quality of life). Thus, NSCs identified were physical function and parameters, health events, upper limb functionality, patients knowledge of disease complications, degree of self-management, need for nursing interventions, self-efficacy, health efficacy, psychological state, depressive mood and QoL.

Disclosure of Interests: Khadija El Aoufy: None declared, Laura Rasero: None declared, Guya Piemonte: None declared, Gianni Vigili: None declared, Serena Guiducci: None declared, Cosimo Bruni: None declared, Silvia Bellando Randone: None declared, Marco Matucci-Cerinic: Grant/Research support from: Actelion, MSD, Pfizer, BMS, Chemomab, Sanpeidia, Speakers bureau: Actelion, BMS, MSD, Janssen DOI: 10.1136/annrheumdis-2019-eular.7685

Figure 1

Conclusion: The results identify outcomes that may allow the structuring of a preliminary behavioural flow chart for nursing SSC case management. Further researches are warranted to examine the multidimensional and complex role of nursing in SSC management.

Flow chart of the SLR:

Abstract AB1356-HPR Table 1. Level of exercise, BASDAI, VAS pain, VAS fatigue and BMI presented with mean scores and standard deviation (SD)

<table>
<thead>
<tr>
<th></th>
<th>Before pregnancy</th>
<th>1st trimester</th>
<th>2nd trimester</th>
<th>3rd trimester</th>
<th>6 weeks postpartum</th>
<th>6 months postpartum</th>
<th>12 months postpartum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regular exercisers: ≥ 3 times a week</td>
<td>32.2% (SD)</td>
<td>19% (SD)</td>
<td>20.3% (SD)</td>
<td>8.5% (SD)</td>
<td>9.5% (SD)</td>
<td>24.5% (SD)</td>
<td>13.6% (SD)</td>
</tr>
<tr>
<td>BASDAI: ≥ 3 times a week</td>
<td>3.0 (2.6)</td>
<td>3.0 (2.5)</td>
<td>2.9 (2.2)</td>
<td>5.5 (1.8)</td>
<td>2.9 (2.5)</td>
<td>3.4 (2.9)</td>
<td>3.2 (2.3)</td>
</tr>
<tr>
<td>VAS pain: ≥ 3 times a week</td>
<td>26.2 (20.5)</td>
<td>56.8 (31.8)</td>
<td>33.4 (26.8)</td>
<td>45.4 (29.2)</td>
<td>28.5 (18.3)</td>
<td>29.9 (29.2)</td>
<td>24.8 (16.6)</td>
</tr>
<tr>
<td>VAS fatigue: ≥ 3 times a week</td>
<td>38.3 (3.8)</td>
<td>36.7 (32.9)</td>
<td>50.8 (24.5)</td>
<td>57.0 (36.4)</td>
<td>42.5 (32.6)</td>
<td>33.3 (37.4)</td>
<td>29.2 (27.1)</td>
</tr>
<tr>
<td>BMI: ≥ 3 times a week</td>
<td>25.3 (4.6)</td>
<td>24.5 (2.2)</td>
<td>26.1 (2.9)</td>
<td>26.0 (2.3)</td>
<td>25.0 (2.5)</td>
<td>25.8 (3.9)</td>
<td>27.7 (7.2)</td>
</tr>
<tr>
<td>Irregular exercisers: ≥ 2 times a week</td>
<td>40.7% (SD)</td>
<td>46.6% (SD)</td>
<td>38% (SD)</td>
<td>35.6% (SD)</td>
<td>25.4% (SD)</td>
<td>36.7% (SD)</td>
<td>34.1% (SD)</td>
</tr>
<tr>
<td>BASDAI: ≥ 2 times a week</td>
<td>2.8 (2.4)</td>
<td>3.4 (2.2)</td>
<td>3.2 (2.6)</td>
<td>3.2 (2.3)</td>
<td>2.5 (1.9)</td>
<td>2.3 (2.1)</td>
<td>3.3 (2.6)</td>
</tr>
<tr>
<td>VAS pain: ≥ 2 times a week</td>
<td>28.1 (25.7)</td>
<td>35.4 (26.2)</td>
<td>38.8 (29.6)</td>
<td>29.4 (27.3)</td>
<td>27.4 (21.0)</td>
<td>24.7 (26.0)</td>
<td>31.8 (25.6)</td>
</tr>
<tr>
<td>VAS fatigue: ≥ 2 times a week</td>
<td>40.4 (33.5)</td>
<td>59.6 (31.3)</td>
<td>53.0 (33.5)</td>
<td>52.3 (33.8)</td>
<td>35.3 (30.3)</td>
<td>27.2 (33.5)</td>
<td>41.4 (32.5)</td>
</tr>
<tr>
<td>BMI: ≥ 2 times a week</td>
<td>26.5 (7.5)</td>
<td>25.5 (4.2)</td>
<td>26.9 (4.8)</td>
<td>28.2 (4.8)</td>
<td>25.2 (3.7)</td>
<td>24.7 (3.6)</td>
<td>25.1 (3.9)</td>
</tr>
<tr>
<td>Non-exercisers: ≥ 3 times a month</td>
<td>27.1% (SD)</td>
<td>34.4% (SD)</td>
<td>41.8% (SD)</td>
<td>55.9% (SD)</td>
<td>65% (SD)</td>
<td>38.7% (SD)</td>
<td>52.2% (SD)</td>
</tr>
<tr>
<td>BASDAI: ≥ 3 times a month</td>
<td>4.0 (3.2)</td>
<td>3.6 (1.9)</td>
<td>2.8 (2.1)</td>
<td>3.9 (2.6)</td>
<td>3.4 (2.7)</td>
<td>4.0 (3.1)</td>
<td>3.8 (2.6)</td>
</tr>
<tr>
<td>VAS pain: ≥ 3 times a month</td>
<td>42.3 (26.7)</td>
<td>34.5 (27.4)</td>
<td>31.4 (24.5)</td>
<td>42.1 (29.8)</td>
<td>36.1 (31.0)</td>
<td>37.7 (25.3)</td>
<td>34.3 (28.3)</td>
</tr>
<tr>
<td>VAS fatigue: ≥ 3 times a month</td>
<td>48.7 (29.0)</td>
<td>55.6 (36.9)</td>
<td>46.2 (30.6)</td>
<td>54.1 (29.3)</td>
<td>43.9 (33.4)</td>
<td>52.3 (30.4)</td>
<td>48.5 (35.7)</td>
</tr>
<tr>
<td>BMI: ≥ 3 times a month</td>
<td>26.5 (5.1)</td>
<td>27.6 (5.6)</td>
<td>27.4 (3.9)</td>
<td>30.8 (6.1)</td>
<td>26.4 (5.2)</td>
<td>26.1 (4.9)</td>
<td>24.7 (5.7)</td>
</tr>
</tbody>
</table>

REFERENCES
Methods: Observational cross-sectional study in patients with intravenous BT from Day Hospital of a tertiary hospital in Madrid. Sociodemographic, disease features (weight, height, work disability (WD), diagnosis, treatment) and PRO (FIRS, FACIT-F, HAD, and GHQ-28) were collected. We defined the Si according to the answer at the 6th and 7th questions of section D of the GHQ-28. The Sa was registered according to the patient’s clinical history. The categorical variables were analyzed with the Chi square test. A logistic regression analysis was performed to evaluate the possible factors associated with suicidal behavior (SB). To evaluate the variance of discrete quantitative variables between groups the Kruskal-Wallis test was used, with a post-hoc analysis with U-Mann Whitney, to determine the difference between pairs.

Results: We included 321 patients, 65% women, with a mean age (range, SD) of 56 years (89-15, 14.1), and a mean disease duration (SD) of 16 years (DS-31-9.7). The sociodemographic and clinical characteristics are described in Table 1 and 2. Of all patients, 4% had had 1 or more Sa and 11% had Si. 23% of patients had associated fibromyalgia (FIRST), 47% fatigue (FACIT-F), 27.4% anxiety (A-HAD), 16.2% depression (D-HAD) and a 48.6% a probable psychic disorder (GHQ-28). The final logistic regression model includes FACIT-F, IL, D-HAD, and first biological with Cox R2 and Snell 20.1% and Nagelkerke 35.5%. The area under the curve was 0.849 with significance p<0.001 [95% CI (0.786 - 0.912)]. Regarding the GHQ-28 score, a significant difference was observed among the diagnostic groups (p<0.001); in post-hoc, a lower score was observed among patients with ankylosing spondylitis p<0.001. We also observed a significant difference among the treatment groups (p<0.001) for the GHQ-28 score. In the post-hoc analysis, the Abatacept group had a significantly higher mean p=0.042 of GHQ-28 score, however, in the multivariate analysis no significant difference was observed p=0.418.

Conclusion: There is a high prevalence of Si and Sa in patients with BT. Depression, fatigue, sleep disorders, fibromyalgia and work disability were associated with a higher prevalence of SB.

Table 1. Demographic characteristics No ideation/No attempt (273) Ideation (36) Attempt (12)

Table 2. Clinical characteristics No ideation/No attempt (273) Ideation (36) Attempt (12)

Disclosure of Interests: Amapro Lopez Esteban : None declared, Roberto Daniel Gonzalez Benitez: None declared, Aurora Alonso Amigo: None declared, Juan Carlos Sanchez Zarotii: None declared, Florentina Garca Colle: None declared, Juan Carlos Nieto: None declared, Belin Serrano Benavente: None declared, Juan Ovales: None declared, Tamara Del Ro Blasco: None declared, Alfonso Ariza: None declared, Daniel Gonzalez Benitez: None declared, Iustina Janta: None declared, Juan Carlos Sanchez Zarotii: None declared, Carlos Gonzalez Consultant for: Celgene, Gilead, Janssen, Merk, Novartis, Pfizer, Speakers bureau: Celgene, Roche, UCB, Indalecio deortegado Sez: None declared.

THE COMBINED EFFECTS OF LIFESTYLE HABITS ON
HEALTH-RELATED QUALITY OF LIFE, PHYSICAL AND
MENTAL FUNCTIONS IN PATIENTS WITH
SPONDYLOARTHROPATHIES

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Background: Earlier studies have found strong correlations between worse health and an unhealthy lifestyle, such as not meeting recommendations of moderate-to-vigorous physical activity, being overweight or obese and the use of tobacco in patients with spondyloarthritides (SpA). The impact of more than one unhealthy lifestyle habit (LSh) is however, scarcely described.

Objectives: To study the combined effects of unhealthy LShs on health-related quality of life (HRQoL) and physical and mental functions in patients with SpA. Differences between SpA subgroups and gender were also studied.

Methods: Postal questionnaires were in 2009 and 2011 sent to all patients diagnosed with SpA and registered in the Skane Healthcare Register. This study included patients who at both time points responded to the survey, were ≥20 years, and had ankylosing spondylitis (AS), psoriatic arthritis (PsA) or undifferentiated spondyloarthritides (USpA). Cross-sectional data from the 2011 questionnaire were available for 1601 patients (AS n=455, PsA n=883, USpA n=263), with a mean age of 58 (13) years (52% women). Self-reported levels of weekly physical activity at moderate or vigorous intensity, (MVPA), use of tobacco (cigarettes and/or snuff) and BMI (overweight or obese) were dichotomized as “healthy” or “unhealthy”. The number of unhealthy LSh were then summarized and straitified into four groups (scoring 0-3, 0=no unhealthy LSh). HRQoL was assessed with EQ-5D (0-1, worst-best), and physical function with BASFI. Disease activity (BASDAI), pain, fatigue (0-10, best-worst), anxiety, and depression (HADa/d) (0-21, no disorder) were available for 1601 patients (AS n=455, PsA n=883, USpA n=263), with a mean age of 58 (13) years (52% women). Self-reported levels of weekly physical activity at moderate or vigorous intensity, (MVPA), use of tobacco (cigarettes and/or snuff) and BMI (overweight or obese) were dichotomized as “healthy” or “unhealthy”.

Results: Fourteen percent (n=226) reported none of the studied unhealthy LSh, while 35% (n=555) reported one, 38% (n=611) two, and 15% (n=209) three unhealthy LSh. Reports of one and more unhealthy LSh had increasing negative impact on HRQoL. (from mean 0.74 (SD 0.19) to 0.57 (0.30)), disease activity (from 3.2 (2.1) to 4.5 (2.3)), physical function (3.2 (2.1) to 4.4 (2.0)), VAS-fatigue (4.2 (2.7) to 5.5 (2.7)), anxiety (4.8 (4.2) to 5.6 (4.4)) and depression (3.3 (3.3) to 4.8 (3.8)) in patients with SpA (p=0.019–5). Our findings support that the combined effect of unhealthy lifestyle habits have negative impact on many aspects of health. There is a need for interventions aiming at screening for not only one but several unhealthy lifestyle habits combined, and to offer coaching to increase behavioral change and promote better health.

Disclosure of Interests: None declared.


HPR Interventions (educational, physical, social and psychological)

AB1359-HPR

THE COMBINED EFFECTS OF LIFESTYLE HABITS ON
HEALTH-RELATED QUALITY OF LIFE, PHYSICAL AND
MENTAL FUNCTIONS IN PATIENTS WITH
SPONDYLOARTHROPATHIES

AB1361-HPR

BENEFITS OF HYDROGINASTICA IN ELDERLY WITH
OSTEOPOROSIS

Mataus Arantes 1, Sonia Bertolini 2, Amelia Pasqual Marques 1, 3, 4, 5, University of Sao Paulo, Department of Physical Therapy, Speech Therapy and Occupational Therapy, Sao Paulo, Brazil; 2 University Center of Maringa, UNESCUMAR, Department of Health Promotion, Maringa – PR, Brazil.

Background: The aging of the population has repercussions in several social sectors, among them health, with a view to increasing the frequency of Chronic Non-Communicable Diseases. It is worth highlighting Osteoporosis, since it is associated with increased mortality and dependencies, becoming a growing public health problem. As a form of maintenance and prevention of osteoporosis it is indicated the performance of physical exercises, among them water gymnastics stands out.

Objectives: The study aimed to present and discuss studies on the benefits of water aerobics for the elderly with osteoporosis.

Methods: For the development of the present study a bibliographic research was carried out in the years 2010 to 2017 through searches in national and international journals indexed in PubMed, Scielo, Lilacs and Medline databases. The descriptors used were: Elderly, Aging Process, Hydrogeology, Aquatic Activity, Osteoporosis and Health Promotion in Portuguese, Spanish and English. The search period was between the months of February and March of 2017 and after selecting the articles, to extract the definitions about the theme, they were read.

Results: We can identify that water aerobics is a practice that addresses these benefits in the elderly with osteoporosis. Another aspect found in the studies is that water gymnastics provides the elderly with improved socio-affective relationships.

Considering the current natural losses due to aging on some physical characteristics, water aerobics is an important exercise practice option. The activities in the aquatic environment are indicated for a considerable gain of muscular mass and reduction of the loss of the same one, aiding in the tonification of the musculature, the loss of fat and the increase of the resistance. For the elderly with osteoporosis this modality is a preventive aid that contributes to improve their quality of life.

Among the studies found, one performed in Japan in the elderly with osteoporosis, found an increase in VO2max, flexibility and increased strength of hydrogymnastics participants; in Israel, the elderly women reduced the Muscle Mass Index and body fat. In Brazil, a study verified the improvement of functional capacity in elderly women practicing water aerobics.

Disclosure of Interests:

Laura Villarreal: None declared, Michael Cabrera: None declared, Pedro Santos-Moreno: Research support from: Dr Santos has received research grants from Janssen, Abbvie and UCB, Speakers bureau: Dr Santos has received speaker fees from Sanofi, Lilly, Bristol, Pfizer, Abbvie, Janssen and UCB, Diana Bultraga-Garcia: None declared.


AB1360-HPR

PREVALENCE OF TOBACCO AND ALCOHOL CONSUMPTION IN PATIENTS WITH RHEUMATOID ARTHRITIS

Laura Villarreal 1, Michael Cabrera 2, Pedro Santos-Moreno 3, Diana Bultraga-Garcia 4, 5, 6, 7, Biomab – Center for rheumatoid arthritis, Psychology, Bogot, Colombia; 2 Biomab – Center for rheumatoid arthritis, EHR administration, Bogot, Colombia; 3 Biomab – Center for rheumatoid arthritis, Rheumatology, Bogot, Colombia; 4 Biomab – Center for rheumatoid arthritis, Nursing research, Bogot, Colombia

Background: Rheumatoid arthritis (RA) is a chronic, inflammatory arthritis leading to progressive joint and organ system damage and disability. It has been demonstrated that smoking and alcohol consumption is a risk factor for poor response to RA treatment.

Objectives: To describe the prevalence of smoking and alcohol consumption in patients with rheumatoid arthritis.

Methods: We conducted a retrospective study, patients were followed during 12 months. Smoking and alcohol consumption were assessed through yearly questionnaires. The disease activity and functional status were measured annually by the DAS28. We calculated means, and standard deviations for continuous variables and categorical variables were presented as rates. We estimated the prevalence smoking and alcohol consumption and explored if there was an association between DAS28 and smoking or alcohol consumption.

Results: We included 6491 patients. patients, 82% were female and 18% male; median age was 60 years (IQ=50-67), regarding disease activity, mean DAS28 was 2.59 ± 1.08. The prevalence of alcohol consumptions was 2.26% while smoking 7.83%. We did not find an statistical association between smoking alcohol consumption and DAS28.

Conclusion: Our study showed a small prevalence of patients with rheumatoid arthritis who smoke or consume alcohol without any associations between smoking or alcohol consumption with disease activity. This could be attributed to a low prevalence in our study. Further research is needed in order to propose other methodological approaches to explore this association.

Disclosure of Interests:

Laura Villarreal: None declared, Michael Cabrera: None declared, Pedro Santos-Moreno: Grant/research support from: Dr Santos has received research grants from Janssen, Abbvie and UCB, Speakers bureau: Dr Santos has received speaker fees from Sanofi, Lilly, Bristol, Pfizer, Abbvie, Janssen and UCB, Diana Bultraga-Garcia: None declared.

Water aerobics for the elderly has been gaining momentum and growing numbers of fans, so much so that in the last 10 years the popularity of exercise in the aquatic environment has increased significantly. **Conclusion:** With the present study it can be verified that the hydrogymnastics presents numerous benefits for maintenance and prevention of osteoporosis in the elderly. Regular practice of water aerobics contributes to good body health, as well as providing physical and mental well-being and social interaction among its practitioners. This study may provide important health professionals with knowledge about the importance of encouraging and intensifying regular physical exercise, including hydrogymnastics, as one of the determinants of elderly health promotion.

**REFERENCES**


Acknowledgement: Instituto Cesumar de Ciência, Tecnologia e Inovação (ICTET)

Disclosure of Interests: None declared


**AB1362-HPR**

**THE EFFECTS OF 4 WEEK REHABILITATION PROGRAM ON PATIENT OUTCOMES IN PATIENTS WITH KNEE OSTEOARTHRITIS**

Orur Aydogdu, Setir Kilikap, Beyzanur Dagpn, Zbeyir San, Marmara University, Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Istanbul, Turkey

**Background:** Osteoarthritis (OA) is the most common form of arthritis and a major cause of pain and disability in older adults (1). Older adults with knee OA report lower physical functioning and increased difficulty in performing activities of daily living compared with older adults without knee OA (2). Knee OA treatment aims to improve physical functions, quality of life, prevent disability, and decrease pain. Therapeutic exercises and physiotherapy treatment applications are recommended for the patients with knee OA (3).

**Objectives:** The purpose of this study was to examine the effects of 4 week physiotherapy and rehabilitation program on range of motion, balance, knee swelling, and activities of daily life, quality of life, and functional status in patients with knee osteoarthritis. It was hypothesized that 4 week rehabilitation program might provide improvements in measures of the patient outcomes in patients with knee osteoarthritis.

**Methods:** Twenty-seven healthy subjects were participated in the study. Subjects had no surgery history of lower extremity. Range of motion, balance, knee swelling, activities of daily life, quality of life, and functional status were assessed by Goniometer, Berg Balance Test, Tape measure, Barthel Index, WHQOL Scale, WOMAC Scale, respectively. The physiotherapy and rehabilitation program started after the first assessment and was applied as 20 sessions for a total of four weeks, five sessions per week. All of the assessments procedures were performed again after the treatment.

**Results:** There were statistically significant improvements in measures of range of motion, balance, knee swelling, and functional status between pre- and post treatment (p<0.05). However, no significant difference was found in activities of daily life and quality of life after the 4-week rehabilitation program (p>0.05).

**Conclusion:** Based on our findings, short-term effects of physiotherapy and rehabilitation program may be beneficial on range of motion, balance, knee swelling, and functional status in patients with knee osteoarthritis. However, 4-week rehabilitation program has no effect on activities of daily life and quality of life in patients with knee osteoarthritis.

**REFERENCES**


Disclosure of Interests: None declared


**AB1363-HPR**

**THE INVESTIGATION OF THE QUALITY OF LIFE AND FUNCTIONAL ABILITIES IN PATIENTS WITH JUVENILE SCLERODERMA**

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**Background:** Juvenile scleroderma (JS) is a rarely seen chronic connective tissue disorder. There are two main disease forms: juvenile localized scleroderma (JLS) and juvenile systemic sclerosis (JSS). These conditions share some common pathophysiologic features which are mainly characterized by inflammation and fibrosis of the skin. In JLS, fibrosis involves restricted areas of the skin, whereas in JSS it also affects the internal organs.

**Objectives:** There have been few studies of quality of life in pediatric scleroderma and these focused predominantly on self-perception and the influence of skin involvement. Our cross-sectional study aimed to describe the influence of juvenile scleroderma on functional ability and quality of life in relation to clinical and demographic measures.

**Methods:** 30 patients (26 girls, 4 boys) with JS between the ages of 6-18 years and 30 healthy controls (20 girls, 10 boys) with similar age and gender were included in our study. Patients with either localized scleroderma or systemic sclerosis (SSc) attending pediatric rheumatology clinics, together with their parents were asked to complete a set of 3 validated measures. Children completed their functional ability status with Childhood Health Assessment Questionnaire (CHAQ) and Jelson Taylor Hand Function Test (JHTFT). The quality of life were evaluated with Scleroderma Health Assessment Questionnaire (SHAQ). Clinical and demographic data were provided by consultant pediatric rheumatologists and physiotherapists.

**Results:** The mean age of the JS group was 14.06 3.24 years (86% female, 14% male, while their 53 localized scleroderma, 47 SSc) and of the control group was 12.43 3.24 years. There were significantly differences between the two groups in functional ability scores (JHTFT), (CHAQ) and quality of life scores (SHAQ) (p<0,05). In JS group, the total-CHAQ score was 0.470.63 (range 03, 0 indicating no impairment), the JHTFT-Total left hand and right hand scores were 44.059.83 and 41.497.42 second respectively, and the median SHAQ-Total score was 0.34 (range 06, 0 indicating no impairment).

**Conclusion:** Functional ability disabilities in JS patients cause limitations in daily living activity. Scleroderma had only a moderate effect on quality of life and functional abilities as measured by the 3 validated instruments. Although a small number of children reported greater impairment, this is an encouraging finding, given its potential disfiguring and debilitating effects.

**REFERENCES**


Disclosure of Interests: None declared

## AB1364-HPR PRELIMINARY CASE REPORT ON SHARING PATIENT HISTORY IN CLINICAL TREATMENT OF RHEUMATOID ARTHRITIS

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**Background:** Rheumatoid arthritis (RA) is a chronic disease with periods of flare-ups and remissions, affecting daily life. Therefore, this disease requires lifelong management and support by the patients, social circle, and health professionals (HP).  

**Objectives:** The aim of this study was to follow up the history of patients with RA, and demonstrate an improved understanding at each point in their disease trajectory, whilst encouraging them to cope, and enabling HP to optimize support provided.

**Methods:** We conducted two 30-minute interviews with patients with RA. Interview questions included the patients’ perspective of their disease and disease information, effects on daily life, as well as psychological considerations using the Corbin and Strauss Chronic Illness Trajectory Framework approach [1].  

This study was approved by the ethics committee of our hospital and informed consent was obtained.

**Results:** The first case: An unmarried 68 year old female living alone. The patients mother also suffered from RA. The patient was vaguely aware of the hereditary nature of RA (pretrajectory phase) and did not result in a big shock to her and she accepted her the diagnosis relatively smoothly (trajectory onset phase). She was prescribed initially pre-scribed methotrexate but this proved ineffective and infliximab was commenced. Remission was achieved and at that time she was satisfied with her relationship with her primary physician (stable phase).

Two years after beginning infliximab, she developed chest pain. However, her primary physician did not explore the problem and advised her that she had depression. She began to distrust him (unstable). She asked for infliximab to be stopped and requested her care be transferred to B university hospital where her mother was being treated. However, she was refused treatment due to the non-severity of her condition. She was unable to come to terms with refusal, and her physical and mental state deteriorated (downward phase).

Her mother advised the patient to go to D hospital, where she was put on Etanercept achieving remission with no complications (comeback phase). At D Hospital; (1) her condition and the need for treatment were clearly explained to her, and she was able to actively participate in shared decision making; and (2) she was given access to support from Health Professionals (HP) such as nurses, who offered a patient centered approach listening to her concerns and advising her appropriately whilst offering general psychological support.

A further 4 patients were interviewed. We will show the key phases of trajectories of their illnesses, the patients opinions about sharing their information with HP through interviewing, and the possibility of behavior change in the patients journeys.

**Conclusion:** This study shows that a patient centered approach taking into account the stages of the illness trajectory benefits patients perceptions of their disease and ability to cope with their condition. It also highlights the importance of having the support of others social circle, particularly at challenging times.

Making a thorough record of the patients disease and QOL trajectory allows the patient to understand their disease process and associated life changes, and assist health professionals to provide the optimal support and resolve problems when they arise.  

This preliminary study focuses on understanding the value of different phases of the trajectory of illness and sheds more light on the relationship between patients and HP and how the disease process and patients perspectives of their disease can facilitate mutual trust and smooth future treatment.

**REFERENCES**


**Disclosure of Interests:** Mie Fusaama: None declared, Susan Oliver: None declared, Hideko Nakahara: None declared, Yvonne van Eijk-Hustings Grant/research support from: UCB, Speakers bureau: Cellgene, Yuriko Kuroe: None declared


## AB1365-HPR INVESTIGATION OF THE ACUTE EFFECTS OF TAPPING ON TISSUE TEMPERATURE, MUSCLE STRENGTH, FUNCTION AND BALANCE IN PATIENTS WITH KNEE OSTEOARTHRITIS

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**Background:** Osteoarthritis (OA) mostly affects knee joint. It causes tissue temperature changes, muscle weakness, functional and balance impairments. Taping can be used to support knee joint. However, contradictory results presented in the literature (1-3).

**Objectives:** The aim of this study was to investigate the acute effects of taping on tissue temperature, muscle strength, function and balance in patients with knee OA.

**Methods:** Thirty-four patients with unilateral OA (34 females, age=60.118.29 years, height =159.765.27m; weight=80.1112.29 kg) were included. The patients were treated with a flexible kinesiology tape (Thera-Band Kinesiology tape, Cramer, USA). Supporting techniques for quadriceps muscle, patellar position and patellar tendon were applied. Before taping and after 30 min of application, tissue temperature with a thermal camera (Testo882, Germany), knee flexor and extensor muscle strength with a dynamometer (Lafayette, USA), function with timed up and go test and balance with computerized balance system (Prokin PK-254P, Tecnobody, Bergamo, Italy) were assessed. The paired samples t-test and Wilcoxon test used for analyses.

**Results:** The tissue temperature of the effected (34.661.16) and non-effected sides (34.871.08) of the cases were different (p=0.033). However, no significant difference was observed for tissue temperature before and after the taping (p=0.145). In the comparison of the effected side and non-effected side muscle strength, a significant difference was found for extensors (p=0.035). After taping the effected side, differences were found for extensor and flexor muscle strength (p=0.00; p=0.001) in comparison to before taping. While there was a significant difference in the time walking test before and after taping (p = 0.026), there was no difference for the balance scores (p> 0.05). The values of the cases before and after taping showed at Table 1.

**Conclusion:** It was observed that taping might not affect tissue temperature and balance. However, muscle strength and function could be affected positively with the acute supporting effect of taping.

**REFERENCES**


**Disclosure of Interests:** None declared

**Disclosure of Interests:** None declared

THE EFFECTS OF LAND AND WATER BASED MULTIDIMENSIONAL FUNCTIONAL MOBILITY EXERCISES ON PULMONARY FUNCTIONS IN ANKYLOSING Spondylitis Patients

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Background: Pulmonary manifestations are common in ankylosing spondylitis (AS) yet there is not enough evidence about the results of different interventions on pulmonary functions.

Objectives: The aim of this study was to evaluate the pulmonary effects of land and water based multidimensional functional mobility exercises on pulmonary functions in AS patients.

Methods: This is a single-blinded, randomized and experimental study conducted in outpatient clinic and thermal center. A total of 38 patients with definite ankylosing spondylitis according to the modified New York criteria were recruited for the study. Patients were randomly allocated to aquatic (AG) and land (LG) exercise group twice in a week for 8 weeks. Pulmonary Function Tests (PFT), maximal inspiratory mouth pressure (MIP), and maximal expiratory mouth pressure (MEP) were measured before and after the intervention.

Results: 3 patients from AG and 6 from LG missed 4 sessions consecutively. In AG, PEF (p<0.004), VC (p=0.025), MVV (p=0.006) and MIP (p=0.001) improved significantly on the other hand in LG FEV1/FVC (0.049), PEF (p<0.007) and MVV (p<0.004) significantly increased.

Conclusion: Performing multidimensional functional mobility exercises in water and on land could have different results. Exercising in water could have additional benefits such as increasing inspiratory muscle strength.

REFERENCES

Disclosure of Interests: None declared

EFFECTIVENESS OF THE BARBERIC TREATMENT ON THE PERCEIVED PAIN, FATIGUE AND FUNCTIONALITY OF WOMEN WITH FIBROMYALGIA

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1Fundacion FIVAN, Valencia, Spain; 2University of Valencia, Physiotherapy, Valencia, Spain; 3Utrecht U, Utrecht, Netherlands

Background: Fibromyalgia (FM) is a chronic pain syndrome accompanied by other symptoms such as fatigue or altered functionality. 1 One of the most common non-pharmacologic treatment is physical exercise because of its known positive influence on pain as a consequence of the physical condition improvement. 2 However, they use to present a lack of adherence to this type of therapeutic programs may be attributable to post-exercise pain. 3 For this reason, alternative approaches that do not involve physical efforts, such as hyperbaric therapy, may be effective to reduce pain, fatigue or functionality in women with FM. 4

Objectives: To compare the effectiveness of hyperbaric therapy and physical exercise on pain, fatigue and functionality in women with FM.

Methods: A randomized control trial was conducted. 28 women with FM were divided in two intervention groups: One group, composed of 14 women, received a low-intensity physical exercise program twice a week for 8 weeks (PEG). The other group received 40 sessions of hyperbaric treatment, 5 times per week (HBTG). To determine the effect of these therapeutic programs, the perceived pain was assessed with an analogue visual scale. Further, the fatigue was measured with the Borg scale and the covered walked distance with The Six minutes walk test. The measurements were conducted two times, before and one week after finishing the treatment. The effect of the treatments was statistically analyzed with a mixed factorial ANOVA with the between-subject factor called group (categories: PEG and HBTG) and with the within-subject factor called intervention (categories: pre and post-intervention).

Results: Our study shows that hyperbaric treatment significantly improved functionality and reduced the levels of pain and fatigue (Table 1). The physical exercise intervention improved functionality, but this program could not reduce the experienced intensity of pain nor the perceived fatigue (p<0.05).

Abstract AB1367HPR Table 1. Effect of the physical exercise program and hyperbaric therapy on pain, fatigue and functionality.

<table>
<thead>
<tr>
<th></th>
<th>Pre-intervention</th>
<th>Post-intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain PEG</td>
<td>6.21 (2.29)</td>
<td>5.57 (2.24)</td>
</tr>
<tr>
<td>Fatigue PEG</td>
<td>6.86 (2.82)</td>
<td>7.21 (2.52)</td>
</tr>
<tr>
<td>Distance PEG</td>
<td>489.21 (76.39)</td>
<td>516.64 (71.58)</td>
</tr>
<tr>
<td>PEG</td>
<td>7.43 (1.70)</td>
<td>5.07 (2.50)</td>
</tr>
<tr>
<td>HBTG</td>
<td>7.79 (2.15)</td>
<td>6.5 (2.24)</td>
</tr>
<tr>
<td>Pain HBTG</td>
<td>557.14 (76.47)</td>
<td>566.79 (71.55)</td>
</tr>
</tbody>
</table>

Data are shown as mean (SD). PEG: physical exercise group; HBTG: hyperbaric treatment group.

Conclusion: Both hyperbaric therapy and physical exercise achieved an improvement in the functionality. Nevertheless, only the hyperbaric therapy achieved a decrease in perceived pain and an improvement in the perceived fatigue.

REFERENCES

Disclosure of Interests: None declared

ENHANCED ROLE OF NURSES AND OTHER HEALTHCARE PROFESSIONALS (HCPs) IN THE CARE OF RHEUMATOID ARTHRITIS AND ASSOCIATED COMORBIDITIES

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Background: Long-term morbidity and mortality in patients with rheumatoid arthritis (RA) are increased11 due to the increased risk of comorbidities
including cardiovascular disease (40-70% incidence\(^2\), 5-12.9% prevalence\(^3\)), diabetes (IR of 8.6 per 1000 person-years\(^4\); 20%\(^5\)), interstitial and within countries\(^10\).

in the roles and responsibilities of healthcare professionals (HCPs) across health care delivery systems throughout Europe, there is also variability in the roles and responsibilities of healthcare professionals (HCPs) across and within countries\(^10\).

Objectives: This study aimed to identify good practices within the roles of HCPs in the care of RA and associated comorbidities and to understand how these practices may be implemented in other centres. Methods: This study interviewed multidisciplinary teams at 12 selected specialist centres across Europe (1 centre per country) and examples of HCPs who had expanded roles and responsibilities were identified. Further, the questions whether these practices improved quality of care and could be implemented in other centres were addressed. Results: This Europe-wide study identified good practice examples of enhanced roles and responsibilities for HCPs such as nurses, physiotherapists, occupational therapists and podiatrists that varied with different categories of patients and their corresponding needs. The scope and depth of extended roles also varied between different countries and health systems. Examples included.

Examples identified

<table>
<thead>
<tr>
<th>Suspected RA</th>
<th>Newly diagnosed RA</th>
<th>Established RA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Providing education on RA and comorbidities</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Conducting history and joint examination</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Coordinating care</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Delivering preliminary comorbidity screening</td>
<td>x</td>
<td></td>
</tr>
<tr>
<td>Providing treatment</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Being first point of contact</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Collaborating with community-based teams</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Providing holistic support</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Empowering self-management</td>
<td>x</td>
<td>x</td>
</tr>
</tbody>
</table>

Conclusion: Expanding the roles of HCP team members can help broaden perspectives on healthcare delivery, relieve the burden put on specialists and enable the provision of well-rounded, patient-centred holistic care that may improve quality of life for patients with RA, especially related to their associated comorbidities.

REFERENCES


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Disclosure of Interests: Alisson Kent: None declared, Cem Gabay Grant/research support from: Eli Lilly Company, Pfizer, AbbVie, and UCB Pharma, Consultant for: Eli Lilly and Company, AbbVie, and UCB Pharma, Patrick Deurez Speakers bureau: Bristol-Myers Squibb, Eli Lilly, Sanofi, Celtrion, Ennio Favalli. None declared, Guillaume Favier: None declared, Tore K. Kven Grant/research support from: AbbVie, BMS, MSD, Pfizer, Roche and UCB., Consultant for: Abb-Vie, Biogen, BMS, Boehringer Ingelheim, Celgene, Celtrion, Eli Lilly, Hospital, Merck-Serono, MSD, Novartis, Oktal, Orion Pharma, Pfizer, Roche, Sandz, Sanofi, Mylan and UCB, Speakers bureau: AbbVie, Biogen, BMS, Boehringer Ingelheim, Celgene, Celtrion, Eli Lilly, Hospira, Merck-Serono, MSD, Novartis, Oktal, Orion Pharma, Pfizer, Roche, Sandz, Sanofi and UCB.


AB1369-HPR

THE EFFECTS OF CLINICAL PILATES TRAINING IN INDIVIDUALS WITH PRIMARY SJOEGREN’S SYNDROME

KESKIN Aylin1, Bilge Basakci Calik1, Elif Gur Kabul1, Murat Tasci2, Veli Cobanakara3, Pamukkale University, School of Physiotherapy and Rehabilitation, DENIZLI, Turkey; Pamukkale University, Department of Rheumatology, DENIZLI, Turkey

Background: Primary Sjogren’s syndrome (PSS), occurs in people with no other rheumatic disease, is a chronic, systemic, autoimmune disease characterized by lymphocytic infiltration of all exocrine glands, especially tears and salivary glands (1,2). Exercise training is commonly recommended in the approach of individuals with rheumatic disease and clinical pilates training have positive effects on endurance, functional mobility and quality of life. Nonetheless there is limited study related exercise training and no study which examined the efficacy of clinical pilates training in individuals with PSS in literature. Therefore, our study is very important. Objectives: The aim of the study was to examine the effects of clinical pilates training on trunk and lower extremity endurance, functional mobility, emosyonel status, sleep quality, functional level and quality of life in individuals with PSS.

Methods: The study included 23 voluntary individuals (22 female,1 male; mean age: 50.529.38 years), with PSS who were diagnosed with primary Sjogren’s syndrome according to 2016 American College of Rheumatology/European League Against Rheumatism Classification Criteria and according to Chisholm-Mason classification between grade 3 and 4 who applied to Pamukkale University Department of Internal Medicine, Department of Rheumatology. Anterior and lateral bridge was used to determine trunk endurance, 30-Second Chair Stand Test (30s-CST) and The Timed Up and Go (TUG) Test for lower extremity endurance, Lower Extremity Functional Scale (LEFS) for functional mobility, Beck Depression Inventory (BDI) and Beck Anxiety Inventory (BAI) for emotional status, Pittsburgh Sleep Quality Index (PSQI) for sleep quality, Health Assessment Questionnaire (HAQ) for functional level and Short Form 36 (SF-36) for quality of life. Light after demographic information and disease related data were recorded. The all assessments were made before and after clinical pilates training. All participants attended 60-min exercises training (5-min warm up, 45-min clinical pilates exercises, 10-min cool down) three times a week for 8 weeks which was progressively challenged and applied by a Physiotherapist with 2 years of experience in this field. Wilcoxon test were used to examine the factors related to functional level.

Results: After training in all evaluations a statistically advanced level of significant improvement compared to pre-training values in individuals with PSS (p<0.001).

Conclusion: Muscular endurance and functional level and the associated with emosyonel status, sleep and quality of life are important for individuals with PSS. Exercise approaches for these parameters are recommended. This study showed that clinical pilates exercises program have positive effects on trunk and lower extremity endurance, functional mobility, emosyonel status, sleep quality, functional level and quality of life in individuals with PSS.

REFERENCES


Disclosure of Interests: None declared.

AB1370-HPR | COMPARISON OF SLEEP, FATIGUE AND SEXUAL PARAMETERS OF RHEUMATIC DISEASES

Fatma Bing Kumburoğlu, Gamze Ann, Nur Baru Karaca, Sule Aşrap Bilgen, Edibe nallı, Hacettepe University Faculty of Physical Therapy and Rehabilitation, Ankara, Turkey; Hacettepe University Faculty of Medicine, Department of Rheumatology, Ankara, Turkey.

Background: Chronic pain, sleep, and fatigue are common complaints in rheumatic disease (1). However, each rheumatic disease has different characteristics. So that it can be thought that individuals can be affected by different diseases in different ways (2).

Objectives: The aim of this study is to compare sleep, fatigue and sexual parameters in different rheumatic diseases.

Methods: Individuals diagnosed with Rheumatoid Arthritis (RA), Ankylosing Spondylitis (AS) and Fibromyalgia (FM) who applied to the Rheumatology Department of the Medical Faculty of Hacettepe University were included in the study. After the demographic characteristics of the individuals were recorded; sexual function, sexual willingness, fatigue, and sleep features were assessed with 11th, 27th, 29th and 30th items of BETY-Biopsychosocial Questionnaire (BETY-BQ) which is developed in rheumatic patients (3).

Results: 160 RA, 108 AS, and 131 FM patients were included in the study. The scores of individuals on scales are shown in Table 1. There was no statistically significant difference among the three groups in terms of BMI (p>0.05), while the mean age of RA patients was statistically different from the other two groups (p<0.05). The sleep, fatigue and sexual parameters (sexual function, sexual willingness) were examined with Kruskal Wallis analysis. When analyzed in terms of differences according to RA, AS and FM, the responses to sleep (p=0.015) and sexual functioning (p=0.003) were found different according to the diseases. However, there was no significant difference in the sexual willingness (p=0.248) and fatigue (p=0.708) related to the disease. Mann-Whitney U test was performed to test the significance of a pairwise difference using Bonferroni correction to adjust for multiple comparisons revealed that the difference between the groups was due to RA patients (Table 2).

Abstract AB1370HPR Table 1. Comparison of three groups.

<table>
<thead>
<tr>
<th></th>
<th>RA (n=160)</th>
<th>AS (n=108)</th>
<th>FM (n=131)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>51.440.83</td>
<td>41.751.19</td>
<td>34.600.78</td>
</tr>
<tr>
<td>BMI</td>
<td>28.650.88</td>
<td>27.490.52</td>
<td>28.641.59</td>
</tr>
<tr>
<td>Fatigue</td>
<td>3.020.10</td>
<td>3.090.10</td>
<td>3.170.87</td>
</tr>
<tr>
<td>Sexual function</td>
<td>1.200.11</td>
<td>1.640.15</td>
<td>1.750.13</td>
</tr>
<tr>
<td>Sexual willingness</td>
<td>1.500.12</td>
<td>1.720.15</td>
<td>1.770.13</td>
</tr>
<tr>
<td>Sleep</td>
<td>2.120.12</td>
<td>2.420.15</td>
<td>2.640.12</td>
</tr>
</tbody>
</table>

Abstract AB1370HPR Table 2. Mann-Whitney U test

<table>
<thead>
<tr>
<th></th>
<th>p</th>
<th>p</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>RA-AS</td>
<td>0.019</td>
<td>0.012</td>
<td></td>
</tr>
<tr>
<td>RA-FM</td>
<td>0.001</td>
<td>0.004</td>
<td>0.278</td>
</tr>
<tr>
<td>AS-FM</td>
<td>0.528</td>
<td>0.276</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: As a result, all the patients who participated in this study have sleep, fatigue, and sexual problems. Although the mean age of RA patients is higher than other patients, it is quite interesting that they have less sleep and sexual function problems. On the other hand, it was expected that symptoms of RA and AS diseases due to their inflammatory nature would be worse than FM. Moreover, it can be estimated that AS patients have spinal involvement and this situation may affect their sexual function, but FM patients results in terms of these parameters were unclear. It was concluded that the psychosocial characteristics were taken into consideration especially in FM patients sexual parameters, fatigue, and sleep features during the disease management.

REFERENCES


Disclosure of Interests: None declared

AB1371-HPR | EFFECTS OF MORNING STIFFNESS ON THE PSYCHOSOCIAL AND FUNCTIONAL STATUS OF PATIENTS WITH JUVENILE IDIOPATHIC ARTHRITIS

Fatma Bing Kumburoğlu, Aykut zadro, Selcan Demir, Yelda Bilgen. Edibe nallı, Seza zen, Hacettepe University Faculty of Physical Therapy and Rehabilitation, Ankara, Turkey; Hacettepe University Faculty of Medicine, Department of Pediatric Rheumatology, Ankara, Turkey.

Background: Juvenile Idiopathic Arthritis (JIA) is a chronic childhood autoimmune disease that has significant implications on a childs physical health and psychosocial integration (1). Common symptoms of JIA include pain, joint stiffness, joint swelling, fatigue, and decreased physical function (2).

Objectives: The aim of this study is to investigate the effects of morning stiffness on the psychosocial and functional status of patients with JIA.

Methods: 387 JIA patients were included in this study. To determine the functional status of the patients functional subscale of The Juvenile Arthritis Biopsychosocial-Questionnaire (JAB-Q) and Childhood Health Assessment Questionnaire (CHAQ) were used. Psychosocial subscale of JAB-Q was used to assess psychosocial status. Finally, morning stiffness was measured as “less than 30 minutes”, “between 30 minutes and 1 hour” and “more than 1 hour”.

Results: A total of 162 boys and 225 girls participated in the study (Table 1). The effect of morning stiffness on functional and psychosocial status was measured as less than 30 minutes”, “between 30 minutes and 1 hour” and “more than 1 hour”. There was statistically significant difference between the functional status (CHAQ Total, p=0.001; CHAQ General VAS, p=0.012; CHAQ Pain VAS, 0.001; Function JAB-Q, p=0.001) of the patients and the duration of morning stiffness. However, there was no significant difference between the duration of morning stiffness and psychosocial status. Mann-Whitney U test was performed to test the significance of a pairwise difference using Bonferroni correction to adjust for multiple comparisons revealed that the difference between the groups was due to the morning stiffness duration “less than 30 minutes” group (Table 2).

Abstract AB1371HPR Table 1. Descriptive statistics

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>12.503.67</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>19.934.34</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female [%]</td>
<td>225 (58.14)</td>
<td></td>
</tr>
<tr>
<td>Male [%]</td>
<td>162 (41.86)</td>
<td></td>
</tr>
</tbody>
</table>

Abstract AB1371HPR Table 2. Mann-Whitney U test

<table>
<thead>
<tr>
<th></th>
<th>CHAQ Total</th>
<th>CHAQ (General VAS)</th>
<th>CHAQ (Pain VAS)</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>p</td>
<td>0.004</td>
<td>0.003</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>p</td>
<td>0.046</td>
<td>0.273</td>
<td>0.028</td>
<td></td>
</tr>
<tr>
<td>p</td>
<td>&lt;0.001</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| 1= <30 min morning stiffness, 2= 30 min-1 hour morning stiffness, 3= >1 hour morning stiffness.

Conclusion: In our study, as a result psychosocial status was not affected by duration of morning stiffness. On the other hand, functionality of patients were getting worse as the duration of morning stiffness increases. It was concluded that psychosocial status should be dealt with independently of functional status, and children should be supported to participate in psychosocial environment such as school attendance, social activities.

REFERENCES

THE INVESTIGATION OF THE RELATIONSHIP BETWEEN PSYCHOSOCIAL STATUS OF CHILDREN WITH JIA AND PARENTS

Aybüke Şerif Yavuz, Aybüke Sevier, Gamze Arnı, Yasin Zel Arslayı, Fatma Birgül Kumburuğlu, Nur Banu Karaca, Şekan Dersin, Yelda Bilgiler, Edibe naı, Seza zenı. 1Hacettepe University Faculty of Physical Therapy and Rehabilitation, Ankara, Turkey; 2Hacettepe University Faculty of Medicine, Department of Pediatric Rheumatology, Ankara, Turkey

Background: Juvenile idiopathic arthritis (JIA) is a heterogeneous group of diseases characterized by unknown origin arthritis that begins before the age of 16 years (1). Therefore, families are often affected by the disease of children. Parents and children often disagree with assessing different aspects of disease activity in JIA (2).

Objectives: The aim of this study is to investigate the relationship between children with JIA and their parents’ psychosocial status.

Methods: A total of 345 children with JIA and their parents were included in the study (n = 690). Juvenile Arthritis Biopsychosocial Questionnaire (JAB-Q) was administered to the subjects (3). The psychosocial status of the individuals was evaluated by this questionnaire.

Results: The mean age of children included in the study (n = 345) was 12.32 ± 3.76 years. While the median value of the Child Psychosocial score was 10 (min: 0 max: 38), the median value of the Parent Psychosocial score was 6 (min: 0 max: 20). Correlation coefficients and statistical significance were calculated by using the Pearson test. A positive low correlation was found between the psychosocial status of the child and parents (r = 0.273, p <0.001) (Table 1).

Table 1. Correlations:

<table>
<thead>
<tr>
<th>JAB-Q</th>
<th>Child</th>
<th>Psychosocial</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>1.00</td>
</tr>
<tr>
<td></td>
<td>p</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td>n</td>
<td>345 345</td>
</tr>
<tr>
<td>Parents</td>
<td></td>
<td>0.283 1.500</td>
</tr>
<tr>
<td>Psychosocial</td>
<td>p</td>
<td>0.000</td>
</tr>
<tr>
<td></td>
<td>n</td>
<td>345 345</td>
</tr>
</tbody>
</table>

Conclusion: It was observed that there was a low relationship between the psychosocial status of children and parents. It was concluded that child and parents psychosocial status may be affected by other variables such as high disease activity, school attendance. Further studies are needed in this area including different variables and interaction psychosocial status.

REFERENCES

Disclosure of Interests: None declared

THE EFFECTIVENESS OF BIOPSYCHOSOCIAL EXERCISE PROGRAM ON PAIN COPING IN PATIENTS WITH ANKYLOSING SPONDYLITIS AND FIBROMYALGIA

Aybüke Sevier, Aybüke Şerif Yavuz, Gamze Arnı, Yunus Zel Arslayı, Fatma Birgül Kumburuğlu, Nur Banu Karaca, Ali Akdogan, Edibe naı. 1Hacettepe University Faculty of Physical Therapy, Ankara, Turkey; 2Hacettepe University Faculty of Medicine, Department of Rheumatology, Ankara, Turkey

Background: Ankylosing spondylitis (AS) and fibromyalgia (FM) are rheumatic diseases with a high incidence in the community. Although many studies have been done on pain in these patient groups, the studies on coping with pain are very limited (1, 2). The aim of this study was to examine the relationship between patients’ biopsychosocial characteristics and coping with pain in AS patients.

Objectives: The aim of this study was to investigate the biopsychosocial characteristics of patients with rheumatic diseases who were inpatients, outpatients and participated in an exercise intervention regularly.

Methods: A total of 105 patients were included in the study (inpatient, outpatient, exercise intervention) (Table 1). For exercise intervention group, BETY as a biopsychosocial exercise model was applied 3 days a week for 3 months [2]. Biopsychosocial characteristics of the patients included in the study were evaluated by BETY-Biopsychosocial Questionnaire (BETY-BQ) (3). In addition to the total score of BETY-BQ, the same time pain, functionality and fatigue, sexuality, emotional status and socialization subcategory of this questionnaire were evaluated on item basis among each patients.

Results: The demographics variables and BETY-BQ scores of the patients were shown in Table 1. There were a statistically significant differences among three groups. After post-hoc analysis, it was determined that there is no difference between the BETY-BQ scores of the inpatients and outpatients (p> 0.05), whereas the BETY-BQ scores of the patients who participated in the group exercise were lower (p<0.05). When the items were analyzed, it was found that patients (items 2, 3, 5, and 12), functional- ity and fatigue (items 6, 7, 11, 26, and 28), emotional status (items 16 and 17), and sleep (item 30) subcategory scores were also lower in patients who participated in BETY programme (p<0.05).

Table 1. Demographic statistics and BETY-BQ scores

<table>
<thead>
<tr>
<th>Inpatient (n=30)</th>
<th>Outpatient (n=44)</th>
<th>Exercise intervention (BETY) (n=31)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (%)</td>
<td>XSD</td>
<td>XSD</td>
</tr>
<tr>
<td>Age (year)</td>
<td>46.3514.56</td>
<td>46.0613.26</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.19 ±7.17</td>
<td>28.98 ±18.85</td>
</tr>
<tr>
<td>BETY-BQ (0-120)</td>
<td>p</td>
<td>XSD</td>
</tr>
<tr>
<td></td>
<td>0.027</td>
<td>49.1017.94</td>
</tr>
<tr>
<td></td>
<td></td>
<td>38.8121.73</td>
</tr>
</tbody>
</table>

Conclusion: It is surprising that the biopsychosocial characteristics of the inpatients and outpatients were similar. According to this result, inpatients shouldn’t be thought as worse than outpatients. On the other hand, the patients who participated in exercise intervention were improved in terms of biopsychosocial aspects. The positive effects of the BETY program on the biopsychosocial status of individuals have been demonstrated formerly [4]. It was concluded that inpatients should be supported to exercise in terms of their biopsychosocial needs during hospitalization period as well as rheumatic outpatients need.

REFERENCES

Disclosure of Interests: None declared
EFFECT OF SCHROTH METHOD AND SCIENTIFIC EXERCISE APPROACH TO SCOLIOSIS (SEAS) ON THE COBB ANGLE AMONG THE ADOLESCENT WITH IDIOPATHIC SCOLIOSIS: A COMPARATIVE STUDY

Jalpa Shah, T Padma Priya, Paliniyan Arunagam, R Kousalya, Sri Venkateshwara Medical College Hospital and Research Centre, physiotherapy, Puducherry, India

Background: Scoliosis is a three-dimensional deformity of the spine and trunk leading to physical and functional disability. Among adolescent, idiopathic scoliosis is the most common (80% - 89%) form of scoliosis with prevalence ranging between 0.47% and 5.2% in general population. As the evidence on the comparative efficacy of various physical therapy in scoliosis is sparse, we conducted a comparative study assessing efficacy of Schroth method of exercise group (SEG) and scientific exercise approach to scoliosis group (SEASG).

Objectives: To compare efficacy of Schroth method and SEAS among adolescent with scoliosis.

Methods: Thirty subjects, both male and female of the age group of 10 to 18 years, with mild-moderate idiopathic scoliosis defined as the spinal radiographic Cobb angle in the range of 20 to 45 and riser sign of 0-2 were randomly allocated to Schroth method of exercise group (SEG, n=15) and scientific exercise approach to scoliosis group (SEASG, n=15). Subjects with diagnosis of spinal injury, previous spinal surgery, gibbus, limb deformity, infection and malignancy were excluded. The SEG and SEASG performed Schroth and scientific exercise respectively, 5 times a week for 7 weeks. To quantify the magnitude of spinal deformity, Cobb angle measurements were obtained by using radiograph to gain pre-post interventional differences. (Figure 1)

Results: SEG showed the significant changes in pre (mean sd 31.2 5.20) and post (mean sd 27.4 5.17) Cobb angle measurements. SEASG also showed the significant changes in pre (mean sd 31.33 5.26) and post (mean sd 29.4 5.9) Cobb angle measurements (Figure 2). Comparing both the groups by unpaired t test suggested SEG to be more efficacious than the SEASG with the t value (4.22) for change in Cobb angle (p < 0.0001) (Figure 3).

Conclusion: The study establishes the role of physical therapy in idiopathic scoliosis of mild to moderate degree among adolescents. Schroth method of exercise performs better compared to the SEAS in patients with mild to moderate scoliosis.

REFERENCES


AB1374-HPR Table 1. Comparison of AS and FM patients before and after treatment

<table>
<thead>
<tr>
<th></th>
<th>AS (n=30)</th>
<th>FM (n=17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>5th question</td>
<td>Pre-treatment</td>
<td>Post-treatment</td>
</tr>
<tr>
<td>(%)</td>
<td>p&lt;0.05</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Yes, always</td>
<td>33.3</td>
<td>10</td>
</tr>
<tr>
<td>Yes, often</td>
<td>20</td>
<td>13.3</td>
</tr>
<tr>
<td>Yes, sometimes</td>
<td>16.7</td>
<td>10</td>
</tr>
<tr>
<td>Yes, rarely</td>
<td>10</td>
<td>13.3</td>
</tr>
<tr>
<td>No, never</td>
<td>20</td>
<td>33.3</td>
</tr>
</tbody>
</table>

Conclusion: Although both AS and FM are rheumatic diseases, it is known that FM patients experience more intense psychosocial stress. They are, therefore, resistant to change (4). We found that the positive change in pain coping skill is not seen in FM group. It is concluded that FM patients regarding in pain coping strategies they need to attend exercise programs and need to be educated about pain coping skills for a longer period.

REFERENCES


Disclosure of Interests: None declared

AB1375-HPR

EFFECT OF SCHROTH METHOD AND SCIENTIFIC EXERCISE APPROACH TO SCOLIOSIS (SEAS) ON THE COBB ANGLE AMONG THE ADOLESCENT WITH IDIOPATHIC SCOLIOSIS: A COMPARATIVE STUDY

Jalpa Shah, T Padma Priya, Paliniyan Arunagam, R Kousalya, Sri Venkateshwara Medical College Hospital and Research Centre, physiotherapy, Puducherry, India

Background: Scoliosis is a three-dimensional deformity of the spine and trunk leading to physical and functional disability. Among adolescent, idiopathic scoliosis is the most common (80% - 89%) form of scoliosis with prevalence ranging between 0.47% and 5.2% in general population. As the evidence on the comparative efficacy of various physical therapy in scoliosis is sparse, we conducted a comparative study assessing efficacy of Schroth method of exercise group (SEG) and scientific exercise approach to scoliosis group (SEASG) in adolescents with idiopathic scoliosis.

Objectives: To compare efficacy of Schroth method and SEAS among adolescent with scoliosis.
Role of Nurse-led Telephone Follow-up to Patient Activation Measure in Patients with Polymyalgia Rheumatica and Giant Cell Arteritis

Pia Toftegaard, Amir Emamifar, Alexandra Brink Walling, Susanne Hjmark Jakobsen, Peter Thye-Rnn

Background: Poor adherence to the osteoporosis prophylaxis medications has been reported before, which may result in treatment failure.

Methods: This is an ongoing 1-year prospective cohort study, 37 consecutive steroid treated patients with newly diagnosed PMR/GCA were included. Patients were seen by the physicians at baseline, 1st and 4th month, where they were interviewed about their compliance towards osteoporosis prophylaxis medications, i.e. Calcium/Vitamin D supplements and Bisphosphonates if Tscore £ -2.5, using a standardized questionnaire.

Results: 85.3% and 75.8% of the patients were completely adherent to their osteoporosis medications at 1st and 4th month, respectively. (figure 1) The difference between level of adherence to the osteoporosis medications at 1st (=week 4) and 4th month (=week 16) was not statistically significant. (P value:0.369). Decreased adherence in patients was mainly due to forgetfulness.

Conclusion: Compared to the earlier findings we found a higher level of adherence in this group of patients. Nurse-led telephone follow up as well as educating the patients respecting the importance of the osteoporosis medications for preventing steroid related side effects, may enhance and subsequently maintain high level of adherence to the osteoporosis medications. Our findings are in line with our earlier study indicating a high level of adherence to the osteoporosis medications in PMR/GCA patients.

References

Disclosure of Interests: None declared

Patient Activation Measure in Patients with Rheumatoid Arthritis

Laura Villarreal, Fernando Rodriguez, Pedro Santos-Moreno, Diana Buitrago-Garcia

Background: The Patient Activation Measure (PAM) is a 13-item measure that assesses patient knowledge, skill, and confidence for self-management. The measure was developed using Rasch analyses and is an interval level, unidimensional, Guttman-like measure. The current analysis is aimed at reducing the number of items in the measure while maintaining adequate precision(1). A Spanish adaptation of the scale was performed in 2017.

Methods: We performed a quantitative, observational, cross-sectional, and questionnaire-based study, convenience sampling was used. Participants were recruited in a specialized RA center, during a patients meeting. We applied the PAM-13 scale validated in Spanish. The scale has a score from 1 to 4 divided in four levels where level 1 represents a disengaged patient and suggests that the doctor is in charge of their health; level 2: the patient becomes aware but struggling; level 3: The patient is taking action and considers himself as a part of the healthcare team, and level 4 represents a patient that maintains behaviors and pushes forward. The maximum score is 52 points.

Results: 322 patients participated, 23 patients generated incomplete PAM scores (response rate 92%) and were excluded. From total 93% of patients were women. Mean age was 60 years 10; mean PAM-13 Was 19.83 6.16. In our study 68% of patients were in level 2 according to PAM-13 scale which means that they are becoming aware of their knowledge, skills and self-management but are still struggling. See table 1. In average 80% of patients answered each question to be in level 1 or 2, 15% in level 3 and only 5% in level 4.

Conclusion: This is the first study in our country where the Patient Activation Measure is applied in patients with rheumatoid arthritis. Thus, it might be useful to implement patient activation monitoring, since the level of activation is low in patients with RA.

Disclosure of Interests: Laura Villarreal: None declared, Fernando Rodriguez: None declared, Pedro Santos-Moreno Grant/research support from: Dr Santos has received research grants from Jansen, Abbvie and UCB, Speakers bureau: Dr Santos has received speaker fees from Sanofi, Lilly, Bristol, Pfizer, Abbvie, Janssen and UCB, Diana Buitrago-Garcia: None declared
EFFECT OF CLINICAL CHARACTERISTICS, HABITS, PHYSICAL ACTIVITY LEVELS AND FUNCTIONAL CAPACITY ON QUALITY OF LIFE IN SYSTEMIC SCLEROSIS PATIENTS

Hazal Yakut1, Sevgi zalevl1, Ahmet Merih Birlik2. 
1Dokuz Eylül niversitesi Fizik Tedavi ve Rehabilitasyon Ynya Kolu, İzmir, Turkey; 2Dokuz Eylül niversity Hastanesi, İmmunoloji-Romatoloji Anabilim dalı, İzmir, Turkey

Background: In patients with Systemic sclerosis (SSc), many factors such as inactivity, smoking, gastrointestinal system involvement are reported to have an adverse effect on overall health related quality of life, and quality of life is in line with the prognosis of the disease (1,2).

Objectives: The aim of this study was to investigate the effect of clinical characteristics, habits, physical activity levels and functional capacity of patients with SSc on quality of life.

Methods: Twenty-three SSc patients were included in the study. The ages of patients, the amount of cigarette consumption, duration of diagnosis and body mass indexes (BMI) were questioned and recorded. Functional capacities of patients were measured by 6 Minute Walking Test (6MWT). Physical activity levels of patients were calculated using the International Physical Activity Questionnaire (IPAQ; using metabolic equivalent-MET). Quality of life was evaluated by the short form SF-36 quality of life questionnaire (SF-36 QoLQ). The SF-36 questionnaire was evaluated as two subscales, physical and mental.

Results: The mean age of the patients was 51.00±11.10 years and the duration of diagnosis was 7.60±4.80 years. BMI was 26±6.07 kg/m² and amount of cigarette consumption was 6.02±3.30 packeyear(s). The mean physical activity levels (IPAQ) were 281.68±60.45 MET, 6MWT distance were 435.39±80.45 m, SF-36 QoLQ-physical were 32.48±13.42 and SF-36 QoLQ-mental were 38.56±11.42 score. It was found that there was a significant correlation between SF-36 QoLQ-physical and BMI (p = 0.043, r = 0.426), 6MWT (p < 0.001, r = 0.737) and IPAQ (p < 0.001, r = 0.647). There was a significant correlation between the SF-36 QoLQ-mental and 6MWT (p < 0.020, r = 0.483) and IPAQ (p = 0.032, r = 0.614).

Conclusion: Reduced levels of physical activity in SSc patients affect functional capacity. Reduced physical activity level and functional capacity decrease the quality of life of patients related to both physical and mental health. Physical health related quality of life of patients is negatively affected by the increase in BMI. Functional capacity, clinical characteristics, habits and physical activity levels should be evaluated and improved in treatment programs aimed at improving the overall health-related quality of life of patients.

REFERENCES


Disclosure of Interests: None declared


EFFECTS OF DIFFERENT EXERCISE MODELS ON PAIN, FUNCTIONALITY, BALANCE, PROPRIOCEPTION AND COGNITION FEATURES OF PATIENTS DIAGNOSED WITH FIBROMYALGIA

Hadi Yavuz1,2, Trker Şahinkaya1, Aysegul Ketenç1, Gikhan Metin1. 1Istanbul University, Physical Medicine and Rehabilitation, Istanbul, Turkey; 2Istanbul University, Sports Medicine, Istanbul, Turkey; 3Istanbul University-Cerrahpusa, Physiology, Istanbul, Turkey

Background: Fibromyalgia syndrome (FMS) is a chronic disease characterized by diffuse pain, fatigue, sleep disturbance, cognitive impairment, and other physical symptoms that adversely affect physical and sensory functions and impair quality of life. Nowadays, in the treatment of FMS, low intensity aerobic exercises and exercise programs combined with other treatment methods are recommended.

Objectives: The aim of this study was to evaluate the effects of aerobic and balance-proprioception exercises on the symptoms of Fibromyalgia (FMS) and the superiority of the two exercise models.

Methods: 51 female patients who adhere to the inclusion criteria were divided into two groups randomly. Aerobic Exercise Group (AEG; n=26) and Balance-Proprioceptive Exercise Group (BPEG; n=25) was applied to the exercise laboratory under the supervision of physiotherapist in Istanbul Medical Faculty, Department of Sports Medicine 3 days a week for 6 weeks. Before and after the program Pain (VAS), functional status (FIO), postural stability (Biodex balance system), knee joint proprioception (Cybex isokinetic dynamometer) were evaluated. Cognitive status was assessed by Standardized Mini Mental State Examination (SMMSE) only before program.

Results: There wasn’t statistically significant difference between demographic (age, weigh, BMI etc.) and clinic (VAS, FIO, Biodex, Cybex, SMMSE) features of the groups at the beginning (p>0.05). Parameters measured in both groups after exercise programs showed progress compared to initial levels (p<0.05). There isn’t the superiority between two exercise groups in terms of VAS, FIO scores (p<0.05). Recovery is found to be better at BPEG in balance parameters (eyes open overall stability index (EOOSSI) and eyes open anteriorposterior stability index (EOAPSSI)) and some parameters that belongs to proprioception (p<0.05).

Conclusion: It is determined that aerobic exercise and balance-proprioception exercise programs at BPEG are effective in positive way methods for functionality, pain, proprioception and balance parameter recovery of the patients. Except EOOSSI and EOAPSSI balance parameter values; according to other parameters it is found that aerobic exercise and balance-proprioception exercises are equal to each other. It is found out that balance-proprioception exercises are superior to aerobic exercises for improving EOOSSI and EOAPSSI. It is revealed that balance proprioception exercises are more effective for curing proprioception. It is observed that patients with FMS had deterioration in cognitive functions.

Disclosure of Interests: None declared


PATIENT SATISFACTION IS HIGH IN PATIENTS TRAINED TO SELF-INJECT WITH A BUTTON FREE AUTO-INJECTION USING VIDEO TRAINING

Dawn Homer, Modality Partnership Community Rheumatology Service, Erdk Medical Practice, Birmingham, United Kingdom

Background: Once-weekly subcutaneous injection of methotrexate can optimize long-term treatment of rheumatic diseases such as rheumatoid arthritis.1 However, available self-injection devices vary in terms of ease of use and level of operational dexterity required.

Objectives: This pilot study compared patient satisfaction with use of a methotrexate pre-filled, button-free, auto-injector pen (Nordic Pharma, UK) for subcutaneous injection with previous use of a button-activated pen device were invited to change to a button-free auto-injector by letter. They were given the option to self-train using an online video or receive one-to-one instruction from a rheumatology nurse. Initial follow-up took place immediately after the first injection; invitation to participate in a 10-minute telephone questionnaire to evaluate their experience of using their new device took place after 3-4 weeks. Satisfaction with the device was assessed overall and according to 7 specific autoinjector attributes: ease of injection; experience of injection; comfort in hand; use with dexterity issues or during flare-ups; confidence in full dose being given; convenience of storage and disposal; and portability.

Results: Thirty-three patients were invited to change to an auto-injector: 22 patients responded (response rate: 64.7%), 19 of which made the assessment and completed the survey. 78% of patients overall were satisfied or very satisfied with administering methotrexate using the auto-injector; 85% of patients were equally or more satisfied with the use of an auto-injector pen compared to their previous device. Patients were equally or
more satisfied with the new device across all 7 autoinjector attributes: convenience of storage and disposal (100.0%), portability (100.0%); comfort in the hand (94.1%); confidence in full dose being given (88.9%); use with dexterity issues or during flare-ups (85.7%); ease of injection (82.4%); experience of injection (68.4%). Self-training via video did not negatively affect satisfaction: 83.3% of those patients confident in their ability to perform self-injection correctly after viewing the video were satisfied or very satisfied with their new autoinjector device. Three patients discontinued with the new device: one switched to oral therapy for reasons unrelated to the device; two returned to their original device.

Conclusion: This pilot study showed that patients were more satisfied with use of a methotrexate button-free auto-injector device than with their previous auto-injector device across all 7 user attributes and that satisfaction was maintained with use of self-training. Patient views regarding acceptability and use of auto-injection devices should be considered when making device switches based on cost and nurse resource allocation to ensure continued adherence with injected medication.

REFERENCES

Disclosure of Interests: Dawn Homer Grant/research support from: This project was supported by an unrestricted educational grant from Nordic Pharma., Consultant for: Participation in an advisory board with Janssen. Cilag in 2016 and will be speaking for Roche-Chugua in March 2019.


HPR Measuring health (development and measurement properties of PROs, tests, devices)

AB1380-HPR THE EFFECTS OF CERVICAL RANGE OF MOTION ON POSTURAL STABILITY IN PATIENTS WITH CHRONIC NECK PAIN

Onur Avşarduoğlu1, Gülşah Kılçı1, Tolga Taşböcek1, Zübeyir San1, 1Marmara University, Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Istanbul, Turkey

Background: Neck pain is a common musculoskeletal problem within chronic pain and it affects up to 71% of adult population during their lifetime (1). Chronic neck pain is related to a series of disabilities: a range of reported pain, postural stability problems, and cognitive dysfunction (2). However, there is no report that investigates the relationship between range of motion and postural stability in patients with chronic neck pain.

Objectives: The purpose of this study was to investigate the relationship between range of motion and postural stability in patients with chronic neck pain.

Methods: Thirty subjects of mean age 28.50 ± 10.95 years who admitted chronic neck pain to a Private Physiotherapy Clinic were participated in this study. While goniometer was used for cervical range of motion, pedalo sensarmove system was used for postural stability. In addition, pain and disability were measured with visual analogue scale, neck disability index, respectively.

Results: It was found that limitation of cervical range of motion was not correlated to postural stability deficits (p>0.05). The neck pain and disability status was not associated with level of postural stability (p>0.05).

Conclusion: The findings of this study showed that postural stability may not be affected by the limitation of cervical range of motion, and also neck pain intensity, neck disability status in patients with chronic neck pain. Further research with larger sample sizes is warranted.

REFERENCES

Disclosure of Interests: None declared


AB1381-HPR ADAPTABILITY, EFFECTIVENESS AND SAFETY OF TOFACITINIB IN PATIENTS WITH RHEUMATOID ARTHRITIS

Fernando Rodriguez1, Anggie Aza2, Michael Cabrera3, Pedro Santos-Moreno4, Diana Buitrago-Garcia5.

1Biomab – Center for rheumatoid arthritis, 2Patient coordinator, Bogot, Colombia; 3Biomab – Center for rheumatoid arthritis, Business administration, Bogot, Colombia; 4Biomab – Center for rheumatoid arthritis, EHR administration, Bogot, Colombia; 5Biomab – Center for rheumatoid arthritis, Rheumatology, Bogot, Colombia; 6Biomab – Center for rheumatoid arthritis, Nursing research, Bogot, Colombia

Background: Tofacitinib is a, selective JAK inhibitor that preferentially inhibits Janus kinase (JAK) 1 and JAK2. Oral tofacitinib 5 mg twice daily or 11 mg once daily is indicated for the treatment of moderate to severe active rheumatoid arthritis (RA) in adult patients who have responded inadequately to, or who are intolerant of, one or more DMARDs. Mainly, one of the strengths of Tofacitinib, is that it is a very suitable medicine for those patients who are afraid of applying a general biologics medicine, or who are of advanced age or are at high risk of adverse events, therefore it’s easy to discontinue it.

Objectives: We aim to describe the tolerance and adaptability of patients to Tofacitinib, as well as the effectiveness and safety in patients with RA in a real-life setting in Bogot, Colombia.

Methods: During 2017 and 2018 we followed-up patients from a RA specialized center in Colombia receiving Tofacitinib. Patients were treated with therapeutic goals type T2T and a multidisciplinary approach. Clinical follow-up was designed by the authors according to DAS28 as follows: every 3-5 weeks (DAS28 > 5.1), every 7-9 weeks (DAS28 ≥ 3.1 and < 5.1), and every 11-13 weeks (DAS28 < 3.1). Tender joint count (TJC), swollen joint count (SJC) and HAQ were measured on each visit. Therapy had to be adjusted with DAS28 > 3.2. We divided patients in four groups: remission (REM), low disease activity (LDA), moderate disease activity (MDA) and high disease activity (HDA) patients and one aim of the study was to look at what percentage of patients who were in moderate or severe disease activity reached a low disease activity or remission. On the other hand, we evaluated the tolerance and adaptability of patients to Tofacitinib. Adverse events were classified according the Common Terminology Criteria for Adverse Events (CTCAE) of the World Health Organization. Descriptive epidemiology for continuous variables, measure of central tendency and dispersion for qualitative and categorical variables through percentages and averages were calculated.

Results: We included 59 patients receiving tofacitinib, 92% were women and 8% men during last two years. Mean age was 60.11. From total, 70% of patients received anti-TNF drugs before tofacitinib and the other 30%. In reference to the adaptability, most of the patients up to 95% expressed to be happy with the oral intake and the suitable dosage of the medication. Regarding effectiveness, mean DAS28 at beginning was 4.6.83 and at the end 2.6.63. At the beginning of follow-up 57.6% of patients were in moderate disease activity according to DAS28 and 33.9% in severe disease activity, while at the end of follow up 64% of patients achieved remission and 16.9% low disease activity during the 12 weeks of follow-up. See table 1. Regarding safety 2 patients presented a dermatological adverse event (herpes zoster) with adverse event rate of 3.3%.

<table>
<thead>
<tr>
<th>ACTIVITY LEVEL</th>
<th>BASELINE n</th>
<th>24 MONTH FOLLOW-UP n</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n %</td>
<td>n %</td>
</tr>
<tr>
<td>REM</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDA</td>
<td>5</td>
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</tr>
<tr>
<td>MDA</td>
<td>34</td>
<td>57.63</td>
</tr>
<tr>
<td>HDA</td>
<td>20</td>
<td>33.90</td>
</tr>
</tbody>
</table>

Abstract AB1381HPR Table 1. DAS28 in patients receiving tofacitinib.

Conclusion: Tofacitinib is a very suitable medicine in patients with RA and improved disease activity in impressive way; also proved to be very safe, except the occurrences of herpes zoster, which is an aspect to take into account in its prescription, but none of patients presented another serious adverse events.

Disclosure of Interests: Fernando Rodriguez: None declared, Anggie Aza: None declared, Michael Cabrera: None declared, Pedro Santos-Moreno: Grant/research support from: Dr. Santos has received research grants from Janssen, Abbvie and UCBI, Speakers bureau: Dr Santos has received speaker fees from Sandofi, Lilly, Bristol, Pfizer, Abbvie, Janssen and UCB, Diana Buitrago-Garcia: None declared

AB1382-HPR 1 COMPARISON OF EFFICACY OF DIFFERENT REHABILITATION APPROACHES IN INDIVIDUALS WITH KNEE OSTEOARTHRITIS

Elif Baysal1, Miray Bukarlı2, Esra Atılgan3, Devrim Tanrıkulu1. 1Istanbul Medipol University, Istanbul, Turkey; 2Istanbul Medipol University, Physical Therapy and Rehabilitation, Istanbul, Turkey; 3Istanbul Medipol University, Ergotherapy, Istanbul, Turkey. Background: Osteoarthritis (OA) is the most common rheumatologic disease in the world, resulting primarily in progressive cartilage destruction. OA-induced changes are the main cause of disability and are mostly seen in the knee joint. Objectives: To investigate the effects of different rehabilitation practices on the range of motion, muscle strength, pain, physical function and quality of life in patients with knee OA. Methods: Thirty patients between the ages of 40-65 with knee OA were included in the study and divided into 3 groups. Transcutaneous Electrical Nerve Stimulation (TENS), ultrasound, hotpack/coldpack and home exercise program were given to the 1. group (n=10) for 15 days. 2. group (n=10) received three doses of Platelet-Rich Plasma (PRP) followed by home exercise program for 15 days. The control group (n=10) received only home exercise program for 15 days. All individuals were evaluated using ‘Goniometer’ for Range of Motion (ROM), ‘Manual Muscle Test’ for M. Quadriceps femoris muscle strength, ‘Visual Analogue Scale’ for pain, ‘The Western Ontario and McMaster Universities Arthritis’ (WOMAC) Scale for physical function and ‘Short Form-12 Quality of Life Scale’ Mental (SF-12 - MC) and Physical Component (SF-12 - PC) for quality of life at baseline and end of treatment.

Results: Statistically significant difference was found at pain and WOMAC score at the time of activity in all groups (Table 1). Statistically significant difference was found at ROM and SF-12 PC score in group 1 and 2, at resting pain and SF-12 MC score in control group (p <0.05) (Table 2). Conclusion: In addition to electrotherapy treatment and PRP in knee OA treatment, it is thought that home exercise program can be used to relieve symptoms and improve quality of life in knee OA.

REFERENCES

Disclosure of Interests: None declared

AB1383-HPR THE VALIDITY AND RELIABILITY OF UNSUPPORTED UPPER LIMB EXERCISE TEST IN INDIVIDUALS WITH RHEUMATOID ARTHRITIS

S. Yaprak Cetin1, Bilge Basakci Calik2, Ayse Aydin3, Ugur Cavlak4. 1Akseniz University, University of Physiotherapy and Rehabilitation, Antalya, Turkey; 2Pamukkale University, School of Physiotherapy and Rehabilitation, Denizli, Turkey; Antalya Education and Research Hospital, Rheumatology, Antalya, Turkey; 4European University of Lefke, Physiotherapy and Rehabilitation, Antalya, Turkey. Background: Rheumatoid arthritis (RA) is a systemic, inflammatory disease that causes pain, joint destruction and disability. RA affects the function of the hand and upper extremities; function deteriorates as the disease progresses and affects independence. Unsupported upper-limb exercise (UULEX) test was developed to evaluate upper extremity function and endurance in individuals with Chronic Obstructive Pulmonary Disease. It is suggested that this test can be used in other clinical cases with arm disabilities.

Objectives: The aim of this study was to examine whether the UULEX Test is valid and reliable in individuals with RA.

Methods: 71 individuals with RA (15 male, 56 female) with an average age of 52.15 ± 10.11 were included in the study. The Intraclass Correlation Coefficient (ICC) was used to assess the reliability of the UULEX test. Each individual was assessed by one physiotherapists in two different sessions, a week apart. The correlations of the UULEX test with Disabilities Arm, Shoulder and Hand (DASH), Health Assessment Questionnaire (HAQ), 30 sec Push Up Test and 6 Peg Board Ring Test were assessed for concurrent validity.

Results: Intrarater reliability of final level, final weight, duration of the UULEX Test were determined to be excellent (ICC = 0.922, 0.960, 0.958). A moderate to excellent correlation was found between UULEX Test and DASH, HAQ, 30 sec Push Up Test and 6 Peg Board Ring Test (p<0.05).

Conclusion: The results of this study showed that the UULEX test is a valid and reliable method in the assessment of upper extremity endurance in individuals with RA.

REFERENCES
The relationship between quality of life, trunk strength and spinal mobility in SpA patients

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Background: Spondyloarthritis (SpA) can seriously affect spinal mobility and trunk strength. Even though exercise therapy is considered one of the keystones of non-pharmacological treatment, guidelines on exercise programs remain vague due to a lack of objective measurements of physical parameters such as trunk mobility and strength. Data on these parameters are scarce for both axial and peripheral SpA-patients (axSpA and perSpA pts).

Objectives: The aim of this study was to measure trunk strength and spinal mobility in SpA-pts and compare these parameters to healthy subjects matched for gender and age and to determine differences between the pts when grouped based on symptom duration and on presence of radiographic sacroiliitis.

Methods: SpA-pts of the Be-Giant cohort were consecutively asked to participate in the study. After informed consent, BASDAI, BASFI and BASMI were evaluated. To measure trunk and cervical strength, pts performed 2 repetitions of a maximal isometric contraction for flexion, extension, lateral flexion and rotation on the Daehak II device (Emed). The maximum value of the 2 repetitions was kept for further analysis. For assessments of lateral flexion and rotation, measured with the DBD, the mean was calculated for right and left measurements. Spinal mobility and trunk strength were compared with a healthy reference population, matched for gender and age by mean of Wilcoxon singed-rank tests. When comparing the perSpA with the r-axSpA and the nr-axSpA, a Kruskal Wallis test was used. A Mann-Whitney U test was used to check for differences between groups based on symptom duration.

Results: Thirty-one SpA-pts participated of which 18 were male (58%). Twenty-four (77%) were classified as axSpA and 7 (23%) as perSpA. Six (19%) of the axial pts had radiographic sacroiliitis and 18 (58%) were non-radiographic. Median time since diagnosis was 5 years and median symptom duration was 7.8 year. Mean age of the pts was 41 years (range: 21-58 years) and their BMI was on average 24 (range: 17-33).

Conclusion: Based on the results of the present study, quality of life seems to be related with spinal mobility. On the other hand, no relationship was identified between the physical activity level and spinal pain. In order to determine the exact relationship, further studies with larger samples and with more varied levels of physical activity are needed.

REFERENCES


2156 Scientific Abstracts
Background: For assessing symptoms of depression in systemic sclerosis (SSc), the Patient Health Questionnaire-8 (PHQ-8) may be useful in clinical care as it is short and easy to administer. The English version of PHQ-8 has been found to be reliable and valid in SSc. Objectives: To assess aspects of validity and reliability of PHQ-8 in Swedish (PHQ-8 Swe) for individuals with SSc.

Methods: Patients meeting the 2013 ACR/EULAR SSc criteria were recruited. The PHQ-8 Swe content validity was assessed via individual interviews (11 patients, 10 healthcare professionals, HPs) which was transcribed and analysed by content analysis. Patients ages, disease durations and symptoms of depression varied. The HPs had different occupational backgrounds and experiences in SSc care. Reliability was tested by internal consistency and test-retest reliability. Sixty-seven patients (median age 62 [minmax: 28-87]) completed the PHQ-8 Swe on two different occasions.

Results: Content validity: The instruction, items, and response options were generally considered easy to understand; however, some clarifications were suggested. Among HPs, it was expressed that some items could be perceived as emotionally demanding for patients especially in recent onset disease. Further they experienced that PHQ-8 was problem-rather than possibility-based. Introducing the PHQ-8 to patients and the need for follow-ups of the answers to the questionnaire were stated as essential. It was further expressed that PHQ-8 covered key aspects of symptoms of depression in SSc nevertheless examples of items suggested to be included were purpose in life, thoughts about death, and loneliness. The items were overall experienced as important without redundancy, and that some items could reflect more general SSc-related symptoms.

Cultural adaption: Possible adjustments to the PHQ-8 translation were made. This version was back translated into English and compared with the original English version. Thereafter, minor changes were made. A final PHQ-8 Swe version was tested for reliability. Reliability: Cronbachs alpha was 0.86 and the corrected item-to-total correlation range was 0.420.78. There were no significant differences between test-retest for seven of the eight items. The median weighted kappa coefficient was 0.63. The median PHQ-8 Swe total score was 4 (0-10, no-severe depressive symptoms). There were no significant differences for total scores between test and retest and the ICC was 0.81.

Conclusion: Content validity of PHQ-8 Swe was satisfactory and a positive quality was indicated for aspects of reliability in individuals with SSc tested in this study. Although some items could be interpreted as covering more general SSc-related symptoms, the PHQ-8 could be valuable for detecting patients with symptoms of depression in need of discussing emotional issues, as reflected in our study. Further studies of the PHQ-8 Swe usefulness are currently being undertaken via evaluation of other psychometric aspects.

REFERENCES


ACKNOWLEDGEMENT


AB1387-HPR ASPECTS OF VALIDITY AND RELIABILITY OF THE SWEDISH VERSION OF PATIENT HEALTH QUESTIONNAIRE-8 IN INDIVIDUALS WITH SYSTEMIC SCLEROSIS

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Background: For assessing symptoms of depression in systemic sclerosis (SSc), the Patient Health Questionnaire-8 (PHQ-8) may be useful in clinical care as it is short and easy to administer. The English version of PHQ-8 has been found to be reliable and valid in SSc.

Objectives: To assess aspects of validity and reliability of PHQ-8 in Swedish (PHQ-8 Swe) for individuals with SSc.

Methods: Patients meeting the 2013 ACR/EULAR SSc criteria were recruited. The PHQ-8 Swe content validity was assessed via individual interviews (11 patients, 10 healthcare professionals, HPs) which was transcribed and analysed by content analysis. Patients ages, disease durations and symptoms of depression varied. The HPs had different occupational backgrounds and experiences in SSc care. Reliability was tested by internal consistency and test-retest reliability. Sixty-seven patients (median age 62 [minmax: 28-87]) completed the PHQ-8 Swe on two different occasions.

Results: Content validity: The instruction, items, and response options were generally considered easy to understand; however, some clarifications were suggested. Among HPs, it was expressed that some items could be perceived as emotionally demanding for patients especially in recent onset disease. Further they experienced that PHQ-8 was problem-rather than possibility-based. Introducing the PHQ-8 to patients and the need for follow-ups of the answers to the questionnaire were stated as essential. It was further expressed that PHQ-8 covered key aspects of symptoms of depression in SSc nevertheless examples of items suggested to be included were purpose in life, thoughts about death, and loneliness. The items were overall experienced as important without redundancy, and that some items could reflect more general SSc-related symptoms.

Cultural adaption: Possible adjustments to the PHQ-8 translation were made. This version was back translated into English and compared with the original English version. Thereafter, minor changes were made. A final PHQ-8 Swe version was tested for reliability. Reliability: Cronbachs alpha was 0.86 and the corrected item-to-total correlation range was 0.420.78. There were no significant differences between test-retest for seven of the eight items. The median weighted kappa coefficient was 0.63. The median PHQ-8 Swe total score was 4 (0-10, no-severe depressive symptoms). There were no significant differences for total scores between test and retest and the ICC was 0.81.

Conclusion: Content validity of PHQ-8 Swe was satisfactory and a positive quality was indicated for aspects of reliability in individuals with SSc tested in this study. Although some items could be interpreted as covering more general SSc-related symptoms, the PHQ-8 could be valuable for detecting patients with symptoms of depression in need of discussing emotional issues, as reflected in our study. Further studies of the PHQ-8 Swe usefulness are currently being undertaken via evaluation of other psychometric aspects.

REFERENCES


ACKNOWLEDGEMENT


AB1386-HPR FORCE SENSE EVALUATION OF THE KNEE JOINT FOLLOWING MENISCOTOMY RELATED WITH DEGENERATIVE MENISCAL TEAR

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Background: Meniscal tears are associated with degenerative knee disease, which can range from mild chondral changes not visible on a radiograph to established knee osteoarthritis. Meniscectomy related with degenerative meniscal tear may affect the force sense of the knee joint which is defined as the ability to accurately reproduce a given force. Objectives: The aim of this study was to compare the force sense of the knee joint of the patients with degenerative meniscal tear following meniscectomy with healthy peers.

Methods: Fifteen patients with meniscectomy and 18 healthy aged matched individuals were included in this study. Evaluation of force sense in the knee joint was measured with the use of a pressure biofeedback device, sphygmomonanometer, (Stabilizer, TM, Chattanooga Group Inc., Chattanooga, TN). The pressure bag of this device was placed under the knee joint. All subjects were instructed to extend the knee via Maximal Voluntary Isometric Contraction (MVIC) for 5 s. Each measurement was repeated three times with 1-min rest intervals and the average constant errors observed on the pressure biofeedback device were recorded as mmHg. Subjects were instructed to obtain at 50% of MVIC. They were asked to maintain the contraction (reproduce the target force) for 5 s. The reproduction force was subtracted from the target force to create a trial error score. Higher error scores indicated lower force sense.

RESULTS: There were no difference in terms of mean age, body mass index between patients (53.67.2 years, 26.21.8 kg/m2) and healthy peers (53.47.09 years, 25.63.2 kg/m2), respectively (p=0.05). Lower accuracy of the knee extensions during the 50% MVIC task was significantly seen in patients with meniscectomy (5.422.07 mmHg) compared to healthy group (1.881.11 mmHg) (p<0.001).

Conclusion: Results of this study demonstrated that higher force sense deficits are present in patients with meniscectomy related to degenerative meniscal tear compared to healthy peers. Thus, knee proprioceptive training focus on force sense might be developed to improve functional capabilities of knee joint especially following meniscectomy. It is also important to establish effective and feasible evaluation interventions for health professionals in clinical practice for assessing proprioception in terms of force sense in degenerative knees.

REFERENCES


TREATMENT ADHERENCE AMONG PATIENTS WITH INFLAMMATORY ARTHRITIDES TREATED WITH bDMARDs: AN OBSERVATIONAL STUDY USING I-CQRs QUESTIONNAIRE AND THE ADMINISTRATIVE CLAIMS DATABASE

AB1388-HPR

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Background: Effective treatments have been introduced for inflammatory arthritides (IA)s in the last decades. However, adherence remains suboptimal. Objectives: The aim of the study was to assess treatment adherence among patients with IA treated with bDMARDs in a community hospital with the Italian 5-item Compliance Questionnaire for Rheumatology (I-CQRs) [1] and the hospital administrative claims database. Methods: We conducted a monocentric, cross-sectional, observational study in IA patients (disease duration >1 year, undergoing treatment with self-administered bDMARDs, capable to complete the questionnaire unaided) recruited in a community hospital from February to October 2018. Treatment adherence was defined according to I-CQRs and to the Medication Possession Ratio (MPR) obtained from the claims database. To investigate variables associated with adherence, demographic, social, and clinical characteristics were considered. I-CQRs has 5 questions, with Likert-answering scale ranging from 1 to 4, an algorithm allows to classify the patient as poorly or highly adherent (i.e., likely to take >80% of their medications correctly) [1]. MPR was obtained by dividing the number of dosage units withdrawn by patients by the prescribed number of dosage units. Agreement between the I-CQRs and MPR definition of high adherence definitions was tested with McNemars test, while the association with patients characteristics with chi-square or Fishers exact test. Results: A total 174 patients completed the I-CQRs (median age 60 years, range 51-67; 37% males), affected by ankylosing spondylitis (16%), rheumatoid arthritis (RA) (62%), psoriatic arthritis (22%) with a median duration of 15 years (range 10-20). Etanercept (49%), adalimumab (20%), abatacept (8%) and tocilizumab (7.5%) were the most prescribed first-line biologics. Association with a conventional synthetic DMARDs was prescribed to 3.4% of subjects. High adherence rate, assessed with I-CQRs, was 85% overall, and 85% in RA patients. Significant differences were observed between highly and poorly adherent patients according to I-CQRs: lower educational status (lower primary or secondary school, and the use of cDMARDs were associated with poor adherence (both with p<0.001); while the use of bDMARDs was negatively associated with high adherence (p=0.05). High adherence rate measured with MPR was 72%. The agreement between high adherence, measured with I-CQR5 and MPR, was low (p=0.0005). Conclusion: The study showed that IA patients treated with bDMARDs with a higher educational level are more adherent to physician prescription, as assessed by I-CQR5. I-CQR5 might overestimate adherence compared to MPR. In our study, the high adherence rate measured with I-CQR5 was higher compared with a report from a large outpatient clinic in the same area, which was limited to RA patients (80% vs 40.1%) [1]. Our study may suggest that adherence benefits more from a close and stable relationship with the health care practitioner, such as in our centre, which is smaller than large outpatients clinics in which patients are followed by a health care professionals equipe rather than a single physician.

REFERENCES


Disclosure of Interests: None declared


THE ASSOCIATION BETWEEN THE AMOUNT OF DIASTASIS RECTI ABDOMINIS AND THE STRENGTH OF ABDOMINAL MUSCLES IN PREGNANT WOMEN

AB1389-HPR

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Background: Diastasis recti abdominis (DRA) is a common musculoskeletal problem, which is defined as a separation of the inter-recti distance between the two bellies of the rectus abdominis muscle at the linea alba.1 Due to the hormonal, postural and musculoskeletal changes, and mechanical strain, the anterior abdominal wall becomes stretched and elongated during pregnancy. Studies have shown that DRA may occur between 27% and 100% in the second and third trimesters of pregnancy.2 Although it has been reported that imbalance in the strength of the abdominal wall muscles altered with the facial tension, the role of abdominal muscle strength on DRA has not been clarified yet. Objectives: The present study assessed the relation between the severity/amount of DRA and the degree of abdominal muscle (rectus abdominis (RA), external and internal oblique muscles) strength in pregnant women. Methods: A total of 153 pregnant women between 14 and 35 weeks of a singleton pregnancy were included in the present study. The finger width method was used to measure the amount of DRA. The amount of separation was determined by the palpation of the medial sides of RA at three reference points: on the umbilicus, 4.5 cm above and 4.5 cm below of the umbilicus. After the subject contracts RA in hook lying position when her arms were in extended position, the size of the diastasis was measured by the number of fingers.2 The strength of abdominal muscles was assessed by the manual muscle test in supine hook lying position. The correlation between the amount of DRA and the degree of abdominal muscle strength was analyzed by the Spearman correlation. Results: The mean age was 28.40±3.69 years, mean Body Mass Index was 27.01±1.26 kg/m2, and mean gestational age was 28.12±5.03 weeks. A negative correlation was found between the amount of the diastasis at 4.5 cm below of the umbilicus and the strength of the RA (r=-0.219, p=0.007), right (r=-0.296, p=0.015) and left external oblique muscles (r=-0.293, p=0.017). Conclusion: Based on the findings of the present study, the separation of RA on the lower level of umbilicus may be negatively associated with the strength of RA and oblique abdominal muscles. Therefore, to decrease the severity of DRA, abdominal strengthening programs should be provided to pregnant women.

REFERENCES


Disclosure of Interests: None declared


AB1388-HPR

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Objectives: To investigate variables associated with adherence, demographic, social, and clinical characteristics were considered. I-CQR5 has 5 questions, with Likert-answering scale ranging from 1 to 4, an algorithm allows to classify the patient as poorly or highly adherent (i.e., likely to take ≥80% of their medications correctly) [1]. MPR was obtained by dividing the number of dosage units withdrawn by patients by the prescribed number of dosage units. Agreement between the I-CQR5 and MPR definition of high adherence definitions was tested with McNemars test, while the association with patients characteristics with chi-square or Fishers exact test. Results: A total 174 patients completed the I-CQR5 (median age 60 years, range 51-67; 37% males), affected by ankylosing spondylitis (16%), rheumatoid arthritis (RA) (62%), psoriatic arthritis (22%) with a median duration of 15 years (range 10-20). Etanercept (49%), adalimumab (20%), abatacept (8%) and tocilizumab (7.5%) were the most prescribed first-line biologics. Association with a conventional synthetic DMARDs was prescribed to 3.4% of subjects. High adherence rate, assessed with I-CQR5, was 85% overall, and 85% in RA patients. Significant differences were observed between highly and poorly adherent patients according to I-CQR5: lower educational status (lower primary or secondary school, and the use of cDMARDs were associated with poor adherence (both with p<0.001); while the use of bDMARDs was negatively associated with high adherence (p=0.05). High adherence rate measured with MPR was 72%. The agreement between high adherence, measured with I-CQR5 and MPR, was low (p=0.0005). Conclusion: The study showed that IA patients treated with bDMARDs with a higher educational level are more adherent to physician prescription, as assessed by I-CQR5. I-CQR5 might overestimate adherence compared to MPR. In our study, the high adherence rate measured with I-CQR5 was higher compared with a report from a large outpatient clinic in the same area, which was limited to RA patients (80% vs 40.1%) [1]. Our study may suggest that adherence benefits more from a close and stable relationship with the health care practitioner, such as in our centre, which is smaller than large outpatients clinics in which patients are followed by a health care professionals equipe rather than a single physician.

REFERENCES


Disclosure of Interests: None declared

PASSIVE COPING STRATEGIES BUT NOT PHYSICAL FUNCTION ARE ASSOCIATED WITH WORSE MENTAL HEALTH, IN WOMEN WITH CHRONIC WIDESPREAD PAIN—A MIXED METHOD STUDY

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Background: Chronic widespread pain (CWP) is a common condition (approximately 10% prevalence), that affects women twice as often as men. There is a lack of knowledge in how different coping strategies relates to health status during CWP development in a general population.

Objectives: To explore different ways of coping with CWP and to relate the different coping strategies to health-related factors, before and after developing CWP.

Methods: A sequential explorative mixed methods study including 19 women 45-67 of age, who had reported CWP in a survey 2016, but not in 1995. Individual interviews were analysed with a phenomenographic approach, and resulted in four categories of coping strategies. These categories were further explored with regard to four dimensions of health status (physical function, bodily pain, vitality and mental health) as measured by SF-36 (0-100, a lower score indicates more disability) and sleep problems measured both in 1995, and 2016.

Results: The qualitative analysis revealed four categories representing different coping strategies, where each woman was labelled by the most dominant category; the mastering woman, the persistent woman, the compliant woman and the conquered woman. The first two categories emerged as being active coping strategies, and the latter two as passive. Women with passive strategies reported significantly lower vitality (median 54 vs 93, p=0.021) in 1995, before they had developed CWP compared with those with active coping strategies. No differences were seen between the groups on physical function, bodily pain or sleep.

In 2016, there were still a difference between the passive and active group regarding mental health (median 56 vs 80, p=0.022), but not for vitality (median 35 vs 40, p=0.707). No differences were seen between the groups on physical function or bodily pain. All eight women with passive strategies reported problems with sleep in 2016, as compared to 6 of the 11 women with active strategies (p=0.045).

Conclusion: Women that reported CWP in 2016, but not in 1995, described both active and passive coping strategies. The qualitative findings were associated with differences in vitality and mental health already in 1995, before they had developed CWP. Further, those with passive coping strategies reported worse health with regard to mental health and sleep problems in 2016. Interestingly, the groups did not differ in bodily pain or physical function neither in 1995 nor in 2016, which implicates the importance for the clinician to take the typical coping strategy into consideration, when meeting these patients in clinical settings.

Disclosure of Interests: None declared


GO-BEYOND: A REAL-WORLD PERSISTENCE STUDY WITH GOLIMUMAB IN PATIENTS WITH AXIAL SPONDYLOARTHRITIS AND RHEUMATOID ARTHRITIS IN TURKEY

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Background: Axial spondyloarthritis (axSpA) and rheumatoid arthritis (RA) are chronic inflammatory diseases and associated with substantial health and economic burden since these conditions affect individuals in their productive years. Adherence to treatment is a major problem for inflammatory rheumatic diseases.

Objectives: In the present study, we aimed to evaluate rates of persistence with golimumab (GLM) therapy in axSpA and RA patients using real-world data.

Methods: This multicenter, non-interventional, retrospective study enrolled 329 patients diagnosed with axSpA (n=269) and RA (n=60) who currently receive or have received golimumab therapy for at least 3 months either as first-line treatment (biologic naive group) or as second-line treatment after failure to another anti-TNF or biologic agent (biologic-experienced group). In addition to the patients demographic and clinical characteristics, data on drug continuation and disease activity scores such as ASDAS/BASDAI and DAS-28 scores were retrieved from the patient records. A regression analysis was conducted to determine the factors associated with drug discontinuation including age, gender, smoking status, disease duration, presence of comorbidities, disease activity measures, concomitant csDMARD use.

Results: Only 28 (10.4%) axSpA and 7 (11.6%) RA patients were biologic-experienced. The changes in disease activity scores of RA and axSpA patients on therapy during 2-years of follow-up are presented in figure a and b.

Golimumab therapy provided good and long-term improvement in the disease activity scores in both RA and axSpA patients. At 6, 12 and 24 months treatment persistence rates were 86.4%, 74.5% and 65.5% for RA and 93.5%, 81.9% and 75.5% for axSpA patients, respectively. Persistence with GLM was similar between biologic-nave and experienced patients. GLM persistence was also similar in RA and axSpA groups (figure c). Regression analysis revealed that smoking (HR 0.523; p=0.006), presence of comorbidity (HR 2.731; p<0.001) and disease duration (HR 0.957, p=0.038) were significant predictors of drug persistence in GLM treated patients.

Conclusion: Our results show that GLM therapy is an effective treatment option with high drug retention rates in both RA and axSpA patients independent of previous biologic exposure. Smoking, co-morbidities and disease duration may affect the continuation of golimumab treatment in inflammatory rheumatic diseases.
The aim of this study is to compare the quality of life, function and emotional status of inpatients and outpatients with rheumatic diseases. The study included 78 patients (inpatient, n = 31; outpatient, n = 47) with rheumatic disease. The Health Assessment Questionnaire (HAQ) (2) and SF-36 (3) were used to evaluate the functionality and quality of life, and the Hospital Anxiety and Depression Scale (HADS) (4) was used to determine their emotional status. The variables were investigated using visual and analytical methods to determine whether or not they are normally distributed. Since physical function, mental health and general health perception values of SF-36 and HADS-Anxiety were normally distributed, the Students T-test was used to compare these parameters between two groups. Physical role limitation, pain, social status, emotional difficulty, energy viability of SF-36, HAQ and HADS-Depression were not normally distributed. Thus, Mann-Whitney U test was used to compare these scores between two groups.

**RESULTS**

The mean age of the subjects (n = 78) included in the study was 46.09 ±13.89 years and the mean BMI was 27.59 ± 15.08. There was a significant difference in depression, anxiety and pain and social functioning sub-parameters of SF-36 (p < 0.005) but there was no significant difference in other parameters (p > 0.005).

**Conclusion**

It was thought that during the period of admission to the hospital, inpatients should be supported in terms of pain management, social functioning and anxiety and, depression as well as taking medication. Besides, caregivers in hospitals should encourage inpatients with regard to maintaining physical activity.

**REFERENCES**


**Disclosure of Interests:** None declared

**AB1393-HPR CAN SUPPORT FROM SIGNIFICANT OTHERS RELIEVE SICKNESS ABSENCE IN EARLY RHEUMATOID ARTHRITIS?**

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**Background:** Persons with rheumatoid arthritis (RA) are at higher risk of sickness absence, and the probability of returning to work is lower compared to the general population. In order for persons with RA to continue working, support from the social environment is claimed to be of importance. However, this relation needs to be further investigated.

**Objectives:** To analyze how support from significant others affects the associations between disease related variables (medication, disease activity and activity limitations) at time for RA diagnosis and sickness absence one year after diagnosis.

**Methods:** Data were collected from 326 (71% women) patients in working age (18-63 years) included in the Swedish early RA cohort TIRA-2. Data were collected between 2006-2015. At the time of inclusion, mean age was 50 years (SD=11), 89% were prescribed disease modifying anti-rheumatic drugs (DMARDs), mean disease activity score 28 joint count (DAS28) was 4.73 (SD=1.34), and mean score for activity limitation reported by Health Assessment Questionnaire (HAQ) was 0.91 (SD=0.60). The number of days with sickness absence during the first year after diagnosis and inclusion was retrieved from the Swedish Social Insurance Agency. Perceived support from significant others, family and friends separately, were self-reported

**Results:** The mean age of the subjects (n = 78) included in the study was 46.09 ±13.89 years and the mean BMI was 27.59 ± 15.08. There was a significant difference in depression, anxiety and pain and social functioning sub-parameters of SF-36 (p < 0.005) but there was no significant difference in other parameters (p > 0.005).

**Abstract AB1393HPR Table 1. Comparison of the scores of inpatients and outpatients**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>INPATIENTS (XSD)</th>
<th>OUTPATIENTS (XSD)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAQ</td>
<td>0.930 ± 0.82</td>
<td>0.890 ± 0.68</td>
<td>0.152</td>
</tr>
<tr>
<td>HADS-Anxiety</td>
<td>9.873 ± 8.21</td>
<td>8.215 ± 0.022</td>
<td>0.06</td>
</tr>
<tr>
<td>HADS-Depression</td>
<td>9.935 ± 7.474</td>
<td>3.83 $\pm$ 0.006</td>
<td>0.66</td>
</tr>
<tr>
<td>SF-36 Physical Function</td>
<td>47.942 ± 48.362</td>
<td>81.8 ± 0.66</td>
<td>0.069</td>
</tr>
<tr>
<td>SF-36 Physical Role Limitation</td>
<td>27.533 ± 27.636</td>
<td>2.86</td>
<td>0.068</td>
</tr>
<tr>
<td>SF-36 Pain</td>
<td>33.663 ± 54.072</td>
<td>4.142 ± 0.001</td>
<td>0.111</td>
</tr>
<tr>
<td>SF-36 Social Status</td>
<td>39.582 ± 55.062</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>SF-36 Mental Health</td>
<td>612 ± 62.736</td>
<td>0.761</td>
<td></td>
</tr>
<tr>
<td>SF-36 Emotional Difficulty</td>
<td>31.1038 ± 33.3243</td>
<td>0.717</td>
<td></td>
</tr>
<tr>
<td>SF-36 Energy Vitality</td>
<td>30.8320 ± 43.2820</td>
<td>0.317</td>
<td></td>
</tr>
<tr>
<td>SF-36 General Health</td>
<td>36.1621 ± 47.4716</td>
<td>0.383</td>
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</tr>
</tbody>
</table>

**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.7315
by VAS scales, zero indicating no support and 100 indicating full support. The associations of disease activity, activity limitation and DMARD use with sickness absence and how these associations were moderated by support from significant others, were analyzed using zero-inflated negative binomial regression.

Results: Higher activity limitation (HAQ) was associated with lower risk of sickness absence (p<.001) but more days with sickness absence (p=.001). Higher disease activity (DAS28) was associated with lower risk of sickness absence (p=.003). However, when including family support, this association was not significant (p=.117) and associated with higher risk of sickness absence, but the association was weaker with family support (p=.029). Disease activity was also associated with more days of sickness absence (p=.013). The use of DMARDs had no significant relation to sickness absence (p=.150) or number of days with sickness absence (p=.852). Although, when including support from friends, DMARD use was associated with higher risk of sickness absence (p=.041). However, this association decreased significantly with support from friends (p=.029).

Conclusion: Support from significant others has an impact on previously known relationships between disease activity, use of DMARDs and sickness absence. Hence, support from significant others has the possibility to help decrease sickness absence among persons with RA one year after diagnosis.

REFERENCES

Disclosure of Interests: None declared

**AB1395HPR**

**BURDEN IN CAREGIVERS OF PATIENTS WITH RHEUMATIC CONDITIONS**

Diana Buitrago-Garcia, Laura Villarreal, Michael Cabrera, Pedro Santos, Moreno, Fernando Rodriguez

Background: Rheumatoid arthritis (RA) is a chronic, disease that affects more than 1% of global population, it is a long term condition that causes pain and disability. Evidence had shown that most of the patients are moderately disabled, which brings the necessity of a caregiver to become the patients companion due to its chronic disease. The caregiving role can have an impact in the psychological and physical sphere of the caregivers life.

Objectives: The aim of this study was to explore demographic characteristics and caregiver burden through the Zarit Scale.

Methods: We conducted a cross sectional study in a meeting where caregivers in a rheumatoid arthritis specialized setting. We collected sociodemographic information, and applied the Zarit caregiver burden interview (ZBI) adapted to Spanish. The ZBI includes 22 questions which has 5 responses from 0 (never) to 4 (nearly always), where scores lower than 47 indicated little to no burden, 47 to 55 low burden and >55 intense burden. We calculated means, and standard deviations for continuous variables and categorical variables were presented as rates.

Results: We applied a survey to 132 caregivers. Mean age was 52 years SD 19 and 72% were women, 78% of them were taking care of their pelvic floor symptoms as well. Therefore decrease in the range of motion of the hip joint due to AS complicates pelvic pain and sexual dysfunction.

Objectives: The aim of study was investigation of sexual satisfaction and sexual dysfunction in partner of patients with AS.

Methods: 50 individuals: 21 female partner of patients with AS with an average age of 40.38 5.31, 29 male partner of patients with AS with an average age of 52.37 5.84 were included in this study. The male partners were evaluated with the International Index of Erectile Function (IIEF) and the female partners were evaluated with the Female Sexual Function Index (FSFI).

Results: Total score of FSFI was 52.37 5.84 (Sexual desire:5.472.01, arousal:11.664.97, orgasm: 8.524.74, lubrication:12.005.06, satisfaction: 8.474.49, pain:8.044.17) in female partner. Erectile score of IIEF was 24.35 6.65, orgasm score was 8.85 3.28, sexual desire score was 7.271.70, sexual satisfaction score was 10.373.86 and general sexual score was 6.142.63 in male partner.

Conclusion: According to the results of the study, female partner had moderate sexual dysfunction, male partner had mild erectile function. This study showed that the sexual functions of female and male partners of patients with AS were affected negatively. Further studies need to assess their pelvic floor symptoms as well.

REFERENCES
[AB1397-HPR] CLINICAL FEATURES IN COHORT OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS IN KAZAKHSTAN

Bakytsholpan Issayeva1, Maira Saparbayeva1, Shabaran Kaygaly1, Moldir Kulshymanova1, Kanat Nurgaliev1, Samal Issayeva1, Gulshat Dalibayeva1, Maira Bizhanova1, Balzhan Kulymbetova2, Karlygash Rysbekova2, Moldir Kulshymanova1, Kanat Nurgaliev1, Samal Issayeva1, Gulshat Dalibayeva1, Maira Bizhanova1, Balzhan Kulymbetova2, Karlygash Rysbekova2, Aralym Atasheva2, Elena Aseeva2, Sergey Solovey2.

1: Astana Medical University, Astana, Kazakhstan; 2: V.A. Nasonova Research Institute of Rheumatology, Moscow, Russian Federation

Background: Systemic lupus erythematosus (SLE) refers to socially significant diseases and the improvement of diagnosis, treatment of the disease belongs to the target indicators of the State Program in Kazakhstan.

Objectives: The aim of this study was to assess the demographic, clinical features, the degree of activity, damage to internal organs and therapy in patients with SLE.

Methods: The study involved 89 patients with a documented diagnosis of SLE (ACR, 1997) hospitalized for inpatient treatment in rheumatology centers. The register included an assessment of gender, age, Disease Activity Index (SLEDAI 2K), organ Damage Index (DI, SLICC, 2012), and therapy. For qualitative signs, absolute and relative values (n, %) are presented.

Results: In the studied cohort of patients with SLE prevailed women (98.8%), the mean age of patients was 33.61±4.7 years, 47% of them under 30 years old. The debut of the disease in the overwhelming majority (52%) patients is associated with stress, pregnancy and childbirth. By ethnicity, Kazakhs - 67 (75.2%), Russian - 7 (7.8%), Uighurs - 6 (6.7%), Korean - 5 (5.6%), others 5 (5.6%). 56% of patients had higher and secondary-special education. Only in a third of patients SLE was diagnosed in the first months of the disease, the rest had erroneous diagnoses, such as rheumatoid arthritis, reactive arthritis, and other systemic diseases. The disease activity (SLEDAI 2K) was very high in 9 (10.1%), high in 24 (26.9%), medium in 39 (43.9%), low in 15 (16.8%) patients and without activity were 2 (2.2%) patients.

Among SLE patients, 92% with mucocutaneous manifestations, 64% had photosensitivity, 56.2% had enanthema, 77.5% had arthritis and arthralgia, 28.1% with serositis, 55% had renal involvement, 25.8% had neurological and 58.4% had hematological disorders. Irreversible organ damages (SLICC) were detected in 67.4% of patients: low DI (1 point) - 26 (29.3%), moderate (2-4 points) - 33 (37.1%) and high (> 4 points) - in 3 (3.4%) patients. Medium and high DI were observed in patients with renal and neurological involvement.

Patients were predominantly in therapy: methylprednisolone (98%), cyto- statics and mycophenolate mofetil (42.3%), hydroxychloroquine (39%). Biological therapy (rituximab, belimumab) was performed in patients with a high degree of activity, nephritis, and neutropenia and in 6 (6.7%) patients with good effect and the possibility of reducing glucocorticoids to minimal doses.

Conclusion: Creating a register and forming a cohort allows for a more complete assessment of activity, organ damage and therapy in patients with SLE.

Disclosure of Interests: None declared

[AB1398-HPR] RHEUMATOID ARTHRITIS– BIOLOGICAL DMARDS EXPERIENCE IN TAWAM HOSPITAL, UAE, A 2-YEAR RETROSPECTIVE STUDY

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Background: Arthritis is the leading cause of disability in America, affecting 50 million adults. Although there is currently no cure for rheumatoid arthritis (RA), improved understanding of RA disease pathogenesis in recent years has led to the development of new treatments. Disease Modifying Anti-Rheumatic drugs (DMARDs) are added at early stages in the treatment of RA to suppress inflammation; they may be used as monotherapy or more commonly in combination. The aim of this study was to present more comprehensive profile of RA, psoriatic arthritis (PSA) and ankylosing spondylitis (AS) is aimed at achieving the lowest disease activity and remission. Patient compliance is considered necessary for the success of treatment in chronic diseases.

Objectives: The objective of this study was to assess the patient adherence to their medications and clinic visits in addition to assessing the prescribing, screening and monitoring parameters of biological disease modifying agents (DMARDs) according to the care pathway at Tawam Hospital and EULAR recommendations.

Methods: A retrospective observational review using data from the computer based system at Tawam hospital. All adult patients with RA, PSA and AS starting a biological DMARD during our study period; December 2016 to December 2018 were eligible.

Results: A total of 54 patients were included. Eighty percent were females. Sixty three percent RA patients, 24% PSA patients and 13% AS patients. Indication, dosing and blood monitoring criteria were met for 100% of the patients. Vaccination criteria was met in only 20%. Screening criteria was met by 57%. Ninety two percent of the RA and PSA patients were started on methotrexate for 3 months before biologics initiation as per guidelines. Forty three percent of AS patients used 2 non-steroidal anti-inflammatory drugs before starting biological therapy.

Medication adherence was measure by: the duration of therapy, consistent clinic visits and regular medication refills. Eighty four percent of the number of patients had adherence to therapy for 6 months or more. Twenty six percent were consistent with their monthly clinic visits. Sixty one percent were compliant with their monthly medication refills.

RA patients were further analysed as they made the majority of our patients. Ninety seven percent of the RA patients had a baseline DAS documented. Eighteen percent had a baseline of DAS28<2.6. Fifty percent had a baseline DAS28>3.2. Twenty nine percent had a baseline DAS28>5.2. Three percent of the patients started on a biologic with no documented baseline DAS. One hundred percent of the patients had a documented DAS. One hundred percent of the patients had a documented DAS including the 18% that had DAS28>2.6; however the reasons were clearly stated (example of reasons, contemplating pregnancy, adverse reaction to previous treatment).

The DAS 28 was documented again at the end of the study period. Fifty nine percent of the patients had DAS28<2.6. Twenty six percent had DAS between 2.6-3.2, twelve percent had DAS28>3.2 and three percent of the patients had a DAS28>5.1. All the patients with DAS28>3.2 (15%) changed their treatment regimen.

Conclusion: This audit concluded 100% compliance with the care pathway at Tawam Hospital and EULAR recommendations in the treatment of RA, PSA and AS with regards to starting a biologic treatment, switching treatment, dosing and monitoring. Overall the patients adherence to their clinic visits and medication refills was satisfactory; however improving adherence to therapy could therefore dramatically improve the efficacy of drug therapy. However there was a gap in the vaccination and screening parameter which indicates a need to add a tool in computer system to aid the physicians in fulfilling this gap.

REFERENCES


Disclosure of Interests: None declared
**AB1399-HPR**  
**FOOT AND ANKLE ASSESSMENT IN PATIENTS WITH DIFFERENT GRADES OF KNEE OSTEOARTHRITIS**

**KARAPINAR MERVE1, Ferdi Baskurt1, Zelilha Baskurt1, Meric Unal2.**  
1Faculty of Health Science, Physiotherapy and Rehabilitation, ISPARTA, Turkey; 2Faculty of Medicine, Sports Medicine, ISPARTA, Turkey

**Background:** Foot and ankle profile has long been considered to contribute to the development of knee osteoarthritis (OA). It may alter the mechanical alignment and dynamic function of the lower limb especially knee functions. It is important to determine compensatory changes in the foot and ankle posture in patients with different grades of knee osteoarthritis. Because it may help in understanding the role of foot orthoses, footwear modifications or treatment strategies on alignment and function of knee.

**Objectives:** This present study was designed to assess the changes in foot and ankle profile among different grades of knee OA.

**Methods:** Patients were assessed with physical examination including foot and knee specifically and anteroposterior and lateral direct radiographies. All patients were divided into four groups for medial compartment OA severity by using the Kellgren-Lawrence grading system of knee OA on weight bearing knee radiographies. The Western Ontario and Mc Master University Osteoarthritis Index (WOMAC) questionnaire was performed to assess pain and the functional status of the patients. Structural foot profile was assessed by the Foot Posture Index (FPI) system and American Orthopaedic Foot and Ankle Society (AOFAS)anklehindfoot and midfoot scales.

**Results:** The study included forty-four patients with mean age 57.12±12.2 years. In terms of severity of knee OA groups; percentages for grade 0-1, 2,3 and 4 were 25%, 22.7%, 25%, 27.2% respectively. In the grade 4 and knee specifically and anteroposterior and lateral direct radiographies. All patients were divided into four groups for medial compartment OA severity by using the Kellgren-Lawrence grading system of knee OA on weight bearing knee radiographies. The Western Ontario and Mc Master University Osteoarthritis Index (WOMAC) questionnaire was performed to assess pain and the functional status of the patients. Structural foot profile was assessed by the Foot Posture Index (FPI) system and American Orthopaedic Foot and Ankle Society (AOFAS)anklehindfoot and midfoot scales. The study indicated that differences of the severity of OA were higher (p < 0.001). Besides, foot pronation was also increased as the severity of osteoarthritis increased. In the grade 0-1 and grade 2; AOFAS-hindfoot and midfoot scores were higher (p<0.001) compared to severe OA (grade 3 and grade 4).

**Conclusion:** The study indicates that differences of the severity of OA have influence on the foot and ankle profile to different degrees. Therefore, it is clinically important to give appropriate orthotics advice or treatment to patients with different degrees of OA to correct the pronation of foot to different degrees.

**REFERENCES**

SELF-REPORTED PHYSICAL FUNCTION AND ASSOCIATED FACTORS IN INDIVIDUALS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

Gizem Irem Kinikli1, Susanne Pettersson2, Sevval Karahan3, Elisabet Svennungsson1, Casrina Bostm2,3, Hacettepe University, Faculty of Physical Therapy and Rehabilitation, Ankara, Turkey; 2Karolinska Institute, Inflammation and Infection Theme, Karolinska University Hospital and Department of Neurobiology, care sciences and society, Stockholm, Sweden; 3Hacettepe University, Faculty of Medicine, Department of Biostatistics, Ankara, Turkey; 4Karolinska University Hospital; Unit of Rheumatology, Department of Medicine, Stockholm, Sweden; 5Karolinska Institute, Department of Neurobiology, care sciences and society, Stockholm, Sweden

Background: Physical activity and exercise have many positive effects in patients with Systemic Lupus Erythematosus (SLE) (1) and poor self-reported physical function has been reported to predict mortality (2). To facilitate and improve physical activity/function, it is thus important to investigate what factors are associated with good physical function. Few previous studies have addressed these issues (3).

Objectives: The aim of this study was to identify factors associated with good self-reported physical function, such as walking and running in individuals with SLE.

Methods: A total of 198 patients (mean age: 51.5±16.1 years; BMI: 24.7±7.4 kg/m²) with SLE participated. The outcome, self-reported physical function was assessed with the question: How much do you think you can manage concerning walk, jog, and run? (From Physical Activity Questionnaire, PAQ). Disease activity was assessed using the SLAM-R and organ damage with SLICC/ACR-DI. The VAS part of EQ-5D, was used to assess self-reported health related quality of life (HRQL). Hospital Anxiety and Depression Scale (HADS) was used to assess anxiety/depression levels. Self-reported exercise during the last year was assessed by questions from PAQ and sitting hours as well as physical activity level was determined from International Physical Activity Questionnaire Short Form (IPAQ-SF). Logistic regression analyses estimated the associations of the following independent variables: age, sex, BMI, disease activity, organ damage, HRQL and anxiety/depression levels, exercise last year, sitting hours and physical activity level, on the dependent variable self-reported physical function (PAQ-question). Statistical significance was defined as a p value <0.05.

Results: Median SLAM-R was 6 (IQR:6), SLICC-DI was 1 (IQR:3), EQ-5D VAS was 72.2 (IQR:22.1) and depression level 4 (IQR:5). Median Self-reported exercise during the last year (PAQ) was exercise irregularly. Median sitting hours a day (IPAQ-SF) was <5 hours. Median physical activity level was moderate (IPAQ-SF). Age (p<0.001; Odds ratio:6.40), SLICC-DI (p=0.002; Odds ratio:4.02) and EQ-5D VAS (p<0.001; Odds ratio:4.20) were significantly associated with better self-reported physical function (Nagelkerke R Square=0.437).

Conclusion: The results demonstrated that SLE-patients who report low physical function are older patients with more organ damage. However, patients who reported low HRQL also reported low physical function. Our results imply that patients with low self-reported HRQL are at risk for not being enough physically active. To break this vicious circle is a challenge for physicians and physical therapists that care for patients with SLE.

REFERENCES


[2] Young A, Ismail M, Papatsoris AG, Barua JM, Calleary JG, Masood J. Entonox inhalation to reduce pain in common diagnostic and therapeutic procedures in children. Evidence from a variety of different procedures has shown it to be an effective, safe and patient acceptable form of analgesia for both adults and children (2). It is widely acknowledged that patient satisfaction questionnaires allow clinicians to acquire meaningful and essential information that identifies gaps in care and facilitates the development of effective action plans for quality improvement in healthcare (3).

Disclosure of Interests: None declared

INVESTIGATION OF SPINE POSTURE, MOBILITY AND REDUCED HAND FUNCTION AFFECTS ACTIVITY OF JIA PATIENTS

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Background: Low back pain (LBP) is the most common musculoskeletal complaint especially in women that causing disability and growing as a global burden (1,2). Changes in spine structures and alignment have been important in the occurrence of LBP (3,4).

Objectives: This study aimed to investigate spine posture, mobility and postural competency in women with and without LBP.

Methods: Thirty-four women with LBP having moderate to severe disability (age: 50.509.26 years; body mass index (BMI): 34.765.42 kg/m²) and age-paired matched 37 asymptomatic healthy women (age: 48.948.99 years; BMI: 31.976.88 kg/m²) were included. Oswetry Disability Index (ODI) was used for disability assessment (higher scores indicated more severe disability (0-50)). Overall spine posture, mobility, postural competency and spine check scores were evaluated using the Spinal Mouse (Idig, Fehraltorf, Switzerland) device in standing position. The scores were evaluated between as poor “0” and “100” as perfect. T test was used for analysis.

Results: The mean score of ODI was 32.258.27 (moderate to severe disability). The scores of spine posture, mobility, postural competency and total spine check of women with LBP were found 24.7615.65; 25.1114.60; 36.0421.58; 30.2612.06, respectively; while, the scores of asymptomatic women were found 34.6716.27; 34.4521.47; 38.2115.18; 38.7215.06, respectively. Lower postural (p=0.011), mobility (p=0.037) and total spine check scores (p=0.011) were found in women with LBP compared to the controls; however, the postural competency was similar (p=0.722).

Conclusion: Women with LBP had poor spine posture, mobility and total spine check scores, but similar postural competency in comparison to controls. In the clinics, considering these parameters might be important while planning the optimal treatment for LBP.

REFERENCES

Disclosure of Interests: None declared

JIA TEAMWORK FOR IMPROVING PATIENTS’ ACCEPTANCE OF INTRAARTICULAR GLUCOCORTICOID INJECTIONS IN LOCAL ANESTHESIA IN OUTPATIENT DEDICATED SERVICE

Aurora Pucacco1, Hanan Jadoun1, Angela Aquilani2, Fabio Basta3, Andrea Uva2, Rebecca Nicolai1, Fabrizio De Benedetti1, Silvia Magni-Manzoni1, Gianfranco Rotton1, Fabrizio De Benedetti1, Silvia Magni-Manzoni Consultant for: Abbvie, Speakers bureau: Abbvie

Background: The discomfort and anxiety related to the medical care of patients with juvenile idiopathic arthritis (JIA), ampered by frequent and ongoing visits, diagnostic tests, medications and hospital stays, can negatively impact on the compliance during examinations and procedures, particularly intraarticular glucocorticoid injections (IAGI) in local anesthesia. A dedicated personnel for supporting patients and their caregivers may provide them relief, thus contributing also to a more serene environment for operators.

Objectives: To identify an appropriate approach for the relief of JIA patients most critical issues related to IAGI in local anesthesia. To provide preliminary validation of the approach identified.

Methods: In the first part of the study the nurse of the IAGI outpatient service at the study center had conversation with all consecutive JIA patients and caregivers seen at the service, while preparing them to IAGI in local anesthesia and while on discharge. In agreement with the patient, the nurse synthesized in keywords and registered each patients most relevant feelings with regard to the IAGI procedure. Patients and caregivers were also asked to suggest feasible tools for a better acceptance of the procedure. The results were discussed within the JIA team, who selected in a questionnaire the most frequently reported keywords and identified the most feasible among the proposed supportive tools. Secondly, all consecutive JIA patients seen at the service were asked to complete the feeling-status questionnaire after the IAGI. As the tools were available, the questionnaire was completed after IAGI procedures tool-supported. Statistics included descriptive analysis and Students t-test for comparison between feelings rating by patients with and without supportive tools (significance: p-value<0.05).

Results: From the list of keywords obtained by the first 10 patients with the nurse, the most reported stress, anxiety, fear, and anger were included in a feeling questionnaire composed of a VAS 0-10 (0=none, 10=worst) for each keyword. Among the suggested supportive tools the JIA team identified as feasible: colored drawings/pictures in the procedure room and the availability of favourite songs/videos/cartoons on tablet just prior and during IAGI. Forty-one patients completed the questionnaire in a mean time of 22 seconds. Among them, 24 (59%) were supported by the selected tools, been meantime available, during IAGI procedure.

Abstract AB1404HPR Table 1. Mean of response to the feeling-questionnaire by JIA patients seen at the IAGI outpatient service without (A) and with (B) supportive tools

<table>
<thead>
<tr>
<th>Feeling</th>
<th>Patients n=17 (A)</th>
<th>Patients n=24 (B)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fear</strong>*</td>
<td>4 (1)</td>
<td>2 (2)</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Anxiety***</td>
<td>4 (2)</td>
<td>2 (2)</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Stress***</td>
<td>9 (1)</td>
<td>4 (2)</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Anger***</td>
<td>5 (2)</td>
<td>1 (2)</td>
<td>&lt;0.005</td>
</tr>
</tbody>
</table>

*VAS 0-10, 0=none, 10=worst

Conclusion: Our preliminary results highlight that a setting for IAGI more comfortable for patients provide an improvement in the JIA patients feelings rating undergoing injection procedures in local anesthesia. The nurses attitude to patients and the teamwork were fundamental in collecting the patients perspective and in adapting their suggestions to the IAGI outpatient service environment.

Acknowledgement: We acknowledge the Associazione Malattie Reumatiche Infantili (AMRIE) Onlus for its support to the initiative

Disclosure of Interests: Aurora Pucacco: None declared, Hanan Jadoun: None declared, Angela Aquilani: None declared, Fabio Basta: None declared, Andrea Uva: None declared, Rebecca Nicolai: None declared, Fabrizio De Benedetti Grant/research support from: Abbvie, SCBi, Novimmune, Roche, Novartis, Sanofi, Pfizer, Silvia Magni-Manzoni Consultant for: Abbvie, Speakers bureau: Abbvie


REDUCED HAND FUNCTION AFFECTS ACTIVITY PERFORMANCE AND QUALITY OF LIFE IN PERSONS WITH SIBM

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Background: Reduced hand function is common in persons with (IBM) (1). Information regarding how hand function deficits affect activities of daily living and quality of life is limited (2,3). There is a need to improve treatment and increase knowledge on how to assess different aspects of SIBM.
AB1406-HPR | DIET AND LUPUS: WHAT DO THE PATIENTS THINK?

George Robinson1, 2, Thomas Moddernell3, Chris Wincup2, Lucia Martin-Gutierrez3, James Wilton3, Anastasia Kalea4, Coiziana Curtin5, Ines Pineda Tarkowski6, John Nepomuceno Staff7. 1Medical School, University of Liverpool, Liverpool, United Kingdom; 2University College London, Neuroscience, London, United Kingdom; 3University College London, Institute for Liver and Digestive Health, London, United Kingdom; 4University College London, Metabolism and Experimental Therapeutics, London, United Kingdom

Background: Cardiovascular disease (CVD) is the leading cause of mortality in patients with systemic lupus erythematosus (lupus). Therefore, using diet to control blood lipid levels and modify CVD risk could be a promising therapeutic strategy to control disease symptoms.

Objectives: The primary objective of this study was to learn about lupus patient experiences with diet including their opinion on considering diet as a therapeutic option. The secondary objective was to obtain this information in a cost and time effective manner.

Methods: A lay summary and a 15 question diet-based online survey was publicly available for 3 weeks. Social media was used to promote the survey through relevant charities, hospitals and research groups.

Results: 300 responses were received, 284 of whom had lupus. Patients reported that there was a lack of clinical counselling regarding diet with only 24% of patients stating that their doctor had spoken to them about diet. Despite this, 100% of patients stated that they would change their diet if they knew it would help their symptoms and 83% would take part in a future diet-based clinical trial. Text analysis of patient research suggestions identified a particular interest in using diet to treat fatigue and manage disease flares.

Conclusion: This project successfully gathered patient information regarding diet and lupus over a short timeframe using an anonymous social media platform. The survey provided evidence that patients support further research and potential diet intervention studies investigating the effect of diet on the symptoms of lupus.

REFERENCES

Disclosure of Interests: None declared


AB1407-HPR | NEUROLOGICAL MANIFESTATIONS DURING THE BEHÇET DISEASE

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Background: Behçet disease MB is a systemic inflammatory disease whose common histopathological substratum is a vasculitis that can reach all vessels. Neurological impairment is one of the diagnostic criteria for MB. A serious condition affects the functional and vital prognosis.

Objectives: The aim of our work was to study the epidemiological, clinical, therapeutic and evolutionary characteristics of patients with BD with neurological involvement.

Methods: This was a retrospective, monocentric, descriptive study of NB from the adult population collected from a population of 150 patients monitored for MB. The study was conducted in the Neurology and Internal Medicine departments over a period of 19 years, from January 1997 to December 2015. Patients meeting the criteria of the international Study Group of the MB of 1990, those of the International Criteria for Behcet Disease (ICBD) and the diagnostic criteria of Neuro-behçet defined proposed by the international consensus of experts of 2014.

Results: We collect 35 patients. The gender ratio was at 6 with 30 men for 5 women. The mean age of our population was 34+ 1.92 years. The neurological manifestations had inaugurated the MB in 55% of the cases. Ninety-four percent of patients had central nervous system involvement, while two patients had peripheral polyradiculoneuritis. Central involvement was parenchymal in 85% of cases, nonparenchymatous in 3% of cases and fixed in 6% of cases. Cerebral imaging showed predominant demyelinating lesions in periventricular and brain stem in 15 patients, a pseudo-tumor appearance in 3 patients, and vascular lesions with arterial aneurysm and cerebral thrombophlebitis in 2 patients. Therapeutically, all patients received corticosteroid therapy with immunosuppressive therapy for 15 patients. Three patients had received an immunomodulatory treatment of anti-TNF a Type. The evolution was by push in 60% of cases, primary progressive in 20% of cases and secondarily progressive in the rest of the cases. Three-quarters of patients with parenchymal brain injury had a favorable outcome. The Outcome was unfavorable in all patients with diffuse disease, brain stem damage, spinal cord injury, angio-behavior, polyradiculo-neuropathy and mixed impairment. The change in visual impairment (NORB) was favorable in one case in two.

Conclusion: Neurological manifestations of MB are serious complications, and are typically poor prognosis both on a vital and functional level. Mortality remains high and neurological sequelae (motor and neuropsychological) are heavy. The prognosis in all the worse because the treatment is instituted late, hence the interest of an early and well conducted treatment.

Disclosure of Interests: None declared

BACKGROUND: The lack of efficacy of biological therapies in rheumatic patients causes a change of treatment, usually to another biological therapy. A significant number of studies have been published in relation to the reasons that cause this inefficacy, however, no studies have evaluated the influence of the weight and lipid profile of patients in this process.

OBJECTIVES: To analyze the influence of weight and lipid profile in the relapse and change of biological therapy.

METHODS: Retrospective-descriptive study. Rheumatic patients in treatment with biological therapies were recruited from January 2016 to December 2018. Sociodemographic data were collected (age and sex), along with anthropometric variables (weight, height, waist circumference and hip perimeter), toxic habits, comorbidities and variables related to the treatment. Associations between variables were analyzed using a Chi-square and T student. P-values < 0.05 were considered statistically significant.

RESULTS: Two hundred and nine patients were enrolled, of which 80 (38.3%) were male and 129 (61.7%) were female. The mean age (SD) was 48.9 ± 12.8 years. One hundred and twenty and twenty patients (57.4%) suffered rheumatoid arthritis, 35 (16.7%) spondyloarthritis, 29 (13.9%) psoriatic arthritis and 10 (4.8%) spondyloarthropathies. One hundred and fifty-three (73.2%) had not switched of biological therapy, 51 (24.4%) switched of biological therapy once and 5 (2.4%) three or more times. Statistically significant differences were found in the obese males who switched of biological therapy in relation to obese males who not switched (35.6% vs. 11.1%). Accordingly, the percentage of patients with hyperlipemia that switched of biological therapy was significantly higher than those who did not (29.4% vs. 13.1%).

The number of evolution and diagnosis we also involved, so that patients with more years of evolution and more years from the diagnosis had a higher percentage of switched (p = 0.006 IC 95% -17.22, - 0.96 and p = 0.042 -18.32; -0.37 respectively).

CONCLUSION: Being obese male and with hyperlipidemia could be a risk factor that would condition the lack of response to a biological therapy and thus the need of switching to another.

REFERENCES
[3] Ganzetti G, Campanati A, Bettacchi A, Brandozzi G, Brisigotti V, Bugatti L, Escudero A, Escudero A. Effectiveness of dog-assisted therapies for people with Alzheimer’s or people with brain injuries, but all of them analyzed a reduced sample number (1) or did not show a good methodological structure (2). Regarding the reduction of pain and quality of life, different studies showed positive results in the use of assisted therapies with dog (6). However, this subject has not been evaluated yet in patients suffering Rheumatologic diseases.

OBJECTIVES: The main objective of this study is to evaluate the influence of companion animals on the perception of outbreaks in rheumatic diseases. Secondary objective: to analyze if having companion animals affected the general state of health or the degree of physical activity.

METHODS: Prospective descriptive study. Consecutive patients attending rheumatology consultation were recruited during the month of October 2018. Sociodemographic data were collected (age, sex, cohabitation with companion animals, type of exercise performed) along with Beck questionnaires to assess depression, SF-12 to assess quality of life, and VREM (Spanish Short Version of the Minnesota Leisure Time Physical Activity Questionnaire) to assess the degree of physical activity. Associations between variables were analyzed using a Chi-square and T student. P-values < 0.05 were considered statistically significant. The main variables: dog, cat and other animals, were analyzed separately and then unified in a new variable called companion animals. The spss v19 program was used for data analysis.

RESULTS: Seventy one patients were enrolled, of which 30 (42.3%) were male and 41 (57.7%) were female. The mean age (SD) was 58.7± 15.31 years. Thirty two patients (45.1%) suffered rheumatoid arthritis, 8 (11.3%) spondyloarthritis, 8 (11.3%) osteoarthritis, and patients with fibromyalgia, becet, gout and scleroderma were present in a lower percentage. Regarding the coexistence with companion animals, 19 (26.6%) lived with dogs and 7 (9.9%) with cats.

The results of this study did not demonstrate any significant relationship between the duration of the outbreaks, the depressive state or the degree of physical activity and the coexistence with companion animals. However, statistically significant differences were found in the quality of live perceived by patients living with dogs in relation to patients without companion animals, so that we found higher scores in the mental SF-12 (56.5 vs 44), (p = 0.036, 95% CI - 24.41, - 0.80), the physical SF-12 (51.7 vs 39), (p = 0.042, 95% CI -25, -0.5) and total SF-12 (56.11 vs 43.85), (p = 0.016, 95% CI 22.4, -2.2).

CONCLUSION: Coexistence with dogs improves the perception of the quality of life of patients, both physically and mentally.

REFERENCES


Disclosure of Interests: None declared

COPING WITH INFLAMMATORY RHEUMATIC DISEASE AND FATIGUE: PATIENTS PERCEPTIONS OF THEIR NEEDS

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Disclosure of Interests: None declared

Acknowledgement: The authors would like to thank the patients who participated in this study.

REFERENCE


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Disclosure of Interests: None declared


THE SELF- AND SHARED-MANAGEMENT OF PAEDIATRIC-ONSET RHEUMATIC AND MUSCULOSKELETAL DISEASES BY CHILDREN, YOUNG PEOPLE AND THEIR FAMILIES: INITIAL FINDINGS FROM A THEORY-GLEANING PROCESS WITH PATIENT ORGANISATION REPRESENTATIVES

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Background: Encouraging children and young people (CYP) with rheumatic and musculoskeletal diseases (RMDs) and their families to adopt self-management behaviours from the point of diagnosis is likely to positively influence the long-term health and wellbeing of CYP. However, there is limited evidence of such interventions targeted at CYP and families.

Objectives: Therefore, the aim of this study was to identify What works, for whom, in what circumstances, and why.

Methods: The study was based on the logic of realist evaluation and the Individual and Family Self-Management Theory. Realist evaluation is a recognised model of theory-driven evaluation which enables an in-depth appreciation of how complex health interventions may or may not work in real-world settings. In this study, a realist evaluation was undertaken using qualitative research methods to explore and refine theories regarding self- and shared-management interventions. The realist evaluation began with a set of initial programme theories, which were initially tested through interviews with one group of stakeholders involved in providing self- and shared-management support. Interviews were transcribed individually and data were analysed in NVivo using a realist logic of analysis to identify contextual influencers, interventions mechanisms and outcomes.

Results: In order to refine and consolidate theories about the self- and shared-management of RMDs by CYP and their families, theory was gleaned from patient organisation representatives with experience of supporting CYP and families. Contextual influencers discussed included the characteristics of: i) individual CYP living with RMDs; ii) the family dynamic; iii) peer and social interaction among both CYP and families; iv) the educational environment; and v) Organisational processes and structures. Patient organisation representatives highlighted the family dynamic and navigating organisation processes and structures as key influencers on CYPs willingness and ability to begin their self-management journey in an age- and developmentally-appropriate manner.

Conclusion: Concepts gleaned during the first phase of the study, particularly around the influence of family dynamic, will be further tested, refined, and consolidated with other groups of stakeholders, including CYP with RMDs; families; healthcare professionals from the paediatric rheumatology multi-disciplinary team; school staff; and patient organisation representatives. In time, it is anticipated that the findings will form a programme specification detailing what works, for whom, in what circumstances, and why with regards to the self- and shared-management of paediatric-onset RMDs.

REFERENCES


Acknowledgement: This work is supported by a University of Leeds School of Healthcare studentship.

Disclosure of Interests: Simon Stones Consultant for: SS has provided consultancy services to Envision Pharma Group, though this is not related to the contents of this abstract., Speakers bureau: SS has under-taken speaking engagements for Actelion, eyeforpharma, Four Health, Janssen and Roche, though these are not related to the contents of this abstract.

**AB1412-HPR** CHANGES OF GAIT SPEED AND PAIN AFTER APPLYING KINESIOTAPE ON QUADRICEPS FEMORIS MUSCLE IN PATIENTS WITH KNEE OSTEOARTHRITIS

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**Background:** Knee osteoarthritis is a chronic degenerative disease, known as the most common cause of difficulty walking in older adults and subsequently is associated with slow walking. Functional decline, increased risk of falls and presence of pain are, in many studies, related to the muscle weakness caused by osteoarthritis especially weakness of the quadriceps muscles. Pain is very noticeable while walking in rugged terrain, during ascent and descent of stairs, when changing from sitting to standing position as well as staying in one position for a long time. Many studies have shown that the strength of the quadriceps femoris muscle can affect gait, by improving or weakening it. Kinesio Tape is a physiotherapeutic technique, which reduces pain and increases muscular strength by irritating the skin receptors.

**Objectives:** The aims of this study was firstly to verify if the application of Kinesio Tape on quadriceps femoris muscle decreases time needed to accomplish the 10 meter walk test in patients with knee osteoarthritis and also in subjects without knee osteoarthritis. Secondly if applying Kinesio Tape on quadriceps femoris muscle reduces pain while walking only in patients with knee osteoarthritis.

**Methods:** In this study we observed the change of gait speed with the help of the 10-meter walk test before, one day and three days after the application of Kinesio Tape in quadriceps femoris muscle. We compared the results of the gait speed in two groups. In the first group, the Patients group, participated 102 out-patients with a clinical diagnosis of primary knee osteoarthritis, while in the second group, the Control group, participated 73 subjects with a main excluding criterion a clinical diagnosis of primary knee osteoarthritis. Secondly, we observed the change of pain, while walking for 10 meters at normal speed for the Patients group, before one day and three days after the application, with the help of Numerical Pain Rating Scale - NRS.

**Results:** Our results indicated that there was a significant increase of gait speed in both groups while walking for 10 meters three days after application of Kinesio Tape on quadriceps femoris muscle. However there was not a significant change one day after the application of Kinesio Tape compared before its application in both groups. Also, there was a significant reduction of pain level 1 and 3 days after application of Kinesio Tape, compared to the level of pain before its application.

**Conclusion:** Our results indicated that there was a significant decrease of time needed to accomplish the 10 meter walk test and also a significant decrease of pain while walking for 10 meters, Kinesio Tape is a technique that can be used especially when changing walking stereotypes is a long term goal of the treatment.

**REFERENCES**


Disclosure of Interests: None declared


**AB1413-HPR** FACTORS AFFECTING ACTIVITIES OF DAILY LIVING IN WOMEN INDIVIDUALS WITH SCLERODERMA

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**Background:** Scleroderma is a multisystemic chronic disease with hand involvement in many patients and responsible for marked disability. Patients with scleroderma have reduced ability to perform activities of daily living (ADL) and several factors may be associated with difficulties in ADL and impairment of upper extremity functions.

**Objectives:** Aim of this study was to indicate the relationship among activities of daily living and pain, fatigue, disease severity, upper extremity strength and functional disability in patients with scleroderma and to identify the factors affecting activities of daily living in individuals with scleroderma.

**Methods:** Thirty five women individuals with scleroderma with mean age 56.46 ± 10.45 were included into the present study. The activities of daily living was evaluated with Miliken ADL questionnaire, pain with visual analog scale (VAS), fatigue with fatigue severity scale (FSS), disease severity with modified Rodnan score (MRS), upper extremity strength with handgrip strength and functional disability with Health Assessment Questionnaire (HAQ). The relationships among the variables were analyzed by the Spearman correlation test. Correlation coefficients between Miliken ADL and other variables were determined by linear regression. The statistics were analyzed by SPSS 23.0 version.

**Results:** The Miliken ADL did not significantly correlated with MRS and VAS (p > 0.05), whereas Miliken ADL did significantly correlated with handgrip strength (r = 0.680, p < 0.001), FSS (r = -0.729, p < 0.001), HAQ (r = -0.867, p < 0.001). Additionally, handgrip strength, fatigue severity scale and HAQ were significant and independent determinants for activities of daily living, accounting for 95.0% of the variance in Miliken ADL in patients with scleroderma.

**Conclusion:** The findings of this study show that scleroderma patients daily life is affected by the disease at different levels. Impaired hand function and difficulties in the performance of ADL are common in scleroderma and may influence an individuals functional disability. Therefore, provide therapeutic interventions at the optimal time it is important to follow the development of these factors in the early stages of the disease.

**REFERENCES**


Disclosure of Interests: None declared

AB1414-HPR  PATIENTS’ EXPERIENCES OF FATIGUE IN AXIAL SPONDYLOARTHRITIS

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Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory arthritis that predominantly affects the spine and the sacroiliac joints. Fatigue is recognised as a central axSpA symptom. AxSpA fatigue is under-explored and often not addressed. Attention in clinical practice seems to be focused on pain and disease activity.

Objectives: The objectives of this study were to explore the meaning, contributing factors and the impact of fatigue on the axSpA patients. Self-management and the role of clinicians were also explored.

Methods: A qualitative phenomenological approach was used. A purposive sample of 10 patients with axSpA, who were experiencing fatigue (≥7cm on a 10cm VAS scale and attending a specialist rheumatology clinic were selected. The participants completed a demographic questionnaire, the Bath ankylosing spondylitis disease activity index (BASDAI) and the Bath ankylosing spondylitis functional index (BASFI) outcome measures. Semi-structured interviews using open-ended questions lasted 30-60 minutes. Interviews were tape-recorded and transcribed verbatim. Data was analysed using Colaizzi’s framework. Two independent reviewers and 5 participants reviewed the data.

Results: Five males and five females were selected to participate in the study. The mean age was 46.6 years (29 - 69). Seven participants were working. The mean BASDAI was 5.4 and mean BASFI was 5. Most of the participants had disease duration of longer than 5 years. The six themes that emerged from the data are:

1. The meaning of fatigue
2. Fatigue patterns
3. Factors that modulate fatigue
4. The impact of fatigue
5. Self-management of fatigue
6. Professional support

Fatigue was defined as an unpredictable, extreme and persistent tiredness. Fatigue had a cognitive and physical component, which was not related to physical activity and did not resolve by rest or sleep. Fatigue was distinguished from tiredness. Tiredness was perceived as a normal feeling which occurred after physical activity and was resolved by rest or sleep.

The severity, duration and frequency of fatigue varied. Fatigue was described as having a multi-factorial aetiology. Fatigue had an overall negative impact upon patients lives affecting their quality of life, leading to psychological and emotional consequences. Participants struggled to self-manage fatigue, receiving no support from health care professionals.

Conclusion: This research has contributed to a better understanding of the patients experiences of axSpA fatigue. Fatigue was described as a huge burden and life-changing. AxSpA fatigue should be acknowledged in clinical practice. AxSpA patients should be asked about fatigue during their clinical consultation. Fatigue should be addressed in its own right and independently from pain and disease activity.

Disclosure of Interests: None declared


AB1415-HPR  PATIENTS PERSPECTIVES ON SELF-MANAGEMENT OF AXIAL SPONDYLOARTHRITIS FATIGUE

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Background: Axial spondyloarthritis (axSpA) is a chronic inflammatory arthritis that mainly affects the axial skeleton and can lead to bony ankyloses. Pain, stiffness and fatigue are the most frequently axSpA-reported symptoms. AxSpA fatigue is multidimensional incorporating physical, psychological and social components, implying that self-management strategies are crucial.

Objectives: This study aimed to explore the self-management of axSpA fatigue. Patients perceptions of whether clinicians give importance to axSpA fatigue were also explored.

Methods: A qualitative phenomenological approach was used. A purposive sample of 10 patients with axSpA, who were experiencing fatigue took part in either a focus group or support day. The focus on the patients’ experiences of axSpA fatigue. Fatigue was not addressed in the clinical setting. Participants felt that they were not guided and supported enough to manage fatigue. More information was needed from health care professionals (HCP) on fatigue management. There was a feeling that HCP focused on the management of pain rather than fatigue.

Conclusion: This research highlighted a clear lack of knowledge about self-management skills to manage axSpA fatigue. Lack of adjustments and coping with fatigue was prominent even in patients who had long disease duration. Furthermore, fatigue was not addressed in clinical practice.

Understanding patients beliefs is an important step towards guiding them to self-manage fatigue. Patients should be guided in implementing self-management plans that would fit their goals, priorities and lifestyle. Self-management is important in improving health outcomes and quality of life.

Disclosure of Interests: None declared


AB1417-HPR  A REVIEW OF PUBLIC PATIENT INVOLVEMENT AND ENGAGEMENT (PPI/E) AT THE ARTHRITIS RESEARCH UK CENTRE FOR ADOLESCENT RHEUMATOLOGY AT UCL, UCLH AND GOSH

James Wilson1, Caitlin Clifford1, Hema Chaplin1, Despina Eleftheriou1, Anna Radrzewska1, Jozianna Curnin1, George Robinson1, Lucia Martin1, Emma Gutierrez1, Deballi Sen1, 1 University College London, Rheumatology, London, United Kingdom; 2 UCL Institute of Child Health, III, London, United Kingdom; 3 University College London Hospital, Adolescent Rheumatology, London, United Kingdom

Background: The adolescent and young adult (AYA) rheumatology clinical service has a well established culture of involving our users in shaping how services are delivered. Since its inception in 2012 the Arthritis Research UK Centre for Adolescent Rheumatology has worked to offer every patient within the clinical service the opportunity to participate in research.

Objectives: This was achieved by 2015 and from 2014 we renewed our focus on an active involvement programme to promote the role of young people in prioritising and designing our research agenda and workstreams. We are currently developing our strategy for the next five years and reviewing our experience to date.

Methods: PPI/E activity records were searched for the period October 2014 to April 2016. This included number of patients involved, their age and diagnosis, and the type of activity along with the number of times they have been involved.

Results: 19 PPI/E activities were organised. From a total of 1554 adolescent and young adult patients 150 patients having been involved in PPI/E the age range was 11-27 and 118 were female.

The activities consisted of focus groups (79%) and support days (11%) all but two of which were disease specific groups.

The disease specific PPI/E activities have been focused on JIA, JSLE, and JDM. The number of patients involved in these activities were 24.62% (n=99), 24% (n=17) and 66% (n=25) respectively. The mean instances of involvement per disease were 2.09 for JIA, 2.53 for JSLE and 3.96 for JDM.

Conclusion: Our results show that many of our patients have taken part in PPI/E activities (11.19%) with over 65% of our JDM patients having taken part in either a focus group or support day. The focus on
inflammatory rheumatic disease is in keeping with the stated aims of our Centre. The mean instances of involvement ranging from 2.09 to 3.56 suggest that patients feel PPVE is worthwhile. We aim to share our results with the young people who have driven this work and will consider how we might move forward. We aim to consult with the group of patients we serve who have not been part of this process to date.

Disclosure of Interests: None declared

HPR Professional education, training and competencies

AB1417-HPR  RHEUMATOLOGY NURSE PRACTICE: EDUCATION TO IMPROVE THE UNDERSTANDING OF RHEUMATIC DISEASES

Linda Grinnell-Merrick1, Iris Zink1, Elizabeth Kirchner1, Jacqueline Fritz1, Monica Richey2, Cathy Patty-Resk1, Carrie Beach1, Vickie Sayles1, Eileen McCullagh1, Eileen Lydon1, Sheree Carter1, Scott Kober2.

Rheumatology Nurse Practice. Looking at the Horizon: What Does the Future Hold in the Treatment of Rheumatoid Arthritis?

Methods: Each print issue contained a combination of evidence-based content related to the main theme, along with a series of individual essays written by faculty members. These essays all linked to the main theme of the issue. Live broadcasts were intended to bring a real-life, case-based perspective to the education.

Results: Improvements of >25% in both knowledge and competence were found in any of patient outcome variables between the groups post treatment in both groups (p<0.05). However, no significant differences were found in any of patient outcome variables between the groups (p>0.05).

Conclusion: We could report that mobile-phone-based home exercise training program decreases systemic inflammation in COPD: a pilot study.

REFERENCES

Disclosure of Interests: None declared

HPR Service developments, innovation and economics in healthcare

AB1418-HPR  MOBILE-PHONE-BASED HOME EXERCISE TRAINING PROGRAM IN PATIENTS WITH KNEE OSTEOARTHRITIS

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Background: Most rehabilitation programs are hospital-based and rely on regular supervision (1). However, mobile health technologies such as smartphone applications may provide lower-cost ways to monitor and train the patients (2). We have developed a mobile-phone application for monitoring and training the patients at home.

Objectives: The purpose of this study was to compare a mobile-phone-based home exercise training program along with supervised physiotherapy program to a brochure-based home exercise training program along with supervised physiotherapy program in patients with knee osteoarthritis. We hypothesized that the patients who received mobile-phone-based home exercise training program along with supervised physiotherapy program over 3 weeks would have better balance, quality of life and less pain and disability score versus the patients who received brochure-based home exercise training program along with supervised physiotherapy program.

Methods: This was a randomized, prospective, comparative clinical study. The study included 40 patients, aged 45-65 years, who diagnosed with a grade 2-3 knee osteoarthritis. The patients were randomly divided into two groups. While one group (n=20) received a mobile-phone-based home exercise training program along with supervised physiotherapy program, the second group (n=20) received a brochure-based home exercise training program along with supervised physiotherapy program as 15 sessions for a total of three weeks, five sessions per week. Pain intensity, balance, disability, and quality of life were measured with Visual Analogue Scale, Berg Balance Scale, WOMAC, and SF-36, respectively. All of the assessments procedures were performed again after the treatment.

Results: There were statistically significant improvements in measures of pain intensity, balance, disability, and quality of life between pre- and post treatment in both groups (p<0.05). However, no significant differences were found in any of patient outcome variables between the groups (p>0.05).

Conclusion: We could report that mobile-phone-based home exercise training program is not superior to brochure-based home exercise training program in terms of patient outcomes over 3-week program.

REFERENCES

Disclosure of Interests: None declared
EFFICIENCY OF INDIVIDUAL STEEL ORTHESIS IN
THE USE OF SUBCUTANEOUS METHOTREXATE IN
MANAGEMENT OF INFLAMMATORY ARTHRITIS

Methods: During the year, under our supervision there were 156 patients aged from 32 to 67 years. Gender composition - 123 (79%) - women, and 32 (21%) - men. The average time between the onset of clinical symptoms and the first day of treatment was 134 days. The average spur size was 4.3 mm. In 80% of patients, a history of pain lasted for more than 3 months. Patients were divided into 2 groups. The experimental group (G1) used individually manufactured insoles (78 people: 61 - women, 17 - men). The control group (G2) used factory insoles (78 people: 58 - women, 20 - men). 152 patients (98%) completed the protocol: 78 (100%) in G1 and 74 (96%) in G2. The criterion for inclusion in the study was the diagnosis of the heel spur. The diagnosis was made based on anamnesis, ultrasound of the plantar aponeurosis, and radiography of the heel region. The exclusion criteria were patients with heel spurs without heel pain, as well as systemic diseases: rheumatoid arthritis, diabetes mellitus, and severe vascular pathology. The degree of longitudinal flat-footedness, stability of the foot, individual deformities of the feet were clinically evaluated using clinical and functional methods and the method of vacuum trace modeling [2]. Individual insoles were made based on frame materials in the projection of the arches of the foot. Dense materials maintain a constant tension of the plantar aponeurosis. G1 patients were made full contact insoles with a correction of the transverse arch, without adding relief elements under the heel. The control group used factory-made insoles from different manufacturers, with soft elements under the heel. Measurement parameters: average pain intensity on a VAS scale; duration of pain throughout the day; distance traveled; subjective comfort when using insoles. The observation period is 12 calendar months.

Results: The average VAS score in G1 decreased from 5.4 ± 0.3 at the beginning of the study to 1.01 in 62 patients (81%). 15 patients reported pain reduction, the average VAS score was 2.1 ± 0.3. Complete relief of G1 pain has been reported in patients with an osteophyte size of less than 5 mm. G1 patients regained their usual movement distance of 3.9 km per day. Cases of recurrence of heel pain is not recorded. No patients experienced discomfort from the use of insoles throughout the entire period of adaptation. In G2, the VAS score decreased from 5.6 ± 0.3 at the beginning of the study to 2.9 ± 0.3. Patients of the G2 group were able to increase the distance of movement to 1.2 km per day.

Conclusion: When using individual insoles, 93% of patients reported complete relief of pain. 7% of patients noted a significant reduction in pain. The use of individual insoles in the treatment of plantar fasciitis made it possible to reduce pain in a shorter time.

REFERENCES

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.8007

THE USE OF SUBCUTANEOUS METHOTREXATE IN
INFLAMMATORY ARTHRITIS: TRANSLATING
RESEARCH INTO PRACTICE USING QUALITY
IMPROVEMENT METHODOLOGY.

Aicha Bouraoui1, Evgenia Guryanova2, Chuvash State University, Cheboksary, Russian Federation, Chuvash State University, Rheabilitation, Cheboksary, Russian Federation

Background: The most common cause of heel pain is the heel spur, which is 75% of patients with heel pain. The intensity of the pain does not depend on the size of the spur, as determined on the radiographs. Often sharp in shape and large in size, the spurs are a random X-ray finding. At the same time, severe pains in the heel region are possible with a normal radiograph [1].

Objectives: The purpose of this study is to establish the effectiveness of the treatment of patients with pain syndrome in the heel spur, by affecting the main components of the pathogenesis of individually manufactured orthopedic insoles.


Results: The majority of patients with inflammatory arthritis should have trial of s/c methotrexate before starting biologics unless there is contraindication. We reviewed the data of 50 patients to assess management of patients with IA using our biologic register. We used the 5 why strategy to have better understanding of the lack of prescribing of s/c mtx and variations in clinical practice. By applying improvement science we standardized our pathway, included methotrexate s/c trial prior to biologics. We also conducted a number of interventions including multidisciplinary educational events and one to one meetings, we mobilized and organised our resources in better way to meet our patients needs. We monitored our data over time and reviewed our practice accordingly.

Conclusion: In summary, our baseline data showed poor use of s/c Mtx in patients with IA despite the growing evidence of its benefit. In order to translate research findings into practice we used 5 whys methodology to have better understanding of the barriers within our systems, we applied QI methodology and standardized our practice for better use of resources at lower cost.

REFERENCES

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.8298

VIRTUAL CLINICS IN THE PRESENT- A PREDICTOR FOR THE FUTURE?

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Background: There is great interest in non face to face (F2F), Internet or app based patient interact at the moment. As these become established, we look at the non F2F appointments already happening in telephone and virtual clinics in a busy urban rheumatology department. Here we look at the type of diagnoses dealt with in a non F2F environment and potential outcomes from these non F2F appointments.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2021-eular.8007

AB1419-HPR

AB1420-HPR
Objectives: To assess the efficiency and utilization of virtual and telephone clinics in a general rheumatology department.

Methods: Data was collected from electronic (Cerner) patient records on 240 patients who had a virtual appointment in May 2018. The data was analysed using Excel 2010.

Results: 240 patients had virtual appointments in one month. 121 (50.4%) were via telephone and 119 (49.6%) via patient letter. 34 (14.1%) patients had multiple virtual/telephone appointments. 129 (54%) were carried out by consultants, 78 (32%) by nurses and 33 (14%) by registrars. 37% had rheumatoid arthritis. 32 (13%) appointments lead to a prescription. Virtual appointments produced 44 referrals, including 18 to another specialty, 16 to physiotherapy, and the rest to hand therapy or podiatry. Most patients had a F2F appointment before and after their virtual appointment in May 2018. 1 patient had died before having a second face to face appointment and 13 (5%) were discharged from their virtual appointment.

Conclusion: Consultants undertook the bulk of virtual clinics, and these appointments resulted in the majority of referrals and prescriptions. Virtual appointments reduce the waiting times for contact with a healthcare professional between appointments. Many patients had several virtual appointments between face to face appointments and this cohort may benefit from more scrutiny. Current technology already improves communication and leads to significant changes in patient care without requiring face to face appointments.

Appointments reduce the waiting times for contact with a healthcare professional between appointments. Many patients had several virtual appointments between face to face appointments.

Disclosure of Interests: None declared


Abstract AB1421HPR Table 1. The mean number of days between each type of appointment.

<table>
<thead>
<tr>
<th>Appointment Type</th>
<th>Mean Number of Days</th>
</tr>
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<tbody>
<tr>
<td>From 1st Face to Virtual Face</td>
<td>44</td>
</tr>
<tr>
<td>From Virtual Appointment to 2nd Virtual Face</td>
<td>53</td>
</tr>
<tr>
<td>From 1st Face to 2nd Face</td>
<td>94</td>
</tr>
</tbody>
</table>

Conclusion: Consultants undertook the bulk of virtual clinics, and these appointments resulted in the majority of referrals and prescriptions. Virtual appointments reduce the waiting times for contact with a healthcare professional between appointments. Many patients had several virtual appointments between face to face appointments and this cohort may benefit from more scrutiny. Current technology already improves communication and leads to significant changes in patient care without requiring face to face appointments.

Disclosure of Interests: None declared


Abstract AB1422-HPR MODERATE AND HIGH ADHERENCE TO A DISEASE MANAGEMENT MODEL IN PATIENTS WITH RHEUMATOID ARTHRITIS IMPROVES CLINICAL RESULTS IN A BIG UNICENTRIC COHORT

Laura Villareal1, Fernando Rodriguez2, Michael Cabrera3, Pedro Santos-Moreno4.

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Background: Rheumatoid arthritis (RA) is an inflammatory, chronic disease of unknown etiology. Usually it leads to deformity and destruction of joints through the erosion of cartilage and bone. Over 90% of patients with RA report to suffer symptoms in hands and joints, swelling, loss of motion, muscle weakness among others. These symptoms affect all aspects in a patients life. Therefore, management of a patient with RA should not only include evaluate outcomes related to the rheumatology specialty, on the contrary, aspects such as physical disability, nutrition, mental health, among others should be taken into account. Centers of excellence in rheumatoid arthritis have proposed a multidisciplinary model of care with an initial diagnosis, treatment prescription and follow-up with a rheumatologist, periodic consultations with a physiatrist, psychologist, physiotherapist, occupational therapy nutrition, and, a patient focused program. With a multidisciplinary model of care the patient is seen as a whole, and the expectation is to achieve the best results in the management of RA.

Objectives: The aim of this research was to define adherence/attendance to a multidisciplinary model of care for patients with RA that attend to a RA specialized center in Colombia.

Methods: We implemented the center of excellence model program proposed by REAL-PANLAR group in 2015 (3). In order to define adherence to the multidisciplinary model the authors performed an informal expert consensus to propose a model to measure adherence to the model. The authors proposed three levels of adherence. We proposed three levels of adherence as follows: High adherence: For rheumatology patients had to attend between 6 and 12 consultations in one year. For physical therapy, physiatry, psychology, occupational therapy and nutrition patients had to attend to 3 or more consultations during one year per each specialty. Moderate adherence: For rheumatology patients had to attend between 3 and 5 consultations in one year. For physical therapy, physiatry, psychology, occupational therapy and nutrition patients had to attend to 2 or 4 consultations during one year per each specialty. Low adherence: For rheumatology patients had to attend between 1 and 2 consultations. For physical therapy, physiatry, psychology, occupational therapy and nutrition patients achieved only 1 consultation or less during one year per each specialty. We performed a descriptive analysis and compared the level of adherence and disease activity.

Results: During 2018 we reviewed the medical charts of 6851 patients diagnosed with rheumatoid arthritis; 82% were female and 18% were male. Mean age was 59 years 13 years old. Regarding disease activity mean DAS28 was 2.69 0.84. Most of patients that were considered as Moderate or High adherent achieve remission or LDA. See table 1. Levels of Adherence in Patients with RA

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Conclusion: This is an initial approach in order to evaluate patients adherence and attendance to a new implemented multidisciplinary disease management model of attention for patients with RA in Colombia. Our descriptive study demonstrated that patients with moderate or high adherence can achieve better clinical outcomes compared to those who aren’t adherent to the model.

Disclosure of Interests: Laura Villareal: None declared, Fernando Rodriguez: None declared, Michael Cabrera: None declared, Pedro Santos-Mereno Grant/research support from: Dr Santos has received research grants from Janssen, Abbvie and UCB, Speakers bureau: Dr Santos has received speaker fees from Sanofi, Lilly, Bristol, Pfizer, Abbvie, Janssen and UCB


Abstract AB1423-HPR ELICITING THE AGENDA OF PATIENTS WITH MUSCULOSKELETAL DISORDERS; THE PHYSIOTHERAPIST-PATIENT INTERACTION

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Background: Eliciting main concerns via interview is important for patient-centered care and for planning individualized rehabilitation program (1, 2). Recently, it has been shown that clinicians often fail to elicit the patients agenda and, when they do, they interrupt the patients discourse (3). However, the prevalence of agenda setting in physiotherapy as a health care provider and the physiotherapist-patient interaction remains relatively unexplored.

Objectives: The aim of this study was to describe agenda elicitation in rehabilitation, to determine the frequency of encounters in which physiotherapists elicited the patients with musculoskeletal disorders agenda, the proportion and timing of interrupted answers.

Methods: An audio-recording analysis of 52 clinical encounters recorded during first physiotherapist-patient interaction were performed. The elicitation of the patient agenda characteristics as the time to interruption or to complete statement were analyzed.

Results: Physiotherapists elicited the patients agenda in all (96.1%) clinical encounters. Interestingly, in those encounters in which physiotherapists elicited patient concerns, the clinician interrupted the patient after a median of 15 seconds (interquartile range 6 to 22 seconds). In the uninterrupted encounters in which physiotherapists elicited patient concerns, the patients with musculoskeletal disorders was state their agenda in 241.45 seconds.

Conclusion: Physiotherapist emphasize to elicit the patients agenda, however, they interrupt expression very sooner. Eventually, the failure to elicit the patients agenda inhibits the physiotherapists-patient communication and this would lead to failure to plan rehabilitation program based on the needs of each patient.

REFERENCES

*EFFECTING A CHANGE AS A PATIENT INSIGHT PARTNER*

Stephanie Skelfington1, Emma Dorris2, 1University College Dublin, Patient Voice in Arthritis Research, Dublin, Ireland; 2University College Dublin, Centre for Arthritis Research, Dublin, Ireland

**Background:** In my patient advocacy work I had experience in every aspect except research, so it was an opportunity to talk to another or former PIP to build my PPI within UCD CAR.

**Objectives:** To prepare patient insight partners (PIPs) with no or limited experience of PPI there should be an opportunity to talk to another or former PIP about their experience or perhaps a leaflet detailing such experience which can be given to new PIPs. This is something not currently done within UCD, but, in response to my suggestion, Im working with UCD CAR to produce.

**Methods:** A personal perspective

**Results:** My formal involvement in this project started with my being invited to be a member of the interview panel choosing the postdoctoral researcher for the project. My remit was to ask the candidates about the impact of the project beyond just the science aspect, to try to figure out who just wanted a job, and who was interested and passionate about this project. I was not only choosing someone for the position but someone I was committing to work with for three years.

One of my first tasks was to act as a mentor in plain English to help the chosen researcher prepare a lay summary of the project. This helped both of us get to grips with the project and its objectives, as well as working out our working dynamic. I work most closely with the project researcher, who has worked in rare disease but not in rheumatology. She has been very receptive and not only took an interest in learning more about the disease area but me as well. I was introduced me to her first as a mentor, and second as a patient advocate. This helped us get to know each other and opened discussions including how PPI could aid her work and how invaluable it is from the patient perspective. This has given our relationship a great start and in a relatively short period we have built the great foundations for an excellent working relationship on a project we are both share a passion for.

For the researchers, to improve the process of PPI I would like some honest feedback on my performance as a patient insight partner. It may not be every patients ideal, but PPI is a knowledge exchange and we learn from each other even more along the way. The reciprocal learning nature of this blog is the number one reason for its creation.

**Conclusion:** Anyone thinking about being a PIP should be aware of how important it is to share their expert knowledge in such as setting and shouldn’t let their fear or perceived lack of knowledge hold them back. They should be willing to be an equal and expect to be treated as such and be willing to contribute fully to the knowledge exchange process including giving honest constructive feedback.

Despite this relationship still being quite new we have plans to grow and build my PPI within UCD CAR.

Disclosure of Interests: None declared

The Global Osteoarthritis Patient Perception Survey (GOAPPS)-The First Global Survey to Directly Compare Patient Perceptions Regarding Their OA Care: A Pilot Study

Angie Botto-van Benden1, Guy Eakin1, Rosa Scortino1, Maritza Quintero1, Jordi Monfort3, Patrick du Souich4, Francisco de Abajo5, Ingrid Müller6, Elke van Delft1,2, Harold van Garderen3, Rob Braamburg1, Raymond Pieters4.

Background: Globally, osteoarthritis (OA) is the third condition associated with disability. Science holds the key to finding better treatments and a cure. Still, it is essential to learn what is important to patients from the patients to implement the most effective global management of OA. The International Osteoarthritis Task Force, an initiative of the Osteoarthritis Foundation International (Barcelona, Spain) and the Arthritis Foundation (Atlanta, United States) with participation from member organizations in additional countries created the Global Osteoarthritis Patient Perception Survey (GOAPPS) - the first global survey to directly compare quality of life (QoL) & patient perceptions of care in the same OA patient survey across languages and cultures.

Objectives: The goal of the survey was to help all stakeholders in OA healthcare develop a better understanding of patients perceptions and how they may differ between cultures by collecting data on adult OA patient perceptions regarding their OA care. The survey will also collect data on patient demographics, OA symptomology, and impact of OA on daily functioning and QoL. Understanding patients needs and perceptions of care is the first step in optimizing global OA management.

Methods: Observational, cross-sectional study by online survey data collection translated into three languages. We collected data on patient demographics, symptomology, OA impact on daily activity and QoL to investigate the relationship between patient perceptions of their OA care, symptoms and impacts, and QoL. The questionnaire comprised of 4 sections: clinical characteristics, relationship with physicians and treatment, perception of attention, treatment and information received and auto-evaluation of QoL. Inclusion criteria included resident age 18 or older with an OA.

Results: A total of 1485 surveys were completed from 7 countries. 1264 surveys were answered in English, 218 in Spanish and 3 in Italian; analysis of cultural differences was unable to be carried out in this pilot. Data show that the majority of the respondents were female (90%) and more than 55 years of age (82%). The majority (73%) of patients had knee OA, followed by hand (57%) and spine (54%). Comorbidities included hypertension (50%) and obesity (43%). Nearly all patients reported limitations related to physical activities (97%), followed by work activities (49%), social interaction (43%) and sex life (23%). 37% of patients experience emotional or mental health issues. The 58% says their doctor adequately explained their diagnosis and 55% understand the treatment options. Importantly, 41% of respondents are not satisfied with their OA treatment and 79% would like access to non-drug/non-surgical treatments. While 52% of respondents rate their QoL as good, 95% would rate it better if their OA was eliminated.

Conclusion: The results emphasize the significant impact of OA disease on patients daily activities and their desire to play an active role in managing their disease. Notably the majority asks for access to additional options for non-drug/non-surgical treatments stressing the need for an OA management improvement. This is a pilot survey and the results do not permit analysis of cultural differences. Continued survey distribution & analysis will determine differences in patient perception of QoL between OA patients living in different countries to further optimize global OA management.

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AB1427-PARE PATIENTS AS RESEARCHERS OF TIETZES SYNDROME AND COSTOCHONDRITIS USING PARTICIPATORY NARRATIVE METHODS OF INQUIRY

Elke van Delft1,2, Harold van Garderen3, Rob Braamburg4, Raymond Pieters4.

1 Association of Tietze and costochondritis patients, Heukelum, Netherlands; 2 Maassstad Hospital, Rotterdam, Netherlands; 3 StoryConnect, Wageningen, Netherlands; 4 University of Applied Sciences Utrecht, Utrecht, Netherlands

Background: Tietzes syndrome and costochondritis are rare, inflammatory rheumatic disorders characterised by chest pain. Pain is most commonly localised unilaterally at the costochondral junctions, with more than one junction generally affected (1). Whereas the conditions are considered self-limiting and in two-thirds of the cases resolve within one year (2,3), they can last up to several years or be recurring (4), limiting the patients ability to function in occupational demands and activities of daily living. The exact cause is not known and therefore it remains a challenge to take on an effective treatment approach.

Objectives: This study aims to gain more insight into patients and medical professionals experiences with and handling of Tietzes syndrome and costochondritis.

Methods: It was noticed that hardly any research is done on Tietzes syndrome and costochondritis and hardly any medical professionals are specialised in these conditions. This sparked the idea to involve patients themselves as researchers of the conditions. To that end an online platform called a StoryPoint was designed, based on the Participatory Narrative Inquiry (PNI) approach (5). This StoryPoint allowed patients and medical professionals to anonymously share and do research on their personal experiences with the conditions. This online assessment was followed by a live meeting with patients suffering from Tietzes syndrome or costochondritis. During this meeting the online gathered narratives were evaluated using group narrative evaluation methods (5).

Results: In total 53 experiences were retrieved. Approximately 60% of patients experienced complaints on a daily basis (figure 1). The reported limitations in daily living were inability to perform physical exercise, a lack of energy and incommprehension from the environment.

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Treatments advised by specialists that relieved complaints were physical therapy, breathing techniques and NSAIDs. Relaxation, low impact movement and warmth were solutions that patients initiated themselves and were perceived helpful. Of all treatments advised by a medical professional, 70% improved complaints, 22% had no effect at all, and 8% worsened the complaints (figure 2). Of the treatments that patients initiated themselves, 76% improved complaints and 22% had no effect (figure 2). We are currently involving a wide variety of medical professionals and researchers for further evaluation of the narratives.

**Conclusion:** Tietzes syndrome and costochondritis can be very limiting conditions, especially when complaints become chronic. Treatments advised by medical professionals are hardly any more effective than treatments initiated by patients themselves. Since both conditions are rare and relatively unknown, medical specialists have difficulties recognising, diagnosing and treating these conditions. It is important that medical professionals become more familiar with Tietzes syndrome and costochondritis and become involved in this type of patient-driven research approaches.

**REFERENCES**


**Disclosure of Interests:** None declared


**REFERENCES**


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**Disclosure of Interests:** None declared

Arthritis research

CANNABIS-BASED PRODUCTS FOR MEDICINAL USE: EXPLORING THE VIEWS AND EXPERIENCES OF PEOPLE WITH FIBROMYALGIA

Simon Stones 1,2,3, Des Quinn4, Fibromyalgia Action United Kingdom, 1University of Leeds, School of Healthcare, Leeds, United Kingdom; 2Fibromyalgia Action United Kingdom, Paisley, United Kingdom; 3European Network of Fibromyalgia Associations, Hest-op-den-Berg, Belgium

Background: A review by the Chief Medical Officer (CMO) of the United Kingdom (UK) in 2014 recommended moving cannabis-based products (CBP) from Schedule 1 of the Misuse of Drugs Regulations 2001 into Schedule 2, allowing CBP to be prescribed for medicinal purposes under controlled conditions by doctors on the Specialist Register of the General Medical Council. This prompted the National Institute for Health and Care Excellence (NICE) to develop guidance on prescribing CBP for medicinal use, which Fibromyalgia Action UK were invited to comment on. Anecdotally, we know that some people with fibromyalgia use CBP to help with pain relief; however, we wanted to explore these experiences further, while summarising people’s thoughts of the draft scope guidelines.

Objectives: The aim of the survey was to understand experiences of CBP among people with fibromyalgia, including people’s opinions of the NICE draft scope guidelines.

Methods: An online survey, hosted through Microsoft Forms, was disseminated via social media and Fibromyalgia Action UK’s website between November and December 2018.

Results: A total of 69 people initially responded; with 66 eligible to participate. The average time to complete was 14.05 minutes. Over three-quarters (77%) reported using CBP. The types of CBP that people had used are shown in Fig 1. Over half reported using Cannabidiol (CBD)/Hemp oil (55%), currently marketed as a food supplement. Around one quarter (26%) used herbal cannabis, with few reporting use of plant-derived/synthetic delta-9-tetrahydrocannabinol (THC) or THC/CBD sprays (3-5%). Of the 50 who responded, 52% reported using CBP for medicinal purposes on a daily basis; 28% stated they used CBP during a fibromyalgia flare. While some people did not report any benefits, one of the clear benefits reported by people was pain relief. People also reported improved sleep and mood, less fatigue, and reduced anxiety. When asked to score the current NICE draft scope guidelines, 48 people responded, with an average rating of 3.88 (1=very poor; 5 = excellent). Some felt that the scope was quite vague, difficult to digest, unclear as to who should and shouldn’t be prescribed CBP, and lacked specific reference to conditions like fibromyalgia. There were also concerns in the time it takes to develop guidance. When asked about confusion among society distinguishing CBP for medicinal purposes from food supplements marketed as CBD/Hemp oil, of 63 respondents, 86% felt there was confusion which needs addressing. Individuals felt that alternative treatment options like CBP should be available to people with fibromyalgia, with additional research to identify the evidence for its potential benefit and safety.

Conclusion: The survey highlights that people with fibromyalgia are using CBP, but not necessarily those that are prescribed by a medical professional. There is an appetite among patients with fibromyalgia to explore the option of alternative treatment using CBP. There is widespread confusion among society distinguishing CBP from CBD/Hemp oil marketed as food supplements, which could be leaving certain individuals vulnerable. The development of national guidance is welcomed; however, investment in research to prove the efficacy and safety of CBP in people with fibromyalgia is also needed, to ensure that patients have appropriate access to safe treatments.

REFERENCES

Best practice campaigning

ME AND MY DILEMMA – A DANISH CAMPAIGN

Connie Ziegler, Gigførgenringen – Danish Rheumatism Association, Gentofte, Denmark

Background: The Danish Rheumatism Association wanted to raise awareness on the challenges people face on a daily basis living with an invisible disease like some RMDs. In addition, the fact that many people are living with a RMD experience that their surroundings have a lack of understanding the daily struggles they have living with a chronic disease.

Objectives: We wanted to increase the general awareness of RMDs and to show our presence in another context than expected. In addition, the campaign should open up for some difficult talks in an entertaining way giving people an occasion to continue the talks at home. Finally the campaign should show that RMDs are not only related to old people and that consist of a wide range of different stories about living with RMDs. Just getting the word out about a disease that rarely receives a lot of focus in the public.

We received about 100 dilemmas, most of them we had to moderate a lot in order to be real dilemmas that could be discussed, have pros and cons and also to make sure that there was a variation in age, gender, diagnose and subject. Between 200-300 people attended each show, which was less than we expected, however Denmark experienced one of the warmest months of May ever and since the shows were planned inside the malls that explained the limited attendance.

The people who did attend the shows were all in the target group, having either a RMD or were related to someone with a RMD.

Conclusion: It was quite a bit of work getting the shows ready, but they fulfilled their purpose in raising awareness to the public and still reach our target group in a new way and in a new context.

By recording all the shows we were able to make 5 great podcasts on different dilemmas, which people with RMD and their relatives can relate to and discuss.

REFERENCES
None

Disclosure of Interests: None declared

Patient information and education

**ESTABLISHING A PATIENT TRAINING CENTER OF RHEUMATOLOGY**

Souzi Makri, CYPLAR, Limassol, Cyprus

**Background:** Patient education is considered of pivotal importance for the Organization. Patients should be informed, educated and well trained to acquire the necessary skills needed to deal with the challenges of living with a chronic disease. Equally important is the need of patients to acquire certain skills, necessary for advocating for their rights and representing their Organizations, both at the National but also at the European level. Realizing the above issues, the National Organization decided to create this training centre at its own premises, as it was noted that there was a lack of expertise in the above area, and that patients needed to be empowered to be equal partners in health decisions, but also effective Self managers of their condition.

**Objectives:** One main objective is to educate individual patients to Self manage their disease by accepting the new situation in their life, but also by learning how to effectively communicate with HPs, to be adherent to treatment, to cope with family work and social environments, and to regain self-confidence. The other objective is to train expert patients, enhance their knowledge and empower them for representing the Organization on all relevant Health committees and participate on all stages of the decision making process.

**Methods:** First step was to create a Brand name and acquire the relevant certificate of the establishment of the training centre. After the certification process had been finished, two volunteers from the Organization were trained by the National Authority of Human Resources and after successfully passing the 8-hour examination, they became certified trainers. A committee, under the two coordinators is now in the process of revising the modules of the first 5 courses which are offered initially, by restating the aims and objectives of each course as well as the training procedure, teaching techniques, methods and evaluation process. The courses are: The self-management (running), the expert patient (running) Self Diagnosis (running), Training for parents of Children with Rheumatic diseases (Coming before the end of Year), “Rebuilding the story of our life” – Systemic Sculpture method (Running from October 2019- April 2019)

The plans for the next steps include the creation of training course on building patient advocacy skills (Participation in Health committees, HTA, Advisory committees etc) and one on recruiting and training of volunteers.

**Results:** The experience from the implementation at the initial stage of the three training courses (Self-management, expert patient and self-diagnosis) shows that patients are happy to join, to share experiences and feelings and they successfully attempt to use the skills acquired in their everyday life. Some of the Organization’s members have now become members on National Health committees. These include the Committee for Pricing of Medical products, National Health Insurance, ad hoc for updating the rights of patients, rare diseases, for digital Health etc. Success of the existing modules has led the Organization to decide on building an online portal for digital learning.

**Conclusion:** The creation of a rheumatology training centre for patients, although at its initial stage, has shown positive results for patients, by enhancing their ability to deal in an effective way with the chronic disease but also in improving their skills and knowledge to strive for effective advocacy and for being part of all in decisions that affect their rights in health.

**Disclosure of Interests:** None declared


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**EASY TO OPEN/EASY TO USE: ACCESSIBILITY FOR PEOPLE WITH REDUCED HAND FUNCTION**

Nina Utens, Stockholm, Stockholm, Sweden

**Background:** One fifth of Sweden’s population, more than 1.5 million people, has reduced hand function.[1] For the European population, it would equal well over 60 million people.

People with reduced hand function, for example due to illness or age, are often unable to handle products or packaging without additional daily living aids. In addition to the 20 percent of the population with reduced hand function, often due to rheumatic disease, women on average have 40 percent lower hand strength than men. In other words, the market for inclusive design is huge and concerns a large portion of all consumers. The Swedish Rheumatism Association, SRA, has for many years fought for accessibility of products and services for our members. The SRA has a history spanning over 15 years of activism for inclusive design. The highlight being the launch of the universal standard SS-ISO 17480:2015 Packaging - Accessible design - Ease of opening, of which the SRA was a big contributor. However, the aim for this abstract is not to put emphasis on previous successes but to describe current attempts to make the packaging industry adapt a more inclusive design for the many people with reduced hand function.

Every third year thousands of delegates visit Scanpack, Northern Europe’s biggest packaging fair. Last year was the first time the SRA attended as an exhibitor, making the SRA the only non-profit organisation working for people with rheumatic diseases, to participate. 463 exhibitors from around 30 countries attended, with 16,500 delegates in total, of which 12,900 were visitors. The fair took place on October 23-26, 2018 in Gothenburg, Sweden.

**Objectives:** “Products that are functional and easy-to-use for people with reduced hand function, are suitable for everyone”. This tagline defined our work for inclusive design. We focused on three objectives in order to make our stand more visible and to participate. The three initiatives are:

1. Individuals with reduced hand function in Sweden.
2. Women have weaker hand strength, compared to men. How much weaker? 56 percent of the survey responses were correct. Correct answer: about 20 percent.
3. Results: Representatives from leading packaging companies and visitors to Northern Europe’s biggest packaging fair learnt that there is room for improvement in the packaging industry to adapt a more inclusive approach towards design that benefits people with rheumatic diseases.

**Conclusion:** Half of the participants who visited the SRA’s exhibition answered correctly to our questionnaire regarding reduced hand function, suggesting there is room for improvement in the packaging industry to adapt a more inclusive approach towards design that benefits people with rheumatic diseases.

**REFERENCE**


**Disclosure of Interests:** None declared

**DOI:** 10.1136/annrheumdis-2019-eular.5265
Building patient led organisations.

PARE0005 REFRESHING THE SOCIAL MEDIA STRATEGY OF FIBROMYALGIA ACTION UK: RESULTS OF A NATIONAL PATIENT ORGANISATION SURVEY

Simon Stones1,2,3, Reece Henderson1, Des Quinn1. Fibromyalgia Action United Kingdom, Paisley, United Kingdom; 2European Network of Fibromyalgia Associations, Hassel-op-den-Berg, Belgium; 3University of Leeds, School of Healthcare, Leeds, United Kingdom

Background: Patient organisations have traditionally provided support for patients. However, the method by which people seek support is increasingly desired across social media, particularly among certain populations within the fibromyalgia community who rely on social media as a key form of communication. In addition, the activity of patient organisations on social media is evolving to encompass greater advocacy and awareness activities with a growing target population of different stakeholders. To address this growing demand, Fibromyalgia Action UK conducted an online survey to inform the organisation’s future social media strategy.

Objectives: The aim of the survey was to understand the preferences of people interacting with Fibromyalgia Action UK’s social media platforms, in order to inform the organisation’s evolving social media and wider communications strategy.

Methods: An online survey was disseminated via Facebook, Twitter and a post on Fibromyalgia Action UK’s website over a one-month period, between October and November 2018. Questions focused on general demographics, social media branding, style and content.

Results: A total of 301 people responded to the survey, 89% of whom had been diagnosed with fibromyalgia and 5% of whom were a friend or relative. More than half of respondents (60%) were aged between 45 and 64 years, with only 13% of respondents aged under the age of 35 years. 91% of respondents felt happy with the organisation’s current branding, with 78% rating the organisation’s social media sites as ‘Good’ or ‘Excellent’. While 92% of respondents were happy with the organisation’s current social media content, around half (51%) suggested an increase in the amount of visual posts (such as infographics), and two thirds (66%) suggested an increase in news articles and patient/carer stories.

Conclusion: The survey highlights the need for more visual, engaging content to inform and educate people about fibromyalgia and related activities. Respondent demographics also highlighted a limited interaction on social media with younger people under the age of 35 years. Together, these findings have prompted the organisation to launch a new campaign, titled ‘BecomeFibroAware’, using visual content to inform, educate and empower the community, as well as an increased focus on engaging younger people with fibromyalgia.

REFERENCE

Acknowledgement: Fibromyalgia Action UK thanks the Board of Trustees and staff for their involvement, and to all of those who participated in the survey.

Disclosure of Interests: Simon Stones Consultant for: SS has provided consultancy services to Envision Pharma Group, though this is not related to the contents of this abstract., Speakers bureau: SS has under- taken speaking engagements for Actelion, eyeforpharma, Four Health, Janssen and Roche, though these are not related to the contents of this abstract., Reece Henderson: None declared, Des Quinn: None declared DOI: 10.1136/annrheumdis-2019-eular.1044

PARE0006 LIVING WITH A RHEUMATIC DISEASE: A RESEARCH ABOUT QUALITY OF LIFE AND WORK CONDITIONS

Antonella Celano1, Serena Mingolla1, Matteo Santopietro2. 1APMAR Onlus, Lecce, Italy; 2WeResearch, Milan, Italy

Background: There are 5 million people who suffer from rheumatic diseases in Italy with an annual expenditure of the health system, estimated for the chronic forms, around 4 billion euros. During the World Arthritis Day 2018 the Association of Persons with Rheumatic and Rare Diseases - Apmar Onlus presented the results of the survey “Living with a rheumatic disease” with the aim of raising public awareness by disseminating data useful to understand the quality of lives of people living with one of the 150 rheumatic diseases.

Objectives: The research investigated:
- The quality of life of people with a rheumatic disease
- The work problems and conditions experimented by people suffering from a rheumatic disease.

Methods: The survey was both qualitative and quantitative. The qualitative phase was held in Milan and was preparatory to the development of the questionnaire distributed at national level. In the first phase two groups of five people were interviewed for two hours. The people interviewed in the focus groups were women and men, age 25-55 years (50% 25-40; 50% 41-55) with at least one rheumatic disease, currently workers/ laborers at least part-time.

In the quantitative phase, a questionnaire was administered throughout the national territory to a sample of 1,020 people, women and men, age 18-75 years with at least one rheumatic disease, currently workers/ laborers at least part-time or who worked for a period preceding the diagnosis of rheumatic disease. The used methodology of on-line investigation was the Cawi (Computer Aided Web Interview).

Results:
- 89,1% of separated and/or divorced interviewed reported that the disease caused problems in the sexual relationship with the partner as to cause their divorce/separation;
- 61% of the sample had to reduce working activities significantly, in many cases abandoning the job completely;
- 26.3% of the sample stated that he prefers not to speak about his illness either with his work colleagues or with his boss and/or superiors.

Conclusion: Rheumatic diseases affect relationships and social life negatively. The research shows how the rheumatic disease can have a particularly critical effect in the relationship with the partner. The problems arising in the relationship of the couple are so meaningful, and cause of misunderstandings and psychological suffering to be considered among the main causes of divorce and separations.

Rheumatic diseases heavily affect the working life. From the research emerges that people with rheumatic diseases that have managed to preserve their work despite the disease, are often reluctant to talk about their health conditions at work. The main reason is the fear of worsening and/or compromising their relations with colleagues and superiors with consequent negative effects on work tasks and the risk of losing their workplace.

People suffering from rheumatic diseases in Italy declare that their condition of difficulty due to the pain, is often underestimated, this leads them to take a closing attitude for the fear of not being understood. The respondents also expressed the fear that in the highly competitive society we live in, there is no place for people to express their pain: they are afraid of being considered weak and in a certain way “to be put aside” and so they must therefore “show themselves strong”.

REFERENCE


PARE0007 RHEUMATISM CHALLENGE 2018 – “RHEUMATISM IN MOTION” WE ARE GOING IN THAT TOGETHER!

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Background: Czech League Against Rheumatism plays an important role in promoting rheumatic patients in the Czech Republic. Its activity is aimed at:
- raising awareness about RA for early diagnosis and RA treatment
- improve an attitude of the Czech patients to the modern treatment, including the biological treatment
- co-operate on the change together with the professional community, regulatory authorities and Health Insurance Companies.
- striving to qualify the people with so called “moderate activity” of the disease for the biological treatment.
• the struggle for full and equal life for people with rheumatic and musculoskeletal diseases
• the establishment of regional clubs and specific patient groups of Czech League Against Rheumatism

Objectives: Creating a campaign Rheumatism Challenge 2018 - “Rheumatism in motion” We are going in that together! The aim of this campaign is improving the health condition of people with RMDs. To motivate patients to move regularly and raising patient awareness about the importance of physical activity.

Methods: Walking as a means to reach a goal is the main content of this campaign. The aim of each participant in this campaign is to reach as much as possible steps and kilometers every months. Exiting challenges prompts patients to higher goals and giving them courage. Through walking Czech League Against Rheumatism wants to improve physical and mental health of people with RMDs. Wants to maintain a joint mobility and reduce a pain. Know and find the right kind of movement for each patient.

Information about this campaign is published on the webpage, Facebook and Instagram of Czech League Against Rheumatism.

Results: This campaign managed to raise awareness about the importance of physical activity. On-line and off-line, more than 500 HCPs and patients with rheumatic and musculoskeletal diseases among the general public. Information about the campaign was in press and television. The campaign continues in 2019. In response to the campaign has increased the number of members in Czech League Against Rheumatism.

Conclusion: This campaign seems to be very useful in promoting how important physical activity is for patients with RMDs. This campaign can support patients be more healthy and more physically active. Active approach to one another life can inspire other patients and their families and friends. Very important is also the support of this campaign from the professional community, medical doctors and health professionals.

Disclosure of Interests: None declared


PARE0008 UNDERSTANDING THE IMPACT OF ANKYLOSING SPONDYLITIS IN DAILY LIFE OF THE PORTUGUESE PATIENTS: RESULTS FROM THE ASSESSMENT OF RESULTS IN ANKYLOSING SPONDYLITIS (AREA) STUDY

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Background: AS is known to have a significant burden upon the individual and family life. It is essential to assess the impact of AS in patients’ lives, to raise awareness and improve early referral, diagnosis and treatment, for a better quality of life.

Objectives: To assess the impact of AS in the life of Portuguese patients (work, daily activities, social life).

Methods: The Assessment of Results in Ankylosing Spondylitis (aERA) study was developed by the NOVA-IMS in cooperation with: Portuguese Society of Rheumatology, Portuguese Association of Family Physicians, National Association of Primary Care Units, National Association of AS Patients and the Portuguese League Against Rheumatic Diseases. The aERA aimed at assessing reasons for delayed referral of suspicious cases of AS to the rheumatologist, as well as disease impact in patients’ lives, global health and work. A comprehensive online survey was developed with the collaboration of LPCDR and sent to AS patients. Data on demographics, lifestyle habits, daily life activities, working habits, disease indexes and healthcare utilization, health status/quality of life indicators, EQ-5D and BASDAI scales. A generalized linear model was adjusted in order to identify the factors impacting on quality of life of patients.

Results: 354 patients responded the survey, 42.1% female, most frequently from the 35-44 year-old age group. Mean age at disease onset was 27 years old, while the diagnosis was confirmed 7 years later. In the previous 12 months, the average of working days lost due to AS issues was 37 (including sick leaves). During that period, AS has affected work productivity in average around 73 days. Cumulatively, patients’ relatives or friends had also lost about 13 days of work, to provide them assistance. Regarding limitations in daily life activities, house cleaning (55.5%), physical exercise (46.5%), getting in/out of bed (45.6%), using stairs (37.9%), shopping (37.4%) and tying shoes (35.2%) were reported as being highly limiting by AS. As for the social life, family and friends’ relationships were reported as not being affected by over 60% of AS patients. However, 19.8% of the respondents have reported a worse relationship with their partners after diagnosis, and 29.7% reported having decreased the frequency of sexual intercourse. Leisure activities, were only reported as not being affected by 34.6% and 40.5% of patients, while the practice of sports has much decreased in 40.7% of the respondents. Almost 80% had mobility issues during the last year, and of 65% had their usual activities/routes affected by AS. The average BASDAS score is 5.5 and the EQ visual analogue scale 55. Analyzing the impact of treatment, biologics and biosimilars were reported as having significantly improved patients’ quality of life, except for physical or sexual activity.

Conclusion: AS has a major impact in the daily life of patients, work productivity, social relationships and leisure activities. Early diagnosis and treatment, along with physical rehabilitation/exercise plans, can reduce this impact and improve their quality of life.

Disclosure of Interests: None declared


Best practice campaigning

PARE0009 THE PHYSIOLOGIC AND EMOTIONAL BURDEN OF RHEUMATOID ARTHRITIS: DATA FROM RA MATTERS, A WEB-BASED SURVEY OF PATIENTS AND PHYSICIANS IN EUROPE AND CANADA

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Background: Rheumatoid Arthritis (RA) is a chronic inflammatory disorder that negatively affects the patients’ health-related quality of life (QOL).1 Despite much progress in addressing the burden of RA, a gap exists in terms of understanding ‘what really matters’ to patients with RA, and balancing patients’ QOL aspirations with clinical targets in key treatment decisions.

Objectives: This international survey investigated how RA affects the lives of patients according to the perceptions of both patients and healthcare providers (HCPs), in order to help health professionals attune their care on the domains that really matter to patients.

Methods: Data were collected from patients with RA, and rheumatologists or HCPs who treat RA in Canada, France, Germany, Italy, Netherlands, Spain, Sweden, and UK using a structured, closed-ended questionnaire in their local language. Respondents for the survey were recruited from survey panels of verified unique respondents, as well as through social media. Data were summarized in terms of both frequency and percentages of patients to understand the experience of patients living with RA on daily activities, relationships, work, and aspirations.

Results: Overall, 5400 adult patients (81% female; mean age 52 years), and 808 rheumatologists or HCPs participated in the survey between November 2016 and February 2017. Of these, the highest proportion of patient and HCP respondents were from the UK (n=1250) and France (n=230), respectively. Overall, 52% of patients and 62% of HCPs believed that the emotional impact of RA is not well understood by people without the disease; whereas 46% of patients and 52% of HCPs had a similar belief with regards to the physical impact of the disease. Patients who felt that the impact of RA is less well understood by others expressed more negative feelings about every aspect of their life with RA. Important relationships with spouse or partner, children, family, friends, and colleagues were generally affected negatively. Almost half of the patients (48%) who participated in the survey reported that they were forced to take long-term leave/retirement or experienced slow career progress since being diagnosed with RA; more than 3 in 5 patients found exercising to be difficult; and almost 1 in 4 patients found difficulties in taking care of personal grooming. Aching/stiff joints, pain, and fatigue were the key physical barriers to daily life for patients, and 65% of patients felt frustrated when they were unable to undertake or complete daily activities due to their disease. Two-thirds of patients wished to be able to accept their life with RA and do what they can to cope with it in the future. Over half of
the patients (52%) had a hope that the physical impact of RA will be better understood in the future.

Conclusion: Despite major advancements in the treatment of RA, the chronic disease continues to significantly affect many aspects of patients’ lives, including relationships, career progression, daily activities, and ability to work. Both patients and HCPs felt that the physical and emotional impact of RA is not well understood by people without the disease. In line with a recently published study, pain, fatigue, and physical function remain primary barriers for patients to live a normal life and to participate fully.2 In RA treatment decisions, patients’ personal goals and patient-reported outcomes should be given greater consideration along with clinical targets.

REFERENCES


PARE0010 INSIDE OUT – A PHOTO CAMPAIGN TO CREATE AWARENESS FOR YOUNG PEOPLE WITH RHEUMATIC AND MUSCULOSKELETAL DISEASES

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Background: Inside Out is a photo campaign of Youth-R-Well.com, the organisation for young people (16-30 years) with rheumatic and musculoskeletal diseases (RMDs) in the Netherlands. The project was inspired by Unga Reumatiker, the youth organisation in Sweden and their campaign Against the invisible side of RMDs. The campaign of Unga Reumatiker showed that young people can suffer from rheumatic diseases, even though these diseases are invisible. Youth-R-Well.com recognized that the invisibility of an RMD can have a major impact on the lives of young people and wanted to create a similar photo campaign to show the invisible side of RMDs.

Objectives: The main objective of this project was to create more awareness for rheumatic and musculoskeletal diseases affecting young people.

One of the hardest parts of living with an RMD is the invisibility of the disease in daily life. We wanted to show that even though you cannot see it, young people have to deal with the consequences of having an RMD on a daily basis. We also wanted to show other young people who are in a similar situation, that they are not the only one.

Methods: To make the invisible side of an RMD visible for others, Youth-R-Well.com created Inside Out, an eight part photo campaign. Eight young people with different types of RMDs, took part in this project. From each individual, two photos were taken: one photo in daylight and one photo in the dark with their rheumatic-spots highlighted by blacklight paint. Next to the photos, the participants introduced themselves in a few sentences and ended with a life quote with a focus on the positive side of life. They were all telling very different and very personal stories. The general quote of the photo campaign was “Although you cannot see it from the outside, it is still there”. The photo campaign was posted on Facebook and Instagram. The photo campaign was released the week before World Arthritis Day, in which the photos of one person were shared on each day. The final photo, a group photo with all the young people and their black light photos, was shared on World Arthritis Day 12 October 2018.

Results: It was a successful campaign, in which we reached almost 30.000 people on Facebook and 5.000 people on Instagram. The success of the project and all the shares and great comments it received were overwhelming. The power of two photos next to each other had a large impact on people who were not familiar with the fact that RMDs do exist among young people. As a result of the great comments, this photo campaign is going to be exhibited in Reade, the center for Rehabilitation and Rheumatology in Amsterdam, to reach more people and make them more aware of the invisibility of RMDs.

Conclusion: Based on inspiration from a youth organisation in Sweden, Youth-R-Well.com created the successful campaign Inside Out. We managed to create more awareness for young people with RMDs and the invisible side of having an RMD. We will continue to spread this campaign and show that young people with RMDs are not alone.

Acknowledgement: First of all, we want to thank all our brave participants who took part in this campaign. Secondly, we want to thank Unga Reumatiker, who inspired Youth-R-Well.com to launch this amazing photo campaign.

Disclosure of Interests: None declared

Innovations in arthritis health care

PARE0011 PILOTING THE FIRST PATIENT PARTNERS PROGRAM FOR AXIAL SPONDYLOARTHRITIS: THE JOURNEY OF BELGIAN PATIENTSTOCOME EXPERT TEACHERS IN RHEUMATOLOGY

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Background: Patients with axial spondyloarthritis (axSpA) were trained to deliver experience-based workshops to medical students, general practicioners, physiotherapists and other healthcare providers concerning axSpA. The most important aims of these workshops are to improve the early diagnosis and to increase awareness of axSpA in the medical sector. Taking an expert role as a patient however requires an extensive training.

Objectives: To describe the training program in detail and to illustrate both the less successful and the optimal implementation steps taken thus far.

Methods: In its first iteration, the training program was developed as a resource book including a curriculum, significant amounts of homework, without enough time for practical exercises. This resulted in a drop-out of a large portion of trainees. Thereafter, the training method has been adapted by copying successful parts of the approach of The Patient Partner® Program for Rheumatoid Arthritis (launched in 1999). Also, more concrete training opportunities via a DVD demonstrating the complete course and training materials, as well as offering hands-on trainings during a three day overnight stay were added. Besides creating opportunities for intensive practicing with each other, there was also more time for informal contacts and it allowed for proper group dynamics. So there is more time for sharing among them with a similar background. A comfortable environment was created for the candidates, enabling them to go through a complete process and giving them sufficient time to train all the components of the program.

Results: On February 22nd 2018, five fresh SpA-patients started the training, all five of them successfully completed the training on June 2nd 2018. On a first evening of familiarization, trainers tried to know more about the motivation of the trainees, while in an individual interview a rheumatologist reassured that the candidates have the correct diagnosis, as their story should be consistent. The selected candidates received part 1 of the training manual by mail and they were invited to profoundly study the terminology and the anatomy, related to their disease. During the first full day of the training, the trainers took time to explain the terminology and anatomy. Later on this constituted the building blocks of the course. The trainers closed this first day demonstrating the history taking and they asked the trainees to study at home their personal medical file.

On day 2, the homework of the previous day was first discussed, followed by related exercises. Day 2 finished with the demonstration of the clinical examination.

The training program was completed with three days with overnight stay. During these days a lot of practical exercises of the clinical examination were organized, followed by a discussion of the impact of the disease and the importance of active participation. The program ended with a general rehearsal and a written as well as an oral test to evaluate how each trainee had assimilated all this.
Conclusion: In the training program PPP SpA, the trainees learn to tell a uniform and academically correct story. This contains an accurate history taking and a correct clinical examination reinforced by the personal history of the Patient Partner. Moreover the whole process helps each Patient Partner to have a better insight in their own illness, a better capacity to cope and to develop more skills in the dialogue with medical practitioners. The experienced positive feedback of the trainees after every course is the best motivation to continue with this approach.

Disclosure of Interests: None declared


INVOLVEMENT OF PATIENTS IN ERN RECONNET: A SUCCESSFUL INITIATIVE RAISING PATIENTS' LEADERSHIP AT EUROPEAN LEVEL

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Background: European Reference Networks (ERNs) are virtual networks involving centres of expertise across EU Member States with the aim of tackling rare and complex diseases. The ERN ReCONNET involves currently 26 healthcare professionals (HCPs) from 8 countries and cover rare and complex connective tissue and musculoskeletal diseases (rCTDs). Patient participation and involvement, also through EURORDIS, is a characteristic of ERNs.

Objectives: To demonstrate that patients’ involvement and collaboration across disease and geographic borders via the ERN ReCONNET effectively brings better care for people living with rCTDs.

Methods: The European Patient Advocacy Groups (ePAGs) provide patients’ opinion and input in all activities of the ERN. They relay the views of their wider communities, evaluate how the ERN acts on patient views, contribute to projects and research, develop and disseminate patients’ information, ensure that patient rights and choices are taken into account in decision-making and identify national groups to work with the ERN’s HCPs. To structure the patients’ involvement, a Patients’ Organizations Working Group led by a Senior and a Junior Coordinator, developed and approved its own Terms of Reference. Patients’ Representative Disease Coordinator (PDR) have been identified for most diseases. They bring patient perspective, liaise with HCPs and their wider patient community. Three ePAGs are voting members of the Steering Committee.

Results: ePAGs have collaborated intensely in ERN activities, organising and participating to regular meetings, providing their input into projects. They co-designed and disseminated surveys on clinical practice guidelines (cPGs) to patients and their families, evaluate how the ERN acts on patient views, contribute to projects and research, develop and disseminate patients’ information, ensure that patient rights and choices are taken into account in decision-making and identify national groups to work with the ERN’s HCPs. To structure the patients’ involvement, a Patients’ Organizations Working Group led by a Senior and a Junior Coordinator, developed and approved its own Terms of Reference. Patients’ Representative Disease Coordinator (PDR) have been identified for most diseases. They bring patient perspective, liaise with HCPs and their wider patient community. Three ePAGs are voting members of the Steering Committee.

Conclusion: The ERN ReCONNET is a great opportunity for patients’ leadership, bridging from EULAR and its PRP program to ERN and other EU initiatives. It will make a tremendous impact on the EU diagnostic and treatment landscape bringing a better quality of life to people with rCTDs.

REFERENCES
[2] https://rmdopen.bmj.com/content/4/Suppl_1

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CORRECT DIET: AN INNOVATIVE 3 STEPS PROJECT

PENDO DEI


None declared, Jürgen Grunert: None declared, vera guimaraes: None declared, lisa matthews: None declared, Sander Otter: None declared, Ana Vieira: None declared


EDUCATING PEOPLE WITH RMDs TO FOLLOW A CORRECT DIET: AN INNOVATIVE 3 STEPS PROJECT

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Background: Patients associations in Italy as in all the European countries have a strong role not only in empowering people with Rheumatic and Muscle-skeletal Diseases (RMDs), but also in educating them to new healthier lifestyles, comprehending physical activity and diet.

In Italy, the special relationship between people and food make our job more difficult than in other countries and it needs to try new ways driving people with RMDs to a correct diet without feeling different from the healthy population.

Objectives: 1. to make patients, their families & care givers and the society aware of how much important is to follow a correct diet to prevent some of the damages that may be related to rheumatic diseases; 2. to make patients and their families aware of the importance to rely on experts in setting up correct dietary regimes; 3. to educate people with RMDs to a correct diet and healthy lifestyle, showing them it is possible to eat meals appetizing, tasty and also appearing beautiful even if following an appropriate and healthy regimen.

Methods: STEP 1 - ANMAR published “RMDs and diet”. The booklet written by dr. Annalisa Olivotti, biologist and nutritionist, contains all topics concerning diet and RMDs; the Rheumatologist position and some suggestions by patients are present too. The booklet has been sent to all people receiving the ANMAR magazine “Sinergia” and was available for free in all ANMAR events and on its website.

STEP 2 – Since September 2018, through the regional associations, ANMAR organized a series of events to educate all the population and especially patients, their families and care givers, to follow a healthy diet, as a first aid to the pharmacological therapies.

STEP 3 - To complete the educational pathway of each meeting, all participants can experience how fun may be eating in a healthy way, having a dinner cooked by local chefs who have previously received a complete list of the most suitable foods for proper nutrition for people with RMDs.

Results: The project is still ongoing: nowadays we can refer these data:

- 15.000 copies of the booklet “RMDs and Diet” were published and distributed
- 5 meetings were organized, directly approaching a total of 450 people
- All participant highly appreciated the healthy menu cooked in the dinners
- 54 new recipes have been sent to the regional Association of Piemonte, leader of the project
- Using a “free – offer” request to enjoy the dinner, the project may also become a good fundraising way for the regional association organizer.

Conclusion: Data collected seem to confirm this one may be a suitable way to overcome the Italian cultural gap which leads to live diet as a bad and depressing lifestyle, as in Italy eating is not only a way to feed on, but an enjoyable moment. We hope further data will enforce this first impressions and definitely confirm it.

Disclosure of Interests: UGO VIORA Employee of: Wyeth Lederle, Sara Severoni: None declared, Silvia Tonolo: None declared


SUCCESSFUL INITIATIVE RAISING PATIENTS AWARENESS AND SUPPORT, London, United Kingdom


None declared, Jürgen Grunert: None declared, vera guimaraes: None declared, lisa matthews: None declared, Sander Otter: None declared, Ana Vieira: None declared


EDUCATING PEOPLE WITH RMDS TO FOLLOW A CORRECT DIET: AN INNOVATIVE 3 STEPS PROJECT

PARE0013

Patient information and education
PATIENT VOICE IN GOUT – A EUROPEAN PATIENT SURVEY TO UNDERSTAND THE NEEDS OF PEOPLE LIVING WITH GOUT

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Background: Gout is one of the most common forms of inflammatory arthritis in Europe, but awareness of it is relatively low. There is limited information available about the impact of gout on patients, and more generally on society.

Objectives: To give gout patients a voice to better understand the impact that the disease has on their lives.

Methods: From June to September 2018, gout patients from 14 European countries were invited to complete a 15 minutes online survey. Adult (18+) patients diagnosed with gout who met the criteria and finished the survey were included in the analysis. The design and content of the survey has been developed together with several patient and clinical experts to ensure that the most relevant aspects of the disease were covered. The questionnaire was translated into 11 different languages and checked that patient-friendly language was used. Patients were recruited via patient associations, leaflets provided to doctors and consumer online market research panels to reach the targeted number of patients.

Results: 1,100 gout patients completed the survey, 78% of respondents were male and 22% female. The mean age of participating patients was 55 years, 56% were employed or studying. The mean age of patients at diagnosis was 45 years and 38% were diagnosed during their first flare. The patients had on average 2.9 flares per year and the length of their last flare was 5 days on average. 84% of patients experienced moderate to severe pain with their most recent flare, 63% had severe pain with their worst flare ever. Patients reported that gout has a significant impact on their daily activities: on their ability to walk (59%), changes in mood and mental well-being (43%) and difficulties relating to their partner (26%). 27% of patients reported that their self-esteem has dropped.

Inconvenience (53% of patients), agony (37%) and frustration (32%) were the words patients most often associated with gout. 10% of patients (or a family member) have retired or lost a job because of their gout.

Despite reporting these not-insignificant impacts of gout on their lives, 79% of patients said that they are satisfied with their current treatment. However, two-thirds (68%) of younger patients (18-35 years) reported that they are satisfied with their current treatment. Despite reporting these not-insignificant impacts of gout on their lives, 79% of patients said that they are satisfied with their current treatment. However, two-thirds (68%) of younger patients (18-35 years) reported that they are satisfied with their current treatment.

Conclusion: The results of this survey demonstrate that gout has a significant impact not only on patients, but also on their families and society. Gout seems to lead to stigma and many patients may feel guilty about their lifestyle choices. Actions need to be taken to manage dissatisfaction of patients and to encourage them to speak up to request better management of the disease. There seems to be an urgent need to educate both patients and the general public about the seriousness of gout and the burden on patients and their families. The results of this survey will be used for communication with healthcare professionals to better address patients’ unmet needs.


EMOTIONAL HEALTH AND WELL-BEING MATTERS

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Background: The most common co-morbidities amongst people with RA are mental health conditions, such as depression and anxiety, as evidenced by previous surveys and reports by the NRAS. NRAS also understands, through interaction with its membership across the UK, that mental health and well-being are important issues for people living with RA and JIA. NRAS therefore partnered with City University to undertake a survey exploring the impact of RA and adult JIA on mental health.

Objectives: To explore the psychological impact of Rheumatoid Arthritis (RA) and Juvenile Idiopathic Arthritis (JIA), along with any psychological support people may have received or would like to have access to, to help manage the anxiety, emotions and stresses that come with being diagnosed with and living with RA or JIA and its treatment.

Methods: Following a focus group held in Central London in early 2018 with a dozen NRAS members, NRAS and City University designed a survey to look at a range of aspects relating to emotional health and well-being, including validated questionnaires to compare data to existing research. The survey was open between May and July 2018, with participants recruited via NRAS newsletters, social media platforms, the NRAS HealthUnlocked forum and via healthcare professionals at rheumatology units. A total of 1,999 people participated in the survey and a final sample of 1,650 was used for analysis.

Results: The survey found that people with RA and adult JIA were less satisfied with their life, believed the things in their life were less worthwhile, and were less happy. The proportion of people who scored poorly on life satisfaction and life worth was over 7 times greater in those with RA and adult JIA than the national average. Despite this, the survey found that 2 in 5 people had never been asked by a health professional about their emotional and psychological well-being, and 1 in 3 people who had requested or been offered support had never received it. Positive experiences that respondents shared of psychological support, such as GP’s and rheumatologists being very supportive, the importance of family, and services offered by NRAS, demonstrate the benefits of good and appropriate support being available. Negative experiences, such as lack of health professional understanding about mental health, lack of understanding of RA by counsellors, and lack of personalised care demonstrate the future work that must be done to help adequately support people with RA and adult JIA.

Conclusion: The survey has demonstrated the need to provide more effective self-management techniques of emotional as well as physical well-being, ultimately leading to overall improved health outcomes. In line with NICE guidelines, other additional support is needed, such as the availability of cognitive behavioural therapy and the implementation of mental health and well-being assessments at annual review. Further research is needed into specific areas, such as health inequalities and why people with severe mental health issues experience poorer disease activity, understanding why adults with JIA have poorer life quality than people with RA, and understanding the impact of psychological interventions for people with adult JIA.

Disclosure of Interests: None declared.


Psychosocial support
**Arthritis research**

**PARE0017** EXPLORING DIFFERENCES IN THE AGE ON ONSET OF JIA BETWEEN MALES AND FEMALES: A PARENT-LED SURVEY

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**Background:** The etiology of juvenile idiopathic arthritis (JIA) remains unknown, despite a range of proposed mechanisms under investigation [1]. However, previous research has revealed biological differences depending on the age of onset of JIA, independent of the classification based on the number of joints involved [2].

**Objectives:** In this parent-led study, the age of onset of JIA by both disease subtype and sex of the child were explored, to identify whether there is a difference in age of onset of JIA between males and females.

**Methods:** An online survey was shared via social media, targeted at parents of children and young people (CYP) with JIA. Questions probed the age of symptom-onset and diagnosis (by single year of age), JIA subtype and Rheumatoid Factor (RF) status.

**Results:** Of the 409 CYP included, 296 had polyarticular (poly) or oligoarticular (oligo) JIA, including extended-oligo JIA (72% of all respondents). There were no differences between onset among these subtypes; therefore, they were grouped for further analysis, given comparable disease progression and genetic markers among these subtypes. There was no significant difference regarding age of symptom onset between RF-positive and RF-negative CYP. Amongst those with poly/oligo JIA, there was a clear peak of symptom-onset in the first few years of life, with over half experiencing symptoms before their third birthday, and 73% before the age of five years. Interestingly, the distribution of symptom-onset was significantly different in the poly/oligo JIA group between males and females (P = 0.0093), with the onset of poly/oligo JIA appearing to occur earlier in females (Figure 1). Given that some CYP with older-onset JIA are sometimes reclassified as having enthesitis-related arthritis (ERA) when examined in adolescent services, the Mann-Whitney U Test was repeated with only those CYP with JIA onset before the age of seven years. In this case, there remained a significant difference in age of onset of poly/oligo JIA between males and females (P = 0.0061).

**Conclusion:** The age of symptom-onset among CYP with poly/oligo JIA differs between males and females, with females tending to exhibit symptom-onset earlier. This appears not to be attributable to misclassification of JIA subtype, and so this knowledge may assist future diagnoses of JIA. Further research is required to identify which temporal-associated factors may be critical in JIA onset and development.

**REFERENCES**


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Building patient led organisations

PARE0018 ENABLING PATIENT-CENTRED CARE IN RHEUMATOID ARTHRITIS AND ASSOCIATED COMORBITIES

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Background: Patients with rheumatoid arthritis (RA) have an increased risk of comorbidities such as diabetes (IR of 8.6 per 1000 person-years11; 20% prevalence2), interstitial lung disease (7.7% incidence3; up to 60% (interstitial lung abnormalities in early RA)4), depression (up to 200%; 16.8%5), and cardiovascular disease (40-70%; 5-12.9%6). However, despite advances in treatment there are few established recommendations on the management of RA-related comorbidities.

Objectives: This study aimed to identify examples of good practice in the care of RA and associated comorbidities meeting standards of patient-centred care, and consider how these could be implemented in other European centres.

Methods: Following a literature review, multidisciplinary teams including specialists in rheumatology, cardiology and internal medicine, nurses, physiotherapists, psychologists, patient liaisons and care coordinators at 12 selected specialist centres across Europe (1 centre per country) were interviewed (approx. 180 interviews). The models identified were critically reviewed by a group of experts including a patient representative, and the degree to which the interventions impacted patient care and could be implemented in other centres was evaluated.

Results: Several care model interventions were identified which may improve quality and the patient’s experience of care, e.g. fully integrates screening and diagnosis of comorbidities; coordination and sharing of care across different disciplines of comorbidity management; tailored individual education of patients and family members on lifestyle; enabling virtual engagement between patients on lifestyle management; and optimised con- venience for patients having to attend multiple specialty appointments.

Conclusion: This study identified and evaluated interventions that may improve patient outcomes and quality of care in RA and associated comorbidities. The next steps will be to disseminate and implement these examples of good practices in a variety of European healthcare systems and settings.

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Patient information and education

PARE0019 LIVING WITH SYSTEMIC SCLEROSIS: EXPLORING ITS IMPACT ON CAREGIVERS: A QUALITATIVE STUDY

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Background: Systemic sclerosis (SSc) is a rare, chronic and heteroge- nous disease with many possible outcomes and an uncertain horizon which presents difficulties not only for patients, but also for caregivers.

Objectives: To gain more insight in the experiences and unmet needs of caregivers for people with SSc in the Netherlands.

Methods: The study had a qualitative design. Participants were recruited by the Dutch patient organization (NVLE) using social media. One focus group and two individual interviews with a semi structured approach were held. Participants were asked to note down their associations with the disease, which lead on to a group conversation moderated by two researchers (MRS, CHE). The focus group was audiotaped and trans-cribed. Individual telephone interviews were summarized. All participants verified and approved the reports afterwards.

Results: Eight caregivers (4 males, 4 females: 4 partners, 2 widowers, 1 parent and 1 friend) of patients with SSc participated. Six attended the focus group session, two were interviewed over the phone. The chal- lenges were reported by the participants. The first challenge is coping with the chronic disease course, unawareness of treatment options and lack of information about limitations in treatment modalities. Furthermore, the distress of patients’ decline, decreased independence, low energy levels and poor energy levels without being able to provide a cure, was experienced as a huge burden by caregivers. Aside from this distress, caregivers per- sonal lives are also affected; future opportunities are cut off, such as starting a family or continuing an active life style.

Caregivers addressed invalidation and the decrease in support from others due to misjudgment and misconceptions about severity, duration
EXERCISE FOR LUPUS PATIENTS

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Background: Up to 80% of all Lupus patients experience fatigue and most of them report this as the most severe symptom. One of the major causes of morbidity in SLE patients is chronic, debilitating fatigue, decreasing quality of life, increasing risk of work disability with associated cumbersome healthcare costs. Several research papers show that the only thing clinically proven to have an effect on Lupus fatigue is moderate exercise. If you tell this to a Lupus patient experiencing fatigue, however, you will find it very difficult to motivate them to exercise. The challenge is to make them realise that exercise does not necessarily mean running a marathon or going to the gym – a little movement goes a long way.

**Objectives:** To get lupus patients to exercise and thereby experience less fatigue/better manage their disease.

**Methods:** Develop an exercise program, that is approved by physiotherapists and leading lupologists, easy to do and inspires Lupus patients to keep active even when they feel exhausted.

**Results:** In collaboration with physical therapists Lupus Europe has developed an exercise program from our own experiences and had it approved by leading European lupologists. The program has five levels; from lying in bed up until being able to run and jump. All exercises can be done at home without training tools. In order to make it accessible we have planned to make five videos (with Lupus patients), showing how to do each exercise and five connected pamphlets. We have already recorded the first three levels and are planning to finish the entire “package” in 2019. The materials will be made available to all Lupus patients on the Lupus Europe web site and YouTube channel free of charge.

**Conclusion:** We have already seen good results within the Lupus community, where people are finding the program easy to use and a help to keeping them active. Our hope is, that researchers will use our program to investigate its effectiveness on Lupus fatigue.

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